

Thank you

for purchasing this e-book.

To receive special offers and news
about our latest products,
sign up below.

Sign Up

Or visit LWW.com



Wolters Kluwer

NINTH EDITION

Handbook of
Clinical Anesthesia
Procedures of the
Massachusetts
General Hospital

کتاب پزشکی کام

تامین منابع علمی تخصصی پزشکی



کتاب پزشکی دات کام

www.ketabpezeshti.com

+98 21 6648 5438

+98 21 6648 5457

This page intentionally left blank.

NINTH EDITION

Handbook of Clinical Anesthesia Procedures of the Massachusetts General Hospital

Senior Editor

Richard M. Pino, MD, PhD, FCCM

Associate Editors

Meredith A. Albrecht, MD

Edward A. Bittner, MD, PhD, FCCP, FCCM

Hovig V. Chitilian, MD

Wilton C. Levine, MD

Susan A. Vassallo, MD

Department of Anesthesia, Critical Care, and Pain Medicine
Massachusetts General Hospital
Harvard Medical School
Boston, Massachusetts



Wolters Kluwer

Philadelphia • Baltimore • New York • London
Buenos Aires • Hong Kong • Sydney • Tokyo

Acquisitions Editor: Keith Donnellan
Product Development Editor: Nicole Dernoski
Editorial Assistant: Kathryn Leyendecker
Marketing Manager: Dan Dressler
Production Project Manager: Bridgett Dougherty
Design Coordinator: Teresa Mallon
Senior Manufacturing Coordinator: Beth Welsh
Prepress Vendor: SPi Global

9th Edition

Copyright © 2016 Wolters Kluwer

All rights reserved. This book is protected by copyright. No part of this book may be reproduced or transmitted in any form or by any means, including as photocopies or scanned-in or other electronic copies, or utilized by any information storage and retrieval system without written permission from the copyright owner, except for brief quotations embodied in critical articles and reviews. Materials appearing in this book prepared by individuals as part of their official duties as U.S. government employees are not covered by the above mentioned copyright. To request permission, please contact Wolters Kluwer at Two Commerce Square, 2001 Market Street, Philadelphia, PA 19103, via email at permissions@lww.com, or via our website at lww.com (products and services).

9 8 7 6 5 4 3 2 1

Printed in China

Library of Congress Cataloging-in-Publication Data

Handbook of clinical anesthesia procedures of the Massachusetts General Hospital / [edited by] Richard M. Pino ; associate editors, Edward A. Bittner, Hovig V. Chitilian, Wilton C. Levine, Susan A. Vassallo. — 9th edition.
p. ; cm.

Includes bibliographical references.

ISBN 978-1-4511-9515-6

I. Pino, Richard M., editor. II. Bittner, Edward A., 1967- , editor. III. Chitilian, Hovig V., editor. IV. Levine, Wilton C., editor. V. Vassallo, Susan A., editor. VI. Massachusetts General Hospital.

[DNLM: 1. Anesthesia—methods—Handbooks. 2. Anesthetics—administration & dosage—Handbooks. 3. Perioperative Care—methods—Handbooks. WO 231] RD82.2

617.9'6—dc23

2015015460

This work is provided "as is," and the publisher disclaims any and all warranties, express or implied, including any warranties as to accuracy, comprehensiveness, or currency of the content of this work.

This work is no substitute for individual patient assessment based upon healthcare professionals' examination of each patient and consideration of, among other things, age, weight, gender, current or prior medical conditions, medication history, laboratory data and other factors unique to the patient. The publisher does not provide medical advice or guidance and this work is merely a reference tool. Healthcare professionals, and not the publisher, are solely responsible for the use of this work including all medical judgments and for any resulting diagnosis and treatments.

Given continuous, rapid advances in medical science and health information, independent professional verification of medical diagnoses, indications, appropriate pharmaceutical selections and dosages, and treatment options should be made and healthcare professionals should consult a variety of sources. When prescribing medication, healthcare professionals are advised to consult the product information sheet (the manufacturer's package insert) accompanying each drug to verify, among other things, conditions of use, warnings and side effects and identify any changes in dosage schedule or contraindications, particularly if the medication to be administered is new, infrequently used or has a narrow therapeutic range. To the maximum extent permitted under applicable law, no responsibility is assumed by the publisher for any injury and/or damage to persons or property, as a matter of products liability, negligence law or otherwise, or from any reference to or use by any person of this work.

LWW.com

Paul H. Alfille, MD

Chief, Division of Thoracic, Vascular and Neuroanesthesia
Department of Anesthesia, Critical Care, and Pain Medicine
Massachusetts General Hospital
Boston, Massachusetts

Richard W. Anderson, MD

Resident in Anesthesia
Department of Anesthesia, Critical Care, and Pain Medicine
Massachusetts General Hospital
Boston, Massachusetts

Keith Baker, MD, PhD

Associate Professor of Anesthesia
Department of Anesthesia, Critical Care, and Pain Medicine
Massachusetts General Hospital
Harvard Medical School
Boston, Massachusetts

Xiaodong Bao, MD, PhD

Instructor in Anesthesia
Department of Anesthesia, Critical Care, and Pain Medicine
Massachusetts General Hospital
Boston, Massachusetts

Peter L. Bekker, MD

Resident in Anesthesia
Department of Anesthesia, Critical Care, and Pain Medicine
Massachusetts General Hospital
Clinical Fellow
Harvard Medical School
Boston, Massachusetts

William Benedetto, MD

Instructor in Anesthesia
Harvard Medical School
Department of Anesthesia, Critical Care, and Pain Medicine
Massachusetts General Hospital
Boston, Massachusetts

Sheri Berg, MD

Instructor of Anesthesia
Harvard Medical School
Assistant Anesthetist
Department of Anesthesia, Critical Care, and Pain Medicine
Massachusetts General Hospital
Boston, Massachusetts

Somaletha Bhattacharya, MD, FFARCSI

Instructor in Anesthesia
Harvard Medical School
Assistant in Anesthesia
Department of Anesthesia, Critical Care, and Pain Medicine
Massachusetts General Hospital
Boston, Massachusetts

Edward A. Bittner, MD, PhD, FCCP, FCCM

Assistant Professor of Anesthesia
Harvard Medical School
Assistant Anesthetist
Department of Anesthesia, Critical Care, and Pain Medicine
Program Director, Critical Care-Anesthesiology Fellowship
Associate Director, Surgical Intensive Care Unit
Massachusetts General Hospital
Boston, Massachusetts

Emery N. Brown, MD

Warren M. Zapol Professor of Anesthesia
Department of Anesthesia, Critical Care, and Pain Medicine
Massachusetts General Hospital
Harvard Medical School
Edward Hood Taplin Professor of Medical Engineering
Institute for Medical Engineering and Science
Professor of Computational Neuroscience
Department of Brain and Cognitive Sciences
Massachusetts Institute of Technology
Cambridge, Massachusetts

Jessie L. Cassada, MD

Resident in Anesthesia
Department of Anesthesia, Critical Care, and Pain Medicine
Massachusetts General Hospital
Boston, Massachusetts

Khan Chaichana, MD

Resident in Anesthesia
Department of Anesthesiology, Critical Care, and Pain Medicine
Massachusetts General Hospital
Boston, Massachusetts

Jonathan E. Charnin, MD

Instructor in Anesthesia
Harvard Medical School
Assistant in Anesthesia
Department of Anesthesia, Critical Care, and Pain Medicine
Massachusetts General Hospital
Boston, Massachusetts

Hovig V. Chitilian, MD

Assistant Professor of Anesthesia
Harvard Medical School
Assistant Anesthetist
Director, Liver Transplant Anesthesia
Massachusetts General Hospital
Boston, Massachusetts

Naida Cole, MD, MM

Resident in Anesthesia
Department of Anesthesia, Critical Care, and Pain Medicine
Massachusetts General Hospital
Boston, Massachusetts

Jessica A. Cox, DACCPM

Resident in Anesthesia
Department of Anesthesia, Critical Care, and Pain Medicine
Massachusetts General Hospital
Boston, Massachusetts

Lane C. Crawford, MD

Resident in Anesthesia
Department of Anesthesia, Critical Care, and Pain Medicine
Massachusetts General Hospital
Boston, Massachusetts

Negin Daneshpayeh, MD

Resident in Anesthesia

Department of Anesthesiology, Critical Care, and Pain Medicine

Massachusetts General Hospital

Boston, Massachusetts

Mitchell Donner, MD

Resident in Anesthesia

Department of Anesthesia, Critical Care, and Pain Medicine

Massachusetts General Hospital

Boston, Massachusetts

Dan Drzymalski, MD

Resident in Anesthesia

Department of Anesthesia, Critical Care, and Pain Medicine

Harvard Medical School

Boston, Massachusetts

Oleg V. Evgenov, MD, PhD

Instructor in Anesthesia

Harvard Medical School

Assistant in Anesthesia

Department of Anesthesia, Critical Care, and Pain Medicine

Massachusetts General Hospital

Boston, Massachusetts

Stuart A. Forman, MD, PhD

Associate Professor of Anesthesia

Harvard Medical School

Associate Anesthetist

Department of Anesthesia, Critical Care, and Pain Medicine

Massachusetts General Hospital

Boston, Massachusetts

David G. Frazer, MD

Resident in Anesthesia

Department of Anesthesia, Critical Care, and Pain Medicine

Massachusetts General Hospital

Boston, Massachusetts

Margaret Gargarian, MD

Assistant Professor of Anesthesia

Harvard Medical School

Department of Anesthesia, Critical Care, and Pain Medicine

Massachusetts General Hospital

Boston, Massachusetts

Edward E. George, MD, PhD

Assistant Professor
Harvard Medical School
Medical Director of Post Anesthesia Care Unit
Department of Anesthesia, Critical Care, and Pain Medicine
Massachusetts General Hospital
Boston, Massachusetts

Matthew C. Gertsch, MD

Resident in Anesthesia
Department of Anesthesia, Critical Care, and Pain Medicine
Massachusetts General Hospital
Boston, Massachusetts

Gregory Ginsburg, MD

Instructor in Anesthesia
Harvard Medical School
Assistant in Anesthesia
Department of Anesthesia, Critical Care, and Pain Medicine
Massachusetts General Hospital
Boston, Massachusetts

Jeremy Goldfarb, MD

Director
Post Anesthesia Care Unit
Director
Preoperative Medical Evaluation Center
Chief, Inpatient Hospitalist Service, Staff Anesthesiologist
Massachusetts Eye and Ear Infirmary
Clinical Instructor
Harvard Medical School
Boston, Massachusetts

Gaganpreet Grewal, MD

Resident in Anesthesia
Department of Anesthesiology, Critical Care, and Pain Medicine
Massachusetts General Hospital
Boston, Massachusetts

George M. Hanna, MD

Instructor of Anesthesia
Harvard Medical School
Assistant in Anesthesia
Department of Anesthesia, Critical Care, and Pain Medicine
Massachusetts General Hospital
Boston, Massachusetts

P. Grace Harrell, MD

Assistant Professor
Harvard Medical School
Assistant Anesthetist
Department of Anesthesia, Critical Care, and Pain Medicine
Massachusetts General Hospital
Boston, Massachusetts

Ryan J. Horvath, MD, PhD

Resident in Anesthesia
Department of Anesthesia, Critical Care, and Pain Medicine
Massachusetts General Hospital
Boston, Massachusetts

Caroline B. G. Hunter, MD

Resident in Anesthesia
Department of Anesthesia, Critical Care, and Pain Medicine
Massachusetts General Hospital
Boston, Massachusetts

Christina Anne Jelly, MD, MSc

Resident in Anesthesia
Department of Anesthesia, Critical Care, and Pain Medicine
Massachusetts General Hospital
Boston, Massachusetts

Rebecca Kalman, MD

Instructor in Anesthesia
Department of Anesthesia, Critical Care, and Pain Medicine
Massachusetts General Hospital
Boston, Massachusetts

Tara L. Kelly, MD

Resident in Anesthesia
Department of Anesthesia, Critical Care, and Pain Medicine
Massachusetts General Hospital
Boston, Massachusetts

Cindy Kim, MD

Resident in Anesthesia
Department of Anesthesia, Critical Care, and Pain Medicine
Massachusetts General Hospital
Boston, Massachusetts

David J. Kim, MD, MS

Resident in Anesthesia
Department of Anesthesiology, Critical Care, and Pain Medicine
Massachusetts General Hospital
Boston, Massachusetts

William R. Kimball, MD, PhD

Assistant Professor of Anesthesia
Harvard Medical School
Associate Anesthetist
Department of Anesthesia, Critical Care, and Pain Medicine
Massachusetts General Hospital
Boston, Massachusetts

Michael R. King, MD

Resident in Anesthesia
Department of Anesthesia, Critical Care, and Pain Medicine
Massachusetts General Hospital
Boston, Massachusetts

Stephanie L. Lee, MD, PhD

Associate Professor of Medicine
Boston University School of Medicine
Director
Thyroid Health Center
Boston Medical Center
Boston, Massachusetts

Jason S. Lee, MD

Resident in Anesthesia
Department of Anesthesia, Critical Care, and Pain Medicine
Massachusetts General Hospital
Boston, Massachusetts

Alexander Y. B. Lee, MD, MBA

Resident in Anesthesia
Department of Anesthesia, Critical Care, and Pain Medicine
Massachusetts General Hospital
Boston, Massachusetts

Yiuka Leung, MD

Resident in Anesthesia
Department of Anesthesia, Critical Care, and Pain Medicine
Massachusetts General Hospital
Boston, Massachusetts

Wilton C. Levine, MD

Assistant Professor of Anesthesia
Harvard Medical School
Assistant Anesthetist
Department of Anesthesia, Critical Care, and Pain Medicine
Associate Medical Director
Perioperative Services
Massachusetts General Hospital
Boston, Massachusetts

Jason M. Lewis, MD

Instructor in Anesthesia
Harvard Medical School
Assistant in Anesthesia
Department of Anesthesia, Critical Care, and Pain Medicine
Massachusetts General Hospital
Boston, Massachusetts

Amber Liu, MD

Resident in Anesthesia
Department of Anesthesia, Critical Care, and Pain Medicine
Massachusetts General Hospital
Boston, Massachusetts

Ayumi Maeda, MD

Resident in Anesthesia
Department of Anesthesia, Critical Care, and Pain Medicine
Massachusetts General Hospital
Boston, Massachusetts

Solmaz Poorsattar Manuel, MD

Resident in Anesthesia
Department of Anesthesia, Critical Care, and Pain Medicine
Massachusetts General Hospital
Boston, Massachusetts

John J. A. Marota MD, PhD

Assistant Professor
Harvard Medical School
Associate Anesthetist
Department of Anesthesia, Critical Care, and Pain Medicine
Massachusetts General Hospital
Boston, Massachusetts

Courtney Maxey-Jones, MD

Resident in Anesthesia
Department of Anesthesia, Critical Care, and Pain Medicine
Massachusetts General Hospital
Boston, Massachusetts

Matthew J. Meyer, MD

Resident in Anesthesia
Department of Anesthesia, Critical Care, and Pain Medicine
Massachusetts General Hospital
Boston, Massachusetts

Rebecca D. Minehart, MD, MSHPEd

Assistant Professor of Anesthesia
Harvard Medical School
Assistant Program Director, Anesthesia Residency
Program Director, Obstetric Anesthesia Fellowship
Department of Anesthesia, Critical Care, and Pain Medicine
Massachusetts General Hospital
Boston, Massachusetts

Alexander D. Moore, MD

Resident in Anesthesia
Department of Anesthesia, Critical Care, and Pain Medicine
Massachusetts General Hospital
Boston, Massachusetts

Robert A. Peterfreund, MD, PhD

Associate Professor of Anesthesia
Harvard Medical School
Anesthetist
Department of Anesthesia, Critical Care, and Pain Medicine
Massachusetts General Hospital
Boston, Massachusetts

May C. M. Pian-Smith, MD, MS

Associate Professor of Anesthesia
Harvard Medical School
Assistant Anesthetist
Director of Quality and Safety
Department of Anesthesia, Critical Care, and Pain Medicine
Massachusetts General Hospital
Boston, Massachusetts

Richard M. Pino, MD, PhD, FCCM

Associate Professor of Anesthesia
Harvard Medical School
Vice Chairman for Clinical Affairs
Associate Anesthetist
Department of Anesthesia, Critical Care, and Pain Medicine
Massachusetts General Hospital
Boston, Massachusetts

Michael P. Puglia, MD, PhD

Resident in Anesthesia
Department of Anesthesia, Critical Care, and Pain Medicine
Massachusetts General Hospital
Boston, Massachusetts

Jason Z. Qu, MD

Assistant Professor of Anesthesia
Harvard Medical School
Department of Anesthesia, Critical Care, and Pain Medicine
Massachusetts General Hospital
Boston, Massachusetts

James P. Rathmell, MD

Professor of Anesthesia
Harvard Medical School
Executive Vice Chairman
Chief, Division of Pain Medicine
Department of Anesthesia, Critical Care, and Pain Medicine
Massachusetts General Hospital
Boston, Massachusetts

Jessie D. Roberts, Jr., MD

Associate Professor of Anesthesia
Harvard Medical School
Associate Anesthetist
Department of Anesthesia, Critical Care, and Pain Medicine
Massachusetts General Hospital
Boston, Massachusetts

Jamie Rubin, MD

Resident in Anesthesia
Department of Anesthesia, Critical Care, and Pain Medicine
Massachusetts General Hospital
Boston, Massachusetts

Adeola Sadik, MD

Resident in Anesthesia
Department of Anesthesia, Critical Care, and Pain Medicine
Massachusetts General Hospital
Boston, Massachusetts

William J. Sauer, MD

Resident in Anesthesia
Department of Anesthesia, Critical Care, and Pain Medicine
Massachusetts General Hospital
Boston, Massachusetts

Puneet Sayal, MD, MSc

Resident in Anesthesia
Department of Anesthesia, Critical Care, and Pain Medicine
Massachusetts General Hospital
Boston, Massachusetts

Ulrich Schmidt, MD, PhD, FCCM

Associate Professor of Anesthesia
Harvard Medical School
Associate Anesthetist
Department of Anesthesia, Critical Care, and Pain Medicine
Massachusetts General Hospital
Boston, Massachusetts

William B. Schoenfeld, MD

Instructor in Anesthesia
Department of Anesthesia, Critical Care, and Pain Medicine
Massachusetts General Hospital
Harvard Medical School
Boston, Massachusetts

Laurie Shapiro, MD

Assistant Professor
Harvard Medical School
Director
Perioperative Inpatient Evaluation Service
Department of Anesthesia, Critical Care, and Pain Medicine
Massachusetts General Hospital
Boston, Massachusetts

Milad Sharifpour, MD, MS

Resident in Anesthesia
Department of Anesthesia, Critical Care, and Pain Medicine
Massachusetts General Hospital
Boston, Massachusetts

Tao Shen, MBBS

Resident in Anesthesia
Department of Anesthesia, Critical Care, and Pain Medicine
Massachusetts General Hospital
Boston, Massachusetts

Kenneth E. Shepherd, MD

Assistant Anesthetist
Department of Anesthesia, Critical Care, and Pain Medicine
Massachusetts General Hospital
Assistant Professor of Anesthesia
Harvard Medical School
Boston, Massachusetts

Bryan Simmons, MD

Resident in Anesthesia

Department of Anesthesia, Critical Care, and Pain Medicine

Massachusetts General Hospital

Boston, Massachusetts

Ken Solt, MD

Associate Professor of Anesthesia

Harvard Medical School

Assistant Anesthetist

Department of Anesthesia, Critical Care, and Pain Medicine

Massachusetts General Hospital

Boston, Massachusetts

Katherine A. Sparger, MD

Department of Pediatrics

Harvard Medical School

Neonatal and Newborn Medicine Unit

Massachusetts General Hospital

Boston, Massachusetts

Genevieve Staudt, MD

Resident in Anesthesia

Department of Anesthesia, Critical Care, and Pain Medicine

Massachusetts General Hospital

Boston, Massachusetts

Michele Szabo, MD

Assistant Professor

Harvard Medical School

Associate Anesthetist

Department of Anesthesia, Critical Care, and Pain Medicine

Massachusetts General Hospital

Boston, Massachusetts

Andrea Torri, MD

Assistant Professor of Anesthesia

Harvard University School of Medicine

Attending Anesthesiologist

Department of Anesthesia, Critical Care, and Pain Medicine

Massachusetts General Hospital

Boston, Massachusetts

Becky Ying Ki Tsui, MD, MPH

Resident in Anesthesia

Department of Anesthesia, Critical Care, and Pain Medicine

Massachusetts General Hospital

Boston, Massachusetts

Samuel M. Vanderhoek, MD

Resident in Anesthesia
Department of Anesthesia, Critical Care, and Pain Medicine
Massachusetts General Hospital
Boston, Massachusetts

Susan A. Vassallo, MD

Assistant Professor of Anesthesia
Harvard Medical School
Anesthetist
Department of Anesthesia, Critical Care, and Pain Medicine
Massachusetts General Hospital
Boston, Massachusetts

Rafael Vazquez, MD

Instructor in Anesthesia
Harvard Medical School
Assistant in Anesthesia
Department of Anesthesia, Critical Care, and Pain Medicine
Massachusetts General Hospital
Boston, Massachusetts

Olof Viktorsdottir, MD

Instructor in Anesthesia
Harvard Medical School
Assistant in Anesthesia
Department of Anesthesia, Critical Care, and Pain Medicine
Massachusetts General Hospital
Boston, Massachusetts

Lisa Warren, MD

Assistant Professor of Anesthesia
Harvard Medical School
Department of Anesthesia, Critical Care, and Pain Medicine
Massachusetts General Hospital
Boston, Massachusetts

Elizabeth Cox Williams, MD

Instructor in Anesthesia
Department of Anesthesia, Critical Care, and Pain Medicine
Massachusetts General Hospital
Boston, Massachusetts

Zhongcong Xie, MD, PhD

Professor of Anesthesia

Harvard Medical School

Associate Anesthetist

Department of Anesthesia, Critical Care, and Pain Medicine

Massachusetts General Hospital

Boston, Massachusetts

Marc D. Yelle, MD, PhD

Resident in Anesthesia

Department of Anesthesia, Critical Care, and Pain Medicine

Massachusetts General Hospital

Boston, Massachusetts

In the late 1970s, Dr. Richard Kitz, as the Anaesthetist-in-Chief at Massachusetts General Hospital, had a vision for a “manual of anesthetic practice, written primarily by recent house staff” that was “intended to be the foundation of practical knowledge for the inexperienced or incompletely trained anesthetist.” The ninth edition of *Clinical Anesthesia Procedures of the Massachusetts General Hospital* continues this tradition. It was written by residents and attending staff of the Department of Anesthesia, Critical Care, and Pain Medicine at the Massachusetts General Hospital. Often, the senior author, now a board certified anesthesiologist, was the “resident author” for the previous edition. For almost 40 years and with the help of over 200 people, the *Clinical Anesthesia Procedures of the Massachusetts General Hospital* has been routinely updated to meet the needs of our ever-changing field.

Similar to the past editions, this manual continues to emphasize the clinical fundamentals needed for the safe administration of anesthesia and perioperative care for our patients. The suggestions reflect the current clinical practice at MGH, represent the foundation of the educational programs for our residency and fellowship programs, and complement more extensive readings in other published works and Internet sources. It is designed to be an easily accessible and accurate source of information for practicing anesthesiologists, nurse anesthetists, anesthesia assistants, trainees in anesthesia and other disciplines, medical students, and health care professionals interested in perioperative care. It is intended to augment experienced clinical teaching and inspire more detailed study stimulated by updated references for each chapter.

I wish to gratefully acknowledge the many past editors of, and contributors to, the previous editions of this handbook. I have enjoyed working with Ms. Nicole Dernoski and her talented editorial staff at Lippincott Williams & Wilkins. I am indebted to Richard J. Kitz, MD, and Hassan Ali, MD, for their mentorship and friendship over the years and to Jeanine Wiener-Kronish, MD, Anesthetist-in-Chief, for her ongoing support. Mack Thomas, MD, inspired me to start on the path to anesthesia and critical care when I was a medical student at LSUMC and purchased the third edition of the handbook. I never remotely dreamed that I would eventually be given the privilege of being one of the editors.

I hope that you find this edition helpful as you pursue the very rewarding and evolving field of anesthesia.

Finally, this handbook could not have been revised without the endless love, support, and patience of my wife, Patti, and son, Daniel.

Richard M. Pino, MD, PhD, FCCM

<i>Contributors</i>	v
<i>Preface</i>	xix

PART I: EVALUATING THE PATIENT BEFORE ANESTHESIA 1

1	Evaluating the Patient Before Anesthesia	1
	Jessie L. Cassada and Laurie Shapiro	
2	Specific Considerations with Cardiac Disease	17
	Christina Anne Jelly and Olof Viktorsdottir	
3	Specific Considerations with Pulmonary Disease	33
	Yiuka Leung and Kenneth E. Shepherd	
4	Specific Considerations with Renal Disease	44
	Samuel Vanderhoek and William Benedetto	
5	Specific Considerations with Liver Disease	64
	Matthew C. Gertsch and Wilton C. Levine	
6	Specific Considerations with Endocrine Disease	76
	Becky Y.K. Tsui, Robert A. Peterfreund, and Stephanie L. Lee	
7	Infectious Diseases and Infection Control in Anesthesia	101
	Courtney Maxey-Jones and Elizabeth Cox Williams	

PART II: ADMINISTRATION OF ANESTHESIA 113

8	Safety in Anesthesia	113
	Solmaz Poorsattar Manuel and May Pian-Smith	

9	The Anesthesia Machine	122
	Adeola O. Sadik and Gregory Ginsburg	
10	Monitoring	133
	Mitchell Donner and William Schoenfeld	
11	Monitoring Anesthetic Brain States	152
	Negin Daneshpayeh and Emery N. Brown	
12	Intravenous and Inhalation Anesthetics	162
	Jason S. Lee and Ken Solt	
13	Neuromuscular Blockade	177
	Bryan Simmons and Oleg V. Evgenov	
14	Airway Evaluation and Management	192
	David G. Frazer and Ulrich Schmidt	
15	Administration of General Anesthesia	211
	William J. Sauer and Stuart A. Forman	
16	Local Anesthetics	222
	Ayumi Maeda and Rebecca D. Minehart	
17	Spinal, Epidural, and Caudal Anesthesia	231
	David J. Kim and Jason M. Lewis	
18	Regional Anesthesia	255
	Lane C. Crawford and Lisa Warren	
19	Intra-anesthetic Problems	290
	Ryan J. Horvath and Keith Baker	
20	Perioperative Hemodynamic Control	312
	Genevieve E. Staudt and Rafael Vazquez	
21	Anesthesia for Abdominal Surgery	328
	Richard W. Anderson and Xiaodong Bao	
22	Anesthesia for Thoracic Surgery	348
	Caroline B.G. Hunter and Paul H. Alfille	

23	Anesthesia for Vascular Surgery	368
	Jessica A. Cox and Hovig V. Chitilian	
24	Anesthesia for Cardiac Surgery	388
	Tao Shen and Jason Zhensheng Qu	
25	Anesthesia for Neurosurgery	422
	Gaganpreet Grewal and Michele Szabo	
26	Anesthesia for Head and Neck Surgery	442
	Chang Amber Liu and Jeremy Goldfarb	
27	Anesthesia for Spine Surgery	455
	Puneet Sayal and George M. Hanna	
28	Anesthesia for Urologic Surgery	460
	Alexander D. Moore and William R. Kimball	
29	Anesthesia for Geriatric Patients	468
	Zhongcong Xie and Khan Chaichana	
30	Care of the Neonate	475
	Jamie Rubin, Katherine A. Sparger, and Jesse D. Roberts Jr.	
31	Anesthesia for Pediatric Surgery	500
	Susan A. Vassallo and Michael P. Puglia	
32	Anesthesia for Obstetrics and Gynecology	523
	Naida Cole and Andrea Torri	
33	Anesthesia Outside of the Operating Room	543
	Alexander Y.B. Lee and John J.A. Marota	
34	Anesthesia for Trauma and Burns	557
	Cindy Kim and Rebecca Kalman	
35	Transfusion Therapy	577
	Michael R. King and Jonathan E. Charnin	

PART III: PERIOPERATIVE ISSUES	594
36 The Postanesthesia Care Unit Matthew J. Meyer and Edward E. George	594
37 Postoperative Pulmonary Complications Milad Sharifpour and Edward A. Bittner	614
38 Adult, Pediatric, and Newborn Resuscitation Peter L. Bekker, Somalettha Bhattacharya, and Richard M. Pino	622
39 Pain Management Marc D. Yelle and James P. Rathmell	639
40 Complementary and Alternative Medicine Dan Drzymalski, Margaret Gargarian, and P. Grace Harrell	658
41 Ethical and End-of-Life Issues Tara L. Kelly and Sheri Berg	665
APPENDIX I: Drugs with Narrow Therapeutic Ranges and Potential for Harm	673
APPENDIX II: Commonly Used Drugs	677
APPENDIX III: Common Intravenous Antibiotics	695
<i>Index</i>	697



Evaluating the Patient Before Anesthesia

Jessie L. Cassada and Laurie Shapiro

I. OVERVIEW

The objectives of the preanesthetic evaluation include establishing rapport, becoming familiar with the patient's surgical illness and coexisting medical conditions, medically optimizing the patient's comorbidities, developing a management strategy for perioperative anesthetic care, and obtaining informed consent for the anesthetic plan. The consultation is then detailed in the patient's medical record and concludes with the anesthetic options, including attendant risks and benefits of discussed options. The overall goals of the preoperative assessment are to reduce perioperative morbidity and mortality and to assuage patient anxiety.

II. HISTORY

Relevant information should be first obtained through chart review followed by corroboration with the patient interview. Prior knowledge of the patient's history when beginning the interview is reassuring to the anxious patient. When the medical record is not available, a history obtained from the patient may be supplemented through discussions with the patient's other physicians. Information gathered should include the following:

- A. History of Presenting Illness.** The anesthesiologist must comprehensively review the symptoms of the present surgical illness, presumptive diagnosis, initial treatment, response to treatment, and diagnostic studies.
- B. Medications.** The interviewer must establish the current dosing and schedules of all the patient's medications. Of particular importance are antihypertensive, antianginal, antiarrhythmic, anticoagulant, anticonvulsant, and specific endocrine (e.g., insulin and hypoglycemics) medications. The decision to continue medication during the preoperative period depends on the severity of the underlying illness, the potential consequences of discontinuing treatment, the half-life of the medication, and the likelihood of deleterious interactions with proposed anesthetic agents. As a general rule, most medications may be continued up through the time of surgery (see section VI).
- C. Allergies and Drug Reactions.** True allergic reactions are relatively uncommon. Nonallergic adverse reactions to perioperative medications are not infrequent and may be perceived as an allergic reaction by the patient. Therefore, it is important to obtain a careful description of the exact nature of the reaction.

1. **True allergic reactions.** This can be presumed based upon a history of drug reaction that (by direct observation, chart documentation, or patient description) produced skin manifestations (pruritus with hives and/or flushing), facial or oral swelling, shortness of breath, choking, wheezing, or vascular collapse.
 2. **Antibiotic allergy.** Allergies to antibiotics, especially to sulfonamides, penicillins, and cephalosporin derivatives, are the most common drug allergies. Notably, a patient reporting allergy is 90% to 99% likely not to be allergic when skin tested. With true penicillin allergy, there is a 2% to 4% cross-reactivity rate seen with first-generation cephalosporins. Cross-reactivity rates are lower for other generations.
 3. **Soybean oil and/or egg yolk allergy.** Most egg allergies are to the white, rather than the yolk, and may not pose any anesthetic issues. Likewise, the vast majority of soy allergies are to the protein rather than to the oil and may not cause any complications. Use of propofol in a patient with these allergies is up to the discretion of the provider as current data on reactivity are mixed.
 4. **Inhalational agent or succinylcholine "allergy."** A history of allergy to "anesthesia," inhalational agents, or succinylcholine (in the patient or any close relative) warrants special attention as this may represent a history of malignant hyperthermia (which is of autosomal dominant inheritance) or prolonged paralysis caused by atypical plasma cholinesterase (see Chapter 13). The metabolism of halothane has been associated with severe hepatitis. Although halothane is no longer used in most countries, it is still an anesthetic in Argentina, Brazil, Greece, India, Russia, and Turkey.
 5. **Local anesthetic allergy.** Allergy to ester-type local anesthetics can be anaphylactic (see Chapter 16), while true allergy to the amide-type local anesthetics is exceedingly rare. Syncopal episodes, tachycardia, or palpitations associated with the injection of a local anesthetic/epinephrine preparation may be falsely labeled as an allergic reaction.
 6. **Shellfish or seafood allergy.** Neither shellfish nor seafood allergy has been linked to an allergy to intravenous iodine contrast. (It had been presumed that shellfish allergies stemmed from high levels of iodine in the shellfish, but this has proven not true.) However, a history of dermatitis after exposure to topical iodine may preclude the use of intravenous iodine.
 7. **Latex allergy or hypersensitivity reactions.** Latex allergy must be ascertained preoperatively to allow for preparation of a latex-free operating room. Additionally, banana, avocado, chestnut, apricot, kiwi, or papaya allergy should be elicited as 30% to 50% of individuals with these allergies have cross-reactive allergies to latex. Other risk factors for latex allergy include repeated exposure to latex (e.g., health care workers or patients with multiple prior surgeries), atopy, and certain medical disorders, such as spina bifida. If these risk factors exist, and no prior skin or serologic tests have been conducted, extra precautions may be warranted.
 8. **Adverse reactions and side effects.** Many perioperative medications are capable of producing memorable and unpleasant side effects (e.g., nausea, vomiting, pruritus) in the conscious patient, but these are not true drug allergies.
- D. Anesthetic History.** Question the patient regarding his or her experience with prior anesthetics, including common complaints, such as postoperative nausea and vomiting (PONV), hoarseness, myopathy, or neuropathy.

Also examine the patient's medical record for specific cautions from previous anesthesiologists. Additionally, review previous anesthetic records for the following information:

1. **Response to medications.** Patient response to sedative, analgesic, and anesthetic agents varies widely among individuals.
 2. **Vascular access and invasive monitoring.** Determine that which has been used in the past, as well as any difficulties encountered.
 3. **Airway management.** Determine past ease of mask ventilation, view obtained on direct laryngoscopy, size and type of laryngoscope blade and endotracheal tube, and depth of endotracheal tube insertion.
 4. **Perianesthetic complications.** Review for complications such as adverse drug reactions, intraoperative awareness, dental injury, protracted PONV, hemodynamic issues, respiratory issues, postoperative myocardial infarction (MI), congestive heart failure, unexpected admission to an intensive care unit (ICU), prolonged emergence, or need for reintubation.
 5. **Narcotic requirements.** Narcotic administration both intraoperatively and in the postoperative recovery unit is useful information, which will lend insight into future requirements.
- E. Family History.** A history of adverse anesthetic outcomes in family members should be assessed with open-ended questions, such as "Has anyone in your family experienced unusual or serious reactions to anesthesia?" Additionally, patients should be specifically asked about a family history of malignant hyperthermia.
- F. Social History and Habits**
1. **Smoking.** Although the complications of smoking may place the patient at a higher risk for perioperative pulmonary complications, cigarette smoking, itself, is no longer viewed as a major risk factor. Patients should, however, be counseled about smoking cessation as recent data have shown that patients are more likely to make a commitment to stop smoking around life-changing events, such as major surgery. A history of exercise intolerance or the presence of a productive cough or hemoptysis may indicate the need for further evaluation.
 2. **Drug and alcohol use.** Although self-reporting of drug and alcohol intake typically underestimates use, it is a helpful start to define the type of drugs used, routes of administration, frequency, and timing of most recent use. Stimulant abuse may lead to palpitations, angina, weight loss, and lowered thresholds for serious arrhythmias and seizures. Acute alcohol intoxication decreases anesthetic requirement and predisposes to hypothermia and hypoglycemia. Alcohol withdrawal may precipitate severe hypertension (HTN), tremors, delirium, and seizures and may markedly increase anesthetic and analgesic requirements. Risk of intraoperative awareness is also increased with chronic opioid or benzodiazepine use.

III. REVIEW OF SYSTEMS

The purpose of review of systems is to elicit symptoms of occult disease and to determine the stability of current disease processes. Coexisting illnesses may complicate the surgical and anesthetic course. These illnesses should be evaluated in a systematic organ systems approach with an emphasis on recent changes in symptoms, signs, and treatment (see, also, Chapters 2 through 6). In certain circumstances, preoperative specialty consultation may be needed to answer specific questions about the interpretation of unusual laboratory tests, unfamiliar drug therapies, or changes in the patient's baseline status.

Consultants should not be asked for a general “clearance” for anesthesia because this is the specific responsibility of the anesthesiologist. A minimum review of systems should seek to elicit the following information:

A. Cardiovascular.

1. **Coronary artery disease.** Preexisting coronary artery disease (CAD) may predispose the patient to myocardial ischemia, ventricular dysfunction, or MI with the stress of surgery and anesthesia. Elicitation of symptoms of angina, dyspnea on exertion (DOE), paroxysmal nocturnal dyspnea, and an assessment of the patient's exercise capacity can help characterize the severity of disease.
2. **Pacemakers and implanted cardioverter–defibrillators.** Pacemakers and/or cardioverter–defibrillator devices implanted for a history of rhythm disturbances require consultation with an electrophysiologist. It is recommended that the device be interrogated within 6 months of surgery. The decision to leave on or deactivate (via transcutaneous magnet placement) the defibrillating mode should be made preoperatively.
3. **Hypertension.** Poorly treated HTN is frequently associated with blood pressure lability during anesthesia. Uncontrolled HTN is also considered a minor risk factor for perioperative major adverse cardiac events.
4. **Dyspnea on exertion.** DOE is an important sign that can be caused by myriad underlying etiologies, including physical deconditioning, obesity, or cardiopulmonary pathology. Knowledge of the latter is of great import for obvious reasons. If the DOE is chronic, it may prove prudent to contact the patient's primary care provider, as often this provider will have insight regarding the etiology. If the DOE is an acute change from baseline, it is advisable to refer the patient to cardiology for further evaluation.
5. **Exercise capacity.** Although patient age and American Society of Anesthesiologists (ASA) physical status classification are more accurate predictors of adverse outcomes, knowledge of the patient's activities of daily living, including maximum activity level, may help predict overall outcome in the perioperative period.

B. Respiratory.

1. **Upper respiratory infection.** Upper respiratory infection (URI), especially in children, can predispose patients to pulmonary complications including bronchospasm and laryngospasm during induction and emergence from general anesthesia. The patient with current signs and symptoms of a URI (e.g., productive cough, rhinorrhea, sore throat, fever) may benefit from postponement of an elective procedure.
2. **Asthma.** Reactive airway disease may result in acute bronchospasm in the perioperative period. Specific questions about previous asthma-related hospitalizations, intubations, emergency room visits, and medication requirement (specifically, steroid use) can help delineate the severity of asthma.
3. **Obstructive sleep apnea.** Symptoms of obstructive sleep apnea (OSA) should be elicited as they may lead to intermittent perioperative hypoxia in adults and children. The patient with OSA will need a comprehensive cardiovascular, pulmonary, and airway evaluation. Opioid dosing should likely be decreased in the patient with OSA, especially children. Further evaluation is warranted if there is evidence of end organ damage, such as pulmonary HTN or right heart strain.

C. Endocrine.

1. **Diabetes mellitus.** Diabetes is a risk factor for CAD. The patient with autonomic nervous system dysfunction may have silent myocardial

ischemia. Alterations in autonomic regulation may also lead to gastroparesis and reflux. Endotracheal intubation may prove difficult in some of the diabetic patients secondary to arthritis of the temporomandibular joints and cervical spine (as a result of glycosylation of synovium). Home blood glucose measurements, hemoglobin A1c level, and question of recent symptomatic hyper- or hypoglycemia may further elucidate if the diabetes is well controlled.

2. **Thyroid disease.** It is important to discuss thyroid disorder as thyroid storm can lead to an intraoperative emergency. Thyroid storm occurs most commonly in patients with thyrotoxicosis secondary to Graves disease and as well in those with untreated disease.

D. Gastrointestinal.

1. **Gastroesophageal reflux disease.** Symptoms of reflux with or without hiatal hernia increase the risk of pulmonary aspiration and may alter the anesthetic plan; an awake intubation or a “rapid sequence” induction may be indicated. The patient should be asked specifically about chest pain/burning sensation, sour taste in the mouth after meals, frank regurgitation of food, or unexplained cough. It can also be important to delineate aggravating factors, such as provocation only with spicy foods versus with lying in the supine position.

2. **Motion sickness or PONV history.** A history of motion sickness and/or PONV increases the risk for PONV. Other factors associated with increased PONV risk include, but are not limited to, history of vertigo, female gender, nonsmoking status, gynecologic and laparoscopic procedures, strabismus surgery, and the need for large doses of perioperative or postoperative opioids. A different anesthetic technique, such as total intravenous anesthesia, may be warranted in the patient with multiple risk factors.

- E. **Musculoskeletal.** A history of radiation to the head or neck may increase the risk of distorted airway anatomy and may alter intubation technique. The patient should also be questioned about joint pain for purposes of intraoperative positioning.

- F. **Obstetric/Gynecologic.** Possibility of pregnancy and timing of last menses should be elicited in women of childbearing age as premedications and anesthetic agents may adversely affect uteroplacental blood flow, act as teratogens, or trigger spontaneous abortion.

- G. **Hematologic.** A history of easy bruising, bleeding, or significantly heavy menses warrants further questioning and may require additional workup as coagulopathies necessitate intraoperative and neuraxial changes in management.

IV. THE PHYSICAL EXAMINATION

The physical examination should be thorough, but focused. Special attention is directed toward evaluation of the airway, heart, lungs, and neurologic status. A detailed assessment of the block site is warranted when a regional anesthetic technique is planned. At a minimum, the physical examination should include the following:

A. Vital Signs.

1. **Blood pressure.** Blood pressure measurement should be taken in both arms with any disparity noted (significant differences may imply disease of the thoracic aorta or its major branches). If hypovolemia is suspected, it is prudent to also measure postural vital signs.
2. **Pulse.** Resting heart rate should be noted for rhythm and rate.

3. **Respiratory rate.** Respirations should be observed for rate, depth, and pattern while at rest.
4. **Oxygen saturation.**
- B. **Height and Weight.** Height and weight measurement are necessary for determining drug dosages, fluid requirements, adequate urine output, and ventilator settings. Ideal body weight should be calculated in the obese patient using the formula $50 + (2.3 \times [\text{height in inches over } 60])$ for men and $45.5 + (2.3 \times [\text{height in inches over } 60])$ for women.
- C. **Head and Neck.** Details of a thorough head and neck examination are outlined in Chapter 14. During the basic preoperative examination, the anesthesiologist should evaluate the following:
 1. **Maximal mouth opening.** Comment on predicted adequacy for intubation.
 2. **Tongue size.**
 3. **Mallampati classification** (see Chapter 14).
 4. **Thyromental distance.** Thyromental distance is the distance between the tip of the chin and the thyroid notch. Approximately three finger-breadths distance is considered normal. Shorter or longer distances may be a sign of a difficult intubation.
 5. **Dentition.** Evaluate for loose or chipped teeth, artificial crowns, dentures, and other dental appliances.
 6. **Facial hair.** A large beard or mustache may interfere with achieving a good seal with mask ventilation and should be noted.
 7. **Cervical spine.** Evaluate and document range of motion in flexion, extension, and rotation of the cervical spine.
 8. **Superficial neck.** Comment on any tracheal deviation, cervical masses, and jugular venous distention. The presence of a carotid bruit is non-specific but may suggest a need for further workup.
 9. **Neck circumference.** A neck circumference measurement of 17" for men and 16" for women are associated with OSA.
- D. **Precordium.** Auscultation of the heart may reveal murmurs, S3, S4, or a pericardial rub.
- E. **Lungs.** Auscultate for wheezing, rhonchi, or rales, which should be correlated with observations regarding the ease of breathing and the use of accessory muscles of respiration.
- F. **Abdomen.** Any evidence of abdominal distention, masses, or ascites should be noted as these may predispose the patient to regurgitation or ventilatory compromise.
- G. **Extremities.** Evaluate for muscle wasting and weakness, distal perfusion, clubbing, cyanosis, edema, and the presence of any cutaneous infections (especially over sites of planned vascular cannulation or regional nerve block). Ecchymosis or unexplained injury, especially in children, women, and elderly patients, can be an indication of an abusive relationship.
- H. **Back.** Note any deformity, bruising, or infection or any factors that could lead to difficulty in patient positioning or performance of neuraxial analgesia.
- I. **Neurologic Examination.** Briefly document mental status, cranial nerve function, cognition, and peripheral sensorimotor function.

V. LABORATORY STUDIES

Routine laboratory screening tests are generally not indicated. Tests should be selected based on the patient's medical condition and the proposed surgical procedure. A brief review of current guidelines follows.

- A. **Hematologic Studies.** Hematologic studies may be indicated if there are concerns regarding significant preoperative or intraoperative blood loss, anemia, or coagulopathy.

1. **Recent hematocrit/hemoglobin level.** There is no universally accepted minimum hematocrit before anesthesia. Hematocrits of 25% to 30% (approximate hemoglobin 8 g/dL) are well tolerated by the otherwise healthy individual but could result in ischemia in the patient with CAD. The etiology and duration of anemia should be ascertained. If the cause is not readily apparent, a surgical delay may be indicated to allow for further workup. The healthy patient undergoing a minimally invasive procedure does not need a routine hematocrit screen.
 2. **Platelet studies.** Platelet function may be assessed by a history of easy bruising, excessive bleeding from gums and minor cuts, and family history. A positive finding in this category warrants additional laboratory evaluation and, possibly, consultation with a hematologist.
 3. **Coagulation studies.** Coagulation studies are ordered only when clinically indicated (e.g., history of a bleeding diathesis, anticoagulant use, liver disease, serious systemic illness) or if postoperative anticoagulation is planned. Coagulation status of the patient on low molecular weight heparin may be monitored through measurement of anti-factor Xa levels.
 4. **Blood type/antibody screen.** Type and screen must be obtained if a significant amount of blood loss is anticipated.
- B. Serum Chemistry.** A metabolic panel should be ordered only when specifically indicated by history and physical examination. For example, measurements of blood urea nitrogen and creatinine are indicated for the patient with chronic renal, cardiovascular, or hepatic disease, as well as for the patient with diabetes or morbid obesity. Serum chemistries are also indicated in the patient taking diuretics, digoxin, steroids, or aminoglycoside antibiotics.
1. **Hypokalemia.** Low potassium levels are common in the patient receiving diuretics and are usually readily corrected by preoperative oral potassium supplementation. Mild hypokalemia (2.8 to 3.5 mEq/L) should not preclude elective surgery. Rapid correction with intravenous potassium may lead to dysrhythmias and cardiac arrest. It is reasonable to delay surgery for cautious correction of marked hypokalemia, particularly if the patient is taking digoxin or experiencing dysrhythmias (see Chapter 4).
 2. **Hyperkalemia.** Elevated potassium is often seen in the patient with end-stage renal disease. In this setting, mild elevations in serum potassium are well tolerated, but it may be prudent to choose replacement fluids that do not contain additional potassium. Large increases in potassium may also predispose to dysrhythmias. Treatment of hyperkalemia is warranted if concentrations exceed 6 mEq/L or if electrocardiogram (ECG) changes are seen.
- C. Electrocardiogram.** ECG should be obtained in the patient with CAD risk factors (age ≥ 65 years, HTN, diabetes mellitus, hypercholesterolemia, family history of CAD, and current cigarette use). It can also detect new dysrhythmias and is useful to evaluate the stability of known abnormal rhythms. An ECG should not be done simply because of advanced patient age. ECG abnormalities in older patients are prevalent, but not specific and, thus, do not have added predictive value over clinical risk factors (see Chapter 10). Although the resting ECG is not a sensitive test for occult myocardial ischemia, an abnormal ECG mandates correlation with history, physical examination, and prior ECGs.
- D. Chest Radiography.** A chest x-ray (CXR) should be obtained in the patient with signs or symptoms of acute cardiopulmonary disease or chronic cardiopulmonary disease that could show radiographic evidence of change in status.

- E. Pulmonary Function Tests.** Pulmonary function tests (PFTs) are used to evaluate the severity of lung disease and the response to bronchodilators. They have a recognized role in the evaluation of patients undergoing lung resection surgery, however, they have not been shown to be predictive of post-operative pulmonary complications in surgeries other than lung resection (see Chapters 3 and 22).

VI. PREOPERATIVE MEDICAL OPTIMIZATION

Preexisting medical conditions should be controlled or stabilized before surgery. Many of the complications associated with these conditions may be prevented by thoughtful administration of standard medications. Some medications should be discontinued or changed in the perioperative period.

- A. Hypertension.** Untreated HTN can cause end-organ damage in the perioperative period. Acute treatment of chronic HTN may be indicated in the patient with systolic blood pressures greater than 20% his or her baseline pressure. If HTN persists despite treatment or if the blood pressure is greater than 180/110 mm Hg, elective surgery should be postponed until the blood pressure is better controlled. Angiotensin-converting enzyme inhibitors and angiotensin receptor blocking agents may cause refractory hypotension intraoperatively and should be held on the day of surgery. β -blockers, calcium channel blockers, and clonidine may be continued in the perioperative period.
- B. Coronary Artery Disease.** A patient with known CAD (history of previous coronary artery bypass grafting or stents, previous MI, or angina with ischemia evidenced on stress testing) or one at risk for CAD may benefit from premedication with β -blockers. A recent study (Devereaux PJ, et al., 2006) suggests the routine use of perioperative β -blockade (previously believed to decrease perioperative mortality) may actually be harmful. However, a patient on chronic β -blocker therapy should continue his or her medication through the day of surgery to avoid withdrawal effects. A second study (Devereaux PJ, et al., 2014) also suggested that perioperative aspirin was associated with problematic side effects. More evidence is required before current guidelines are changed. Current guidelines at the Massachusetts General Hospital state that aspirin for primary and secondary prevention be continued up to and including the day of surgery, except in the case of intracranial neurosurgical procedures, intramedullary spine surgery, surgery of the middle ear or posterior eye and possibly prostate surgery. Discontinuing aspirin in the patient receiving the drug for secondary prophylaxis necessitates an explicit discussion with the patient's primary care physician, cardiologist or vascular physician. The discussion should weigh the cardiovascular risks of stopping aspirin versus the risk of bleeding from the procedure. This decision should be documented in the patient's record.
- C. Anticoagulation Therapy.** Depending on the indication for the anticoagulation, a patient on warfarin may need to be transitioned to low molecular weight heparin or unfractionated heparin regimens prior to surgery. This is a discussion that should occur directly between the surgeon and cardiologist (or whomever manages the patient's anticoagulation).
- D. Chronic Nonsteroidal Anti-inflammatory Use.** The modest inhibition of platelet function seen with nonsteroidal anti-inflammatory drugs (NSAID) use does not increase bleeding risk in many surgeries nor does it increase the risk associated with spinal or epidural anesthesia. Despite this, some surgeons may hesitate to continue NSAIDs given preliminary research results

suggesting deleterious effects on bone healing. More data on this are needed. Given the oppositional literature, a discussion with the surgeon regarding NSAID use may be justified. Complete reversal of aspirin effects requires 7 to 10 days for new platelet synthesis, while the effect of other NSAIDs resolves in three or four half-lives. Celecoxib likely does not affect platelet function and therefore can be continued perioperatively.

- E. Opioid Tolerance.** Usual doses of opioids should be continued in the perioperative period. A patient who is taking methadone should continue his or her normal dosing up through the day of surgery. If on Suboxone, a perioperative treatment plan should be formulated by the patient's prescribing physician, surgeon, and anesthesiologist consultant. The anesthesiologist must take into consideration the risks versus benefits of continuing versus stopping the medication, and optimal timing for the latter, before instructing the patient.
- F. Asthma.** A patient with moderate-to-severe asthma may require treatment with albuterol or ipratropium via metered dose inhaler immediately prior to surgery. A wheezing patient should be referred to pulmonology or his or her primary care provider for medical optimization and symptom control before proceeding with surgery. All asthma medications (inhaled and oral) ought to be continued in the perioperative period.
- G. Diabetes Mellitus.** A diabetic patient may be hyperglycemic or hypoglycemic perioperatively. Hyperglycemia can predispose the patient to a hyperosmolar state that can result in impaired enzyme (e.g., nitric oxide synthase, leukocyte elastase, amylase, lipase) function, diabetic ketoacidosis, or a hyperosmolar hyperglycemic nonketotic state. Finger-stick glucose level should be obtained preoperatively and abnormal levels treated as necessary (see Chapter 6).
- H. High Aspiration Risk.** Guidelines to reduce the risk of pulmonary aspiration have been published by the ASA and should be considered for the patient with a high risk of aspiration, including any patient with a hiatal hernia with reflux symptoms, a difficult airway, ileus, obesity, poorly controlled diabetes, depressed sensorium, or pregnancy, and any trauma patient. Routine use of aspiration prophylaxis in the patient without risk factors is not recommended. The following medications are effective in increasing the pH of gastric acid, but there is little conclusive evidence that they decrease the frequency of pulmonary aspiration or reduce morbidity and mortality in patients who aspirate gastric contents.
 - 1. Histamine antagonists.** Histamine antagonists produce a dose-related decrease in gastric acid production. Cimetidine (Tagamet), 200 to 400 mg orally or intravenously, and ranitidine (Zantac), 150 to 300 mg orally or 50 to 100 mg intravenously or intramuscularly, significantly reduce the volume and the acidity of gastric secretions. Multidose regimens (i.e., the night before and the morning of surgery) are the most effective, although parenteral administration may be used to achieve a rapid (<1 hour) onset. Cimetidine prolongs the elimination of many drugs, including theophylline, diazepam, propranolol, and lidocaine, potentially increasing the toxicity of these agents. Ranitidine has not been associated with such side effects.
 - 2. Proton pump inhibitors.** Examples of proton pump inhibitors are omeprazole (Prilosec) and esomeprazole (Nexium). These drugs are highly effective in reducing acid production but do not work quickly enough to be used in the immediate preoperative period. A patient taking one of these medications chronically should receive a dose the night before and/or the morning of surgery.

3. **Antacids.** Colloidal antacid suspensions (e.g., Mylanta) effectively neutralize stomach acid but can cause a pneumonitis if aspirated. A non-particulate antacid, such as sodium citrate and citric acid (Bicitra), 30 to 60 mL, 30 minutes prior to induction, is less effective in raising gastric pH but is also less injurious if aspirated.
4. **Metoclopramide.** Metoclopramide (Reglan) enhances gastric emptying by increasing lower esophageal sphincter tone and simultaneously relaxing the pylorus. An oral dose of 10 mg may be given 1 to 2 hours prior to induction of anesthesia. The intravenous dose, 10 to 20 mg, can be given in the induction area. When administered intravenously, metoclopramide should be given slowly to avoid abdominal cramping. As with all dopamine antagonists, metoclopramide may produce dystonia or other extrapyramidal effects. It should not be given in the event of a suspected bowel obstruction.
1. **Other Medications.** In general, anticonvulsants, antiarrhythmics, steroids, and hormonal supplements may be continued through the perioperative period.

VII. ANESTHETIC ASSESSMENT AND PLAN

- A. **ASA Physical Status Class.** ASA class provides an overall impression of the complexity of the patient's medical condition. The patient should be assigned to one of the following physical status classes:
 1. **Class 1.** A healthy patient (no physiologic, physical, or psychological abnormalities).
 2. **Class 2.** A patient with mild systemic disease without limitation of daily activities.
 3. **Class 3.** A patient with severe systemic disease that limits activity but is not incapacitating.
 4. **Class 4.** A patient with incapacitating systemic disease that is a constant threat to life.
 5. **Class 5.** A moribund patient not expected to survive 24 hours with or without the operation.
 6. **Class 6.** A brain-dead patient whose organs are being removed for donation purposes.
 7. **Emergent.** If the procedure is performed as an emergency, an E is added to the previously defined ASA Physical Status.
- B. **Airway Management.** Take into consideration the patient's current airway exam, past airway management, aspiration risk, and the planned procedure (including positioning and estimated duration).
- C. **Monitoring.** Evaluate the need for invasive monitoring. The healthy patient undergoing minimally invasive surgery needs only the standard ASA monitors. If the patient, however, has significant cardiovascular disease or may experience large hemodynamic fluctuations intraoperatively, invasive monitoring should be considered (e.g., central venous pressure for volume monitoring, arterial line for potential hemodynamic instability).
- D. **Anesthetic Options.** Numerous methods are available for providing anesthesia, analgesia, and hemodynamic stability for any given type of surgery. General anesthesia, regional anesthesia, and combinations thereof should be reviewed and considered.

VIII. PATIENT DISCUSSION

The perioperative period is emotionally stressful for the patient who may have fears about surgery and anesthesia. The anesthesiologist can alleviate many of these fears by way of a thorough discussion with the patient. If the

TABLE
1.1

ASA Guidelines for Preoperative NPO Status

Age	Clear Liquids (Hours)	Breast Milk (Hours)	Nonhuman Milk/ Light Snack (Hours)	Fried Fatty Foods/Meat (Hours)
Infant	2	4	6	8
Child	2	4	6	8
Adult	2	N/A	6	8

provider performing the assessment will not be the anesthetizing provider, the patient should be reassured that his or her concerns and needs will be relayed and addressed. Moreover, the anesthesiologist should explain, in detail, the events of the perioperative period. It would behoove the anesthesiologist to give instruction and information on the following:

- A. Perioperative Procedures.** Explanation of the procedures that will occur prior to induction (e.g., placement of intravenous, arterial or epidural catheters, placement of routine monitors, preoxygenation, cricoid pressure) with reassurance that supplemental sedation and analgesia (local and intravenous) will be provided as necessary during this period.
- B. Perioperative Medication Use.** Maintenance or discontinuation of medications in the perioperative period should be thoroughly explained to the patient (see section VI).
- C. Preoperative Fasting.** See Table 1.1.
- D. Postoperative Recovery.** Explain the intended plan for postoperative recovery in the postanesthesia care unit or ICU.
- E. Pain Control.** Detail the plan for perioperative pain control.
- F. Autologous Blood Donation.** Autologous donation may be considered in the stable patient scheduled for surgery in which blood transfusion is likely, such as total joint arthroplasty and radical prostatectomy. This donation can be arranged through the American Red Cross if in-house resources do not support it.

IX. INFORMED CONSENT

Informed consent involves discussing with the patient the anesthetic plan, alternatives to said plan, and potential complications. This discussion ought to be conducted in terms understandable to the layperson and tailored to the patient's level of comfort. It should be conducted in the patient's native language with interpreters trained in medical interpretation. For some rare languages, it may be necessary to conduct the interview with the assistance of an interpreter via telephone. Young children must not be used as interpreters in obtaining informed consents, although adult family members may serve as interpreters if the patient signs a waiver of disclosure stating the patient chooses to waive his or her access to a hospital-appointed translator.

- A. Explanation of General Anesthesia.** Certain aspects of anesthetic management are outside the realm of common experience and must be explicitly defined and discussed beforehand. Examples of this include endotracheal intubation, mechanical ventilation, invasive hemodynamic monitoring, regional anesthesia techniques, blood product transfusion, and postoperative ICU care.

- B. Alternatives.** Alternatives to the suggested management plan should be presented as they may become necessary if the planned procedure fails or if there is a change in clinical circumstances.
- C. Risks.** Risks associated with anesthesia-related procedures should be disclosed in a manner that the reasonable person would find helpful in making a decision. In general, disclosure applies to complications that occur with a relatively high frequency—not to all remotely possible risks. The anesthesiologist should familiarize the patient with the most frequent and severe complications of the following common procedures:
- 1. Regional anesthesia.** The risks of regional anesthesia include headache, infection, local bleeding, nerve injury, drug reactions, and possible failure to provide adequate anesthesia. Certain regional anesthetic techniques may carry more specific risks (e.g., pneumothorax after an infraclavicular nerve block) and should be weighed against the associated benefits specific to the patient. General anesthesia and its attendant risks should also be discussed as it could become necessary.
 - 2. General anesthesia.** The risks of general anesthesia include sore throat, hoarseness, nausea and vomiting, dental injury, and allergic reactions to drugs administered. The possibility of intraoperative awareness, pulmonary or cardiac injury, stroke or death, postoperative visual loss, postoperative cognitive dysfunction, postoperative intubation, or ICU admission should be discussed when appropriate.
 - 3. Blood transfusion.** The risks associated with blood transfusion are fever, hemolytic reactions, and infection. Currently, the risk of transmission of the hepatitis B virus is 1 in 360,000, whereas the risk of transmission of the human immunodeficiency and hepatitis C viruses is 1 in 2,000,000 units transfused.
 - 4. Vascular cannulation.** The risks of intravenous catheters include injury of peripheral nerves, tendons, or blood vessels. Hemothorax, pneumothorax, and infection are risks associated with central venous access.
 - 5. Undefined risks.** In cases in which the risk has not been objectively defined, the patient should be so informed.
- D. Extenuating Circumstances.** Anesthetic procedures may proceed without informed consent in emergency situations.
- E. Religious/Personal Beliefs.** Certain personal beliefs and desires may warrant special consideration prior to surgery. The Jehovah's Witness patient undergoing elective surgery should have a clear plan that is understood and agreed to by the patient and the entire surgical team. The same considerations apply to the patient with "do not resuscitate" orders (see Chapter 41).

X. DOCUMENTATION

The preoperative anesthesia note is a medicolegal document in the permanent hospital record. As such, it should be a concise, legible statement, which includes the date and time of the interview, the planned procedure, and laterality (if applicable). It should include relevant positive and negative findings from the history, physical examination, and laboratory studies including a list of allergies and relevant medications as discussed above. A problem list that delineates all disease processes, their treatments, and current functional limitations must also be included.

The note should also detail the discussion that occurred with the patient including anesthetic options, particular risks, monitoring needs, and postoperative plans.

XI. DAY OF SURGERY PREMEDICATION

A. Sedatives and Analgesics. The goal for administering sedatives and analgesics before surgery is to allay the patient's anxiety, to decrease pain during administration of regional anesthesia and preoperative line placement, and to facilitate smooth induction of anesthesia. It has been shown that the requirement for these drugs can be reduced by a thorough preoperative visit by an anesthesiologist. The dose of sedatives and analgesics must be reduced or withheld in a patient who is elderly, debilitated, or acutely intoxicated. The dose should also be decreased in a patient with upper airway obstruction, central apnea, neurologic deterioration, severe pulmonary disease, or valvular heart disease.

1. Benzodiazepines. Benzodiazepines are highly effective in the treatment of anxiety. They also produce exceptional amnesia.

a. Midazolam. Midazolam (Versed), 1 to 3 mg intravenously or intramuscularly, is a short-acting benzodiazepine that provides excellent anterograde amnesia and sedation. It should not be given to a sedated patient with an unsecured airway as it may cause significant respiratory depression, especially in combination with an opioid.

b. Lorazepam. Lorazepam (Ativan), 1 to 2 mg orally or intravenously, may also be used but may cause more prolonged amnesia and postoperative sedation. It should not be given intramuscularly.

2. Barbiturates. Barbiturates are rarely used for preoperative sedation; however, pentobarbital (Nembutal) is occasionally used by nonanesthesiologists for sedation during diagnostic procedures.

3. Opioids. Opioids may be given preoperatively to a patient who has, or is anticipated to have, significant pain or to a patient who is opioid dependent. A patient coming from an inpatient ward may already be on morphine, hydromorphone, or meperidine and thus have a higher perioperative opioid requirement. The opioid-dependent patient should receive sufficient premedication to overcome tolerance and to prevent perioperative withdrawal. Intravenous fentanyl is appropriate for use immediately prior to induction as its effects are rapid and intense, but short lived.

B. Anticholinergics. Anticholinergics are not frequently used for premedication. Glycopyrrolate, 0.2 to 0.4 mg intravenously for adults and 10 to 20 $\mu\text{g}/\text{kg}$ for pediatric patients, may be given in conjunction with ketamine as an antisialagogue. Occasionally, this antisialagogue effect is desirable during oral surgery, bronchoscopy, or fiberoptic intubation.

C. Antiemetics. Antiemetics may be given prior to induction or intraoperatively to prevent PONV (see Chapter 36). Prophylactic antiemetic agents should be considered for the patient with at least two risk factors (see section III.D.2). Adequate prophylaxis includes the use of at least two antiemetics with differing mechanisms of action (see Table 1.2). The first-line agent should be the safest and least expensive drug.

D. Aspiration Risk-Mitigating Agents. Aspiration risk-mitigating agents may be warranted on the day of surgery in the at-risk patient (see section VI.H).

TABLE 12	Antiemetic Agents

Antiemetic Agent	Mechanism of Action	Side Effects	Dose
Ondansetron	Serotonin (5-HT ₃) receptor antagonist	Dizziness, headache, and QTc prolongation	4 mg intravenously
Droperidol ^a	Dopamine (D ₂) receptor antagonist	Dystonia, prolonged QTc, and decreased seizure threshold	0.5–1.25 mg intravenously
Haloperidol	D ₂ receptor antagonist	Dystonia, prolonged QTc, and decreased seizure threshold	1 mg intravenously
Dexamethasone	Unknown	Anal/vulvar pruritus and hyperglycemia	4 mg intravenously
Metoclopramide	Dopamine receptor antagonist	GI upset with abdominal cramping and dystonia	10 mg intravenously
Promethazine	Antihistamine	Sedation and decreased seizure threshold	6.25 mg intravenously
Scopolamine	Anticholinergic	Dry mouth, blurred vision, confusion, and urinary retention	1.5 mg transdermally

^a The Food and Drug Administration requires 2–3 h of ECG monitoring following administration given the risk of QTc prolongation and Torsades de Pointes.

XII. DELAYING SURGICAL PROCEDURES

Occasionally, it is in the best interest of the patient to delay elective surgical procedures for further medical evaluation and optimization. Some conditions can significantly increase morbidity and mortality if not appropriately evaluated and treated.

- A. Recent Myocardial Infarction.** If the patient has had an MI within the past 30 days, elective surgery should be postponed.
- B. New Dysrhythmia.** New-onset atrial fibrillation, atrial flutter, supraventricular tachycardia, sustained ventricular tachycardia, and second-degree, type II or third-degree heart block must be evaluated with an ECG, rhythm strip, electrolyte replenishment, and a cardiology consultation. Surgery should be postponed until workup is complete, etiology determined, and stability established.
- C. Coagulopathy.** Coagulopathies can predispose the patient to massive intraoperative blood loss. As such, surgery should be postponed until all possible etiologies have been thoroughly investigated and treated. Coagulopathy can be the result of myriad etiologies including, but not restricted to, liver dysfunction, medication use, and sepsis. The patient must have a platelet count greater than 50,000 prior to proceeding with elective surgery.
- D. Hypoxia.** If hypoxia is of unclear etiology, surgery should be postponed until the cause is investigated and the patient optimized. There are many causes of hypoxia, ranging from decreased fraction of inspired oxygen to a large ventricular septal defect. The workup should begin with an arterial blood gas and CXR. Further diagnostic studies may be conducted as warranted.

- E. New Cardiovascular Symptoms.** Unstable angina, new or changed chest pain, and new or changed shortness of breath or dyspnea on exertion are worrisome. Surgery should be postponed until these symptoms can be fully evaluated by a cardiologist or other appropriate specialist. New ECG changes, especially those indicative of silent MI (e.g., bifascicular block, or new, significant Q waves), must be evaluated prior to elective procedures.
- F. New Murmurs.** New heart murmurs of auscultatory significance may be indicative of a change in valvular pathology and should be evaluated by ECHO and/or cardiology before proceeding with elective surgery.

Suggested Readings

- American Society of Anesthesiologists. Practice Advisory for the Perioperative Management of Patients with Cardiac Rhythm Management Devices: Pacemakers and Implantable Cardioverter-Defibrillators. Available from: <https://www.asahq.org/For-Members/Practice-Management/Practice-Parameters.aspx>
- American Society of Anesthesiologists. Practice Advisory for Preanesthesia Evaluation. Available from: <https://www.asahq.org/For-Members/Practice-Management/Practice-Parameters.aspx>
- American Society of Anesthesiologists. Practice Guidelines for the Management of Patients with Obstructive Sleep Apnea. Available from: <https://www.asahq.org/For-Members/Practice-management/Practice-Parameters.aspx>
- American Society of Anesthesiologists. Practice Guidelines for Preoperative Fasting and the Use of Pharmacologic Agents to Reduce the Risk of Pulmonary Aspiration: Application to Healthy Patients Undergoing Elective Procedures. Available from: <https://www.asahq.org/For-Members/Practice-Management/Practice-Parameters.aspx>
- American Society of Anesthesiologists. Practice Guidelines for Management of the Difficult Airway. Available from: <https://www.asahq.org/For-Members/Practice-Management/Practice-Parameters.aspx>
- Apfel CC, Heidrich FM, Jukar-Rao S, et al. Evidence-based analysis of risk factors for postoperative nausea and vomiting. *Br J Anaesth* 2012;109:742–753.
- Apfel CC, Korttila K, Abdalla M, et al. A factorial trial of six interventions for the prevention of postoperative nausea and vomiting. *N Engl J Med* 2004;350:2441–2451.
- Baron TH, Kamath PS, McBane RD. Management of antithrombotic therapy in patients undergoing invasive procedures. *N Engl J Med* 2013;368:2113–2124.
- Bradley AE, Tober KE, Brown RE. Use of propofol in patients with food allergies. *Anaesthesia* 2008;63:439.
- Brown KA. Intermittent hypoxia and the practice of anesthesia. *Anesthesiology* 2009;110:922–927.
- Chen KY, Chen L, Mao J. Buprenorphine–naloxone therapy in pain management. *Anesthesiology* 2014;120:1262–1274.
- Crossley GH, Poole JE, Rozner MA, et al. The Heart Rhythm Society (HRS)/American Society of Anesthesiologists (ASA) Expert Consensus Statement on the perioperative management of patients with implantable defibrillators, pacemakers and arrhythmia monitors: facilities and patient management. *Heart Rhythm* 2011;8:1114–1154.
- DePestel DD, Benninger MS, Danziger L, et al. Cephalosporin use in treatment of patients with penicillin allergies. *J Am Pharm Assoc* 2008;48:530–540.
- Devereaux PJ, Mrkobrada M, Sessler DI, et al. Aspirin in patients undergoing noncardiac surgery. *N Engl J Med* 2014;370:1494–1503.
- Devereaux PJ, Yang H, Guyatt GH, et al. Rationale, design, and organization of the Perioperative Ischemic Evaluation (POISE) trial: a randomized controlled trial of metoprolol versus placebo in patients undergoing noncardiac surgery. *Am Heart J* 2006;152:223–230.
- Egbert LD, Battit GE, Turndorf H, et al. The value of the preoperative visit by an anesthetist. A study of doctor–patient rapport. *JAMA* 1963;185:553–555.
- Fleisher LA, Fleischmann KE, Auerbach AD, et al. 2014 ACC/AHA guideline on perioperative cardiovascular evaluation and management of patients undergoing noncardiac surgery: executive summary: a report of the American College of Cardiology/American Heart Association Task Force on Practice Guidelines. *Circulation* 2014;130:1–141.

- Gan TJ. Risk factors for postoperative nausea and vomiting. *Anesth Analg* 2006;102:1884–1898.
- Liu LL, Dzankic S, Leung JM. Preoperative electrocardiogram abnormalities do not predict postoperative cardiac complications in geriatric surgical patients. *J Am Geriatr Soc* 2002;50:1186–1191.
- MGH Guidelines for perioperative aspirin administration. Consensus Statement from the Departments of Anesthesia, Medicine, Cardiology, and Surgery. 12/2011.
- Murphy A, Campbell DE, Baines D, et al. Allergic reactions to propofol in egg-allergic children. *Anesth Analg* 2011;113:140–144.
- Pichichero ME. Use of selected cephalosporins in penicillin-allergic patients: a paradigm shift. *Diagn Microbiol Infect Dis* 2007;57:13S–18S.
- Raith K, Hochhaus G. Drugs used in the treatment of opioid tolerance and physical dependence: a review. *Int J Clin Pharmacol Ther* 2004;42:191–203.
- Sadr Azodi O. The efficacy of a smoking cessation programme in patients undergoing elective surgery: a randomised clinical trial. *Anesthesiology* 2009;64:259–265.
- Smetana GW. Preoperative pulmonary evaluation: identifying and reducing risks for pulmonary complications. *Cleve Clin J Med* 2006;73:S36–S41.
- Twersky RS, Goel V, Narayan P, et al. The risk of hypertension after preoperative discontinuation of angiotensin-converting enzyme inhibitors or angiotensin receptor antagonists in ambulatory and same-day admission patients. *Anesth Analg* 2014;118:938–944.
- Wagner S, Breiteneder H. The latex-fruit syndrome. *Biochem Soc Trans* 2002;30:935–940.

Specific Considerations with Cardiac Disease

Christina Anne Jelly and Olof Viktorsdottir

I. GENERAL CONSIDERATIONS

An estimated one in three of Americans has one or more types of cardiovascular disease (CVD). Mortality data show that one of every three deaths in the United States is secondary to CVD.

II. CORONARY ANATOMY

The coronary arteries perfuse the myocardium. The left and right coronary arteries originate from the coronary sinuses distal to the aortic valve. The left main coronary artery (LMCA) branches into the left anterior descending artery (LAD) and the left circumflex artery (LCX) to supply most of the left ventricle (LV), interventricular septum (IVS), and the left atrium (LA). The right coronary artery (RCA) supplies the right atrium (RA) and ventricle (RV). It also supplies portions of the IVS, including the sinoatrial (SA) and atrioventricular (AV) nodes (Fig. 2.1). In approximately 70% of the population, the posterior descending artery (PDA) is supplied by the RCA. This circulation is described as “right dominant.” The remainder of the population is either “left dominant,” with the PDA emerging from the LCX (10% of the population), or “codominant,” with the PDA receiving contributions from both the LCX and RCA (20% of population).

III. PREOPERATIVE CARDIOVASCULAR EVALUATION FOR NONCARDIAC SURGERY

The American College of Cardiology and the American Heart Association (ACC/AHA) have developed joint guidelines for the preoperative cardiovascular evaluation of patients undergoing noncardiac surgery. The initial evaluation consists of the patient's history, focused physical examination, and routine laboratory investigation. Based on the patient's history, cardiac risk factors, functional status, and the nature of the surgical procedure, the ACC/AHA guidelines provide a stepwise approach for identifying patients who may benefit from further cardiovascular testing (Fig. 2.2).

A. Initial Screening

1. The need for **emergency surgery** preempts further cardiac workup. The ACC/AHA guidelines define an emergency procedure as one that must be started within 6 hours. As there is little to no time, the patient must proceed often with no or very limited clinical preoperative evaluation. Emergent surgery should proceed with appropriate patient monitoring and management strategies based on the patient's clinical risk factors for CAD.
2. If the **surgery is not emergent**, determine whether the patient has an acute coronary syndrome (ACS). An ACS is unstable angina or a myocardial infarction (MI). The patient may present with chest pain, shortness of breath, diaphoresis, or nausea. The EKG may show ST segment depressions or elevations. If the patient has an ACS, the surgical procedure should be postponed and the patient should immediately undergo cardiac evaluation and guideline-directed medical therapy (GDMT).

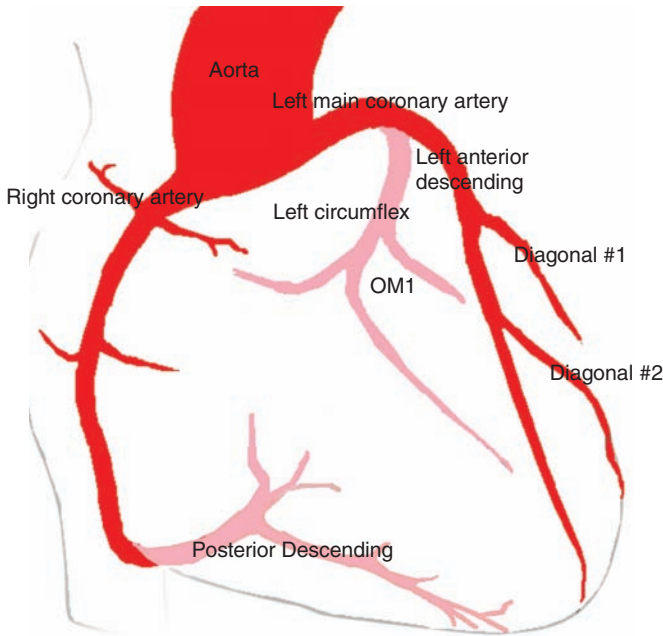


FIGURE 2.1 Coronary anatomy.

If the patient does not have an ACS, then proceed with an assessment of the patient's postoperative risk for a major adverse cardiac event (MACE).

B. Risk of MACE. The patient's risk of MACE should be determined based on clinical characteristics and the surgical procedure. Clinical risk factors for MACE include a history of heart failure, coronary artery disease, cerebrovascular disease, diabetes, and chronic kidney disease. Validated risk prediction tools, such as the Revised Cardiac Risk Index (RCRI) and the American College of Surgeons National Surgical Quality Improvement Program (ACS NSQIP) Surgical Risk Calculator (riskcalculator.facs.org), can be used to help predict the risk of perioperative MACE.

1. If the patient has a **low risk of MACE** ($<1\%$), then **no further testing** is needed and the patient may **proceed to surgery**.
2. If the patient has an **elevated risk of MACE** ($\geq 1\%$), then the **functional capacity** should be determined. **Functional capacity** can be expressed as metabolic equivalents (METs). A single MET represents oxygen consumption at rest. If the patient has moderate or excellent functional capacity without cardiac symptoms, then the patient may proceed to surgery without further evaluation. **Moderate or excellent functional capacity** is defined as **exercise capacity greater than or equal to 4 METs**. Activities that correspond to moderate functional capacity include climbing two flights of stairs, walking on level ground at 4 mph, running a short distance, scrubbing floors, or playing a game of golf without a cart. The ability to participate in strenuous sports such as swimming, singles tennis, or football generally corresponds to excellent functional capacity.

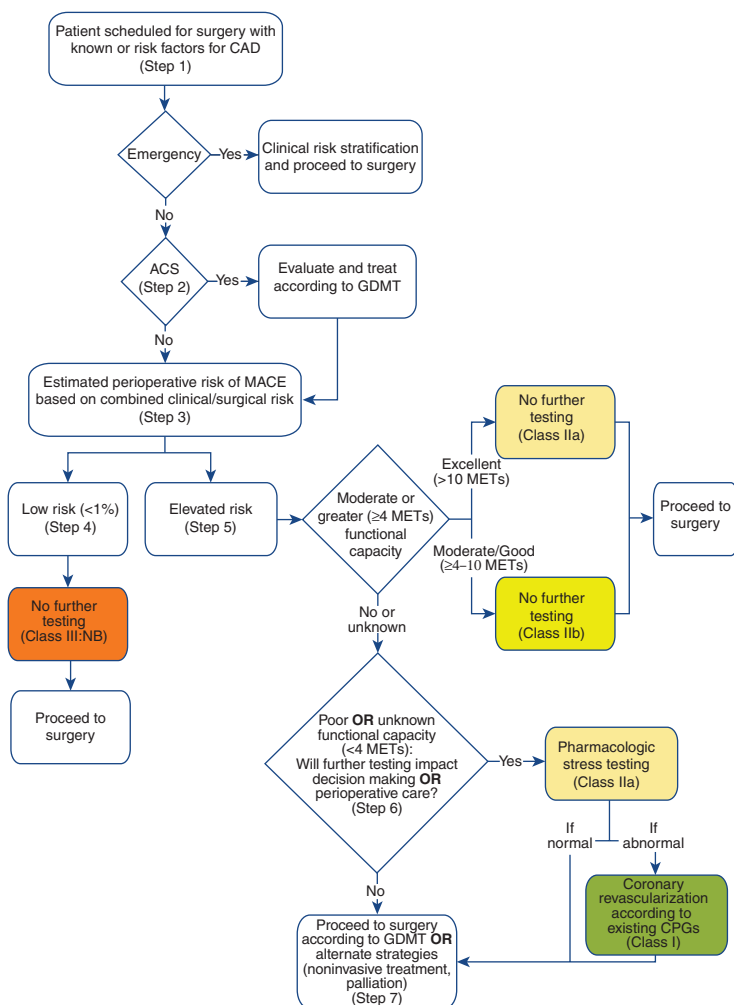


FIGURE 2.2 Stepwise approach to perioperative cardiac assessment for CAD. Colors correspond to classes of recommendations. (Reprinted with permission from 2014 ACC/AHA guidelines on perioperative cardiovascular evaluation and management of patients undergoing noncardiac surgery. *J Am Coll Cardiol* 2014;64(22):e77–e137.)

3. If the patient has **poor or unknown functional capacity**, then further testing may be needed if the results will change a patient's management. **Poor functional capacity** is defined as an exercise capacity **less than 4 METs**. Examples include the inability to walk more than two blocks on level ground without stopping due to symptoms and activity limited to eating, dressing, and walking indoors. Further testing may include exercise or pharmacologic stress testing. If abnormal, coronary angiography may be considered. The patient can then proceed to surgery with

GDMT. Testing may not be necessary if the results will not alter patient management.

C. Supplemental Cardiac Evaluation. Supplemental cardiac evaluation should be performed when indicated to measure functional capacity, identify the presence of cardiac dysfunction, and provide an estimate of the perioperative cardiac risk.

1. **Preoperative resting 12-lead ECG** should be considered for patients with known coronary heart disease, significant arrhythmia, peripheral arterial disease, cerebrovascular disease, or other structural heart disease, except for those undergoing low-risk surgery. Routine preoperative ECG is not indicated for asymptomatic patients undergoing low-risk surgery.
2. **Rest echocardiography** may be used to evaluate ventricular function in patients with history of heart failure or dyspnea of unknown origin. It is also useful to assess valvular pathology in patients with a history of valvular disease or a newly identified heart murmur.
3. **Stress testing** is recommended for patients with elevated risk of MACE and poor or unknown functional capacity if outcome will change management. Patients who have an elevated risk of MACE and moderate to good (4 to 10 METs) functional capacity may proceed to surgery without stress testing. Routine screening with stress testing is not useful for patients undergoing low-risk noncardiac surgery.
 - a. **Exercise stress testing** provides an objective measure of functional capacity. It is the preferred modality in patients who are capable of achieving adequate workloads. Sensitivity and specificity for multivessel CAD are 81% and 66%, respectively. Exercise stress tests are highly predictive when ST segment changes are characteristic of ischemia (>2 mm, sustained into recovery, and/or associated with hypotension). The risk of perioperative cardiac events is increased significantly in patients who have abnormal exercise ECGs at low workloads. Radionuclide imaging or echocardiography can be combined with exercise stress testing for patients whose baseline ECGs render interpretation invalid.
 - b. **Pharmacologic stress testing** can be conducted with either an agent that increases myocardial oxygen demand (dobutamine) or dilates coronary arteries (dipyridamole or adenosine). Pharmacologic stress tests are suitable for patients who are unable to exercise. Dobutamine stress testing is typically combined with echocardiography to detect wall motion abnormalities brought about by the increased myocardial workload. Dipyridamole or adenosine stress tests are typically combined with radionuclide imaging to detect areas of myocardium that are at risk. Pharmacologic vasodilation has the risk of a false-negative test in patients with multivessel CAD where all vessels are already maximally vasodilated. In both cases, perioperative cardiac risk is directly proportional to the extent of myocardium that is found to be at risk on imaging.
4. **Cardiac catheterization** is considered the “gold standard” for evaluating CAD. Information obtained includes coronary anatomy with visualization of direction and distribution of flow, hemodynamics, and overall function of the heart. Routine preoperative coronary angiography is not recommended. Revascularization before noncardiac surgery is recommended in circumstances in which revascularization is indicated according to existing clinical practice guidelines.
5. **Cardiac consultation** may be helpful in determining which tests will be useful and in interpreting the results. The consultant can help optimize

the patient's preoperative medical therapy and provide follow-up in the postoperative period. Such follow-up is crucial with the initiation of new drug therapies and often for patients with pacemakers and implantable cardioverter-defibrillator (ICD) devices (see section V-VI).

- D. Indications for preoperative coronary revascularization with either **coronary artery bypass grafting** or **percutaneous coronary intervention (PCI)** are in general the same as in the nonoperative setting. Surgery, in and of itself, is not an indication for coronary revascularization, regardless of extent of vessel disease or left ventricular dysfunction.

IV. PREANESTHETIC CONSIDERATIONS

- A. Patients are likely to be anxious. Reassurance during the preoperative visit has been shown to be useful in decreasing anxiety. **Anxiolytics** may blunt rises in sympathetic tone and may be invaluable.
- B. **Cardiac medications** are usually continued perioperatively. Possible exceptions include angiotensin-converting enzyme inhibitors (due to prolonged vasodilation), sustained-release or long-acting medications, and diuretics.
1. **β -Blockers.** The preponderance of evidence suggests that the perioperative administration of β -blockers is associated with a reduction in perioperative cardiac events but not surgical mortality. Preoperative β -blocker administration has been associated with an increased incidence of adverse effects such as bradycardia and stroke, especially when larger doses have been given. Patients who are on chronic β -blocker therapy preoperatively should continue to receive them in the perioperative period. In patients with moderate to high risk of perioperative myocardial ischemia or with three or more RCRI risk factors (e.g., diabetes mellitus, HF, coronary artery disease, renal insufficiency, cerebrovascular accident), it may be reasonable to start β -blockers before surgery. When possible, β -blockers should be started days to weeks before elective surgery and titrated cautiously. They should not be started on the day of surgery.
 2. **Statins.** Patients taking statins should continue to receive statins perioperatively. Preoperative initiation of statin therapy is reasonable in patients undergoing vascular surgery as well as in patients with standard clinical indications for statin therapy who are undergoing elevated-risk procedures.
 3. **Aspirin.** The efficacy of aspirin for the secondary prevention of MI in patients with ischemic heart disease has been well documented. Data on the risk of discontinuing antiplatelet therapy in patients with coronary stents have strongly suggested continuing aspirin in the perioperative period. See Chapter 1. The data on continuing aspirin in patients undergoing elective noncardiac, noncarotid surgery who have not had previous coronary stenting, however, are controversial. Some publications recommend that aspirin should not be stopped routinely in the perioperative period at all, while a recent randomized controlled trial concludes that aspirin has no significant effect on the rate of death or nonfatal MI but increases the risk of bleeding.
- C. **Timing of elective surgery in the setting of previous PCI** presents a special challenge. Management decisions should be made in consultation with the patient's cardiologist and surgeon.
1. **Balloon angioplasty without stent placement.** The ACC/AHA recommend that elective noncardiac surgery should be **delayed 14 days** after balloon angioplasty. Aspirin therapy should be continued in the perioperative period.

2. **Bare metal coronary stents (BMS).** Current recommendations are to **delay elective noncardiac surgery for 30 days** following PCI with BMS. This time period allows for the completion of thienopyridine therapy and the endothelialization of the stent. The risk of ischemic events is greatest within 30 days of PCI, significantly lower at 30 to 90 days, and lowest after 90 days. Aspirin therapy should be continued perioperatively.
3. **Drug-eluting stents (DES).** Thrombosis of DES can occur months after placement and is often related to the omission of thienopyridine therapy perioperatively. The current consensus recommendation is to **defer elective surgery for 365 days** following placement. Aspirin therapy should be continued perioperatively. Elective noncardiac surgery after DES implantation **may be considered after 180 days** if the risk of further delay is greater than the expected risks of ischemia and stent thrombosis.
4. Should a noncardiac surgical procedure be required within the time frame recommended for dual-antiplatelet therapy following PCI, consider continuing the therapy throughout the perioperative period. If bleeding risk necessitates the discontinuation of thienopyridine therapy, continue aspirin therapy and restart thienopyridines as soon as possible.
- D. **Supplemental oxygen** should be provided to all patients who have a significant risk of ischemia.
- E. **Monitoring** is discussed in Chapter 10.
- F. **Anesthetic Technique.** No convincing outcome data support the superiority of one particular anesthetic technique over another in the management of patients at risk for perioperative cardiac events.

V. ISCHEMIC HEART DISEASE

Coronary artery disease afflicts an estimated 30% of patients undergoing surgery in the United States. CAD increases in prevalence with age. Other risk factors include hypercholesterolemia, male gender, hypertension, cigarette smoking, diabetes mellitus, obesity, and family history of premature development of ischemic heart disease. CAD is a risk factor for perioperative cardiac complications, including MI, unstable angina, congestive heart failure (CHF), and serious dysrhythmias.

- A. **Pathophysiology.** Myocardial ischemia occurs when oxygen demand exceeds oxygen delivery.
- B. **Supply.** The myocardium is supplied via coronary arteries. Myocardial oxygen supply depends on coronary artery diameter, LV diastolic pressure, aortic diastolic pressure, and arterial oxygen content.
 1. **Coronary blood flow** is dependent on the aortic root-to-downstream coronary pressure gradient. Most coronary blood flow **occurs during diastole**. Coronary artery blood flow in normal individuals is controlled primarily through local mediators. The coronary arteries of patients with significant CAD may be maximally dilated at rest.
 2. **Heart rate** is inversely proportional to the length of diastole. Faster heart rates decrease the duration of maximal coronary perfusion.
 3. **Blood oxygen** content is determined by hemoglobin concentration, oxygen saturation, and dissolved oxygen content. Increasing inspired oxygen fraction and/or hemoglobin concentration increases blood oxygen content.
- C. **Demand.** Myocardial oxygen consumption (MVO_2) is increased by increases in ventricular wall tension and heart rate (velocity of shortening) and, to a lesser degree, contractility.
 1. **Ventricular wall tension** is modeled by Laplace law: wall tension is directly proportional to the ventricular transmural pressure and the

ventricular radius, and inversely proportional to the ventricular wall thickness. Changes in these parameters affect oxygen demand.

2. **Heart rate.** Tachycardia is well tolerated in normal hearts. Atherosclerotic coronary arteries may not adequately dilate to meet increased demands of faster heart rates.
 3. **Contractility** increases with the increased chronotropy, myocardial stretch, calcium, and catecholamines. Increasing contractility increases oxygen consumption.
- D. Supply and Demand Balance.** Atherosclerosis is the most common etiology for supply-demand imbalances. Conditions such as aortic stenosis, systemic hypertension, and hypertrophic cardiomyopathy, which are characterized by marked ventricular hypertrophy and high intraventricular pressures, may also increase MVO_2 . These conditions may create imbalances, even in the setting of normal coronary arteries. The goal of treatment is to improve the myocardial oxygen supply-demand balance.
1. **Increase supply**
 - a. **Increase coronary perfusion pressure** with the administration of volume or α -adrenergic agonists to increase aortic root diastolic pressure.
 - b. **Increase coronary blood flow** with nitrates to dilate coronary arteries.
 - c. **Increase oxygen content** by raising hemoglobin concentration or oxygen partial pressure.
 2. **Decrease demand**
 - a. **Decrease heart rate** either directly with β -adrenergic antagonists or indirectly by decreasing sympathetic tone with opioids and anxiolytics.
 - b. **Decrease ventricular size** (decrease wall tension) by decreasing preload with nitrates, calcium channel antagonists, or diuretics. Occasionally, increasing inotropy may decrease demand by decreasing ventricular size and wall tension.
 - c. **Decreasing contractility** may decrease MVO_2 if ventricular size and wall tension do not increase excessively. Calcium channel blockers and volatile anesthetics decrease contractility.
 - d. **Intra-aortic balloon counter pulsation** increases coronary perfusion pressure by augmenting diastolic pressure. It also reduces resistance to LV ejection, thereby reducing LV size and wall tension.

VI. VALVULAR HEART DISEASE

A. Aortic Stenosis

1. **The etiology** is usually progressive calcification and narrowing of a tricuspid or bicuspid valve. A valve area less than 1.0 cm^2 or mean gradient greater than 40 mm Hg defines severe stenosis. Mild stenosis is defined as a valve area of greater than 1.5 cm^2 or mean gradient of less than 25 mm Hg. Moderate stenosis is defined as a valve area between 1.0 and 1.5 cm^2 or a gradient between 25 and 40 mm Hg.
2. **Symptoms** of angina, syncope, or heart failure develop late in the disease process. In the absence of surgical intervention, the average survival is 2 to 3 years following the onset of symptoms.
3. **Pathophysiology**
The ventricle becomes **hypertrophied** and stiff in response to the increased pressure load. Coordinated atrial contraction becomes critical to maintaining adequate ventricular filling and stroke volume. The ventricle is susceptible to ischemia due to increased muscle mass and decreased coronary perfusion in the setting of increased intraventricular pressure.

4. **Anesthetic considerations.** Aortic stenosis is the only valvular lesion associated with an increased risk of perioperative ischemia, MI, and death.
 - a. **Normal sinus rhythm** and adequate **volume status** should be maintained.
 - b. **Avoid systemic hypotension.** Hypotension should be treated immediately and aggressively with an α -agonist such as phenylephrine to maintain adequate coronary perfusion pressure.
 - c. **Avoid tachycardia.** Tachycardia results in increased oxygen demand along with a shorter period of diastole leading to decreased coronary perfusion and reduced cardiac output. Severe bradycardia can lead to reduced cardiac output and should be avoided as well. **Cardiac pacing** capabilities should be considered to treat severe bradycardia. Supraventricular tachydysrhythmias should be treated aggressively with direct current cardioversion.
 - d. **Nitrates** and **peripheral vasodilators** should be administered with extreme caution.
 - e. The **treatment of ischemia** in these patients is directed at increasing oxygen delivery by raising coronary perfusion pressure and decreasing oxygen consumption (by increasing blood pressure and lowering heart rate).
- B. **Aortic Regurgitation**
 1. **Etiologies** include rheumatic heart disease, endocarditis, trauma, collagen vascular diseases, and processes that dilate the aortic root (e.g., aneurysm, Marfan syndrome, and syphilis).
 2. **Pathophysiology**
 - a. Acute aortic regurgitation may cause sudden LV volume overload with increased LV end-diastolic pressure and pulmonary capillary occlusion pressure. Manifestations include decreased cardiac output, CHF, tachycardia, and vasoconstriction.
 - b. Chronic aortic regurgitation leads to LV dilation and eccentric hypertrophy. Symptoms may be minimal until late in the disease process when left heart failure occurs.
 3. **Anesthetic considerations**
 - a. Maintain a normal to slightly increased heart rate to minimize regurgitation and maintain aortic diastolic and coronary artery perfusion pressure.
 - b. Maintain adequate volume status.
 - c. Improve forward flow and decrease LV end-diastolic pressure and ventricular wall tension with vasodilators.
 - d. Avoid peripheral arterial constrictors. They may worsen regurgitation.
 - e. Consider pacing. These patients have an increased incidence of conduction abnormalities.
 - f. Intra-aortic balloon counter pulsation is generally contraindicated in the setting of aortic regurgitation.
- C. **Mitral Stenosis**
 1. **The etiology** is almost always rheumatic.
 2. **Pathophysiology**
 - a. Increased left atrial pressure and volume overload increase left atrial size and may cause **atrial fibrillation** and **pulmonary edema**.
 - b. **Elevated left atrial pressure** increases pulmonary venous pressure and pulmonary vascular resistance. In turn, right ventricular (RV) pressure is increased for a given cardiac output. Chronic pulmonary hypertension produces pulmonary vascular remodeling. **Pulmonary hypertension** may lead to tricuspid regurgitation, RV failure, and decreased cardiac output.

3. Anesthetic considerations

- a. **Avoid tachycardia.** Tachycardia is poorly tolerated because of decreased diastolic filling time leading to decreased cardiac output and increases in left atrial pressure. Control ventricular response pharmacologically or consider cardioversion for patients with atrial fibrillation. Continue digoxin, calcium channel blockers, and β -adrenergic blockers perioperatively.
- b. **Avoid pulmonary hypertension.** Hypoxia, hypercarbia, acidosis, atelectasis, and sympathomimetics increase pulmonary vascular resistance. Oxygen, hypocarbia, alkalosis, nitrates, prostaglandin E_1 , and inhaled nitric oxide decrease pulmonary vascular resistance.
- c. **Hypotension** may indicate RV failure. Inotropes and agents that decrease pulmonary hypertension may be useful (e.g., dobutamine, milrinone, amrinone, nitrates, prostaglandin E_1 , and inhaled nitric oxide).
- d. **Pulmonary artery catheter** may assist in the perioperative evaluation of volume status, intracardiac pressures, and cardiac output.
- e. **Premedication** should be adequate to prevent anxiety and tachycardia. Exercise caution in patients with hypotension, pulmonary hypertension, or low cardiac output.

D. Mitral Regurgitation

1. **Etiologies** include mitral valve prolapse, ischemic heart disease, endocarditis, and post-MI papillary muscle rupture.
2. **Pathophysiology.** Mitral regurgitation allows blood to be ejected into the left atrium during systole. The amount of regurgitant flow depends on the ventricular-atrial pressure gradient, size of the mitral orifice, and duration of systole.
 - a. **Acute mitral regurgitation** usually occurs in the setting of MI. Acute volume overload of the left heart leads to LV dysfunction with increased ventricular wall tension.
 - b. **Chronic mitral regurgitation** causes gradual left atrial and LV overload and dilation with compensatory hypertrophy.
 - c. **Measurement of ejection fraction** does not accurately reflect forward flow, because the incompetent valve permits immediate bidirectional ejection with systole.
3. **Anesthetic considerations**
 - a. **Relative tachycardia** is desirable to decrease ventricular filling time and ventricular volume.
 - b. **Afterload reduction** is beneficial. Increased systemic vascular resistance will increase regurgitation.
 - c. **Maintain preload.**

VII. CONGESTIVE HEART FAILURE

Heart failure results from impairment of ventricular function. Heart failure manifests as dyspnea, fatigue, decreased exercise tolerance, and pulmonary or peripheral edema. Heart failure can be classified into two categories: (1) heart failure with reduced ejection fraction (HFrEF) that is associated with variable degrees of LV enlargement and depressed ventricular ejection and (2) heart failure with preserved EF (HFpEF) in which diastolic dysfunction is pronounced.

- A. **Etiologies** include ischemic cardiomyopathy; hypertension; valvular heart disease; endocrine and metabolic causes such as diabetes, thyroid disease, and acromegaly; toxic cardiomyopathies due to alcohol, cocaine, or chemotherapy; nutritional causes such as carnitine deficiency; infective

causes such as viral myocarditis, HIV, and Chagas disease; iron overload states; amyloidosis; sarcoidosis; and catecholamine-induced (takotsubo).

- B. Pathophysiology** of heart failure is the culmination of progressive changes in myocyte architecture that result in changes in ventricular shape, chamber size, ventricular wall thickness, and stiffness that lead to reduced myocardial function and cardiac output.

C. Anesthetic Considerations

Hemodynamic goals aim to preserve cardiac output and minimize myocardial work. Medical management should be optimized preoperatively.

- 1. Maintain preload but with caution.** Patients with impaired LV function depend on preload to maintain cardiac output; however, they are at risk of pulmonary edema with fluid overload.
- 2. Avoid tachycardia** to minimize myocardial work and preserve ventricular filling during diastole.
- 3. Aggressively treat arrhythmias** as they may lead to reduction in cardiac output. In a failing ventricle, left ventricular end-diastolic volume (LVEDV) is heavily dependent on atrial contraction. The absence of coordinated atrial contractions (such as in atrial fibrillation) can lead to significant compromise of ventricular preload.
- 4. Preserve contractility.** Patients with heart failure may rely on increased sympathetic tone to maintain cardiac output. As a result, they may become profoundly hypotensive following induction. Inotropic support may be required.
- 5. Afterload reduction** is favorable as it reduces myocardial work. If vasopressors are needed, they should be used with caution.

VIII. HYPERTROPHIC CARDIOMYOPATHY

Hypertrophic cardiomyopathy is a cardiac disorder characterized by **asymmetric LV hypertrophy and impaired relaxation in diastole**. Although most patients with hypertrophic cardiomyopathy do not have an increased LV outflow tract gradient at rest, many of them develop **dynamic outflow tract obstruction** with decreased filling and increased contractility. Under these conditions, as flow accelerates through the narrowed LV outflow tract, it creates drag, which pulls the anterior leaflet of the mitral valve toward the septum. This systolic anterior motion (SAM) of the anterior mitral leaflet leads to further outflow obstruction and mitral regurgitation.

A. Anesthetic Considerations:

Factors that **worsen the outflow obstruction** include decreased arterial pressure, decreased intraventricular volume, increased contractility, and increased heart rate.

- 1. Maintain normal volume status.**
- 2. Avoid tachycardia.** Continue β -adrenergic and calcium channel blocker therapy for heart rate control.
- 3. Maintain normal sinus rhythm.** Consider cardioversion for supraventricular tachycardia.
- 4. Avoid hypotension.** Correct vasodilation with α -adrenergic agonists to avoid tachycardia and marked changes in contractility. Use nitrates and peripheral dilators with extreme caution.
- 5. Use inotropes with caution.** Increased inotropy may exacerbate the outflow obstruction.

IX. CONGENITAL HEART DISEASE

With improvement in the survival of congenital heart disease (CHD) patients, anesthesiologists are encountering them with greater frequency as adults in noncardiac surgical settings. Depending on the underlying

lesion, an adult with a history of CHD (ACHD) may have an **uncorrected** lesion or may have undergone a **reparative** or **palliative** procedure in the past. As the medical and surgical management of these conditions continues to evolve, different patients with the same original congenital defect may present having undergone significantly different procedures and, as a result, may differ in their anatomy and physiology. Transferring patient care to institutions with extensive experience in managing these disorders should be considered.

A. General Considerations

1. A thorough understanding of the patient's **cardiac anatomy, physiology, and functional status** along with the **physiologic stresses** associated with the surgical procedure is essential.
2. **Myocardial dysfunction** may be present as a long-term consequence of the physiology of the original lesion or the subsequent reparative or palliative procedure. It may also be a consequence of chronic hypoxemia.
3. **Dysrhythmias** are common and may be due to the pathophysiology of the cardiovascular defect or scarring from prior surgery. Intra-atrial reentrant tachycardia and ventricular tachycardia are commonly encountered in this patient population.
4. **Cyanotic patients** are often polycythemic and at risk for stroke and thrombosis. Intravenous hydration is important. Hemodilution may be considered in the instance of a preoperative hematocrit greater than 60%. **Abnormal hemostasis**, usually mild in severity, has been noted in patients with cyanotic CHD.
5. **Systemic air emboli** are a constant danger in the presence of bidirectional or right-to-left shunts. Intravenous lines must be purged of air bubbles, and air filters should be used.
6. **Infective endocarditis prophylaxis.** Some CHD patients require antibiotic prophylaxis for infective endocarditis with certain procedures. See Chapter 7.
7. A complete discussion of the specific lesions common in ACHD patients is beyond the scope of this chapter. For a more thorough treatment of the subject, the reader is referred to the Suggested Readings.

X. CARDIAC TRANSPLANT PATIENT

Globally, more than 5,000 cardiac transplants are performed each year. The 1-year survival rate is over 85%, and the 3-year survival rate is approximately 75%. These patients are increasingly encountered in the noncardiac surgical setting.

A. Physiology of the Transplanted Heart

1. Sympathetic reinnervation may occur over time. Parasympathetic reinnervation is not thought to occur; however, bradycardia related to the administration of neostigmine has been reported.
2. Transplanted hearts exhibit accelerated graft atherosclerosis and are at increased risk for myocardial ischemia.
3. **Hemodynamics of the transplanted heart**
 - a. Cardiac impulse formation and conduction are normal, although the resting heart rate is increased.
 - b. The Frank-Starling mechanism remains intact. Transplanted hearts respond normally to circulating catecholamines.
 - c. Autoregulation of coronary blood flow is intact.
 - d. Due to autonomic denervation, the transplanted heart meets the demand for increased cardiac output initially by increasing stroke volume and subsequently by increasing heart rate in response to circulating catecholamines.

4. Drug effects

- a. Drugs that act via the autonomic system (e.g., atropine and digoxin) are ineffective.
- b. Direct-acting agents are effective. Isoproterenol, dopamine, or epinephrine may be used to increase heart rate. Norepinephrine or phenylephrine may be used to increase blood pressure. Response to epinephrine is blunted.
- c. β -Adrenergic receptors are intact and may be present in increased density.
- d. Traditional teaching dictates that anticholinesterases have no effect on the rate of a denervated heart; however, over time, other receptor-related mechanisms may take over and allow anticholinesterases to exert bradycardic effect. A muscarinic antagonist should always be coadministered to block the cardiac and other muscarinic side effects.

B. Anesthetic Considerations

1. The patient's activity level and exercise capacity should be determined. A cardiology consultant may provide data concerning cardiac function and anatomy as measured by echocardiography and catheterization.
2. Underlying CAD may be asymptomatic. Evidence of ischemia may include a history of dyspnea, signs of reduced cardiac function, and dysrhythmias.
3. A baseline 12-lead ECG should be obtained and may demonstrate multiple P waves and right bundle branch block.
4. To assess the effect of immunosuppression and concomitant drug therapy, baseline laboratory studies should include complete blood count, serum electrolytes, blood urea nitrogen, serum creatinine, glucose, and liver function tests.
5. Strict aseptic technique is required for all interventions (e.g., intravenous access), because the patient may be receiving long-term immunosuppression.
6. **Monitoring.** Invasive monitoring is used when indicated by the patient's cardiopulmonary status and the surgical procedure. The right internal jugular vein is often the access site for repetitive endocardial biopsies and may need to be reserved for this purpose.

7. Anesthesia

- a. General, regional, and spinal anesthesia have been administered to cardiac transplant patients. Selection of a specific anesthetic technique should be guided by considerations other than the patient's history of cardiac transplantation.
- b. **Hemodynamic goals**
 1. Maintain preload.
 2. Avoid sudden vasodilation. Initial compensatory changes in cardiac output depend on the Frank-Starling mechanism because of the delayed heart rate response.
 3. If sudden hypotension occurs, administer volume and direct-acting vasopressors such as phenylephrine and norepinephrine.

XI. PACEMAKERS

- A. A standardized five-letter code is used to describe the function of each pacemaker.
 1. The first letter designates the **chamber paced** (O, none; A, atrium; V, ventricle; D, dual [both atrium and ventricle]).

2. The second letter describes the **chamber sensed** (O, none; A, atrium; V, ventricle; D, dual).
 3. The third letter describes the **pacemaker's response** to sensed events (O, none; I, inhibition of pacemaker output; T, triggering of pacemaker output; D, dual response: spontaneous atrial and ventricular activity inhibit atrial and ventricular pacing and atrial activity triggers a ventricular response).
 4. The fourth letter indicates the presence or absence of **rate modulation** (O, no rate modulation; R, rate modulation present).
 5. The fifth letter specifies the presence and type of multisite **pacing** (O, none; A, more than one stimulation site in either atrium, stimulation sites in each atrium, or a combination of the two; V, more than one stimulation site in either ventricle, stimulation sites in each ventricle, or a combination of the two; D, any combination of A and V).
 6. For example, a **VVI** pacemaker will sense and pace the ventricle yet will be inhibited and will not fire if an R wave is detected. A **DDD** pacemaker senses and paces both the atrium and ventricle. A **VVIRV** pacemaker has ventricular inhibitory pacing with rate modulation and multisite ventricular pacing. This mode is often used in patients with heart failure, chronic atrial fibrillation, or intraventricular conduction delay. A **DDDRD** pacemaker has dual-chamber pacing with rate modulation and multisite pacing in both the atrium (or atria) and ventricle(s).
- B. Indications.** See ACC/AHA/North American Society of Pacing and Electrophysiology (NASPE) practice guidelines (see Suggested Readings) for additional information.
1. Symptomatic bradycardia
 2. Third-degree (complete) AV block
 3. Type II, second-degree AV block
 4. Cardiac resynchronization therapy. Biventricular pacing to synchronize RV and LV depolarization in patients with depressed ejection fraction and symptomatic heart failure who also have an interventricular conduction abnormality. Such therapy has been shown to improve functional capacity and reduce hospitalization and mortality in patients who are otherwise optimally medically managed.
- C. Preoperative Evaluation of Patients with Permanent Pacemakers**
1. Determine the **indication** for the pacemaker and **device dependency**.
 2. Determine the **location** of the pulse generator. Most are currently placed in the upper chest. Older models may be located in the abdomen.
 3. Determine the **model** and programmed **mode** of the pacemaker. If the information is not readily available, the manufacturer and model number may be obtained from a radiograph of the generator. The manufacturer of the device must be identified in order to be able to program the pacemaker, as each manufacturer has a unique programming device. Determine whether rate modulation is active. Also, determine the response of the device to a magnet.
 4. Determine proper functioning of the device by patient history, electrophysiology clinic follow-up records, and ECG. Device interrogation is the only reliable method for determining the settings and battery function of the device.
 5. Patients with a pacemaker should not enter a room with a magnetic resonance imaging machine because of the potential for pacemaker dysfunction.

D. Intraoperative Management

1. **Modern pacemakers** are extremely resistant to electromagnetic interference (EMI) associated with the use of electrocautery. If interference does occur, the pacemaker output may be inhibited or the pacemaker may be reset to a committed pacing mode (i.e., DOO or VOO).
2. Applying a **magnet** to most pacemakers will cause them to function in an asynchronous mode. This will prevent pacemaker output inhibition by EMI associated with electrocautery use. Typically, normal pacemaker function is restored upon removal of the magnet. Most pacemakers will go into VOO mode when a magnet is placed; however, **the magnet response of a pacemaker is most reliably determined by device interrogation**. Use of a magnet during surgical procedures is necessary only if a patient is pacemaker dependent and inhibition of pacemaker output is noted coincident with EMI. If used, the magnet should be placed directly over the pacemaker. It is best to tape the magnet in place to avoid inadvertent dislodgment.
3. **Resetting of pacemakers** by EMI will produce asynchronous pacing that can be noted on the ECG.
4. Intraoperative exposure of the device to EMI can be reduced by placing the current return pad ("**grounding pad**") in a location on the patient such that the **current path from the electrocautery does not pass near the pulse generator**. Other measures include the use of **short, intermittent bursts** at the lowest possible energy level and the use of a **bipolar electrocautery** system or an **ultrasonic (harmonic) scalpel**. Consider inactivating rate-responsive features during the procedure.
5. **Monitor heart rate** during electrocautery with a pulse oximeter, arterial line, precordial or esophageal stethoscope, or a finger on the pulse.
6. **Postoperative evaluation of pacemaker function** is recommended by most manufacturers if electrocautery is used or if settings are changed perioperatively.

E. Temporary Perioperative Pacing Options

1. **Transcutaneous**. External pacing can be performed via large pads placed on the anterior and posterior thorax. This is an easy and inexpensive method of ventricular pacing. This method of pacing is typically not used for patients undergoing cardiac or thoracic surgery given location of incision, dressings, and drains.
2. **Transvenous**
 - a. A temporary pacing electrode can be inserted via a central vein into the heart.
 - b. Various pulmonary artery catheters that have pacing options exist (see Chapter 10).
3. **Transesophageal**. The left atrium can be paced with a pacing probe placed in the esophagus. Transesophageal pacing requires intact AV nodal conduction.

F. Implantable Cardioverter-Defibrillator (ICD). ICDs have significantly improved the mortality of patients at high risk for sudden cardiac death. The four key ICD functions are antitachycardia pacing (ATP), cardioversion, defibrillation, and backup pacing.

1. The ICD is implanted in the upper chest and is connected to one or two defibrillating transvenous leads that also have sensing and pacing capabilities. These leads sense ventricular tachycardia or fibrillation and can deliver a countershock of up to 40 J. All ICDs are exquisitely sensitive to EMI associated with electrocautery. EMI can be interpreted by an ICD as ventricular fibrillation leading to spurious shocks.

2. Most ICDs are designed to suspend detection in response to a magnet application and resume function upon removal of the magnet. In these models, magnet application will prevent misinterpretation of EMI as ventricular fibrillation. Some models of St. Jude and Boston Scientific ICDs can be programmed to ignore magnet application. Furthermore, some older models of Boston Scientific ICDs may be programmed to suspend function with magnet application but require magnet removal and reapplication to resume function. It is best to have ICD function interrogated preoperatively to determine its settings and response to magnet application.
3. **Intraoperative magnet application**, rather than deactivation of the ICD, is preferred: If ventricular tachycardia or ventricular fibrillation occurs intraoperatively, simply removing the magnet will cause the ICD to resume detection and deliver therapy, typically in less than 10 seconds. This is more certain and faster than applying external defibrillation.
4. ICD failure during anesthesia may occur as a result of changes in defibrillation thresholds. An external defibrillator should be available, and some advocate placing external defibrillator pads preoperatively.
5. Patients with an ICD should not enter a room with a magnetic resonance imaging machine because of the potential for ICD dysfunction.

Suggested Readings

- ASA. Practice advisory for the perioperative management of patients with cardiac rhythm management devices: Pacemakers and implantable cardioverter-defibrillators. *Anesthesiology* 2005;103:186–198.
- Ashary N, Kaye AD, Hegazi AR, et al. Anesthetic considerations in the patient with a heart transplant. *Heart Dis* 2002;4:191–198.
- Bernstein AD, Daubert J-C, Fletcher RD, et al. The revised NASPE/BPEG generic code for antibradycardia, adaptive-rate, and multisite pacing. *Pacing Clin Electrophysiol* 2002;25:260–264.
- Devereaux PJ, Yang H, Yusuf S, et al. Effects of extended-release metoprolol succinate in patients undergoing non-cardiac surgery (POISE trial): a randomised controlled trial. *Lancet* 2008;371:1839–1847.
- Devereaux PJ, Mrkoberada M, Sessler, D, et al. Aspirin in patients undergoing noncardiac surgery. *N Engl J Med* 2014;370:1494–1503.
- Fleisher LA, Fleishmann KE, Auerbach AD, et al. 2014 ACC/AHA guideline on perioperative cardiovascular evaluation and management of patients undergoing noncardiac surgery: a report of the American College of Cardiology/American Heart Association Task Force on practice guidelines. *J Am Coll Cardiol* 2014;64(22):e77–e137.
- Gibbons RJ, Antman EM, Alpert JS, et al. ACC/AHA 2002 guideline update for exercise testing. *Circulation* 2002;106:1883–1892.
- Grines CL, Bonow RO, Caset DE Jr, et al. Prevention of premature discontinuation of dual antiplatelet therapy in patients with coronary artery stents: a science advisory from the American Heart Association, American College of Cardiology, Society for Cardiovascular Angiography and Interventions, American College of Surgeons, and American Dental Association, with representation from the American College of Physicians. *Circulation* 2007;115:813–818.
- Hindler K, Shaw AD, Samuels J, et al. Improved postoperative outcomes associated with preoperative statin therapy. *Anesthesiology* 2006;105:1260–1272.
- Kertai MD. Preoperative coronary revascularization in high-risk patients undergoing vascular surgery: a core review. *Anesth Analg* 2008;106:751–758.
- Lindenauer P, Pekow P, Wang K, et al. Perioperative beta-blocker therapy and mortality after major noncardiac surgery. *N Engl J Med* 2005;353:349–336.
- Lovell A. Anaesthetic implications of grown-up congenital heart disease. *Br J Anaesth* 2004;93:129–139.

- Nishimura RA, Carabello BA, Faxon DP, et al. ACC/AHA 2008 guideline update on valvular heart disease: focused update on infective endocarditis. *Circulation* 2008;118:887–896.
- Nuttall GA, Brown MJ, Stombaugh JW, et al. Time and cardiac risk of surgery after bare-metal stent percutaneous coronary intervention. *Anesthesiology* 2008;109:588–595.
- Rabbitts JA, Nuttall GA, Brown MJ, et al. Cardiac risk of noncardiac surgery after percutaneous coronary intervention with drug-eluting stents. *Anesthesiology* 2008;109:596–604.
- Rozner MA. The patient with a cardiac pacemaker or implanted defibrillator and management during anaesthesia. *Curr Opin Anaesthesiol* 2007;20:261–268.
- Slininger KA, Haddadin AS, Mangi AA, et al. Perioperative Management of Patients With Left Ventricular Assist Devices Undergoing Noncardiac Surgery. *Journal of Cardiothoracic and Vascular Anesthesia* 2013;2(4):752–759.
- Warnes CA, Williams RG, Bashore TM, et al. ACC/AHA 2008 guidelines for the management of adults with congenital heart disease: executive summary. *Circulation* 2008;118:1–56.

Specific Considerations with Pulmonary Disease

Yiuka Leung and Kenneth E. Shepherd

I. GENERAL CONSIDERATIONS

Postoperative pulmonary complications (POPCs) such as exacerbation of preexisting lung disease, pneumonia, and/or respiratory failure are as prevalent as cardiac complications and contribute to morbidity, mortality, and increased length of hospital stay. Although more research is needed, currently the risk factors for POPCs can be broadly classified into patient related and procedure related. POPCs can be reduced in all types of procedures by identifying patients at risk, optimizing their medical therapy preoperatively, performing vigilant intraoperative care, and by delivering aggressive postoperative care emphasizing analgesia and lung expansion.

- A. Evidence from a meta-analysis supports risk reduction for specific patients (see section III.A.1)
- B. Procedure-related risk factors include
 - 1. General anesthesia
 - 2. Emergency surgery
 - 3. Surgery lasting more than 3 hours
 - 4. Surgical site (abdominal, thoracic, head and neck, vascular, and neurosurgery)
- C. Recommended postoperative interventions for those at risk include using lung expansion maneuvers and using nasogastric tubes selectively (see section VIII)

II. CLASSIFICATION OF PULMONARY DISEASE

- A. Obstructive airway diseases are characterized by abnormal expiratory gas flow rates. The airflow limitation can be structural or functional. The mechanism of hypoxemia in obstructive disease is primarily through regional mismatching of ventilation and perfusion ($\dot{V}/\dot{Q}$ mismatch). Dyspnea, a major symptom, is multifactorial in origin but is in large part related to loading of the respiratory muscles.
 - 1. Chronic obstructive pulmonary disease (COPD) is a slowly progressive obstructive lung disease involving the airways and/or pulmonary parenchyma, resulting in a gradual loss of lung function. COPD doubles the risk of POPCs and is associated with increased postoperative cardiac and renal complications. It is generally classified as being attributable to either emphysema ("pink puffer") or chronic bronchitis ("blue bloater"). Although these often coexist, below they are considered as separate entities.
 - a. Emphysema is due to abnormal permanent enlargement of the air-spaces distal to the terminal bronchioles accompanied by destructive changes of the alveolar wall. This leads to loss of the normal elastic recoil of the lung with subsequent premature airway closure at higher than normal lung volumes during exhalation.
 - b. Chronic bronchitis is defined as the presence of productive cough for at least 3 months in each of 2 successive years in a person in

whom the excessive secretions are not due to other diseases. The most common precipitant is cigarette smoking.

2. Asthma is a complex and heterogeneous syndrome characterized by variable airflow obstruction, airway inflammation, and increased airway responsiveness to a variety of stimuli that include exercise, cooling, drying and/or instrumentation of the airways, infection, medications, and occupational exposure.
3. Cystic fibrosis (CF) involves the secretion of highly viscous mucus. This results in airway obstruction, fibrosis, chronic pulmonary infection, and cachexia. Late changes include pneumothorax and bronchiectasis with hemoptysis, hypoxemia, carbon dioxide retention, and respiratory failure.
- B. Restrictive pulmonary disease is characterized by a decrease in lung compliance and may be intrinsic or extrinsic. Airway resistance is usually normal, whereas lung volumes and diffusing capacity are reduced. As in obstructive disease, the primary cause of hypoxemia in restrictive states is $\dot{V}/\dot{Q}$ mismatch. Often patients have multiple reasons for pulmonary dysfunction as well as mixed obstructive and restrictive defects. Proper diagnosis requires a careful history and physical examination. Pulmonary function testing may be required to differentiate obstructive from restrictive defects and can be used to assess a patient's response to therapy.
 1. Intrinsic
 - a. Pulmonary edema occurs when fluid accumulates in the interstitium and alveoli by hydrostatic, cardiogenic (e.g., congestive heart failure [CHF]), or "noncardiogenic" (e.g., acute respiratory distress syndrome [ARDS]) mechanisms.
 - b. Pulmonary interstitial disease causes inflammation/fibrosis of interstitium, alveoli, or vascular beds. The latter may lead to pulmonary hypertension and cor pulmonale. Examples include sarcoidosis, chronic hypersensitivity pneumonitis, and radiation fibrosis.
 2. Extrinsic
 - a. Pleural disease, either fibrosis or effusion.
 - b. Chest wall deformity, such as kyphoscoliosis, ankylosing spondylitis, pectus excavatum, trauma, or burns.
 - c. Diaphragmatic compression by obesity, ascites, pregnancy, or from retraction during abdominal surgery.
- C. Pulmonary hypertension is characterized by a mean pulmonary artery pressure of more than 25 mm Hg at rest (or >30 mm Hg with exercise), with a normal pulmonary artery occlusion (capillary wedge) pressure. It can result in right atrial and right ventricular dilatation, hypertrophy and failure, and likely increases POPCs. It is classified as follows:
 1. Primary pulmonary arterial hypertension occurs due to idiopathic fibrin deposition in the pulmonary capillaries and arterioles accompanied by increased thrombogenesis. The total cross-sectional area of the pulmonary vasculature may be markedly decreased
 2. Pulmonary hypertension due to left heart failure
 3. Pulmonary hypertension due to lung diseases and/or hypoxia
 4. Chronic thromboembolic pulmonary hypertension
 5. Pulmonary hypertension with unclear and/or multifactorial mechanisms (e.g., sarcoidosis and vasculitis)

III. IDENTIFICATION OF THE PATIENT AT RISK

A. History

1. Patient-related information to be obtained, per meta-analysis, includes advanced age (>60), preexisting lung disease (e.g., COPD), and nonpulmonary information related to overall physical fitness and conditions

(ASA-PS 2 or greater, poor functional status, malnutrition, and CHF). Other risk factors may include hypoxemia, anemia, obstructive sleep apnea (OSA), recent respiratory infection, and current sepsis. Among laboratory predictors, good evidence exists only for low serum albumin levels (<30 g/L) in predicting POPCs.

2. Symptoms of respiratory disease such as cough, expectoration, hemoptysis, wheezing, dyspnea, and chest pain should be elicited. Occupational exposures, medications, recent changes in clinical status as well as symptoms of OSA should be defined.
3. Chronic cough may suggest bronchitis or asthma. If cough is productive, sputum should be examined for evidence of infection and, if appropriate, sent for Gram stain, culture, or cytology.
4. Smoking history should be quantified in pack years (number of packs smoked per day multiplied by the number of years smoked). The risks of malignancy, COPD, and POPCs are directly proportional to the smoking history.
5. Dyspnea is an uncomfortable sensation of breathing. The activity level should be defined; severe dyspnea (occurring at minimal activity or at rest) may be a predictor of both poor ventilatory reserve and the need for postoperative ventilatory support.

B. Physical Findings

1. Body habitus and general appearance.
 - a. Obesity, pregnancy, and kyphoscoliosis reduce lung volumes and capacities (functional residual capacity [FRC] and total lung capacity [TLC]) and pulmonary compliance and predispose to atelectasis and hypoxemia.
 - b. Cachectic malnourished patients have blunted respiratory drive and decreased muscle strength and are predisposed to pneumonia.
 - c. Cyanosis requires a minimum reduced hemoglobin concentration of 5 g/dL. The appearance of cyanosis depends on many factors, including cardiac output, oxygen uptake by the tissue, and hemoglobin concentration. Cyanosis suggests hypoxemia but can be unreliable.
2. Respiratory signs. Respiratory rate and pattern, diaphragmatic coordination, and the use of accessory muscles should be assessed.
 - a. Tachypnea, a respiratory rate greater than 25 breaths/minute, is usually the earliest sign of respiratory distress.
 - b. Respiratory pattern
 1. Pursed-lip breathing, tripodding, and visible expiratory effort may indicate airway obstruction.
 2. Accessory muscle use increases with load and dysfunction of the diaphragm and intercostal muscles.
 3. Asymmetry of chest wall expansion may result from unilateral bronchial obstruction, trauma, pneumothorax, pleural effusion, lung consolidation, or unilateral phrenic nerve injury (causing an elevated hemidiaphragm).
 4. Tracheal deviation may suggest pneumothorax or mediastinal disease with tracheal compression. Severe cases may cause difficulty during intubation or airway obstruction during induction of general anesthesia.
 5. Inspiratory paradox. Normally, the abdominal wall should move outward with the chest wall during inspiration. Inspiratory paradox occurs when the abdomen collapses as the chest wall expands during inspiration and suggests paralysis or severe dysfunction of the diaphragm.

c. Auscultation

1. Diminished breath sounds may indicate local consolidation, pneumothorax, or pleural effusion.
2. Rales, usually in dependent portions, may indicate atelectasis or CHF.
3. Wheezing may indicate obstructive airway disease.
4. Stridor may indicate upper airway narrowing.

3. Cardiovascular signs

- a. Pulsus paradoxus can be seen in patients with asthma and is defined as a fall in systolic blood pressure of greater than 10 mm Hg during inspiration. It is probably due to selective impairment of left ventricular filling and ejection secondary to the negative pleural pressure generated during spontaneous ventilation. Pulsus paradoxus can also be seen with pericardial tamponade and superior vena cava obstruction, but the physiologic mechanism is different than it is with asthma.
- b. Pulmonary hypertension occurs as a result of elevated pulmonary vascular resistance.
- c. Physical signs may include splitting of the second heart sound with an accentuated pulmonic component, jugular venous distention, hepatomegaly, hepatojugular reflux, and peripheral edema.
- d. Factors that may acutely increase pulmonary vascular resistance include hypoxia, hypercarbia, acidosis, pulmonary embolism, ARDS, and the application of high levels of positive end-expiratory pressure (PEEP).

C. Diagnostic Studies

1. Chest radiograph

- a. Hyperinflation and decreased vascular markings are characteristic of COPD and asthma.
- b. Pleural effusion, pulmonary fibrosis, and skeletal abnormalities (kyphoscoliosis and rib fractures) may predict restrictive disease states.
- c. Air space disease, including CHF, consolidation, atelectasis, lobar collapse (bronchial obstruction), and pneumothorax, is an important predictor of $\dot{V}/\dot{Q}$ mismatch and hypoxemia.
- d. Specific lesions, including pneumothorax, emphysematous blebs, and cysts, may preclude the use of nitrous oxide.
- e. Tracheal narrowing or deviation may occur as a result of mediastinal compression or masses. Further workup with computed tomography or magnetic resonance imaging may be of value in detailing the precise location and degree of obstruction of tracheal and bronchial lesions.

2. Electrocardiogram. Electrocardiographic signs of significant pulmonary dysfunction include the following:

- a. Low voltage and poor R-wave progression attributable to hyperinflation
- b. Signs of pulmonary hypertension and cor pulmonale, such as
 1. Right axis deviation
 2. P pulmonale (P waves >2.5 mm in height in lead II)
 3. Right ventricular hypertrophy (R/S ratio >1 in lead V_1)
 4. Right bundle branch block

3. Arterial blood gas tensions

- a. Partial pressure of oxygen (PaO_2). Hypoxemia is considered severe when PaO_2 is less than 55 mm Hg. Patients with severe hypoxemia

at rest have significant pulmonary dysfunction and are at increased risk for POPCs.

- b. Partial pressure of carbon dioxide (PaCO_2). Hypercarbia occurs when PaCO_2 is greater than 45 mm Hg. Patients who chronically retain carbon dioxide often have end-stage lung disease with little or no reserve and are at increased risk for POPCs.
- c. Measurement of pH in conjunction with PaCO_2 allows determination of acid–base disturbances.
4. Pulmonary function tests (PFTs) measure pulmonary mechanics and functional reserve and provide an objective assessment of lung function. In this context, they are used to estimate residual lung function after pulmonary resection, as measured by split function studies (which quantify dysfunction in each lung). The impact of preoperative PFTs in predicting the risk of clinically important POPCs in other surgical procedures is not as clear. The use of preoperative PFTs in evaluating these patients must be individualized. Normal values for a 70-kg adult male include TLC, 5.5 L; vital capacity (VC), 4 L; FRC, 2.5 L; residual volume (RV), 1.5 L; and forced expiratory volume in the first second (FEV_1), 3.2 L, which is 80% of VC. Obstructive defects are characterized by elevated TLC, FRC, and RV with reduced FEV_1 (<80%). Restrictive defects are characterized by proportional decreases in all lung volumes with a normal or increased FEV_1/FVC ratio.

IV. EFFECTS OF ANESTHESIA AND SURGERY ON PULMONARY FUNCTION

General anesthesia decreases lung volumes and promotes $\dot{V}/\dot{Q}$ mismatch and atelectasis formation. Many anesthetic drugs blunt the ventilatory response to hypercarbia and hypoxia. Postoperatively, atelectasis and hypoxemia are common findings, especially in patients with preexisting pulmonary disease. Pulmonary function is further compromised by postoperative pain, which can limit coughing and lung expansion.

A. Respiratory Mechanics and Gas Exchange

1. General anesthesia and the supine position decrease FRC. Atelectasis occurs when lung volumes during tidal breathing fall below the volume at which airway closure occurs (closing capacity). PEEP can minimize this effect. The supine position causes a cephalad movement of the diaphragm and a reduction in FRC.
2. Positive-pressure ventilation compared with spontaneous breathing leads to $\dot{V}/\dot{Q}$ mismatching. During positive-pressure ventilation, non-dependent portions of the lung receive a greater proportion of ventilation than do dependent portions. In contrast, pulmonary blood flow tends to be increased in dependent portions of the lung; its distribution is affected by gravity and the anatomical distribution of pulmonary vessels. The result is a variable increase in both $\dot{V}/\dot{Q}$ mismatch and physiologic dead space.

B. Regulation of Breathing

1. The ventilatory response to hypercarbia is reduced by inhalation anesthetics, propofol, barbiturates, and opioids. PaCO_2 is elevated with spontaneous ventilation during general anesthesia, as is the apneic threshold (the PaCO_2 at which patients who have had hyperventilation to apnea again resume spontaneous ventilation).
2. The ventilatory response to hypoxia may also be blunted by inhalation anesthetics, propofol, barbiturates, and opioids. This effect may be particularly important in patients with severe chronic lung disease who

normally retain carbon dioxide and depend more on hypoxic drive to increase ventilation.

3. The respiratory depressant effects of anesthetic and analgesic drugs may be more pronounced in patients with OSA.
- C. **Effect of Surgery.** Postoperative pulmonary function is affected by the site of surgery. The ability to cough and breathe deeply is reduced after abdominal operations compared with peripheral procedures and appears to be related to diaphragm dysfunction and to the pain produced by coughing and deep breathing. VC can be reduced by up to 75% after upper abdominal procedures and by approximately 50% after lower abdominal or thoracic operations. Recovery of normal pulmonary function may take several weeks. Peripheral procedures have little impact on VC or the ability to clear secretions.
- D. **Effect on Ciliary Function.** The upper respiratory tract normally warms and humidifies inspired air, providing an ideal environment for normal function of respiratory tract cilia and mucus. General anesthesia, often conducted with unhumidified gases at high flow rates, dries secretions and can easily damage respiratory epithelium. Endotracheal intubation exacerbates this problem by bypassing the nasopharynx. Secretions become thickened, ciliary function is reduced, and the patient's resistance to pulmonary infections is decreased.

V. PERIOPERATIVE TREATMENT IN PULMONARY DISEASE

- A. The goals of preoperative treatment are to improve the aspects of disease that may be reversible.
 1. Cessation of smoking for 12 hours before surgery may reduce nicotine and carboxyhemoglobin levels, promoting better tissue oxygen transport. Cessation of smoking for longer periods (at least several weeks) does reduce the risk of wound infection and may reduce the risk of POPCs by improving ciliary function and reducing airway secretions and irritability.
 2. Those with acute exacerbations of COPD or asthma should be treated and elective procedures delayed until resolution. Unfortunately, there are no data on how long after resolution that the patient remains at increased risk.
 3. Identification of the patient with sleep apnea and institution of and optimization of continuous airway pressure/bilevel positive airway pressure (CPAP/BIPAP) preoperatively may be associated with improved outcomes.
 4. Measures aimed at preventing perioperative thromboembolism (such as compression stockings or anticoagulants) are important for all major surgeries. These may be instituted, preoperatively, intraoperatively, or postoperatively.
 5. Lung expansion maneuvers (voluntary deep breathing, coughing, incentive spirometry, and chest percussion and vibration combined with postural drainage) improve mobilization of secretions and increase lung volumes, reducing the incidence of POPCs. Training in these methods preoperatively should ideally be done to optimize postoperative outcome.
- B. **Intraoperative Management**
 1. Humidification of inspired gases aids clearance of bronchial secretions.
 2. Protective lung ventilation and conservative fluid management during anesthesia may reduce POPCs.

C. Postoperative management is outlined in section VIII of this chapter.

D. Medical Treatment

1. Sympathomimetics, or β_2 -adrenergic agonist drugs, cause bronchodilation via cyclic AMP-mediated relaxation of bronchial smooth muscle.
 - a. Drugs with β_2 -adrenergic selectivity are generally selected. These are classified as those that are short acting and those with prolonged action.
 1. Short-acting β_2 -agonists such as albuterol by inhalation are used for prophylaxis before instrumentation of the airways and for episodes of acute bronchospasm.
 2. Long-acting β_2 -agonists such as salmeterol and formoterol are used in combination with an inhaled corticosteroid for maintenance therapy. They are not indicated for treating acute exacerbations of bronchoconstriction.
 - b. Drugs with mixed β_1 - and β_2 -adrenergic effects include epinephrine (Adrenalin) and isoproterenol (Isuprel). The chronotropic and arrhythmogenic potential of these drugs is a concern in patients with cardiac disease. The intravenous (IV) use of low doses of epinephrine ($<1 \mu\text{g}/\text{minute}$) may be considered for severe medically refractory bronchospasm. At low doses (0.25 to $1.0 \mu\text{g}/\text{minute}$), β_2 -adrenergic agonist effects predominate, with an increase in heart rate attributable to β_1 -adrenergic stimulation. At higher doses of epinephrine, α -adrenergic effects become predominant, with increases in systolic blood pressure.
2. Parasympatholytics. Anticholinergics have a direct bronchodilating effect by blocking the action of acetylcholine on second messengers, such as cyclic guanine monophosphate. They may improve the FEV₁ in patients with COPD, when administered by inhalation. Specific agents include the following:
 - a. Ipratropium bromide (Atrovent) is a short-acting drug given by metered-dose inhaler (MDI) or by nebulizer.
 - b. Tiotropium (Spiriva) is a long-acting drug administered by dry powder inhaler for maintenance therapy.
 - c. Glycopyrrolate (Robinul), 0.2 to 0.8 mg, is administered by nebulizer.
 - d. Atropine sulfate, which has considerable systemic absorption, may cause tachycardia and thus has limited usefulness.
3. Nonspecific phosphodiesterase (PDE) inhibitors/methylxanthines
 - a. Methylxanthines (e.g., aminophylline and theophylline) cause bronchodilation by multiple mechanisms, including activating histone deacetylases, blocking adenosine receptors, releasing endogenous catecholamines, and increasing the intracellular concentration of cyclic AMP through nonspecific inhibition of phosphodiesterase enzymes. They are also thought to affect direct stimulation of the diaphragm. They should be continued until the morning of surgery but are of no benefit during general anesthesia.
 - b. Toxicity occurs frequently when drug levels exceed $20 \mu\text{g}/\text{mL}$; symptoms and signs include nausea, vomiting, headache, anxiety, tachycardia, arrhythmias, and seizures. Dosing requires close monitoring, as smokers and adolescents (patients with rapid drug metabolism) may require higher doses, while patients who are elderly, who have CHF or liver disease, or who are taking cimetidine, propranolol, or erythromycin, should receive reduced doses, reflecting slower drug metabolism.

- c. Patients who will remain on “nothing by mouth” or NPO status for an extended period may receive IV theophylline or aminophylline (a soluble ethylenediamine salt containing 85% theophylline by weight). Oral theophylline preparations can be restarted once enteral intake of medications is tolerated.
- 4. PDE4 inhibitor. Roflumilast is an oral therapy approved to reduce the risk of exacerbation in severe COPD.
- 5. Corticosteroids are often used in patients not responding to bronchodilators. Their mechanisms of action are complex and not completely understood; however, they appear to reduce airway inflammation and responsiveness, edema, mucus secretion, and smooth muscle constriction. Although they are useful for acute severe exacerbations, their clinical effect may take several hours.
 - a. Steroids are preferably administered by inhalation (e.g., Flunisolide [Aerobid] by MDI, 2 puffs every 6 hours) because of decreased systemic side effects.
 - b. Commonly used IV steroids include hydrocortisone (Solu-Cortef), 100 mg IV every 8 hours, and methylprednisolone (Solu-Medrol), up to 0.5 mg/kg IV every 6 hours, in asthmatic bronchitis and often higher doses in an exacerbation of severe asthma. Perioperative regimens are usually tapered in dose, frequency, and route of administration as dictated by clinical response.
 - c. “Stress dose” replacement may be needed in patients currently or recently taking corticosteroids (see Chapter 6).
- 6. Cromolyn is an inhaled medication used as prophylactic therapy for asthma. Its precise mechanisms of action remain unknown, but it appears to act by stabilizing the mast cell membranes and blunting the acute release of preformed bronchoactive mediators. It is of no utility in the acute treatment of bronchospasm.
- 7. Mucolytics
 - a. Acetylcysteine (Mucomyst), administered by nebulizer, can decrease the viscosity of mucus by breaking the disulfide bonds in mucoproteins.
 - b. Hypertonic saline is sometimes used to decrease mucus viscosity. When it is given by nebulizer, an osmotic shift of water to mucus enhances mucus volume and promotes clearance. Inhalation of hypertonic saline, like acetylcysteine—and even occasionally β -adrenergic agonists, anticholinergics, and steroid preparations—may increase airway resistance.
 - c. Recombinant deoxyribonuclease (DNase or Pulmozyme), 10 to 40 mg inhaled daily, is used in some patients with CF to decrease the viscosity of bronchial secretions by cleaving DNA strands in sputum. This improves airway clearance and pulmonary function by 5% to 20% in many patients with CF.
- 8. Leukotriene (LT) modifying drugs have anti-inflammatory effects that act by blocking LT receptors (Zafirlukast and Montelukast). These are approved currently for prophylaxis and maintenance therapy of chronic asthma. A specific benefit in the perioperative period has not yet been determined. Potential adverse reactions include liver function abnormalities and eosinophilic vasculitis (Churg-Strauss syndrome).
- 9. Anti-IgE antibody (Omalizumab), by injection, is used as a maintenance therapy for asthmatic patients with a strong allergic component and poorly controlled symptoms despite otherwise maximal therapy.

10. Ketamine is a bronchial smooth muscle relaxant. Its mechanism is thought to be sympathomimetic and/or antagonism of spasmogenic carbachol and histamine. Ketamine has been used for medically unresponsive bronchospasm, or status asthmaticus.
11. Ivacaftor is a CFTR potentiator that improves chloride transport and mucus transport in the airways in CF patients with the G5510 mutation.

VI. PREMEDICATION

The goals of premedication are to allay anxiety, minimize reflex bronchoconstriction to airway irritants (dry gases and instrumentation), and facilitate the smooth induction of anesthesia.

- A. Oxygen therapy, if required preoperatively, should be continued while the patient is being transported to the operating room and clearly written as a preoperative "order."
- B. If the patient is taking inhaled β -adrenergic agonists or anticholinergics, these should accompany the patient to the operating room; their preoperative use may decrease airway responsiveness.
- C. Anticholinergics are often indicated by inhalation to prevent bronchospasm secondary to vagal stimulation caused by airway manipulations such as laryngoscopy and endotracheal intubation. Some of these agents can be given parenterally. Parenteral administration, however, may cause drying of secretions, increasing the viscosity of mucus.
- D. Histamine (H_2) antagonists (cimetidine, ranitidine) may exacerbate bronchospasm in patients with asthma, because blockage of H_2 receptors may result in unopposed H_1 -mediated bronchoconstriction. Coadministration of an H_1 -blocking agent (diphenhydramine, 25 mg IV) should be considered.
- E. Benzodiazepines are effective anxiolytics but may cause excessive sedation and respiratory depression in compromised patients, especially when used with opioids.
- F. Opioids provide analgesia and sedation but must be carefully titrated to avoid respiratory depression, especially in patients with severe pulmonary dysfunction and/or OSA.

VII. ANESTHETIC TECHNIQUE

- A. Peripheral nerve blockade or local anesthesia may be the best choice of anesthetic for patients with pulmonary disease when the site of operation is peripheral, such as eye or extremity procedures. Some upper extremity blocks may compromise the function of the phrenic nerves (e.g., interscalene and supraclavicular blocks) and should be avoided in patients with severe preexisting lung disease.
- B. Spinal or epidural anesthesia is a reasonable choice for lower extremity surgery. Patients with severe COPD depend on accessory muscle use, including intercostals for inspiration and abdominal muscles for forced exhalation. Spinal anesthesia may be deleterious if motor blockade decreases FRC, reduces a patient's ability to cough and clear secretions, or precipitates respiratory insufficiency or failure. Combined epidural and general anesthetic techniques ensure airway control, provide adequate ventilation, and prevent hypoxemia and atelectasis. Prolonged peripheral procedures are probably best performed with a general anesthetic or a combined technique.
- C. General anesthesia, often in combination with epidural anesthesia, is indicated for upper abdominal and thoracic procedures.

1. Most volatile agents provide bronchodilation and an adequate depth of anesthesia to decrease the hyperreactivity of sensitive airways. However, desflurane can cause airway irritation and coughing with inhalation and is not an optimal choice in patients with reactive airways.
2. Dynamic lung hyperinflation (auto-PEEP) is also important to avoid during general endotracheal anesthesia in patients with reactive airways or elevated lung compliance (severe COPD). Auto-PEEP, which can result in hypotension and decreased cardiac output, often occurs when not enough expiratory time is given to completely empty the lungs.
3. The use of a laryngeal mask airway (LMA) reduces but does not eliminate the risk of bronchospasm, as laryngoscopy or instrumentation of the larynx alone can elicit a laryngobronchospastic response in these patients. An additional risk of using the LMA is the inability to ventilate during bronchospasm, as inspiratory pressure may exceed the sealing force of the LMA in the larynx. The ProSeal LMA was recently developed to overcome this limitation and can be considered.

VIII. POSTOPERATIVE CARE

Residual neuromuscular blockade should be addressed. Lung expansion maneuvers (deep breathing, incentive spirometry, chest physiotherapy, suctioning, and/or noninvasive ventilation with CPAP/BiPAP) should be immediately available to all patients who are identified to be at high risk. Thromboembolism prophylaxis, effective pain management, and selective use of nasogastric tubes are also important to reduce POPCs. The possibility of (invasive or noninvasive) postoperative ventilatory support should be anticipated and discussed with the patient. In those requiring this, a lung protective strategy should be considered.

Suggested Readings

- Bohadana A, Izbicki G, Kraman SS. Fundamentals of lung auscultation. *N Engl J Med* 2014;370:2053.
- Brueckmann B, Villa-Urbe JL, Bateman BT, et al. Development and validation of a score for prediction of postoperative respiratory complications. *Anesthesiology* 2013;118:1276–1285.
- Canet J, Gallart L, Gomar C, et al. Prediction of postoperative pulmonary complications in a population-based surgical cohort. *Anesthesiology* 2010;113:1338–1350.
- Futier E, Constantin J-M, Paugam-Burtz C, et al. A trial of intraoperative low- tidal-volume ventilation in abdominal surgery. *N Engl J Med* 2013;369:428–437.
- Global Initiative for Asthma. Global strategy for asthma management and prevention. 2006. <http://www.ginasthma.org>
- Global Initiative for chronic obstructive lung disease; Global strategy for diagnosis, management, and prevention of COPD. 2014. <http://www.goldcopd.org>
- Gross JB, Apfelbaum JL, Caplan RA, et al. Practice guidelines for the perioperative management of patients with obstructive sleep apnea: a report by the American Society of Anesthesiologists Task Force on Perioperative Management of patients with obstructive sleep apnea. *Anesthesiology* 2006;104:1081–1093.
- Huffmeyer JL, Littlewood KE, Nemergut EC. Perioperative management of the adult with cystic fibrosis. *Anesth Analg* 2009;109:1949–1961.
- Jaber S, Chanques G, Jung B. Postoperative noninvasive ventilation. *Anesthesiology* 2010;112:453–461.
- Kaw R, Pasupuleti V, Walker E, et al. Postoperative complications in patients with obstructive sleep apnea. *Chest* 2012;141:436–441.
- Kor DJ, Lingineni RK, Gajic O, et al. Predicting risk of postoperative lung injury in high-risk surgical patients: a multicenter cohort study. *Anesthesiology* 2014;120:1168–1181.

- Kumar GV, Nair AP, Murthy HS, et al. Residual neuromuscular blockade affects postoperative pulmonary function. *Anesthesiology* 2012;117:1234–1244.
- Mills E, Eyawo O, Lockhart I, et al. Smoking cessation reduces postoperative complications: a systematic review and meta-analysis. *Am J Med* 2011;124:144–154.e148.
- Pritts CD, Pearl RG. Anesthesia for patients with pulmonary hypertension. *Curr Opin Anaesthesiol* 2010;23:411–416.
- Qaseem A, Snow V, Fitterman N, et al. Risk assessment for and strategies to reduce perioperative pulmonary complications for patients undergoing noncardiothoracic surgery: a guideline from the American College of Physicians. *Ann Intern Med* 2006;144:575–580.
- Sasaki N, Meyer MJ, Eikermann M. Postoperative respiratory muscle dysfunction: pathophysiology and preventive strategies. *Anesthesiology* 2013;118:961–978.
- Wiener-Kronish JP, Shepherd KE, Bapolje S, et al. Perioperative evaluation. In: Mason RJ, Broaddus VC, Martin TR, eds. *Murray & Nadel's Textbook of Respiratory Medicine*, 5th ed. Philadelphia: Saunders, 2010: 578–589.

Specific Considerations with Renal Disease

Samuel Vanderhoek and William Benedetto

I. GENERAL CONSIDERATIONS

Approximately 5% of the population has renal disease, with a trend toward increasing prevalence with age. Perioperative renal dysfunction complicates patient management and results in increased morbidity and mortality. Aside from optimizing intravascular volume status, there is no definite consensus on prophylaxis for the development of acute kidney injury (AKI). However, morbidity and mortality may be decreased by a thorough understanding of considerations related to renal disease.

II. PHYSIOLOGY

Blood flow to the kidneys is regulated by intrinsic autoregulatory mechanisms, which help maintain volume and composition of body fluids and aid in excretion of metabolites and toxins and retention of nutrients. The kidneys maintain a stable internal balance despite large fluctuations in fluid and solute intake. They regulate intravascular volume, osmolality, acid–base and electrolyte balance, and they excrete hormones as well as the end products of metabolism and drugs.

A. Regulation of Blood Flow

1. The kidneys receive 20% of total cardiac output, with the renal cortex receiving 94% of total blood flow. The renal medulla receives only 6% of total renal blood flow but extracts approximately 80% of the oxygen that it receives, making it very susceptible to ischemia, particularly the medullary thick ascending loop of Henle.
2. **Renal blood flow** is autoregulated between mean arterial pressures of 60 to 150 mm Hg by intrinsic mechanisms balancing afferent and efferent arteriolar tone. Extrinsic factors such as sympathetic vasoconstrictor innervation, dopaminergic receptors, and the renin–angiotensin system can also alter renal blood flow. Autoregulation can be impaired in states of severe sepsis, AKI, and possibly cardiopulmonary bypass. The kidney is largely devoid of β_2 -receptors.

B. Fluid Regulation

1. **Total body water** (TBW) is approximately 60% of body weight. In obese patients, it may be more precise and practical to calculate TBW based on ideal body weight.
 - a. Two thirds of TBW is **intracellular**.
 - b. One third of TBW is extracellular.
 1. Two thirds of extracellular fluid is **interstitial** and one third is **intravascular**.
 2. **Estimated blood volume** is 70 mL/kg with an estimated plasma volume of 50 mL/kg.
2. The cells of the **macula densa** of the thick ascending limb are chemoreceptors that sense the tubular concentration of sodium and can help to regulate volume status.
3. **Hypovolemia** is managed by the activation of vasoconstrictor and salt-retaining neurohormonal systems including the following:

a. Renin–angiotensin–aldosterone system

1. The **juxtaglomerular apparatus** of the kidney secretes renin in response to renal hypoperfusion, decreased sodium chloride delivery to the distal nephron, and increased sympathetic activity. Renin cleaves angiotensinogen to form angiotensin I, which is then converted to angiotensin II by angiotensin-converting enzyme (ACE) in the lung and other tissues.
2. **Angiotensin II** produces arteriolar vasoconstriction and stimulates aldosterone release.
3. **Aldosterone** is a mineralocorticoid released by the adrenal cortex in response to angiotensin II, increased potassium levels, decreased sodium content, and adrenocorticotropic hormone. Aldosterone acts on the distal tubules to increase reabsorption of sodium in exchange for potassium and protons.
4. **Diuretics** abolish the kidneys' ability to concentrate urine by washing out the renal medullary concentration gradient. Acute tubular necrosis (ATN) presents early as an inability to concentrate urine caused by the breakdown of the Na^+/K^+ -ATPase pump in the medullary thick ascending loop of Henle because of a loss of cell polarity.
- b. **Arginine vasopressin (AVP)** (also called antidiuretic hormone [ADH]) is released by the posterior pituitary gland in response to increased osmolality, decreased extracellular volume, positive pressure ventilation, and surgical stimuli, including pain. AVP increases the permeability of the collecting duct to water through insertion of water channel "aquaporins." Thus, ADH conserves water and concentrates urine.

4. Hypervolemia

- a. **Atrial natriuretic peptide**, a neuropeptide, is the predominant salt-excreting stimulus along with decreases in angiotensin II and sympathetic activity resulting in decreased sodium resorption, thus producing a dilute urine (300 mOsm/kg) and abundant urine sodium (80 mEq/L). Loop diuretics may produce a similar picture even in the face of hypovolemia.
- b. **Kinins** are converted from kininogens by kallikreins and are regulated by salt intake, renin release, and hormone levels. They cause renal vasodilatation and natriuresis.

5. Osmotic equilibrium

- a. The **medullary interstitium** is kept hypertonic by the countercurrent multiplier effect of the loop of Henle.
- b. **Calculated osmolality** (mOsm/kg) = $2[\text{Na}^+] + ([\text{blood urea nitrogen}] (\text{mg/dL})/2.8) + ([\text{glucose}] (\text{mg/dL})/18)$. Normal osmolality = 290 mOsm/kg.
- c. **Osmolal gap** = $\text{Osm (measured)} - \text{Osm (calculated)}$ is normally less than 10. An increased osmolal gap occurs when osmotically active but unmeasured substances (e.g., ethanol, mannitol, methanol, and sorbitol) are present in the blood.
6. **Daily adult water intake** is approximately 2,600 mL: 1,400 mL in liquids, 800 mL in solid food, and 400 mL from metabolism. The minimum water intake to excrete solute load is about 600 mL/day.

C. Electrolyte Balance

1. Disorders of sodium homeostasis

- a. **Hyponatremia**: Plasma sodium concentration less than 134 mEq/L.
 1. **TBW** may be high, low, or normal (usually a sign of free water excess).
 2. **Hyponatremia** often results in reduced plasma osmolality.

3. **Pseudohyponatremia** from hyperglycemia (uncontrolled diabetes mellitus), hyperlipidemia, or hyperproteinemia (multiple myeloma) should be ruled out to avoid mistreatment.
4. **Clinical features** vary with the degree of hyponatremia and the rapidity of onset. Symptoms generally do not appear until the sodium concentration falls below 125 mEq/L.
 - a. **Moderate hyponatremia or gradual onset:** Confusion, muscle cramps, lethargy, anorexia, and nausea.
 - b. **Severe hyponatremia or rapid onset:** Seizures and coma.
5. Generally, acute normalization of the serum $[\text{Na}^+]$ is not necessary. It should be **corrected at a rate of 0.5 mEq/L/h** until 120 mEq/L is reached to prevent complications from rapid correction (e.g., cerebral edema, central pontine myelinolysis, and seizures). At this point, the patient should be out of danger, and the $[\text{Na}^+]$ should be normalized slowly over a period of days. Treatment depends on the volume status of the patient.
 - a. **Hypervolemic hyponatremia** due to renal failure, congestive heart failure, cirrhosis, or nephrotic syndrome is treated by sodium and water restriction and possibly with diuresis.
 - b. **Hypovolemic hyponatremia** from diuretics, vomiting, or bowel preparations is treated with normal saline. For severe hypovolemic hyponatremia, the $[\text{Na}^+]$ may be partially corrected to 125 mEq/L or a serum osmolality of 250 mmol/L over 6 to 8 hours with 3.5% hypertonic saline. Hypertonic saline is dangerous in volume-expanded salt-retaining states such as congestive heart failure.
 - c. **Normovolemic hyponatremia** from the syndrome of inappropriate ADH secretion, hypothyroidism, drugs that impair renal water excretion, or water intoxication is treated by fluid restriction.
- b. **Hypernatremia:** Plasma sodium concentration greater than 144 mEq/L. It is usually caused by impairment of thirst or the ability to obtain water.
 1. **TBW** may be high, low, or normal (usually a sign of free water deficit).
 2. **Clinical features** vary with the degree of hypernatremia and rapidity of onset, ranging from tremulousness, weakness, irritability, and mental confusion to seizures and coma.
 3. **Treatment** depends on determining the volume status of the patient. Rapid correction can induce cerebral edema, seizures, permanent neurologic damage, and death. Plasma $[\text{Na}^+]$ should be corrected at a maximum rate of 0.5 mEq/L/h. The water deficit, if present, can be calculated as follows:

$$\text{Volume to be replaced (L)} = [(0.6 \times \text{body weight [kg]}) \times ([\text{Na}^+] - 140)/140]$$
 - a. **Hypervolemic hypernatremia** occurs secondary to Na^+ overload from mineralocorticoid excess, dialysis with hypertonic solutions, or treatment with hypertonic saline or sodium bicarbonate (NaHCO_3). The excess total body Na^+ (i.e., volume) may be removed by dialysis or with diuretic therapy, and the water loss is replaced with 5% dextrose in water (D5W).
 - b. **Hypovolemic hypernatremia** occurs secondary to water loss exceeding Na^+ loss (e.g., diarrhea, vomiting, and osmotic diuresis) or inadequate water intake (e.g., impaired thirst mechanism and altered mental status). If **hemodynamic instability or**

evidence of hypoperfusion is present, initial volume therapy should consist of 0.45% or even 0.9% NaCl. **After volume replenishment**, the remaining free water deficit should be replaced with D5W until the Na^+ concentration decreases. Then, 0.45% saline may be substituted.

- c. **Normovolemic hypernatremia** is typically the result of diabetes insipidus in patients with a normal thirst response. Therapy consists of treating the underlying etiology, correcting the free water deficit with D5W, and using exogenous vasopressin in neurogenic diabetes insipidus.

2. Disorders of potassium homeostasis

- a. **Hypokalemia:** Plasma $[\text{K}^+]$ less than 3.3 mEq/L.

- 1. Serum $[\text{K}^+]$ is a poor index of **total body potassium** stores, because 98% of body potassium is located intracellularly. Thus, large $[\text{K}^+]$ deficits must be present before seeing a decrease in serum $[\text{K}^+]$. In a 70-kg man with normal pH, a fall in serum $[\text{K}^+]$ from 4 to 3 mEq/L reflects a deficit of 100 to 200 mEq. Below 3 mEq/L, each decrease of 1 mEq/L reflects an additional deficit of 200 to 400 mEq.

2. Etiologies

- a. **Total body K^+ deficit.**
- b. **Shifts in distribution** of K^+ (extracellular to intracellular).
- 3. **$[\text{K}^+]$ loss** may be from the following:
 - a. **Gastrointestinal tract** (e.g., vomiting, diarrhea, nasogastric suctioning, chronic malnutrition, or obstructed ileal loops).
 - b. **Kidney** (e.g., diuretics, mineralocorticoid and glucocorticoid excess, and some types of renal tubular acidosis).
- 4. Changes in **K^+ distribution** occur with alkalosis (H^+ shifts to the extracellular fluid and K^+ moves intracellularly). Thus, rapid correction of acidosis, by hyperventilation or NaHCO_3 administration, may produce undesirable hypokalemia.
- 5. **Clinical features** rarely appear unless $[\text{K}^+]$ is less than 3 mEq/L or the rate of fall is rapid.
 - a. **Signs** include weakness, augmentation of neuromuscular block, ileus, and disturbances of cardiac contractility.
 - b. Hypokalemia increases excitability and predisposes the patient to **arrhythmias** that may be refractory to treatment unless the hypokalemia is resolved. Electrocardiographic (ECG) changes include flattened T waves, U waves, increased PR and QT intervals, ST segment depression, and atrial and ventricular dysrhythmias. Ventricular ectopy is more likely with concomitant digitalis therapy.
 - c. Serum $[\text{K}^+]$ less than 2.0 mEq/L is associated with vasoconstriction and rhabdomyolysis.
- 6. **Treatment.** Rapid replacement of K^+ may cause more problems than hypokalemia. There is no need to correct chronic hypokalemia ($[\text{K}^+] \geq 2.5$ mEq/L) before induction of anesthesia. Hypokalemia-induced conduction disturbances or diminished contractility can be treated with K^+ (0.5 to 1.0 mEq intravenously [IV] every 3 to 5 minutes) until resolution. Serum $[\text{K}^+]$ must be closely followed during correction.
- b. **Hyperkalemia:** plasma $[\text{K}^+]$ greater than 4.9 mEq/L.
 - 1. Certain conditions and drugs can worsen hyperkalemia such as catabolic stress, acidosis, nonsteroidal anti-inflammatory drugs (NSAIDs), ACE-I, potassium-sparing diuretics, and β -blockers.

2. Etiologies

- a. **Decreased excretion** (e.g., renal failure and hypoaldosteronism)
- b. **Extracellular shift** (e.g., acidosis, ischemia, rhabdomyolysis, tumor lysis syndrome, and drugs such as succinylcholine). Acidosis increases the serum $[K^+]$ by 0.5 mEq for every 0.1 unit decrease in the pH
- c. Administration of blood, potassium penicillins, and salt substitutes to renal failure patients
- d. **Pseudohyperkalemia** from a hemolyzed specimen
3. **Clinical features** are more likely with acute changes than with chronic elevation.
 - a. **Signs and symptoms** include muscle weakness, paresthesias, and cardiac conduction abnormalities, which become dangerous as K^+ levels approach 7 mEq/L. Bradycardia, ventricular fibrillation, and cardiac arrest may result.
 - b. Hyperkalemia suppresses electrical conduction. **ECG findings** include peaked T waves, ST segment depression, prolonged PR interval, loss of the P wave, diminished R-wave amplitude, QRS widening, and prolongation of the QT interval.
4. **Treatment** depends on the nature of ECG changes and serum levels.
 - a. **ECG changes** are treated with slow IV administration of 0.5 to 1.0 g of calcium chloride ($CaCl_2$). The dose may be repeated in 5 minutes if changes persist.
 - b. **Hyperventilation and $NaHCO_3$** administration shifts K^+ intracellularly. Between 50 and 100 mEq of $NaHCO_3$ may be given IV over 5 minutes, with a repeated dose in 10 to 15 minutes.
 - c. **Insulin** also shifts K^+ intracellularly. Regular insulin (10 units) is given IV simultaneously with 25 g of glucose (one ampule of a 50% solution) over 5 minutes. Check the glucose level 30 minutes later to avoid hypoglycemia.
 - d. The above therapies are short-term measures to decrease $[K^+]$ via cellular shifts. Cation exchange resins (sodium polystyrene sulfonate [Kayexalate], 20 to 50 g with sorbitol) given orally or rectally will slowly remove K^+ from the body and should be used as soon as possible. Serum $[K^+]$ can also be lowered by dialysis.

D. Extrarenal Regulatory and Metabolic Functions

1. **Erythropoietin** is produced to stimulate red blood cell production. Treatment of patients with exogenous recombinant erythropoietin can prevent the anemia due to chronic kidney disease (CKD) and its sequelae.
2. **Vitamin D** is converted to its most active form, 1,25-dihydroxy-vitamin D by the kidney.
3. **Parathyroid hormone** acts on the kidney to conserve calcium, to inhibit phosphate resorption, and to increase conversion of vitamin D by the kidney.
4. Peptides and protein hormones such as insulin are metabolized, accounting for the generally decreased insulin requirements as renal failure progresses.

III. RENAL FAILURE

The definition varies but has been reported as an increase in serum creatinine by 0.5 mg/dL, increase in serum creatinine by 50%, or serum creatinine greater than 2 mg/dL.

A. Acute Kidney Injury. Incidence varies according to etiology, definition, and type of surgery but is 4% to 24% with mortality rates as high as 60% to 90%. Postoperative renal dysfunction is associated with higher incidence of gastrointestinal bleeding, respiratory infection, sepsis, and longer ICU and hospital length of stay.

1. Epidemiology. From 2% to 5% of hospitalized patients; increases with age.

2. Etiology

a. Prerenal. Due to decreased circulating volume (hypovolemia) or a perceived decrease in circulating volume (decreased cardiac output or hypotension). Early correction of the underlying cause usually results in rapid reversal of renal dysfunction, but continued renal hypoperfusion may result in intrinsic renal damage.

b. Intrarenal. The most common cause is ATN due to ischemia (see section III.C). Other intrarenal causes include toxins, acute glomerulonephritis, and interstitial nephritis.

c. Postrenal. Obstructive lesions result in disrupted emptying and can be caused by renal calculi, neurogenic bladder, prostatic disease, or an encroaching tumor. Unilateral obstruction rarely causes AKI.

d. Normotensive ischemic acute kidney injury. A low-perfusion state may arise in the absence of frank hypotension in a patient with “normal” appearing blood pressures. These patients typically have underlying risk factors for renal injury including early sepsis or exposure to nephrotoxic agents such as IV contrast or NSAIDs. Additionally, normotension in a patient with baseline chronic hypertension can actually herald a low-perfusion state.

3. Classification. There are three widely used classification systems for AKI (Table 4.1):

a. The RIFLE criteria classifies three levels of kidney injury (risk, injury, or failure) and two outcomes (loss and end-stage renal disease [ESRD]) based upon (1) a percentage increase in serum creatinine over 7 days or (2) a decrease in urine output (UOP).

b. The AKIN criteria modifies the RIFLE criteria by including absolute increases in serum creatinine and limiting the period of injury to a 48-hour window.

c. The KDIGO criteria fuses the RIFLE and AKIN criteria.

4. Diagnosis. Clinical features occurring late in the course of the disease include hypervolemia due to an impaired ability to excrete water and sodium with resultant hypertension and peripheral edema, potential hypovolemia due to lack of urine concentrating ability, potassium retention, impaired excretion of drugs and toxins, and potential progression to CKD. Results of urine and serum indices can help to distinguish prerenal, intrarenal, and postrenal etiologies (Table 4.2).

5. Prevention. Mainly based on tradition, anecdotes, or extrapolation from animal models. A modest goal is to keep UOP greater than 0.5 mL/kg/h and to avoid hypovolemia, hypoxia or decreased O_2 delivery, renovascular constriction, increased renal O_2 demand, and maintenance of renal vasodilation and renal tubular blood flow along with attenuation of renal ischemic reperfusion injury.

6. Treatment

a. Medications such as diuretics, dopamine, and fenoldopam can be used to increase UOP, treat hypertension, and manage electrolyte, fluid, and acid-base disturbances but have not been proven to prevent or treat AKI (see sections IV.A and IV.B).

TABLE 4.1

Criteria for Acute Kidney Injury

	Serum Creatinine Criteria			Urine Output Criteria
	RIFLE	AKIN	KDIGO	
Definition	Increase in serum creatinine of >50% developing over <7 days	Increase in serum creatinine of 0.3 mg/dL or >50% developing over <48 h	Increase in serum creatinine of 0.3 mg/dL over 48 h or >50% developing over 7 days	Urine output of <0.5 mL/kg/h for > 6 h
Staging				
RIFLE-Risk	Increase in serum creatinine >50%	Increase in serum creatinine of 0.3 mg/dL or >50%	Increase in serum creatinine of 0.3 mg/dL or >50%	Urine output of <0.5 mL/kg/h for >6 h
AKIN/KDIGO stage 1				
RIFLE-Injury	Increase in serum creatinine >100%	Increase in serum creatinine >100%	Increase in serum creatinine >100%	Urine output of <0.5 mL/kg/h for >12 h
AKIN/KDIGO stage 2				
RIFLE-Failure	Increase in serum creatinine >200%	Increase in serum creatinine >200%	Increase in serum creatinine >200%	Urine output of <0.3 mL/kg/h for >12 h or anuria for >12 h
AKIN/KDIGO stage 3				
RIFLE-Loss	Need for RRT >4 wk			
RIFLE-End-stage	Need for RRT >3 mo			

Pallevsky PM. Definition of acute kidney injury. In: Curhan GC, ed. *UpToDate*. Waltham: UpToDate. (Accessed August 13, 2014.)

TABLE
42

Urine and Serum Diagnostic Indexes

	Prerenal	Renal	Postrenal
Urine (Na)	<10 mEq/L	>20 mEq/L	>20 mEq/L
Urine (Cl)	<10 mEq/L	>20 mEq/L	
FE _{Na}	<1%	>2%	>2%
Urine osmolality	>500	<350	<350
Urine/serum (creatinine)	>40	<20	<20
Renal failure index	<1%	>2%	>2%
Urine/serum (urea)	>8	<3	<3
Serum (BUN)/creatinine	>20	10	10

BUN, blood urea nitrogen; FE_{Na}, fractional excretion of sodium.

b. Hemodialysis. Incidence of AKI patients requiring dialysis varies depending on the underlying surgical operation (e.g., coronary artery bypass grafting 1.1% versus general surgery 0.6%).

1. **Hemodialysis** uses an artificial semipermeable membrane that separates the patient's blood from dialysate and allows the exchange of solutes by diffusion. Vascular access (via central venous catheters or a surgically created arteriovenous fistula) and systemic or regional anticoagulation are often required. Hemodialysis typically is performed three times a week, and serum electrolyte and volume abnormalities are corrected by adjusting the dialysis bath fluid. Blood samples taken immediately after dialysis will be inaccurate, because redistribution of fluid and electrolytes takes about 6 hours. Continuous arteriovenous or venovenous hemodialysis may also be performed. Complications include arteriovenous fistula infection or thrombosis, dialysis disequilibrium or dementia, hypotension, pericarditis, and hypoxemia.
2. **Hypotension** can occur during hemodialysis with changes in preload, electrolyte changes, acid–base abnormalities, hemodynamic effects of buffering drugs, and impaired sympathetic response.
3. **Indications** for dialysis in AKI and CKD include hyperkalemia, acidosis, volume overload, uremic complications (pericarditis, tamponade, and encephalopathy), and severe azotemia.
4. **Ultrafiltration** and **hemofiltration** allow for the removal of volume with minimal removal of waste products. These techniques are useful in volume-overloaded patients. As with standard hemodialysis, anticoagulation may be required.
 - a. **Ultrafiltration** uses hemodialysis equipment to create a hydrostatic driving force across the membrane without a dialysate on the opposing side. Thus, an ultrafiltrate of serum is removed, and this volume is not replaced. If large volumes of fluid are removed rapidly, hypotension may ensue.
 - b. **Hemofiltration** uses the same principle as ultrafiltration; however, replacement fluid is given to the patient either before or after the membrane filter and solutes/electrolytes are removed by convection. Volume shifts are minimized so that patients can tolerate longer periods of continuous filtration.
- c. **Continuous renal replacement therapy (CRRT)** refers to any continuous mode of extracorporeal solute or fluid removal. Indications

in addition to AKI include fluid clearance, electrolyte imbalances, and managing metabolic acidosis. Slower blood flow rates with CRRT improve hemodynamic stability compared with regular hemodialysis.

B. Chronic kidney disease (CKD) is defined by kidney damage (structural or functional abnormalities of the kidney) for ≥ 3 months as manifested by abnormalities in the composition of blood or urine, abnormalities in imaging tests, or a glomerular filtration rate (GFR) less than 60 mL/minute/1.73 m² for ≥ 3 months.

- 1. Epidemiology.** CKD affects more than 26 million adults in the United States (Table 4.3).
- 2. Etiology.** Common causes include hypertension, diabetes mellitus, chronic glomerulonephritis, tubulointerstitial disease, renovascular disease, and polycystic kidney disease.
- 3. Clinical features**
 - a. Hypervolemia and hypertension,** sometimes resulting in congestive heart failure and edema.
 - b. Accelerated atherosclerosis,** which may increase the risk of coronary artery disease.
 - c. Uremic pericarditis and pericardial effusions,** which may cause cardiac tamponade.
 - d. Hyperkalemia, hypermagnesemia, and hyponatremia** may occur.
 - e. Hypocalcemia and hyperphosphatemia** due to elevated parathyroid hormone, resulting in renal osteodystrophy.
 - f. Metabolic acidosis** due to retained sulfates and phosphates and an inability to excrete products of metabolism.
 - g. Chronic anemia** secondary to decreased erythropoietin production and decreased red blood cell survival.
 - h. Platelet dysfunction,** which can be temporarily treated with desmopressin acetate.
 - i. Gastrointestinal dysfunction is common as a result of accumulated urea that may result in inflammation of the entire GI tract. Increased gastric volume, acid production, and delayed gastric emptying** result in an increased incidence of peptic ulceration, and nausea and vomiting with increased risk of regurgitation and aspiration with anesthesia.
 - j. Increased susceptibility to infection due to leukocyte and immune dysfunction from uremia, malnutrition, and inflammatory reaction to dialysis.**
 - k. Central nervous system changes** range from mild changes in mentation to severe encephalopathy and coma. Peripheral and autonomic neuropathies are common.
 - l. Glucose intolerance and hypertriglyceridemia.**

TABLE 4.3		National Kidney Foundation Classification of CKD	
Stage	Description	GFR	U.S. Prevalence (%)
I	Normal	≥ 90	3.3
II	Mild	60–89	3.0
III	Moderate	30–59	4.3
IV	Severe	15–29	0.2
V	Failure	<15	0.1

4. **Treatment.** When needed, 85% receive hemodialysis and 15% receive peritoneal dialysis. Transplantation is the preferred method of treatment for most CKD patients.

- a. **Hemodialysis (see section III.A.5.b)**

- b. **Peritoneal dialysis** uses the capillaries of the peritoneum as a semi-permeable exchange membrane with the dialysate infused into the peritoneal cavity via an indwelling peritoneal catheter. Advantages over hemodialysis include less hypotension or disequilibrium and no need for heparin treatment. However, peritoneal dialysis is less efficient and limited in catabolic states compared with hemodialysis. Complications include infection, hyperglycemia from the dextran in the dialysate, and increased protein loss into the dialysate.

- C. **Specific Causes of Renal Failure**

1. **ATN** may be produced by ischemic or toxin injuries and is the major intrinsic form of AKI. ATN is the most common cause of perioperative renal failure, and its development is associated with high mortality. The major risk factors for ATN are a history of preexisting renal insufficiency, administration of radiocontrast agents or aminoglycoside antibiotics, and advanced age. Anesthetic management of patients who are at risk for developing ATN includes meticulous management of fluids and hemodynamics with the goal of maintaining euolemia, normal renal perfusion, and urinary output. No specific therapies have proved consistently beneficial in preventing or treating perioperative ATN.
2. **Glomerulonephropathies** are a diverse family of diseases that may present insidiously or more acutely with fulminant renal failure. Nephrotic syndrome may be the initial presentation with severe proteinuria (3.5 g/day), hypoalbuminemia, hyperlipidemia, and edema. Anesthetic concerns include depleted intravascular volume and protein, accelerated atherosclerotic disease, and increased risk of infection. Glomerulonephropathy may be secondary to autoimmune diseases such as systemic lupus erythematosus or vasculitides such as granulomatosis with polyangiitis. Therapy may include glucocorticoids and cytotoxic agents.
3. **Hypertensive nephrosclerosis** is a major etiology in the development of ESRD and may account for up to 30% of patients beginning dialysis. Treatment of diastolic hypertension reduces disease progression and the associated morbidity and mortality.
4. **Diabetic nephropathy** is the single largest cause of ESRD in the United States. The nephropathy presents with proteinuria, and there is a progressive decline in renal function over 10 to 30 years after the initial diagnosis. Diabetic nephropathy often manifests itself as a type IV renal tubular acidosis (hyporeninemic hypoaldosteronism) or as papillary necrosis. There is a high correlation between renal dysfunction and diabetic retinopathy. Aggressive control of blood glucose and blood pressure may forestall the development and prevent progression of nephropathy.
5. **Tubulointerstitial diseases** primarily affect the renal tubules and interstitium and include acute and chronic forms of interstitial nephritis.
 - a. **Acute interstitial nephritis** is most commonly caused by drugs (e.g., penicillins, cephalosporins, sulfonamides, rifampin, and NSAIDs) in adults. Systemic infections are the most common etiologies in children. Acute interstitial nephritis usually presents as oliguric renal failure with a variable degree of proteinuria. Symptoms of an inflammatory response, such as fever, rash, eosinophilia, and

eosinophiluria, are suggestive of the diagnosis of acute interstitial nephritis. Treatment is supportive and includes discontinuation of suspect drugs.

- b. **Chronic interstitial nephritis** is most commonly due to obstruction of urine flow or reflux, analgesic abuse, or heavy metal intoxications. Early in the disease, patients lose the ability to concentrate urine and have polyuria and nocturia. Later manifestations depend on the specific anatomic lesions. The only specific therapy for chronic interstitial nephritis is treatment of the underlying cause.
6. **Polycystic kidney diseases** are autosomal dominant diseases responsible for 5% to 8% of adult ESRD. Approximately 25% of patients at 50 years of age and 50% of patients at 75 years of age will manifest ESRD. Cystic disease may also affect the liver. Also, there is an association with intracranial and aortic aneurysms. Tuberous sclerosis and von Hippel-Lindau disease may also present as cystic renal disease.
7. **Obesity** is associated with glomerular hyperfiltration, proteinuria, focal segmental glomerulosclerosis and other glomerulopathies. Additionally, obesity places patients at increased risk for hypertension, diabetes, activation of the renin–angiotensin–aldosterone system, and development of CKD. Perioperative renal considerations for the obese patient include altered pharmacokinetics, increased intra-abdominal pressures and associated oliguria, and difficulties in assessing volume status.

IV. PHARMACOLOGY AND THE KIDNEY

- A. **Diuretics** are used to increase UOP (Table 4.4), treat hypertension, and manage electrolyte, fluid, and acid–base disturbances. The use of diuretics (e.g., furosemide) has been shown to decrease the duration of oliguria and the need for hemodialysis but has no effect on mortality or recovery from AKI.
- B. **Dopamine and fenoldopam** dilate renal arterioles, increase renal blood flow, and augment natriuresis and the GFR. Low-dose dopamine (0.5 to 3 $\mu\text{g/kg/min}$) has been proposed to prevent and treat AKI, but efficacy has never been demonstrated. Low-dose fenoldopam, a specific dopamine-1 receptor agonist, may preserve renal function without the toxicity of dopamine.
- C. **Anesthetic Effects on the Kidney.** Patients with normal kidney function experience transient postanesthetic alterations in renal function. These alterations may occur despite insignificant changes in blood pressure and cardiac output, suggesting that changes in intrarenal distribution of blood flow are responsible. With brief exposures to anesthesia, the observed changes in renal function are reversible (renal blood flow and GFR return to baseline within a few hours). With extensive surgery and prolonged anesthesia, impaired ability to excrete a water load or concentrate urine may last for several days.
 1. **Indirect effects.** All inhalational agents and many induction agents cause myocardial depression, hypotension, and a mild-to-moderate increase in renal vascular resistance, leading to the decreased renal blood flow and GFR. Compensatory catecholamine secretion causes redistribution of renal cortical blood flow. AVP levels do not change during halothane or morphine anesthesia but increase with the onset of surgical stimulation. Hydration before the induction of anesthesia attenuates the rise in AVP produced by painful stimuli. Spinal and epidural anesthesia produce decreases in renal blood flow, GFR, and UOP.
 2. **Direct effects.** The direct toxicity of fluorinated agents is of concern, because fluoride (F^-) inhibits metabolic processes, affects urine-

TABLE 44
Diuretics

	Primary Site of Action	Primary Effect	Side Effects	Comments
Nonosmotic				
Loop (furosemide, edectin, and bumetanide)	Thick ascending loop of Henle and $\text{Na}^+/\text{K}^+/\text{Cl}^-$ pump	Moderate-to-severe natriuresis and chloruresis	Hypokalemia, alkalosis, and volume contraction	Interferes with both urinary concentration and dilution
Thiazides (chlorothiazide, dyazide, and metolazone)	Distal tubules and Na^+/Cl^- pump	Mild-to-moderate natriuresis	Hyponatremia, hypokalemia, alkalosis, and volume contraction	Interferes with urinary dilution and tends to be ineffective in renal failure and CHF
Carbonic anhydrase inhibitors (acetazolamide)	Proximal tubule and Na^+-H^+ exchange	Mild natriuresis	Hyperchloremia, hypokalemia, and metabolic acidosis	Used primarily for ophthalmology; self-limiting renal effect
Potassium sparing (aldactone, triamterene, and amiloride)	Collecting duct and Na^+-K^+ , Na^+-H^+ exchange	Mild-to-moderate natriuresis	Hyperkalemia	Used in conjunction with K^+ losing diuretics or in hyperaldosterone states
Osmotic				
Mannitol	Proximal tubule, descending loop of Henle and collecting duct	Moderate-to-severe diuresis	Early vasodilation and volume expansion Late hyperosmolality and volume contraction	Draws intracellular fluid into intravascular space

CHF, congestive heart failure.

concentrating ability, and can cause proximal tubular swelling and necrosis. The magnitude of F^- elevation depends on the concentration and duration of the anesthetic.

- a. **Isoflurane** and **desflurane** are not associated with significant release of F^- .
- b. **Sevoflurane** is also metabolized to F^- . Strong bases that accumulate in the CO_2 absorbent at low gas flows can degrade sevoflurane to a nephrotoxic by-product. Nephrotoxicity has been observed in rats. The Food and Drug Administration warns against using low inspired gas flows with sevoflurane. Some have warned against use in patients with preexisting renal disease.

V. PHARMACOLOGY AND RENAL FAILURE

Many common anesthetic drugs may be affected by renal dysfunction due to changes in compartment volumes, electrolytes, pH (acidemia resulting in a higher percentage of nonionized drug), decreased serum protein concentration resulting in increased bioavailability of protein-bound drugs, and impaired biotransformation and rates of excretion (Table 4.5). Loading doses do not need to be altered significantly in CKD as the duration of action of drugs administered by bolus is determined by redistribution, not elimination. With repeated dosing or long-term infusion, the duration of action is dependent on elimination, and maintenance doses of drugs with significant renal excretion should be reduced.

TABLE
4.5

Pharmacologic Considerations for Perioperative Drugs Used in Patients with Chronic Renal Insufficiency

Drug Class	Pharmacokinetics	Considerations
Volatile anesthetics	Pulmonary metabolism.	Sevoflurane produces compound A, a potentially nephrotoxic metabolite.
Lipid Soluble		
Barbiturates	Free fraction of induction dose is almost doubled in patients with CKD.	Exaggerated hypotension and other clinical effects in CKD. Need to reduce induction dose.
Benzodiazepines	Increased free fraction in CKD.	Potentiates clinical effects in CKD. Active metabolites accumulate with repeated dosing.
Propofol	Rapid, extensive hepatic metabolism. Pharmacokinetics unchanged in CKD.	CKD does not alter clinical effects.
Etomidate	Increased free fraction in CKD.	CKD does not alter clinical effects.
Ketamine	Redistribution and hepatic metabolism largely responsible for termination of anesthetic effects. Minimal change in free fraction in CKD.	CKD does not alter clinical effects.

TABLE 45 Pharmacologic Considerations for Perioperative Drugs Used in Patients with Chronic Renal Insufficiency (<i>continued</i>)		
Drug Class	Pharmacokinetics	Considerations
Opioids	Metabolized in liver.	May have increased and prolonged effect in CKD. Active metabolites may prolong action with chronic administration: Morphine-6-glucuronide (morphine) has potent analgesic and sedative effects. Normeperidine (meperidine) has neurotoxic effects. Hydromorphone-3-glucuronide (hydromorphone) can cause cognitive dysfunction and myoclonus. Fentanyl has no active metabolite.
Ionized Drugs		
Muscle relaxants	Standard dose of succinylcholine increases serum K ⁺ by 0.5–0.8 mEq/L in CKD. Many nonpolarizing NMBs result in prolonged effects due to reliance on renal excretion.	Succinylcholine is not contraindicated in CKD if serum K ⁺ is not elevated. Cisatracurium, mivacurium, and rocuronium are preferable in CKD.
Cholinesterase inhibitors	Decreased elimination in CKD, and half-life is prolonged.	Half-life prolongation is similar or greater than the duration of blockade from long-acting NMB so recurarization is rarely seen.
Digoxin	Excreted in urine.	Increased risk of toxicity in CKD.
Vasoactive Drugs		
Catecholamines		Catecholamines with α -adrenergic effects constrict renal vasculature and may reduce renal blood flow.
Sodium nitroprusside	Metabolized by the kidney and excreted as thiocyanate.	Toxicity from thiocyanate accumulation is more likely in CKD.
Antibiotics		
Penicillin, cephalosporins, aminoglycosides, and vancomycin	Predominately dependent on renal elimination.	Loading dose is unchanged, but maintenance doses need adjustment.

A. Lipid-soluble drugs generally are poorly ionized and must undergo metabolism by the liver to water-soluble forms before elimination by the kidney. With few exceptions, the metabolites have little biologic activity.

1. Benzodiazepines and butyrophenones are metabolized in the liver to both active and inactive compounds, which are then eliminated by the kidney. Benzodiazepines are 90% to 95% protein bound. Great care

must be taken in using diazepam because of its long half-life and its active metabolites. Accumulation of benzodiazepines and their metabolites may occur in severe renal failure. Benzodiazepines are not appreciably removed by dialysis.

2. **Barbiturates, etomidate, and propofol** are highly protein bound, and in hypoalbuminemic patients, a much greater proportion will be available to reach the receptor sites. Acidosis and changes in the blood-brain barrier will further reduce induction requirements. Lower initial doses are recommended in renal failure.
3. **Opioids** are metabolized in the liver but may have a more intense and prolonged effect in patients with renal failure, particularly in hypoalbuminemic patients in whom protein binding will be reduced. Active metabolites of morphine and meperidine may prolong their actions, and accumulation of normeperidine may cause seizures. The pharmacokinetics of fentanyl, sufentanil, alfentanil, and remifentanyl are unchanged in renal failure.
- B. **Ionized Drugs.** Drugs that are highly ionized at physiologic pH tend to be eliminated unchanged by the kidney, and their duration of action may be prolonged by renal dysfunction.
 1. **Muscle relaxants.** Neuromuscular blocking drugs that have a more predictable duration and may be preferable for patients with renal dysfunction include mivacurium, cisatracurium, and rocuronium.
 2. **Cholinesterase inhibitors.** With impaired renal function, elimination of the reversal drugs is decreased and their half-lives are prolonged. Prolongation is similar or greater than the duration of blockade from pancuronium or *d*-tubocurarine, so the return of muscle relaxation after adequate reversal (recurarization) is rarely seen.
 3. **Digoxin** is excreted in the urine, and patients with renal failure are at increased risk of digitalis toxicity.
- C. **Vasoactive agents have certain properties that merit concern in the patient with renal disease.**
 1. **Catecholamines** with α -adrenergic effects (norepinephrine, epinephrine, phenylephrine, and ephedrine) constrict the renal vasculature and may reduce renal blood flow.
 2. **Isoproterenol** also reduces renal blood flow but to a lesser extent.
 3. **Sodium nitroprusside** contains cyanide and is metabolized by the kidney and excreted as thiocyanate. Toxicity, primarily neurologic, from excessive accumulation of thiocyanate is more likely in renal failure patients.

VI. ANESTHETIC MANAGEMENT

- A. **Preoperative Assessment.** The etiology of renal disease should be elucidated (e.g., diabetes mellitus, glomerulonephritis, and polycystic kidney disease). Elective surgery should be postponed, therefore pending resolution of acute disease processes. The degree of residual renal function is best estimated by creatinine clearance (see section VI.A.3.e) and is the most important consideration for anesthetic management. A thorough, systems-based history and physical should be performed (see Chapter 1).
 1. **History**
 - a. **Signs and symptoms** of polyuria, polydipsia, dysuria, edema, and dyspnea should be sought.
 - b. **Relevant medications** should be detailed: diuretics, antihypertensives, potassium supplements, digitalis, and nephrotoxic agents (NSAIDs, aminoglycosides, exposure to heavy metals, and recent radiographic dye).

c. **Schedule of hemodialysis** should be noted and coordinated with elective procedures.

2. Physical examination

a. Patients should be thoroughly examined for the stigmata of renal failure as described in section III.B.3.

b. **Arteriovenous fistula** should be evaluated for patency (by the presence of a thrill or bruit). Intravenous access and blood pressure determinations should be performed on the opposite limb.

3. Laboratory studies

a. **Urinalysis** provides a qualitative assessment of general renal function.

1. Findings suggestive of renal disease include abnormal pH, proteinuria, pyuria, hematuria, and casts.

2. The kidney's ability to concentrate urine is often lost before other changes become apparent. A specific gravity of 1.018 or greater after an overnight fast suggests that concentrating ability is intact. However, radiographic dye and osmotic agents will elevate specific gravity and invalidate this test.

b. **Urine electrolytes**, osmolality, and urine creatinine can help determine volume status and concentrating ability and are used to help differentiate between prerenal and intrarenal diseases (see Table 4.1).

c. **Blood urea nitrogen** is an insensitive measure of GFR, because it is influenced by volume status, cardiac output, diet, and body habitus. The ratio of blood urea nitrogen to creatinine is normally 10–20:1; disproportionate elevation of the blood urea nitrogen may reflect hypovolemia, low cardiac output, gastrointestinal bleeding, or steroid use.

d. **Serum creatinine** normally is 0.6 to 1.2 mg/dL but is affected by the patient's skeletal muscle mass and activity level. Creatinine concentration is inversely proportional to GFR so that a doubling of the creatinine generally corresponds to a 50% reduction in GFR.

e. **Creatinine clearance** is used to estimate GFR and provides the best estimate of renal reserve. It is normally 80 to 120 mL/min. A gross estimate of creatinine clearance can be calculated with the following equation:

$$\{[140 - \text{age (years)}] \times \text{weight (kg)}\} / [72 \times \text{serum creatinine (mg/dL)}]$$

f. Multiply by 0.85 for women. In obese individuals, ideal body weight should be used to estimate creatinine clearance. This formula is invalid in the presence of gross renal insufficiency or changing renal function. Medications such as trimethoprim, H_2 receptor antagonists, and salicylates block the secretion of creatinine and may elevate serum creatinine and decrease creatinine clearance.

g. Serum Na^+ , K^+ , Cl^- , and HCO_3^- concentrations usually will be normal until renal failure is advanced. Careful consideration of the risk and benefit of proceeding with elective surgery should be made if $[Na^+]$ is less than 131 or greater than 150 mEq/L or $[K^+]$ is less than 2.5 or greater than 5.9 mEq/L, because these abnormalities may exacerbate arrhythmias and compromise cardiac function.

h. Serum Ca^{2+} , PO_4^- , and Mg^{2+} concentrations are altered.

i. **Hematologic studies** should assess anemia and coagulation abnormalities.

j. **ECG** may reveal myocardial ischemia or infarction, pericarditis, and the effects of electrolyte abnormalities (see section II.C).

- k. **Chest radiographs** may reveal evidence of fluid overload, pericardial effusion, infection, uremic pneumonitis, or cardiomegaly.
- 4. **Risk assessment.** Risk factors for postoperative renal dysfunction are as follows:
 - a. **Preexisting renal insufficiency**
 - b. **Diabetes mellitus**, Types 1 and 2 (see section III.C.4)
 - c. **Age greater than 65 years** due to an age-related decline in renal reserve and GFR.
 - d. **Congestive heart failure**
 - e. **High-risk surgery** such as renal artery surgery, thoracic and abdominal aortic surgery, and prolonged (>3 hours) cardiopulmonary bypass.
 - f. **Recent exposure to toxins**
 - 1. **Contrast media** cause a decrease in O_2 supply, by causing intrarenal vasoconstriction and a decreased medullary blood supply, and an increase in O_2 demand. The osmotic load increases work to the medullary nephrons
 - 2. Bile pigments
 - 3. Endotoxemia
 - 4. Aminoglycoside antibiotics
 - 5. NSAID
 - g. **Prolonged renal hypoperfusion** resulting from shock, sepsis, nephritic syndrome, and cirrhosis.
- 5. **Optimization**
 - a. Patients on hemodialysis should be dialyzed before surgery, allowing time between dialysis and surgery to permit equilibration of fluids and electrolytes. Blood samples taken immediately after hemodialysis may be inaccurate due to redistribution of fluid and electrolytes. Equilibration may take up to 6 hours.
 - b. If the patient is on CRRT, the decision to continue intraoperatively must be based on the underlying reason for the CRRT, the duration of the procedure, and the type of procedure. Most patients will be able to tolerate discontinuation of CRRT before surgery and reinstitution afterward. However, certain patients may not be able to tolerate even a short period off CRRT, usually because of increased K^+ or acidosis, and one may need to decide whether the surgery can be postponed or to arrange for CRRT in the operating room or even during transport to the operating room. Major surgical procedures or prolonged surgical procedures may also dictate the need for intraoperative CRRT.
 - c. It may be prudent to postpone major elective vascular surgery for a few days after contrast media exposure. In addition, pretreatment with ***N*-acetylcysteine (NAC)** and **sodium bicarbonate infusion (SBI)** before radiographic contrast administration may prevent contrast-induced nephropathy.
 - 1. **NAC** 20% (200 mg/mL) 1,200 mg is given orally every 12 hours, on the day before and on the day of contrast administration, for a total of 2 days. There is conflicting data regarding the effectiveness of NAC in preventing contrast-induced nephropathy.
 - 2. **SBI** of 150 mEq/L of sodium bicarbonate (three ampules of 50 mEq sodium bicarbonate in 1 L of D5W or free water) is administered at 3 mL/kg/h for 1 hour before contrast administration and followed by an infusion of 1 mL/kg/h for 6 hours after the procedure.

B. Intraoperative Management. Either general or regional anesthesia with standard monitoring is acceptable. When regional anesthesia is considered, coexisting neuropathies should be determined (and documented) and the coagulation profile checked for coagulopathies.

1. **Premedication** should be administered carefully because renal failure patients may have increased sensitivity to central nervous system depressants especially if significant uremia is present (see section V.A.1).
2. The dose of **induction agents** may need to be reduced and their rate of administration slowed down to avoid hypotension (see section V.A.2). Serum potassium should be checked before administration of succinylcholine.
3. Most anesthetics cause peripheral vasodilation and myocardial depression with the need for vasoconstrictors or fluid replacement to compensate. Angiotensin II increases efferent arteriolar vasoconstriction to maintain glomerular filtration pressure. However, in patients taking ACE-I or angiotensin receptor blocker, this compensatory mechanism may be decreased, which could cause a decrease in renal perfusion pressure and urine production.
 - a. **Narcotics** increase ADH release, which may further reduce UOP (see section V.A.3).
 - b. Halogenated **volatile anesthetics** may have direct renal toxicity (see section IV.C.2).
4. Surgical stimulation results in an increase in circulating catecholamine, catabolic hormones, and cytokines that increase ADH. Stimulation increases aldosterone as well as glucocorticoids, which result in sodium/water retention and potassium loss.
5. **Positioning** should be done carefully because these patients are prone to fractures secondary to renal osteodystrophy.
6. **Fluid replacement** should take into account maintenance fluid requirements, evaporative/insensible losses (e.g., open abdominal procedures with losses up to 10 mL/kg/h), extravasation/third-space losses of fluids, and intravascular/blood loss.
 - a. Fluid replacement should proceed cautiously with isotonic crystalloids. Potassium-containing fluids should be avoided in anuric patients.
 - b. Large volumes of 0.9% sodium chloride administration may result in a hyperchloremic metabolic acidosis. Limited data suggest that lactated Ringer solution is associated with less metabolic acidosis and hyperkalemia, especially in patients undergoing renal transplant surgery.
 - c. For more extensive procedures, a central venous pressure or pulmonary artery catheter may help guide fluid management (see Chapter 10).
7. CKD gives rise to a variety of hematologic disturbances, including anemia, leukocyte dysfunction, and coagulopathy. Accordingly, these patients are at an increased risk for intraoperative bleeding. Interventions to reduce bleeding include the following:
 - a. Recombinant erythropoietin corrects anemia, normalizes starting hemoglobin, and may restore platelet function.
 - b. DDAVP normalizes bleeding time and improves platelet function by stimulating release of von Willebrand-Factor VIII complex from the endothelium into the plasma where it binds and activates platelets. Effects are seen 1 to 2 hours postinfusion and last approximately 6 to 12 hours.

- c. Cryoprecipitate contains von Willebrand-Factor VIII complex, which corrects the prolonged bleeding time in about 50% of cases. However, there is a risk of bloodborne infection.
 - d. Conjugated estrogens may shorten the bleeding times and have a longer duration of action than DDAVP.
 - e. Aggressive dialysis regimen.
 - f. Heparin-free or low-dose heparin hemodialysis.
8. **Renal transplantation** is performed for patients with ESRD. Recipients generally have hypertension and/or diabetes mellitus, are at increased risk for cardiac disease, and may have disturbances in electrolytes, acid-base balance, platelet function, and volume status. Specific considerations include the following:
- a. IV access may be limited, and placement in extremities with fistulas or shunts should be avoided. The benefits of additional invasive monitors (central venous or arterial lines) should be weighed against the risks of catheter-related infections in functionally immunosuppressed patients.
 - b. Patients may have delayed gastric emptying from diabetes, uremic neuropathy, and preoperative opioids, so a rapid sequence induction may be indicated.
 - c. If a rapid sequence induction is not indicated, benzylisoquinolinium muscle relaxants are preferable given their metabolism independent of renal function. However, benzylisoquinolinium metabolism is pH dependent, and acidosis in ESRD may prolong their effects.
 - d. Graft function depends on adequate intravascular volume before and after vascular anastomosis to maintain perfusion to the transplanted kidney. Mannitol, crystalloid, and albumin are useful volume expanders. If pharmacologic support is necessary, inotropes may be preferable to α -agonists, but data are limited.
 - e. Most patients receive immunosuppressants to prevent graft rejection, including induction therapy with antithymocyte globulin that can induce an anaphylactic reaction.

C. Postoperative Management

- 1. Postoperative fluid replacement should take into account effusions and drainage tube losses and mobilization of third-space fluid back into the vascular compartment.
 - a. **Replacement fluid** should consist of isotonic fluid and dextrose until the patient is able to take adequate fluid orally.
- 2. **Hypertension** is a common postoperative problem and is aggravated by fluid overload. For those not on dialysis, diuretics and short-acting antihypertensives are effective. For those on dialysis, postoperative dialysis may be required.

Suggested Readings

- Abuelo, JG. Normotensive ischemic acute renal failure. *N Engl J Med* 2007;357:797–805.
- Colson P, Ryckwaert F, Coriat P. Renin angiotensin system antagonists and anesthesia. *Anesth Analg* 1999;89:1143–1155.
- Craig RG, Hunter JM. Recent developments in the perioperative management of adult patients with chronic kidney disease. *Br J Anaesth* 2008;101:296–310.
- Merten GJ, Burgess P, Gray LV. Prevention of contrast induced nephropathy with sodium bicarbonate. *JAMA* 2004;291:2328–2334.
- Petroni KC, Cohen NH. Continuous renal replacement therapy: anesthetic implications. *Anesth Analg* 2002;94:1288–1297.

- Sear JW. Kidney dysfunction in the postoperative period. *Br J Anaesth* 2005;95:20–32.
- Schmid S, Jungwirth B. Anaesthesia for renal transplant surgery: an update. *Eur J Anaesthesiol* 2013;29:552–558.
- Sladen RN. Renal physiology. In: Miller R, ed. *Anesthesiology*, 7th ed. New York: Churchill Livingstone; 2010:441–476.
- Suneja M, Kumar AB. Obesity and perioperative acute kidney injury: a focused review. *J Crit Care* 2014;29:694e1–694e6.
- Thakar CV. Perioperative acute kidney injury. *Adv Chronic Kidney Dis* 2013;20:67–75.
- Wagener G, Brentjens TE. Anesthetic concerns in patients presenting with renal failure. *Anesthesiol Clin* 2010;28:39–54.
- Weldon BC, Monk TG. The patient at risk for acute renal failure. *Anesthesiol Clin North Am* 2000;18(4):705–737.

Specific Considerations with Liver Disease

Matthew C. Gertsch and Wilton C. Levine

I. HEPATIC ANATOMY

A. Liver Structure

1. The anatomic unit of the liver is **lobule**. The lobule is composed of hexagonal plates of hepatocytes and portal triads (terminal portal vein, hepatic artery, and bile duct branch) surrounding a central hepatic vein.
2. Hepatocytes are classified by their position in relation to their portal triad. Those closest to the triad are labeled **Zone 1 cells (periportal)**. These cells receive the most oxygen and nutrients and are responsible for most nitrogen metabolism, oxidation, and gluconeogenesis. **Zone 2** is a transitional area. **Zone 3 hepatocytes (pericentral)** are the farthest from the triad and are at the greatest risk for ischemic injury.
3. **Hepatic Blood Supply.** The liver composes only 2% of the total body mass, but it receives 20% to 25% of the cardiac output.

1. The **hepatic artery** supplies 25% of the total liver blood flow and 50% of the liver's oxygen requirement.
2. The **portal vein** drains the stomach, spleen, pancreas, and intestine. It supplies 75% of the hepatic blood flow and 50% of hepatic oxygen.
3. **Total hepatic blood flow** depends greatly on venous return from the pre-portal organs. Flow in the hepatic artery is regulated by sympathetic tone and local adenosine concentration and is inversely related to portal vein flow (PVF). A reduction in PVF will lead to an increased adenosine concentration in the liver, which causes local arteriole dilation and an increase in hepatic artery flow. Total hepatic blood flow may be reduced in diseases causing increased hepatic vascular resistance (e.g., cirrhosis, infiltrative disease as in metastatic liver disease, and Budd-Chiari syndrome).

II. HEPATIC FUNCTION

A. Synthesis and Storage

1. **Proteins.** The normal adult liver produces 12 to 15 g of protein per day including the following:
 - a. **Albumin** is manufactured exclusively in the liver and has a half-life of approximately 20 days. It comprises 50% of all circulating plasma proteins and is the most important drug-binding protein, especially for organic acids such as penicillins and barbiturates. Albumin contributes to oncotic pressure and also serves as a carrier protein for bilirubin and hormones.
 - b. **α_1 -Acid glycoprotein** is an "acute phase reactant" and is responsible for binding basic drugs such as amide local anesthetics, propranolol, and opioids.
 - c. **Pseudocholinesterase** is responsible for the degradation of succinylcholine, mivacurium, and ester-type local anesthetics. In the presence of severely depressed hepatocellular function or a

genetically mediated enzyme deficiency, decreased plasma levels may cause profound clinical effects.

- d. All proteinaceous **clotting factors** are produced in the liver with the exception of factor VIII, which is produced in the vascular endothelium. Synthesis of factors II (prothrombin), VII, IX, and X as well as proteins C, S, and Z are vitamin K dependent; deficiency of vitamin K or disturbances of liver function may lead to deficiencies of clotting factors and excess bleeding. Factor VII has the shortest half-life (4 to 6 hours) and therefore declines at nearly the same rate as protein C (9 hours). Because factor VII is located in the extrinsic pathway, which is assessed by the prothrombin time (PT), this early decline in the factor VII activity prolongs the PT even though other pathways have not yet been affected. Factors II, IX, and X have half-lives of approximately 60, 24, and 36 hours, respectively. Consequently, it takes 4 to 6 days before their activities are at a minimum level, and an antithrombotic effect is achieved that correlates with the INR.
 2. **Carbohydrates.** The liver is actively involved in the homeostatic regulation of plasma glucose levels (**glycogen synthesis** and **gluconeogenesis**). The normal liver can store enough glycogen to provide glucose during a fast of 12 to 24 hours. After that time, glucose is derived by gluconeogenesis from amino acids, glycerol, and lactate.
 3. **Lipids.** Most of the body's lipoproteins, as well as cholesterol and phospholipids, are formed in the liver.
 4. **Heme and bile.**
 - a. The liver is the primary erythropoietic organ of the fetus and continues to be a major site of hematopoiesis until approximately 2 months of age. In healthy adults, the liver is responsible for 20% of heme production. Abnormalities in **heme synthesis** can result in porphyria.
 - b. The liver forms approximately 800 mL of bile per day. **Bile** salts are detergents that aid in absorbing, transporting, and excreting lipids. Bile also carries metabolic waste products and drug metabolites to the intestine from the liver. As an emulsifier, bile facilitates fat absorption by the small intestine. Failure to produce or release bile causes jaundice and an inability to absorb fat and fat-soluble vitamins (A, D, E, and K) and can result in steatorrhea, vitamin deficiencies, and coagulopathy.
- B. Degradation**
1. **Proteins.** The liver is the major site of protein degradation where amino acids are broken down through a process that generates urea for the elimination of ammonia. Patients with liver disease may lack the ability to form urea, resulting in rapidly rising plasma ammonia levels and hepatic encephalopathy.
 2. **Steroid hormones.** Cholesterol is degraded principally by the liver, and its by-products serve as a substrate for the production of bile salts, steroid hormones, and cell membranes. The liver also serves as the major site of steroid hormone degradation, and **hepatic failure results in steroid excess**. Elevations of serum aldosterone and cortisol result in increased resorption of sodium and water, and loss of potassium in the urine, contributing to the edema, ascites, and electrolyte abnormalities frequently seen with liver disease. Decreased metabolism of estrogens and impaired conversion to androgens causes other clinical stigmata of liver disease including spider angiomas, gynecomastia, palmar erythema, and testicular atrophy.

3. **Heme and bile.** Bilirubin that is bound to albumin is delivered to hepatocytes where it then undergoes conjugation with glucuronic acid, which makes it water soluble. These products are excreted within the bile and are eliminated via the feces or urine.

C. Drug Metabolism

1. The liver has a dual blood supply, receiving blood from the hepatic artery and the portal veins. The hepatic extraction ratio (HER) is a measure of the efficiency of the liver in removing drugs from hepatic inflow. It is defined as the fraction of a drug concentration flowing into the liver that is removed through hepatic elimination and metabolism. High-extraction drugs are absorbed from the gut and delivered to the liver, where they may be metabolized before reaching the systemic circulation (first-pass metabolism). Drugs with a high extraction ratio and significant first-pass metabolism have low oral bioavailability.
2. **Hepatic clearance** = $HER \times \text{hepatic blood flow rate}$. Some drugs are extensively metabolized by the liver and have an HER of close to 1.0 (propofol). In these cases, hepatic metabolism depends predominantly on hepatic blood flow, and moderate changes in hepatic function have little effect on clearance. Other drugs have an HER of less than 1.0, and clearance depends on both hepatic function and changes in hepatic blood flow.
3. **Protein binding.** The degree of protein binding depends on the specific drug's affinity for protein binding and the protein concentration. Decreased concentrations of plasma proteins, as often seen in liver disease, will result in a greater proportion of unbound drug. Only free, unbound drug is pharmacologically active and is available for conversion to a less active form. A decrease in plasma proteins may therefore affect the potency and/or elimination of a drug.
4. **Volume of distribution** is often increased in patients with liver disease, and **portal-systemic shunting** permits orally administered drugs to bypass the liver, reducing the first-pass effect. Both can alter drug effects and metabolism.
5. **Enzyme induction/cytochrome P450** enzymes are produced in the liver and are responsible for much drug metabolism. Certain drugs such as barbiturates, ethanol, and phenytoin induce cytochrome P450 enzymes. Induction of cytochrome P450 increases tolerance to a drug's effect and tolerance to other drugs that are also metabolized by the cytochrome P-450 system.
6. Two steps are involved in **hepatic drug elimination**:
 - a. **Phase I** reactions change a compound's structure via oxidation, reduction, or hydrolysis (primarily via cytochrome P450 enzymes). The products of this phase may be metabolically active. Drugs that have a high affinity for the P450 complex (e.g., ciprofloxacin) may decrease the metabolism of concurrently administered drugs.
 - b. **Phase II** reactions may or may not follow Phase I reactions and are enzymatically enhanced conjugations with glucuronide, sulfate, taurine, or glycine. These conjugations increase the water solubility of the metabolite for excretion via urine.

III. METABOLISM OF ANESTHETICS

A. Intravenous Anesthetics

1. Induction agents

- a. **Propofol** is metabolized by the liver ($HER \sim 1$) to water-soluble compounds that are excreted by the kidneys. Extrahepatic metabolism of propofol also contributes to total propofol clearance.

- b. **Barbiturates** have a duration of action that is determined by redistribution and hepatic metabolism and may have prolonged effects in patients with liver disease. Hypoalbuminemia, as seen in patients with altered liver function, may reduce protein binding and increases the free active fraction of these drugs. Therefore, barbiturates must be titrated carefully in patients with liver disease.
 - c. **Ketamine** is metabolized by the hepatic microsomal enzyme system to norketamine, which has approximately 30% of the activity of the parent drug. Ketamine has an HER of approximately 1.
 - d. **Etomidate** is metabolized by the liver through ester hydrolysis to inactive metabolites. Similar to ketamine, etomidate has a high HER, so clearance is affected by conditions that reduce hepatic blood flow. Recovery from an initial induction dose is primarily due to rapid redistribution.
2. **Benzodiazepines and opioids** are metabolized primarily by the liver and have significantly increased half-lives in patients with liver disease. Additionally, they have increased potency in cases of hypoalbuminemia as these drugs, which are usually protein bound, are now free in the plasma resulting in higher drug levels. This issue may confound the clinical picture of hepatic encephalopathy and should be titrated carefully.
3. **Neuromuscular blocking agents.** Patients with liver disease often demonstrate resistance to nondepolarizing neuromuscular blockers, probably because of increased volume of distribution or increased neuromuscular receptors. However, a slower elimination time may decrease the requirement for maintenance dosing.
- a. **Pancuronium** is excreted primarily in the urine but 10% to 20% is metabolized in the liver. The 3-hydroxymetabolite has neuromuscular blocker activity. Approximately 30% of pancuronium is eliminated through hepatobiliary mechanisms, and its effect may be prolonged in patients with biliary obstruction or cirrhosis.
 - b. **Intermediate-acting neuromuscular blocking drugs, vecuronium and rocuronium**, are highly dependent on hepatobiliary excretion and metabolism (both are excreted, 50% unchanged, in the bile). This translates to a decreased clearance and a prolonged effect in patients with liver disease. Vecuronium undergoes hepatic metabolism to several compounds, one of which is 3-desacetylvecuronium that 50% of vecuronium's neuromuscular blocker activity. **Cisatracurium** and atracurium are degraded via Hofmann elimination and are unaffected by liver disease.
 - c. Succinylcholine and mivacurium (not available in the United States) are completely metabolized in the plasma by pseudocholinesterase. Cholinesterase production may be depressed in severe liver disease, and its duration may be prolonged in patients with hepatic dysfunction.

IV. LIVER DISEASE

A. **Liver disease** is classified by time course and severity.

1. **Parenchymal**

- a. **Acute hepatocellular injury** has many etiologies, including viral infection (hepatitis A, B, C, D, and E; Epstein-Barr virus; cytomegalovirus; herpes simplex virus; ECHO virus; and coxsackievirus), drugs, chemicals and poisons (including alcohol, halothane, phenytoin, propylthiouracil, isoniazid, tetracycline, and acetaminophen), and

inborn errors of metabolism (e.g., Wilson disease and α_1 -antitrypsin deficiency).

- b. **Chronic parenchymal disease** may be associated with varying degrees of functional impairment. **Cirrhosis** may result from many insults, including chronic active hepatitis, alcoholism, hemochromatosis, primary biliary cirrhosis, and congenital disorders. End-stage hepatic fibrosis causes significant resistance to portal blood flow, leading to portal hypertension and esophageal varices. Further complications from the combination of portal hypertension and decreased hepatic function include ascites, coagulopathy, gastrointestinal bleeding, and encephalopathy.

- 2. **Cholestasis** occurs most frequently in cholelithiasis and acute or chronic cholecystitis. Primary biliary cirrhosis and primary sclerosing cholangitis also begin as cholestatic diseases, ultimately leading to parenchymal damage and liver failure. **Hyperbilirubinemia** is an important marker for hepatobiliary disease. **Unconjugated hyperbilirubinemia** is due to excess bilirubin production (e.g., massive transfusion, absorption of large hematomas, or hemolysis) or impaired uptake of unconjugated bilirubin by the hepatocyte (e.g., Gilbert syndrome). **Conjugated hyperbilirubinemia** generally occurs with hepatocellular disease (e.g., alcoholic or viral hepatitis and cirrhosis), disease of the small bile ducts (e.g., primary biliary cirrhosis and Dubin-Johnson syndrome), or obstruction of the extrahepatic bile ducts (e.g., pancreatic carcinoma, cholangiocarcinoma, and gallstones).

B. Manifestations of Liver Disease

- 1. **Central nervous system.** Hepatic dysfunction can lead to **encephalopathy**. Although the exact pathogenesis is unclear, impaired neurotransmission, presence of intrinsic γ -aminobutyric acid-ergic substances, and altered cerebral metabolism may be involved in its pathogenesis. **Ammonia levels** are often elevated in encephalopathic patients but do not correlate with the severity or outcome of encephalopathy. Signs may vary from sleep disturbances to the presence of asterix or coma. Patients with severe acute liver failure often present with a rapidly progressive encephalopathy complicated by **cerebral edema**. Elevated intracranial pressure must be aggressively managed to prevent cerebral ischemia. Extreme hyponatremia or its overly aggressive treatment may lead to fatal **central pontine myelinolysis**. Changes in mental status and increased sensitivity to sedatives mandate caution in dosing premedications.

2. Cardiovascular system

- a. Patients with advanced liver disease exhibit a **hyperdynamic circulatory state** with an elevated **cardiac output**, resting tachycardia, and **decreased systemic vascular resistance**. Elevated levels of nitric oxide, glucagon, and prostaglandins are thought to be responsible for the arteriolar vasodilation. **Arteriovenous shunts**, such as spider angiomas in the skin, can be present in almost all vascular beds.
- b. Patients with advanced liver failure also have a reduced effective intravascular volume due to vasodilation and portosystemic shunting. In addition, hypoalbuminemia, increased levels of aldosterone, and inappropriate secretion of antidiuretic hormone all lead to increased **total body fluid volume** that worsen ascites and edema/anasarca.
- c. **Alcoholic cardiomyopathy (ACM)** should always be considered in patients with a history of alcohol abuse. ACM is characterized by

an increase in myocardial mass, dilation of the ventricles, and wall thinning. Changes in ventricular function may depend on the stage of the disease, in that asymptomatic ACM is associated with diastolic dysfunction, whereas systolic dysfunction is a common finding in symptomatic ACM patients characterized by a dilated left ventricle, normal or reduced left ventricular wall thickness, and increased left ventricular mass.

3. Respiratory system

- a. **Airway protection** is a major concern in patients with liver disease. Patients with the typical stigmata of advanced disease have ascites (increased abdominal pressure—causing a reduction in functional residual capacity [FRC]) and encephalopathy (altered mental status) which can affect their ability to protect their airway and should be considered at increased risk for aspiration. Definitive airway protection with rapid sequence induction and intubation is frequently advisable when general anesthesia is required.
- b. **Chronic hypoxemia** results from many causes. Massive ascites and pleural effusions lead to atelectasis and restrictive lung physiology. Diminished hypoxic pulmonary vasoconstriction results in ventilation-perfusion mismatch; intrapulmonary shunting can be significant (10% to 40%). Pulmonary hypertension can coexist with portal hypertension and can produce right heart failure. The hepatopulmonary syndrome is a triad of liver disease, increased alveolar-arterial oxygen gradient, and intrapulmonary vascular dilations. The syndrome of platypnea-orthodeoxia may be seen (postural hypoxemia and dyspnea induced by upright posture) as the presence of a hyperdynamic circulation, and low pulmonary resistance results in the rapid transit of blood through the lungs and potentiates the transit of deoxygenated blood to the systemic circulation. Because of gravity, shifting of blood to the dilated precapillary beds of the lung bases results in an increased hypoxemic dyspnea when the patient is in the upright position.

4. Gastrointestinal system

- a. The increased pressure in the portal system due to increased volume of blood through these vessels or increased resistance (scarring, fibrosis) to portal blood flow results in **portal hypertension**, splenomegaly, and splanchnic venous congestion. This increases collateral circulation, which is manifested as hemorrhoids, esophageal varices, and dilated abdominal wall veins (caput medusae). **Ascites** is due to splanchnic venous congestions coupled with hypoalbuminemia and decreased oncotic pressure. Ascites may increase the risk of abdominal wound dehiscence, abdominal wall herniation, and respiratory compromise. Ascites can be managed with diuretics, with careful attention to electrolytes and renal function. If a large volume of ascites is uncontrolled prior to surgery, paracentesis may be advisable. Replacement of ascites with albumin, colloids, or blood products is advisable to reduce the risk of hepatorenal syndrome (HRS).
- b. **Variceal bleeding** can progress rapidly to hemorrhagic shock. After volume resuscitation, treatment consists of vasopressin, somatostatin, β -adrenergic blockade, sclerotherapy, or endoscopic ligation.

5. Renal system

- a. Intravascular volume depletion may produce **prerenal azotemia**. The blood urea nitrogen level may be deceptively low because of the liver's inability to synthesize urea from ammonia.

- b. **Water and electrolyte balance** is complicated by frequent use of diuretics. Metabolic alkalosis, hypokalemia, and hyponatremia (despite total body sodium overload) are common in patients with hepatic disease. Hyponatremia may lead to seizures and worsening of hepatic encephalopathy; caution should be used when treating hyponatremia as rapid correction may lead to central pontine myelinosis. Correction of hyponatremia is typically done with fluid restriction and discontinuation of diuretics.
 - c. **Hepatorenal syndrome** is characterized by increased renal vascular resistance, oliguria, and renal failure in the presence of hepatic failure. The sequelae include decreased renal blood flow, sodium retention, and increased sensitivity to nonsteroidal anti-inflammatory medications. Normal renal function returns after liver transplantation or if liver failure resolves.
- 6. **Coagulopathy** is caused by several factors.
 - a. **Synthesis of clotting factors** (II, VII, IX, and X) as well as that of endogenous anticoagulants (proteins C, S, and Z) is impaired in liver failure.
 - b. **Cholestasis** causes impaired absorption of fat and fat-soluble vitamins (A, D, E, and K). **Vitamin K**, produced in the intestinal mucosa, is an important cofactor in the synthesis of clotting factors II, VII, IX, and X.
 - c. **Thrombocytopenia** secondary to hypersplenism, alcohol-induced bone marrow failure, and consumption is frequently seen.
 - d. **Preoperative correction of clotting abnormalities** with fresh frozen plasma (FFP) or vitamin K should be performed as necessary. In emergency situations, vitamin K should be avoided due to its prolonged time of onset (approximately 8 hours). In these situations, FFP can be administered, and cryoprecipitate, DDAVP, factor VIIa, and platelets should be considered for refractory situations. Regional anesthesia may not be appropriate in the setting of liver failure or anticipated liver failure. The potential for postoperative coagulopathy should be taken into account before placing an epidural. Invasive monitoring can help evaluate and guide volume status. The importance of adequate venous access for intraoperative infusion of crystalloid, colloid, blood products, and vasoactive drugs should not be underestimated.
- 7. **Nutritional deficiency**, as manifested by the forms of protein–energy malnutrition marasmus and kwashiorkor, can be part of liver disease, especially in alcoholics. Nutritional deficiency is a risk factor for increased morbidity and mortality postoperatively and should be treated with supplementation high in carbohydrate/lipid content and low in amino acid content to prevent worsening of hepatic encephalopathy. Nutritional supplementation is especially important in alcoholics and should include vitamin B₁ supplementation. If surgery is not urgent, nutritional status should be optimized preoperatively.
- 8. **Glycemic control** depends heavily on the liver. **Hypoglycemia** may occur in end-stage hepatic insufficiency, during the anhepatic phase of liver transplantation, or in liver failure that may accompany an episode of severe circulatory shock. Close monitoring of blood glucose levels should be performed frequently, and glucose-containing solutions should be administered as necessary. Severe hepatic insufficiency leads to diminished **glycogen** stores, requiring gluconeogenesis to maintain normoglycemia. **Gluconeogenesis** is also impaired in severe liver disease and alcoholism.

V. SURGICAL RISK IN PATIENTS WITH LIVER DISEASE

A. Mortality

1. Reported mortality rates in patients with cirrhosis undergoing various nontransplant surgical procedures range from **8.3% to 25%** (in comparison with 1.1% for noncirrhotic patients). Wide range of mortality is related to **severity of the disease, type of surgery, patient demographics, and expertise of the surgical, anesthetic, and ICU teams.**

B. Risk Assessment

1. Preoperative risk assessment can help predict survival and may reduce perioperative morbidity and mortality.
2. The **Child-Turcotte-Pugh (CTP)** classification was designed to evaluate the risk of surgical portosystemic shunt procedures and was subsequently found to predict long-term survival in patients with cirrhosis. This risk stratification system includes **ascites, bilirubin level, albumin level, nutritional status, encephalopathy, and PT** (Table 5.1).
3. Other predictors of perioperative risk include **type of surgery**, presence of **sepsis, reoperation**, and elective versus **emergent** surgery. Procedures involving a laparotomy (greater reduction in hepatic arterial blood flow) or other intra-abdominal incisions (open cholecystectomy, gastric surgery, and colectomies), cardiac surgery, or those associated with increased blood loss have particularly high mortality rates.
4. The **model for end-stage liver disease (MELD)** is a prognostic scoring system also originally designed for the purpose of selecting cirrhotic patients for portosystemic shunt procedures but was found to be superior to the CTP score in predicting 3-month survival in patients with cirrhosis. It uses a patient's values for serum bilirubin, serum creatinine, and the INR to predict survival (Table 5.2).

C. Preoperative Assessment

1. Routine screening of liver function with lab tests has not proven to be useful when applied to a general surgical population.
2. A careful **history** and **physical examination** are the best screening tools in the preoperative period. Symptoms of concern include a history of jaundice, pruritus, malaise, and anorexia. Exposure to drugs, alcohol, and other toxins should be considered. Physical examination may reveal stigmata of liver disease such as hepatosplenomegaly, ascites, peripheral edema, spider angiomas, testicular atrophy, caput medusae, hemorrhoids, asterixis, gynecomastia, and temporal wasting.

TABLE 5.1
Modified Child-Pugh Score

Parameter	Points		
	1	2	3
Albumin (g/dL)	>3.5	2.8–3.5	<2.8
Bilirubin (mg/dL) ^a	<2.0	2.0–3.0	>3.0
Ascites	Absent	Slight	Moderate
Encephalopathy	Absent	Grades I and II	Grades III and IV
PT prolongation (s)	<4.0	4.0–6.0	>6.0

Class A, 5 to 6 points; class B, 7 to 9 points; class C, 10 to 15 points.

^a For primary biliary cirrhosis: 1 point for bilirubin <4.0 mg/dL, 2 points for bilirubin 4–10 mg/dL, and 3 points for bilirubin more than 10 mg/dL.

TABLE
52 MELD Score

$$\text{MELD} = 3.78[\text{Ln serum bilirubin (mg/dL)}] + 11.2[\text{Ln INR}] + 9.57[\text{Ln serum creatinine (mg/dL)}] + 6.43$$

In interpreting the MELD score in hospitalized patients, the 3-month mortality is

- 40 or more—100% mortality
- 30–39—83% mortality
- 20–29—76% mortality
- 10–19—27% mortality
- <10—4% mortality

The maximum score given for MELD is 40. All values higher than 40 are given a score of 40. If the patient has been dialyzed twice within the last 7 d, then the value for serum creatinine used should be 4.0. Any value <1 is given a value of 1 (i.e., if bilirubin is 0.8, a value of 1.0 is used).

3. **Laboratory tests** should be considered for the patient in whom liver disease is suspected (bilirubin, transaminases, alkaline phosphatase, albumin, total protein, PT, and hepatitis serologies).
4. **EKG, chest radiograph, and evaluation of the myocardial function** should be considered when indicated based on age, disease severity, and duration.
5. **Duration** and severity of liver disease have general prognostic implications, and **percutaneous liver biopsy** may be indicated to establish a diagnosis before elective surgery.
- D. Every effort should be made to **correct abnormalities before surgery**, including coagulopathies, poorly controlled ascites, volume and electrolyte imbalances, renal dysfunction, encephalopathy, thrombocytopenia, and inadequate nutritional status.

VI. ANESTHESIA IN PATIENTS WITH LIVER DISEASE

- A. Planning the anesthetic must take into account the surgical procedure, type and severity of liver disease, and alterations to hepatic blood flow due to anesthetics. Meticulous attention must be paid to **maintaining adequate hepatic perfusion** and oxygen delivery. Both **general and regional anesthesia** techniques can decrease total hepatic blood flow. Episodes of perioperative hepatic ischemia (due to surgical manipulation or anesthetics) can exacerbate preexisting liver disease. Hypotension, hemorrhage, and vasopressors can compromise hepatic oxygenation delivery, resulting in increased postoperative hepatic dysfunction. Surgical traction and patient positioning can compromise hepatic blood flow. Positive-pressure ventilation and positive end-expiratory pressure may cause deleterious effects in hepatic venous pressure, resulting in decreased cardiac output and total hepatic blood flow. **Hyperventilation** should be avoided because hypocarbia can independently reduce hepatic blood flow.
- B. Caution must be exercised when **regional anesthesia** is considered in a patient with liver disease. Coagulopathy and thrombocytopenia put these patients at a higher risk for epidural bleeding and hematoma formation. In a recent randomized control trial of 367 patients undergoing partial hepatectomy, epidural analgesia was independently associated with increased risk of packed red blood cell transfusion and did not appear to minimize complications or shorten hospital stay. However, in a patient with well-compensated liver disease and a reasonably normal coagulation profile and platelet count, regional anesthesia may be appropriate, but this must be considered on a case-by-case basis.

- C. Sufficient **venous access** is of paramount importance, especially in surgery involving the liver parenchyma. **Large-bore peripheral intravenous cannulas** are inserted before or after the induction of anesthesia for major surgery (often 12 gauge or larger). In patients with insufficient peripheral access, **large-bore central venous catheters** (i.e., 8.5 French single-lumen or 12 French double-lumen catheters) may be inserted. Universal precautions are mandatory given the high risk of infection in this patient population.
- D. Invasive monitoring is also an important component of anesthetic planning. An **arterial catheter** facilitates blood sampling for monitoring serial blood gases, glucose, and electrolytes and is needed for measuring arterial blood pressure. It is considered routine in major surgery for patients with end-stage liver disease. **Central venous catheterization** is indicated for pressure monitoring and rapid drug administration into the central circulation. **Pulmonary artery catheters** may help guide fluid and vasopressor therapy in some patients. Skillful line placement is important in coagulopathic patients. Ultrasonographic visualization of the vein before or during cannulation will reduce the incidence of carotid arterial puncture and the number of needle passes needed to cannulate the jugular vein.
- E. A low threshold for performing a **rapid sequence induction** should exist for these patients given their elevated intra-abdominal pressure and increased risk of aspiration.
- F. Other physiologic variables that should be taken into consideration include urine output, body temperature, blood sugar levels, electrolyte disturbances, and coagulation status.
- G. Proper **postoperative care** and the timing of **extubation** for patients presenting with severe comorbidities should also be considered.
- H. **Surgical considerations for the anesthesiologist during procedures on the liver.** Excessive bleeding and transfusion requirements have been correlated with increased postoperative morbidity. Management must focus on the balance between reducing blood loss while maintaining adequate liver perfusion. Newer surgical techniques for hepatic resection and other procedures on the liver have been developed to decrease blood loss. **Total hepatic vascular exclusion (TVE)**, the **Pringle maneuver (PM)**, and **low central venous pressure (CVP) anesthesia** are three such techniques.
1. TVE consists of clamping the hepatic inflow vessels (portal vein and hepatic artery) to the liver as well as the outflow vessels (inferior vena cava and suprahepatic inferior vena cava). This can have profound deleterious effects on venous return and the hemodynamics of the patient. This also results in a significant amount of warm ischemic time to the liver and may increase postoperative hepatic dysfunction.
 2. The PM consists of intermittent clamping of the hepatic inflow vessels (portal vein and hepatic artery) causing intermittent hepatic ischemia. There can be significant back bleeding through the hepatic veins and vena cava.
 3. **Low CVP anesthesia.** A low CVP (generally referred to as a CVP lower than 5 mmHg) facilitates control of bleeding from hepatic veins and the inferior vena cava during parenchymal dissection. Low CVP anesthesia reduces the pressure gradient that promotes bleeding through inadvertent extrahepatic venous injuries as well as hepatic venous bleeding during parenchymal dissection.

A recent meta-analysis of all randomized controlled trials investigating the effect of low CVP on blood loss and blood transfusion in patients undergoing hepatectomy showed that both rates of blood loss and transfusion are reduced when low CVP anesthesia is performed. The possibility of complications related

to maintaining a low CVP is real, but they occur infrequently. Most studies have found no difference between low CVP groups and control groups, regarding harm to organs as a result of reduced blood inflow; however, routine measurement of renal and liver function is not sensitive enough to detect mild ischemic injury and reperfusion injury.

VII. POSTOPERATIVE LIVER DYSFUNCTION

Postoperative liver dysfunction after surgery and anesthesia is common and can range from mild enzyme elevations to fulminant hepatic failure. There are many etiologies for postoperative hepatic dysfunction.

- A. Surgical causes** include maneuvers that impair hepatic blood flow or obstruct the biliary system (clamped vessels, retraction, or direct injury). Postoperative elevations of hepatocellular enzymes or bilirubin also can be caused by increased bilirubin loads after massive transfusion, resorption of hematoma, or hemolysis. Overt hepatic failure can occur during or after shock of any etiology.
- B. Nonsurgical** causes of hepatic dysfunction include undiagnosed cases of preoperative viral hepatitis, alcoholism, and cholelithiasis. Drug therapy in the perioperative period must also be evaluated as a cause of jaundice.
- C. Halothane hepatitis** is clinically indistinguishable from viral hepatitis. The diagnosis is one of exclusion. The incidence is 1 in 6,000 to 1 in 35,000 following single exposure to halothane and increases to about 1 in 3,000 following multiple exposures. Halothane is not available in the United States, but it is still in many countries.

Suggested Readings

- Badalamenti S, Graziani G, Salerno F, et al. Hepatorenal syndrome. New perspectives in pathogenesis and treatment. *Arch Intern Med* 1993;153:1957–1967.
- Bhangui P, Laurent A, Amathieu R, et al. Assessment of risk for non-hepatic surgery in cirrhotic patients. *J Hepatol* 2012;57:874–884.
- Carton EG, Plevak DJ, Kranner PW, et al. Perioperative care of the liver transplant patient. Part 2. *Anesth Analg* 1994;78:382–399.
- Carton EG, Rettke SR, Plevak DJ, et al. Perioperative care of the liver transplant patient. Part 1. *Anesth Analg* 1994;78:120–133.
- Chen H, Merchant NB, Didolkar MS. Hepatic resection using intermittent vascular inflow occlusion and low central venous pressure anesthesia improves morbidity and mortality. *J Gastrointest Surg* 2000;4:162–167.
- Child CG, Turcotte JG. Surgery and portal hypertension. *Major Probl Clin Surg* 1964;1:1–85.
- Cook RC. Pharmacokinetics and pharmacodynamics of nondepolarizing muscle relaxants. In: Park GR, Kang Y, eds. *Anesthesia and Intensive Care for Patients with Liver Disease*. New York: Butterworth-Heinemann; 1995:79–88.
- Dershwitz M, Hoke JF, Rosow CE, et al. Pharmacokinetics and pharmacodynamics of remifentanyl in volunteer subjects with severe liver disease. *Anesthesiology* 1996;84:812–820.
- Eid EA, Sheta SA, Mansour E. Low central venous pressure anesthesia in major hepatic resection. *Middle East J Anesthesiol* 2005;18(2):367–377.
- Hoteit MA, Ghazale AH, Bain AJ, et al. Model for end-stage liver disease score versus Child score in predicting the outcome of surgical procedures in patients with cirrhosis. *World J Gastroenterol* 2008;14(11):1774–1780.
- Jones RM, Moulton CE, Hardy, KJ. Central venous pressure and its effect on blood loss during liver resection. *Br J Surg* 1995;85:1058–1060.
- Kamath PS. Clinical approach to the patient with abnormal liver test results. *Mayo Clin Proc* 1996;71:1089–1095.
- Kim YK, Chin JH, Kang SJ, et al. Association between central venous pressure and blood loss during hepatic resection in 984 living donors. *Acta Anaesthesiol Scand* 2009;53(5):601–606.

- Li Z, Sun Y, Wu F, et al. Controlled low central venous pressure reduces blood loss and transfusion requirements in hepatectomy. *World J Gastroenterol* 2014;20(1):303–309.
- Melendez JA, Arslan V, Fisher ME, et al. Perioperative outcomes of major hepatic resections under low central venous pressure anesthesia: blood loss, blood transfusion, and the risk of postoperative renal dysfunction. *J Am Coll Surg* 1998;187:620–625.
- Millwala F, Nguyen GC, Thuluvath PJ. Outcomes of patients with cirrhosis undergoing non-hepatic surgery: risk assessment and management. *World J Gastroenterol* 2007;13(30):4056–4063.
- Page A, Rostad B, Staley CA, et al. Epidural analgesia in hepatic resection. *J Am Coll Surg* 2008;206(3):1184–1192.
- Parks DA, et al. Hepatic physiology. In: Miller RD, ed. *Anesthesia*, 5th ed. New York: Churchill Livingstone, 2000:647–662.
- Patel T. Surgery in the patient with liver disease. *Mayo Clin Proc* 1999;74:593–599.
- Picker O, Beck C, Pannen B. Liver protection in the perioperative setting. *Best Pract Res Clin Anaesthesiol* 2008;22(1):209–224.
- Scott VL, Dodson SF, Kang Y. The hepatopulmonary syndrome. *Surg Clin North Am* 1999;79:23–41.
- Villanueva C, Colomo A, Bosch A, et al. Transfusion strategies for acute upper gastrointestinal bleeding. *N Engl J Med* 2013;368:11–21.
- Wiklund RA. Preoperative preparation of patients with advanced liver disease. *Crit Care Med* 2004;32:S106–S115.

Specific Considerations with Endocrine Disease

Becky Y. K. Tsui, Robert A. Peterfreund,
and Stephanie L. Lee

I. DIABETES MELLITUS

- A. **Diabetes mellitus (DM)** is a chronic systemic disease characterized by an absolute or relative lack of insulin. DM is the most common endocrinopathy encountered in the perioperative period.
- B. **Physiology of DM.** Insulin is synthesized in pancreatic β -cells. Glucose, β -adrenergic agonists, arginine, and acetylcholine stimulate insulin secretion; α -adrenergic agonists and somatostatin inhibit insulin secretion. Insulin facilitates glucose and potassium transport across cell membranes, increases glycogen synthesis, and inhibits lipolysis. Peripheral tissues resist the effects of insulin during times of stress (e.g., surgery, infection, and cardiopulmonary bypass). Normally, low-level insulin production continues during fasting periods, preventing catabolism and ketoacidosis.
- C. **Types of DM**
 1. **DM type 1** is caused by autoimmune destruction of β -cells resulting in an absolute insulin deficiency. Patients are generally thin, diagnosed at a younger age, sensitive to small amounts of insulin, and prone to ketoacidosis. Management is with insulin.
 2. **DM type 2** is the diagnosis in 90% of all adult diabetics. Patients have peripheral resistance to insulin and require high insulin levels to maintain euglycemia. They are generally older, obese, ketosis resistant, and prone to hyperosmolar complications. Initial management is usually with diet and exercise alone. Oral hypoglycemic agents, insulin sensitizers, and/or insulin are added as needed. Type 2 diabetics frequently have metabolic syndrome, a combination of obesity, hyperlipidemia, hypertension (HTN), and insulin resistance. With the increasing prevalence of childhood obesity, DM type 2 is now encountered in teenagers.
 3. **Gestational DM.** Between 2% and 5% of pregnancies are complicated by gestational DM. More than 50% of parturients with gestational DM will develop DM type 2 later in life.
 4. **Secondary DM** is due to other causes of absolute or relative insulin insufficiency. Insulin hyposecretion is seen with pancreatic destruction due to cystic fibrosis, pancreatitis, hemochromatosis, cancer, and after pancreatic surgery. Glucose intolerance may result from glucagonoma, pheochromocytoma, thyrotoxicosis, acromegaly, or glucocorticoid excess.
- D. **Terminology.** The terms “juvenile-onset DM,” “adult-onset DM,” “insulin-treated DM,” and “Insulin-requiring DM” should be avoided. These terminologies fail to specify the actual type of DM and its implications.
- E. **Outpatient Therapy for DM**
 1. **Oral hypoglycemic agents** (Table 6.1)
 - a. **Sulfonylureas** increase pancreatic insulin release and may cause hypoglycemia. Glyburide and glimepiride, the two longest acting of

TABLE 6.1 Noninsulin Agents Used to Treat DM

Agent		Onset (Hours)	Duration (Hours)
Sulfonylurea	Tolbutamide ^a	≤0.25	6–12
	Tolazamide ^a	1	10–24
	Chlorpropamide ^a	1	60
	Glipizide (Glucotrol)	1	10–20
	Glipizide XL	1	20–24
	Gliclazide (glibenclamide)	1–2	12–24
	Glyburide (Micronase, Glynase, and Diabeta)	1	18–24
α-Glucosidase inhibitor^b	Glimepiride (Amaryl)	1	24
	Acarbose (Precose)	Immediate	<0.3
Biguanide^b	Miglitol (Glyset)	Immediate	<0.3
	Metformin (Glucophage, Glumetza, Riomet, and Fortamet)	1	8–12
Thiazolidinedione^b	Pioglitazone (Actos)	1	24
	Rosiglitazone (Avandia)	1	24
Meglitinide	Repaglinide (Prandin)	1	3–4
	Nateglinide (Starlix)	1	4
D-Phenylalanine derivative			
GLP-1 receptor agonists^{b,c}	Exenatide (Byetta)	<0.25	6–12
	Exenatide QW (Bydureon) ^d	2–4 wk ^e	
	Liraglutide (Victoza) ^d		24
	Albiglutide QW (Tanzeum) ^d		
	Dulaglutide (Trulicity) ^d		
Amylin analog^b	Lixisenatide (Lyxumia) ^f		
	Pramlintide (Symlin)	<0.25	2–4
DPP-IV inhibitor^{b,g}	Sitagliptin (Januvia)	1	24
	Saxagliptin (Onglyza)	1–2	24
	Linagliptin (Tradjenta) ^d	1.5	
	Alogliptin (Nesina) ^d		
	Vildagliptin (Galvus) ^{d,f}		
Dopamine agonist	Bromocriptine Mesylate (Cycloset and Parlodel)	1	8–12
SGLT2 inhibitor	Canagliflozin (Invokana)	Within 24 (dose dependent)	24
	Empagliflozin (Jardiance)		
	Dapagliflozin (Farxiga)		
	Ipragliflozin (Suglat) ^f		

^a Historical agents that are no longer widely used.

^b When used as the sole agent for treatment, hypoglycemia while fasting (NPO) is unlikely.

^c Glucagon-like peptide 1.

^d Onset of action and/or duration of action are not reported.

^e Steady state achieved by week 7.

^f Currently not FDA approved.

^g Dipeptidyl peptidase IV.

the currently used sulfonylurea agents, can induce hypoglycemia for more than 24 hours after administration. Sulfonylureas increase the effectiveness of thiazide diuretics, barbiturates, and anticoagulants by displacing these drugs from albumin.

- b. **Meglitinides and D-phenylalanine derivatives** act via a nonsulfonylurea receptor pathway to rapidly increase insulin release from the pancreas. These drugs may also cause hypoglycemia.
 - c. **Biguanides** decrease insulin resistance, decrease hepatic glucose production, and inhibit intestinal glucose absorption. They will not produce hypoglycemia when used as single agent therapy for diabetes. Patients with congestive heart failure, shock, or renal or hepatic dysfunction are at risk for biguanide-induced lactic acidosis. In patients without these risk factors, the risk is close to zero. Diarrhea is a common side effect.
 - d. **Thiazolidinediones** decrease hepatic glucose production, enhance insulin's action in the liver and skeletal muscle, and decrease insulin resistance. Side effects include abdominal obesity, fluid retention leading to edema or congestive heart failure, anemia, hepatotoxicity, and increased creatine phosphokinase. Thiazolidinediones will not produce hypoglycemia when used as single agent therapy.
 - e. **α -Glucosidase inhibitors** delay carbohydrate digestion and reduce postprandial hyperglycemia. Side effects include malabsorption, flatulence, and diarrhea. Drugs in this class will not produce hypoglycemia when used as single agent therapy.
 - f. **Dipeptidyl peptidase IV (DPP-IV) inhibitors** increase the level of endogenous glucagon-like peptide 1 (GLP-1), thereby enhancing insulin secretion and decreasing glucagon secretion in a glucose-dependent manner. They are not associated with significant gastrointestinal (GI) side effects or hypoglycemia. There is a potential increased risk of heart failure in susceptible patients.
 - g. **Dopamine agonists** improve glycemic control by resetting circadian activity in hypothalamic neurons. This reduces fasting and postprandial glucose, triglyceride, and free fatty acid levels. Side effects include fatigue, headache, and dizziness. Single agent therapy is not associated with hypoglycemia.
 - h. **SGLT2 inhibitors** reduce renal reabsorption of filtered glucose by inhibiting sodium-glucose cotransporter 2 (SGLT2). SGLT2 is located in the proximal renal tubules and is responsible for more than 90% of renal glucose reabsorption. By inhibiting this cotransporter, SGLT2 inhibitors increase urinary excretion of glucose and reduce plasma glucose in a glucose-dependent manner.
- 2. Injectable agents**
- a. **Insulin** (Table 6.2). Rapid-acting insulins are given just before meals to prevent postprandial hyperglycemia. Short- and intermediate-acting insulins are often given several times a day to provide basal and peaking levels. Long-acting insulins are given once daily to mimic basal insulin secretion. Regular and rapid-acting insulins can also be administered continuously via a pump. The liver and kidney metabolize insulin. As a result, renal insufficiency may produce clinically significant prolongation of insulin action and reduce insulin requirement.
 - b. **Amylin analogs** (Table 6.1) suppress postprandial glucose release from the liver, suppress glucagon secretion, and reduce appetite by delaying gastric emptying. Amylin analogs do not cause hypoglycemia when given alone but may cause hypoglycemia when given concurrently with insulin. The most common side effect is nausea.
 - c. **GLP-1 analogs** (Table 6.1) enhance glucose-stimulated insulin secretion, reduce glucagon levels, slow gastric emptying, and increase insulin biosynthesis. The most common adverse events include

TABLE
62

Subcutaneous (SC) Insulin Preparations Used to Treat DM

Class	Agent	Onset (Hours)	Peak Effect (Hours)	Duration (Hours)
Rapid Acting	Lispro (Humalog)	0.1–0.25	1–2	2–4
	Aspart (NovoLog)	0.1–0.25	1–2	2–4
	Glulisine (Apidra)	0.1–0.25	1–2	2–4
Short Acting	Regular (Humulin R, Novolin R)	0.5–1	2–4	6–10
	NPH	2–4	6–12	12–18
Intermediate Acting				
Long Acting	Glargine (Lantus)	1–3	No peak	20–24
	Detemir (Levemir)	1–3	No peak	20–24

Note:

1. When regular insulin is administered IV, the onset of action is immediate. The duration of action is ~1 h.
 2. Fixed combinations of insulin are used sometimes with potential consequences of having two drugs with different onset and duration profiles mixed together.
- NPH, neutral protamine hagedorn.

nausea, vomiting, and diarrhea. GLP-1 analogs may also increase the risk of heart failure in susceptible patients. Patients receiving both a GLP-1 analog and a sulfonylurea are at increased risk for hypoglycemia.

F. Acute Complications of Diabetes. Diabetic ketoacidosis (DKA) and hyperglycemic hyperosmolar syndrome (HHS, previously known as hyperglycemic, hyperosmolar nonketotic state [HONK]) are the result of insulin deficiency, resistance to insulin during stress (e.g., infection, surgery, myocardial infarction [MI], dehydration, and trauma), or medications.

1. **DKA** occurs primarily in DM type 1. It may be the initial presentation of DM type 1.
 - a. **DKA** is associated with depressed myocardial contractility, decreased vascular tone, anion gap acidosis due to ketones, electrolyte abnormalities, hyperglycemia, and hyperosmolarity. Patients are often profoundly hypovolemic because of the forced diuresis of hyperglycemia, emesis, and reduced oral intake during illness. Total body K^+ is depressed (3 to 10 mEq/kg of body weight), but serum levels are falsely normal or elevated because acidosis shifts K^+ out of cells. Measured Na^+ concentrations are artifactually lowered by 1.6 mEq/L for every 100 mg/dL that the glucose is elevated. Hypophosphatemia and hypomagnesemia from osmotic diuresis are common. Patients may present with nausea, vomiting, abdominal pain, polyuria, polydipsia, weakness, renal failure, shock, deep rhythmic (Kussmaul) breathing with a fruity odor, or mental status changes. Mortality of DKA is less than 5% when identified and treated early.
 - b. **Treatment of DKA** is with volume replacement, insulin, correction of electrolyte abnormalities, identification and treatment of underlying stressors or precipitants (MI, infection, etc.), and supportive care. The following outline pertains to management in the general

medical environment; management of the patient in the perioperative period may need to be more aggressive.

1. Begin the treatment with 15 to 20 mL/kg of intravenous normal saline (NS) in the first hour followed by NS at 5 to 15 mL/kg/h. If the corrected serum sodium is high or normal, $\frac{1}{2}$ NS can be substituted at the same rate. Monitor the hemodynamics and urine output. Consider invasive monitoring.
 2. Initiate potassium repletion once serum potassium levels fall below 5.5 mEq/L and the patient is making urine. For patients presenting with significant hypokalemia (<3.3 mEq/L), begin potassium repletion immediately with 40 mEq of potassium per hour. Delay insulin therapy briefly until potassium replacement has started.
 3. Treat hyperglycemia and insulin deficiency with regular intravenous (IV) insulin. Give a first bolus of 0.1 to 0.15 U/kg IV and then start an infusion at approximately 0.1 U/kg/h. Monitoring should include hourly glucose and electrolyte determinations and frequent measures of pH, osmolality, and ketones to guide adjustment of insulin dose and electrolyte replacement. If the serum glucose falls less than 50 mg/dL after 1 hour, double the insulin infusion rate every hour until a decline in glucose between 50 and 75 mg/hour is attained. Once glucose is less than 250 mg/dL, reduce the insulin infusion rate to 3 to 6 U/hour and add 5% dextrose to the IV fluids. Continue the insulin infusion until the anion gap and serum bicarbonate are normal. Premature cessation of the insulin infusion may result in recrudescence of DKA.
 4. Replace magnesium and phosphate as needed once normal renal function and urine output have been verified. Consider bicarbonate therapy only for severe acidosis (pH <7), hemodynamic instability, or rhythm disturbances.
 5. Identify and treat the underlying precipitants.
 6. Patients with altered mental status may require intubation for airway protection.
2. **HHS** may be the initial presentation of DM type 2.
- a. **HHS** is often associated with glucose levels exceeding 600 mg/dL, electrolyte abnormalities, central nervous system (CNS) dysfunction (depressed sensorium, seizure, and coma), and severe hyperosmolality, hypovolemia, and hemoconcentration from osmotic diuresis. The typical water deficit may be 8 to 10 L. Patients may present with blurred vision, neurologic deficits, weight loss, leg cramps, polydipsia, or polyuria. Although insulin levels are inadequate to prevent hyperglycemia, they are sufficient to block lipolysis, ketogenesis, and ketoacidosis. Mortality due to HHS may be as high as 15%.
 - b. **Treatment of HHS.** The following outline pertains to management in the general medical environment; management of the patient in the perioperative period may need to be more aggressive.
 1. Begin fluid therapy with 1 to 1.5 L (or 15 to 20 mL/kg) of NS in the first hour followed by 5 to 15 mL/kg/h of either NS or $\frac{1}{2}$ NS, depending on whether the corrected serum sodium concentration is low or normal or high. Approximately 50% of the fluid deficit should be given over the first 12 hours, with the remainder administered more slowly over the following 24 to 36 hours. After the initial resuscitation, correct severe hyperglycemia and hyperosmolality gradually over 24 hours to reduce the risk of

- cerebral edema. The rate of fluid replacement may be adjusted in the elderly or in a patient with a history of congestive heart failure.
2. Start insulin administration after fluid therapy has begun. Glucose concentration can drop as much as 80 to 200 mg/dL/h with fluid therapy alone. Administer insulin as in the treatment of DKA. Begin with a 0.1 to 0.15 U/kg bolus followed by an infusion of 0.1 U/kg/h. The insulin infusion can be doubled hourly until an appropriate response is noted. Titrate insulin infusion rates to maintain glucose levels at less than 250 mg/dL until cardiovascular, electrolyte, and metabolic parameters are normal.
 3. Measure glucose and electrolyte levels hourly. Potassium and electrolyte repletion is similar to that in the treatment of DKA. The absence of acidosis makes potassium deficiency generally less profound than observed with DKA.
 4. It is important to search for and treat precipitants.
 5. Patients with altered mental status may require intubation for airway protection.
 6. Consider venous thrombosis prophylaxis as these patients are at high risk for thrombotic events.
- G. Anesthetic considerations in the patient with DM** focus on risk reduction, maintenance of euglycemia, avoidance or treatment of acute complications of DM, and prevention of perioperative complications related to chronic complications of DM.
1. **DKA, HHS, and metabolic abnormalities** should be treated before elective surgery and actively managed in the operating room if surgery is urgent. For blood glucose level greater than 350 mg/dL, surgery should be postponed if the glucose level can be further optimized. Of note, certain surgical conditions (such as sepsis) or perioperative steroid therapy may be the cause of hyperglycemia and should be considered before postponing elective surgery.
 2. **Glycemic management.** There is no consensus on the ideal blood glucose target. However, there is evidence that tight control of blood glucose may not be desirable as recent studies show an increased mortality rate attributed to hypoglycemia. However, perioperative hyperglycemia is undesirable. It decreases white blood cell chemotaxis and function, increases infection rates, impairs wound healing, leads to dehydration from osmotic diuresis, and promotes a hyperviscous and possibly thrombogenic state. Hyperglycemia is also associated with increased rates of renal allograft rejection and worse outcomes after MI, stroke, burn, traumatic brain injury, and spinal cord injury. The authors of this chapter recommend maintaining serum glucose levels between 120 and 180 mg/dL. However, for short procedures, management of baseline hyperglycemia in patients with poorly controlled diabetes should be deferred to the postoperative period and not be actively corrected intraoperatively as acute alterations may be harmful.
 - a. **Oral hypoglycemic agents** and insulin sensitizers that can cause hypoglycemia (sulfonylureas, meglitinides, and D-phenylalanine derivatives) should be held the day of surgery. Amylin analogs and GLP-1 analogs, which cause delayed gastric emptying, should also be held in order to reduce the likelihood of postoperative nausea and vomiting (PONV). Metformin should be held from the day of surgery until normal postoperative renal function has been confirmed because of its association with lactic acidosis. Thiazolidinediones and DPP-IV inhibitors do not cause hypoglycemia and may be given

the morning of surgery. α -Glucosidase inhibitors also do not produce hypoglycemia, but they are ineffective when patients are NPO (nothing by mouth [nil per os]). SGLT2 inhibitors may cause hypovolemia. This is also the newest class of diabetic medications with little experience in anesthetized patients; there may be unexpected side effects. Patients with well-controlled DM type 2, who are undergoing a minor surgery and have held their oral hypoglycemics, can often be managed without insulin. However, glucose levels should be monitored in all patients to detect hypoglycemia or hyperglycemia. Patients who have taken their oral hypoglycemic agents may require a glucose infusion, and poorly controlled patients or patients undergoing major surgery may require insulin treatment.

- b. **Insulin-treated type 2 diabetics.** Insulin should be continued through the night before surgery. If the patient has a history of hypoglycemia, the dose should be reduced to $\frac{1}{2}$ to $\frac{2}{3}$ of the patient's customary dose.
- c. Patients should receive approximately half of their total normal morning dose of intermediate- or long-acting insulin in a subcutaneous dose. Rapid- and short-acting insulins should not be given. Start a glucose-containing infusion (5% dextrose, 1.5 mL/kg/h) as soon as possible (with the morning insulin dose for hospitalized patients and on arrival to the hospital for same-day admit patients). Patients scheduled for surgery later in the day should arrive early to facilitate glucose and insulin management while they are NPO. The blood glucose should be checked frequently (every 2 to 4 hours). If glucose drops below 120 mg/dL, the glucose infusion rate should be increased. If glucose rises above 180 mg/dL, an infusion of regular insulin should be started and continued throughout the perioperative period. Because of unreliable intraoperative subcutaneous absorption, IV insulin dosing is preferable during surgery, especially in the presence of hypothermia, hemodynamic instability, or a requirement for vasopressors. A guideline for managing intraoperative infusions of regular insulin is presented in Table 6.3. During

TABLE
6.3

Guidelines for Routine Regular IV Insulin Infusion

Begin regular insulin infusion at 0.5–1 unit/h (25 units/25 mL of saline). Check glucose at least hourly until stable and adjust infusion as appropriate. Then check glucose at least every 2 h.

Adjustment of Regular Insulin Infusion Rate, units/hour

Blood Glucose (mg/dL)	Infusion Change	Other Treatment
<70	Hold 30 min	Administer D50, 15–20 mL. Recheck glucose after 30 min. Repeat D50 administration until glucose >70 mg/dL.
70–120	–0.3 U/h	
121–180	No change	
181–240	+0.3 U/h	
241–300	+0.6 U/h	
>300	+1.0 U/h	

Notes: Guidelines assume the patient is fasting and not in DKA or HHS. Dosing must be individually titrated based on frequent blood glucose monitoring. D50 is a solution of dextrose, 50% (weight/volume) in water.

therapy with IV insulin, glucose should be checked at least every hour until stable and every 2 hours thereafter. Monitor potassium levels during insulin infusion. Decrease the insulin infusion rate and avoid potassium administration if renal insufficiency develops.

- d. **Type 1 DM.** These patients must always receive some insulin, despite low or normal glucose levels, to prevent ketoacidosis. Simultaneous infusion of a glucose-containing solution may be necessary to prevent hypoglycemia. Perioperative insulin management for the type 1 diabetic patients receiving the newer intensive regimens of three or more daily insulin injections should be discussed in advance with the physician responsible for managing the patient's diabetes. For the patient with an insulin pump, the following information should be obtained preoperatively: pump identification information, programmed settings information, insertion site, blood sugar measurements, plans for correction dosing, pump failure plan, and diabetes provider contact information. The usual basal rates can be reduced by 10% to 20% while the patient is NPO to avoid hypoglycemia. On the day of surgery, if the insertion site of the pump does not interfere with the site of surgery, the insulin pump should be continued throughout the perioperative period with sleep or "sick day" basal rates. The patient should also be started on a glucose infusion. Blood glucose levels should be checked frequently with target glucose level of 120 to 180 mg/dL. Of note, the use of x-ray and/or defibrillation may interfere with the functioning of the pump. An insulin pump is often not MRI compatible.
- e. **Fixed ratio insulin combinations** are prescribed for the outpatient management of some diabetics. In consultation with the physician managing the diabetes, these patients should be switched to preparations of individual insulins in the immediate preoperative period. An appropriately reduced dose (approximately 50%) of only the long-acting insulin can then be taken on the morning of surgery as described above.
- f. **Combination therapy** is common used in diabetic patients. Untoward effects, such as hypoglycemia, may be more likely.
3. **Vascular disease.** Diabetic patients have a strong predisposition to all types of vascular disease. Macrovascular disease (coronary artery, cerebrovascular, and peripheral vascular) and microvascular disease (retinopathy and nephropathy) occur more frequently, more extensively, and at an earlier age than in the general population. Ischemic heart disease is the most common cause of perioperative morbidity in diabetic patients. Cardiac ischemia may be silent because of autonomic neuropathy. Continuation of aspirin and β -blockade and a high index of suspicion are mainstays of management. DM and HTN are often comorbid diseases. Patients may be hypovolemic due to chronic anti-HTN treatment or hyperglycemic diuresis, resulting in significant hypotension after induction of general anesthesia. This may be exacerbated in patients with autonomic neuropathy due to an inability to compensate for vasodilation. DM is the most common cause of chronic renal insufficiency requiring hemodialysis. Avoid nephrotoxins and consider renal protective treatments in patients exposed to IV contrast loads.
4. **Neuropathy.** Autonomic neuropathy is present in 20% to 40% of patients with long-standing DM. It may result in symptomatically silent cardiac ischemia, decreased lower esophageal sphincter tone, gastroparesis, bladder atony, and labile blood pressure. There is an increased risk of

sudden cardiac death because of autonomic cardiac dysfunction and a diminished central ventilatory response to hypoxia. Patients with autonomic neuropathy may have more intraoperative hypothermia, be at higher risk of aspiration due to increased gastric volumes, and be less able to compensate for the sympathectomy of neuraxial anesthesia. Signs of cardiac autonomic neuropathy include resting tachycardia, orthostatic hypotension, and decreased beat-to-beat variability with deep breathing. Metoclopramide, 10 mg IV preoperatively, may increase gastric emptying in patients with gastroparesis. If the gastroparesis is severe, consider placing the patient on a clear liquid diet 1 to 2 days preoperatively. Peripheral neuropathies may cause pain and/or numbness. Patients with peripheral neuropathy are more vulnerable to positioning injuries and should be padded carefully. Document neuropathies before initiating regional anesthesia.

5. Airway management

- a. **Stiff joint disease** may complicate airway management. Approximately 30% of type 1 diabetics are considered “difficult intubations” because of decreased temporomandibular joint and cervical spine mobility.
- b. **Obesity**, sleep apnea, and redundant pharyngeal tissue are common in patients with metabolic syndrome or DM 2.
6. **Protamine.** Diabetic patients receiving NPH or NPL (Humalog mix) insulin are at increased risk for protamine reactions.

II. HYPOGLYCEMIA

- A. **Etiologies.** Common causes include excessive doses of insulin or oral hypoglycemic agents. Uncommon causes of hypoglycemia include pancreatic adenoma (insulinoma) or carcinoma, cirrhosis, hypopituitarism, adrenal insufficiency, hepatoma, sarcoma, ethanol ingestion, and renal failure (reduced insulin clearance).
- B. **Signs and Symptoms.** Adrenergic responses to hypoglycemia produce tachycardia, diaphoresis, palpitations, HTN, and tremulousness. Neuroglycopenia can result in irritability, headache, confusion, stupor, seizure, and coma. *General anesthesia masks the signs and symptoms of hypoglycemia.* Patients with long-standing DM and previous episodes of hypoglycemia often lose sympathetic responses to hypoglycemia, a condition termed **hypoglycemic unawareness**. Hypoglycemic unawareness is more common in patients with excellent glucose control.
- C. **Anesthetic considerations** include providing a continuous glucose infusion and periodically checking the serum glucose. Anticipate fluctuating glucose levels from surgical stress and with insulinoma manipulation.

III. THYROID DISEASE

Thyroid disease is the second most common endocrine disease encountered perioperatively, occurring in approximately 10% of the adult population. The female to male ratio is 5:1 to 10:1.

- A. **Physiology.** Thyroid-stimulating hormone (TSH) from the anterior pituitary stimulates the thyroid gland to take up iodine and produce the hormones triiodothyronine (T_3) and L-thyroxine (T_4); 80% of serum T_3 is produced by conversion from T_4 by peripheral tissues. T_3 is 20 to 50 times more potent than T_4 but has a shorter half-life. T_3 and T_4 are extensively (>99%) bound to plasma proteins, but only the free (unbound) thyroid hormone is biologically active. T_3 and T_4 are major regulators of metabolic activity. They alter the speed of drug metabolism, biochemical reactions, total body oxygen consumption, and heat production.

B. Evaluation and Laboratory Studies. Serum TSH is currently the best initial screen for the determination of thyroid function in the ambulatory population. TSH levels rise in hypothyroidism and fall in thyrotoxicosis. Evaluation of thyroid function is complex in sick patients. Starvation, glucocorticoids, stress, dopamine and fever may suppress TSH levels. As a result, total T_4 , free thyroxine index, and total T_3 measurements may aid diagnosis in sick patients.

C. Thyrotoxicosis

- 1. Etiologies of thyrotoxicosis**, in order of decreasing frequency, include Graves disease, toxic multinodular goiter, subacute thyroiditis (acute phase), toxic adenoma, TSH receptor stimulation by β -human chorionic gonadotropin overproduction (pituitary or placental tumors), and ovarian tumors secreting thyroid hormone (struma ovarii). Ingestion of excess iodine, amiodarone and iodinated contrast agents in patients with multinodular goiter, or supratherapeutic doses of thyroid hormone can also lead to thyrotoxicosis.
- 2. Thyrotoxicosis is a hypermetabolic state.** Patients present with nervousness, heat intolerance, fatigue, diarrhea, insomnia, increased perspiration, muscle weakness, tremors, irregular menses, and weight loss. Cardiovascular signs include dysrhythmias (sinus tachycardia and atrial fibrillation), palpitations, HTN, and high output or congestive heart failure. Patients may have leukopenia, anemia, or thrombocytopenia. Low clotting factor concentrations from increased metabolism result in increased sensitivity to anticoagulation therapy. Ophthalmic disease occurs only with Graves hyperthyroidism.
- 3. Treatment of thyrotoxicosis.** Chronic thyroid hormone excess is treated by gland ablation with surgery or radioactive iodine or by inhibition of hormone production with specific antithyroid drugs (e.g., propylthiouracil [PTU] and methimazole). Two to six weeks of drug therapy may be required to normalize hormone levels. The most serious side effects of antithyroid agents are hepatitis and agranulocytosis. Urticaria is a common side effect of antithyroid therapy.
- 4. Thyroid storm**, an endocrine emergency, is a state of physiologic decompensation due to severe thyrotoxicosis. Infection, surgery, trauma, cessation of antithyroid medications, excess iodine, iodinated IV contrast agents, and amiodarone may precipitate this condition. Thyroid storm may occur 6 to 18 hours postoperatively. Manifestations include diarrhea, vomiting, hyperpyrexia (38°C to 41°C) leading to hypovolemia, tachycardia, congestive heart failure, shock, weakness, irritability, delirium, and coma. Thyroid storm may mimic malignant hyperthermia, neuroleptic malignant syndrome, sepsis, hemorrhage, pheochromocytoma crisis, or transfusion/drug reaction. The mortality rate of thyroid storm is greater than 20%.
- 5. Treatment for thyroid storm** (Table 6.4) includes blocking thyroid hormone synthesis and release, blocking T_4 to T_3 conversion, suppressing the sympathetic response with β -adrenergic blockade, and supportive therapy (active cooling, meperidine to attenuate heat production from shivering, vigorous hydration, and electrolyte replacement). Steroids should be administered if there is any indication of adrenal insufficiency (including cardiovascular collapse). Iodine must be given **at least 1 hour before** initiation of treatment with PTU or methimazole.
- 6. Anesthetic considerations.** Ideally, patients should be euthyroid prior to surgery to avoid precipitating thyroid storm. Antithyroid drugs, pharmacologic iodine doses, and β -adrenergic antagonist medications should be continued through surgery.

TABLE
64 Treatment of Thyroid Storm

Block Sympathetic Response

Propranolol	1–2 mg IV (repeat as needed) or 40–80 mg orally every 6 h
Verapamil	5–10 mg IV (repeat as needed)
Esmolol	50–100 $\mu\text{g/kg/min}$ IV

Block Thyroid Hormone Synthesis (Thionamides)

PTU	200 mg orally every 4–6 h
Methimazole	20 mg orally or per rectum every 4 h

Block Thyroid Hormone Release

Iopanoic acid ^a	500 mg orally every 12 h
Iodine (SSKI) ^a	100 mg orally every 12 h
Dexamethasone	2 mg orally every 6 h

Block T_4 to T_3 Conversion

Propranolol, PTU, and Iopanoic acid
Steroids (hydrocortisone, 100 mg orally/IV every 8 h or dexamethasone, 2 mg orally/IV every 6 h)

Supportive Therapy

Fluids, cooling (with meperidine to block shivering), electrolyte replacement, antipyretics (no aspirin), treatment of precipitating illness and congestive heart failure, oxygen, nutrition, consider plasmapheresis and airway support

^a Give iopanoic acid or SSKI >1 h after PTU or methimazole to avoid a hormone production surge.
SSKI, saturated solution of potassium iodide.

- In an emergent situation, thyrotoxic patients can be prepared for surgery in less than 1 hour with high-dose IV propranolol or esmolol (100 to 300 $\mu\text{g/kg/min}$) titrated until the heart rate is less than 100 beats/minute. Rapid preparation also includes the administration of dexamethasone.
- Consider generous sedative premedication unless there is concern for airway compromise. Avoid sympathetic stimulation (pain, ketamine, and local anesthetics with epinephrine).
- Regional anesthesia may be beneficial in thyrotoxic patients because it blocks sympathetic responses. The addition of epinephrine to the local anesthetic should be avoided due to the risk of systemic uptake and worsening tachycardia and HTN. Thrombocytopenia sometimes occurs in thyrotoxicosis. Consider checking the platelet count before initiating regional anesthesia.
- Patients may be hypovolemic due to HTN, diarrhea, and perspiration. Hypotension should be treated with vasoconstrictor agents and fluids. Anticipate brisk tachycardic response to anticholinergic drugs.
- Protect the proptotic eyes which may not achieve complete lid closure in patients with Graves disease.
- Drug metabolism and anesthetic requirements appear to be increased because of rapid metabolism in thyrotoxicosis. However, myasthenia gravis may be seen in some patients with Graves disease (30-fold increased incidence), so relaxants should be titrated carefully.
- Large goiters may displace and compress the trachea, compromising the airway. In addition, emergency tracheostomy may be difficult in patients with goiter.

D. Hypothyroidism

1. **Etiologies of hypothyroidism.** Hypothyroidism may be congenital, result from thyroid gland damage (surgery, radioiodine, and radiation), or be secondary to pituitary disease. Other causes include Hashimoto thyroiditis, iodine deficiency, drug therapy (lithium, amiodarone with preexisting chronic thyroiditis, or phenylbutazone), and late-phase subacute thyroiditis. Hashimoto thyroiditis is the most common cause of hypothyroidism in adults and can be associated with other autoimmune processes (systemic lupus, rheumatoid arthritis, primary adrenal insufficiency, pernicious anemia, DM type 1, or Sjögren syndrome).
2. **Clinical features of hypothyroidism** include lethargy, impaired mentation, depression, cold intolerance, facial edema with an enlarged tongue, weight gain, hoarseness, paresthesias, irregular menses, ascites, anemia, coagulation abnormalities, constipation, and adynamic ileus with delayed gastric emptying. Cardiovascular and hemodynamic features include diastolic HTN, pericardial effusion, bradycardia, intravascular hypovolemia, reversible cardiomyopathy, ECG changes with conduction abnormalities, and diminished baroreceptor reflexes. Associated findings include autoimmune adrenal destruction with decreased cortisol and aldosterone production, hyponatremia and fluid overload from decreased water excretion and reduced glomerular filtration rate (GFR), and the syndrome of inappropriate antidiuretic hormone secretion (SIADH).
3. **Treatment of hypothyroidism.** Chronic treatment involves oral supplementation with oral thyroid hormone. T_4 is administered once daily and requires 7 to 10 days to have initial effects; 3 to 4 weeks of therapy are needed to achieve a stable state. T_4 dosing is usually adjusted every 4 to 6 weeks based on serum TSH levels. T_3 is not routinely used as therapy for hypothyroidism because of its short half-life. Cautious IV or oral thyroid hormone loading will hasten normalization of serum T_4 levels. IV thyroid hormone should be given with caution in patients with coronary artery disease because the increased metabolic state and oxygen consumption may induce cardiac ischemia.
4. **Myxedema coma** (profound hypothyroidism) is a clinical diagnosis. Surgery, drugs, trauma, and infection initiate the decompensated state in a severely hypothyroid patient. It is defined by decreased mental status associated with hyporesponsiveness to CO_2 , congestive heart failure, hypothermia, and exaggerated symptoms of hypothyroidism.
5. **Treatment of myxedema coma** is with T_3 , 25 μ g IV every 12 hours, passive rewarming, supportive care (which may include intubation/ventilation), correction of electrolyte abnormalities, hydrocortisone (50 mg IV every 8 hours or by continuous infusion), and management of hypotension, congestive heart failure, effusions, and the precipitating cause (such as MI, cerebral vascular accident [CVA], or infection). Active warming may cause hypotension in these patients who are hypovolumic with peripheral vasoconstriction.
6. **Anesthetic considerations.** Only severe hypothyroidism requires postponing elective surgery.
 - a. Securing the airway may be difficult because of an enlarged tongue, relaxed oropharyngeal tissues, goiter, and poor gastric emptying.
 - b. Patients may be prone to hypotension due to hypovolemia and blunted baroreceptor reflexes (especially with cardiac depressants and vasodilators).
 - c. Patients also manifest CO_2 insensitivity and increased sensitivity to CNS-depressant and paralytic medications.

- d. Corticosteroid supplementation may be necessary.
 - e. There is an increased likelihood of congestive heart failure, hypothermia, hypoglycemia, hyponatremia, and delayed emergence.
- E. Thyroid Surgery.** Indications for thyroid surgery include diagnosis of neoplasms, thyroid malignancy, hyperthyroidism resistant to medical management, retrosternal goiter, and goiter causing obstructive or cosmetic symptoms.
- 1. Anesthetic considerations.** General anesthesia with endotracheal intubation is the most common anesthetic technique.
 - a. Preoperative evaluation should include an assessment of thyroid function as well as evaluation for a potentially difficult airway.
 - b. Some surgeons monitor the integrity of the recurrent laryngeal nerve with electromyography (EMG) testing. Recording electrodes inserted into the laryngeal muscles or external electrodes fitted on the endotracheal tube detect laryngeal muscle activity in response to nerve stimulation. Alternatively, a laryngeal mask airway (LMA) may be used for airway management. The LMA allows intraoperative visualization of vocal cord function with a fiberoptic scope. Neuromuscular blockade must be avoided or minimized in these situations.
 - c. Postoperative complications of thyroid surgery include recurrent laryngeal nerve palsy, hypothyroidism, hypocalcemia from hypoparathyroidism, phrenic nerve injury, pneumothorax, thyroid storm in patients with untreated Graves hyperthyroidism, and airway obstruction from bleeding, edema, preexisting tracheomalacia, or bilateral recurrent laryngeal nerve paresis.

IV. CALCIUM METABOLISM AND PARATHYROID DISEASE

- A. Physiology.** Calcium is essential for neuromuscular excitability, cardiac automaticity, mitotic division, coagulation, muscle contraction, neurotransmitter and hormone secretion and action, and the activity of many enzymes. Parathyroid hormone (PTH) and vitamin D maintain the extracellular calcium concentration within a narrow range. PTH increases intestinal calcium absorption, increases osteoclastic release of calcium and phosphorus from bone, decreases renal clearance of calcium, and enhances formation of 1,25-dihydroxyvitamin D by the kidney. Levels of ionized calcium and magnesium determine the secretion of PTH. Vitamin D augments the effects of PTH and is necessary for calcium absorption from the GI tract. Calcitonin from thyroid "C" cells lowers calcium and phosphorus concentrations by inhibiting renal calcium reabsorption and osteoclast activity but has a limited physiologic role in humans.
- B.** Serum calcium is divided into bound (primarily to albumin) and unbound (free, ionized) forms. Phosphate, citrate, and other anions complex about 6% of the total serum calcium. Hypoalbuminemia produces a decrease in total calcium of approximately 0.8 mg/dL for each gram per deciliter of albumin below normal (4.0 g/dL). Acidosis increases, and alkalosis decreases, ionized calcium due to alterations in albumin binding. Ionized calcium, the physiologically important form, can be measured directly in whole blood.
- C. Hypercalcemia**
 - 1. Etiologies of hypercalcemia** include hyperparathyroidism (50% of ambulatory cases), malignancy, immobilization, granulomatous diseases, vitamin D intoxication, familial hypocalciuric hypercalcemia, thyrotoxicosis, drugs (lithium, thiazides, calcium, vitamin A, and

theophylline), Paget disease, renal disease, AIDS, and adrenal insufficiency. **Hyperparathyroidism** is characterized by hypercalcemia and hypophosphatemia with an elevated intact PTH level, usually caused by a parathyroid adenoma. Four-gland parathyroid hyperplasia causes hyperparathyroidism in only 10% of the cases. Parathyroid hyperplasia can be associated with pituitary adenoma and pancreatic tumors in multiple endocrine neoplasia (MEN) type I or medullary thyroid carcinoma and pheochromocytoma in MEN type IIa. Parathyroid carcinoma is a rare cause of hyperparathyroidism and hypercalcemia. **Hypercalcemia of malignancy** is due to release of a PTH-like molecule (PTH-related protein) from tumors and cytokine-mediated or direct bony destruction resulting in resorption of calcium from the skeleton.

2. **Clinical features of hypercalcemia** are summarized in Table 6.5. Mild hypercalcemia is usually asymptomatic. When total serum calcium (corrected for albumin level) is more than 13 mg/dL, there is increased risk of end-organ calcification, renal calculi, and nephrocalcinosis. A total serum calcium level of greater than 14 to 15 mg/dL is considered an endocrine emergency, as patients may have uremia, coma, cardiac arrest, or death.
3. **Treatment of hypercalcemia**
 - a. **Hydration** with normal saline IV to maintain a urine output of 100 to 150 mL/hour is the initial treatment for hypercalcemia. In patients with symptoms of volume overload, furosemide may be added. The patient must be monitored for hypokalemia, hypomagnesemia, fluid overload, and diuresis-induced hypovolemia. In patients with renal or cardiac failure, dialysis should be considered. Goals should also include treatment of the underlying cause of hypercalcemia. ICU care may be necessary.
 - b. **Bisphosphonates** (Pamidronate 60 to 90 mg IV over 4 hours or Zoledronate 4 mg IV over 15 minutes) decrease bone resorption

TABLE
6.5

Hypercalcemia: Signs and Symptoms

Gastrointestinal

- Nausea/vomiting
- Anorexia
- Constipation
- Pancreatitis
- Peptic ulcers
- Abdominal pain

Hemodynamic

- Dehydration
- HTN
- ECG/conduction changes
- Digitalis sensitivity
- Dysrhythmias
- Catecholamine resistance

Hematologic

- Anemia
- Thrombosis

Osteopenia/osteoporosis

Weakness/atrophy/fatigability

Central nervous system

- Seizures
- Disorientation/psychosis
- Memory loss
- Sedation/lethargy/coma
- Anxiety/depression

Renal

- Polyuria
- Nephrolithiasis
- Decreased renal blood flow
- Oliguric failure (late)

and are the treatment of choice in severe or life-threatening hypercalcemia and in hypercalcemia of malignancy. The maximum effect occurs in 2 to 4 days. Side effects include renal insufficiency, fever, myalgias, uveitis, and osteonecrosis of the jaw. Lower bisphosphonate doses are used in patients with renal insufficiency.

- c. **Salmon calcitonin** (4 to 8 international units [IU]/kg subcutaneously [SC] every 12 hours) will lower serum calcium concentrations by 1 to 2 mg/dL in 4 to 6 hours, but its effects are transient.
 - d. **Gallium nitrate** (100 to 200 mg/m²/d IV × 5 days) inhibits bone resorption and is effective in humoral hypercalcemia of malignancy, but its use is limited by nephrotoxicity and the need for continuous infusion over 5 days.
 - e. **Glucocorticoid therapy** (prednisone 40 to 100 mg/day PO for 3 to 5 days) is effective in some cases of multiple myeloma, vitamin D toxicity, and granulomatous diseases, although not in other causes of hypercalcemia.
 - f. Alternative therapies for severe hypercalcemia resistant to other therapies include denosumab (60 to 120 mg SC) and cinacalcet (30 to 60 mg PO BID).
4. **Anesthetic considerations.** Hypercalcemia greater than 12 mg/dL warrants correction preoperatively. Intravascular volume and other electrolyte abnormalities should be normalized and monitored. Hypercalcemia has an unpredictable effect on neuromuscular blockade, so relaxants should be carefully titrated. Muscular weakness due to hypercalcemia may worsen respiratory function. Careful positioning is required because patients can be osteoporotic. Patients with hypercalcemia are predisposed to digitalis toxicity and may have conduction abnormalities. Avoid hypoventilation because acidosis increases free calcium levels.
- D. **Hypocalcemia** is serum calcium less than 8.5 mg/dL in the absence of hypoalbuminemia or abnormalities in pH.

1. **Etiologies of hypocalcemia.** A major cause of hypocalcemia is hypoparathyroidism due to underproduction of PTH or, rarely, resistance to PTH effects by end-organ tissues. PTH underproduction may occur after gland damage during neck surgery or severe magnesium deficiency. Symptoms may be seen in the immediate postoperative period or days to weeks later. Other causes of PTH underproduction include radiation, hemosiderosis, infiltrative processes (malignancy and amyloidosis), and severe hypomagnesemia (<1 mg/dL). Less common causes of hypocalcemia include severe vitamin D deficiency and sequestration of calcium from extensive burns, fat emboli, and pancreatitis. furosemide, hyperphosphatemia, and antiepileptic drugs can cause hypocalcemia. In the operating room, **massive transfusion** (30 mL/kg/h), especially in patients with liver failure, results in hypocalcemia when citrate binds to calcium.
2. **Clinical features of hypocalcemia.** Patients are usually asymptomatic until total calcium is less than 7.0 mg/dL or ionized calcium is less than 2.8 mg/dL (0.7 mmol/L) especially if the onset is insidious.
 - a. Chronic hypocalcemia causes lethargy, muscle cramps, a prolonged QT interval, renal failure, cataracts, dementia, and personality changes.
 - b. Acute hypocalcemia produces neuromuscular irritability with muscle cramps and hand, foot, and circumoral paresthesias. Patients may demonstrate facial nerve irritability to percussion (Chvostek sign) or carpal spasm with tourniquet ischemia for 3 minutes (Trousseau sign).

- c. Severe hypocalcemia results in stridor, laryngospasm, tetany, apnea, coagulopathy, hypotension with catecholamine resistance, psychosis/confusion, and seizures unresponsive to conventional therapy.

3. Treatment of hypocalcemia

- a. Severe or symptomatic hypocalcemia should be treated with IV calcium. Calcium irritates the veins; administer calcium centrally whenever possible. A 10 mL ampule of calcium gluconate contains 93 mg of elemental calcium; a 10 mL ampule of calcium chloride contains 273 mg of calcium. For urgent therapy, two ampules of calcium gluconate or one ampule of calcium chloride may be given IV over 10 to 20 minutes. Less urgent situations are treated with a 15 mg/kg infusion of elemental calcium IV over 8 to 12 hours. During parenteral therapy, calcium levels, creatinine, the ECG, and hemodynamic status must be monitored. Therapeutic goals are a total serum calcium level near 8 mg/dL and a low urinary calcium level. Evaluate phosphorus, potassium, and magnesium levels and correct the abnormalities. Treat elevated phosphorus levels with oral phosphate binders; treat low magnesium levels (<1 mg/dL) with parenteral magnesium sulfate.
 - b. Mild-to-moderate hypocalcemia may be managed with oral calcium and activated vitamin D analogue. Patients require elemental calcium at 1.5 to 3 g/day (3,750 to 7,500 mg of calcium carbonate) and 1, 25-dihydroxyvitamin D (calcitriol, 0.25 to 3.0 μ g/day) in 4 to 6 divided doses.
 - c. For chronic replacement, patients receive calcitriol or vitamin D (ergocalciferol 50,000 IU, one to three times/week) in addition to calcium.
4. **Anesthetic considerations.** Correct calcium and other electrolyte abnormalities. Respiratory or metabolic alkalosis, hypothermia, rapid infusions of blood products (especially with hepatic insufficiency), and renal dysfunction can worsen hypocalcemia. Follow coagulation status. Patients may have hypotension with insensitivity to β -adrenergic agonists, a prolonged QT interval, advanced atrioventricular block, and digitalis insensitivity. Response to neuromuscular blocking drugs is unpredictable. Careful positioning is required, as patients may be osteoporotic.

E. Parathyroid Surgery

- 1. **Anesthetic considerations** and surgical complications in parathyroid surgery are similar to those for thyroid surgery. General anesthesia or regional techniques can be used. Surgeons may perform recurrent laryngeal monitoring intraoperatively. To ensure the appropriate removal of parathyroid tissue, blood may be sent intraoperatively for PTH levels with a 50% reduction and normalization of PTH level predicting surgical success. The circulating half-life of PTH is just a few minutes.

V. ADRENAL CORTICAL DISEASE

- A. **Physiology.** The adrenal gland consists of a cortex secreting glucocorticoids, mineralocorticoids, and androgens and a medulla secreting catecholamines. These hormones maintain homeostasis in stress states.
- 1. **Glucocorticoids.** Cortisol is the principal hormone of this class. It is produced daily in a diurnal manner in response to adrenocorticotrophic hormone (ACTH) from the anterior pituitary. Cortisol is required for converting norepinephrine to epinephrine in the adrenal medulla and for producing angiotensin. It acts as an

anti-inflammatory agent and has multiple effects on carbohydrate, protein, and fatty acid metabolism. Stress stimulates increased cortisol release. Cortisol raises blood pressure by augmenting catecholamine-induced vasoconstriction.

2. **Mineralocorticoids.** Aldosterone is the principle hormone of this class and the major regulator of extracellular fluid volume and potassium homeostasis. Its production is regulated by the renin-angiotensin system and blood potassium concentration (see Chapter 4). Increased renin levels promote the conversion of angiotensinogen to angiotensin I. Angiotensin-converting enzyme (ACE) cleaves angiotensin I to generate angiotensin II. Angiotensin II then stimulates aldosterone secretion. Aldosterone causes reabsorption of Na^+ and excretion of K^+ and H^+ in the distal tubule. ACE inhibitors reduce the production of angiotensin II and aldosterone. Angiotensin II receptor blockers (ARBs) are competitive antagonists of the angiotensin II receptors and also reduce aldosterone secretion.
 3. **Androgens.** Abnormalities in androgen secretion are rarely pertinent to anesthetic management.
- B. Pharmacology.** Synthetic steroids are available with different potencies and ratios of glucocorticoid to mineralocorticoid effect (Table 6.6).
- C. Primary Hyperaldosteronism (Conn Syndrome)**
1. **Etiologies.** Causes include aldosterone-producing adrenal adenomas or aldosterone excess from bilateral adrenal hyperplasia.
 2. **Clinical features.** Patients present with diastolic HTN, hypokalemic alkalosis, headaches, and muscle weakness.
 3. **Treatment.** The definitive treatment for aldosterone-producing adrenal adenomas is adrenalectomy. The standard treatment for bilateral adrenal hyperplasia is with the aldosterone receptor inhibitor spironolactone or eplerenone.
- D. Glucocorticoid Excess (Cushing Syndrome)**
1. **Etiologies.** The most common cause of Cushing syndrome is exogenous steroid administration. Endogenous causes include excess ACTH secretion from the pituitary (defined as Cushing disease), ectopic ACTH secretion from tumors elsewhere in the body, and excess

TABLE 6.6 Glucocorticoid and Mineralocorticoid Hormones

Steroid	Relative Potency			Duration (Hours)
	Glucocorticoid	Mineralocorticoid	Equivalent Dose (mg)	
Short acting				8–12
Cortisol	1.0	1.0	20	
Cortisone	0.8	0.8	25	
Aldosterone	0.3	3,000	—	
Intermediate acting				12–36
Prednisone	4.0	0.8	5	
Prednisolone	4.0	0.8	5	
Methylprednisolone	5.0	0.5	4	
Fludrocortisone	10.0	125	—	
Long acting				>24
Dexamethasone	25–40	0	0.75	

cortisol secretion secondary to adrenal adenoma or bilateral adrenal micronodular hyperplasia (BAMH).

2. **Clinical features.** Patients present with truncal obesity, moon face, gastroesophageal reflux disease, HTN, hypernatremia, excess intravascular volume, hyperglycemia, hypokalemia, red or purple cutaneous striae, poor wound healing, muscle wasting and weakness, osteopenia/osteoporosis, hypercoagulability with thromboembolism, mental status changes and emotional lability, aseptic osteonecrosis, pancreatitis, benign intracranial HTN, peptic ulceration, glaucoma, or infection.
3. **Anesthetic considerations.** Patients often exhibit HTN refractory to treatment. Excess intravascular volume can be reduced with diuretics, but potassium must be replaced. Monitor serum glucose levels and treat as needed. Osteoporosis makes careful positioning necessary. Patients may have unrecognized coronary artery disease. Consider venous thrombosis prophylaxis. Adrenalectomy is performed for adrenal adenoma or BAMH and may be open or laparoscopic. Glucocorticoid replacement should begin postoperatively for both unilateral and bilateral adrenalectomies. Mineralocorticoid replacement is necessary only after bilateral adrenalectomy. Excess ACTH secretion is treated by excision of the secreting tumor. Anesthesia for transsphenoidal pituitary surgery is discussed in Chapter 25.

E. Adrenal Cortical Hypofunction

1. **Etiologies.** Idiopathic hypofunction, autoimmune destruction, surgical removal, radiation, metastatic destruction, infection, hemorrhage, drugs (ketoconazole, rifampin, and metyrapone), granulomatous infiltration, vasculitis, adrenal vein thrombosis, or loss of ACTH stimulation can produce adrenal cortical hypofunction. Exogenous steroid administration may suppress the hypothalamic–pituitary–adrenal axis for up to 12 months after treatment has been stopped.
2. **Clinical features.** Lack of glucocorticoids may produce episodic fever, abdominal pain, and hypotension that are difficult to distinguish from an acute surgical abdomen. Mineralocorticoid deficiency will lead to decreased urinary sodium conservation, decreased response to circulating catecholamines, and hyperkalemia.
 - a. **Primary adrenal insufficiency (Addison disease)** is associated with both low cortisol and low aldosterone levels resulting in weight loss, headache, weakness, fatigue, anorexia, nausea/vomiting, abdominal pain, postural hypotension, diarrhea or constipation, and hyperpigmentation.
 - b. **Secondary adrenal insufficiency**, precipitated by abnormalities in ACTH secretion, results in low cortisol levels but normal aldosterone function. Patients may have panhypopituitarism, with symptoms of TSH, growth hormone (GH), or gonadotropin deficiency.
 - c. **Acute adrenal insufficiency** (Addisonian crisis) is a medical emergency that can occur in the context of stress such as surgery, trauma, or infection. Patients present with tachycardia and hypotension unresponsive to fluid, along with nausea, abdominal pain, and mental status changes.
3. **Treatment.** Under basal conditions, the hydrocortisone replacement dose is 10 to 20 mg daily (10 to 15 mg upon awakening and 5 to 10 mg at 4 PM) or prednisone at 4 to 7.5 mg once daily. During times of stress, the glucocorticoid dose must be increased. Treatment of Addisonian crisis includes fluids (5% dextrose in normal saline), steroid replacement (hydrocortisone 100 IV or dexamethasone 6 mg IV, and then

hydrocortisone 30 to 50 mg IV every 8 hours or as a continuous infusion), inotropes as necessary, and electrolyte correction. Patients may be hypoglycemic and have changes in mental status. Precipitating causes must be sought and treated. Hydrocortisone dosage may be decreased by 50% every 1 to 2 days, depending on the clinical status. In primary adrenal insufficiency, daily fludrocortisone (Florinef), 0.05 to 0.1 mg orally, is required once the hydrocortisone dose is below 50 to 75 mg daily.

4. **Anesthetic considerations.** Evaluate and treat volume with isotonic saline, hemodynamic, glucose, and electrolyte status as necessary. Avoid etomidate in the hypoadrenal patient because of the potential for further adrenal suppression. Patients with adrenal hypofunction may exhibit marked sensitivity to sedative, anesthetic, or vasodilator drugs. Titrate drug doses carefully to avoid cardiovascular depression. Perioperative steroid replacement is controversial and should be individualized. Any patient who has received more than a 14-day course of supraphysiologic steroid dosing in the past year may need glucocorticoid supplementation perioperatively. Following is one recommendation for perioperative IV hydrocortisone dosing:
 - a. **Minor surgery** (inguinal herniorrhaphy, minor urologic or gynecologic procedures, and oral or minor plastic surgery), hydrocortisone 25 mg or usual daily steroid dose (whichever is higher) preoperatively. Resume usual regimen on postoperative day 1.
 - b. **Moderate surgery** (open cholecystectomy, joint replacement, and extremity revascularization), hydrocortisone 50 to 75 mg or usual daily steroid dose (whichever is higher) preoperatively, 50 mg every 8 hours intraoperatively, and 20 mg every 8 hours on postoperative day 1. Resume usual regimen on postoperative day 2.
 - c. **Major surgery** (cardiothoracic or major abdominal surgery), hydrocortisone 100 mg or usual daily dose (whichever is higher) within 2 hours preoperatively, 50 mg every 8 hours until postoperative day 2 or 3, and then reduce by 50% daily until preoperative regimen is reached.

VI. ADRENAL MEDULLARY DISEASE

- A. **Physiology.** Preganglionic fibers of the sympathetic nervous system stimulate release of catecholamines from the adrenal medulla. Peripheral effects of catecholamines include chronotropic and inotropic stimulation of the heart, vasomotor changes, enhanced hepatic glycogenolysis, and inhibition of insulin release. Catecholamines are biotransformed in the kidney and liver to metanephrine, normetanephrine, and vanillylmandelic acid.

B. Pheochromocytoma

1. **Epidemiology.** Pheochromocytomas are functionally active catecholamine-secreting tumors of the adrenal medulla; 10% are bilateral, 10% are metastatic, and 10% to 25% are familial (occurring as part of MEN IIa and MEN IIb or in association with neurofibromatosis, tuberous sclerosis, von Hippel-Lindau or Sturge-Weber syndromes). Ten percent of tumors occur extra-adrenally (known as paraganglioma). Pheochromocytoma is a rare cause of HTN (approximately 0.1%). Most tumors secrete epinephrine, norepinephrine, and dopamine. Secretion is independent of neurogenic control.
2. **Clinical features.** Signs and symptoms are due to excess catecholamine release. The classic presentation includes palpitations, headache, and

diaphoresis in an episodically hypertensive patient, but 10% do not have HTN. Other symptoms include anxiety, tremor, hyperglycemia, orthostatic hypotension, and weight loss. Patients with pheochromocytoma are usually dehydrated and hemoconcentrated. A plasma fractionated metanephrines or 24-hour urine collection for catecholamines and their metabolites are the routine screening tests. Preoperative diagnosis is important, as intraoperative diagnosis is associated with a mortality approaching 50%. Treatment is with excision.

3. **Preoperative evaluation and preparation.** Preoperative recognition of end-organ damage is important for optimization. Catecholamine-induced dilated or hypertrophic cardiomyopathy occurs in 20% to 30% of patients. Congestive heart failure, hypovolemia, intracranial hemorrhage, hyperglycemia, and renal failure are other potential concerns. Comorbid endocrinopathies should be sought and treated. Goals of preoperative treatment are to restore intravascular volume and reduce the end-organ effects of catecholamines.
 - a. α -Receptor blockade is often started with oral phenoxybenzamine, a long-acting irreversible α_1 -adrenergic and α_2 -adrenergic blocker (starting with 20 to 30 mg/day and increasing to 60 to 250 mg/day until blood pressure is controlled), or prazosin (1 to 6 mg orally, four times a day) or doxazosin (2 to 5 mg, two to three times), which are shorter-acting competitive α_1 -blockers. A calcium-channel blocker is an option as a supplemental or an alternative therapy, especially if the patient cannot tolerate α -receptor blockers due to hypotension or other severe side effects. Achieving adequate α -receptor blockade may require 7 to 14 days. Clinical end points that suggest a patient is ready for surgery include blood pressure less than 120/80 mm Hg (seated) for at least 24 hours, postural hypotension (but blood pressure >80/45 (standing)), a maximum of five premature ventricular contraction (PVC) per minute, no changes on ECG for 1 to 2 weeks, and nasal stuffiness. Prazosin/doxazosin and phenoxybenzamine should be stopped approximately 12 and 48 hours preoperatively, respectively.
 - b. Adequate volume repletion is reflected by weight gain and decreasing hematocrit. After adequate alpha blockade, the patients without congestive heart failure or renal insufficiency are encourage to start a high sodium diet (>5000 mg daily) for volume expansion.
 - c. β -Blockade is instituted with caution (due to potential cardiomyopathy) and only *after* the onset of adequate α -blockade (to prevent unopposed vascular α -receptor stimulation and worsening HTN).
 - d. A less common preoperative management strategy is to deplete the adrenal medulla of stored catecholamine with metyrosine, a catecholamine synthesis inhibitor (1 to 4 g/day). Clinical end points are the same as with prazosin, doxazosin, and phenoxybenzamine.
4. **Anesthetic considerations.** The goal is to avoid hypotension or sympathetic outflow, as either scenario can produce adrenergic crisis. Preoperative sedation may be helpful. Avoid sympathomimetic, vagolytic, or histamine-releasing drugs as well as sympathetic responses to induction, intubation, pneumoperitoneum, and surgical stimulation. A combined technique using an epidural is effective in ablating sympathetic responses (but not catecholamine surges), but hypotension should be actively avoided.
 - a. Blood pressure should be measured directly. The need for other invasive monitoring depends on the patient's medical status.

- b. Magnesium blocks catecholamine receptors and catecholamine release from the adrenal medulla and peripheral adrenergic nerve terminals. It can be a useful adjunct (40 to 60 mg/kg IV loading dose, infusion 2 g/hour, and 20 mg/kg boluses p.r.n), but it may delay awakening and cause muscle weakness.
- c. Dysrhythmias and severe HTN (hypertensive crisis) may occur intraoperatively. Treatment options include IV boluses of sodium nitroprusside (NTP), 50 to 100 μ g; nicardipine, 1 to 2 mg; magnesium, 20 mg/kg; or phentolamine, 1 to 5 mg. β -Blockade with labetalol or esmolol may be required after HTN has been treated.
- d. Once the tumor's venous supply is ligated, a sudden decrease in blood pressure may occur due to the decrease in circulating catecholamine levels and residual α -blockade and β -blockade. Vigorous volume support and treatment with a direct-acting vasopressor such as phenylephrine is customary. Vasopressin may be helpful.
- e. Glucose should be monitored perioperatively, as patients may have hyperglycemia preoperatively and hypoglycemia postoperatively.
- f. Endogenous catecholamine levels should return to normal shortly after tumor removal, but blood pressure may take much longer to normalize. ICU care may be required in the postoperative period. Patients undergoing bilateral adrenalectomy will require glucocorticoid and mineralocorticoid replacement therapy.

VII. PITUITARY DISEASE

A. Anterior Pituitary Gland

1. **Physiology.** The anterior pituitary regulates the thyroid and adrenal glands, the ovaries and testes, growth, and lactation by producing TSH, ACTH, follicle-stimulating hormone, luteinizing hormone, GH, and prolactin. A negative feedback system mediated by peripheral hormones tightly controls anterior pituitary secretion. Anterior pituitary adenomas may lead to hormone excess or hypopituitarism. Macroadenomas (>1 cm in diameter) can compress adjacent structures producing visual disturbances, seizures, or increased intracranial pressure (ICP).
2. **Anterior pituitary hyperfunction.** Pituitary adenoma is the most common cause of anterior pituitary hyperfunction. Prolactinomas generally do not affect anesthetic management. The hyperthyroidism of a TSH-secreting adenoma and the hyperadrenalism of an ACTH-secreting adenoma are treated as described above (see sections III and V). The anatomic and physiologic changes seen with GH-secreting tumors warrant careful consideration.
- a. **Acromegaly (excess GH)**
 1. **Clinical features.** GH stimulates bone, cartilage, and soft tissue growth leading to prognathism, subglottic narrowing of the trachea, and soft tissue overgrowth of the lips, tongue, epiglottis, and vocal cords. Connective tissue overgrowth can cause recurrent laryngeal nerve paralysis, carpal tunnel syndrome, and other peripheral neuropathies. These patients often develop glucose intolerance, muscle weakness, arthritis, osteoporosis, HTN, obstructive sleep apnea (OSA), congestive heart failure, and arrhythmias. They also have an increased incidence of coronary artery disease and colon carcinoma. The primary treatment is surgical removal of the tumor. Medical management for persistent disease after surgery includes dopamine agonists (bromocriptine and cabergoline), somatostatin analogs (octreotide

and lanreotide), GH receptor antagonists (pegvisomant) and radiation therapy. Excision of GH-secreting pituitary adenomas is often performed transsphenoidally (see Chapter 25).

2. **Anesthetic considerations.** Patients should be evaluated for other endocrinopathies and cardiac disease preoperatively. Conventional mask airways are often difficult to achieve, and endotracheal intubation can be challenging. Advanced airway and tracheostomy equipment should be available, and awake fiberoptic intubation should be considered. Small-diameter endotracheal tubes may be required. Serum glucose levels should be carefully monitored and muscle relaxants titrated using a peripheral nerve stimulator. Patients may be osteoporotic and have increased susceptibility to peripheral neuropathies. Careful positioning is necessary. Patients with OSA are at high risk for postoperative obstruction.

3. Anterior pituitary hypofunction

- a. **Etiologies.** Pituitary adenoma is the most common cause of anterior pituitary hypofunction. Other causes of pituitary failure include trauma, radiation, pituitary apoplexy, tumors, infiltrative disease, and surgical hypophysectomy. Sheehan syndrome is a condition of pituitary failure in which hemorrhagic shock causes vasospasm and subsequent pituitary necrosis in postpartum women.
- b. **Anesthetic considerations.** Adrenal insufficiency develops over 4 to 14 days after destruction of the pituitary. Perioperative glucocorticoid supplementation may be necessary. Because the half-life of thyroid hormone is 7 to 10 days, symptomatic hypothyroidism does not occur until 3 to 4 weeks after pituitary surgery or apoplexy.

B. Posterior Pituitary Gland

1. **Physiology.** The posterior pituitary is composed of the nerve terminals of neurons originating in the hypothalamus. Antidiuretic hormone (ADH; vasopressin) and oxytocin are stored in the posterior pituitary. ADH regulates plasma osmolality and extracellular fluid volume and facilitates renal tubular resorption of water. Intravascular hypovolemia, pain from trauma or surgery, nausea, and positive airway pressure stimulate ADH secretion. Oxytocin stimulates uterine contraction in labor and milk ejection in lactation.
2. **Diabetes insipidus (DI)**
 - a. **Etiologies.** DI results from insufficient ADH secretion by the posterior pituitary (central DI) or failure of the renal tubules to respond to ADH (nephrogenic DI). Causes of central DI include intracranial trauma, hypophysectomy, hypophysitis, metastatic disease to the pituitary or hypothalamus, and infiltrative diseases. Causes of nephrogenic DI include hypokalemia, hypercalcemia, sickle cell anemia, chronic myeloma, obstructive uropathy, chronic renal insufficiency, and lithium therapy. Nephrogenic DI may be seen in the third trimester of pregnancy and may also be congenital.
 - b. **Clinical features** include polydipsia and polyuria. The urine is inappropriately dilute, and serum osmolality is high. Urine output is greater than 2 L/day.
 - c. **Anesthetic considerations.** Mild DI (daily urinary volumes of 2 to 6 L in patients with an adequate thirst mechanism) does not require treatment. In patients who cannot drink, initial therapy should be with isotonic fluids (normal saline) to reverse shock. Once osmolality is less than 290 mOsm/kg, hypotonic fluids (half normal saline) are necessary. Total body water deficit can be estimated as follows:

$$\text{Water deficit (L)} = [0.6 \times \text{body weight (kg)}] \times [([Na^+] - 140)/140]$$

Body weight is the initial weight before dehydration. Careful monitoring and titration of urine output and plasma volume, sodium, and osmolality are necessary.

- d. **Central DI** may be treated with the synthetic vasopressin analog desmopressin (DDAVP) at 1 to 2 μg SC or IV every 6 to 24 hours as needed (or with an infusion intraoperatively). Side effects of DDAVP include hyponatremia, HTN, and coronary artery vasospasm.
 - e. **Nephrogenic DI** is associated with failure of vasopressin to reduce urinary volume. Adequate oral or parenteral hydration must be assured. Chlorpropamide (an oral hypoglycemic) potentiates the effects of ADH on renal tubules and may be helpful. Inhibition of prostaglandin synthesis (by ibuprofen, indomethacin, or aspirin) or mild salt depletion with a thiazide diuretic may reduce urine volume.
3. **SIADH** is persistent secretion of ADH in the absence of an osmotic stimulus.
 - a. SIADH can be caused by malignancy, CNS disorders (trauma, infection, and tumor), pulmonary disorders (tuberculosis, pneumonia, positive-pressure ventilation, and chronic obstructive pulmonary disease), and drugs (nicotine, narcotics, chlorpropamide, clofibrate, vincristine, vinblastine, cyclophosphamide, and serotonin reuptake inhibitors). Other etiologies include lupus, HIV, Guillain-Barre, hypothyroidism, Addison disease, congestive heart failure, cirrhosis, and porphyria. SIADH is associated with urine osmolality greater than serum osmolality (with a low serum osmolality), urine sodium greater than 20 mEq/L, and serum sodium less than 130 mEq/L. If serum sodium falls below 110 mEq/L, cerebral edema and seizures may result.
 - b. Fluid restriction (800 to 1,000 mL daily) is the primary treatment for the mild hyponatremia of SIADH. Chronic hyponatremia without symptoms has virtually no mortality. Thus, resuscitation with sodium-containing solutions is reserved for symptomatic, severe hyponatremia (serum $\text{Na}^+ < 120$ mEq/L). Hyponatremia should be corrected no faster than 0.5 mEq/L/h because overly aggressive correction may produce central pontine myelinolysis, an irreversible neurologic disorder (see Chapter 4). Demeclocycline antagonizes the effects of ADH on renal tubules and may be helpful.

VIII. CARCINOID

- A. **Carcinoid Tumors.** Most carcinoid tumors arise in the GI tract (appendix, ileum, and rectum), but they can also be seen in the lungs and elsewhere. Carcinoid tumors are capable of secreting substances that affect vascular, bronchial, and GI smooth muscle tone. Serotonin and histamine are the most commonly secreted hormones, but carcinoid tumors are capable of secreting 35 peptides and hormones, including bradykinin, prostaglandins, kallikrein, and others. Stimuli for the release of mediators include catecholamines, histamine, hypotension, and tumor manipulation.
- B. **Carcinoid syndrome** is seen in 2% to 5% of patients with carcinoid tumors. This syndrome develops when substances produced by the tumor reach the systemic circulation. Substances secreted from GI tumors are metabolized in the liver (preventing carcinoid syndrome) until the secretion overwhelms the liver's neutralizing ability, either because of the quantity produced or because of decreased liver activity from metastases. Tumors

located outside the GI tract may produce the syndrome by direct release of mediators into the systemic circulation; 40% to 50% of small bowel and proximal colon carcinoids produce carcinoid syndrome. Symptoms are less frequent with carcinoids of the bronchus, rarely seen with appendiceal carcinoids, and never seen with rectal carcinoid tumors.

C. Clinical features of carcinoid syndrome depend on which mediators a tumor releases. Common symptoms include flushing, bronchoconstriction, GI hypermotility, and hypoglycemia or hyperglycemia. Peripheral vasodilation and vasoconstriction can produce profound hypotension and HTN. Right-sided valvular lesions resulting in tricuspid regurgitation and pulmonic stenosis are seen in 20% to 40% of patients with carcinoid syndrome. Left-sided valvular disease is unusual.

D. Treatment is by surgical removal of the tumor. Liver metastases may be surgically resected or embolized. Medical treatment is used in preparation for surgery or embolization, in patients with unresectable disease, and in patients who are not surgical candidates. Octreotide, a long-acting somatostatin analog, is the mainstay of medical treatment.

E. Anesthetic Considerations

1. Hypovolemia, glucose abnormalities, and electrolyte disturbances should be treated preoperatively. Patients should be evaluated for valvular heart disease and may require endocarditis prophylaxis. Octreotide at 50 to 100 μg SC is usually given preoperatively. Peak levels are achieved in 30 minutes. Preoperative sedation may be helpful to minimize mediator release due to anxiety.
2. Large blood loss should be expected as tumors are vascular, and there may be liver dysfunction or metastases. Invasive blood pressure monitoring should be used in anticipation of large blood pressure swings. Central venous pressure monitoring may help differentiate the cause of hypotension (hypovolemia versus carcinoid crisis).
3. Triggers of mediator release should be avoided (hypotension, anxiety, pain, hypoxia, hypercarbia, tumor compression, drugs that cause histamine or catecholamine release, or sympathetic stimulation). Anticipate intraoperative mediator release; treat with octreotide boluses (25 to 50 μg IV, diluted to 10 $\mu\text{g}/\text{mL}$) or infusion (50 to 100 $\mu\text{g}/\text{hour}$ IV). Flushing is a warning sign of potential cardiovascular instability and should be treated with octreotide boluses. Hypotension or HTN should be treated with octreotide, fluids, and direct-acting vasoconstrictors (phenylephrine) or vasodilators (nitrates) as needed. Conventional therapies for these conditions (β -agonists, epinephrine, and NTP) can stimulate mediator release and exacerbate symptoms. Bronchospasm is less common but may be severe and should be treated with octreotide, antihistamines, and nebulized ipratropium.
4. Patients with carcinoid syndrome may have delayed awakening due to excess serotonin. Postoperative ICU care may be appropriate, especially if an octreotide taper is required.

Suggested Readings

General

Peterfreund RA, Lee SL. Endocrine surgery and intraoperative management of endocrine conditions. In: Longnecker D, Brown D, Newman M, et al., eds. *Anesthesiology*. New York: McGraw-Hill; 2012:1112–1132.

Diabetes

Abdelmalak B, Ibrahim M, Yared J, et al. Perioperative glycemic management in insulin pump patients undergoing noncardiac surgery. *Curr Pharm Des* 2012;18(38):6204–6214.

Cefalu WT, Buse JB, et al. Beyond metformin: safety considerations in the decision-making process for selecting a second medication for type 2 diabetes management. *Diabetes Care* 2014;37(9):2647–2659.

Girard M, Schricker T. Perioperative glucose control: living in uncertain times. *Can J Anaesth* 2011;58(3):312–320, 320–329.

Russo N. Perioperative glycemic control. *Anesthesiol Clin* 2012;30(3):445–466.

Sebranek J, Kopp Lugli A, Coursin DB. Glycaemic control in the perioperative period. *Br J Anaesth* 2013;111(suppl 1):i18–i34.

Thyroid

Bajwa SJS, Sehgal V. Anesthesia and thyroid surgery: the never ending challenges. *Indian J Endocrinol Metab* 2013;17(2):228–234.

Langley RW, Burch HB. Perioperative management of the thyrotoxic patient. *Endocrinol Metab Clin North Am* 2003;32:519–534.

Mathew V, Misgar RA, Ghosh S, et al. Myxedema coma: a new look into an old crisis. *J Thyroid Res* 2011;2011:493462.

Stathatos N, Wartofsky L. Perioperative management of patients with hypothyroidism. *Endocrinol Metab Clin North Am* 2003;32:503–518.

Calcium

Aguilera IM, Vaughan RS. Calcium and the anaesthetist. *Anaesthesia* 2000;55:779–790.

Bajwa SJS, Sehgal V. Anesthetic management of primary hyperparathyroidism: a role rarely noticed and appreciated so far. *Indian J Endocrinol Metab* 2013;17(2):235–239.

Adrenals

Ganguly A. Primary aldosteronism. *N Engl J Med* 1998;339:1828–1834.

Marik PE, Varon J. Requirement of perioperative stress doses of corticosteroids: a systematic review of the literature. *Arch Surg* 2008;143:1222–1226.

Pivonello R, De Martino MC, De Leo M, et al. Cushing's syndrome. *Endocrinol Metab Clin North Am* 2008;37:135–149.

Salvatori R. Adrenal insufficiency. *JAMA* 2005;294:2481–2488.

Pheochromocytoma

Bajwa SJS, Bajwa SK. Implications and considerations during pheochromocytoma resection: a challenge to the anesthesiologist. *Indian J Endocrinol Metab* 2011;15(suppl 4):S337–S344.

Hariskov S, Schumann R. Intraoperative management of patients with incidental catecholamine producing tumors: a literature review and analysis. *J Anaesthesiol Clin Pharmacol* 2013;29(1):41–46.

Kinney MAO, Bradley JN, Warner MA. Perioperative management of pheochromocytoma. *J Cardiovasc Anesth* 2002;16:359–369.

Shen J, Yu R. Perioperative management of pheochromocytoma: the heart of the issue. *Minerva Endocrinol* 2013;38(1):77–93.

Pituitary

Bajwa SS, Bajwa SK. Anesthesia and Intensive care implications for pituitary surgery: recent trends and advancements. *Indian J Endocrinol Metab* 2011;15(suppl 3):S224–S232.

Dunn LK, Nemergut EC. Anesthesia for transsphenoidal pituitary surgery. *Curr Opin Anaesthesiol* 2013; 26(5):549–554.

Horvat A, Kolak J, Gopcević A, et al. Anesthetic management of patients undergoing pituitary surgery. *Acta Clin Croat* 2011;50(2):209–216.

Seidman PA, Kofke WA, Policare R, et al. Anaesthetic complications of acromegaly. *Br J Anaesth* 2000;84(2):179–182.

Carcinoid

Dierdorf SF. Carcinoid tumor and carcinoid syndrome. *Curr Opin Anaesthesiol* 2003; 16:343–347.

Mancuso K, Kaye AD, Boudreaux JP, et al. Carcinoid syndrome and perioperative anesthetic considerations. *J Clin Anesth* 2011;23(4):329–341.



Infectious Diseases and Infection Control in Anesthesia

Courtney Maxey-Jones and Elizabeth Cox Williams

- I. The Centers for Disease Control and Prevention estimates that in the United States, there are approximately 1.7 million nosocomial infections per year which cause or contribute to 99,000 deaths per year. In addition to the morbidity and mortality, these complications cost billions of dollars annually.

A. Infection Control Responsibilities of Anesthesia Providers

1. **Participate in infection control** to prevent transmission of infectious agents between patients and between patients and operating room (OR) personnel.
2. **Prevent or avoid infectious complications associated with anesthetic procedures** such as central venous catheter (CVC) insertion and epidural placement.
3. **Participate in prevention of surgical wound infections and antibiotic stewardship** with timely and appropriate perioperative antibiotic selection.

II. INFECTION CONTROL IN THE OR

A. Methods of Infection Spread

1. **Contact** with a colonized person, an actively infected person, a host, or a fomite is the most frequent route of transmission in the OR.
2. **Body fluids** (blood, urine, CSF) are a method of transmission that depends on access to a mucosal surface or a break in the integrity of the skin barrier.
3. **Droplet transmission** is the transfer of infectious particles via suspension in large fluid droplets such as those released during coughing or sneezing which travel short distances.
4. **Airborne transmission** is similar to droplet transmission with the exception that the particles are small enough to remain suspended in air and travel in air currents.

- B. **Standard or Universal precautions** constitute a minimum of acceptable guidelines that should be used for all patient populations regardless of infectious status.

1. **Hand hygiene** has consistently been shown to be the single most important method for preventing nosocomial infections. Basic hand hygiene requires that alcohol-based hand rub be used before and after any patient contact including any contact with equipment in the immediate vicinity of the patient.
2. **Personal protective gear** including gloves, gowns, masks, eye protection, and face shields should be readily available. Gloves should be used any time there is potential for contact with body fluids and additional protective gear should be used when indicated based on precaution requirements.

3. **Appropriate OR attire** to prevent infectious spread includes clean scrubs that have not been worn outside of the OR, a cap or bonnet that covers all hair including beards, a mask, and either OR dedicated closed toed shoes or shoe covers over general use closed toed shoes.
- C. **Specific precautions** are necessary based on specific pathogens and their mode of transmission.
 1. **Contact precautions** are applied to patients with pathogens that can be transmitted by direct or indirect contact. The most frequently encountered organisms are methicillin-resistant *Staphylococcus aureus* (MRSA) and vancomycin-resistant *Enterococcus* (VRE). Routine screening via rectal (VRE) and nasal (MRSA) swabs has increased the identification of colonized patients, thus increasing the number of patients on contact precautions.
 - a. **Gloves and gown** should be donned prior to entering and removed upon exiting the patient room.
 - b. **Alcohol based hand cleanser or hand washing** should occur prior to gowning and gloving and immediately following gown and glove removal.
 - c. During **transportation**, gowns and gloves should only be worn if providing direct patient care necessitating contact with the patient.
 - d. **Medical records** should be kept outside of the patient room and transported in a plastic bag.
 - e. **Removal of contact precautions** is hospital specific and organism specific. Typical standards include cessation of antibiotics for at least 48 hours, negative cultures from the infected site if applicable and three negative cultures on different dates from the common site of colonization (MRSA—nasal, VRE—rectal).
 2. **Contact precautions plus** is for patients with known or suspected infection with spore forming or alcohol-resistant organisms that can be transmitted by direct or indirect contact. The most frequently encountered is *Clostridium difficile*. In addition to standard contact precautions, hands must be washed with water and soap after glove and gown removal. These precautions may be discontinued after completion of an appropriate antibiotic course and resolution of symptoms.
 3. **Strict contact precautions** are for patients with infection or colonization with *S. aureus* that has reduced sensitivity to vancomycin (vancomycin intermediate sensitivity [VISA]) or vancomycin-resistant *Staphylococcus aureus* (VRSA). In addition to contact precautions plus, patients should have dedicated staff assigned to their care, and patients should only be transported for essential purposes. In order to discharge the patient, transfer the patient to another facility, or discontinue strict contact precautions, the local health department must be contacted.
 4. **Droplet precautions** are for patients with known or suspected infection with organisms that are transmissible via large respiratory droplets. The most frequently encountered organisms/diseases include meningococcal meningitis, *Mycoplasma pneumoniae*, and influenza.
 - a. **Disposable surgical masks** should be worn by providers when within 3 feet of the patient and should be disposed of immediately after exiting the room. **Hand hygiene** should be completed after disposing of the mask.
 - b. **Transportation** of the patient requires the patient to wear a surgical mask.

5. **Airborne precautions** are for patients with known or suspected infection with organisms that may remain suspended in the air and be dispersed by air currents. The most frequently encountered organisms include pulmonary tuberculosis and *Varicella*.
 - a. **N95 respirators** should be worn whenever in the patient's room. These are specialized masks that require fit testing and training prior to use.
 - b. **Negative pressure** isolation rooms are required and doors should remain closed.
 - c. **Transportation** of the patient requires the patient to wear a surgical mask and those providing direct care to wear an N95 respirator.
- D. **Operating Room Hygiene Standards**
 1. **Bactericidal cleaning agents** should be used between all cases on the anesthesia machine, monitors, and work station.
 2. **Clean workstation standards** at MGH mandate that any item that has touched the anesthesia machine tray will be discarded between cases to prevent cross contamination.
 3. **Sterilization of reusable equipment** between uses is necessary (i.e., laryngoscopes, reusable laryngeal mask airways (LMAs), bronchoscopes, reusable stylets).
 4. **Bacterial contamination of the anesthesia machine** and the possibility of cross contamination between patients is a controversial topic. Available data have shown no significant difference in postoperative pulmonary infection rate between reusable circuits that are appropriately cleaned and disposable circuits. The addition of a bacterial filter does not prevent infectious transmission. The high oxygen content, metallic ions, and the shifts in temperature and humidity present within the machine are bactericidal.
 5. **Air exchanges** in the OR should occur at a minimum of 15 times per hour, and the OR should be maintained at a positive pressure relative to surrounding areas with few exceptions (i.e., airborne precaution patient).
- E. **Avoid Anesthesia Associated Infectious Complications**
 1. **Peripheral intravenous lines** should be placed after cleaning of the insertion site with an approved cleaning solution (at MGH, these include 70% isopropyl alcohol, povidone iodine, or 2% chlorhexidine/70% isopropyl alcohol) and covered with a transparent occlusive dressing.
 2. **Strict sterile technique** including site cleaning, drapes, mask, and sterile gloves should be used for other invasive procedures including epidural placement, spinals, arterial lines, and peripheral nerve blocks.
 3. **Central venous catheters (CVC)** are a major source of potentially avoidable nosocomial infections. The most common sites of venous cannulation are the femoral, internal jugular, and subclavian veins. It was traditionally taught that femoral lines were the "dirtiest," and subclavian lines the "cleanest," but recent studies indicate that sterile technique in placement and daily assessment is more important than site choice. Central line-associated blood stream infection (CLABSI) is a source of major morbidity and health care expenditure. Causes include infection from skin flora at the site, contamination of infusions or catheter hubs, and seeding from distant sites. Emergency insertion, long duration in situ, use for total parenteral nutrition, and an increased number of lumens heighten the risk of CLABSI. The most common pathogens

are bacteria including *Staphylococcus* and *Streptococcus* spp. as well as *Candida* spp.

- a. **Protocols** for placement and daily care decrease CLABSI. Use of a checklist and dedicated monitoring personnel during placement ensures strict sterile technique including full draping of the patient, aseptic technique (hand prep, site prep, sterile gown and gloves, mask), and appropriate dressing. Use of a daily care checklist ensures site skin integrity, maintenance of a transparent occlusive dressing, and ongoing evaluation for necessity of central access as well as appropriateness of removal. Routine replacement of CVC has not shown any clinical benefit.
 - b. **Diagnosis** of CLABSI is based on clinical manifestations, ranging from localized signs of infection to septic shock, combined with laboratory culture data. Blood, sputum, and urine cultures as well as wound cultures if applicable should be obtained prior to antibiotic initiation. If further clarity is required, simultaneous quantitative blood cultures, one from a peripheral site and one from the CVC, should be obtained. A 5- to 10-fold higher colony count on the culture from the CVC supports the diagnosis of CLABSI.
 - c. **Treatment** of CLABSI. The CVC should be removed and replaced at a new site. Changing the catheter over a guide wire is increasingly considered a suboptimal management technique. Empiric antibiotic coverage is appropriate with narrowing of coverage as soon as Gram stain and culture data allows. Typical antibiotic courses for uncomplicated CLABSI are 7 to 14 days, but longer courses may be indicated for fungal infections and immunocompromised hosts.
4. **Aspiration pneumonia** is a potentially lethal infectious anesthetic complication as a result of aspiration of oropharyngeal or gastric contents that can occur at any point when the airway is not secured.
- a. **Aspiration pneumonia** indicates an actual infectious etiology while **aspiration pneumonitis** reflects a noninfectious chemical pneumonitis. Differentiation between the two can be challenging and as such antibiotic therapy should not be reflexively initiated for all aspiration events.
 - b. **Risk factors for aspiration** include emergency surgery, insufficient time spent NPO prior to induction, pregnancy, gastroparesis or other functional obstruction, bowel obstruction, and severe gastroesophageal reflux.
 - c. **Risk factors for aspiration pneumonia** include large volume of aspiration, aspiration of low pH content matter, aspiration of particulate matter, immunocompromised status, and known colonization of secretions.
 - d. **Treatment** of aspiration pneumonia should target the most frequent bacteria encountered: *S. aureus*, *Escherichia coli*, *Pseudomonas aeruginosa*, *Klebsiella pneumoniae*, and anaerobes. Broad spectrum antibiotics may be indicated if pneumonitis has not improved in the first 48 hours. Narrowing of antibiotics should be accomplished as soon as possible based on respiratory Gram stain and culture.
5. **Transfusion-related infections** have been minimized by using increasingly stringent testing protocols for all donated blood products. Use of appropriate transfusion thresholds can decrease the frequency and quantity of transfusion to additionally decrease related infection rates. (Table 7.1)

TABLE
7.1

Transfusion-Related Infection Risk

Transfusion-Related Infection	Risk
Bacterial infection (seen in platelet transfusion)	1 in 10,000
Parvovirus	1 in 35,000
Hepatitis C	1 in 150,000–400,000
Hepatitis B	1 in 200,000–500,000
Hepatitis A	1 in 1,000,000
HIV	1 in 1,500,000–2,000,000
Human T-lymphocytic virus 1 and 2	1 in 2,000,000–3,000,000
Syphilis	1 in 4,000,000

III. PERIOPERATIVE ANTIBIOTICS

A. Indications for Administration of Antibiotics in the OR

1. **Continuation of ongoing treatment** for active infection
2. **Prophylaxis against surgical site infection**
3. **Prophylaxis against endocarditis**

B. Principles of Prophylaxis

1. Surgical site infections occur approximately 500,000 times per year in the United States, according to the Centers for Disease Control and Prevention. These result in increased hospital stays, increased ICU admissions, increased health care expenses, and, most importantly, an increase in mortality of up to 50%.
2. **Surgical Care Improvement Project (SCIP)** is a national initiative to improve surgical outcomes. Antibiotics prophylaxis and stewardship are a major part of the measures.
 - a. **SCIP-1:** Preoperative antibiotic dosed within 1 hour before incision time. Of note, not all procedures warrant routine antibiotic prophylaxis.
 - b. **SCIP-2:** Prophylactic antibiotic must be SCIP recommended. See Table 7.2 for SCIP-recommended regimens.
 - c. **SCIP-3:** Prophylactic antibiotics must be discontinued within 24 hours of the anesthetic end time (exception is 48 hours for cardiac surgery).
3. **Timing and Administration**
 - a. As noted above, **antibiotic administration must occur within 60 minutes of incision** to allow appropriate blood and tissue levels. Care must be taken to ensure this, as administration may occur in an inpatient unit, in the preoperative area, in the emergency department, or in the OR. The institutional guidelines for the correct dose of antibiotics should be followed.
 - b. **Repeated dosing** is indicated for surgeries of long duration, surgeries with large blood loss, or large fluid replacement. Redosing is antibiotic specific. Cefazolin is the most frequently used perioperative antibiotic with a typical redosing schedule of every 4 hours intraoperatively.
 - c. Parenteral administration is standard. Slow intravenous push is appropriate for some antibiotics (i.e., cefazolin), and prolonged infusions are required for others (i.e., vancomycin).
 - d. Observation for **adverse reactions**.

TABLE
72
SCIP-Recommended Perioperative Prophylactic Antibiotics

Surgical Procedure/Site	SCIP-Approved Antibiotics
Coronary artery bypass grafting (CABG), other cardiac, or vascular Hip/knee arthroplasty	Cefazolin, cefuroxime, OR vancomycin ^a If β -lactam allergy: vancomycin ^b OR clindamycin Cefazolin, cefuroxime, OR vancomycin ^a If β -lactam allergy: vancomycin ^b OR clindamycin ^b
Colon	Cefotetan, cefoxitin, ampicillin/sulbactam, OR ertapenem ^c OR cefazolin OR cefuroxime <i>and</i> metronidazole If β -lactam allergy: clindamycin <i>and</i> aminoglycoside OR clindamycin <i>and</i> quinolone OR clindamycin <i>and</i> aztreonam OR metronidazole <i>and</i> aminoglycoside OR metronidazole <i>and</i> quinolone
Hysterectomy	Cefotetan, cefazolin, cefoxitin, cefuroxime, OR ampicillin/sulbactam If β -lactam allergy: clindamycin OR metronidazole

^a Justification for vancomycin is acceptable with provider documentation.

^b Cardiac, orthopedic, and vascular surgery, if patient is allergic to β -lactam antibiotics, vancomycin, or clindamycin are acceptable substitutes.

^c Single dose only.

1. Antibiotics are the second leading cause of anaphylaxis in the OR.
2. Agent-specific hypersensitivity reactions may be encountered (i.e., red man syndrome with vancomycin).
- e. As noted above, antibiotics should be discontinued within 24 hours to prevent development of drug-resistant organisms.
- C. Endocarditis Prophylaxis.** Patients with certain congenital and acquired cardiac conditions are at increased risk for infective endocarditis following specific surgical and dental procedures. In 2007, the American Heart Association released updated guidelines for endocarditis prophylaxis. This update narrowed both the list of cardiac abnormalities and the list of procedures for which prophylaxis is indicated. The reasoning behind this was the rarity of postoperative infective endocarditis and inconclusive evidence to support the use of prophylactic antibiotics.
 - 1. Prophylaxis for High-Risk Patients Only.** High-risk patients include (i) prosthetic cardiac valves or prosthetic material used in cardiac valve repair, (ii) history of infectious endocarditis, (iii) specific congenital heart diseases (CHD): unrepaired cyanotic CHD including palliative shunts and conduits, completely repaired CHD with prosthetic material or device in the initial 6 months after the procedure, or repaired CHD with residual defects at the site or adjacent to the site of the prosthetic device, and (iv) cardiac transplant recipients who develop valvulopathies. All other cardiac abnormalities do not need endocarditis prophylaxis.
 - 2. Prophylaxis for High-Risk Procedures Only.** High-risk procedures include (i) dental procedures that involve manipulation of gingival tissue, periapical region of the teeth, or perforation of the oral mucosa,

(ii) respiratory tract procedures only if there is incision or biopsy of respiratory mucosa, and (iii) skin and musculoskeletal tissue procedures only if the site is infected. Specifically gastrointestinal and genitourinary procedures are no longer considered high risk.

D. Surgical Wound Classification. Surgical wounds are classified based on risk of infection and help to guide antibiotic therapy.

1. **Clean** wounds are uninfected, show no signs of inflammation, do not enter the respiratory, gastrointestinal, or genitourinary tracts, and are closed primarily. The biggest risk for postoperative infections is from skin-colonizing bacteria such as *Staphylococcus* and *Streptococcus* spp.
2. **Clean-contaminated** wounds enter the respiratory, gastrointestinal, or genitourinary tracts without spillage of contents. Common pathogens are site dependent. Common respiratory pathogens include *Streptococcus pneumoniae*, *K. pneumoniae*, *S. aureus*, and *P. aeruginosa*. Common gastrointestinal pathogens include *E. coli*, *Proteus* spp., *Bacteroides* spp., and *Enterococcus* spp. Common genitourinary pathogens include *E. coli*, *Proteus* spp., *Klebsiella* spp., and *Staphylococcus saprophyticus*.
3. **Contaminated** wounds include gross spillage of nonpurulent contents and those with breaks in sterile technique. Common pathogens are site dependent.
4. **Dirty** wounds include gross spillage of purulent contents, existing infection or perforation, and organisms known to be present prior to the procedure. Again, common pathogens are site dependent.

E. Commonly Encountered Perioperative Antibiotics

1. **β -Lactams** include penicillins, carbapenems, monobactams, and cephalosporins. The common mechanism of action is inhibition of cell wall synthesis.
 - a. **Cefazolin**, a first-generation cephalosporin, is the most commonly administered perioperative antibiotic as it provides coverage of most of the gram-positive and many of the gram-negative bacteria that are seen with clean wounds. **Cefoxitin and cefotetan**, second-generation cephalosporins, extended coverage of gram-negative bacteria and anaerobic bacteria making them appropriate selections for clean-contaminated and contaminated wounds. **Ceftriaxone** and **ceftazidime**, third-generation cephalosporins, and **cefepime**, a fourth-generation cephalosporin, extend coverage further over gram-negative bacteria making them appropriate selections for dirty wounds in particular.
 - b. **Adverse reactions** include (i) hypersensitivity reactions from rash to anaphylaxis (10% of penicillin allergic patients are allergic to first-generation cephalosporins), (ii) central nervous system toxicity (especially high-dose penicillin), (iii) hematologic (platelet dysfunction with piperacillin or ticarcillin and impairment of clotting factor production with cefotetan), and (iv) interstitial nephritis (especially with methicillin or nafcillin).
2. **Clindamycin** inhibits protein synthesis at ribosomal subunits and is an appropriate alternative for β -lactam allergic patients. Coverage includes most gram-positive bacteria as well as many anaerobes. **Adverse reactions** include (i) rash (anaphylaxis is rare), (ii) hypotension with rapid administration, (iii) gastrointestinal distress, (iv) *C. difficile* colitis, and (v) potentiation of neuromuscular blockade.
3. **Vancomycin** inhibits cell wall synthesis at a different site than the β -lactams. It covers most gram-positive bacteria including MRSA but

provides no coverage of gram-negative bacteria, making it an appropriate selection for β -lactam allergic patients and patients colonized or infected with MRSA. **Adverse reactions** include (i) red man syndrome and hypotension from histamine release with rapid administration, (ii) hypersensitivity reactions, and (iii) increased nephrotoxicity and ototoxicity when administered with other agents at risk for causing nephrotoxicity and ototoxicity.

4. **Aminoglycosides** include gentamicin, tobramycin, streptomycin, and amikacin. The mechanism of action is inhibition of protein synthesis at a ribosomal subunit different from clindamycin. Coverage includes gram-positive and gram-negative aerobes and *Mycobacteria* spp. making them appropriate choices for combination therapy in wounds other than clean. **Adverse reactions** include (i) nephrotoxicity especially in patients with baseline renal impairment or other risk factors for renal impairment, (ii) ototoxicity, and (iii) potentiation of neuromuscular blockade.
5. **Fluoroquinolones** include ciprofloxacin, levofloxacin, and moxifloxacin. Mechanism of action is inhibition of bacterial DNA replication. Coverage includes extensive gram-negative bacteria, many gram-positive bacteria, and atypical bacteria making them appropriate choices for combination therapy in wounds other than clean. **Adverse reactions** include (i) gastrointestinal distress, (ii) hepatotoxicity, (iii) central nervous system effects especially in the elderly, and (iv) variable QT prolongation.
6. **Metronidazole** inhibits nucleic acid synthesis. Coverage includes most anaerobic organisms making it appropriate for combination therapy in wounds other than clean. **Adverse reactions** include (i) gastrointestinal distress, (ii) thrombophlebitis, (iii) hypersensitivity reactions, (iv) neurologic effects including peripheral neuropathy and (v) disulfiram-like reaction when combined with alcohol.

IV. PATHOGENIC ORGANISMS OF ANESTHETIC CONCERN

The Centers for Disease Control and Prevention (www.cdc.org) has current reviews of common pathogens, including all reviewed here.

A. Viruses

1. **Human immunodeficiency virus (HIV)**
 - a. **Transmission.** HIV is transmitted through percutaneous or mucosal exposure to infected blood or body fluids via needlestick or other sharps injury, blood transfusion, sexual contact, and perinatally from infected mother to neonate.
 - b. **Occupationally acquired HIV.** Risk is low for occupationally acquired HIV in health care workers. Risk of seroconversion after percutaneous exposure to blood from an HIV-positive patient is 0.3%. Risk is increased with deep injury, visible patient blood on the injurious device, a needle that was within a vein or artery in the HIV-positive patient, patients in the terminal stages of HIV, and larger bore hollow needles.
 - c. **Post-Exposure Prophylaxis (PEP).** In case of exposure, the Occupational Health Service of the institution should be contacted. Frequently updated guidelines are available for management of exposed health care workers on the CDC Web site (www.cdc.gov) and from the National Clinicians' PEP Hotline (888-448-4911). PEP must be initiated within 3 days of exposure making immediate reporting of exposure to occupational health of paramount importance. The decision to initiate PEP and the choice and duration of the PEP regimen are

based on numerous factors including type of exposure, volume of exposure, and sensitivity of the virus to antiretroviral agents. PEP is not 100% effective, and follow-up testing is necessary.

2. Hepatitis B Virus (HBV)

- a. **Transmission.** HBV is transmitted through percutaneous or mucosal exposure to infected blood or body fluids via needlestick or other sharps injury, blood transfusion, sexual contact, and perinatally from infected mother to neonate.
- b. **Occupationally acquired HBV.** Risk depends on immunization status of the health care provider, hepatitis Be antigen (HBeAg) status of the HBV-positive patient, and quantity of inoculate. Risk is increased in unimmunized health care workers (currently most hospitals and health care facilities require HBV vaccination and antibody titers prior to employment), source patients who are HBeAg positive, and when percutaneous exposure is via a hollow large bore needle. Risk of clinical hepatitis from HBeAg-negative percutaneous exposure via needlestick is 1% to 6%, but is 22% to 31% with HBeAg-positive percutaneous exposure via needlestick. 90% of acute HBV hepatitis resolves without sequelae; however, 10% become chronically infected and are at risk for chronic hepatitis, cirrhosis, and hepatocellular carcinoma.
- c. **HBV Vaccination.** Recombinant vaccination consisting of three vaccinations over 3 months is effective at least 90% of the time. As the nonresponder rate is 10%, verification of antibody titers should be completed for those who will be in contact with blood or bloody body fluids.
- d. **PEP.** Exposure to blood or body fluids from patients who are known to be hepatitis B surface antigen (HBsAg) positive or patients with unknown status who are high risk for HBV may require PEP. Immediate reporting of the event is of utmost importance. Vaccinated health care workers who have appropriate levels of hepatitis B surface antigen antibodies (HBsAb) (≥ 10 mIU/mL) require no treatment. Vaccinated health care workers who have low levels of HBsAb (< 10 mIU/mL) and previously unvaccinated health care workers are treated with hepatitis B immunoglobulin (HBIG) and vaccination/revaccination.

3. Hepatitis C Virus (HCV)

- a. **Transmission.** HCV is typically transmitted through large volume or repeated percutaneous exposure to blood, blood transfusion, perinatally from infected mother to neonate, and less commonly from sexual contact.
- b. **Occupationally acquired HCV.** HCV seroconversion from percutaneous exposure via needlestick or other sharps injury is approximately 1.8%. Of those infected with HCV, 80% become chronically infected and are at risk for chronic hepatitis, cirrhosis, and hepatocellular carcinoma.
- c. **PEP.** No PEP is currently recommended for HCV exposure. Close clinical and laboratory follow-up should continue to evaluate for necessity of treatment for chronic infection.

4. Herpes simplex virus (HSV) I and II

- a. **Transmission.** HSV is transmitted by direct contact between infected individuals, whether symptomatic or not, of infected secretions and mucosa or damaged skin.
- b. **Occupationally acquired HSV.** Herpetic whitlow is HSV infection of the finger that can occur in the health care setting from contact

with oral secretions of an infected individual. Symptoms include fever, painful and inflamed lesions, and localized lymphadenopathy. Persons with active herpetic whitlow can transmit HSV, so patient contact should be avoided.

5. **Cytomegalovirus (CMV).** CMV is a herpesvirus that in healthy patients is usually asymptomatic; however, it can be life threatening in immunocompromised patients and in utero. Transmission of CMV occurs via direct contact between a susceptible host (severely ill or immunocompromised) and infected source in the form of blood transfusion or organ transplantation. Infection can be acute or reactivation of a latent infection. To reduce this risk, CMV-negative immunosuppressed patients and CMV-negative pregnant patients should receive blood transfusions from CMV-negative donors if transfusion is required.

6. **Varicella-Zoster Virus (VZV)**

- a. **Transmission.** VZV (chicken pox and shingles) is transmitted via direct contact or airborne routes. Anesthesia providers can be exposed or expose others to VZV. Like CMV, VZV can be life threatening to immunocompromised patients and in utero.
- b. **VZV Vaccination.** VZV vaccination is indicated for all nonimmune health care workers who may come into contact with high-risk patient populations. A history of chicken pox as a child and/or antibody titers may be required by health care facilities as preemployment screening.

7. **Influenza Virus**

- a. **Transmission.** Influenza is transmitted via respiratory secretions in the droplet route. Anesthesia providers can acquire and spread influenza via their close involvement with respiratory secretions. Influenza is generally not life threatening in healthy individuals but may be life threatening in the immunocompromised, the chronically ill, and elderly patients.
- b. **Influenza Vaccination.** Most health care facilities now require annual vaccinations for health care workers.

B. Bacteria

1. **Mycobacterium tuberculosis.**

- a. **Transmission of tuberculosis (TB).** TB is transmitted via respiratory secretions via an airborne route. TB is often a latent or inactive disease that may be asymptomatic. Active TB most often occurs in immunocompromised and chronically ill patients.
- b. **Occupational TB.** Most health care facilities require annual testing of health care workers for TB via purified protein derivative (PPD) skin testing. Recent seroconversion warrants treatment with a course of isoniazid. Additionally, health care workers need to be fitted and trained for N95 respirators.

2. **Antibiotic resistant bacteria** is a growing problem in medicine. The rate of growth in antibiotic resistant bacteria is currently outpacing the development of new antimicrobial drugs. Poor antibiotic stewardship, prolonged hospitalizations, presence of indwelling catheters, and prolonged mechanical ventilation have contributed to the increase in antibiotic-resistant bacteria. Anesthesia providers can help prevent the transmission of and slow the rate of growth of antibiotic-resistant bacteria with strict infection control policies and antibiotic stewardship.

C. Prion Diseases

1. **Protein-containing infectious particles (prions)** cause diseases such as **Creutzfeldt-Jakob** and **kuru**. Transmission is from direct inoculation of

infected material into a host, with most commonly reported transmission being from dura transplantation. Epidemiologic studies are limited due to the long incubation time and rarity of the disease. Although the occupational risk for health care workers is believed to be very low, following a surgical procedure of confirmed or suspected disease decontamination of equipment is per specific protocols.

V. OCCUPATIONAL EXPOSURE TO INFECTIOUS DISEASE

A. Prevention of Exposure

1. Use **standard or universal precautions** as above.
2. **Observe needle safety.** The Centers for Disease Control and Prevention estimate that 385,000 needlestick and other sharps-related injuries occur in health care workers each year. Many safety needle and needleless systems have been designed and should be used preferentially over standard needles. Needles should never be recapped, and needles should be discarded in a labeled sharps container immediately after use.

B. Management of Exposure

1. **Wash exposed area.** Soap and water or sterile saline should be used to wash skin, and water or sterile saline should be used to flush mucous membranes. Specialized eye washing stations should be available.
2. **Immediate reporting of exposure** to occupational health or the emergency room (if after normal work hours) to ensure initiation of protocols for testing, PEP, and counseling.

VI. IMMUNOCOMPROMISED PATIENTS

A. Immunocompromised patients are at increased risk for community-acquired, nosocomial, and opportunistic infections. Immunocompromise can be due to malignancy, chemotherapy, HIV infection, corticosteroids, severe malnutrition, and immunosuppressive therapy for solid organ and bone marrow transplant recipients or severe autoimmune disease.

1. **Elective surgery** should be delayed if possible in the severely immunocompromised (i.e., total neutrophil count <500 cells/mm³).
2. Strict adherence to **sterile technique** is essential.
3. **Providers with respiratory infections** should not be involved in the care of severely immunocompromised patients. If unavoidable, the provider should wear a surgical mask during any contact with the patient.
4. Patients may be on **neutropenic precautions** that include specific dietary and environmental restrictions as well as the wearing of masks during transport.
5. **Antibiotic prophylaxis** is used in various immunocompromised patients for prophylaxis against postoperative wound infection and for long-term prophylaxis against opportunistic infections. It is important to verify which immunosuppressant drugs a patient is taking as many may interact with common perioperative medications. Cyclosporine, in particular, is associated with metabolism alteration and toxicity when combined with various antibiotics.

Suggested Readings

AHA Guideline. Prevention of Infective Endocarditis. *Circulation* 2007;116:1736–1754.
Centers for Disease Control and Prevention. Guidelines for preventing the transmission of *Mycobacterium tuberculosis* in health care facilities. *MMWR Morb Mortal Wkly Rep* 1994;43:1–132.

- Centers for Disease Control and Prevention. Updated U.S. Public Health Service Guidelines for the Management of Occupational Exposures to HBV, HCV, and HIV and Recommendations for Postexposure Prophylaxis. Available at: <http://www.cdc.gov/mmwr/preview/mmwrhtml/rr5011a1.htm>
- Centers for Disease Control and Prevention. Workbook for Designing, Implementing, and Evaluating a Sharps Injury Prevention Program. Available at: http://www.cdc.gov/sharpsafety/pdf/sharpsworkbook_2008.pdf
- Harbath S, Frankhauser C, Schrenzel J, et al. Universal screening for methicillin-resistant *Staphylococcus aureus* at hospital admission and nosocomial infection in surgical patients. *JAMA* 2008;299:1149–1157.
- Loftus R, Brown J, Koff M, et al. Multiple reservoirs contribute to intraoperative bacterial transmission. *Anesth Analg* 2012;114:1236–1245.
- Loftus R, Koff M, Burchman C, et al. Transmission of pathogenic bacterial organisms in the anesthesia work area. *Anesthesiology* 2008;109:399–407.
- The Joint Commission. Specifications Manual for National Hospital Inpatient Quality Measures. Available at: http://www.jointcommission.org/specifications_manual_for_national_hospital_inpatient_quality_measures.aspx

8

Safety in Anesthesia

Solmaz Poorsattar Manuel and May Pian-Smith

I. SAFETY IN ANESTHESIA

- A. Anesthesiology has led the patient safety movement, and anesthesia-related adverse outcomes have drastically declined since the 1960s. Despite this decline, the risks of both general and regional anesthesia remain. Recent data suggest that anesthetic-related mortality is 0.5 to 1/100,000 in the developed world.
- B. Adverse events are injuries resulting from medical care. Many systems and human factor errors can contribute to adverse events. Reason's "Swiss cheese model" of adverse event causation describes how, although many layers of defense lie between hazards and adverse events, there are gaps in each layer that, if aligned perfectly, can allow an event to occur.
- C. Errors can occur despite a practitioner's expertise, experience, and good intention. In the perioperative arena, errors can result from the following:
 - 1. **Organizational influences** including production pressure or improperly maintained equipment
 - 2. **Inadequate supervision**, which includes the unavailability of attending anesthesiologists to immediately assist junior residents
 - 3. **Preconditions** for unsafe acts include fatigued clinicians or improper communication practices
 - 4. **Specific individual acts**
- D. **Preventing adverse events** therefore relies on optimizing practitioners' understanding of the system and resources of their workplace, in addition to individual practice improvement. Strategies to create safer systems include the following:
 - 1. **Simplification**
 - 2. **Standardization**
 - 3. **Improving teamwork and communication**
 - 4. Developing an organizational culture that promotes **learning from past mistakes**. Strategies for individuals to decrease various types of errors are described below.

II. TYPES OF ERRORS

Errors are acts of commission (doing something wrong) or omission (failing to do the right thing) leading to an undesirable outcome. Anesthesiologists should be aware of, and actively work to mitigate, common types of errors.

A. Medication Errors. It is estimated that at least 5% of hospital patients experience an adverse drug event. The cost of preventable medication errors in US hospitals has been estimated at \$16.4 billion annually.

1. Examples of medication errors include administration of an inappropriate dose, administration through an inappropriate route, administration at an inappropriate rate, and administration to the incorrect patient. Some specific examples as follows:

- a. The rapid intravenous (IV) administration of undiluted dilantin or undiluted potassium can cause cardiovascular collapse or death.
- b. Neostigmine administered without a corresponding antimuscarinic drug can lead to severe bradycardia, asystole, and death.
- c. Inadvertent administration of a medication to which a patient has a known allergy.

2. Strategies to decrease medication errors:

- a. Have a thorough understanding of the pharmacokinetics, pharmacodynamics, and effects of each medication administered.
- b. Exercise extreme vigilance in drug administration. Double-check medications prior to administration and consider implementing the “Five Rights” checklist: right patient, right route, right dose, right time, and right drug prior to each administration.
- c. Have only **unit dosing** available in the patient care area. Unit dosing refers to packaging medications in quantities and concentrations that are safe and appropriate for administration without dilution.
- d. Involve clinical pharmacists during ICU rounds. Pharmacists can provide assistance with drug dosing questions and help identify medication errors immediately.
- e. Perform careful medication reconciliation when transitioning care between the floor, ICU, and OR. Medical reconciliation is the process of reviewing a patient’s complete medication regimen on both ends of care to avoid unintended inconsistencies.
Avoid confusing and potentially hazardous abbreviations. The Joint Commission has issued a list of high-risk “do not use” abbreviations. http://www.jointcommission.org/assets/1/18/Do_Not_Use_List.pdf
- f. Consider bar coding technology to decrease medication identification errors.

B. Procedure Errors

1. Examples of procedure errors include wrong-site surgery, retained instruments, and operating room fires. Higher volumes of certain surgeries or procedures being performed by a single physician or institution have been associated with better outcomes.

2. Strategies to reduce procedure errors:

- a. “Universal Protocols” should be implemented including signing site of surgery, using preprocedural time-outs, and using checklists.
- b. Intraoperative surgical instrument and sponge counts are used to prevent retention of surgical instruments in the patient. If the instrument counts at the end of the procedure indicate that an instrument is missing, radiography of the operative field is conducted in the OR to determine whether the instrument is in the patient.
- c. Recognize and avoid the fire safety triangle: ignition source (electrocautery, lasers) plus fuel source (gauze, drapes, ETT) plus oxidizers (oxygen, nitrous oxide) equals fire.
- d. The positive volume–outcome relationship for procedures argues for simulation training and specialization. Robust competency

training should take place for procedures such as vascular catheterization, advanced intubation techniques, and bedside ultrasound use.

- C. Cognitive errors** are not due to faulty knowledge, but involve faulty thought processes and subconscious biases. Cognitive errors are important contributors to missed diagnoses and patient injury.

1. Examples of cognitive errors: Table 8.1 lists 14 common cognitive errors.

TABLE 8.1 Cognitive Error Catalogue		
Cognitive Error	Definition	Illustration
Anchoring	Focusing on one issue at the expense of understanding the whole situation	While troubleshooting an alarm on an infusion pump, you are unaware of sudden surgical bleeding and hypotension
Availability bias	Choosing a diagnosis because it is in the forefront of your mind due to an emotionally charged memory of a bad experience	Diagnosing simple bronchospasm as anaphylaxis because you once had a case of anaphylaxis that had a very poor outcome
Premature closure	Accepting a diagnosis prematurely, failure to consider reasonable differential of possibilities	Assuming that hypotension in a trauma patient is due to bleeding, and missing the pneumothorax
Feedback bias	Misinterpretation of no feedback as “positive” feedback	Belief that you have never had a case of unintentional awareness, because you have never received a complaint about it
Confirmation bias	Seeking or acknowledging only information that confirms the desired or suspected diagnosis	Repeatedly cycling an arterial pressure cuff, changing cuff sizes, and locations, because you “do not believe” the low reading
Framing effect	Subsequent thinking is swayed by leading aspects of initial presentation	After being told by a colleague, “this patient was extremely anxious preoperatively,” you attribute postoperative agitation to her personality rather than low blood sugar
Commission bias	Tendency toward action rather than inaction. Performing unindicated maneuvers, deviating from protocol. May be due to overconfidence, desperation, or pressure from others	“Better safe than sorry” insertion of additional unnecessary invasive monitors or access; potentially resulting in a complication
Overconfidence bias	Inappropriate boldness, not recognizing the need for help, tendency to believe we are infallible	Delay in calling for help when you have trouble intubating, because you are sure you will eventually succeed

(continued)

TABLE
8.1

Cognitive Error Catalogue (*continued*)

Cognitive Error	Definition	Illustration
Omission bias	Hesitation to start emergency maneuvers for fear of being wrong or causing harm, tendency toward inaction	Delay in calling for chest tube placements when you suspect a pneumothorax, because you may be wrong and you will be responsible for that procedure
Sunk costs	Unwillingness to let go of a failing diagnosis or decision, especially if much time/resources have already been allocated. Ego may play a role	Having decided that a patient needs an awake fiberoptic intubation, refusing to consider alternative plans despite multiple unsuccessful attempts
Visceral bias	Countertransference; our negative or positive feelings about a patient influencing our decisions	Not troubleshooting on epidural for a laboring patient, because she is "high maintenance" or a "complainer"
Zebra retreat	Rare diagnosis figures prominently among possibilities, but physician is hesitant to pursue it	Try to "explain away" hypercarbia when MH should be considered
Unpacking principle	Failure to elicit all relevant information, especially during transfer of care	Omission of key test results, medical history, or surgical event
Psych-out error	Medical causes for behavioral problems are missed in favor of psychological diagnosis	Elderly patient in PACU is combative—prescribing restraints instead of considering hypoxia

From Stiegler MP, Neelankavil JP, Canales C, et al. Cognitive errors detected in anaesthesiology: a literature review and pilot study. *Br J Anaesth* 2012;108(2):229–235.

2. Strategies to decrease cognitive errors:

- a. Use **Bayesian reasoning** and **iterative hypothesis testing**. In Bayesian reasoning, probability estimate for a hypothesis is updated as additional evidence is acquired. With iterative hypothesis testing, a list of differential diagnoses is modified and re-ranked as more information becomes available. Each piece of new information triggers a recalibration of the probability of various diagnoses.
 - b. Be aware of performance-shaping factors that may adversely affect anesthesiologists' diagnostic abilities: noise, illness, aging, and especially sleep deprivation and fatigue.
 - c. Continually learn from experience: self-reflect, discuss with senior clinicians, and participate in M&M conferences.
- D. Human Factors Errors.** Human factors engineering is the applied science of systems design. It is concerned with the interplay between people and their work environments. Pioneering studies of human factors in anesthesia were integral to the redesign of anesthesia equipment, significantly reducing the risk of injury or death in the operating room. Experts in this field perform usability tests and heuristic analyses to identify error-prone devices or systems before they lead to harm.
- E. Care Transition and Handoff Errors**
1. **Examples of handoff errors:** The most common errors at the time of transitions and handoffs are medication errors and failure to follow-up diagnostic results.

2. Strategies to decrease handoff errors:

- Handoffs should occur at designated times and without distractions. The anesthetic record should indicate the time of the change.
- If possible, care transitions should be avoided during short procedures. They should be used carefully in complex cases.
- During a handoff, the following information should be clearly and accurately presented:
 - Prior clinical details.** The patient's diagnosis, surgical procedure, allergies, past medical and surgical history, relevant medications, and any pertinent laboratory values or studies.
 - Intraoperative management.** Status of the surgical procedure, airway assessment and management techniques, anesthetic plan, current vital signs with an explanation for any apparent abnormalities or trends, details of IV access and monitoring, blood loss and volume status assessment, status of the patient's blood bank sample plus blood product availability, anticipated need for additional intraoperative, and plan for postoperative recovery of the patient.
 - Handoffs should also address likely clinical scenarios and contingency plans.
- A handoff checklist may be used to ensure that complete information is communicated to the next responsible clinician. See Figure 8.1 for an example of the handoff checklist utilized at MGH.

F. Teamwork and Communication Errors. The operating room and intensive care unit are team environments. Teamwork enhances safety and may be essential for preventing or recovering from a critical situation.

Hand-Off Checklist

06:31 AM Refresh

☒ **Demographics**
 Age 60 Year ☒ Scheduled Procedure test
☒ Weight 68.18 Kg ☒ BMI 21.57 kg/m²

☒ **Past Medical History and Medications**
☒ Allergies: nkda Possible ☒ Diabetes Yes ☐ No Last Glucose Value 100 mg/dL

☒ **Airway**
☒ Airway Management ETT ☒ Mask Quality Good without adju ☒ View Grade 1, vocal cord see

☒ **Access**
☒ IV-1 Location Right forearm ☒ IV-1 Size 20G

☒ **Fluids**
 Total Urine 200 ml Total EBL 140 ml
 Total Crystalloids 1,000 ml

☒ **Perioperative Medications (pain relievers, muscle relaxants, vasoactive drugs)**
 Regional Anesthesia used: Epidural Insertion

☒ **Antibiotics**

Last Start Time	Last Dose	Last Antibiotic Name
Nov 9 2012 6:30AM	600 mg	Clindamycin

☒ **Intraoperative Concerns (tourniquet, clamp time, redosing of heparin)**

☒ **Postoperative Plan (emergence, disposition, pain control)**

☒ **Introduction of Incoming Anesthesia Provider**

Save + Close Save Close

FIGURE 8.1 Handoff checklist. This is an example of a tool to guide the transfer of patient care intraoperatively, from one anesthetist to another. EBL, estimated blood loss; HPI, history of present illness; PMH, past medical history; PSH, past surgical history; UO, urine output.

1. **Strategies to enhance teamwork and decrease communication errors:**
 - a. Start each day with effective introductions and end with debriefings.
 - b. Well-functioning teams are characterized by appropriate authority gradients and hierarchies that do not stifle the free flow of information. Authority Gradient refers to the established or perceived power hierarchy within a team, and how the distribution of power is balanced. Concentration of power in one person or in overbearing team leaders leads to a steep and inappropriate authority gradient. Expressing concerns, questioning, or even clarifying instructions would require considerable determination on the part of team members who perceive their input as devalued or frankly unwelcome. In contrast, inclusive leadership, where input from team members is invited and appreciated, is thought to allow for improved collaboration.
 - c. Develop an understanding of the responsibilities and functions of the other team members. During a crisis, maintain awareness of the other team members' actions.
 - d. Make requests and delegate tasks clearly and specifically by name. Delegate tasks to those who can best perform them.
 - e. Utilize **closed-loop communication** to avoid misunderstandings. When one individual gives a message, the receiver should repeat the message back to ensure it was heard correctly. Always confirm that critical interventions have been made as planned.
 - f. **Always communicate any concerns** early and clearly.

III. GENERAL SAFETY STRATEGIES

In addition to the specific measures to avoid common errors discussed above, an anesthesiologist's practice needs to include general daily strategies to maintain safety.

A. Prepare Comprehensive and Sound Preoperative Plans.

1. Prioritize goals and include contingencies for crises.
2. Become familiar with any new procedure, equipment, and/or anesthetic technique.
3. Prepare the patient.
4. Prepare the workspace. Pay specific attention to provider maneuverability, maintenance of an unobstructed visual field and adequacy of access to the patient and the anesthesia machine.
5. Obtain any additional medications or equipment that may be needed.
6. Label all medications.
7. Perform a complete checkout of the anesthesia workstation, monitors, and other devices.
8. Check backup equipment.
9. Know the location of emergency supplies and equipment.

B. Develop Situational Awareness.

1. Use a systematic approach to scanning the anesthesia machine, monitors, patient, surgical field, and surroundings. Arrange equipment and appropriate monitors in a way that facilitates scanning.
2. Continuously evaluate the patient's condition and the progress of the surgical procedure. Construct differential diagnoses to explain the observed events. Develop plans for different possible interventions.

C. Compensate for Stressors.

1. Recognize conditions that decrease personal performance: production pressure, noise, poor lighting, fatigue, boredom, illness, hunger, and interpersonal tension.
2. Optimize the work environment.

3. Recognize one's own limitations by asking for needed relief when overtired or ill.

D. Verify Observations.

1. Cross-check observations with redundant systems (e.g., check heart rate with both the electrocardiogram [EKG] and with the pulse oximeter) and assess covarying variables (e.g., look for a concomitant change in heart rate with an increase in blood pressure). When a situation does not make sense, review it with a second person.

E. Prepare for Crisis.

1. Be prepared for critical events. Make sure the entire care team is aware of the most likely critical events, actively plan for contingencies, and be prepared to revise the plan.
2. Review, practice, and use accepted protocols for emergencies and resuscitation.
3. Know where emergency checklists are located and have a low threshold for consulting them. Alternatively, "just in time" learning refers to reviewing cognitive aids just prior to a case, in anticipation of potential complications.
4. **Calling for help is an appropriate response when confronted with potentially overwhelming circumstances.** Learn to call for help early because it may not be available immediately.

F. Recognize and Address Production Pressures including Time and Economic Constraints.

These constraints sometimes conflict with adequate preoperative evaluation, preparation, and monitoring as well as create pressure to avoid canceling cases. If you are uncertain about proceeding with a case or believe it is unsafe to anesthetize a patient, address concerns explicitly to your colleagues. Pressure to put efficiency and output ahead of safety has caused catastrophic accidents in various industries. Patient safety must remain the highest priority, despite overt or covert pressures and incentives to emphasize production. Ultimately making quality a priority should also enhance efficiency.

- G. **Learn From Close Calls.** An event that nearly results in an adverse outcome should be used to improve future performance under similar circumstances. Develop institutional processes that enable mistakes to be analyzed and used as guides for education and process improvement.

IV. QUALITY ASSURANCE AND SAFETY IMPROVEMENT PROGRAMS

Institutional quality assurance programs must include a spectrum of activities aimed at maintaining and improving the quality of care and minimizing the risk of injury from anesthesia.

- A. **Just Culture.** Health care organizations should strive to create a **just culture**. A just culture is one that recognizes that even competent professionals make mistakes and that individual practitioners should not be held accountable for system failings over which they have no control. A just culture does not tolerate the conscious disregard of clear risks to patients; reckless behavior or gross misconduct. Personnel should always feel comfortable disclosing their own errors while maintaining professional accountability.
- B. **Standards and Guidelines.** Anesthesiologists should be aware of national and local safety policies and procedures. This includes policies for monitoring, response to adverse events, resuscitation protocols, perioperative testing protocols, and any special procedures or practices for the use of drugs, equipment, and supplies. The American Society of Anesthesiologists' standards and practice guidelines can be found at www.asahq.org.
- C. **Safety Training.** Anesthesia providers should obtain training in fire safety; electrical safety; OR evacuation; infection control procedures; and crisis

management. They should also be certified in advanced cardiac life support and, under certain circumstances, pediatric advanced life support and advanced trauma life support. Simulation techniques should be used wherever practical to allow practice under controlled conditions.

- D. Documentation.** Many systems depend on voluntary error reporting by providers. A safety report or quality assurance incident report should be completed for any unusual occurrence, unforeseen outcome, patient injury, or near miss, especially if follow-up action may be required to prevent recurrence. Incidents are reviewed by the departmental quality assurance committee, which receives additional information from those involved in the event and may suggest compensatory mechanisms as systematic factors are identified. Cases with special educational value should be presented at departmental case conferences. There should be ongoing analysis of all adverse events to identify and assess system problems and developing patterns.
- E. Guidelines for Action Following an Adverse Anesthesia Event.** Despite best efforts, errors may still occur. The objective of these guidelines is to limit patient harm from errors when they do occur, to ensure the causes of the event are identified, and to help prevent recurrence (Fig. 8.2).



FIGURE 8.2 Connections between review, improvement, and regulation help assure success. The ultimate goal of investigating critical events is to have fewer events. This goal is met when reviewers generate ideas about potential interventions to avoid similar events from occurring in the future. These ideas are then passed to the improvement and innovation arm, which tests the ideas and implements solutions to reduce the risk of future events. Interventions shown to be effective may be adopted by policymakers. (From Agarwala AV, McCarty LK, Pian-Smith MC. Anesthesia quality and safety: advancing on a legacy of leadership. *Anesthesiology* 2014;120(2):253–256.)

1. **The anesthesiologist** involved in an adverse event should do the following:
 - a. Continue to provide care for the patient.
 - b. Notify the anesthesia operating room administrator as soon as possible. If a resident or certified registered nurse anesthetist was involved in the event, he or she should notify the attending staff.
 - c. Document events in the patient record. If appropriate, include serial numbers or lot numbers of equipment or medication that was involved.
 - d. Do not alter the record.
 - e. Stay involved with the follow-up care.
 - f. Contact consultants as needed.
 - g. Submit a follow-up report to the department quality assurance committee.
 - h. Participate in apology and disclosure with the patient or patient's family.
 - i. Obtain support as needed.

Suggested Readings

- Agarwala AV, McCarty LK, Pian-Smith MC. Anesthesia quality and safety: advancing on a legacy of leadership. *Anesthesiology* 2014;120(2):253–6.
- American Society of Anesthesiologists. <http://www.asahq.org/publicationsAndServices/sgstoc.htm>. Accessed on August 2, 2014.
- Anesthesia Patient Safety Foundation. www.asahq.org. Accessed on August 2, 2014.
- Arriaga AF, Bader AM, Wong JM, et al. Simulation-based trial of surgical-crisis checklists. *N Engl J Med* 2013;368:246–53.
- Cooper JB, Gaba DM. A strategy for preventing anesthesia accidents. *Int Anesthesiol Clin* 1989;27:148–152.
- Cooper JB, Longnecker D. Safety and quality: The guiding principles of patient-centered care. In Longnecker D, ed. *Principles of Anesthesiology*, 2nd ed. New York: McGraw Hill Medical Publishing; 2012:16–26.
- Cooper JB, Newbower RS, Kitz RJ. An analysis of major errors and equipment failures in anesthesia management: considerations for prevention and detection. *Anesthesiology* 1984;60:34–42.
- Gaba DM. Anaesthesiology as a model for patient safety in health care. *BMJ* 2000;320:785–788. Available at: www.bmj.com/cgi/content/full/320/7237/785
- Gaba DM, Fish K, Howard S. *Anesthesia crisis management*. New York: Churchill Livingstone; 1994.
- Guohua L, Warner M, Lang BH, et al. Epidemiology of anesthesia-related mortality in the United States, 1999–2005. *Anesthesiology* 2009;110:759–765.
- Institute for Safe Medication Practice. www.ISMP.org. Accessed on August 2, 2014.
- Kohn LT, Corrigan JM, Donaldson MS, eds. *To Err is Human: Building a Safer Healthcare System*. Washington: National Academy Press; 1999.
- Leape LL. Error in medicine. *JAMA* 1994;272:1851–1857.
- Rall M, Gaba DM. Human performance and patient safety. In: Miller RD, ed. *Miller's Anesthesia*. New York: Elsevier Churchill Livingstone; 2010:93–150.
- Stiegler MP, Neelankavil JP, Canales C, et al. Cognitive errors detected in anaesthesiology: a literature review and pilot study. *Br J Anaesth* 2012;108(2):229–35.
- Watcher RM. *Understanding Patient Safety*, 2nd ed. New York: McGraw Hill Medical Publishing; 2012.

The Anesthesia Machine

Adeola O. Sadik and Gregory Ginsburg

I. OVERVIEW

The basic function of the anesthesia machine is to prepare a gas mixture of precisely known and variable composition for delivery to the patient. The machine delivers a controlled flow of oxygen, nitrous oxide, air, and anesthetic vapors. These are delivered to a breathing system, which provides a means to deliver positive-pressure ventilation and to control alveolar carbon dioxide by minimizing rebreathing and/or by absorbing exhaled carbon dioxide. A mechanical ventilator is connected to the breathing system, freeing the anesthetist's hands for other tasks. Various monitors are used to survey the functioning of the ventilation system, to detect equipment malfunctions, and to provide information about the patient.

II. THE GAS DELIVERY SYSTEM (FIG. 9.1)

A. Gas Supplies

1. **Piped gases.** Wall outlets deliver oxygen, nitrous oxide, and air, from a central supply source, at a pressure of 50 to 55 pounds/in² (psi). These outlets and the supply hoses to the machine are diameter indexed and color coded in order to safeguard against the administration of a hypoxic gas mixture.
2. **Cylinders.** Gas cylinders are used as backup sources when wall delivery fails or in locations where piped anesthesia gases are not available. Anesthesia machines use the size E cylinder. In a similar fashion to the gas supply hoses, cylinder colors are specific for each gas and pin indexed to prevent connection to the wrong regulator. It is important to make sure that each anesthesia machine has a cylinder wrench to enable the flow of gas when piped gases are not available.
 - a. **A full cylinder of oxygen** (green) has a pressure of 2,000 to 2,200 psi and contains the equivalent of 660 L of gas at atmospheric pressure and room temperature. The oxygen cylinder pressure decreases in direct proportion to the amount of oxygen remaining in the cylinder.
 - b. **A full cylinder of nitrous oxide** (blue) has a pressure of 745 psi and contains the equivalent of 1,500 L of gas at atmospheric pressure and room temperature. The nitrous oxide in the full cylinder is primarily in the liquid phase; the cylinder pressure does not decrease until the liquid content is exhausted, at which time approximately one fourth of the total volume of gas remains.
 - c. **Air cylinders** are present on some machines. A full cylinder (yellow) has a pressure of 1,800 psi and contains the equivalent of 630 L at atmospheric pressure and room temperature.
 - d. **Pressure regulators** reduce the high pressure from the cylinders to about 45 psi (just below pipeline pressure) so that, when cylinder gases are used, adjustments at the flow valves (rotameters) are not needed to compensate for the changing pressure that occurs as the cylinders empty. If both cylinders and pipelines are connected and open, gas flows preferentially from the pipeline because its pressure is slightly higher than the regulated cylinder pressure.

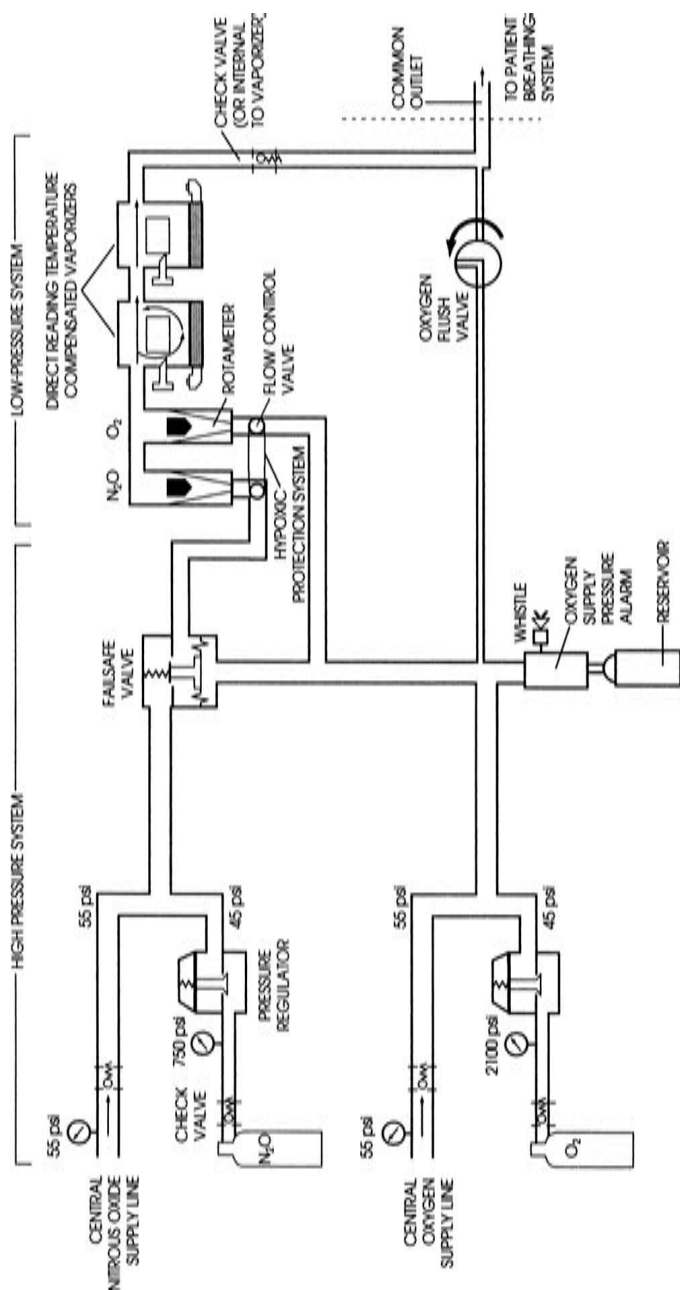


FIGURE 9.1 Schematic of an anesthesia machine. There are many variations in the design depending on vintage and manufacturer.

The regulators divide the machine into high-pressure (proximal to the regulator) and low-pressure (distal to the regulator) systems. In the event that the pipeline pressure fails or is less than the cylinder pressure, the cylinder will supply the gas until it is emptied.

B. Flow control valves and flowmeters control and measure gas flows.

1. **A needle valve** controls the flow of each gas. As a safety feature, the oxygen control knob has a different texture and, occasionally, protrudes more than the nitrous oxide and air controls. The needle valves also reduce gas pressures from 45 to 55 psi (high pressure) to near atmospheric pressure (low pressure).
2. **Flowmeters.** The traditional flowmeter is a calibrated tapered glass tube in which a bobbin or a ball float is used to indicate the flow of gas. Flowmeters with a ball float should be read in the middle of the ball. Meters with a bobbin should be read at the top of the bobbin. Newer anesthesia machines have electronic flowmeters and displays that often provide a digital readout. The oxygen flowmeter is always placed downstream so that a leak will be less likely to result in delivery of a hypoxic gas mixture.

C. Vaporizers. Anesthesia machines are outfitted with one or more temperature-compensated flow-over vaporizers calibrated to deliver a specific concentration of anesthetic measured as percent by volume. These vaporizers operate on the principle that a small proportion of the total gas mixture delivered to them is diverted into a vaporizing chamber, where it becomes fully saturated with anesthetic before it is added back to the main flow. The concentration of anesthetic delivered by the vaporizer is therefore proportional to the amount of gas passing through the vaporizing chamber, which is controlled primarily by the vaporizer dial. Because saturated vapor pressure varies with temperature, a secondary mechanism alters the amount of gas diverted through the chamber to compensate for temperature changes. The vaporizers are calibrated for a specific anesthetic and have pin-indexed filling adapters to prevent inadvertent addition of an incorrect anesthetic to a vaporizer. The vaporizing chamber is enclosed in a metal case to enhance heat transfer and to compensate for the heat lost from cooling as the anesthetic evaporates. The desflurane vaporizer is heated and pressurized to compensate for the anesthetic's relatively high vapor pressure and the extreme cooling that occurs when high concentrations are vaporized.

- D. **The Common Gas Outlet** is the port where gases exit the machine; it is connected to the breathing system via the fresh gas hose.
- E. **Oxygen Flush Valve.** One hundred percent oxygen at 45 to 55 psi comes directly from the high-pressure system to the common gas outlet. Oxygen flow can be as high as 40 to 60 L/minute. Caution should be taken when using this valve for intubated patients in order to prevent barotrauma.

III. BREATHING SYSTEMS

The circle system is most commonly used. The T-piece systems (Mapleson D and F) are used in infants because of low resistance and small dead space.

- A. **The Circle System.** The circle system incorporates a carbon dioxide absorber and prevents rebreathing of exhaled carbon dioxide. The system allows low fresh gas flows that conserve use of expensive inhalation anesthetics and maintain higher humidity and temperature within the breathing circuit. The circle consists of an absorber, two one-way valves, a Y-piece adapter, a reservoir bag, and an adjustable pressure limiting (APL) "pop-off" valve (Fig. 9.2).

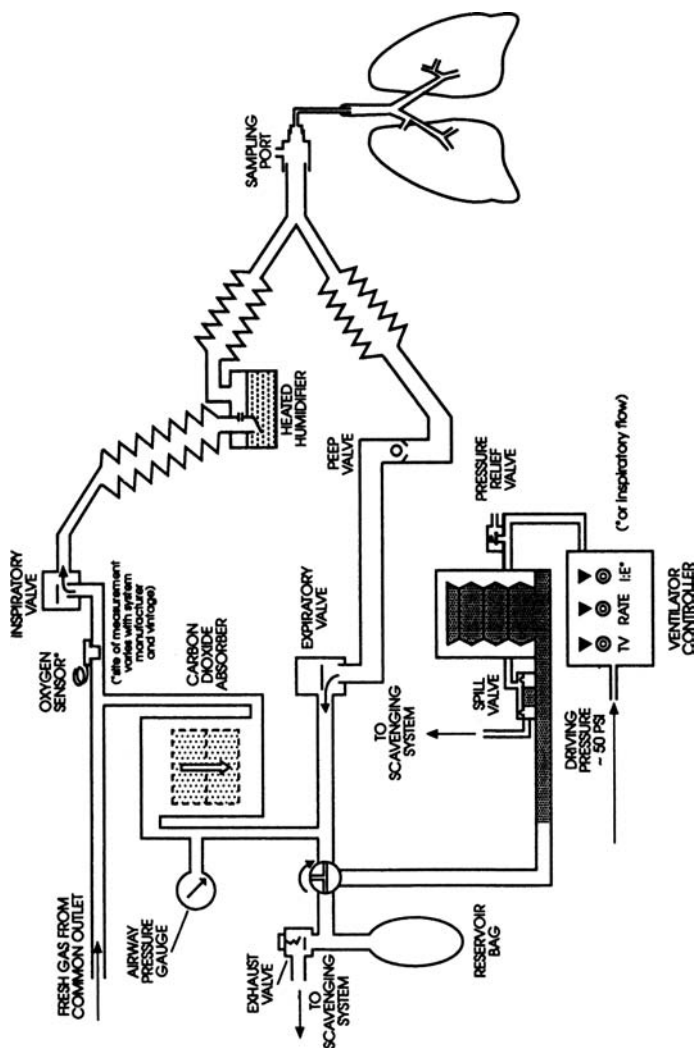


FIGURE 9.2 Representative circle breathing system with ventilator. The airway pressure gauge may sense on the patient side of the inspiratory valve. The PEEP valve may be integral to the ventilator. Other variations are possible depending on the manufacturer.

1. The **carbon dioxide absorber**. Soda lime ($\text{CaOH}_2 + \text{NaOH} + \text{KOH} + \text{silica}$) or Baralyme ($\text{Ba}[\text{OH}]_2 + \text{Ca}[\text{OH}]_2$) contained in the absorber combines with carbon dioxide, forming CaCO_3 and liberating heat and moisture (H_2O). A pH-sensitive dye changes to blue-violet, indicating exhaustion of the absorbing capacity. In older machines with a two-tiered canister system, the top canister should be changed when 25% to 50% of the pellets have changed color, although a second canister provides a safety margin. The size of the container used should accommodate a patient's tidal volume for maximum efficiency.
 2. Two **one-way valves** (inspiratory and expiratory) ensure that exhaled gas is not rebreathed without passing through the carbon dioxide absorber.
 3. The **Y-piece adapter** is used to connect the inspiratory and expiratory sides of the system to the patient.
 4. The **reservoir bag and APL valve** are located on the expiratory limb. The reservoir bag accumulates gas between inspirations. It is used to visualize spontaneous ventilation and to assist ventilation manually. Typically, a 3 L reservoir bag is used for adult patients; smaller bags may be appropriate for pediatric patients. The APL valve is used to control the pressure in the breathing system and allows excess gas to escape. The valve can be adjusted from fully open (for spontaneous ventilation, minimal peak pressure 1 to 3 cm H_2O) to fully closed (maximum pressure 75 cm H_2O or greater). Dangerously high pressures that may produce barotrauma and hemodynamic compromise can occur if the valve is left unattended in the fully or partially closed position.
- B. The T-Piece Systems.** The T-piece systems are single-limbed rebreathing systems. Because there is no CO_2 absorber, rebreathing of CO_2 is inevitable unless a fresh gas flow at least equal to the patient's peak flow is used. Inspired CO_2 concentration is controlled by the fresh gas flow and/or by varying the minute ventilation. Mapleson classified all possible configurations of single-limbed rebreathing systems (the T-pieces included) according to the relative position of the patient, fresh gas flow, reservoir bag, and valve. The Mapleson D and F systems are used most frequently and are both T-piece systems. All the T-piece systems require high fresh gas flows (at least two to three times minute ventilation) to prevent rebreathing during spontaneous ventilation. Capnography is useful to verify sufficient washout of carbon dioxide.
1. The **Mapleson D** circuit is a semiclosed system with a reservoir bag and APL valve at the machine end with fresh gas entering at the patient end (Fig. 9.3).
 2. The **Bain** circuit is a coaxial version of the Mapleson D. The fresh gas delivery tube is a small-diameter uncorrugated tube that runs inside the corrugated wide-diameter expiratory limb. Inspired gases are warmed, and the system appears simpler, but there is a risk of hypoxia if leaks develop, so the circuit should always be carefully checked for leaks before use.
 3. The **Mapleson F** circuit (Jackson-Rees modification of the Ayres T-piece or Mapleson E) is particularly useful in neonates and small infants. It consists simply of an open-ended reservoir bag and a defined length of corrugated breathing tube, with fresh gas entering the system at the patient end. Manual ventilation of small patients is accomplished well with this system because the anesthetist can adjust the filling of the open-ended reservoir bag with his or her hand, making the bag a sensitive indicator of lung compliance. The system also allows the anesthetist to be near the infant while manually ventilating. The advantages of this system have been reduced by the introduction of scavenging

systems that increase its weight and by improvements in alternative systems (e.g., low-compliance breathing tubes and improvements in mechanical ventilators).

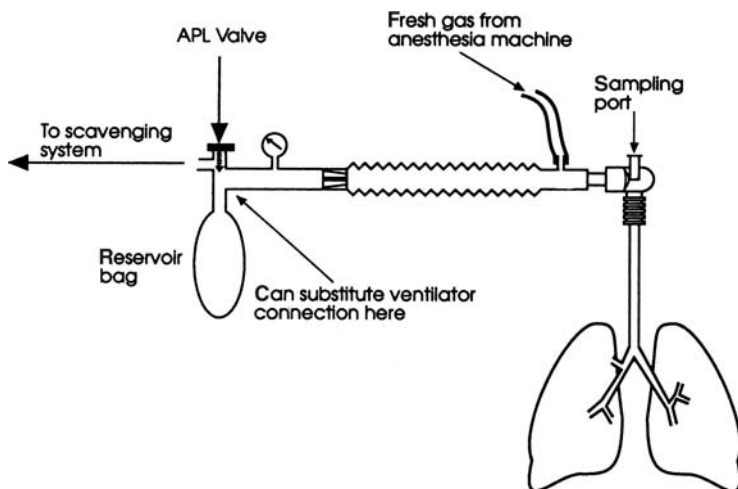


FIGURE 9.3 Schematic of a Mapleson D breathing system. In the Bain modification, the fresh gas flows through a tube that runs through the corrugated tubing.

IV. ANESTHESIA VENTILATORS

- A. Conventional anesthesia machines** are fitted with a mechanical ventilator that uses a **collapsible bellows within a closed chamber**. The bellows is compressed intermittently when oxygen or air is directed into the chamber, thereby pressurizing it. The ventilators are time-cycled flow (as opposed to pressure) generators, controlled both mechanically and electronically and pneumatically driven (requiring 10 to 20 L of driving gas per minute). Ventilator controls vary among makes and models. Some ventilators require setting of minute ventilation, rate, and inspiratory/expiratory (*I/E*) ratio to produce the desired tidal volume; other ventilators allow direct adjustment of the tidal volume, with *I/E* ratio dependent on the inspiratory flow rate (which is set independently). A portion of the fresh gas flow delivered by the machine adds to the set tidal volume during the inhalation phase. For example, an increase in total fresh gas flow from 3 to 6 L/minute will increase delivered minute ventilation by an additional 1 L/minute at an *I/E* ratio of 1:2 or by 1.5 L/minute at an *I/E* ratio of 1:1 (more inspiratory time in the latter). Although gas-driven ventilators can be safely driven with either oxygen or air, most often oxygen is chosen and is supplied by pipeline. Whether cylinder gases are used to drive the ventilator in the event of pipeline failure is usually determined by the user. If the machine is set up to drive the ventilator using cylinder oxygen, mechanical ventilation should be discontinued in the event of pipeline failure to conserve oxygen supplies.
- B. Flow generators** deliver a set tidal volume regardless of changes in patient's compliance (unlike pressure generators) but will not compensate for system leaks and may produce barotrauma because high pressures can be

generated. They reliably deliver the preset tidal volume (even in the presence of a small leak). The risk of barotrauma is minimal when patients have healthy and normally compliant lungs.

- C. For infants and patients with diseased lungs, maintaining preset tidal volumes may produce unacceptably high airway pressures and increased risk of barotrauma. **Pressure generators** are more appropriate in these situations, because airway pressure is controlled.
- D. The lack of flexibility of many older anesthesia machine ventilators severely limits their use in the setting of abnormal lung mechanics. In these situations, the use of manual ventilation or a critical care ventilator may be preferred. Modern anesthesia machines feature versatile **microprocessor-controlled ventilators**, which allow for sophisticated manipulation and monitoring of airway pressures (e.g., variable positive end-expiratory pressure [PEEP]) and flow rates. These ventilators incorporate a piston rather than a bellows and are also notable for more consistent delivery of set tidal volumes independent of fresh gas flow rates. As is the case with ICU ventilators, newer anesthesia machines are capable of multiple modes (such as pressure control, pressure support, synchronized mandatory, and inverse ratio ventilation), thereby enabling the anesthetist to optimize ventilation, oxygenation, hemodynamics, and weaning.

V. SAFETY FEATURES

- A. An **Audible Oxygen Alarm** is fitted in the oxygen supply line of the high-pressure system. It consists of a pressure regulator and a reed or whistle that will sound when the pressure in the supply line is greater than 0 and less than about 25 psi.
- B. A pressure-operated **"fail-safe" valve** in the high-pressure system of the nitrous oxide supply line opens only when oxygen pressure in the high-pressure system is above 25 psi. If the oxygen pressure falls below that, nitrous oxide will cease to flow. Because both the audible oxygen alarm and the fail-safe valve respond specifically to low pressure in the oxygen supply line of the high-pressure system, neither protects against the delivery of a hypoxic mixture downstream in the low-pressure system (e.g., if the oxygen flow control valve is accidentally shut off).
- C. **Oxygen Ratio Control.** Anesthesia machines are typically fitted with a device to control the proportion of oxygen delivered. This may take the form of a mechanical link between the oxygen and nitrous oxide flow control knobs that will not allow a fraction of inspired oxygen (F_{IO_2}) of less than 25% to be set. Alternatively, some machines incorporate an oxygen ratio monitor that sounds an alarm if a low F_{IO_2} is set.
- D. **Pressure alarms** are incorporated into all anesthesia machines.
 1. A **low-pressure alarm** is triggered by a period of no pressure in the system or by a sustained pressure drop below atmospheric pressure. Low pressure may be caused by a disconnection or a large leak in the system. Negative pressure usually indicates a scavenging system malfunction or that the patient is inhaling against an obstruction.
 2. A **high-pressure alarm** may have a variable or a preset (e.g., 65 cm H₂O) limit. A high-pressure alarm may indicate obstruction in the tubing or endotracheal tube or a change in the pulmonary compliance (e.g., bronchospasm, pneumothorax, laparoscopic insufflation, or "light anesthesia").
 3. A **continuing pressure alarm** alerts the user in the event of high pressure being sustained for more than a few seconds. A blocked or closed pop-off valve, a malfunctioning ventilator pressure relief valve, or an obstruction in the scavenging system could create this condition.

VI. SCAVENGING

A scavenging system channels waste gases away from the operating room to a location outside the hospital building or a location where the gases can be discharged safely (e.g., to a nonrecirculating exhaust ventilating system). The ambient concentration of anesthetic gases in the operating room should not exceed 25 parts per million (ppm) for nitrous oxide and 2 ppm for halogenated agents. Specific anesthetic gas-scavenging systems should be used routinely. These systems consist of a collecting system, a transfer system, a receiving system, and a disposal system.

- A. The **Collecting System** delivers waste gases to the transfer system and operates from the APL valve and from the expiratory valve of the ventilator. In addition, waste gases may be collected from the gas analyzers.
- B. The **Transfer System** consists of tubing that connects the collecting and receiving systems.
- C. The **Receiving System** ensures that neither positive nor negative pressure builds at the patient end of the system. The system may be open or closed. An open system consists of a reservoir canister opened to atmosphere at one end. Suction usually is applied to the canister, exhausting the waste gas. A closed system consists of a reservoir bag with positive and negative pressure relief valves to maintain the pressure in the bag within an acceptable range.
- D. The **Disposal System** may be passive or active, although passive systems are inadequate for modern hospitals. A passive system consists of wide-bore tubing that carries gases directly to the exterior or into the exhaust ventilation ducts. Active systems can be powered by vacuum systems, fans, pumps, or Venturi systems.

VII. GAS ANALYSIS

Several methods are used to monitor concentrations of O_2 , CO_2 , and anesthetic gases in the breathing system. The oxygen analyzer is the most important monitor for detecting a hypoxic gas mixture. Capnometry, the measurement of CO_2 , has many uses, including monitoring the adequacy of ventilation and detecting breathing system faults. Breath-to-breath monitoring of anesthetic concentrations provides tracking of anesthetic uptake and distribution. Most gas analyzers incorporate alarms. Among the techniques for measurement are the following:

- A. **Mass spectrometry** was first used to provide rapid response measurement of the concentration of any gas. The major limitation was the large size of that required housing in a central location to serve multiple operating rooms. A sample of gas withdrawn through a side port in the breathing system near the Y-piece was carried through a nylon catheter to the mass spectrometer. After ionization in an electron beam, the resulting fragments are accelerated through a high-voltage field and then subjected to a deflecting magnetic field. The specific fragments are detected on collectors, and the relative concentration of each agent is determined. Calibration is performed automatically at the central system. By a switching system, the mass spectrometer can sample from numerous locations. The time between measurements in each room may be one or several minutes depending on the number of rooms "on line." A "stat" sample may be requested.
- B. **Infrared analysis** uses spectrophotometry and Beer law to provide continuous measurement of the concentration of gas or anesthetic in a gas mixture. Gases that have two or more different atoms in the molecule absorb infrared radiation; thus, infrared analysis can be used to

measure concentrations of CO_2 , N_2O , and halogenated anesthetics but not O_2 . Typically, some gas is withdrawn from the breathing system at a steady rate (50 to 300 mL/minute) and passed into a small measurement chamber in the instrument. Pulses of infrared energy at a wavelength that is absorbed only by the gas of interest are beamed through the gas, and the difference in energy absorbed is used to determine the gas concentration. In some capnographs, a miniaturized measurement chamber and sensor are placed in the breathing system. In most infrared instruments, only one preselected volatile anesthetic can be measured at a time.

- C. Oxygen Analyzers.** Continuous measurements of oxygen concentrations in a mixture of gases can be provided by mass spectrometry; polarographic, galvanic, or fuel cell analysis; or paramagnetic analysis.

- 1. Polarographic oxygen analyzers** are placed in the inspiratory limb of the circuit. The sensor consists of an anode and a cathode in an electrolyte solution with a polarizing voltage. Oxygen diffuses through a semipermeable membrane into the electrolyte solution, after which a current flows that depend on the uptake of oxygen at the cathode and thus on the partial pressure of oxygen. Sensors have a limited life span and should be placed in the upright position to avoid accumulation of moisture.
- 2. Galvanic or fuel cell analyzers** are similar to polarographic cell analyzers except that different anode, cathode, and electrolyte materials are used, and no polarizing voltage is applied. This cell is similar to a battery that consumes oxygen.
- 3. Paramagnetic analyzers.** These analyzers are based on the principle that oxygen is paramagnetic and therefore attracted to a magnetic field, whereas most other gases are weakly diamagnetic and therefore repelled from a magnetic field. Modern miniaturized paramagnetic analyzers incorporate a rapidly oscillating magnetic chamber and are capable of **breath-to-breath analysis**. They are often combined with another gas analysis technique in an anesthetic agent monitor.

VIII. ACCESSORIES

- A. A backup means of positive-pressure ventilation** (self-inflating bag) should be available for any anesthetic procedure. In many operating rooms, these bags can be found on the back of the anesthesia machine.
- B. A humidifier** may be used and is indicated especially for infants and small children and during high-flow anesthesia. Two types are used during anesthesia: water bath and condenser humidifiers. Water bath humidifiers are associated with a risk of overheating (with consequent injury to the patient) and with risk of infection. Condenser humidifiers increase the resistance of the breathing system but are simpler to use than water bath humidifiers. High resistance makes them unsuitable for use with small children.
- C.** Many new machines have built-in **PEEP** capability.
- D. A flashlight** should be available in case of power failure.
- E. Computerized information management systems**, including electronic anesthetic records, are increasingly replacing written medical and anesthetic records. Advantages may include enhanced documentation including automated perioperative patient data collection, accessible databases that facilitate quality improvement and resource utilization, enhanced billing accuracy and completeness, and efficient compliance with various regulatory and accreditation requirements.

IX. NEXT-GENERATION ANESTHESIA MACHINES

The conventional anesthesia machine works well and meets almost all needs. Machine-related morbidity and mortality are usually attributable to human misuse (e.g., unrecognized breathing circuit disconnection) rather than to true equipment failure. Conventional machines are at the end of their evolutionary cycle, however, and the introduction of a new generation of machines is well under way. **Next-generation anesthesia machines** present many challenges to anesthetists in terms of their increased complexity, changed layout and function, and integration of new technologies. Notable advantages of some newer machines include the following:

- A. **Electronic interfaces** that facilitate more versatile and precise measurement and manipulation of gas concentrations, airway pressures, and ventilation (controlled and assisted).
- B. More numerous and adaptable alarms.
- C. **Fewer external connections**, possibly reducing the incidence of disconnections, misconnections, kinking, and other mishaps.
- D. **Automated machine self-checkout**, which likely enhances the detection rate of malfunctions while also freeing the anesthetist to perform other tasks.
- E. **Enhanced data collection** to facilitate integration with computerized information management systems.

X. ANESTHESIA MACHINE CHECKOUT RECOMMENDATIONS

This checkout, or a reasonable equivalent, should be conducted before administering anesthesia. These recommendations are valid only for an anesthesia system that conforms to current and relevant standards and the following monitors: capnograph, pulse oximeter, oxygen analyzer, respiratory volume monitor (spirometer), and breathing system pressure monitor with high- and low-pressure alarms. This is a guideline that users are encouraged to modify to accommodate differences in equipment design and variations in local clinical practice. Such local modifications should have appropriate peer review. Users should refer to the operator's manual for the manufacturer's specific procedures and precautions, specifically the manufacturer's low-pressure leak test. (**Note:** If an anesthesia provider uses the same machine in successive cases, the steps denoted by an asterisk [*] below may not need to be repeated and may be abbreviated after the initial checkout.)

- A. **Emergency Ventilation Equipment.** Verify that backup ventilation equipment is available and functioning.*
- B. **Suction Device.** Verify that a suction device is available and of adequate pressure remove airway fluids.
- C. **High-Pressure System**
 1. **Check oxygen cylinder supply.*** Verify oxygen cylinder supply
 2. **Check central pipeline supplies.*** Check if hoses are connected properly, and pipeline pressure gauges read approximately 50 psi.
- D. **Low-Pressure System**
 1. **Check initial status of low-pressure system.***
 - a. Close flow control valves and turn vaporizers off.
 - b. Check fill level and tighten vaporizers' filler caps.
 2. **Turn on the machine's master switch and all other necessary electrical equipment.***
 3. **Test flowmeters.*** Adjust flow of all gases through their full range, checking for smooth operation of floats and undamaged flow tubes.
- E. **Scavenging System.** Check and adjust the scavenging system.*
- F. **Breathing System**
 1. **Calibrate O₂ monitor.** Verify that low O₂ alarm is enabled and functioning.

2. **Check initial status of the breathing system.**
 - a. Check that breathing circuit is complete, undamaged, and unobstructed.
 - b. Verify that CO₂ absorbent is adequate.
3. **Perform leak check of the breathing system (some or all portions of this section may be automated and/or require different values per manufacturer recommendation).**
 - a. Set all flowmeters to 0 (or the minimum value).
 - b. Close APL (pop-off) valve and occlude Y-piece.
 - c. Pressurize breathing system to 30 cm H₂O with O₂ flush.
 - d. Ensure that pressure remains fixed for at least 10 seconds.
 - e. Open APL (pop-off) valve and ensure that pressure decreases.
- G. **Manual and Automatic Ventilation Systems.** Test ventilation systems and uni-directional valves.
- H. **Monitors.** Check, calibrate, and/or set alarm limits of all monitors.
- I. **Final Position.** Check final status of the machine.
 1. Vaporizers off
 2. APL valve open
 3. Selector switch to "Bag"
 4. All flowmeters to 0
 5. Breathing system is now ready to use

Suggested Readings

- Dorsch JA, Dorsch SE, eds. *A Practical Approach to Anesthesia Equipment*. Philadelphia: Lippincott Williams & Wilkins; 2011.
- Dorsch JA, Dorsch SE, eds. *Understanding Anesthesia Equipment*, 5th ed. Philadelphia: Lippincott Williams & Wilkins; 2008.
- Ehrenwerth J, Eisenkraft J, Berry J, eds. *Anesthesia Equipment: Principles and Applications*, 2nd ed. Philadelphia: Elsevier Saunders; 2013.
- Olympio MA. Modern anesthesia machines offer new safety features. *Anesth Patient Saf Found News* 2003;18:17–32.
- Sandberg WS, Urman RD, Ehrenfeld JM. *The MGH Textbook of Anesthesia Equipment*. Philadelphia: Elsevier Saunders; 2011.

I. STANDARD MONITORING

The ASA Standards for Basic Anesthetic Monitoring state that an anesthetist should be present and that oxygenation, ventilation, circulation, and temperature should be continually evaluated during all anesthetics.

A. Standard Monitoring for General Anesthesia

For all anesthetics, the monitoring of circulation, oxygenation, ventilation temperature is required. The minimal requirements for general anesthesia include an oxygen analyzer to confirm the administered FIO_2 , pulse oximetry, electrocardiogram (ECG), blood pressure measurement, and the ability to assess temperature. Capnography (Chapters 14 and 15) is mandatory for general anesthesia and recommended for monitored anesthesia care and regional anesthesia.

B. Additional Monitoring

The patient's comorbidities and operative procedure may require additional monitors to measure arterial and venous pressures, cardiac function (Chapters 2 and 24), neuromuscular blockade (Chapter 13), and central nervous system activity (Chapters 11 and 25).

II. CARDIOVASCULAR SYSTEM

Circulation may be assessed with clinical signs, ECG, noninvasive and invasive blood pressure monitoring, central venous pressure (CVP), pulmonary artery cannulation, and echocardiography.

- A. Clinical signs and symptoms of perfusion abnormalities** are often limited during general anesthetics but are important to assess in the preoperative period (Chapter 1) and may include alterations in mental status, neurologic deficits, dyspnea, chest pain, cool limbs, diminished pulses, and poor capillary refill.
- B. ECG.** The ECG is used to determine the heart rate and to detect and diagnose dysrhythmias, myocardial ischemia, pacemaker function, and electrolyte abnormalities. The presence of an ECG signal does not guarantee cardiac contraction and output.

1. Mechanism of monitoring

- a. Electrode pads.** ECG electrodes measure a small electrical signal (about 1 mV). This makes the ECG prone to electrical interference from outside sources and requires proper electrode application to clean, dry skin.
- b. Electrode locations.** To effectively detect dysrhythmias and ischemia, the pads must be placed in consistent locations on the body. Limb leads must be placed on or near their appropriate limbs and the precordial lead (V5) at the fifth intercostal space, anterior axillary line.
- c. Modes and options**
 - 1. Monitors often have several choices for filtering of noise, most commonly called “diagnostic” and “monitor” modes. The monitor mode filters out noise by using a narrowed bandpass (0.5 to 40 Hz), while the diagnostic mode filters less signal and noise by using a wider bandpass (0.05 to 100 Hz). The diagnostic mode should be used when monitoring for ischemia.

2. Automatic trending of ST segment changes is useful monitoring for the development of ischemia over time.
2. **Rhythm detection.** The relationship between the P and QRS waves allows for dysrhythmia diagnosis; the P wave is best seen in lead II.
3. **Ischemia detection.** Monitoring leads II and V5 allows for detection of ischemia in 95% of patients since it monitors a large area of the myocardium. Lead II monitors the inferior portion of the heart, supplied by the right coronary artery. Lead V5 monitors the bulk of the left ventricle, supplied by the left anterior descending artery. Lead I may be monitored on patients in whom the left circumflex artery is at risk.

C. Arterial Blood Pressure

Arterial blood pressure is composed of vascular resistance and blood flow. Blood supply to an organ may be low despite adequate blood pressure because of high vascular resistance. Autoregulation in an individual organ may cause local changes in resistance in order to maintain a constant blood flow.

1. **Mean arterial pressure (MAP)** may be measured directly or calculated ($\text{MAP} = \text{diastolic pressure} + 1/3 \text{ pulse pressure (systolic} - \text{diastolic)}$).
2. **Automated noninvasive blood pressure** is the most common noninvasive method of measuring blood pressure in the operating room. **Manual blood pressure** directly measures the systolic and diastolic blood pressures by auscultation of Korotkoff sounds, palpation, or Doppler.

a. Limitations

1. An appropriate cuff size is required for correct determinations of blood pressure. A cuff that is too small may result in falsely high blood pressures while a cuff that is too large may result in falsely low blood pressures. The cuff width should cover two thirds of the upper arm or thigh.
2. Dysrhythmias and motion artifact may result in erroneous values or may not give any values at all, resulting in a delay in accurate measurements when using an automated cuff.
3. Venous congestion and ischemia may result from frequent blood pressure measurements during rapid or large blood pressure fluctuations.
4. Very low or high blood pressures may not correlate with intra-arterial measurements; noninvasive blood pressure measurement often overestimates low blood pressure (i.e., systolic blood pressure below 80 mm Hg).
3. **Palpation may be used to estimate systolic blood pressure** based on whether the pulse may be palpated at key points: radial artery (80 mm Hg), femoral artery (60 mm Hg), or carotid artery (50 mm Hg). This method is inaccurate and is only an estimation when the blood pressure is very low.
4. **Invasive blood pressure monitoring** uses an indwelling arterial catheter coupled through fluid-filled tubing to a pressure transducer. The transducer converts pressure into an electrical signal to be displayed.

a. Indications

1. Need for tight blood pressure control (e.g., induced hypertension or hypotension).
2. Hemodynamically unstable patient.
3. Frequent arterial blood sampling.
4. Inability to utilize noninvasive blood pressure measurements.

b. Interpretation

1. Systolic blood pressure is often monitored in situations when high pressure may cause rupture (e.g., aneurysm).

2. MAP is often monitored for assessing adequate perfusion pressure of vital organs.
- c. **Materials** include appropriately sized arterial catheter and transducer apparatus. Generally, the catheter size is 22 to 24 gauge for infants, 20 to 22 gauge for children, and 18 to 20 gauge for adults.
 1. **Transducer** is connected to fluid-filled tubing and a pressurized bag of saline. The pressurized saline enables a continuous infusion at 3 mL/hour to prevent clotting. The signal should have a flat frequency response below 20 Hz to monitor all physiologic heart rates.
 2. **Tubing** should be rigid and as short as possible, with no kinks or air bubbles.
 3. **Setup.** The transducer should be electronically zeroed while open to air and placed at the height of the coronary sinus for most patients (phlebostatic axis). Exceptions include placing the transducer at the level of the head during cerebral aneurysm surgery.
5. **Procedure: Arterial cannulation**
 - a. **Locations.** The radial artery is the most common site of insertion. Other locations include ulnar, brachial, axillary, femoral, and dorsalis pedis arteries. As distance from the heart increases, systolic blood pressure increases, diastolic pressure decreases, and MAP generally has little variation.
 - b. **Procedure: Radial artery cannulation.** (<https://www.youtube.com/watch?v=7coTBnJt4iA>)
 1. The wrist is hyperextended with an arm board and the skin prepped. The procedure should be performed aseptically. Local anesthetic may be used to raise a skin wheal if the patient is awake (Fig. 10.1).

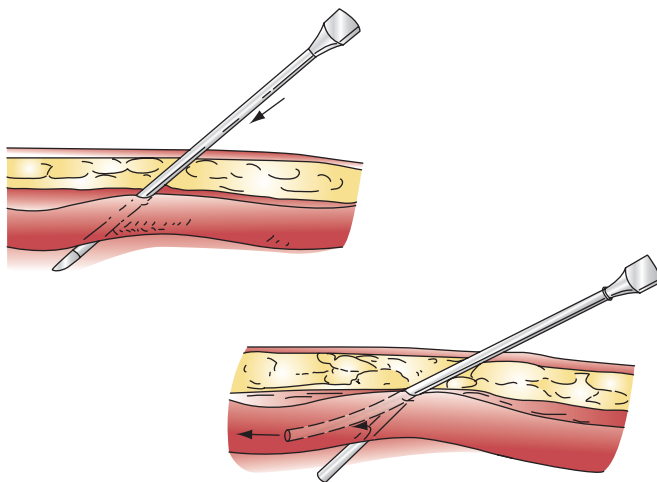


FIGURE 10.1 Radial artery cannulation using the transfixing technique. As shown in the upper drawing, the needle catheter is advanced through the artery. The lower drawing shows the needle withdrawn and the catheter removed until pulsatile flow is obtained. The catheter then is advanced into the artery with a guide wire using the Seldinger technique. (Reused from Gerhardt MA, Walosik-Arenall KM. *Monitoring the cardiac surgical patient.* In: Hensley FA, Gravlee GP, Martin DE, eds. *Practical Approach to Cardiac Anesthesia*. 5th ed. Philadelphia: Wolters Kluwer Health; 2013:117–155.)

2. The needle is advanced until the artery is entered, and blood flow is observed. The catheter is then advanced over the needle into the artery as in inserting an intravenous catheter. The needle is removed once the catheter is in the vessel, and the catheter is connected to the transducer tubing. An alternative method (transarterial) is when the arterial catheter enters the artery confirmed by a small flash of arterial blood and then advanced through the back wall of the artery. The needle is removed, the catheter is slowly withdrawn, and when there is a spurt of arterial blood, a sterile guide wire is used to ease catheter insertion.
 3. Ultrasound guidance is helpful for arterial line placement in patients with poor arterial access.
 4. Do not flush the line with more than 3 mL since retrograde flow into the cerebral circulation has been demonstrated.
- c. **Considerations for Placement**
1. Femoral and axillary artery cannulation is best performed with an 18- or 20-gauge catheter to enter the vessel and then inserting a longer 6-inch 18-gauge catheter via the Seldinger technique.
 2. The **modified Allen test** may assess the relative contribution of the radial and ulnar arteries to the blood supply to the hand, but the results are unreliable.
 3. Blood pressure and pulse should be assessed in both right and left sides; if disparity exists, the catheter should be placed on the side with the higher pressure since pressure artifacts tend to underestimate the correct blood pressure.
 4. Prior cannulation may result in thrombosis. Proximal pulsation should be assessed before placement. Distal pulsation may simply indicate collateral flow.
- d. **Complications**
1. An **overdamped waveform** will cause an artifactual low blood pressure measurement. This may result from arterial obstruction, catheter occlusion, excess tubing, stopcocks, air bubbles, or kinking of the pressure tubing.
 2. An **underdamped waveform** will result in an artifactually high systolic blood pressure measurement. This may result from use of nonrigid tubing or hyperresonance caused by reverberation of pressure waves.
 3. Rare complications include arterial thrombosis, ischemia, infection, and fistula or aneurysm formation. Pulse oximetry on the same hand as the arterial catheter may help to indicate impending vascular compromise. The catheter should be removed, and the opposite side used if new placement is indicated. The ipsilateral ulnar artery should not be cannulated in the event of radial artery complications.

III. CVP AND CARDIAC OUTPUT

A. **CVP.** CVP is measured by coupling the intravascular space to a pressure transducer using a fluid-filled tubing.

1. Pressure is monitored at the level of the vena cava or the right atrium. The transducer apparatus (see section II.C.4.c.) is placed at the level of the coronary sinus.

a. **Indications**

1. Measurement of right heart filling pressures to assess intravascular volume and right heart function

2. Drug administration to the central circulation
 3. Intravenous access for patients with poor peripheral access
 4. Indicator injection for cardiac output determination
 5. Access for insertion of pulmonary artery catheter (PAC)
- b. Waveform.** The CVP tracing contains three positive deflections—the **a**, **c**, and **v** waves—and two negative slopes—the **x** and **y descents** (Fig. 10.2). The waves correspond to atrial contraction, isovolemic ventricular contraction including tricuspid bulging, and right atrial filling, respectively. The x descent corresponds to atrial relaxation and systolic collapse. The y descent corresponds to early ventricular filling and diastolic collapse.
- c. Analysis**
1. **Range.** The CVP is read between the **a** and **c** waves at end-expiration, thus minimizing the interaction of respiration. The **normal CVP is 2 to 6 mm Hg**.
 2. **Decreases in CVP.** When a CVP decrease is associated with an increase in blood pressure, without changes to the systemic vascular resistance, the CVP has fallen because of increased cardiac performance. If blood pressure is decreased, decreased CVP is due to decreased intravascular volume or venous return.
 3. **Increases in CVP.** When this increase is associated with increased blood pressure, without changes to the systemic vascular resistance, the cause of increased CVP is an increase in volume or venous return. With an associated decrease in blood pressure, the increased CVP is due to decreased cardiac performance.
- d. Pathology and CVP**
1. **Cannon a waves** are caused by the atrium contracting against a closed tricuspid valve, as during atrioventricular dissociation.
 2. **Large v waves** are caused by regurgitant flow during ventricular contraction, as with tricuspid regurgitation.
- e. Positive-pressure ventilation** affects both cardiac output and venous return. According to the Starling rule, the transmural pressure, which is the difference between the atrial pressure and extracardiac pressure, correlates with the cardiac output. At low levels of PEEP,

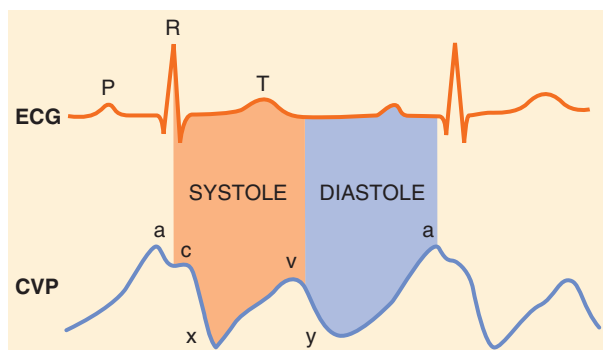


FIGURE 10.2 The normal central venous pressure (CVP) trace and electrocardiogram (ECG). (Reused from Connor CW. Commonly used monitoring techniques. In: Barash PG, Cullen BF, Stoelting RK, et al., eds. *Clinical Anesthesia*. 7th ed. Philadelphia: Wolters Kluwer Health; 2013:711, with permission.)

the CVP increases with increased PEEP. At high levels of PEEP (over about 15 cm H₂O), CVP increases as the cardiac output is depressed because of impaired right ventricular output.

2. Procedure: CVP

a. Locations. Common locations include the following veins: internal jugular (IJ), subclavian, external jugular, axillary, cephalic, and femoral.

b. Materials include a saline bag under pressure, fluid-filled tubing, and transducer. The transducer is placed at the level of the coronary sinus.

1. Multiple lumen catheters are directly inserted and are available with one to four lumens to provide access for multiple drugs, pressure monitoring, and blood sampling.

2. An introducer is a large-bore catheter with a septum valve. A special multiple lumen catheter or a PAC is then placed through the introducer as described below.

3. Ultrasound can be used to identify anatomy, assist catheter insertion, and verify placement.

c. Complications

1. Dysrhythmias, caused by the guide wire irritating the endocardium, are temporary and resolve with withdrawal of the wire.

2. Arterial puncture can cause significant vessel damage and bleeding if the dilator or catheter is placed into the artery. Before dilation, intravenous position should be verified by color, blood gas, or pressure measurement through the finder needle, thin-walled needle, or 18-gauge catheter. If an artery is punctured before dilation, the needle should be removed and pressure applied for at least 5 minutes (10 minutes in the case of coagulopathy) and a new site chosen. If the catheter is placed in the artery, it should remain in place and a vascular surgeon should be consulted.

3. The guide wire should not feel tethered with dilator placement, as this may signify venous damage or puncture of the posterior wall. Do not continue to advance a guide wire if it does not pass easily.

4. Pneumothorax, hemothorax, hydrothorax, chylothorax, or pericardial tamponade may become evident with vital sign changes. They are in part ruled out with chest radiography. The risk of pneumothorax is highest with subclavian vein insertion.

5. Infection and air embolism may occur at any time before removal of the catheter. The risk of infection is higher with femoral venous placement. To reduce the chance of air embolism upon catheter removal, the site is occluded with the patient performing a Valsalva maneuver. The Trendelenburg position helps to prevent air entrainment at neck and subclavian sites.

d. For the **internal jugular Seldinger technique**, the **right side** is preferred because the vessels run a straighter course to the right atrium (Fig. 10.4). (<https://www.youtube.com/watch?v=KSgw1V4bchM>; https://www.youtube.com/watch?v=2VYp0rEr_cE)

1. Position and preparation. There are three positions for placement of the CVP catheter into the IJ: anterior, medial, and posterior based on the location of insertion relative to the sternocleidomastoid muscle. The most common is the medial position. The patient is supine or in the Trendelenburg position with the head extended and turned toward the contralateral side of insertion. To reduce catheter-related infections, sterile drapes should cover the

patient from head to toe, the procedurist should wear sterile gown and gloves, and the neck should be prepped with chlorhexidine.

2. **Landmarks** include the suprasternal notch, clavicle, lateral border of sternocleidomastoid (SCM) muscle, and angle of the mandible. For insertion, locate the midpoint between the mastoid process and the sternal attachment of the SCM. Ultrasound is routinely used for visualizing anatomy and locating the vein (Fig. 10.3).

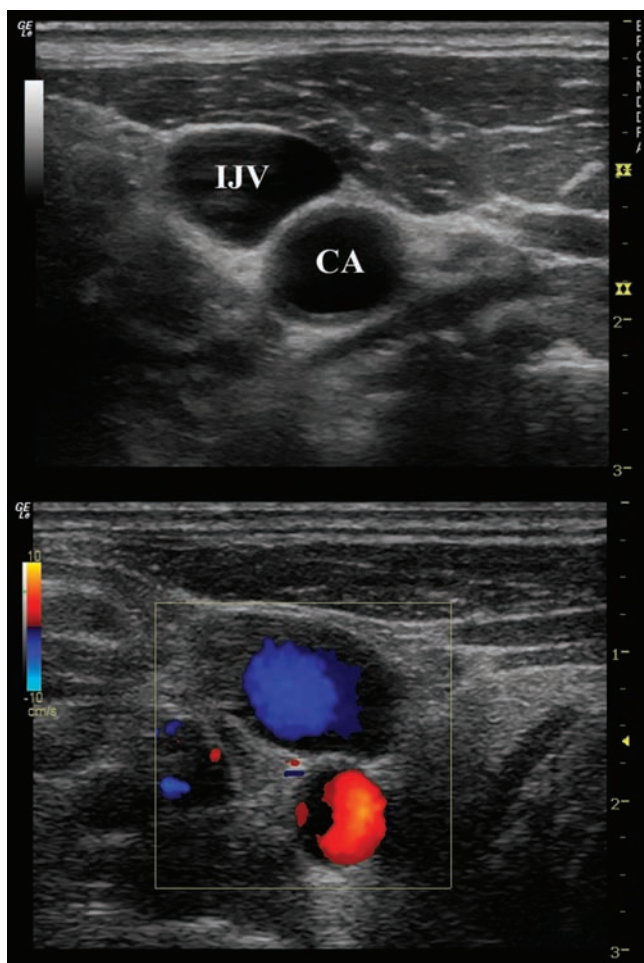


FIGURE 10.3 Ultrasound-guided internal jugular catheterization. The top picture demonstrates the two-dimensional examination showing the internal jugular vein (IJV) lateral to the carotid artery (CA). The bottom picture with the transducer-oriented caudad using color Doppler demonstrates the IJV with blue flow and CA with red flow. (From Barash P, Cullen, BF, Stoelting, RK, et al. *Clinical Anesthesia*. Philadelphia: Lippincott Williams & Wilkins; 2009.)

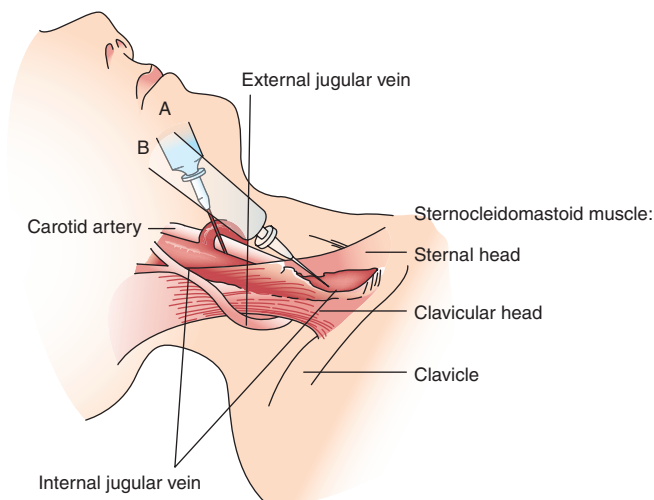


FIGURE 10.4 Two methods for internal jugular cannulation. **A:** Anterior approach—insertion at the medial border of the sternocleidomastoid muscle medial head, 5 cm above the clavicle, directed toward the ipsilateral nipple. **B:** Central approach—insertion at the apex of the triangle formed by the lateral and medial head of the sternocleidomastoid muscle, directed toward the ipsilateral nipple. (Reused from Gerhardt MA, Walosik-Arenall KM. Monitoring the cardiac surgical patient. In: Hensley FA, Gravlee GP, Martin DE, eds. *Practical Approach to Cardiac Anesthesia*. 5th ed. Philadelphia: Wolters Kluwer Health; 2013:117–155.)

3. **Placement** can vary based upon the needle insertion site in relation to the patient's neck anatomy (Fig. 10.4). While aspirating, a finder needle is inserted at a 45° angle to the skin and advanced toward the ipsilateral nipple until venous blood is aspirated. Once the vein is located, the syringe is removed and a guide wire is passed through the needle or catheter.
4. Intravenous position must be verified by ultrasound, color, blood gas, or pressure measurement. The needle or catheter is then removed, and the site enlarged laterally with a scalpel.
5. For triple and quadruple lumen catheters, a dilator is often not necessary when accessing the internal jugular vein. With countertraction, a rigid dilator is advanced over the wire with gentle twisting; the guide wire should still be easily mobile, indicating preserved intravascular position.
6. The dilator is removed while maintaining the guide wire, and a central catheter or introducer is inserted over the wire. Alternatively, an introducer and dilator are inserted simultaneously. The wire is removed, the ports are aspirated and flushed, and the catheter is secured to the skin.
7. A chest radiograph is required to confirm the position and exclude complications, such as pneumothorax. The tip of the catheter should be at the junction of the superior vena cava (SVC) and right atrium and should not encounter the wall of the SVC at a right angle.

- e. The **SCV** (<https://www.youtube.com/watch?v=RDtgzNWmYBw>) may be easily accessed as the vessel passes under the clavicle at the midclavicular line. It is one of the most common central venous line locations. Although the artery is not compressible in case of puncture, coagulopathy is not a contraindication to placement. The SCV is often preferred for patient comfort, and the left SCV is often chosen because of the natural course of the brachial cephalic vein into the SVC.
 1. **Landmarks** include the clavicle, suprasternal notch, and lateral border of the SCM as it inserts onto the clavicle. The insertion site is medial to the midclavicular line.
 2. The thin-walled needle is placed at the insertion site and aimed at the suprasternal notch. It is used to identify the clavicle, and the tip is then “walked” posteriorly under the clavicle. The key to avoid a pneumothorax is to always keep the needle parallel to the floor during insertion. Total insertion of the catheter should not be greater than 16 to 17 cm, as this may place the tip in the right atrium.
- f. **Femoral vein** is one of the most easily accessible central veins and using it does not carry a risk of pneumothorax. Limitations include hip immobility and limited utility during cardiopulmonary resuscitation.
 1. **Landmarks** include the femoral artery, inguinal ligament, anterior superior iliac spine (ASIS), and pubic tubercle. The femoral vein is immediately medial to the femoral artery. If the artery is not palpable, the vein is reliably located one third of the distance from the pubic tubercle to the ASIS. In either case, the insertion point is just inferior to the inguinal ligament, 1 to 2 cm medial to the artery.
 2. **Placement** uses the Seldinger technique.
- g. **External jugular vein** is cannulated similarly to an internal jugular vein placement described in section II.D.2.b. It runs obliquely across the SCM, along a line running from the angle of the mandible to the midpoint of the clavicle. Occlusive pressure at the inferior portion of the vein near the clavicle may ease cannulation. Because the vessel bends to join the SCV, threading of a guide wire may be difficult and should not be forced. For this reason, internal jugular cannulation may be easier for central catheter placement.
- h. **Basilic vein** may be used to access the central circulation with a long catheter. Passing the guide wire into the SCV may be difficult but may be facilitated by abducting the ipsilateral arm and turning the head toward the side of insertion.
3. **Pulmonary artery catheterization and pulmonary artery occlusion pressures.** The PAC gives information about ventricular function and vascular volume by measuring CVP, pulmonary artery pressure (PAP), pulmonary artery occlusion pressure (PAOP), mixed venous sampling, and cardiac output.
 - a. **Mechanism.** The PAC is inserted through a central venous introducer catheter. It passes through the vena cava, right atrium, and right ventricle and into the pulmonary artery. Transducers are connected to separate ports to allow CVP and PAP measurements. Inflating the balloon at the tip of the catheter allows measurement of PAOP, or “wedge” pressure, reflecting the left atrial pressure and left ventricular preload. To minimize the effect of alveolar pressure

on PAOP, the tip should rest in West zone III, where pulmonary venous pressure is greater than alveolar pressure. Fortunately, the tip usually ends up in this location.

b. Indications

1. Unexplained hypotension
2. Access for cardiac pacing
3. Surgical procedures with significant physiologic changes (e.g., open aortic aneurysm repair, and lung or liver transplant)
4. Acute myocardial infarction with shock

c. PA and PAOP

1. **Waveform.** The PAP waveform is similar in shape to the systemic arterial waveform. Because of the location, the waveform is smaller and precedes the systemic waveform. With the balloon inflated, the PAC will measure the PAOP recording, which is similar to the CVP waveform, with **a** and **v** waves. This waveform approximates the left atrial pressures and is slightly delayed because of the interposed lung.

2. **Range.** The **normal PAP is 15 to 30 mm Hg systolic and 5 to 12 mm Hg diastolic.** The **normal range for PAOP is 5 to 12 mm Hg.** At end expiration, this approximates the left atrial pressure and correlates with the left ventricular end diastolic volume.

d. PAOP analysis is used to assess the left heart performance. A basic model of left heart function is given by the relationship between the end-systolic pressure–volume curve and end-diastolic pressure–volume curve. Because the left ventricular end-diastolic pressure (LVEDP), which correlates with the left ventricular end-diastolic volume, is known, the following deductions are possible (Fig. 10.5).

1. **Increase in PAOP** can be due to an increase in end-diastolic volume, decrease in compliance, or both.
2. **Decrease in PAOP** can be due to a decrease in end-diastolic volume, increase in compliance, or both.

e. Pathology and PAOP

1. **Large a waves** may be due to either left ventricular hypertrophy (LVH) or atrioventricular dissociation. LVH will decrease the compliance of the left ventricle and will elevate the LVEDP. Thus, the PAOP should be measured at the peak of the **a** wave. During atrioventricular dissociation, pressure should be measured before the **a** wave.
2. **Large v waves** are the result of mitral regurgitation.
3. **Right heart dilatation** can cause shifting of the interventricular septum into the left ventricle, effectively decreasing the left ventricular end-diastolic compliance. Thus, LVEDP will be elevated.
4. **Pulmonary embolism** may cause an elevation of the PAP without a concomitant elevation of the PAOP.

f. Materials/catheter types. Most catheters are available with or without bonded heparin. Types of PACs include the following:

1. **Venous infusion** (VIP, VIP+) catheters provide extra ports for infusion and sampling.
2. **Paceports** allow placement of cardiac pacing wires.
3. **Continuous cardiac output** catheters perform frequent automated determinations of cardiac output by using frequent low-heat pulses to obtain a thermodilution curve; the values are usually an average over time.
4. **Oximetric** catheters monitor mixed venous O_2 saturation.

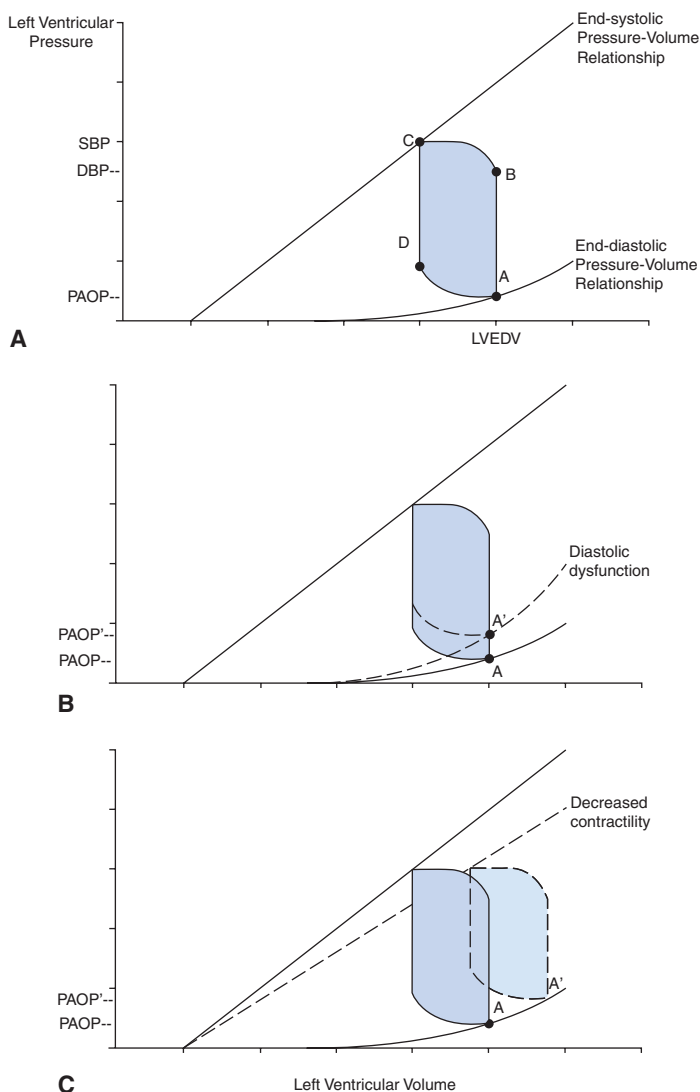


FIGURE 10.5 Left ventricular pressure–volume relationships. **A:** The cardiac cycle (A-B-C-D-A) is limited by the end-systolic pressure–volume relationship (describing the contractility) and the end-diastolic pressure–volume relationship. The PAOP approximates the LVEDP. An increase in PAOP may be ascribed to decreased diastolic compliance (**B**), an increase in left ventricular end-diastolic volume (LVEDV) (**C**), or a combination of both. An increase in LVEDV often results from decreased contractility in the setting of a properly performing right ventricle (**C**). SBP, systolic blood pressure; DBP, diastolic blood pressure.

5. **Right ventricular ejection fraction catheters** use a rapid response thermistor to calculate the right ventricular ejection fraction in addition to cardiac output.
4. **Procedure: pulmonary artery catheter**
 - a. **Locations and preparation** are similar to those of the central venous catheter described in section II.D.2. The PAC is invariably placed through an introducer catheter. The operator typically dons a fresh pair of sterile gloves between the introducer and PAC placement.
 - b. **Technique.** The PAC is prepared and examined as follows:
 1. **Sheath placement** is done before balloon examination and placed at 70 cm. The sheath allows movement of the PAC to adjust to the optimum position while maintaining sterility.
 2. **Balloon examination** includes inflating the balloon with 1.5 mL of air. The balloon should be symmetrical, inflate and deflate smoothly, and the tip of the PAC should not protrude past the tip of the balloon.
 3. All ports are flushed to ensure patency and are attached to calibrated pressure transducers. Raising and lowering the PAC distal end should produce changes on the pressure tracing and serve as a quick test of the system before insertion.
 4. **Placement** (Fig. 10.6). The PAC is held so that it follows a natural curve through the heart during passage through the introducer.

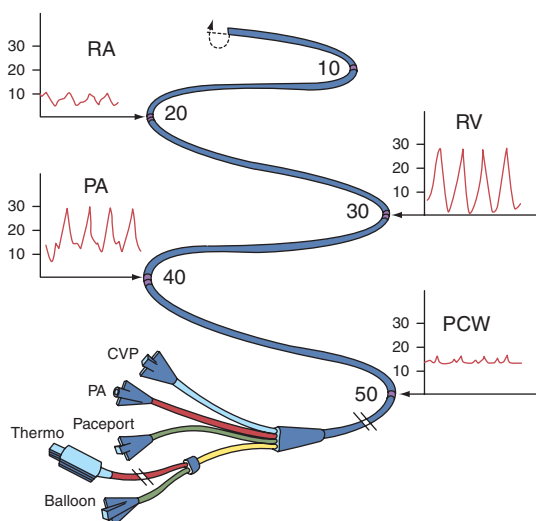


FIGURE 10.6 Pulmonary artery catheter (PAC) and pressure waveforms that will be encountered as it is inserted into the wedged position from the right internal jugular vein. Distances in centimeters on the catheter correspond to insertion distances read at the diaphragm of the introducer and are approximate. CVP, central venous pressure; PCW, pulmonary capillary wedge; RA, right atrium; RV, right ventricle; Thermo, thermistor connection for cardiac output determination. (Reused from Gerhardt MA, Walosik-Arenall KM. Monitoring the cardiac surgical patient. In: Hensley FA, Gravlee GP, Martin DE, eds. *Practical Approach to Cardiac Anesthesia*. 5th ed. Philadelphia: Wolters Kluwer Health; 2013:117–155.)

Once the 20-cm mark is reached, the balloon is inflated with 1.5 mL of air, and the CVP waveform is confirmed. As the catheter is advanced, the waveform will change to a right ventricular waveform and then to a pulmonary artery waveform (with a diastolic pressure step-up and down-sloping diastolic plateau). The PAC is advanced until a PAOP waveform is seen, and the balloon is then deflated. The waveform should return to a pulmonary artery tracing upon deflation. If it does not, then the PAC should be withdrawn about 5 cm with the balloon deflated, the balloon should be reinflated, and the PAC should be advanced until a PAOP tracing is encountered. The balloon should remain deflated normally.

5. **Securing** the sheath to the introducer proximally and at the 70-cm mark distally ensures the ability to manipulate the PAC aseptically. The introducer and PAC are secured to the patient, and an occlusive dressing is applied.
- c. **Distances.** From the right internal jugular vein, each location appears “on the tens.” The right atrium is reached at 20 cm, the right ventricle is reached at 30 cm, the pulmonary artery is reached at 40 cm, and the PAOP should be at 50 cm. For subclavian vein placement, subtract 5 cm from these distances; for femoral vein placement, add 20 cm to these distances.
- d. During PAC insertion, difficulty in passing the catheter into the right ventricle and pulmonary artery may be encountered because of balloon malfunction, valvular lesions, a low-flow state, or a dilated right ventricle. The monitoring equipment should be rechecked for calibration and scale. Inflating the balloon with a full 1.5 mL of air, slow PAC advancement, and large inspirations by the patient to augment venous return may be helpful. The PAC may have to be withdrawn to a depth of 20 to 30 cm, rotated slightly, and readvanced.
- e. **Complications**
 1. **Pneumothorax** during placement of the PAC is the most common complication.
 2. **Dysrhythmias** are possible because of direct stimulation of the atrium, ventricle, and pulmonary outflow tract in 50% to 70% of placements. They are usually transient and resolve spontaneously with continued passage or with withdrawal of the PAC. Complete heart block and ventricular tachycardia are possible (up to 0.3% of placements) and should be treated appropriately.
 3. **Right bundle branch block** is a specific risk in patients with either a left bundle branch block or a first-degree heart block, as this may result in complete heart block. In this event, the PAC should be withdrawn and temporary pacing initiated.
 4. **Pulmonary artery rupture or infarction** is possible from overinflation or prolonged inflation of the balloon or from direct pressure by the PAC. Thus, the balloon should be slowly inflated, and volume to achieve PAOP should be monitored. Furthermore, the PAP should be monitored by default; if a persistent PAOP appears, the catheter should be pulled back immediately and repositioned.
 5. **Pacemakers** do not contraindicate PAC placement, although fluoroscopic guidance should be used if the pacemaker is less than 6 weeks old.
 6. **Balloon rupture** may occur with overinflation with more than the recommended 1.5 mL.

7. **Valve damage, thrombus formation, and infection** can occur with PACs. Knotting of the catheter can happen when the catheter will not pass through the pulmonary valve and turns back on itself in the right ventricle.
5. **Cardiac output** is typically 4 to 8 L/minute, while the cardiac index (CO/body surface area [BSA]) is 2.4 to 4.0 L/min/m². CO is conventionally measured with a PAC using thermodilution. The risks of PAC placement have generated interest in alternative CO methods such as pulse contour analysis, whole body dilution techniques, esophageal Doppler, Fick methods, and impedance cardiography.
 - a. **Thermodilution with a PAC** is the gold standard for CO measurement. A known volume of cold saline is injected into the CVP port. The resulting temperature change is monitored by the thermistor located at the PAC tip. The area under the temperature–time curve correlates with cardiac output.
 1. **CO should be measured at end expiration.** Changes in intrathoracic pressure affect the CO measurement. Negative intrathoracic pressure during the inspiration phase of spontaneous breathing increases venous return and left ventricular transmural pressure. Positive intrathoracic pressure during the inspiration phase of positive-pressure ventilation decreases venous return and left ventricular transmural pressure.
 2. **Tricuspid regurgitation** often causes CO and cardiac index to be underestimated by prolonging the time and increasing the area under the CO curve. Though underestimation is the most common error, values may be overestimated as well.
 3. **Errors in CO measurement** may also be caused by injectate spillage, very slow injection, use of the wrong catheter constant, and intra-cardiac shunt.
 - b. **Pulse contour analysis** determines stroke volume and cardiac output by computer analysis of the arterial pulse pressure waveform. This method assumes aortic pulse pressure is proportional to stroke volume. The effects of vascular tone are included in the calculation as a conversion factor calculated from heart rate, MAP, and vessel compliance. The advantage is that central venous access is not needed. Available systems utilize patient demographics and physical characteristics for arterial impedance estimation (FloTrac System, Edwards Lifesciences, Irvine, CA) or injected indicators for calculation (see below). Limitations include:
 1. **Nonlinearity of aortic compliance changes.** The compliance of the aorta changes nonlinearly with pressure. This may limit the accuracy of stroke volume estimates.
 2. **Resonance and damping** may occur, as with use of any arterial catheter for invasive blood pressure monitoring.
 3. **Does not accurately track changes in stroke volume.** Limited ability to clinically assess changes in SV after a volume challenge or the use of vasopressors.
 - c. **Whole body dilution techniques** were originally done using indocyanine green dye dilution. Currently available methods combine the use of an indicator dilution CO measurement for calibration and pulse contour analysis, examples include PiCCO and LiDCO.
 1. **Transpulmonary thermodilution (PiCCO)** requires a central venous catheter and a specialized femoral arterial catheter with a thermistor. A cold saline bolus is injected through the central venous

catheter. The femoral arterial thermistor records the temperature changes downstream. Analysis of the curve yields estimates of cardiac output and blood volume in the heart.

2. **Lithium dilution (LiDCO)** may be used with a radial or brachial artery catheter with a lithium sensor at the tip. A known concentration and volume of lithium chloride solution is injected through a central or peripheral vein. An arterial lithium concentration–time curve is generated. CO is calculated from the area under the curve.
 3. **Limitations of dilution techniques.** Intracardiac shunt and aortic insufficiency may cause CO to be underestimated.
 - d. **Esophageal Doppler** measures descending thoracic aortic blood flow (ABF) with a Doppler beam and sensor positioned at a known angle in the esophagus. This measures ABF, but not CO, directly. Since ABF is roughly 70% of CO, CO may be estimated while avoiding the invasive risks of PAC placement. The probe requires minimal training to place and may be left in place for days. However, it cannot be performed easily on awake patients and does not provide direct information about cardiac filling pressures.
 - e. **Modified Fick techniques.** NICO (Philips Respironics, Pittsburgh, PA) uses sensors in the breathing circuit attached to an intubated patient to measure flow, airway pressure, and CO_2 concentration. During periods of rebreathing, CO_2 elimination is calculated from these measurements. The Fick principle is applied to calculate cardiac output, which is proportional to the change in CO_2 elimination divided by the change in end-tidal CO_2 .
 - f. **Thoracic Bioimpedance** uses skin electrodes placed along the neck and thorax to measure changes in voltage and impedance. Because blood is a stronger conductor than muscle, bone, and skin, changes in thoracic blood volume during the cardiac cycle result in impedance changes. Ohm's law is applied to use the change in impedance to determine CO. This method is completely noninvasive and the electrodes require minimal training to place. A large body habitus and fluid overload may result in inaccurate measurements.
 - g. **Thoracic Bioreactance** (NICOM device, Cheetah Medical, Portland, OR) uses outer electrodes that apply an electric current of known frequency across the thorax and inner electrodes that record the signal after it interacts with the pulsatile blood flow within the thorax resulting in a time delay, or phase shift. The volume of pulsatile blood (stroke volume) that caused the specific time delay can be calculated and continually detected to create the NICOM signal. The continual, dynamic sensing results in less signal distortion than bioimpedance systems. Although further studies are needed, the CO as measured by bioreactance has been shown to be highly correlated with that measured by thermodilution.
6. **Echocardiography**
- a. **Mechanism.** Echocardiography is performed with ultrasonic waves to create a two-dimensional image of the heart and surrounding structures. This may be done from a transthoracic or transesophageal approach, depending on the targeted structures, patient compliance, and conditions during placement. It provides independent assessments of the same parameters that a PAC measures, but it also reveals cardiac valve function, ventricular contractility, diastolic function, and intracardiac structures.

b. Indications

1. **Hypotension** of unknown cause
2. **Uninterpretable PAC values**
3. **Suspected intracardiac masses or vegetations**
4. **Valvular abnormalities**
5. **Shunts**
6. **Air embolism**
7. **Pericardial disease**
8. **Thoracic aneurysm/dissection**

c. Methods

1. **Transthoracic echocardiogram** can be performed with the patient awake and provides good visualization of right heart structures and qualitative estimates of contractile performance, although visualization of the left heart is limited and may not be allowed by the surgical location.
2. **Transesophageal echocardiogram** requires that the patient be topically, locally, or generally anesthetized, but it may be performed intraoperatively and allows superior visualization of the left heart.

IV. RESPIRATORY SYSTEM

The respiratory system is responsible for oxygen uptake and carbon dioxide removal and provides a conduit for delivery of anesthetic agents.

A. Mandatory respiratory monitors during general anesthesia include pulse oximetry, capnography, inspired oxygen analyzer, and a disconnect alarm. Direct visualization of the chest and a precordial or esophageal stethoscope may provide additional information. During regional anesthesia, respiration may be monitored with direct visualization, oximetry, and capnography.

B. Oxygenation is most easily measured by **pulse oximetry**. Other methods include qualitative assessment of skin color, transcutaneous oximetry, and arterial blood gas sampling.

1. **Method.** Oxygenated and deoxygenated hemoglobin absorb light differently at most wavelengths, including 660 and 960 nm, the wavelengths examined by most devices. The Beer-Lambert law allows the concentration of each species to be calculated from the absorption of light at those wavelengths. The ratio of absorption is processed to give the oxygen saturation of hemoglobin. The sensor has at least two light-emitting diodes (960 and 660 nm) and a light detector. This may be applied to fingers, toes, earlobes, tongue, or, with a special probe, the nose.
2. **Interpretation.** Normal range in a healthy adult is 96% to 99%, while values above 88% may be acceptable in patients with lung disease. A high pulse oximeter reading (SpO_2) generally indicates that oxygen is available in the lungs, taken up in the blood, and delivered to distal tissues. A low SpO_2 may be due to a problem along the above pathway or due to an error in monitoring.
3. **Limitations.**
 - a. Oximetry may be a late reporter of inadequate gas exchange.
 - b. **Carboxyhemoglobin** absorbs light similarly to oxygenated hemoglobin at 660 nm and will provide falsely elevated readings, although it does not contribute to oxygenation.
 - c. **Methemoglobin** absorbs light at both 660 and 940 nm, resulting in a saturation of 85%, which does not correlate with the true saturation. Methemoglobinemia may often be treated with methylene blue.
 - d. **Methylene blue, indocyanine green, indigo carmine, and isosulfan blue** injections transiently result in falsely low saturation readings.

- e. SpO_2 tends to be falsely overestimated at low saturations (below 80%).
 - f. Low perfusion, motion, and nail polish (especially blue) may cause SpO_2 measurements to be uninterpretable or unreliable.
- C. Ventilation** is assessed by end-tidal carbon dioxide measurements (i.e., capnography) and spirometry. Capnometry and capnography are often used as synonyms, as both analyze and record carbon dioxide, with the latter including a waveform. Capnography not only evaluates respiration but also confirms of endotracheal intubation and is diagnostic of pathologic conditions.
- 1. Method.** The measurement of carbon dioxide is often based on infrared light absorption to determine concentration. Carbon dioxide may be measured either at the breathing circuit (mainstream capnograph) or via aspiration of gas samples by the capnograph (sidestream capnograph). Mainstream capnographs often cause traction on the endotracheal tube and can cause burns by radiant heat, while sidestream capnographs have a measurement delay based on sample volumes and may result in significant leaks from sampling. Sidestream capnography may also be used on a nonintubated patient to give a qualitative assessment of respiration.
 - 2. Waveform.** The normal end-tidal carbon dioxide (PetCO_2) waveform (Fig. 10.7) contains the expiratory portion (phases I, II, III, and

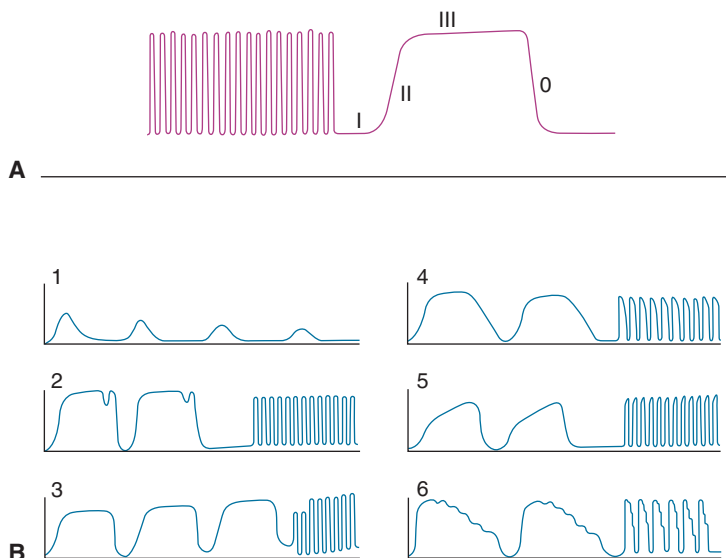


FIGURE 10.7 **A:** Normal capnograph. *I*, dead space expiration; *II*, mixed dead space and alveolar gas expiration; *III*, alveolar gas expiration and plateau; *0*, inspiration. Phase IV is an upswing that occurs at the end of phase III. **B:** Capnographs that may be seen in practice. 1, rapidly extinguishing uncharacteristic waveform, compatible with esophageal intubation; 2, regular dips in end-expiratory plateau, seen in underventilated lungs or in patients recovering from neuromuscular blockade; 3, upward shift in baseline and plateau, seen with rebreathing of carbon dioxide, miscalibration, and so forth; 4, restrictive pulmonary disease; 5, obstructive pulmonary disease; 6, cardiogenic oscillations.

occasionally IV) and inspiratory portion (phase 0). Two angles, the α angle (between phases II and III) and the β angle (between phases III and 0), also aide in interpretation.

- a. **Phase 0** is the inspiratory segment.
 - b. **Phase I** is the carbon dioxide-free gas that is not involved in gas exchange (dead space).
 - c. **Phase II** is the rapid upswing and includes both alveolar gas and dead space gas.
 - d. **Phase III** is a plateau that involves alveolar gas and has a small positive slope. Petco_2 is measured at the end of phase III.
 - e. **Phase IV** is a terminal upswing seen in obese and pregnant patients with reduced thoracic compliance.
 - f. **α Angle** is between phases II and III and is related to the ventilation: perfusion matching of the lung. The **β angle** is between phases III and 0 and usually is about 90 degrees, and it may be used to assess rebreathing.
3. **Range and analysis**
- a. Normally, Petco_2 is 2 to 5 mm Hg lower than arterial CO_2 pressure, so the typical range for end-tidal carbon dioxide during general anesthesia is 30 to 40 mm Hg.
 - b. Due to swallowed gas, **esophageal intubation** may result in carbon dioxide return similar to that of endotracheal intubation, except that Petco_2 diminishes to zero with a few breaths.
 - c. **An early sign of malignant hyperthermia** is a rapidly rising end-tidal carbon dioxide, especially if it is unresponsive to hyperventilation.
 - d. Shock/low perfusion, embolism, auto-PEEP, airway obstruction, and system leaks will result in diminishing end-tidal carbon dioxide.
 - e. Carbon dioxide absorption during laparoscopic procedures, reperfusion after releasing an arterial clamp or tourniquet, and absorbent exhaustion or channeling will result in rising end-tidal carbon dioxide.
 - f. Widening of the β angle with an elevation of both phases 0/I and III is a sign of **inspiratory valve failure**.
 - g. Elevation of both phase 0/I and phase III is a sign of **expiratory valve failure** or **absorbent malfunction**.

V. TEMPERATURE MONITORING

- A. **Mechanism.** Temperature may be measured intermittently or continuously. The limitation of more external methods of temperature determination is that they may not reflect changes in the core body temperature, especially in the presence of vasoconstriction.
- B. **Indications**
 1. **Need to control temperature** during induced hypothermia and rewarming (e.g., during cardiopulmonary bypass or vascular neurosurgery).
 2. **Infants and small children** are prone to thermal lability due to their high surface area-to-volume ratio.
 3. **Adults subjected to large evaporative losses or low ambient temperatures** (as occur with exposed body cavity, large volume transfusion of unwarmed fluids, or burns) are prone to hypothermia.
 4. **Febrile patients** need to be monitored because of the risk of hyper- or hypothermia.
 5. Patients with **autonomic dysfunction** are unable to autoregulate their body temperature.

6. **Malignant hyperthermia** is always a possible complication, and temperature monitoring should always be available.

C. Monitoring Sites

1. **Skin temperature**, as measured on the forehead, is normally 3°F to 4°F below core temperature, and this gradient may increase with further cooling.
2. **The axilla** is a common site for noninvasive temperature determination and is usually 1°F below body temperature. The probe needs to be placed at the axillary artery with the arm adducted.
3. **Tympanic membrane temperature** correlates well with core temperature. Intervening cerumen may enlarge the gradient with respect to core temperature.
4. **Rectal temperature** changes lag behind those of core body temperature. This phenomenon is often noted during rewarming after hypothermia and indicates the slower peripheral, or “shell,” rewarming. The risk of rectal perforation is a rare complication.
5. **Nasopharyngeal temperature**, measured at the posterior nasopharynx, reflects the brain temperature. This measurement is performed by measuring the distance from the external meatus of the ear to the external naris and inserting the temperature probe to that distance. This method may be associated with epistaxis in coagulopathic or pregnant patients or may result in skin necrosis if the probe is allowed to press on the naris during longer procedures. This method is discouraged in patients with head trauma or cerebrospinal fluid rhinorrhea.
6. **Esophageal temperature** monitoring reflects the core temperature well. The probe should be located at the lower third of the esophagus and rarely may be misplaced in the airway.
7. **Blood temperature** measurements may be obtained with the thermistor of a PAC.

Suggested Readings

- Jacobsohn E, Chorn R, O'Connor M. The role of the vasculature in regulating venous return and cardiac output: historical and graphical approach. *Can J Anaesth* 1997;44:849–867.
- Kodali BS. *Capnography: A Comprehensive Educational Website*, May 2005. Harvard Medical School. 30 September 2005. <http://www.capnography.com>
- Lake CL. *Clinical Monitoring: Practical Applications for Anesthesia & Critical Care*, 1st ed. Philadelphia: WB Saunders; 2001.
- Marik PE. Noninvasive cardiac output monitors: a state-of-the-art review. *J Cardiothorac Vasc Anesth* 2012;27(1):121–134.
- Mark JB. *Atlas of Cardiovascular Monitoring*. New York: Churchill Livingstone; 1998.
- Pagel PS, Grossman W, Haering JM, et al. Left ventricular diastolic function in the normal and diseased heart (pt 1). *Anesthesiology* 1993;79:836–854.
- Pagel PS, Grossman W, Haering JM, et al. Left ventricular diastolic function in the normal and diseased heart (pt 2). *Anesthesiology* 1993;79:1104–1120.
- Perret C, Tagan D, Feihl F, et al. *The Pulmonary Artery Catheter in Critical Care*. Oxford: Blackwell Science; 1996.
- Sagawa K, Maughan L, Suga H, et al. *Cardiac contraction and the pressure-volume relationship*. Oxford: Oxford University Press; 1988.



Monitoring Anesthetic Brain States

Negin Daneshpayeh and Emery N. Brown

I. GENERAL CONSIDERATIONS

General anesthesia is defined as a drug-induced reversible condition composed of unconsciousness, amnesia, analgesia, immobility and stability of the autonomic, cardiovascular, respiratory and thermoregulatory systems. Monitoring behavioral states during general anesthesia is challenging. During general anesthesia, amnesia is not monitored directly but implicitly by the extent to which unconsciousness is achieved.

- A. The physiologic signs of changes in heart rate, arterial blood pressure, and movement are the measures most commonly used to track the anesthetic during maintenance of general anesthesia.
- B. The changes in heart rate and arterial blood pressure that anesthetized patients show in response to a nociceptive stimulus can be explained in terms of the **nociceptive–medullary–autonomic (NMA) circuit**, which is comprised of the spinoreticular tract, the brainstem arousal circuits, and the sympathetic and parasympathetic efferent pathways.
 1. The **ascending nociceptive (pain) pathway** begins with A-delta and C-fibers whose free nerve endings bring nociceptive (painful) information from the periphery to the spinal cord.
 2. In the spinal cord, these fibers synapse in the dorsal horn on projection neurons that travel through the anterolateral fasciculus and synapse at multiple sites in the brainstem, including the nucleus of the tractus solitarius in the medulla.
 - a. The **autonomic response to a painful stimulus** is initiated within the nucleus of the tractus solitarius, which mediates sympathetic output through the rostral ventral lateral medulla and the caudal ventral lateral medulla to the heart and peripheral blood vessels through projections to the thoracolumbar sympathetic ganglia.
 - b. The parasympathetic output from the nucleus of the tractus solitarius is mediated through the nucleus ambiguus, which projects through the vagus nerve to the sinoatrial node of the heart.
- C. Thus, a potentially nociceptive operative stimulus initiates an increase in sympathetic output and a decrease in parasympathetic output through the NMA circuit that rapidly results in the increase in heart rate and arterial blood pressure.
 1. The NMA circuit explains why increases in heart rate and arterial blood pressure are used as a rapid indicator of an inadequate level of analgesia.
- D. There are several additional approaches for monitoring unconsciousness and analgesia.
 1. **Electroencephalogram (EEG)**-based indices are among the most commonly used methods for tracking altered levels of consciousness induced by general anesthesia and sedation.

II. ELECTROENCEPHALOGRAM-BASED INDICES OF LEVEL OF CONSCIOUSNESS

- A. It is recognized that the EEG changes systematically in relation to the dose of anesthetic drug administered. As a consequence, the unprocessed EEG and various forms of processed EEG have been used to track

the level of consciousness of patients receiving general anesthesia and sedation.

1. Basic Biophysics of EEG

- a. The EEG detects postsynaptic potentials in the cerebral cortex. As neurons synapse in a region of the cortex, they produce macroscopic extracellular currents that can be detected as potential differences by surface electrodes. The cortex is tied to subcortical structures like the thalamus.
- b. Therefore with the EEG, inferences can be made about both cortical and subcortical dynamics.
- c. The EEG signals are comprised of oscillations or waves with a variety of frequencies.
 1. The signal typically consists of many frequencies with different amplitudes (Figs. 11.1 and 11.2).

B. Several EEG-based index systems have been studied and used in clinical practice. These systems process the EEG and provide an index value or set of values in real time or near real time to track the level of consciousness. In general, the indices are designed to decrease with decreasing levels of consciousness and increase as consciousness returns. The anesthesia provider can use these indices along with physiologic signs such as changes in heart rate and blood pressure to track the patient's state of unconsciousness and to some degree antinociception.

C. Bispectral Index (BIS) is an EEG-based index system. A sensor is placed on the forehead that transmits EEG signals to a digital signal converter, which sends the information to the monitor for processing and analysis.

1. Bispectral Index (BIS)

- a. The BIS uses a proprietary algorithm that processes the EEG in near real time and computes an index between 0 and 100 that indicates the patient's level of consciousness. A value of 100 corresponds to being completely awake, whereas 0 corresponds to a profound state of coma or unconsciousness that is reflected by an isoelectric or flat EEG.
- b. Measures specific features of the spectrogram, the bispectrum, and the level of burst suppression and uses a predetermined weighting scheme to convert these features into the *index value*.
- c. Along with the index value, the BIS monitor also displays the unprocessed EEG, the spectrogram, and the level of electromyographic activity.
- d. The electromyography indicator displays in decibels the power in the frequency range of 70 to 110 H that is believed to be attributable to muscle activity. The power range is 30 to 55 dB.

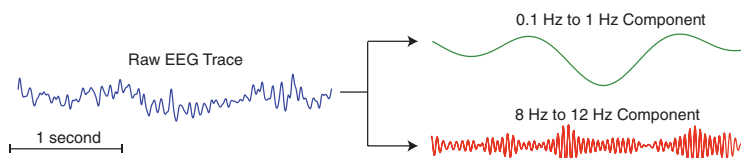


FIGURE 11.1 A typical electroencephalogram trace can be split into a slower oscillatory (0.1 to 1 Hz component [top]) with an overlying higher frequency (8 to 12 Hz component [bottom]).

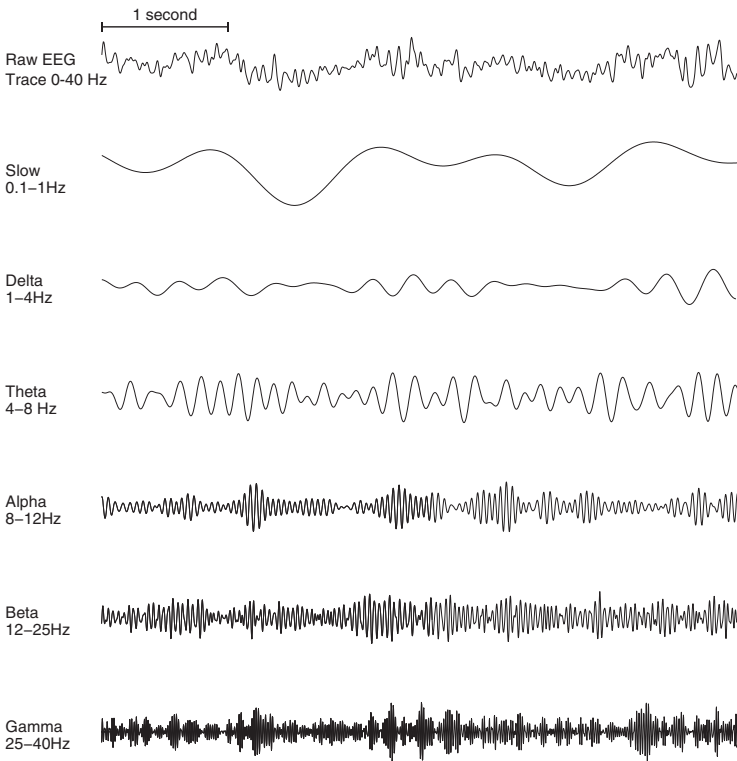


FIGURE 11.2 Anesthetic states and electroencephalogram signatures. Slow (<1 Hz), delta (1 to 4 Hz) and theta (4 to 8 Hz) oscillations are typically seen during unconsciousness at surgical planes. Alpha (8 to 12 Hz) and beta (12 to 25 Hz) oscillations are frequently associated with an arousable state of sedation. Gamma (25 to 40 Hz) is associated with an awake pattern with eyes open.

- e. A patient is considered to be appropriately anesthetized when the BIS value is between 40 and 60.
 - f. The BAG-RECALL Trial, which focused on patients at high risk for intraoperative awareness, found that patients with BIS-guided general anesthesia experienced a small but statistically significant increase in intraoperative awareness relative to patients receiving general anesthesia guided by an end-tidal anesthetic criterion.
- 2. Patient Safety Index (PSI)**
- a. The PSI uses a proprietary algorithm that assesses level of consciousness based on the EEG for patients receiving general anesthesia.
 - b. Like the BIS, it is also scaled from 0 to 100, but the numeric range to ensure that the patient is unconscious is between 25 and 50.
 - c. In addition to displaying the numeric value, the PSI monitor also shows the unprocessed EEG in real time with its spectrogram from both the left and right sides of the head, the level of electromyographic

activity, an artifact index, and the suppression ratio which measures the amount of time the EEG is in burst suppression.

- d. This monitor has been less frequently studied in clinical investigations and has not received the same level of clinical use as the BIS monitor.

3. Narcotrend

- a. Like the BIS and the PSI, the Narcotrend uses a proprietary algorithm that converts the EEG into different states denoted as A to F. Stage A corresponds to the patient being wide-awake, whereas stage F corresponds to increasing burst suppression down to an isoelectric state. The Narcotrend monitor displays the Narcotrend Index, which is scaled between 0 and 100, the unprocessed EEG signal and its spectrogram.
- D. Although the EEG-based indices have been available for nearly 20 years, there are several reasons why they are not part of standard practice in anesthesiology. First, use of EEG-based indices does not ensure that awareness under general anesthesia can be prevented. Second, these indices are considered less reliable in pediatric populations. Third, the indices do not relate directly to the neurophysiology of how a specific anesthetic exerts its effects in the brain. Therefore, they cannot give an accurate picture of the brain's responses to the drugs. Finally, the indices assume that the same index value reflects the same level of unconsciousness for all anesthetics.

III. END-TIDAL ANESTHETIC CRITERION

- A. The **median minimal alveolar concentration (MAC)** value (the MAC of inhaled anesthetic required for immobility in 50% of patients) remains the gold standard for dosing inhaled anesthetics. However, MAC cannot be used to define or predict brain states in anesthetized patients. Animal experiments have demonstrated that there is no clear association between anesthetic-induced EEG patterns and immobility, and that inhaled anesthetics produce immobility primarily by acting in the spinal cord, rather than the brain.
- B. Regardless, end-tidal anesthetic concentration is widely used as a way to monitor the level of consciousness induced by inhaled anesthetics and guide anesthetic dosing.
 - a. This use of MAC has been supported by the B-Unaware Trial that reported no difference in the incidence of intraoperative awareness with an anesthetic protocol that maintained the BIS between 40 and 60 and a protocol that maintained the end-tidal anesthetic between 0.7 and 1.3 MAC.
- C. Unlike the BIS, PSI and Narcotrend, which provide EEG-based measures of brain activity, the end-tidal anesthetic criterion is related very indirectly to brain activity through the concentration of anesthetic expired in the lungs.
- D. A key drawback is that it cannot be used with a total intravenous anesthetic.

IV. THE SPECTRAL ANALYSIS OF THE EEG

- A. A segment of EEG can be decomposed into a plot of its power (usually in dB) as a function of frequency. This plot is termed the power spectrum. Because the spectrum captures only one instance in time it has limited utility during a dynamic anesthetic state (Fig. 11.3).

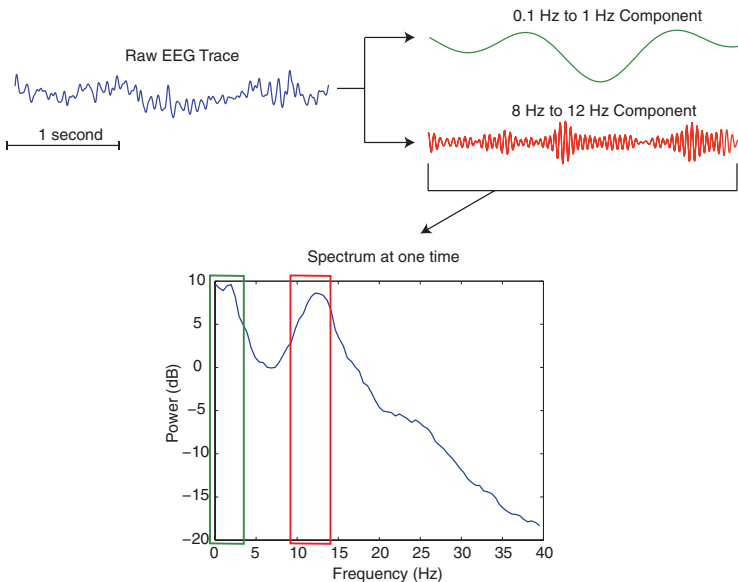


FIGURE 11.3 The plot of power (usually in decibels, dB), against the frequencies being analyzed is the power spectrum.

- B. Taking the spectrum plots at several adjacent time intervals and stacking them together forms a **3D spectrogram**. The spectrogram is a plot of power by frequency as a function of time.
 1. Red = high power, blue = low power.
 2. The 3D spectrogram can be flattened into to a 2D plot which is displayed on monitors in the operating room (Fig. 11.4). The 2D spectrogram plot is also termed the density spectral array. The 3D spectrogram is also termed the compressed spectral array.

V. EFFECTS OF DIFFERENT ANESTHETICS ON THE BRAIN

A. Propofol

1. Neurophysiology: Agonist at the gamma-aminobutyricacid (GABA_A) receptors which function to enhance inhibition
 - a. There is usually a balance between excitatory and inhibitory control of pyramidal neurons. Propofol enhances the inhibitory effects.
 - b. Affects the thalamus by increasing inhibition which decreases excitatory inputs to the cortex.
2. EEG signatures
 - a. The EEG signatures are markers of altered arousal states induced by each anesthetic.
 - b. Propofol displays a characteristic alpha oscillation (8 to 12 Hz) and a slow oscillation (0.5 to 1 Hz).
3. Putative mechanism EEG effect
 - a. During the normal awake state there is a constant exchange of information between the thalamus and cortex. Modeling studies have shown that the EEG alpha oscillations (8 to 12 Hz) observed

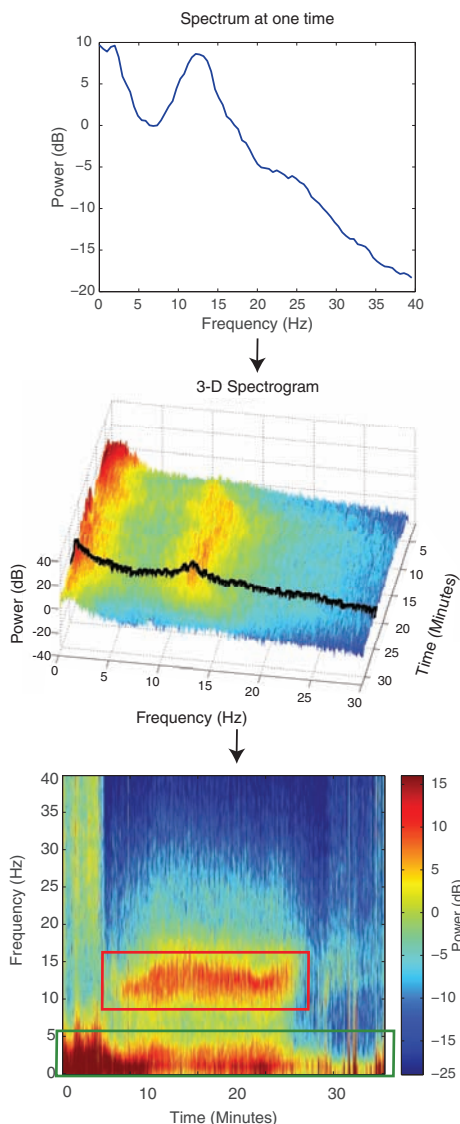


FIGURE 11.4 Construction of the spectrogram: The power spectrum plot at several points in time can be stacked together to form a 3D spectrogram (**middle**). The spectrogram still retains the frequency and power axes but has the helpful addition of a time axis. The 3D spectrogram flattened into a 2D plot (**bottom**) is what is displayed intraoperatively on brain function monitors.

with propofol likely represent an alpha oscillation between the thalamus and the frontal cortex.

- b. The slow oscillation seen with propofol is associated with neurons across the cortex being activated and inactivated at different times (up-down states). This fragments brain activity into asynchronous windows and impairs communication, which is also referred to as “cortical fragmentation” (Fig. 11.5).

B. Ether-Derived Anesthetics (sevoflurane, isoflurane, desflurane)

1. Neurophysiology: Unknown mechanism of action
2. EEG signatures: The raw EEG tracing of the ether-derived inhaled anesthetics appears similar to propofol with an alpha oscillation and a slow oscillation.
 - a. However, at higher concentrations of ether-derived anesthetics, the alpha waves appear to blend with the slow oscillations. This is called the “fill in” effect (Fig. 11.6).

C. Dexmedetomidine (Precedex)

1. Neurophysiology: the locus coeruleus synapses with multiple areas of the brain, including excitatory inputs to the cortex, preoptic area of the thalamus, basal forebrain, and intralaminar nucleus of the thalamus
 - a. Dexmedetomidine acts as an agonist at α_2 receptors which decreases the release of NE from locus coeruleus projections to the cortex, preoptic area of the thalamus, basal forebrain, and intralaminar nucleus of the thalamus.
 - b. This leads to disinhibition of GABA-ergic projections of the preoptic area leading to inhibition of the arousal centers in the midbrain, pons, and hypothalamus, causing sedation.

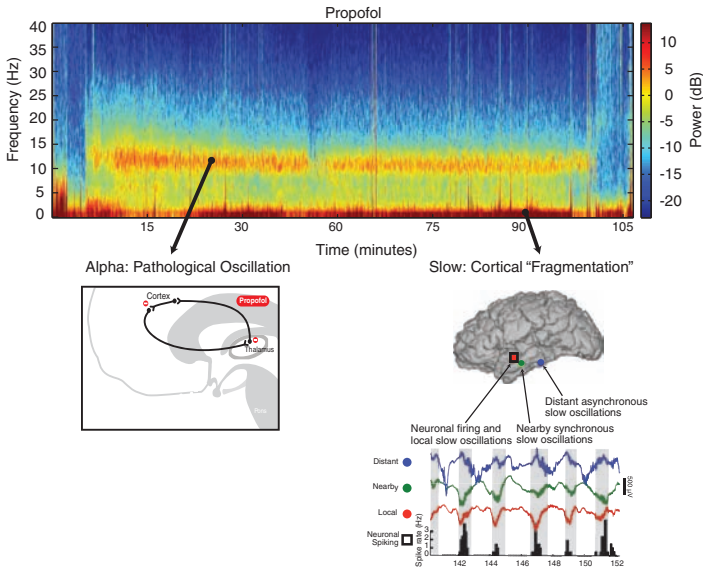


FIGURE 11.5 Spectrogram of propofol showing a pathologic alpha oscillation (8 to 12 Hz), which corresponds with prevention of communication between the thalamus and cortex, and slow wave (0.5 to 1 Hz) cortical fragmentation.

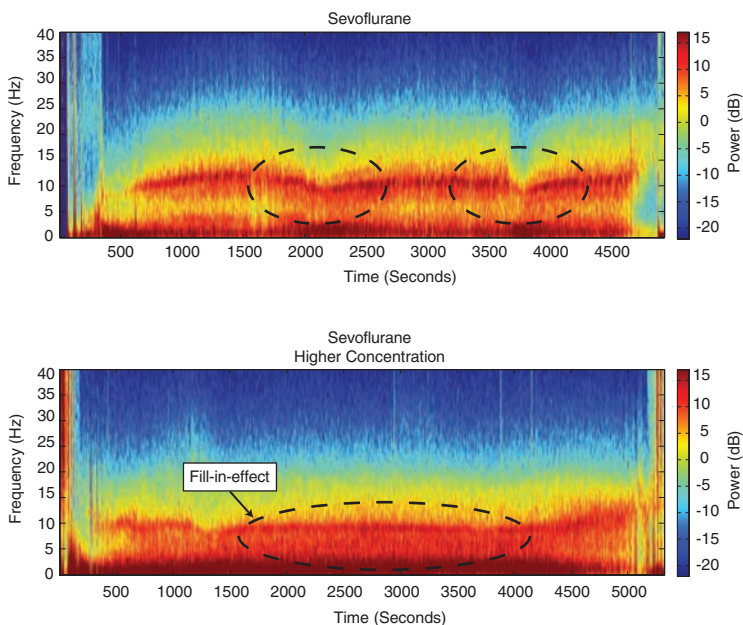


FIGURE 11.6 Spectrogram of sevoflurane showing an alpha (8 to 12 Hz) and slow wave (0.5 to 1 Hz) oscillation at low concentration, and the “fill in” effect at high concentrations of anesthetic.

- c. Dexmedetomidine-induced inhibition of brain stem arousal centers decreases their excitatory inputs to the cortex.
- d. Dexmedetomidine sedation is similar in this way to non-REM sleep.
2. EEG signatures:
 - a. Low dose: Slow waves and spindles (intermittent 9 to 15 Hz oscillations)
 - b. High dose: Slow waves around 1 Hz only
 1. Very similar in appearance to slow wave sleep
 2. Profound brainstem effects
3. Putative mechanism EEG effect
 - a. Slow waves most likely result from decreased excitatory inputs from the brainstem induced by dexmedetomidine's actions in the brainstem.
 - b. Spindles most likely result from diminished excitatory inputs to the cortex and to the thalamus.
4. While EEG patterns observed during sedation with dexmedetomidine appear similar to those observed during general anesthesia with propofol, dexmedetomidine is characterized by spindles whereas propofol is characterized with frontal alpha oscillations. The drugs have different molecular mechanisms and behavioral properties and are likely accompanied by distinguishing neural circuit dynamics (Fig. 11.7).
- D. Ketamine
 1. Neurophysiology: Ketamine binds to *N*-methyl-D-aspartate (NMDA) receptors on inhibitory interneurons present in the cortex, limbic system, and hippocampus
 - a. This leads to disinhibition of the interneurons, leading to an altered arousal state.

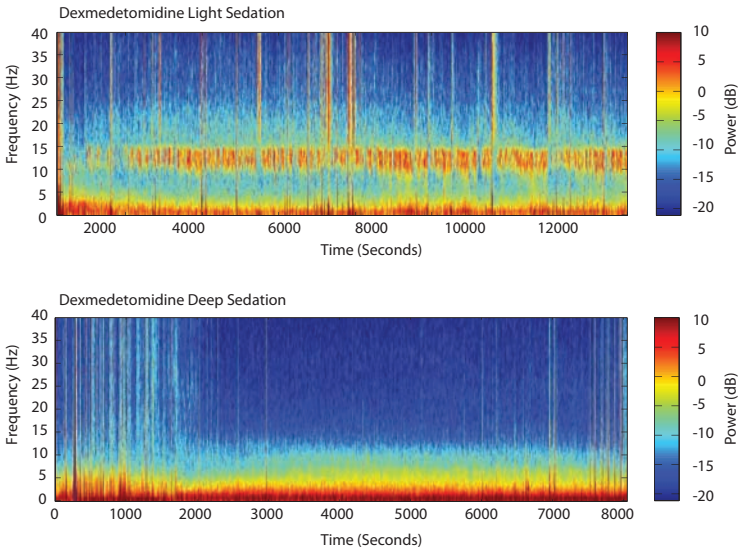


FIGURE 11.7 Spectrogram of dexmedetomidine showing both spindles (9 to 15 Hz) and slow wave (0.5 to 1 Hz) oscillations at low doses and a predominance of slow wave oscillations at high doses

2. EEG signatures: The raw EEG trace is very active and very fast
 - a. On the spectrogram, a 30 Hz gamma oscillation is notable.
 - b. For this reason, the numeric index value associated with a ketamine anesthetic can be read and displayed as a higher value despite adequate anesthesia (Fig. 11.8).

E. Nitrous Oxide

1. Neurophysiology: Thought to have NMDA actions, which is represented by fast beta/gamma oscillation

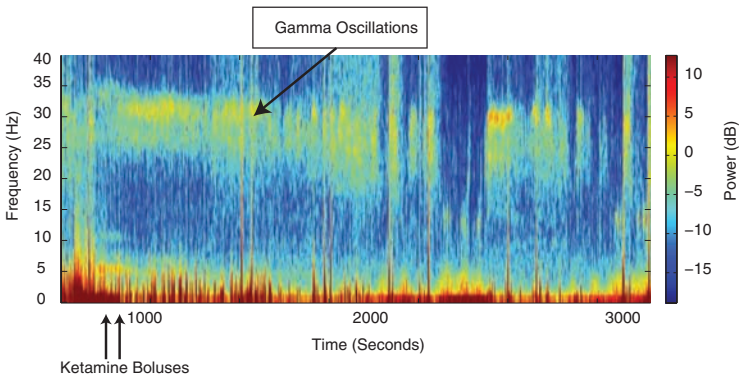


FIGURE 11.8 Spectrogram of ketamine showing a notable 30 Hz gamma oscillation.

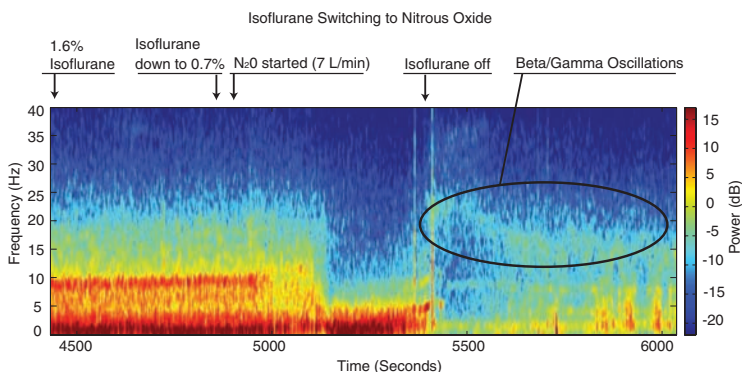


FIGURE 11.9 Spectrogram of nitrous oxide during a transition from isoflurane as the anesthetic to nitrous oxide, as may occur clinically toward the end of surgery to facilitate emergence. The spectrogram of nitrous oxide profound slow-delta oscillations that transition to gamma oscillations.

2. EEG signatures: Fast beta/gamma oscillations as above
 - a. Initial high concentrations of nitrous oxide can induce slow oscillations (Fig. 11.9).
3. Putative mechanism EEG effect: blocking of brainstem glutamatergic inputs to the thalamus and basal forebrain, most likely from the parabrachial nucleus and the medial pontine reticular formation.

VI. CONCLUSION

- A. Although the unprocessed EEG recordings of the anesthetics can look similar, the spectrograms make clear that each anesthetic has a distinct EEG signature. These signatures can be related to the mechanisms by which the drugs act at specific receptors in specific neural circuits to alter arousal.

Suggested Readings

- Akeju O, et al. Effects of sevoflurane and propofol on frontal electroencephalogram power and coherence. *Anesthesiology* 2014;121:990–998.
- Akeju O, et al. A comparison of propofol- and dexmedetomidine- induced electroencephalogram dynamics using spectral and coherence analysis. *Anesthesiology* 2014;121:978–989.
- Avidan, MS, et al. Prevention of intraoperative awareness in a high-risk surgical population. *N Engl J Med* 2011;365:591–600.
- Avidan, MS, et al. Anesthesia awareness and the bispectral index. *N Engl J Med* 2008;358:1097–1108.
- Brown EN, Solt K, Purdon PL, Akeju O. Monitoring the brain state during general anesthesia and sedation. Chapter 50. In: *Miller's Anesthesia*, in press.
- Brown EN, Lydie R, Schiff ND. General anesthesia, sleep and coma. *N Engl J Med* 2010;363:2638–2650.
- Brown EN, Purdon PL, Van Dort CJ. General anesthesia and altered states of arousal: a systems neuroscience analysis. *Annu Rev Neurosci* 2011;34:601–628.
- Clinical Electroencephalography for the Anesthesiologist. www.eeganesthesia.com. Accessed February 12, 2015.
- Lewis LD, Weiner VS, Mukamel EA, et al. Rapid fragmentation of neuronal networks at the onset of propofol-induced unconsciousness. *Proc Natl Acad Sci U S A* 2012;109:E3377–E3386.
- Purdon PL, et al. Electroencephalogram signatures of loss and recovery of consciousness from propofol. *Proc Natl Acad Sci U S A* 2013;110:E1142–E1151.

I. PHARMACOLOGY OF INTRAVENOUS ANESTHETICS

Intravenous (IV) anesthetics are commonly used for the induction and maintenance of general anesthesia and for sedation. The rapid onset and offset of these drugs are due to their physical translocation into and out of the brain. After a bolus IV injection, lipid-soluble drugs such as propofol, thio-pental (not available in the United States), and etomidate rapidly distribute into the **vessel-rich group** of highly perfused tissues (e.g., brain, heart, liver, and kidneys), causing an extremely rapid onset of effect. Plasma concentrations decrease as the drug is taken up by the less well-perfused tissues (e.g., muscle and fat), and the drug rapidly leaves the brain. This **redistribution** from the brain is responsible for the termination of effects, but the **clearance** of the active drug must still occur, typically by hepatic **metabolism** and renal **elimination**. **Elimination half-life** is defined as the time required for the plasma concentration of a drug to decrease by 50% during the elimination phase of clearance. **Context-sensitive half-time (CSHT)** is defined as the time required for a 50% decrease in the central compartment drug concentration after a steady-state infusion of specified duration (duration is the “context”).

A. Propofol (2, 6-diisopropylphenol) is used for the induction or maintenance of general anesthesia and for procedural sedation. It is prepared as a 1% isotonic oil-in-water emulsion, which contains egg lecithin, glycerol, and soybean oil. Bacterial growth is inhibited by ethylenediaminetetraacetic acid (EDTA), diethylenetriamine pentaacetic acid (DTPA), sulfite, or benzyl alcohol depending on the manufacturer.

- 1. Mode of action.** Facilitates inhibitory neurotransmission by enhancing the function of γ -aminobutyric acid type A (GABA_A) receptors in the central nervous system (CNS). The modulation of glycine receptors, *N*-methyl-D-aspartate (NMDA) receptors, cannabinoid receptors, and voltage-gated ion channels may also contribute to propofol's actions.
- 2. Pharmacokinetics**
 - a.** Hepatic and extrahepatic metabolism to inactive metabolites which are renally excreted.
 - b.** CSHT remains short (15 minutes after a 2-hour infusion), making propofol infusions useful for the maintenance of anesthesia.
- 3. Pharmacodynamics**
 - a. CNS**
 - 1.** Induction doses rapidly produce unconsciousness (30 to 45 seconds), followed by a rapid termination of effect due to redistribution. Emergence is rapid and often accompanied by mood elevation. Low doses produce sedation and amnesia.
 - 2.** Weak analgesic effects at hypnotic concentrations.
 - 3.** Decreases intracranial pressure (ICP) and also cerebral perfusion pressure (CPP) due to markedly decreased mean arterial pressure (MAP). Cerebral autoregulation as well as vasoconstriction in response to hyperventilation are unaffected.

4. Propofol is an anticonvulsant and raises the seizure threshold more than that with methohexital.
 5. Frontal alpha oscillations (8 to 12 Hz), delta oscillations (1 to 4 Hz), and slow oscillations (<1 Hz) appear on the electroencephalogram (EEG). Higher doses cause burst suppression and isoelectric EEG.
 6. Depresses somatosensory-evoked potentials (SSEPs) and motor-evoked potentials (MEPs), but little effect on brainstem auditory-evoked potentials (BAEPs).
 7. Postoperative nausea and vomiting (PONV) occurs less frequently after a propofol-based anesthetic compared with other techniques, and subhypnotic doses have antiemetic effects.
- b. Cardiovascular system**
1. Dose-dependent decreases in preload, afterload, and contractility lead to decreases in blood pressure (BP) and cardiac output. Hypotension may be marked in hypovolemic, elderly, or hemodynamically compromised patients.
 2. Heart rate (HR) is minimally affected, and baroreceptor reflex is blunted.
- c. Respiratory system**
1. Dose-dependent decreases in respiratory rate (RR) and tidal volume (TV).
 2. Ventilatory responses to hypoxia and hypercarbia are diminished.
- 4. Dosage and administration.** Table 12.1.
- a. Titrate with reduced incremental doses in hypovolemic, elderly, or hemodynamically compromised patients or if administered with other anesthetics.
 - b. Relatively larger induction and maintenance doses are required in infants and small children.
 - c. Propofol emulsion supports bacterial growth despite the addition of antimicrobials; prepare drug under sterile conditions, label with date and time, and discard unused, opened propofol after **6 hours** to prevent inadvertent bacterial contamination.
- 5. Adverse effects**
- a. **Venous irritation.** May cause pain during IV administration, which can be reduced by administration in a large vein or by adding

TABLE
12.1

Dosages of Commonly Used IV Anesthetics

Drug	Dose		
	Induction (mg/kg)	Maintenance (μ g/kg/min)	Sedation (Titrate to Effect)
Propofol IV	2.0–2.5	100–150	25–75 μ g/kg/min
Midazolam IV	0.1–0.4	0.5–1.5	0.5–1.0 mg
Midazolam IM			0.07–0.1 mg/kg
Ketamine IV	0.5–2	15–90	0.1–0.8 mg/kg
Ketamine IM	5–10		2–4 mg/kg
Etomidate IV	0.2–0.4	10	5–8 μ g/kg/min ^a
Dexmedetomidine IV			0.2–0.7 μ g/kg/h ^b

^a For brief periods.

^b After loading dose of 0.5–1.0 μ g/kg over 10 min.

lidocaine to the solution (e.g., 20 mg of lidocaine to 200 mg of propofol). The most effective method to reduce pain is to give lidocaine (0.5 mg/kg, IV) 1 to 2 minutes before propofol injection with a tourniquet proximal to the IV site.

- b. **Lipid disorders.** Propofol is a lipid emulsion and should be used cautiously in patients with disorders of lipid metabolism (e.g., hyperlipidemia and pancreatitis).
 - c. **Myoclonus and hiccups** can occur after induction doses, although less frequently than with methohexital or etomidate.
 - d. **Propofol infusion syndrome** is a rare and often fatal disorder that occurs in critically ill patients (usually children) subjected to prolonged, high-dose propofol infusions. Typical features include rhabdomyolysis, metabolic acidosis, cardiac failure, and renal failure.
- B. Barbiturates** such as thiopental and methohexital rapidly produce unconsciousness (30 to 45 seconds) after IV administration, followed by rapid termination of effects due to redistribution. Barbiturate preparations for IV administration are highly alkaline (pH >10) and are usually prepared as dilute solutions (1.0% to 2.5%).
1. **Mode of action.** Similar to propofol, barbiturates facilitate inhibitory neurotransmission by enhancing GABA_A receptor function. They also inhibit excitatory neurotransmission via glutamate and nicotinic acetylcholine receptors.
 2. **Pharmacokinetics**
 - a. Hepatic metabolism. Methohexital has a much higher clearance than thiopental. Thiopental is metabolized to pentobarbital, an active metabolite with a longer half-life.
 - b. Multiple doses or prolonged infusions may produce prolonged sedation or unconsciousness due to the reduced rate of redistribution, the return of the drug to the central compartment, and slow hepatic metabolism. The CSHT of thiopental is long, even after short infusions.
 3. **Pharmacodynamics**
 - a. **CNS**
 1. Dose-dependent CNS depression ranging from sedation to unconsciousness. Much higher doses are required to suppress responses to painful stimuli.
 2. Dose-dependent cerebral vasoconstriction and decrease in cerebral metabolic rate (CMRO₂) cause reductions in ICP and cerebral blood flow (CBF). Cerebral autoregulation remains unaffected.
 3. At high doses, thiopental will produce an isoelectric EEG. In contrast, methohexital can elicit seizure activity.
 4. Minimal effects on SSEPs or MEPs, but dose-dependent depression of BAEPs.
 - b. **Cardiovascular system**
 1. Cause venodilation and depress myocardial contractility, leading to dose-dependent decreases in BP and cardiac output, especially in patients who are preload dependent. Decrease in BP is less pronounced than with propofol.
 2. Baroreceptor reflexes remain largely intact; therefore, HR may increase in response to hypotension.
 - c. **Respiratory system**
 1. Dose-dependent decreases in RR and TV. Ventilatory responses to hypoxia and hypercarbia are markedly depressed. Apnea may result for 30 to 90 seconds after an induction dose.

2. Laryngeal reflexes remain more intact compared with propofol; therefore, the incidence of cough and laryngospasm is higher.
4. **Dosage and administration.** See Table 12.1.
 - a. Reduce doses in hypovolemic, elderly, or hemodynamically compromised patients.
 - b. May precipitate when mixed with drugs in lower pH solution (e.g., succinylcholine) and cause the precipitation of other drugs (e.g., vecuronium). Therefore, it is prudent to use a free-running IV and avoid simultaneous injection with other drugs.
5. **Adverse effects**
 - a. **Allergy.** True allergies are unusual. Thiopental occasionally causes anaphylactoid reactions (i.e., hives, flushing, and hypotension) due to histamine release.
 - b. **Porphyria**
 1. **Absolutely contraindicated** in patients with acute intermittent porphyria, variegate porphyria, and hereditary coproporphyria.
 2. Barbiturates induce porphyrin synthetic enzymes such as δ -aminolevulinic acid synthetase; patients with porphyria may accumulate toxic heme precursors and suffer an acute attack.
 - c. **Venous irritation and tissue damage**
 1. May cause pain at the site of administration due to venous irritation.
 2. Thiopental can cause severe pain and tissue necrosis if injected extravascularly or intra-arterially. If intra-arterial administration occurs, phentolamine (α -blocker), heparin, vasodilators, and regional sympathetic blockade may be helpful in treatment.
 - d. **Myoclonus and hiccups** are often seen during induction with methohexital.
- C. **Benzodiazepines** include midazolam, lorazepam, and diazepam. They are often used for sedation, amnesia, anxiolysis, or as adjuncts to general anesthesia. Midazolam is prepared in a water-soluble form at pH 3.5, while diazepam and lorazepam are dissolved in propylene glycol and polyethylene glycol, respectively.
 1. **Mode of action.** Enhance inhibitory neurotransmission by increasing the affinity of GABA_A receptors for GABA. Different clinical effects (e.g., amnesia, sedation, and anxiolysis) appear to be mediated by different GABA_A receptor subtypes.
 2. **Pharmacokinetics**
 - a. After IV administration, the onset of CNS effects occurs in 2 to 3 minutes for midazolam and diazepam (slightly longer for lorazepam). Effects are terminated by redistribution; therefore, durations of a single dose of diazepam and midazolam are similar. The effects of lorazepam are somewhat more prolonged.
 - b. All three drugs are metabolized in the liver. Elimination half-lives for midazolam, lorazepam, and diazepam are approximately 2, 11, and 20 hours, respectively. The active metabolites of diazepam last longer than the parent drug and accumulate with repeated dosing. Hydroxymidazolam can accumulate and cause sedation in patients with renal failure.
 - c. Diazepam clearance is reduced in the elderly, but this is less of a problem with midazolam and lorazepam. Obese patients may require higher initial doses of benzodiazepines, but clearance is not markedly different.

3. Pharmacodynamics

a. CNS

1. Amnestic, anticonvulsant, anxiolytic, muscle relaxant, and sedative-hypnotic effects in a dose-dependent manner. Amnesia may last for only 1 hour after a single premedicant dose of midazolam. Sedation may sometimes be prolonged.
2. Do not produce significant analgesia.
3. Dose-dependent reduction of CBF and CMRO₂.
4. Do not produce burst suppression or isoelectric EEG pattern, even at very high doses.

b. Cardiovascular system

1. Mild systemic vasodilation and decrease in cardiac output. HR is usually unchanged.
2. Hemodynamic changes may be pronounced in hypovolemic or critically ill patients if rapidly administered in a large dose or with an opioid.

c. Respiratory system

1. Mild dose-dependent decreases in RR and TV. Some decrease in hypoxic ventilatory drive.
2. Respiratory depression may be pronounced if administered with an opioid, in patients with pulmonary disease or in debilitated patients.

4. Dosage and administration. See Table 12.1 for midazolam.

- a. Incremental IV doses of diazepam (2.5 mg) or lorazepam (0.25 mg) may be used for sedation.
- b. Appropriate oral doses are 5 to 10 mg of diazepam or 2 to 4 mg of lorazepam.

5. Adverse effects

- a. **Drug interactions.** Administration of a benzodiazepine to a patient receiving the anticonvulsant **valproate** may precipitate a psychotic episode.

b. Pregnancy and labor

1. May be associated with a slightly increased risk of cleft lip and palate when administered during the first trimester.
2. Cross the placenta and may lead to CNS depression in the neonate.

- c. **Superficial thrombophlebitis and injection pain** may be produced by the vehicles in diazepam and lorazepam.

6. Flumazenil (imidazobenzodiazepine) is a competitive antagonist at the benzodiazepine binding site of GABA_A receptors in the CNS.

- a. Reversal of benzodiazepine-induced sedative effects occurs within 2 minutes; peak effects occur at approximately 10 minutes. Does not completely antagonize the respiratory depressant effects of benzodiazepines.
- b. Half-life is shorter than the benzodiazepine agonists, so repeated administration may be necessary.
- c. Metabolized to inactive metabolites in the liver.
- d. **Dose.** 0.3 mg IV every 30 to 60 seconds (to a maximum dose of 5 mg).
- e. **Contraindicated** in patients with tricyclic antidepressant (TCA) overdose (thought to be the unmasking of TCA-induced seizure activity) and in those receiving benzodiazepines for the control of seizures or elevated ICP. Use cautiously in patients who have had long-term treatment with benzodiazepines because acute withdrawal may be precipitated.

D. Etomidate is a sedative–hypnotic agent most commonly used for IV induction of general anesthesia. It is supplied in a solution containing 35% of propylene glycol.

1. Mode of action. Facilitates inhibitory neurotransmission by enhancing GABA_A receptor function.

2. Pharmacokinetics

- After an induction dose, times to loss of consciousness and return of consciousness are similar to that for propofol. Effects of a single bolus dose are terminated by redistribution.
- Very high clearance in the liver and by circulating esterases to inactive metabolites.

3. Pharmacodynamics

a. CNS

- No analgesic properties.
- CBF, CMRO₂, and ICP decrease while CPP is usually maintained. Cerebral vasoconstriction in response to hyperventilation is preserved.
- Induces burst suppression at high doses.
- Less depression of evoked potentials compared to that with propofol or thiopental. BAEPs are unaffected, while SSEPs are enhanced.

b. Cardiovascular system

- Minimal changes in HR, BP, and cardiac output. Often chosen to induce general anesthesia in hemodynamically compromised patients.
- Does not affect the sympathetic tone or the baroreceptor function. Will not effectively suppress hemodynamic responses to pain.

c. Respiratory system

- Dose-dependent decreases in RR and TV; transient apnea may occur.
- The respiratory depressant effects of etomidate are less pronounced than those of propofol or barbiturates.

4. Dosage and administration. See Table 12.1.

5. Adverse effects

- Myoclonus** may occur after administration, particularly in response to stimulation.
- Nausea and vomiting** occur more frequently in the postoperative period than with other anesthetic agents.
- Venous irritation and superficial thrombophlebitis** may be caused by the propylene glycol vehicle. Minimized by administration into a free-flowing IV carrier infusion.
- Adrenal suppression.** Inhibits 11 β -hydroxylase; a single induction dose suppresses adrenal steroid synthesis for up to 24 hours. May not be clinically significant after a single dose, but repeated doses/infusions have been associated with increased mortality in the ICU.

E. Ketamine is a sedative–hypnotic agent with potent analgesic properties. It is used for the induction of general anesthesia and for sedation and analgesia in the perioperative setting.

- Mode of action.** Anesthetic effects are mainly attributed to noncompetitive antagonism of NMDA receptors in the CNS, although effects on opioid receptors, acetylcholine receptors, and voltage-gated sodium and calcium channels also have been reported.

2. Pharmacokinetics

- a. Produces unconsciousness in 30 to 60 seconds after an IV induction dose. Effects are terminated by redistribution in 15 to 20 minutes. After intramuscular (IM) administration, the onset of CNS effects is delayed for approximately 5 minutes, with peak effect at approximately 15 minutes.
- b. Metabolized rapidly in the liver to multiple metabolites, some of which have modest activity (e.g., norketamine). Elimination half-life is 2 to 3 hours.
- c. Repeated bolus doses or prolonged infusions result in accumulation.

3. Pharmacodynamics

a. CNS

1. Produces a “dissociative” state accompanied by amnesia and profound analgesia. Analgesia occurs at much lower concentrations than hypnosis, so analgesic effects persist after the return of consciousness.
2. Increases CBF, ICP, and CMRO₂; cerebral vasoconstriction in response to hyperventilation is preserved.
3. Enhancement of SSEPs; depression of brainstem auditory-evoked potentials (BAEPs) and visual-evoked potentials (VEPs).
4. Dose-dependent EEG changes that differ from other anesthetics; high doses do not produce an isoelectric EEG. Gamma oscillations (25 to 40 Hz) are often observed.

b. Cardiovascular system

1. Increases HR, cardiac output, and BP of systemic and pulmonary arteries by causing the release of endogenous catecholamines.
2. Often used to induce general anesthesia in hemodynamically compromised patients, particularly those for whom HR, preload, and afterload should remain high. Should be used cautiously in patients with CAD or pulmonary hypertension.
3. May act as a direct myocardial depressant in patients with maximal sympathetic nervous system stimulation or in patients with autonomic blockade.

c. Respiratory system

1. Usually depresses RR and TV only mildly and has minimal effect on CO₂ response.
2. Potent bronchodilator due to sympathomimetic effects.
3. Laryngeal protective reflexes are relatively well maintained, although aspiration can still occur.

4. Dosage and administration. See Table 12.1.

- a. Useful for IM induction in patients with no IV access (e.g., children).
- b. A concentrated 10% solution is available for IM use only.

5. Adverse effects

- a. **Oral secretions** are markedly stimulated. The coadministration of an antisialagogue (e.g., glycopyrrolate) may be helpful.
- b. **Emotional disturbance.** May cause agitation and unpleasant hallucinations during the early postoperative period. Incidence is higher with increased age, female gender, and dosages greater than 2 mg/kg but may be greatly reduced with the coadministration of a benzodiazepine or propofol. Children seem to be less troubled than adults by the hallucinations. Alternatives should be considered in patients with psychiatric disorders.

- c. **Muscle tone.** May lead to random myoclonic movements, especially in response to stimulation. Muscle tone is often increased.
 - d. **Increases ICP** and is relatively contraindicated in patients with head trauma or intracranial hypertension.
 - e. **Ocular effects.** May lead to mydriasis, vertical nystagmus, diplopia, blepharospasm, and increased intraocular pressure.
 - f. **Anesthetic depth may be difficult to assess.** Common clinical signs of anesthetic depth (e.g., HR, BP, and RR) as well as EEG-based monitors of anesthetic depth are less reliable when ketamine is used.
- F. Dexmedetomidine.** Dexmedetomidine is a sedative agent with analgesic properties. It is used as an adjunct to general and regional anesthesia and for sedation in the ICU and the OR.
- 1. **Mode of action.** Highly selective α_2 -adrenergic receptor agonist (α_2/α_1 1,600:1). **Clonidine** is a less-selective and longer-acting α_2 agonist (α_2/α_1 200:1) with similar sedating and analgesic properties.
 - 2. **Pharmacokinetics**
 - a. Undergoes rapid redistribution after IV administration. Elimination half-life is approximately 2 hours.
 - b. Metabolized extensively in the liver.
 - 3. **Pharmacodynamics**
 - a. **CNS**
 - 1. Elicits a sedated but arousable state similar to natural sleep.
 - 2. Potentiates CNS effects of propofol, volatile anesthetics, benzodiazepines, and opioids.
 - 3. Weak amnestic; no anticonvulsant properties.
 - 4. Low doses produce spindles on the EEG that are similar to those observed during non-REM stage 2 sleep. Higher doses produce delta and slow oscillations similar to non-REM stage 3 sleep.
 - b. **Cardiovascular system**
 - 1. Decreases HR and BP, although transient hypertension may occur after an IV bolus.
 - 2. Baroreflex is well preserved.
 - c. **Respiratory system**
 - 1. Minimal respiratory depression, although it may add to respiratory depressant effects of other anesthetics.
 - 2. Airway reflexes remain intact, making it useful for awake fiberoptic intubation.
 - d. **Endocrine system.** May decrease adrenal response to adrenocorticotrophic hormone after prolonged infusions, although clinical significance is unclear.
 - 4. **Dosage and administration.** See Table 12.1.
 - a. Decreased dosage should be considered in patients with significant hepatic dysfunction. Because the activity of dexmedetomidine metabolites has not been studied, decreased dosage may be prudent for patients with severe renal dysfunction.
 - b. Indicated only for infusions lasting less than 24 hours.
 - 5. **Adverse effects.** Antimuscarinic effects (e.g., dry mouth and blurred vision) may occur due to α_2 adrenal receptor-mediated inhibition of acetylcholine release.
- G. Opioids.** Morphine, meperidine, hydromorphone, fentanyl, sufentanil, alfentanil, and remifentanil are opioids commonly used in general anesthesia. Their primary effect is analgesia, and, therefore, they are used to supplement other agents during the induction or maintenance of general anesthesia. In high doses, opioids are occasionally used as the primary

anesthetic (e.g., cardiac surgery). Opioids differ in their potencies, pharmacokinetics, and side effects.

1. Mode of action. Bind to specific receptors in the brain, spinal cord, and on peripheral neurons. The opioids listed above are all relatively selective for μ -opioid receptors.

2. Pharmacokinetics

a. Pharmacokinetic data are presented in Table 12.2.

b. After IV administration, the onset of action is within minutes for the fentanyl derivatives; hydromorphone and morphine may take 20 to 30 minutes for peak effect due to their lower lipid solubilities. The termination of effects for all opioids except remifentanyl is by redistribution.

c. Elimination is primarily by the liver and depends on hepatic blood flow. Remifentanyl is metabolized by nonspecific esterases in tissues (primarily skeletal muscle). Morphine and meperidine have active metabolites, whereas hydromorphone and the fentanyl derivatives do not.

d. Metabolites are primarily excreted in the urine. In patients with renal failure, the accumulation of morphine-6-glucuronide may cause prolonged narcosis and respiratory depression. Renal failure may also cause the accumulation of normeperidine, an active meperidine metabolite associated with seizure activity.

3. Pharmacodynamics

a. CNS

1. Produce sedation and analgesia in a dose-dependent manner; euphoria is common. Very large doses may produce amnesia and loss of consciousness, but opioids are not reliable hypnotics.

2. Reduce the minimum alveolar concentration (MAC) of inhalational anesthetics and the requirements for IV sedative-hypnotic drugs.

TABLE
12.2

Dose, Time to Peak Effect, and the Duration of Analgesia for IV Opioid Agonists and Agonist-Antagonists^a

Opioid	Dose (mg) ^b	Peak (minute)	Duration (hour) ^c
Morphine	10	30–60	3–4
Meperidine	80	5–7	2–3
Hydromorphone	1.5	15–30	2–3
Oxymorphone	1.0	15–30	3–4
Methadone	10	15–30	3–4
Fentanyl	0.1	3–5	0.5–1
Sufentanyl	0.01	3–5	0.5–1
Alfentanyl	0.75	1.5–2	0.2–0.3
Remifentanyl	0.1	1.5–2	0.1–0.2
Pentazocine	60	15–30	2–3
Butorphanol	2	15–30	2–3
Nalbuphine	10	15–30	3–4
Buprenorphine ^d	0.3	<30	5–6

^a Data for fentanyl derivatives are derived from intraoperative studies, the remainder from postoperative pain studies.

^b Approximately equianalgesic doses (see text).

^c Average duration of first single dose.

^d Buprenorphine is not available for analgesic use in the United States. Sole use is high-dose maintenance for previous opioid addicts.

3. Decrease CBF and $CMRO_2$.
4. Produce miosis by the stimulation of the Edinger-Westphal nucleus of the oculomotor nerve.
- b. Cardiovascular system**
 1. All opioids except meperidine produce minimal changes in cardiac contractility. Baroreceptor reflexes are preserved.
 2. Systemic vascular resistance (SVR) usually is moderately reduced because of reduced medullary sympathetic outflow. Bolus doses of meperidine or morphine may reduce SVR secondary to histamine release.
 3. Produce bradycardia in a dose-dependent manner by the stimulation of the central vagal nuclei. Meperidine has a weak atropine-like effect and does not cause bradycardia.
 4. The relative hemodynamic stability offered by opioids often leads to their use in sedation or anesthesia for hemodynamically compromised or critically ill patients.
- c. Respiratory system**
 1. Produce dose-dependent respiratory depression. RR decreases initially; TV decreases with larger doses. The effect is accentuated in the presence of sedatives, other respiratory depressants, or pre-existing pulmonary disease.
 2. Decrease ventilatory response to hypercapnia and hypoxia. Effects are markedly increased if the patient falls asleep.
 3. Opioids dose dependently decrease the cough reflex. Higher doses suppress tracheal and bronchial foreign body reflexes, so endotracheal intubation and mechanical ventilation are better tolerated.
- d. Gastrointestinal system**
 1. Decrease gastric emptying and intestinal secretions. Colonic tone and sphincter tone increase and propulsive contractions decrease, resulting in constipation.
 2. Increase biliary pressure and may produce biliary colic; the spasm of the sphincter of Oddi may prevent cannulation of the common bile duct. The incidence is lower with agonist-antagonist opioids.
- 4. Dosage and administration.** Opioids are usually administered IV, either by bolus or by infusion. Appropriate dosages are presented in Table 12.2. Clinical dosing must be individualized and based on the patient's underlying condition and clinical response. Larger doses may be required in patients chronically receiving opioids.
- 5. Adverse effects**
 - a. Allergic reactions** are rare, although anaphylactoid reactions may occur with morphine and meperidine secondary to histamine release.
 - b. Drug interactions.** The administration of meperidine or tramadol to a patient who has received a monoamine oxidase inhibitor may result in delirium or hyperthermia and may be fatal.
 - c. Nausea and vomiting** can occur because of the direct stimulation of the chemoreceptor trigger zone. Nausea is more likely if the patient is moving.
 - d. Muscle rigidity** may occur, especially in the chest, abdomen, and upper airway, resulting in the inability to ventilate the patient. The incidence increases with drug potency, dose, rate of administration, and presence of nitrous oxide. Rigidity may be reversed

by administering neuromuscular relaxants or opioid antagonists and is less likely after pretreatment with a benzodiazepine or propofol.

- e. **Urinary retention** may occur because of increased tone in the vesical sphincter and inhibition of the detrusor (voiding) reflex. May also decrease awareness of the need to urinate.
6. **Naloxone** is a pure opioid antagonist used to reverse unanticipated or undesired opioid-induced effects such as respiratory or CNS depression.
 - a. **Mode of action.** Competitive antagonist at opioid receptors in the brain and spinal cord.
 - b. **Pharmacokinetics**
 1. Peak effects are seen within 1 to 2 minutes; a significant decrease in its clinical effects occurs after 30 minutes because of redistribution.
 2. Metabolized in the liver.
 - c. **Pharmacodynamics**
 1. Reverses the pharmacologic effects of opioids such as CNS and respiratory depression.
 2. Crosses the placenta; administration to the parturient before delivery will decrease opioid-induced respiratory depression in the neonate.
 - d. **Dosage and administration.** Perioperative respiratory depression in an adult can be treated with 0.04 mg IV every 2 to 3 minutes as needed. **Repeated administration may be necessary** due to short duration of action.
 - e. **Adverse effects**
 1. May lead to the abrupt onset of **pain** as opioid analgesia is reversed. This may be accompanied by sudden hemodynamic changes (e.g., hypertension and tachycardia).
 2. May precipitate **pulmonary edema** and **cardiac arrest** in rare cases.

II. PHARMACOLOGY OF INHALATION ANESTHETICS

Inhalation anesthetics are usually administered for the maintenance of general anesthesia but also can be used for induction, especially in pediatric patients. General properties of commonly used inhalation anesthetics are summarized in Table 12.3. Dosages of inhalation anesthetics are expressed as **MAC**, the **minimum alveolar concentration** at 1 atm at which 50% of patients do not move in response to a surgical stimulus. MAC is additive (e.g., 0.5 MAC nitrous oxide + 0.5 MAC isoflurane = 1 MAC total).

TABLE
12.3

Properties of Inhalation Anesthetics

Anesthetic	Vapor Pressure (mm Hg, 20°C)	Partition Coefficients		MAC (% With O ₂ Only)
		Blood–gas ^a (37°C)	Brain–blood (37°C)	
Isoflurane	239	1.41.6	1.6	1.15
Desflurane	664	0.42	1.3	6.0
Sevoflurane	157	0.69	1.7	2.05
Nitrous oxide	39,000	0.47	1.1	104

^a The blood–gas partition coefficient is inversely related to the rate of induction.

A. Mode of Action

- 1. Nitrous oxide.** Although exact mechanisms are unknown, anesthetic effects are mainly attributed to the antagonism of NMDA receptors in the CNS.
- 2. Volatile anesthetics.** Exact mechanisms are unknown. Various ion channels in the CNS involved in synaptic transmission (including GABA_A, glycine, and glutamate receptors) have been shown to be sensitive to inhalation anesthetics and may play a role.

B. Pharmacokinetics

- 1. Determinants of the speed of onset and offset.** The alveolar anesthetic concentration (F_A) may differ significantly from the inspired anesthetic concentration (F_I). The rate of rise of the ratio of these two concentrations (F_A/F_I) determines the speed of induction of general anesthesia (Fig. 12.1). Two opposing processes, anesthetic delivery to and uptake from alveoli, determine the F_A/F_I at a given time. Determinants of uptake include the following:
 - a. Blood–gas partition coefficient.** A lower solubility in blood will lead to lower uptake of anesthetic into the bloodstream, thereby increasing the rate of rise of F_A/F_I . The solubility of halogenated volatile anesthetics in blood is increased somewhat with hypothermia and hyperlipidemia.
 - b. Inspired anesthetic concentration.** This is influenced by the volume of the breathing circuit, fresh gas inflow rate, and the absorption of the volatile anesthetic by circuit components.
 - c. Alveolar ventilation.** Increased minute ventilation, without the alteration of other processes that affect anesthetic delivery or uptake, increases F_A/F_I . This effect is more pronounced with the more blood-soluble agents.
 - d. Concentration effect.** As F_I increases, the rate of rise of F_A/F_I also increases. For a gas with a high F_I like nitrous oxide, a large amount is taken up into blood, but this causes a large loss of the total gas volume. The remaining nitrous oxide is thus “concentrated,” and the addition of more anesthetic with the next breath will increase the concentration further. The uptake of a large gas volume also creates

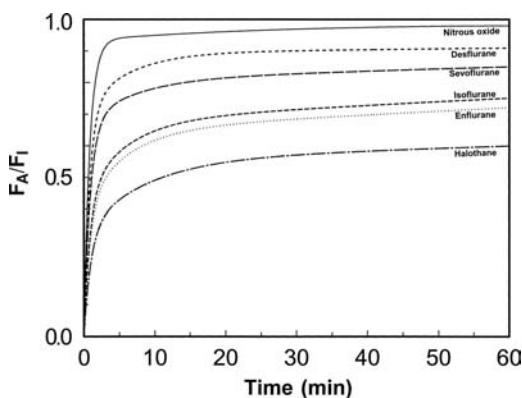


FIGURE 12.1 Ratio of alveolar to inspired gas concentration (F_A/F_I) as a function of time at constant cardiac output and minute ventilation.

a void that draws more fresh gas into the alveoli, thereby increasing F_A and augmenting the inspired TV . The concentration effect explains why the rate of rise of F_A/F_I is faster for nitrous oxide than for desflurane (see Fig. 12.1), even though the blood–gas partition coefficient for desflurane is smaller.

- e. **The second gas effect.** This is a direct outcome of the concentration effect. When nitrous oxide and a potent inhalation anesthetic are administered together, the uptake of nitrous oxide concentrates the “second” gas (e.g., isoflurane) and increases the input of additional second gas into the alveoli via the augmentation of inspired volume.
 - f. **Cardiac output.** An increase in the cardiac output (and therefore pulmonary blood flow) will increase anesthetic uptake and thus decrease the rate of rise in F_A/F_I . A decrease in the cardiac output will have the opposite effect. This effect of cardiac output is more pronounced with nonbreathing circuits or highly soluble anesthetics and is most prominent early in the course of anesthetic administration.
 - g. **Gradient between alveolar and venous blood.** The uptake of anesthetic into the bloodstream will decrease as the anesthetic partial pressure gradient between the alveolar gas and the venous blood decreases. This gradient is particularly large early in the course of anesthetic administration.
2. **Distribution in tissues.** The rate of equilibration of anesthetic partial pressure between blood and a particular organ system depends on the following factors:
 - a. **Tissue blood flow.** Equilibration occurs more rapidly in tissues receiving increased perfusion. The **vessel-rich group** of highly perfused organ systems receives approximately 75% of the cardiac output. The remainder of the cardiac output perfuses predominantly into muscle and fat.
 - b. **Tissue solubility.** For a given arterial anesthetic partial pressure, anesthetic agents with high-tissue solubility are slower to equilibrate. Solubilities of anesthetic agents differ among tissues. Brain–blood partition coefficients of inhalation agents are shown in Table 12.3.
 - c. **Gradient between arterial blood and tissue.** Until equilibration is reached between the anesthetic partial pressure in the blood and a particular tissue, a gradient exists that leads to the uptake of anesthetic by the tissue. The rate of uptake will decrease as the gradient decreases.
 3. **Elimination**
 - a. **Exhalation.** This is the predominant route of elimination. After discontinuation, an anesthetic’s tissue and alveolar partial pressures decrease by reversing the processes that occurred when the anesthetic was introduced.
 - b. **Metabolism.** Significant biotransformation of nitrous oxide has not been demonstrated. Volatile anesthetics may undergo different degrees of hepatic metabolism.
 - c. **Anesthetic loss.** Inhalation anesthetics may be lost both percutaneously and through visceral membranes, although such losses are probably negligible.
- C. **Pharmacodynamics**
1. **Nitrous oxide**
 - a. **CNS**
 1. Thought to act primarily by inhibiting NMDA receptors.

2. Concentrations greater than 60% may produce amnesia, although not reliably.
 3. Because of its high MAC (104%), it is usually combined with other anesthetics to attain surgical anesthesia.
- b. Cardiovascular system**
1. Mild myocardial depressant and a mild sympathetic nervous system stimulant.
 2. HR and BP are usually unchanged.
 3. May increase pulmonary vascular resistance in adults.
- c. Respiratory system.** Mild respiratory depressant, although less so than the volatile anesthetics.
- 2. Volatile anesthetics**
- a. CNS**
1. Produce unconsciousness and amnesia at relatively low inspired concentrations (25% to 35% of MAC).
 2. At lower doses of halogenated ether anesthetics (isoflurane, sevoflurane, desflurane), alpha, delta, and slow oscillations are present. At higher doses, theta oscillations (4 to 8 Hz) appear, followed by burst suppression.
 3. Decreased amplitude and increased latency of SSEPs.
 4. Increase CBF and decrease CMRO₂; uncouple autoregulation of CBF.
- b. Cardiovascular system**
1. Produce dose-dependent myocardial depression and systemic vasodilation.
 2. HR tends to be unchanged, although desflurane can cause sympathetic stimulation, tachycardia, and hypertension at induction or when the inspired concentration is abruptly increased.
 3. Sensitize the myocardium to the arrhythmogenic effects of catecholamines, which is of particular concern during the infiltration of epinephrine-containing solutions or the administration of sympathomimetic agents.
- c. Respiratory system**
1. Produce dose-dependent respiratory depression with decrease in TV, increase in RR, and increase in arterial CO₂ pressure.
 2. Produce airway irritation and, during light levels of anesthesia, may precipitate coughing, laryngospasm, or bronchospasm, particularly in patients who smoke or have asthma. The lower pungency of sevoflurane makes it more suitable for use as an inhalation induction agent.
 3. Equipotent doses of volatile agents possess similar bronchodilator effects, with the exception of desflurane, which has mild bronchoconstricting activity.
 4. Inhibit hypoxic pulmonary vasoconstriction, which may contribute to pulmonary shunting.
- d. Neuromuscular system**
1. Dose-dependent decrease in skeletal muscle tone, often enhancing surgical conditions.
 2. May precipitate **malignant hyperthermia** in a susceptible patient.
- e. Hepatic system.** May cause a decrease in hepatic perfusion. Rarely, a patient may develop hepatitis secondary to exposure to a volatile agent, most notably halothane ("halothane hepatitis").
- f. Renal system.** Decrease renal blood flow through either a decrease in MAP or an increase in renal vascular resistance.

D. Adverse Effects Related to Specific Agents

1. Nitrous oxide

- a. **Expansion of closed gas spaces.** The predominant constituent in closed gas-containing spaces in the body is nitrogen. Because nitrous oxide is 35 times more soluble in blood than nitrogen, closed air spaces will expand as the amount of nitrous oxide diffusing into these spaces is greater than the amount of nitrogen diffusing out. Spaces containing air such as a pneumothorax, occluded middle ear, bowel lumen, or pneumocephalus will markedly enlarge if nitrous oxide is administered. Nitrous oxide will diffuse into the cuff of an endotracheal tube and may increase pressure within the cuff; this pressure should be assessed intermittently and, if necessary, adjusted.
 - b. **Diffusion hypoxia.** After discontinuation of nitrous oxide, its rapid elimination from the blood into the lung may lead to a low partial pressure of oxygen in the alveoli, resulting in hypoxia and hypoxemia if supplemental oxygen is not administered.
 - c. **Inhibition of tetrahydrofolate synthesis.** N_2O inhibits methionine synthase, a vitamin B_{12} -dependent enzyme necessary for the synthesis of DNA. It should be used with caution in pregnant patients and those deficient in vitamin B_{12} .
2. **Desflurane** can be degraded to carbon monoxide in carbon dioxide absorbents (especially Baralyme). This is most likely to occur when the absorbent is new or dry.
 3. **Sevoflurane** can be degraded in CO_2 absorbents (especially Baralyme) to fluoromethyl-2,2-difluoro-1-vinyl ether (**Compound A**), which has been shown to produce renal toxicity in animal models. Compound A concentrations increase at low fresh gas rates. So far, there has been no evidence of consistent renal toxicity with sevoflurane usage in humans.

Suggested Readings

- Brown EN, Purdon PL, Van Dort CJ. General anesthesia and altered states of arousal: a systems neuroscience analysis. *Annu Rev Neurosci* 2011;34:601–28.
- Dershwitz M, Rosow CE. Pharmacology of intravenous anesthetics. In: Longnecker DE, Brown DL, Newman MF, et al., eds. *Anesthesiology*. 1st ed. New York: McGraw-Hill Professional; 2007:849–868.
- Eger EI. Uptake and distribution. In: Miller RD, ed. *Anesthesia*. 6th ed. New York: Churchill Livingstone; 2005:131–153.
- Forman SA, Mashour GA. Pharmacology of inhalational anesthetics. In: Longnecker DE, Brown DL, Newman MF, et al., eds. *Anesthesiology*. 1st ed. New York: McGraw-Hill Professional; 2007:739–766.

The principal pharmacologic effect of **neuromuscular-blocking drugs (NMBDs)** is to interrupt transmission of synaptic signaling at the **neuromuscular junction (NMJ)** by interacting with the **nicotinic acetylcholine receptor (AChR)**.

I. NEUROMUSCULAR JUNCTION

- A. The NMJ (Fig. 13.1) is a chemical synapse located in the peripheral nervous system. The NMJ is composed of the **neuronal presynaptic terminal**, where **acetylcholine (ACh)** is stored in specialized organelles known as **synaptic vesicles**, and the postsynaptic muscle cell (**motor endplate**), where high densities (up to $10,000/\mu\text{m}^2$ at the synapse) of the nicotinic AChRs are found.
- B. In response to an action potential in the nerve, **voltage-dependent calcium channels**, which are highly concentrated in close proximity to synaptic vesicles, open and cause a rapid influx of calcium into the nerve terminal increasing its intracellular concentrations to approximately $100\ \mu\text{M}$. This influx of calcium lasts only about 0.5 milliseconds but is sufficient enough to induce fusion of synaptic vesicles with the plasma membrane to release stored ACh. ACh then diffuses across the synaptic cleft where two molecules of ACh bind to a single nicotinic AChR.
- C. **Postjunctional nicotinic AChRs** are glycoproteins composed of five subunits (two α and one each of β , δ , and ϵ) with the two α -subunits constituting the binding sites for ACh and NMBDs. When two molecules of ACh are bound, the AChR undergoes a conformational change (activation) that allows influx of sodium and calcium into the muscle cell to depolarize the membrane and causes contraction. Once depolarization occurs, repolarization begins with the efflux of potassium and the cessation of sodium and calcium entry. At this point, the AChR becomes inactivated. The amount of ACh released and the number of postsynaptic AChRs is much greater than that actually needed to induce contraction. This is termed the “safety factor” for neuromuscular transmission and plays a crucial role in certain pathologic conditions. After triggering depolarization, ACh diffuses into the synaptic cleft where it is rapidly hydrolyzed (within 15 milliseconds) by **acetylcholinesterase (AChE)** into choline and acetate. Choline is subsequently recycled to synthesize new ACh in the motor nerve terminal.
- D. **Prejunctional nicotinic AChRs** are located on the presynaptic nerve terminal and are responsible for augmenting depolarization of the nerve terminal during high frequency stimulation, thereby enhancing ACh release. Antagonism of these receptors by nondepolarizing NMBDs is the mechanism by which these agents produce fade on the train of four (TOF).

II. GENERAL PHARMACOLOGY

- A. **Cholinergic receptors** are categorized as **nicotinic** and **muscarinic** by their responses to the alkaloids nicotine and muscarine, respectively. There are two main classes of nicotinic cholinergic receptors, muscular (found at the NMJ) and neuronal (found in autonomic ganglia, at end-organ sites of parasympathetic nerves, and in the central nervous system). Since the cholinergic receptors have different subunit composition, most drugs bind to

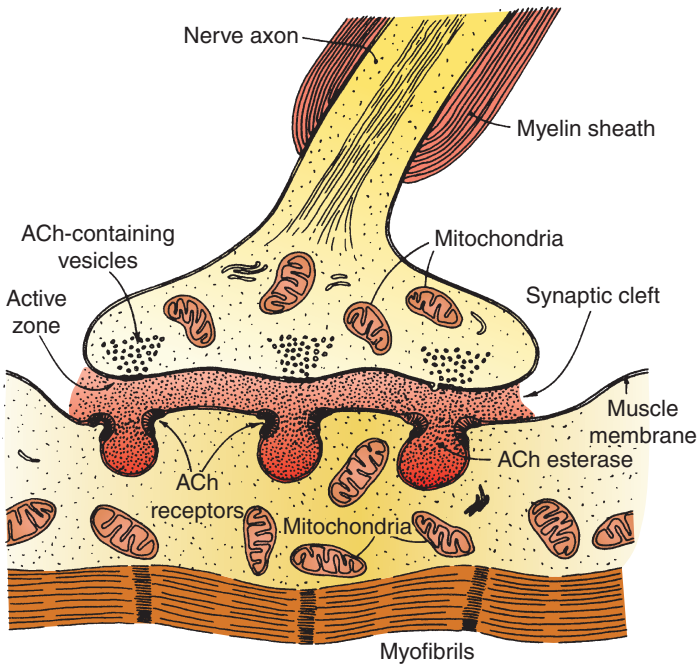


FIGURE 13.1 The neuromuscular junction.

them with different affinity and have different effects. Only ACh and drugs working by producing ACh (AChE inhibitors) are agonists at all of them.

- B. There are well-described signaling systems that regulate the **distribution and density of AChRs** at the NMJ. Pathologic conditions that affect AChR distribution are quite common. For example, denervation, prolonged inactivity, or prolonged mechanical ventilation decreases the density of AChRs at the NMJ, whereas extrajunctional AChRs (often referred to as immature or fetal postjunctional nicotinic AChRs) proliferate over the surface of the muscle membrane. This "**up-regulation**" of AChRs increases sensitivity to agonists such as ACh and succinylcholine, but it decreases the sensitivity to competitive antagonists such as nondepolarizing NMBDs. In contrast, increased sensitivity to antagonists and decreased sensitivity to agonists develop under conditions associated with **down-regulation of AChRs**. This can occur when the NMJ is exposed to excess ACh (e.g., following chronic use of AChE inhibitors).
- C. NMBDs can be classified by the duration of effect: **ultrashort-acting** (<10 minutes; succinylcholine), **short-acting** (<20 minutes; mivacurium [not available in the United States]), **intermediate-acting** (45 to 60 minutes; atracurium, cisatracurium, rocuronium, and vecuronium), and **long-acting** (>1 hour; pancuronium). Nondepolarizing NMBDs can be further classified by chemical class: **aminosteroid derivatives** (e.g., pancuronium, rocuronium, and vecuronium) and **benzylisoquinolines** (e.g., atracurium, cisatracurium, and mivacurium). NMBDs differ substantially in their onset, duration of blockade, metabolism, side effects, and interactions with other drugs (Tables 13.1 and 13.2).

TABLE
131Comparative Clinical Pharmacology of NMBDs^a

	ED ₉₅ (mg/kg) ^b	Intubating Dose (mg/kg) ^c	Time to Intubation (minutes) ^d	Time to 25% Recovery (minutes) ^e	Infusion Rate (μg/kg/min) ^f	Elimination
Depolarizing drug						
Succinylcholine	0.25	1–1.5	1	4–6	60–100	Plasma cholinesterase
Nondepolarizing drugs						
Atracurium	0.25	0.4–0.6	2–3	20–35	4–12	Ester hydrolysis, Hofmann elimination
Cisatracurium	0.05	0.15–0.2	2–3	40–60	1–3	Hofmann elimination
Mivacurium	0.08	0.15–0.25	2–3	15–25	3–15	Plasma cholinesterase
Pancuronium	0.06	0.06–0.1	3–4	60–100		Kidneys (70%–80%), biliary and hepatic (20%–30%)
Rocuronium	0.3	0.6–1.2	1–1.5	30–150	4–12	Primarily by liver
Vecuronium	0.05	0.08–0.12	2–3	25–40	0.8–2	Biliary and hepatic (70%–90%), kidneys (10%–30%)

^a There is a large variability in the response to all relaxants, especially at the extremes of age and with profound illness. Therefore, all patients should be carefully monitored as described in the text. Doses shown here are intended for intravenous administration in adult patients.

^b An ED₉₅ dose of a relaxant provides adequate surgical relaxation with nitrous oxide–opioid anesthesia.

^c These are customary intubating doses and not all equipotent. Neuromuscular blockade is potentiated by volatile anesthetics. For nondepolarizing agents, the intubating dose can be approximately double of the ED₉₅.

^d These times reflect the use of customary intubating doses and may be substantially altered by the depth of anesthesia. For a rapid sequence induction with nondepolarizing agents, onset time can be shortened by administering a priming dose 3–5 minutes before the full dose. Alternatively, a dose of a nondepolarizing agent four times higher than the ED₉₅ dose can be used.

^e Maintenance bolus doses to be given when the TOF count reaches 2–3 are generally 20%–25% of the initial bolus dose.

^f Continuous infusion should be initiated only after early evidence of spontaneous recovery from the initial bolus dose.

TABLE
132
Cardiovascular Side Effects of NMBDs

Drugs	Histamine Release ^a	Ganglionic Effects	Vagolytic Activity	Sympathetic Stimulation
Atracurium	+	0	0	0
Cisatracurium	0	0	0	0
Mivacurium	+	0	0	0
Pancuronium	0	0	++	++
Rocuronium	0	0	+	0
Succinylcholine	+/-	+	0	0
Vecuronium	0	0	0	0

^a Histamine release is dose and rate dependent and, therefore, less pronounced if drugs are injected slowly.

III. NEUROMUSCULAR BLOCKADE

A. Depolarizing Blockade

Succinylcholine (SCh), the only depolarizing NMBD, is composed of two ACh molecules linked together via an acetyl moiety. SCh binds to the α -subunits of the nicotinic AChR leading to depolarization of the postjunctional membrane. Because SCh is not degraded by AChE as rapidly as ACh, it persistently depolarizes the motor endplate, leading to inactivation of the voltage-gated sodium channels in the perijunctional zone that are necessary for propagation of the depolarization. Induction doses of SCh produce a rapid onset (about 1 minute) of a transient agonist effect (e.g., muscle twitch) followed by skeletal muscle paralysis lasting 4 to 6 minutes. These characteristics make SCh a common choice for facilitating rapid tracheal intubation.

1. SCh effect terminates when the drug diffuses away from the AChRs and is rapidly hydrolyzed by **plasma cholinesterase** (produced in the liver and also referred to as pseudocholinesterase) to succinylmonocholine and then, more slowly, to succinic acid and choline. This enzyme is not the same as AChE and is not found in the synaptic cleft. However, inhibitors of AChE affect both enzymes to different degrees.
2. **Side effects of SCh** are related to its agonist effects at both the nicotinic and muscarinic AChRs.
 - a. **Myalgia** is common postoperatively, especially in the muscles of the abdomen, back, and neck. It is attributed to muscle fasciculations and observed more frequently in females and younger patients after minor surgical procedures.
 - b. **Cardiac dysrhythmias.** SCh has no direct effect on the myocardium. However, ganglionic stimulation may increase heart rate and blood pressure in adults. Alternatively, SCh may stimulate muscarinic receptors at the sinus node, producing sinus bradycardia, a junctional rhythm, or even asystole, particularly in children and following repeated exposure within a short time interval (i.e., 5 minutes) in adults. Pretreatment of children with intravenous (IV) atropine immediately before SCh reduces the occurrence of bradyarrhythmias.
 - c. SCh depolarization exaggerates the usual transmembrane ionic flux and normally induces elevation of serum potassium by 0.5 to 1.0 mEq/L. However, life-threatening **hyperkalemia** and cardiovascular collapse may occur in patients with major burns, massive tissue

injuries, extensive denervation of skeletal muscle, or upper motor neuron diseases. This effect is attributed to a proliferation of extra-junctional AChRs or damaged muscle membranes and a massive release of potassium upon stimulation. In patients with burns, the period of greatest risk is from 2 weeks to 6 months after the burn has been sustained. However, it is recommended to avoid Sch after the first 24 hours and for 2 years from the time of the injury. Patients with mild elevations of potassium related to renal failure may usually safely receive Sch.

- d. A transient **increase in intraocular pressure** occurs 2 to 4 minutes following Sch, presumably due to contractions of the extraocular muscles with associated compression of the globe or cycloplegia causing obstruction of aqueous outflow via the trabecular meshwork. However, the use of Sch in open eye injuries is still acceptable for rapid sequence inductions (see Chapter 26).
 - e. **Increased intragastric pressure** results from fasciculations of abdominal muscles. The pressure increase (averaging 15 to 20 mm Hg in an adult) is counterbalanced by an even greater increase in the lower esophageal sphincter tone.
 - f. Sch produces a mild transient **increase in intracranial pressure** (see Chapter 25).
 - g. **A history of malignant hyperthermia (MH) is an absolute contraindication to the use of Sch.** Some degree of masseter muscle spasm may be a normal response to Sch, but severe jaw rigidity increases the risk that a fulminant MH episode may follow. Generalized muscle rigidity, tachycardia, tachypnea, and profound hyperpyrexia after Sch should alert the clinician to this condition (see Chapter 19).
 - h. **Pretreatment with a subparalyzing dose of a nondepolarizing NMBD** (e.g., cisatracurium 1 mg IV or rocuronium 3 mg IV) 2 to 4 minutes before Sch may blunt visible fasciculations but is not uniformly effective in attenuating the above-mentioned side effects. Moreover, awake patients pretreated with a nondepolarizing NMBD may experience diplopia, weakness, or dyspnea. When pretreating for a rapid sequence induction, the subsequent IV dose of Sch should be increased to 1.5 mg/kg.
3. **Phase I blockade.** Neuromuscular blockade produced by Sch can be separated into two phases. Phase I blockade (Fig. 13.2) is the usual response to Sch as previously described and is characterized by the following:
- a. Transient muscle fasciculations followed by relaxation.
 - b. Absence of fade to tetanic or TOF stimulation (see section IV.C).
 - c. Absence of posttetanic potentiation (PTP; see section IV.C)
 - d. AChE inhibitors potentiate rather than reverse the block.
4. **Phase II blockade** is most likely to occur after repeated or continuous administration of Sch when the total dose exceeds 3 to 5 mg/kg. Phase II blockade is thought to be secondary to repeated channel opening, causing distortion of the normal electrolyte balance and desensitizing the junctional membrane to further depolarization. It has some of the characteristics of a nondepolarizing blockade:
- a. Fade after tetanic or TOF stimulation (see section IV.C)
 - b. Presence of PTP (see section IV.C)
 - c. Tachyphylaxis (increasing dose requirement)
 - d. Prolonged recovery
 - e. Partial or complete reversal by AChE inhibitors

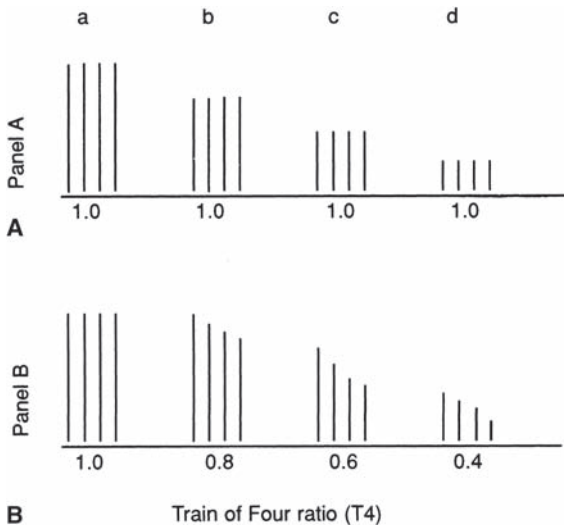


FIGURE 13.2 Schematic representation of TOF responses to a depolarizing (**A**) and a nondepolarizing (**B**) muscle relaxant, showing the control response before the relaxant (a) and afterward (b, c, d). Note no fade with the depolarizing relaxant and progressive fade with the nondepolarizing relaxant.

5. **Prolonged blockade** following SCh may be caused by low levels of plasma cholinesterase, a drug-induced inhibition of its activity, or a genetically atypical enzyme.
 - a. **Decreased plasma cholinesterase levels** are found in the last trimester of pregnancy and for several days postpartum, severe liver or kidney disease, starvation, carcinomas, hypothyroidism, burn patients, decompensated cardiac failure, and after therapeutic radiation.
 - b. **Inhibition of plasma cholinesterase** occurs with the use of organophosphorus compounds (e.g., echothiophate eye drops and insecticides) and other drugs that inhibit AChE (e.g., neostigmine, pyridostigmine, and donepezil), chemotherapeutic agents (e.g., cyclophosphamide and nitrogen mustard), oral contraceptives, glucocorticoids, esmolol, and monoamine oxidase inhibitors. Plasma cholinesterase levels are not usually altered by hemodialysis.
 - c. **Several genetic variants of plasma cholinesterase** exist: normal (N), atypical (A), fluoride resistant (F), and silent (S). **Homozygous atypical cholinesterase** (A–A, prevalence 0.04%) results in prolonged (2 to 3 hours) skeletal muscle paralysis and respiratory insufficiency following a conventional dose of SCh. Heterozygous atypical cholinesterase (N–A, prevalence 4%) results in only modest prolongation of effect.
 - d. The **dibucaine number** is a laboratory assay used to characterize plasma cholinesterase abnormality. Normally, the local anesthetic dibucaine inhibits plasma cholinesterase activity by about 80% (dibucaine number of 80), whereas A–A plasma cholinesterase is inhibited by about 20% (dibucaine number of 20). In N–A, dibucaine numbers range from 30 to 65. The comparable **fluoride number** ranges

from 0 to 60. N-F individuals (prevalence 0.005%) have slight prolongation of Sch effect, a normal dibucaine number, and a reduced fluoride number. A heterozygous silent N-S individual (incidence 0.005%) has slightly prolonged effect, but dibucaine and fluoride numbers are normal. Homozygotes F-F and S-S are extremely rare.

- e. Patients exhibiting prolonged blocks after a single administration of succinylcholine require sedation and continued intubation until there is a return of twitches. The neuromuscular blockade at this point is similar to that seen with nondepolarizing NMBD. Once fade with TOF is observed, reversal with neostigmine/glycopyrrolate is possible. Blood assays should be performed to determine total cholinesterase and, dibucaine number, and fluoride numbers.

B. Nondepolarizing blockade is produced by reversible competitive antagonism of ACh at the α -subunits of the AChRs.

1. It is **characterized** by the following (Figs. 13.2 and 13.3):
 - a. Absence of fasciculations
 - b. Fade during tetanic and TOF stimulation (see section IV.C)
 - c. Presence of PTP (see section IV.C)
 - d. Antagonism of depolarizing blockade
 - e. Potentiation by other nondepolarizing NMBDs and volatile anesthetic agents
 - f. Reversal by AChE inhibitors
2. **The clinical pharmacology** of the commonly used nondepolarizing NMBDs is outlined in Table 13.1. Synergistic blockade may occur when aminosteroid NMBDs are administered together with benzylisoquinolines. When NMBDs with similar chemical structure are combined, the effect is additive.
3. **Mivacurium** is a short-acting nondepolarizing NMBD composed of three stereoisomers (trans-trans, cis-trans, and cis-cis diesters). It is rapidly hydrolyzed by plasma cholinesterase. The onset time may be shortened by using a divided dose (1.5 mg/kg followed by 1.0 mg/kg 30 seconds after the first dose) or increasing its 95% effective dose (ED_{95}) by three-fold. The divided dose also minimizes histamine release than can occur with the rapid administration of higher doses. It should be used with

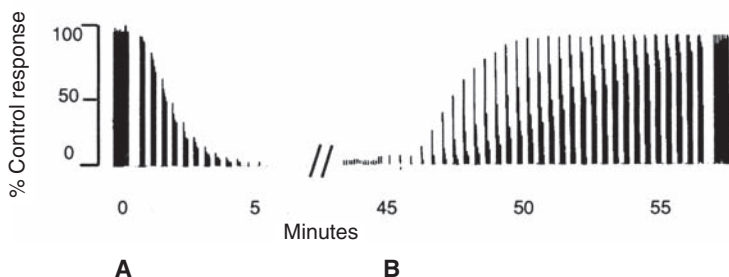


FIGURE 13.3 **A:** Electromyographic response to repeated TOF stimulation after injection of a nondepolarizing agent. Each vertical bar is composed of four individual twitch responses. Fade of TOF response eventually leaves only one twitch (approximately 90% blockade). **B:** Reversal of the blockade by neostigmine and atropine given 45 minutes later shows a progressive recovery of the TOF response and reduction in fade with a TOF ratio of 0.9.

caution in patients with known atypical plasma cholinesterase activity or using cholinesterase inhibitors. If blockade following mivacurium must be reversed with an anticholinesterase agent, edrophonium may be preferred to neostigmine because it has much less effect on plasma cholinesterase activity. Mivacurium is still commonly used in Europe but no longer being marketed in the United States.

4. **Atracurium** is a mixture of 10 stereoisomers. The drug undergoes ester hydrolysis by nonspecific plasma esterases and **Hofmann elimination** (nonbiologic process independent of renal, hepatic, or enzymatic function). Laudanosine, its major metabolite, is a CNS stimulant at high plasma levels. Atracurium is recommended for patients with significant hepatic or renal disease. Rapid IV administration at doses greater than 2.5 times the ED_{95} causes a transient release of histamine and hypotension.
5. **Cisatracurium** is one of 10 stereoisomers that constitute atracurium. It is approximately four times as potent as atracurium. High molar potency results in a relatively slow onset time (see Rocuronium). The drug is cleared primarily by Hofmann elimination, and its duration of action is largely independent of renal or hepatic function. Unlike atracurium, it does not produce histamine release or hemodynamic effects after rapid injection of doses as high as eight times its ED_{95} .
6. **Vecuronium** is a lipophilic NMBD that is readily absorbed by the liver and excreted into the bile. One of the metabolites, 3-desacetylvecuronium, has neuromuscular-blocking properties (about 50% to 70% of the potency of vecuronium) and eliminated by the kidneys. Vecuronium has a prolonged clinical effect in elderly patients and those with liver disease and renal failure, as a result of reduced clearance and extended elimination half-life. Vecuronium has no significant effects on heart rate and blood pressure, but it inhibits histamine *N*-methyltransferase and might potentiate effects such as flushing and hypotension when histamine is released by drugs such as morphine.
7. **Rocuronium** is an analog of vecuronium that has lower potency. The large intubating dose results in a fast onset time because a larger number of molecules reach the NMJ per circulation time. At a dose of 0.6 mg/kg, good to excellent intubating conditions are achieved within 60 seconds. Increasing the dose to 1.2 mg/kg (four times the ED_{95}) shortens the time even more but significantly prolongs the duration of action, which can be highly variable among patients. This drug is often chosen when a rapid sequence induction is required but SCH is contraindicated. Clearance of rocuronium occurs as unchanged drug in bile and through renal excretion. Administration of the drug to patients with renal failure could result in a longer duration of action, especially after repeated doses or continuous infusion. Rocuronium does not induce the release of histamine or produce cardiovascular effects, even after administration of large doses.
8. **Pancuronium** is a long-acting NMBD. Because it is predominantly eliminated by the kidneys, the drug has a prolonged duration of neuromuscular blockade in patients with renal failure. In patients with hepatic cirrhosis or biliary tract dysfunction, the initial dose of pancuronium to achieve adequate relaxation may be higher due to increased volume of distribution, whereas the duration of action is greater than usual due to decreased plasma clearance. Pancuronium can increase systemic blood pressure, heart rate, and cardiac output by inhibition of catecholamine reuptake at sympathetic nerve terminals and a vagolytic action

at cardiac muscarinic receptors. These cardiac stimulating effects may contribute to myocardial ischemia due to increased myocardial oxygen requirements in patients with coronary artery disease.

9. The **cardiovascular side effects** of nondepolarizing NMBDs are summarized in Table 13.2. Hypotension caused by histamine release can be reduced or prevented by slow administration of the drug (>30 seconds).
- C. Clinical Choice of NMBD**
1. **Many factors** must be considered simultaneously when selecting a NMBD: the urgency for tracheal intubation, the duration of the procedure, coexisting medical conditions that may affect the NMJ, and side effects and metabolism of the drug. For example, the rapid onset of SCH makes it a good choice for rapid intubation of the trachea, but rocuronium will decrease the risk of hyperkalemia in patients with burns. Pancuronium can produce a tachycardia that is undesirable in patients with severe ischemic heart disease, but its vagolytic effects may be appropriate in pediatric patients. When compared to intermediate-acting NMBDs, studies have shown that the incidence of residual neuromuscular blockade is greater with long-acting NMBDs.
 2. **Cost-effectiveness** is also a consideration in the choice of drug. The additional expense of newer short-acting NMBDs may not be justified in longer cases. On the other hand, the incidence of postoperative residual blockade and costs of postoperative drug-induced morbidity should be part of assessing cost-effectiveness.

IV. MONITORING OF NEUROMUSCULAR FUNCTION

- A. There are several reasons to monitor neuromuscular function under anesthesia:
 1. To facilitate timing of intubation
 2. To provide an objective measurement of relaxation during surgery and degree of recovery before extubation
 3. To titrate NMBD dosage according to patient response
 4. To monitor for the development of phase II block
 5. To permit early recognition of patients with abnormal plasma cholinesterase activity
 6. To prevent sequelae of residual postoperative neuromuscular blockade
- B. **Peripheral nerve stimulators** use various patterns of stimulation: single twitch, tetanus, TOF, and double-burst stimulation as well as the “posttetanic count.” The **adductor pollicis response to ulnar nerve stimulation** at the wrist is most often used, because it is easily accessible, and the results are not confused with direct muscle activation. Cutaneous electrodes are placed at the wrist over the ulnar nerve and attached to a battery-driven pulse generator, which delivers a graded impulse of electrical current at a specified frequency. For maximal twitch response, the negative pole (active) should be placed distally over the ulnar nerve at the wrist. Evoked muscle tension can be estimated by feeling for thumb adduction or measured by using a force transducer attached to the thumb. After administration of a NMBD, the developed tension and twitch height decrease with the onset of blockade. If the ulnar nerve is unavailable, other sites may be used (e.g., facial, posterior tibial, peroneal, or lateral popliteal nerves). It is difficult to estimate twitch strength accurately by palpation, so significant residual muscular blockade may be missed by all these techniques.
- C. The twitch response to various patterns of stimulation has been correlated with clinical end points, and these data are summarized in Table 13.3.

TABLE
133
Clinical Assessment of Neuromuscular Blockade

Twitch Response	Clinical Correlate
95% suppression of single twitch at 0.15–0.1 Hz	Adequate intubating conditions
90% suppression of single twitch; TOF count of one twitch	Surgical relaxation with nitrous oxide–opioid anesthesia
75% suppression of single twitch; TOF count of three twitches	Adequate relaxation with volatile agents
25% suppression of single twitch	Decreased vital capacity
TOF ratio > 0.75; sustained tetanus at 50 Hz for 5 s	Head lift for 5 s; vital capacity of 15–20 mL/kg; inspiratory force of –25 cm H ₂ O; effective cough
TOF ratio > 0.9	Sit up unassisted; intact carotid body response to hypoxemia; normal pharyngeal function
TOF ratio of 1.0	Normal expiratory flow rate, vital capacity, and inspiratory force; diplopia resolves

1. **Single twitch** is a supramaximal stimulus, typically lasting 0.2 milliseconds at a frequency of 0.1 Hz (one impulse every 10 seconds). The height of the muscle twitch (its amplitude for a given load and peak tension) is determined as a percent of control. A supramaximal stimulus ensures recruitment of all muscle fibers, while a short duration prevents repetitive nerve firing. The stimulus frequency is important because it affects twitch height and degree of fade. Single twitch is not a sensitive measure of onset or recovery from blockade because 75% of AChRs must be blocked before twitch height begins to decrease, and 75% of the receptors may still be blocked when it returns to control height.
2. **Tetanic stimulus** frequencies vary from 50 to 200 Hz. All NMBDs reduce twitch height, but with nondepolarizing and phase II blockades, a tetanic fade is also demonstrated. This occurs when NMBDs bind to presynaptic receptors and decrease mobilization of ACh during high-frequency stimulation. A tetanic stimulus at 50 Hz for 5 seconds is clinically useful, because a sustained tension at this frequency corresponds to that achieved with maximum voluntary effort. However, tetanic stimuli are painful and can speed up recovery in the stimulated muscle, thus misleading the clinician with respect to the degree of recovery in respiratory and upper airway muscles.
3. **Posttetanic single twitch** is measured by single-twitch stimulation 6 to 10 seconds after a tetanic stimulus. An increase in this twitch is called **Posttetanic Potentiation (PTP)**, and it is due to increased mobilization and synthesis of ACh during and after tetanic stimulation. Both nondepolarizing and phase II blockade cause PTP, but depolarizing blockade does not.
4. **The TOF** is four supramaximal stimuli given at a frequency of 2 Hz (Fig. 13.2). They could be repeated at intervals of at least 10 seconds. Responses at this frequency show fade during the onset and recovery of neuromuscular blockade. During nondepolarizing neuromuscular blockade, elimination of the fourth response corresponds to 75% depression of a single twitch. Disappearance of the third, second, and first responses correspond to 80%, 90%, and 100% depression of a single twitch, respectively. The ratio of the height of the fourth to the

first twitch (**TOF ratio**) correlates with several clinical parameters (see Table 13.3). However, clinicians often overestimate TOF ratios and are unable to detect fade when the TOF ratio is greater than 0.4. Functional impairment of the muscles of the upper airway may exist up to TOF ratios as high as 0.9, with a significant risk of regurgitation and aspiration. NMBDs may also impair the carotid body hypoxic response, even at a TOF ratio of 0.7. Nevertheless, TOF is a very useful method for clinical monitoring, because it does not require a control measurement, it is less painful than tetanic stimulation (may be performed in an awake patient to identify residual block), and it does not affect subsequent recovery. It provides a good measure of blockade required for surgical relaxation and is also useful in assessing recovery from blockade. It is not helpful in quantifying the degree of depolarizing blockade because no fade will be evident. However, TOF monitoring may be used to detect fade, indicating the onset of phase II blockade during continuous or repeated administration of Sch.

5. **Posttetanic count** is used to quantify *deep* levels of nondepolarizing block. A 50-Hz tetanic stimulus is given for 5 seconds, followed 3 seconds later by repeated single stimuli at 1 Hz. The number of detectable responses predicts the time for spontaneous recovery. A response to posttetanic twitch stimulation precedes the return of TOF responses.
6. **Double-burst stimulation** uses a burst of two or three tetanic stimuli at 50 Hz followed 750 milliseconds later by a second burst. A decrease in the second response indicates residual curarization. When using tactile evaluation, fade in response to double-burst stimulation is more easily detected than fade in response to TOF stimulation.
- D. Recording instruments are the only objective means to accurately quantify muscle contraction in response to nerve stimulation. **Mechanomyography** and **electromyography** are research tools. Mechanomyography uses a force transducer to convert isometric muscle contractions into electric signals while electromyography measures the electrical activity of the muscle action potential. **Acceleromyography** measures acceleration of muscle contraction and is the only recording monitor commercially available for clinical use.

V. REVERSAL OF NEUROMUSCULAR BLOCKADE

- A. **Recovery from Sch-induced depolarizing blockade** usually occurs within 5 to 10 minutes following a 1 mg/kg IV dose. Patients with atypical or inhibited plasma cholinesterase could have a greatly prolonged duration of blockade. Reversal of phase II blockade occurs spontaneously within 10 to 15 minutes in approximately 50% of patients. It is advisable to allow patients with prolonged blockade to recover spontaneously for 20 to 25 minutes and then reversal with an anticholinesterase agent may be attempted if there is no further improvement in twitch strength. Earlier reversal could potentiate the block.
- B. **Nondepolarizing blockade** spontaneously recovers when the drugs diffuse from their sites of action. Reversal can be accelerated by administering agents that inhibit AChE, thereby increasing the ACh available to compete for binding sites.
- C. The most commonly used anticholinesterase drugs are **edrophonium** (0.05 to 1 mg/kg) and **neostigmine** (0.03 to 0.07 mg/kg; maximum dose up to a total of 5 mg). The drugs act by increasing ACh levels and, thus, produce nicotinic and muscarinic effects. Bradycardia, bronchoconstriction, salivation, tearing, and miosis can be minimized by administering

an antimuscarinic drug. Atropine (0.01 mg/kg) is used with edrophonium because the time course of the two drugs is similar. For the same reason, glycopyrrolate (0.02 mg/kg) is used with neostigmine. Higher doses of neostigmine (>2.5 mg) have been associated with increased incidence of postoperative nausea and vomiting. However, the potential harm associated with lack of reversal outweighs the risk of side effects.

- D. Encapsulating reversal agents** are novel muscle relaxant binding drugs that form tight water-soluble complexes with NMBDs, thereby reducing the amount of neuromuscular-blocking agent available to bind AChRs at the NMJ. **Sugammadex**, a modified γ -cyclodextrin, is currently approved for clinical use in several countries but not in the United States. Following IV administration, it binds steroidal NMBDs (rocuronium > vecuronium > pancuronium) in a 1:1 ratio. In clinical trials, sugammadex has demonstrated the ability to rapidly reverse rocuronium- or vecuronium-induced neuromuscular blockade. For routine reversal, a dose of 4 mg/kg is recommended if recovery has reached at least 1–2 posttetanic counts. If immediate reversal of rocuronium-induced blockade is required, a dose of 16 mg/kg is recommended. In patients with severe renal failure (creatinine clearance <30 mL/minute), the excretion of sugammadex or the sugammadex–rocuronium complexes is delayed, but no signs of recurrent neuromuscular blockade are observed. If readministration of rocuronium or vecuronium is required, a waiting time of 24 hours is recommended.
- E. Time to adequate reversal** is related to the degree of spontaneous recovery. Reversal may be more difficult with the use of long-acting NMBDs, large total doses, and high concentrations of inhalation anesthetics. Other factors that may prolong the blockade include hypothermia, antibiotics (particularly aminoglycosides, clindamycin, and tetracyclines), electrolyte disturbances (hypokalemia, hypocalcemia, and hypermagnesemia), and acid–base disturbances (alkalosis prolongs blockade, and acidosis impairs reversal). Reversal with an anticholinesterase agent should not be attempted unless at least one response to TOF stimulation is present. Attempts to reverse a deep or resistant block with excessive doses of neostigmine may increase the degree of residual weakness. If residual weakness is present after attempted reversal, the endotracheal tube should be left in place to provide adequate ventilation and airway protection.
- F. Evidence of Neuromuscular Recovery**
 - 1. Signs of adequate neuromuscular recovery** include maintenance of a patient airway without assistance, adequate ventilation and oxygenation, sustained grip strength, the ability to sustain head lift or movement of an extremity without fade, the ability to clench down on an oral airway and prevent its withdrawal, and the absence of disorganized muscle activity.
 - 2. The TOF ratio corresponding to adequate neuromuscular recovery** has been a matter of debate. Historically, TOF ratios between 0.7 and 0.8 were deemed adequate; however, recent studies have demonstrated significant pharyngeal dysfunction associated with postoperative pulmonary complications at these TOF ratios. A more stringent criterion, particularly for at-risk patients, would be a TOF ratio of >0.9.

VI. DISORDERS THAT INFLUENCE THE RESPONSE TO NMBDS

Certain illnesses, both those confined to the NMJ and those affecting more general systems, dramatically affect the response to and safety of NMBDs. In general, transmission at the NMJ is abnormal in these disorders, and there are ultrastructural and biochemical changes in motor nerves, muscle, or both.

A. Burns and Immobilization

1. **Thermal injury** affects fluid and electrolyte balance, cardiovascular and pulmonary function, drug metabolism, and musculoskeletal structure and function.
2. **Burn patients** and many **immobilized patients** have a greatly exaggerated response to depolarizing agents and a decreased responsiveness to nondepolarizing agents. Burn patients exhibit ultrastructural and biochemical alterations in both muscle cells and neuromuscular contacts. These effects can be seen for more than 1 year after the initial thermal insult. Administration of SCH can cause fatal hyperkalemia. Similar problems have been reported in patients with major crush injuries or large areas of devitalized tissue.

B. Critical Illness

1. **Myopathy of critical illness** is a collective group of disorders that can cause weakness in intensive care unit (ICU) patients. The prevalence is exceedingly high (30% to 70%). The underlying pathology is quite heterogeneous, ranging from pure neuropathies and myopathies to mixed neuromuscular transmission disorders. Sepsis and multiorgan system failure are commonly associated with myopathy of critical illness.
2. **Weakness** is the common manifestation of all these myopathic disorders, and they contribute to ventilator dependence and increased morbidity and mortality. Myopathy may also produce altered deep tendon reflexes, increased creatine kinase levels, and electrophysiologic alterations in nerves, muscles, or both.
3. **Corticosteroids, NMBDs, and certain antibiotics** can contribute to or precipitate weakness in ICU patients. One subtype of myopathy of critical illness, acute necrotizing myopathy, has been linked to the repeated administration of NMBDs, often in conjunction with high doses of corticosteroids. Therefore, limiting steroid and NMBD use in critically ill patients is advisable.

C. Myasthenia Gravis

1. Myasthenia gravis (MG) is an **autoimmune disease** with a prevalence of 14 to 20 per 100,000 population in the United States. It is most common in young adult women.
2. **The loss of AChRs at motor endplates** in MG is induced by **antireceptor antibodies**. These antibodies are detectable in the serum of 90% of MG patients, but antibody titers correlate poorly with clinical signs.
3. MG often presents with the gradual onset of **pharyngeal or ocular weakness**. All muscle groups may be affected. The hallmark of MG is weakness that becomes worse with exercise.
4. The **diagnosis** is supported by the clinical history and confirmed by the presence of anti-AChR serum antibodies, by transiently improved muscle strength after 10 mg of IV edrophonium (the Tensilon test), and by characteristic electromyographic findings.
5. **Treatment** includes anticholinesterases (e.g., pyridostigmine), corticosteroids, immunosuppressive drugs (e.g., azathioprine and cyclophosphamide), plasmapheresis, and thymectomy. Remission of the disease is common after thymectomy.
6. Special attention needs to be given to MG patients receiving either regional anesthetic or general anesthetic.
 - a. **Anticholinesterase therapy** should not be discontinued before surgery.
 - b. **Neuraxial regional anesthesia** is associated with skeletal muscle relaxation and some degree of diaphragmatic weakness. This normal

effect of regional anesthesia often unmasks underlying weakness. These patients, therefore, may suffer from profound respiratory weakness and need careful respiratory monitoring throughout anesthesia and recovery.

- c. These patients are often **resistant to depolarizing agents**, although clearance of SCh is inhibited by pyridostigmine. They are also **extremely sensitive to nondepolarizing agents**. Both longer-acting agents such as pancuronium and shorter-acting agents such as cis-atracurium have been associated with prolonged blockade, refractoriness to reversal agents, and profound postoperative weakness. NMBDs are best avoided, if possible.
 - d. **Monitoring of the degree of neuromuscular blockade is strongly recommended**, although complete recovery of the TOF does not ensure recovery of the muscles of the upper airway or adequate spontaneous ventilation.
 - e. **Surgery and anesthesia may exacerbate the underlying illness**. Postoperative ventilatory support may be required even after minor surgical procedures.
- D. Muscular dystrophies** are a heterogeneous group of inherited muscle disorders characterized by a progressive loss of skeletal muscle function. **Duchene muscular dystrophy** is the most common and the most severe of the disorders. The responsible gene encodes a membrane-associated protein known as dystrophin that is critical for the stability of the muscular membrane. The disorder is X-linked recessive and clinically evident in males. The clinical course is characterized by painless degeneration and atrophy of skeletal muscle, which manifests as weakness by the age of 5 years. By the preteen years, the patient often is confined to a wheelchair, and death usually occurs by the mid-20s secondary to congestive heart failure.
1. **Serum creatine kinase levels** are elevated and track the progression of muscular degeneration. By the late stages of the disease, creatine kinase levels are near normal because of significant loss of muscle mass.
 2. Cardiac (progressive systolic dysfunction and ventricular thinning) and smooth muscles (gastrointestinal hypomotility with delayed gastric emptying) are affected to various degrees. Although the diaphragm is spared, accessory muscle weakness produces a restrictive pattern on pulmonary function testing. Because coughing is impaired, pneumonia is a frequent complication.
 3. **SCh** can cause massive rhabdomyolysis, hyperkalemia, and death. Because the intensity and duration of drug effect are hard to predict, short-acting NMBDs may be preferable. **Volatile inhalational agents**, particularly halothane, can have exaggerated myocardial depressant effects. **MH** occurs with increased frequency. The delayed gastric emptying and ineffective cough place these patients at greater risk for regurgitation and aspiration. Postoperatively, these patients require aggressive pulmonary physiotherapy to ensure adequate secretion clearance. **Opioids**, which may further depress deep breathing and coughing, should be used cautiously.
- E. The myotonic syndromes** are a group of disorders characterized by a defect in skeletal muscle relaxation and persistent contraction of skeletal muscles after stimulation. The persistent contraction is a consequence of ineffective calcium removal from the cytoplasm to the sarcoplasmic

reticulum. **Myotonic dystrophy** is the most common syndrome in this group of disorders.

1. Myotonic dystrophy patients have progressive involvement and deterioration of skeletal, cardiac, and smooth muscles throughout the body, with weakened respiratory effort, a restrictive pattern on pulmonary function testing, and diminished gastrointestinal motility. Other symptoms include cataracts, cardiac conduction abnormalities, baldness, and mental retardation.
2. **Regional anesthesia, neuromuscular-blocking agents, and increasing depth of general anesthesia do not relieve myotonic muscle rigidity.** Pregnancy exacerbates this condition, and cesarean section is often indicated because of uterine muscle dysfunction. These patients are exquisitely sensitive to the respiratory depressant effects of opioids, benzodiazepines, and inhalational agents. Neuraxial opiates that have minimal effect on respiratory function in normal persons can have a substantial effect in these patients. Similar to patients with Duchenne muscular dystrophy, these patients have frequent cardiac arrhythmias and are at increased risk for cardiac arrest during general anesthesia.
3. **SCh** should be avoided as it induces prolonged skeletal muscle contraction. **Nondepolarizing agents** can be used; however, the use of short-acting agents and careful titration of reversal agents are recommended.

Suggested Readings

- Ali HH, Savarese JJ. Monitoring of neuromuscular function. *Anesthesiology* 1976;45:216–249.
- Berg H, Roed J, Viby-Mogensen J, et al. Residual neuromuscular block is a risk factor for postoperative pulmonary complications: a prospective, randomised, and blinded study of postoperative pulmonary complications after atracurium, vecuronium and pancuronium. *Acta Anaesthesiol Scand* 1997;41:1095–1103.
- Briggs ED, Kirsch JR. Anesthetic implications of neuromuscular disease. *J Anesth* 2003;17:177–185.
- Chiu JW, White PF. The pharmacoeconomics of neuromuscular blocking drugs. *Anesth Analg* 2000;90:S19–S23.
- Eriksson LI. Residual neuromuscular blockade. Incidence and relevance. *Anaesthesist* 2000;49:S18–S19.
- Eriksson LI. The effects of residual neuromuscular blockade and volatile anesthetics on the control of ventilation. *Anesth Analg* 1999;89:243–251.
- Kopman AF, Yee PS, Neuman GG. Relationship of the train-of-four fade ratio to clinical signs and symptoms of residual paralysis in awake volunteers. *Anesthesiology* 1997;86:765–771.
- Lien C. Development and potential clinical impact of ultra-short acting neuromuscular blocking agents. *Br J Anaesth* 2011;107:i60–i71.
- Martyn JA, Richtsfeld M. Succinylcholine-induced hyperkalemia in acquired pathologic states: etiologic factors and molecular mechanisms. *Anesthesiology* 2006;104:158–169.
- Murphy GS, Szokol JW, Marymont JH, et al. Residual paralysis at the time of tracheal extubation. *Anesth Analg* 2005;100:1840–1845.
- Murphy GS, Szokol JW. Monitoring neuromuscular blockade. *Int Anesthesiol Clin* 2004;42:25–40.
- Pandit L, Agrawal A. Neuromuscular disorders in critical illness. *Clin Neurol Neurosurg* 2006;108:621–627.
- Plaud B, Meretoja O, Hofmockel R, et al. Reversal of rocuronium-induced neuromuscular blockade with sugammadex in pediatric and adult surgical patients. *Anesthesiology* 2009;110:284–294.
- Shear TD, Martyn JA. Physiology and biology of neuromuscular transmission in health and disease. *J Crit Care* 2009;24:5–10.

I. APPLIED ANATOMY

A. The **pharynx** is divided into the nasopharynx, the oropharynx, and the laryngopharynx.

1. The **nasopharynx** consists of the nasal passages, including the septum, turbinates, and adenoids.
2. The **oropharynx** consists of the oral cavity, including the dentition and tongue.
3. The epiglottis separates the **laryngopharynx** into the larynx (leading to the trachea) and the **hypopharynx** (leading to the esophagus).

B. The Larynx

1. The **larynx**, located at the level of the fourth to the sixth cervical vertebrae, originates at the laryngeal inlet and ends at the inferior border of the cricoid cartilage. It consists of nine cartilages; three unpaired (thyroid, cricoid, and epiglottis) and three paired (corniculates, cuneiforms, and arytenoids); ligaments; and muscles.
2. The **cricoid cartilage**, located just inferior to the **thyroid cartilage at the C5-6 vertebral level**, is the only complete cartilaginous ring in the respiratory tree.
3. The **cricothyroid membrane** connects the thyroid and cricoid cartilages and measures 0.9×3.0 cm in adults. The membrane is superficial, thin, and devoid of major vessels in the midline, making it an important site for emergent surgical airway access (see Cricothyroidotomy below).
4. The **laryngeal muscles** can be divided into two groups: muscles that open and close the glottis (lateral cricoarytenoid [adduction], posterior cricoarytenoid [abduction], and transverse arytenoid) and muscles that control the tension of the vocal ligaments (cricothyroid, vocalis, and thyroarytenoid).

5. Innervation

- a. **Sensory.** The **glossopharyngeal nerve** (cranial nerve IX) provides sensory innervation to the posterior one third of the tongue, the oropharynx from its junction with the nasopharynx, including the pharyngeal surfaces of the soft palate, epiglottis, and the fauces, to the junction of the pharynx and esophagus. The **internal branch of the superior laryngeal nerve**, a branch of the vagus nerve (cranial nerve X), provides sensory innervation to the mucosa from the epiglottis to and including the vocal cords. The sensory fibers of the **inferior laryngeal nerve**, a branch of the recurrent laryngeal nerve (also a branch of the vagus nerve), provides sensory innervation to the mucosa of the subglottic larynx and trachea.
- b. **Motor.** The external branch of the **superior laryngeal nerve** provides motor innervation to the cricothyroid muscle. Activation of this muscle results in tensing of the vocal cords. The motor fibers of the **inferior laryngeal nerve** provide motor innervation to all other intrinsic muscles of the larynx. **Bilateral injury to the inferior laryngeal**

nerves (e.g., via injury to the recurrent laryngeal nerves) can produce unopposed activation of the cricothyroideus, leading to tensing of the vocal cords and airway closure.

- C. The **glottis** is composed of the vocal folds (true and “false” cords) and the rima glottidis.
 - 1. The **rima glottidis** describes the aperture between the true vocal cords.
 - 2. The **glottis** represents the narrowest point in the adult airway (more than 8 years of age), whereas the cricoid cartilage represents the narrowest point in the infant airway (birth to 1 year of age).
- D. The **lower airway** extends from the subglottic larynx to the bronchi.
 - 1. The subglottic larynx extends from the vocal folds to the inferior border of the cricoid cartilage (C6).
 - 2. The **trachea** is a fibromuscular tube that is 10 to 12 cm long with a diameter of approximately 20 mm in adults. It extends from the cricoid cartilage to the carina. The trachea is supported by 16 to 20 U-shaped cartilages, with the open end facing posteriorly. Noting the posterior absence of cartilaginous rings provides anterior–posterior orientation during fiberoptic exam of the tracheobronchial tree.
 - 3. The trachea bifurcates into the right and left main stem bronchi at the carina. The right main stem bronchus is approximately 2.5 cm long with a takeoff angle of approximately 25 degrees. The left main stem bronchus is approximately 5 cm long with a takeoff angle of approximately 45 degrees.

II. EVALUATION

- A. **History.** A history of difficult airway management in the past may be the best predictor of a challenging airway. If old medical records are available, prior anesthetic records should be reviewed for the ease of intubation and ventilation (the ability to mask ventilate, and whether adjuncts to mask ventilation were required; the number of intubation attempts; the type of laryngoscope blade used; the size of the endotracheal tube (ETT); or if any specialty airway equipment, i.e., video laryngoscopy or a fiberoptic scope were required). Particular importance should also be placed on diseases that may affect the airway. Specific symptoms related to airway compromise should be sought, including hoarseness, stridor, wheezing, dysphagia, dyspnea, and positional airway obstruction.
 - 1. **Arthritis or cervical disk disease** may decrease neck mobility. Cervical spine instability and limitation of mandibular motion are common in rheumatoid arthritis. The temporomandibular and cricoarytenoid joints may also be involved. Aggressive neck manipulation in these patients may lead to atlantoaxial subluxation and spinal cord injury. The risk of atlantoaxial subluxation is highest in patients with severe hand deformities and skin nodules.
 - 2. **Infections** of the floor of the mouth, salivary glands, tonsils, or pharynx may cause pain, edema, and trismus with limited mouth opening.
 - 3. **Tumors** may obstruct the airway or cause extrinsic compression and tracheal deviation.
 - 4. **Increased body mass index (BMI) is often a challenge during the induction of anesthesia.** The increased BMI coupled with other anatomical findings (Mallampati score, increased neck circumference, short thyromental distance) can be predictive for difficult ventilation by mask and a high probability for a difficult tracheal intubation. The decreased functional residual capacity (FRC) associated with an increased in BMI can result in a precipitous desaturation with the apnea of induction.

5. **Trauma** may be associated with airway injuries, cervical spine injury, basilar skull fracture, or intracranial injury.
6. **Previous surgery, radiation, or burns** may produce scarring, contractures, and limited tissue mobility and narrow the oral aperture.
7. **Acromegaly** may cause mandibular hypertrophy and overgrowth and enlargement of the tongue and epiglottis. The glottic opening may be narrowed because of enlargement of the vocal cords.
8. **Scleroderma** may produce skin tightness and decrease mandibular motion and narrow the oral aperture.
9. **Trisomy 21 patients** may have atlantoaxial instability and macroglossia.
10. **Dwarfism and achondroplasia** patients may be associated with atlantoaxial instability and potentially difficult airway management because of mandibular hypoplasia (micrognathia).
11. **Other congenital anomalies** may complicate airway management, particularly pediatric and adult patients with craniofacial abnormalities such as Pierre Robin, Treacher Collins, Klippel-Feil, and Goldenhar syndromes. In contrast, children with isolated cleft palates are not specifically difficult to intubate if the condition is not associated with other airway or craniofacial abnormalities, but nasotracheal intubation should be avoided.

B. Physical Examination

1. **Specific findings** that may indicate a difficult airway include the following:
 - a. Inability to open the mouth
 - b. Poor cervical spine mobility
 - c. Receding chin (micrognathia)
 - d. Large tongue (macroglossia)
 - e. Prominent incisors
 - f. Short muscular neck
2. **Injuries** to the face, neck, or chest must be evaluated to assess their contribution to airway compromise.
3. **Head and neck examination.** There is no single best predictor of difficult airway management on the physical exam, so a detailed exam is in order. Multiple predictors of difficult airway will increase the specificity of the exam.
 - a. **Nose.** The patency of the nares or the presence of a deviated septum should be determined by occluding one nostril at a time and assessing ease of ventilation through the other nostril. This is especially important should nasotracheal intubation be required.
 - b. **Mouth.** Identify macroglossia and conditions that reduce mouth opening (e.g., facial scars or contractures, scleroderma, and temporomandibular joint disease). **Poor dentition** may increase the risk of tooth injury or avulsion during airway manipulation. Loose teeth should be identified preoperatively and protected or removed before initiation of airway management.
 - c. **Neck**
 1. If the **thyromental distance** (the distance from the lower border of the mandible to the thyroid notch with the neck fully extended) is less than 6 cm (three to four finger breadths), there may be difficulty visualizing the glottis. The mobility of laryngeal structures should be assessed, and the trachea should be palpable in the midline above the sternal notch. Look for scars from previous neck surgery, an enlarged thyroid, other paratracheal masses, and indurated tissues suggestive of radiation therapy.

2. **Cervical spine mobility.** Patients should be able to touch their chin to their chest and extend their neck posteriorly. Lateral rotation should not produce pain or paresthesia.
3. The presence of a healed or patent **tracheostomy** stoma may be a clue to subglottic stenosis or prior complications with airway management. Smaller diameter ETTs should be available for these patients.
4. The **Mallampati classification** to predict difficult intubation is based on the finding that visualization of the glottis is impaired when the base of the tongue is disproportionately large. Assessment is made with the patient sitting upright, with the head in the neutral position, the mouth open as wide as possible, and the tongue protruded maximally without phonation. The modified classification includes the following four categories (Fig. 14.1):
 - a. **Class I.** Faucial pillars, soft palate, and uvula are visible.
 - b. **Class II.** Faucial pillars and soft palate may be seen, but the uvula is masked by the base of the tongue.
 - c. **Class III.** Only soft palate is visible. Intubation is predicted to be difficult.
 - d. **Class IV.** Soft palate is not visible. Intubation is predicted to be difficult.
- C. **Special Studies.** In most patients, a careful history and physical examination will be all that are needed to evaluate an airway. Useful adjuncts may include the following:
 1. **Laryngoscopy** (direct, indirect, video, or flexible fiberoptic) will provide information about the hypopharynx, laryngeal inlet, and vocal cord function. It can be performed in a conscious patient with topical anesthesia or nerve blocks.
 2. **Chest or cervical imaging** may reveal tracheal deviation or narrowing and bony deformities in the neck. Cervical spine films are particularly important in trauma cases and should be performed in case of an injury above the clavicle or serious multiple traumatic injuries. In patients with altered mental status or distracting injuries, a normal cervical radiograph cannot rule out a significant ligamentous injury. Cervical spine precautions should be applied during intubation and computed

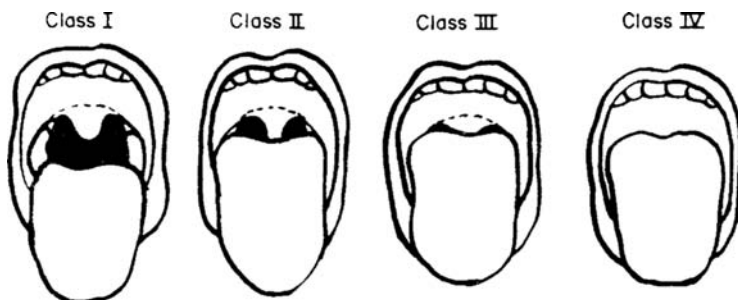


FIGURE 14.1 Mallampati classification of the oropharyngeal structures as modified by Samsoon and Young, as defined in a patient sitting upright with mouth maximally opened and tongue protruded without phonation. (From Samsoon GLT, Young JRB. Difficult tracheal intubation, a retrospective study. *Anaesthesia* 1987;42:487–490, with permission.)

tomography (CT) or MRI scans should be obtained, depending on local protocols. Lateral cervical spine films may be useful in symptomatic patients with rheumatoid arthritis or Down syndrome to assess for atlantoaxial subluxation.

3. **Tracheal tomograms or CT scan** can delineate masses obstructing the airway.
4. **Pulmonary function tests** and flow volume loops can help determine the degree and site of airway obstruction (see Chapters 1 and 3).
5. **Baseline arterial blood gas tensions** can indicate the functional consequences of airway abnormalities and alert the clinician to patients who are chronically hypoxemic or hypercarbic.

III. MASK AIRWAY

A. Indications

1. To preoxygenate (denitrogenate) a patient before endotracheal intubation
2. To assist or control ventilation as part of initial resuscitation before an ETT is placed
3. To provide inhalation anesthesia in patients not at risk for regurgitation of gastric contents

B. Technique involves placing a face mask and maintaining a patent airway.

1. **The mask** should fit snugly around the bridge of the nose, cheeks, and mouth. Clear plastic masks allow for observation of the lips (for color) and mouth (for secretions or vomitus).
2. **Mask placement.** The mask is held in the left hand so that the little finger is at the angle of the mandible, the third and fourth fingers are along the mandible, and the index finger and thumb are placed on the mask in the shape of the letter "C." The right hand is available to control the reservoir bag. Two hands may be required to maintain a good mask fit, necessitating an assistant to control the bag. Head straps may be used to assist mask fit. Peak inspiratory pressures should be kept below 20 cm H₂O in order to minimize gastric insufflation. There are certain airway environments that may require a reversal of the handedness of mask ventilation described above, where the mask will be held in the right hand, and the left hand will control the reservoir bag. This should become an ambidextrous skill.
3. **Edentulous patients** may present a problem when attempting to achieve an adequate seal with the face mask because of decreased distance between the mandible and the maxilla. An oral airway will often correct this problem, and the cheeks may be compressed against the mask to decrease leaks. Two hands may be required to do this. Alternatively, dentures may be left in place during mask ventilation, but have often been removed prior to induction.
4. **Airway obstruction** during spontaneous ventilation may be recognized by a paradoxical "rocking" motion of the chest and abdomen. During spontaneous ventilation, if the upper airway is obstructed as the diaphragm contracts, the abdomen distends as it normally does for each breath, but the thorax collapses instead of being insufflated. Stridor is a high-pitched noise associated with an extreme narrowing of an upper airway and may be caused by diseases such as croup but is most commonly observed with laryngospasm after extubation. With airway obstruction, respiratory excursions in the reservoir bag will be decreased or absent, and peak airway pressures will be increased when positive-pressure ventilation is attempted.

5. **Airway patency** may be restored by the following:
 - a. Neck extension.
 - b. Jaw thrust, by placing the fingers under the angles of the mandible and lifting forward.
 - c. Turning the head to one side.
 - d. Insertion of an oral airway. An airway may not be well tolerated if the gag reflex is intact. Complications from the use of oral airways include vomiting, laryngospasm, and dental trauma. The wrong-size oral airway may worsen obstruction. If the oral airway is too short, it may compress the tongue; if it is too long, it may lie against the epiglottis.
 - e. A nasal airway helps maintain upper airway patency in a patient with minimal-to-moderate obstruction and is reasonably tolerated by awake or sedated patients. Nasal airways can cause epistaxis and should be avoided in patients who are anticoagulated.
- C. **Difficult mask ventilation** may be anticipated in patients who have the following: obesity, edentition, beards, cervical arthritis, or obstructive sleep apnea. Appropriate oral and nasal airways and laryngeal mask airways (LMAs) should be available.
- D. **Complications.** The mask may cause pressure injuries to soft tissues around the mouth, mandible, eyes, or nose. Loss of the airway may result from laryngospasm or vomiting. Mask ventilation does not protect the airway from aspiration of gastric contents. **Laryngospasm**, a tonic contraction of the laryngeal and pharyngeal muscles, causes airway obstruction and closure of the vocal cords that may be relieved by jaw thrust and the application of constant positive airway pressure. If this fails, a small dose of succinylcholine (20 mg intravenously or intramuscularly in the adult) may be required.

IV. LARYNGEAL MASK AIRWAY

- A. The classic LMA and its multiple variations are disposable supraglottic airway management devices that can be used as an alternative to both mask ventilation and endotracheal intubation in appropriate patients. The LMA also plays an important role in the management of the difficult airway. When inserted appropriately, the LMA lies with its tip resting over the upper esophageal sphincter, cuff sides lying over the pyriform fossae, and cuff upper border resting against the base of the tongue. Such positioning allows for effective ventilation with minimal inflation of the stomach.
1. **Indications**
 - a. As an alternative to mask ventilation or endotracheal intubation for airway management. The LMA is not a replacement for endotracheal intubation when endotracheal intubation is indicated.
 - b. In the management of a known or unexpected difficult airway.
 - c. In airway management during the resuscitation of an unconscious patient.
2. **Contraindications**
 - a. Patients at risk of aspiration of gastric contents, such as patients with a full stomach, or symptomatic gastroesophageal reflux disease.
 - b. Patients with decreased respiratory system compliance, because the low-pressure seal of the LMA cuff will leak at high inspiratory pressures, and gastric insufflation may occur. Peak inspiratory pressures should be maintained at less than 20 cm H₂O to minimize cuff leaks and gastric insufflation.
 - c. Patients in whom long-term mechanical ventilatory support is anticipated or required.
 - d. Patients with intact upper airway reflexes, because insertion can precipitate laryngospasm.

TABLE 14.1
Laryngeal Mask Airway Sizes

Patient Age/Size	LMA Size	Cuff Volume	ETT Size (ID)
Neonates/infants to 5 kg	1	Up to 4 mL	3.5 mm
Infants, 5–10 kg	1.5	Up to 7 mL	4.0 mm
Infants/children, 10–20 kg	2.0	Up to 10 mL	4.5 mm
Children, 20–30 kg	2.5	Up to 14 mL	5.0 mm
Children, 30 kg to small adults	3.0	Up to 20 mL	6.0 cuffed
Average adults	4.0	Up to 30 mL	6.0 cuffed
Large adults	5.0	Up to 40 mL	7.0 cuffed

3. Use

- a. LMAs are available in a variety of pediatric and adult sizes (see Table 14.1). Using the proper size maximizes the probability of appropriate cuff fit. Maneuvers for appropriate insertion of the LMA are shown in Figure 14.2.
 - b. Ensure correct cuff deflation and lubrication. Lubrication of the LMA inner surface should be avoided because any lubricant dripping into the larynx can precipitate laryngospasm.
 - c. Follow usual preoxygenation and monitoring requirements.
 - d. Ensure an adequate level of anesthesia and suppression of upper airway reflexes.
 - e. Position the patient's head appropriately. The "sniffing" position (slight flexion of the lower cervical spine with extension of C1-2) used to optimize endotracheal intubation also typically provides the best positioning for LMA insertion.
 - f. Insert the LMA (see Fig. 14.2). A soft bite block can be used to protect against a patient biting down on the LMA tube.
 - g. Inflate cuff (see Table 14.1). Typically, one sees a smooth ovoid expansion of the tissues above the thyroid cartilage with adequate inflation of the appropriately positioned LMA.
 - h. Ensure adequate ventilation.
 - i. Connect to anesthetic circuit. The LMA can be secured with tape, if necessary.
 - j. LMA removal. The LMA generally is well tolerated by a patient emerging from general anesthesia as long as the cuff is not overinflated (cuff pressure less than 60 cm H₂O). The LMA can be removed by deflating the cuff once the patient has emerged from general anesthesia and has return of upper airway reflexes.
 - k. The LMA is a suitable airway for some patients having procedures in the prone position. If this technique is chosen, patients can position themselves on the operating table before induction. After induction of anesthesia, the LMA can be inserted with the patient's head turned to the side and resting on a pillow or blankets.
- 4. Intubating LMAs.** There are multiple brands and styles of LMAs that are designed to facilitate intubation of the patient by passing an ETT through them, either blindly or with flexible fiberoptic guidance. The disposable single use air-Q LMA is similar in style to a standard LMA, but has a larger reinforced tube, and removable airway connector that allows the placement of any standard ETT that has been lubricated with water gel lubricant. The reusable LMA Fastrach includes a curved stainless steel tube covered with silicone, a 15-mm end connector, cuff,

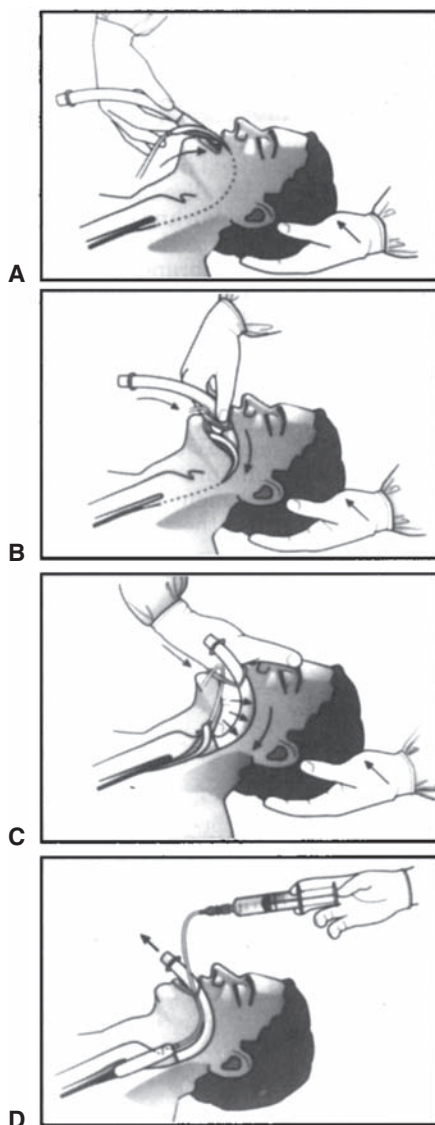


FIGURE 14.2 **A:** With the head extended and the neck flexed, carefully flatten the LMA tip against the hard palate. **B:** With the index finger, push the LMA in a cranial direction following the contours of the hard and soft palates. **C:** Maintaining pressure with the finger on the tube in the cranial direction, advance the mask until definite resistance is felt at the base of the hypopharynx. **D:** Inflation without holding the tube allows the mask to seat itself optimally. (From Brain AJ, Denman WY, Goudsouzian NG. *Laryngeal Mask Airway Instructional Manual*. Berkshire, UK: Brain Medical Ltd.; 1996:21–25.)

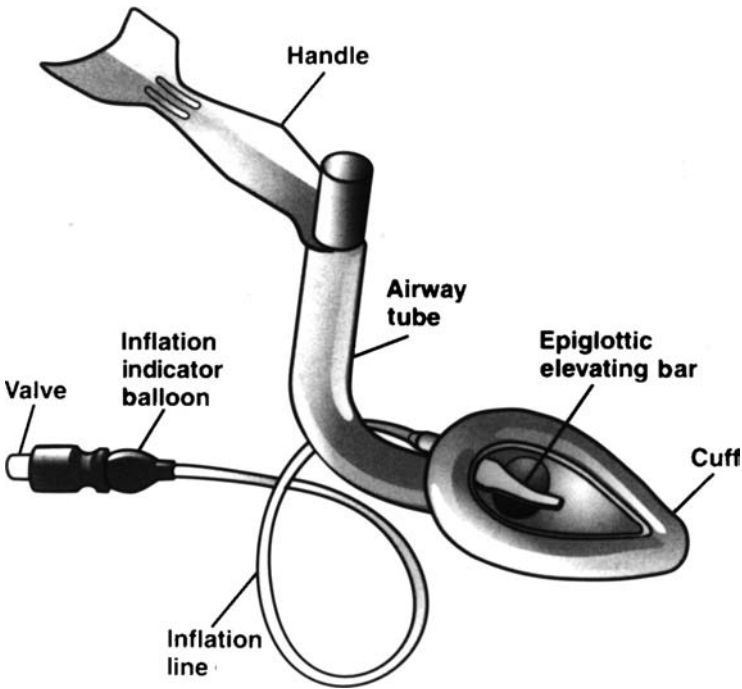


FIGURE 14.3 Features of the LMA Fastrach. (From Brain AIJ, Verghese C. *LMA-Fastrach Instruction Manual*. San Diego: LMA North America, Inc.; 1998.)

and an epiglottic lifting bar (Fig. 14.3). The tube is of sufficient diameter to accept a cuffed 8-mm ID ETT and is short enough to ensure that the ETT cuff will rest beyond the vocal cords.

5. **Adverse effects.** The most common adverse effect of using any LMA is a sore throat, with an estimated incidence of 10%, and is most often related to over inflation of the LMA cuff. The primary major adverse effect is aspiration, which has been estimated to occur at a comparable incidence as with mask or endotracheal anesthesia.

V. ENDOTRACHEAL INTUBATION

A. Orotracheal Intubation

1. **Indications.** Endotracheal intubation is required to provide a patent airway when patients are at risk for aspiration, when airway maintenance by mask is difficult, and for prolonged controlled ventilation. Intubation also may be required for specific surgical procedures (e.g., head/neck, intrathoracic, or intra-abdominal procedures).
2. **Technique.** Intubation is usually performed with a laryngoscope. The Macintosh and Miller blades are most commonly used.
 - a. The **Macintosh blade** is curved, and the tip is inserted into the vallecula (the space between the base of the tongue and the pharyngeal surface of the epiglottis) (Fig. 14.4A). It provides a good view

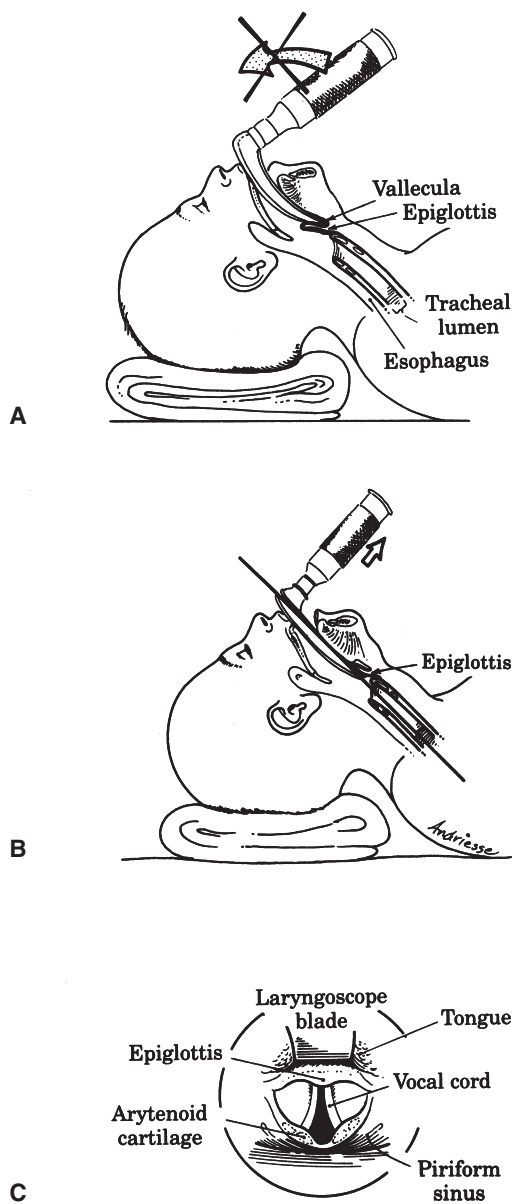


FIGURE 14.4 Anatomic relations for laryngoscopy and endotracheal intubation. **A:** Curved blade placement. **B:** Straight blade placement. **C:** Glottic exposure with curved blade placement.

of the oropharynx and hypopharynx, thus allowing more room for passage of the ETT with decreased epiglottic trauma. Size ranges are designated as no. 1 to 4, with most adults requiring a Macintosh no. 3 blade.

- b. The **Miller blade** is straight, and it is passed so that the tip lies beneath the laryngeal surface of the epiglottis (Fig. 14.4B). The epiglottis is then lifted to expose the vocal cords. The Miller blade provides excellent exposure of the glottic opening but provides a smaller passageway through the oropharynx and hypopharynx. Sizes are designated as no. 0 to 4, with most adults requiring a Miller no. 2 or 3 blade.
- c. Various modified laryngoscope blades provide better visualization of the cords through epiglottis lifting (Mc Coy) or indirect visualization of the cords (Siker and Trueview EVO).
- d. The classic intubation position is the so-called **sniffing position**, with the occiput elevated by pads or folded blankets and the neck extended. On average, this improves the laryngoscopic view, although intubation and mouth opening may be facilitated in some patients by simple neck extension. Neck flexion may make it more difficult to open the mouth.
- e. The laryngoscope is held in the left hand near the junction between the handle and blade. After propping the mouth open with a scissoring motion of the right thumb and index finger, the laryngoscope is inserted into the right side of the patient's mouth while sweeping the tongue to the left. The lips should not be pinched by the blade, and the teeth should be avoided. The blade is then advanced toward the midline until the epiglottis comes into view. The tongue and pharyngeal soft tissues are then lifted to expose the glottic opening. The laryngoscope should be used to lift (see Fig. 14.4B) rather than act as a lever (see Fig. 14.4A), to prevent damage to the maxillary incisors or gingiva.
- f. An appropriate ETT size depends on the patient's age, body habitus, and type of surgery. A 7.0-mm ETT is used for most women, and an 8.0-mm ETT is used for most men. The ETT is held in the right hand as one would hold a pencil and advanced through the oral cavity from the right corner of the mouth and then through the vocal cords. The anatomic view for visualization with a Macintosh laryngoscope is shown in Figure 14.4C. If visualization of the glottic opening is incomplete, it may be necessary to use the epiglottis as a landmark, passing the ETT immediately beneath it and into the trachea. External pressure on the cricoid and/or thyroid cartilage may aid in visualization. The proximal end of the ETT cuff is placed just below the vocal cords, and the markings on the tube are noted in relation to the patient's incisors (or lips). The cuff is inflated just to the point of obtaining a seal in the presence of 20 to 30 cm H₂O positive airway pressure.
- g. **Proper placement of the ETT** needs to be verified by the detection of carbon dioxide in end-tidal or mixed expiratory gas as well as inspection and auscultation of the stomach and both lung fields during positive-pressure ventilation. If an ETT is inserted too deeply, it usually passes into the right mainstem bronchus. When breath sounds are heard on one side of the thorax only, an endobronchial intubation should be suspected, and the ETT should be withdrawn until breath sounds are heard bilaterally. (In trauma

patients, unilateral breath sounds may be indicative of a pneumothorax.) Listening for breath sounds high in each axilla may decrease the chances of being misled by transmitted breath sounds from the opposite lung. A high index of suspicion of an esophageal intubation should be maintained until adequate oxygenation and ventilation are ensured.

h. The ETT should be fastened securely with tape, preferably to taut the skin overlying bony structures.

3. **Complications of orotracheal intubation** include injury of the lips or tongue, teeth, pharynx, or tracheal mucosa. There may rarely be avulsion of arytenoid cartilages or damage to vocal cords or trachea.

B. Nasotracheal Intubation

1. **Indications.** Nasotracheal intubations are uncommon but may be required in patients undergoing an intraoral or oral maxillofacial facial procedure. Compared with oral ETTs, the maximal diameter that can be accommodated is usually smaller, and, accordingly, the resistance to breathing may be higher. The nasotracheal route is rarely used for long-term intubation because of increased airway resistance and the increased risk of sinusitis.

2. **Contraindications.** Basilar skull fractures, especially of the ethmoid bone, nasal fractures, epistaxis, nasal polyps, coagulopathy, and planned systemic anticoagulation and/or thrombolysis (i.e., the patient with acute myocardial infarction), are relative contraindications to nasal intubation.

3. **Technique.** Topical anesthesia and vasoconstriction of the nasal mucosa may be achieved by applying a mixture of 2% lidocaine and 0.25% phenylephrine, using cotton-tipped pledgets. If both nares are patent, the right side is preferred because this will direct the bevel of most ETTs toward the flat nasal septum, reducing damage to the turbinates. The inferior turbinates can interfere with passage and limit the size of the ETT. Usually, a 6.0- to 6.5-mm ETT is used for women and a 7.0- to 7.5-mm ETT is used for men. After it passes through the naris into the pharynx, the tube is advanced through the glottic opening. Intubation may be performed blindly on awake patients, anesthetized but breathing spontaneously, and anesthetized and apneic using direct laryngoscopy assisted by Magill forceps, or with by fiberoptic bronchoscopic assistance.

4. **Complications** are similar to those described for orotracheal intubation (see section V.A.3). Additionally, epistaxis, submucosal dissection, and dislodgement of enlarged tonsils and adenoids may occur. Compared with orotracheal intubation, the nasotracheal route has been associated with an increased incidence of sinusitis and bacteremia.

- C. **Fiberoptic Intubation.** The flexible fiberoptic bronchoscope consists of glass fibers that are bound together to provide a flexible unit for the transmission of light and images. The fiberoptic bundle is fragile, and excessive bending can damage the fibers. Working channels are usually present and can be used to administer topical anesthetics and provide suction or oxygen. The visual field often becomes limited as the fiberoptic bronchoscope nears the glottic opening. Secretions, blood, or fogging of the lens may obscure the view. Immersing the tip of the fiberoptic scope in warm water helps to prevent fogging.

1. **Standard equipment** for oral or nasal fiberoptic intubation includes an oral bite block or Ovassapian airway, topical anesthetics and vasoconstrictors, suction, and a sterile fiberoptic scope with a light source.

2. Indications

- a. The flexible fiberoptic bronchoscope can be used in both awake and anesthetized patients to evaluate and intubate their airways. It can be used for both nasal and oral endotracheal intubations and should be used as a first option in an anticipated difficult airway rather than as a "last resort."
 - b. Initial fiberoptic intubation is recommended for patients with known or suspected cervical spine pathology, head and neck tumors, morbid obesity, or a history of difficult ventilation or intubation.
3. **Technique.** An ETT is placed over a lubricated fiberoptic scope, suction or oxygen tubing is attached to the working port, and the control lever is grasped with one hand while the scope is advanced or maneuvered with the other hand. The use of oxygen through the suction port is often helpful to blow away secretions that may obstruct the view. An oral OvaSsapien airway is helpful and well tolerated for oral fiberoptic intubation. It is important to keep the fiberoptic scope in the midline to prevent entering the piriform fossa. The tip of the scope is positioned anteriorly when in the hypopharynx and advanced toward the epiglottis. If mucous or secretions impair the view, the scope should be retracted or removed to clean the tip and then reinserted in the midline. As the scope slides beneath the epiglottis, the vocal cords are seen. The scope is advanced with the tip in a neutral position until the tracheal rings are noted. The scope is stabilized within the trachea, and the ETT is advanced over it and into the trachea. If there is resistance to the passage, the ETT may need to be turned 90 degrees counterclockwise to avoid the anterior commissure and permit passage through the vocal cords. The tracheal carina should be visualized before withdrawing the fiberoptic scope to ensure proper positioning of the tube.

D. Alternative Intubation Equipment and Techniques

1. **Video Laryngoscopy.** There are many specially designed laryngoscopes that incorporate fiberoptic video or optical prisms to further refine the concept of indirect visualization of the vocal cords on a video screen. These laryngoscopes include multiple reusable or disposable versions of the GlydeScope, Storz C-MAC, AIRQ, Pentax AWS, as well as others, that all result in vocal cords visualization in nearly 100% of the patients. Despite optimal visualization of the vocal cords, ETT advancement can still occasionally be difficult. The different models of video laryngoscopes are all slightly different from each other, and proficiency with one model does not ensure proficiency with them all. It is advisable to familiarize yourself with the video laryngoscope you will be using, by initially performing intubations on patients whose airway could confidently be secured by direct laryngoscopy, or another intubation technique.
2. **The gum elastic bougie,** a 60-cm long, 15-French semi-rigid device with a slight J angle at its distal tip, exemplifies the various types of hollow and solid introducers that may facilitate passage of the ETT into the trachea when direct laryngoscopy is difficult. During direct laryngoscopy, the bougie is advanced under the epiglottis, and its angled end is directed anteriorly toward the glottic opening. If the bougie is inserted into the trachea, often the tracheal rings will be felt as a characteristic "clicking" sensation. The ETT is then advanced over the bougie, and proper placement is confirmed as described above (see section V.A.2.g). The bougie may also be slides as an ETT exchanger.

3. **The light wand** consists of a malleable lighted stylet over which an oral ETT can be passed blindly into the trachea. To insert, the operating room lights are dimmed, and the light wand and ETT are advanced following the curve of the tongue. A glow noted in the lateral neck indicates that the tip of the ETT lies in the piriform fossa. If the tip enters the esophagus, there is a marked diminution in the light's brightness. When the tip is correctly positioned in the trachea, a glow is noted in the anterior neck. At this point, the ETT is slid off the stylet and into the trachea.
4. **Retrograde tracheal intubation** can be performed when previously described techniques have been unsuccessful. It is performed in a conscious patient who is ventilating with a stable airway. For this technique, the cricothyroid membrane is identified and punctured in the midline with an 18-gauge intravenous (IV) catheter. An 80-cm, 0.025-in. guidewire is introduced and directed cephalad. A laryngoscope is used to visualize and retrieve the wire. An ETT is passed over the wire, which serves as a guide through the vocal cords.

VI. THE DIFFICULT AIRWAY AND EMERGENCY AIRWAY TECHNIQUES

A. Difficult Airway. The 2013 revision of the American Society of Anesthesiologists (ASA) algorithm for managing difficult airways is shown in Figure 14.5. Familiarity with this algorithm is crucial for the anesthesiologist. Since its adoption in 1993, the number of death or brain death claims associated with airway-related events during induction of anesthesia has decreased significantly.

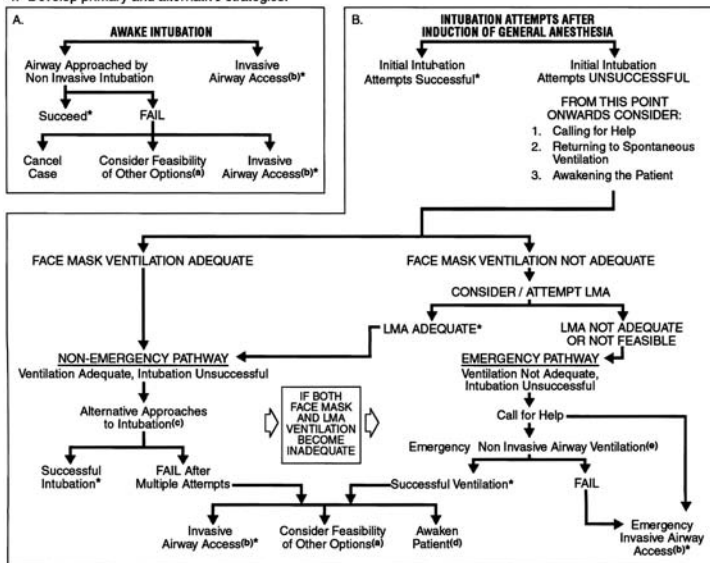
1. The difficult airway can be divided into the recognized difficult airway and the unrecognized difficult airway; the latter presents the greater challenge for the anesthesiologist.
2. The ASA defines a **difficult airway** as failure to intubate with conventional laryngoscopy after three attempts and/or failure to intubate with conventional laryngoscopy for more than 10 minutes. Others have suggested that a more appropriate definition of a difficult airway would be that of failure to intubate with conventional laryngoscopy after an optimal/best attempt. This optimal/best attempt is defined as an attempt with a reasonably experienced laryngoscopist, no significant resistive muscle tone, use of optimal sniffing position, use of external laryngeal manipulation, change of laryngoscope blade type a single time, and change of laryngoscope blade length a single time.
3. The use of **regional anesthesia** as a way to avoid the known or anticipated difficult airway deserves special mention. Although the difficult airway algorithm advocates considering regional anesthesia, it must be kept in mind that the regional block can fail, or the patient may require rapid conversion to a general anesthetic for other reasons. Regional anesthesia generally should not be elected for a patient with a known difficult airway if the surgery cannot be terminated rapidly (in case of failed or inadequate block) or access to the patient's airway is compromised.
4. The supraglottic airway device or LMA is a prominent airway option throughout the 2013 ASA difficult airway algorithm:
 - a. **Nonemergency**
 1. An airway in patients who can be mask ventilated after general anesthesia is induced but cannot be intubated. It is also an alternative if awake intubation has failed (but only when general anesthesia and mask ventilation are not considered problematic).
 2. A conduit for intubation in patients who can be mask ventilated but cannot be intubated with conventional laryngoscopy.



DIFFICULT AIRWAY ALGORITHM

1. Assess the likelihood and clinical impact of basic management problems:
 - A. Difficult Ventilation
 - B. Difficult Intubation
 - C. Difficulty with Patient Cooperation or Consent
 - D. Difficult Tracheostomy
2. Actively pursue opportunities to deliver supplemental oxygen throughout the process of difficult airway management
3. Consider the relative merits and feasibility of basic management choices:

A. Awake Intubation	vs.	Intubation Attempts After Induction of General Anesthesia
B. Non Invasive Technique for Initial Approach to Intubation	vs.	Invasive Technique for Initial Approach to Intubation
C. Preservation of Spontaneous Ventilation	vs.	Ablation of Spontaneous Ventilation
4. Develop primary and alternative strategies:



* Confirm ventilation, tracheal intubation, or LMA placement with exhaled CO₂

a. Other options include (but are not limited to): surgery utilizing face mask or LMA anesthesia, local anesthesia infiltration or regional nerve blockade. Pursuit of these options usually implies that mask ventilation will not be problematic. Therefore, these options may be of limited value if this step in the algorithm has been reached via the Emergency Pathway.

b. Invasive airway access includes surgical or percutaneous tracheostomy or cricothyrotomy.

c. Alternative non-invasive approaches to difficult intubation include (but are not limited to): use of different laryngoscope blades, LMA as an intubation conduit (with or without fiberoptic guidance), fiberoptic intubation, intubating stylet or tube changer, light wand, retrograde intubation, and blind oral or nasal intubation.

d. Options re-preparation of the patient for awake intubation or canceling surgery.

e. Options for emergency non-invasive airway ventilation include (but are not limited to): rigid bronchoscope, esophageal-tracheal combite ventilation, or transtracheal jet ventilation.

FIGURE 14.5 ASA difficult airway algorithm. (From ASA. Practice guidelines for management of the difficult airway: an updated report by the American Society of Anesthesiologists Task Force on Management of the Difficult Airway. *Anesthesiology* 2003;98:1269–1277.)

b. Emergency

1. An airway in patients who cannot be intubated and cannot be ventilated. The Combitube and transtracheal jet ventilation are other options.
2. A conduit for intubation in patients who cannot be intubated and cannot be ventilated (when a supraglottic airway is insufficient and intubation per se is needed).

B. Emergency Airway Techniques

1. **Percutaneous needle cricothyroidotomy** involves placing a 14-gauge IV catheter or 7.5-French introducer through the cricothyroid membrane into the trachea. Oxygen can be administered by connecting the breathing circuit to a 3-mm ID ETT adapter inserted directly into the IV catheter or to a 7.0-mm ID ETT adapter inserted into a 3-mL syringe barrel and connected to the IV catheter. Dedicated cricothyroidotomy catheters are preferred, as the IV catheters have a very high rate of kinking and obstruction.
 - a. **Oxygenation**, but not ventilation, can be achieved by administering oxygen through the catheter at flow rates of 10 to 12 L/min. This is a temporary maneuver and is absolutely contraindicated in cases of complete upper airway obstruction, because severe barotrauma may result.
 - b. **Some ventilation** may be achieved by pressing the oxygen flush valve for 1 second and allowing for passive exhalation over 2 to 3 seconds.
 - c. Once in place, the catheter must be carefully and firmly held in position to **avoid dislodgment**, which can be life threatening.
 - d. **Complications** include barotrauma, pneumothorax, subcutaneous emphysema of the neck and anterior chest, loss of the airway, and death. Furthermore, the airway is not “protected,” and aspiration is a possibility.
2. **Rigid bronchoscopy** by a surgeon or interventional pulmonologist may be necessary to support an airway partially obstructed by a foreign body, traumatic disruption, stenosis, or mediastinal mass. General anesthesia will usually be required for insertion. It is important to have a range of bronchoscope sizes available (including pediatric sizes) (see Chapter 22).
3. **Cricothyroidotomy** is a rapid effective method for relieving severe upper airway obstruction. With the neck extended, a small incision is made in the cricothyroid membrane in the midline. The handle of a scalpel or a Kelley forceps is used to separate the tissues while a tracheostomy tube or ETT is inserted percutaneously.
4. **Tracheostomy** may be performed under local anesthesia before the induction of general anesthesia for a patient with a particularly difficult airway.
 - a. **Technique.** After careful dissection of vessels, nerves, and the thyroid isthmus, a tracheal incision is made, usually between the third and fourth cartilaginous rings. Percutaneous dilational tracheostomy, using commercially available techniques and a modified Seldinger technique, may also be performed.
 - b. **Complications** include hemorrhage, false passage, and pneumothorax.

VII. SPECIAL CONSIDERATIONS

A. Rapid Sequence Induction

1. **Indications.** Patients at risk for aspiration include those who have recently eaten (full stomach), pregnant patients, and those with bowel obstruction, morbid obesity, or symptomatic reflux.
2. **Technique**
 - a. **Equipment** necessary for a rapid sequence induction should include the following:
 1. Functioning tonsil-tip (Yankauer) suction
 2. Several different laryngoscope blades (Macintosh and Miller)
 3. Several styletted ETTs, including one that is of size smaller than normal
 4. An assistant who can apply cricoid pressure effectively

- b. The patient is **preoxygenated** using high flow rates of 100% oxygen for 3 to 5 minutes (denitrogenation). Four to five vital capacity breaths of 100% oxygen achieve nearly similar results when time is of the essence. The patient can also be placed in a head up, reverse Trendelenburg position during preoxygenation, which will delay the onset of desaturation upon apnea.
- c. The neck is extended so the trachea is directly anterior to the esophagus. The administration of an induction agent (e.g., propofol or ketamine) is immediately followed by succinylcholine (1 to 1.5 mg/kg IV). When succinylcholine is contraindicated, the use of a high dose nondepolarizing neuromuscular blockers or remifentanyl (3 to 5 μ g/kg) as an additional induction agent is warranted. An assistant places firm downward digital pressure on the cricoid cartilage, effectively compressing and occluding the esophagus (**Sellick maneuver**). This maneuver theoretically reduces the risk of passive regurgitation of gastric contents into the pharynx and may bring the vocal cords into better view by displacing them posteriorly. It should not be used if the patient is actively vomiting, because high pressures could injure the esophagus.
- d. There should be no attempt to ventilate the patient by mask. Cricoid pressure is maintained until successful endotracheal intubation is verified.
- e. Intubation can usually be performed within 30 seconds. If intubation attempts are unsuccessful, cricoid pressure should be maintained continuously during subsequent intubation maneuvers and while mask ventilation is in progress.

B. Awake Intubation

1. **Indications.** Awake oral or nasal intubation should be considered when there is

- a. A difficult intubation anticipated in a patient at risk for aspiration
- b. Uncertainty about the ability to ventilate or intubate after induction of general anesthesia (e.g., morbidly obese patients)
- c. A need to assess neurologic function after intubation or positioning for surgery

2. **Technique**

- a. To perform an awake intubation, a 4% lidocaine gargle, followed by a lidocaine spray or nebulizer, is used to decrease upper airway sensation.
 1. **Superior laryngeal nerve block** may be used to anesthetize supraglottic structures. A 25-gauge needle is directed anterior to the greater cornu of the hyoid bone and inserted in the thyrohyoid membrane. After negative aspiration, 2 mL of 2% lidocaine is injected on each side.
 2. **Translaryngeal injection of local anesthetic** can anesthetize the glottis and upper trachea. A 25-gauge needle is inserted through the cricothyroid membrane in the midline. After aspiration of air to confirm placement within the tracheal lumen, 2 mL of 2% lidocaine is injected, and the needle is withdrawn. The patient will cough when local anesthetic is injected, aiding in anesthetic spread. This block may increase the risk for aspiration in a patient with a full stomach or may be difficult in a patient with a large neck where precise palpation of the cricothyroid membrane is difficult.

- b. **Awake oral laryngoscopy** often allows one to assess the airway. Sedatives such as midazolam, propofol, and fentanyl may be used in addition to the nerve blocks described above.
- c. **Awake (blind) nasal intubation** may be performed after adequate topical anesthesia and regional airway blocks.
 - 1. Incremental doses of sedatives are useful adjuncts.
 - 2. A well-lubricated ETT is passed into the nasopharynx with gentle pressure.
 - 3. Deep resonant breath sounds may be noted as the tube is advanced toward the glottis. An exaggerated sniffing position may be useful. The ETT is usually passed into the trachea during inspiration.
 - 4. Successful intubation is noted when the patient is unable to phonate, breath sounds and humidification within the ETT are noted with ventilation, and carbon dioxide is noted on the capnograph.
- 3. **Complications** are as described in section V.B.4.
- c. **ETT Changes.** Occasionally, ETT cuff leaks or partial obstruction of the ETT necessitates changing an ETT in a patient with a difficult airway.
 - 1. The oropharynx is suctioned and the patient is ventilated with 100% oxygen.
 - 2. A **tracheal tube exchanger** is a specialized stylet that is placed through the ETT and into the trachea. The depth of insertion is carefully measured. While one person holds the tube changer and assures that it does not pass too distally, the second anesthetist slides the original ETT off the changer and passes a new one over the stylet into the trachea. The risks of using this technique are pneumothorax if the tube changer enters a distal airway and failure to pass the ETT through the cords.
 - 3. A **fiberoptic bronchoscope** can also be used for reintubation. An ETT is placed over the bronchoscope, the tip of which is passed into the trachea alongside the existing tube. The cuff of the existing ETT is deflated, the bronchoscope is advanced, and tracheal rings are noted to confirm position. The existing ETT is removed (a tracheal tube changer may be left in its place), and the new one is advanced as described in section V.C. The advantages of this technique are that the trachea is directly seen, and the patient can be oxygenated through the working port of the bronchoscope if there is difficulty passing the ETT through the vocal cords.

Suggested Readings

- Adnet F, Baillard C, Borron SW, et al. Randomized study comparing the “sniffing position” with simple head extension for laryngoscopic view in elective surgery patients. *Anesthesiology* 2001;95:836–841.
- ASA. Practice guidelines for management of the difficult airway: an updated report by the American Society of Anesthesiologists Task Force on Management of the Difficult Airway. *Anesthesiology* 2013;118(2):251–270.
- Brain AJ, Vergheze C, Strube PJ. The LMA “ProSeal”—a laryngeal mask with an oesophageal vent. *Br J Anaesth* 2000;84:650–654.
- Cormack RS, Lehane J. Difficult tracheal intubation in obstetrics. *Anaesthesia* 1984;39:1105–1111.
- Ferson DZ, Rosenblatt WH, Johansen MJ, et al. Use of the intubating LMA Fastrach in 254 patients with difficult-to-manage airways. *Anesthesiology* 2001;95:1175–1181.
- Hurford WE. Nasotracheal intubation. *Respir Care* 1999;44:643–649.

- Langeron O, Masso E, Huraux C, et al. Prediction of difficult mask ventilation. *Anesthesiology* 2000;92:1229–1236.
- Peterson GN, Domino KB, Caplan RA, et al. Management of the difficult airway: a closed claims analysis. *Anesthesiology* 2005;103:33–39.
- Samsoon GLT, Young JRB. Difficult tracheal intubation: a retrospective study. *Anaesthesia* 1987;42:490–497.
- Scmitt H, Buchfelder M, Radespil-Troger M, et al. Difficult intubation in acromegalic patients. *Anesthesiology* 2000;93:110–114.
- Sellick B. Cricoid pressure to control regurgitation of stomach contents during induction of anesthesia. *Lancet* 1961;2:404–406.

The **primary goals** of general anesthesia are to maintain the health of the patient while safely providing amnesia, hypnosis (lack of awareness), analgesia, and immobility. **Secondary goals** may vary depending on the patient's medical condition, the surgical procedure, and the surgical setting (e.g., outpatient surgical unit versus inpatient operating room [OR]). Perioperative planning involves the integration of preoperative, intraoperative, and postoperative care. Flexibility, the ability to anticipate problems before they occur, and the ability to execute contingency plans are skills that define the expert anesthetist.

The Anesthetic Plan. An anesthetic plan helps the anesthetist marshal appropriate resources and anticipate potential difficulties. Important elements include the following:

1. Risk Assessment (e.g., ASA classification and cardiovascular risk stratification—see 2014 ACC/AHA Guidelines)
2. Specific homeostatic challenges (organ systems, temperature, and coagulation)
3. Intravenous (IV) access (anticipated blood loss)
4. Monitoring
5. Airway management
6. Medications (allergies, antibiotics, anxiolysis, anesthesia induction and maintenance, PONV prophylaxis, and pain)
7. Perioperative analgesia (opioids, NSAIDs, and nerve blocks)
8. Postoperative transport and disposition

Before entering the OR, specific airway, blood loss, or other surgical concerns should be discussed with other members of the care team (see WHO Surgical Safety Checklist). For the patient at high risk for life-threatening complications (e.g., airway loss, nonperfusing arrhythmia, massive hemorrhage, or air embolus), specialized equipment and/or extra help should be immediately available and preoperatively reviewing pertinent sections of an emergency manual is recommended.

I. PREOPERATIVE PREPARATION

The anesthetist assumes responsibility for the patient when the preoperative medication is administered. An anesthetist or other responsible clinician should accompany an unstable patient during transport to the OR.

A. Preoperative evaluations may be performed minutes to weeks before the administration of the anesthetic and sometimes not by the anesthetist of record. A detailed history and physical exam should be performed, and preoperative optimization should be completed. The administering anesthetist performs an airway examination and checks for interim changes in the patient's condition, medications, laboratory data, and consultant notes. Time of last oral intake is confirmed (see Table 15.1). Tube feeds in critically ill intubated patients may be continued before and during procedures outside the abdomen and thorax. Allergies and the anesthetic

TABLE
15.1
ASA Practice Guidelines for Preoperative Fasting

Ingested Material	Minimum Fasting Period ^a
Clear liquids	2 h
Breast milk	4 h
Infant formula, nonhuman milk, light meals	6 h
Full meal	8 h

^a Healthy patients, elective cases.

plan are reviewed with the patient, and proper informed consent for the administration of anesthesia is obtained from either the patient or his or her legal proxy.

- B. Intravascular Volume.** Patients may arrive in the OR with intravascular or total body hypovolemia due to prolonged NPO status, severe inflammatory illness, hemorrhage, fever, vomiting, or diuretic use. Currently available isotonic bowel preparations may not directly induce water loss but can decrease absorption of fluids ingested before surgery. The patient's volume status is evaluated either clinically or with appropriate monitors. If a **fluid deficit** is present, the patient should be adequately hydrated before the induction of anesthesia. The fluid deficit for fasting adults is estimated at 60 mL/h + 1 mL/kg/h for each kilogram greater than 20 kg (maintenance fluids). In general, at least half of this deficit is corrected before induction; the remainder may be corrected intraoperatively. The type and amount of fluids given may be modified in the presence of systemic diseases (see Chapters 2 to 6) or for specific types of surgery (Chapters 22 and 25).
- C. IV Access.** The size and number of IV catheters placed varies with the procedure, anticipated blood loss, and the need for continuous drug infusions. At least one large bore IV (>16-gauge) catheter should be placed when rapid fluid or blood infusion is anticipated. When continuous drug infusions are to be delivered concurrently with rapid fluid infusion, an additional IV catheter often is dedicated for this purpose. Some medications used for cardiovascular support (e.g., norepinephrine) are best delivered via a central venous catheter placed either before induction, if indicated, or after (see below under Monitoring).
- D. Preoperative Medications**
 - 1. Anxiety.** The preoperative period is one of high anxiety, especially for patients who have not had a prior interview with an anesthetist. Anxiety may be managed effectively with calm reassurance and expression of interest in the patient's well-being. When deemed appropriate, a benzodiazepine (e.g., diazepam and midazolam) with or without a small dose of an opioid (e.g., fentanyl and morphine) may be administered. Oral diazepam or lorazepam may be given with a small amount of water 30 to 60 minutes before the procedure. Patients complaining of pain on arrival in the OR may be given analgesics in incremental amounts to alleviate symptoms. Dosages are based on the patient's age, medical condition, and anticipated time of discharge (see Chapters 1 and 12). Appropriate monitoring should be used and resuscitative equipment available.
 - 2. Drugs to neutralize gastric acid** (H_2 -antagonists, PPIs, nonparticulate antacids) **and decrease gastric volume** (metoclopramide, H_2 -antagonists, PPIs) should be used only when the patient is at increased risk of

aspiration of gastric contents (i.e., recent meal, trauma, bowel obstruction, pregnancy, history of gastric surgery, increased intra-abdominal pressure, difficult airway, or history of active reflux; see Chapter 1). When bowel obstruction is present, promotility drugs may increase retrograde peristalsis and are contraindicated.

- E. Monitoring.** Standard ASA monitoring (see Chapter 10) is established before the induction of anesthesia. Invasive hemodynamic monitors (e.g., arterial catheter, central venous line, and pulmonary artery catheter) should be placed before induction of anesthesia when indicated by the patient's medical condition and potential anesthetic effects (e.g., an arterial line for a patient at risk for cerebral ischemia). Invasive monitors may be placed after induction of anesthesia when indicated primarily by the surgical procedure (e.g., a central line for a patient undergoing elective aortic surgery). Surgical-specific monitoring (e.g., evoked potentials) should be discussed with the surgical team to ensure compatibility with anesthetic plans.

II. INDUCTION OF ANESTHESIA

Induction of anesthesia produces an unconscious patient with depressed reflexes who is dependent on the anesthetist for maintenance of homeostatic mechanisms and safety.

- A. The environment** in the OR should be warm and with minimal noise. All members of the OR team (scrub nurse, circulating nurse, and surgeon) should focus their attention on the patient and be ready to give immediate assistance to the anesthetist if needed.
- B. The patient's position** for induction is usually supine, with extremities resting comfortably on padded surfaces. The head should rest on a raised firm padded support, and tilted back in a "sniff" position (see Chapter 14). Routine preinduction administration of oxygen (denitrogenation) minimizes the risk of hypoxia developing during induction of anesthesia. High flow (8 to 10 L/min) oxygen should be delivered via a face mask placed gently on the patient's face. The patient can be instructed to take deep breaths and exhale fully to speed the exchange of oxygen. Angling upward the OR table back (semisitting position) or the entire table (reverse Trendelenburg position) can improve the ventilatory function and comfort of obese patients or those who experience orthopnea. These positions also reduce the risk of pulmonary aspiration of gastric contents.
- C. Induction Techniques.** The choice of induction technique is guided by the patient's medical condition, anticipated airway management (i.e., risk of aspiration, difficult intubation, or compromised airway), and patient preference.
- 1. IV induction** begins with administration of a potent short-acting hypnotic drug (specific agents and doses are given in Chapter 12). After loss of consciousness, inhalation or additional IV agents are administered to maintain anesthesia. Most of the IV induction agents are powerful respiratory depressants, so loss of consciousness is often accompanied by a short period of apnea requiring controlled ventilation. Depending upon the choice and dose of maintenance anesthetics, ventilation may be controlled, or the patient may breathe spontaneously or with assistance (see section III.C).
 - 2. An induction using only inhalational anesthetics** may be used to maintain spontaneous ventilation when there is a compromised airway or to defer the placement of an IV catheter (e.g., in pediatric patients). After preoxygenation, inhalational anesthetics are added at low concentration (0.5 times minimum alveolar concentration [MAC]) and

then increased every three to four breaths until the depth of anesthesia is adequate for IV placement or airway manipulation. Alternatively, a “single vital capacity breath” inhalation induction can be achieved using a high concentration of a less pungent agent like halothane or sevoflurane. Physiologic signs should be closely observed to assess anesthetic depth (Table 15.2).

3. Intramuscular injection of ketamine, rectal methohexital, oral transmucosal fentanyl, and oral midazolam are induction techniques more commonly used in uncooperative patients or young children (see Chapters 11 and 31).
- D. **Airway Management** (see Chapter 14). The patency of the patient’s airway is critically important during induction of anesthesia. Patients with difficult or unstable airways may be intubated safely before the induction of anesthesia. The anesthetized patient’s airway may be managed using a face mask, oral or nasopharyngeal airway, cuffed oropharyngeal airway, laryngeal mask airway (LMA), or endotracheal tube (ETT). If tracheal intubation is planned, a muscle relaxant may be given to facilitate laryngoscopy and intubation. The ability to ventilate the patient via face mask should be demonstrated before muscle relaxant administration. An exception to this rule is the “rapid sequence induction” for patients at risk for pulmonary aspiration (see Chapter 14). Remifentanyl at 4 $\mu\text{g}/\text{kg}$ also has been shown effective in facilitating rapid intubation but frequently causes bradycardia and hypotension.
- E. **Laryngoscopy and intubation** cause strong sympathetic responses such as hypertension and tachycardia; these can be attenuated by the prior administration of additional hypnotics, volatile anesthetics, opioids, lidocaine (1 to 2 mg/kg), or β -adrenergic blockers.

TABLE
15.2

States of General Anesthesia

Stage I: Amnesia	This period begins with induction of anesthesia and continues to loss of consciousness. The threshold of pain perception is lowered during stage I.
Stage II: Delirium	This period characterized by uninhibited excitation and potentially injurious responses to noxious stimuli, including vomiting, laryngospasm, hypertension, tachycardia, and uncontrolled movement. The pupils are often dilated, gaze may be divergent, respiration is frequently irregular, and breath holding is common. Desirable induction drugs accelerate transition through this stage.
Stage III: Surgical anesthesia	In this target depth for anesthesia, the gaze is central, pupils are constricted, and respirations are regular. Anesthesia is considered sufficient when painful stimulation does not elicit somatic reflexes or deleterious autonomic responses (e.g., hypertension and tachycardia).
Stage IV: Overdosage	Commonly described as “too deep,” this stage is marked by shallow or absent respirations, dilated and nonreactive pupils, and hypotension that may progress to circulatory failure. Anesthesia should be lightened immediately.

The “stages” or planes of anesthesia were defined by Guedel after careful observation of patient responses during induction with diethyl ether. Induction with modern anesthetic agents is sufficiently rapid that these descriptions of individual stages are often not applicable or appreciated. However, modification of these categories still provides useful terminology to describe progression from the awake to the anesthetized state.

- F. Positioning for surgery** usually occurs after the induction of general anesthesia. Patients at risk for neurologic injury during positioning may undergo awake intubation and then be assisted into their surgical position before induction of anesthesia. Movement of a supine, anesthetized patient into a different position may cause hypotension because of the lack of intact hemodynamic reflexes. Positioning should occur at a controlled pace with frequent assessments of the patient's cardiovascular status and with close attention to the patient's airway and ventilation. The entire OR team (anesthetists, surgeons, nurses) should ensure that the patient's head and limbs are protected and sufficiently padded to prevent compressive ischemia or nerve injury. Hyperextension or over-rotation of the patient's neck and joints must be avoided. Throughout the case, the padding, position and status of the patient's eyes, ears, nose, and limbs should be periodically reassessed and documented.
- G.** A "time-out" (see WHO Surgical Safety checklist) during which the patient ID, procedure, location, and laterality are confirmed, and specific anesthetic and surgical concerns are readdressed, is performed immediately prior to surgical incision.

III. MAINTENANCE

Maintenance begins when the patient is sufficiently anesthetized to block awareness and movements in response to surgery. Vigilance on the part of the anesthetist is required to maintain homeostasis (vital signs, acid-base balance, temperature, coagulation, and volume status) and regulate anesthetic depth.

A. Ensuring hypnosis (lack of awareness) and amnesia are implicit goals of a general anesthetic. **Intraoperative awareness** with recall is estimated to occur in 0.1% to 0.2% of general anesthetics and is more frequent in certain high-risk surgical populations (e.g., trauma, cardiac surgery, and obstetrics). Factors that increase the risk of awareness include the use of muscle relaxants together with "light" anesthesia techniques such as nitrous oxide–narcotic. Alcoholism or long-term use of sedatives and/or opioids may increase patient dosage requirements for general anesthetics. Preoperative discussion with the patient prior to obtaining consent is recommended when such risk factors are present. The **depth of anesthesia** should be continuously assessed from induction through emergence. Changes in the intensity of surgical stimulation may cause rapid changes in anesthetic depth, which should be anticipated. Responses suggesting inadequate anesthetic depth are nonspecific. These may be somatic (movement, coughing, and changes of respiratory pattern) or autonomic (tachycardia, hypertension, mydriasis, sweating, or tearing). Purposeful movements in response to surgical stimulation or voice command are evidence of "perceptive awareness" but most often occur without recall. These should be attenuated by first ensuring adequate hypnosis and analgesia and then, if indicated, by the administration of muscle relaxants. In paralyzed patients, changes in physiologic signs (Table 15.2) can indicate inadequate anesthesia, but these are unreliable. Awareness can occur without any autonomic signs, and sympathetic activation may be caused by stimuli other than awareness or pain (e.g., hypoxia, hypercarbia, hypovolemia, caval compression, and adrenal manipulation). Furthermore, autonomic responses are modified by IV analgesics, regional anesthesia, angiotensin blockers, β -blockers, calcium channel blockers, adrenergic drugs, and other drugs. Intraoperative monitors that analyze features of the cortical electroencephalogram and auditory-evoked potentials have

been shown to help predict the hypnotic state under many, but not all, types of general anesthesia. When hypnosis is maintained with inhaled anesthetics, keeping total end-tidal drug concentrations above $0.7 \times \text{MAC}$ is also associated with a low incidence of awareness.

B. Methods

1. **The use of volatile agents** with minimal opioid use usually permits spontaneous ventilation. The concentration of the volatile anesthetic is titrated to patient movement (if muscle relaxants are not used), blood pressure (which decreases with increasing depth), and ventilation. Nitrous oxide, if used, is adjusted to ensure adequate oxygenation. High concentrations of nitrous oxide are contraindicated in patients with closed air-filled compartments (e.g., pneumothorax, pneumocephalus, bowel obstruction, and intravitreal bubbles in eye surgery). Nitrous oxide has the potential to exacerbate hematologic or neurologic diseases in patients with vitamin B₁₂ or folate deficiency or methionine synthase abnormalities.
 2. **Total Intravenous Anesthesia (TIVA)** uses the continuous infusion or repeated boluses of a short-acting hypnotic drug (e.g., propofol) with or without opioids (e.g., remifentanyl) and a muscle relaxant. This technique is particularly useful in situations where ventilation is frequently interrupted (e.g., bronchoscopy, tracheal surgery, and laser airway surgery) and for patients at high risk for PONV.
 3. **Balanced anesthesia**, which combines the above methods, is often used. A low concentration of a volatile or IV anesthetic (0.3 to $0.5 \times \text{MAC}$ or ED_{50}) may be combined with nitrous oxide, opioids, and relaxant. Continuous ketamine or dexmedetomidine infusions can be combined with inhaled or IV anesthetics to reduce the need for intraoperative and postoperative opioids. Combining anesthetics reduces the need for and the potential toxicity of large doses of single agents but increases the risk of adverse drug interactions.
 4. **General anesthesia can be combined with a regional anesthetic technique** (i.e., peripheral or neuraxial nerve block). The required depth of general anesthesia is significantly reduced with blockade of painful surgical stimulation but still needs to be sufficient to ensure hypnosis, particularly when muscle relaxants are used.
- C. **Ventilation** of the patient during general anesthesia may be spontaneous, assisted, or controlled.
1. **Spontaneous or assisted ventilation** may help assess the depth of anesthesia by observing the respiratory rate and pattern. A patient may breathe spontaneously with or without assistance, via a mask, LMA, or ETT. Intraoperative respiratory function may be significantly compromised because of the patient's medical condition, positioning, external pressure on the thorax and abdomen, surgical maneuvers (e.g., peritoneal insufflation, open chest, and surgical packing), and medications (e.g., opioids). Most inhaled and IV anesthetic agents depress respiration in a dose-dependent manner, with a moderate rise in arterial partial pressure of carbon dioxide (PaCO_2).
 2. **Controlled ventilation.** Although a mask or LMA may be used, an ETT and mechanical ventilator are generally used if ventilation is to be controlled for a significant period of time. Minute ventilation is adjusted to maintain an appropriate level of end-tidal CO_2 (ETCO_2). In patients having major surgery or otherwise at risk for ventilator-induced lung injury, lung protective ventilation with low tidal volumes ($\leq 6 \text{ mL/kg}$) and positive end-expiratory pressure (PEEP) should be used

(see Chapter 36). Peak inspiratory pressure (PIP) should be noted. High airway pressure (>25 to 30 cm H_2O in nonobese patients) or changes of PIP must be immediately investigated. Low PIP may signal a breathing circuit leak, while high PIP may indicate ETT obstruction or movement, altered lung compliance or resistance, change in muscle relaxation, or surgical compression.

3. **Assessment of ventilation.** Adequate ventilation is confirmed by continual observation of the patient, auscultation of breath sounds, inspection of the anesthesia machine (e.g., reservoir breathing bag, ventilator bellows, airway pressures, and gas flows), and patient monitors (e.g., capnograph and pulse oximeter). Arterial blood gas analysis and adjustments in the patient's ventilation may be required intraoperatively. If gas exchange is inadequate, manual controlled ventilation, increased inspired oxygen concentrations, PEEP, or special ventilator modes (sometimes requiring a stand-alone ventilator) may be used (see Chapter 36) while the source of the problem is sought and treated.

D. Fluids

1. Intraoperative IV fluid requirements

- a. **Maintenance fluid requirements** as described in section I.B should be continued intraoperatively. In some instances (e.g., extremity surgery with tourniquet use), this may be the major component of the fluid requirement.
- b. **"Third space losses"** are due to tissue edema from surgical trauma, whereas **"insensible losses"** are due to evaporation from the airways and surgical wounds. These losses are difficult to assess and may be substantial (up to 20 mL/kg/h) depending on the site and extent of the surgery. The rate of evaporative loss is increased in febrile patients.
- c. **Blood losses may be difficult to estimate.** The amount present in the suction canisters should be monitored, taking into consideration the presence of other fluids (e.g., irrigation and ascites). Used surgical sponges should be checked and may be weighed to improve estimates of blood loss. Blood lost on the surgical field (e.g., surgical drapes) and on the floor should be estimated. If blood loss is substantial, serial monitoring of hematocrit is warranted.

2. IV fluids are administered to correct preoperative deficits and intraoperative losses.

- a. **Crystalloid solutions** are used to replace maintenance fluid requirements, evaporative losses, and third space losses. When administered in large volumes, commonly used crystalloids (e.g., lactated Ringer's, normal saline, and Plasmalyte) have different effects on electrolyte levels, acid-base status, coagulation, and organ function. If hemoglobin levels are adequate, blood loss also may be replaced with IV crystalloid, administered in a 3:1 ratio of volume to estimated blood loss. With continued blood loss, this ratio will increase.
- b. **Colloid solutions** (e.g., 5% or 25% albumin) may be used to replace blood loss or restore intravascular volume. To replace blood loss, colloid solutions should be administered in an approximately 1:1 ratio of volume to estimated blood loss (see Chapter 34). Hydroxyethyl starch solutions are alternative colloids that are associated with increased morbidity and mortality in critically ill patients.

- c. **Other IV solutions** may be indicated for patients with specific metabolic conditions (e.g., TPN for malnourished patients and added glucose for diabetic patients receiving insulin).
- d. **Blood transfusion** is discussed in Chapter 35.
- 3. **Assessment.** Trends in heart rate, blood pressure, and urine output ($> 0.5 \text{ mL/kg/h}$) may serve as guides to intravascular volume status and adequacy of replacement therapy. Measurement of CVP, pulmonary artery occlusion pressure, right and left end-diastolic volumes (using transesophageal echocardiography), and cardiac output provide additional data to guide fluid administration when intraoperative losses are large or when cardiopulmonary disease mandates strict control of the patient's central pressures. Hematocrit, platelet count, fibrinogen concentration, prothrombin time, and partial thromboplastin time are used to assess adequacy of blood product therapy.

IV. EMERGENCE

During this period, the patient makes the transition from an unconscious state to an awake state with intact protective reflexes. This is a critical, understudied, and often underemphasized phase of the anesthetic plan. Claims data reveals that untoward events occur frequently during emergence from general anesthesia.

- A. **Goals.** Patients should be awake and responsive, with full muscle strength and adequate pain control. Full recovery of airway reflexes and muscle function minimizes the risk of airway obstruction or pulmonary aspiration upon extubation and facilitates immediate neurologic assessment. In patients with cardiovascular disease, hemodynamics should be controlled.
- B. **Technique.** Surgical stimulation diminishes as the procedure nears completion and anesthetic depth is reduced, enabling rapid emergence. Residual muscle relaxation is reversed, and the patient starts to breathe spontaneously. Analgesic requirements should be estimated and addressed before awakening.
- C. **Environment.** The OR should be warmed, blankets placed on the patient, and noise and conversation minimized. All members of the OR team (scrub nurse, circulating nurse, and surgeon) should be ready to give immediate assistance to the anesthetist if needed.
- D. **Positioning.** The patient is usually returned to the supine position before extubation. Semi-sitting or reverse Trendelenburg positions may facilitate spontaneous ventilation during emergence. The patient may be extubated in a lateral or prone position if the anesthetist is confident that the airway can be maintained and protected. A method for quickly returning the patient to the supine position must be available.
- E. **Mask Ventilation.** A patient who has received mask ventilation should continue to breathe 100% oxygen by mask during emergence. A period of light anesthesia (stage II; Table 15.2) often occurs before regaining consciousness. Stimulation (especially of the airway) during this period may precipitate vomiting or laryngospasm and is best avoided. The patient can be moved when fully awake, following verbal commands, breathing spontaneously, and oxygenating adequately.
- F. **Extubation.** Removal of the ETT from the trachea of an intubated patient is a critical moment. Patients with respiratory failure, hypothermia, impaired sensorium, and marked hemodynamic instability, or patients whose airway may be significantly jeopardized (e.g., with extensive oral surgery or possible glottic edema after neck surgery or prolonged head-down positioning) may remain intubated postoperatively until these conditions have improved.

1. **Awake extubation.** Extubation of the airway usually occurs after the patient fully regains protective reflexes. Awake extubation is indicated in patients at risk of aspiration of gastric contents, patients who have difficult airways, and patients who have just undergone tracheal or maxillofacial surgery.
 - a. **Criteria.** Before extubation, the patient should be awake and hemodynamically stable. The patient should have regained full muscle strength (see Chapter 13), follow simple verbal commands (e.g., lift head), and breathe spontaneously with acceptable oxygenation and ventilation.
 - b. **Technique.** The presence of an ETT may be irritating to patients emerging from anesthesia. Lidocaine (0.5 to 1.0 mg/kg IV) can be given to suppress coughing but may prolong emergence. The patient breathes 100% oxygen, and the oropharynx is suctioned. Mild positive airway pressure (20 cm H₂O) is applied via the ETT, the ETT cuff is deflated, and the tube is removed. Oxygen (100%) administration is continued by face mask. The anesthetist's attention should remain focused on the patient until the patient's ability to ventilate, oxygenate, and protect the airway is confirmed. The extubated patient may become unconscious again and lose protective airway reflexes when stimulation decreases.
 - c. **Removal of the ETT over a flexible stylet** (e.g., airway exchange catheter [AEC], jet stylet, and fiberoptic bronchoscope) can be performed when the patency of the patient's airway is uncertain or reintubation may be difficult. The airway is first anesthetized with 0.3 to 0.5 mg/kg lidocaine administered via the ETT, and the patient is allowed to breathe spontaneously. A lubricated AEC is passed into the trachea through the ETT, the ETT cuff is deflated, and the ETT removed, leaving the exchange device in place until the anesthetist is certain that the patient's airway is stable. If airway obstruction develops, oxygen can be insufflated via the hollow exchange device or an ETT can be reinserted over the device, which acts as a guide.
2. **Deep extubation.** Stimulation of airway reflexes by the ETT during emergence can be avoided by extubating the trachea while the patient is still deeply anesthetized (stage III). This reduces the risk of laryngospasm and bronchospasm, making it a useful technique for severely asthmatic patients. It also avoids coughing and straining that may be undesirable after middle-ear surgery, open-eye procedures, and abdominal or inguinal herniorrhaphy.
 - a. **Criteria.** Contraindications to deep extubation are noted above (section IV.F.1). Anesthetic depth must be sufficient to avoid responses to airway stimulation. Anesthesia may be deepened with a short-acting IV anesthetic or ventilation with a high concentration of a volatile agent.
 - b. **Technique.** All necessary airway equipment and medications should be readily available for replacement of the ETT. Surgical positioning must allow unrestricted access to the head for airway management. The oropharynx should be suctioned, the ETT cuff deflated, and, if there is no response to cuff deflation, the ETT is removed. Airway management is continued by face mask, and emergence is managed as described above (section IV.F).
- G. Agitation.** Severe agitation is occasionally seen on emergence from general anesthesia. Physiologic causes (e.g., hypoxia, hypercarbia, airway

obstruction, or a full bladder) must be excluded. Pain, a common reason for agitation, may be treated with cautious titration of opioids (e.g., fentanyl, 0.025 mg IV, or meperidine, 25-mg IV increments) if vital signs and oxygenation are reassuring.

H. Delayed Awakening. On occasion, a patient will not awaken promptly after the administration of general anesthesia. Ventilatory support and airway protection should be continued, and specific etiologies should be investigated in the broad categories of pharmacologic, neurologic, or metabolic.

V. TRANSPORT

The anesthetist should accompany the patient from the OR to the postanesthesia care unit (PACU) or ICU. Monitoring of blood pressure, hemoglobin saturation, and electrocardiogram is continued during transport to an ICU but generally is not needed for transport of stable patients to the PACU. Supplemental oxygen should be available, and the patient's airway, ventilation, and overall condition should be continually observed. Placing the patient in the lateral position may help to prevent aspiration and upper airway obstruction. Medications and airway equipment should be available during transport if the patient is unstable or if transport is over a significant distance. Upon transfer of responsibility for patient care in the PACU or ICU, the anesthetist should provide a concise but thorough summary of the patient's past medical history, intraoperative course, postoperative condition, current therapy, and plans or concerns going forward.

VI. POSTOPERATIVE VISIT

A postoperative evaluation of the patient should be performed by the anesthetist within 48 hours of surgery and documented in the patient's medical record. The visit should include a review of the medical record, examination of the patient, and discussion of the patient's perioperative experience. Specific complications such as nausea, sore throat, dental injury, nerve injury, ocular injury, altered pulmonary function, or change in mental status should be sought. Questions to elicit evidence of awareness during the general anesthetic (Table 15.3) should be asked. Responses, along with an evaluation and plan if needed, should be recorded in the patient's chart. Complications that require further therapy or consultations should be actively managed, and the patient's course should be followed until these issues are resolved.

TABLE 15.3 Postoperative Assessment for Awareness During General Anesthesia

The Modified Brice Interview^a

1. What is the last thing you remember before going to sleep?
2. What is the first thing you remember after waking up?
3. Do you remember anything between going to sleep and waking up?
4. Did you dream during your procedure?
5. What was the worst thing about your operation?

^a These questions are a modification of the interview approach first reported by Brice DD, Hetherington RR, Utting JE. *Br J Anaesth* 1970;42:535–541. Responses to this type of postoperative interview have been reported to vary depending on the interval after surgery and the setting (hospital versus home).

Suggested Readings

- ASA Committee. Practice guidelines for preoperative fasting and the use of pharmacologic agents to reduce the risk of pulmonary aspiration: application to healthy patients undergoing elective procedures: an updated report by the American Society of Anesthesiologists Committee on Standards and Practice Parameters. *Anesthesiology* 2011;114(3):495–511.
- Avidan MS, Jacobsohn E, Glick D, et al. Prevention of intraoperative awareness in a high-risk surgical population. *N Engl J Med* 2011;365:591–600.
- Avidan MS, Zhang L, Burnside BA, et al. Anesthesia awareness and the bispectral index. *N Engl J Med* 2008;358:1097–1108.
- Cavallone LF, Vannucci A. Review article: extubation of the difficult airway and extubation failure. *Anesth Analg* 2013;116(2):368–383.
- Fleisher LA, Fleischmann KE, Auerbach AD, et al. 2014 ACC/AHA guideline on perioperative cardiovascular evaluation and management of patients undergoing noncardiac surgery: a report of the ACC/AHA Task Force on Practice Guidelines. *J Am Coll Cardiol* 2014;67:944.
- Forman SA. Awareness during general anesthesia: concepts and controversies. *Semin Anesth Perioper Med Pain* 2006;25:211–218.
- Myles PS, Leslie K, McNeil J, et al. Bispectral index monitoring to prevent awareness during anaesthesia: the B-Aware randomised controlled trial. *Lancet* 2004;363:1757–1763.
- Sebel PS, Bowdle TA, Ghoneim MM, et al. The incidence of awareness during anesthesia: a multicenter United States study. *Anesth Analg* 2004;99:833–839.
- Stanski DR, Shafer SL. Monitoring depth of anesthesia. In: Miller RD, ed. *Anesthesia*. 6th ed. Philadelphia: Churchill Livingstone; 2005:1227–1264.
- Willenkin RL, Polk SL. Management of general anesthesia. In: Miller RD, ed. *Anesthesia*. 4th ed. New York: Churchill Livingstone; 1994:1045–1056.
- World Alliance for Patient Safety. WHO surgical safety checklist and implementation manual. 2008. http://www.who.int/patientsafety/safesurgery/ss_checklist/en/

I. GENERAL PRINCIPLES

A. Chemistry. Local anesthetics are weak bases whose structure consists of an aromatic moiety connected to a substituted amine through an ester or amide linkage. The pK_a values of local anesthetics are near physiologic pH; thus, in vivo, both charged (protonated) and uncharged (unprotonated) forms are present. The degree of ionization is important because the uncharged form is more lipophilic and is able to gain access to the axon. The clinical differences between the ester and amide local anesthetics involve their potential for producing adverse effects and the mechanisms by which they are metabolized.

- 1. Esters.** Procaine, cocaine, chlorprocaine, and tetracaine. The ester linkage is cleaved by plasma cholinesterase. The half-life of esters in the circulation is very short (about 1 minute). The degradation product of ester metabolism is *p*-aminobenzoic acid.
- 2. Amides.** Lidocaine, mepivacaine, bupivacaine, etidocaine, and ropivacaine. The amide linkage is cleaved through initial *N*-dealkylation followed by hydrolysis, which occurs primarily in the liver. Patients with severe hepatic disease may be more susceptible to adverse reactions from amide local anesthetics. The elimination half-life for most amide local anesthetics is 2 to 3 hours.

B. Mechanism of Action

- 1. Local anesthetics block nerve conduction** by impairing propagation of the action potential in axons. They have no effect on the resting or threshold potentials but decrease the rate of rise of the action potential so that the threshold potential is not reached.
- 2. Local anesthetics interact directly with specific receptors** on the Na^+ channel, inhibiting Na^+ ion influx. The anesthetic molecule must traverse the cell membrane through passive nonionic diffusion in the uncharged state and then becomes protonated and binds to the axoplasmic side of the sodium channel. K^+ and Ca^{2+} channels are also found to be blocked by local anesthetics.
- 3. Physicochemical properties** of the local anesthetics affect neural blockade.
 - a. Lipid solubility.** Higher lipophilicity increases potency by increasing the rate of diffusion through axonal membranes and other tissues.
 - b. Protein binding.** More protein binding prolongs the duration of effect.
 - c. pK_a .** Agents with a lower pK_a value will have a faster onset because a greater fraction of these weak bases will exist in the uncharged form at pH 7.4 and thus will more readily diffuse across nerve membranes.
 - d. pH of the drug solution.** Higher pH will speed up the onset by increasing the proportion of molecules in the uncharged form.
 - e. Drug concentration.** Higher concentration speeds up the onset of action due to mass effect.
- 4. Differential blockade of nerve fibers**
 - a. Peripheral nerves** are classified according to size and function (Table 16.1). Traditionally, thin nerve fibers were believed to be more easily blocked than thick ones; however, the opposite susceptibility

TABLE
16.1 Classification of Nerve Fibers

Class	Myelin	Diameter (μm)	Local Anesthetic Sensitivity	Function
A- α	+++	12–20	++	Motor
A- β	+++	5–12	++	Touch/pressure
A- γ	++	1–4	+++	Proprioception/motor tone
A- δ	++	1–4	+++	Pain/temperature
B	+	1–3	++	Preganglionic autonomic
C	–	0.5–1	+	Pain/temperature

has been found. Myelinated fibers are more readily blocked than unmyelinated ones, as myelinated fibers need to be blocked only at the nodes of Ranvier.

- b. **Differential blockade** refers to the fact that a specific concentration of local anesthetic may produce a different intensity of block for pain, temperature sensation, and motor function. This reflects the different sensitivities of nerve fibers to local anesthetics, and it may be due to different ion channel composition or different arrangement of channels within the axon. A dilute solution of local anesthetic cannot be relied upon to block a specific sensory or motor function in a reproducible manner.

5. **Sequence of clinical anesthesia.** Complete blockade of peripheral nerves usually progresses in the following order:

- a. Sympathetic block with peripheral vasodilatation and skin temperature elevation.
- b. Loss of pain and temperature sensation.
- c. Loss of proprioception.
- d. Loss of touch and pressure sensation.
- e. Motor paralysis.

6. **Pathophysiologic factors affecting the neural block**

- a. **A decrease in the cardiac output** reduces the plasma and tissue clearance of local anesthetics, increasing plasma concentration and the potential for toxicity.
- b. **Severe hepatic disease** may prolong the duration of action of amino amides.
- c. **Renal disease** has minimal effect.
- d. Patients with **reduced cholinesterase activity** (newborns and pregnant patients) and patients with **atypical cholinesterase** may have decreased clearance of ester-type anesthetics, but this will not generally lead to toxicity unless a very high percentage of enzyme activity is lost.
- e. **Fetal acidosis** may cause ionization of local anesthetics and thereby “trap” drug molecules transferred from the mother to the fetus. The increased fetal versus maternal concentration may increase the possibility of fetal toxicity, particularly with amide forms that are not cleared rapidly by the maternal circulation like the ester forms, and therefore reach the fetus in greater concentrations.
- f. Pathologic conditions such as **sepsis, malignancy, and cardiac ischemia** can increase the concentration of the binding protein α_1 -acid glycoprotein, and this may decrease the plasma concentration of free local anesthetics.

C. Commercial Preparations

1. Commercially available solutions of local anesthetics are supplied as **hydrochloride salts** to promote ionization and increase solubility in water. Plain solutions usually are adjusted to pH 6. Those containing epinephrine are adjusted to pH 4 because of the instability of catecholamine molecules at alkaline pH.
2. **Antimicrobial preservatives** (paraben derivatives) are added to multi-dose vials. Only preservative-free solutions should be used in spinal, epidural, or caudal anesthesia to prevent potentially neurotoxic effects from preservatives.
3. **Antioxidants** (sodium metabisulfite, sodium ethylenediaminetetraacetic acid [EDTA]) may be added to slow breakdown of local anesthetics.

II. CLINICAL USES OF LOCAL ANESTHETICS

The choice of local anesthetic must take into account the duration of surgery, regional technique used, surgical requirements, the potential for local or systemic toxicity, and any metabolic constraints (Tables 16.2 and 16.3).

A. Combinations of Local Anesthetics

1. Chloroprocaine–bupivacaine, lidocaine–bupivacaine, and mepivacaine–bupivacaine mixtures are reported to have a rapid onset and long duration; however, it has been shown with chloroprocaine–bupivacaine mixtures that the onset is slower than chloroprocaine, but the duration is shorter than bupivacaine when administered epidurally in obstetrics. The systemic toxicity appears to be additive.
2. **Eutectic mixture of local anesthetics (EMLA)** cream is a mixture of 2.5% lidocaine and 2.5% prilocaine for use as a topical skin anesthetic. It must be applied to unbroken, healthy skin for at least 30 minutes for an effect.

B. Epinephrine

1. **Epinephrine** may be added to local anesthetics for the following reasons:
 - a. To prolong the duration of anesthesia. This varies with the specific agent and its concentration as well as the type of regional block.
 - b. To decrease systemic toxicity by decreasing the rate of absorption of anesthetic into the circulation, thus minimizing peak blood levels of local anesthetics. Addition of 5 μg for every mL of local anesthetic decreases systemic absorption by up to one third.
 - c. To increase intensity of the block by a direct α -agonist effect on antinociceptive neurons in the spinal cord.
 - d. To provide local vasoconstriction and decrease surgical bleeding.
 - e. To assist in detection of intravascular injections (see Chapter 16, section III.C.2.b).
2. **Adding epinephrine** (to make a 1:200,000 solution, or 5 $\mu\text{g}/\text{mL}$) to plain solutions of local anesthetics just before administration permits the use of a solution with a high pH, which speeds up the onset of the block. A 1:200,000 dilution is achieved by adding 0.1 mL of 1:1,000 (1 mg/mL) epinephrine (with a tuberculin syringe) to 20 mL of local anesthetic solution.
3. The **maximum dose of epinephrine** should not exceed 10 $\mu\text{g}/\text{kg}$ in pediatric patients and 5 $\mu\text{g}/\text{kg}$ in adults to avoid ventricular arrhythmias.
4. Epinephrine should **not be used** in peripheral nerve blocks in areas with poor collateral blood flow (e.g., digits, penis, and nose) or in intravenous regional techniques. Caution is advised in patients with severe coronary artery disease, arrhythmias, uncontrolled hypertension, and hyperthyroidism.

TABLE 16.2
Clinical Uses of Local Anesthetics

Anesthetics	pK _a	Onset	Duration ^a	Relative Toxicity	Officially Recommended Highest Doses (mg) ^b	Clinical Use/Comments
Esters						
Procaine (Novocaine)	8.9	Slow	Short	Low	500 (600)	Infiltration, spinal Allergic potential
Chlorprocaine (Nesacaine)	9.1	Fast	Short	Low	800 (1,000)	Infiltration, nerve blocks, epidural, spinal Rapid hydrolysis in plasma
Tetracaine (Pontocaine)	8.5	Slow	Long	High	10 (20)	Spinal, topical
Benzocaine	2.5	Moderate	Short	n/a ^c	n/a ^c	Exclusively for topical use Methemoglobinemia
Amides						
Lidocaine (Xylocaine)	7.9	Fast	Medium	Medium	300 (500)	All types of local and regional anesthesia
Prilocaine (Citanest)	7.7	Fast	Medium	Medium	400 (600)	Infiltration, nerve blocks, epidural Methemoglobinemia
Mepivacaine (Carbocaine)	7.6	Fast	Medium	Medium	400 (550)	Infiltration, nerve blocks, epidural, spinal
Bupivacaine (Marcaine, Sensorcaine)	8.1	Moderate	Long	High	175 (225)	All types of local and regional anesthesia Lower concentration provide differential sensory/motor block
L-Bupivacaine (Chirocaine)	8.1	Moderate	Long	High	150 (n/a)	All types of local and regional anesthesia S-Isomer of bupivacaine—probably less cardiac toxicity than bupivacaine
Ropivacaine (Naropin)	8.1	Moderate	Long	High	225 (n/a)	Infiltration, nerve blocks, epidural S-Isomer enantiomer of bupivacaine—less cardiac toxicity than bupivacaine
Etidocaine (Duranest)	7.7	Moderate	Long	High	300 (400)	Infiltration, nerve blocks, epidural Motor greater than sensory blockade

^a Duration of dose depends on site of administration and proximity to vasculature (see Table 15.3).

^b Dose in epinephrine-containing solution in parenthesis. The maximum dose to be employed as a single injection should be determined on the basis of the status of the patient and the type of regional anesthetic technique to be performed.

^c 20% spray has a high risk of methemoglobinemia and has been removed from practice by many hospitals in the United States.

TABLE
163

Local Anesthetic Agents

Anesthetic Technique	Anesthetic	Concentration (%)	Duration (minutes) ^a	Usual Volume (mL; 70-kg Patient) ^b
Local infiltration	Procaine	1–2	20–30 (30–45)	
	Lidocaine	0.5–1	30–60 (120)	
	Mepivacaine	0.5–1	45–90 (120)	
	Bupivacaine	0.25–0.5	120–240 (180–240)	
	Ropivacaine	0.2–0.5	120–240 (180–240)	
Peripheral nerve blocks (drug with epinephrine 1:200,000)	Lidocaine	1–2	(120–240)	30–50
	Mepivacaine	1–1.5	(180–300)	30–50
	Bupivacaine	0.25–0.5	(360–720)	30–50
	Ropivacaine	0.2–0.5	(360–720)	30–50
Epidural (drug with epinephrine 1:200,000)	Chloroprocaine	2–3	(30–90)	15–30
	Lidocaine	1–2	(60–120)	15–30
	Mepivacaine	1–2	(60–180)	15–30
	Bupivacaine	0.25–0.5	(180–350)	15–30
	Levobupivacaine	0.25–0.75	(180–350)	15–30
	Ropivacaine	0.2–0.75	(180–350)	15–30
Spinal	Lidocaine + glucose (hyperbaric)	1.5, 5.0	30–60	1–2
	Bupivacaine (isobaric)	0.5	90–200	3–4
	Bupivacaine + glucose (hyperbaric)	0.75	90–200	2–3
	Tetracaine (hypobaric)	0.25	90–200	2–6
	Tetracaine (isobaric)	1.0	90–200	1–2
	Tetracaine + glucose (hyperbaric)	0.25–1.0	90–200	1–4

^a Duration in epinephrine-containing solution in parenthesis. Adding epinephrine to local anesthetic solution prolongs the analgesia duration of lidocaine, mepivacaine, and tetracaine. However, the analgesia duration of bupivacaine and ropivacaine is not significantly affected by epinephrine, partly because of the vasoconstriction produced by these agents.

^b Doses should be reduced for patients with specific risk factors and when non-epinephrine-containing solutions are used.

- C. Phenylephrine** has been used like epinephrine, but no particular advantages have been demonstrated; anywhere from 2 to 5 mg of phenylephrine can be added to solutions of local anesthetics to prolong spinal anesthesia.
- D. Opioids** such as fentanyl and hydromorphone have been used together with local anesthetics in spinal/epidural anesthesia with improved analgesia and may allow for decreased dosing of local anesthetics.
- E. Sodium bicarbonate** added to local anesthetic solutions raises the pH and increases the concentration of nonionized free base. The increased percentage of uncharged drug will increase the rate of diffusion and speed

up the onset of neural blockade. Typically, 1 mEq of sodium bicarbonate is added to each 10 mL of lidocaine, chloroprocaine, or mepivacaine; only 0.1 mEq of sodium bicarbonate may be added to each 10 mL of bupivacaine to avoid precipitation. Carbonated local anesthetics (e.g., lidocaine carbonate) are thought to augment neural block by lowering intraneural pH and promoting formation of the active (charged) species.

- F. Meperidine** has local anesthetic properties, and it has been used as the sole anesthetic agent in spinal anesthesia for cesarean delivery. There is no proven advantage to routinely using the drug this way.

III. TOXICITY

A. Allergic Reactions

True allergic reactions to local anesthetics are uncommon. It is important to differentiate them from common nonallergic responses such as vasovagal episodes and responses to intravascular injection of local anesthetic and/or epinephrine.

- 1. Ester-type local anesthetics** may cause allergic reactions from the metabolite *p*-aminobenzoic acid. These anesthetics also may produce allergic reactions in persons sensitive to sulfa drugs (e.g., sulfonamides or thiazide diuretics).
- 2. Amide-type local anesthetics** are nearly devoid of allergic potential. Multidose vials of anesthetic solutions containing **methylparaben** as the preservative may produce an allergic reaction in patients sensitive to *p*-aminobenzoic acid.
- 3. Local hypersensitivity reactions** may produce local erythema, urticaria, edema, or dermatitis.
- 4. Systemic hypersensitivity reactions** are rare and can present with generalized erythema, urticaria, edema, bronchoconstriction, hypotension, and cardiovascular collapse.
- 5. Treatment** is supportive (see Chapter 18).

B. Local Toxicity

- 1. Tissue toxicity** is rare with short-term use.
- 2. Post spinal pain syndrome (PSPS)**, previously known as “transient radicular irritation” (TRI) or “transient neurologic symptoms” (TNS), may occur after subarachnoid injection of local anesthetics. This usually manifests as pain or dyesthesia in the buttocks or legs. (Please see Chapter 16 for more details.)
- 3.** Reports of sensory and motor deficits after intrathecal chloroprocaine solutions containing the antioxidant sodium bisulfite resulted in a change in its formulation. EDTA has replaced bisulfite. Nevertheless, intense back pain has been reported after epidural administration of large volumes (≥ 40 mL) of solution. The back pain is thought to be caused by spasms of the paraspinal muscles due to the calcium-binding properties of EDTA.

- C. Local Anesthetic Systemic Toxicity (LAST)** usually results from intravascular injection or overdose. However, toxicity can also occur from rapid absorption from tissue depot, especially in highly vascular areas.

- 1.** Incidence of systemic toxic reaction is reported to be 7.5 to 20/10,000 peripheral nerve blocks.
- 2. Intravascular injection** most commonly occurs during nerve blockade in areas with large blood vessels (e.g., axillary or vertebral artery and epidural veins). This can be minimized by the following:
 - a.** Aspiration before injection
 - b.** Use of epinephrine-containing solutions for test doses

- c. Use of small incremental volumes in establishing the block (e.g., 5 mL for each injection)
- d. Use of proper technique during intravenous regional anesthesia (see Chapter 17)
- 3. **CNS toxicity**
 - a. Clinical features
 - 1. An initial excitatory phase may be due to blockade of inhibitory pathways, as well as release of glutamate (an excitatory neurotransmitter).
 - 2. Early signs include **dizziness, lightheadedness, tinnitus, perioral numbness, metallic taste.**
 - 3. Late signs include **muscle twitching, tremors, seizures, and coma.**
 - b. Respiratory and metabolic **acidosis will decrease seizure threshold**; therefore, airway management should take precedence in suspected LAST.
 - c. Transversus abdominis plane block techniques after cesarean delivery recently have been linked to CNS toxicity in patients.
- 4. **CVS toxicity**
 - a. Toxicity of the cardiovascular system is due to a decrease in rate of depolarization of Purkinje fibers and ventricular muscle, due to sodium channel blockade.
 - b. EKG changes are common.
 - 1. Early changes include a prolonged PR interval and an increase in QRS duration.
 - 2. Late changes include sinus bradycardia and asystole.
 - c. Cardiodepressant potency correlates with nerve block potency.
 - 1. Bupivacaine > lidocaine > chlorprocaine
 - d. **Pregnancy** increases sensitivity to cardiotoxicity.
 - e. **Acidosis and hypoxia** markedly worsen cardiotoxicity, making airway management a priority for treatment.
- 5. Treatment of LAST (see Table 16.4)
 - a. **Initial Focus**
 - 1. **Airway management:** ventilate with 100% O₂ and consider advanced airway techniques as acidemia may worsen the clinical picture.
 - b. **Seizure suppression:** benzodiazepines are preferred. **Avoid propofol** in patients having signs of cardiovascular instability.
 - c. Alert the nearest facility having **cardiopulmonary bypass capability**
 - d. **Management of cardiac arrhythmia**
 - 1. **BLS/ACLS** will require adjustment of common medications (below) and perhaps prolonged effort
 - 2. **Avoid vasopressin, calcium channel blockers, β -blockers, or local anesthetic**
 - 3. **Reduce individual epinephrine doses to <1 mcg/kg**
 - e. **Lipid emulsion (intralipid 20%),** particularly after intravascular injection of bupivacaine
 - 1. **Bolus 1.5 mL/kg** (lean body mass) intravenously over 1 minute (~100 mL for a 70-kg patient).
 - 2. **Continuous infusion at 0.25 mL/kg/min**
 - 3. Repeat bolus once or twice for persistent cardiovascular collapse
 - 4. Double the infusion rate to 0.5 mL/kg/min if blood pressure remains low
 - 5. **Continue infusion** for at least 10 minutes after attaining circulatory stability
 - 6. Recommended upper limit: approximately 10 mL/kg lipid emulsion over the first 30 minutes

TABLE
164

ASRA Check List for Managing LAST. 2012 Version



AMERICAN SOCIETY OF
REGIONAL ANESTHESIA AND PAIN MEDICINE

Checklist for Treatment of Local Anesthetic Systemic Toxicity

**The Pharmacologic Treatment of Local Anesthetic Systemic Toxicity (LAST)
is Different from Other Cardiac Arrest Scenarios**

- ☐ **Get Help**
- ☐ **Initial Focus**
 - ☐ **Airway management:** ventilate with 100% oxygen
 - ☐ **Seizures uppression:** benzodiazepines are preferred; **AVOID propofol** in patients having signs of cardiovascular instability
 - ☐ Alert the nearest facility having **cardiopulmonary bypass** capability
- ☐ **Management of Cardiac Arrhythmias**
 - ☐ **Basic and Advanced Cardiac Life Support (ACLS)** will require adjustment of medications and perhaps prolonged effort
 - ☐ **AVOID** vasopressin, calcium channel blockers, beta blockers, or local anesthetic
 - ☐ **REDUCE** individual epinephrine doses to <1 mcg/kg
- ☐ **Lipid Emulsion (20%) Therapy** (values in parenthesis are for 70kg patient)
 - ☐ **Bolus 1.5 mL/kg** (lean body mass) intravenously over 1 minute (~100mL)
 - ☐ **Continuous infusion 0.25 mL/kg/min** (~18 mL/min; adjust by roller clamp)
 - ☐ Repeat bolus once or twice for persistent cardiovascular collapse
 - ☐ Double the infusion rate to 0.5 mL/kg/min if blood pressure remains low
 - ☐ **Continue infusion** for at least 10 minutes after attaining circulatory stability
 - ☐ Recommended upper limit: Approximately 10 mL/kg lipid emulsion over the first 30 minutes
- ☐ **Post LAST events** at www.lipidrescue.org and report use of lipid to www.lipidregistry.org

Used with permission from Neal JM, Mulroy MF, Weinberg GL; ASRA. American Society of Regional Anesthesia and Pain Medicine checklist for managing local anesthetic systemic toxicity: 2012 version. *Reg Anesth Pain Med* 2012;37:16–18.

D. Methemoglobinemia

1. Pathophysiology: The oxidation of heme groups within deoxyhemoglobin (Fe^{2+}) results in methemoglobinemia (Fe^{3+}), which cannot transport oxygen and thus produces a functional anemia.

2. Common local anesthetics that cause methemoglobinemia include **prilocaine** (an ingredient of EMLA cream), which is metabolized to *o*-toluidine in the liver and oxidizes hemoglobin to methemoglobin, and **benzocaine**, which is found in topical sprays.
3. **Treatment** is with **methylene blue** (1 to 2 mg/kg intravenously over 5 minutes), which converts methemoglobin back to reduced hemoglobin.

Suggested Readings

- Berde CB, Strichartz GR. Local anesthetics. In: Miller RE, ed. *Anesthesia*. 7th ed. New York: Churchill Livingstone; 2009:913–939.
- Camann WR, Bader AM. Spinal anesthesia for cesarean delivery with meperidine as the sole agent. *Int J Obstet Anesth* 1992;1:156–158.
- Cousins MJ, Bridenbaugh PO, Carr DB, et al., eds. *Cousins & Bridenbaugh's Neural Blockade in Clinical Anesthesia and Management of Pain*. 4th ed. Philadelphia: Lippincott Williams & Wilkins, 2009.
- Di Gregorio G, Schwartz D, Ripper R, et al. Lipid emulsion is superior to vasopressin in a rodent model of resuscitation from toxin-induced cardiac arrest. *Crit Care Med* 2009;37(3):993–999.
- Hiller DB, Gregorio GD, Ripper R, et al. Epinephrine impairs lipid resuscitation from bupivacaine overdose: a threshold effect. *Anesthesiology* 2009;111(3):498–505.
- Milligan KR. Recent advances in local anesthetics for spinal anaesthesia. *Eur J Anaesthesiol* 2004;21(11):837–847.
- Mulroy MF. Systemic toxicity and cardiotoxicity from local anesthetics: incidence and preventive measures. *Reg Anesth Pain Med* 2002;27(6):556–561.
- Neal JM, Mulroy MF, Weinberg GL; American Society of Regional Anesthesia and Pain Medicine. American Society of Regional Anesthesia and Pain Medicine checklist for managing local anesthetic systemic toxicity: 2012 version. *Reg Anesth Pain Med* 2012;37(1):16–18.
- Reiz S, Nath S. Cardiotoxicity of local anaesthetic agents. *Br J Anaesth* 1986;58:736–746.
- Rosenberg PH, Veering BT, Urmey WF. Maximum recommended doses of local anesthetics: a multifactorial concept. *Reg Anesth Pain Med* 2004;29(6):564–575.
- Scholz A. Mechanisms of (local) anaesthetics on voltage-gated sodium and other ion channels. *Br J Anaesth* 2002;89:52–61.
- Stevens RA, Urmey WF, Urquhart BL, et al. Back pain after epidural anesthesia with chloroprocaine. *Anesthesiology* 1993;78(3):492–497.
- Vaida G. Prolongation of lidocaine spinal anesthesia with phenylephrine. *Anesth Analg* 1986;65:781–785.
- Weiss E, Jolly C, Dumoulin JL, et al. Convulsions in 2 patients after bilateral ultrasound-guided transversus abdominis plane blocks for cesarean analgesia. *Reg Anesth Pain Med* 2014;39:248–251.



Spinal, Epidural, and Caudal Anesthesia

David J. Kim and Jason M. Lewis

I. GENERAL CONSIDERATIONS

- A. **Preoperative assessment** of the patient for regional anesthesia is similar to that for general anesthesia. The details of the procedure to be performed, including its anticipated length, patient position, and a complete review of any coexisting diseases, should be taken into account in determining the appropriateness of a regional technique.
- B. The area where the block is to be administered should be examined for potential difficulties or pathology. Preexisting neurologic abnormalities should be well documented and the presence of kyphoscoliosis determined.
- C. A history of abnormal bleeding and a review of the patient's medications may indicate a need for additional coagulation studies.
- D. **Informed consent** should be obtained including a detailed explanation of the planned procedure, with risks and benefits. Patients should be reassured that additional sedation and anesthesia can be given during the operation and that general anesthesia is an option if the block fails or the operation becomes more prolonged or extensive than originally thought. In some instances, it is planned from the onset to have a combination of regional and general anesthesia.
- E. As with general anesthesia, patients should receive appropriate monitoring (see Chapter 10) and have an intravenous (IV) line in place. Oxygen, equipment for intubation and positive-pressure ventilation, and drugs to provide hemodynamic support must be available.

II. SEGMENTAL LEVEL REQUIRED FOR SURGERY

- A. Knowledge of the sensory, motor, and autonomic distributions of spinal nerves will help the anesthetist determine the correct segmental level required for a particular operation and anticipate the potential physiologic effects of producing a block to that level. Figure 17.1 illustrates the dermatomal distribution of the spinal nerves.
- B. Afferent autonomic nerves innervate visceral sensation and viscerosomatic reflexes at spinal segmental levels much higher than would be predicted from skin dermatomes.
- C. Minimal suggested levels for common surgical procedures are listed in Table 17.1.

III. CONTRAINDICATIONS TO NEURAXIAL ANESTHESIA

A. Absolute

- 1. Patient refusal
- 2. Localized infection at skin puncture site
- 3. Significant coagulopathy
- 4. Increased intracranial pressure

B. Relative

- 1. Septicemia or bacteremia
- 2. Hypovolemia
- 3. Central nervous system disease

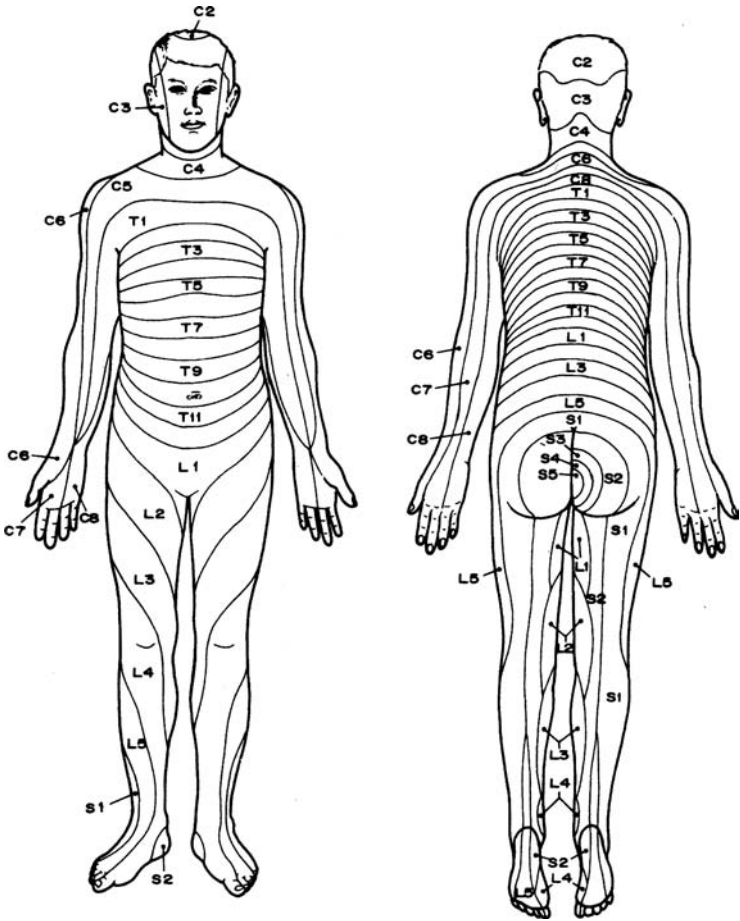


FIGURE 17.1 Skin dermatomes corresponding to respective sensory innervation by spinal nerves.

TABLE 17.1 Suggested Minimum Cutaneous Levels for Spinal Anesthesia	
Operative Site	Level
Lower extremities	T12
Hip	T10
Vagina, uterus	T10
Bladder, prostate	T10
Lower extremities with tourniquet	T8
Testis, ovaries	T8
Lower intra-abdominal	T6
Other intra-abdominal	T4

IV. SPINAL ANESTHESIA

Spinal anesthesia involves administering local anesthetic into the subarachnoid space.

A. Anatomy

1. The **spinal canal** extends from the foramen magnum to the sacral hiatus. The boundaries of the bony canal are the vertebral body anteriorly, the pedicles laterally, and the spinous processes and laminae posteriorly (Fig. 17.2).
2. Three **interlaminar ligaments** bind the vertebral processes together:
 - a. Superficially, the **supraspinous ligament** connects the apices of the spinous processes.
 - b. The **interspinous ligament** connects the spinous processes on their horizontal surface.
 - c. The **ligamentum flavum** connects the caudal edge of the vertebrae above to the cephalad edge of the lamina below. This ligament is composed of elastic fibers and is usually recognized by its increased resistance to the passage of a needle.
3. The **spinal cord** extends the length of the vertebral canal during fetal life, ends at about L3 at birth, and is moved progressively to a cephalad position as the vertebral column grows to reach near the adult L1 level by 2 years of age. The conus medullaris, lumbar, sacral, and coccygeal nerve roots branch out distally to form the cauda equina. Spinal needles are placed in this area of the canal (below L2) because the mobility of the nerves reduces the danger of trauma from the needle.

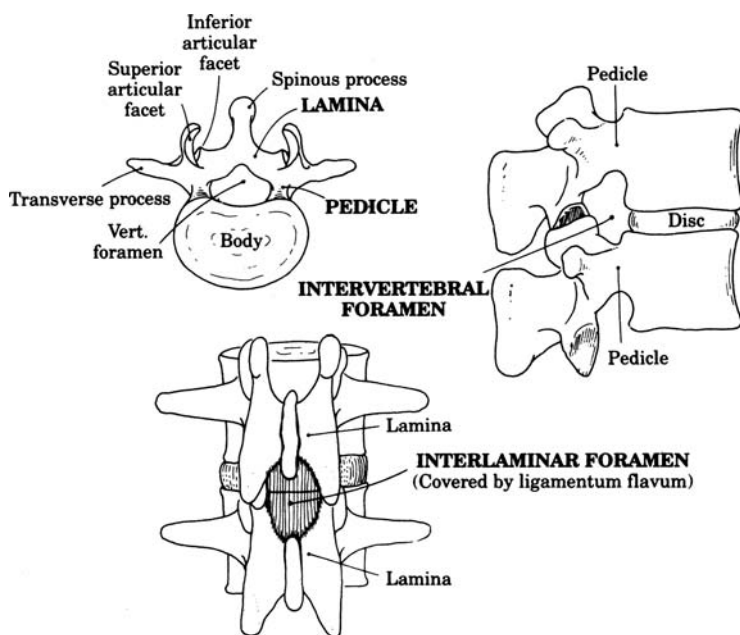


FIGURE 17.2 Vertebral anatomy.

4. The spinal cord is invested in three **meninges**:
 - a. The **pia mater**
 - b. The **arachnoid**, which lies between the pia and the dura mater
 - c. The **dura mater**, which is a tough fibrous sheath running longitudinally the length of the spinal cord and is tethered caudally at S2
 5. The **subarachnoid space** lies between the pia mater and the arachnoid mater and extends from the attachment of the dura at S2 to the cerebral ventricles above. The space contains the spinal cord, nerves, cerebrospinal fluid (CSF), and blood vessels that supply the spinal cord.
 6. **CSF** is a clear colorless fluid that fills the subarachnoid space. The total volume of CSF is 100 to 150 mL, whereas the volume in the spinal subarachnoid space is 25 to 35 mL. CSF is continuously formed at a rate of 450 mL/day by secretion or ultrafiltration of plasma from the choroid arterial plexuses located in the lateral, third, and fourth ventricles. CSF is reabsorbed into the bloodstream through the arachnoid villi and granulations that protrude through the dura to lie in contact with the endothelium of the cerebral venous sinuses.
- B. Physiologic Changes**
1. **Neural Blockade. Differential blockade** refers to the varying sensitivity of different types of nerve fibers to the effects of local anesthetics. Smaller C fibers conveying autonomic impulses are more easily blocked than the larger sensory and motor fibers. As a result, the level of autonomic blockade extends above the level of the sensory blockade by two to six segments. Similarly, fibers conveying sensation are more easily blocked than the larger motor fibers so that the sensory blockade will extend above the level of the motor blockade. Traditionally, it was believed that this differential blockade was solely due to difference in nerve fiber diameter. However, it is possible that the causes of this phenomenon are multifactorial.
 2. **Cardiovascular. Hypotension** is directly proportional to the degree of **sympathetic blockade** produced. Sympathetic blockade results in dilatation of arteries and venous capacitance vessels, leading to decreased systemic vascular resistance and decreased venous return. If the block is below T4, increased baroreceptor activity produces an increase in activity to the cardiac sympathetic fibers and vasoconstriction of the upper extremities. Blockade above T4 interrupts cardiac sympathetic fibers, leading to bradycardia, decreased cardiac output, and a further decrease in blood pressure. These changes are more marked in patients who are hypovolemic, are elderly, or have obstruction to venous return (e.g., pregnancy). Risk factors for bradycardia after spinal anesthesia include baseline bradycardia, the American Society of Anesthesiologists physical status 1, use of β -blockers, age less than 50, prolonged PR interval, and sensory level above T6.
 3. **Respiratory.** Low spinal anesthesia has no effect on ventilation. With ascending height of the block into the thoracic area, there is progressive ascending intercostal muscle paralysis. This has little effect on ventilation in the supine surgical patient with intact diaphragmatic function mediated by the phrenic nerve (C3 to C5), but patients may report a sensation of dyspnea due to decreased sensation of chest wall expansion. Conversely, ventilation in patients with poor respiratory reserve, such as the morbidly obese, may be profoundly impaired. Paralysis of both intercostal and abdominal muscles decreases the efficiency of coughing, which may be important in patients with chronic obstructive pulmonary disease. Usually, a spinal level of T4 does not result in impaired ventilation, but respiratory compromise may happen in patients with limited respiratory reserve or higher spinal levels.

4. Visceral Effects

a. **Bladder.** Sacral blockade (S2 to S4) results in an atonic bladder that can retain large volumes of urine. Blockade of sympathetic afferent and efferent innervation of the sphincter and detrusor muscle produces urinary retention.

b. **Intestine.** Sympathetic blockade (T5 to L1) produced by spinal anesthesia leads to contraction of the small and large intestines because of a predominance of parasympathetic tone.

5. **Neuroendocrine.** Peridural block to T5 inhibits part of the neural component of the stress response through its blockade of sympathetic afferents to the adrenal medulla and blockade of sympathetic and somatic pathways mediating pain. Other components of the stress response and central release of humoral factors are unaffected. Vagal afferent fibers from the upper abdominal viscera are not blocked and can stimulate release of hypothalamic and pituitary hormones, such as antidiuretic hormone and adrenocorticotrophic hormone. Glucose tolerance and insulin release are normal.

6. **Thermoregulation.** Hypothermia may occur due to several mechanisms. The predominant cause is redistribution of the central heat to the periphery secondary to vasodilatation, which makes forced air warming particularly effective at raising the patient's temperature. Core temperature may drop even though surface temperature is preserved and patients can feel warm despite a decrease in temperature. Thermoregulation is impaired given the loss of vasoconstriction to preserve heat below the level of sympathectomy. Shivering is common.

7. **Central Nervous System Effects.** Spinal anesthesia may have direct effects to suppress the consciousness, probably secondary to decreased afferent stimulation of the reticular activating system. During spinal or epidural anesthesia, doses of sedative agents may be decreased.

C. Technique

1. **Spinal Needle.** There are two main categories of spinal needles: those with a beveled tip that cut the dura ("cutting tip") and those with a conical tip ("pencil-point") with a lateral opening. The former includes the Quincke needle while the latter includes the **Sprotte** and **Whitacre** needles. Pencil-point needles may reduce the incidence of postdural puncture headache (<1%) compared with traditional cutting-tip needles by splitting rather than cutting dural fibers during insertion. Twenty-four- and 25-gauge needles are easily bent and are often inserted through a 19-gauge introducer needle. The 22-gauge **Quincke** needle is more rigid and is easily directed when inserted. It can be useful in older patients in whom access may be more difficult and the incidence of postdural puncture headache is low.

2. **Patient position.** The lateral decubitus, prone, and sitting positions can be used for administration of spinal anesthesia.

a. In the **lateral position**, the patient is placed with the affected side up if a hypobaric or isobaric technique is to be used and with the affected side down if a hyperbaric technique is to be used. The spine is horizontal and parallel to the edge of the table. The knees are drawn up toward the chest, and the chin is flexed downward onto the chest to obtain maximal flexion of the spine.

b. The **sitting position** is useful for low spinal blocks required in certain gynecologic and urologic procedures and is commonly used in obese patients to assist in identification of the midline. It is often used in conjunction with hyperbaric anesthetics. The head and shoulders are flexed downward onto the trunk with the arms resting on a stand. An assistant should be available to stabilize the patient, and the patient should not be oversedated.

- c. The **prone position** is used in conjunction with hypobaric or isobaric anesthetics for procedures on the rectum, perineum, and anus. A prone jackknife position can be used for administration of spinal anesthesia and the subsequent surgery.

3. Procedure

- a. With all regional anesthetic procedures, the patient should be monitored with standard ASA monitors including EKG, blood pressure, and oxygen saturation.
- b. The L2–L3, L3–L4, or L4–L5 interspaces are commonly used for spinal anesthesia. The L3 to L4 interspace or the spinous process of L4 is aligned with the upper borders of the superior iliac crests.
- c. Disinfect a large area of skin with an appropriate antiseptic solution. Care must be taken to avoid contamination of the spinal kit with antiseptic solution as the solution is potentially neurotoxic.
- d. Check the stylet for correct fit within the needle.
- e. Raise a skin wheal with 1% lidocaine and a 25-gauge needle at the spinal puncture site.

f. Approaches

1. **Midline.** Place the spinal needle (or introducer) through the skin wheal and into the interspinous ligament. The needle should be in the same plane as the spinous processes and angulated slightly cephalad toward the interlaminar space (Fig. 17.3).

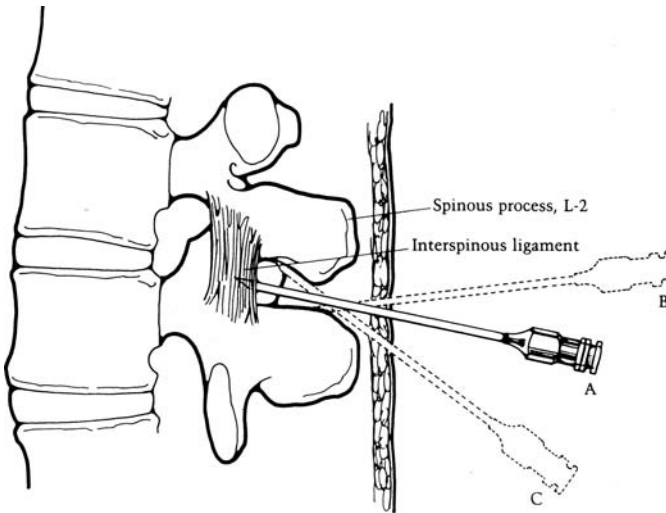


FIGURE 17.3 Spinal needle insertion, lateral view. For the classic midline approach, the needle is introduced in the middle of the interspace and advanced with a slight cephalad angulation. If correctly angled (**A**), it will enter the interspinous ligament, ligamentum flavum, and epidural space. If bone is contacted, it may be the inferior spinous process (**B**), and cephalad redirection will identify the correct path. If angling cephalad causes contact with bone again at a shallower depth (**C**), it is probably the superior spinous process. If bone is encountered at the same depth after several attempts at redirection (not shown), the needle is most likely on the lamina lateral to the interspace, and the position of the true midline should be reassessed. (From Mulroy MF. *Regional Anesthesia: An Illustrated Procedural Guide*. 2nd ed. Boston: Little, Brown and Company; 1996:79, with permission.)

2. **Paramedian.** This approach is useful in patients who cannot adequately flex their backs because of pain or whose interspinous ligaments may be ossified. Place the spinal needle approximately 1 cm lateral and 1 cm caudad to the center of the selected interspace. Aim the needle medially and slightly cephalad, passing lateral to the supraspinous ligament. If the lamina is contacted, redirect the needle and walk the tip off the lamina in a medial and cephalad direction.
 3. **Needle Placement.** Always keep the stylet in place when advancing the needle so that the needle's lumen does not become plugged with tissue. If paresthesias occur during placement, immediately withdraw the needle. Allow the paresthesia to pass and reposition the needle before proceeding again. Advance the needle until increased resistance is felt as it passes through the ligamentum flavum. As the needle is advanced beyond this ligament, a sudden loss of resistance will occur as the needle "pops" through the dura.
 4. Remove the stylet and confirm correct placement by noting free flow of CSF into the hub of the needle. Rotate the needle in 90-degree increments if necessary to confirm or reestablish good flow of CSF.
 5. **Administration of anesthetic.** Connect the syringe containing the predetermined dose of local anesthetic to the needle. Gently aspirate CSF into the syringe, which produces birefringence within dextrose-containing solutions and confirms free flow. Inject the drug slowly. Repeat aspiration of CSF at the end of the injection confirms that the needle point is still within the subarachnoid space. Remove the needle and place the patient gently into the desired position.
 - g. **Closely monitor** (every 60 to 90 seconds) blood pressure, pulse, and respiratory function for 10 to 15 minutes. Determine the ascending anesthetic level by noting the response to a gentle pinprick or an alcohol swab. Stabilization of the local anesthetic level takes approximately 20 minutes.
 - h. **Continuous spinal anesthesia** allows small aliquots of drug to be injected repeatedly to produce the desired level of sensory blockade. With this technique, a high or rapid sympathetic block can be avoided (of particular concern in the compromised patient). A 20-gauge catheter is inserted through a 17-gauge epidural needle. The catheter is advanced 2 to 4 cm into the subarachnoid space. Stimulation of nerve roots during catheter insertion necessitates repositioning of the catheter. **Neurotoxicity** from hyperbaric glucose-containing local anesthetic solutions injected through microbore spinal catheters (26 to 32 gauge) has been reported and may be due to the development of very high concentrations of local anesthetic around the nerves of the cauda equina. There are currently no such approved microbore catheters marketed in the United States.
 - i. **Layered Spinal.** This technique is frequently used in orthopedic surgery procedures at MGH to extend the duration of anesthesia by administering a dose of 0.5% bupivacaine through the spinal needle, waiting several minutes, and then adding additional drug incrementally.
- D. Determinants of the Level of Spinal Blockade**
1. **Major**
 - a. **Baricity of Local Anesthetic Solution.** Local anesthetic solutions can be described as hyperbaric, hypobaric, or isobaric in relation to the specific gravity of CSF (1.004 to 1.007 g/mL).

TABLE
17.2
Drugs and Dosages for Hyperbaric Spinal Anesthesia

Drug	Level (mg)			Duration (minutes)
	T10	T8	T6	
Tetracaine ^a	10	12	14	90–120
Bupivacaine ^{a,b}	7.5	9.0	10.5	90–120
Mepivacaine	30	45	60	60–90

^a Doses are based on a 66-inch patient. An additional 2 mg of tetracaine or 1.5 mg of bupivacaine should be added or subtracted for each 6 inches in height above or below 66 inches.

^b 0.5% isobaric bupivacaine is not FDA-approved for spinal anesthesia and should be considered “off label use.”

1. **Hyperbaric solutions** are typically prepared by mixing the drug with dextrose. They settle by gravity to the most dependent parts of the CSF column (Table 17.2).
2. **Hypobaric solutions** are prepared by mixing the drug with sterile water. They slowly rise to the highest part of the CSF column.
3. **Isobaric solutions** may have the advantage of a predictable spread through the CSF that is less dependent on patient position. Increasing the dose of an isobaric anesthetic has more of an effect on the duration of anesthesia than on the dermatomal spread. Patient positioning can be altered to limit or increase the spread of these mixtures.
- b. **Drug dose.** The anesthetic level varies directly with the dose of the agent used.
- c. **Drug volume.** The greater the volume of the injected drug, the further the drug will spread within the CSF. This is especially applicable to hyperbaric solutions.
- d. **Patient Position.** This does not affect the spread of isobaric solutions.
2. **Minor**
 - a. **Turbulence of CSF.** Turbulence created within the CSF during or after the injection will increase the spread of the drug and the level obtained. Turbulence is created by rapid injection, barbotage (the repeated aspiration and reinjection of small amounts of CSF mixed with drug), coughing, and excessive patient movement.
 - b. **CSF volume.** Lumbosacral CSF volume is inversely correlated with the extent of the spread of local anesthetic. There are no good predictors of lumbosacral CSF volume, but weight has some correlation.
 - c. **Increased intra-abdominal pressure.** Pregnancy, obesity, ascites, and abdominal tumors increase pressure within the inferior vena cava. This pressure increases blood volume within the epidural venous plexus, concomitantly reducing the volume of CSF within the vertebral column, which permits greater spread of injected local anesthetic. In obese patients, this effect is potentiated by increased fat within the epidural space.
 - d. **Spinal curvatures.** Lumbar lordosis and thoracic kyphosis influence the spread of hyperbaric solutions. Drug injected above the L3 level while the patient is in the lateral position will spread cephalad and will be limited by the thoracic curvature at T4 (Fig. 17.4).

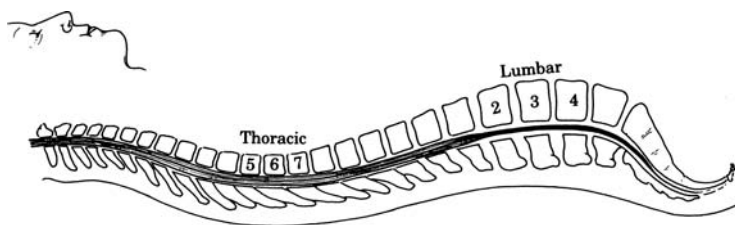


FIGURE 17.4 Spinal column curvatures that influence the spread of anesthetic solutions.

E. Determinants of the Duration of the Spinal Blockade

1. **Drugs and dose.** A characteristic duration is specific for each drug (see Chapter 16). The addition of opioids to the injected solution can modify the character of the block (see also Chapter 39). **Hydrophilic opioids** (e.g., morphine) offer analgesia that is slow in onset and long in duration. Delayed respiratory depression may occur. If hydrophilic opioids are given intrathecally, patients should be closely observed for at least 24 hours. **Lipophilic opioids** (e.g., fentanyl) have lower risk of delayed respiratory depression. Onset is fast and duration is moderate.
2. **Vasoconstrictors.** The addition of epinephrine, 0.2 mg (0.2 mL of 1:1,000), or phenylephrine, 2 to 5 mg, can prolong the duration of some spinal anesthetics by up to 50%. This effect has not been definitively demonstrated for bupivacaine, although there is evidence that epinephrine prolongs the analgesic effects of low-dose bupivacaine and fentanyl combinations used for labor analgesia.

F. Complications and Side Effects

1. **Neurologic.** Nerve injury is infrequent but can be a serious problem. Several types of nerve injury may occur.
 - a. Direct nerve injury related to needle or catheter placement. Pain during insertion of the catheter or injection of the drug is a warning sign for potential nerve injury resulting from needle or catheter placement and requires repositioning of the needle or catheter. **Transient paresthesias**, which can occur during placement of neuraxial blocks, typically resolve immediately and are usually without any long-term sequelae.
 - b. **Transient neurologic syndrome (TNS)** is a spontaneous severe radicular pain that occurs after resolution of the spinal anesthetic and may last for 2 to 7 days. Symptoms include buttock and thigh pain described as achy or burning in quality. TNS is usually responsive to conservative measures, such as nonsteroidal anti-inflammatory drugs and warm compresses. The incidence is highest with lidocaine administration but has also been observed with tetracaine, bupivacaine, and mepivacaine. Obesity, ambulatory surgery, knee arthroscopic surgery, and lithotomy position are additional risk factors.
 - c. Separately, there is an incidence of **back pain** following spinal anesthesia that may be related to the relaxation of the ligaments that occurs with the anesthesia. There is a similar incidence of back pain following general anesthesia, again likely related to the effects of anesthetic agents and muscle relaxants on the structures of the back.

d. **Bloody tap.** Puncture of an epidural vein during needle insertion may result in either blood or a mixture of blood and CSF emerging from the spinal needle. If the fluid does not rapidly clear, the needle should be withdrawn and reinserted.

e. **Spinal hematoma** is a surgical emergency. Overall incidence is around 1/150,000. The signs and symptoms of severe back pain and persistent neurologic deficit usually present within 48 hours. Risk is higher among patients who are coagulopathic or anticoagulated. Bloody taps are not generally thought to cause a spinal hematoma in patients with normal coagulation. A bloody tap may be a risk factor for spinal hematoma in patients who undergo subsequent anticoagulation, but there are no data to support the mandatory cancellation of a case under these circumstances. Instead, we advocate direct communication with the surgeon and that a specific risk-benefit decision about proceeding be made on an individual basis.

Close postoperative monitoring for signs consistent with hematoma is warranted. Diagnosis is usually made with magnetic resonance imaging (MRI), and treatment is via emergent hematoma evacuation. Because catheter removal as well as needle placement may cause spinal hematoma, anesthesiologists need to check a patient's coagulation status and the use of anticoagulants not only at the time of needle placement but also at the time of catheter removal. The approach to the use of anticoagulants, antiplatelet agents, and nonsteroidal anti-inflammatory drugs at Massachusetts General Hospital is listed in Table 17.3.

f. **Postdural puncture headache** usually develops within 3 days; 70% of headaches resolve within 7 days, and 90% within 6 months. The classic "spinal headache" is frontal and occipital in distribution; less frequently, the temporal area is affected. The headache is exacerbated by upright posture and relieved by lying supine. Other manifestations include visual disturbances or hearing impairment. Risk factors include younger age, female gender, larger needle size, pregnancy, multiple dural punctures, and a history of previous postdural puncture headache. The incidence may be reduced by using smaller needles and noncutting needles (e.g., pencil-point needles). Initial treatments of symptoms include rehydration, maintenance of supine position, pain medication including opioids, and caffeine. Maintenance of supine position as a prevention is neither proven nor recommended. Caffeine exerts its effect by vasoconstriction of cerebral vessels. The recommended dose of caffeine is 300 to 500 mg orally or IV. One cup of coffee contains 50 to 100 mg of caffeine. If initial therapy fails and severe symptoms persist more than 24 hours, an **epidural blood patch** can be done. Epidural needle insertion is done at the level of presumed dural puncture. Blood is drawn in a sterile fashion and injected into the epidural space. The typical blood volume is 20 to 30 mL or less if the patient complains of back discomfort during injection. The success rate ranges from 65% to 98%, and results are often immediate. A second blood patch can be tried with a success rate about the same as the first attempt. The use of a prophylactic epidural blood patch before the onset of headache symptoms is of doubtful benefit and not recommended.

2. Cardiovascular

a. **Hypotension.** The incidence of hypotension may be reduced by IV administration of 500 to 1,000 mL of Ringer lactate solution before

Anticoagulation and Epidural Anesthesia/Analgesia Guidelines

Drug (Generic)	Common Trade Names	Time Interval for Catheter Placement or Neuraxial Procedure After Last Dose	Time Interval for Catheter Removal After Most Recent Dose	Time Interval to Restart Med After Neuraxial Procedure or Catheter Removal
Abciximab	Reopro	48 h	48 h	24 h
Argatroban	Acova	At least 6 h; check for normal PTT or ACT	Check for normal PTT or ACT	2 h
Cilostazol ^a	Pletal	48 h	48 h	2 h
Clopidogrel ^b	Plavix	5–7 d	Depends on the dose	24 h
Eptifibatide	Integrilin	8 h	8 h	24 h
Fondaparinux ^c	Arixtra	4 d	4 d	2 h
Heparin subcutaneously (twice daily)	Heparin	No significant risk		
Heparin IV	Heparin	2–4 h, PTT < 35	2–4 h, PTT < 35	2 h
Dalteparin (low-dose) ^d	Fragmin (<5,000 units daily)	12 h	12 h	4 h
Dalteparin (high-dose) ^d	Fragmin (5,000 units twice daily or 120 units/kg twice daily or 175 units/kg daily)	24 h	24 h	4 h
Enoxaparin (low-dose) ^d	Lovenox (<60 mg daily)	12 h	12 h	4 h
Enoxaparin (high-dose) ^d	Lovenox (>60 mg daily or 1 mg/kg twice daily)	24 h	24 h	4 h
NSAID, ASA	Celebrex, Motrin, Naprosyn, Vioxx, etc.	No significant risk		

(continued)

TABLE

173

Anticoagulation and Epidural Anesthesia/Analgesia Guidelines (continued)

Drug (Generic)	Common Trade Names	Time Interval for Catheter Placement or Neuraxial Procedure After Last Dose	Time Interval for Catheter Removal After Most Recent Dose	Time Interval to Restart Med After Neuraxial Procedure or Catheter Removal
Thrombolytics: streptokinase, alteplase (tPA)	Streptase, Activase	10 d	10 d	10 d
Ticlopidine	Ticlid	14 d	14 d	24 h
Tirofiban	Aggrastat	8 h	8 h	24 h
Warfarin	Coumadin	3–5 d, INR ≤ 1.5	Check INR if treatment >24 h, INR ≤ 1.5	Same day

^aIf cilostazol (Pletal) is the only anticoagulant given, then an epidural catheter placement is most likely safe. If cilostazol (Pletal) is combined with other anticoagulant medicines (e.g., aspirin), neuraxial procedure or catheter placement should be delayed for at least 48 h.

^bClopidogrel (Plavix) has a 24- to 48-hour window to remove an epidural catheter once the medication is given. If it has been more than 48 h since dosing of clopidogrel, you must wait for 7 d.

^cFondaparinux should not be given if regional anesthesia is anticipated or has been used. If, however, fondaparinux 2.5 mg is given, we suggest the above guidelines. For larger doses (5–10 mg), neuraxial procedure should not be done for 7 d.

^dLow molecular weight heparin: single daily dosing may be started 6–8 h postoperatively. Twice-daily dosing should be started at least 24 h postoperatively. Epidural catheters should be removed before initiation of therapy.

ACT, activated clotting time; ASA, aspirin; NSAID, nonsteroidal anti-inflammatory drug; PTT, partial thromboplastin time.

performing the block. Patients with decreased cardiac function require care in administering large volumes of IV fluid, because translocation of fluid from the peripheral to the central circulation during recession of the block and return of systemic vascular tone could produce volume overload and pulmonary edema. Treatment of hypotension includes increasing venous return and treating severe bradycardia. Trendelenburg position, fluid administration, raising lower extremities to autotransfuse blood, or the use of vasopressors may be necessary.

- b. **Bradycardia.** Bradycardia can be treated with atropine or glycopyrrolate. If bradycardia is severe and accompanied by hypotension, epinephrine or epinephrine may be used.

3. Respiratory

- a. **Dyspnea** is a common complaint with high spinal levels. It is caused by the proprioceptive blockade of afferent fibers from abdominal and chest wall muscles. Reassuring the patient may be all that is required, although adequate ventilation must be ensured.
- b. **Apnea** can be caused by reduced medullary blood flow accompanying severe hypotension or from direct blockade of C3 to C5 ("total spinal"), inhibiting phrenic nerve output. Immediate ventilatory support is required.

4. Visceral

- a. **Urinary retention.** The mechanism of urinary retention is described in section IV.B.4.a. Urinary retention may outlast the sensory and motor blockade. A urinary catheter should be placed if anesthesia or analgesia is maintained for a prolonged period.
 - b. **Nausea and vomiting** are usually caused by hypotension or unopposed vagal stimulation. Treatment involves restoring blood pressure, administering oxygen, and IV atropine.
5. **Infection** after spinal anesthesia is exceedingly rare. Nevertheless, meningitis, arachnoiditis, and epidural abscess can occur. Possible etiologies include chemical contamination and viral or bacterial infection. Consultation and prompt diagnosis and treatment are essential.
6. **Pruritis** commonly occurs with the use of neuraxial opioids and is more frequent with intrathecal administration as opposed to epidural. The exact mechanism is unclear. Pharmacologic treatments include nalbuphine (5 to 10 mg IV), naloxone (1 to 2 $\mu\text{g/kg/h}$), naltrexone (6 to 9 mg PO), diphenhydramine (25 to 50 mg IV/PO), ondansetron (4 to 8 mg IV), and propofol (10 to 20 mg IV bolus).
7. **Shivering** has a high incidence and may be treated with IV meperidine (25 mg IV). Clonidine (65 to 300 $\mu\text{g IV}$) has been shown to have a similar efficacy.

V. EPIDURAL ANESTHESIA

Epidural anesthesia is achieved by introducing local anesthetics into the epidural space.

- A. **Anatomy.** The epidural space is a potential space extending from the base of the skull to the sacrococcygeal membrane. Posteriorly, it is bounded by the ligamentum flavum, the anterior surfaces of the laminae, and the articular processes. Anteriorly, it is bounded by the posterior longitudinal ligament covering the vertebral bodies and intervertebral discs. Laterally, it is bounded by intervertebral foramina and the pedicles. It has direct communications with the paravertebral space. It contains fat and

lymphatic tissue as well as epidural veins, which are most prominent in the lateral aspects of the space. The veins have no valves and directly communicate with the intracranial veins. The veins also communicate with the thoracic and abdominal veins through the intervertebral foramina and with the pelvic veins through the sacral venous plexus. The epidural space is widest in the midline and tapers off laterally. In the lumbar region, it is 5- to 6-mm wide in the midline; in the midthoracic region, the space is 3- to 5-mm wide.

B. Physiology

1. **Neural blockade.** Local anesthetic placed in the epidural space acts directly on the spinal nerve roots located in the lateral part of the space. These nerve roots are covered by the dural sheath, and the local anesthetic gains access to the CSF by uptake through the dura. The onset of the block is slower than with spinal anesthesia, and the intensity of the sensory and motor block is less. Anesthesia develops in a segmental manner, and selective blockade can be achieved.
2. **Cardiovascular.** Physiologic changes from sympathetic blockade are similar to those described for spinal anesthesia (see section IV.B.2), but usually, hemodynamic change is slower. Large doses of local anesthetic may be absorbed or inadvertently injected into the systemic circulation and depress the myocardium. Epinephrine used to prolong the duration of the local anesthetics may also be absorbed or injected into the systemic circulation, producing tachycardia and hypertension.
3. **Respiratory.** Physiologic changes are similar to those described for spinal anesthesia. When we use postoperative epidural analgesia with dilute local anesthetics after major abdominal, upper abdominal, or thoracic surgery, the reduction in functional residual capacity and impairment of diaphragm function are minimized, which improves overall pulmonary outcome. With epidural anesthesia, the incidence of postoperative hypoxemia can be decreased by reducing the dose and effects of systemic opioids.
4. **Coagulation.** Epidural anesthesia has been reported to reduce venous thrombosis and subsequent pulmonary embolism. Proposed mechanisms include increased pelvic blood flow, decreased sympathetic response to surgery, and earlier mobility. Epidural anesthesia may reduce intraoperative blood loss during hip, pelvic, and lower abdominal surgeries.
5. **Gastrointestinal.** Epidural anesthesia can be administered for patients undergoing bowel resection with anastomosis. As with spinal anesthesia, the predominance of the parasympathetic system may cause contraction of the bowel. Patients often have earlier return of bowel function with the use of an epidural.
6. Other physiologic changes seen are similar to those described for spinal anesthesia (see section IV.B).

C. Technique

1. **Epidural needles.** Most commonly, the 17-gauge **Tuohy** or **Weiss** needle is used for identification of the epidural space. These needles are styletted, have a blunt leading edge with a lateral opening, and have a thin wall to allow passage of a 20-gauge catheter.
2. **Patient position.** Patients can be positioned for epidural anesthesia in either the sitting or the lateral position. The same considerations apply as for spinal anesthesia (see section IV.C.2).

3. **Monitoring.** The patient should be monitored with standard monitors including EKG, blood pressure, and oxygen saturation.
4. **Approaches.** Whether from a midline or a paramedian approach, the needle should enter the epidural space in the midline, because the space is widest here and there is a decreased risk of puncturing epidural veins, spinal arteries, or spinal nerve roots, all of which lie predominantly in the lateral aspects of the epidural space. Palpation of landmarks, skin preparation, and draping are as described for spinal anesthesia (see section IV.C.3) (Fig. 17.5).
- a. **Lumbar.** Use a long 25-gauge needle for superficial and deep infiltration of local anesthetic into the supraspinous and interspinous ligaments. This needle also assists in defining the direction in which the epidural needle should be inserted. Advance the epidural needle through the supraspinous and interspinous ligaments in a slightly cephalad direction, until it comes to lie within the “rubbery” ligamentum flavum.
1. **Loss-of-resistance techniques.** Remove the stylet and attach a glass or plastic loss-of-resistance syringe containing approximately 3 mL of air or saline to the needle hub. Apply constant pressure to the plunger of the syringe while slowly advancing the needle. When the bevel enters the epidural space, there is a marked “loss of resistance” to plunger displacement. Alternatively, an

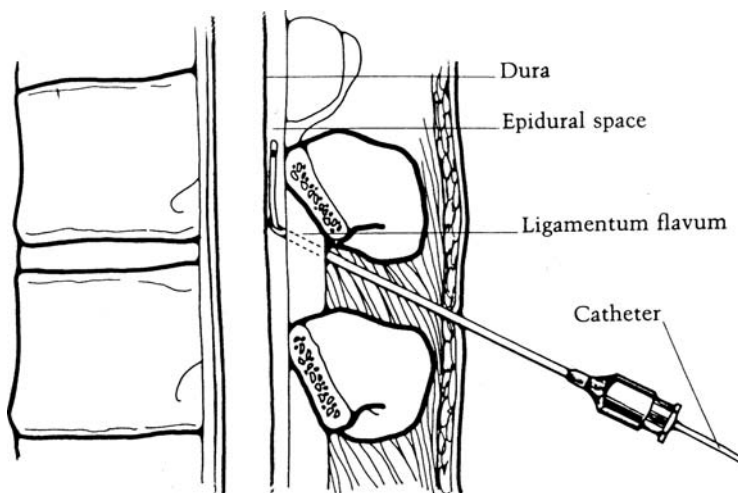


FIGURE 17.5 Insertion of an epidural catheter. The needle is secured by resting one hand on the back and grasping the hub firmly (not shown) while the other hand inserts the catheter into the hub and gently advances it beyond the tip of the needle. The bevel is usually directed cephalad, which produces the most reliable insertion; caudad orientation may allow the catheter to exit one of the intervertebral foramina. Ideally, the catheter is advanced 3 to 4 cm beyond the needle tip; further placement increases the potential for lateral misdirection or foraminal exit. (From Mulroy MF. *Regional Anesthesia: An Illustrated Procedural Guide*. Boston: Little, Brown and Company; 1996:109, with permission.)

“intermittent” technique can be used, where the change in resistance is tested repeatedly in between small careful advances of the epidural needle. When air is used for loss of resistance, the amount of air injection should be minimized. Patchy block, pneumocephalus, and air embolism have been reported with loss of resistance with the air technique.

2. The **hanging drop technique** relies on the principle that a drop of fluid placed on the hub of the epidural needle (once the ligamentum flavum has been entered) will retract into the needle as the tip of the needle is advanced into the epidural space. This negative pressure is provided by “tenting” of the dura by the needle tip but may be altered by transmitted changes in intra-abdominal and intrathoracic pressure (e.g., pregnancy and obesity). Drop retraction occurs only about 80% of the time, so if a change in compliance is felt while advancing through the ligamentum flavum, it should be checked by “loss of resistance.”
- b. **Thoracic epidural anesthesia** provides upper abdominal and thoracic anesthesia with a smaller dose of local anesthetic. Postoperative analgesia can be produced without lower extremity blockade. Although the technique is the same as for lumbar placement, the thoracic vertebral spinous processes are much more sharply angulated downward so that the tip of the superior spinous process overlies the lamina of the vertebra below, and the epidural needle should be directed in a more acute cephalad direction. In addition, there is a risk of producing trauma to the underlying spinal cord if dural puncture occurs. Occasionally, a paramedian approach is necessary.
- c. **Technique for catheter placement.** An epidural catheter permits repeated injections of local anesthetic for prolonged procedures and provides a route for postoperative analgesia.
 1. Thread a 20-gauge radiopaque catheter with 1-cm graduations through the epidural needle. If the catheter contains a wire stylet, the stylet should first be withdrawn 1 to 2 cm before insertion of the catheter to decrease the incidence of paresthesia and dural or venous puncture. Many individuals prefer to completely remove the stylet since it is stiff enough allow placement into extraepidural tissue. If the catheter passes easily without the stylet, it usually is located in the epidural space. Polyvinyl chloride catheters are relatively stiff and resist kinking but can be associated with dural and venous puncture. Teflon catheters are very soft and flexible but may be more likely to kink and occlude. Newer catheters of nylon, polyamide, and polyvinyl offer compromises between flexibility and rigidity. Wire-reinforced soft catheters do not kink and are much less prone to slipping out. When multipore catheters are used, the distance from the catheter tip to the most proximal lateral hole should be noted to ensure that all injected medication reaches the epidural space.
 2. Slowly advance the catheter approximately 5 cm into the epidural space. The patient may experience an abrupt paresthesia, which is usually transient. If it is sustained, the catheter must be repositioned. If the catheter must be withdrawn, the catheter and needle should be removed together to avoid shearing the catheter tip.

3. Measure the distance from the surface of the patient's back to a mark on the catheter.
 4. Carefully withdraw the needle over the catheter and remeasure the distance from the patient's back to the mark on the catheter. If the catheter was advanced, withdraw it, leaving 4 to 5 cm within the epidural space.
 - d. Administer a **test dose** of local anesthetic agent through the needle if a single-dose technique is used or through the catheter for continuous techniques. A test dose usually consists of 3 mL of 1.5% lidocaine with 1:200,000 epinephrine. This should have little effect in the epidural space. If the solution has been injected into the CSF, a spinal block will occur rapidly. If the solution has been injected into an epidural vein, a 20% to 30% increase in heart rate may be seen. Other symptoms of an intravascular injection include perioral numbness, a metallic taste, tinnitus, and palpitations. A corresponding increase in blood pressure can also be seen if the patient's heart rate is controlled with β -blockers.
 - e. **Injection of anesthetic.** Administer the anesthetic solution in 3- to 5-mL increments every 3 to 5 minutes until the desired total dose has been given. Aspirate the catheter or needle, checking for the appearance of blood or CSF, before each injection.
- D. Determinants of the Level of the Epidural Blockade**
1. **Volume of local anesthetic.** A maximum dose of 1.6 mL of local anesthetic per segment has been suggested for the induction of epidural blockade. This maximum can be exceeded if dilute mixtures of medications are used, as for postoperative or labor analgesia.
 2. **Age.** The volume of local anesthetic should be reduced by approximately 50% in the elderly and in neonates. Stenosis of intervertebral foramina in the elderly reduces the lateral paravertebral spread of the injected drug, allowing for a more cephalad spread.
 3. **Pregnancy.** A 30% reduction in dose is expected in pregnant women. Hormonal effects during pregnancy render nerves more sensitive to the effects of local anesthetic, and inferior vena cava compression increases blood volume within the epidural venous plexus, reducing the potential volume of the epidural space.
 4. **Speed of injection.** Rapid injection of drug into the epidural space may produce a less reliable block than a slow, steady injection at approximately 0.5 mL/s. Very rapid injection of large volumes of drug has the potentially hazardous effect of increasing pressure within the epidural space. Such a rise in pressure can produce headache, increased intracranial pressure, and possibly spinal cord ischemia by decreasing spinal cord blood flow.
 5. **Position.** The position of the patient has a slight effect on the level of the epidural blockade. Patients sitting upright have greater caudad spread of blockade; patients in the lateral position have a higher level of block on the dependent side.
 6. **Spread of epidural blockade.** Onset of blockade occurs first and is most dense at the level of injection. Spread of the block usually occurs faster in a cephalad than in a caudad direction. This is likely because of the relative difference in size between the large lower lumbar and sacral nerve roots compared with the smaller thoracic nerve roots. L5–S1 are large nerve roots making them difficult to anesthetize and often leading to sparing of this area during epidural block.

E. Determinants of the Onset and Duration of the Epidural Blockade

1. **Selection of drug** (see Chapter 15).
2. **Addition of epinephrine.** Epinephrine, added at a concentration of 1:200,000, decreases the systemic uptake and plasma levels of local anesthetic and prolongs its duration of action (see Chapter 16).
3. **Addition of opioid.** The addition of fentanyl, 50 to 100 μg , to the local anesthetic solution speeds the onset, increases the level, prolongs the duration, and improves the quality of the block. Fentanyl is thought to produce this effect by having a selective action at the substantia gelatinosa of the dorsal horn of the spinal cord to modulate pain transmission. This action appears to be synergistic with the actions of the local anesthetics.
4. **pH adjustment of solution.** The addition of sodium bicarbonate to the local anesthetic solution in a ratio of 1 mL of 8.4% sodium bicarbonate to each 10 mL of lidocaine (0.1 mL for each 10 mL of bupivacaine as excess bicarbonate will precipitate in bupivacaine) decreases the onset time for the blockade. It is thought that this effect is due to an increased amount of local anesthetic base, which increases the rate at which non-ionized drug crosses axonal membranes.

F. Complications

1. **Dural puncture** occurs in about 1% of epidural catheter placements. If dural puncture occurs during attempted epidural catheter insertion, the chance of postdural puncture headache is higher than with spinal anesthesia. Furthermore, it is important to minimize the amount of CSF leakage from the epidural needle by either covering the proximal hole of the needle with your finger or reinserting the stylet. Several management options are available after dural puncture. A conversion to spinal anesthesia can be made by injecting an appropriate amount of anesthetic into the CSF. Continuous spinal anesthesia can be performed by inserting an epidural catheter into the subarachnoid space through the epidural needle. If epidural anesthesia is required (e.g., for postoperative analgesia), the catheter can be repositioned at a different interspace so that the tip of the epidural catheter lies well away from the site of dural puncture. The possibility of spinal anesthesia occurring with injection of the epidural catheter should be considered.
2. **Bloody tap.** If a bloody tap occurs during epidural needle placement, some practitioners advocate for epidural placement at a different interspace. Advantages include minimizing confounding effects of visualized blood on determination of correct catheter placement and potentially decreasing amounts of systemically absorbed local anesthetic that may be falsely interpreted as a positive test dose. In patients with normal coagulation function, such bloody taps rarely lead to serious sequelae (e.g., epidural hematoma). Bloody epidural taps may be risk factors for epidural hematoma in patients who undergo subsequent anticoagulation, but there are no data to support the mandatory cancellation of a case under these circumstances. Instead, we advocate direct communication with the surgeon and that a specific risk–benefit decision about proceeding be made on an individual basis. Close postoperative monitoring for signs consistent with hematoma is warranted.
3. **Catheter complications**
 - a. **Inability to thread the epidural catheter** is relatively common. This problem can occur if the epidural needle is inserted into the lateral

aspect of the epidural space rather than the midline or if the bevel of the needle is at too acute an angle to the epidural space for the catheter to emerge. It can also occur if the level of the needle is only partially through the ligamentum flavum when loss of resistance is found. In the latter case, slight (1 mm) advancement of the needle into the epidural space may facilitate catheter insertion.

- b. The catheter can be inserted into an epidural vein.** Blood cannot always be aspirated back through the catheter. This may be noticed only when an initial test dose with epinephrine is administered, and tachycardia is noted. The catheter should be withdrawn until blood can no longer be aspirated, flushed with saline, and then retested. Withdrawal of the catheter more than 1 to 2 cm should prompt removal and reinsertion.
- c. Catheters can break off or become knotted** within the epidural space. In the absence of infection, a retained catheter is no more reactive than a surgical suture. The patient should be informed of the problem and reassured. The complications of surgical exploration and removal of an asymptomatic catheter are greater than in conservative management.
- d. Cannulation of the subdural space.** The subdural space is a potential space between the dura and the arachnoid membranes and may be entered with a needle or with a catheter. CSF is not aspirated but the effects of the local anesthetic are quite different from usual epidural anesthesia and are often quite variable. In the absence of myelography, it is a diagnosis of exclusion. It can result in dissociation of blocked modalities (e.g., full sensory anesthesia without motor block or motor block with minimal sensory block). It should be suspected whenever an epidural dose produces a more extensive spread than expected. Subdural catheters should be removed and an epidural catheter should be placed.
- 4. Unintentional subarachnoid injection.** The injection of a large volume of local anesthetic into the subarachnoid space can produce total spinal anesthesia. Treatment is similar to that described for spinal complications (see section IVF).
- 5. Intravascular injection** of local anesthetic into an epidural vein causes central nervous system and cardiovascular toxicity and may result in convulsions and cardiopulmonary arrest. Resistant ventricular fibrillation with IV bupivacaine has been described. Animal data and case reports suggest benefit of IV lipid emulsion for local anesthetic-related cardiotoxicity. A bolus of Intralipid 20%, 1.5 mL/kg, over 1 minute followed by a continuous infusion (0.25 mL/kg/min) with repeat bolus doses every 3 to 5 minutes for a total maximum dose of 8 mL/kg has been proposed on www.lipidrescue.org as a treatment regimen. Cardiopulmonary bypass is an option if ventricular fibrillation or cardiac arrest is resistant to pharmacologic therapy (see Chapters 16 and 38).
- 6. Local anesthetic overdose.** Systemic local anesthetic toxicity may occur due to the relatively large amounts of drug required for anesthesia. Inadvertent intravascular injection is the most common cause of local anesthetic overdose. Vasoconstrictors such as epinephrine decrease the incidences of toxicity by decreasing the rate of absorption of the local anesthetic. Therapy is geared toward support of compromised functions.

7. **Direct spinal cord injury** is more likely if the epidural injection is above L2. The onset of a unilateral paresthesia during needle insertion suggests lateral entry into the epidural space. Further injection or insertion of a catheter at this point may produce trauma to a nerve root. Small feeder arteries to the anterior spinal artery also run in this area as they pass through the intervertebral foramen. Trauma to these arteries potentially may result in anterior spinal cord ischemia or an epidural hematoma. Placement of epidural catheters after the induction of general anesthesia negates the ability to appreciate symptoms of paresthesia and is done only when such potential risk is deemed necessary. Pediatric patients frequently have catheters placed after induction of general anesthesia, often at the caudal level.
8. **Postdural puncture headache.** If the dura is punctured with a 17-gauge epidural needle, there is a greater than 75% chance of a young patient developing a postdural puncture headache. Management is the same as that described under spinal anesthesia (see section IV.F.1.f.).
9. **Epidural abscess** is an extremely rare complication of epidural anesthesia. The source of infection usually is from hematogenous spread to the epidural space from an infection in another area. Infection can also arise from contamination during insertion, contamination of an indwelling catheter used for postoperative pain relief, or a cutaneous infection at the insertion site. The patient presents with fever, severe back pain, and localized back tenderness. Progression to nerve root pain and paralysis can occur. Initial laboratory investigations include evaluation for a leukocytosis and a lumbar puncture suggestive of a parameningeal infection. Definitive diagnosis is by MRI. Treatment includes antibiotics and sometimes urgent decompression laminectomy. Rapid diagnosis and treatment are associated with good neurologic recovery. Epidural catheter dressings should be inspected daily for signs of leakage and inflammation.
10. **Epidural hematoma** is an extremely rare complication of epidural anesthesia. An epidural hematoma is a surgical emergency. Trauma to epidural veins in the presence of a coagulopathy may result in a large epidural hematoma. The patient can present with severe back pain and persistent neurologic deficit after epidural anesthesia. Diagnosis is confirmed by MRI. A decompressive laminectomy within about 8 hours from the onset of symptoms is required to preserve neurologic function.
11. **Horner syndrome** is seen in 1% to 4% of epidural anesthetics. The constellation of ptosis, miosis, anhidrosis, and enophthalmos occurs due to the sympathetic blockade of the upper thoracic spinal segments. Reassurance is provided to the patient as these symptoms resolve.

VI. COMBINED SPINAL–EPIDURAL ANESTHESIA

- A. Spinal anesthesia offers the benefits of rapid onset. Placement of an epidural catheter at the same time offers the advantage of prolonged anesthesia and analgesia for longer procedures or postoperative pain management. This technique often is used in the labor and delivery setting (see Chapter 32).
- B. **Technique.** Prepare the patient as for epidural placement (see section V.C). After placing the epidural needle in the epidural space, advance a long spinal needle (Sprotte 24 gauge $\times$ 120 mm or Whitacre 25 gauge) through the epidural needle until the characteristic pop of dural penetration occurs. At this point, withdraw the stylet from the spinal needle and confirm free flow of CSF. Inject medication into the subarachnoid space and withdraw

the spinal needle. Thread an epidural catheter through the epidural needle in the standard fashion. If epidural anesthesia is used subsequently, a test dose is required.

VII. CAUDAL ANESTHESIA

Caudal anesthesia is obtained by placing local anesthetic into the epidural space in the sacral region. This technique is often used for pediatric anesthesia. The details below are intended for the adult population.

- A. Anatomy.** The caudal space is an extension of the epidural space. The sacral hiatus is formed by the failure of the laminae of S5 to fuse. The hiatus is bounded laterally by the sacral cornua, which are the inferior articulating processes of S5. The **sacroccoccygeal membrane** is a thin layer of fibrous tissue that covers the sacral hiatus. The caudal canal contains the sacral nerves, the sacral venous plexus, the filum terminale, and the dural sac, which usually ends at the lower border of S2. In neonates, the dural sac may extend to S4.
- B. Physiology.** The physiology of caudal anesthesia is similar to that described for epidural anesthesia (see section V.B). It is indicated for surgical and obstetric procedures of the perineal and sacral areas.
- C. Technique**
 1. Caudal epidural anesthesia is performed with the patient in the lateral, prone, or jackknife position.
 2. Palpate the sacral cornua. If they are difficult to palpate directly, the location of the sacral hiatus in adults can be estimated by measuring 5 cm from the tip of the coccyx in the midline.
 3. Skin preparation and draping are as described for spinal anesthesia (see section IV.C.3).
 4. Raise a skin wheal with 1% lidocaine between the sacral cornua.
 5. Insert a 22-gauge spinal needle at an angle of 70 to 80 degrees to the skin. Advance the needle through the sacroccoccygeal membrane, which is identified by a characteristic pop. Avoid attempting to thread the needle up the caudal canal, because this increases the likelihood of puncturing an epidural vein (Fig. 17.6).
 6. Withdraw the stylet and inspect the hub of the needle for passive CSF or blood flow. The needle can be aspirated as a further check. Reposition the needle if either blood or CSF appears.
 7. Administer a test dose of 3 mL of local anesthetic solution with epinephrine (1:200,000), similar to that used for lumbar epidural anesthesia (see section V.C.3.d), observing the patient for signs of subarachnoid or IV injection. Because the caudal canal has a rich epidural venous plexus, IV injections are seen frequently and can occur even though blood cannot be aspirated from the needle.
 8. A caudal catheter can be placed in a manner analogous to that for lumbar epidural anesthesia with a 17-gauge Tuohy needle (see section V.C.3.a). The catheter can be used for postoperative analgesia.
 9. The level, onset, and duration for caudal anesthesia follow the same principles outlined for epidural anesthesia (see sections V.D and V.E). The extent of caudal block is less predictable than other epidural techniques because of the variability in content and volume of the caudal canal and the amount of local anesthetic solution that leaks out of the sacral foramina. To obtain sacral anesthesia, a volume of 12 to 15 mL should be sufficient.
- D. Complications.** The complications of caudal anesthesia are similar to those of epidural anesthesia (see section V.F).

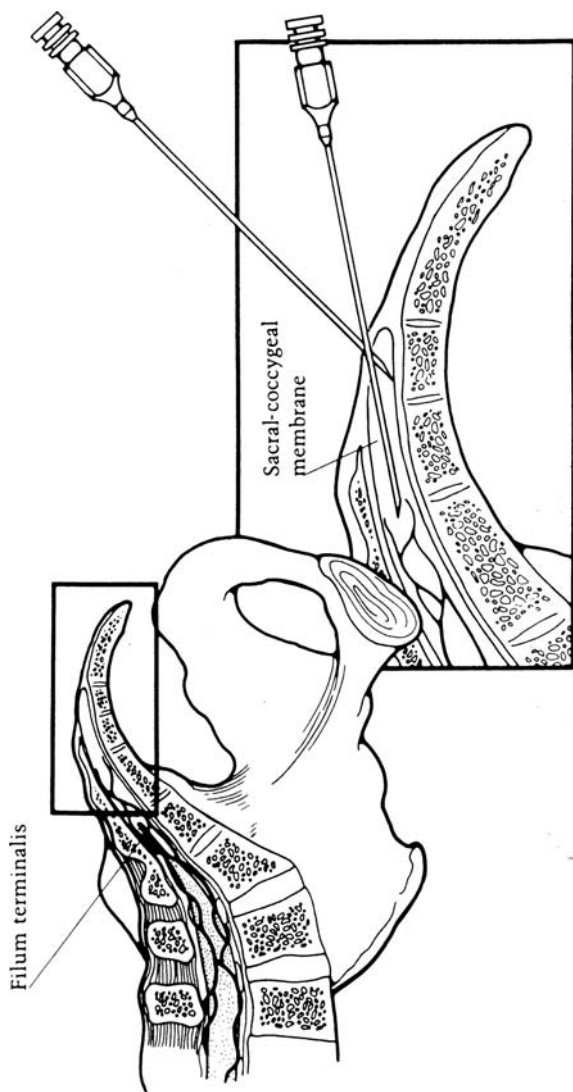


FIGURE 17.6 Sacral anatomy, lateral view. A needle directed through the sacral–coccygeal membrane at a 45-degree angle will usually “pop” through the ligament and contact the anterior bone of the sacral canal. The needle needs to be rotated so that the bevel does not scrape the periosteum of this layer, and the angle of advancement changed to allow passage directly 2 to 3 cm up the canal without contacting the bone again. This space is generously endowed with blood vessels, and the terminal point of the dural sac extends a variable distance in the sacral canal but usually lies at the S2 level. (From Mulroy MF. *Regional Anesthesia: An Illustrated Procedural Guide*. Boston: Little, Brown and Company; 1996:124, with permission.)

VIII. ANTICOAGULATION AND NEURAXIAL BLOCKADE

Neuraxial blockade should be avoided in the presence of prophylactic or therapeutic anticoagulation because of the increased risk of epidural hematoma formation. Massachusetts General Hospital guidelines regarding neuraxial anesthesia in anticoagulated patients are listed in Table 17.3.

- A. Oral Anticoagulants.** In patients receiving low-dose oral anticoagulants (warfarin), regional techniques may be performed if the thromboprophylaxis was initiated less than 24 hours previously. If epidural or spinal anesthesia is planned, hold warfarin 3 to 5 days before the operation, and the patient's international normalized ratio (INR) should be checked before the operation. An INR less than or equal to 1.5 is generally acceptable for many anesthesiologists, but there is no definite cutoff value above which epidural or spinal anesthesia is specifically discouraged.
- B. Unfractionated Heparin.** Twice-daily subcutaneous heparin prophylaxis is not a contraindication for the use of neuraxial techniques. There is an unknown risk with prophylactic subcutaneous heparin dosed three times per day. In these cases, a coagulation profile should be obtained. Caution should be used in debilitated patients, in whom the action of the drug may be prolonged and in whom neurologic monitoring may be difficult. IV heparin should be stopped 2 to 4 hours before the initiation of neuraxial blockade, and a repeat coagulation profile should be obtained if there is any question about the state of anticoagulation. Administration of heparin should be delayed for at least 2 hours after placement. Removal of a catheter should be treated with the same anticoagulation guidelines as the placement of a catheter.
- C. Low Molecular Weight Heparin.** Patients receiving low molecular weight heparin (LMWH) for thromboembolism prophylaxis have altered coagulation parameters. Spinal or epidural needle placement should not be done for at least 12 hours after the last dose. Patients receiving higher doses of LMWH (enoxaparin 1 mg/kg twice daily) will require longer delays (24 hours). In patients requiring continuing LMWH administration, spinal or epidural catheters should be removed before administration of LMWH. The subsequent administration of LMWH should be delayed for 4 hours after catheter removal.
- D. Antiplatelet Drugs.** Patients receiving aspirin or nonsteroidal anti-inflammatory drugs do not appear to be at higher risk for epidural hematoma formation. These drugs could contribute to an increased bleeding risk, however, if they are used concurrently with other anticoagulants. With regard to thienopyridine derivatives (ticlopidine and clopidogrel), the suggested time interval between discontinuation of medication and initiation of neuraxial block is 14 days for ticlopidine and 5 to 7 days for clopidogrel. Following platelet GPIIb/IIIa inhibitors, normal platelet function returns in 24 to 48 hours with abciximab and in 4 to 8 hours with eptifibatide and tirofiban.
- E. Fibrinolytic and Thrombolytic Agents.** Although the plasma half-life of thrombolytic drugs is only for hours, it takes several days before thrombolytic effects disappear. Surgery or puncture of noncompressible vessels within 10 days of thrombolytic therapy is contraindicated. There is no definitive guideline regarding the neuraxial anesthesia and thrombolytic therapy. Measurement of the fibrinogen level may be helpful in guiding the decision.

F. Herbal Medication (see Chapter 40). Herbal medications including garlic, ginkgo, and ginseng are all known to affect coagulation. Currently, there are no specific guidelines for timing the neuraxial block in relation to herbal medication use. Because it is not known at which doses potential coagulopathies occur, management decisions are often based more on a clinical history of abnormal bleeding. Herbal medications are thought to be more problematic when taken concurrently with other conventional anticoagulant medications.

Suggested Readings

- Aida S, Taga K, Yamakura T, et al. Headache after attempted epidural block: the role of intrathecal air. *Anesthesiology* 1998;88:76–81.
- Horlocker TT, Wedel DJ, Rowlingson JC, et al. Regional anesthesia in the patient receiving antithrombotic or thrombolytic therapy: American Society of Regional Anesthesia and Pain Medicine Evidence-Based Guidelines (Third Edition). *Reg Anesth Pain Med* 2010;35(1):64–101.
- Moen V, Dahlgren N, Irestedt L. Severe neurological complications after central neuraxial blockades in Sweden 1990–1999. *Anesthesiology* 2004;101:950–959.
- Moraca RJ, Sheldon DG, Thirlby RC, et al. The role of epidural anesthesia and analgesia in surgical practice. *Ann Surg* 2003;238:663–673.
- Turnbull DK, Sheperd DB. Post-dural puncture headache: pathogenesis, prevention and treatment. *Br J Anaesth* 2003;91(5):718–729.

I. GENERAL CONSIDERATIONS

- A. Peripheral nerve blockade** can be an excellent addition or alternative to general anesthesia for many surgical procedures. Regional anesthesia provides optimal surgical conditions of sensory and motor blockade without significantly disrupting autonomic function. Single-shot blocks can provide prolonged postoperative analgesia for up to 24 hours, while continuous catheter techniques can provide analgesia for days. The benefits of regional anesthesia include patient satisfaction, faster initial recovery, and the ability to avoid general anesthesia if desired.
- B. The preoperative assessment,** preparation of the patient, and degree of monitoring are the same as for general anesthesia. Patients should follow fasting (nothing by mouth) guidelines whenever possible, and regional anesthesia should not be chosen simply to avoid complications related to a full-stomach or difficult airway. Baseline neurologic examination and any preexisting conditions should be documented before any block is performed.
- C. Consent for regional anesthesia** should include a thorough description of the risks, benefits, options, and common side effects. **Need for supplemental** local anesthesia, sedation, or potential for general anesthesia should also be discussed.
- D. Preoperative anxiolysis** may be appropriate as long as the patient remains cooperative and alert. Usually, short-acting agents such as fentanyl and midazolam are adequate. Performing blocks on heavily sedated patients or on adults under general anesthesia is not optimal.
- E. Standard ASA monitoring** of blood pressure, ECG, and pulse oximetry should be used during performance of all regional blocks. Resuscitation equipment should be readily available, including intralipid for local anesthetic systemic toxicity (LAST) (see Chapter 16).
- F. Aseptic technique** should be employed during performance of all blocks. Although the definition of essential aseptic technique is robust, evidence-based studies are lacking. Recent reviews and the ASA practice advisory for prevention of infectious complications in neuraxial anesthesia emphasize the following: removal of jewelry and watches, hand hygiene with an alcohol-based antiseptic, use of cap, mask, and sterile gloves, use of individual packets of chlorhexidine solution (preferably alcohol based) for skin preparation, sterile drape of the patient and maintenance of a sterile procedural field, placement of a sterile occlusive dressing over catheter insertion sites, and proper preparation of local anesthetic solutions. The use of a sterile gown has not been shown to reduce bacterial contamination rates compared to the use of gloves alone in several ICU-based studies and remains controversial.
- G. Postoperative follow-up** should include assessment of block efficacy and duration, patient satisfaction, and presence of residual sensory or motor blockade, paresthesia, and other side effects.

II. GENERAL CONTRAINDICATIONS

Not all patients are suitable for regional anesthesia. Absolute contraindications to regional anesthesia include lack of patient consent, skin infection

at the site of needle insertion, or when nerve blockade would hinder the proposed surgery or desired postoperative neurologic exam. Relative contraindications include coagulopathy, neuropathy, systemic infection, excessive patient anxiety, mental illness, and anatomic distortion. Neuromuscular diseases such as multiple sclerosis, polio, and muscular dystrophy may be aggravated by peripheral nerve blockade.

III. COMPLICATIONS COMMON TO ALL NERVE BLOCKS

- A. Complications of local anesthetics** include intravascular injection (Fig. 18.1), local anesthetic systemic toxicity (LAST) (see Chapter 16 Local Anesthetics), and allergic responses. Use of ultrasound, epinephrine in local anesthetic solutions, and intermittent aspiration during injection may help identify intravascular injection. Benzodiazepine premedication increases the seizure threshold and may decrease the central nervous system toxicity of local anesthetics as well as patient anxiety. However, this may also reduce early recognition of toxicity and therefore should be titrated carefully to prevent oversedation.
- B. Nerve damage is a rare complication that may result from** direct needle trauma, nerve compression and ischemia, or local anesthetic-induced neurotoxicity. Pain with needle advancement or local anesthetic injection suggests an intraneural needle position but is not a reliable predictor. Although pain or paresthesia may also result from external nerve compression by local anesthetic, if encountered during injection, one must consider this complication and redirect needle position.
- C. Hematomas** may result from vascular puncture but usually resolve without residual problems. When considering regional anesthesia for an anticoagulated or coagulopathic patient, one should consider following neuraxial guidelines, particularly for the deeper blocks (e.g., infraclavicular, lumbar

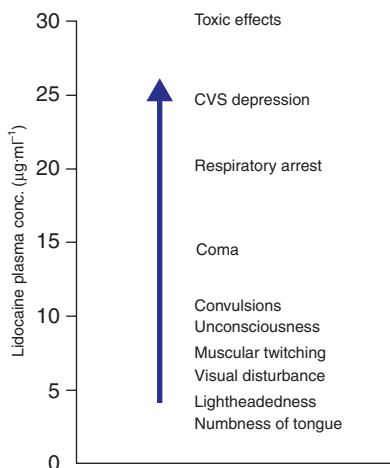


FIGURE 18.1 Progressive continuum of symptoms of lidocaine local anesthetic toxicity. These symptoms are seen in roughly the same progression and proportion with the other local anesthetics, except that cardiovascular system (CVS) toxicity may be seen with the more potent amino amides at blood levels closer to the convulsion threshold. (From Barash PG, Cullen BF, Stoelting RK, eds. *Clinical Anesthesia*. Philadelphia: JB Lippincott; 2009:389, with permission.)

plexus, paravertebral) where vessel compression for bleeding control is challenging (see Chapter 17).

- D. **Infection** risk is reduced with the use of antiseptic skin preparation and the use of sterile equipment and techniques.
- E. **Failure/incomplete block** can be identified with a careful neurologic examination prior to the beginning of the surgical procedure.

IV. EQUIPMENT

A. Needles Used for Nerve Blockade

1. **A block needle** should be the smallest diameter possible for patient comfort. However, block needles often are inserted into deep tissue and therefore need a more rigid shaft. For most peripheral regional blocks, a 22-gauge needle is preferable. For superficial blocks, such as axillary blocks, a 23-gauge needle is suitable.
 2. **Short bevel needles** (30 to 45 degrees) are associated with decreased nerve trauma and intravascular injection compared with standard A bevel needles and have become standard for peripheral nerve blocks. However, some data suggest that the use of smaller, sharp needles may be associated with less damage in the event of a nerve injury because of a “clean cut” of the nerve. Newer needles with a Sprotte or Whitacre tip may be less traumatic.
 3. **Insulated needles** designed for use in nerve stimulator-guided techniques have a small conductive area at the needle tip, which allows for more accurate nerve stimulation at lower amplitudes of current compared to noninsulated needles.
 4. **Echogenic needles** designed for use in ultrasound-guided techniques feature modifications such as texturing or scoring of the needle's surface to enhance reflection of ultrasound waves and improve needle visibility under ultrasound.
 5. **Ideal needle length** varies by block. Upper- and lower-extremity blocks are best performed with a 50- to 150-mm needle depending on the nerve depth. Brachial plexus blocks usually do not require more than a 100-mm needle and can frequently be accomplished, in the case of interscalene block, with a 25- to 50-mm needle.
- B. Many blocks require depositing a large volume of local anesthetic with a single injection. Connecting a large-volume (20-mL) syringe to the block needle with sterile extension tubing ensures stable needle position during aspiration and injection. For larger volumes of local anesthesia, multiple syringes can be attached with a stopcock.
- C. **Nerve stimulators** (Fig. 18.2) designed for regional anesthesia deliver a current of 0.1 to 10.0 mA at a frequency of 1 to 2 Hz and a stimulus duration of 0.1 to 0.3 milliseconds.
- D. **Ultrasound equipment** that is portable and utilizes transducers of various shapes, sizes, and frequencies facilitates imaging of relevant anatomy and serves as an alternative/adjuvant to nerve stimulator approaches. Sterile ultrasound gel and transducer sheaths allow for real-time imaging within a sterile field.
- E. A variety of **continuous catheter kits** and infusion pumps for continuous nerve blockade are commercially available.
- F. **Selection of local anesthetic** should depend upon the desired speed of block onset and duration of block (see Chapter 16 Local Anesthetics).

V. NERVE LOCALIZATION TECHNIQUES

Several techniques may be used to localize target nerves. The classic approach uses anatomical landmarks, tactile feedback from fascial clicks, and elicited paresthesias to guide needle advancement and injection. Nerve

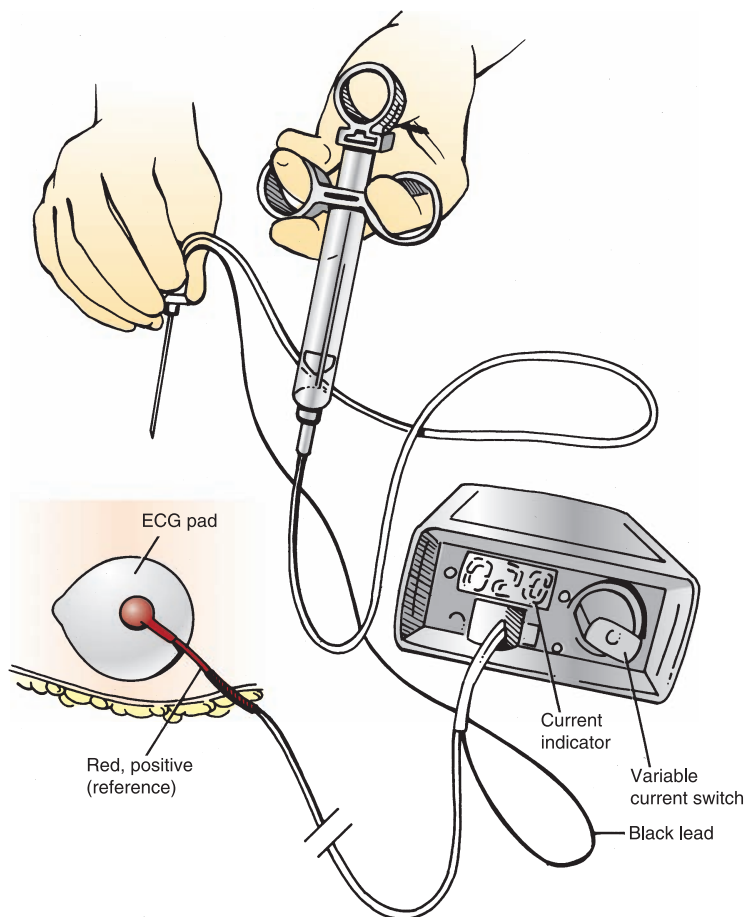


FIGURE 18.2 Nerve stimulator attached to the regional block needle. The negative (*black*) lead is attached to the exploring needle, whereas the positive (*red*) is connected to a reference electrocardiogram pad used as a “ground.” The stimulator is set to deliver 1 to 2 mA of current to detect the nerve. The current is reduced further as the needle approaches the nerve. A current of 0.5 mA will produce motor stimulation when the needle is adjacent to the nerve. (From Mulroy MF, Bernard CM, McDonald SB, et al. *A Practical Approach to Regional Anesthesia*. 4th ed. Philadelphia: Wolters Kluwer; 2009, with permission.)

stimulator-guided techniques allow the operator to estimate the distance of the needle tip from the target nerve based on the magnitude of current required to elicit the desired motor response. Ultrasound-guided techniques allow for real-time visualization of the needle tip, relevant anatomy, and local anesthetic spread and have become widely used in recent years. Studies have shown that the use of ultrasound may reduce block performance time, number of needle passes, and volume of local anesthetic required for successful block and may also reduce the incidence of vascular puncture. Nevertheless, complications such as intravascular and intraneural injection have occurred even with the use of ultrasound.

- A. Eliciting a paresthesia** by contacting a nerve with a needle is a time-honored method of nerve localization. However, this may cause patient discomfort and possibly a higher incidence of postanesthetic dysesthesia or neuropathy. This technique has become less popular as many anesthetists have transitioned practice to either nerve stimulation or ultrasound guidance.
- B. Electrical stimulation** of a mixed nerve produces a motor response without significant pain.
1. Ground the positive lead of the stimulator to the patient and attach the negative terminal of the stimulator to the needle.
 2. Set the nerve stimulator to an initial current of 0.5 to 1.0 mA and move the needle toward the nerve until a motor response in the desired muscle group occurs. If a twitch is uncomfortable, the current should be reduced. Stimulation of the target nerve at a current of 0.2 to 0.5 mA suggests accurate needle placement for local anesthetic administration. Motor response at less than 0.2 mA is suggestive of intraneural placement, and the needle should be withdrawn slightly.
- C. Ultrasound guidance** may replace or supplement the above techniques for peripheral nerve blockade.
1. **Ultrasound** uses high-frequency sound waves to visualize structures and tissues in real-time without ionizing radiation. Within the ultrasound transducer, electric current is applied to a piezoelectric crystal array, which vibrates at high frequency to generate sound waves. As these waves travel out through the tissue being imaged, some are reflected back to the transducer. The intensity and delay in return of the reflected sound waves are used to construct a 2D gray-scale image. Denser substances such as bone reflect more sound waves and appear brighter or **hyperechoic**. Less-dense substances such as air or fluid reflect less and appear darker or **hypoechoic**.
 2. **"Knobology"**: Commercially available ultrasound machines allow the operator to adjust a number of parameters to optimize visualization. **Depth** should be set to the minimum that allows visualization of target structures. **Focus** should be placed just beyond the depth of the target structures. **Gain** determines the overall brightness of the image and may be increased or decreased as needed. **Frequency** affects both image resolution and depth of penetration. Higher frequencies increase the resolution at the expense of penetration (suitable for highly detailed examination of superficial tissues such as the breast and thyroid). Conversely, lower frequencies increase the depth of penetration at the expense of resolution (suitable for examination of deep structures such as the heart, abdominal viscera, and uterus). Most nerve blocks (e.g., infraclavicular, femoral, and sciatic nerve at the popliteal fossa) are performed at an intermediate depth and thus utilize intermediate frequencies. Axillary and interscalene blocks are more superficial and are best imaged at higher frequencies. In obese patients, frequencies may need to be decreased to favor penetration, particularly for infraclavicular, neuraxial, and popliteal fossa blocks. **Color Doppler** is useful for identification of vascular structures.
 3. **Performance** of the block depends on optimal visualization of target structures, proper needle positioning, and adequate spread of local anesthetic around the nerve(s).
 - a. Initial positioning of the ultrasound transducer is determined by surface landmarks and refined by scanning to obtain the optimal view of the anatomy in question. The left–right orientation of the transducer in relation to the image display should be confirmed prior to scanning. Basic scanning maneuvers include sliding the

transducer in the horizontal plane, tilting its vertical axis to various angles in relation to the skin surface, rotating it around its vertical axis, and applying more or less vertical pressure to it. Color Doppler may be employed to identify vascular structures in the intended needle trajectory. Anatomic structures may be viewed in a sagittal, transverse or an oblique plane to facilitate performance of a directly guided nerve block.

- b. There are two options for needle visualization. In the “out-of-plane” approach, the needle is inserted immediately above or below the midline of the transducer and is then advanced perpendicular to the plane of the ultrasound beam. This provides a cross-sectional view of the needle tip as a hyperechoic dot. Alternatively, in the “in-plane” approach, the needle is inserted several centimeters lateral to the transducer and is then advanced in the plane of the ultrasound beam, allowing continuous visualization of the length of the needle as a hyperechoic line. While the in-plane approach results in the needle traversing a longer distance, it may minimize the likelihood of contacting nerves, blood vessels, pleura, and other vital structures during needle passage.
- c. The needle tip should be positioned in close proximity to the target nerve. Spread of local anesthetic should be observed both for evidence of intraneural injection, which may result in nerve injury and should prompt adjustment of needle position, and for adequacy of spread. Circumferential spread of local anesthetic around the target nerve suggests injection in the proper fascial plane. For some blocks, multiple injection sites may be needed to achieve the desired distribution of local anesthetic.

VI. CERVICAL PLEXUS BLOCK FOR REGIONAL ANESTHESIA OF THE NECK

- A. **Anatomy.** The cervical plexus lies in the paravertebral region of the upper four cervical vertebrae (Fig. 18.3). It is formed from the ventral rami of the C1–C4 spinal nerve roots. It is deep to the sternocleidomastoid muscle

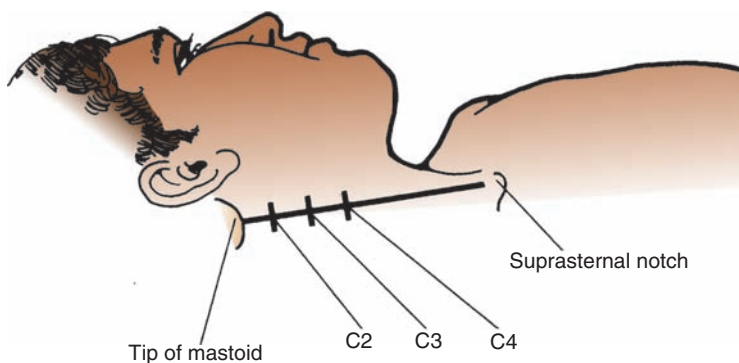


FIGURE 18.3 Superficial landmarks for cervical plexus block. A line is drawn from the mastoid process to the prominent tubercle of the sixth cervical vertebra. The transverse processes of the second, third, and fourth cervical vertebrae lie 0.5 cm posterior to this line and at 1.5-cm intervals below the mastoid. (From Mulroy MF, Bernard CM, McDonald SB, et al. *A Practical Approach to Regional Anesthesia*. 4th ed. Philadelphia: Wolters Kluwer; 2009, with permission.)

(SCM) and anterior to the middle scalene muscle, in continuity with the nerve roots forming the brachial plexus (see section VII.A). The plexus has superficial and deep branches. The **superficial branches** pierce the cervical fascia anteriorly, just posterior to the SCM, and supply the skin of the back of the head, side of the neck, and anterior and lateral shoulder. The **deep branches** supply the muscles and deep structures of the neck and form the phrenic nerve.

- B. Indications. Superficial cervical plexus block** produces only cutaneous anesthesia and is useful for superficial procedures on the neck and shoulder. **Deep cervical plexus block** is a paravertebral block of the C1–C4 nerve roots; anesthetizing both the deep and the superficial branches. Common indications for cervical plexus block are as follows:

1. Cervical lymph node biopsy/excision
2. Carotid endarterectomy
3. Thyroid operations
4. Tracheostomy (when combined with topical airway anesthesia)

- C. Complications** are possible with deep cervical plexus block because of the close proximity of the needle to neural and vascular structures.

1. **Phrenic nerve block** is the most common complication. This block should be used cautiously in patients with diminished pulmonary reserve. Bilateral deep cervical plexus block will produce bilateral phrenic and recurrent laryngeal nerve blockade and therefore should be avoided.
2. **Subarachnoid injection** resulting in total spinal anesthesia.
3. **Epidural injection** with resultant bilateral cervical epidural anesthesia.
4. **Vertebral artery injection** causing central nervous system toxicity with very small doses of local anesthetic.
5. **Recurrent laryngeal nerve block** causing hoarseness and vocal cord dysfunction.
6. **Cervical sympathetic nerve block** producing an ipsilateral Horner syndrome.

D. Techniques

1. **Superficial block with landmark technique:** Position the patient supine with the neck slightly extended and the head turned toward the opposite side. Use a 50-mm, 23- to 25-gauge needle to inject 10 mL of local anesthetic subcutaneously along the posterior border of the SCM.
2. **Superficial block with ultrasound guidance:** Position the patient as above. Place the ultrasound probe transversely over the SCM at the level of the cricoid cartilage and scan posteriorly until the posterior edge of the SCM is visualized in the center of the screen. The supraclavicular nerves may be visualized as two to three small hypoechoic structures between the SCM and scalene muscles. Identify the brachial plexus between the anterior and middle scalene muscles. Insert a 50-mm, 23- to 25-gauge needle just lateral to the probe and advance in plane until the needle tip is beneath the posterior border of the SCM and adjacent or lateral to the plexus. After negative aspiration, inject 10 to 15 mL of local anesthetic and observe spread between the SCM and the underlying prevertebral fascia.
3. **Deep block with landmark technique:** Position the patient as above. Draw a line connecting the tip of the mastoid process and **Chassaignac tubercle** (the most prominent of the cervical transverse processes, located at C6, the level of the cricoid cartilage). Draw a second line 1 cm posterior to the first line. The C2 transverse process can be palpated 1- to 2-cm caudad to the mastoid process, with the C3 and C4 processes lying at 1.5-cm intervals along the second line. At each level, insert a 22-gauge 50-mm

needle perpendicular to the skin with caudal angulation. Advance the needle 1.5 to 3.0 cm until it contacts the transverse process. After careful negative aspiration for cerebrospinal fluid (CSF) or blood, inject 3 to 5 mL of local anesthetic solution at each transverse process.

4. **Deep block with ultrasound guidance:** Ultrasound may be used to guide performance of the deep cervical block. Although no specific technique has emerged as superior, the goal is to identify the pertinent transverse processes, nerve roots, and boundaries of the cervical paravertebral space and to deposit 3 to 5 mL of local anesthetic adjacent to the nerve roots.

VII. REGIONAL ANESTHESIA OF THE UPPER EXTREMITY

A. Anatomy

1. The shoulder, axilla, and upper extremity are innervated by the brachial plexus except for the medial aspect of the upper arm that is innervated by the intercostobrachial nerve formed by the second thoracic nerve root.
2. The **brachial plexus** is formed from the anterior roots of the spinal nerves from C5–C8 and T1, with frequent contributions from C4 and T2.
3. Each **root** exits posterior to the vertebral artery and travels laterally in the trough of its cervical transverse process, where it is directed toward the first rib and fuses with the other four roots to form the three trunks (upper, middle, and lower) of the plexus. The roots are sandwiched between the fascial sheaths of the anterior and middle scalene muscles.
4. The **trunks** pass over the first rib through the space between the anterior and middle scalene muscles, in association with the subclavian artery, which shares the same fascial sheath. The roots and trunks have several branches, innervating the neck, shoulder girdle, and chest wall.
5. As the trunks pass over the first rib and under the clavicle, they split into **divisions**, which then reorganize to form the three **cords** (lateral, medial, and posterior) of the plexus. The cords descend into the axilla, where each has one major branch in addition to several minor branches, before becoming a major terminal nerve of the upper extremity. Branches of the lateral and medial cords form the **median nerve**. The lateral cord gives off a branch that forms the **musculocutaneous nerve**, whereas the posterior cord becomes the **axillary and radial nerves**. The medial cord also forms the **ulnar, medial antebrachial, and brachial cutaneous nerves**. In the axilla, the median nerve classically lies lateral to the axillary artery, the radial nerve posterior, and the ulnar nerve medial, but variation in these relative positions may occur. The axillary and musculocutaneous nerves exit the sheath high up in the axilla, the musculocutaneous nerve traveling through the substance of the coracobrachialis muscle before becoming subcutaneous below the elbow, and the axillary nerve traveling through the quadrilateral space (bordered by the humeral shaft, long head of the triceps, and teres major and minor muscles) before dividing into its terminal branches. The median cutaneous nerves of the arm and forearm are minor branches of the medial cord (Fig. 18.4). The cutaneous peripheral nerve supply of the upper extremity is summarized in Figure 18.5.
6. The **dermatome and sclerotome distribution of the nerves** of the body is summarized in Figure 18.6. Cutaneous innervation does not necessarily correlate with deep structures; therefore, knowledge of the sclerotomes can be very useful in predicting the ultimate success of any regional technique.

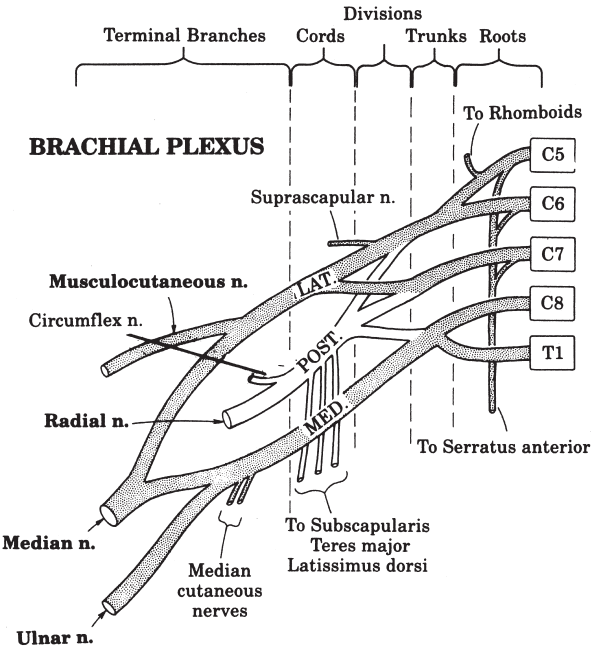


FIGURE 18.4 Diagram of the brachial plexus and peripheral nerve formation.

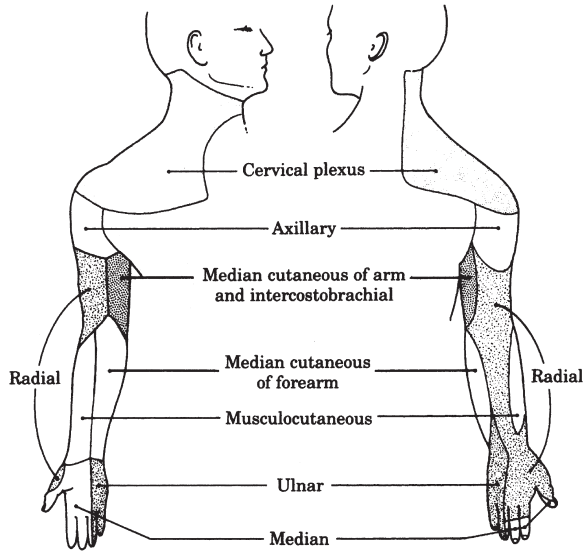


FIGURE 18.5 Cutaneous peripheral nerve supply of the upper extremity.

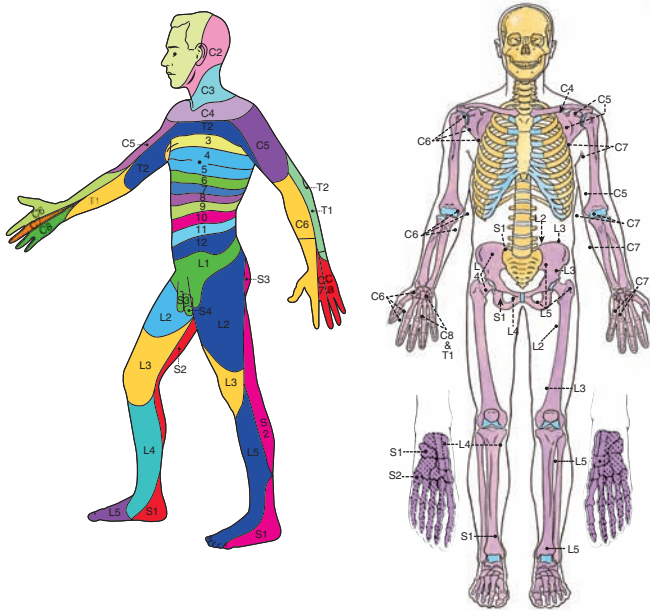


FIGURE 18.6 A side view of the dermatomes (**left**) and an anterior view of the sclerotomes indicated by the different styles of shading (**right**).

7. The major motor functions of the five nerves are as follows:

- a. Axillary (circumflex nerve):** shoulder abduction (deltoid contraction)
- b. Musculocutaneous:** elbow flexion (biceps contraction)
- c. Radial:** elbow (triceps contraction), wrist, and finger extension (extensor carpi radialis longus)
- d. Median:** wrist and finger flexion (flexor carpi radialis).
- e. Ulnar:** wrist and finger flexion (flexor carpi ulnaris)

B. Indications

- 1. Brachial plexus blockade** anesthetizes various areas of the upper extremity, depending on which anatomic level of the brachial plexus is blocked. The preferred approach to the plexus depends on the surgical site, the risk of complications, and the experience of the individual anesthetist.
 - a. The interscalene approach** blocks the brachial plexus at the level of the nerve roots to upper trunks. It also blocks the superficial cervical plexus at local anesthetic volumes above 5 to 10 mL, thereby anesthetizing the skin over the shoulder. The ulnar nerve is frequently spared. This approach is most useful for shoulder and proximal humerus surgery. It is less useful for forearm and hand operations, unless supplemented by an ulnar nerve block.
 - b. The supraclavicular approach** blocks the plexus at the level of the trunks to divisions. Because of the compact nature of the plexus at this point of injection and the fact that very few nerves have yet left the plexus, this approach allows for reliable anesthesia of the entire arm distal to the shoulder.

- c. The **infraclavicular approach** blocks the plexus at the level of the cords and provides excellent coverage for surgery distal to the midhumerus.
- d. The **axillary approach** blocks the terminal branches of the brachial plexus. However, because the musculocutaneous and medial cutaneous nerves of the arm exit the sheath more proximally, they are not consistently blocked by this approach, making it unreliable for operations proximal to the elbow.
- e. The **intercostobrachial nerve, T2**, must be blocked in addition to the plexus for procedures involving the medial arm or using a proximal humeral tourniquet. This is accomplished by subcutaneous infiltration with local anesthetic of the medial aspect of the arm at the level of the axillary fossa.
- f. **Blockade of an individual peripheral nerve** may be useful when limited anesthesia is required or a plexus block is incomplete. The musculocutaneous nerve may be blocked at the axilla or the elbow. Each of the other major terminal nerves may be blocked at the elbow, forearm, or the wrist.

C. Techniques and Complications

1. Interscalene

- a. **Interscalene block using landmark/nerve stimulator technique** (Fig. 18.7): Position the patient supine with the head turned slightly away from

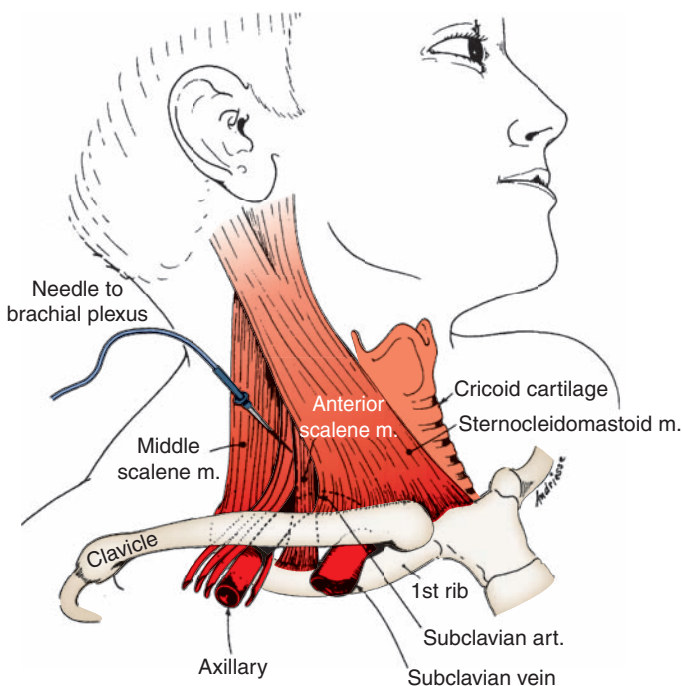


FIGURE 18.7 Interscalene approach to brachial plexus block.

the side to be blocked. Identify the lateral border of the sternocleidomastoid by having the patient lift his or her head off the bed. The anterior scalene muscle lies below the posterior edge of the sternocleidomastoid. By rolling one's fingers posteriorly over the anterior scalene muscle, a groove between the anterior and middle scalenes can be palpated. The intersection of this groove with a transverse plane at the level of the cricoid cartilage is the point at which the needle should enter the skin in a slightly caudad and posterior direction. Because the scalenes are accessory muscles of respiration, asking the patient to take slow deep breaths while palpating for the groove may be helpful. The external jugular vein frequently crosses the groove at the level of the C6 vertebra and may also be a useful landmark. Advance a 25- to 50-mm needle into the groove at a 45-degree angle in a caudal and posterior direction. Stimulation of the plexus will result in a paresthesia or muscle twitch in the deltoid, biceps, triceps, or pectoris major muscles. Paresthesia or twitches confined to the shoulder may result from suprascapular or cervical plexus stimulation and indicate that the needle is posterior to the plexus. Paresthesia or twitches of the diaphragm (hiccoughs) indicate that the needle is just anterior to the plexus. Despite being accurately placed in the groove, the needle will sometimes contact the cervical transverse process without stimulating the plexus. If this happens, withdrawing the needle and redirecting it slightly will likely elicit the correct response. A volume of 30 to 40 mL of anesthetic solution should be injected incrementally after negative aspiration of heme or CSF.

- b. **Interscalene block using ultrasound guidance:** Position the patient supine, semireclined with the arms at the side, or in the lateral decubitus position. Place the probe over the SCM at the level of the cricoid cartilage (C6), and identify the internal carotid artery and internal jugular vein (Fig. 18.8). Move the probe laterally and identify the anterior and middle scalene muscles. At this time, the roots/trunks will come into view as hypoechoic nodular structures often stacked in a "stoplight" configuration between the anterior and middle scalenes. They should be centered on the screen, and a needle insertion point should be chosen just lateral to the probe site. After infiltration with local anesthetic, insert a 22-gauge 50-mm facet-tip needle and advance within the plane of the ultrasound beam toward the target nerves. The middle scalene muscle may or may not be directly traversed. With the former, a distinct increase in resistance followed by a pop will be seen and felt as the needle enters and exits the middle scalene muscle. Another tissue "pop" may be felt when entering the prevertebral fascia. After negative aspiration, deposit 15 to 20 mL of local anesthetic solution between the two scalene muscles. Hypoechoic local anesthetic spread should be visualized in the ultrasound image.
 - c. **Complications** are identical to those of the cervical plexus block (see section VI.D).
2. **Supraclavicular**
 - a. **Supraclavicular block using landmark/nerve stimulator technique:** Position the patient supine with the head turned away from the operative side. Identify the interscalene groove as described above (see section VII.C.1.a.). Palpate the pulse of the subclavian artery inferiorly in this space. Insert a 22-gauge 25- to 50-mm needle just cephalad to the palpating finger in the interscalene groove at the

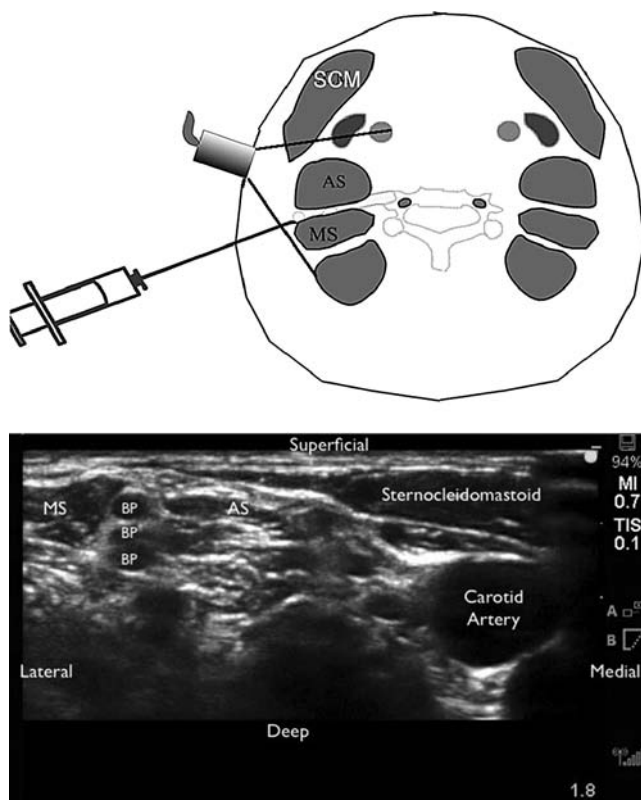


FIGURE 18.8 Interscalene block using ultrasound guidance. SCM, sternocleidomastoid muscle; AS, anterior scalene muscle; MS, middle scalene muscle.

level of the clavicle and advance caudally. The “click” of the needle entering the plexus may be felt, and the plexus may be identified with a nerve stimulator or by the paresthesia technique. Deltoid twitch indicates proximity to the upper trunk, while biceps, triceps, or pectoralis twitch indicates proximity to the medial trunk. The ideal needle position is in close proximity to the lower trunk, which is manifested by a twitch of the fingers in flexion or extension. After negative aspiration, inject 20 to 30 mL of local anesthetic solution.

- b. Supraclavicular block using ultrasound guidance** (Fig. 18.9): Position the patient supine with the head turned to the contralateral side. A blanket roll or pillow behind the shoulder may help facilitate visualization. Place a linear probe in the coronal oblique plane in the supraclavicular fossa. The brachial plexus will be visualized as a hypoechoic group of nerves located laterally and caudally to the prominent subclavian artery. Deep to the artery, the hyperechoic first rib is typically seen; however, the pleura is obscured by the

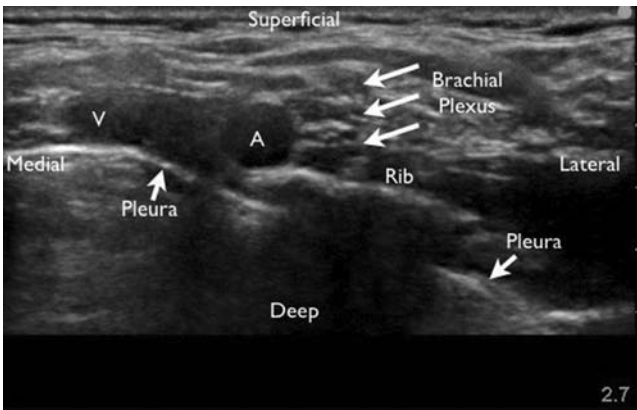


FIGURE 18.9 Supraclavicular block using ultrasound guidance. A, subclavian artery; B, brachial plexus; V, subclavian vein; R, rib; P, Pleura.

rib's acoustic shadow. Insert a 22-gauge 25- to 50-mm needle just lateral to the probe and within the plane of the ultrasound beam, and advance until it reaches the brachial plexus. After negative aspiration, slowly administer 15 to 20 mL of local anesthetic solution. The ideal site of local anesthetic deposition is in the "eight pocket" between the plexus and subclavian artery, just above the first rib. Spread of local anesthetic should be observed throughout the "bunch of grapes" (cluster of nerves). If not, additional injection of local anesthetic may be necessary after repositioning the needle.

- c. **Complications** include pneumothorax, phrenic nerve block, and Horner syndrome in addition to those mentioned in section V.

3. Infraclavicular

a. **Infraclavicular block using landmark/nerve stimulator technique:**

Position the patient supine with the extremity slightly abducted and the palm upward. Landmarks to be palpated include the clavicle, coracoid process, and chest wall. After identifying the coracoid process, mark 2 cm inferior and 2 cm medial, making sure this needle insertion mark is superior to the chest wall (between coracoid process and chest wall). Using a 100-mm insulated needle with a nerve stimulator starting 0.5 and 1.0 mA, advance the needle in a plumb-bob direction until motor stimulation indicates contact with the cord level of the brachial plexus. If no contact is made, the first redirection should be away from the chest wall. Stimulation of the lateral cord will give flexor carpi radialis stimulation and/or some wrist and finger flexion (median nerve). Stimulation of the posterior cord will produce extension at the elbow and/or wrist (radial nerve). Stimulation of the medial cord produces flexor carpi ulnaris movement with some flexion of the wrist and/or fingers (median and ulnar nerves). A successful block can occur with loss of motor stimulation at 0.3 to 0.5 mA in any of the three cords; however, stimulation of the posterior cord generally results in a higher success rate. After aspiration is performed and deemed negative for blood, inject 30 to 40 mL of local anesthetic in 3- to 5-mL increments, aspirating prior to each injection.

- b. Infraclavicular block using ultrasound guidance:** Position the patient supine with the arm abducted 90 degrees at the shoulder and the forearm supinated so the palm faces up. Place the probe in the infraclavicular fossa (at the deltopectoral groove); identify the axillary artery and vein and hyperechoic cords of the brachial plexus lying in lateral, posterior, and medial positions to the artery (Fig. 18.10). A needle insertion site is identified approximately 1 cm. superior to the probe. A 22-gauge 100- to 150-mm needle is appropriate for use in obese or muscular patients. Smaller 50- to 80- mm needles are best for smaller or thinner patients. Insert the needle and advance at a 45-degree angle to the skin, keeping in the plane of the ultrasound

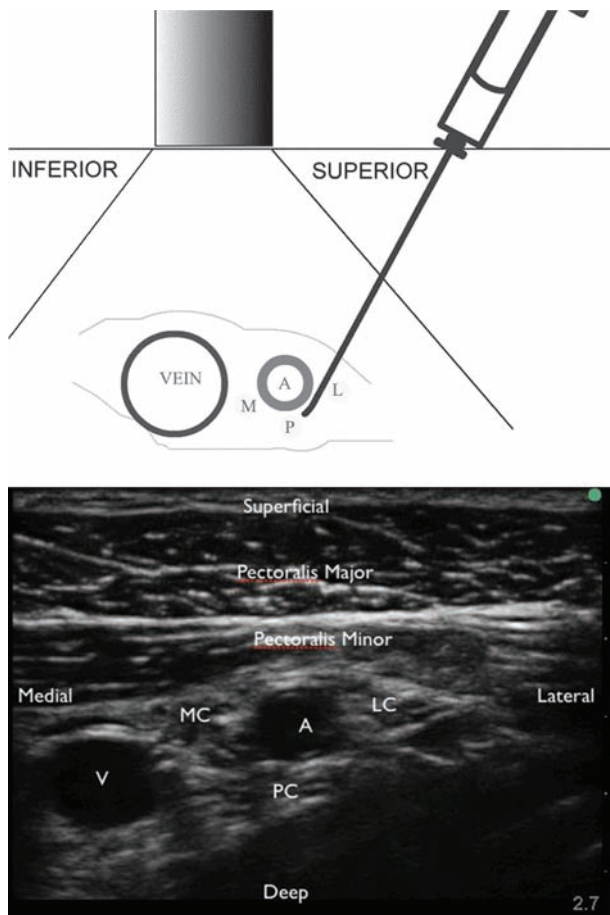


FIGURE 18.10 Infraclavicular block using ultrasound guidance. V, axillary vein; A, axillary artery; M, medial cord of brachial plexus; P, posterior cord of brachial plexus; L, lateral cord of brachial plexus.

beam, until the tip is positioned posterior to the axillary artery (i.e., in the 6 o'clock position). After negative aspiration, deposit 20 to 30 mL of local anesthetic solution with a goal of distribution around the axillary artery. This may require repositioning the needle after partial injection to achieve spread in both locations.

c. **Complications** include pneumothorax in addition to those mentioned in section V.

4. Axillary (Fig. 18.11)

a. **Axillary block using landmark/nerve stimulator technique:** Position the patient supine with the arm abducted 90 degrees at the shoulder, externally rotated and flexed at the elbow. Palpate the axillary artery at its most proximal location in the axilla. If the artery is difficult to palpate, move the patient's hand laterally or reduce the degree of abduction at the shoulder. Advance a 23-gauge, 25- to 50-mm needle through the skin just superior to the palpating fingertip, directing the needle toward the apex of the axilla. Localization of one of the nerves of the plexus by either paresthesia or nerve stimulation confirms that the needle tip is within the

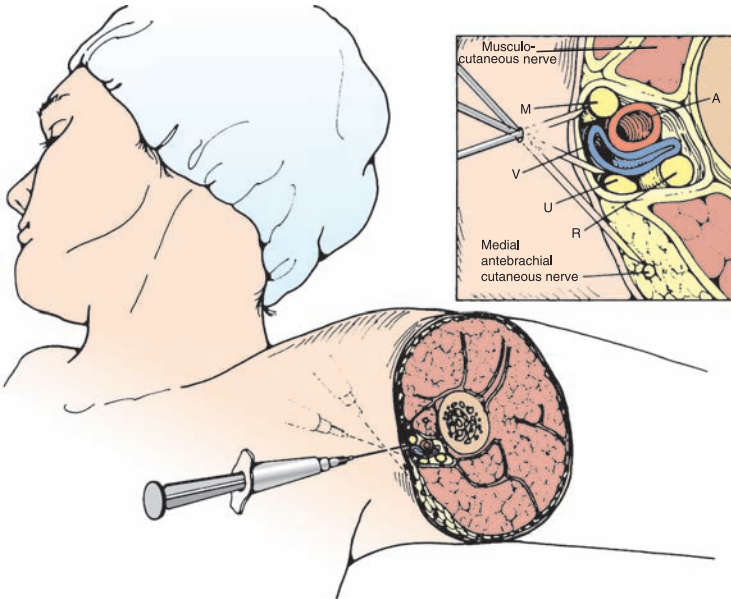


FIGURE 18.11 Needle position for axillary injection. The median (M) and musculocutaneous nerves lie on the superior side of the artery (A). The latter usually lies within the body of the coracobrachialis muscle at this point. The ulnar (U) nerve lies inferior and the radial (R) nerve is inferior and posterior to the artery. These positions may vary with individual patients. The medial antebrachial cutaneous nerve usually lies in the subcutaneous tissues just inferior to the neurovascular bundle and is anesthetized by a subcutaneous wheal along that area, along with the intercostobrachial fibers. (From Mulroy MF, Bernard CM, McDonald SB, et al. *A Practical Approach to Regional Anesthesia*. 4th ed. Philadelphia: Wolters Kluwer; 2009, with permission.)

plexus sheath; 30 to 40 mL of local anesthetic may be injected. If the axillary artery is penetrated, advance the needle through the posterior wall of the artery.

Frequently, a “pop” will be felt as the sheath is penetrated. If this occurs and the needle pulsates in synchrony with the pulse, the tip of the needle is located within the sheath and the anesthetic may be injected. For greater confidence, confirmation of needle location through the use of ultrasound or nerve stimulator will improve the quality and duration of block.

- b. Redirect the needle so that the tip of the needle is just superior to the artery and perpendicular to the skin in all planes. Advance the needle until the humerus is contacted and then, moving the tip through a 30-degree arc superiorly, 5 mL of local anesthetic solution can be injected in a fanwise pattern. This will block the **musculocutaneous nerve** in the body of coracobrachialis muscle.
- c. **Intercostobrachial nerve block** requires subcutaneous injection of 5 mL of anesthetic, directly inferior to the axillary artery and extending to the inferior border of the axilla.
- d. **Axillary nerve block using ultrasound guidance:** Position the patient supine with the arm abducted 90 degrees at the shoulder, externally rotated and flexed at the elbow. Place the transducer over the axillary artery to obtain a cross-sectional view, and position the artery in the center of the screen (Fig. 18.12). Three hyperechoic nerves can be appreciated in the perivascular area. Special care should be taken to identify veins as pressure from the transducer may easily compress and obscure them from view. Insert a 22-gauge 25- to 50-mm needle superior to the transducer and advance toward the nerves within the plane of the ultrasound beam. After negative aspiration, inject a total of 20 to 30 mL of local anesthetic in close proximity to the axillary artery. The goal is 360-degree spread around the axillary artery, which may be achieved by single injection at the “6 o’clock” position relative to the artery or by injection at multiple sites.
- e. Next, identify the **musculocutaneous nerve** as a hyperechoic oval or triangular structure between the coracobrachialis and biceps muscles. Without changing the needle entry site, using a more perpendicular trajectory, position the needle tip adjacent to the nerve and inject 2 to 5 mL of local anesthetic solution.
- f. **Complications** include injection of local anesthetic into the axillary artery in addition to those mentioned in section V.

5. Ulnar nerve block

- a. **At the elbow**, locate the ulnar groove in the medial epicondyle and inject 5 to 10 mL of local anesthetic solution 3 to 5 cm proximal to the groove in a fanwise pattern.
- b. **At the wrist** (Fig. 18.13), the ulnar nerve is just lateral to the flexor carpi ulnaris tendon at the level of the ulnar styloid process. Pierce the deep fascia with the needle oriented perpendicular to the skin, just lateral to the tendon, and inject 3 to 6 mL of solution.

6. Median nerve block

- a. **At the elbow** (see Fig. 18.13), the median nerve is just medial to the brachial artery. Palpate the artery 1 to 2 cm proximal to the elbow crease and inject 3 to 5 mL of anesthetic just medial to it in a fanwise pattern.

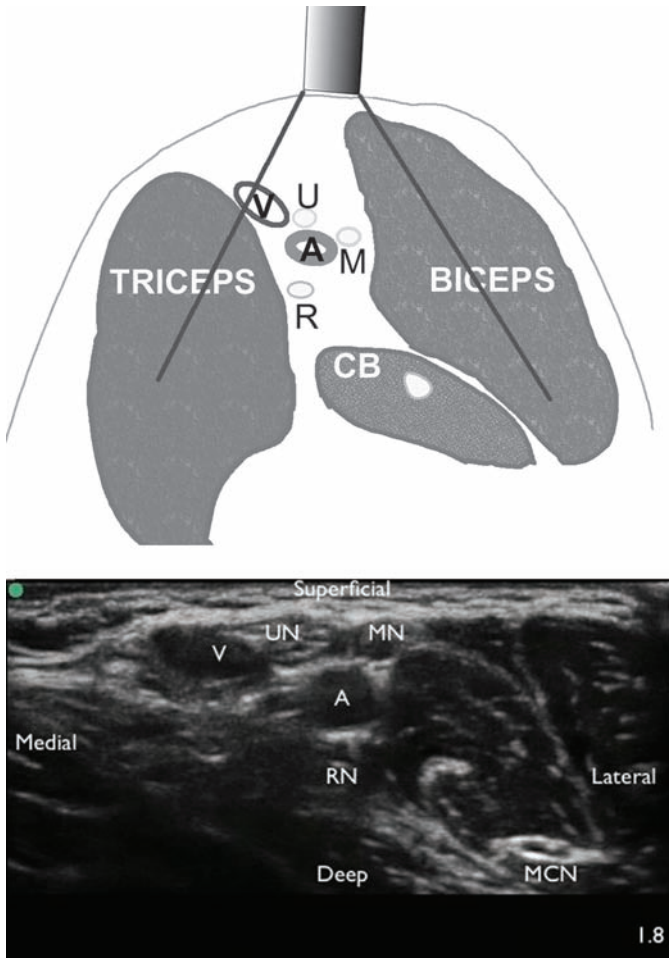


FIGURE 18.12 Axillary nerve block using ultrasound guidance. V, axillary vein; A, axillary artery; M, median nerve; U, ulnar nerve; R, radial nerve; CB, coracobrachialis muscle.

- b. **At the wrist** (see Fig. 18.13), the median nerve lies between the palmaris longus tendon and the flexor carpi radialis tendon, 2 to 3 cm proximal to the wrist crease. Pierce the deep fascia with the needle oriented perpendicular to the skin close to the lateral border of the palmaris longus and inject 3 to 5 mL of anesthetic.

7. Radial nerve block

- a. **At the elbow** (see Fig. 18.13), the radial nerve lies lateral to the biceps tendon, medial to the brachioradialis muscle, at the level of the lateral epicondyle of the humerus. Insert the needle 1 to 2 cm lateral to the tendon and advance until it contacts the lateral epicondyle. Inject 3 to 5 mL of anesthetic solution.

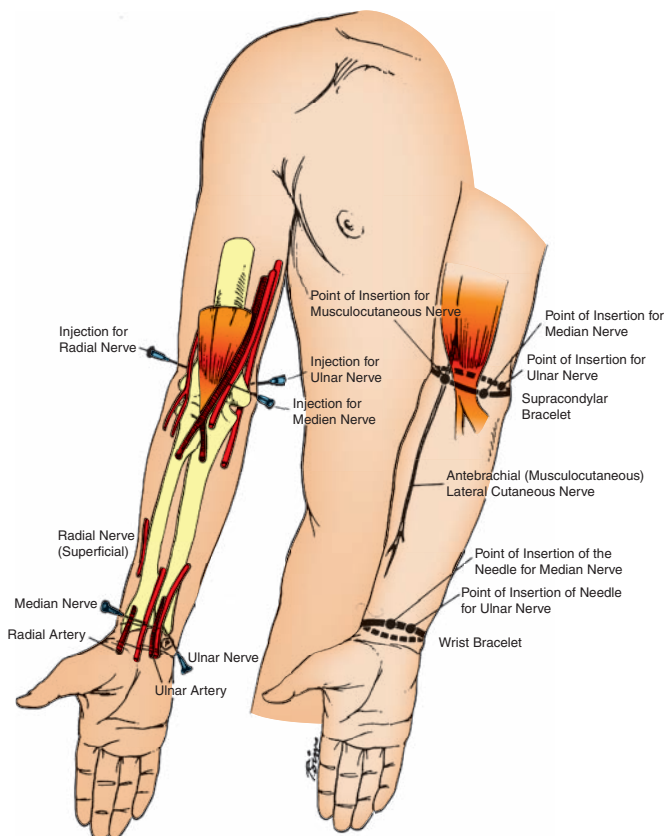


FIGURE 18.13 Deep anatomy for elbow and wrist block of musculocutaneous, radial, ulnar, and median nerves. (Modified from Raj PP. *Clinical Practice of Regional Anesthesia*. New York: Churchill Livingstone; 1991, with permission.)

- b. **At the wrist**, the radial nerve divides into its terminal branches in the superficial fascia. Inject 5 to 10 mL of local anesthetic subcutaneously, extending from the radial artery anteriorly to the extensor carpi radialis posteriorly, beginning just proximal to the wrist.
8. **Musculocutaneous nerve block**: The musculocutaneous nerve may be blocked in the axilla, as described in section VII.C.4.b. Its terminal cutaneous component is blocked concomitantly with the radial nerve block at the elbow.
9. **Block of the terminal nerves of the brachial plexus with ultrasound guidance** can be accomplished at the level of the elbow and the wrist. Utilizing the anatomical landmarks described above, the peripheral nerves can be seen as hyperechoic structures and targeted with 5 to 10 mL of local anesthetic.

- 10. Intravenous (IV) regional anesthesia (Bier block):** IV administration of local anesthetic distal to a tourniquet is a simple way to anesthetize an extremity for short-duration procedures (60 minutes or less).
- Place a 20- to 22-gauge IV catheter (heplock) as distally as possible in the extremity to be blocked. Apply a pneumatic double tourniquet proximally and exsanguinate the extremity by elevating it and wrapping it distally to proximally with an Esmarch bandage.
 - Both tourniquet cuffs should be checked. Inflate the proximal cuff to 150 mm Hg greater than systolic pressure. Absence of pulses after inflation ensures arterial occlusion. Remove the Esmarch bandage and slowly inject the anesthetic into the previously placed IV catheter. High-pressure injection can overcome the tourniquet and lead to systemic spread of local anesthetic. Average drug doses are 50 mL of 0.5% lidocaine for an arm. Although Bier block has been described for the leg, it is generally not utilized for two primary reasons. It is difficult to achieve complete vascular occlusion with a tourniquet, and the volume of local anesthetic required increases the potential of systemic toxicity.
 - Anesthesia occurs within 5 minutes of local anesthetic injection. Tourniquet pain generally becomes unbearable after 1 hour and is the limiting factor for the success of this technique. When the patient complains of pain, the distal tourniquet that overlies the anesthetized skin should be inflated and the proximal tourniquet released. Some advocate changing cuffs at 45 minutes, before the onset of pain.
 - For shorter procedures of the hand, wrist, and distal forearm, a single-cuffed tourniquet may be applied proximally on the forearm. Generally, 25 to 30 mL of 0.5% lidocaine provides sufficient anesthesia and facilitates early deflation of the tourniquet.
 - The major **complication** associated with IV regional anesthesia is local anesthetic toxicity. It may occur during injection if the tourniquet fails or after tourniquet deflation, particularly with a short inflation time. Careful attention to drug dosage and to the adequacy of vascular occlusion will minimize the risk of local anesthetic toxicity. During injection and deflation of the tourniquet, the patient should be observed closely for evidence of toxicity.

VIII. REGIONAL ANESTHESIA OF THE LOWER EXTREMITY

- A. Anatomy.** There are two major plexuses that innervate the lower extremity: the lumbar plexus and the sacral plexus.
- The **lumbar plexus** (Fig. 18.14) is formed within the psoas muscle from the anterior rami of the L1–L4 spinal nerves, with a contribution from the 12th thoracic nerve. The most cephalad nerves of the plexus are the **iliohypogastric**, **ilioinguinal**, and **genitofemoral nerves**. These nerves pierce the abdominal musculature anteriorly before supplying the skin of the hip and groin. The remainder of the lower abdomen is supplied by intercostal nerves. The three caudal nerves of the lumbar plexus are the **lateral femoral cutaneous (LFC)**, **femoral**, and **obturator nerves**.
 - The **LFC nerve** passes under the lateral end of the inguinal ligament, supplying sensory innervation to the lateral thigh and buttock.
 - The **femoral nerve** passes under the inguinal ligament just lateral to the femoral artery and supplies the muscles and skin of the anterior thigh as well as the knee and hip joints. From there, it courses with the femoral artery and vein through the **adductor canal**, an anatomic

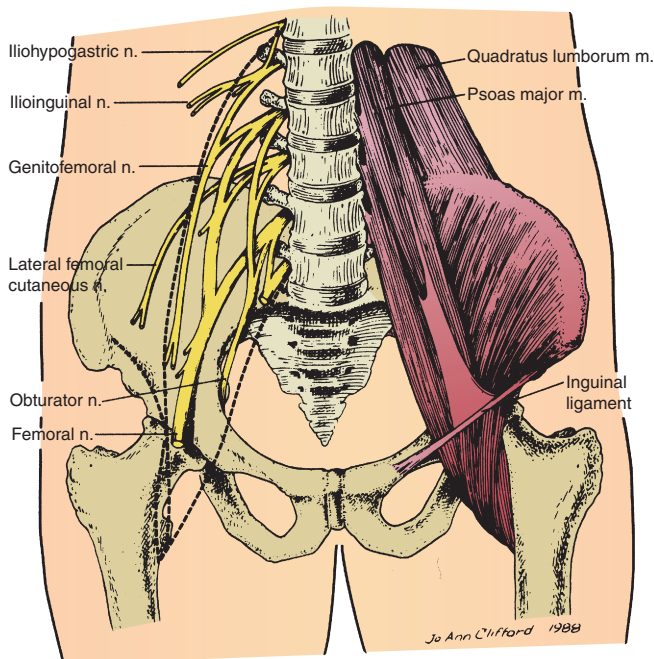


FIGURE 18.14 The lumbar plexus lies in the psoas compartment between the psoas major and quadratus lumborum. (Modified from Miller RD. *Anesthesia*. 6th ed. New York: Churchill Livingstone; 2004.)

tunnel bounded by the fascial planes of the sartorius, the vastus medialis, and the adductor longus and magnus. The nerve and vessels exit the canal at the adductor hiatus just above the medial femoral condyle. The **saphenous nerve** is the cutaneous termination of the femoral nerve, supplying the skin of the medial leg and foot. It is the only nerve of the lumbar plexus that innervates the leg below the knee.

- c. The **obturator nerve** exits from the pelvis through the obturator canal of the ischium, innervating the adductor muscles of the thigh, the hip and knee joints, and a portion of the skin of the medial thigh.
2. The **sacral plexus** is formed from the anterior rami of the L4–L5 lumbar nerves and the S1–S3 sacral nerves. The two major nerves of the sacral plexus are the sciatic nerve and the posterior cutaneous nerve of the thigh.
 - a. The **posterior cutaneous nerve of the thigh** travels with the sciatic nerve in its proximal extent and supplies the skin of the posterior thigh. Techniques for blocking the sciatic nerve will also block the posterior cutaneous nerve of the thigh.
 - b. The **sciatic nerve** passes out of the pelvis through the greater sciatic foramen, becomes superficial at the lower border of the gluteus maximus, descends along the medial aspect of the femur supplying

branches to the hamstrings, and becomes superficial again at the popliteal fossa. There, it divides into the tibial nerve and the common peroneal nerve.

1. The **tibial nerve** travels down the posterior calf and passes under the medial malleolus before dividing into its terminal branches. It supplies the skin of the medial and plantar foot and causes plantar flexion.
2. The **common peroneal nerve** winds around the head of the fibula before dividing into the superficial and deep peroneal nerves.
 - a. The **superficial peroneal nerve** is a sensory nerve that passes down the lateral calf, dividing into its terminal branches just medial to the lateral malleolus, supplying the anterior foot.
 - b. The **deep peroneal nerve** enters the foot just lateral to the anterior tibial artery, lying at the superior border of the malleolus, in between the anterior tibialis tendon and the extensor hallucis longus tendon. Although primarily a motor nerve causing dorsiflexion of the foot, it also sends a sensory branch to the web space between the first and second toes.
 - c. The **sural nerve** is a sensory nerve formed from branches of the common peroneal and tibial nerves. It passes under the lateral malleolus, supplying the lateral foot.
- B. **Indications.** Anesthetizing the entire lower extremity requires blocking components of both the lumbar and sacral plexuses. When choosing which blocks to utilize, considerations include surgical site, use of tourniquet, and whether the goal is surgical anesthesia or postoperative analgesia.
 1. The **ilioinguinal–iliohypogastric block** is a simple and very useful block, providing excellent analgesia for **groin operations** (e.g., hernia repair). Lower-abdominal operations can also be performed with combined lumbar plexus block and intercostal nerve blocks or paravertebral blocks.
 2. **Hip operations** require anesthesia of the entire lumbar plexus with the exception of the iliohypogastric and ilioinguinal nerves. This is most easily accomplished with a **lumbar plexus block (psoas block)**.
 3. **Major thigh operations** (e.g., placement of a femoral rod) require anesthesia of the LFC, femoral, obturator, and sciatic nerves. These operations may be performed with a **combined psoas–sciatic block**.
 4. **Operations limited to the anterior thigh** may be performed with a **combined LFC–femoral block**. The nerves may be blocked separately or together with a “3-in-1” block (see section IX.C.2). Alone, an LFC block gives excellent analgesia for skin graft donor sites on the anterior thigh. An isolated femoral nerve block is particularly useful for providing postoperative analgesia for femoral shaft fractures or as the sole anesthetic for quadricepsplasty or repair of a patellar fracture.
 5. **For thigh tourniquet pain**, a combined LFC–femoral nerve block, in concert with a sciatic block, will usually provide adequate analgesia. This is because the area of skin that the obturator nerve supplies is generally small.
 6. **Open operations on the knee** require anesthesia of the LFC, femoral, obturator, and sciatic nerves, which is most easily accomplished with a **combined psoas–sciatic block**. For knee arthroscopy, combined 3-in-1 and femoral–sciatic nerve blocks provide adequate anesthesia. Single-shot or continuous **femoral nerve block** or **adductor canal block** is an alternative for postoperative analgesia to cover the discomfort of the skin incision.
 7. **Operations distal to the knee** require **sciatic block and block of the saphenous** component of the femoral nerve. The branches of the sciatic nerve can be

blocked with multiple injections at the ankle or with a single injection at the gluteal, subgluteal or midfemoral level or in the popliteal fossa. The latter is particularly useful when cellulitis is present at the ankle. Ankle block will provide reliable anesthesia for transmetatarsal and toe amputations.

- C. Complications** specific to lower-extremity blocks include epidural blockade with potential sympathectomy, vascular injury, perforated viscus, and renal injury (lumbar plexus block).
- D. Techniques** for localization for lower-extremity block procedures can be performed by paresthesia nerve stimulation, and ultrasound-guided techniques.

1. Ilioinguinal–iliohypogastric block

- a. Ilioinguinal–iliohypogastric block using landmark technique:** Insert a 25-mm 22-gauge needle perpendicular to the skin and 3 cm medial to the anterior superior iliac spine (ASIS). Contact the ASIS and inject 10 to 15 mL of local anesthetic while withdrawing the needle to the skin.
- b. Ilioinguinal–iliohypogastric block using ultrasound guidance:** Place the transducer medial to the ASIS along a line connecting the ASIS and umbilicus. Identify the nerves as hyperechoic structures in the fascial plane between the internal oblique and transversus abdominus muscles. Insert a 25-mm 22-gauge needle medial to the probe and advance in a medial-to-lateral direction in the plane of the ultrasound beam until the needle tip is within the previously described fascial plane. After negative aspiration, inject 10 mL of local anesthetic.

2. Lumbar plexus block (psoas block)

- a. Lumbar plexus block using landmark/nerve stimulator technique:** Local anesthetic deposited into the substance of the psoas muscle will be confined by its fascia and will anesthetize the entire plexus. Place the patient in the lateral position, hips flexed, with the surgical side uppermost. Insert a 22-gauge 150-mm needle perpendicular to the skin at a point 3-cm cephalad to a line connecting the iliac crests and 4 to 5 cm lateral to the midline. If the transverse process of L4 is contacted, redirect the needle. Localize the plexus by using a nerve stimulator, which will produce a quadriceps muscle twitch. Inject 30 to 40 mL of local anesthetic. **Epidural blockade** is a complication of this approach, occurring with an incidence of approximately 10%. Rare, but catastrophic, bleeding into the retroperitoneum has also been described.
- b. Lumbar plexus block using ultrasound guidance:** Position the patient as above. Place a curved 2- to 5-MHz transducer in the longitudinal plane at the desired level of blockade (L2–4). Scan from medial to lateral and identify the transverse processes, paraspinal muscles (superficial to the transverse processes), psoas muscle (deep to the transverse processes), and peritoneum (deep to the psoas muscle), noting the depth of all structures. Next, turn the transducer in the transverse or sagittal oblique plane. Identify the posterior one third of the psoas muscle, where the lumbar plexus is located. The plexus itself is unlikely to be visualized. Insert a 22-gauge 150-mm needle medial to the transducer and advance from medial to lateral within the plane of the ultrasound beam until the needle tip lies in the posterior one third of the psoas muscle. After negative aspiration, inject 30 to 40 mL of local anesthetic.
- 3. A 3-in-1 block** attempts to block the three branches of the lumbar plexus with a single injection. However, 3-in-1 block most often anesthetizes only the femoral and obturator nerves, sparing the LFC. The fascia iliaca block anesthetizes the femoral and LFC nerves but rarely the obturator nerve.

- a. With the patient in the supine position, insert a 50- to 80-mm 22-gauge needle just caudad to the inguinal ligament and lateral to the femoral artery. Direct the needle cephalad at a 45-degree angle until a quadriceps twitch or paresthesia is elicited. After negative aspiration, inject 30 to 40 mL of local anesthetic.
4. An alternative approach is the **fascia iliaca compartment block**. It consists of injecting local anesthetic behind the fascia iliaca at the junction of the lateral and middle thirds of a line drawn from the pubic tubercle to the ASIS.
5. **LFC nerve block** (Fig. 18.16). Insert a 25-mm 22-gauge needle 1 to 2 cm caudal and medial to the ASIS. Direct the needle in a slightly lateral and cephalad direction, striking the iliac bone medially just below the ASIS, and inject 5 to 10 mL of local anesthetic.
6. **Femoral nerve block** (see Fig. 18.15)

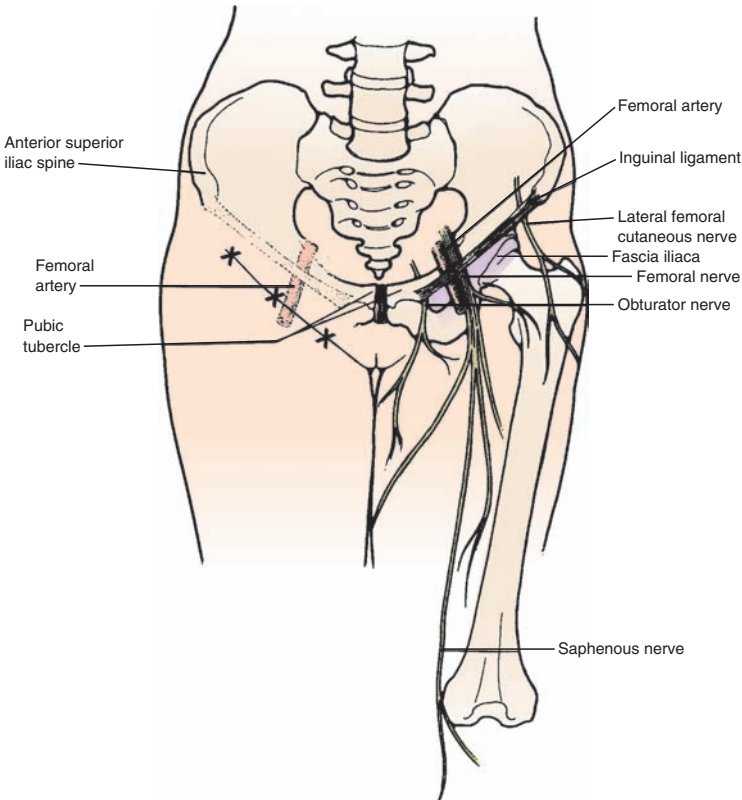


FIGURE 18.15 Block of the anterior lumbosacral branches in the groin. The LFC nerve emerges approximately 1 to 2 cm medial to the ASIS and is best blocked along the line 1-2 cm caudad to the ASIS. The femoral nerve emerges alongside and slightly posterior to the femoral artery and is again easily approached approximately 2.5 cm below the inguinal ligament. On that same line, the obturator nerve emerges from the obturator canal but is deeper and less reliably located. (From Mulroy MF, Bernard CM, McDonald SB, et al. *A Practical Approach to Regional Anesthesia*. 4th ed. Philadelphia: Wolters Kluwer; 2009, with permission.)

- a. **Femoral nerve block using landmark/nerve stimulator technique** is carried out identically to the 3-in-1 block (see section IX.C.2), with elicitation of quadriceps or patella tendon contraction. A volume of 15 to 20 mL of local anesthetic suffices.
- b. **Fascia iliaca/femoral nerve block using ultrasound guidance** is performed with the patient supine. Place the ultrasound probe over the femoral artery at the level of the femoral crease and move approximately 1 cm laterally so that the femoral artery is at the medial edge of the image (Fig. 18.16). Two separate fascial layers can be visualized overlying the iliopsoas muscle: the superficial fascia lata and the deeper fascia iliaca. The femoral nerve can be visualized just deep to the fascia iliaca and lateral to the femoral artery. Insert a 22-gauge needle at least 50-mm long and advance medially at a 60-degree angle to the skin. As the needle is advanced, two distinct “pops” are felt and seen (each an initial increase of resistance followed by sudden loss of resistance as the two fascial layers are traversed). At this point, having passed through the fascia lata and the fascia iliaca, the needle tip should lie between the fascia iliaca and the iliopsoas muscle. After negative aspiration, inject local anesthetic. Approximately 20 mL is sufficient to block the femoral nerve alone, while more volume is generally required to additionally block the LFC and obturator nerves. Note that it is not necessary for the needle tip to be directly next to the femoral artery or nerve for the block to be successful. If the needle is in the proper plane, local anesthetic spread is seen mostly in the horizontal direction, easily reaching the femoral and LFC nerves.
7. **Adductor canal block using ultrasound guidance** anesthetizes the femoral nerve at the level of the mid thigh as it courses through the adductor canal. Blocking the femoral nerve here as opposed to at the inguinal crease has

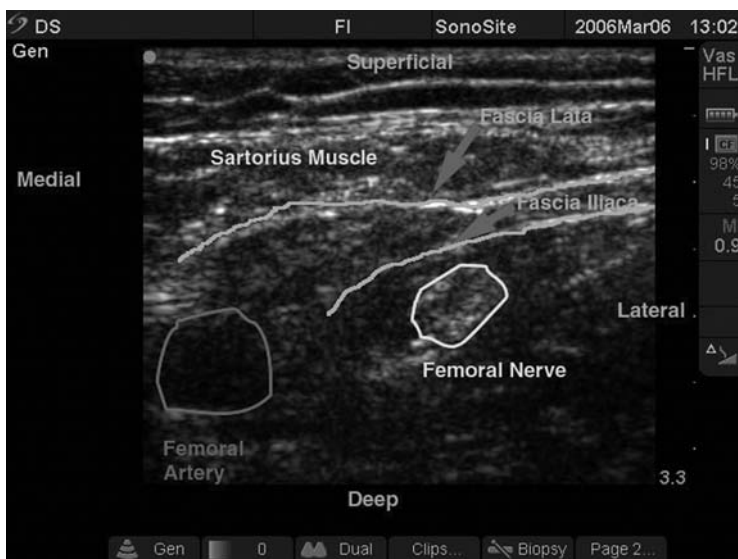


FIGURE 18.16 Fascia iliaca/femoral nerve block using ultrasound guidance.

been shown to result in equivalent analgesia with potentially less motor blockade of the quadriceps. Place the patient in the supine position, with the operative leg externally rotated and slightly flexed at the knee. Scan with the ultrasound probe to identify the femoral artery deep to the sartorius at the medial aspect of the midthigh. The femoral nerve bundles can be visualized as echodense structures adjacent to the femoral artery. Insert a 80- to 100-mm 22-gauge needle lateral to the probe, and advance toward the target structures. After negative aspiration, deposit 5 to 10 mL of local anesthetic on each side of the femoral artery.

8. Obturator nerve block (Fig. 18.15).

a. Obturator nerve block with landmark/nerve stimulator technique: With the patient in the supine position, identify the pubic tubercle and insert an 80-mm 22-gauge needle 1.5 cm caudal and 1.5 cm lateral to the tubercle. After contacting the bone, withdraw the needle and redirect it slightly lateral and caudal while advancing 2 to 3 cm into the obturator foramen. Electrical stimulation of the obturator nerve will elicit an adductor twitch. After negative aspiration, inject 20 mL of local anesthetic while fanning laterally.

b. Obturator nerve block with ultrasound guidance: Position the patient supine. Place the transducer on the medial thigh just below the inguinal crease. Identify the anterior branch of the obturator nerve in the fascial plane between the adductor longus and brevis muscles. Identify the posterior branch in the fascial plane between the adductor brevis and magnus muscles. Advance an 80-mm 22-gauge needle until the tip lies in the appropriate fascial plane, and inject 5 to 10 mL of local anesthetic around each branch. Both in-plane and out-of-plane approaches may be used.

9. Sciatic nerve block may be used for surgery of the thigh when blocked proximally in combination with femoral nerve blockade, surgery of the knee when combined with blockade of the femoral, LFC, and obturator nerves, or foot and ankle surgery when combined with saphenous nerve (femoral) blockade.

a. Classic posterior/gluteal approach using landmark/nerve stimulator technique: Place the patient in the Sims position (the lateral decubitus position with the leg to be blocked uppermost and flexed at the hip and knee; Fig. 18.17). Identify the posterior superior iliac spine and greater trochanter and draw a straight line connecting the two structures. At its midpoint, draw a perpendicular line inferiorly for 3 to 4 cm. Insert an 80- to 100-mm 22-gauge needle perpendicularly to the skin, 3 cm below the midpoint, and connect the needle to a nerve stimulator set at an initial current of 2.5 mA. Advance the needle to a depth of approximately 3 cm to elicit a motor response in the sciatic distribution (contraction of hamstring or gastrocnemius; foot dorsiflexion or plantar flexion) or paresthesia in the leg or foot. If buttock contraction is observed, the inferior or superior gluteal nerves are being stimulated, and the needle is simply redirected. When an appropriate motor response is noted, decrease the stimulus current in a stepwise fashion to determine the threshold for stimulation. Reposition the needle until the goal of a stimulus threshold less than 1.0 mA is reached. After a test dose, inject 20 to 30 mL of local anesthetic, aspirating the syringe after each 5 mL is injected. A double-injection technique identifies and injects the tibial and peroneal components of the sciatic nerve separately, through the same skin insertion site.

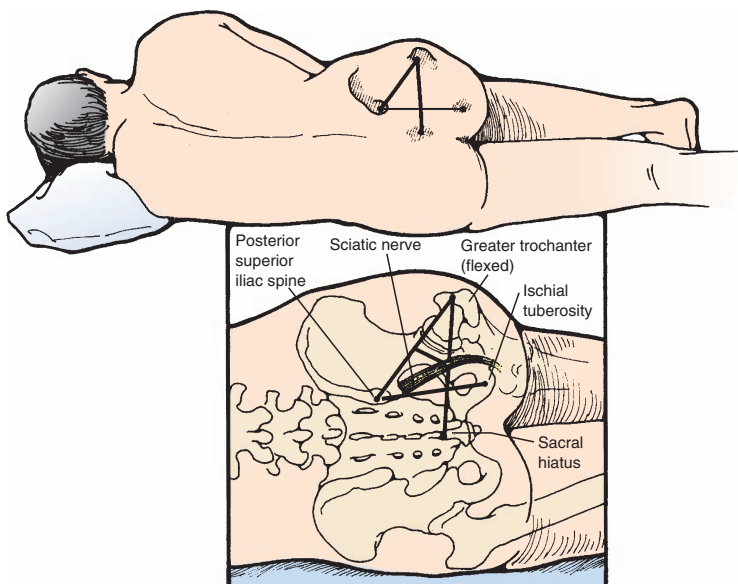


FIGURE 18.17 Sciatic nerve block, classic posterior approach. With the patient in the lateral position and the hip and knee flexed, the muscles overlying the sciatic nerve are stretched to allow easier identification. The nerve lies beneath a point 5-cm caudad along the perpendicular line that bisects the line joining the posterior superior iliac spine and the greater trochanter of the femur. This is also usually the intersection of that perpendicular with another line joining the greater trochanter and the sacral hiatus. (From Mulroy MF, Bernard CM, McDonald SB, et al. *A Practical Approach to Regional Anesthesia*. 4th ed. Philadelphia: Wolters Kluwer; 2009, with permission.)

- b. Classic posterior/gluteal approach using ultrasound guidance:** Position the patient as above. Place a curved transducer between the greater trochanter and ischial tuberosity. Visualize the hyperechoic sciatic nerve in the transverse plane at the level of the ischial spine, deep to the gluteus maximus muscle and superficial to the quadratus femoris muscle. Insert an 80- to 100-mm 22-gauge needle lateral to the transducer and advance in plane until the needle tip is in proximity to the nerve. After negative aspiration, inject 15 to 20 mL of local anesthetic with the goal of circumferential spread around the nerve.
- c. Lithotomy/subgluteal approach using landmark/nerve stimulator technique:** With the patient supine, flex the lower extremity as far as possible at the hip and support it by stirrups or an assistant. The Sims, or lateral recumbent, position is another option. Locate the midpoint of a line between the greater trochanter and the ischial tuberosity. Insert an 80- to 100-mm 22-gauge needle attached to a nerve stimulator perpendicular to the skin at this point and advance the needle until a motor response is seen, indicating sciatic nerve stimulation. Inject 20 to 30 mL of local anesthetic, aspirating intermittently.
- d. Subgluteal approach using ultrasound guidance:** Position the patient in the Sims position, or prone. Perform as gluteal approach above,

but a few centimeters more distally where the gluteus maximus is thinner and the sciatic nerve is more superficial.

- e. **Anterior approach using landmark/nerve stimulator technique:** Position the patient supine with both legs extended. Draw a line connecting the ASIS and the pubic tubercle. Palpate the femoral pulse along this line. Draw a second line overlying the femoral pulse and perpendicular to the first line, extending 4 to 5 cm caudally. The end of the second line is the needle insertion point. Insert a 100- to 150-mm 22-gauge needle at this point and advance perpendicular to the skin, stabilizing the soft tissue and quadriceps muscle with the other hand. Foot or toe twitch is usually elicited at a depth of 10 to 12 cm. After negative aspiration, inject 15 to 20 mL of local anesthetic.
- f. **Anterior approach using ultrasound guidance:** Position the patient as above. Place a curved transducer in the transverse plane on the antero-medial aspect of the proximal thigh at the level of the minor trochanter. The femoral artery is visualized just deep to the sartorius muscle, and the femur is seen deep to the vastus intermedius. Medial to the femur is the adductor magnus muscle. The sciatic nerve appears as a hyperechoic oval deep to the adductor magnus, typically at a depth of 6 to 8 cm. Insert a 100- to 150-mm 22-gauge needle (in-plane or out-of-plane) and advance until the needle tip is in proximity to the sciatic nerve. After negative aspiration, inject 15 to 20 mL of local anesthetic with the goal of circumferential spread around the nerve.
- g. **Popliteal approach using landmark/nerve stimulator technique** (Fig. 18.18). With the patient prone, flex the knee at 30 degrees. This outlines the borders of the popliteal fossa, which is bounded by the knee crease inferiorly, the long head of the biceps femoris laterally, and the superimposed tendons of the semimembranosus and semitendinosus muscles medially. Draw a vertical line on the skin, dividing the fossa into two triangles. Insert an 80-mm 22-gauge needle 6 cm superior to the knee crease and 1 cm lateral to the line bisecting the fossa. Use a nerve stimulator to localize the nerve and inject 30 to 40 mL of local anesthetic, aspirating intermittently.
- h. **Popliteal approach using ultrasound guidance** may be performed posteriorly with the patient in the prone position, although a lateral approach in a supine patient may also be utilized. The probe is placed at the level of the popliteal crease, and the popliteal artery should be seen in cross-section. The artery is then followed cephalad 5 to 7 cm. The popliteal vein classically lies superficial and lateral to the artery, and the sciatic nerve lies even more superficial and lateral to the vein. The sciatic nerve appears as a bright, hyperechoic structure 10 to 18 mm in diameter (Fig. 18.19). The semimembranosus muscle is seen medial, and the biceps femoris is seen lateral to the nerve. These muscles become more prominent with cephalad movement of the probe. The nerve should be traced cephalad and caudad to identify the site of bifurcation into the tibial and common peroneal nerves. In the prone position, with the sciatic nerve centered in the image, and taking an in-plane approach, a needle insertion site is chosen approximately 1 cm lateral to the probe. A 22-gauge 80-mm block needle is appropriate (although larger 17- to 20-gauge needles may be needed for more muscular or obese patients) and is inserted and advanced at an appropriate angle to the skin to allow positioning of the needle tip adjacent to the nerve at the point of bifurcation. After aspiration is performed and deemed negative for

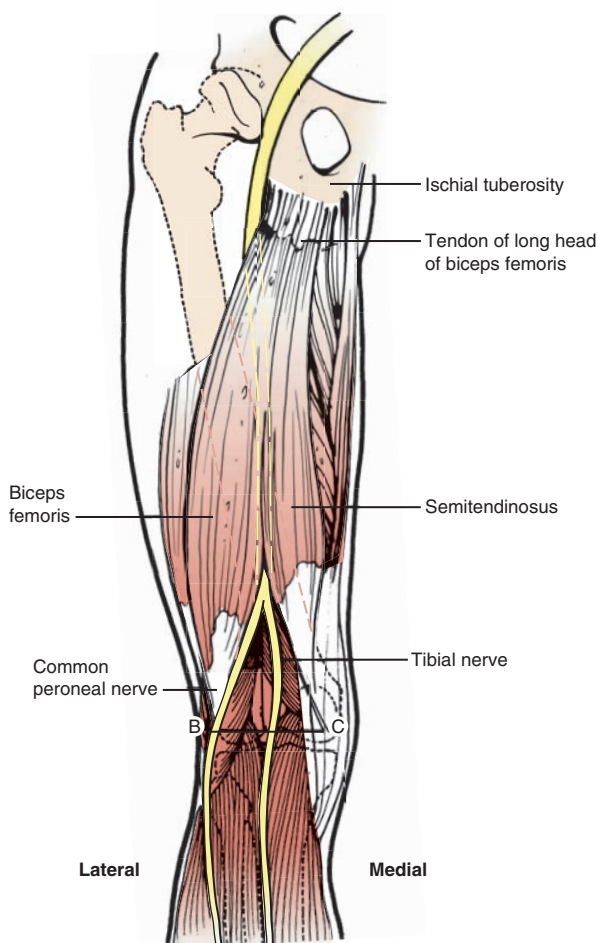


FIGURE 18.18 Popliteal fossa block. The two major trunks of the sciatic nerve bifurcate in the popliteal fossa 7 to 10 cm above the knee. A triangle is drawn using the heads of the biceps femoris and the semitendinosus muscles and the skin crease of the knee; a long needle is inserted 1 cm lateral to a point 6-cm cephalad on the line from the skin crease that bisects this triangle. (From Mulroy MF, Bernard CM, McDonald SB, et al. *A Practical Approach to Regional Anesthesia*. 4th ed. Philadelphia: Wolters Kluwer; 2009, with permission.)

blood, 20 to 30 mL of local anesthetic is injected with a goal of circumferential spread around the nerve.

- 10. Saphenous nerve block.** The saphenous nerve (femoral) can be blocked at the ankle (see section IX.C.9) or at the knee. At the knee, inject 10 mL of local anesthetic in the deep subcutaneous tissue, extending from the medial surface of the tibial condyle to the superimposed tendons of

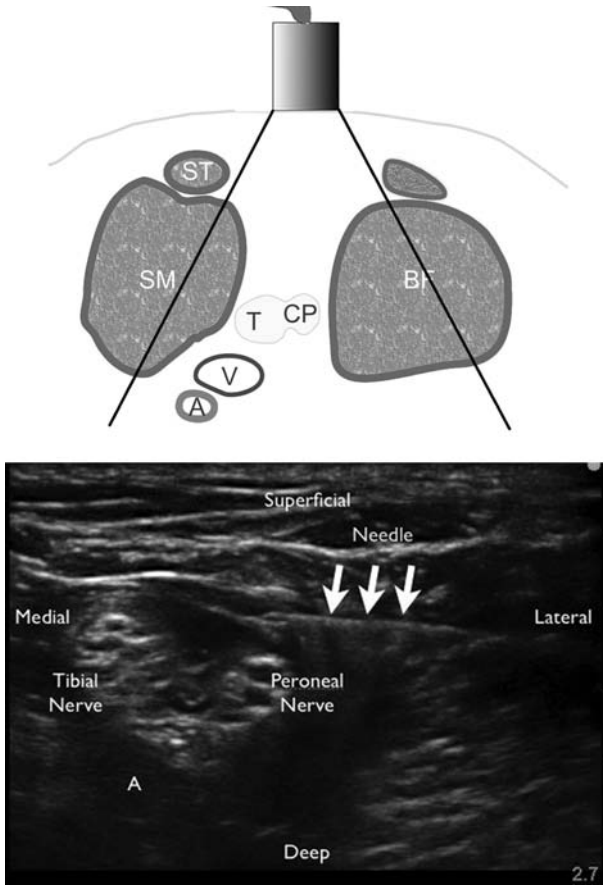


FIGURE 18.19 Sciatic nerve block at the knee using ultrasound guidance. *T*, tibial nerve; *CP*, common peroneal nerve; *SM*, semimembranosus muscle; *BF*, biceps femoris muscle; *ST*, semitendinosus muscle; *A*, popliteal artery; *V*, popliteal vein.

the semimembranosus and semitendinosus muscles. At the level of the knee, the saphenous nerve may be visualized with ultrasound guidance as a hyperechoic structure next to the saphenous vein.

11. Ankle block (Fig. 18.20)

- a. The five nerves supplying the foot can be blocked at the ankle. Elevate the foot on a pillow to provide easy access to both sides of the ankle.
- b. At the superior border of the malleoli, the **deep peroneal nerve** is situated between the anterior tibialis tendon and the extensor hallucis longus tendon, which are easily palpable with the dorsiflexion of the foot and extension of the great toe. Insert a 25-mm needle just lateral to the anterior tibial artery between the two tendons until

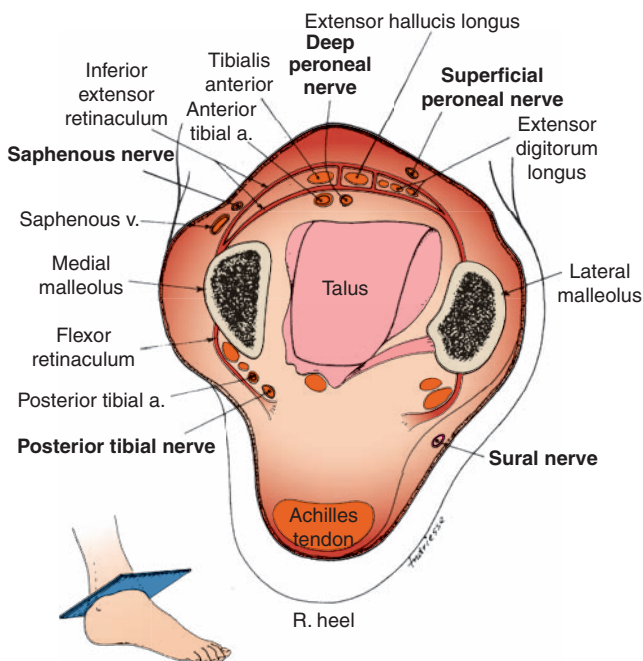


FIGURE 18.20 Cross-section at the level of the ankle.

- contacting the tibia and then withdraw the needle while depositing 5 to 10 mL of local anesthetic.
- c. Then, inject a 10-mL volume of local anesthetic subcutaneously across the anterior surface of the tibia, from malleolus to malleolus. This will block the **superficial peroneal nerve** laterally and the **saphenous nerve** medially.
 - d. To block the **posterior tibial nerve**, insert a needle posterior to the medial malleolus, directed toward the inferior border of the posterior tibial artery. A paresthesia may be noted in the sole of the foot. Withdraw the needle 1 cm from the point of bony contact and inject 5 to 10 mL of local anesthetic in a fan-shaped area.
 - e. Block the **sural nerve** by inserting the needle midway between the Achilles tendon and the lateral malleolus, directing it toward the posterior surface of the lateral malleolus. After contacting the bone, withdraw the needle and inject 5 mL of local anesthetic.
 - f. **Ultrasound guided ankle block** can be performed with a small linear high-frequency probe. The posterior tibial, sural, and deep peroneal nerves are easily identified as hyperechoic structures along their typical anatomical distribution. The saphenous nerve may be indentified adjacent to the saphenous vein. The superficial peroneal nerve is best blocked by a field block as the terminal nerves at the level of the ankle are not easily visualized. Local anesthetic, 3 to 5 mL may be deposited adjacent to each nerve.

IX. THORACIC PARAVERTEBRAL BLOCK FOR REGIONAL ANESTHESIA OF THE THORAX AND ABDOMEN

- A. Anatomy.** The thoracic paravertebral space is a wedge-shaped space containing the intercostal nerves, dorsal rami, sympathetic chain, as well as adipose tissue and the intercostal vessels (Fig. 18.21). The boundaries of this space are formed anteriorly by the parietal pleura and posteriorly by the superior costotransverse ligament, which adjoins the lower border of the transverse process from above to the upper border of the rib below. The base of this wedge is formed by the lateral border of the vertebral body, intervertebral foramen, and intervertebral disk. The apex of this wedge continues laterally in conjunction with the intercostal space. The left and right paravertebral spaces at a specific level are in continuity with each other medially via the intervertebral foramen and epidural space and anteriorly via the prevertebral space.
- B. Indications.** Thoracic paravertebral block produces unilateral somatic and sympathetic sensory loss and is useful for surgical procedures involving the chest and upper abdomen. Indications for paravertebral blocks include rib fractures, thoracotomy, breast surgery, and herniorrhaphy.
- C. Contraindications.** In addition to those already specified for regional anesthesia, relative contraindications for paravertebral block include previous thoracotomy or thoracic spine surgery, kyphoscoliosis, or chest wall deformity, all of which may predispose to pneumothorax.
- D. Complications** specific to this block include pneumothorax, and intrathecal or epidural injection.
- E. Technique**

- 1. Paravertebral block using landmark technique:** Place the patient in the sitting or prone position. Identify the spinous processes of the appropriate dermatomal levels and mark the skin 2.5 cm laterally to approximate the transverse process (of the inferior vertebra). While infiltrating the skin with local anesthetic over the transverse process, a 25-gauge needle can be advanced to identify the depth and plane at which the process is encountered. Advance a Tuohy needle (18- to 20-gauge) until contact

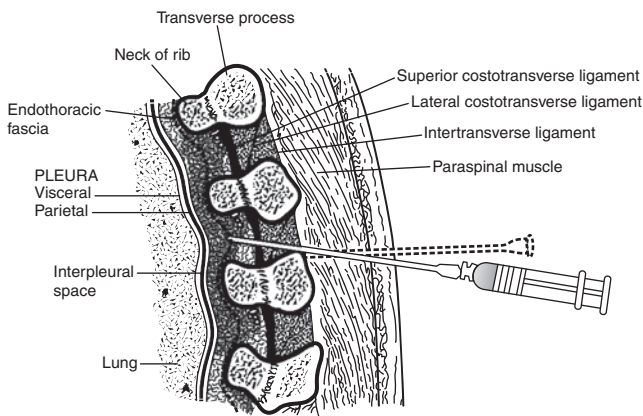


FIGURE 18.21 Sagittal section through the thoracic paravertebral space showing a needle that has been advanced above the transverse process. (From Karmakar MJ. Thoracic paravertebral block. *Anesthesiology* 2001;95:771–780.)

with the transverse process is made. Withdraw the needle slightly and advance 1 to 1.5 cm in a cephalad or caudad direction walking off of the transverse process. A subtle pop may be appreciated as the needle tip traverses the superior costotransverse ligament. Some authors advocate using a loss-of-resistance technique as an alternative to localizing the paravertebral space. Nerve stimulation has been found to improve the efficacy of landmark technique paravertebral block. After gentle aspiration for CSF, air, or blood, inject 3 to 5 mL of local anesthetic at each level. Alternatively, a continuous catheter may be advanced into the space to provide prolonged analgesia. Typically a single-level injection will spread up to three dermatomes; therefore, injection at multiple levels may be necessary for wider coverage.

2. **Thoracic Paravertebral block using ultrasound guidance** may be performed with an **out of plane or paramedian approach**. Place the probe parasagittally several centimeters lateral to the spinous processes, and scan medially until the transverse processes and thoracic paravertebral space (TPVS) are visualized. Insert a Tuohy or facet-tip needle at the midline of the probe, and walk off the transverse process as above. A subtle fascial click may be appreciated, and depression of the pleura with local anesthetic injection should be visualized if the costotransverse ligament has been traversed. An in-plane paramedian approach may also be used; however, steep insertion angles make needle visualization challenging. Tissue hydrodissection with local anesthetic may aid in confirming the position of the needle tip as it is advanced into the paravertebral space. Alternately, an **in-plane or intercostal approach** may be used to allow continuous visualization of the needle. Place the ultrasound probe transversely just lateral to the spinous processes at the level of the rib of the desired thoracic level. The rib is easily visualized as a shallow hyperechoic structure with acoustic shadowing below it. Move the probe slightly cranially or caudally off the rib into the intercostal space and visualize the hyperechoic pleura and the shadow of the transverse process. The TPVS appears as a hypoechoic triangle bounded by the pleura below, the hyperechoic innermost intercostal membrane (contiguous with the costotransverse ligament medially) above, and the transverse process medially. Insert an 80- to 100-mm 22-gauge facet-tip or larger Tuohy needle laterally to the probe, and advance medially toward the TPVS. Continuous visualization of the needle tip is essential to avoid pleural puncture. After negative aspiration, 3 to 5 mL of local anesthetic may be injected at a multiple single levels, or alternatively a larger volume (up to 20 mL) may be injected at a single midpoint level. A catheter may be placed to provide continuous analgesia. Depression of the pleura is observed with injection of local anesthetic, and spread can be traced cranially and caudally.

X. TRANSVERSUS ABDOMINIS PLANE (TAP) BLOCK FOR REGIONAL ANESTHESIA OF THE ABDOMEN

- A. **Anatomy.** The anterior abdominal wall receives sensory innervation from the anterior (ventral) rami of the T7–T12 and L1 spinal nerves. The terminal branches of these nerves travel through the lateral abdominal wall within the transversus abdominis plane (TAP), the fascial plane between the internal oblique and the transversus abdominis muscles. Of note, just deep to the transversus abdominis lies the transversalis fascia and parietal peritoneum.
- B. **Indications.** TAP block provides unilateral analgesia of the anterior abdominal wall including the skin, muscles, and parietal peritoneum. Theoretically, block of T7–L1 can be achieved, but in clinical practice

extent of the block is variable. TAP block is most reliable for providing postoperative analgesia for abdominal incisions below the umbilicus (e.g., laparotomy for colorectal surgery, appendectomy, radical retropubic prostatectomy, abdominal hysterectomy, Cesarean section, laparoscopy). Bilateral block is required for midline incisions.

C. Complications specific to TAP block include perforated viscus.

D. Technique

- 1. TAP block using landmark technique:** Position the patient supine with the abdomen exposed from costal margin to iliac crest. For obese patients, padding or tilting the bed to raise the operative side up 30 degrees can be helpful. Identify the Triangle of Petit, an anatomic triangle between the lower costal margin and iliac crest. It is bounded by the iliac crest at its base, the external oblique anteriorly, and the latissimus dorsi posteriorly. Insert an 80- to 100-mm 22-gauge blunt-tipped needle perpendicular to the skin within the Triangle of Petit. Advance the needle until two “pops” are felt. The first indicates needle passage through the external oblique fascia, and the second through the internal oblique fascia into the TAP. After negative aspiration, inject 20 to 30 mL of local anesthetic per side or thread a catheter for continuous analgesia.
- 2. TAP block using ultrasound guidance** is performed in the same position as the landmark approach. Place the ultrasound probe transversely between the lower costal margin and the iliac crest over the anterior axillary line. Identify the three muscular layers of the abdominal wall: the external oblique (EOM), internal oblique (IOM), and transversus abdominis (TAM). Deep to the TAM, the parietal peritoneum may be visualized with loops of bowel sliding beneath it. Insert an 80- to 100-mm 22-gauge blunt-tipped needle 2 cm medial to the probe at a 30-degree angle to the skin. Advance in the plane of the ultrasound beam until the needle tip lies in the fascial plane between the IOM and TAM. After negative aspiration, inject 20 to 30 mL of local anesthetic per side or thread a catheter for continuous analgesia. Spread can be traced between the IOM and TAM superiorly and inferiorly.

XI. RECTUS SHEATH BLOCK FOR REGIONAL ANESTHESIA OF THE ABDOMEN

- A. Anatomy.** The rectus abdominis muscle (RAM) is located beneath the superficial fascia of the abdomen. Laterally, the aponeurosis of the EOM, IOM, and TAM splits to form the anterior and posterior rectus sheath, which then rejoin in the midline at the linea alba. The terminal branches of the 9th, 10th, and 11th intercostal nerves run between the IOM and TAM to penetrate the posterior wall of the RAM and end in an anterior cutaneous branch supplying the skin of the umbilical area.
- B. Indications.** Rectus sheath block anesthetizes the periumbilical area from T9 to T11. It is useful for analgesia after umbilical hernia repair and other midline abdominal incisions.
- C. Complications** specific to rectus sheath block include perforated viscus and intravascular injection into the epigastric arteries.
- D. Technique**

- 1. Rectus sheath block using landmark technique:** Position the patient supine with the abdomen exposed. Insert an 80- to 100-mm 22-gauge blunt-tipped needle perpendicular to the skin at a point 2 to 3 cm lateral to and just cephalad to the umbilicus. Advance the needle until the “pop” of passage through the anterior rectus sheath is felt. Advance further until the resistance of the posterior rectus sheath is felt. After negative aspiration, inject 10 to 20 mL of local anesthetic per side.

2. **Rectus sheath block using ultrasound guidance:** Position the patient supine with the abdomen exposed. Place the ultrasound probe transversely just lateral to the umbilicus. Insert an 80- to 100-mm 22-gauge blunt-tipped needle medial to the probe and advance in plane in a medial-to-lateral direction through the anterior rectus sheath and RAM until the tip rests against the posterior rectus sheath. After negative aspiration, inject 10 to 20 mL of local anesthetic per side.

Suggested Readings

- ASA Task Force. Practice advisory for the prevention, diagnosis, and management of infectious complications associated with neuraxial techniques. *Anesthesiology* 2010;112:530–545.
- Awad I, Duggan E. Posterior lumbar plexus block: anatomy, approaches, and techniques. *Reg Anesth Pain Med* 2005;30:143–149.
- Chan VS, Perlas A, Rawson R, et al. Ultrasound-guided supraclavicular brachial plexus block. *Anesth Analg* 2003;97:1514–1517.
- Chan VS. *Ultrasound Imaging for Regional Anesthesia: A Practical Guide Booklet*. USRA, <http://www.usra.ca/booklet.php>.
- Cousins MJ, Bridenbaugh PO. *Neural Blockade in Clinical Anesthesia and Management of Pain*. 3rd ed. Philadelphia: Lippincott-Raven; 1998.
- Dalens B, Vanneville G, Tanguy A. Comparison of the fascia iliaca compartment block with the 3-in-1 block in children. *Anesth Analg* 1989;69:705–713.
- De Andres J, Sala-Blanch X. Peripheral nerve stimulation in the practice of brachial plexus anesthesia: a review. *Reg Anesth Pain Med* 2001;26:478–483.
- Gray, A. *Atlas of Ultrasound-Guided Regional Anesthesia*. 2nd ed. Philadelphia: Elsevier, Saunders; 2013.
- Halaszynski TM. Ultrasound brachial plexus anesthesia and analgesia for upper extremity surgery: essentials of our current understanding, 2011. *Curr Opin Anaesthesiol* 2011;24(5):581–591.
- Hebl J, Niesen A. Infectious complications of regional anesthesia. *Curr Opin Anaesthesiol* 2011;24:573–580.
- Karmakar MJ. Thoracic paravertebral block. *Anesthesiology* 2001;95:771–780.
- Kim D, Lin Y, Goytizolo EA, et al. Adductor canal block versus femoral nerve block for total knee arthroplasty: a prospective, randomized, controlled trial. *Anesthesiology* 2014;120(3):540–550.
- Ihnatsenka B, Boezaart A. Applied sonoanatomy of the posterior triangle of the neck. *Int J Shoulder Surg* 2010;4(3):63–74.
- Lissauer J, Mancuso K, Merritt C, et al. Evolution of the transversus abdominis plane block and its role in postoperative analgesia. *Best Pract Res Clin Anaesthesiol* 2014;28(2):117–126.
- Neal JM, Bernards CM, Hadzic A, et al. ASRA practice advisory on neurologic complications in regional anesthesia and pain medicine. *Reg Anesth Pain Med* 2008;33:404–415. NYSORA.com/techniques.
- Raj PP. *Textbook of Regional Anesthesia*. New York: Churchill Livingstone, 2002.
- Sala Blanch X, Lopez AM, et al. Intraneural injection during nerve stimulator-guided sciatic nerve block at the popliteal fossa. *Br J Anaesth* 2009;102:855–861.
- Shriki J. Ultrasound physics. *Crit Care Clin* 2014;30(1):1–24.
- Sites BD, Taenzer AH, Herrick MD, et al. Incidence of local anesthetic systemic toxicity and postoperative neurologic symptoms associated with 12,668 ultrasound-guided nerve blocks: an analysis from a prospective clinical registry. *Reg Anesth Pain Med* 2012;37(5):478–482.
- Spence BC, Beach ML, Gallagher JD, et al. Ultrasound-guided interscalene blocks: understanding where to inject the local anaesthetic. *Anaesthesia* 2011;66(6):509–514.
- Sripada R, Bowens C. Regional anesthesia procedures for shoulder and upper arm surgery: upper extremity update- 2005 to present. *Int Anesthesiol Clin* 2012;50(1):26–46.
- Vloka JD, Hadzic A, April E, et al. The division of the sciatic nerve in the popliteal fossa: anatomical implications for popliteal nerve blockade. *Anesth Analg* 2001;92:215–217.
- Warman P, Nicholls B. Ultrasound-guided nerve blocks: efficacy and safety. *Best Pract Res Clin Anaesthesiol* 2009;23(3):313–326.

I. HYPOTENSION

Hypotension is a significant decrease of arterial blood pressure below the patient's usual range. It may be due to a decrease in cardiac function (contractility), systemic vascular resistance (SVR or afterload), venous return (preload), or to the presence of dysrhythmias.

A. Contractility

1. Most anesthetic agents, including **inhalational agents**, **barbiturates** and **benzodiazepines** (see Chapter 12) cause dose-dependent direct myocardial depression. **Opiates** are not direct myocardial depressants in usual clinical doses, though clinically significant bradycardia and hypotension may be observed due to decreased sympathetic outflow.
2. **Cardiac medications** such as β -adrenergic antagonists, calcium channel blockers and lidocaine, are myocardial depressants.
3. **Acute cardiac dysfunction** may occur with myocardial ischemia or myocardial infarction (MI), hypocalcemia, severe acidosis or alkalosis, hypothermia of less than 32°C, cor pulmonale, vagal reflexes, and systemic toxicity from local anesthetics (particularly bupivacaine).

B. Decreased SVR

1. A decrease in SVR can be seen with many of the drugs administered during anesthesia.
 - a. **Isoflurane** and, to a lesser extent, sevoflurane and desflurane produce a dose-dependent decrease in SVR.
 - b. **Opiates** and **propofol** produce loss of vascular tone by reducing sympathetic nervous system outflow.
 - c. **Benzodiazepines** may decrease SVR, particularly when administered at high doses in conjunction with opiates.
 - d. **Direct vasodilators** (e.g., nitroprusside, nitroglycerin, and hydralazine).
 - e. α_1 -**Adrenergic blockers** (e.g., droperidol, chlorpromazine, phentolamine, and labetalol).
 - f. α_2 -**Adrenergic agonists** (e.g., clonidine).
 - g. **Histamine-releasing medications** (e.g., *d*-tubocurarine, mivacurium, and morphine).
 - h. **Ganglionic inhibitors** (e.g., trimethaphan).
 - i. **Calcium channel blockers**.
 - j. **Angiotensin-converting enzyme inhibitors** and **angiotensin receptor blockers**.
 - k. **Inodilators** (e.g., milrinone).
2. **Sympathetic blockade** frequently occurs during spinal and epidural anesthesia, leading to a reduction in SVR.
3. **Sepsis** causes release of vasoactive substances that mediate peripheral vasodilation and cause hypotension.
4. **Vasoactive metabolites** released during bowel manipulation, aortic cross-clamp release, or tourniquet release may cause hypotension.
5. **Allergic reactions** (see section XVIII) may cause profound hypotension.
6. **Profound hypoxia**
7. **Adrenal insufficiency** (including iatrogenic causes)

C. Inadequate Venous Return (Preload)

1. **Hypovolemia** may be caused by blood loss, insensible evaporative losses, preoperative deficits (e.g., nothing-by-mouth status, vomiting, diarrhea, nasogastric tube suction, enteric drains, and certain bowel preparations), or polyuria (e.g., diuretic use, diabetes mellitus, diabetes insipidus, or postobstructive diuresis). In patients undergoing positive-pressure ventilation changes in the intra-arterial blood pressure trace are correlated with volume responsiveness. Hypovolemia can be considered when the delta-down component (the difference between the systolic blood pressure during apnea and the lowest systolic blood pressure after a positive pressure breath) of the systolic pressure variation is greater than about 10 mm Hg in a paralyzed and mechanically ventilated patient.
 2. **Caval compression** may result from a gravid uterus, massive ascites, tumor, surgical maneuvers or during laparoscopic insufflation of greater than 10 mm Hg leading to increased intra-abdominal pressure.
 3. **Increased venous capacitance** may occur with the following:
 - a. Sympathetic blockade (e.g., ganglionic blockers or regional anesthesia)
 - b. Direct vasodilators (e.g., nitroglycerin)
 - c. Histamine-releasing medications (e.g., morphine, mivacurium)
 - d. Medications that reduce sympathetic outflow (e.g., propofol, inhalational agents, and opioids).
 4. **Increased intrathoracic pressure** will impair venous return. Possible causes include tension pneumothorax (section XIII), mechanical ventilation with large tidal volumes, positive end-expiratory pressure (PEEP), auto-PEEP (air trapping or dynamic hyperinflation) and continuous positive airway pressure (CPAP).
 5. **Acute primary increases in central venous pressure (CVP)** can cause a decrease in venous return as the increased CVP reduces the pressure gradient that drives blood from the periphery into the right heart.
 - a. **Tension pneumothorax** leads to compression of the heart and great vessels. The resulting elevation in CVP decreases preload and gives rise to hypotension.
 - b. **Cardiac tamponade** is a collection of fluid in the pericardial space causing compression of the heart, resulting in decreased filling due to elevated intrapericardial pressures.
 - c. **Pulmonary embolism** obstructs right ventricular ejection and in turn raises right atrial pressure, which can drastically reduce venous return.
 - d. **Intra-abdominal hypertension** causes increased intrathoracic pressure which then compresses the heart and raise the CVP. Thus the CVP can be elevated while the heart is severely underfilled.
- D. Dysrhythmias (also see section III)**
1. **Tachydysrhythmias** often result in hypotension secondary to a decreased diastolic filling time.
 2. **Atrial fibrillation, atrial flutter, and junctional rhythms** cause hypotension from loss of the atrial contribution to diastolic filling. This is particularly pronounced in patients with valvular heart disease or diastolic dysfunction, in whom atrial contraction may augment end-diastolic volume by more than 30%.
 3. **Bradycardias** may cause hypotension if preload reserve is inadequate to maintain a compensatory increase in stroke volume.

- E. Treatment of hypotension** should be directed toward correcting the underlying cause. Depending on the etiology, appropriate maneuvers include:
- 1. Decreasing anesthetic depth**
 - 2. Volume expansion** (e.g., administration of blood products, colloids or crystalloids)
 - 3. Vasopressor support** to increase vascular resistance or decrease venous capacitance (e.g., phenylephrine and vasopressin if acidemic) and increase stroke volume (e.g., epinephrine).
 - 4. Correction of mechanical causes**, such as relief of pericardial tamponade, placement of a needle thoracostomy and chest tube for pneumothorax, reducing or eliminating PEEP or CPAP, decreasing mean airway pressure, relieving obstruction of the vena cava (e.g., left uterine displacement for a pregnant patient), surgically relieving intra-abdominal hypertension, or surgically removing a massive pulmonary embolism.
 - 5. Antidysrhythmic (see section III)** may include β -blockers, calcium channel blockers, and amiodarone.
 - 6. Inotropic support** (e.g., dobutamine, dopamine, norepinephrine, milrinone, and epinephrine).
 - 7. Anti-ischemic therapy** may include raising the systemic blood pressure with vasopressors and then treating the underlying ischemic myocardium (see section XIV).
 - 8. In the case of refractory hypotension**, consider the use of additional non-invasive monitors (e.g., transthoracic or transesophageal echocardiography) and the placement of invasive monitors (e.g., arterial line, central venous catheter or pulmonary artery catheter) to aid diagnosis.

II. HYPERTENSION

A. Etiologies

- 1. Catecholamine excess** may be seen with inadequate anesthesia, especially during laryngoscopy, intubation, incision, emergence, hypoxia, hypercarbia, patient anxiety, pain, and prolonged tourniquet use.
 - 2. Preexisting disease** such as essential hypertension or pheochromocytoma.
 - 3. Increased intracranial pressure**
 - 4. Systemic absorption of vasoconstrictors** such as epinephrine and phenylephrine.
 - 5. Aortic cross-clamping** which leads to a significant increase in SVR.
 - 6. Rebound hypertension** from discontinuation of clonidine or β -adrenergic blockers.
 - 7. Drug interactions.** The administration of ephedrine to patients receiving tricyclic antidepressants (e.g., amitriptyline, nortriptyline, doxepin) and monoamine oxidase inhibitors (e.g., isoniazid, rasagiline, selegiline) may cause an exaggerated hypertensive response.
 - 8. Bladder distention**
 - 9. Administration of indigo carmine dye** (via an α -adrenergic effect).
- B. The treatment** of hypertension is directed toward correcting the underlying cause. It may include the following:
- 1. Improving oxygenation and ventilation.**
 - 2. Increasing the depth of anesthesia** (e.g., volatile and IV anesthetics and analgesics).
 - 3. Sedating an anxious patient or emptying a full bladder.**
 - 4. Medications** (for further discussion, see Chapter 20).
 - a. Combined α and β -Adrenergic blocking agents:** labetalol in 5 to 10 mg increments intravenously [IV].

- b. **β -Adrenergic blocking agents:** propranolol, 0.5- to 1.0-mg increments IV; metoprolol, 1.0–5.0 mg IV; or esmolol, 5- to 10-mg increments IV.
- c. **Vasodilators:** hydralazine, 2.5- to 5-mg increments IV; nitroglycerin infusion, starting at 30 to 50 $\mu\text{g}/\text{minute}$ IV and titrating to effect; nitroprusside infusion, 30 to 50 $\mu\text{g}/\text{minute}$ IV and titrating to effect.
- d. **Calcium channel blockers:** verapamil, 2.5 to 5 mg IV; diltiazem, 5 to 10 mg IV.

III. DYSRHYTHMIAS

A. Sinus bradycardia is a sinus node–driven heart rate of less than 60 beats/minute. Unless there is severe underlying heart disease, hemodynamic changes are minimal. With very slow rates, atrial and ventricular ectopic escape beats or rhythms may occur.

1. Etiologies

- a. **Hypoxia**
- b. **Intrinsic cardiac disease** such as sick sinus syndrome or acute MI (particularly inferior wall MI).
- c. **Medications** such as succinylcholine (especially in young children via a direct cholinergic effect), anticholinesterases, β -adrenergic blockers, calcium channel blockers, digoxin, and synthetic narcotics (e.g., fentanyl and remifentanyl).
- d. **Increased vagal tone** occurs with traction on the peritoneum or spermatic cord; pressure on the globe via the oculocardiac reflex; pressure near the brainstem during craniotomies for posterior fossa lesions; direct pressure on the vagus nerve or carotid sinus during neck or intrathoracic surgery; acute distension of the peritoneal cavity during laparoscopy; centrally mediated vagal response from anxiety or pain (vasovagal reaction); and valsalva maneuvers.

e. Increased intracranial pressure

2. Treatment of sinus bradycardia

- a. Verify adequate oxygenation and ventilation.
- b. Bradycardia due to increased vagal tone requires discontinuation of the provocative stimulus. Atropine (0.5 mg IV) or low-dose epinephrine (10 to 50 μg IV) may be needed if the patient is hypotensive. Glycopyrrolate (0.2 to 0.6 mg IV) or ephedrine (5 to 10 mg IV) may be given for hemodynamically stable bradycardia, the latter may be more appropriate for settings of brief surgical stimulation of the vagus.
- c. In patients with intrinsic cardiac disease, treatment should proceed with atropine (0.5 mg IV), chronotropes (e.g., ephedrine, dopamine), or cardiac pacing.

B. Sinus tachycardia is a sinus node–driven heart rate greater than 100 beats/minute. The rate is regular and rarely exceeds 160 beats/minute. Electrocardiogram (ECG) should demonstrate a P wave preceding each QRS complex with a fixed PR interval.

- #### 1. Etiologies
- include catecholamine excess, inadequate anesthesia or analgesia; hypercarbia; hypoxia; hypotension; hypovolemia; medications (e.g., pancuronium, desflurane, atropine, and ephedrine); fever; MI; pulmonary embolism; tamponade; tension pneumothorax; malignant hyperthermia; pheochromocytoma; and thyrotoxicosis.

- #### 2. Treatment
- should be directed toward correcting the underlying cause and may include the following:

- a. Correcting oxygenation and ventilation abnormalities.
- b. Increasing the depth of anesthesia and treating pain with analgesics.
- c. Correcting hypovolemia.

- d. Medications such as opioids and β -adrenergic blockers. Patients with active coronary artery disease and adequate blood pressure may benefit by treatment with β -adrenergic blockers to control the heart rate while the cause is being determined.

C. Heart Block

1. **First-degree atrioventricular (AV) block** is characterized by a PR interval of 0.2 seconds or longer. In first-degree block, every atrial pulse is transmitted to the ventricle.
2. **Second-degree AV block** is divided into two types: Mobitz type 1 (Wenckebach) and Mobitz type 2.
 - a. **Mobitz type 1** (Wenckebach) usually occurs when a conduction defect is in the AV node and is manifest by a progressive PR prolongation culminating in a nonconducted P wave. It is generally benign.
 - b. **Mobitz type 2** is a conduction defect in or distal to the AV node. It presents with a constant PR interval and frequent nonconducted P waves. It is more likely to progress to third-degree block.
3. **Third-degree AV block** (complete heart block) is usually due to lesions distal to the His bundle and is characterized by the absence of AV conduction. Usually, a slow ventricular rate is seen (fewer than 45 beats/minute). P waves occur regularly but are independent of QRS complexes (AV dissociation).
4. **Treatment of heart block**
 - a. **First-degree AV block** does not usually require specific treatment, however, temporary pacing should be available in the case of first-degree heart block in combination with a bifascicular block (so-called “trifascicular block”).
 - b. **Second-degree AV block**
 1. **Mobitz type 1** requires treatment only if symptomatic bradycardia, congestive heart failure, or bundle branch block occurs. Transcutaneous or transvenous pacing may be necessary, particularly during an inferior MI.
 2. **Mobitz type 2** may progress to complete heart block and is an indication for pacemaker placement.
 - c. **Third-degree AV block** is treated with transcutaneous, transvenous, or epicardial pacing.
- D. **Supraventricular tachycardias** originate at or above the bundle of His. The resulting QRS complexes are narrow (<120 milliseconds) except during aberrant conduction.
 1. **Atrial premature contractions (APCs)** occur when ectopic foci in the atria fire before the next expected impulse from the sinus node. The P wave of an APC characteristically looks different from preceding P waves, and the PR interval may vary from normal. APCs may cause aberrant QRS complexes. If the AV node is still in a refractory period, an APC will not elicit a ventricular response. APCs are common, usually benign, and typically require no treatment.
 2. **Junctional or AV nodal rhythms** are characterized by absent or abnormal P waves and normal QRS complexes. Although they may indicate ischemic cardiac disease, junctional rhythms are commonly seen in healthy individuals receiving inhalational anesthesia. In the patient whose cardiac output depends heavily on the contribution from atrial contraction, stroke volume and blood pressure may decline precipitously. Treatment may include the following:
 - a. Reduction of anesthetic depth.
 - b. Increasing intravascular volume.

- c. Atropine in increments of 0.2 mg IV may convert a slow junctional rhythm to sinus rhythm, particularly if secondary to a vagal mechanism.
 - d. Paradoxically, β -blockers may be used cautiously (e.g., propranolol, 0.5 mg IV and metoprolol, 1 to 3 mg), especially with isorhythmic AV dissociation (independent atrial and ventricular rhythms that are similar in rate).
 - e. If the dysrhythmia is associated with hypotension, increasing the blood pressure with vasopressors (e.g., ephedrine or norepinephrine) may be required as a temporizing measure.
 - f. If necessary, atrial pacing may be instituted to restore atrial contraction.
3. **Atrial fibrillation** is an irregular rhythm with an atrial rate of 350 to 600 beats/minute and a variable ventricular response. It may be seen with myocardial ischemia, mitral valvular disease, hyperthyroidism, pulmonary embolism, excessive sympathetic stimulation, digitalis toxicity, after thoracic surgery, or when the heart has been manipulated. Treatment is based on the hemodynamic status.
- a. **Rapid ventricular rate with stable hemodynamics** can be treated initially with β -adrenergic blockade, such as propranolol (0.5 mg increments IV), metoprolol (2.5- to 5-mg increments), esmolol (5 to 10 mg increments), or a calcium channel blocker such as verapamil (2.5- to 5-mg increments) or diltiazem (10 to 20 mg IV) (see Chapter 38). Amiodarone (150 mg IV) can be used to promote conversion back to sinus rhythm (anticoagulation prior to cardioversion is recommended in patients with atrial fibrillation for longer than 24 hours).
 - b. **Rapid ventricular rate with unstable hemodynamics** requires synchronized cardioversion (50 to 100 J if biphasic or 200 J if monophasic) (see Chapter 38).
4. **Atrial flutter** is usually a regular rhythm with an atrial rate of 250 to 350 beats/minute and a characteristic sawtooth ECG configuration. It is often seen with underlying heart disease (i.e., rheumatic heart disease and mitral stenosis). A 2:1 block will result in a rapid ventricular rate (usually 150 beats/minute). Treatment usually includes β -adrenergic, calcium channel blockade or synchronized cardioversion (see Chapter 38).
5. **Paroxysmal supraventricular tachycardia** is an abrupt onset tachydysrhythmia (atrial and ventricular rates of 150 to 250 beats/minute) with reentry usually through the AV node. This rhythm may be associated with **Wolff-Parkinson-White [WPW] syndrome**, thyrotoxicosis, or mitral valve prolapse. Patients without heart disease may develop this dysrhythmia due to stress, caffeine, or excess catecholamines. Treatment includes **adenosine** (6 to 18 mg IV, 3 mg if given centrally), Valsalva maneuvers, carotid sinus massage, or propranolol (1 to 2 mg IV). AV nodal blockers (calcium channel and β -blockers) are contraindicated for the treatment of atrial fibrillation or atrial flutter in patients with WPW syndrome as they selectively slow conduction through the AV node, which can lead to increased conduction through the accessory pathway and cause ventricular fibrillation. Synchronized cardioversion may be required for the hemodynamically unstable patient (also see Chapter 38).
- E. **Ventricular Dysrhythmias**
- 1. **Ventricular premature contractions (VPCs)** occur when ectopic foci in the ventricle fire before the next expected impulse arrives. They are characterized by widened QRS (>120 milliseconds) complexes.

When coupled alternately with normal beats, ventricular bigeminy exists. VPCs are occasionally seen in healthy individuals. Under anesthesia, they frequently occur during states of catecholamine excess, hypoxia, or hypercarbia. They may also signify myocardial ischemia or infarction, digitalis toxicity, or hypokalemia. **VPCs may require therapy when they are multifocal, occur in runs (>2 sequentially), increase in frequency (>10% of all ventricular depolarizations), or occur on or near the preceding T wave (R-on-T phenomenon);** these situations may precede the development of ventricular tachycardia, ventricular fibrillation, and cardiac arrest. Treatment in an otherwise healthy individual may include deepening anesthesia and ensuring adequate oxygenation, ventilation while assessing for electrolyte abnormalities (especially potassium, and magnesium). Patients with coronary artery disease who continue to have ventricular irritability should have any ischemia treated. If the ectopy continues, then **amiodarone** (150 mg IV over 10 minutes followed by an infusion at 1 mg/minute for 6 hours then 0.5 mg/minute thereafter) may be considered. Refractory ventricular ectopy may require further treatment (see Chapter 38).

2. **Ventricular tachycardia** is a wide-complex tachydysrhythmia at a rate of 150 to 250 beats/minute. Hemodynamically unstable patients with a pulse should be treated as outlined in the ACLS guidelines with cardiopulmonary resuscitation and cardioversion (100 J if biphasic, or 200 J if monophasic; if unresponsive, may increase energy in a stepwise fashion). For stable patients the first-line treatment depends on whether the ventricular tachycardia is monomorphic or polymorphic. If polymorphic, treat as if unstable. In addition, the treatment may depend on the ejection fraction (see Chapter 38 for specific recommendations).
3. **Ventricular fibrillation** is chaotic ventricular activity resulting in ineffective ventricular contractions. Cardiopulmonary resuscitation and defibrillation are required (see Chapter 38 for specific recommendations).
4. **Ventricular preexcitation.** WPW syndrome is due to an accessory pathway connecting the atria and ventricle. The most common mechanism is characterized by antegrade conduction through the normal AV conduction system and retrograde conduction through the accessory pathway. Characteristic ECG findings include a short PR interval and a slurred "delta wave" at the upstroke of the QRS. Tachydysrhythmias are common. The treatment depends on whether the patient is hemodynamically stable (see Chapter 38). Unstable patients should receive synchronized cardioversion starting at 50 J (monophasic or biphasic). These patients are at high risk for ventricular fibrillation.

IV. HYPOXEMIA

Hypoxemia occurs when oxygen delivery to the tissues is insufficient to meet metabolic demands.

A. Intraoperative Etiologies

1. Inadequate oxygen supply

- a. Loss of the main pipeline supply with an empty reserve oxygen tank.
- b. An oxygen flowmeter that is not turned to a sufficient flow.
- c. Breathing system disconnection.
- d. Large leaks in the anesthesia machine, ventilator, carbon dioxide absorber, breathing circuit, or around the endotracheal tube or laryngeal mask airway (LMA). This condition may be managed acutely by increasing oxygen flow or using a self-inflating (Ambu) bag to deliver oxygen to the patient.

- e. Obstructed endotracheal tube (e.g., kinked or mucus plug).
 - f. Malpositioned endotracheal tubes (e.g., esophageal or mainstem bronchial intubation).
 - g. Upper airway obstruction.
 - h. Laryngospasm in the unintubated patient (see section X).
 - 2. **Hypoventilation** (see section V.A)
 - 3. **Ventilation–perfusion inequalities or shunting**
 - a. **Pulmonary.** as seen with atelectasis, pneumonia, pulmonary edema, aspiration, pneumothorax, bronchospasm, mucous plugging, and other parenchymal pathologic states as well as with single lung ventilation. In some cases, these inequalities may be corrected by increasing mean airway pressure or applying PEEP.
 - b. **Cardiac.** right-to-left cardiac shunt, as in VSD, ASD and tetralogy of Fallot.
 - 4. **Reduction in oxygen carrying capacity.** Oxygen carrying capacity is reduced with anemia, carbon monoxide poisoning, and hemoglobinopathies, despite a normal oxygen saturation as measured by pulse oximetry. Methemoglobin reduces oxygen carrying capacity and at high levels will reduce oxygen saturation reading via pulse oximetry.
 - 5. **Leftward shift of the hemoglobin–oxygen dissociation curve** results from hypothermia, decreased 2,3-diphosphoglycerate concentration, alkalosis, hypocarbia, and carbon monoxide poisoning.
- B. Treatment of Hypoxemia**
- 1. If the patient is being mechanically ventilated, begin manual ventilation with 100% oxygen to assess pulmonary compliance. Evaluate breath sounds, check the surgical field for mechanical interference with ventilation, examine the endotracheal tube for obstruction or dislodgement, and confirm adequate movement of the chest wall or diaphragm. Elevated peak airway pressures may indicate bronchospasm, pneumothorax, an obstructed endotracheal tube, or endobronchial intubation.
 - 2. The breathing circuit, ventilator, and anesthesia machine should be checked for leaks. If present, ventilation should be started with high flow 100% oxygen via an alternative source such as a self-inflating bag until the problem is rectified.
 - 3. Adequate oxygen delivery to the patient should be confirmed with an inline oxygen analyzer.
 - 4. Bronchoscopy may be valuable to help rule out obstructive causes.
 - 5. Further treatment is outlined in Chapter 37.

V. HYPERCARBIA

Hypercarbia is due either to inadequate ventilation or to increased carbon dioxide production and can lead to respiratory acidosis, increased pulmonary artery pressure, and increased intracranial pressure.

A. Inadequate Ventilation

- 1. **Central depression of the medullary respiratory center** can be caused by medications (e.g., opioids, barbiturates, benzodiazepines, and volatile anesthetics) or primary central nervous system pathology (e.g., tumor, ischemia, and edema). Controlled ventilation and the administration of reversal agents (e.g., naloxone and flumazenil) may be required.
- 2. **Neuromuscular depression** may be seen with a high level of spinal anesthesia, phrenic nerve paralysis, and inadequate reversal of neuromuscular blockade.

3. **Inappropriate ventilator settings** may result in low minute ventilation.
4. **Increased airway resistance** may occur with bronchospasm, upper airway obstruction, mainstem intubation, obstructed endotracheal tube, severe chronic obstructive lung disease, congestive heart failure, and hemothorax or pneumothorax.
5. **Rebreathing of exhaled gases** may occur due to an exhausted carbon dioxide absorber, inspiratory or expiratory valve failure, or inadequate fresh gas flows in nonrebreathing systems.
6. **One-lung ventilation** in patients with preexisting pulmonary pathology can lead to significant hypercarbia.
- B. **Increased carbon dioxide production** results from exogenous carbon dioxide (e.g., absorption of carbon dioxide from insufflation during laparoscopy); reperfusion of ischemic tissue; and hypermetabolic states (e.g., hyperthermia, sepsis, burns and malignant hyperthermia).
- C. **Treatment of hypercarbia** should be targeted to the cause. Depending on the etiology, treatment may include intubation, increasing minute ventilation, repositioning the endotracheal tube, suctioning, treatment of bronchospasm, diuresis, or placing a chest tube.

VI. ABNORMAL URINE OUTPUT

- A. **Oliguria** is defined as urine output less than 0.5 mL/kg/h. Prerenal, renal, and postrenal causes are described in Chapter 4.
 1. **Treatment** includes ruling out mechanical causes (e.g., malpositioned, kinked, or obstructed Foley catheter) and renal dysfunction (can be accessed through renal ultrasound).
 2. **Hypotension** should be corrected to ensure adequate renal perfusion pressure.
 3. **Volume status should be assessed.** A fluid bolus may be given if hypovolemia is suspected. If oliguria persists, CVP measurement or systolic variation in arterial tracing in mechanically ventilated patients may help guide further fluid management. Patients with reduced ventricular function may require placement of a pulmonary artery catheter.
 4. **If oliguria persists** despite an adequate volume status, urine output can be increased with the following drugs. Current evidence suggests that these medications do not affect renal function or outcome, however they may aid in toxin elimination and reduce the formation of casts.
 - a. Furosemide, 2 to 20 mg IV.
 - b. Dopamine infusion, 1 to 3 $\mu\text{g/kg/min}$ IV.
 - c. Mannitol, 12.5 to 25.0 g IV.
 - d. Fenoldopam, 0.1 to 0.4 $\mu\text{g/kg/min}$ IV.
 5. **Intraoperative diuretics** may be required to preserve urine output in patients on chronic diuretic therapy.
- B. **Anuria** is a rare occurrence in the perioperative period. Mechanical causes, including Foley catheter malfunction or ureteral damage or transection, must be excluded and hemodynamic instability must be treated.
- C. **High urine output** may occur in response to iatrogenic causes (e.g., vigorous fluid administration, mannitol, and Lasix), but other causes must be considered, including hyperglycemia, and both neurogenic and nephrogenic diabetes insipidus (see Chapter 6). High urine output is not a problem unless associated with hypovolemia or electrolyte abnormalities. Treatment should be directed at the underlying cause, maintaining volume status, and correcting electrolyte abnormalities.

VII. HYPOTHERMIA

Hypothermia is a common problem in the perioperative period.

- A. **Heat loss** during general anesthesia and surgery may occur from any or all of the following mechanisms:
 1. **Redistribution of heat from core areas** (e.g., brain, heart, etc.) to peripheral tissues (e.g., limbs, skin, etc.). Redistribution results in a reduction in the core temperature with maintenance of the mean body temperature.
 2. **Radiation.** Radiant heat loss depends on cutaneous blood flow and exposed body surface area.
 3. **Evaporation.** Energy is lost as liquid vaporizes from mucosal and serosal surfaces, skin, and lungs. Evaporative losses depend on the exposed surface area and the relative humidity of ambient gas.
 4. **Conduction,** which is heat transfer from a warm to a cool object. This heat loss is proportional to the area exposed, difference in temperature, and thermal conductivity.
 5. **Convection,** which is the loss of heat by conduction to a moving gas. High airflow rates in the operating rooms (10 to 15 room volume changes/hour) may result in significant heat loss.
- B. **Pediatric patients** are particularly susceptible to intraoperative hypothermia (see Chapters 30 and 31).
- C. **Geriatric patients** are also more prone to hypothermia (see Chapter 29).
- D. **Anesthetic Effects.** Volatile anesthetics impair the thermoregulatory center located in the posterior hypothalamus and predispose to heat redistribution and heat loss due to their vasodilatory properties. Opioids will reduce the vasoconstriction mechanism for heat conservation because of their sympatholytic properties. Muscle relaxants reduce muscle tone and prevent shivering. Regional anesthesia produces sympathetic blockade, muscle relaxation, and sensory blockade of thermal receptors, which inhibit compensatory responses.
- E. **Severe hypothermia** is associated with a number of physiologic changes.
 1. **Cardiovascular.** Increased SVR, ventricular dysrhythmias, and myocardial depression may occur with severe hypothermia.
 2. **Metabolic.** Decreased metabolic rate and decreased tissue perfusion (from catecholamine response) may occur.
 3. **Hematologic.** Increased blood viscosity, leftward shift of the hemoglobin dissociation curve, impaired coagulation, and platelet dysfunction occur.
 4. **Neurologic.** Decreased cerebral blood flow, increased cerebrovascular resistance, decreased minimum alveolar concentration, delayed emergence from anesthesia, drowsiness, and confusion may occur.
 5. **Drug disposition.** Decreased hepatic blood flow and metabolism coupled with decreased renal blood flow and clearance result in decreased anesthetic requirement.
 6. **Shivering.** Can increase heat production, oxygen consumption and sympathetic tone.
- F. **Prevention and Treatment of Hypothermia**
 1. **Maintain or increase ambient temperature.** Anesthetized patients frequently become hypothermic if the room temperature is below 21°C.
 2. **Cover exposed surfaces** to minimize conductive and convective losses. Forced warmed air blankets placed over the patient can provide both insulation and active warming. Active warming should not be attempted on ischemic tissues such as those found distal to the level of an aortic cross-clamp.

3. **Warming transfused fluids and blood** is essential in cases with large fluid requirements or rapid infusion rates (see Chapter 15). Doing so will reduce heat loss by about 0.25°C per liter of crystalloid.
4. **Use of closed or low-flow semiclosed circuit anesthesia** will decrease evaporative losses and modestly reduce heat loss.
5. **Heated humidifiers** can be added to the anesthetic circuit when high gas flows are used. These will warm and humidify the inspired gas, minimizing evaporative loss from the lungs. The temperature of inspired gas must be monitored and kept below 41°C; otherwise, there is potential for airway burns. Alternatively, “artificial noses” (passive heat and moisture exchangers) can be placed between the endotracheal tube and the breathing circuit. These are hygroscopic membrane filters with large surface areas that trap the humidity of expired air.
6. **Warming blankets** placed beneath the patient can increase body temperature by conduction from warm water pumped through the blanket. This method is most effective in children weighing less than 10 kg. The temperature should be kept below 40°C to avoid burns.
7. **Radiant warmers and heating lamps** warm the patients by infrared radiation and are useful only for infants. The warming lamps should be kept at least 70 cm from the patient to avoid burns.
8. **Warming irrigation solutions** prior to use.

VIII. HYPERTHERMIA

Hyperthermia is an increase in temperature of 2°C/hour or 0.5°C/15 minute. It is uncommon for a patient to become hyperthermic based solely on maneuvers to conserve body heat in the operating room. Therefore, any increase in temperature must be investigated. Hyperthermia and its accompanying hypermetabolic state produce an increase in oxygen consumption, cardiac work, glucose demand, and compensatory minute ventilation. Sweating and vasodilation may result in decreased intravascular volume and venous return.

A. Etiologies

1. **Malignant hyperthermia** must be considered during any perioperative temperature increase (see section XVII).
2. **Inflammation, infection, and sepsis** with release of inflammatory mediators may cause hyperthermia.
3. **Hypermetabolic states** such as thyrotoxicosis may cause hyperthermia.
4. **Injury to the hypothalamic thermoregulatory center** from anoxia, edema, trauma, or tumor may affect temperature set points in the hypothalamus.
5. **Neuroleptic malignant syndrome (NMS)** triggered by neuroleptics such as phenothiazines (e.g., haloperidol) and is a rare cause.
6. **Sympathomimetics**, such as monoamine oxidase inhibitors, amphetamines, cocaine, and tricyclic antidepressants may produce a hypermetabolic state.
7. **Anticholinergics**, such as atropine, may suppress sweating.

B. Treatment

1. **If malignant hyperthermia is suspected**, dantrolene treatment must be initiated (see section XVII).
2. **Severe hyperthermia** can be treated by cooling exposed body surfaces (e.g., skin) with ice, cooling blankets, and reduced ambient temperature or by performing internal lavage (e.g., stomach, bladder, bowel, and peritoneum) with cold saline. Volatile liquids, such as alcohol, applied to the skin will promote evaporative heat loss. Conductive heat loss can be increased with vasodilators such as nitroprusside and nitroglycerin.

Centrally active agents such as aspirin and acetaminophen can be given by nasogastric tube or rectally. Shivering can be prevented by maintaining neuromuscular blockade. When hyperthermia is profound, **extra-corporeal cooling** can be used. Cooling should be stopped when body temperature reaches 38°C to avoid hypothermia.

IX. DIAPHORESIS (SWEATING)

Diaphoresis (sweating) may occur in response to the sympathetic discharge caused by anxiety, pain, hypercarbia, or noxious stimuli in the presence of inadequate anesthesia. It may also be seen in conjunction with bradycardia, nausea, and hypotension as part of a generalized vagal reaction or as a thermoregulatory response to hyperthermia.

X. LARYNGOSPASM

- A. **Laryngospasm** is most commonly caused by an irritative stimulus to the airway during a light plane of anesthesia. Common noxious airway stimuli that may elicit this reflex include secretions, vomitus, blood, inhalation of pungent volatile anesthetics, oropharyngeal or nasopharyngeal airway placement, laryngoscopy, painful peripheral stimuli, and peritoneal traction during light anesthesia. Laryngospasm can also result from sudden administration of high doses of synthetic narcotics (e.g., fentanyl) during induction of anesthesia.
- B. **Reflex closure of the vocal cords**, causing partial or total glottic obstruction, may be manifest in less severe cases by stridor and, when complete, by an obstructed pattern of breathing. In this situation, the abdominal wall rises with contraction of the diaphragm during inspiration, but because air entry is blocked the chest retracts or fails to expand. During attempted expiration, the abdomen falls as the diaphragm relaxes and the chest returns to its original position. With complete obstruction, the anesthetist will not be able to ventilate the patient.
- C. The hypoxia, hypercarbia, and acidosis that result can cause hypertension and tachycardia. Hypotension, bradycardia, and ventricular dysrhythmias leading to cardiac arrest will ensue unless airway patency is restored within minutes. Children and pregnant women are particularly prone to these complications because of their small functional residual capacity and relatively high oxygen consumption.
- D. **Treatment.** Deepening the anesthetic level and removing the stimulus (e.g., by suction, withdrawal of an artificial airway, or stopping peripheral stimulation) while administering 100% oxygen may be adequate to relieve laryngospasm. If laryngospasm is not relieved, **continuous positive pressure on the airway** with a jaw thrust may relieve the spasm; if not, a small dose of **succinylcholine** (e.g., 10 to 20 mg IV in an adult) will relax the striated muscles of the larynx. The lungs should be ventilated with 100% oxygen, and the anesthetic level deepened before the noxious stimulation is resumed or the patient may be allowed to awaken if laryngospasm has occurred during emergence. Infrequently, laryngospasm may require reintubation. Laryngospasm can result in negative pressure pulmonary edema which may need treatment after the laryngospasm resolves.

XI. BRONCHOSPASM

- A. **Reflex bronchiolar constriction** may be centrally mediated or may be a local response to airway irritation. Bronchospasm is common in anaphylactoid or anaphylactic drug and blood transfusion reactions as well as in cigarette smokers and those with chronic bronchitis. Like laryngospasm,

bronchospasm may be elicited by noxious stimuli such as secretions and endotracheal intubation.

- B. Wheezing** (usually more pronounced on expiration) characterizes bronchospasm and is associated with tachypnea and dyspnea in the awake patient. An anesthetized patient may be difficult to ventilate because of increased airway resistance. Decreased expiratory flow rates may produce air trapping and increase intrathoracic pressure, decreasing venous return, cardiac output, and blood pressure. End-tidal carbon dioxide curves often have an obstructive pattern (continual rise) during exhalation.
- C. Histamine-releasing drugs** (e.g., morphine, mivacurium, vancomycin, and atracurium) may exacerbate bronchoconstriction.

D. Treatment

- 1. The endotracheal tube position** should be checked and, if carinal stimulation is the cause, withdrawn slightly.
- 2. Deepening the anesthetic level** will frequently reverse bronchospasm that is secondary to inadequate anesthesia. Deepening the level of anesthesia can usually be accomplished with an inhalational agent. An IV agent may be necessary when ventilation is significantly impaired. Propofol produces fewer symptoms of bronchoconstriction than barbiturates and is usually preferable. Ketamine has the advantage of causing bronchodilation by releasing endogenous catecholamines. The inspired oxygen concentration should be increased until adequate oxygenation is achieved.
- 3. Medical treatment** includes administering inhaled or intravenous β_2 -adrenergic agonists (see Chapter 3). Inhaled bronchodilators have limited systemic absorption, which may minimize cardiovascular side effects. Nebulized forms may contain large particles, which deposit to a large extent in tubing and upper airways. The dosage of metered dose inhalers should be titrated to effect when administered into a breathing circuit. Large doses (10 to 20 puffs) may be necessary. If severe, low-dose ketamine (0.1 to 0.15 mg/kg/h based on case reports) or low-dose IV epinephrine (0.02 to 0.05 μ g/kg/min based on case reports) should be started.
- 4. Adequate hydration and humidification** of inspired gases will minimize inspissation of secretions.

XII. ASPIRATION

General anesthesia causes depression of airway reflexes that predisposes patients to aspiration. Aspiration of gastric contents from vomiting or regurgitation may cause bronchospasm, hypoxemia, atelectasis, tachypnea, tachycardia, and hypotension. The severity of symptoms depends on the volume and pH of the gastric material aspirated. Conditions that predispose to aspiration include gastric dysmotility, gastric outlet obstruction, gastroesophageal reflux, small-bowel obstruction, symptomatic hiatal hernia, pregnancy, and recent food ingestion.

- A. If vomiting or regurgitation occurs** in an anesthetized patient whose airway is not protected by an endotracheal tube, the patient should be placed in the Trendelenburg position to minimize passive flow of gastric contents into the trachea, the head should be turned to the side, the upper airway suctioned, and an endotracheal tube placed. Suctioning the endotracheal tube before instituting positive-pressure ventilation avoids forcing gastric contents into the distal airways. Evidence of significant aspiration includes wheezing, decreased lung compliance, and hypoxemia. A chest radiograph should be obtained, however, radiographic evidence of infiltrates may be delayed. Bronchodilators may be useful.

- B. Bronchoscopy** should be performed if a clinically significant aspiration is suspected. The airways should be suctioned clear, and foreign bodies such as teeth and food removed. Lavage with large volumes of saline is not helpful.
- C. Aspiration of blood**, unless of large volume, is usually benign.
- D. Administration of antibiotics** usually is not warranted unless the material aspirated contains a high bacterial load such as with bowel obstruction (see Chapter 7).
- E. A sputum specimen** should be obtained for Gram stain and culture.
- F. Steroids** are not useful for treating aspiration.
- G. If significant aspiration has occurred**, close postoperative observation should be undertaken. This includes pulse oximetry and repeat chest radiography. Ventilatory support and supplemental oxygen may be necessary (see Chapter 37).

XIII. PNEUMOTHORAX

Pneumothorax is the accumulation of gas within the pleural space.

A. Etiologies

1. Spontaneous rupture of blebs and bullae.
 2. Blunt or penetrating chest trauma.
 3. Surgical entrance into the pleural space during thoracic, upper abdominal, or retroperitoneal surgery, tracheostomy, or surgery of the chest wall or neck.
 4. Iatrogenic complication of procedures such as subclavian or internal jugular vein catheter placement, thoracentesis, pericardiocentesis, or upper extremity nerve block.
 5. During positive-pressure ventilation using high pressures and volumes, causing barotrauma and alveolar rupture. Patients with chronic obstructive pulmonary disease are at particularly high risk.
 6. Malfunction of chest tubes.
- B. Physiologic effects** of a pneumothorax is largely a function of the gas volume and the rate of expansion. A small pneumothorax may have no significant cardiopulmonary effect while a larger one may result in significant lung collapse and hypoxemia. A tension pneumothorax occurs when there is a one-way leak into the pleural space, causing a significant increase in intrapleural pressure. This can result in decreased venous return, mediastinal shift, and compression of the heart. A small tension pneumothorax can cause hypotension, whereas a large tension pneumothorax can cause a cardiac arrest.
- C. The diagnosis** of pneumothorax can be difficult. Signs of pneumothorax include decreased breath sounds on the affected side, a reduction in lung compliance, an increase in peak inspiratory pressure, and hypoxemia. Hypotension reflects the presence of a tension pneumothorax. A chest radiograph can usually reveal a pneumothorax as a hyperlucency between the chest wall, mediastinum or diaphragm and lung parenchyma. Ultrasound of the chest wall which reveals no evidence of parietal and visceral pleura sliding against each other with respirations is also evidence of a pneumothorax and ultrasound can provide a reliable and rapid diagnosis. Treatment of an unstable patient should not be delayed while waiting for a chest radiograph.
- D. Treatment.** Nitrous oxide should be discontinued, and the patient should be ventilated with 100% oxygen. A tension pneumothorax requires immediate decompression. A large-bore catheter (14 to 16 gauge) can be inserted into the pleural space at the second intercostal space in the midclavicular line. A chest tube then can be placed at the fifth or sixth intercostal space in the midaxillary line.

XIV. MYOCARDIAL ISCHEMIA

A. Etiology

Myocardial ischemia is the result of an imbalance between myocardial oxygen supply and consumption and, if persistent, may lead to MI.

B. Clinical Features

1. In the awake patient, myocardial ischemia may manifest as chest pain, dyspnea, nausea and vomiting, diaphoresis, or shoulder and jaw pain. **Asymptomatic ischemia is common** in the perioperative period, particularly in diabetic patients. In patients under general anesthesia, hemodynamic instability and ECG changes may occur with ischemia.
2. **ECG changes** such as **ST segment depression** greater than 1 mm or acute T-wave inversion may indicate subendocardial ischemia. **ST segment elevation** is usually seen with transmural myocardial ischemia. T-wave changes may also be seen with electrolyte abnormalities and thus are not particularly diagnostic of ischemia. Lead V₅ is the single most sensitive lead for detecting left ventricular ischemia (see Chapter 10).
3. **Other indicators of ischemia** include the following:
 - a. Hypotension.
 - b. Changes in central filling pressures or cardiac output.
 - c. Regional wall motion abnormalities as detected with TEE.
 - d. Dysrhythmias, particularly ventricular ectopy.

C. Treatment

1. **Hypoxemia and anemia should be corrected** to maximize myocardial oxygen delivery.
2. **β -Adrenergic antagonists** (e.g., metoprolol in 1 to 3 mg increments IV or propranolol in 0.5- to 1.0-mg increments IV or esmolol in 5- to 10-mg increments IV) decrease myocardial oxygen consumption by decreasing heart rate and contractility. These medications are contraindicated, however, in acute heart failure.
3. **Nitroglycerin** (starting at 25 to 50 μ g/minute IV or 0.15 mg sublingually) reduces ventricular diastolic pressure and volume through venodilation and thus decreases myocardial oxygen demand. Additionally, nitroglycerin may improve oxygen delivery by enhancing collateral coronary flow.
4. **Myocardial ischemia occurring in the setting of hypotension** may require a vasopressor such as phenylephrine (40 to 80 μ g/minute IV) or norepinephrine (2 to 20 μ g/minute IV) to improve myocardial perfusion pressure. Anesthetic depth may need to be decreased and intravascular volume optimized.
5. When myocardial ischemia results in a significant reduction in cardiac output and hypotension (cardiogenic shock), positive **inotropes** such as dopamine (5 to 20 μ g/kg/min IV), dobutamine (5 to 20 μ g/kg/min IV), milrinone (0.375 to 0.75 μ g/kg/min after loading dose of 50 μ g/kg) and norepinephrine (2 to 20 μ g/minute IV) are indicated. Intra-aortic balloon counterpulsation may be lifesaving. A pulmonary artery catheter or transesophageal echocardiogram may be helpful in assessing ventricular function and response to therapy.
6. **Aspirin** should be administered.
7. **Heparin treatment, thrombolytic therapy, angioplasty, and coronary revascularization** may be considered in selected patients under the guidance of a cardiologist.

XV. PULMONARY EMBOLISM

Pulmonary embolism is the obstruction of pulmonary arterial blood flow by thrombus, air, fat, or amniotic fluid. Large emboli may lead to a sudden decrease in end-tidal carbon dioxide tension due to an **acute increase in dead space**. Other signs include an increase in end-tidal nitrogen tension, as well as an increased CVP, hypoxemia, hypotension, tachyarrhythmias or bradyarrhythmias, and ventricular ectopy.

A. Thromboemboli most commonly arise from the deep venous system of the pelvis and lower extremities. Predisposing factors for the development of thrombi are stasis, hypercoagulability, and vascular wall abnormalities. Associated conditions include pregnancy, trauma, carcinoma, prolonged bed rest, and vasculitis.

- 1. Physical findings** are nonspecific and may include tachypnea and tachycardia, dyspnea, bronchospasm, and fever.
- 2. Laboratory studies.** The ECG reveals a nonspecific tachycardia unless embolization is severe, in which case right-axis deviation, right bundle branch block, and anterior T-wave changes may be seen. Pulmonary embolism may cause atrial fibrillation. The chest radiograph may be unremarkable unless pulmonary infarction has occurred. Typically, hypotension and hypoxemia are present. In spontaneously breathing patients, hypocapnia and respiratory alkalosis may result from the increased respiratory rate. Definitive diagnosis requires a pulmonary angiogram or high-resolution computed tomography of the chest (spiral computed tomography).
- 3. Intraoperative treatment** of a suspected pulmonary embolism is supportive. Oxygenation may be increased with increased FiO_2 . Intraoperative heparin treatment may be considered, but thrombolytic therapy is usually not an option because of the risk of hemorrhage. In patients who are severely hypoxic or hypotensive, cardiopulmonary bypass and pulmonary embolectomy may be considered.

B. Air embolism occurs during entrainment of air into a vein or venous sinus. It occurs most commonly during intracranial surgery in the sitting position, where dural venous sinuses are stented open. Air embolism may also occur during liver transplantation, open cardiac procedures, and insufflation during laparoscopy.

- 1. Additional signs indicating air embolism** include air seen by TEE or heard with a precordial Doppler.
- 2. Treatment** begins with limiting the entrainment of additional air by flooding the surgical field with saline or repositioning the patient so that venous pressure is increased. Nitrous oxide should be discontinued to avoid enlarging air bubbles within the circulation. Placing the patient in a head-down and left lateral decubitus position may help reduce an air collection from blocking right ventricular filling and limit air entering the pulmonary artery. If a central venous catheter is in place, it should be aspirated in an attempt to remove air. Fluid and especially vasopressors (such as norepinephrine) are used to maintain blood pressure.
- 3. The use of PEEP** in the setting of air embolism is controversial. It will limit the entrainment of air by raising CVP but at the expense of reducing venous return and possibly cardiac output. **Hyperbaric oxygen** may be considered in cases where a large amount of gas has been entrained.

C. Fat embolism occurs after trauma or surgery involving the long bones, pelvis, or ribs.

1. **Clinical features** are related to mechanical obstruction of the pulmonary circulation and are similar to those found with pulmonary thromboembolism. The release of free fatty acids may lead to diminished mental status, worsening hypoxemia, fat globules in the urine, disseminated intravascular coagulation (DIC), thrombocytopenia, and petechial hemorrhages.
2. **Treatment is supportive**, with the administration of circulatory support plus supplemental oxygen and ventilation as necessary.

D. **Amniotic fluid emboli** (see Chapter 32).

XVI. CARDIAC TAMPONADE

Accumulation of blood or other fluid within the pericardial sac may prevent adequate ventricular filling and reduce stroke volume and cardiac output. When the accumulation is rapid, cardiovascular collapse may occur within minutes.

- A. **Cardiac tamponade** may be associated with the following: chest trauma, cardiac or thoracic surgery, pericardial tumor, pericarditis (acute viral, pyogenic, uremic, or postradiation), myocardial perforation by a central venous or pulmonary artery catheter, and aortic dissection.
- B. **Clinical features** include tachycardia, hypotension, jugular venous distention, muffled heart sounds, and a decrease in pulse pressure. An ECG may reveal **electrical alternans** (EKG finding of alternating QRS amplitude or axis) and diffusely low voltage. **Pulsus paradoxus** (> a 10 mm Hg inspiratory decrease in systolic blood pressure) may be appreciated. There is **equalization of right and left heart pressures** as reflected in identical CVP, right ventricular end-diastolic pressure, pulmonary artery diastolic pressure, and pulmonary capillary wedge pressures. Radiographic findings may include an enlarged cardiac silhouette. An **echocardiogram** is diagnostic.
- C. The **treatment** of a hemodynamically unstable patient with suspected cardiac tamponade is pericardiocentesis. Intravascular volume should be augmented, and vasopressors that maintain chronotropy and inotropy (e.g., dopamine) are administered to maintain blood pressure. A long needle is inserted between the xiphoid process and the left costal margin and directed toward the left shoulder. If the precordial lead of the ECG is attached to the needle, an injury current (ST segment elevation) will be observed when the needle contacts the epicardium. The needle should be withdrawn slightly and aspirated. Ultrasound guided pericardiocentesis in the hands of a skilled operator can be accomplished by introducing a needle through the chest wall and aspirating the fluid accumulation where it is closest to the skin under continuous visualization. **Complications of pericardiocentesis** include pneumothorax, coronary artery laceration, and myocardial perforation. A surgical pericardial window is a more permanent approach to alleviating tamponade.

XVII. MALIGNANT HYPERTHERMIA

- A. **Etiology.** Malignant hyperthermia is a hypermetabolic syndrome occurring in genetically susceptible patients after exposure to an anesthetic triggering agent. **Triggering anesthetics** include all potent inhalational agents (e.g., halothane, isoflurane, desflurane, and sevoflurane) and succinylcholine. The syndrome is thought to be due to a reduction in the reuptake of Ca^{2+} by the sarcoplasmic reticulum necessary for the termination of muscle contraction. Consequently, muscle contraction is sustained, resulting in signs of hypermetabolism, including tachycardia, acidosis, hypercarbia, muscle rigidity, tachypnea, hypoxemia, and hyperthermia. Malignant hyperthermia usually occurs in the operating room but onset may be delayed until the patient reaches the postanesthesia care unit or even the postoperative floor.

B. Clinical Features

1. Unexplained tachycardia.
2. Hypercarbia in the mechanically ventilated patient or tachypnea in the spontaneously breathing patient that is unresponsive to increased minute ventilation.
3. Metabolic acidosis.
4. Muscle rigidity even in the presence of neuromuscular blockade. Masseter spasm after giving succinylcholine is associated with malignant hyperthermia. However, not all patients who develop masseter spasm will develop malignant hyperthermia.
5. Hypoxemia.
6. Ventricular dysrhythmias.
7. Hyperkalemia.
8. Fever is a late sign.
9. Myoglobinuria.

C. Treatment

1. **Summon help** as soon as malignant hyperthermia is suspected. Discontinue all triggering anesthetics, and hyperventilate with 100% oxygen from a new source such as wall oxygen via an Ambu bag. Convert to a total intravenous anesthetic such as propofol. Surgery should be concluded as quickly as possible, and the anesthesia machine should be changed when feasible.
2. Administer Dantrolene or Ryanodex. **Dantrolene** (Dantrium), 2.5 mg/kg IV initially and repeated to a total of 10 mg/kg or more if signs of malignant hyperthermia persist. Dantrolene is the only known specific treatment for malignant hyperthermia. Its efficacy is due to its ability to inhibit Ca^{2+} release from the sarcoplasmic reticulum. Each ampule contains 20 mg of dantrolene and 3 g of mannitol and should be reconstituted with 50 mL of warm sterile water. **Ryanodex** is newer formulation of dantrolene sodium with increased solubility. Each vial of Ryanodex contains 250mg Dantrolene sodium and 125mg mannitol and should be reconstituted with 5ml sterile water. Ryanodex dosing is the same as for the less soluble Dantrolene.
3. **Sodium bicarbonate administration** should be guided by pH and partial pressure of carbon dioxide (PCO_2) measurements.
4. **Hyperkalemia** may be corrected with insulin, glucose and an inhaled β -agonist (e.g., albuterol). However, hypokalemia may occur as the hypermetabolic state is brought under control. Calcium administration should be avoided.
5. **Dysrhythmias** generally subside with resolution of the hypermetabolic phase of malignant hyperthermia. Persistent dysrhythmias should be treated.
6. **Hyperthermia** is treated by a variety of methods (see section VIII).
7. **Urine output** ideally should be maintained at 2 mL/kg/min to avoid renal tubular damage from myoglobin. A Foley catheter should be placed as soon as possible.
8. **Recrudescence, disseminated intravascular coagulation, and acute tubular necrosis** may occur after an acute episode of malignant hyperthermia. Therefore, dantrolene therapy (1 mg/kg IV or orally every 6 hours) and observation should be continued for 48 to 72 hours after an episode of malignant hyperthermia.
9. Contact the MH hotline if necessary at 1-800-MH-HYPER (1-800-644-9737) from within the United States. Information can also be obtained at www.mhaus.org.

D. Anesthesia for Malignant Hyperthermia–Susceptible Patients

1. A **family history** of anesthetic problems suggesting susceptibility, such as unexplained fevers or death during anesthesia, should be sought in every patient.
2. **Malignant hyperthermia (MH)** may be triggered in susceptible patients who have had previous uneventful exposures to triggering agents.
3. **Pretreatment with dantrolene** is not recommended for malignant hyperthermia–susceptible patients. A MH cart or other dantrolene supply, however, should be immediately available.
4. **The anesthesia machine** should be prepared by changing the carbon dioxide absorbent and fresh gas tubing, disconnecting the vaporizers, using a disposable breathing circuit with charcoal filters if available, and flushing the machine with oxygen at a rate of 10 L/minute for at least 20 minutes. The preparation of modern anesthesia machines is variable. Some are more difficult to prepare and may require prolonged flushing times with maximal fresh gas flows while others only require carbon filters in inspiratory and expiratory limbs of the circuit.
5. **Local or regional anesthesia** should be considered, but general anesthesia with nontriggering agents is acceptable. **Safe drugs** for induction and maintenance of general anesthesia include barbiturates, propofol, benzodiazepines, opioids, and nitrous oxide. Nondepolarizing neuromuscular blockers may be used and safely reversed.
6. **Close monitoring** for early signs of malignant hyperthermia such as unexplained hypercarbia or tachycardia is crucial.

E. Associated Syndromes. An increased risk of malignant hyperthermia has been reported in association with a number of disorders. In many of these cases, the association is not well established. However, patients with the following disorders should be treated as though they are susceptible to malignant hyperthermia:

1. **King-Denborough syndrome**, characterized by dwarfism, mental retardation, and musculoskeletal abnormalities.
2. **Central core disease**, a rare myopathy.
3. **Multiminicore disease**, another rare myopathy
4. **Duchenne muscular dystrophy** and other **muscular dystrophies** are not associated with Malignant Hyperthermia, but may be associated with hyperkalemia.

F. Neuroleptic malignant syndrome (NMS) is associated with the administration of neuroleptic drugs and shares many of the features of malignant hyperthermia.

1. **Clinical features.** NMS typically develops over 24 to 72 hours and is clinically similar to malignant hyperthermia, presenting as a hypermetabolic episode consisting of hyperthermia, autonomic nervous system instability, pronounced muscle rigidity, and rhabdomyolysis. Creatine kinase and hepatic transaminases often are increased, and mortality approaches 30%.
2. **Treatment** of NMS is with dantrolene, although benzodiazepines, dopamine antagonists such as bromocriptine, and nondepolarizing muscle relaxants will also decrease muscle rigidity.
3. **Anesthetic implications.** The exact relationship between NMS and malignant hyperthermia is unclear. Some patients with a history of NMS may be at risk for malignant hyperthermia, and a conservative approach may be warranted (e.g., avoidance of known triggering agents). Patients with NMS must be appropriately monitored for malignant hyperthermia during all anesthetics (e.g., temperature and end-tidal carbon dioxide). They should not be pretreated with dantrolene.

XVIII. ANAPHYLACTIC AND ANAPHYLACTOID REACTIONS

- A. Anaphylaxis** is a life-threatening allergic reaction. It is initiated by antigen binding to preformed IgE antibodies on the surface of mast cells and basophils, which cause release of vasoactive substances (e.g., histamine, leukotrienes, prostaglandins, kinins, and platelet-activating factor). Anaphylaxis is characterized by an acute elevation in tryptase levels.
- B. Anaphylactoid reactions** are clinically similar to anaphylactic reactions, but they are not mediated by IgE and do not require prior sensitization to an antigen.
- C. Clinical features** of anaphylactic or anaphylactoid reactions may include the following:
1. Urticaria and flushing.
 2. Bronchospasm or airway edema, which can produce respiratory failure.
 3. Hypotension and shock due to peripheral vasodilation and increased capillary permeability.
 4. Pulmonary edema.
- D. Treatment**
1. **Discontinue anesthetic agents** if circulatory collapse is present.
 2. **Administer 100% oxygen.** Assess the need to intubate and support ventilation. Airway edema can persist beyond the acute event.
 3. **Begin intravascular volume expansion.**
 4. **Treat hypotension by giving epinephrine** (50 to 100 μ g IV). For overt cardiovascular collapse, epinephrine (0.5 to 1.0 mg IV) is indicated, followed by an infusion if hypotension persists. Epinephrine is useful for treating hypotension and bronchospasm, and for limiting mast cell degranulation. Other catecholamines such as norepinephrine may be added. Vasopressin should be added in refractory causes.
 5. **Steroids** (e.g., hydrocortisone, 250 mg to 1.0 g IV, or methylprednisolone, 1 to 2 g IV) may reduce the inflammatory response.
 6. **Histamine antagonists** (e.g., diphenhydramine, 50 mg IV, and ranitidine, 50 mg IV in the adult) may be useful as second-line therapy.
- E. Prophylaxis for Drug Hypersensitivity Reactions**
1. **Histamine (H_1) antagonists.** Diphenhydramine (0.5 to 1.0 mg/kg or 50 mg IV in the adult) the night before and morning of exposure.
 2. **H_2 antagonists.** Ranitidine (50 mg IV or 150 mg orally in the adult) the night before and the morning of exposure.
 3. **Corticosteroids.** Prednisone (1 mg/kg or 50 mg for adults), four doses every 6 hours before exposure.

XIX. FIRE AND ELECTRICAL HAZARDS IN THE OPERATING ROOM

- A. Fire** in the operating room is a rare event that requires the presence of an ignition source, fuel, and an oxidizing agent.
1. **Lasers and electrocautery devices** are the most common ignition sources.
 2. **Fuels** include alcohol, solvents, sheets, drapes, and plastic or rubber materials (including endotracheal tubes). Modern potent inhalation anesthetics are not fuels. During an electrical fire, it is important to unplug the electrical source.
 3. **Oxygen** is by far the most common oxidizing agent, although nitrous oxide also supports combustion. Materials that are only marginally combustible in air can produce a massive flame in the presence of a high oxygen concentration. Supplemental oxygen can accumulate under surgical drapes and should be administered only when medically indicated.

4. **Fire extinguishers** should be readily available in all anesthetizing locations. Carbon dioxide and halon fire extinguishers offer the advantage of efficacy against a variety of fires without producing the particulate contamination associated with dry chemical extinguishers.

B. Electrical Safety

1. **Macroshock** is an electrical injury caused when a large current passes through intact skin producing a thermal, neural, or muscular injury. It may disrupt normal physiologic function and cause cardiac or respiratory arrest. The level of injury varies with source frequency and individuals, but, in general, the following guidelines can be applied for an alternating current of 60 cycles/second:
 - a. **1 mA for 1 second:** threshold of perception
 - b. **5 mA for 1 second:** accepted as maximum harmless current intensity. Level at which line isolation monitors alarm.
 - c. **10 to 20 mA for 1 second:** current that results in sustained muscular contraction, referred to as the "Let go current."
 - d. **100 mA for 1 second:** threshold for ventricular fibrillation.
2. **Microshock** occurs when small currents pass directly to the heart. This occurs intentionally when using cardiac pacemakers but can be harmful if it occurs inadvertently. Ventricular fibrillation can be produced by as little as **100 μ A** of current applied to the myocardium. This current is well below the 2 to 5 mA threshold of the line isolation monitor alarm, thus line isolation monitors do not protect a patient from microshock. To minimize the likelihood of microshock, all equipment should be properly grounded with a three-prong plug, and connections to the patient should be electrically isolated. Battery operation does not ensure electrical isolation.
3. **Line isolation monitors** are designed to alert the anesthesiologist when faulty ground connections place patients and operating room personnel at risk of potential exposure to large currents (2 to 5 mA). The line isolation monitor alarms when one of the two "hot" power lines becomes grounded, creating a first fault. This event signals that someone in the operating room may receive a macroshock if they touch any electrical equipment supplied by this circuit, as they now serve as the ground for the system, creating the second fault. If the line isolation monitor alarms, unplug the last appliance that was plugged in. Further investigation into the appliance or circuit will be necessary. Although line isolation monitors continue to be used in operating rooms, most electrical equipment used today has built-in electrical isolation and many modern operating rooms contain ground fault interrupters on electrical outlets.
4. **Burns from electrosurgical units (ESU)** may result from poor contact between the dispersive electrode (grounding pad) and the patient. Under such conditions, anything that is grounded may provide an alternative pathway for current, resulting in a burn at these sites. The risk of burns can be minimized by ensuring that the electrode gel is adequate, that the dispersive electrode is placed near the surgical site, and that the patient is insulated from possible alternative pathways for current flow.

Suggested Readings

- Chacko T, Ledford D. Peri-anesthetic anaphylaxis. *Immunol Allergy Clin North Am* 2007; 27(2):213–230.
- Cotton N, Larcher C, Sommet A, et al. The sevoflurane washout profile of seven recent anesthesia workstations for malignant hyperthermia-susceptible adults and infants: a bench test study. *Anesth Analg* 2014;119:67–75.

- Ebo DG, Fisher MM, Hagendorens MM, et al. Anaphylaxis during anaesthesia: diagnostic approach. *Allergy* 2007;62:471–487.
- Flood P, Rathmell JP, Shafer S. *Stoelting's Pharmacology and Physiology in Anesthetic Practice*. 5th ed. Philadelphia: Wolters Kluwer; 2014.
- Fuchshuber P, Jones S, Josens D, et al. Ensuring safety in the operating room—the “fundamental use of surgical energy” (FUSE) program. *Int Anesthesiol Clin* 2013;51:65–80.
- Gaba DM, Fish KJ, Howard SN, et al. *Crisis Management in Anesthesiology*. 2nd ed. Philadelphia: Churchill Livingstone; 2014.
- Hines RL, Marschall KE. *Stoelting's Anesthesia and Co-Existing Disease*. 6th ed. Philadelphia: Saunders; 2012.
- Kim TW, Nemergut ME. Preparation of modern anesthesia workstations for malignant hyperthermia-susceptible patients: a review of past and present practice. *Anesthesiology* 2011;114:205–212.
- Lobato EB, Gravenstein N, Kirby RR. *Complications in Anesthesiology*. Philadelphia: Lippincott; 2007.
- Marik PE. Aspiration pneumonitis and aspiration pneumonia. *N Engl J Med* 2001;344:665–671.
- Marik PE, Cavallazzi R, Vasu T, et al. Dynamic changes in arterial waveform derived variables and fluid responsiveness in mechanically ventilated patients: a systematic review of the literature. *Crit Care Med* 2009;36:2642–2647.
- Simons ER, Arduso LR, Bilo MB, et al. International consensus on (ICON) anaphylaxis. *World Allergy Organ J* 2014;7:1–19.
- Zacharias M, Mugawar M, Herbison GP, et al. Interventions for protecting renal function in the perioperative period. *Cochrane Database Syst Rev* 2013;(9):CD003590.

I. BLOOD PRESSURE

The goal of hemodynamic management is to maintain adequate organ perfusion. Since organ perfusion is difficult to measure in vivo, systemic blood pressure is monitored as an indicator of blood flow and organ perfusion. The relationship between systemic blood pressure and systemic perfusion can be modeled by the mechanical analogue of Ohm's Law: $MAP - CVP = SVR \times CO$. Where MAP represents mean arterial pressure, CVP represents central venous pressure, SVR represents systemic vascular resistance, and CO represents cardiac output. As illustrated by the equation, changes in MAP do not always reflect changes in CO.

A. Cardiac output is influenced by heart rate, preload, afterload, and myocardial compliance and contractility. These separate variables are intimately interdependent and controlled by the autonomic nervous system and humoral mechanisms.

II. AUTOREGULATION

The ability of an organ or vascular bed to maintain adequate blood flow despite varying blood pressure is termed autoregulation. Metabolic regulation controls about 75% of all local blood flow in the body. Organs have differing ability (autoregulatory reserve) to increase or decrease their vascular resistance to provide tight coupling between metabolic demand and organ blood flow. Anesthetic agents that cause vasodilation inhibit organ autoregulation. Under these conditions, organ perfusion is more dependent on systemic blood pressure.

III. ADRENERGIC RECEPTOR PHYSIOLOGY (TABLE 20.1)

Adrenergic receptors can be distinguished by their response to a series of catecholamines. α -Adrenergic receptors are activated by norepinephrine, epinephrine, and isoproterenol in descending order of responsiveness. Beta-adrenergic receptors demonstrate the inverse, with the greatest activity in response to isoproterenol, followed by epinephrine and finally norepinephrine. Receptors that interact exclusively with dopamine are termed **dopaminergic**. Adrenergic receptors can be further subdivided based on their anatomic location and downstream effects.

A. α_1 Receptors are located postsynaptically in vascular smooth muscle and in the smooth muscle of the coronary arteries, uterus, skin, intestinal mucosa, iris, and splanchnic bed. Activation causes arteriolar and venous constriction, mydriasis, and relaxation of the intestinal tract. Cardiac α_1 receptors increase inotropy and decrease heart rate.

B. α_2 Receptors

1. Presynaptic α_2 receptors are located in the locus ceruleus and substantia gelatinosa within the central nervous system. Activation of these receptors inhibits the release of norepinephrine, acetylcholine, serotonin, dopamine, and substance P. Activation has been associated with hypnotic and sedative effects, antinociceptive action, hypotension, and bradycardia.

TABLE
20.1

Adrenergic Receptors and Their Effect Sites^d

Receptor	Site of Action	Effect	Agonists	Antagonists
α_1	Vascular smooth muscle	Increase inotropy	Phenylephrine ^a	Phenoxybenzamine
	Uterus	Vasoconstriction	Epinephrine	Phentolamine
	Skin	Mydriasis	Norepinephrine	Terazosin
	Intestinal mucosa	Uterine contraction	Methyldopa	Prazosin
	Iris	Sphincter constriction	Clonidine	Carvedilol
	Splanchnic bed	Bronchoconstriction	Dexmedetomidine	
	Coronary arteries	Inhibition of insulin secretion		
α_2	Presynaptic: Central nervous system	Inhibit release of neurotransmitters (NE, Ach, dopamine, serotonin)	Dexmedetomidine	Phenoxybenzamine
		Hypnosis, sedation	Clonidine	Phentolamine
		Bradycardia, hypotension	Epinephrine	Labetalol
			Norepinephrine	
			Phenylephrine	
			Methyldopa	
	Postsynaptic: Vascular smooth muscle	Vasoconstriction		
		Decreased insulin release		
	Gastrointestinal tract	Decreased salivation		
	Pancreatic β cells	Analgesia		
	Central nervous system			
β_1	Myocardium	Increased inotropy	Isoproterenol	Atenolol ^c
	SA node	Increased chronotropy	Epinephrine	Esmolol ^c
	Cardiac conduction system	Increased renin release	Dobutamine	Metoprolol ^c
	Kidneys	Lipolysis	Norepinephrine	Propranolol
	Adipose tissue		Dopamine	Labetalol
β_2	Vascular smooth muscle	Vasodilation	Ephedrine ^b	
		Bronchodilation	Terbutaline	Labetalol
	Bronchial smooth muscle	Uterine relaxation	Isoproterenol	Propranolol
		Increased inotropy	Terbutaline	Esmolol (at high doses)
		Insulin release	Epinephrine	
	Myocardium		Ephedrine	
	Uterus		Dopamine	
DA ₁	Renal smooth muscle	Vasodilation	Fenoldopam	^d
	Mesenteric smooth muscle		Dopamine	
			Dopexamine	
DA ₂	Presynaptic	Inhibit norepinephrine release	Dopamine	^d
			Dopexamine	

^a Agonists listed in descending order of effect.

^b Primary mode of action for ephedrine is indirect stimulation of receptor release.

^c Selective for β_1 -receptors.

^d Only hemodynamically significant drugs included in table.

2. **Postsynaptic α_2 receptors** are located within the central nervous system, as well as peripherally in vascular smooth muscle, the gastrointestinal tract, and pancreatic β cells. Activation of the peripheral postsynaptic α_2 receptors causes vasoconstriction, hypertension, decreased salivation, and decreased insulin release. Activation of the central receptors is associated with analgesia and an anesthetic-sparing effect.
- C. **β_1 Receptors** are located in the myocardium, sinoatrial node, ventricular conduction system, adipose tissue, and renal tissue. Activation causes an increase in inotropy, chronotropy, myocardial conduction velocity, renin release, and lipolysis.
- D. **β_2 Receptors** are located in vascular, bronchial, dermal, and uterine smooth muscle, as well as in the myocardium. Stimulation leads to vasodilation, bronchodilation, uterine relaxation, and, possibly, an increase in inotropy. β_2 Receptor activation also promotes gluconeogenesis, insulin release, and potassium uptake by cells.
- E. **β_3 Receptors** are involved in lipolysis and regulation of metabolic rate.
- F. **Dopaminergic Receptors** are divided into five subtypes (D1, D2, D3, D4, and D5). These are further classified into a D1-like family, consisting of D1 and D5 receptors, and D2-like family, consisting of D2, D3, and D4 receptors.
 1. **Dopaminergic-1 receptors** are located postsynaptically on renal and mesenteric vascular smooth muscle cells. They mediate vasodilation.
 2. **Dopaminergic-2 receptors** are located presynaptically in the central nervous system and inhibit norepinephrine release.
- G. **Receptor Regulation.** There is an inverse relationship between the receptor number and the concentration and duration of exposure to circulating adrenergic agonists. This is termed receptor up-regulation and down-regulation. For example, chronic β -blocker therapy leads to the up-regulation of β -adrenergic receptors. As a result, the sudden cessation of β -blocker therapy may be associated with rebound hypertension and tachycardia with resulting myocardial ischemia due to hypersensitivity to endogenous catecholamines.

IV. ADRENERGIC PHARMACOLOGY (TABLE 20.2)

A. α -Agonists

1. **Phenylephrine** is a direct-acting α_1 -agonist at typical clinical doses (40 to 200 mcg/min infusion), with some β -receptor activity at higher doses or with concurrent α -blockade. Phenylephrine causes both arterial and venous vasoconstriction. This dual action increases venous return and mean arterial blood pressure, frequently resulting in reflex bradycardia. Phenylephrine maintains cardiac output in patients with normal myocardial function but may decrease cardiac performance in the presence of myocardial ischemia. Phenylephrine has a short duration of action, which makes it easily titratable.
2. **Clonidine** is a centrally acting antihypertensive with relative selectivity for α_2 -adrenoreceptors. Its actions include reducing sympathetic tone, increasing parasympathetic activity, reducing anesthetic and analgesic requirements, causing sedation, and decreasing salivation. It can be administered intravenously, intramuscularly, orally, transcutaneously, and into the intrathecal and epidural spaces.
3. **Dexmedetomidine** is a selective α_2 -adrenoreceptor agonist currently approved for the short-term (<24 hours) intravenous sedation of mechanically ventilated patients in an intensive care setting. Its action

Drug Dosages of Commonly Used Vasopressors and Inotropes

Drug Name (Trade Name)	IV Bolus	IV Infusion	Dose	Adrenergic Effects			
				α	β	DA	V
Arginine vasopressin (Pitressin)	NR (septic shock) 40 units (cardiac arrest)	1. 50 units/250 mL 2. 0.2 units/mL 3. 0.01–0.1 unit/min 4. 10–20 min					+++
Dobutamine (Dobutrex)	NR	1. 250 mg/250 mL 2. 1,000 μ g/mL 3. 2–20 μ g/kg/min 4. 5–10 min		+	+++		
Dopamine (Inotropin)	NR	1. 200 mg/250 mL 2. 800 μ g/mL 3. 1–20 μ g/kg/min 4. 5–10 min	Low High	++	++	+++	+++
Ephedrine Epinephrine (Adrenaline)	5–10 mg 20–100 μ g (hypotension) 0.5–1 mg (cardiac arrest)	NR 1. 1 mg/250 mL 2. 4 μ g/mL 3. 0.5–5 μ g/min 4. 1–2 min	++ Low High	++ + ++	+++ +++ +++++		
Isoproterenol (Isuprel)	NR	1. 1 mg/250 mL 2. 4 μ g/mL 3. 2–10 μ g/min 4. 5–10 min			++++		

(continued)

TABLE
202

Drug Dosages of Commonly Used Vasopressors and Inotropes (continued)

Drug Name (Trade Name)	IV Bolus	IV Infusion	Dose	Adrenergic Effects			
				α	β	DA	V
Milrinone	NR	20 mg/250 mL of 0.9% NaCl; 50 μ g/kg IV load over 10 min, then 0.375–0.75 μ g/kg/min; dosage adjustment required for renally impaired patients				Nonsympathomimetic	
Norepinephrine (Levophed)	NR	1. 4 mg/250 mL 2. 16 μ g/mL 3. 1–30 μ g/min 4. 1–2 min	Low High	++ ++++	+ ++		
Phenylephrine (Neosynephrine)	40–100 μ g	1. 10 mg/250 mL 2. 40 μ g/mL 3. 10–150 μ g/min 4. 5–10 min		++++			

DA, dopaminergic; V, vasopressin; NR, not recommended.

on presynaptic receptors inhibits the release of norepinephrine, and its activation of postsynaptic α_2 -receptors in the CNS inhibits sympathetic activity. These effects decrease blood pressure and heart rate. Dexmedetomidine offers potential advantages over other sedatives, including lack of respiratory depression, lower rates of associated delirium, and a decreased incidence of hypotension.

B. β -Agonists (Please refer to Table 20.2 for recommended dose ranges.)

1. **Isoproterenol** is a direct-acting, nonselective β -adrenergic agonist. It gives rise to an increase in heart rate and contractility through its actions at β_1 -receptors and reduces SVR through its actions on β_2 -receptors. It has a neutral effect on cardiac output. It is also a pulmonary vasodilator and a bronchodilator.

a. Indications

1. Hemodynamically significant, atropine-resistant bradycardia
 2. Atrioventricular block until temporary pacing can be instituted
 3. Maintenance of an elevated heart rate such as in pediatric patients who have a fixed stroke volume and cardiac transplant recipients
 4. Status asthmaticus
 5. β -blocker overdose
- b. Continuous electrocardiographic monitoring is recommended with intravenous administration. It may be through a peripheral intravenous line.
- c. Adverse effects include vasodilation, hypotension, and tachyarrhythmias. It may contribute to an imbalance in myocardial oxygen supply and demand, leading to myocardial ischemia.

C. Mixed Agonists

1. **Epinephrine** is a direct-acting α - and β -receptor agonist, produced by the adrenal medulla.

a. Indications

1. Cardiac arrest
2. Anaphylaxis
3. Bronchospasm
4. Cardiogenic shock
5. Symptomatic bradycardia or heart block
6. Prolongation of the duration of action of local anesthetics

- b. **The clinical effect of epinephrine** is determined by its activation of both α - and β -receptors, with β -effects predominating at lower doses. At very low doses (e.g., 0.25 to 0.5 $\mu\text{g}/\text{min}$), epinephrine primarily causes bronchodilation and is the most effective bronchodilator available. Increasing doses cause increases in inotropy, chronotropy, and vasoconstriction. At even higher doses, α -effects predominate, and stroke volume may fall as SVR increases. Significant tachycardia, dysrhythmias, and myocardial ischemia may limit the usefulness of epinephrine in the clinical setting. Volatile anesthetics, especially halothane, can sensitize the myocardium to circulating catecholamines leading to potentially life-threatening dysrhythmias. Epinephrine should be administered through a central venous line whenever possible because severe tissue necrosis can occur if it extravasates.

2. **Norepinephrine**, the neurotransmitter of the sympathetic nervous system, is the biosynthetic precursor of epinephrine. Norepinephrine is a potent α - and β_1 -receptor agonist, with α effects predominating at lower doses. Compared to epinephrine, it has minimal effects on β_2 receptors. Norepinephrine increases blood pressure by increasing

SVR, whereas cardiac output remains relatively unchanged. Myocardial performance may improve, if the increased blood pressure improves coronary blood flow and relieves myocardial ischemia. Norepinephrine increases the vascular resistance of most organs, thereby diminishing organ perfusion despite increases in MAP. As with most vasoactive agents, intra-arterial blood pressure monitoring as well as continuous cardiac rhythm monitoring should be instituted to guide dose titration. Norepinephrine should be administered centrally. Possible side effects include arrhythmias and worsening microvascular perfusion, particularly at higher doses.

3. **Dopamine**, the immediate precursor of norepinephrine, produces a dose-related combination of α -, β -, and dopamine receptor effects. It also serves as a neurotransmitter in the basal ganglia and chemoreceptor trigger zone. At lower doses (approximately $<4 \mu\text{g/kg/min}$), renal and splanchnic vessel dopamine receptors are activated primarily, resulting in increased renal blood flow, glomerular filtration, and sodium (Na^+) excretion. As the dose of dopamine is increased (4 to $10 \mu\text{g/kg/min}$), β effects become apparent, leading to increases in myocardial contractility, heart rate, and arterial blood pressure. At high doses ($>10 \mu\text{g/kg/min}$), α_1 effects predominate, leading to marked increases in arterial and venous blood pressure and decreases in renal blood flow. Dopamine also causes the release of norepinephrine from nerve terminals. Dopamine administration often increases urine output but does not prevent or alter the course of renal injury. Dopamine may be indicated in cardiogenic or vasodilatory shock, heart failure, and refractory bradycardia. Tachycardia (often seen even at lower doses), ventricular arrhythmias, increased myocardial oxygen consumption, and profound vasoconstriction are adverse effects associated with its administration.
4. **Dobutamine** is a synthetic catecholamine that has β_1 -, β_2 -, and α_1 -adrenergic receptor activity. Dobutamine is a mixture of stereoisomers; the L(-)-isomer stimulates α_1 -receptors and the D(+)-isomer has β_1 - and β_2 -receptor activity. Dobutamine increases myocardial contractility through its effect on cardiac α_1 - and β_1 -receptors. In the peripheral vasculature, dobutamine has vasodilatory effects because its β_2 -effect overshadows its α_1 -properties. Dobutamine increases heart rate secondary to the positive chronotropic effects of β_1 activation. It is a useful agent for treating low cardiac output states caused by myocardial dysfunction secondary to acute infarction, cardiomyopathy, or myocardial depression after cardiac surgery. Dobutamine typically increases cardiac output and decreases SVR with minimal effects on arterial blood pressure and heart rate. Its hemodynamic effects are similar to those resulting from a combination of dopamine and nitroprusside. Pulmonary vascular resistance (PVR) also decreases, making dobutamine beneficial for patients with right heart failure. Systemic hypotension, increased myocardial oxygen consumption, and tachyarrhythmias are the most common side effects.
5. **Ephedrine** is a plant-derived, noncatecholamine, direct, and indirect adrenergic agonist. Ephedrine causes the release of norepinephrine and other endogenous catecholamines stored within nerve terminals. It is utilized for the temporary treatment of hypotension associated with hypovolemia, sympathetic blockage, myocardial depression secondary to anesthetic overdose and bradycardia. Tachyphylaxis quickly develops, which limits its use to bolus administration.

D. Nonadrenergic Agents

1. **Inamrinone** (name changed from amrinone to prevent confusion with amiodarone), milrinone, and enoximone are synthetic, noncatecholamine, nonglycosidic, bipyridine derivatives. They act by inhibiting type III phosphodiesterase, thereby increasing cyclic adenosine monophosphate (cAMP) levels and causing increased contractility and peripheral vasodilation. Their action is independent of adrenergic receptors and, as such, their effects are synergistic with those of adrenergic agents.
 - a. Inamrinone produces a dose-dependent improvement in cardiac index, left ventricular work index, and ejection fraction. Heart rate and MAP remain constant. The time to peak effect is about 5 minutes. Inamrinone undergoes hepatic elimination with a half-life of 5 to 12 hours. Adverse effects include dose dependent but reversible hypotension, thrombocytopenia, hypokalemia, dysrhythmias, liver function test abnormalities, fever, and gastrointestinal distress.
 - b. **Milrinone** is a derivative of inamrinone and has the same hemodynamic profile. Milrinone is **twenty times more potent** than inamrinone and is not associated with thrombocytopenia. A typical dosing strategy would include a bolus of 50 $\mu\text{g}/\text{kg}$ followed by an infusion of 0.375 to 0.75 $\mu\text{g}/\text{kg}/\text{min}$. Adverse effects include hypotension, ventricular arrhythmias, cardiac ischemia, and torsades de pointes. It has a half-life of 2 to 4 hours, such that it needs to be introduced with caution in unstable patients. Coadministration with a vasopressor is often necessary given the potential for significant hypotension. Milrinone is frequently used for inotropic support following coronary artery bypass grafting.
 - c. **Enoximone** is an orally available imidazolone derivative. At low dose (25 to 50 mg three times daily), it improves the exercise capacity of patients with chronic heart failure.
2. **Levosimendan** is both a positive inotrope and a vasodilator. It binds to cardiac troponin C, sensitizing the myofilament to calcium, and facilitating ATP-dependent potassium channel opening. Its primary role is in the treatment of decompensated low output heart failure. Its use has been investigated in a series of trials containing approximately 3,500 patients with one of the most recent trials, the SURVIVE trial published in 2007 showing no difference in mortality at 180 days when compared to patients treated with dobutamine. A Cochrane review on its use in low output cardiac failure included only four trials and 66 patients. However, it did reveal a trend toward hemodynamic benefit and improved mortality in the levosimendan arm. A much larger meta-analysis of 27 trials and 3,350 patients found a significant improvement in mortality and the rate of myocardial infarction in the levosimendan arm. Possible adverse effects include hypotension, arrhythmias, myocardial ischemia, and hypokalemia.
3. **Arginine vasopressin (AVP)** is a synthetic analog of antidiuretic hormone. AVP causes vasoconstriction by direct stimulation of vascular smooth muscle V1 receptors. It is a recommended alternative to epinephrine in the treatment of adult shock-refractory ventricular fibrillation as a one-time bolus (40 units intravenously [IV]). It may also be beneficial as a low-dose (0.04 unit/min) IV infusion in the setting of catecholamine-resistant vasodilatory shock, such as that seen in patients on chronic ACE inhibitor therapy. AVP may also be used in the setting of pulmonary hypertension as it preferentially constricts peripheral vasculature to increase SVP while it has no effect on pulmonary vasculature.

AVP has a rapid onset with a duration of action of 10 to 20 minutes. Administration through a central venous catheter is recommended.

4. **Terlipressin** is a vasopressin analog that has been studied as a first-line agent for the treatment of hypotension associated with catecholamine-resistant septic shock, as well as hepatorenal syndrome. However, case reports implicating terlipressin with both profound symptomatic hyponatremia and IV failure suggest that its risk profile may render it difficult to use clinically.
5. **Methylene blue** is an indicator dye commonly used in urologic surgery to assess the integrity of the urinary system, as well as in the treatment of methemoglobinemia. Methylene blue acts by competitively inhibiting guanylate cyclase, which in turn decreases the production of cGMP. This renders the vascular endothelium less sensitive to cGMP-mediated vasodilators, such as nitric oxide. Methylene blue has been shown to be effective in the treatment of vasoplegia following cardiopulmonary bypass. The most commonly described dosing regimen includes a slow bolus of 2 mg/kg, which may be followed by an infusion of 2 mg/kg/h. Adverse effects include transient dysrhythmias, increased PVR, and coronary vasoconstriction. It may precipitate acute hemolytic anemia in patients with glucose-6-phosphate dehydrogenase deficiency. Administration of methylene blue may interfere with pulse oximetry, producing falsely low readings.

V. β -ADRENERGIC ANTAGONISTS (TABLE 20.3)

- A. **Propranolol** is a nonselective β_1 - and β_2 -adrenergic receptor antagonist available in both IV and oral forms. Propranolol is highly lipophilic; it is almost entirely absorbed following oral administration and undergoes up to 75% first-pass clearance by the liver. Hemodynamic effects of propranolol and other β -adrenergic antagonists are secondary to the reduction of cardiac output and suppression of the renin-angiotensin system. β -Adrenergic antagonists can be distinguished by their relative β_1 selectivity, their intrinsic sympathomimetic activity, and their pharmacologic half-lives.
- B. **Metoprolol** is a selective β_1 -adrenergic receptor antagonist available in both oral and IV forms. It may be used to treat supraventricular tachycardias. It is also effective in the treatment of angina pectoris, in reducing mortality from myocardial infarction, and in treating mild-to-moderate hypertension. Its role in the prevention of perioperative adverse cardiac events remains somewhat controversial. According to the most recent AHA/ACC guidelines published in 2014, patients who are chronically on a β -blocker should continue this therapy in the perioperative as abrupt cessation is associated with increased adverse cardiac events. Preoperative initiation of β -blocker therapy may also be considered in patients with three or more RCSI risk factors. Both of these guidelines have level B evidence to support them.
- C. **Esmolol** is a selective β_1 -adrenergic receptor antagonist that is metabolized rapidly by esterases located in the cytoplasm of red blood cells. The red blood cell esterase is different from plasma pseudocholinesterase and is not affected by anticholinesterases. The time to its peak effect is 5 minutes, and its elimination half-life is 9 minutes. Esmolol is valuable perioperatively because it can be administered intravenously, it has a rapid onset, a very short duration of action, and it can be administered to patients with asthma, chronic obstructive pulmonary disease, and myocardial dysfunction. Its diluent contains propylene glycol, which may cause an osmolar gap metabolic acidosis during prolonged infusions.

TABLE
20.3 β -Adrenergic Antagonists

Drug Name (Trade Name)	β_1 -Selectivity	Bioavailability (%)	β Half-Life ^a	Elimination	Usual Oral Dose	IV Dose
Atenolol (Tenormin)	++	55	6–9 h	R (85%)	50–100 mg	5-mg increments
Esmolol (Brevibloc)	++	–	9 min	Red blood cell esterase		10- to 20-mg bolus; 0.25–0.5 mg/kg load, then 50–200 μ g/kg/min
Labetalol (Trandate, Normodyne)	0	25	3–8 h	H	100 mg	5- to 10-mg bolus; 10–40 mg/h titrated upward
Metoprolol (Lopressor)	++	50	3–6 h	H	25–100 mg qd-qid	5- to 25-mg increments
Nadolol (Corgard)	0	20	14–24 h	R (75%)	40–240 mg qd	NR
Propranolol (Inderal)	0	33	3–4 h	H	10–40 mg bid-qid	0.25- to 1-mg increments
Timolol (Blocadren)	0	75	4–5 h	H (80%) R (20%)	5–15 mg qd-bid	NR

^a β Half-life may not be predictive of clinical duration of action.

H, hepatic elimination; R, renal elimination; NR, not recommended.

D. Labetalol is a combined α - and β -adrenergic receptor antagonist. It has a β - to α -adrenergic receptor blockade ratio of 3:1 when given orally and 7:1 when administered intravenously. Its combined effect on both α - and β -receptors leads to decreased blood pressure without a reflexive increase in heart rate. Labetalol also decreases PVR and minimally affects cardiac output. Labetalol is useful intraoperatively to blunt the sympathetic response to tracheal intubation and to treat hypertension. Labetalol is also used in the management of patients with pheochromocytomas and rebound hypertension secondary to clonidine withdrawal.

VI. VASODILATORS (TABLE 20.4)

A. Sodium nitroprusside is a direct-acting vasodilator that acts on arterial and venous smooth muscle.

1. The mechanism of action of sodium nitroprusside is common to all nitrates. The nitroso moiety decomposes to release nitric oxide. Nitric oxide is an unstable, short-lived free radical that activates guanylate

TABLE
20.4

Vasodilator Drugs

Drug Name (Trade Name)	IV Bolus	IV Infusion	Mechanism of Action
Fenoldopam (Corlopan)	NR	1. 10 mg/250 mL 2. 40 μ g/mL 3. 0.05–1.5 μ g/kg/min 4. 1–4 h	D ₁ -Receptor agonist; moderate α_2 - receptor affinity
Hydralazine (Apresoline)	2.5–5 mg q15min, 20–40 mg IV q4–6 h	NR	Direct-acting vascular smooth muscle dilation
Labetalol (Trandate, Normodyne)	5–10 mg q5min	1. 200 mg/250 mL 2. 0.8 mg/mL 3. 10–40 mg/h 4. 15 min	α -receptor and β -receptor blockade
Nitroglycerin	50–100 μ g	1. 30 mg/250 mL ^a 2. 120 μ g/mL 3. 0.5–15 μ g/kg/min 4. 4 min	Venous vasodilator
Nitroprusside (Nipride)	NR	1. 30 mg/250 mL ^a 2. 120 μ g/mL 3. 0.2 μ g/kg/min ^b 4. 4 min	Arterial > venous vasodilator
Phentolamine (Regitine)	1–5 mg	NR	α -Receptor blockade
Prostaglandin E ₁ (Alprostadil)	NR	1. 1–2 mg/250 mL 2. 4–8 μ g/mL 3. 0.05 μ g/kg/min ^b 4. 1 min	Direct vasodilator via prostaglandin receptors in vascular smooth muscle

^a Massachusetts General Hospital infusion mix: 30 mg/250 mL of saline = 120 mg/1,000 mL = 120 μ g/mL. Infusion pump set at 20 mL/h = 20/60 mL/min = 1/3 mL/min = 40 μ g/min. Therefore, dose in μ g/min is 2 $\times$ the set infusion rate (2 $\times$ mL/h = μ g/min).

^b Dose may be titrated higher to desired effect.

a, mix in 5% dextrose in water; b, concentration; c, usual IV dosage range; d, duration; NR, not recommended.

cyclase. This activation leads to an increase in the concentration of cyclic guanosine monophosphate, which causes smooth muscle relaxation.

2. Sodium nitroprusside reduces afterload through arteriolar dilation and reduces preload through venous dilation. These effects typically cause a reflex increase in heart rate and myocardial contractility, an increase in cardiac output, and marked decreases in SVR and PVR. Sodium nitroprusside dilates cerebral blood vessels and should be used with caution in patients with decreased intracranial compliance.
3. Sodium nitroprusside dilates all vascular beds equally, increasing overall blood flow. A vascular steal phenomenon may be created when perfusion to an ischemic region that is already maximally vasodilated may be shunted to a nonischemic region that is able to vasodilate further. This is especially important in the coronary vasculature where regional ischemia may be exacerbated despite the decrease in overall myocardial oxygen consumption created by afterload reduction.
4. Sodium nitroprusside is useful perioperatively because it has a fast onset time (1 to 2 minutes), and its effects dissipate within 2 minutes of discontinuation.
5. **Cyanide toxicity.** In vivo, sodium nitroprusside reacts nonenzymatically with the sulfhydryl groups in hemoglobin to release five cyanide radicals per molecule. Some of these radicals can be converted to **thiocyanate** by tissue and liver rhodanese and excreted in the urine. Thiocyanate has a half-life of 4 days and will accumulate in the presence of renal failure. Cyanide radicals may also bind to intracellular cytochrome oxidase and disrupt the electron transport chain. This disruption can lead to cell hypoxia and death even in the face of adequate oxygen tensions.
 - a. **Clinical features.** Cyanide toxicity typically occurs when more than 1 mg/kg has been administered within 2.5 hours or when the blood concentration of cyanide ion is greater than 100 $\mu\text{g/dL}$. Tachyphylaxis, metabolic acidosis, and elevated mixed venous oxygen tensions are early signs of cyanide toxicity. Symptoms of cyanide toxicity include fatigue, nausea, muscle spasms, angina, and mental confusion.
 - b. **Treatment.** Cyanide toxicity is treated by discontinuing the sodium nitroprusside infusion and administering 100% oxygen and **sodium thiosulfate**. Sodium thiosulfate is a sulfur donor in the rhodanese reaction that converts cyanide to thiocyanate. It is administered as an infusion over 15 minutes at a dose of 150 mg/kg dissolved in 50 mL of water. Severe cyanide toxicity (base deficit >10 mEq, hemodynamic instability) may require the additional administration of **amyl nitrate** (0.3 mL by inhalation) or **sodium nitrate** (5 mg/kg IV over 5 minutes). These two compounds create methemoglobin, which will bind to the cyanide ion and form inactive cyanmethemoglobin.
- B. **Nitroglycerin** is a potent venodilator that also relaxes arterial, pulmonary, ureteral, uterine, gastrointestinal, and bronchial smooth muscles. Nitroglycerin decreases MAP primarily by increasing venous capacitance.
 1. **Indications.** Nitroglycerin is useful for treating congestive heart failure and myocardial ischemia by increasing coronary flow and improving left ventricular performance. Nitroglycerin increases venous capacitance, decreases venous return, and consequently decreases ventricular end-diastolic volume. A decrease in end-diastolic volume is associated with a decrease in ventricular wall tension, which reduces myocardial oxygen consumption.

2. **Reflex tachycardia** frequently occurs and must be treated with β -blockers to avoid increasing myocardial oxygen consumption and negating nitroglycerin's beneficial effects.
 3. **Tachyphylaxis** develops with continuous infusion.
 4. **Complications.** Nitroglycerin is metabolized by the liver and has no known toxicity in the clinical dose range. Extremely high doses (>250 to 300 mcg/min) and prolonged continuous use may produce methemoglobinemia. Nitroglycerin produces cerebral vasodilation and should be used with caution in patients with low intracranial compliance, for example, patients with cerebral tumors, hemorrhage, or edema.
- C. Hydralazine** is a direct-acting arterial vasodilator. It decreases MAP by reducing arteriolar tone in the coronary, cerebral, renal, uterine, and splanchnic beds. This helps preserve blood flow to these organs. The vasodilation induced by hydralazine triggers a reflex increase in heart rate and causes activation of the renin-angiotensin system. These effects can be attenuated by the concomitant use of a β -blocker. Hydralazine can be administered as an IV bolus of 20 to 80 mg given over 2 minutes to treat hypertensive emergencies or to augment the effect of other hypotensive agents. The time to peak effect of IV hydralazine is 15 to 20 minutes with an elimination half-life of 4 hours. Long-term use over months to years has been associated with a lupus-like syndrome, skin rash, drug fever, pancytopenia, and peripheral neuropathy.
- D. Calcium channel antagonists (verapamil, diltiazem, nifedipine, and clevidipine)** alter calcium flux across cell membranes and cause various degrees of arterial vasodilation with minimal effect on venous capacitance. They decrease the vascular resistance of peripheral organs and cause coronary artery vasodilation. They are also myocardial depressants. Verapamil and diltiazem also depress atrioventricular nodal conduction (see Chapter 38). **Nifedipine** is limited to oral administration for the treatment of hypertension. **Verapamil** and **diltiazem** are also indicated for the treatment of hemodynamically stable narrow complex supraventricular tachyarrhythmias. The initial verapamil dose is 2.5 to 5.0 mg IV, with subsequent doses of 5 to 10 mg IV administered every 15 to 30 minutes. Diltiazem is given as an initial bolus of 20 mg. An additional dose of 25 mg and an infusion of 5 to 15 mg/h can be administered if needed. Oral diltiazem is commonly used for chronic therapy of myocardial ischemia. Its vasodilatory and negative inotropic properties can cause hypotension, exacerbation of congestive heart failure, bradycardia, and enhancement of accessory conduction in patients with Wolff-Parkinson-White (WPW) syndrome. **Clevidipine** is an ultrashort-acting, intravenously administered dihydropyridine calcium channel antagonist. It may be used to treat hypertension when oral agents cannot be used as well as perioperative hypertension. It is rapid in onset, with a half life of approximately 60 seconds and can be rapidly titrated for effective blood pressure control. It relies only on serum esterase activity for metabolism. Its dosing is therefore independent of renal and hepatic function. Effects on blood pressure last between 5 and 10 minutes, with a 90% return to baseline blood pressure by 7 minutes. A suggested dosing regimen starts with an infusion of 1 to 2 mg/h, which may be doubled every 90 seconds until the blood pressure approaches target range. A dose of 6 to 8 mg/h is adequate for most patients.
- E. Enalaprilat, an active metabolite of enalapril,** is currently the only angiotensin-converting enzyme inhibitor available for IV use. It reduces systolic and diastolic blood pressure by inhibiting the conversion of angiotensin I to angiotensin II. Enalaprilat may be used to treat perioperative

hypertension. It has an onset of action of approximately 15 minutes, peak effect of 1 to 4 hours, and overall duration of action of about 4 hours. Elimination is primarily renal, and caution is recommended when used in the setting of renal dysfunction.

- F. Fenoldopam** is a synthetic dopamine (DA-1) receptor agonist. A continuous IV infusion may be used perioperatively for the management of severe hypertension in patients with impaired renal function. Fenoldopam acts by dilation of selective arterial beds while maintaining renal perfusion. Selective renal dose to increase renal blood flow without inducing hypotension is 3 $\mu\text{g/kg/min}$. It also has diuretic and natriuretic properties. The hemodynamic response occurs within 5 to 15 minutes. The dose should be adjusted every 15 to 20 minutes until optimal blood pressure control is achieved. Adverse effects include dose-dependent tachycardia and occasional hypokalemia. Bolus administration is not recommended, and hypotension may occur with concomitant use of β -adrenergic receptor blockade.
- G. Adenosine** is an endogenous nucleotide that, in high doses, has inhibitory effects on cardiac impulse conduction through the atrioventricular node. Adenosine dilates cerebral blood vessels, impairs autoregulation, and is metabolized to uric acid. Its ability to slow conduction through the atrioventricular node has led to its use in diagnosing and treating supraventricular tachydysrhythmias. However, if atrial fibrillation/flutter is present in a patient with WPW syndrome, adenosine should be avoided as it may allow preferential conduction through the accessory pathway (WPW syndrome; see Chapter 38).
- H. Prostaglandin E_1 (PGE_1)** is a stable metabolite of arachidonic acid that causes peripheral and pulmonary vasodilation. It is used to dilate the ductus arteriosus in neonates and infants with ductal-dependent congenital heart disease (e.g., transposition of the great arteries, coarctation of the aorta, or tetralogy of Fallot). PGE_1 also has been used to treat pulmonary hypertension in patients with severe right ventricular failure.
- I. Sildenafil** is a selective phosphodiesterase-5 inhibitor that can be used as a pulmonary vasodilator. By inhibiting phosphodiesterase-5, it stabilizes cGMP, leading to an increase in pulmonary levels of nitric oxide. It has been shown to improve exercise capacity and hemodynamics in patients with pulmonary hypertension.
- J. Phentolamine** is a short-acting selective α -adrenergic receptor antagonist that causes predominantly arterial and some venous vasodilation. Phentolamine is used to treat states of norepinephrine excess (e.g., pheochromocytoma); as an adjuvant for induced hypotension; and for infiltration into the skin where norepinephrine has been extravasated (5 to 10 mg diluted in 10 mL of saline).

VII. INDUCED HYPOTENSION

Induced hypotension is a somewhat controversial technique used when control of bleeding improves operating conditions and facilitates surgical technique (e.g., middle ear microsurgery, cerebral aneurysm clipping, and plastic surgery) or reduces the need for transfusion (e.g., orthopedic surgery, patients with rare blood groups, and religious constraints). An acceptable blood pressure goal is a target MAP of 30% below a patient's baseline, with a MAP no lower than 50 mm Hg in an otherwise healthy patient and 80 mm Hg in an elderly patient. This technique is not appropriate for patients with a history of vascular insufficiency to the heart, brain, or kidneys; cardiac instability (unless afterload reduction improves performance); uncontrolled

hypertension; anemia; or hypovolemia. It should be utilized with caution as serious complications, while rare in healthy patients, include cerebral infarct, myocardial infarction, and acute kidney injury. Hypotension can be achieved using neuraxial blockade, high concentrations of volatile anesthetics, potent short-acting opioids (e.g., remifentanyl), and peripheral vasodilators (e.g., nitroprusside or nitroglycerin). While this technique was first described in the 1940s and gained widespread popularity over the past 40 years, there is a paucity of data to support or refute this hemodynamic technique as efficacious.

VIII. DRUG DOSAGE CALCULATIONS

Drug concentrations frequently require conversion between various units of measurement before bolus or continuous infusion administration to the patient.

- A.** A drug concentration expressed as $Z\%$ contains:

$$Z \text{ mg/dL} = Z \text{ g/100 mL} = (10 \times Z) \text{ g/L} = (10 \times Z) \text{ mg/mL}$$

Example: A 2.5% solution of sodium thiopental is equivalent to 25 g/L or 25 mg/mL.

- B.** A drug concentration that is expressed as a ratio is converted as follows:

$$1:1,000 = 1 \text{ g/1,000 mL} = 1 \text{ mg/mL}$$

$$1:10,000 = 1 \text{ g/10,000 mL} = 0.1 \text{ mg/mL}$$

$$1:100,000 = 1 \text{ g/100,000 mL} = 0.01 \text{ mg/mL}$$

- C.** Continuous drug infusions are calculated based on a simple formula:

$$Z \text{ mg/250 mL} = Z \text{ } \mu\text{g/min at an infusion rate of 15 mL/h}$$

Standard drug mixes in use at Massachusetts General Hospital are shown in Table 20.1. The desired rate of infusion for any drug is easily calculated as a fraction or multiple of 15 mL/h.

Example: An 80-kg patient needs dopamine at 5 $\mu\text{g/kg/min}$:

$$5 \text{ } \mu\text{g/kg/min} \times 80 \text{ kg} = 400 \text{ } \mu\text{g/min}$$

$$400/200 \text{ (number of milligrams in 250 mL solution)} \times 15 \text{ mL/h} = 30 \text{ mL/h}$$

Suggested Readings

- Barak M, Yoav L, Abu el-Naaj I. Hypotensive anesthesia versus normotensive anesthesia during major maxillofacial surgery: a review of the literature. *Sci World J* 2015;2015:1–7.
- Barnes P. β -Adrenergic receptors and their regulation. *Am J Respir Crit Care Med* 1995;152:838–860.
- De Backer D, Biston P, Devriendt J, et al. Comparison of dopamine and norepinephrine in the treatment of shock. *N Engl J Med* 2010;362(9):779–789.
- Deeks ED, Keating GM, Keam SJ. Clevidipine: a review of its use in the management of acute hypertension. *Am J Cardiovasc Drugs* 2009;9(2):117–134.
- Dellinger RP, Levy MM, Rhodes A, et al. The Surviving Sepsis Campaign Guidelines Committee including The Pediatric Subgroup. Surviving sepsis campaign: international guidelines for management of severe sepsis and septic shock. *Int Care Med* 2013;39(2):165–228.
- Gordon AC, Wang N, Walley KR, et al. The cardiopulmonary effects of vasopressin compared with norepinephrine in septic shock. *Chest* 2012;142(3):593–605.
- Jadadzadeh M, Hosseini SH, Mostafavi Pour Manshadi SM, et al. Effect of milrinone on short term outcome of patients with myocardial dysfunction undergoing off-pump coronary artery bypass graft: a randomized clinical trial. *Acta Med Iran* 2013;51(10):681–686.
- Kamibayashi T, Maze M. Clinical uses of α_2 -adrenergic agonists. *Anesthesiology* 2000;93:1345–1349.
- Lavigne D. Vasopressin and methylene blue: alternate therapies in vasodilatory shock. *Semin Cardiothorac Vasc Anesth* 2010;14:186–189.
- Lawson N, Meyer D. Autonomic nervous system: physiology and pharmacology. In: Barash PG, Cullen BF, Stoelting RK, eds. *Clinical Anesthesia*. 3rd ed. Philadelphia: Lippincott-Raven Publishers; 1997:243–309.

- Mebazaa A, Nieminen MS, Packer M, et al. Levosimendan versus dobutamine for patients with acute decompensated heart failure: the SURVIVE randomized trial. *JAMA* 2007;297(17):1883–1891.
- Mousavi S. Vasopressin and septic shock. *J Pharm Care* 2013;1(2):65–73.
- Ndefo UA, Erowele GI, Ebiasah R, et al. Clevidipine: a new intravenous option for the management of acute hypertension. *Am J Health Syst Pharm* 2010;67(5):351–360.
- Overgaard CB, Dzavik V. Inotropes and vasopressors: review of physiology and clinical use in cardiovascular disease. *Circulation* 2008;118:1047–1056.
- Pasin L, Landoni G, Nardelli P, et al. Dexmedetomidine reduces the risk of delirium, agitation and confusion in critically ill patients: a meta-analysis of randomized controlled trials. *J Cardiothorac Vasc Anesth* 2014;28(6):1459–1466.
- Rodriguez MA, Kumar SK, De Caro M. Hypertensive crisis. *Cardiol Rev* 2010;18(2):102–107.
- Serpo Neto A, Nassar AP, Cardoso SO, et al. Vasopressin and terlipressin in adult vasodilatory shock: a systematic review and meta-analysis of nine randomized controlled trials. *Crit Care* 2012;16:R154.
- Srivastava U, Sarkar ME, Kumar A, et al. Comparison of clonidine and dexmedetomidine for short-term sedation of intensive care unit patients. *Indian J Crit Care Med* 2014;18(7):431–436.
- Treschan TA, Peters J. The vasopressin system: physiology and clinical strategies. *Anesthesiology* 2006;105(3):599–612.
- Unverzagt S, Wachsmuth L, Hirsch K, et al. Inotropic agents and vasodilator strategies for acute myocardial infarction complicated by cardiogenic shock or low cardiac output syndrome. *Cochrane Database Syst Rev* 2014;1:CD009669.

I. PREANESTHETIC CONSIDERATIONS

Patients undergoing abdominal surgery require a complete history and physical examination as outlined in Chapter 1. The following issues germane to abdominal surgery should be considered as well.

A. Preoperative Fluid Status. Surgical pathology may cause severe derangement in volume homeostasis, producing both hypovolemia and anemia. The main sources of fluid deficits are inadequate intake, sequestration of water and electrolytes into abdominal structures and fluid loss.

1. Assessment of volume status

- a. Postural changes in vital signs (increased heart rate and decreased blood pressure) may reveal mild-to-moderate hypovolemia; severe hypovolemia will produce tachycardia and hypotension. Dry mucous membranes, decreased skin turgor and temperature, delayed capillary refill, and skin mottling indicate decreased peripheral perfusion secondary to hypovolemia.
- b. Laboratory analysis including base excess, hematocrit, serum osmolality, BUN–creatinine ratio, serum and urine electrolyte concentrations, and urine output are helpful in estimating volume deficits.
- c. If the intravascular volume status of a patient cannot be determined by clinical assessment alone, then invasive monitoring may be required. In addition to monitoring systemic pressures, an arterial line may be used to assess pulse pressure variation (PPV) and systolic pressure variation (SPV) that can aid in estimating volume status without the risks associated with central line placement. In general, a delta-down component of SPV of 5 mm Hg and a PPV of 13% to 15% indicates that a patient will be volume responsive. Central venous pressure (CVP) measurement that has been the customary way to estimate volume status has fallen out of favor for several reasons. A pulmonary artery catheter may be placed in patients who will have ongoing volume requirements to optimize cardiovascular performance (see Chapter 10). Esophageal Doppler monitors can also be used to assess.

2. Etiology of hypovolemia

- a. **Reduced Intake:** NPO guidelines are reviewed in earlier chapters. Patients may have reduced or no oral intake before surgery. However, for elective cases, they may not be hypovolemic if following new NPO guidelines. Gastrointestinal tract obstruction may prevent adequate oral intake, and malabsorption may preclude absorption of adequate fluids. Despite IV hydration in the preoperative period, patients could arrive to the operating room with signs of hypovolemia and symptoms of dehydration.
- b. **Emesis or gastric drainage** may produce significant fluid losses, particularly in patients with bowel obstruction. Quantity, quality (bloody), duration, and frequency of emesis should be assessed.
- c. **Diarrhea** from intestinal disease, infection, or cathartic bowel preparation can cause significant extracellular fluid loss.

- d. Bleeding from gastrointestinal sources includes ulcers, neoplasms, esophageal varices, diverticula, angiodysplasia, and hemorrhoids.
 - e. Sequestration of fluid may occur either into the bowel lumen from ileus or into the interstitium from peritonitis.
 - f. Fever increases insensible fluid loss.
- B. Metabolic and hematologic derangements** occur frequently in patients requiring emergency abdominal surgery. Hypokalemic metabolic alkalosis is common in patients with large gastric losses (emesis or nasogastric [NG] tube drainage). Severe hypovolemia or septicemia can cause metabolic acidosis. Sepsis can produce disseminated intravascular coagulopathy.
- C. Length of surgery** is influenced by the history of previous abdominal surgery, intra-abdominal infection, radiation therapy, steroid use, surgical technique, and surgeon experience. This is often unpredictable, particularly if the pathology is unclear preoperatively.
- D. Anticipated postoperative course** will determine the type of anesthetic, fluid administration, analgesic considerations, and immediate postoperative management.
- E. All patients for emergency abdominal procedures are considered to have full stomachs.** A rapid sequence induction (RSI), potentially with the use of cricoid pressure or an awake intubation technique, is indicated with the goal of minimizing aspiration risk. It is worth noting that cricoid pressure has not been shown to reduce the risk of aspiration on induction. Premedication with histamine (H_2) antagonist and oral nonparticulate antacid can decrease gastric acidity. Metoclopramide decreases gastric volume, though the efficacy to reduce the risk of aspiration has never been proven. Metoclopramide also should not be used in cases of bowel obstruction.

II. ANESTHETIC TECHNIQUES

- A. General anesthesia (GA)** remains the most commonly employed technique.
1. Advantages include protection of the airway, assurance of adequate ventilation, and rapid induction of anesthesia with controlled depth and duration.
 2. Disadvantages include loss of airway reflexes, which increases the risk of aspiration during routine or emergency surgery, potential adverse hemodynamic consequences of general anesthetics, and potentially increased time for recovery.
- B. Regional anesthetic techniques** for abdominal surgery include neuraxial anesthetics (i.e., spinal, epidural, and caudal anesthesia) and peripheral nerve blocks performed on the trunk including rectus sheath, transverse abdominal plane (TAP), subcostal TAP, and ilioinguinal and iliohypogastric nerve blocks. The innervation of the abdominal wall is via the anterior divisions of the thoracolumbar nerves (T6–L1), and these blocks provide anesthesia and analgesia by blocking various divisions of these nerves. Thorough discussion of the risks and benefits of regional anesthesia are discussed in Chapter 18. Patients who undergo surgery via regional anesthesia typically require supplementation with anxiolytic/sedative medications to tolerate the operating room experience.
1. **Lower abdominal procedures** (e.g., inguinal hernia repair) can be performed with regional anesthesia techniques
 - a. Epidural anesthesia usually is performed with a continuous catheter technique. A “single-dose” technique is applicable for surgery of less than 3 hours but rarely used.

- b. Spinal anesthesia usually is performed with a single-dose technique, although spinal catheters can be placed. The duration of block is determined by the choice of local anesthetic and adjuvants (see Chapter 17).
 - c. Peripheral nerve blocks (discussed below) can also provide adequate anesthesia for abdominal surgery but are more commonly used as adjuvant techniques for postoperative analgesia.
 - d. Blockade of the ilioinguinal, iliohypogastric, and genitofemoral nerves produces a satisfactory field block for herniorrhaphy. These nerve blocks are easily performed by the anesthesiologist but may require direct supplementation of spermatic cord structures by the surgeon.
- 2. Upper abdominal procedures** (above the umbilicus, T10) are not well tolerated under regional anesthesia alone. Spinal or epidural anesthesia for upper abdominal procedures may require a sensory level to T2–T4. Paralysis of intercostal muscles from a high thoracic level impairs deep breathing. Although minute ventilation is maintained, patients often complain of dyspnea. Intraperitoneal air or upper abdominal exploration produces a dull pain referred to a C₅ distribution (usually over the shoulders) that is not prevented by regional anesthesia and may require supplementation with intravenous (IV) analgesics.
- 3. Advantages**
- a. If awake for the procedure, patients maintain the ability to communicate symptoms (e.g., chest pain).
 - b. Airway reflexes are maintained.
 - c. Profound muscle relaxation and bowel contraction optimize surgical exposure.
 - d. Sympathectomy increases blood flow to bowel.
 - e. Continuous catheter techniques provide a ready means for postoperative analgesia.
 - f. Regional techniques are opioid sparing.
 - g. There is some evidence to support earlier return of bowel function in patients with prolonged postoperative ileus when epidural catheters are used for postoperative analgesia.
- 4. Disadvantages**
- a. Local anesthetic toxicity from inadvertent IV injection or rapid absorption.
 - b. Patient cooperation is necessary for the institution of block and positioning during surgery.
 - c. Failure necessitates intraoperative conversion to GA.
 - d. Regional nerve blockade may be contraindicated in patients with abnormal bleeding profile or localized infection at the site of injection.
 - e. Sympathectomy with neuraxial techniques may lead to vaso/venodilation and bradycardia that can precipitate profound hypotension. Unopposed parasympathetic activity causes the bowel to contract and may make construction of bowel anastomoses more difficult; this can be reversed with glycopyrrolate, 0.2 to 0.4 mg IV, or 1 mg glucagon.
 - f. Blockade of upper thoracic nerves may compromise pulmonary function.
 - g. Awake patients often require frequent communication and reassurance; this may distract the anesthesiologist during complicated cases.

C. A combined technique makes use of a regional technique along with a general anesthetic. This technique is commonly used for extensive upper abdominal surgeries and may include an epidural or a nerve block + GA. Peripheral nerve blocks of the abdominal wall may be done awake, but more commonly immediately after induction or just prior to emergence (postprocedure) from GA. The nerve blocks can provide significant intra-operative and postoperative analgesia, creating an opioid-sparing technique. The blocks may be viable options when neuraxial techniques are contraindicated due to concerns for sepsis, severe spinal stenosis, severe peripheral nerve disease, or patient refusal.

The common peripheral nerve blocks that are performed on the abdominal wall include the following:

- 1. TAP blocks** can be used for most lower abdominal procedures, often as an alternative for epidural anesthesia. A regional needle is placed in the anterior axillary line, between the costal margin and the iliac crest. The local anesthetic spreads between the transversus abdominis and internal oblique muscle planes. Catheters are often used for TAP blocks to provide postoperative analgesia, providing a significant opioid-sparing effect.
- 2. Rectus sheath blocks** are appropriate for midline procedures, particularly periumbilical procedures. Local anesthetic is deposited via a regional needle between the rectus muscle and posterior rectus sheath.
- 3. Subcostal TAP blocks** are similar to the TAP block described above but the needle is placed more superiorly and laterally, below the costal margin. The upper nerve fibers, in particular T8–T10, are more likely anesthetized with this modification of the TAP block.

III. MANAGEMENT OF ANESTHESIA

A. Standard monitors are used as described in Chapter 10.

B. Induction of Anesthesia

1. Restoration of volume deficits before induction should be considered (discussed below).
2. RSI or awake intubation is required for all patients considered with full stomachs. Indications include conditions in which gastric emptying is delayed, intra-abdominal pressure is increased, or lower esophageal tone is compromised. Examples include trauma, bowel obstruction or ileus, hiatal hernia, gastroesophageal reflux disease, pregnancy beyond the first trimester, significant obesity, ascites, and diabetes with gastroparesis and autonomic dysfunction.

C. Maintenance of Anesthesia

1. Fluid replacement is guided by clinical judgment and/or invasive monitoring. Traditionally, very long cases with significant bowel exposure and preoperative hypovolemia required fluid replacement of up to 10 to 15 mL/kg/h. New evidence, however, suggests that a more restrictive approach may be associated with faster recovery and fewer complications.
2. Using a “protocol-based” strategy for fluid administration appears to reduce impairment of bowel motility, cardiopulmonary complications, and bowel edema; improve anastomosis healing; and reduce hospital stay time. There is not a strict definition of fluid restriction, nor is there agreed-upon protocol for fluid restriction. Literature has been published using differing protocols based on a variety of measured parameters including volume of fluid administered, perioperative weight gain, and volume based on hemodynamic responsiveness. The key point is

that more restrictive administration of intraoperative fluids in a deliberate, planned manner appears to improve outcomes. Patients with severe burns, severe hypotension, or major fluid shifts should not be significantly fluid restricted.

- a. Bleeding should be estimated both by direct observation of the surgical field and suction traps and by weighing sponges. Blood loss may be concealed (e.g., beneath drapes or within the patient). Labs should be checked appropriately.
 - b. Insensible losses likely range from 0.5 mL/kg/h to 1 mL/kg/h for larger abdominal cases, much less than many anesthesia providers believe.
 - c. After an overnight NPO period, blood volume is likely near normal in most patients and may not require IV fluid to make up for the fluid deficit. Clinical judgment will guide the need for resuscitation prior to starting the case.
 - d. Abrupt drainage of ascitic fluid with surgical entry into the peritoneum can produce acute hypotension from sudden decreases of intra-abdominal pressure and pooling of blood in mesenteric vessels, thus reducing venous return to the right heart. Postoperative reaccumulation of ascitic fluid can produce significant intravascular fluid losses.
 - e. NG and other enteric drainage should be quantified and replaced appropriately.
3. Fluid losses should be replaced with crystalloids, colloids, or blood products.
- a. Initially, fluid should be replaced by administration of an isotonic salt solution. When an isotonic crystalloid solution is used to replace blood loss, goal directed therapy and fluid response probably is better than traditional 3:1 replacement. Growing evidence shows aggressive normal saline use may cause non-anion gap metabolic acidosis.
 - b. Colloids are fluids containing particles large enough to exert oncotic pressure. They remain in the intravascular space longer than crystalloids. Multiple studies comparing fluid resuscitation with crystalloids to colloids have reported no benefit with colloids. Colloid solutions are more expensive than crystalloids, and their routine use may not be justified. Albumin may be superior to crystalloid in patients with significant burns, hepatorenal disease, or acute lung injury. Hydroxyethyl starch solutions (e.g., Hextend or Hespan) are non-blood-derived colloids that may also be used as methods of volume expansion but are falling out of favor due to deleterious effects on renal function, coagulation, and potentially all-cause mortality.
4. Muscle relaxation is required for all but the most superficial intra-abdominal procedures. Sufficient relaxation is critical during abdominal closure because bowel distention, edema, and organ transplantation can increase the volume of abdominal contents.
- a. Titrating relaxants to obtain a single twitch by train-of-four monitoring should provide enough relaxation for surgical closure yet allow for reversal of muscle relaxants for extubation.
 - b. Potent inhalational agents block neuromuscular conduction and are synergistic with relaxants.
 - c. Neuraxial blockade with local anesthetics provides excellent abdominal muscle relaxation.

- d. Flexing the operating table may decrease tension on transverse abdominal and subcostal incisions and facilitate surgical closure without need for profound muscular relaxation which is often requested by the surgeons.
- 5. Use of nitrous oxide (N_2O) may cause bowel distention because N_2O diffuses into the bowel lumen faster than nitrogen can diffuse out with the amount of distention depending on the concentration of N_2O delivered, the blood flow to the bowel, and the duration of N_2O administration. Under normal conditions, the initial volume of bowel gas is small; doubling or tripling of this volume does not pose a significant problem. Studies have shown that N_2O may be used in shorter (<3 hours) open and laparoscopic surgeries, without causing clinically significant bowel distention. Use of N_2O is relatively contraindicated in bowel obstruction because the initial volume of bowel gas may be large. Most recent ENIGMA trial did not prove nitrous oxide related to any significant adverse outcomes.
- 6. NG tubes are frequently placed in the perioperative period.
 - a. Preoperative placement is indicated for decompression of the stomach, especially in trauma victims and patients with obstructed bowel. Although suction via a large-bore NG tube can reduce the volume of gastric contents, it does not completely evacuate the stomach and may facilitate aspiration by stenting open the lower esophageal sphincter. NG tubes may also compromise mask fit. Before induction, suction should be applied to NG tubes. During induction, tubes should be allowed to drain. Cricoid pressure may help to prevent passive reflux when an NG tube is present.
 - b. Intraoperative placement is required to drain gastric fluid and air during abdominal surgery. NG and orogastric tubes should never be placed with excessive force; lubrication and head flexion facilitate insertion. Tubes can be directed into the esophagus by using a finger within the oropharynx or using Magill forceps under direct visualization with a laryngoscope.
 - c. Complications of NG tube insertion include bleeding, submucosal dissection of the retropharynx, and placement in the trachea. Intracranial placement has been described in patients with basilar skull fracture. The NG tube should be secured carefully to avoid excessive pressure on the nasal septum or nares, as this may cause ischemic necrosis.
 - d. As discussed above, the need for a gastric tube should be discussed with the surgeon as placement for elective procedures is not recommended in many cases.
- 7. Common intraoperative problems associated with abdominal surgery include the following:
 - a. Pulmonary compromise can be caused by surgical retraction of abdominal viscera to improve exposure, insufflation of gas during laparoscopy, or Trendelenburg positioning. These maneuvers may elevate the diaphragm, decrease functional residual capacity (FRC), and produce hypoxemia. Application of positive end-expiratory pressure (PEEP) may counter these effects.
 - b. Temperature control. Heat loss in open abdominal procedures is common. Potential sources and treatment are discussed in Chapter 19.
 - c. Hemodynamic changes as a result of bowel manipulation (i.e., hypotension, tachycardia, and facial flushing) and abdomen inflation.

- d. Fecal contamination from perforation of the gastrointestinal tract can cause infection and sepsis.
- e. Ischemic bowel patients can have intractable hypotension from SIRS and sepsis.
- f. Hemodynamic instability and difficult ventilation during abdomen closures may be early warnings for postoperative abdominal compartment syndrome.

D. Enhanced Recovery After Surgery (ERAS)

Popularized in Europe and now growing in use in the United States, patients are optimized to allow the fastest recovery and discharge postoperatively. The basic tenets include frequent use of epidurals and other regional techniques (regardless of open vs. laparoscopic), multimodal analgesia, goal-directed fluid therapy, reduced NPO times, and early feeding and early ambulation postoperatively. Many of the recommendations challenge the traditional approaches to perioperative management, both from an anesthetic and surgical standpoint.

1. With the ERAS protocols, there is enhanced recovery of bowel function, earlier feeding, reduced overall minor complication rates and reduced length of stay. Readmission rates and mortality are similar.
2. Guidelines have been published for many of the major types of abdominal surgery.
3. Notable highlights of ERAS protocols for elective colonic surgery
 - a. Premedications are generally not given.
 - b. Mechanical bowel preparations (MBPs) should not routinely be used as there is no clear evidence of benefit, but they may increase bowel spillage.
 - c. Clear fluids containing significant carbohydrate content are given 2 to 3 hours before surgery, and NPO times for solids are generally 6 hours. Modifications based on disease state are taken into consideration.
 - d. NG tubes should not be routinely used for elective colonic surgery.
4. Goal-directed therapy with respect to intraoperative fluid management is based on objective measurements of fluid status, often making use of an esophageal Doppler in many of the published studies. Fluid challenges are given to increase stroke volume until the patient is no longer volume responsive. The arterial waveform can potentially be used in a similar manner.
5. Postoperative fluids are minimized, and total perioperative fluids are significantly reduced.
6. Balanced solutions (i.e., lactated Ringers, Plasmalyte) are preferred to NS, which causes a metabolic acidosis.

IV. ANESTHETIC CONSIDERATIONS FOR SPECIFIC ABDOMINAL PROCEDURES

A. Laparoscopic Surgery. Laparoscopic approaches are applied to an increasing number of surgical procedures, including appendectomy, cholecystectomy, hernia repair, fundoplication, nephrectomy, weight loss surgery, liver resection, and colon resection. Benefits of laparoscopic surgery include smaller incision, reduced postoperative pain, decreased postoperative ileus, early ambulation, shorter hospital stay, and earlier return to normal activities.

1. Operative technique involves intraperitoneal insufflation of CO₂ through a needle inserted into the abdomen via a small infraumbilical incision until intra-abdominal pressure reaches 12 to 15 mm Hg. Patient positioning is used to facilitate operative exposure: steep reverse Trendelenburg improves visualization of upper abdominal structures; Trendelenburg helps to visualize lower abdominal structures.

2. Anesthetic considerations

- a. Hemodynamic changes associated with laparoscopy are influenced by the intra-abdominal pressure needed for the creation of pneumoperitoneum, volume of CO_2 absorbed, the patient's intravascular volume status, positioning, and anesthetic agents used. Generally, intra-abdominal pressures of 12 to 15 mm Hg are well tolerated in healthy patients. Mean arterial pressure and systemic vascular resistance usually increase with the creation of pneumoperitoneum in healthy patients; cardiac output is unaffected. Patients with coexisting cardiac disease may develop decreased cardiac output and hypotension associated with pneumoperitoneum. Absorption of CO_2 across the peritoneal surface can cause hypercarbia, resulting in sympathetic nervous system stimulation and increased blood pressure, heart rate, and cardiac output.
- b. The reduction in FRC associated with GA is compounded by the creation of pneumoperitoneum. FRC may be further compromised by the Trendelenburg position and patient body habitus. Frequent recruitment and high PEEP may be necessary to treat alveolar collapse.
- c. Because patients may be positioned in steep Trendelenburg or reverse Trendelenburg, changes in venous return must be anticipated and monitored. Also, frequent attention must be given to patients' arms to prevent brachial plexus injury.
- d. Temperature control. Heat loss may occur from intraperitoneal insufflation of cold gas.
- e. Embryonic channels between the peritoneal and pleural/pericardial cavities may open with increased intraperitoneal pressure, resulting in pneumomediastinum, pneumopericardium, and pneumothorax. Diffusion of gas cephalad from the mediastinum can lead to subcutaneous emphysema of the face and neck.
- f. Vascular injuries secondary to the introduction of the needle or trocar can produce sudden blood loss and necessitate conversion to an open procedure to control bleeding.
- g. Venous gas embolism is rare but may occur on induction of pneumoperitoneum if the needle or trocar is placed into a vessel or an abdominal organ or if gas is trapped in the portal circulation. The high capacity of blood to absorb CO_2 and its rapid elimination in the lungs increases the margin of safety in case of accidental IV injection of CO_2 . Insufflation of gas under high pressure can lead to a "gas lock" in the vena cava and right atrium; this will decrease venous return and cardiac output and produce circulatory collapse. Embolization of gas into the pulmonary circulation leads to increased dead space, ventilation/perfusion mismatch, and hypoxemia. Systemic gas embolization (with occasionally devastating effects on cerebral and coronary circulation) can occur with massive gas entrainment or via a patent foramen ovale. Treatment consists of immediately stopping gas insufflation, placing the patient on 100% O_2 to relieve hypoxemia, and positioning the patient in steep head-down left lateral decubitus to displace gas from the right ventricular outflow tract (see Chapter 19), open up IV fluid and inotropic RV support.
3. Anesthetic management. Although laparoscopy procedures have been performed under neuraxial techniques, GA is usually required for laparoscopy. Creation of pneumoperitoneum and steep Trendelenburg

positioning can compromise ventilatory function and is not tolerated in an awake patient. A urinary bladder catheter and a gastric tube are inserted (usually after induction of GA) to improve visualization and reduce the risk of trauma to bladder and stomach with trocar insertion.

B. Esophageal surgery for gastroesophageal reflux disease can be performed via either an abdominal approach (see below) or a thoracic approach.

1. The Nissen fundoplication is the most common surgical treatment for reflux disease. It involves wrapping the fundus of the stomach around the lower part of the esophagus. This creates a collar in which intra-gastric pressure serves to constrict the wrapped esophagus rather than push the gastric contents into the esophagus. Hiatal hernias, if present, are repaired at the time of surgery. This procedure is often performed using laparoscopic techniques to decrease the duration of postsurgical hospitalization.

- a. Anesthetic considerations. This procedure is performed most commonly with GA or combined GA–epidural (for open procedures). Patients who come to surgery often have been treated medically with proton pump inhibitors, H_2 -receptor antagonists, or prokinetic agents. These should be continued until the day of surgery. An RSI or awake intubation is indicated because of the high risk of gastro-esophageal reflux and the potential for aspiration.

- b. An esophageal bougie may be placed to calibrate fundoplication; this ensures an adequate esophageal lumen to minimize postoperative dysphagia. The stomach or esophagus may be perforated by passage of the bougie or NG tube. With the laparoscopic method, the bougie is directed into the stomach by observation alone. Correct angulation of the esophagus or stomach during this maneuver is extremely important in preventing injury. The dilator or NG tube should be passed slowly and should be directly visualized. Particular attention should be paid to patients with esophageal strictures.

C. Gastric surgery for gastric cancer, lymphoma, and uncontrolled bleeding is usually performed with combined GA–epidural. The high likelihood of aspiration in these patients necessitates rapid-sequence or awake intubation.

1. Gastrectomy or hemigastrectomy with gastroduodenostomy (Billroth I) or gastrojejunostomy (Billroth II) is usually performed for gastric adenocarcinoma, lymphoma, or intractable bleeding from gastric or duodenal ulcers. Rarely, it is necessary in Zollinger-Ellison syndrome.

2. Gastrotomy tube placement can be performed through a small upper abdominal incision or percutaneously with an endoscope. Local anesthesia with sedation is often adequate in the debilitated elderly patient, although some require GA.

D. Intestinal and Peritoneal Surgery. Indications for small bowel resection include infection, penetrating trauma, Crohn disease, obstructing adhesions, Meckel diverticulum, carcinoma, and infarction (from volvulus, intussusception, or thromboemboli). Patients are often hypovolemic and are considered to have a full stomach.

1. Appendectomy is performed through a small lower abdominal incision or via laparoscopy. IV hydration before induction is indicated because fever, poor oral intake, and vomiting may produce hypovolemia. GA with rapid-sequence or awake intubation is necessary. TAP blocks may be opioid sparing and should be considered as an adjuvant for this procedure.

2. Colectomy or hemicolectomy is used to treat colon cancer, diverticular disease, Crohn disease, ulcerative colitis, trauma, ischemic colitis, and abscess. Emergency colectomy on unprepared bowel carries a high risk of peritonitis from fecal contamination. Some emergencies involving the colon are treated with an initial diverting colostomy, followed later by bowel preparation and elective colectomy. Patients must be evaluated for hypovolemia, anemia, and sepsis. All emergency colectomies and colostomies should be treated as if at risk for aspiration. Combination general/regional anesthetics are preferable.
3. Perirectal abscess drainage, hemorrhoidectomy, and pilonidal cystectomy are relatively noninvasive and brief procedures. Pilonidal cysts are excised with patients positioned prone; abscess drainage and hemorrhoidectomy can be performed in either a prone or a lithotomy position. If GA is used, deep planes of anesthesia or use of muscle relaxants may be necessary to achieve adequate sphincter relaxation. Hyperbaric spinal anesthesia is used for procedures in the lithotomy position, whereas a hypobaric technique is useful for the flexed prone (jackknife) or knee-chest position. A caudal block may be performed for either position.
4. Inguinal, femoral, or ventral herniorrhaphies can be performed under local anesthesia, regional anesthesia (spinal, epidural, caudal, or nerve block), or GA. Maximum stimulation and profound vagal responses may occur during spermatic cord or peritoneal retraction. Communication with surgeons is important, as they may need to reduce traction if necessary. Care should be given to minimize coughing on emergence that can strain the repair.

E. Hepatic Surgery

1. Partial hepatectomy is performed for hepatoma, unilobar metastasis of a carcinoma, arteriovenous malformation, or echinococcal cysts. Extensive hemorrhage should be anticipated and standard monitors are supplemented with placement of arterial and large-bore IV access and/or central venous catheters. Blood loss during hepatic parenchymal division can be reduced by temporary occlusion of portal venous and arterial inflow at the level of the hepatic pedicle (Pringle maneuver). Low CVP has been shown to reduce blood loss during the case and improve survival. The CVP is generally kept in the range of 2 to 5 mm Hg. CVP essentially represents the back pressure which causes bleeding during the resection. Fluids should be restricted with a goal of maintaining urine output of 0.5 mL/kg/h and an acceptable blood pressure (variable depending on patient). If fluid restriction is not adequate, nitrates and opioids can be used as well.
The normal liver has considerable reserve, and extensive resection is required before clinical impairment of drug metabolism is evident. The effects of liver disease on anesthetic management are discussed in Chapter 5. Epidural or paravertebral catheters can be placed in patients with normal coagulation status.
2. Transjugular intrahepatic portosystemic shunts (TIPS) procedure has replaced portacaval or splenorenal shunt procedure for patients with portal hypertension because of superior outcome. The procedure entails access of internal jugular vein (most on right side). A shunt between portal vein and hepatic vein will be created after verifying position with both contrast and pressure measurement. TIPS procedure can be performed under either MAC or GA. Although the anesthetic for a TIPS is simple, a high-level vigilance is required because of potential bleeding.

F. Biliary Tract Procedures

1. Cholecystectomy is a common procedure performed via either open laparotomy or laparoscopic techniques. GA is favored for either technique. During laparoscopic cholecystectomy, the patient is placed in a steep reverse Trendelenburg position, and the gallbladder is dissected from the liver bed by using either cautery or laser. Muscle relaxants are required for adequate abdominal wall relaxation. The amount of hemorrhage is difficult to assess because of the limited field of view and high magnification of the laparoscope; heavy bleeding from the cystic or hepatic arteries may occur.
2. Biliary drainage procedures include transduodenal sphincteroplasty for extensive choledocholithiasis; cholecystojejunostomy for distal common bile duct obstruction from pancreatic cancer; and choledochojejunostomy for chronic pancreatitis, stone disease, and benign strictures of the distal bile duct. Endoscopic and transhepatic techniques are increasingly common, but open surgical drainage is occasionally required. Blood loss is usually minimal but fluid loss may be significant.

G. Pancreatic Surgery

1. Although the initial treatment of acute pancreatitis is supportive, surgical intervention may be necessary for complications of pancreatitis. Surgical management is indicated for infected pancreatic necrosis and hemorrhagic pancreatitis unresponsive to resuscitation with blood products and correction of coagulopathy. Pancreatic pseudocysts may require drainage either surgically or via endoscopy. The cyst may be anastomosed to a Roux-en-Y limb of jejunum, the posterior wall of the stomach, or duodenum. Surgical intervention can produce significant bleeding and third-space fluid losses. In severe acute pancreatitis, activation of inflammatory mediators can produce sepsis and multiple organ dysfunction that require fluid resuscitation, mechanical ventilation, and vasopressor support.
2. Pancreatojejunostomy with gastrojejunostomy and choledochojejunostomy (Whipple procedure) is performed for resection of adenocarcinoma of the pancreas, malignant cystadenoma, or refractory pancreatitis confined to the head of the pancreas. These procedures have a high potential for hemorrhage and fluid loss. Epidural catheters and intraoperative celiac plexus block are generally helpful for postoperative pain control in the absence of contraindications.

H. Splenectomy may be performed emergently after blunt or penetrating trauma or electively for the treatment of idiopathic thrombocytopenic purpura or staging Hodgkin lymphoma. GA and muscle relaxation are required. Large-bore IV access is necessary because major blood loss requiring transfusion can be encountered. A combined epidural and general anesthetic technique is appropriate with the caveat that a sympathectomy may significantly potentiate hypotension from hemorrhage. Occasionally, a transthoracic approach to gain control of the hilar vessels of a very large spleen may be necessary. Splenectomy patients should receive polyvalent pneumococcal vaccine in the postoperative period.

1. **Intraoperative radiation therapy** for pancreatic or colonic adenocarcinoma may be performed during laparotomy for primary resection or tumor debulking. Specially designed operating rooms have been constructed to facilitate intraoperative radiotherapy. If transport to a separate radiation therapy suite is necessary, however, the anesthetized patient is transported before wound closure. The patients must be hemodynamically

stable and have a stable ventilatory status as they are monitored by remote television outside the radiation area. Aortic or inferior vena cava (IVC) compression may occur when the sterile cone of the radiation therapy device is positioned in the abdominal wound. Ventilation with 100% oxygen can maximize the sensitivity of the tumor to radiation therapy. Treatments usually require 5 to 20 minutes but can be interrupted in the event of problems with hemodynamics or ventilation. Wound closure may be performed either in the radiation suite or after transport back to the operating room.

- J. Surgery for the Obese.** With more than 60% of the U.S. population considered overweight, obesity is a major health issue. The body mass index (BMI) is correlated to the relative amount of adipose tissue and is calculated as follows: $BMI = \text{body weight (kg)} / \text{height (m}^2\text{)}$. Patients are considered overweight if BMI is greater than 25, obese if BMI is greater than 30, and morbidly obese if BMI is greater than 35 to 40.

1. Preanesthetic considerations

- a. Obese patients have increased circulating blood volume and increased cardiac output to meet increased oxygen consumption. Depressed left ventricular function can be found even in young asymptomatic patients and is correlated to the degree of obesity. Hypertension is also significantly correlated with obesity.
- b. Obese individuals have a higher risk for hypercholesterolemia, a risk factor for development of atherosclerosis and coronary artery disease. Patients with several cardiac risk factors may require cardiology consultation to optimize medical therapy in the perioperative period and to determine the necessity for further cardiac evaluation.
- c. Respiratory system compliance is decreased in obesity due to decreased chest wall compliance from extra weight. There is a slight decrease in lung compliance due to increased pulmonary blood volume. FRC is reduced. In the supine position, FRC may fall within the closing volume, leading to ventilation perfusion mismatch and hypoxemia. The higher metabolic demand of the obese person with concomitant increased oxygen consumption and CO_2 production requires increased minute ventilation to maintain normocapnia.
- d. Increased submucosal fat in the pharynx predisposes to collapse of the hypopharynx during sleep, leading to obstructive sleep apnea. Long-standing hypoxemia can result in pulmonary hypertension and right heart failure. Patients with severe sleep apnea may benefit from intensive monitoring in the immediate postoperative period.
- e. Increased gastric emptying time and elevated intra-abdominal pressure and volume predispose to a higher incidence of symptomatic gastroesophageal reflux.
- f. Type 2 diabetes with hyperglycemia, hyperinsulinemia, and insulin resistance is common in the obese. Because perfusion of adipose tissue is variable, IV insulin infusion may be necessary to control hyperglycemia. Guidelines for the management of glucose and insulin are covered in Chapter 6.
- g. Airway management traditionally has been considered a challenge in the obese because of the large size of the neck and face. Studies have reported that obesity or BMI alone are not a predictor for difficult intubation, although increasing neck circumference and a Mallampati score ≥ 3 have been associated with problematic intubation. Careful assessment of neck and jaw mobility, inspection of

the oropharynx, and examination of dental status are required. If intubation is expected to be difficult, awake intubation should be considered and discussed with the patient.

- h. Positioning of the upper body so that the external auditory meatus is in line with the sternal notch has been shown to provide a better view for direct laryngoscopy. This is often accomplished by making a “ramp” of blankets under the thorax, which facilitates aligning the thorax with the trachea. In addition, the reverse Trendelenburg position should always be used in morbidly obese patients to increase their FRC and utilize gravity to displace soft tissue away from the neck/airway.
 - i. Significant psychological problems, such as depression and low self-esteem, may occur in many of these patients.
- 2. Surgical techniques** Bariatric surgery is currently the most effective treatment of morbid obesity. Patients with a BMI ≥ 40 or with a BMI ≥ 35 with obesity-related comorbidities are candidates for surgery. Currently, two basic types of bariatric surgery are performed.
- a. Vertical banded gastroplasty produces a small gastric pouch that restricts the volume of food that can be ingested. Long-term weight loss may be limited by maladaptive eating patterns (liquids with high caloric content) or by staple line disruption. Gastroplasty procedures, particularly the laparoscopic sleeve gastrectomy, are becoming more popular due to lower complications than a formal bypass procedure.
 - b. Roux-en-Y gastric bypass surgery consists of formation of a small gastric pouch and anastomosis of the pouch to the proximal jejunum. Weight loss occurs due to both a restrictive anatomy as well as decreased absorption of calories because of the bypassed small intestine. Patients who undergo this surgery may experience a “dumping” syndrome in which ingestion of high-energy-density food leads to nausea, abdominal cramping, and diarrhea. The Roux-en-Y gastric bypass can also be performed laparoscopically.
- 3. Anesthetic management**
- a. Standard operating tables are often unable to accommodate the size and weight of the obese patient; tables specifically designed for obese patients should be used. Extra padding and skin protection are necessary even for short procedures.
 - b. Standard noninvasive monitoring, with a urinary catheter, is acceptable in patients who are generally healthy. An appropriately sized blood pressure cuff is critical; a regular-sized cuff placed on the forearm may be more effective than an oversized cuff on the upper arm. IV access may be challenging.
 - c. Clinical evaluation of hydration and blood volume in the obese patient is difficult. While they have an increased total circulating blood volume, it is less than in normal-sized patients as calculated per kilogram of body weight. Technical difficulties during surgery can lead to increased blood and fluid losses. Although fluid replacement guided by hemodynamics and urine output is generally safe in healthy individuals, invasive monitoring to guide fluid management may be necessary in some patients.
 - d. Regional anesthetic techniques can be challenging because of difficulties in identifying anatomic landmarks. Nevertheless, use of epidural anesthesia in combination with a general anesthetic may be advantageous. The midline of the spine may be more readily

apparent in the sitting position than in lateral decubitus, thus facilitating catheter placement. Long epidural needles (5 inches) may be necessary. Tegaderm should be applied after patients return to straight sitting position to prevent inadvertently pulling out catheters. The volume of local anesthetic volume injected may need to be decreased in obese patients; the volume of the epidural space is decreased because of fatty infiltration and increased blood volume in the epidural venous system based on OB literature.

- e. The combination of an increased metabolic demand and decreased FRC leads to rapid, dramatic, and sometimes refractory desaturation during apnea. Preoxygenation for 3 to 5 minutes is recommended; established oxygen reserve remains small. Mask ventilation may be difficult with limited gas exchange. Use of an oral or nasopharyngeal airway or two-person bag-mask technique is frequently required.
- f. Morbidly obese patients have a greater reduction in lung volume than nonobese patients during GA; this promotes more atelectasis, airway closure, and hypoxemia. High PEEP is needed to counteract it.
- g. Drug dosages are difficult to estimate in the obese patient. Obese patients have increased total body weight, with increases in both fat body weight as well as lean body weight (LBW). However, the ratio of lean body weight to total body weight decreases with increase in total body weight. Physiologically, obese patients have an increase in cardiac output, total body volume, GFR, and other regional alterations in blood flow that alter pharmacokinetics and dynamics. In general, lipid-soluble drugs have an increased volume of distribution, but significant exceptions exist. An increased volume of distribution can also result in an increased half-life.
 1. In general, in obese patient, LBW is highly correlated with cardiac output, which determines early distribution kinetics, and drug clearance. Most anesthetic drugs should dose based on LBW.
 2. LBW is determined by individual's height and weight and is best determined in obese patients by a modified LBW2005 equation: $LBW_{men} = [9 \times 10^3 \times \text{body weight} / 7 \times 10^3 + (216 \times \text{BMI})]$; $LBW_{women} = [9 \times 10^3 \times \text{body weight} / 9 \times 10^3 + (244 \times \text{BMI})]$.
 3. Induction doses of propofol should be based on LBW, and maintenance dosing should be based on TBW.
 4. Doses of opioids, including remifentanyl, should be based on LBW.
 5. With increased amount of pseudocholinesterase and extracellular fluid, succinylcholine administration should be based on TBW.
 6. Nondepolarizing muscle relaxants should dose on IBW base.
- h. The patient should be extubated in the operating room when awake, with adequate cough reflexes, and after confirmation of adequate reversal of muscle relaxation. Because the supine position decreases FRC, obese patients should be placed in a sitting position as soon as possible. Patients requiring continuous positive airway pressure for sleep apnea can resume this treatment as soon as necessary; gastric distention does not appear to be a problem.
- i. Postoperative intensive care or step down unit should be considered for patients with severe coronary artery disease, poorly controlled diabetes, and severe sleep apnea. Studies have shown that patients who are male, older (>50 years), heavier (BMI > 60 kg/m²), and who have complications requiring reoperation likely need intensive care.

K. Orthotopic Liver Transplantation. Orthotopic liver transplantation is a curative procedure for end-stage liver disease. Common etiologies include nonalcoholic steatohepatitis (NASH), alcoholic cirrhosis, hepatocellular carcinoma, sclerosing cholangitis, Wilson disease, α_1 -antitrypsin deficiency, primary biliary cirrhosis, and viral hepatitis.

1. Preanesthetic considerations for the patient with liver disease are discussed in Chapter 5.

2. Surgery for hepatic transplantation proceeds in three distinct stages.

- a. Recipient hepatectomy includes resection of the gallbladder, hepatic veins, and sometimes a section of IVC.
- b. Anhepatic phase marked by decreased venous return from interruption of the IVC. Venovenous bypass (typically left femoral and portal to left axillary vein) can improve venous return when collateral circulation is not sufficient.
- c. Postanhepatic phase marked by reperfusion of the donor liver that delivers hyperkalemic, hypothermic, and acidic solution to the central circulation. The patient's condition usually stabilizes after completion of vascular anastomoses. After biliary anastomoses are completed, donor cholecystectomy, choledochojejunostomy, and placement of a choledochal tube complete the surgery.

3. Anesthetic considerations

- a. Hemorrhage in the presence of baseline coagulopathy can produce dramatic blood loss (multiple blood volumes); recipient hepatectomy is usually the period of greatest hemorrhage. Fibrinolysis during the anhepatic and postperfusion phases, due to release of tissue plasminogen activator, may exacerbate preexisting coagulopathy. Aminocaproic acid (Amicar) and/or aprotinin may be helpful in reducing blood product transfusion requirements.
- b. Hypothermia should be avoided by aggressive warming starting before induction.
- c. Metabolic derangements are common.
 1. Oliguria secondary to hypovolemia and hypoperfusion may produce renal failure and hyperkalemia.
 2. Large-volume transfusion of citrated blood products may lead to hypocalcemia and hyperkalemia.
 3. During the anhepatic phase, there is a theoretical risk of hypoglycemia, although hyperglycemia from administration of dextrose-containing solutions is more common. This phase of surgery is often marked by a progressive metabolic acidosis.
- d. Hypoxia can occur from intrapulmonary shunting, thoracic restriction from surgical retraction, and Trendelenburg position. Adequate oxygenation may require a high fraction of inspired oxygen (FiO_2) and application of PEEP.
- e. Hypotension from hypovolemia or cardiac dysfunction should be anticipated. Vasopressors and inotropes are necessary until the underlying problem is corrected.

4. Anesthetic management

- a. Standard monitors plus an intra-arterial blood pressure monitor and a urinary catheter are essential. Many patients require pulmonary artery catheter placement. Transesophageal echocardiography has been used to monitor cardiac function and volume status and to assess the right heart if a venous air embolism is suspected when working on the IVC placement of an NG tube, and a TEE probe must be done with caution because of esophageal varices.

- b. RSI of anesthesia is advised because these patients are at risk of reflux from a full stomach, ascites, or obtundation.
- c. Maintenance of anesthesia is accomplished with a balanced technique including moderate- to high-dose opioids and a volatile agent. N_2O is avoided because of potential air embolism during venovenous bypass and to minimize bowel distention. Large-bore IV access is also necessary via central and peripheral means. A rapid transfusion system capable of delivering 1.0 to 1.5 L/min at 38°C should supply the largest catheter.
- d. Intraoperative laboratory studies including arterial blood gas tensions, glucose, electrolytes, hematocrit, platelets, and coagulation profiles should guide therapy. Labs are sent very frequently during the anhepatic and reperfusion phases as the fluid shifts and acid-base changes occur very rapidly.
- e. Transfusion therapy rests on both autologous transfusion of blood salvaged from the surgical field and banked products. Laboratory and clinical assessment of coagulation will determine the need for packed red blood cells, fresh-frozen plasma, or other blood products. Cryoprecipitate and aminocaproic acid are potential therapeutic adjuncts.
- f. Malignant arrhythmias or cardiac arrest can result from the cold, hyperkalemic, acidemic washout of the donor organ, hypoperfused gut, and lower extremities. Metabolic derangements should be corrected prior to reperfusion. Resuscitation from hemodynamic collapse with high-volume transfusion may be required.
- g. After surgery, the donor liver resumes function, coagulopathy generally improves, and ongoing fluid requirements diminish. Patients require additional opioids for analgesia and sedation.

L. Renal Transplantation (see Chapter 28)

M. Heterotopic pancreatic transplantation is performed usually in conjunction with heterotopic renal transplantation. Although recipients may undergo a nephrectomy, their native pancreas is left intact. Anesthetic considerations are primarily related to renal transplantation and management of diabetes. Surgery often entails anastomosis of the donor pancreas to the recipient's bladder via a portion of duodenum allowing exocrine pancreatic secretions to drain into the bladder. Blood glucose should be determined frequently because it falls rapidly with perfusion of the pancreas. Because there is no pepsin present, trypsinogen and chymotrypsinogen are not activated. Gram-negative urinary tract infection can activate these enzymes and lead to bladder damage, requiring emergency removal of the transplanted pancreas. The pancreas secretes bicarbonate that is lost in the urine.

N. Recovery of Organs for Transplantation After Brain Death

1. A significant gap exists between the supply of suitable donated organs and the demand for these organs to treat end-stage disease. To increase the donor pool, strict exclusion criteria (age and coexisting illnesses) are no longer used. In addition, some centers use aggressive care regimens for potential donors to prevent common perturbations in homeostasis that accompany brain death. An alternative is the non-heart-beating donor, who does not meet brain death criteria but has such a poor prognosis that the family might consider withdrawing life support. A transplant coordinator from an organ procurement organization must screen all potential donors.

2. Organs may be deemed unsuitable based on donor age, organ injury, disease, or gross abnormalities.
3. Hormonal therapy using methylprednisolone, arginine vasopressin, and triiodothyronine can increase the number of successfully implanted organs and reduce graft dysfunction when administered to brain-dead donors who demonstrate resistance to conventional resuscitation as manifested by low cardiac output, inadequate organ perfusion, or worsening lactic acidosis.
4. Anesthetic management for harvesting organs should focus on optimizing organ perfusion and oxygenation. Volatile anesthetics may help to blunt spinal reflex, reduce the adrenergic storm, and provide some ischemic preconditioning to the vital organs, though studies have not been done to confirm clinical significance. Opioids will also help with reduction in response to stimulation.
 - a. Dissection of organs usually occurs in the following order: heart (30 minutes), lungs (1 to 1.5 hours), liver (1 to 1.5 hours), pancreas (1 to 1.5 hours), and kidneys (30 minutes to 1 hour).
 - b. Once all organs are mobilized, heparin (20,000 to 30,000 units IV in adult donors) is administered and the aorta is cross-clamped. The distal aorta and IVC are cannulated, and the harvested organs are perfused in situ, topically cooled, and exsanguinated via the IVC.
 - c. Ventilatory support is discontinued after the aorta is cross-clamped, and the anesthesiologist's role is completed with the discontinuation of all monitoring and supportive care, except during heart and lung procurement.
 - d. Non-heart-beating organ donation, also referred to as donation after cardiac death (DCD), is reserved for patients who are not declared brain dead but whose family has chosen to remove them from life support because their condition is considered "hopeless." Life-sustaining treatment (mechanical ventilation and vasopressors) is discontinued after the patient is prepared for surgery to remove the organs. Five minutes after asystole occurs, a physician who is not part of the transplant team declares death. The body is rapidly cooled with preservative solution via an aortic cannula, and the abdomen entered and organs removed expeditiously. This technique has the disadvantage of significant warm ischemia time before organ procurement begins. In addition, there are ethical debates about the appropriateness of interventions (heparin treatment) aimed at improving grafts before the donor's death. Usually, anesthesiologists are not involved in DCD. However, if the lungs are donated, an anesthesiologist may be asked to intubate the deceased and briefly ventilate.
5. Specific management problems
 - a. Hypoxemia may be caused by atelectasis, pulmonary edema, aspiration, or pneumonia. The FiO_2 and minute ventilation should be adjusted to maintain a $\text{PaO}_2 \leq 100$ mm Hg and $\text{PaCO}_2 = 35$ to 45 with pH 7.35 to 7.45. Arterial blood gases should be determined every 30 to 60 minutes. High levels of PEEP should be avoided to preserve cardiac output and avoid barotrauma. High FiO_2 should be avoided in potential lung donors to minimize possible oxygen toxicity.
 - b. Poikilothermia is common, and early aggressive measures should be taken to minimize heat loss.

- c. Hypertension often transiently accompanies brain death and can be dramatic. Reflex hypertensive responses to surgical stimulation may occur. Short-acting agents such as nitroprusside or esmolol should be used anticipating hypotension that is often more challenging to control during organ procurement.
- d. Hypotension is common and is due to a combination of hypovolemia and neurogenic derangement of vasomotor control. Central venous or pulmonary artery catheterization may be necessary to optimize filling pressures. Hypovolemia can be treated with crystalloid, colloid solutions, and blood products as necessary. Hematocrit should be maintained greater than 30%. After restoration of intravascular volume, a vasopressor such as dopamine, epinephrine, or norepinephrine may be necessary.
- e. Dysrhythmias occur frequently, especially in the setting of electrolyte imbalance, hypothermia, increased intracranial pressure, hypoxemia and acidosis, and derangement of brainstem cardiovascular control centers. Standard therapy is indicated. Bradycardia is often resistant to atropine and may require pacing therapy.
- f. Polyuria may be secondary to volume overload, osmotic diuresis, or the diabetes insipidus resulting from derangement of the hypothalamic–pituitary axis. An IV infusion of vasopressin or desmopressin may be titrated to treat severe diabetes insipidus (see Chapter 6) and should be done in consultation with the surgical team. If used, it is prudent to discontinue these infusions 1 hour before aortic cross-clamping to minimize the risk of uneven distribution or ischemic injury with the infusion of preservative solution.
- g. Oliguria should be treated by ensuring adequate intravascular volume. Dopamine is preferred for the initial treatment of hypotension. A brisk diuresis is preferred when the kidneys are to be harvested. If volume repletion and pressors are not effective in restoring adequate urine output, mannitol and/or furosemide may be used.

Suggested Readings

- Ahmad S, Nagle A, McCarthy RJ, et al. Postoperative hypoxemia in morbidly obese patients with and without obstructive sleep apnea undergoing laparoscopic bariatric surgery. *Anesth Analg* 2008;107(1):138–143.
- Akca O, Lenhardt R, Fleischmann E, et al. Nitrous oxide increases the incidence of bowel distention in patients undergoing elective colon resection. *Acta Anaesthesiol Scand* 2004;48:894–898.
- Ballantyne JC, Carr DB, deFerranti S, et al. The comparative effects of postoperative analgesic therapies on pulmonary outcome: cumulative meta-analyses of randomized, controlled trials. *Anesth Analg* 1998;86:598–612.
- Boldt J, Haisch G, Suttner S, et al. Effects of a new modified, balanced hydroxyethyl starch preparation (Hextend) on measures of coagulation. *Br J Anaesth* 2002;89:722–728.
- Brodsky JB, Lemmens HJ, Brock-Utne JG, et al. Morbid obesity and tracheal intubation. *Anesth Analg* 2002;94(3):732–736.
- Brodsky JB, Lemmens HJ, Collins JS, et al. Nitrous oxide and laparoscopic bariatric surgery. *Obes Surg* 2005;15:494–496.
- Carton EG, Plevak DJ, Kranner PW, et al. Perioperative care of the liver transplant patient. Part 2. *Anesth Analg* 1994;78:382–399.
- Carton EG, Rettke SR, Plevak DJ, et al. Perioperative care of the liver transplant patient. Part 1. *Anesth Analg* 1994;78:120–133.
- Chappell D, Jacob M, Hofmann-Kiefer K, et al. A rational approach to perioperative fluid management. *Anesthesiology* 2008;109(4):723–740.

- Choi PT, Yip G, Quinonez LG, et al. Crystalloids vs. colloids in fluid resuscitation: a systematic review. *Crit Care Med* 1999;27:200–210.
- Corcoran T, Rhodes J, Clarke S, et al. Perioperative fluid management strategies in major surgery: a stratified meta-analysis. *Anesth Analg* 2012;114(3):640–651.
- Doherty M, Buggy DJ. Intraoperative fluids: how much is too much? *Br J Anaesth* 2012;109(1):69–79.
- Ebert TJ, Shankar H, Haake RM. Perioperative considerations for patients with morbid obesity. *Anesthesiol Clin* 2006;24(3):621–636.
- Gridelli B, Remuzzi G. Strategies for making more organs available for transplantation. *N Engl J Med* 2000;343:404–410.
- Gustafsson UO, Scott MJ, Schwenk W, et al.; Enhanced Recovery After Surgery Society. Guidelines for perioperative care in elective colonic surgery: Enhanced Recovery After Surgery (ERAS[®]) Society recommendations. *World J Surg* 2013;37(2):259–284.
- Hartog CS, Bauer M, Reinhart K. The efficacy and safety of colloid resuscitation in the critically ill. *Anesth Analg* 2011;112:156–164.
- Hebbard PD, Barrington MJ, Vasey C. Ultrasound-guided continuous oblique subcostal transversus abdominis plane blockade: description of anatomy and clinical technique. *Reg Anesth Pain Med* 2010;35(5):436–441.
- Hovagimian F, Lysakowski C, Elia N, et al. Effect of intraoperative high inspired oxygen fraction on surgical site infection, postoperative nausea and vomiting, and pulmonary function: systematic review and meta-analysis of randomized controlled trials. *Anesthesiology* 2013;119(2):303–316.
- Huntington JT, Royall NA, Schmidt CR. Minimizing blood loss during hepatectomy: a literature review. *J Surg Oncol* 2014;109:81–88.
- Ingrande J, Lemmens HJ. Dose adjustment of the anaesthetics in the morbidly obese. *Br J Anaesth* 2010;105(Suppl 1):i16–i23.
- Jaffe RA, Samuels SL. *Anesthesiologist's manual of surgical procedures*. 2nd ed. Philadelphia: Lippincott Williams & Wilkins; 1999.
- Lobo SM, Ronchi LS, Oliveira NE, et al. Restrictive strategy of intraoperative fluid maintenance during optimization of oxygen delivery decreases major complications after high-risk surgery. *Crit Care* 2011;15(5):R226.
- Lowham AS, Filipi CJ, Hinder RA, et al. Mechanisms and avoidance of esophageal perforation by anesthesia personnel during laparoscopic foregut surgery. *Surg Endosc* 1996;10:979–982.
- McKeown DW, Bonser RS, Kellum JA. Management of the heart beating brain-dead organ donor. *Br J Anaesth* 2012;108(Suppl 1):i96–i107.
- Molenaar IQ, Wanaar N, Groen H, et al. Efficacy and safety of antifibrinolytic drugs in liver transplantation: a systematic review and meta-analysis. *Am J Transplant* 2007;7:185–194.
- Myles PS, Leslie K, Chan MT, et al.; the ANZCA Trials Group for the ENIGMA-II investigators. The safety of addition of nitrous oxide to general anesthesia in at-risk patients having major non-cardiac surgery (ENIGMA II): a randomised, single blind trial. *Lancet* 2014;384(9952):1446–1454.
- Neligan PJ, Porter S, Max B, et al. Obstructive sleep apnea is not a risk factor for difficult intubation in morbidly obese patients. *Anesth Analg* 2009;109(4):1182–1186.
- Ogunnaiké BO, Jones SB, Jones DB, et al. Anesthetic considerations for bariatric surgery. *Anesth Analg* 2002;95(6):1793–1805.
- Patel T. Surgery in the patient with liver disease. *Mayo Clin Proc* 1999;74:593–599.
- Pelosi P, Ravagnan I, Giurati G, et al. Positive end-expiratory pressure improves respiratory function in obese but not in normal subjects during anesthesia and paralysis. *Anesthesiology* 1999;91:1221–1231.
- Qadan M, Akca O, Mahid SS, et al. Perioperative supplemental oxygen therapy and surgical site infection: a meta-analysis of randomized controlled trials. *Arch Surg* 2009;144:359–366.
- Robertson KM, Cook DR. Perioperative management of the multiorgan donor. *Anesth Analg* 1990;70:546–556.
- Shenkman Z, Shir Y, Brodsky JB. Perioperative management of the obese patient. *Br J Anaesth* 1993;70:349–359.
- Sinha AC. Some anesthetic aspects of morbid obesity. *Curr Opin Anaesthesiol* 2009;22(3):442–446.

- Spanjersberg WR, Reurings J, Keus F, et al. Fast track surgery versus conventional recovery strategies for colorectal surgery. *Cochrane Database Syst Rev* 2011;(2):CD007635
- Strunden MS, Heckel K, Goetz AE, et al. Perioperative fluid and volume management: physiological basis, tools and strategies. *Ann Intensive Care* 2011;1(1):2.
- Tympa A, Theodoraki K, Tsaroucha A, et al. Anesthetic considerations in hepatectomies under hepatic vascular control. *HPB Surg* 2012;2012:720–754.
- White PF. The changing role of non-opioid analgesic techniques in the management of postoperative pain. *Anesth Analg* 2005;101(5 Suppl):S5–S22.
- Zhuang CL, Ye XZ, Zhang XD, et al. Enhanced recovery after surgery programs versus traditional care for colorectal surgery: a meta-analysis of randomized controlled trials. *Dis Colon Rectum* 2013;56(5):667–678.

I. PREOPERATIVE EVALUATION

- A. Patients scheduled for thoracic surgery** should undergo the usual preoperative assessment as detailed in Chapter 1.
 1. Any patient undergoing elective thoracic surgery should be carefully screened for underlying bronchitis or pneumonia and treated appropriately before surgery.
 - a. Diagnostic procedures** such as bronchoscopy and lung biopsy may be indicated for persistent infection.
 - b. Infection beyond an obstructing lesion** may not resolve without surgery.
 2. In patients with **tracheal stenosis**, the history should focus on symptoms or signs of positional dyspnea, static versus dynamic airway collapse, and evidence of hypoxemia. The history may also suggest the probable location of the lesion.
- B. An arterial blood gas (ABG)** may help clarify the severity of underlying pulmonary disease but is not routinely necessary.
- C. Pulmonary function tests** are useful for assessing the pulmonary risk of lung resection. Forced expiratory volume in 1 second (FEV1) and diffusion capacity of the lung for carbon monoxide (DLCO) serve as initial predictors of postoperative outcomes. Marginal results of these tests may prompt additional studies, including postoperative predicted FEV1, ventilation/perfusion (V/Q) scans, and exercise function testing of maximal oxygen uptake ($\dot{V}_{O_{2max}}$) to stratify risks of resection.
- D. Cardiac function** should be assessed if there is a question about the relative contribution of cardiac and pulmonary diseases to the patient's functional impairment. Echocardiography can be used to assess right ventricular function. Echocardiographic estimation of right ventricular systolic pressure can be used as a screening tool for pulmonary hypertension, although, right heart catheterization is required for definitive diagnosis.
- E. Chest radiography, computed tomography (CT), and magnetic resonance imaging (MRI)** are useful to determine the presence and extent of tracheobronchial, pulmonary and mediastinal pathology. Imaging studies can also reveal the nature and degree of involvement of other thoracic structures in the disease process.
- F. Three-dimensional reconstruction** from CT is used to assess the caliber of stenotic airways and can be used to predict the size and length of the endotracheal tube that will be appropriate for the patient. Severe airway stenosis may change the anesthetist's plans for induction and intubation.

II. PREOPERATIVE PREPARATION

- A. Preoperative sedation** should be given carefully to patients with tracheal or pulmonary disease.
 1. **Heavy sedation** may impair postoperative deep breathing, coughing, and airway protection. Patients with poor pulmonary function will be more prone to hypoxemia when their respiratory drive is suppressed. When sedating these patients, it is prudent to monitor oxygenation and administer supplemental oxygen.

2. **In the presence of airway obstruction**, sedation must be carefully balanced. It is crucial to maintain spontaneous ventilation. Oversedation may profoundly suppress ventilation, but an anxious patient may make exaggerated respiratory efforts. In this case, the increased turbulence may worsen airway obstruction, leading to increased anxiety. Benzodiazepines, reassuring words, careful monitoring, and an expeditious start to the procedure are the best approach. In patients with airway stenosis, Heliox, a mixture of 79% helium and 21% oxygen, will lower the density of the respiratory gas and reduce airway resistance.
- B. **Glycopyrrolate** (0.2 mg intravenously) may be given to decrease oral secretions.

III. MONITORING

- A. **Standard monitoring** should be used as described in Chapter 10.
- B. Intra-arterial blood pressure monitoring should be used if, based on the patient's condition or the nature of the surgical procedure, rapid hemodynamic alterations are anticipated, or frequent ABG evaluation is needed.
 1. Compression of the heart and great vessels may occur during thoracic surgical exposure. Continuous blood pressure monitoring allows for the immediate diagnosis of hemodynamic instability.
 2. Manipulations during surgical procedures on peripheral lung tissue, such as thorascopic wedge resection, are less likely to compress the heart or great vessels. Intermittent blood pressure monitoring may be sufficient in these cases.
 3. ABG measurements are helpful for the management of patients undergoing tracheal surgery, especially in the postoperative period.
 4. In the lateral position, it is possible for blood flow to the dependent arm to be impaired. Pulsatile flow to the dependent arm should be monitored with an arterial catheter or a pulse oximeter.
 5. During mediastinal surgery (e.g., tracheal reconstruction or mediastinoscopy), it is possible for the innominate artery to be compressed, restricting flow to the right carotid and brachial arteries. Perfusion to the right arm should be monitored by pulse oximeter or blood pressure cuff. Immediate feedback to the surgeon will allow decompression of the innominate artery. Blood pressure monitoring of the left arm should be available to allow monitoring of systemic arterial pressure in the event that the surgeon is unable to relieve compression of the innominate artery.
- C. The use of additional invasive monitors is dictated by the patient's comorbidities. If a pulmonary artery catheter is placed:
 1. It is customarily inserted from the nondependent side of the neck. If the catheter interferes with the surgical resection, it can be retracted into the main pulmonary artery and readvanced when the artery on the operative side is clamped.
 2. Pressure measurements referenced to the atmosphere may be affected by lateral positioning and opening the chest. Trends in central venous pressure, pulmonary artery pressure, and pulmonary artery occlusion pressure should be monitored. Cardiac output and stroke volume measurements remain accurate.

IV. ENDOSCOPIC PROCEDURES

Endoscopic procedures include direct or indirect visualization of the pharynx, larynx, esophagus, trachea, and bronchi. Endoscopy may be undertaken to obtain biopsy samples, delineate upper airway anatomy, remove obstructing foreign bodies, assess hemoptysis, place stents and guidewires, position radiation catheters, apply photodynamic therapy, and perform laser surgery.

- A. Flexible bronchoscopy** permits visualization from the larynx to the segmental bronchi.
1. A “working lumen” is used for suctioning, administering drugs, and passing wire instruments.
 2. Ventilation must occur around the flexible bronchoscope. Bronchoscopes range in external diameter from approximately 5 mm (standard adult size) to 2 mm (neonatal bronchoscopes that lack a working lumen). Larger “therapeutic” bronchoscopes and ultrasound-equipped scopes have diameters ranging to 7 mm.
 3. **Topical anesthesia** is a common anesthetic approach.
 - a. The patient should meet the American Society of Anesthesiologists preoperative fasting guidelines.
 - b. Lidocaine (various formulations from 1% to 4%) is applied to the oropharynx or nasopharynx, larynx, and vocal cords. The trachea can be sprayed with anesthetic through the bronchoscope or by transtracheal injection. If good topicalization of the airway is achieved, no further anesthesia is required.
 - c. Care should be taken with the total dose of local anesthetic due to high systemic absorption from the orotracheal mucosa.
 - d. Premedication with atropine or glycopyrrolate will limit salivary dilution of the anesthetic and may improve the onset and efficacy of the anesthetic.
 - e. Nerve blocks may be used to supplement airway anesthesia (see Chapter 14).
 - f. The patient should have nothing by mouth until tracheal and laryngeal reflexes return, 2 to 3 hours following administration, to prevent postprocedure aspiration.
 4. **General anesthesia** may be indicated in anxious or uncooperative patients; in more extensive bronchoscopic procedures; or if bronchoscopy is part of a larger surgical procedure.
 - a. Bronchoscopy is very stimulating but does not cause postoperative pain, so a potent short-acting anesthetic is preferable.
 - b. Muscle relaxation or topical anesthesia to the trachea is generally needed to prevent coughing during the procedure.
 - c. The endotracheal tube used should be sufficiently large (7 mm inner diameter for a standard scope, 8.5 or 9 mm if ultrasound will be used) to permit ventilation in the annular space around the scope.
 - d. If there are no contraindications to its use, a laryngeal mask airway (LMA) offers the advantages of a large lumen and the ability to visualize the vocal cords and proximal trachea.
- B. Rigid bronchoscopy** permits visualization of the larynx to the mainstem bronchi.
1. A rigid bronchoscope has better optics and a larger working channel than a flexible bronchoscope. It can be used to establish an airway, visualize the trachea, and treat tracheal pathologies such as obstruction, stenosis, and hemorrhage.
 2. Ventilation is accomplished through the lumen of the scope, allowing better control of a marginal airway.
 3. Rigid scopes are not cuffed, so a variable leak will occur depending on the size of the scope, lumen of the airway, and depth of insertion.
 4. General anesthesia is required for rigid bronchoscopy. It is important to prevent coughing or movement to avoid tracheal disruption. Either deep inhalation anesthesia or muscle relaxation is required to prevent movement and coughing.

5. Conventional ventilation can be used, with the anesthesia circuit attached to a side arm of the rigid bronchoscope. The proximal end of the rigid bronchoscope is closed by a clear lens or by a gasket through which telescopes may be passed.
 - a. The potentially large leak requires an anesthesia machine capable of delivering high oxygen flows.
 - b. An intravenous or a potent inhalational anesthetic technique can be used, but intravenous technique is preferred. It can be difficult to maintain adequate anesthesia with an inhalational technique due to leak and interruption of ventilation. There will also be considerable operating room contamination with volatile anesthetics.
 - c. Close coordination between the surgeon and anesthesiologist is needed because ventilation may need to be interrupted for surgery, and surgery in turn may be interrupted by the need to ventilate.
 6. In cases of severely compromised airways (e.g., severe airway stenosis or airway disruption), maintenance of spontaneous ventilation is indicated. The patient may be given an inhalational induction with sevoflurane, and the rigid bronchoscope may be introduced under a deep plane of anesthesia. After securing the airway, intravenous agents could be substituted.
 7. Ventilating gas usually leaks out around the bronchoscope so that measurements of end-tidal carbon dioxide may be inaccurate. Adequacy of ventilation should be assessed by observation of chest excursion, pulse oximetry, and, if necessary, blood gas analysis.
 8. **Rigid bronchoscopes** are available that are designed for jet ventilation through a special small side lumen.
 - a. The central lumen remains open. Severe barotrauma may occur if gas is not allowed to escape. Observation of chest movement during the expiratory phase is critical. Conversely, ventilation may be ineffective with noncompliant lungs.
 - b. An intravenous anesthetic technique (see Chapter 15) must be used. Muscle relaxation is required for the jet to inflate the lungs adequately.
 - c. Additional gas is added to the inspired gas by the Venturi effect. The inspired oxygen concentration is uncertain because the amount of room air entrained cannot be controlled.
 - d. During laser surgery, the inspired oxygen concentration should be reduced to below 0.3, either by jetting air or by using a gas blender for the jet intake.
 - e. The advantage of the jet technique is that ventilation is not interrupted by suctioning or surgical manipulations because the proximal end of the bronchoscope is always open. This makes the bronchoscope suitable for use during laser surgery of the larynx, vocal cords, or proximal trachea.
 - f. Automated jet ventilators carry the added safety feature of automatic hold when the expiratory airway pressure rises above a set threshold. This prevents breath stacking and subsequent barotrauma.
 9. **Complications** of bronchoscopy include dental and laryngeal damage from intubation, injuries to the eyes or lips, airway rupture, pneumothorax, and hemorrhage. Airway obstruction may be caused by hemorrhage, a foreign body, or a dislodged mass.
- C. Flexible esophagoscopy** may be performed under local anesthesia as described for flexible bronchoscopy (see section IVA) or after the induction

of general anesthesia and endotracheal intubation. Use of a smaller caliber endotracheal tube will allow the surgeon more room to work in the pharynx and proximal esophagus.

- D. **Rigid esophagoscopy** is commonly performed under general anesthesia with muscle relaxation. As with flexible esophagoscopy, a smaller endotracheal tube is used.
- E. **Laser surgery** is performed on upper and lower airway lesions, including laryngeal tumors, subglottic webs, and laryngeal papillomatosis. A laser's wavelength determines its penetration and biologic effect. The surgery may be performed via rigid bronchoscopy, laryngoscopy with jet ventilation, or traditional endotracheal intubation. The patient is often in laryngeal suspension, and this requires muscle relaxation. Postoperative pain is minimal.

V. MEDIASTINAL OPERATIONS

A. **Mediastinoscopy** is conducted to evaluate the extrapulmonary spread of pulmonary tumors and to investigate mediastinal masses. Mediastinoscopy is performed through an incision just superior to the manubrium. A rigid endoscope is then introduced beneath the sternum, and the anterior surfaces of the trachea and the hilum are examined. The patient is supine with the neck extended.

- 1. Any general anesthetic technique may be used, provided the patient remains immobile. Although the procedure is not very painful, intermittent stimulation of the trachea, carina, and mainstem bronchi occurs.
- 2. **Complications** include pneumothorax, rupture of the great vessels, and damage to the airways. Large-bore IV access is required, and the patient should have blood cross-matched in the case of hemorrhage. IV access should be placed in the right upper extremity as the left innominate vein may be compressed during mediastinoscopy. There is a risk of stroke from innominate artery occlusion by compression between the mediastinoscope and the posterior surface of the sternum. As stated previously, perfusion to the right arm should be monitored by pulse oximetry or blood pressure measurement. Blood pressure monitoring in the left arm is essential to monitor systemic blood pressure in the event of innominate arterial compression. Should innominate arterial compression occur and the surgeon be incapable of relieving the pressure (i.e., while managing hemorrhage through the mediastinoscope), the mean systemic pressure must be increased to encourage collateral flow to the right cerebral hemisphere. The trachea may be intermittently compressed by the mediastinoscope, and the position of the patient and surgeon increases the chance of accidental disconnection of the breathing circuit.

B. **Chamberlain procedure** uses an anterior parasternal incision to obtain lung or anterior mediastinal tissue for biopsy or to drain abscesses. The incision is typically in the left second intercostal interspace. The patient is supine.

- 1. Following the induction of general anesthesia, the procedure is performed with the patient in the supine position. If no ribs are resected, the procedure is usually not very painful. Infiltration of the incision with local anesthetic or administration of small doses of opioids and/or IV nonsteroidal anti-inflammatories is usually sufficient for analgesia.
- 2. One-lung ventilation is not required for lung biopsy, but manual ventilation in cooperation with the surgeon(s) can facilitate the procedure.
- 3. If the pleural space is evacuated as it is closed, a chest tube generally is not required postoperatively, although the patient should be monitored carefully for any signs of pneumothorax.

C. Mediastinal Surgery

1. **Median sternotomy** is performed for resection of mediastinal tumors and for bilateral pulmonary resections. In descending order of frequency, mediastinal masses include neurogenic tumors, cysts, teratodermoids, lymphomas, thymomas, parathyroid tumors, and retrosternal thyroids.
2. **Thymectomy** is performed by median sternotomy and may be performed to treat myasthenia gravis. Anesthetic considerations for the patient with myasthenia gravis are detailed in Chapter 13.
3. **General anesthesia** may be induced and maintained with any technique.
 - a. **Neuromuscular blockers** are not required to maintain surgical exposure but may be a useful adjunct to general anesthesia. Both non-depolarizing and depolarizing muscle relaxants are best avoided in the myasthenic patient.
 - b. During the actual sternotomy, the patient's lungs should be deflated and motionless. Even so, complications of sternotomy include laceration of the right ventricle, atrium, or great vessels (particularly the innominate artery) and unrecognized pneumothorax in either side of the chest.
 - c. **Postoperative pain** from a median sternotomy is significantly less than from a thoracotomy and may be managed with either an epidural or parenteral opioids.

VI. PULMONARY RESECTION

A. Surgical Techniques

1. **Lateral or posterolateral thoracotomy** is an approach for the resection of large pulmonary neoplasms or abscesses. Thoracotomy is often preceded by staging procedures such as bronchoscopy, mediastinoscopy, or thoracoscopy. If the staging procedures are performed at the same sitting, the anesthetic should be planned to accommodate the possibility of a shortened procedure if metastatic disease is discovered.
 2. **Video-assisted thoracoscopic surgery (VATS)** is a common approach for wedge resection, segmentectomy, and lobectomy. Thoracoscopic surgery may result in less postoperative pain and a shorter recovery time. Lung isolation is required for adequate visualization of the surgical field.
 3. **Robot-assisted thoracoscopic surgery** is an emerging technique that is theoretically superior to VATS in that the accuracy of the robotic arm facilitates lymph node resection with the conservation of nerves and improved cure rates.
 - a. Good pressure point padding must be ensured due to extremes of positioning with robotic surgery.
 - b. When the robot is docked, the surgical bed must not be moved at all.
 - c. As with VATS, complete collapse of the operative lung must be maintained.
- B. Endobronchial Tubes.** Placement of a double-lumen tube is indicated for lung protection (for significant hemoptysis or unilateral infection), bronchoalveolar lavage, or surgical exposure.

1. Choice

- a. Double-lumen tubes range in size from 26 to 41 French. In general, a 39- or 41-French tube is chosen for adult males and a 35- or 37-French is chosen for adult females. Selection is also based on the patient's height. In general, for men, 70 inches is used for a cutoff height between the 39- or 41-French tubes. For women, 65 inches is a cutoff between 35 or 37 French.

- b. **Right- and left-sided double-lumen tubes** are available and are designed to conform to either the right or the left mainstem bronchus. Each tube has separate channels: one for ventilation of the bronchus and the other for the trachea and nonintubated bronchus. Right-sided tubes have a separate opening in the bronchial lumen to permit ventilation of the right upper lobe.
- c. **The choice of a left- or right-sided tube** depends on the type and side of operation. If a mainstem bronchus is absent, stenotic, disrupted, or obstructed, the double-lumen tube must be placed on the opposite side, preferably under direct fiberoptic guidance. In most cases, the choice of a left- versus right-sided tube is not so absolute. Most surgical procedures can be performed with a left-sided double-lumen tube. It is our practice, however, to selectively intubate the dependent (nonoperative) bronchus. This ensures that the endobronchial tube will not interfere with resection of the mainstem bronchus if this is necessary. Also, if the nondependent lung is intubated, ventilation of the dependent lung through the tracheal lumen may be compromised by mediastinal pressure pushing the tube against the tracheal wall and creating a “ball-valve” obstruction.

2. Insertion

- a. The endobronchial tube, including both cuffs and all necessary connectors, should be carefully checked before placement. The tube may be lubricated, and a stylet should be placed in the bronchial lumen.
- b. After laryngoscopy, the endobronchial tube should be inserted initially with the distal curve facing anteriorly. Once in the trachea, the stylet should be removed and the tube rotated so that the bronchial lumen is toward the appropriate side. The tube is then advanced to an average depth of 29 cm at the incisors or gums (27 cm in females) or less if resistance is met.
- c. Alternatively, a fiberoptic bronchoscope can be passed down the bronchial lumen as soon as the tube is in the trachea and then used to guide the tube into the correct mainstem bronchus.
- d. Once the tube has been inserted and connected to the anesthesia circuit, the tracheal cuff is inflated, and manual ventilation is initiated. Endotracheal placement is confirmed by the presence of end-tidal CO_2 and the auscultation of bilateral breath sounds and no detectable air leak. The tracheal side of the adapter is then clamped, and the distal tracheal lumen is opened to atmospheric pressure via the access port. The bronchial cuff is inflated to a point just sufficient to eliminate air leak from the tracheal lumen, and the chest is auscultated. Breath sounds should now be limited to the side that has been endobronchially intubated. Moving the clamp to the bronchial side of the adapter and closing the tracheal access port should cause only the nonintubated side to be ventilated.
- e. Once adequate lung isolation is achieved, the fiberoptic bronchoscope should be used to confirm position because physical examination may be difficult or misleading. When passed down the tracheal lumen, the bronchoscope should reveal the carina with the proximal edge of the bronchial cuff just visible in the mainstem bronchus. Passing the bronchoscope down the bronchial lumen should reveal either the left mainstem bronchus or the bronchus intermedius, depending on whether a left- or right-sided tube has been placed. The orifice of the right upper lobe should be visible

- through the side lumen of a right-sided tube. A bronchoscope should be kept available throughout the case.
- f. Lung isolation can be monitored continuously if the anesthesia machine is able to measure inspiratory and expiratory volumes independently and display the leak.
3. Double-lumen tube malposition commonly has a few patterns.
 - a. The tube is placed too far into the bronchus so that the distal lumen ventilates a single lobe.
 - b. The tube is too shallow such that the bronchial balloon obstructs the entire tracheal lumen.
 - c. A left-sided tube is misplaced into the right mainstem bronchus, with the right upper lobe mistakenly thought to be the entire right bronchus. This malposition can be corrected under bronchoscopic guidance via the bronchial lumen, withdrawing the tube to the trachea and directing towards the left mainstem bronchus.
 4. Prior to extubation or any significant manipulation of the endobronchial tube, the bronchial cuff should be deflated.
 5. The procedure for passing an endobronchial tube through an existing tracheostomy stoma is identical. Bronchoscopy will help to determine how far the tube should be advanced once it is in the trachea.
- C. Univent tubes** are large-caliber endotracheal tubes encompassing a small integrated channel for a built-in bronchial blocker. Indications for a Univent tube include the need for post-op intubation, the desire to avoid changing from a double-lumen tube to a single-lumen tube, and situations in which placement of a double-lumen tube is difficult or contraindicated. A potential complication is inadvertent advancement and insufflation of the bronchial blocker into the trachea, causing complete obstruction to ventilation.
1. **Insertion.** The Univent tube is inserted into the trachea in the usual fashion and is rotated toward the operative lung. After inflation of the tracheal cuff, the bronchial blocker is advanced into the operative mainstem bronchus under fiberoptic guidance. After appropriate positioning, the cuff of the bronchial blocker is inflated. Because the Univent tube is made of Silastic rather than polyvinyl chloride, thorough lubrication of the bronchoscope is required.
 2. **Collapse of the operative lung** occurs through both exhalation via the small distal opening in the blocker and progressive absorption of oxygen from the lung, which will produce alveolar collapse. This is a slow process but may be hastened by deflating the blocker and disconnecting the anesthesia circuit while observing the lung. Once collapse has occurred, the blocker can be reinflated and the circuit reconnected.
- D. Bronchial blockers** may be used routinely, but especially in situations in which it is not possible to place an endobronchial tube, including in pediatric patients, in those with difficult airway anatomy, or where satisfactory lung isolation cannot be achieved by other means.
1. **Vascular occlusion catheters, such as the Fogarty, is an older source for bronchial blocker.** An appropriately sized Fogarty catheter (8- to 14-French venous occlusion catheter with a 10-mL balloon) is selected and placed into the trachea before endotracheal intubation. After intubation, the balloon tip is positioned with a fiberoptic bronchoscope in the appropriate mainstem bronchus and inflated. Lung collapse occurs slowly, via absorption of gases. There is no ability to suction or perform maneuvers such as continuous positive airway pressure (CPAP) to the nonventilated lung.

2. The **Arndt blocker** is a bronchial blocker especially designed for lung isolation. Placement is facilitated by a distal loop that can be snared with a bronchoscope. The airway connector is well designed, with separate access ports for the blocker, bronchoscope, and ventilation circuit. Like the Univent tube, the blocker has a small central lumen that can be used for lung collapse or CPAP.
3. The Y-shaped EZ-blocker is designed to simplify positioning. Like the Arndt blocker, it includes an airway connector that allows simultaneous ventilation, bronchoscopic visualization, and blocker placement. This blocker terminates at a Y shape that mimics the carinal division into the mainstem bronchi, terminating with a cuff on each extension. The blocker is placed such that the Y sits at the carina with the extensions in each mainstem bronchus. Each cuff can be inflated by its corresponding balloon. Like the other blockers, each extension has a small central lumen.
- E. **Complications of lung isolation techniques** include collapse of obstructed segments of the lung, airway trauma including bronchial rupture, bleeding, and aspiration during prolonged efforts at intubation. Hypoxia and hypoventilation may occur both during placement efforts and as a result of malpositioning.
- F. **Positioning.** Thoracotomies for lung resection are most commonly performed in the lateral decubitus position with the bed sharply flexed and the hemithorax of interest parallel to the floor.
 1. The arms are usually extended in front of the patient and must be carefully padded to avoid compression on the radial and ulnar nerves or obstruction of arterial and venous cannulas. This can usually be avoided by placing cannulas in the arm contralateral to the incision. The dependent brachial plexus must be checked for excessive tension. Various devices exist for supporting the upper arm securely above the lower, leaving the anesthetist with good access to the lower arm. Neither arm should be abducted more than 90 degrees.
 2. The neck should remain in a neutral position, which requires constant support of the head during the movement of the bed into the flexed position. The dependent eye and ear should be carefully checked to ensure that they are not under any direct pressure.
 3. The lower extremities should be padded appropriately to avoid compression injuries. In male patients, the scrotum should be free of compressive forces.
 4. During the positioning process, the vital signs should be closely observed because pooling of blood in dependent extremities may cause hypotension.
 5. Changes in position can move the endobronchial tube or blocker and change $\dot{V}/Q$ relationships. Lung compliance, lung isolation, and oxygenation should be reassessed after any change in position.
- G. **One-lung Ventilation.** General anesthesia, the lateral position, an open chest, surgical manipulations, and one-lung ventilation all alter ventilation and perfusion.
 1. **Oxygenation**
 - a. The amount of pulmonary blood flow passing through the unventilated lung (pulmonary shunt) is the most important factor determining arterial oxygenation during one-lung ventilation.
 - b. Diseased lungs often have reduced perfusion secondary to vascular occlusion or vasoconstriction. This may limit shunting of blood through the nonventilated operative lung during one-lung ventilation.

- c. Perfusion of the unventilated lung is also reduced by hypoxic pulmonary vasoconstriction (HPV). HPV is the pulmonary vascular mechanism that diverts blood flow away from poorly ventilated areas of the lung, minimizing $\dot{V}/\dot{Q}$ mismatch.
- d. **PEEP** has variable effect on the PVR, and positive end-expiratory pressure (PEEP) has not been definitively shown to improve oxygenation during one lung ventilation, but it is used as part of lung-protective strategies.
- e. The lateral position (as opposed to supine) reduces pulmonary shunting, because gravity decreases blood flowing to the nondependent lung.
- f. Oxygenation should be continuously monitored by pulse oximetry.

2. Ventilation

- a. **Arterial carbon dioxide tension** during one-lung ventilation is generally maintained at the same level as on two lungs. This should not be at the expense of hyperinflating or overdistending the ventilated lung.
- b. **Controlled ventilation** is mandatory during open-chest operations.
- c. **Plateau (or end-inspiratory) airway pressure** should generally be maintained below 25 cm H₂O to avoid overdistention of the lung. The occurrence of high airway pressure should be investigated immediately, including with a fiberoptic bronchoscope and is usually due to malpositioning of the endobronchial tube or the presence of secretions.
- d. **Tidal volume** should be maintained in the 3 to 6 mL/kg range for protective one lung ventilation
- e. A moderate increase of partial pressure of carbon dioxide in arterial blood is usually well tolerated. Respiratory rate can be increased to maintain minute ventilation if necessary (as long as intrinsic PEEP) and air trapping are minimal).
- f. When switching from two-lung to one-lung ventilation, manual ventilation allows instantaneous adaptation to the expected changes in compliance and facilitates assessment of lung isolation. Once tidal volume and compliance have been assessed by hand and lung collapse has been confirmed visually, mechanical ventilation can be reinstituted.

H. Management of One-Lung Ventilation

- 1. **Anesthetic management.** During one-lung ventilation, the use of nitrous oxide is limited or discontinued if there is any evidence of a significant decrease in partial pressure of oxygen in arterial blood (e.g., a decrease in oxygen saturation).
- 2. **Difficulties with oxygenation during one-lung ventilation** may be treated with a variety of maneuvers directed at decreasing blood flow to the nonventilated lung (decreasing shunt fraction), minimizing atelectasis in the ventilated lung, or providing additional oxygen to the operative lung.
 - a. **Tube position** should be reassessed by fiberoptic bronchoscopy and repositioned if necessary. Additionally, the bronchial lumen should be suctioned to clear secretions and ensure patency.
 - b. **CPAP** can be applied to the nonventilated lung with a separate circuit. Under direct visualization, the collapsed lung is inflated and then allowed to deflate to a volume that will not interfere with surgical exposure (usually 2 to 5 cm H₂O CPAP).
 - c. **PEEP** may be increased to the ventilated lung to treat atelectasis, but this may lower arterial oxygen saturation if a greater proportion of blood flow is forced into the unventilated lung as a result.

- d. Recruitment maneuvers to overcome atelectasis have been shown to be effective.
- e. **Apneic oxygenation** may be provided to the nonventilated lung by partially inflating it with 100% oxygen and then capping the exhalation port. In this way, a motionless partially collapsed lung is maintained. **Reinstallation** of oxygen will be necessary every 10 to 20 minutes.
- f. **In the event of persistent hypoxemia** that is uncorrectable by combinations of the aforementioned therapies or a sudden precipitous desaturation, the surgeon must be notified and the operative lung reinflated with 100% oxygen. Two-lung ventilation should be maintained until the situation has stabilized, after which the operative lung can be allowed to collapse again. Periodic reinflations or manual two-lung ventilation may be required to maintain an adequate arterial oxygen saturation throughout some procedures.
- g. **A total intravenous anesthetic (TIVA) technique** may be preferred to the administration of a volatile anesthetic, because it is easier to maintain a constant depth of anesthesia while performing maneuvers to improve oxygenation and ventilation. TIVA has not been shown to decrease hypoxia and, unlike inhalation agents, it does not attenuate the inflammatory response.
- h. **If hypoxemia persists**, the surgeon can minimize shunt by compressing or clamping the pulmonary artery of the surgical lung or any of its available lobes.
- i. **Cardiopulmonary bypass (CPB)** or Extracorporeal oxygenation (ECMO) can be instituted to provide oxygenation (see Chapter 24) in extreme situations.
3. When switching from one-lung back to two-lung ventilation, a few manual breaths with a prolonged inspiratory hold will help to reexpand collapsed alveoli.
- I. **Anesthetic Technique.** General anesthesia, in combination with epidural or regional anesthesia, is the preferred technique. If an epidural is used, it should be placed at the thoracic level (see Chapter 17).
1. **General anesthesia** is typically induced with propofol, a short-acting opioid, and maintained with a volatile agent in oxygen. A neuromuscular blocking agent is administered to induce paralysis.
 - a. At the conclusion of the procedure with both lungs ventilated, nitrous oxide, in concentrations up to 70%, will provide a smoother emergence than a volatile agent alone. It is essential that the chest tubes are functioning.
 - b. Muscle relaxants are useful adjuncts to general anesthesia. Although surgical exposure does not require muscle relaxation, movement and coughing carry some risk.
2. **Epidural analgesia** is an effective method for postoperative pain relief after thoracotomy. The epidural may be used intraoperatively to augment the general anesthetic.
- J. **Emergence and Extubation.** The goal of the anesthetic technique selected is to have an awake, comfortable, and extubated patient at the end of the procedure.
 1. **Before closing the chest**, the lungs are recruited to 20 to 30 cm H₂O pressure for 15 to 30 seconds to reinflate the atelectatic areas and check for significant air leaks.
 2. **Chest tubes** are inserted to drain the pleural cavity and promote lung expansion. Chest tubes usually are placed under water seal and up to

20 cm H₂O suction, except after a pneumonectomy. After pneumonectomy, a chest tube, if used, should be placed under water seal only. Applying suction could shift the mediastinum to the draining side and reduce venous return.

3. **Prompt extubation** avoids the potential disruptive effects of endotracheal intubation and positive-pressure ventilation on fresh suture lines. If postoperative mechanical ventilation is required, the double-lumen tube should be exchanged for a conventional endotracheal tube with a high-volume low-pressure cuff. Inspiratory pressures should be kept as low as possible.
- K. Postoperative Analgesia.** Posterolateral thoracotomy is a painful incision, involving multiple muscle layers, rib resection, and continuous motion as the patient breathes. Therapy for postoperative pain should begin before the patient emerges from general anesthesia.
 1. **Epidural analgesia** has been long considered the preferred approach for postthoracotomy pain management (see Chapter 39). Ipsilateral shoulder pain that thoracotomy patients commonly note is referred pain from phrenic nerve irritation and is not covered by epidural analgesia but is well treated with adjuncts, such as nonsteroidal analgesics and acetaminophen.
 2. **Paravertebral nerve blocks**
 - a. Recent studies have suggested that paravertebral nerve blocks are an effective alternative to epidural analgesia in thoracotomy patients.
 - b. Preoperative blocks are usually performed to provide sensory block from approximately T4 to T9. These blocks can be placed intraoperatively in the surgical field or percutaneously using anatomic landmarks, or ultrasound for guidance. The block may be conducted with the patient in either the sitting or prone position. Ultrasound-guided paramedian sagittal or transverse intercostal techniques may be used. For both ultrasound percutaneous techniques, the end point of the block is visualization of depression of the pleura by the local anesthetic into the paravertebral space. If landmark technique is used, the endpoint of the block is loss of resistance. A single-shot block provides analgesia for 12 to 24 hours depending on choice of local anesthetic. Additionally, an infusion catheter may be placed in the paravertebral space for continuous postoperative analgesia.
 - c. Intercostal nerve blocks can be placed under direct thoracoscopic guidance, or percutaneously by following landmarks. The neurovascular bundle travels in a groove inferior to each rib. These nerve blocks provide analgesia for 6 to 8 hours. Care to avoid intravascular injection is important.
 3. Parenteral opioids, if required, should be administered judiciously.
 4. **Nonsteroidal anti-inflammatory agents.** **Ketorolac** has proved effective as a supplemental analgesic but should be used with caution in the elderly, in patients with renal insufficiency, and in those with a history of gastric bleeding. Acetaminophen is also effective for the treatment of referred shoulder pain.

VII. TRACHEAL RESECTION AND RECONSTRUCTION

- A. General Considerations.** Surgery of the trachea and mainstem bronchi involves significant anesthetic risks, including interruption of airway continuity and the potential for total obstruction of an already stenotic airway.

1. The surgical approach depends on the location and extent of the lesion. Lesions of the cervical trachea are approached through a transverse neck incision. Lower lesions necessitate an upper sternal split. Lesions of the distal trachea and carina may require a median sternotomy or a right thoracotomy.
 2. Extubation at the conclusion of the surgical procedure is the goal of the anesthetic because it will put less strain on the fresh tracheal anastomosis.
 - a. Induction
 3. **The anesthetic technique** must include a plan for preserving airway patency throughout induction and intubation and emergency plans and equipment for dealing with any sudden loss of airway control, ranging from rigid bronchoscopy to CPB based on the clinical assessment and experience of the team.
 4. **If the airway is critically stenotic**, spontaneous ventilation should be maintained throughout the induction because it may not be possible to ventilate the lungs by mask ventilation if apnea occurs. A volatile agent in oxygen is the preferred anesthetic, and no muscle relaxants are used. Sevoflurane, with its lack of airway irritability, is suitable for inhalational induction. A deep plane of anesthesia must be achieved before instrumentation, and this may require 15 to 20 minutes in a patient with small tidal volumes and a large functional residual capacity. Hemodynamic support with phenylephrine may be required for an elderly or debilitated patient to tolerate the necessary high concentration of volatile agent.
 5. **Patients with preexisting mature tracheostomies** may be induced with intravenous agents followed by cannulation of the tracheostomy with a cuffed, flexible, armored endotracheal tube. The surgical field around the tube is prepared, and the tube is removed and replaced with a sterile one by the surgeon.
- B. Intraoperative management** is complicated by periodic interruption of airway continuity by the surgical procedure.
1. **Rigid bronchoscopy** is commonly performed before the surgical incision to delineate tracheal anatomy and caliber.
 - a. If the surgeon determines that an endotracheal tube can be placed through the stenotic segment, this should be done as soon as the bronchoscope is withdrawn. Controlled ventilation can then be used safely.
 - b. If the stenotic segment is too narrow or friable to allow intubation, spontaneous ventilation and anesthesia must continue through the bronchoscope until surgical access to the distal trachea is achieved. Alternatives include having the surgeon “core out” the tracheal lesion with the rigid bronchoscope, placing a tracheostomy distal to the stenotic segment, intubating the trachea above the lesion or placing a LMA and allowing spontaneous ventilation to continue, or using a jet ventilation system to ventilate the patient from above the lesion.
 - c. Flexible Bronchoscopy via an LMA is an alternative to rigid bronchoscopy immediately prior to tracheal resection.
 2. When the airway is in jeopardy or ventilation is intermittent, 100% oxygen should be administered.
 3. **For lower tracheal or carinal resections**, a long endotracheal tube with a flexible armored wall can be used. This allows the surgeon to position the tip in the trachea or either mainstem bronchus and to operate around it without interrupting ventilation.

4. **When the trachea is surgically divided**, the endotracheal tube must be retracted proximal to the division and a sterile armored tube placed into the distal trachea by the surgeon. A suture may be placed in the distal end of the orotracheal tube before pulling it back into the pharynx to facilitate replacing it in the trachea at the end of the procedure.
 - a. The tube is frequently removed and reinserted by the surgeons as they work around it. Close coordination during this portion of the procedure will help avoid leakage of gas from the circuit.
 - b. Once the stenotic segment has been removed and the posterior tracheal reanastomosis completed, the transtracheal tube is removed, and the endotracheal tube is readvanced from above. The distal trachea should be suctioned to remove accumulated blood and secretions. The patient's neck is then flexed forward, reducing tension on the trachea, and the anterior portion of the anastomosis is completed.
 5. **Jet ventilation** through a catheter held by one of the surgeons may be required during carinal resection if the distal airways are too small to accommodate an endotracheal tube.
 - a. It is difficult to administer volatile agents by a jet ventilator so intravenous agents are needed during this portion of the surgery.
 - b. Jet ventilation rate and pressure should be carefully titrated by direct observation of the surgical field. Obstruction of exhalation will lead to "stacking" of breaths, increased airway pressure, and barotrauma.
 6. **At the conclusion of the procedure**, a single large suture is placed from the chin to the anterior chest to preserve neck flexion and thereby minimize tension on the tracheal suture line. Several blankets under the head will help maintain flexion. Close attention to neck position during emergence, extubation, and transfer is essential.
- C. Emergence and Extubation**
1. **Spontaneous ventilation** should be resumed as soon as possible after the procedure to minimize trauma to the tracheal suture line. Most patients may be safely extubated, but in those for whom difficult anatomy or copious secretions make this undesirable, a small tracheostomy may be placed below the tracheal repair.
 - a. The patient should be awake enough to maintain spontaneous ventilation and avoid aspiration but should be extubated before excessive head movement can damage the surgical repair.
 - b. Fiberoptic examination of the surgical repair via LMA may be planned for the conclusion of the case, or done if there is suspicion of obstruction after extubation.
 - c. If tracheal collapse, airway edema, or secretions cause persistent respiratory distress after extubation, the patient should be reintubated fiberoptically with a small uncuffed endotracheal tube, preferably with the head maintained in forward flexion.
 2. Frequent bronchoscopies at the bedside under local anesthesia may be required to remove secretions from the lungs in the postoperative period.
 3. Only relatively small amounts of intravenous opioids are usually needed to treat the mild pain from the neck incision. Analgesia usually is administered after the patient is wide awake and responsive and while monitoring for undesirable respiratory depression.

D. Tracheal disruption may be caused by airway instrumentation or thoracic trauma and may be signaled by hypoxia, dyspnea, subcutaneous emphysema, pneumomediastinum, or pneumothorax.

1. **The point of injury** is commonly at the cricoid, midtrachea, carina, or either mainstem bronchus. Several mechanisms of injury have been proposed, including high airway pressures, lateral stretch of the thoracic cavity, and deceleration injury.
2. **Positive-pressure ventilation** will exacerbate the air leak and rapidly worsen symptoms from pneumothorax or pneumomediastinum. If possible, the patient should be allowed to breathe spontaneously, following the protocol for the patient with critical tracheal stenosis.
3. **Tracheal damage** in the already anesthetized patient may be treated initially by advancement of a small endotracheal tube past the point of injury. In the case of a difficult airway in which the tube causes the injury, an immediate surgical tracheostomy must be performed and access to the distal trachea secured.
4. Once a tube has been placed across or distal to the site of tracheal disruption, controlled positive-pressure ventilation can begin. Further management is as for the patient undergoing elective airway surgery.

VIII. INTRAPULMONARY HEMORRHAGE

Massive hemoptysis may be caused by thoracic trauma, pulmonary artery rupture secondary to catheterization, or erosion into a vessel by a tracheostomy, abscess, or airway tumor.

- A. The trachea must be immediately intubated and the lungs ventilated with 100% oxygen.
- B. An attempt should be made to suction the airway clear, ideally by rigid bronchoscopy.
- C. **If a unilateral source is identified**, lung isolation may be undertaken to protect the uninvolved lung and facilitate corrective surgery.
 1. **Lung isolation** may be achieved by placing an endobronchial blocker or a double-lumen endobronchial tube. Choice of technique depends on experience, equipment at hand, and the extent of active bleeding. Active bleeding may obscure airway visualization during flexible bronchoscopy. Obstruction of the endotracheal tube is an ever-present danger, and frequent suctioning may be necessary.
 2. In an emergency, the existing endotracheal tube can be advanced into the mainstem bronchus of the uninvolved lung and the cuff inflated.
 3. **Fiberoptic bronchoscopy** is essential for suctioning blood and confirming isolation.
 - a. Frequently, the source of bleeding is from the bronchial circulation. **Embolization** in the radiology suite is often attempted if the patient is stable.
 - b. Definitive treatment may require a thoracotomy and surgical repair.

IX. BRONCHOPLEURAL FISTULA

Bronchopleural fistula is a connection between a bronchial stump and the surrounding pleura. Symptoms include dyspnea, subcutaneous emphysema, persistent air leak, and purulent discharge from the chest tube.

A. General Considerations

1. Small fistulas may close spontaneously; a persistent leak indicates involvement of a larger bronchus.

2. Treatment of subsequent sepsis involves antibiotics and chest tube drainage.
3. Surgical approach varies, ranging from application of fibrin glue via bronchoscopy to thoracoplasty with a pedicled muscle flap.

B. Anesthetic Management

1. Positive-pressure ventilation may be inadequate if most ventilation escapes through the fistula. A functional chest tube must be in place before induction and positive-pressure ventilation.
2. Patients often undergo inhalation induction with spontaneous ventilation and lung isolation via endobronchial intubation to minimize the amount of time spent ventilating the fistula.
3. **High-frequency jet ventilation (HFJV)** has been used as an alternative to lung isolation to successfully decrease gas leak through the fistula by providing lower peak and mean airway pressures than with traditional positive-pressure ventilation. HFJV is not as effective in patients with noncompliant lungs such as acute respiratory distress syndrome patients. If mechanical ventilation via a standard endotracheal tube is to be used, flow redistribution may not be used to signal the end of a breath: the fistula will allow for gas flow at a constant velocity, causing the mechanical breath to continue indefinitely.

X. ESOPHAGEAL SURGERY

Esophageal surgery includes procedures for resecting esophageal neoplasms, for treating reflux, and for repairing traumatic or congenital lesions.

A. General Considerations

1. Patients may be chronically malnourished both from systemic illness (carcinoma) and anatomic interference with swallowing. Enteral or parenteral nutrition may have been initiated preoperatively.
2. Both esophageal carcinoma and traumatic disruption of the distal esophagus are associated with ethanol abuse; patients may have impaired liver function, elevated portal pressures, anemia, cardiomyopathy, and bleeding disorders.
3. Patients who have difficulty swallowing may be significantly hypovolemic. Cardiovascular instability may be further exacerbated by preoperative chemotherapy with cardiotoxins.
4. Most patients presenting for esophageal procedures will be at risk for aspiration. Rapid sequence induction or awake intubation should be planned.
5. Monitors should include a radial artery and urinary catheters. Central venous access may be desirable.
6. Temperature conservation measures should be aggressively pursued. The use of a warmed air blanket over the lower body is routine.

B. Operative Approach and Anesthesia

1. **An upper esophageal diverticulum** (Zenker diverticulum) is approached through a lateral cervical incision, similar to that for carotid surgery. This incision may also be used for upper esophageal myotomies for swallowing disorders.
2. **Positioning.** The patient is positioned supine with the neck extended and the head turned to the contralateral side.
3. **General anesthesia** may be induced and maintained with any technique after rapid sequence intubation. Postoperative pain and fluid shifts are usually minimal with a cervical incision, and patients may be safely extubated at the conclusion of the procedure. The surgeons may or may not elect to leave a nasogastric tube in place.

4. Carcinoma

- a. Lesions of the upper esophagus are approached by a “three-hole” approach, which includes a transverse cervical incision, a laparotomy, and a right thoracotomy. Sometimes the lesion is high enough to be removed with a transhiatal approach, including only the anterior cervical incision and the laparotomy, avoiding the thoracotomy. The laparotomy (and sometimes the right thoracotomy) are required to mobilize the stomach and lower esophagus. A cervical incision allows for anastomosis of the proximal esophagus and distal stomach.
- b. **Lesions of the middle esophagus** are commonly approached with a laparotomy followed by a right-sided thoracotomy. This procedure is known as an **Ivor Lewis esophagectomy**. Mobilization of the stomach or jejunum is accomplished through a midline abdominal incision. The right thoracotomy allows for a proximal anastomosis above the level of the aortic arch. There are also minimally invasive versions of this procedure that use laparoscopic and thoracoscopic equipment for the abdominal and thoracic portions of the procedure, respectively.
- c. **Lower esophageal lesions** are approached through an extended left thoracoabdominal incision. After resection, the surgeon will perform a primary anastomosis of the esophagus and stomach. Occasionally, the stomach does not provide an adequate distal anastomosis, and the surgeon instead brings up a Roux-en-Y loop of jejunum.
- d. Postoperative endotracheal extubation is performed when patients can protect their own airway from aspiration and they are fully awake. Immediate postoperative extubation can be considered in healthier patients after uncomplicated procedures.
- e. Virtually, any anesthetic technique may be used. Epidural analgesia is commonly used in the postoperative period both for analgesia from large incisions and to avoid any risk of aspiration from somnolence secondary to parenteral narcotics.
- f. Epidural analgesia has been shown to improve esophageal blood flow, as long as hypotension and hypovolemia are treated.
- g. If postoperative intubation is deemed necessary, it is usual to change from a double-lumen to a conventional endotracheal tube at the conclusion of the resection. Dependent tissue edema may significantly narrow the airway, rendering reintubation difficult.
5. **Trauma to the entire esophagus**, as with lye ingestion, may necessitate a total esophagectomy with subsequent interposition of a segment of colon or jejunum to serve as a conduit between the pharynx and stomach.
 - a. Surgical exposure may require two or three incisions, as described previously.
 - b. These patients may have a prolonged postoperative course with significant fluid shifts and nutritional depletion and are at risk for aspiration pneumonia. The trachea may remain intubated at the conclusion of the surgery, if a complex procedure has been done.
6. **Fundoplication** (e.g., Belsey Mark IV, Hill, or Nissen) is performed to relieve gastroesophageal reflux; the specific procedure depends on the surgeon's preference and the patient's anatomy.
 - a. The surgical approach is transabdominal for the Hill and Nissen procedures, and transthoracic for the Belsey. Collapse of the left lung is required for the latter procedure.

- b. Fluid shifts are usually less than after other esophageal surgeries, and the patients may be safely extubated at the conclusion of the procedure. Postoperative analgesic requirements are determined by the specific incision made; most patients benefit from epidural medications.

XI. LUNG TRANSPLANTATION

Lung transplantation is performed for end-stage nonmalignant lung disease. The most common indications are severe emphysema, α_1 -antitrypsin deficiency, cystic fibrosis, pulmonary fibrosis, and pulmonary hypertension. Specific operations include living-related lobar lung transplant (LRLTx), single-lung transplant (SLTx), double-lung transplant (DLTx), sequential SLTx, and combined heart–lung transplantation. The etiology of the lung disease usually dictates the specific operation to be performed and the likelihood that CPB will be required. Furthermore, the patient's position depends on the incision required for adequate surgical exposure (lateral decub/thoracotomy for SLTx and clamshell incision/supine for DLTx or LRLTx). Hence, knowing the patient's preoperative diagnosis will suggest the required approach. Patients will have undergone preoperative counseling, exercise and cardiac testing, and a conditioning program along with other assessments outlined in section I. Because the optimal donor ischemic time is less than 4 hours, time is of the essence.

A. Monitors and Equipment

1. Transplant patients will be actively immunosuppressed; therefore, sterile technique for all procedures is paramount. In addition to the usual monitoring for pulmonary resection, a pulmonary artery catheter with atrioventricular pacing capabilities is placed. A femoral arterial line is contemplated for patients who have a high likelihood of requiring CPB. A large-bore femoral venous access line is also of use when CPB is contemplated.
2. Medications should be immediately available to treat bronchospasm, electrolyte disturbances, pulmonary hypertension, and right ventricular failure. Immunosuppressants, steroids, and antibiotics should also be administered. All blood products must be leukocyte depleted and transfused via a filter. Anticipation of a large transfusion requirement and maintenance of an ample supply of blood products are important.
3. An epidural catheter should be placed for postoperative pain management, unless there is a strong possibility that the patient will need CPB and full heparin treatment.
4. Rarely, an additional mechanical ventilator may be required to optimally ventilate each lung.
5. Equipment should be available for peripheral arteriovenous or venovenous bypass through an oxygenator if hypoxemia becomes a significant problem (see Chapter 24).

B. Anesthetic Technique. Any technique that provides cardiovascular stability is appropriate. An intravenous technique may be preferable in the face of compromised ventilation. Organ availability is rarely planned, so most recipients will be considered “full stomachs.”

1. **Lung isolation** is best achieved with a contralateral endobronchial tube. In the event of a DLT, a left-sided tube is used with the left-sided bronchial anastomosis performed distal to the tip. The endobronchial tube may be exchanged for a single-lumen endotracheal tube at the end of operation if the patient is expected to require postoperative ventilation.
2. **Capnography** may be misleading because of severe mismatching of ventilation to perfusion. Frequent measurements of ABG tensions are warranted to assess ventilation. Worsening acidemia may also signal inadequate tissue perfusion from a variety of causes (hypovolemia, airtrapping, and decreased cardiac output).

3. **Transesophageal echocardiography (TEE) is useful for assessing right heart function and pulmonary blood flow after implantation.**
4. **Full CPB** may be necessary for the patient with pulmonary hypertension who cannot tolerate unilateral pulmonary artery clamping. Indications for bypass include arterial oxygen saturation less than 90% after clamping of the pulmonary artery, cardiac index less than 3.0 L/min/m² despite therapy with dopamine and nitroglycerin, or a systolic blood pressure less than 90 mm Hg. Continuous cardiac output monitors may be used to assess cardiac function. Management of CPB is discussed in Chapter 24.
5. The newly transplanted lung has impaired surfactant production and vascular endothelial permeability.
 - a. PEEP and frequent recruitment maneuvers will be needed to prevent atelectasis.
 - b. Pulmonary hypertension will cause increased hydrostatic pulmonary edema and worsening gas exchange and lung compliance.
- C. **Following surgery**, the patient will require intensive care.
 1. **Extubation** is possible in some patients after SLT and smooth intraoperative courses.
 2. **Many** patients will remain intubated until the transplanted lung begins to function well, and symptoms of reperfusion edema and acute rejection are controlled. The trachea is extubated only when the patient is hemodynamically stable and breathing comfortably.
 3. **Serial ABGs** are followed to document the function of the transplanted lung. Acute rejection may manifest as decreasing pulmonary compliance with worsening arterial oxygenation.
 4. **The patient** must be observed for signs of toxicity from the immunosuppressive regimen, including acute renal failure.
- D. **Repeated bronchoscopies and biopsies** of the transplanted lung are necessary after surgery and are often managed under local anesthesia with intravenous sedation.

XII. LUNG VOLUME REDUCTION SURGERY

Lung volume reduction surgery is performed on patients with severe bullous emphysema who experience incapacitating dyspnea despite maximal medical therapy and is often performed as a “bridge” to lung transplantation. The goal is to relieve thoracic distention and improve the mechanics of ventilation. Patients are selected under strict criteria and undergo a period of cardiopulmonary conditioning before surgery. Patients have extremely limited respiratory reserve, complicating induction and extubation.

- A. **The surgical approach** is via VATS, thoracostomy, or median sternotomy. The least functional part of the lung, as determined by CT and intraoperative observation, is resected. Postop air leaks decrease with lung sealants and lower pleural suction pressure.
- B. **The anesthetic technique** is similar to lung resection (see section VI). Postoperatively, epidural or paravertebral analgesia is essential.
- C. **Postoperative Course.** The trachea should be extubated postoperatively and the patients admitted to an intensive care unit.
 1. Patients will not usually meet classic extubation criteria.
 2. Maneuvers such as sitting position, air admixture, nebulized bronchodilators, and deep extubation with assisted ventilation via mask or LMA as a bridge to full extubation may help.
- D. A number of alternative endobronchial treatments for severe emphysema are being developed, including glues, endobronchial valves, and parenchymal staples.

Suggested Readings

- Alfille PH. Anesthesia for tracheal surgery. In Grillo HC, ed. *Surgery of the Trachea and Bronchi*. Hamilton: BD Decker; 2004:433–470.
- Bernard A, Deschamps C, Allen MS, et al. Pneumonectomy for malignant disease: factors affecting early morbidity and mortality. *J Thorac Cardiovasc Surg* 2001;121:1076–1082.
- Bracken CA, Gurkowski MA, Naples JJ. Lung transplantation: historical perspective, current concepts, and anesthetic considerations. *J Cardiothorac Vasc Anesth* 1997;11:220–241.
- Cicala RS, Kudsk KA, Butts A, et al. Initial evaluation and management of upper airway injuries in trauma patients. *J Clin Anesth* 1991;3:91–98.
- Colice GL, Shafazand S, Griffin JP, et al.; American College of Chest Physicians. Physiologic evaluation of the patient with lung cancer being considered for resectional surgery: ACCP evidenced-based clinical practice guidelines (2nd edition). *Chest* 2007;132:161S–177S.
- Devitt JH, Boulanger BR. Lower airway injuries and anaesthesia. *Can J Anaesth* 1996;43:148–159.
- Duthie DJ. Anesthetic agents for thoracic surgery: what's best? *Curr Opin Anaesthesiol* 2013;25:53–57.
- Gruchnik KP, Clark JA. Pathophysiology of one-lung ventilation. *Thorac Surg Clin* 2005;15(1):85–103.
- Hartigan PM, Pedoto A. Anesthetic considerations for lung volume reduction surgery and lung transplant. *Thorac Surg Clin* 2005;15(1):143–157.
- Hobai IA, Chhangani SV, Alfille PH. Anesthesia for tracheal resection and reconstruction. *Anesthesiol Clin* 2012;30:709–730.
- Joshi GP, Bonnet F, Shah R, et al. A systematic review of randomized trials evaluating regional techniques for postthoracotomy analgesia. *Anesth Analg* 2008;107(3):1026–1040.
- Lennox PH, Umedaly HS, Grant RP, et al. A pulsatile pressure waveform is a sensitive marker for confirming the location of the thoracic epidural space. *J Cardiothorac Vasc Anesth* 2006;20(5):659–663.
- MacDougall P. Postthoracotomy shoulder pain: diagnosis and management. *Curr Opin Anaesthesiol* 2008;21(1):12–15.
- Pawlowski J. Anesthetic considerations for interventional pulmonary procedures. *Curr Opin Anaesthesiol* 2013;25:6–12.
- Soto RG, Fu ES. Acute pain management for patients undergoing thoracotomy. *Ann Thorac Surg* 2003;75(4):1349–1357.
- Vidal Melo MF, Musch G, Kaczka DW. Pulmonary pathophysiology and lung mechanics in anesthesiology: a case-based overview. *Anesthesiol Clin* 2012;30:759–784.

I. PREOPERATIVE ASSESSMENT AND MANAGEMENT

Patients undergoing vascular surgery frequently have multiple comorbid conditions that should be optimized prior to surgery.

A. Cardiovascular System

Cardiac events such as myocardial infarction, arrhythmia, and heart failure are the leading cause of morbidity and mortality in patients undergoing vascular surgery. Myocardial infarction (MI) accounts for about one half of early postoperative deaths. According to the ACC/AHA guidelines for preoperative cardiac evaluation, these patients are considered to be at an elevated ($>1\%$) risk for postoperative major adverse cardiac events (MACE). Preoperative cardiac evaluation is addressed in greater detail in Chapter 2. Below are some specific considerations with regard to vascular surgical patients.

- 1. Cardiac stress testing.** For nonemergent cases, in patients with poor functional capacity (<4 METS), cardiac stress testing should be carried out if the results will impact patient care. Pharmacologic stress testing will be necessary for patients with physical limitations such as claudication or disability from prior stroke. The need for coronary artery catheterization is determined based on the results of the stress test, in consultation with a cardiologist.
- 2. Echocardiography** may be indicated if the patient has a new murmur, dyspnea of unknown etiology, valvular heart disease, or compensated heart failure with new, or worsening, symptomatology.
- 3. Blood pressures** should be measured in both arms to determine whether there is a difference. Due to the systemic nature of atherosclerosis, patients may have subclavian or axillary arterial stenoses. Blood pressure should be monitored in the extremity with the higher reading.
- 4. Coronary revascularization** should be carried out only if medically indicated. According to the CARP trial (Coronary Artery Revascularization Prophylaxis), coronary revascularization in advance of major vascular surgery has not been shown to improve outcome when compared with medical management. This trial excluded patients with left main coronary artery disease, ejection fraction less than 20%, and severe AS.
- 5. β -blocker therapy** should be maintained in patients who are on it chronically. Initiation of β -blocker therapy is reasonable in patients with three or more RCRI (revised cardiac risk index) risk factors or in patients with reversible ischemia on preoperative testing. However, improper timing and dose titration may increase risk of stroke and mortality. β -blocker therapy should be started at least 2 days prior to surgery; 7 days is preferred. Therapy should be started at a low dose and titrated slowly to achieve target heart rate of 60 to 80 bpm. They should be held for hypotension.
- 6. Antiplatelet therapy.** Aspirin therapy should be continued in patients with coronary stents, those with cerebrovascular disease, or those with high-risk CAD. Continuation should be considered in all

vascular surgical procedures in discussion with the surgeon. Aspirin therapy is associated with an increased risk of bleeding. POISE-2, a randomized, controlled trial of 10,000 patients undergoing noncardiac surgery, did not show a benefit of aspirin initiation or continuation with respect to MACE or death. However, it excluded patients who had recently received coronary stents and those undergoing carotid endarterectomy (CEA). Furthermore, only a small proportion of the study population underwent vascular surgery. Continuation of **clopidogrel** therapy depends on patient factors (e.g., presence and type of coronary stents and when they were placed) as well as surgical factors.

7. **Statins** should be continued perioperatively. The initiation of statin therapy is reasonable in patients undergoing vascular surgery. The statin should ideally be started 1 week to 30 days prior to the surgical procedure. There is evidence that statins decrease coronary inflammation regardless of low-density lipoprotein level. Withdrawal prior to surgery has been associated with increased cardiac events.
8. **Warfarin** should be discontinued at least 3 to 5 days before surgery, and, if indicated, heparin therapy started.
9. If **regional anesthesia** is planned, anticoagulant and antiplatelet agents should be held according to guidelines (see Chapter 18) and in consultation with the surgeon and cardiologist.

B. Respiratory System

Many vascular patients have histories of significant tobacco use and may have compromised pulmonary function (see Chapter 3). Routine pulmonary function testing is not indicated. Aortic cross-clamping and associated ischemia–reperfusion can produce a systemic inflammatory response that may contribute to postoperative lung injury.

C. Renal System

Preexisting renal dysfunction is common. It is related to atherosclerosis, hypertension, diabetes, and advanced age and may exist even in the absence of an abnormal serum creatinine value. Due to a decreased number of functioning glomeruli, these patients have a reduced capacity to autoregulate renal perfusion in the setting of hypotension and are often intolerant to perioperative insults such as ischemia–reperfusion, atheroembolism, and nephrotoxins like contrast dye. Patients with chronically elevated serum creatinine levels (>2 mg/dL) have substantially greater morbidity and mortality following vascular surgery. Open aortic and renal arterial surgeries carry the highest risk for postoperative renal dysfunction. Patients undergoing endovascular procedures are at risk for **contrast-induced nephropathy (CIN)**. **CIN** is diagnosed by an increase in serum creatinine beginning 24 to 48 hours following contrast exposure in a patient with no other reason for acute kidney injury. Risk factors for CIN include chronic kidney disease, diabetes, anemia, heart failure, the use of high-osmolar contrast, and the use of high volumes of contrast. In patients at risk, crystalloid administration and the use of low volumes of iso-osmolar or low-osmolar contrast agents are recommended. Pretreatment with **sodium bicarbonate** may also be considered, although the data regarding its benefit are inconsistent. Sodium bicarbonate (150 mEq/L) can be given as a bolus infusion of 3 mL/kg over 1 hour followed by 1 mL/kg/h. The duration should extend for 6 hours after the last dose of contrast. **N-acetylcysteine (NAC)** administration may also be considered at a dose of 1,200 mg orally every 12 hours, on the day before and on the day of contrast exposure, for a total of 2 days.

D. Central Nervous System

Patients should be examined for carotid bruits and questioned for a history of transient ischemic attacks (TIAs) and cerebrovascular accidents. Symptomatic carotid disease may warrant revascularization prior to other elective procedures.

E. Endocrine System

In addition to accelerated atherosclerosis, long-standing diabetics may have extensive microvascular disease resulting in autonomic dysfunction, silent myocardial ischemia, and nephropathy. In consultation with the patient's endocrinologist, **metformin** should be discontinued prior to procedures that involve IV contrast dye, or renal or hepatic ischemia due to the potential for the development of severe lactic acidosis. It should also be held in patients with preexisting renal dysfunction or heart failure.

F. Hematologic System

The vascular surgical patient is at particularly high risk to develop **heparin-induced thrombocytopenia (HIT)** due to the need for repeated and occasionally prolonged exposure to heparin (see Chapter 24). This syndrome is characterized by thrombocytopenia and/or thrombosis in the setting of heparin exposure and is due to the formation of antibodies to the heparin-platelet factor 4 (PF4) complex. In patients with a recent diagnosis of HIT who require vascular surgery with intraoperative anticoagulation, an anti-PF4 antibody level should be checked. If elevated, a serotonin release assay (SRA) is recommended. If the SRA is negative, heparin can be used intraoperatively irrespective of the result of the anti-PF4 antibody test. If both the anti-PF4 antibody test and the SRA are positive, surgery should be delayed or an alternative anticoagulant should be used. The **acute management** of the patient with HIT includes discontinuation of all heparins, suspension of warfarin, avoidance of platelet transfusions, and the initiation of alternative, nonheparin, anticoagulant therapy.

II. PERIPHERAL ARTERIAL SURGERY

A. General Considerations

Peripheral arterial procedures include the bypass or stenting of stenotic arteries; embolectomy of occluded arteries; and the repair of peripheral arterial aneurysms. Endovascular approaches are employed whenever possible and are typically performed in the operating room, angiography suites, or hybrid operating rooms. Special considerations for the provision of anesthesia outside of the operating room are discussed in Chapter 33.

B. Percutaneous Balloon Angioplasty and Stenting

Limb patency and amputation-free survival rates are similar to open bypass surgery. Patients must have a target lesion amenable to the endovascular approach: typically a focal short-segment occlusion with patent vessels distal to the treated lesion (i.e., "good runoff"). Advantages of percutaneous therapy include faster patient recovery, shorter hospital stay, smaller wounds with lower complication rates, and potential cost savings. Procedures on the upper and lower extremities are typically performed in the operating room angiography suites and are frequently done under local anesthesia with sedation.

1. **Surgical approach** may be percutaneous or through a cutdown to the artery. Brachial artery access may be required necessitating IV placement and blood pressure monitoring on the contralateral arm.
2. **Large amounts of intravenous contrast dye** may be administered and may require prophylaxis for CIN (see "Renal System" under section I, above).
3. **Anesthetic technique** frequently involves monitored anesthesia care with standard monitors. Local anesthesia typically provides sufficient

analgesia. Provisions should be made to allow for conversion to general anesthesia in the case of an unplanned conversion to open repair.

4. **IV unfractionated heparin** is often used as an adjunct and is given prior to arterial cannulation. A **vasodilator** may be administered intra-arterially by the surgeon to treat catheter or wire-induced vasospasm. Treatment of systemic effects may be required.
5. **Distal embolization** is a potential serious complication with aggressive endovascular instrumentation.

C. Lower-Extremity Bypass Grafting

In the presence of multisegment disease or poor distal runoff, open **surgical bypass** of the lower extremity is preferred over the endovascular approach. An autologous saphenous vein graft is the most commonly used conduit. If this is not available, or is of unacceptable quality, an upper extremity vein from the patient or cryopreserved cadaveric vein may be used. Preparation of the vein and subsequent anastomoses to the arterial circulation may be time consuming but rarely place significant hemodynamic stress on the patient. The use of synthetic grafts in selected patients may reduce the length of these procedures. **Blood loss is usually minimal**, but it may be significant with revision of a previous bypass. **Routine monitoring** is usually sufficient. Patient comorbidities or surgical complexity may warrant placement of invasive monitors. **No significant differences in morbidity or mortality have been demonstrated between regional anesthesia and general anesthesia** for lower limb revascularization.

1. **General anesthesia.** Any technique is appropriate provided hemodynamic stability is maintained.
2. **Regional anesthesia.** Potential advantages may include sympathetic blockade, improved pain control, lack of airway instrumentation, improved ability to detect symptoms of myocardial ischemia in an awake patient, and reduced incidence of pneumonia. However, long procedures under regional anesthesia can pose a challenge for patients who may become uncomfortable and restless.
 - a. A continuous **lumbar epidural catheter** is commonly used. It provides excellent analgesia and muscle relaxation as well as the ability to administer postoperative analgesia. Spinal anesthesia may be used if the length of the procedure is appropriate. For **femoral–popliteal** and distal lower extremity bypass limited to a single limb, combined lumbar plexus and sciatic nerve block may be used as an alternative to neuraxial anesthesia. For **iliofemoral bypass**, a spinal or epidural will require a higher level (i.e., T8–T10) because of proximal extension of the incision and peritoneal retraction for exposure of the iliac artery. **Femoral–femoral bypass grafting** is used to treat symptomatic unilateral iliac occlusive disease.
 - b. An **α -adrenergic agent** (e.g., phenylephrine) should be available to treat the hypotension associated with sympathetic blockade.
 - c. **Neuraxial anesthesia is contraindicated in anticoagulated patients.** Clotting abnormalities must be corrected (with fresh-frozen plasma [FFP], vitamin K, or protamine) before catheter insertion, or the patient must receive a general anesthetic. See Chapter 17 for specific medication guidelines. Of note, there is no evidence that the subcutaneous administration of unfractionated heparin for DVT prophylaxis increases the risk of epidural hematoma. If postoperative warfarin therapy is needed, the epidural should be removed before the onset of the anticoagulant effect (within 24 hours of administration of the first dose).

D. Peripheral Embolectomy and Femoral Pseudoaneurysm

Femoral pseudoaneurysms are most often iatrogenic, occurring in the setting of femoral artery catheterization (e.g., for coronary angiography or intra-aortic balloon pump placement). As such, these patients often have unstable cardiovascular disease (e.g., recent MI with stent placement). Some are anticoagulated or have recently received thrombolytic agents, thus precluding regional anesthesia. Field blocks with local anesthesia may be most appropriate in the setting of cardiovascular instability. Embolectomy of an obstructed artery may be associated with significant blood loss and hypotension.

E. Peripheral Aneurysms

Peripheral arterial aneurysms, such as popliteal artery aneurysms, rarely rupture but are associated with a high rate of thrombosis and embolism. Either general or neuraxial anesthesia may be used to manage their repair.

F. Axillofemoral Bypass Grafting

An axillofemoral bypass graft restores arterial blood flow to the lower extremities in patients with occluded aortoiliac vessels who are not candidates for aortic reconstruction for various reasons including high anesthetic risk, significant intra-abdominal adhesions due to prior abdominal surgeries, active abdominal infection, or an infected aortic prosthesis. A prosthetic graft is tunneled under the pectoralis muscle and positioned in the subcutaneous layer of the thorax and abdomen and anastomosed distally to the femoral artery. General anesthesia is most appropriate.

G. Vascular Surgery of the Upper Extremity

Vascular surgery of the upper extremity usually includes distal embolectomy and repair of traumatic injuries. The surgery is localized, but there may be a need to harvest a vein graft at a site distant from the vascular repair. Possible anesthetic techniques include field block and regional or general anesthesia.

III. CAROTID REVASCULARIZATION**A. General Considerations**

Carotid revascularization is performed in patients with stenotic lesions of the internal carotid artery. These lesions often present as carotid bruits and may produce TIAs or strokes. The indication for surgical revascularization takes into account patient life expectancy, surgical complication rates, the presence of symptoms, and the degree of stenosis. CEA is indicated for patients with nondisabling stroke or TIA who have greater than 70% stenosis by noninvasive imaging, as long as their life expectancy is greater than or equal to 5 years and the surgeon's perioperative stroke and death risk is less than 6%. The data are less clear for patients with asymptomatic disease. CEA may be indicated in asymptomatic males with greater than 70% stenosis and a life expectancy in excess of 5 years if the surgeon's perioperative stroke and death risk is less than 3%. It is not clear that CEA is more effective than medical therapy in women with asymptomatic carotid artery stenosis. If the patient does not meet criteria for surgical revascularization, risk factor modification with medical therapy and lifestyle changes is instituted. This consists of statin and antiplatelet therapy, smoking cessation, blood pressure control, and management of diabetes. CEA is the preferred modality for operative therapy of carotid artery stenosis. The role of carotid artery stenting (CAS) is still being defined. Evidence suggests that CAS and CEA have similar long-term results, but CAS is associated with a higher rate of periprocedural morbidity and mortality. In symptomatic patients, CAS is recommended

for patients with difficult surgical access (i.e., prior neck dissections) or radiation-induced carotid stenosis as long as the surgeon's postoperative stroke and death risk is less than 6%. CAS is not recommended for patients with asymptomatic carotid artery stenosis.

Along with the standard history and physical, the preoperative anesthetic assessment should focus on the documentation of **existing neurologic deficits** as well as the **range of motion of the patient's neck**.

B. Carotid Artery Stenting

1. Indications

CAS may be preferred over CEA in patients with neck anatomy that is unfavorable for open surgery, such as with prior neck surgery or radiation, or in patients with higher operative risk due to severe cardiac or pulmonary disease. Due to the potential for CIN, CAS is generally avoided in patients with renal dysfunction.

2. **Monitoring.** An arterial catheter is indicated for continuous hemodynamic monitoring and facilitates frequent blood draws for monitoring of activated clotting time (ACT). Close observation of the patient's **mental status** is necessary to detect new-onset stroke resulting from plaque embolization.

3. **Anesthetic management** usually consists of monitored anesthesia care combined with local anesthesia at the vascular access site. Care should be taken to maintain the patient's level of alertness to facilitate intraoperative neurologic monitoring. The femoral artery is typically accessed percutaneously. The awake patient may feel pain during balloon angioplasty and arterial dilation that resolves immediately with balloon deflation.

4. **IV contrast dye** and fluoroscopy are used intermittently throughout the procedure.

5. **Heparin** is administered prior to arteriotomy.

6. Vagally mediated **bradycardia** can occur following stent deployment. Pretreatment with glycopyrrolate is helpful.

7. **Complications** include stroke, vascular access site injuries, device malfunction, restenosis, and CIN. Microembolic injuries are more frequent after CAS compared with CEA; embolic protection devices (EPDs) can reduce neurologic injuries if the operator is experienced with the apparatus.

C. Carotid Endarterectomy

1. Monitoring.

a. **Intra-arterial blood pressure monitoring** is necessary.

b. **CNS monitoring** is necessary during carotid cross-clamp application, to evaluate the adequacy of cerebral perfusion and to identify patients who may require **shunting**. The awake patient is the gold standard for intraoperative CNS monitoring. If the procedure is being conducted under general anesthesia, the CNS can be monitored using **electroencephalography** (EEG), transcranial Doppler ultrasound, or arterial stump pressure measurement. CEA can also be conducted with routine shunting without continuous CNS monitoring. There are no data to support the use of routine versus selective shunting. No particular method of CNS monitoring in selective shunting has been shown to produce better outcomes.

2. **Anesthetic technique.** The choice of anesthetic technique has no significant impact on patient outcome. The decision to proceed with general anesthesia or regional anesthesia is usually based on the preferences of the surgeon and the patient.

a. Regional Anesthesia

1. Regional anesthesia may be performed with a combined **superficial and deep cervical plexus block** or with a superficial plexus block that is supplemented in the field by the surgeon (see Chapter 18). Both have potential complications.
2. CEA under regional anesthesia **requires an alert, cooperative patient** who is able to tolerate lying still, with the head rotated to the side, under the drapes.
3. **Access to the airway** may be necessary at any time, and the patient should be properly positioned and draped with this in mind. An appropriately sized laryngeal mask airway should be readily available.
4. **Continuous neurologic** assessment is possible in the awake patient.

b. General anesthesia

1. Ventilation and oxygenation is controlled leading to reduced cerebral metabolic demand.
2. **Prior to induction, neuromonitoring baselines** are established.
3. **Blood pressure** should be maintained at the patient's **high-normal** range that may require a vasopressor such as phenylephrine.
4. **A hemodynamically stable induction** is desired to preserve cerebral perfusion. Minute ventilation should be adjusted to avoid hypocapnic cerebral vasoconstriction. Hypercarbia, however, has no clinical benefit.
5. A steady state of **light anesthesia** is generally compatible with EEG monitoring. **Muscle relaxants** are helpful to minimize movement that can interfere with EEG interpretation as well as the procedure.
6. Anesthetic techniques to facilitate **early postoperative extubation** and **neurologic examination** are desirable.

3. Carotid Cross-clamping

- a. **Systemic heparin** (5,000 units IV) is administered before cross-clamping.
- b. Prior to cross-clamp, **blood pressure** is typically increased by the use of a vasopressor, with the intention of maintaining ipsilateral cerebral perfusion from the contralateral carotid through the Circle of Willis.
- c. **Surgical manipulation of the carotid sinus** may cause intense vagal stimulation, leading to hypotension and bradycardia. Release of traction or infiltration with local anesthetic will typically abolish the response. Administration of anticholinergics is seldom required. Prophylactic infiltration of local anesthetic infiltration should be considered for patients with significant preoperative cardiac conduction delay, critical aortic stenosis, and significant coronary disease.
- d. **Routine shunting, selective shunting, or nonshunting.** Shunting involves the placement of a plastic tube intra-arterially to span the arteriotomy and preserve ipsilateral, antegrade cerebral perfusion during carotid artery cross-clamping. The approach to shunting is based on surgical preference. A number of case series have shown similar stroke risk with the three approaches. In selective shunting, a shunt is placed when neuromonitoring reveals evidence of cerebral ischemia following carotid cross-clamping.
- e. **Unclamping** may produce reflex vasodilation and bradycardia. Vasopressors may be required as the baroreceptors adapt. Their use may also be required in the postoperative period.

D. Postoperative Considerations

1. Immediate postoperative complications include **neurologic deficits, blood pressure lability, and airway obstruction**.
2. **Neurologic deficits** are typically due to emboli related to the surgical procedure. They should be managed aggressively with increased blood pressure and consultation with the surgeon and a stroke specialist.
3. **Labile blood pressures** may be observed secondary to alterations in the carotid baroreceptor response brought about by the endarterectomy. Hypertension requiring a vasodilator (labetalol or nitroglycerin) may be a result of surgical denervation of the carotid sinus. Hypotension requiring a vasopressor (phenylephrine) may be a result of baroreceptor hypersensitivity and typically does not reflect hypovolemia.
4. **Acute airway obstruction** may occur secondary to hemorrhage at the suture line and an expanding hematoma. The immediate release of the superficial sutures with evacuation of the hematoma is necessary to prevent airway compromise.
5. **Injury to the recurrent laryngeal, superior laryngeal, or hypoglossal nerves** can occur and is usually transient. Injury to the recurrent laryngeal nerve is characterized by a hoarse voice. Bilateral recurrent laryngeal nerve injury is rare but must be considered in patients who have undergone previous contralateral CEA or neck surgery. It will present with acute upper airway obstruction.
6. **Cerebral hyperperfusion syndrome (CHS)** typically occurs several days postoperatively and may manifest as ipsilateral headache, seizure, focal neurologic signs, or intracranial hemorrhage. It is related to an abrupt increase in blood flow with loss of autoregulation in the surgically reperfused brain. Based on the pathophysiology of the syndrome, **it is reasonable to target postoperative blood pressures in the normal to slightly subnormal range** for prevention.

IV. ABDOMINAL AORTIC REPAIR

Abdominal aortic repair may be required for atherosclerotic occlusive disease or aneurysmal dilation of the aorta. Aorto-occlusive disease usually presents as claudication. An abdominal aortic aneurysm (AAA) may be found incidentally. Alternatively, it may present with back pain or, if ruptured, severe shock. Ninety-five percent of all AAAs occur below the level of the renal arteries. Indications for repair are largest diameter greater than 5.5 cm in men and 5.2 cm in women; rate of expansion exceeding 1 cm/year; or symptoms secondary to the AAA. The annual risk of rupture of an expanding 5-cm aneurysm is about 4%. The operative mortality for elective AAA repair is less than 2%, while the overall mortality of aneurysm rupture is 70% to 80%.

A. Endovascular Abdominal Aortic Repair (EVAR)

1. **Overview.** The majority of infrarenal AAA are treated by EVAR. The procedure involves the endovascular placement of an expandable stent graft spanning the aneurysm under fluoroscopic guidance. The stent graft excludes the aneurysm from the circulation preventing its expansion and rupture. The application of an aortic **cross clamp is not required** consequently. **EVAR leads to greater intraoperative hemodynamic stability.** There is a lower incidence of postoperative pulmonary, cardiovascular, and renal morbidity and significantly reduced 30-day operative mortality for EVAR compared to open surgery. The early survival benefit is lost over time. At about 2 years postprocedure, mortality rates are the same as those for patients who have undergone open

aneurysm resection. Patients with endovascular repair also require regular follow-up imaging and may require additional EVAR-related interventions.

2. **Patient suitability** for EVAR depends on the size and morphology of the AAA. Most infrarenal AAAs with favorable neck anatomy are repaired endovascularly. EVAR has lower short-term, perioperative mortality, but higher incidence of leak and other long-term complications, and requires a lifetime of imaging surveillance. Younger patients with better risk profile may more suited for open repair.
3. **Monitoring and access.** Intra-arterial blood pressure monitoring is required in addition to standard monitors. Large bore peripheral access (16 gauge or 14 gauge) is desirable. Central venous access is rarely required.
4. **Surgical considerations.** Systemic **heparinization** is required. If the aneurysm involves the renal or mesenteric arteries, a more complex endovascular stent graft with branches or fenestrations can be used. For infrarenal aneurysms, **surgical access is usually via bilateral common femoral arteries**. Exposure of the arteries followed by arteriotomies is typically performed with surgical repair afterward. Percutaneous access with subsequent closure using a specialized device is possible for select patients in the absence of femoral artery disease or stenosis. There is significant **radiation exposure** with **fluoroscopy** and a **contrast dye** load. **Ensuring the patient does not move** during digital subtraction angiography will reduce the patient's exposure by minimizing the need for repeated studies. Following stent graft deployment, an intra-aortic balloon is inflated to expand the stent graft and anchor it in place. Balloon inflation leads to temporary aortic occlusion. The occlusion is short lived, typically lasting 3 to 4 heartbeats. Hypertension may be observed during the period of balloon occlusion; however, it usually does not last long enough to warrant therapy. **Controlled hypotension** may be requested by the surgeon during stent graft deployment to prevent proximal hypertension and stent graft displacement.
5. **Anesthetic technique.** EVAR may be performed under **local, regional, or general anesthesia**. Factors such as anticoagulant use, patient comfort, surgeon preference, and anticipated length of surgery will influence the choice of anesthetic. There is some evidence to suggest lower morbidity and mortality, shorter hospital stays, and fewer ICU admissions with local or regional anesthesia as compared to general anesthesia. Bilateral ilioinguinal or iliohypogastric nerve blocks are alternatives along with local infiltration. Of note, in contrast to neuraxial anesthesia, local anesthesia will not alleviate the ischemia pain associated with femoral artery occlusion, and supplementation with systemic analgesics may be required.
6. **Conversion to open repair is rare (<1%).** It may be necessary in the setting of difficult arterial access (e.g., with severely atherosclerotic arteries); vessel dissection at the arterial access site; tortuous iliac arteries that prevent passage of the deployment system; stent malposition or migration; and aneurysm rupture. Resuscitation equipment such as a red blood cell salvage device and a rapid infusion device should be available in centers performing EVAR.
7. **Bleeding** may occur around the femoral sheaths and is often difficult to quantify or track. Massive hemorrhage is rare.

8. Complications of EVAR include failure to exclude the AAA from the arterial system (endoleak), embolism, arterial injury, graft kinking, groin access injury, limb ischemia and infection. Patients with impaired renal function are at risk for CIN. *N*-acetylcysteine and crystalloid infusion may be considered (see “Renal System” under section I, above).

a. Endoleak (Fig. 23.1) is the persistence of blood flow into the aneurysm sac leading to expansion. It occurs in 20% to 25% of EVARs. Types I and III endoleaks are considered at high risk for aneurysm sac pressurization and rupture and should be treated as soon as diagnosed. Type II endoleaks may spontaneously resolve and are followed closely with serial imaging. If they persist, they may require a subsequent procedure to embolize the responsible vessel. Treatment is not recommended for type IV endoleaks.

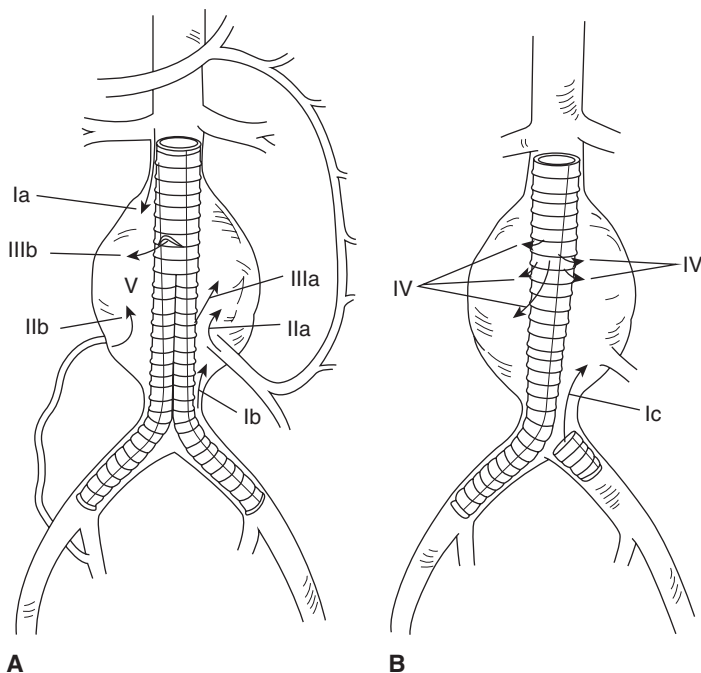


FIGURE 23.1 A, B: Schematic demonstrating the different types of endoleak after endovascular aneurysm repair. Type I endoleaks occur because of inadequate graft seal resulting in perigraft flow and include (Ia) perigraft flow occurring proximally, (Ib) perigraft flow occurring distally, and (Ic) perigraft flow around an iliac artery occlusion device. Type II endoleaks occur when branch arteries backbleed because of collateral flow. These endoleaks include (IIa) backbleeding inferior mesenteric artery and (IIb) backbleeding lumbar artery. Type III endoleaks occur when flow persists between the segments of a modular graft and include (IIIa) leaks between iliac limbs or an iliac limb and main body component and (IIIb) leaks between main body components. Type IV endoleaks (IV) occur when flow is present through endograft material (graft porosity). Type V endoleak, or, “endotension” (V), occurs when persistent or recurrent pressurization of the aortic aneurysm exists in the absence of demonstrable endoleak. (Drawings prepared by H. Fischer, MFA.)

B. Open Abdominal Aortic Surgery

1. **Patient selection.** Open surgical repair is indicated for patients whose aortic anatomy does not meet the specified minimum requirements for standard, commercially available endografts; for patients in whom delaying repair to wait for a custom-made endograft may result in significant risk of rupture; and for patients unlikely to comply with long-term imaging surveillance protocols following EVAR.
2. **Surgical approach.** Compared with a **transabdominal** approach, the **retroperitoneal (RP)** approach may result in a lower incidence of postoperative ileus, pulmonary complications, cardiovascular complications, and fluid shifts. The RP approach is technically advantageous in morbidly obese patients and in those who have had previous abdominal procedures.
3. **Monitoring.** A large peripheral IV, arterial line, central venous catheter, and Foley catheter are indicated. Procedures that require a supraceliac cross-clamp entail greater hemodynamic perturbations and blood loss. Enhanced intraoperative monitoring of cardiac function with TEE or PA catheter may be beneficial. Vasopressors and vasodilators must be available.
4. **Anesthetic technique.** Most patients receive combined general and epidural anesthesia using a low-thoracic to midthoracic epidural catheter. Although general anesthesia alone is acceptable, a combined technique reduces anesthetic requirements, facilitates earlier extubation, and provides effective postoperative analgesia.
5. The hemodynamic goal of **induction** is to **avoid hypertension**. It is helpful to establish a sensory level with the epidural catheter prior to the induction of general anesthesia.
6. **Heat conservation.** Heat loss during aortic procedures may be considerable. Strategies for heat conservation are discussed in Chapter 19. Forced air warmers should **never** be used **below the level of the aortic cross-clamp**. Severe burns may develop during cross-clamping due to the absence of heat redistribution by normal blood flow.
7. **Bowel manipulation** is necessary to gain access to the aorta during the transabdominal approach and may be accompanied by skin flushing, decreased systemic vascular resistance, and profound hypotension. These changes may be caused by the release of prostaglandins and vasoactive peptides from the bowel and last for 20 to 30 minutes. Treatment consists of vasopressor administration and volume expansion.
8. **Fluid management.** There is the potential for significant intravascular volume depletion due to hemorrhage; insensible losses into the bowel and peritoneal cavity; and evaporative losses associated with the laparotomy. Volume resuscitation is guided by the patient's hemodynamics. Aortic cross-clamp application will give rise to renal insufficiency, even with an infrarenal cross-clamp.
9. **Blood product administration** should be guided by the patient's laboratory values.
10. **Aortic Cross-Clamping**
 - a. **Heparin** (5,000 units IV) is administered several minutes prior to the application of the aortic cross-clamp.
 - b. **Hypertension** will occur with aortic cross-clamping. The degree of hypertension is a function of the cross-clamp location. A more proximal cross-clamp is associated with a greater increase in blood pressure. Consideration can be given to inducing mild hypotension prior to the application of the cross-clamp. The **increased afterload**

is well tolerated by patients with normal cardiac function, but those with compromised left ventricular function may develop myocardial ischemia and hypotension. Hypotension with the application of the aortic cross-clamp may indicate left ventricular failure secondary to increased afterload or retrograde dissection into the coronary arteries. Cardiac function must be evaluated and supported.

- c. Avoidance of excessive hypertension is important during aortic cross-clamp to minimize the **risk of retrograde aortic dissection**.
- d. Following proximal clamping, **vascular control distal to the aneurysm** is established. If the vasculature distal to the aneurysm has been surgically exposed, distal control may be achieved via the application of a cross-clamp on the aorta or common iliac arteries distal to the aneurysm. If the distal vasculature is not exposed, endovascular control is achieved. Once the aneurysm sac is opened, a balloon-tipped catheter is advanced distal to the aneurysm. Balloon inflation occludes the vessel and prevents backbleeding, establishing distal control. Significant retrograde hemorrhage may occur during this maneuver.
- e. There is no compelling evidence to support the use of renal protective adjuncts such as **mannitol and fenoldopam**. The application of an aortic cross-clamp at any level may lead to decreased renal cortical blood flow and urine output. With suprarenal clamping, renal perfusion is at even greater risk due to longer cross-clamp times and potential for cholesterol embolization. The maintenance of adequate hydration and urine output is paramount.

11. Aortic Unclamping

- a. Unclamping will produce immediate **hypotension** due to a fall in systemic vascular resistance.
- b. The degree of hypotension is a function of clamp duration and the proximal extent of the clamp.
- c. In preparation for the release of the aortic cross-clamp, steps should be taken to optimize the patient's intravascular **volume status** and **increase vascular tone**. Inspired oxygen concentration should be increased to 100%. Having the surgeon release the clamp in a slow, controlled fashion can help to minimize hypotension.
- d. Following unclamping, reperfusion of the ischemic organs and tissues leads to acidemia and systemic vasodilation. The magnitude of these disturbances is a function of the duration of the aortic cross-clamp and the metabolic activity of the organs that were ischemic. **Cross-clamping above the celiac or superior mesenteric artery (SMA) can produce profound visceral ischemia and acidosis. Sodium bicarbonate** may be administered at unclamping to mitigate the effects of acidosis. **Minute ventilation** may also be increased to induce a mild respiratory alkalosis. In the setting of profound hypotension that is unresponsive to fluids or vasopressors, the aortic cross-clamp may be reapplied to maintain adequate perfusion pressure while additional volume and vasopressors are administered.

- 12. **Emergence.** Most patients with working epidurals and infrarenal or juxtarenal cross-clamps can be extubated at the end of the procedure. Patients with hemodynamic instability, persistent hemorrhage, persistent acidosis, or severe hypothermia (<33°C) are left intubated. Hypertension, tachycardia, pain, and shivering should be anticipated and treated.

C. Emergent Repair of a Ruptured Abdominal Aortic Aneurysm

Patients may be **hemodynamically stable or unstable** depending on the degree to which the rupture is contained. Rupture can occur into the peritoneal cavity or the RP space. Some measure of tamponade will temporarily reduce the volume of blood loss.

1. The priority for anesthetic management is the establishment of adequate **IV access** for large volume resuscitation.
2. **Blood products** should be ordered immediately. If type-specific blood and FFP are unavailable, universal donor-type blood (type O negative for women of childbearing age and type O positive for all others) and FFP (type AB) should be obtained, and a **blood bank sample** should be sent immediately to the lab for cross-matching. **Colloid solutions** should be ordered. A red blood cell salvage system as well as a rapid transfuser should be immediately available.
3. **Standard monitors** should initially be applied if the patient is unstable, so as not to delay definitive surgical control. The immediate priority is to control bleeding surgically by cross-clamping the aorta through a laparotomy or thoracotomy. Alternatively, the aorta may be occluded endovascularly using a balloon-tipped catheter. Invasive monitors (arterial line, central line, PA catheter) may be placed as time and hemodynamics permit. **Clear communication with the surgical team** regarding the surgical and anesthetic plans is essential. If the patient's hemodynamics permit, placement of a central venous catheter is often performed while the patient is awake.
4. **Hypotensive resuscitation should be conducted** by restricting intravascular volume administration to maintain systolic blood pressure in the 70 to 100 mm Hg range. Restricting crystalloid resuscitation will also reduce the incidence of iatrogenic coagulopathy.
5. Based on the clinical circumstances, the surgical plan, and the available equipment, it may be preferable to insert an occlusive balloon-tipped catheter into the aorta above the level of the aneurysm prior to the induction of general anesthesia. Such a catheter may be inserted percutaneously using local anesthesia. It can then be used to occlude the aorta in the event of circulatory collapse following anesthetic induction.

6. Surgical technique: Endovascular versus Open

a. Open repair

1. **Induction.** In moribund patients, endotracheal intubation should be performed immediately. Hypotensive patients should be pre-oxygenated and induced expeditiously. Hemodynamics may allow for only small doses of scopolamine, etomidate, ketamine, and a benzodiazepine. **Severe hypotension on induction may occur** as a result of vasodilation, loss of sympathetic drive, and loss of peritoneal tamponade with abdominal wall relaxation. The patient should be prepped and draped prior to induction and the surgeon ready to make incision if needed.
2. Care must be taken to **avoid hypertension** during induction.
3. Once the aorta has been clamped and hemodynamic stability achieved, incremental doses of opioids and supplemental anesthetics may be given as tolerated.
4. Blood component therapy should be guided by the laboratory values. In the event of massive hemorrhage, packed red blood cells (PRBCs) and FFP should be administered in a ratio of at least 2:1.

5. **Hypothermia** (as discussed in Chapter 19) contributes to acidosis, coagulopathy, and myocardial dysfunction and should be treated (as discussed in Chapter 19).
6. **Renal protective strategies** such as aggressive hydration and the maintenance of appropriate perfusion pressure should be instituted. The administration of mannitol and fenoldopam may be considered, although there is no compelling evidence to support their use. Mortality in patients developing renal failure following a ruptured AAA is high.
- b. **Endovascular repair** can be considered as an alternative to open repair provided anatomy is suitable, the center is appropriately equipped, and the team is appropriately experienced. The procedure may be performed under local anesthesia. Although retrospective studies have shown significant survival benefit in patients treated with EVAR, prospective, randomized trials have shown no difference in mortality for patients with ruptured AAA treated with open versus endovascular repair.
7. **Complications and prognosis.** Under the best of circumstances, there is a 40% to 50% mortality rate. The incidence of MI, acute renal failure, respiratory failure, and coagulopathy is high.

V. THORACOABDOMINAL AORTIC ANEURYSM REPAIR

A. Etiology of Thoracic Aortic Disease

Causes of thoracic aortic disease include atherosclerosis, degenerative disorders of connective tissue (e.g., Marfan and Ehlers-Danlos syndromes and cystic necrosis), infection (e.g., syphilis), congenital defects (e.g., coarctation and congenital aneurysms of the sinus of Valsalva), trauma (e.g., penetrating and deceleration injuries), and inflammatory processes (e.g., Takayasu aortitis).

The most common problem affecting the thoracic aorta is **atherosclerotic aneurysm** of the descending portion, accounting for about 20% of all aortic aneurysms. When such aneurysms dissect proximally, they may involve the aortic valve or coronary ostia. Distal dissection may involve the abdominal aorta with renal or mesenteric involvement.

The next most frequent problem is **traumatic disruption** of the thoracic aorta. Adventitial false aneurysms may form distal to the left subclavian artery at the insertion of the ligamentum arteriosum, because of penetrating or deceleration injuries. These false aneurysms may dissect proximally and involve the arch and its major branches.

B. Crawford classification of thoracoabdominal aneurysms (Fig. 23.2).

1. **Type I.** Aneurysm of the descending thoracic aorta distal to the subclavian artery, ending at or above the origin of the visceral vessels.
2. **Type II.** Aneurysm from the origin of the subclavian artery to the distal abdominal aorta. This is the highest risk type in terms of paralysis, renal failure, and mortality.
3. **Type III.** Aneurysm from the mid-descending thoracic aorta to the distal abdominal aorta.
4. **Type IV.** Aneurysm from the diaphragm down to the distal aorta.

C. Associated Findings

1. **Airway deviation or compression**, particularly of the left mainstem bronchus, producing atelectasis.
2. **Tracheal displacement or disruption**, producing difficulties with endotracheal intubation and ventilation. Long-standing aneurysms may give rise to recurrent laryngeal nerve damage, resulting in vocal cord paralysis and hoarseness.

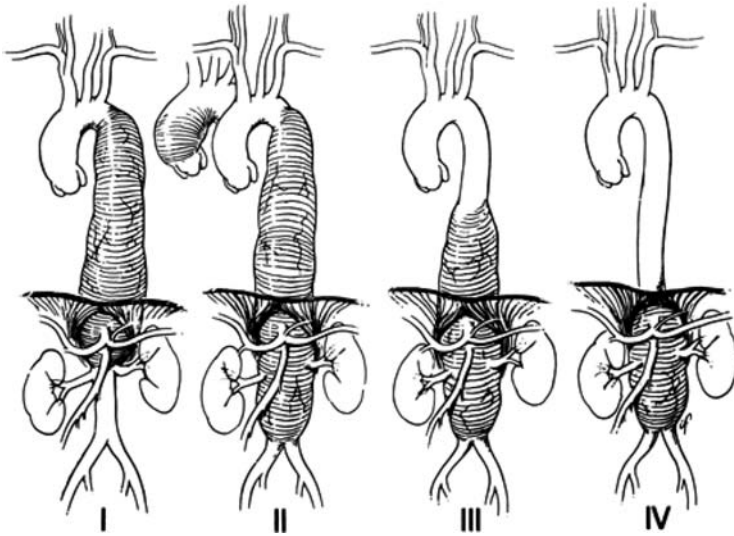


FIGURE 23.2 Crawford classification of thoracic and thoracoabdominal aortic aneurysms. (From Crawford, ES, Crawford, JL, Safi, HJ et al. Thoracoabdominal aortic aneurysms preoperative and intraoperative factors determining immediate and long-term results of operations in 605 patients. *J Vasc Surg* 1986;3:389–404.)

3. **Hemoptysis**, due to the erosion of the aneurysm into an adjacent bronchus.
 4. **Esophageal compression** with dysphagia and an increased risk of aspiration.
 5. **Distortion and compression of the central venous and arterial anatomy**, producing markedly asymmetric pulses and difficult internal jugular vein cannulation.
 6. **Hemothorax and mediastinal shift** from rupture or leakage, producing respiratory and circulatory compromise.
 7. **Reduced distal perfusion** secondary to aortic branch vessel occlusion, producing renal, mesenteric, spinal cord, or extremity ischemia.
- D. Open Thoracic Aortic Aneurysm Repair**
1. **Surgical technique.** During repair of the aneurysm, the affected aortic segment is isolated, and an interposition graft is inserted. During aortic cross-clamping, distal aortic perfusion may be provided by atrial-femoral bypass. The **inclusion technique** involves using the portion of native aorta containing the celiac, superior mesenteric, and renal ostia as a component of the bypass graft.
 2. **Spinal cord protection**
 - a. **Anatomy**
 1. **Aortic radicular arteries**, arising segmentally from the lumbar and lower thoracic regions of the aorta, contribute to the blood supply of the anterior spinal cord through anastomoses with the anterior spinal artery, which arises from the vertebral arteries at the base of the skull.

2. The most dominant of the aortic radicular arteries is the **artery of Adamkiewicz**, which usually originates between T8 and T12.
3. Cross-clamping of the thoracic aorta may compromise flow through these vessels and result in anterior spinal cord ischemia giving rise to anterior spinal artery syndrome.
- b. **Anterior spinal artery syndrome.** Manifestations include paraplegia, rectal and urinary incontinence, and loss of pain and temperature sensation. Vibratory and proprioceptive sensations are maintained. Paraplegia occurs in 2% to 4% of descending thoracic aortic aneurysm repairs and 3% to 10% of thoracoabdominal aortic aneurysm repairs. **Risk factors** include the location of proximal and distal cross-clamps; the duration of the cross-clamp; increased body temperature; the degree of collateralization of the spinal cord circulation; and previous abdominal aneurysm surgery.
- c. **Spinal Cord Protection Strategies**
 1. **CSF drainage** lowers the CSF pressure (CSFP) and promotes spinal cord perfusion. It has been shown to reduce the incidence of anterior spinal artery syndrome and is recommended for all patients undergoing thoracic aortic procedures (both open and endovascular). The CSF drainage catheter is inserted at the L4-5 level and advanced 8 to 12 cm into the subarachnoid space. CSFP is monitored throughout the procedure and CSF drained to a goal pressure of less than 10 mm Hg. Complications include spinal headache, intracranial hypotension, subdural hemorrhage, epidural or spinal hematoma, meningitis, and persistent CSF leak.
 2. **Maintaining a MAP greater than 80 mm Hg** is recommended. Spinal cord perfusion pressure (SCPP) is the difference between MAP and CSFP (or CVP if it is greater). The target SCPP is greater than 70 mm Hg. This goal can be achieved by maintaining a MAP greater than 80 mm Hg, CSFP less than 10 mm Hg, and CVP less than 10 mm Hg.
 3. **Moderate systemic hypothermia** is reasonable for spinal cord protection.
 4. **Distal aortic perfusion** using atrial–femoral bypass may be used to minimize ischemic time to the spinal cord and visceral organs.
 5. **Motor-evoked potential (MEPs) monitoring** and/or somatosensory-evoked potentials (SSEPs) monitoring can be used to detect spinal cord ischemia. In response to the degradation of MEPs or SSEPs, MAP can be raised to encourage collateral perfusion to the spinal cord. Furthermore, the surgeon may reimplant intercostal arteries into the graft.
3. **Renal protection.** Lasix, mannitol, and dopamine have not been demonstrated to reduce the incidence of renal insufficiency. Distal aortic perfusion when the distal clamp is proximal to the renal arteries reduces renal ischemic time. Perfusion of cold crystalloid directly into the renal arteries has been shown to reduce the incidence of renal insufficiency.
4. **Monitoring** includes a right radial arterial cannula as application of the aortic cross-clamp proximal to the left subclavian artery is occasionally necessary. A femoral arterial catheter is used to monitor distal aortic perfusion pressures during atrial–femoral bypass. CSF pressure transducer is necessary. TEE or PA catheter may be used to monitor cardiac function. Care must be exercised with insertion of the TEE probe as the aneurysm may compress the esophagus.

5. Anesthetic technique

- a. **Vasopressors** (phenylephrine and norepinephrine) and **vasodilators** (nitroglycerin and nitroprusside) should be available prior to induction.
- b. **General anesthesia** is induced as detailed in section IV.B.5-6. When MEPs are used for spinal cord monitoring, paralytics and volatile anesthetics must be avoided. Total intravenous anesthesia (TIVA) is required.
- c. **Lung isolation** is achieved to facilitate surgical access and protect the left lung from trauma during left thoracotomy. Lung isolation can be accomplished using a double-lumen tube (DLT) or an endobronchial blocker (see Chapter 22). A right-sided DLT is preferred in case where the aneurysm distorts the left bronchial anatomy. The advantage of using a bronchial blocker is that it avoids the need to change from a DLT to a single-lumen endotracheal tube at the conclusion of the procedure.
- d. **Positioning.** The patient is turned to the right lateral decubitus position with the pelvis at a small degree of tilt to facilitate femoral access. Bite blocks are placed between the molars bilaterally with the tongue free to prevent injury during MEP monitoring.

6. Maintenance

- a. **TIVA** with propofol and opioid is used for these cases because volatile anesthetics can interfere with spinal cord monitoring.
- b. **Fluid management** is based on the patient's hemodynamics. Fluid administration is limited to FFP, red blood cells, platelets, and colloids in an attempt to limit the development of a coagulopathy and edema brought about by excessive crystalloid administration. A red blood cell salvage system and a rapid infuser should be used.

7. Aortic cross-clamping

- a. Prior to cross-clamping, a target CSFP of 6 to 10 mm Hg is maintained.
- b. **Marked hypertension** is universal with a proximal aortic cross-clamp application and is treated with nitroglycerin and nitroprusside.
- c. **Renal ischemia is minimized** by the infusion of cold crystalloid directly into the renal arteries.

8. Use of shunts

- a. Perfusion of the mesentery can be maintained either using a shunt from a limb of the atrial-femoral bypass circuit or through a side-arm shunt (Gott shunt) on the graft.
- b. Distal aortic perfusion through atrial-femoral bypass maintains blood flow to organs distal to the distal aortic clamp. The adequacy of perfusion is monitored using a femoral arterial line. Table 23.1 summarizes the management consideration for atrial-femoral bypass.

TABLE 23.1 Management of Flow through the Atrial-to-Left-Femoral-Artery Bypass Shunt

Radial Artery Pressure	Femoral Artery Pressure	Intervention
↑	↓	Increase pump flow
↓	↑	Decrease pump flow
↓	↓	Administer volume or vasopressor
↑	↑	Administer vasodilator

9. **Aortic unclamping** produces hypotension by the mechanism discussed in section IV.B.13. Volume administration before and during unclamping, slow release of the cross-clamp, and use of vasopressors are continued until myocardial function and vascular tone have returned to baseline.
 10. **Systemic acidosis** is universal after the release of the aortic cross-clamp. The degree of acidosis depends on the ischemic time to the organs. An infusion of bicarbonate during the cross-clamping period may minimize the acidemia and preserve the function of the myocardium and vasopressor agents.
 11. At the conclusion of the procedure, the patient is kept intubated and sedated. Consideration should be given to the replacement of the DLT with a single-lumen tube. Caution is advised as there may be significant airway and oropharyngeal edema. An elevated MAP should be maintained to maximize collateral perfusion to the spinal cord.
- E. Endovascular Thoracic/Thoracoabdominal Aortic Aneurysm Repair (TEVAR)**
1. **Benefits and patient selection.** Endovascular thoracic aortic aneurysm repair leads to significantly lower morbidity than open repair. Patients with significant comorbidities who would be poor candidates for open surgical repair may particularly benefit from endovascular repair. Patients must have suitable aortic anatomy to accommodate a stent graft as well as suitable vascular access sites free from significant atherosclerotic disease to allow large-bore sheath insertion.
 2. **Spinal cord and bowel preservation.** To minimize risk of spinal cord ischemia and paraplegia, **CSF monitoring and drainage** are recommended for all thoracic aortic procedures (see section V.D.2.c. above). For thoracoabdominal aortic aneurysm repairs, preservation of mesenteric perfusion may be achieved through the construction of extra-anatomic bypass grafts prior to endograft implantation. Creation of these extra-anatomic grafts via open surgical techniques, performed in combination with endovascular aortic stent grafting, is referred to as **hybrid repair**.
 3. **Monitoring** includes an arterial line and central venous or PA catheter, based on patient indications. **TEE** is reasonable for cardiac monitoring as well as for procedural guidance.
 4. **Surgical considerations** for TEVAR are similar to those for EVAR (section IV.A.4).
 5. **Anesthetic technique** TEVAR may be performed under local, regional, or general anesthesia, but general anesthesia is typically preferred. Neuraxial anesthesia may interfere with postoperative motor examination and neurologic monitoring.
 6. Following the deployment of the stent graft, an elevated MAP should be maintained to encourage collateral perfusion to the spinal cord.
 7. **Complications of TEVAR** include **paraplegia** as well as those discussed in section IV.A.6-7 for EVAR: injury to the vascular access site and thromboemboli to the lower extremities, kidneys or mesentery. Endoleaks occur in 10% to 20% of patients. Six to seven percent of patients require reintervention. Hypotension in the postoperative period increases the risk of delayed-onset paraplegia and should be avoided.

VI. AMPUTATIONS

A. General Considerations

Amputations can be performed under general or regional anesthesia. While regional techniques suffice physiologically as a primary anesthetic, most patients strongly prefer general anesthesia due to the emotional

nature of the operation. There is no mortality difference between regional and general anesthesia. Regardless, insertion of an epidural catheter or perineural block is typically recommended for postoperative pain control. Postoperative stump pain is effectively treated with either continuous perineural infusion of bupivacaine or epidural infusion of bupivacaine combined with an opioid.

B. Phantom Limb Pain

Phantom limb pain (PLP) has been reported to occur in 60% to 70% of patients undergoing amputation. It is controversial whether the use of perioperative neuraxial anesthesia decreases the risk of development of chronic PLP. The literature suggests that good perioperative pain control, starting in the preoperative period and extending postoperatively, may be associated with a reduced incidence of PLP. Further studies are needed.

Suggested Readings

- Brott TG, Halperin JL, Abbara S, et al. 2011 ASA/ACCF/AHA/AANN/AANS/ACRA/ASNR/CNS/SAIP/SCAI/SIR/SNIA/SVM/SVS guideline on the management of patients with extracranial carotid and vertebral artery disease: executive summary. *J Am Coll Cardiol* 2011;57(8):1002–1044.
- Chaikof EL, Brewster DC, Dalman RL, et al. Society for Vascular Surgery practice guidelines for the care of patients with an abdominal aortic aneurysm: executive summary. *J Vasc Surg* 2009;50(4):880–896.
- Chery J, Semaan E, Darji S, et al. Impact of regional versus general anesthesia on the clinical outcomes of patients undergoing major lower extremity amputation. *Ann Vasc Surg* 2014;28(5):1149–1156.
- De Bruin JL, Baas AF, Buth J, et al. Long-term outcome of open or endovascular repair abdominal aortic aneurysm. *N Engl J Med* 2010;362:1881–1889.
- Erickson KM, Cole DJ. Carotid artery disease: stenting vs. endarterectomy. *Br J Anaesth* 2010;105:i34–i49.
- Fedorow CA, Moon MC, Mutch AC, et al. Lumbar cerebrospinal fluid drainage for thoracoabdominal aortic surgery: rationale and practical considerations for management. *Anesth Analg* 2010;111:46–58.
- Fleisher LA, Beckman JA, Brown KA, et al. 2009 ACCF/AHA focused update on perioperative beta blockade incorporated into the ACC/AHA 2007 guidelines on perioperative cardiovascular evaluation and care for noncardiac surgery. *J Am Coll Cardiol* 2009;54(22):e13–e118.
- Fleisher LA, Fleischmann KE, Auerbach AD, et al. 2014 ACC/AHA guideline on perioperative cardiovascular evaluation and management of patients undergoing noncardiac surgery: executive summary: a report of the American College of Cardiology/American Heart Association Task Force on Practice Guidelines. *J Am Coll Cardiol* 2014;130(24):2215–2245.
- GALA Trial Collaborative Group; Lewis SC, Warlow CP, Bodenham AR, et al. General anaesthesia versus local anaesthesia for carotid surgery (GALA): a multicentre, randomised controlled trial. *Lancet* 2008;372:2132–2142.
- Gelman S. The pathophysiology of aortic cross-clamping and unclamping. *Anesthesiology* 1995;82:1026–1060.
- Guarracino F. Cerebral monitoring during cardiovascular surgery. *Curr Opin Anaesthesiol* 2008;21(1):50–54.
- Gutsche JT, Szeto W, Cheung AT. Endovascular stenting of thoracic aortic aneurysm. *Anesthesiol Clin* 2008;26(3):481–499.
- Hiratzka LF, Bakris GL, Beckman JA, et al. 2010 ACCF/AHA/AATS/ACR/ASA/SCA/SCAI/SIR/STS/SVM guidelines for the diagnosis and management of patients with thoracic aortic disease. *Circulation* 2010;121(13):e266–e369.
- IMPROVE Trial Investigators. Endovascular or open repair strategy for ruptured abdominal aortic aneurysm: 30 day outcomes from IMPROVE randomised trial. *BMJ* 2014;348:f7661.
- Kent KC. Abdominal aortic aneurysms. *N Engl J Med* 2014;371:2101–2108.

- Lamuraglia GM, Houbballah R, Laposata M. The identification and management of heparin-induced thrombocytopenia in the vascular patient. *J Vasc Surg* 2012;55:562–570.
- McFalls EO, Ward HB, Moritz TE, et al. Coronary artery revascularization before elective major vascular surgery. *N Engl J Med* 2004;351:2795–2804.
- Moll FL, Powell JT, Fraedrich G, et al. Management of abdominal aortic aneurysms clinical practice guidelines of the European society for vascular surgery. *Eur J Vasc Endovasc Surg* 2011;41(Suppl 1):S1–S58.
- Nicolaou G, Ismail M, Cheng D. Thoracic endovascular aortic repair: update on indications and guidelines. *Anesthesiol Clin* 2013;31(2):451–478.
- Reddy U, Smith M. Anesthetic management of endovascular procedures for cerebrovascular atherosclerosis. *Curr Opin Anaesthesiol* 2012;25(4):486–492.
- Smaka TJ, Cobas M, Velazquez OC, et al. Perioperative management of endovascular abdominal aortic aneurysm repair: update 2010. *J Cardiothorac Vasc Anesth* 2011;25(1):166–176.
- United Kingdom EVAR Trial Investigators. Endovascular versus open repair of abdominal aortic aneurysm. *N Engl J Med* 2010;362:1863–1871.
- United Kingdom EVAR Trial Investigators. Endovascular repair of aortic aneurysm in patients physically ineligible for open repair. *N Engl J Med* 2010;362:1872–1880.
- Vaughn SB, LeMaire SA, Collard CD. Case scenario: Anesthetic considerations for thoracoabdominal aortic aneurysm repair. *Anesthesiology* 2011;115:1093–1102.
- Vaniyapong T, Chongruksut W, Rerkasem K. Local versus general anaesthesia for carotid endarterectomy. *Cochrane Database Syst Rev* 2013;12:CD000126.
- Wesner L, Marone LK, Dennehy KC. Anesthesia for lower extremity bypass. *Int Anesthesiol Clin* 2005;43(1):93–110.

I. CARDIOPULMONARY BYPASS (CPB)

CPB is used to temporarily perform the functions of the heart (circulation of blood) and lungs (gas exchange) during surgical procedures on the heart and great vessels. It involves a pump and oxygenator connected through an extracorporeal circuit that provides oxygenated blood flow to the systemic circulation, bypassing the heart and lungs.

A. Components of Circuit

1. Venous blood is drained from the venous cannula (inserted into the right atrium) to a **venous reservoir**. Vacuum assist can augment flow but is associated with hemolysis and the risk of air entrainment. Maintaining an adequate fluid level in the venous reservoir is critical to prevent air entrainment.
2. A **pump** (roller or centrifugal) propels the venous blood forward. Unlike roller pumps, centrifugal pumps are afterload sensitive and will decrease flow if resistance increases (e.g., with outflow obstruction). Centrifugal pumps are less traumatic to blood and do not pump air.
3. Venous blood enters a **heat exchanger** and an **oxygenator** (membrane or bubble) that adds oxygen and removes carbon dioxide by adjusting the FiO_2 and sweep rate. A volatile anesthetic (e.g., isoflurane) is added to the oxygenator gas mixture. The arterialized blood passes through an **arterial filter** before entering the systemic circulation via an aortic cannula, which is usually inserted in the ascending aorta. The femoral artery is sometimes used for aortic cannulation for emergency or redo sternotomy situations.
4. Cardioplegic solution containing high potassium is infused into the coronary circulation to induce and maintain cardiac arrest. Cardioplegia can be infused via the aortic root or coronary ostia (antegrade) or through the coronary sinus (retrograde).
5. **Left Ventricular (LV) vent** removes blood that accumulates in the LV to decrease wall tension. Venting is achieved by suctioning on the same catheter placed for antegrade cardioplegia or one specifically inserted into the LV via the right pulmonary vein across the mitral valve.
6. **Additional components** can be connected to the circuit, including a red blood cell salvage device, an ultrafiltration unit, and an in-line unit for monitoring blood gas tensions as well as hemoglobin and electrolyte concentrations.

- B. CPB pathophysiology.** Contact of blood with the CPB circuit can lead to an intense systemic inflammatory response through the activation of the complement, kallikrein and coagulation cascades. A prolonged CPB time is associated with multisystem compromise including neurologic dysfunction, ARDS, coagulopathy, hepatic insufficiency, and acute kidney injury. A number of approaches have been tested to decrease inflammation in CPB including: leukocyte depletion, hemofiltration, administration of monoclonal antibodies against inflammatory mediators, and the coating of circuitry with heparin. None have shown definitive clinical benefit in humans.

- C. CPB effects on pharmacokinetics.** CPB results in increased volume of distribution and decreased protein binding. Acid–base shifts can affect the ionized and unionized concentrations of drugs. Decreased perfusion pressures during CPB can lead to reduced hepatic and renal clearance. Hypothermia further decreases hepatic enzyme function.

II. PREOPERATIVE ASSESSMENT FOR CARDIAC SURGERY

- A. Issues pertinent to the cardiac procedure and the physiologic impact of CPB and circulatory arrest include the following:**
- 1. Prior surgery** in the chest, which technically complicates surgery
 - 2. Evidence of aortic and cerebrovascular disease**—symptomatic or documented carotid arterial disease may warrant endarterectomy beforehand. Aortic disease can affect cannulation strategies for bypass and may sometimes require concomitant repair with the cardiac operation.
 - 3. History of bleeding, anticoagulation regimens, and prothrombotic tendencies** may reveal a condition responsive to perioperative therapy.
 - 4. A history of heparin-induced thrombocytopenia (HIT)** alerts to the potential for the development of life-threatening thrombotic complications when exposed to heparin. See section on *anticoagulation for cannulation and bypass* for management of patients with HIT.
 - 5. Renal insufficiency** may indicate the need for intraoperative renal protective measures.
 - Patients with **pulmonary disease** can develop severe **post-CPB pulmonary dysfunction** and may benefit from preoperative antibiotics, bronchodilators, steroids, or chest physical therapy.
 - 7. Liver dysfunction** (e.g., cardiac cirrhosis) may indicate derangements in coagulation and platelet function and the need for transfusion of coagulation factors, platelets, and fibrinogen.
- B. Cardiac evaluation** should determine the major anatomic and physiologic characteristics of the cardiovascular system, to facilitate prediction of the likelihood of intraoperative ischemia and to determine the functional reserve of the heart.
- 1. Radionuclide imaging** may demonstrate the regions and extent of myocardium at risk for ischemia. Radionuclide ventriculography characterizes cardiac chamber volume, ejection fraction, and right-to-left stroke volume ratios.
 - 2. Viability studies** in patients with severe LV dysfunction can help distinguish areas of myocardial necrosis from hibernation; the latter may recover after revascularization. Current modalities include nuclear imaging (SPECT or PET), dobutamine stress echocardiography, and magnetic resonance imaging (MRI).
 - 3. Echocardiography** provides an assessment of ventricular function and valve function. Regional wall motion abnormalities may reflect ischemia or prior myocardial infarction.
 - 4. High-resolution (64-slice) computed tomographic scanning and functional MRI** are noninvasive modalities to assess for coronary vascular disease. These modalities may be useful in patients who are not candidates for cardiac catheterization.
 - 5. Cardiac catheterization** remains the gold standard diagnostic test for most forms of cardiac disease.
 - a. Anatomic data.** Coronary angiography reveals the location and extent of coronary stenoses, distal runoff, collateral flow, and coronary dominance. **Significant stenosis** implies a greater than 70% reduction in luminal diameter. The **dominant coronary artery** supplies the atrioventricular node and the posterior descending coronary artery.

TABLE
24.1

Normal Intracardiac Pressure and Oxygen Saturation

	Pressure (mm Hg)	O ₂ Saturation (%)
Superior vena cava	—	71
Inferior vena cava	—	77
Right atrium (mean)	1–8	75
RV (systolic/diastolic)	15–30/0–8	75
PA (systolic/diastolic)	15–30/4–12	75
PA occlusion pressure (mean)	2–12	—
Left atrium (mean)	2–12	98
LV (systolic/diastolic/end diastolic)	100–140/0–8/2–12	98
Aorta (systolic/diastolic)	100–140/60–90	98

b. Functional data. Ventriculography may demonstrate wall motion abnormalities, mitral regurgitation (MR), and intracardiac shunts. LV ejection fraction is normally greater than 0.6. Impaired ventricular performance is a useful predictor of increased surgical risk.

c. Hemodynamic data are compiled from both right and left heart catheterization. Intracardiac and pulmonary vascular pressures reflect volume status, cardiac valve function, and the presence of pulmonary vascular disease (normal values are presented in Table 24.1). An elevated LV end-diastolic pressure (LVEDP) may be due to ventricular failure and dilation, volume overload (mitral or aortic insufficiency [AI]), poor compliance from ischemia or hypertrophy, or a constrictive process. The LVEDP may rise substantially in patients with coronary artery disease (CAD) after dye injection for ventriculography or coronary angiography, despite otherwise normal hemodynamic values.

d. Left-to-right intracardiac shunts are demonstrated by an arterial oxygen saturation (SaO₂) “step up” in the right heart. Systemic and pulmonary flow and flow ratios can be calculated using the Fick equation.

e. Cardiac output is determined by thermodilution and can be used to derive the hemodynamic indices (Table 24.2).

C. Other Studies

1. Routine laboratory studies for patients undergoing a cardiac operation usually include a complete blood count, prothrombin time (PT), activated partial thromboplastin time (aPTT), platelet count, electrolytes, blood urea nitrogen, creatinine, glucose, liver function tests, and thyroid-stimulating hormone level. A heparin–Platelet Factor 4 (PF4) antibody detection assay should be considered for patients with a low or rapidly falling platelet count associated with heparin, as these patients are at risk for developing HIT.

2. Chest radiograph and a 12-lead electrocardiogram (ECG) with a rhythm strip.

3. Pulmonary function tests may be appropriate in patients with underlying lung disease.

4. Vascular studies such as carotid duplex and vein mapping.

D. Cardiac Medications

1. β -Adrenergic antagonists, calcium channel blockers, and nitrates, including intravenous nitroglycerin, are routinely continued on schedule until the patient's arrival in the operating room (OR).

TABLE
24.2 Ventricular Function Indices

Formula	Units	Normal Value
$SV = \frac{CO}{HR} \times 1,000$	mL/beat	60–90
$SI = \frac{SV}{BSA}$	mL/beat/m ²	40–60
$LVS\!WI = \frac{1.36(MAP - PCWP)}{100} \times SI$	g-m/m ² /beat	45–60
$RVS\!WI = \frac{1.36(PAP - CVP)}{100} \times SI$	g-m/m ² /beat	5–10
$SVR = \frac{(MAP - CVP)}{CO} \times 80$	dyne-s/cm ⁵	900–1,500
$PVR = \frac{(PAP - PCWP)}{CO} \times 80$	dyne-s/cm ⁵	50–150

BSA, body surface area; CO, cardiac output; CVP, mean central venous pressure; HR, heart rate; LVSWI, left ventricular stroke work index; MAP, mean systemic arterial pressure; PAP, mean pulmonary artery pressure; PCWP, pulmonary capillary wedge pressure; PVR, pulmonary vascular resistance; RVSWI, right ventricular stroke work index; SI, stroke index; SV, stroke volume; SVR, systemic vascular resistance.

- Digoxin** is commonly held for 24 hours preoperatively due to potential toxicity (especially in the presence of hypokalemia) and a long elimination half-life. When rate control is critical, however, as in mitral stenosis (MS), digoxin should be continued.
- Angiotensin-converting enzyme (ACE) inhibitors**, angiotensin receptor blockers (ARBs), and **diuretics** are usually held before surgery. Patients with significant LV dysfunction are prone to vasodilatory shock when they receive an ACE inhibitor preoperatively.
- Antiarrhythmics** are generally continued until the time of surgery.
- Aspirin** has a positive effect on graft patency and should be continued in most patients who have significant CAD. Bleeding related solely to aspirin therapy can be overcome with platelet transfusion provided the drug has been cleared from the circulation. Patients with cardiovascular pathology may be receiving multiple antiplatelet agents that may or may not be rapidly reversible (Table 24.3). Clopidogrel or prasugrel is stopped 5 to 7 days prior to surgery. If a bare-metal stent was placed within the past month or a drug-eluting stent within the last year, clopidogrel is often continued up until the time of surgery. Short-acting IIb/IIIa inhibitors should be stopped 4 hours preoperatively.
- Warfarin** is held 3 to 5 days preoperatively to allow normalization of the International Normalization Ratio (INR). Intravenous vitamin K (5 to 10 mg) or 2 to 4 units of fresh-frozen plasma (FFP) may be used emergently to correct coagulopathy. However, FFP will only transiently correct a warfarin-induced coagulopathy due to the relatively longer half-life of warfarin compared with the vitamin K-dependent cofactors (factors II, VII, IX, and X), thus putting the patient at risk for rebound coagulopathy. Oral anticoagulants such as dabigatran, rivaroxaban, and apixaban should be stopped 5 days before cardiac surgery.

Antiplatelet Agents					
Drug	Inhibits	Half-life	Duration	Reversible	Methods to Restore Function
Aspirin	Cyclooxygenase	15–20 min	7 d	No	Platelet transfusion
Abciximab (Reopro)	Glycoprotein IIb/IIIa receptor	30 min	48 h	Partially	Platelet transfusion
Eptifibatide (Integrilin)	Glycoprotein IIb/IIIa receptor	2.5 h	4–8 h	Yes	Delay surgery 2 h after stopping drug
Tirofiban (Aggrastat)	Glycoprotein IIb/IIIa receptor	1.5–3 h	4–8 h	Yes	Discontinue drug as soon as possible
Clopidogrel (Plavix)	Adenosine diphosphate receptor	8 h	7 d	No	before surgery Platelet transfusion
Prasugrel (Effient)	Adenosine diphosphate receptor	2–15 h	7 d	No	Platelet transfusion
Ticagrelor (Brilinta)	Adenosine diphosphate receptor	6–9 h	5 d	No	Platelet transfusion
Ticlopidine (Ticlid)	Adenosine diphosphate receptor	12 h to 5 d with repeated dosing	7 d	No	Platelet transfusion
Dipyridamole ^a (Persantine)	Adenosine uptake; phosphodiesterase	9–13 h	4–10 h	Yes	Platelet transfusion
Cilostazol (Pletal)	Phosphodiesterase III	11–13 h	48 h	Yes	Platelet transfusion
Herbal therapies ^b	Platelet aggregation	Variable	Variable	Variable	Limited data available

^a Dipyridamole is available in a formulation with aspirin (Aggrenox).

^b Includes garlic, ginkgo, ginseng, ginger, feverfew, fish oil, and dong quai.

Unlike warfarin, their actions cannot be reversed by the administration of vitamin K or FFP. Emergent reversal requires the administration of four-component prothrombin complex concentrates. In the case of dabigatran, hemodialysis may be used. Rivaroxaban and apixaban are too highly protein bound to be removed by dialysis.

7. **Heparin** infusions initiated for unstable angina or left main CAD are continued preoperatively. The anticoagulant effects of unfractionated heparin are acutely reversible with IV protamine administration. In contrast, the anticoagulant effects of low molecular weight heparin (LMWH) preparations are not fully reversible with protamine. LMWH has been associated with increased perioperative hemorrhage in cardiac surgical patients.

III. ANESTHETIC MANAGEMENT

A. Monitoring

1. **Standard monitors** (see Chapter 10).
 - a. Continuous **ECG** display of both leads II and V₅ with ST segment trend analysis
 - b. **Temperature monitoring** includes that of the nasopharynx (reflective of the core), the blood temperature (measured from pulmonary artery [PA] catheter), and bladder or rectal temperature, which represents the average body temperature.
2. **Central venous and PA pressures**
 - a. **Patients with normal ventricular function** can be effectively managed with either central venous pressure (CVP) monitoring with or without transesophageal echocardiography (TEE) or a PA catheter.
 - b. **Pacing PA catheters** provide pacing capability. They can be used to maintain a suitably high heart rate in patients with regurgitant valvular lesions (AI and MR) management of a variety of valvular lesions (AI and MR) and intraoperative conduction disorders. They can also be used during procedures in patients with prior sternotomies during which rapid access for epicardial pacing may not be possible. They are also used for rapid ventricular pacing or backup pacing for transcatheter aortic valve replacement (TAVR). **Mixed venous oxygen saturation** (SmvO₂) monitoring is available continuously with PA catheters specially equipped with a fiberoptic-linked oximeter. A decrease in SmvO₂ is the result of decreased cardiac output, decreased hemoglobin, increased oxygen consumption, or decreased SaO₂.
3. **Intraoperative TEE** is a useful tool to provide real-time information on cardiac anatomy and functional status, which can inform surgical and anesthetic decision making. The Society of Cardiovascular Anesthesiologists/American Society of Echocardiography TEE guidelines recommend the use of intraoperative in all open heart (e.g., valvular procedure) and thoracic aortic surgical procedures and to be considered in coronary artery bypass grafting (CABG) surgery. TEE may also be used to guide management during catheter-based intracardiac procedures (e.g., TAVR and MitraClips).
 - a. The routine examination consists of **20 standard views**. The probe is advanced into the esophagus (upper and mid-esophageal views) and then into the stomach for transgastric views.
 - b. **Application** of intraoperative TEE includes assessment of global and regional LV and RV function, chamber sizes and valvular anatomy and function. TEE is very sensitive for detecting ischemia. Upon termination of CPB, it can be used to assess ventricular function, the presence of intracardiac air, and the presence of paravalvular leaks.

- c. **Absolute contraindications** to TEE are the presence of an esophageal stricture, tracheoesophageal fistula, and a history of esophageal surgery and esophageal trauma. TEE must be used cautiously in patients with esophageal varices and altered anatomy (e.g., from gastric bypass surgery) and in those who have had radiation therapy to the neck and mediastinum. The incidence of severe complications such as esophageal perforation is on the order of 0.1%.
- d. **3-Dimensional TEE** can provide visualization of complex valvular features.
- 4. **Neurologic monitors** such as transcranial Doppler, multichannel electroencephalography, and near-infrared spectroscopy (NIRS) may improve neurologic outcome by alerting the clinician to perfusion imbalances during CPB. BIS monitor is a useful guide to titrate anesthetic agents for cardiac surgical patients being considered for early extubation.

B. Preinduction

1. **Peripheral venous access** is established. In adults, one large-bore (14- or 16-gauge) peripheral intravenous (IV) catheter is sufficient. If excessive bleeding is expected (e.g., a redo operation or a patient with a preexisting coagulopathy), a second volume line will facilitate blood product administration.
2. **Sedation and analgesia** are warranted in almost all cardiac surgical patients. Combinations of benzodiazepines and opioids provide excellent amnesia and analgesia for preinduction catheter insertion, with an acceptable degree of cardiorespiratory depression in all but the most debilitated patients. Patients with severe aortic stenosis (AS), MS, pulmonary hypertension, or left main CAD may not tolerate even small degrees of hypotension and respiratory depression; minimal or no premedication is administered until the patient arrives in the OR.
3. **Arterial cannulation** is performed with a 20-gauge catheter.
 - a. Left radial or femoral artery cannulation is used for systemic blood pressure monitoring when right axillary artery cannulation is planned by the surgeon for antegrade cerebral protection during DHCA.
 - b. Cannulation distal to a previous brachial artery cutdown site should be avoided. Pressure gradients may occur across arteriotomies, especially during and after CPB.
 - c. If blood pressure measurements are asymmetric, the arterial catheter should be placed on the side with the higher value.
 - d. Be certain to note whether the surgeon will use the radial artery for CABG surgery.
 - e. Femoral artery cannulation is a safe and reliable alternative to radial artery cannulation. Preoperative femoral artery cannulation in patients with severe CAD and poor LV function provides a site for postoperative intra-aortic balloon pump (IABP) insertion, if it becomes necessary. Brachial and axillary artery cannulations are third and fourth choices.
 - f. Intra-aortic balloon central lumen pressure can be transduced as a monitor of central arterial pressure.
4. **Central venous access** may be established before or after induction.
5. **A defibrillator and an external pacemaker generator** must be available. If the patient has a permanent pacemaker or implantable cardioverter defibrillator (ICD), a magnet should be available.
6. **Typed and cross-matched packed red blood cells** (2 to 4 units) must be present and checked.

7. **Baseline hemodynamics values**, including cardiac output, are recorded.
8. Readily available medications should include heparin, calcium chloride, lidocaine, amiodarone, inotropes, vasopressors, vasodilators, and nitroglycerin. Protamine should never be drawn up until the patient is safely separated from CPB.

IV. INDUCTION

- A. Induction is a critical time in the anesthetic management of the patient. A surgeon should be available, and the CPB pump should be ready in the event of severe hemodynamic instability during induction. A systematic and gradual induction involves minimizing the degree of cardiovascular depression while maintaining an adequate anesthetic depth.
1. **Agents** useful in the induction and maintenance of anesthesia in the cardiac surgical patient include the following:
 - a. **IV opioids** produce various degrees of vasodilation and bradycardia without significant myocardial depression. Fentanyl (50 to 100 $\mu\text{g/kg}$) or sufentanil (10 to 20 $\mu\text{g/kg}$) can be used as both the induction and primary maintenance agents. Alternatively, a smaller induction bolus (fentanyl 25 to 50 $\mu\text{g/kg}$) may be supplemented with a continuous opioid infusion. Alternatively, even lower doses (fentanyl 10 to 25 $\mu\text{g/kg}$, or sufentanil 1 to 5 $\mu\text{g/kg}$) may be used in conjunction with other central nervous system depressants as part of a balanced technique.
 - b. **Sedative hypnotics and amnestics**, including benzodiazepines, propofol, and etomidate, may be useful as coinduction agents in particular situations. Of these drugs, etomidate causes the least myocardial depression.
 - c. **Volatile inhalation anesthetics** are useful supplementary agents, especially in the treatment of hypertension.
 - d. **Muscle relaxants** with minimal cardiovascular effects are commonly chosen (e.g., vecuronium, cisatracurium, and rocuronium). Pretreatment with a "priming dose" and early relaxant administration help to counteract chest wall rigidity often encountered during opioid-based inductions. **Succinylcholine** is used for rapid sequence inductions for patients with reflux or a full stomach. The parasympatholytic actions of **pancuronium** can counteract the bradycardic effects of opioids.
2. **Specific considerations for valvular heart disease** (see also Chapter 2).
 - a. **Aortic stenosis (AS)**. Physiologic goals include the maintenance of adequate intravascular volume, sinus rhythm, contractility and systemic vascular resistance (SVR) and the avoidance of tachycardia. Patients with AS typically have a hypertrophied and noncompliant ventricle and require higher filling pressures (LVEDP of 20 to 30 mm Hg). Anesthetic agents that reduce vascular tone or myocardial contractility should be avoided. An infusion of phenylephrine can be started 1 to 2 minutes before induction to decrease the risk of developing significant hypotension associated with induction. Dysrhythmias must be treated aggressively.
 - b. **Aortic insufficiency (AI)**. Physiologic goals include the maintenance of adequate intravascular volume and adequate contractility. Bradycardia and increases in SVR must be avoided. Patients with AI are often highly dependent on endogenous sympathetic tone. Patients with coexisting CAD may decompensate with significant bradycardia due to very low diastolic perfusion pressure. A means for rapid pacing should be available.

- c. **Mitral stenosis (MS).** Hemodynamic goals mandate the maintenance of a slow rhythm, preferably sinus, and adequate intravascular volume, contractility, and SVR. Patients with severe MS and elevated pulmonary vascular resistance (PVR) are challenging to induce. Elevated PVR, often secondary to hypoventilation or positive end-expiratory pressure (PEEP), must be avoided. Atrial fibrillation with rapid ventricular response must be treated aggressively, such as with immediate cardioversion.
 - d. **Mitral regurgitation (MR).** Physiologic goals include the maintenance of adequate intravascular volume, myocardial contractility, a normal or elevated heart rate, and a reduction of systemic vascular tone. Increased SVR should be avoided. Anesthesia-induced decreases in SVR are usually well tolerated.
 - e. **In patients with mixed valvular lesions,** the most hemodynamically significant lesion will dominate the management goals. The addition of CAD to mixed valvular lesions makes planning even more complex (e.g., AS with AI and CAD). In all situations, determine the three most likely problems that could occur during induction and plan the management for each.
3. **Specific considerations for emergent inductions**
- a. **Pulmonary embolus.** Induction of general anesthesia and the institution of positive-pressure ventilation can precipitate cardiovascular collapse. It is prudent to prepare and drape the unstable patient prior to induction. In patients with compromised RV function, cannulation of the femoral vessels under local anesthesia should be performed prior to induction to allow for the emergent institution of CPB if needed.
 - b. **Pericardial tamponade.** Similar concerns are present for patients with pericardial tamponade. Adequate volume administration is essential. Starting an inotropic agent and a vasopressor before induction may be helpful. A rapid sternotomy may be required if hemodynamic collapse occurs with anesthesia induction. If possible, the pericardial effusion should be drained under local anesthesia prior to induction.
 - c. **Aortic dissection.** Hypertension can precipitate aortic rupture. Packed red blood cells must be available in the OR before induction. Proximal extension of the dissection into the coronary arteries can occur leading to myocardial ischemia or tamponade.
 - d. **Ventricular septal defect (VSD) and papillary muscle rupture after myocardial infarction.** Patients may present with extreme hypotension. Rapid initiation of CPB is essential. Preinduction initiation of intra-aortic balloon counterpulsation therapy is indicated in many of these patients.
- B. **The prebypass period** is characterized by variable levels of stimulation during the preparation for CPB initiation. Stimulating periods include sternotomy and sternal retraction, pericardiotomy, and aortic cannulation.
- 1. **Baseline** P_{aO_2} , P_{aCO_2} , pH, hematocrit (Hct), and activated clotting time (ACT) should be obtained.
 - 2. Consider **autologous blood procurement** in otherwise healthy patients with a starting Hct of 40% or greater. 1 to 2 units of whole blood may be drained passively into sterile blood bags and later transfused into the patient following conclusion of CPB and heparin reversal.
 - 3. **The lungs are deflated** during sternotomy. Physical alterations of the chest wall can produce ECG changes (especially T-wave changes), which should be noted to avoid confusion with ischemia.

4. **Left internal mammary artery dissection** may cause ipsilateral hemothorax and negatively affect pulmonary mechanics in patients with reduced pulmonary reserve.
5. **Anticoagulation for cannulation and bypass**
 - a. **Prior to the induction of anesthesia**, heparin at a dose of 350 units/kg should be drawn up and kept readily available in case the emergent initiation of CPB is necessary. The dose may be increased to 500 units/kg if the patient has been receiving heparin infusion or is being treated with IABP counterpulsation. The heparin should be administered through a centrally placed catheter.
 - b. **Vasodilation** often follows the heparin bolus and should be anticipated.
 - c. The **ACT** is used to monitor the degree of anticoagulation. It should be measured approximately 5 minutes after heparin administration. Baseline values are 80 to 150 seconds. Heparin treatment sufficient to prevent microthrombus formation during CPB correlates with an ACT of more than 400 seconds (at higher than 35°C). An ACT value of greater than 450 seconds is preferred, given the variability that exists in this point-of-care test. Patients on continuous IV heparin preoperatively may become relatively "heparin resistant." If an ACT longer than 400 seconds is not achieved with the standard heparin dose, an additional 200 to 300 units/kg is administered. If this fails, antithrombin concentrate (500 to 1,000 units) or 2 to 4 units of FFP may be necessary to correct a probable antithrombin III deficiency.
 - d. **Patients with a diagnosis of HIT type 2 (also known as HIT with thrombotic syndrome [HITS])** require alternative anticoagulation management during CPB. The classification of HIT is determined by immune involvement. HIT type 1 is a nonimmunologic reaction of heparin with platelets that causes a mild thrombocytopenia. HIT type 2 is an immune-mediated phenomenon that activates platelets, resulting in platelet aggregation. Biochemical mediators from activated platelets can induce the generation of thrombin, leading to diffuse arterial and venous clotting. The diagnosis requires serologic and clinical evidence. Patients with a positive functional assay (serotonin release assay or platelet aggregation study), greater than 50% reduction in platelets (irrespective of starting platelet count), drop in platelet count less than 150k, or history of a thrombotic event associated with heparin use are more likely to have an adverse outcome when re-expose to heparin. Patients with a positive ELISA test in the absence of a positive functional assay or clinical symptoms have a lower likelihood of having an adverse reaction to heparin.
 - e. For patients with HIT type 2 or HITS, **alternatives to standard heparin treatment** exist (Table 24.4); each has significant limitations that should be discussed with the surgeon and a hematologist before use.
 1. All forms of heparin are removed preoperatively. Saline is used to flush pressure transducers, and citrated saline is used to wash salvaged blood during the centrifugation process.
 2. A heparin-free PA catheter is used.
 3. Alternative anticoagulant regimens may be used. These include bivalirudin, or unfractionated heparin in combination with an antiplatelet agent (see Table 24.4).

TABLE
24.4

Alternative CPB Anticoagulation in Patients with HIT

Drug	Mechanism	Half-life	Lab Monitor	Reversible?
Bivalirudin (Angiomax)	Direct thrombin inhibitor	25 min (normal renal function)	ACT	No
Argatroban	Direct thrombin inhibitor	40–50 min (prolonged in hepatic insufficiency)	ACT	No
Tirofiban (Aggrastat) + unfractionated heparin ^a	Glycoprotein IIb/IIIa receptor inhibitor prevents platelet aggregation in HIT	1.5–3 h	ACT (platelets and D-dimer if heparin-induced thrombosis is suspected)	No

^a Additional training is required to safely use this anticoagulation technique for patients requiring CPB.

4. If unfractionated heparin is used, then a bypass dose of porcine heparin is administered before aortic cannulation (to minimize the likelihood of a repeat dose of heparin).
5. Aspirin is administered early in the postoperative period, and initiation of systemic anticoagulation with a direct thrombin inhibitor and warfarin may be indicated to prevent both early and late postoperative thromboembolic complications.
6. **Antifibrinolytic drugs** such as ϵ -aminocaproic acid (Amicar) are usually given as a bolus 10 g followed by an infusion 2 g/h during all on-pump procedures, with the intention of inhibiting excessive fibrinolysis (i.e., plasmin activity and D-dimer formation) and possibly preserving platelet function.
7. **Aortic cannulation** is conducted in the ascending aorta just proximal to the innominate artery. **Epiaortic scanning** is used to sonographically direct the cannulation site in patients with known atherosclerotic disease. Maintaining a systolic blood pressure near 100 mm Hg during aortic cannulation decreases the risk of dissection.
8. Some surgeons will perform the **proximal saphenous vein graft anastomoses** before initiating CPB. An improperly placed side-biting clamp may occlude more than 50% of the aortic lumen and markedly increase afterload, causing myocardial decompensation. The early signs are hypotension, elevation of PA pressures and ST-segment changes.
9. One or two **venous return cannulas** are inserted via the right atrium. A single cavoatrial catheter is placed in the right atrial appendage, with the tip in the IVC and fenestrations in the mid-atrium. For open-heart procedures (i.e., mitral and tricuspid valve surgeries), bicaval cannulation, consisting of separate superior vena cava (SVC) and IVC cannulas is conducted.
10. **Retrograde autologous priming (RAP)** can be used to reduce the hemodilution from the crystalloid priming solutions (typically 1,600 mL) of the bypass circuit. During RAP, the patient's blood pushes the crystalloid prime out of the circuit, often necessitating use of α -agonist agents to maintain vascular tone and prevent hypotension. RAP is most beneficial in patients with small blood volumes and low hemoglobin concentrations.

C. Cardiopulmonary Bypass

1. Initiation of CPB. After an ACT greater than or equal to 450 seconds is obtained, the clamp on the venous line is released and CPB is initiated. After the perfusionist is convinced that the venous return is adequate, he or she will turn on the pump and progressively increase the rate to a flow of 2.0 to 2.4 L/min/m² or roughly 50 mL/kg/min for adults. Depending on the vascular resistance, intravascular volume, and blood viscosity, a mean arterial pressure (MAP) of 40 to 120 mm Hg may be achieved by such flow. Observe the bright red blood entering the aorta during this initiation to confirm that the membrane oxygenator is working properly. Once adequate flows and venous drainage are established, volatile anesthetics from the anesthesia machine, IV fluids, and pulmonary ventilation are discontinued. Muscle relaxants are readministered to prevent shivering. Anesthesia is maintained using IV agents or inhalational agents administered through a vaporizer in the fresh gas line of the circuit. It is advisable to withdraw the PA catheter 1 to 5 cm to prevent the catheter tip from migrating into a wedge position during CPB. If two venous return lines are used and tourniquets are applied to achieve complete CPB, the CVP measured above the tourniquet is the SVC pressure. High CVP may indicate obstruction of SVC cannula. After fibrillation or arrest, mean PA pressures are displayed. A vent cannula may be inserted into the left ventricle to prevent LV distention.

2. Maintenance of CPB

a. Myocardial protection during the cross-clamp period is achieved primarily by reducing myocardial oxygen consumption through hypothermia, hyperkalemic arrest, or both.

1. Intermittent cold cardioplegia is a commonly used technique. Cold (4°C to 6°C) hyperkalemic solution with or without blood is delivered to the coronary circulation approximately every 20 minutes (or sooner if cardiac electrical activity returns). Systemic cooling of the patient and topical cooling of the heart augment myocardial protection.

2. The warm cardioplegia technique delivers a warm (32°C to 37°C) hyperkalemic solution mixed with blood at approximately a 1:5 ratio. The solution is delivered continuously during the cross-clamp period with a few interruptions to allow visualization of the anastomotic sites. Mild systemic cooling to 32°C to 34°C is frequently performed. Serum glucose levels will increase dramatically and are treated with IV insulin.

b. Hypothermia (20°C to 34°C) is commonly used during CPB. Oxygen consumption and blood flow requirements are reduced while blood viscosity is increased, thus counteracting prime-induced hypoviscosity. Adverse effects of hypothermia include impaired autoregulatory, enzymatic, and cellular membrane function; decreased oxygen delivery (leftward shift of the hemoglobin oxygen dissociation curve); and potentiation of coagulopathy. Metabolic requirements decrease about 7% for every degree Celsius reduction in body temperature below 37°C.

c. Hemodynamic monitoring during CPB is the shared responsibility of the perfusionist, anesthesiologist, and surgeon.

1. Hypotension during the initiation of CPB is usually due to hemodilution and hypoviscosity. Other important causes include inadequate pump flow, vasodilation, acute aortic dissection, and incorrect placement of the aortic cannula (e.g., directing flow

toward the innominate artery not supplying the cannulated radial artery). The PA pressure and LV vent flow rate should be inspected to ensure that aortic incompetence has not compromised forward pump flow. A phenylephrine infusion may be required to treat transient hypotension. During the course of CPB, a pressure gradient (as high as 40 mm Hg) may develop between the radial artery and the aorta. The lower radial artery pressure could lead to unnecessary administration of vasopressors if the discrepancy is not recognized. In the presence of carotid stenosis, MAP should be maintained at a higher level than usual (e.g., 80 to 90 mm Hg), and hypocarbia should be avoided.

2. **Hypertension** (MAP > 90 mm Hg) may be due to excessive flow rates or increased vascular resistance, which may be treated with vasodilators or anesthetics.
3. **Elevated PA pressures** indicate left heart distention, which may be due to inadequate venting, AI, or inadequate isolation of venous return. Severe distention may result in myocardial injury.
- d. **Acid-base Management.** In the setting of hypothermia, gas solubility increases and the dissociation constant for water decreases, resulting in a lower $[H^+]$ and $[OH^-]$ and a higher pH. While total CO_2 content remains constant, the partial pressure of CO_2 decreases.
 1. **pH-stat** corrects the patient's blood gas for temperature and strives to maintain a neutral pH of 7.4 and CO_2 near 40 mmHg by adding CO_2 to the CPB circuit. This strategy results in cerebral vasodilatation and more uniform cerebral cooling, however at an increased risk of cerebral microembolism.
 2. **Alpha-stat** involves the use of uncorrected gas tensions during hypothermia. No CO_2 is added to the oxygenator. The basis of the approach is that the total CO_2 content of blood and the intracellular electroneutrality (as primarily governed by the imidazole rings of histidine residues) are unchanged during hypothermia. Cerebral blood flow is autoregulated and coupled to cerebral oxygen demand.
 3. Most studies fail to reveal any significant difference in patient outcomes between the two methods. Generally, α -stat is used in adults and pH-stat in children when circulatory arrest is used.
- e. **Metabolic acidosis and oliguria** suggest inadequate systemic perfusion. Additional volume (blood or crystalloid depending on Hct) may be required to achieve increased flow. Brisk urine output should be established within the first 10 minutes of CPB.
 1. **Oliguria** (<1 mL/kg/h) should be treated with a trial of increased perfusion pressure and/or flow, mannitol (0.25 to 0.5 g/kg), or dopamine (1 to 5 μ g/kg/min). Patients on chronic furosemide therapy may require their usual dose during CPB to sustain diuresis. Fenoldopam, a selective dopamine agonist, will promote natriuresis and may provide renoprotective effects during CPB.
 2. **Hemolysis** during CPB is usually due to mechanical trauma to red blood cells from the bypass machine and the pump suction. Released pigments may cause acute renal failure postoperatively. For hemoglobinuria, diuresis is maintained using IV fluids with mannitol or furosemide. In severe cases, the urine is alkalinized by administering sodium bicarbonate at 0.5 to 1.0 mEq/kg.
- f. **Additional heparin** bolus and/or infusion may be needed for prolonged CPB. The duration of heparin anticoagulation may be

shorter in patients on chronic heparin therapy or during cases in which systemic hypothermia is not used. The ACT does not correlate well with plasma heparin levels when the patient is on CPB, but many centers routinely monitor the ACT during hypothermic (25°C to 34°C) CPB.

- g. **Blood glucose** should be controlled between 80 and 200 mg/dL during bypass. Hyperglycemia may be associated with an increased risk of neurologic injury. Diabetic patients following a warm cardioplegia technique will typically require an insulin infusion.
 - h. Table 24.5 lists some of the **problems** that can be encountered during CPB. Anesthesiologists should be alerted to these issues as they may significantly affect subsequent separation from CPB.
- D. Discontinuing CPB** implies transferring cardiopulmonary function from the bypass system back to the patient. In preparation for this transition, the anesthesiologist must examine and optimize the patient's metabolic, anesthetic, and cardiorespiratory conditions.
1. **Preparation for discontinuing CPB begins during rewarming.** The arterial blood is warmed. The core (nasopharyngeal) temperature should reach but not exceed 38°C before discontinuation from CPB.
 - a. **Laboratory data** to be acquired during rewarming include P_aO_2 , P_aCO_2 , pH, potassium, calcium, glucose, Hgb, and ACT. Clinical decisions concerning pH are usually made according to the values measured at 37°C (alpha-stat management).
 - b. **Adequate anticoagulation** during rewarming and separation from CPB is ensured with additional heparin if necessary.
 - c. **Metabolic acidosis** should be treated with sodium bicarbonate, and the perfusionist may elect to increase the sweep rate to remove CO_2 . **Hyperkalemia**, commonly seen following the use of cardioplegia, frequently corrects spontaneously by redistribution and diuresis. If not, the administration of IV insulin/glucose or sodium bicarbonate will lower serum potassium.
 - d. Usually, a **Hct** of over 20% should be achieved before separation, either by transfusion or by hemoconcentration, as indicated by the CPB reservoir volume.
 - e. **FFP** should be thawed before separation from bypass (requiring 30 to 45 minutes) if the patient is at risk for postoperative bleeding. **Platelets** should also be readily available for these patients.

TABLE
24.5 Potential Problems during CPB

Problem	Possible Cause
Inadequate systemic pressures	Vasoplegia, inadequate flow, hemodilution
Poor gas exchange	Oxygenator failure, hypoxic gas mixture, inadequate coagulation, poor perfusion
High arterial line pressure	Mechanical obstruction, malpositioned aortic cannula, aortic dissection, inadequate anticoagulation, or cold agglutination
Distension of heart	Poor venous drainage, inadequate venting, increased regurgitation, or shunting
High coronary sinus pressure (during retrograde cardioplegia)	Small coronary sinus, malpositioning of catheter

2. **Anesthetic considerations** during rewarming include maintenance of adequate neuromuscular blockade, analgesia, and amnesia. Supplementary relaxants, opioids, and benzodiazepines may be given. If MAP is elevated, nitroglycerin or sodium nitroprusside may be used for blood pressure control as well as to facilitate rewarming.

3. **Separation from CPB**

- a. After procedures in which the heart has been opened (e.g., valve replacements), **de-airing maneuvers** under TEE guidance are used to prevent air embolism to the cerebral or coronary circulations. Positive-pressure ventilation accompanied by clamping of the venous return lines will move air forward from the pulmonary veins. Air in the ventricular trabeculae can be liberated by shifting the OR table from side to side and lifting the apex of the heart; it can then be evacuated by needle aspiration of the apex. Direct aspiration of air bubbles visible within coronary artery vein grafts may help prevent myocardial ischemia.
- b. **Aortic cross-clamp removal** reestablishes coronary perfusion. A nitroglycerin infusion may be started in CABG patients to reduce coronary vasospasm and reperfusion injury.
- c. **Defibrillation** may be spontaneous; ventricular fibrillation is treated with internal paddles delivering 5 to 10 J of energy with a biphasic waveform defibrillator. Failure may indicate inadequate warming, graft problems, a metabolic disturbance, or inadequate myocardial protection. Additional lidocaine, magnesium (1 g IV slowly), or amiodarone (150-mg IV bolus followed by infusion at 1 mg/min for 6 hours, then 0.5 mg/min) may be required.
- d. **Rhythm is assessed.** With bradycardia, atrial pacing is established through epicardial wires. Ventricular pacing is added if there are atrioventricular conduction abnormalities. Hypothermia as well as hypocalcemia, hyperkalemia, and hypermagnesemia caused by cardioplegia solutions may contribute to a high incidence of reversible heart block immediately after CPB. Atrial tachycardia may also indicate inadequate anesthesia and may be treated with fentanyl. Other atrial dysrhythmias may be treated with overdrive pacing, cardioversion, and antiarrhythmics (e.g., esmolol, propranolol, amiodarone, verapamil, or rarely digoxin).
- e. **The ECG should be inspected** for evidence of ischemia possibly related to intracoronary air or inadequate revascularization.
- f. During separation from CPB, volume administration may be guided by monitoring LV filling using TEE, mean PA pressure, PA occlusion pressure, or a surgically placed LA line. RV filling is indicated by the CVP or direct RV visualization. The determination of target post-bypass filling pressures should consider the patient's preoperative pressures, the degree of left ventricular hypertrophy (LVH), the adequacy of the myocardial revascularization, and the anticipated physiologic effects of corrective valvular surgery. A normotensive patient without LVH will most likely need an LA pressure of 10 mm Hg or a mean PA pressure of 20 mm Hg. A patient with severe LVH and inadequate revascularization may need an LA pressure of 20 mm Hg or a mean PA pressure of 30 mm Hg. TEE is particularly helpful in assessing LV filling.
- g. **Comparison** is made between central (aortic) and peripheral (radial) arterial pressures to ensure that no significant pressure gradient exists. If a significant gradient exists, a femoral arterial line can be placed.

- h. **Compliance and resistance of the lungs** are tested with a few trial breaths. Ventilation should be reestablished when LV ejection begins even if the patient is still on CPB. To facilitate reexpansion of the lungs, the stomach is suctioned, and, if previously opened, the pleural cavities are drained. If the lungs are difficult to ventilate, tracheobronchial suctioning and the administration of bronchodilators may be indicated.
 - i. **Visual inspection of the heart** confirms atrioventricular synchrony. Contractility is assessed both by gross appearance and by systolic performance, as estimated by peak systolic and pulse pressure (taking into account pump flow and LA and PA pressures). If poor myocardial performance is demonstrated or anticipated (e.g., impaired preoperative function or intraoperative ischemia), initiation of inotropic support before separation from CPB may be indicated. Pump flow rate is checked and compared with the patient's preoperative cardiac output. Significantly higher flows indicate the need to increase vascular tone (using agents such as norepinephrine and phenylephrine).
 - j. **Ionized Ca^{2+}** may be corrected slowly 15 minutes after cross-clamp removal. Rapid Ca^{2+} administration, especially in the presence of myocardial ischemia, is associated with Ca^{2+} -induced myocardial injury. Calcium will increase both contractility and SVR.
- E. At the time of actual separation from CPB**, venous lines to the pump are slowly clamped, allowing the heart to gradually fill and eject with each contraction. Prolonged partial venous line occlusion allows for "**partial bypass**," during which time cardiopulmonary function is shared and hemodynamics are assessed. After complete venous line occlusion, once adequate filling pressures are achieved, perfusion through the aortic cannula is stopped, and the heart alone provides systemic perfusion.
1. **Pressure maintenance.** Transfusion from the CPB reservoir maintains the LA pressure or mean PA pressure at an optimal level. Care is taken not to overdistend the heart. Should overdistention occur, the surgeon may "empty" the heart by transiently unclamping a venous line. Alternatively, the patient may be temporarily placed in reverse Trendelenburg position to decrease venous return to the overdistended heart.
 2. **At termination of bypass, it is important to assess** the ECG, systemic blood pressure, left-sided filling pressure, right-sided filling pressure, and the cardiac output. These values are compared with target values for the patient. If the patient is unstable, correct any pacing problems, have the surgeon assess the patency of the grafts, and use TEE to assess the valve replacement or repair. Assuming there is no surgical cause for hemodynamic instability, the unstable patient will usually fall into one of the categories listed in Table 24.6. **If a return to CPB is necessary**, adequate anticoagulation must be ensured. **A full dose** of heparin is indicated if protamine has been administered.
- F. Postbypass Period**
1. **Hemodynamic stability** is the primary goal. CPB gives rise to myocardial functional impairment and a systemic inflammatory response. Maintain adequate volume status, perfusion pressure, and appropriate rate and rhythm. Continuously monitor and reassess the surgical field.
 2. **Hemostasis.** Once cardiovascular stability has been achieved and the surgeon is confident that the bleeding is controlled, **protamine** administration begins. Initially, 25 to 50 mg is given over 2 to 3 minutes, and the hemodynamic response is observed. Protamine often causes systemic

TABLE
246
Hemodynamic Changes and Management After CPB

Clinical Scenarios	SBP	CO	PAP	CVP	Management Options
Hypovolemia	↓	↓	↓	↓	Volume administration
LV failure	↓	↓	↑	↑	Inotropes, IABP, CPB, and LVAD
RV failure	↓	↓	↓	↑	Inotropes, increase MAP, decrease PVR, CPB, and RVAD
Biventricular failure	↓	↓	↑	↑	Treatment for LV and RV failure
Low SVR	↓	↑	Normal	Normal	Vasopressors; decrease anesthetic
High SVR	↑	↓	Normal	Normal	Vasodilators; deepen anesthetic
pHTN	↓	↓	↑	↑	Inotropes with pulmonary dilating properties (e.g., milrinone), nitrous oxide; reinstitute CPB

MAP, mean arterial pressure; CO, cardiac output; PA, pulmonary artery pressure; CVP, central venous pressure; LV, left ventricle; RV, right ventricle; IABP, intra-aortic balloon pump; CPB, cardiopulmonary bypass; LVAD, left ventricular assist device; RVAD, right ventricular assist device; PVR, pulmonary vascular resistance; pHTN, pulmonary hypertension.

vasodilation (type I reaction) that can be avoided by slow administration over 10 to 15 minutes and reversed with α -agonist support. Rarely, an anaphylactic or anaphylactoid reaction (type II reaction) resulting in hypotension, bronchospasm and pulmonary edema is encountered. Type II reactions are more likely observed in diabetic patients taking subcutaneous injections of protamine-containing insulin preparations (i.e., NPH) and men who have had a vasectomy. Finally, catastrophic pulmonary hypertension (type III reaction) can occur, manifested by elevated PA pressures, right ventricular dilatation, systemic hypotension, and myocardial depression. Upon severe reaction, protamine is immediately discontinued, appropriate resuscitative measures are used, and, if necessary, the patient is retreated with heparin (with a full loading dose), and CPB is reinitiated. If forward flow is compromised, ask the surgeon to inject the heparin into the right atrium.

- It is advisable to monitor PA pressures while administering protamine (even if LA pressure is available).
- In general, 1 to 1.3 mg of protamine is administered for each 100 units of heparin administered throughout the procedure. Alternatively, the protamine dose can be calculated based on the patient's whole blood heparin level. Automated heparin-protamine titration assays are available to calculate the protamine dose for complete heparin neutralization; this method is associated with reduced protamine requirement.
- Four to five minutes following protamine administration, the ACT is compared with baseline. Additional protamine is given to return the ACT toward control. The aPTT also serves as a sensitive indicator of residual circulating heparin. Thromboelastography may be used to provide information about coagulation factor activity, platelet function, and degree of fibrinolysis during and after CPB.
- During transfusion of blood obtained from the hemoconcentrator, additional protamine (25 to 50 mg) is given to reverse the heparin.

Blood obtained from red blood cell salvage devices is devoid of heparin.

- e. Antifibrinolytic agents, such as aminocaproic acid and tranexamic acid, are used to decrease postoperative bleeding and transfusion requirements.
- f. Achievement of normothermia reduces the severity of post-CPB coagulopathy.
3. **Pulmonary dysfunction may follow CPB.** Aggressive treatment of bronchospasm before sternal closure is imperative.
4. **Pulmonary hypertension** may arise during the post-CPB period. See Table 24.6 for approaches to management.
5. **Sternal closure** may precipitate acute cardiovascular decompensation. **Cardiac tamponade** may develop from compression of the heart and great vessels in the mediastinum.
 - a. Volatile anesthetics and other negative inotropes are reduced in anticipation of sternal closure. Intravascular volume should be optimized.
 - b. Immediately after sternal closure, the filling pressures and cardiac output are compared with preclosure values, and appropriate adjustments in volume or drug infusions are made.
 - c. Mediastinal and pleural tubes are placed on suction to prevent tamponade and quantify blood loss.
 - d. The LA waveform and the ability of pacemakers to capture are rechecked to verify that displacement has not occurred.
 - e. If the patient is hemodynamically unstable or ventilation is inadequate, the sternum should be reopened. The patient may require transfer to the intensive care unit (ICU) with the sternum open.
- G. **Transfer to the ICU**
 1. Patients should always be hemodynamically stable before transport. Transport involves standard transport monitoring, defibrillator, and a transport ventilator if the patient remains intubated.
 2. Upon arrival to the ICU, mediastinal and pleural drainage tubes are attached to suction. An anteroposterior chest radiograph and a 12-lead ECG are obtained, and blood samples are sent for ABG, electrolytes, Hct, platelet count, PT, and aPTT. Before leaving the ICU, the anesthesiologist should review the ECG and ABG and check the chest radiograph for the presence of abnormal findings (e.g., atelectasis, pneumothorax, malpositioned tubes and catheters, widened mediastinum, or pleural effusion).

V. POSTOPERATIVE CARE

- A. **Warming.** Most cardiac surgical patients will be hypothermic upon arrival to the ICU, and their initial course is notable for warming and vasodilation. Pressor and volume requirements should be anticipated. Adequate sedation, by either periodic bolus or continuous infusion, will prevent early waking and shivering during this period.
- B. **Complications**
 1. **Dysrhythmias and myocardial ischemia** are common in the immediate postoperative period. Diagnosis and management are discussed in Chapter 36.
 2. **Unexplained profound hypotension**, unresponsive to volume and pharmacologic resuscitation, is an indication for immediate reopening of the chest in the ICU. The OR should be notified and blood products requisitioned.

3. **Cardiac tamponade** may occur insidiously. Most often, an accumulation of blood in the mediastinum and inadequate chest tube drainage secondary to clot are responsible. Placing mediastinal tubes on suction as soon as the sternum is closed will help to prevent the development of tamponade. Reopening the sternum may be lifesaving. The diagnosis is considered with hypotension or low-output state. Equilibration of mean CVP, PA, and PA occlusion pressures is rarely present because the pericardium is open.

VI. PEDIATRIC CARDIAC ANESTHESIA

A. Transition from Fetal to Adult Circulation. The transition from fetal to adult circulation is a transformation from a parallel to a series circulation. In utero, there is right-to-left shunting of blood across the ductus arteriosus. After birth, as the lungs are expanded and alveolar oxygen tension rises, the PVR decreases. Simultaneously, the SVR increases in association with the loss of the low-resistance placental circulation. The net effect of the PVR falling beneath the SVR is a reversal of ductus flow. The ductus arteriosus will contract and functionally close in the first 10 to 15 hours of life. This is caused by a loss of placental-produced prostaglandins and an increase in neonatal blood oxygen tension. Accompanying the decrease in PVR is an increase in pulmonary blood flow, an improvement in RV compliance, and a decrease in right-sided pressures relative to the left. This drop in right atrial pressure results in the closure of the foramen ovale. With the closure of the ductus arteriosus and the foramen ovale, the circulation assumes an adult configuration. These changes in the neonatal period are tentative; however, and reversion to a fetal circulation can occur during periods of abnormal physiologic stress. Persistence of elements of fetal circulation is common in many cases of congenital heart disease (CHD) and can occasionally be lifesaving.

B. Differences between Neonatal and Adult Cardiac Physiology

1. In infants, there is **parasympathetic nervous system dominance** that reflects the relative immaturity of the sympathetic nervous system. Infant hearts are more responsive to circulating catecholamines than to sympathetic nervous stimulation.
2. Neonatal hearts have more inelastic membrane mass than elastic contractile mass. Consequently, infant hearts have less myocardial reserve, a greater sensitivity to myocardial depressants, and a greater sensitivity to volume overload. The relatively noncompliant ventricles make stroke volume less responsive to increases in preload or demand. As such, **increases in cardiac output largely depend on increases in heart rate.**
3. The RV and LV are equal in muscle mass at birth. A left-to-right muscle mass ratio of 2:1 is not achieved until the age of 4 to 5 months.

C. Congenital Heart Disease (CHD). The clinical presentation depends on both the anatomy and the physiologic changes secondary to intracardiac shunts and obstructive lesions. In general, there are three categories of lesions: shunt, mixing lesion, and flow obstruction.

1. **Shunt.** A shunt is an abnormal communication between the systemic and pulmonary circulations. Examples are atrial septal defect (ASD), VSD, and patent ductus arteriosus (PDA). The direction of blood flow is dependent on the pressures on either side of the shunt and the size of the shunt orifice.
 - a. **Left-to-right shunt**—occurs when the PVR is lower than the SVR, resulting in increased pulmonary blood flow. This can cause

pulmonary circulation congestion, volume overload, and increased work for the LV. Prolonged exposure to increased pulmonary blood flow results in progressive elevations in PVR, eventually leading to pulmonary vascular obstructive disease.

- b. **Right-to-left shunt**—occurs when PVR or RV outflow tract resistance exceeds SVR, thereby reducing pulmonary blood flow and manifesting as hypoxemia and cyanosis. Pure right-to-left shunting due to high PVR is seen in Eisenmenger syndrome and persistent pulmonary hypertension of the newborn with atrial and ductal shunting.
- c. **Simple versus Complex shunts:** Simple shunts are not associated with anatomic obstruction to ventricular outflow. Pulmonary and systemic blood flow is determined by both the size of the shunt and the relative PVR/SVR ratio. Most left-to-right shunts are simple shunts. In contrast, most right-to-left shunts are **complex shunts**. These shunts are accompanied by an anatomic obstruction to blood flow. Shunt flow depends less on the PVR/SVR ratio and more on the resistance of the obstructive lesion. For example, tetralogy of Fallot is a complex right-to-left shunt since shunting occurs through the VSD because of pulmonary outflow obstruction while PVR remains low.
- d. **Shunt flow calculation.** Measuring the Q_p/Q_s (ratio of pulmonary to systemic blood flow) quantifies the direction and degree of shunting.

$$Q_p / Q_s = (SaO_2 - SmvO_2) / (SpvO_2 - SpaO_2)$$

$$Q_p / Q_s > 1 \text{ indicates left-to-right shunt}$$

$$(1-1.5 \text{ small shunt}; 1.5-2.0 \text{ moderate shunt}; > 2.0 \text{ large shunt}).$$

$$Q_p / Q_s < 1 \text{ indicates right-to-left shunt}$$

where Q_p is pulmonary blood flow, $SmvO_2$ is mixed venous oxygen saturation, Q_s is systemic blood flow, $SpvO_2$ is pulmonary venous oxygen saturation, SaO_2 is systemic arterial oxygen saturation, and $SpaO_2$ is PA oxygen saturation. When calculating the ratio, oxygen saturation can be conveniently used instead of oxygen content. To simplify the calculation, if systemic blood is fully saturated, one can approximate that there is no significant right-to-left shunting and that pulmonary venous oxygen saturation is equal to systemic oxygen saturation ($SpvO_2 = SaO_2$).

2. **Mixing lesions.** In these lesions, there is large mixing between the pulmonary and systemic circulation as if they act as a common chamber. The Q_p/Q_s is independent of the shunt size and entirely dependent on relative vascular resistance or outflow obstruction. In cases of LV outflow obstruction, the pulmonary blood flow may be excessive enough to impair systemic perfusion. Examples of mixing lesions include truncus arteriosus, single ventricle, and total anomalous pulmonary venous return.
3. **Obstructive lesions.** These include AS, pulmonic stenosis, coarctation of the aorta, and asymmetrical septal hypertrophy. These lesions have ductal-dependent circulations. For example, in left-sided obstructive defects, systemic perfusion is dependent on blood flow from the RV via the PDA. In right-sided obstructive lesions, pulmonary blood flow is supplied from the aorta via the PDA.

D. Anesthetic Management

1. Preoperative evaluation

- a. The **history** should provide an assessment of the extent of cardiopulmonary impairment. Documentation should be made of the presence of cyanosis or CHF, exercise tolerance, cyanotic spells, activity level, feeding and growth patterns, associated syndromes, and anatomic abnormalities.
- b. **Physical examination** should make note of skin color, activity level, respiratory pattern and frequency, and appropriateness of development for given age. The heart and lungs should be auscultated. Close attention given to the patient's airway and IV access. Peripheral pulses should be palpated and blood pressure measurements obtained in both arms as well as the lower extremities to rule out coarctation.
- c. The **chest radiograph** should be examined for evidence of cardiomegaly, CHF, abnormalities in heart position, and the presence of any thoracic cage abnormalities.
- d. The **ECG** may be normal even in the presence of CHD. However, abnormalities can be important clues to underlying cardiac lesions.
- e. **Echocardiography** will show anatomic abnormalities and provide information about flow patterns and pressure gradients.
- f. **Cardiac catheterization** can be used to define the cardiopulmonary anatomy and quantify pulmonary and systemic shunt flows, vascular resistance, and intracardiac chamber pressures.

2. **Premedication.** Infants younger than 6 months of age, cyanotic or dyspneic children, and patients who are critically ill should generally receive no premedication. Older or more vigorous children may be given oral midazolam (0.5 to 1.0 mg/kg). Oral ketamine (5 to 7 mg/kg) may be added for a deeper level of sedation. An alternative intramuscular regimen is ketamine (3 to 5 mg/kg) in combination with midazolam (0.5 to 1.0 mg) and glycopyrrolate (0.1 to 0.2 mg) administered in the preanesthetic holding area. With the exception of ketamine, doses of sedatives are reduced in cases decreasing SVR would increase right-to-left shunting. Cyanotic infants are usually polycythemic and may be prone to thromboses of vital organs if they are not adequately hydrated with IV fluids preoperatively.

3. **Monitoring and equipment.** In addition to the standard monitoring required for all patients, a precordial or esophageal stethoscope and three temperature probes (tympanic membrane, esophageal, and rectal) should be available. Intra-arterial pressure monitoring is usually necessary. Prior surgical procedures such as Blalock-Taussig shunt construction or coarctation repair, may influence the choice of site for radial artery cannulation. **Central venous catheters** are typically inserted for the infusion of vasoactive drugs, the monitoring of CVP and the administration of fluids. A 4 Fr double-lumen catheter can be used for infants weighing less than 10 kg, and a 5-French triple-lumen catheter can be used for larger children. A warming blanket, radiant heating lamps, and a heated humidifier are useful perioperatively. TEE is an important diagnostic and intraoperative management tool.

4. **Resuscitation drugs** and infusions of inotropic medications appropriate for pediatric use must be available. Commonly used inotropes include dopamine (2 to 10 $\mu\text{g/kg/min}$), epinephrine (0.01 to 0.1 $\mu\text{g/kg/min}$), and dobutamine 2 to 10 $\mu\text{g/kg/min}$). **Air bubbles** must be meticulously removed from IV tubing and syringes. **Air filters** should be used

whenever possible. Even in the absence of shunts, paradoxical air emboli may traverse a probe-patent foramen ovale (PFO).

5. **Induction.** The choice between an inhalational and IV induction is based primarily on ventricular function and the degree of patient cooperation. A slow, carefully titrated induction by either technique usually provides a safe and stable anesthetic. Theoretically, patients with right-to-left shunts may have a slower rate of induction with volatile anesthetics because blood is shunted past the lungs. Similarly, arterial concentrations of IV anesthetics may increase more rapidly in patients with a significant right-to-left shunt. For the uncooperative child or a child surviving primarily on sympathetic stimulation, intramuscular ketamine (3 to 5 mg/kg) along with an antisialagogue such as atropine (0.02 mg/kg) or glycopyrrolate (0.01 mg/kg) may be used.
- E. Cardiopulmonary Bypass**
1. **Pump prime volume** ranges between 150 and 1,200 mL. Packed red blood cells are frequently added to the prime to yield an initial Hct of approximately 25% when on bypass. For smaller children, the red cells may be washed to remove potassium, lactic acid, and citrate-phosphate-dextrose-adenine preservative. Cells may be leukocyte depleted to decrease patient exposure to cytomegalovirus. Typical constituents of pump prime include sodium bicarbonate (to counteract acidosis), mannitol (to promote diuresis), heparin, and calcium (to offset the effects of the citrate in blood). Albumin solutions and FFP may be added to the prime for neonates.
 2. **Infants and children** generally lack vasooclusive disease. Consequently, blood flow during CPB is more important than arterial pressure. Flows as high as 150 mL/kg/min may be used in infants weighing less than 5 kg, while MAP as low as 30 mm Hg is well tolerated provided that SVC pressure is low (indicating that venous drainage is adequate).
 3. **Deep hypothermic circulatory arrest** is used extensively for infants weighing less than 10 kg. Up to 1 hour of circulatory arrest is tolerated without neurologic injury at a core and brain temperature of 15°C to 20°C. Where appropriate, low-flow CPB may offer advantages over circulatory arrest. Management points include adequate brain hypothermia (e.g., packing the head with ice packs), hemodilution, acid-base balance, muscle relaxation, and blood glucose control.
- F. Procedures that do not require CPB** include PDA ligation, aortic coarctation repair, PA banding, and most procedures, which create shunts designed to increase pulmonary blood flow (e.g., modified Blalock-Taussig shunt). Procedures such as pulmonary valvotomy, aortic valvotomy, and the creation of ASDs can be accomplished with percutaneous techniques.
- G. Management of Specific CHD Lesions (Table 24.7)**
1. **Cyanotic lesions** are secondary to **right-to-left shunting** either alone or in the presence of an obstruction to pulmonary blood flow. Typical conditions include tetralogy of Fallot, tricuspid atresia, pulmonary atresia, and pulmonary hypertension.
 - a. **Management goals** are to decrease PVR, increase pulmonary blood flow, maintain SVR, and maintain central volume.
 - b. **Ventilation management** include using modest hypocarbia, increasing inspired oxygen concentration, maintaining normal functional residual capacity, and avoiding acidosis.
 - c. Patients with **tetralogy of Fallot** are prone to hypercyanotic spells (rapid desaturation usually in response to surgical or other stimulation). Management of these spells includes measures that reduce infundibular spasm and improve pulmonary blood flow

Specific Congenital Cardiac Lesions

Lesion	Anatomy	Pathophysiology	Surgical Correction	Anesthetic Considerations
ASD	Three varieties: 1. Ostium secundum: defect in septum (most common) 2. Ostium primum: endocardial cushion defect. 3. Sinus venosus: caval-atrial defect often with partial anomalous pulmonary venous return.	Left-to-right shunt. RV volume overload. Potential for right-to-left shunting (e.g., during Valsalva maneuver) with paradoxical embolus risk. Minimal symptoms until later age, when CHF may develop.	Suture or patch closure. Percutaneous catheterization device closure.	Inhalation or intravenous induction. Potential extubation at end of procedure. Avoid air bubbles.
VSD	Supracristal, membranous canal, and muscular subtypes.	Left-to-right shunt. Increased pulmonary blood flow. Pulmonary hypertension and reversal of shunt as a late effect (Eisenmenger syndrome).	Dacron patch closure of singular or multiple defects. Muscular defects may be difficult to locate. Selected defects may be amenable to percutaneous catheterization device closure.	Hypoxemia and low FiO_2 to decrease pulmonary blood flow. Avoid myocardial depressants. Avoid air bubbles. Potential for postoperative AV block and pacing requirement. Potential need for postrepair inotropic support. Non-CPB case. Arterial line on right Suitable for regional anesthesia supplementation. Potential for postrepair hypertension.
Coarctation of the aorta	Narrowing usually distal to origin of left subclavian artery May be preductal or postductal in location. Often associated with a VSD.	Increased blood flow to upper extremities and head. Systemic hypoperfusion. Pressure overload of LV.	Left thoracotomy approach. Subclavian artery flap angioplasty or resection and end-to-end anastomosis.	

PDA	PDA.	Right-to-left shunt when PVR is high. Left-to-right shunt as PVR decreases. Necessary for survival with certain lesions (e.g., hypoplastic left heart syndrome).	Left thoracotomy versus thoracoscopic approach. Ligation and occasional division of PDA. Potential for percutaneous catheterization coil embolization.	Usually premature infants with concomitant pulmonary disease. Avoid high FiO_2 (risk of retrolental fibroplasia). Risk of recurrent laryngeal nerve damage.
Tetralogy of Fallot	1. VSD. 2. Pulmonary outflow tract obstruction. 3. RV hypertrophy. Overriding aorta	Right-to-left shunting through VSD into overriding aorta. Fixed (pulmonic stenosis) and dynamic (infundibular hypertrophy) RV outflow obstruction components. Systemic desaturation ("Tet" spell).	Patch closure of VSD. RV outflow tract reconstruction/augmentation. Excision of infundibular muscle band (when appropriate).	Management of "Tet spell": augment intravascular volume, minimize PVR (increase FiO_2 and decrease PaCO_2), increase SVR (knee-chest position and phenylephrine), and consider negative inotropes (halothane and β -blockade). Potential need for postoperative pacing.
Transposition of the great arteries	Transposition of both the aorta to the RV and the PA to the LV resulting in isolation of pulmonary and systemic circulations.	ASD, VSD, and/or PDA required for pulmonary and systemic blood mixing and, hence, survival.	Atrial switch procedure (Mustard and Senning): rarely performed. Arterial switch procedure (Jatene). When associated with a VSD and pulmonic stenosis, a Rastelli procedure (LV to aorta baffle closure via the VSD, and RV to PA allograft conduit).	Ductus/mixing lesion-dependent CHD lesion. Prostaglandin E_2 to maintain ductus patency (when appropriate).
Truncus arteriosus	Single great artery that gives rise to the aorta, PA, and coronary arteries. Associated VSD.	Mixing of pulmonary and systemic blood. Most commonly presents with pulmonary overcirculation. Valvuloplasty of truncal valve.	VSD closure. RV to PA valved conduit.	Increase PVR or decrease pulmonary blood flow precorrection (based on the degree of pulmonary overcirculation). Normalize PVR postcorrection. Potential need for inotropic support postrepair.

(continued)

Specific Congenital Cardiac Lesions (*continued*)

Lesion	Anatomy	Pathophysiology	Surgical Correction	Anesthetic Considerations
Atrioventricular canal defect Hypoplastic left heart syndrome	Common AV valve. Deficiency of atrial and ventricular septae. Atrietic/hypoplastic mitral valve, aortic valve, LV, and ascending aorta.	Mixing of blood at the atrial and ventricular levels. Usually presents with pulmonary overcirculation. Left-to-right shunt (obligatory) at atrial or ventricular level for mixing. Ductus arteriosus dependent for right-to-left (i.e., systemic) perfusion.	Closure of ASD and VSD. Mitral/tricuspid valvuloplasty. Palliative, staged repair: 1. Norwood I: atrial septectomy, reconstruction of aortic arch, PA plasty, and creation of systemic to pulmonary shunt. 2. Bidirectional Glenn: takedown of systemic to pulmonary shunt, creation of SVC to PA (cavopulmonary) shunt. 3. Modified Fontan procedure: creation of an IVC to PA anastomosis via an intra-atrial baffle; creates total cavopulmonary continuity. Alternatively, cardiac transplantation is an option.	Manipulate PVR to balance/optimize pulmonary systemic blood flow. Anticipate need for inotropic support postrepair. Associated with Down syndrome (potentially airway issues). Critically ill neonates. Preoperative (ICU) management will impact outcome. Prostaglandin E_1 to maintain ductal patency. Inotropes often necessary prerepair and postrepair. Avoid myocardial depressants. Fentanyl $>50 \mu\text{g/kg}$ prior to sternotomy. Manipulate PVR via adjustments in FiO_2 and PCO_2 to balance/optimize pulmonary versus systemic perfusion. Target goal: $\text{MAP} = 40$, $\text{pH} = 7.40$, $\text{PaO}_2 = 40$, $\text{PaCO}_2 = 40$.

ASD, atrial septal defect; AV, atrioventricular; CHD, congenital heart disease; CHF, congestive heart failure; CPB, cardiopulmonary bypass; FiO_2 , fraction of inspired oxygen; ICU, intensive care unit; IVC, inferior vena cava; LV, left ventricle; MAP, mean arterial pressure; PA, pulmonary artery; PaO_2 , partial pressure of oxygen; PaCO_2 , partial pressure of carbon dioxide; PDA, patent ductus arteriosus; PVR, pulmonary vascular resistance; RV, right ventricle; SVC, superior vena cava; SVR, systemic vascular resistance; VSD, ventricular septal defect.

(e.g., β -blockers such as propranolol), volume loading (15 to 20 mL/kg), and use of α -agonists (e.g., phenylephrine) to increase SVR. Alprostadil (prostaglandin E_1 0.05 to 0.1 $\mu\text{g/kg/min IV}$) may be used to maintain ductus arteriosus patency, decrease PVR, and increase pulmonary blood flow.

2. **Lesions with increased pulmonary blood flow** and left-to-right shunting include atrial septal defects (ASDs), ventricular septal defects (VSDs), and patent ductus arteriosus (PDA).
 - a. **Management goals** are to avoid negative inotropes and excessive pulmonary blood flow.
 - b. **Anesthetic maneuvers** include minimizing myocardial depressants (e.g., volatile anesthetics) and increasing PVR and decrease pulmonary blood flow in favor of systemic blood flow through maintaining normocarbida to slight hypercarbia, limiting inspired oxygen concentration and using PEEP.
3. **Balanced shunts** have the potential for a ventricle's output to be directed to the pulmonary or systemic circulation and include hypoplastic left heart syndrome, truncus arteriosus, double-outlet RV, and complete AV canal defect. The direction of blood flow is governed by the relative resistances of the pulmonary and systemic vasculatures (PVR/SVR ratio).
 - a. **Management goals** are to manipulate pulmonary blood flow to maintain adequate systemic perfusion. Often both a low-normal blood pressure (e.g., MAP of 40 mm Hg) and a low PaO_2 (e.g., 40 mm Hg) must be tolerated.
 - b. **Anesthetic maneuvers** depend on the balance of systemic versus pulmonary blood flow, which can be affected by altering P_aCO_2 , inspired oxygen concentration, and PEEP.

VII. OTHER CARDIAC PROCEDURES

- A. **Off-bypass CABG** is performed to avoid the complications associated with CPB and to minimize aortic manipulation. Proximal grafts are performed using either a partial aortic cross-clamp technique or a specifically designed proximal anastomotic device that precludes aortic clamping. Distal grafts are performed using one of several heart stabilizing devices. Considerations for this procedure include the following:
 1. Consider tailoring anesthetic management to allow possible **early extubation** after surgery (e.g., fentanyl 5 to 10 $\mu\text{g/kg}$, volatile anesthetic followed by an infusion of propofol or dexmedetomidine).
 2. **Heparin** 350 units/kg IV is given, and the ACT is maintained above 400 seconds. This allows the patient to be emergently initiated on CPB if necessary. Antifibrinolytic therapy is avoided. A small dose of protamine (50 to 100 mg) is given after the procedure.
 3. **ECG monitoring** can be difficult because the heart is placed in nonanatomic positions. Nonetheless, it is important to establish a baseline ECG (for each position) and to monitor the ST segments.
 4. **Hemodynamic instability** is common, particularly when the surgeon is performing the distal anastomoses. Grafts to vessels with less disease tend to be associated with more instability than those to vessels that are occluded. Increasing MAP to optimize coronary perfusion is critical for the ischemic heart during creation of the distal anastomosis. If hemodynamically intolerable ischemia results, coronary shunting may be indicated. Occasionally, repositioning of the heart is required to permit augmented right-sided filling when hemodynamic instability is due to obstruction of right heart inflow.

5. **Volume requirements** tend to be high. A full heart tends to tolerate physical manipulation better.
 6. **Ventricular dysrhythmias** may be treated with amiodarone 150 mg IV bolus and then followed with 1 mg/min infusion. Acid–base and electrolyte abnormalities should be corrected.
- B. “Redo” Cardiac Surgery**
1. **Mediastinal structures**, including the heart, major vessels, prior coronary bypass grafts, as well as the lungs may be adherent to the underside of the sternum. They can be lacerated during sternotomy. Usually, 2 to 4 units of blood must be in the OR before sternotomy begins. An additional 14 g IV catheter or a rapid infusion catheter should be placed to facilitate volume resuscitation. Because the patient may need to go on CPB emergently, 350 units/kg of heparin must be in a syringe ready to administer immediately. In emergency situations, venous return may be supplied from the pump suction line on the field (“sucker bypass”).
 2. Central venous and arterial catheter insertions may be difficult at sites previously used for catheters.
 3. Insertion of a PA catheter equipped with pacing capability is prudent as epicardial pacing may not be possible during chest opening. Transcutaneous defibrillation pads should be applied to the lateral aspects of the chest in the event of malignant arrhythmias during opening (e.g., from tearing of pericardium and myocardium and rapid bleeding).
 4. **Diffuse bleeding** from dissection of scar tissue may occur after CPB. Use of an antifibrinolytic drug such as ϵ -aminocaproic acid (Amicar) at 10-g bolus followed by 2 g/h infusion is encouraged.
 5. **Careful ECG monitoring** is imperative because manipulation of atheromatous grafts may send emboli to the coronary circulation. Because myocardial protection is more challenging in patients with previous coronary grafts, postbypass myocardial dysfunction is more likely.
- C. Cardiac Tamponade and Constrictive Pericarditis**
1. Avoid decreases in myocardial contractility, peripheral vascular resistance, and heart rate. **Pericardiocentesis** prior to induction may be advisable in patients with tamponade unless the condition is secondary to aortic dissection.
 2. An arterial catheter, a large-bore IV catheter should be inserted. A central venous catheter or PA catheter may be used if the patient can tolerate insertion.
 3. Useful **induction agents** include etomidate and ketamine.
 4. A method for **backup atrial pacing** (transesophageal or transvenous) should be available.
 5. Patients should be prepped and draped for surgery prior to induction. In **severe cases**, awake intubation with maintenance of spontaneous ventilation should be considered.
- D. Cardiac Transplantation**
1. **Management of the donor** (see Chapter 21).
 2. **Anesthetic management of the recipient**
 - a. **The key to patient survival** is minimizing the ischemic time of the donated heart. Consequently, expeditious preparation of the recipient and communication with the surgical team are essential.
 - b. **Preoperative evaluation** of the recipient should determine whether the patient has had previous chest surgery, has an elevated PVR (>6 Wood units, transpulmonary gradient >12 mm Hg), has pulmonary hypertension responsive to venodilators, or is coagulopathic.

- c. **Invasive monitoring** should include an arterial line and a triple-lumen central venous catheter. A PA catheter should be used when the patient has severe pulmonary hypertension. **Aseptic technique** is critical because the patient will be immunosuppressed following the procedure.
 - d. **Precautions for a full stomach** may be necessary during induction. Etomidate and fentanyl are good choices to provide hypnosis and analgesia, respectively. If the patient is receiving inotropic infusions, consider increasing their doses before induction. If a ventricular assist devices (VAD) is present, venous return must be maintained for the pump to maintain its flow rate.
 - e. **Right heart failure and coagulopathy** are common during the rewarming phase of bypass. Cellular blood products should be irradiated or leukocyte depleted to minimize foreign HLA antigen exposure.
 - f. The donor heart will be unresponsive to drugs whose actions are mediated by the recipient's cholinergic nervous system (e.g., atropine and glycopyrrolate). Upon termination of CPB, the recipient's heart rate should be maintained between 80 and 110 beats/min. This can be accomplished with epicardial pacing or pharmacologically with a dopamine (2 to 10 $\mu\text{g}/\text{kg}/\text{min}$), epinephrine (0.01 to 0.1 $\mu\text{g}/\text{kg}/\text{min}$), or isoproterenol infusion (0.5 to 5 $\mu\text{g}/\text{min}$). If a biatrial implantation technique was used, there may be two distinct P waves during sinus rhythm.
 - g. **Immunosuppressants** will be necessary and are administered in consultation with the surgeon and transplant cardiologist.
- E. Deep Hypothermic Circulatory Arrest (DHCA).** DHCA may be necessary for surgery on the distal ascending aorta or aortic arch (e.g., for an aneurysm or aortic dissection). Circulatory arrest provides a bloodless field inside the aorta. Hypothermia decreases the metabolic rate and minimizes the risk of cerebral and organ ischemia during circulatory arrest. Problems associated with DHCA include increased CBP time, coagulopathy, and end-organ dysfunction. The risk of permanent neurologic injury after aortic arch surgery using DHCA is approximately 3% to 12%. Most patients tolerate 30 minutes of DHCA without significant neurologic dysfunction. Management issues include the following:
- 1. Organ protection during DHCA**
- a. **Hypothermia.** Systemic cooling to 18°C produces electrical silence on the EEG in most patients. There is no outcomes evidence to support topical cooling of the head in humans.
 - b. **Antegrade cerebral perfusion (ACP)** via the right axillary artery or **retrograde cerebral perfusion (RCP)** via the SVC cannula can be used to extend the duration of safe DHCA. ACP is thought to be superior to RCP for cerebral protection; however, it carries the risk of arterial wall dissection and cerebral embolism.
 - c. **Pharmacologic interventions.** Animal studies have suggested a protective effect of certain agents such as barbiturates, steroids, mannitol, lidocaine, magnesium, dexmedetomidine, and calcium channel antagonists. These agents have not been shown to have conclusive benefits in human randomized controlled trials.
 - d. **Glycemic control** is important. Glucose metabolism is impaired under DHCA. Blood glucose concentration should be maintained below 180 mg/dL to avoid worsening neurologic injury.
 - e. **Temperature Monitoring.** It is commonly preferred to use more than one site for core body temperature monitoring. Tympanic membrane

temperature provides the closest assessment of brain temperature. During rewarming, the perfusate temperature is kept at a maximum of 10°C above core body temperature and never above 36°C.

1. **Neurophysiologic monitoring** includes EEG, bispectral index, somatosensory-evoked potentials, NIRS, and jugular venous bulb saturation (SjO₂).

2. **Acid–base management** depends on whether α -stat or pH-stat is used (see *Maintenance of CPB*). The pediatric literature generally recommends the use of pH-stat management during DHCA for both cerebral and myocardial protection.

F. **Ventricular assist devices (VAD)** may be classified as extracorporeal, implantable, or percutaneous. Extracorporeal devices employ a pump that is positioned outside of the patient.

1. Extracorporeal devices

a. **Indications** include postcardiotomy support, cardiogenic shock, bridge to recovery, and bridge to transplant.

b. These devices can provide biventricular support. Inflow cannulation sites include the LV or LA for left-sided support and the RV or RA for right-sided support. Corresponding outflow cannulae are inserted into the aorta or main PA. The cannulae (inflow and outflow) are connected to an external pump. Surgical time and dissection are significantly less with these than with implanted devices.

c. Both the Abiomed BVS 5000 and the Thoratec VAD utilize pneumatically driven pumping sacs. Whereas the Abiomed BVS 5000 depends on gravity for venous drainage, the Thoratec VAD is equipped with vacuum-assisted drainage. The primary difference between the two devices is patient mobility. Patients with the Abiomed BVS 5000 must lie supine while patients with the Thoratec may ambulate.

2. Implantable devices (e.g., Novacor LVAS, HeartMate VXE, HeartMate Pneumatic, Heartmate II, and Thoratec IVAD).

a. These devices are used as a bridge to cardiac transplantation or for destination therapy.

b. Except for the Thoratec IVAD, these devices are designed for LV support only. They consist of an inflow cannula, a pump, and an outflow cannula. The inflow cannula is inserted into the LV apex while the outflow cannula is inserted into the ascending aorta. A driveline is tunneled through the skin to connect the implanted pump to the external console. CPB is always necessary for placement.

c. The Novacor LVAS, HeartMate VXE, and Heartmate devices are electrically drive. A rechargeable power source fits into a backpack or holsters and allows the patient to leave the hospital. The Heartmate II is smaller than the others, making it appropriate for use in a wider range of patients. Because of its axial flow characteristics, it provides a significantly reduced degree of pulsatile arterial perfusion.

3. Anesthetic considerations for VAD insertion

a. Patients will have **marginal cardiac function**. Extreme care is required during induction to minimize decreases in contractility and preload.

b. **Bleeding** can be problematic, especially with the implanted devices. Establish adequate IV access for volume administration and consider using an antifibrinolytic agent. All the pumps except for the Heartmate VXE require anticoagulation.

c. If the patient is receiving the device as a bridge to transplantation, transfuse with leukocyte-depleted cellular blood products to minimize HLA antigen exposure.

- d. **TEE is required.** TEE can determine the degree of AI, which, if significant, may warrant insertion of a tissue valve. It can also detect the degree of tricuspid regurgitation; presence of PFO, ASD, or VSD; the degree of right heart dysfunction (which may require mechanical RV support); and the presence of intracardiac thrombus. Postoperative TEE examination is used to assess whether the inflow cannula is properly inserted, by assessing for the absence of turbulent flow, and to ensure that all air is removed from the heart.
 - e. Patients receiving an LVAD frequently require RV support. Inotropes, inhaled nitric oxide, and occasionally an RVAD are required.
 - f. Most devices function best in the automatic mode after chest closure. The flow will then depend largely on venous return. Decreased venous return will be signaled by a decreased pumping rate because the devices will pump only when adequately filled. Volume or a vasopressor should be administered.
- G. Extracorporeal membrane oxygenation (ECMO)** is an alternative form of extracorporeal life support to VADs. ECMO is indicated for the short-term management of severe but reversible cardiogenic shock or respiratory failure that is refractory to conventional treatment. It is an option for treatment of severe postcardiotomy ventricular dysfunction with or without hypoxemia. It consists of an external pump that pushes venous blood through a membrane allowing gas exchange before returning the blood to the circulation via a warmer.
1. Venous drainage usually occurs from the internal jugular vein or femoral vein. Blood is returned either to an artery (venoarterial ECMO) or a central vein (venovenous ECMO).
 2. **Venoarterial (VA) ECMO** bypasses the patient's heart and lungs with diversion of complete or partial flow through the ECMO circuit, providing both respiratory and hemodynamic support. It can be used for refractory postcardiotomy cardiogenic shock. The same cannulation setup during CPB can be used for ECMO. If considered subsequently, ECMO can be established from the femoral artery and vein. A condition called **differential hypoxemia** can occur in VA ECMO when a proportion of venous blood in a patient with some return of cardiac function is pumped into the diseased lungs, with subsequent ejection of hypoxic blood to the coronaries and great vessels. This may be revealed by a difference in oxygenation from sampling of left-sided and right-sided arterial lines.
 3. **Venovenous (VV) ECMO** provides gas exchange support in patients with good cardiac function. Venous cannulae are usually placed in the right femoral vein for drainage and right internal jugular for infusion. Alternatively, a dual-lumen cannula (from Avalon Laboratories) can be inserted into the internal jugular vein. Similar to a hemodialysis catheter, this cannula drains blood from IVC and SVC and returns blood directly into the RA, reducing the incidence of recirculation and allowing greater patient movement.
 4. **Aggressive medical support** is required to optimize the results of ECMO and facilitate weaning. Interventions may include the use of pulmonary vasodilators for pulmonary hypertension, lung-protective ventilation strategies; optimization of preload to provide pulmonary perfusion; and the use of renal replacement therapy. To avoid thrombus formation in the ECMO circuit, heparin is administered to maintain the ACT at 1.5 to 2.0 times normal.

5. **Continual assessment** of native cardiopulmonary function is essential. If the heart and lungs do not recover within the expected timeframe (1 to 2 weeks), the decision should be made to convert to long-term support such as a VAD or transplant. A discussion of the goals of care is important if the disease process is believed to be nonreversible.

VIII. ANESTHESIA FOR “OFF-SITE” CARDIAC PROCEDURES

The goal of anesthesia is to provide sufficient sedation to allow the procedure to be completed without excessive movement while avoiding cardiopulmonary instability. The issues pertinent to anesthesia outside of the OR for non-cardiac procedures apply to cardiac procedures as well.

A. The IABP is normally placed in the cardiac catheterization lab under sedation. It provides circulatory assistance for the failing or ischemic heart. Inflation of the intra-aortic balloon augments aortic diastolic pressure and thus coronary perfusion. The effect is most beneficial for the LV that receives most of its blood supply during diastole. Deflation of the balloon reduces the impedance to LV ejection, thereby reducing myocardial oxygen consumption. **Preoperative indications** for placement include unstable angina that is refractory to medical therapy; LV failure due to myocardial infarction, ruptured papillary muscle, or VSD; and prophylaxis for a high-risk patient with severe left main disease. **Postbypass indications** include refractory LV failure preventing successful termination of CPB and refractory ST-segment elevation.

1. The IABP is inserted through a femoral artery and advanced until the tip is 1 to 2 cm distal to the left subclavian artery in the descending thoracic aorta. Positioning can be guided by TEE. It can be placed in a transthoracic manner if iliofemoral disease precludes the use of a femoral artery.
 2. **Inflation of the IABP** is synchronized with the patient's ECG, a pacemaker potential, or the arterial blood pressure trace. Balloon inflation occurs early in diastole either at the dicrotic notch of the arterial pressure waveform or following a time delay after the R wave on ECG. **Balloon deflation** occurs during isovolumic contraction. Intraoperative triggering directly from a pacemaker generator will eliminate interference otherwise caused by electrocautery or blood sampling from an arterial catheter.
 3. **Relative contraindications** include severe AI, aortic aneurysm, and severe peripheral vascular disease.
 4. **Complications** of the IABP include distal embolization, aortic dissection, aortic rupture, and lower extremity ischemia. **Anticoagulation** is indicated for extended IABP use. Heparin is usually used with a target ACT or aPTT that is 1.5 to 2 times the baseline.
- B. Percutaneous Device Closure of Patent Foramen Ovale (PFO) or ASD.** Following induction of general endotracheal anesthesia, right heart catheterization is performed, and a guidewire is threaded across the PFO or ASD. TEE is used to define the intracardiac anatomy and size of the defect. It is also used to guide the placement of the device and assess whether deployment of the device is successful in closing the defect.
- C. Implantable Cardioverter Defibrillator (ICD).** Modern ICDs consist of an endocardial lead system and a pectoral pulse generator. Older systems used epicardial lead systems and abdominal generators.
1. ICDs are used for primary prevention of sudden cardiac death in patients with systolic heart failure (EF < 35%) refractory to medical therapy or in those with high-risk conditions such as long QT syndrome,

hypertrophic cardiomyopathy, Brugada syndrome, and arrhythmogenic right ventricular dysplasia. In addition to ICD placement, patients with dilated cardiomyopathy and a widened QRS have been shown to also benefit from cardiac resynchronization therapy (CRT).

2. Devices are placed under local anesthesia in the electrophysiology laboratory. A brief period of general anesthesia is necessary for testing of the device once it is implanted. A propofol infusion titrated to maintain spontaneous respiration is generally suitable. Patients with severe reflux, a difficult airway, or agitation may require endotracheal intubation. Standard monitors are used. Intubation equipment, a bag-valve-mask resuscitator, emergency drugs, oxygen, suction apparatus, and an external defibrillator must be present.
 3. If intracardiac electrodes are inadequate, patients may require intraoperative epicardial electrode placement. These patients are often hemodynamically compromised. They should have an arterial catheter and catheter for vasoactive medication administration. Emergency drugs, including epinephrine, must be immediately available.
 4. **Noninvasive programmed stimulation** is used to test the function of an ICD after it has been implanted. An ICD programmer is used to induce the irregular rhythm (ventricular fibrillation or tachycardia). The device is then checked for proper sensing and dysrhythmia termination. Because this is an elective procedure, the patient should be fasting, and propofol anesthesia is used as described in section VI.C.1.
- D. Cardioversion.** A short-acting sedative (e.g., propofol or etomidate) can be administered for brief loss of consciousness. The combination of fentanyl and midazolam is an alternative but not ideal due to prolonged duration of action. Routine fasting guidelines should be followed for all elective cardioversions. Hemodynamically unstable patients often warrant immediate cardioversion, and a small dose of amnestic may be all that can be tolerated.
- E. Percutaneous aortic valve replacement** is conducted for patients who are not surgical candidates. An expanding bioprosthetic valve is placed over the native aortic valve. The procedure may be carried out using a transfemoral arterial, transvenous transseptal, or open transapical approach. The procedure is typically carried out in a hybrid OR or cardiac catheterization laboratory.
1. **General anesthesia with endotracheal intubation** is required for the procedure. The anesthetic management of these patients may be challenging as they usually have multiple medical comorbidities in addition to critical AS.
 - a. **Rapid ventricular pacing** is used to minimize cardiac motion during valve deployment. A transvenous pacing lead is inserted into the right ventricle. A pacing rate of 140 to 200 beats/min frequently results in 1:1 ventricular capture and sufficiently lowers the pulse pressure and cardiac output. The rapid pacing periods must be minimized to avoid hemodynamic instability, especially in patients with depressed LV function and CAD.
 - b. **TEE** is particularly useful to assess adequate placement and function of the valve. It is crucial to ensure accurate positioning of the valve with TEE and fluoroscopy prior to deployment to avoid embolization of the valve or a large perivalvular leaks. Once the valve is deployed, TEE can inform on the stability, location, and function of the valve as well as any degree of perivalvular regurgitation.

2. **Complications** include tamponade (due to wire perforation), cerebral vascular accident, aortic rupture or dissection, AI, conversion to emergent surgical aortic valve replacement, myocardial infarction, suboptimal valve deployment, and AV block.
- F. **Percutaneous mitral valve repair** is effective for both degenerative and functional MR in patients who are not suitable surgical candidates. The mechanical device (MitraClip, Abbott Vascular) is advanced through the IVC and delivered into the LA through transseptal access; it then grasps and approximates the valve leaflets. Short- and medium-term outcomes have been favorable in the randomized EVEREST II study. Compared to surgical repair, there is less reduction in MR with the percutaneous approach.
 1. **General endotracheal anesthesia** with TEE and fluoroscopic guidance is required for the procedure. In some centers, the procedure is done under sedation and local anesthesia.
 - a. Right heart catheterization or PA catheter placement is often performed to monitor right- and left-sided hemodynamics before and after the procedure.
 - b. TEE guidance is crucial for the transseptal puncture and device positioning.
 - c. Brief periods of apnea may be required to allow precise placement of the device.
 - d. Vasoactive agents and inotropes may be required to raise the blood pressure to adequately assess the severity of residual MR.
 2. **Complications** include tamponade, systemic embolization, worsening of MR and arrhythmias (especially atrial fibrillation).

Suggested Readings

- American Society of Anesthesiologists and Society of Cardiovascular Anesthesiologists Task Force on Transesophageal Echocardiography. Practice guidelines for perioperative transesophageal echocardiography. An updated report by the American Society of Anesthesiologists and the Society of Cardiovascular Anesthesiologists Task Force on Transesophageal Echocardiography. *Anesthesiology* 2010;112:1084–1096.
- Diaz LK, Andropoulos DB. New developments in pediatric cardiac anesthesia. *Anesthesiol Clin North America* 2005;23:655–676.
- El-Marghabel I. Ventricular assist devices and anesthesia. *Semin Cardiothorac Vasc Anesth* 2005;9:241–249.
- Feldman T, Foster E, Glower D, et al. Percutaneous repair or surgery for mitral regurgitation. *N Engl J Med* 2011;364(15):1395–1406.
- Ferraris VA, Ferraris SP, Saha SP, et al. Perioperative blood transfusion and blood conservation in cardiac surgery: the STS and SCA clinical practice guideline. *Ann Thorac Surg* 2007;83:S27–S86.
- Gravlee GP, Davis RF, Kurusz M, et al., eds. *Cardiopulmonary Bypass*. 2nd ed. Philadelphia: Lippincott Williams & Wilkins; 2000.
- Hensley FA, Martin DE, Gravlee GP, eds. *A Practical Approach to Cardiac Anesthesia*. 3rd ed. Philadelphia: Lippincott Williams & Wilkins; 2002.
- Karl TR. Neonatal cardiac surgery. Anatomic, physiologic, and technical considerations. *Clin Perinatol* 2001;28:159–185.
- Konstadt S, Shernan S, Oka Y. *Clinical Transesophageal Echocardiography: A Problem-Oriented Approach*. 2nd ed. Philadelphia: Lippincott Williams & Wilkins; 2003.
- Kothandan H, Ho VK, Yeo KK, et al. Anesthesia management for MitraClip device implantation. *Ann Card Anaesth* 2014;17(1):17–22.
- Murkin JM. Perioperative multimodality neuromonitoring: an overview. *Semin Cardiothorac Vasc Anesth* 2004;8:167–171.

- Murkin JM, Arango M. Near-infrared spectroscopy as an index of brain and tissue oxygenation. *Br J Anaesth* 2009;103(Suppl 1):i3–i13.
- Myles PS, McLroy D. Fast-track cardiac anesthesia: choice of anesthetic agents and techniques. *Semin Cardiothorac Vasc Anesth* 2005;9:5–16.
- Piquette D, Deschamps A, Belisle S, et al. Effect of intravenous nitroglycerin on cerebral saturation in high-risk cardiac surgery. *Can J Anaesth* 2007;54:718–727.
- Reul H, Akdis M. Temporary or permanent support and replacement of cardiac function. *Expert Rev Med Devices* 2004;1:215–227.
- Riess FC. Anticoagulation management and cardiac surgery in patients with heparin-induced thrombocytopenia. *Semin Thorac Cardiovasc Surg* 2005;17:85–96.
- Roasio A, Lobreglio R, Santin A, et al. Fenoldopam reduces the incidence of renal replacement therapy after cardiac surgery. *J Cardiothorac Vasc Anesth* 2008;22:23–26.
- Serna DL, Thourani VH, Puskas JD. Antifibrinolytic agents in cardiac surgery: current controversies. *Semin Thorac Cardiovasc Surg* 2005;17:52–58.
- Speiss BD. *Perioperative Transfusion Medicine*. 2nd ed. Philadelphia: Lippincott Williams & Wilkins; 2005.
- Thys D. *Textbook of Cardiothoracic Anesthesiology*. New York: McGraw-Hill; 2001.
- Wan S, LeClerc JL, Vincent JL. Inflammatory response to cardiopulmonary bypass: mechanisms involved and possible therapeutic strategies. *Chest* 1997;112:676–692.
- Warkentin TE, Koster A. Bivalirudin: a review. *Expert Opin Pharmacother* 2005;6:1349–1371.
- Woo YJ. Cardiac surgery in patients on antiplatelet and antithrombotic agents. *Semin Thorac Cardiovasc Surg* 2005;17:66–72.

I. PHYSIOLOGY

- A. Cerebral blood flow (CBF)** is equal to cerebral perfusion pressure (CPP) divided by the cerebral vascular resistance. **CPP is defined as the difference between the mean arterial pressure (MAP) and intracranial pressure (ICP) or central venous pressure, whichever is higher.** CBF averages 50 mL/100 g of brain tissue per minute in the normal brain and is affected by blood pressure, metabolic demands, PaCO_2 , PaO_2 , blood viscosity, vasoactive agents, and neurogenic regulation. The brain receives approximately 15% of the cardiac output.
- 1. CBF** is maintained at a constant level by constriction and dilation of arterioles (autoregulation) (Fig. 25.1) when the MAP is between 50 and 150 mm Hg. When MAP is outside these limits, CBF varies directly with the MAP. Chronic hypertension shifts the autoregulatory curve to the right, rendering hypertensive patients susceptible to cerebral ischemia at blood pressures considered normal in healthy individuals. Chronic antihypertensive therapy may normalize the autoregulatory range. Cerebral ischemia, trauma, hypoxia, hypercarbia, edema, mass effect, and volatile anesthetics attenuate or abolish autoregulation and may make blood flow to the affected area dependent on MAP.
 - 2. PaCO_2** has profound effects on CBF by its effect on the pH of the brain extracellular fluid (ECF). CBF increases linearly with increasing PaCO_2 in the range from 20 to 80 mm Hg, with an absolute change of 1 to 2 mL/100 g/min for each mm Hg change in PaCO_2 . The effect of PaCO_2 on CBF decreases over 6 to 24 hours because of slow adaptive changes in the brain ECF bicarbonate concentration. Sustained hyperventilation causes cerebrospinal fluid (CSF) bicarbonate production to decrease, allowing CSF pH to gradually normalize. Rapid normalization of PaCO_2 after a period of hyperventilation results in a significant CSF acidosis with vasodilation and increased ICP.
 - 3. PaO_2 .** Hypoxia is a potent cerebral vasodilator. CBF increases markedly below a PaO_2 of 60 mm Hg. PaO_2 above 60 mm Hg has little influence on CBF.
 - 4. Neurogenic regulation.** The cerebral vasculature receives extensive cholinergic, adrenergic, serotonergic, and VIPergic innervation, although the exact role these systems play in regulation of CBF is not clear. Evidence suggests, however, that increased sympathetic tone in hemorrhagic shock shifts the lower end of the autoregulatory curve to the right and results in lower CBF at a given MAP.
 - 5. Viscosity.** Normal hematocrit (33% to 45%) in a normal brain has little influence on CBF. During focal cerebral ischemia, however, reduction in viscosity by hemodilution (hematocrit 30% to 34%) may increase CBF to ischemic territories.
- B. Cerebral metabolic rate (CMRO_2)** and CBF are tightly coupled, because the brain requires a constant supply of substrate to meet its high metabolic demands. Regional or global increases in CMRO_2 elicit a corresponding increase in CBF, probably mediated by signaling molecules such as

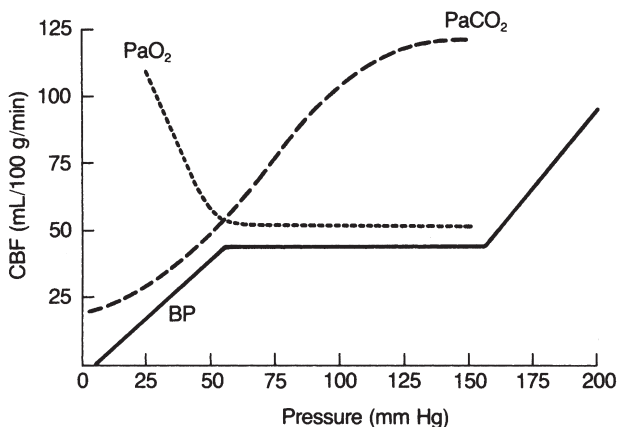


FIGURE 25.1 Autoregulation maintains a constant level of CBF over a wide range of carotid artery mean blood pressures. Independent of this effect, CBF is elevated by hypercarbia (PaCO_2) and hypoxemia (PaO_2); hypocarbia diminishes CBF.

nitric oxide. Other factors that modulate CMRO_2 (and CBF through this mechanism) include the following:

- 1. Anesthetics.** Variable effect (see sections II.A and B).
- 2. Temperature.** Hypothermia decreases CMRO_2 by 7% per 1°C below 37°C . Hyperthermia increases CMRO_2 .
- 3. Seizures.** Increases CMRO_2 .
- 4. Pain or arousal.** Increases CMRO_2 .
- C. ICP** reflects the relationship between the volume of the intracranial contents (brain, blood, and CSF) and the volume of the cranial vault. **Normal ICP is 5 to 15 mm Hg.** A sustained elevation of ICP greater than 15 to 20 mm Hg in the setting of intracranial pathology is considered abnormal.
 - 1. The cranial vault is rigid,** and its capacity to accommodate increases in intracranial volume is limited. A developing intracranial mass (e.g., tumor, edema, hematoma, or hydrocephalus) initially displaces blood and CSF, and ICP remains relatively normal (Fig. 25.2). As intracranial volume increases further, intracranial compliance decreases, and ICP rises rapidly (see Fig. 25.2). Thus, patients with decreased compliance may develop marked increases in ICP even with small increases in intracranial volume (e.g., cerebral vasodilation due to anesthesia, hypertension, or carbon dioxide retention) (see Fig. 25.2).
 - 2. Clinical features of elevated ICP.** ICP elevation usually decreases CPP and may cause ischemia in regions of the brain where autoregulation is defective and CBF depends on CPP. Early signs and symptoms of increased ICP include headache, nausea, vomiting, blurred vision, papilledema, and decreased levels of consciousness. As ICP increases, brain herniation may occur causing mechanical injury and/or ischemia to the brainstem and cranial nerves. This may result in hypertension with bradycardia or tachycardia, irregular respiration, oculomotor (third cranial) nerve palsy leading to ipsilateral pupillary dilation with no light reflex, abducens (sixth cranial) nerve palsy, contralateral hemiparesis or hemiplegia, and ultimately, coma and respiratory arrest.

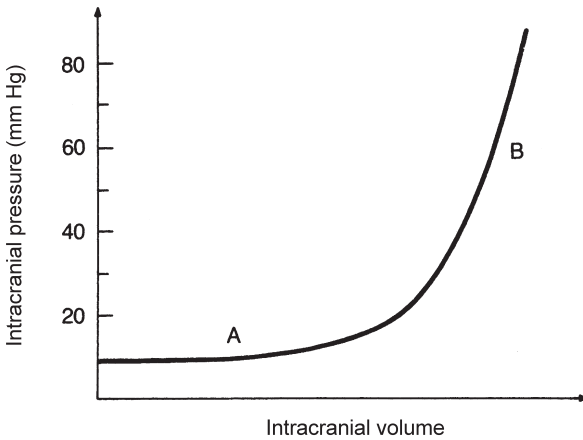


FIGURE 25.2 The intracranial compliance curve. In the normal ICP range (A), increases in intracranial volume produce minimal changes in ICP. Further, small increases in ICP after the “elbow” of the curve can produce abrupt increases in ICP (B).

3. Treatment of elevated ICP involves strategies aimed at decreasing the volume of the intracranial components:

- a. **Hypoxia and hypercarbia cause cerebral vasodilation** and should be avoided. Hyperventilation to a PaCO_2 of 25 to 30 mm Hg produces cerebral vasoconstriction and may be used as a temporizing measure in the management of acutely increased ICP. Hyperventilation is potentially deleterious, however, and can cause ischemia in injured brain where CBF is low. Therefore, it should be withdrawn when effective definite therapy is established. Additionally, the effect of hyperventilation on ICP decreases as CSF pH normalizes.
- b. **Decrease jugular venous pressure.** Elevating the head at least 30 degrees promotes venous drainage and decreases intracranial venous blood volume. Avoid excessive flexion or rotation of the neck and prevent increases in the intrathoracic pressure (e.g., coughing, straining, and elevated intrathoracic pressure). Positive end-expiratory pressure should be minimized to the lowest level that maintains adequate lung recruitment.
- c. **Control CMRO_2 .** Barbiturates are potent vasoconstrictors that decrease cerebral blood volume while decreasing CMRO_2 . Prevent increases in CMRO_2 due to arousal/seizures with adequate sedation and seizure prophylaxis where indicated.
- d. **Maintaining high serum osmolality** (305 to 320 mOsm/kg) may reduce cerebral edema and decrease brain volume. Fluid management is designed to achieve this goal (see section VD). In addition, **mannitol** (0.5 to 2.0 g/kg intravenous [IV]) and **furosemide** produce a hyperosmolar state and are effective in the acute reduction of ICP. **Hypertonic saline** is an alternative to mannitol for managing raised ICP.
- e. **CSF volume can be reduced by** draining the CSF through ventriculostomy catheter or needle aspiration intraoperatively.
- f. Surgical removal of tumor, hematoma, or decompressive craniectomy reduces intracranial volume and ICP.
- g. Steroids may reduce cerebral edema associated with tumors.

II. PHARMACOLOGY

Agents used in anesthesia may affect $CMRO_2$ and CBF.

A. Inhalation anesthetics produce a dose-related reduction in $CMRO_2$ while causing an increase in CBF.

- 1. Nitrous oxide** can cause increases in $CMRO_2$, CBF, and ICP. These effects can be greatly attenuated or abolished when it is administered in conjunction with IV anesthetic agents. Nitrous oxide should be avoided when intracranial airspaces (e.g., pneumocephalus) exist, because it diffuses more rapidly into such spaces than nitrogen diffuses out and may produce an acute increase in ICP.
 - 2. Volatile agents** cause increases in CBF due to their direct vasodilatory actions. Autoregulation can be attenuated or abolished by increasing the concentrations of these drugs, but responsiveness to carbon dioxide seems to be preserved (Table 25.1). The vasodilatory effect of inhalational agents is clinically insignificant in patients with normal intracranial compliance. These agents should be used with caution in patients with compromised intracranial compliance (e.g., large intracranial mass lesion and acute intracranial hematoma).
 - 3. Volatile anesthetics** produce dose-dependent reductions in metabolism ($CMRO_2$), probably by depressing neuronal electrical activity. Isoflurane is the most potent in this respect and is the only volatile agent that induces an isoelectric electroencephalogram (EEG) at clinically relevant concentrations ($2 \times MAC$).
- B. IV anesthetics** generally cause coupled reduction in CBF and $CMRO_2$ in a dose-dependent manner. This is due to the depression of cerebral metabolism. **Barbiturates**, **etomidate**, and **propofol** markedly decrease CBF and $CMRO_2$ and can produce isoelectric EEGs. Etomidate has been associated with seizures and is best avoided in seizure-prone patients. **Lidocaine** in therapeutic doses decreases both CBF and $CMRO_2$. **Ketamine**, by contrast, increases CBF and $CMRO_2$ and is used infrequently in neuroanesthesia. **Opioids** and **benzodiazepines** produce minimal changes in CBF and $CMRO_2$. Autoregulation and carbon dioxide responsiveness appear to be preserved with IV agents.
- C. Muscle relaxants** have no direct effect on CBF and $CMRO_2$. They may alter cerebral hemodynamics indirectly through their effects on blood pressure. **Succinylcholine** produces a transient increase in ICP, likely caused by arousal phenomena, which can be attenuated by prior administration of a barbiturate or a defasciculating dose of a nondepolarizing muscle relaxant.
- D. Vasoactive Drugs**

- 1. Adrenergic agonists.** α -Adrenergic agonists and low-dose β -adrenergic agonists have little influence on CBF if MAP is within the limits of

TABLE
25.1

Cerebral Physiologic Effects of Inhalational Anesthetics

	Nitrous Oxide	Desflurane	Sevoflurane	Isoflurane
CBF	↑	↑↑	↑	↑↑
CPP	↓	↓↓	↓	↓↓
ICP	↔/↑	↔/↑	↔/↑	↔/↑
Metabolic demands	↑	↓	↓	↓
CO ₂ reactivity	↔	↔	↔	↔
Seizure threshold	↓	↓	↓	↓

autoregulation. Larger doses of β -adrenergic agonists can produce an increase in CMRO₂ and CBF that can be exaggerated in the setting of a defect in the blood–brain barrier. Dopamine causes an increase in CBF with little change in CMRO₂.

2. **Vasodilators.** Sodium nitroprusside, nitroglycerin, hydralazine, nimodipine, and nicardipine can increase CBF and ICP by direct cerebral vasodilation if MAP is maintained. β -Adrenergic–blocking agents probably have minimal effects. Despite these profiles, all these agents have been used safely during neuroanesthesia, particularly if CPP is maintained.

E. Cerebral Protection

1. Focal versus global cerebral ischemia

- a. **Focal ischemia** is characterized by an area of densely ischemic tissue that is surrounded by nonischemic brain, which may provide collateral flow to the penumbral margins. This residual blood flow may allow neurons to survive for varied periods of time (e.g., thrombolysis within 3 hours after stroke onset may prevent a full infarct due to reperfusion).
- b. **Complete global ischemia** is characterized by absent CBF (e.g., cardiac arrest). Tolerance for surviving global ischemia is on the order of minutes.

2. Agents

- a. **IV anesthetic agents:** High-dose **barbiturates** may slightly improve neurologic recovery from focal ischemia, possibly by decreasing metabolic rate or more likely by a direct pharmacologic effect. **Propofol** may also reduce focal ischemic cerebral injury, although it is not as extensively studied as the barbiturates. Etomidate aggravates ischemic brain injury. Early clinical reports suggest that prophylactic low-dose **lidocaine** may have neuroprotective effects in nondiabetic patients.
- b. **Volatile anesthetic agents** may provide some cerebral protection, but data are conflicting, and it is unclear whether this neuroprotection is sustained.
- c. **Nimodipine's** beneficial effects on vasospasm after subarachnoid hemorrhage (SAH) are well established and are likely mediated through neuronal, rather than vascular, effects. Clinical trials failed to detect a beneficial effect for acute stroke patients.
- d. **Steroids** have not been found to be beneficial after stroke or severe head injury.
- e. **Magnesium** confers significant neuroprotection in animal studies. However, a large clinical trial did not show protection in acute stroke victims.
- f. **Hypothermia** reduces metabolism for both neuronal and cellular functions and therefore may be beneficial in the setting of decreased cerebral perfusion. Induced mild hypothermia (12 to 24 hours) has been shown to be effective in reducing morbidity in patients who sustain cardiac arrest. By contrast, two clinical studies did not demonstrate improved outcome when induced mild hypothermia was used in patients after significant head injury or intraoperatively for aneurysm surgery.
- g. **Hyperthermia** profoundly worsens outcome from focal cerebral ischemia and should be avoided.
- h. Moderate **hyperglycemia** (>170 mg/dL) exacerbates neurologic injury after an ischemic insult. There are human data suggesting that normalizing blood glucose causes higher incidence of good outcome in stroke patients.

- i. **Other physiologic variables:** In addition to the above-mentioned variables of temperature and glucose, meticulous management of perfusion pressure, $p\text{CO}_2$, $p\text{O}_2$, pH normalization, and seizure prophylaxis contribute significantly to improved neurologic outcome in the setting of cerebral ischemia. Maintenance of a high-normal CPP can augment collateral CBF. By contrast, hypotension reduces CBF and exacerbates the injury. Normocapnia should be maintained. Seizures, which can increase CBF and ICP and decrease CPP, should be prevented and rapidly treated.
3. There is preliminary evidence that female sex hormones may confer some neuroprotection after TBI.

III. ELECTROPHYSIOLOGIC MONITORING

A. Electroencephalography (EEG) measures electrical activity of the neurons of the cerebral cortex and is thus used as a threshold marker for detecting ischemia due to inadequate CBF. It is used frequently during procedures that jeopardize cerebral perfusion, such as carotid endarterectomy, or to ensure electrical silence before circulatory arrest.

1. Normal CBF in gray and white matter averages 50 mL/100 g/min. With most anesthetic techniques, the EEG starts to become abnormal when the CBF decreases to 20 mL/100 g/min. Isoflurane is distinct as the EEG becomes abnormal when CBF is much lower at 8 to 10 mL/100 g/min. Cellular survival is endangered when CBF decreases to 12 mL/100 g/min (lower with isoflurane). Thus, EEG changes can warn of ischemia before CBF becomes insufficient to maintain tissue viability. Prompt detection of EEG changes may be treated with increases in perfusion pressure or shunting to restore CBF to prevent infarction.
2. The EEG may exhibit changes intraoperatively with no demonstrable neurologic deficit during postoperative examination. Cerebral ischemia can produce electrical dysfunction without causing neuronal cell damage because the blood flow threshold for electrical failure is higher than that needed to maintain cellular integrity.
3. Factors other than anesthetics that may affect the EEG include hypothermia (which may limit the usefulness of EEG during cardiopulmonary bypass), hypotension, hypoglycemia, hypoxia, tumors, vascular abnormalities, and epilepsy. An abnormal EEG in patients with pre-existing neurologic deficits, strokes in evolution, and recent reversible ischemic neurologic deficits can also make it difficult to interpret new changes.
4. **Anesthetic effects on the EEG** are generally global, which often helps distinguish them from the focal changes of ischemia. A predominance of slow activity is seen as the anesthetic depth increases. "Deep" anesthesia may cause marked EEG slowing, making detection of superimposed ischemic changes during critical periods difficult to interpret. Maintaining a constant level of anesthesia during critical periods (e.g., carotid clamping) facilitates EEG interpretation.

B. Evoked Potential Monitoring

1. **Sensory-evoked potentials (SEPs)** are electrical potentials generated within the neuraxis in response to stimulation of a peripheral or cranial nerve. As they travel from the periphery to the brain, these potentials can be recorded by electrodes placed over the scalp and along the transmission pathway. Evoked potentials (EPs) have lower voltage than background EEG activity, but summation of hundreds of signals using computerized devices makes it possible to extract them by averaging

out the random background EEG. A normal response implies that the conduction pathway is intact. **Damage to the pathway generally decreases the amplitude or prolongs latency** (i.e., the time from peripheral stimulus to arrival of potentials at the recording site) of the waveform peaks. EPs are classified according to the nerve tract being evaluated.

- a. **Somatosensory-evoked potentials (SSEPs)** are obtained by stimulating a peripheral nerve (e.g., median nerve at the wrist or posterior tibial nerve at the ankle or in the popliteal fossa) and recording the elicited signals over the spinal cord (spinal SSEPs) or cerebral cortex (cortical SSEPs). SSEPs are used most commonly to monitor spinal cord function during spinal cord or vertebral column surgery (e.g., major spine surgery with instrumentation) and may be used during peripheral nerve, brachial plexus, or thoracic aortic surgery (to detect spinal ischemia during aortic cross-clamping). Because SSEPs are conducted primarily by the dorsal column in the spinal cord, there are concerns about the reliability of SSEP monitoring for detecting threatened motor function (i.e., anterior spinal cord ischemia). For this reason, the “wake-up test” is used in some centers (see section VII.B.2), as well as motor-evoked potential (MEP) monitoring.
- b. **Brainstem-auditory evoked potentials (BAEPs)** are recorded by delivering an auditory stimulus to one ear through an ear-insert headphone. BAEPs reflect the transmission of electrical impulses along the auditory pathway and are monitored during posterior fossa surgery in an attempt to avoid brainstem or auditory (eighth cranial) nerve damage.
2. **MEPs.** Monitoring the integrity of the motor tracts within the spinal cord may be more reliable than SSEP monitoring during spinal surgery. The ventral motor columns of the spinal cord may be more susceptible to ischemia than the posterior proprioceptive fibers. Motor impulses can be generated by transcranial electrical stimulation. The evoked responses are measured as a potential over the spinal cord below the surgical field and in the muscle of interest. Anesthetics substantially modify transcranially induced potentials but less so if the stimulus is measured in the spinal cord below the surgical field.
3. **Electromyography (EMG)** records muscle responses to the stimulation of motor nerves. EMG is used frequently when there is risk of facial nerve injury during cerebellopontine angle surgery (e.g., posterior fossa surgery for meningioma). Because the EMG records motor responses to stimulation, neuromuscular-blocking agents are avoided during the periods of electrical stimulation.
4. **Confounding factors.** Interpretation of EP changes is confounded by factors similar to those that affect the EEG (e.g., anesthetics, temperature, hypotension, hypoxia, anemia, and preexisting neurologic lesions). Volatile anesthetics can depress SSEPs by reducing the amplitude or prolonging the latency of the SSEPs and can abolish the far more sensitive MEPs. BAEPs appear to be more resistant to the depressive effects of anesthetics than cortical SSEPs. IV anesthetics have less of an effect; barbiturates, propofol, and fentanyl/or remifentanyl are compatible with effective monitoring of cortical SSEPs, BAEPs, and MEPs.
5. **False positives.** Changes in EPs occur frequently and often are not associated with postoperative neurologic complications. Further work is required to establish the nature, magnitude, and duration of EP changes associated with irreversible damage.

IV. PREOPERATIVE CONSIDERATIONS FOR NEUROSURGIC PROCEDURES

- A. Intracranial compliance** may be decreased by intracranial mass lesions (e.g., tumor, hematoma, or abscess). Surrounding normal brain tissue may be compressed, leading to blood–brain barrier compromise, cerebral edema, and loss of cerebral autoregulation. Signs and symptoms of increased ICP are discussed in section I.C.3.
- B. A computed tomography (CT) or magnetic resonance imaging scan** should be reviewed. Midline shift, basal cistern obliteration, loss of sulci, and ventricular effacement suggest the presence of increased ICP. The degree of brain edema surrounding the mass and the site of the lesion in relation to major intracranial vessels and structures should be noted. Lesions near the dural venous sinuses may require exposure of the sinuses to the atmosphere and may be associated with a higher risk of venous air embolism (see section V.I.D.3).
- C. The pathology of the mass** is important in anticipating possible perioperative problems. Vascular lesions (e.g., meningiomas and some metastatic brain tumors) may bleed profusely. Infiltrating malignant tumors may render the patient particularly prone to postoperative cerebral edema.
- D. Preoperative fluid and electrolyte imbalances and glucose intolerance may be present due to poor oral intake, use of diuretics and steroids, and centrally mediated endocrine abnormalities.**
- E. Anticonvulsants** may be required to control seizures. **Corticosteroids** may be necessary to treat edema. These drugs should be continued perioperatively.
- F. Premedication** should be prescribed cautiously, because patients with intracranial disease may be extremely sensitive to the effects of central nervous system (CNS) depressants. Frequently, no premedication is given. If sedation is needed, diazepam (0.1 to 0.2 mg/kg orally) can be used. Additional sedation can be given once the patient arrives in the operating room. If the patient has impaired intracranial compliance and/or a high ICP, opioids should be avoided because of their respiratory-depressant effects and the increases in CBF that occur with hypercarbia.
- G.** In addition to standard monitoring (see Chapter 10), arterial catheters are used in most patients undergoing craniotomy. Capnography is particularly useful when reducing ICP by hyperventilation. A urinary catheter is placed to aid fluid management and diuretic therapy. Invasive monitoring (e.g., pulmonary artery catheter) may be indicated for patients with severe cardiac, renal, or pulmonary disease in the context of marked diuretic-induced fluid shifts. Because access to the neck is limited during neurosurgery, placing central lines by brachial or subclavian approaches should be considered. A second IV catheter for drug administration is often useful.

V. INTRAOPERATIVE MANAGEMENT

Anesthetic goals for intracranial procedures include hypnosis, amnesia, immobility, control of ICP and CPP, and a “relaxed brain” (i.e., optimal surgical conditions). Whenever possible, the anesthetic plan should provide an awake, extubated patient who can be evaluated neurologically at the end of the procedure.

- A. Induction of anesthesia** must be accomplished without increasing ICP or compromising CBF. Hypertension, hypotension, hypoxia, hypercarbia, and coughing should be avoided.
 - 1.** While thiopental ([not available in the United States] 3 to 7 mg/kg), propofol (2.0 to 2.5 mg/kg), midazolam (0.2 to 0.4 mg/kg), and etomidate (0.3 to 0.4 mg/kg) are all reasonable IV induction agents, the hemodynamic effects caused by these agents should be anticipated.

2. **An adequate mask airway** is essential to prevent hypoventilation and increased PaCO_2 . After induction, hyperventilation by mask can be started with either a nitrous oxide–oxygen mixture or 100% oxygen.
3. An intubating dose of muscle relaxant is given. Nondepolarizing agents are commonly chosen. Adequate relaxation should be obtained before laryngoscopy and intubation to avoid coughing and straining.
4. **Opioids** cause minimal changes in cerebral hemodynamics and are useful in blunting responses to intubation and craniotomy. Because intubation, placement of head pins, and craniotomy (skin incision and manipulation of the periosteum) represent the most stimulating periods during intracranial procedures, generous doses of narcotics are given before these manipulations. Fentanyl (5 to 10 $\mu\text{g}/\text{kg}$) and remifentanyl are most commonly used, because both have rapid onset and high potency. Lidocaine (1.5 mg/kg IV) can also be used to attenuate the cardiovascular and ICP responses to intubation.
5. **Low concentrations of a potent volatile agent** are occasionally added to prevent hypertension during the initial surgical stimulation.
6. After intubation, the eyes are covered with watertight patches to prevent irritation from surgical preparation solutions, and the head is carefully checked after final positioning to ensure good venous return. Because **access to the airway is limited during neurosurgic procedures**, breath sounds and ventilation should be checked after final positioning to ensure proper placement of the endotracheal tube, the tube should be adequately secured, and all connections in the breathing circuit should be securely tightened.

B. Maintenance

1. **Adequate brain relaxation** is necessary before opening the dura. This is achieved by ensuring adequate oxygenation, venous return, muscle relaxation, anesthetic depth, a PaCO_2 of 33 to 35 mm Hg (hyperventilation if dictated by surgical field), and often the administration of furosemide (10 to 20 mg IV), mannitol (0.5 to 1.5 g/kg IV), and dexamethasone before the craniotomy is completed. The surgeon can assess the need for further brain relaxation by checking the tension of the dura. If necessary, additional IV thiopental can be administered or CSF can be drained through a previously placed lumbar subarachnoid catheter.
 2. **Anesthetic requirements** are substantially lower after craniotomy and dural opening, because the brain parenchyma is devoid of sensation. If supplemental narcotics are needed, small doses of morphine or fentanyl can be given. A continuous infusion of propofol (50 to 150 $\mu\text{g}/\text{kg}/\text{min}$) and/or remifentanyl (0.1 to 0.5 $\mu\text{g}/\text{kg}/\text{min}$) produces a stable level of anesthesia and allows a rapid emergence. Large doses of **long-acting narcotics and sedatives are usually avoided during the last 1 to 2 hours of the procedure** to facilitate neurologic examination at the end of surgery and avoid potential drowsiness and hypoventilation.
 3. **Muscle relaxants** are frequently continued throughout the procedure to prevent movement. Patients receiving anticonvulsants (e.g., phenytoin) may require more frequent administration of muscle relaxants.
- C. **Emergence** should occur promptly without straining or coughing. IV lidocaine may be administered to suppress the cough reflex but may delay emergence. Toward the end of the procedure, PaCO_2 is normalized gradually if hyperventilation was employed. Hypertension should be controlled to minimize bleeding; rapidly acting IV agents such as labetalol, esmolol, sodium nitroprusside, and nitroglycerin are often used. Muscle relaxation is usually maintained until the head dressing is completed and then

reversal agents are administered. Before leaving the operating room, the patient should be awake so that a brief neurologic examination can be performed. The differential diagnosis of persisting unconsciousness after discontinuation of all anesthetics should include residual anesthesia, narcosis, hypothermia, hypoxia, hypercapnia, partial neuromuscular blockade, metabolic causes, and surgically induced increases in ICP (bleeding, edema, and hydrocephalus). Physostigmine (0.01 to 0.03 mg/kg IV) or naloxone (0.04 to 0.4 mg IV) may help antagonize pharmacologically induced CNS depression. The presence of new localized or generalized neurologic deficits should be immediately addressed and may be evaluated by CT and/or surgical reexploration.

- D. Perioperative fluid management** is designed to decrease brain water content, thereby reducing ICP and providing adequate brain relaxation, while maintaining hemodynamic stability and CPP.
 - 1. The blood–brain barrier** is selectively permeable. Gradients for osmotically active substances ultimately determine the distribution of fluids between the brain and intravascular spaces.
 - a. Water freely passes through the blood–brain barrier.** Intravascular infusion of free water may increase brain water content and may elevate ICP. Iso-osmotic glucose solutions (e.g., 5% dextrose in water) have the same effect, because the glucose is metabolized and free water remains. These are usually avoided during neurosurgery.
 - b. The blood–brain barrier is impermeable to most ions** including Na^+ . Unlike the peripheral vasculature, total osmolality, rather than colloid oncotic pressure, determines the osmotic pressure gradient across the blood–brain barrier. Consequently, maintenance of high-normal serum osmolality can decrease brain water content, while administration of a large amount of hyposmolar crystalloid solution may increase it.
 - c. Large, polar substances cross the blood–brain barrier poorly.** Albumin has little effect on brain ECF, because the colloid oncotic pressure contributes to only a small portion of total plasma osmolality (approximately 1 mOsm/L).
 - d.** If the blood–brain barrier is disrupted (e.g., by ischemia, head trauma, or tumor), permeability to mannitol, albumin, and saline increases so that these molecules have equal access to brain ECF. Under such circumstances, iso-osmolar colloid and crystalloid solutions seem to have similar effects on edema formation and ICP.
 - 2. Severe fluid restriction** can produce marked hypovolemia, leading to hypotension, reduced CBF, and ischemia of the brain and other organs, while only modestly decreasing brain water content. **Excessive hypervolemia** may cause hypertension and cerebral edema.
 - 3. Specific treatment recommendations.** The overall goal is to maintain normal intravascular volume and to produce a hyperosmolar state.
 - a. Fluid losses.** The fluid deficit incurred by an overnight fast is usually not replaced. Physiologic maintenance fluids are given. Third spacing of fluids during intracranial surgery is minimal and usually does not warrant replacement. Two thirds to total intraoperative urine output is replaced with crystalloid. If signs of hypovolemia develop, additional fluid is administered.
 - b. Assessment of blood loss** may be difficult during intracranial procedures because significant amounts can be hidden under the drapes. Also, irrigating solutions are used generously by the neurosurgeon.

- c. **The serum osmolality** is increased to 305 to 320 mOsm/kg. If large fluid requirements are anticipated, iso-osmolar crystalloid solutions such as 0.9% normal saline (309 mOsm/kg) may be preferable to hyposmolar solutions such as lactated Ringer's (272 mOsm/kg). However, large volumes of 0.9% normal saline may cause a metabolic acidosis. Therefore, it is prudent to follow the arterial blood gases and change to lactated Ringer's if indicated. Mannitol (0.5 to 2.0 g/kg IV) and/or furosemide (5 to 20 mg IV) are also administered. The marked diuresis produced by these agents demands close monitoring of intravascular volume and electrolytes.
 - d. **Hypokalemia** may develop from the use of steroids or potassium-wasting diuretics and is exacerbated by hyperventilation. Nevertheless, intraoperative administration of potassium is rarely necessary.
 - e. **Hyponatremia** may be produced by diuretics or syndrome of inappropriate antidiuretic hormone secretion (SIADH).
 - f. **Hyperglycemia** may worsen neurologic outcome after ischemia (see section II.E.2.d). Glucose-containing solutions are avoided in patients at risk for CNS ischemia.
- E. Immediate Postoperative Care.** Patients are observed closely in an intensive care setting after most intracranial neurosurgic procedures.
1. **The head of the bed** should be elevated 30 degrees to promote venous drainage.
 2. **Neurologic function**, including the level of consciousness, orientation, pupillary size, and motor strength, should be assessed frequently. Deterioration of any of these may indicate development of cerebral edema, hematoma, hydrocephalus, or herniation.
 3. **Adequate ventilation and oxygenation** are essential in patients with reduced consciousness.
 4. **Continuous monitoring of ICP** may be indicated if intracranial hypertension exists at the time of dural closure or is anticipated in the postoperative period.
 5. **Serum electrolytes and osmolality** should be checked.
 6. **SIADH** can be diagnosed by hyponatremia and serum hyposmolality with high urine osmolality and is treated by restricting free water intake.
 7. **Cerebral Salt Wasting Syndrome** can occur in the setting of injury to the brain or brain tumors. It is characterized by hyponatremia and polyuria. Polydipsia, extreme salt cravings, and dehydration may also be seen. It is a diagnosis of exclusion and can be difficult to distinguish from SIADH, with the main difference being volume status (hypovolemia in cerebral salt wasting syndrome and normal to hypervolemia in SIADH).
 8. **Diabetes insipidus** may occur after any intracranial procedure but is most common after pituitary surgery. **Polyuria** is associated with hyponatremia, serum hyperosmolality, and urine hyposmolality. Conscious patients can compensate by increasing their fluid intake; otherwise, adequate IV replacement is mandatory. **Aqueous vasopressin** (5 to 10 USP units subcutaneously or 3 units/h by IV infusion) may be given. Larger doses may cause hypertension. Alternatively, **desmopressin** (1 to 2 mg IV or subcutaneously every 6 to 12 hours) can be used and is associated with a lower incidence of hypertension.
 9. **Seizures** may indicate the presence of an expanding intracranial hematoma or cerebral edema. If a seizure occurs, airway patency, oxygenation, and ventilation must be ensured. The patient should be protected

from injury and the IV secured. For acute therapy, thiopental (50 to 100 mg IV), midazolam (2 to 4 mg IV), or lorazepam (2 mg) may be used. Fosphenytoin (15 to 20 mg/kg IV, 100 to 150 mg/min) can be administered to prevent recurrence.

10. **Tension pneumocephalus** may occur and should be suspected after failure to awaken from anesthesia. Skull radiographs or head CT scans confirm the diagnosis; treatment consists of opening the dura to release the air.

VI. SPECIFIC NEUROSURGICAL PROCEDURES

- A. Patients with **intracranial aneurysms** present for surgery electively or emergently following **SAH**.

1. Preoperative evaluation of patients with SAH should include all components of a routine preoperative evaluation (see Chapter 1), with attention to known associated physiologic perturbations. These include the **neurologic grade** (Table 25.2), presence of **vasospasm** (and the hemodynamic parameters that have been effective in relieving clinical symptoms), degree of hydrocephalus, ICP elevation, and concurrent drug therapy such as calcium channel blockade with nimodipine, which may cause moderately lower systemic pressures intraoperatively. **Electrocardiographic changes** are common after SAH and include arrhythmias and fluctuating ST-segment, QT-interval, and T-wave changes. These are probably caused by subendocardial injury following the autonomic discharge that occurs in association with the initial SAH. Provided these are not associated with cardiac dysfunction, no modification of patient management is necessary although recent data suggest that a heart rate of either less than 60 or greater than 80 or the presence of nonspecific ST/T wave abnormalities are independently associated with increased mortality in SAH patients receiving aneurysm clipping. Cardiac biomarkers may be increased as well.
2. Current practice is to intervene early during the first 72 hours after SAH for patients with neurologic grades I to III, which decreases the risk of rebleeding and facilitates the hypertensive management of vasospasm.
3. **Specific anesthetic considerations** include the following:
 - a. **Avoidance of hypertension**, which may increase the risk of aneurysm rupture, before aneurysm clipping. Prophylactic use of agents such as IV nicardipine, fentanyl, β -adrenergic blockers, lidocaine, or additional doses of barbiturates or propofol will often attenuate the blood pressure response to noxious stimulus such as laryngoscopy and intubation.

TABLE 25.2 Classification of Patients with Intracranial Aneurysms According to Surgical Risk (Hunt and Hess Classification)

Grade	Characteristics
I	Asymptomatic or minimal headache and slight nuchal rigidity
II	Moderate-to-severe headache, nuchal rigidity, no neurologic deficit other than cranial nerve palsy
III	Drowsiness, confusion, mild focal deficit
IV	Stupor, moderate-to-severe hemiparesis, possibly early decerebrate rigidity, vegetative disturbances
V	Deep coma, decerebrate rigidity, moribund

- b. **Avoidance of hypotension** to maintain adequate CPP in the recently insulted brain with resultant altered autoregulation and often marginally perfused areas of brain.
 - c. **Providing adequate brain relaxation** to optimize surgical exposure. Rapid reductions in ICP may affect transmural pressure and increase the risk of aneurysm rupture. This should be done cautiously before dural opening.
 - d. **Induced hypertension** may be requested during temporary clipping to improve collateral blood flow to regions that were perfused by the clipped arteries. Often, IV phenylephrine is used for this purpose. It is critical that hypertension be induced only **after** the temporary clip has been placed.
 - e. **Intraoperative aneurysm rupture** can produce rapid and **massive blood loss** requiring large-bore IV access for volume resuscitation. Accurate estimation of blood loss is essential to guide volume repletion. Induced hypotension, adenosine planned arrest, or, occasionally, manual pressure on the ipsilateral carotid artery in the neck may be helpful during the desperate situation of a large and uncontrolled premature rupture.
 - f. **Mild hypothermia** (34°C) has been traditionally used as a protective strategy for the brain during periods of cerebral ischemia. **Data from the Intraoperative Hypothermia for Aneurysm Surgery Trial (IHAST), however, suggest that hypothermia does not improve either neurologic or neuropsychologic outcome in good-grade surgical SAH patients.** Given the cardiac and infectious morbidity associated with hypothermia, it is now a matter of controversy whether hypothermia is the desired physiologic goal for aneurysm surgery.
 - g. Once the permanent clips have been placed on the aneurysm, prevention of postoperative vasospasm becomes important. Blood pressure is increased moderately, and fluids are administered to achieve a mildly positive fluid balance.
 - h. When appropriate, the anesthetic should be designed for a prompt emergence from anesthesia to enable an immediate neurologic examination to ensure that clip placement does not compromise the parent vessel.
- B. An arteriovenous malformation (AVM)** is a direct communication between cerebral arteries and veins without an intervening capillary bed. Because an AVM is a high-flow, low-resistance system, surrounding brain regions may be hypoperfused by the diversion of blood through the AVM ("steal" phenomenon). The most common presentations of an AVM are SAH, seizures, headaches, and, rarely, progressive neurologic deficits due to steal phenomenon.
- 1. Patients with AVMs may require anesthetic care for embolization procedures or surgical resection.
 - a. **Embolizations** are usually done to decrease blood flow to the AVM before surgical resection. Embolization may decrease the risk of intraoperative bleeding and postoperative reperfusion hyperemia.
 - b. Embolizations can be done under general anesthesia or monitored anesthesia care, which has the advantage of permitting continuous neurologic evaluation.
 - c. The anesthetist should be prepared for adverse reactions to the contrast dye (e.g., anaphylaxis and osmotic load that may cause congestive heart failure), vessel perforation (sudden and rapid blood loss requiring immediate craniotomy), and neurologic changes.

2. **Anesthetic management for surgical resection** of an AVM is similar to that for cerebral aneurysms.
 - a. The primary focus is on tight blood pressure control, because hypotension can lead to ischemia of hypoperfused regions. Hypertension can exacerbate perfusion pressure breakthrough, a poorly understood phenomenon that is thought to be caused by abrupt diversion of the AVM's blood flow to adjacent, previously marginally perfused brain, which produces sudden cerebral engorgement and hemorrhage. Should perfusion pressure breakthrough and brain swelling occur, they are commonly treated with barbiturates, hypothermia, and modest lowering of blood pressure.
 - b. Potential for large blood loss occurs in cases in which the AVM is large and has arterial feeders from more than one part of the cerebral arterial vasculature or when the preoperative embolization has been unsuccessful.
 - c. **Postoperative angiography** to confirm complete AVM resection is usually done immediately after surgery, sometimes within the operating room. Should any residual AVM be detected, further resection is indicated.
- C. **Posterior Fossa Surgery**
 1. **Posterior fossa tumors** may cause cranial nerve palsies, cerebellar dysfunction, and hydrocephalus due to obstruction of the fourth ventricle. Tumors or surgery around the glossopharyngeal and vagus nerves may impair the gag reflex and increase the risk of aspiration. Tumor resection that results in edema in the floor of the fourth ventricle may damage respiratory centers and necessitate postoperative mechanical ventilation.
 2. **Cardiovascular instability** resulting from surgical manipulation is common. Sudden severe bradycardia and hypertension occur if the trigeminal nerve is stimulated. Bradycardia, asystole, or hypotension may follow stimulation of the glossopharyngeal or vagus nerve. In such cases, the surgeon should be notified immediately, because the instability usually resolves with cessation of the stimulus. Pharmacologic treatment (e.g., atropine, glycopyrrolate, or ephedrine) is rarely necessary.
 3. **A sitting position** is occasionally used for posterior fossa surgery. The advantages include better surgical exposure, improved venous and CSF drainage, diminished bleeding due to lower venous pressures, and improved access to the airway, chest, and extremities for the anesthetist. The sitting position is also associated with a higher incidence of venous air embolism and cardiovascular instability. Modified supine, prone, and three-quarter prone positioning may be substituted for the sitting position because of these concerns.
 - a. **Venous air embolism** is a risk whenever the operative site is above the level of the heart and there is an open noncollapsible vein. Under these circumstances, an open venous sinus can entrain air and produce hypoxia, hypercarbia, bronchoconstriction, hypotension, and ultimately, cardiovascular collapse. Systemic arterial air embolism is a risk whenever right-to-left shunts occur and can cause myocardial and cerebral ischemia. Monitoring devices for the detection of air embolism and central venous catheters for aspiration of air are often placed when there is risk for venous air embolism.
 - b. **Methods used to monitor for venous air embolism** include Doppler ultrasound (which reveals a characteristic "mill wheel" murmur when air is entrained), capnography (which may reveal a sudden

decrease in end-tidal CO_2), end-tidal nitrogen monitoring, and transesophageal echocardiography (TEE). Of these, TEE is the most sensitive of the invasive monitors and Doppler ultrasound the most sensitive of noninvasive monitors.

- c. **If air is detected**, the focus is to prevent further air aspiration and treatment of the adverse consequences. First, the surgeons are notified so they can eliminate the source of air (close the dural opening, place bone wax, or flood the surgical field), nitrous oxide is discontinued, and air is aspirated from the central venous pressure catheter. If the patient remains stable, the prevention of further air entry may be all that is needed. If hypotension develops, Trendelenburg positioning, fluid administration, and inotropic support may be required.
4. At the end of surgery, the adequacy of the airway and respiration should be verified before extubation. Surgical manipulation may have caused damage to the cranial nerves or respiratory centers in the brainstem with resulting pharyngeal or respiratory dysfunction. Postoperative infarction, edema, or hematoma formation in the posterior fossa can cause rapid clinical deterioration. Close observation and prompt support including intubation, mechanical ventilation, and circulatory management may be required.

D. Awake Craniotomy

1. Recommended for removal of tumors involving or adjacent to speech and/or motor cortex and for epileptogenic focus resection. Intraoperative cortical mapping allows maximal resection with minimal postoperative neurologic dysfunction.
 2. The goals are to provide adequate analgesia and sedation as well as to ensure hemodynamic stability, a patent airway, and patient cooperation with neurologic testing during cortical stimulation. Adequate local anesthesia is required. Conscious sedation with propofol, dexmedetomidine, remifentanyl, or other agents may be used. Alternatively, an “asleep-awake-asleep” technique may be used as long as the patient is fully cooperative during testing. An LMA may be necessary for airway patency during the “asleep” portions of the case.
 3. Be prepared to treat a **cortical stimulation-induced seizure**. If one occurs, ask the neurosurgeons to irrigate the cortex with iced saline. Next, the seizure may be aborted with either midazolam or a small amount of barbiturate (thiopental 50 mg IV). These small doses may stop the seizure and not overly sedate the patient so that testing may continue. It is important that the IV catheter is not placed across a joint, which may be flexed and ineffective during a grand mal seizure. Before the procedure, the patient’s anticonvulsant level should be checked to ensure that it is therapeutic.
 4. **Allow adequate access to the patient’s airway**. This should include sufficient room to provide mask ventilation and laryngeal mask airway insertion should the circumstances require these interventions.
- E. **Transsphenoidal resection of the pituitary gland** is performed through either a nasal or a labial incision.

1. Although nonfunctioning **pituitary adenomas** are the most common tumor type, some patients have endocrine deficiencies due to hypothalamic-pituitary compression. Various hyperpituitarism syndromes may accompany functioning adenomas, including Cushing syndrome, acromegaly (with associated airway difficulties), and amenorrhea-galactorrhea.

2. ICP is not a concern as these tumors are usually small and unlikely to compromise intracranial compliance.
 3. **Uncontrollable bleeding** is rare but can be massive and catastrophic due to lack of exposure. Frontal craniotomy ultimately may be required to achieve hemostasis.
 4. **Monitoring.** The operating microscope obstructs access to the patient's head, so the endotracheal tube must be firmly secured. Continuous monitoring of ventilation is essential. Arterial monitors are usually not indicated unless indicated by other medical comorbidities.
 5. **Throat packs** will prevent blood from accumulating in the stomach and may reduce postoperative vomiting. The throat pack must be removed before extubation.
 6. At the conclusion of surgery, nasal breathing will be obstructed by packs. Patients should be prepared for this preoperatively.
 7. **Diabetes insipidus** may occur after transsphenoidal hypophysectomy (usually 4 to 12 hours postoperatively). Treatment with IV fluids or vasopressin may be necessary (see section VE.7). Some patients may develop postoperative adrenal insufficiency and require corticosteroids postoperatively.
- F. Stereotactic surgery** is performed through a burr hole, using a three-dimensional reference grid attached to the head with pins placed in the outer table of the skull. This approach allows localization of a discrete area of brain for biopsy or ablation. In most cases, the procedure can be performed under local anesthesia with IV sedation. Because the stereotactic apparatus precludes full access to the airway, sedation must be given with caution. If general anesthesia is needed after the frame is placed, the technique for securing the airway is selected based on the urgency of airway management and whether the stereotactic frame interferes with the mask or laryngeal mask airway. Because the frame may also prevent optimal head positioning for mask ventilation and direct laryngoscopy, laryngeal mask airways and equipment for awake intubation, preferably with a fiberoptic laryngoscope, should be available. The stereotactic frame can be removed in an emergency; newer models can be quickly removed to provide access to the airway.
- G. Deep brain stimulators** are inserted in patients with movement disorders (mostly Parkinson disease) who have failed medical therapy. Microelectrodes are inserted through burr holes to a precise location in the subthalamic nuclei, globus pallidum, or thalamus. A stereotactic headframe is required to identify and locate the electrode target.
1. Patients do not receive their morning dose of either dopaminergic or anticholinergic medications to improve electrode recordings that guide electrode placement to a specific cell layer.
 2. Patients are awake and not sedated during the electrode placement. Sedatives alter the electrode recordings. Once the electrodes are secure, appropriate sedation is desirable.
- H. Epilepsy surgery** is performed in patients with epilepsy of focal origin who are refractory to medical therapy or intolerant of the side effects of anticonvulsants.
1. **Excision of a seizure focus.** Electrophysiologic mapping of the epileptic focus and other cortical areas (e.g., language, memory, or sensorimotor) is often performed to maximize the resection of the epileptogenic lesion while minimizing the neurologic deficits. Awake craniotomy with IV sedation and local anesthesia of the scalp permits performance of the mapping procedure, which requires patient cooperation.

General anesthesia offers the advantages of patient comfort, immobility, a secure airway, and ability to control PaCO₂ and other variables. The anesthetic technique is chosen for its ability to augment (e.g., enflurane, methohexital, etomidate, or ketamine) or attenuate (e.g., benzodiazepines, barbiturates, or isoflurane) the seizure focus and its compatibility with intraoperative monitoring (see section III). Because there is often an initial increase in seizure activity postoperatively, anti-convulsants should be resumed promptly.

2. **Vagal nerve stimulators (VNS)** may be placed for medically refractory epilepsy. The electrodes are typically placed through an incision in the left neck and then tunneled to a generator located above the left pectoralis fascia. VNS are typically placed under general anesthesia with endotracheal intubation. Patients frequently are taking multiple antiepileptic drugs, which may cause resistance to neuromuscular-blocking drugs. Additionally, medications that may trigger seizure activity (e.g., ketamine) should be avoided. Postoperatively, monitoring for peritracheal hematoma and vocal cord paralysis should be performed.
- I. **Head trauma.** Anesthetic management of the patient with head trauma is complicated by the challenging combination of a “tight” head, full stomach, and potentially unstable cervical spine. While following the “ABCs” of resuscitation, the anesthesiologist should ascertain the mechanism and extent of injury. **Cervical spinal cord injury** must be suspected and the neck stabilized until cervical vertebral fracture is excluded.
 1. Patients who are responsive and ventilating adequately should receive supplemental oxygen and be observed closely for evidence of neurologic deterioration.
 2. Comatose patients require immediate endotracheal intubation for airway protection and to avoid hypercarbia and hypoxia, which can exacerbate increases in ICP and contribute to secondary brain injury.
 3. **Endotracheal intubation** should be accomplished rapidly, with blood pressure stability and without coughing or straining.
 - a. **A rapid sequence induction** is usually performed. If a cervical spine fracture has not been excluded, the neck should be immobilized with manual in-line stabilization (MILS). The anterior part of the cervical collar may be removed to apply gentle cricoid pressure (excessive pressure may displace a fracture) and obtain sufficient mouth opening. A short-acting induction agent such as propofol, thiopental, or etomidate is used to induce anesthesia, which is immediately followed by an intubating dose of muscle relaxant. Succinylcholine can be used safely unless contraindicated for other reasons (see section II.C and Chapter 13). Nondepolarizing relaxants also may be used. When MILS is used, the laryngoscopist should anticipate an increased likelihood of poor glottic visualization due to limited extension of the occiput, C1, and C2.
 - b. **Awake intubation** (e.g., blind nasal or fiberoptic) may be advocated because of full-stomach considerations, the potential for worsening neck injuries during manipulation of the airway, and anticipation of a difficult airway due to associated facial injuries. Awake approaches are often impractical or unwise in head-injured patients because of lack of cooperation, airway bleeding, and increases in ICP that can be induced by hypertension, coughing, and straining.
 - c. **Nasal intubation and nasogastric tube placement** are relatively contraindicated in the presence of a basilar skull fracture (e.g., CSF rhinorrhea, otorrhea, or Le Fort III facial fracture).

4. **Hypertension** in head-injured patients may be the body's compensatory effort to maintain CPP in the face of increased ICP. CPP should be maintained at 60 mm Hg. **Hypotension can be detrimental** in patients with elevated ICP and, when combined with tachycardia, should lead one to suspect bleeding from other injuries. Interventions to stop bleeding and restore intravascular volume should precede or proceed in concert with surgical treatment of the head injury.
5. **Hypoxia should be aggressively treated** as its presence dramatically worsens neurologic outcome in head-injured patients.
6. **Hyperglycemia should be treated** to improve neurologic outcome.
7. **ICP monitoring** can be performed if severe or progressive intracranial hypertension is suspected.
8. **Seizures** may accompany direct cerebral injury or signal the expansion of an intracranial hematoma.
9. **Brain contusion** is the most common type of head injury. Surgery is usually reserved for acute epidural hematomas and acute subdural hematomas. Subdural hematomas are much more common than epidural hematomas and carry a worse prognosis. Intracranial hypertension is frequently seen even after evacuation of hematomas because of severe brain swelling.
10. **Penetrating brain injuries** require early debridement of injured tissue and removal of bone fragments and hematoma. Skull fractures may require debridement, cranioplasty, and repair of dural lacerations.
11. **Anesthetic management** follows the general rules of maintaining CPP and reducing ICP and cerebral edema. Postoperative intubation and ventilatory support are frequently required for ICP control and airway protection in patients with prolonged loss of consciousness or an inadequate gag reflex. Preoperative alteration in the level of consciousness is helpful in predicting the need for postoperative intubation.
12. **Disseminated intravascular coagulation** is a frequent complication of an acute head injury, particularly those associated with a subdural hematoma. Frequent monitoring of the patient's coagulation status is recommended throughout the procedure.
13. **Corticosteroids are not indicated for head trauma** and may increase morbidity and mortality.
- J. **CSF shunts** are inserted in patients with hydrocephalus. A VP shunt is the most common treatment for hydrocephalus. A ventricular catheter is placed through a frontal burr hole and is attached to a subcutaneous reservoir and valve. These are then attached to the draining catheter which is tunneled subcutaneously to the upper abdomen where a minilaparotomy is performed to insert the catheter under direct supervision.
 1. The anesthetic management of these patients is determined primarily by the acuity of their disease. Acute hydrocephalus is a neurosurgic emergency where rapidly rising ICP could cause ischemic neurologic damage. Management should focus on measures, which will reduce the patient's ICP, maintain a CPP of at least 60 mm Hg, and enable rapid neurosurgic decompression. Anesthetic management of elective VP shunt insertion or revision employs a standard, well-managed, and safe anesthetic where factors that cause extreme ICP elevation are avoided.
 2. Some patients with a trapped ventricle can be treated with a ventriculostomy that is inserted through a frontal burr hole. A perforation is made in the ventricular septum under direct vision. These patients are anesthetized with general anesthesia as the ICP sometimes increases with the infused irrigating solution. This could potentially cause patient discomfort or altered consciousness.

VII. SURGERY ON THE SPINE AND SPINAL CORD

Surgery on the spine and spinal cord is undertaken for a variety of conditions, including intervertebral disk disease, spondylosis, stenosis, neoplasm, scoliosis, and trauma. The physiology of the spinal cord and brain is similar, even though absolute rates of blood flow and metabolism are lower in the spinal cord. Maintaining spinal cord perfusion pressure (which equals MAP minus extrinsic pressure on the cord) and reducing cord compression are clinical management objectives.

- A. **The prone position** is frequently used. Most patients can be anesthetized on a stretcher and “logrolled” onto the operating room table after endotracheal intubation. Awake intubation should be considered for patients with tenuous neurologic conditions that may be worsened by laryngoscopy/intubation or positioning (e.g., patients with unstable cervical or thoracic spine injuries). Under these circumstances, an abbreviated neurologic examination should be performed after intubation and transfer to ensure that injury has not occurred. The anesthetist should ensure that all pressure points are padded; neck and extremities are in neutral positions; eyes, ears, nose, and genitalia are free from pressure; and all monitors and lines are secured in place and functioning. Special attention should be paid to the endotracheal tube, since it can move or kink in the process of positioning. **Ischemic optic neuropathy is a potential complication** of prone cases associated with length of procedure (usually >5 hours), blood loss (usually >2 L), hypotension, and fluid resuscitation. Increased facial swelling may alter venous hemodynamics in the globe, leading to optic nerve ischemia and postoperative visual deficits. There are no standard preventive guidelines, but maintenance of systemic blood pressure near baseline values, frequent eye checks to assess for direct pressure on the globe, and maintenance of adequate perfusion are likely beneficial.
- B. **Surgery to correct scoliosis** can be accompanied by significant blood loss. Various techniques can be used to reduce homologous blood transfusion, including preoperative autologous donation, intraoperative hemodilution, use of intraoperative blood-scrubbing techniques, and meticulous patient positioning to prevent increased abdominal and intrathoracic pressures that can increase venous bleeding. Because of concern of neurologic sequelae, induced hypotension may not be advantageous in this procedure. Scoliosis surgery is accompanied by a 1% to 4% incidence of serious postoperative neurologic complications. Spinal instrumentation and distraction can cause spinal cord ischemia and result in paraplegia. Intraoperative monitoring of spinal cord function is used routinely.
 1. **SSEP and MEP monitoring** provide continuous evaluation of spinal cord function (see section III.B).
 2. **The selective wake-up test.** Intraoperatively, if there is uncertainty about the neurophysiologic monitoring, the presence of neuromuscular function is assured when patients are awakened briefly and asked to move their legs. If there is no leg movement, the spine distraction is released until movement is observed. Patients should be prepared for this event preoperatively. Wake-up tests can be performed in older children.
 3. **Total IV anesthesia** with remifentanyl and propofol is often selected because it is less likely to interfere with neurophysiologic monitoring than volatile anesthetics; however, it does not provide for a reliably fast intraoperative wake-up test. Alternatively, children, who often have robust nerve conduction, may be anesthetized with desflurane, with or without nitrous oxide and short-acting narcotics to achieve a much faster intraoperative wake-up. Communication of anesthetic interventions with the clinical neurophysiologist or technician is important.

C. After acute spinal cord injury, surgery may be required to decompress and stabilize the spinal cord. The primary goal in the initial management of acute spinal cord injury is to prevent secondary damage to the injured cord. This is accomplished by stabilizing the spine and correcting circulatory and ventilatory abnormalities that can exacerbate the primary injury. The presence of cervical cord injury should lead one to suspect associated head, face, or tracheal trauma; thoracic and lumbar spine injuries often are associated with chest or intra-abdominal trauma.

1. **Spinal shock** is characterized by vasodilation and hypotension. If the lesion involves the sympathetic cardiac accelerator nerves (T1–T4), bradycardia, bradyarrhythmias, atrioventricular block, and cardiac arrest can occur due to unopposed vagal activity. Spinal shock occurs because of functional transection of sympathetic innervation below the level of the injury and may persist for days to weeks. Bradycardia can be treated by atropine. Hypotension can be treated by fluid, vasopressors, or both. A pulmonary artery catheter may be helpful when other injuries are present and volume status is uncertain. Patients with high spinal cord injury may be unusually sensitive to the cardiovascular depressant effects of anesthetics because of an inability to increase sympathetic tone.
 2. **Lesions above C3–C4 necessitate intubation and mechanical ventilatory support** because of loss of innervation to the diaphragm (C3–C5). Lesions below C5–C6 may still cause as much as 70% reduction in vital capacity and FEV₁ with impaired ventilation and oxygenation.
 3. **Atony of the gastrointestinal tract and urinary bladder** necessitates a nasogastric tube and indwelling urinary catheter, respectively. These patients are also **prone to heat loss** because of inability to vasoconstrict.
 4. **Methylprednisolone** (30 mg/kg IV loading dose, followed by an infusion of 5.4 mg/kg/h for 23 hours) may improve the functional recovery of patients with acute spinal cord injuries if treatment is begun within the first 3 hours after injury. There is some controversy surrounding this therapy for spinal cord injury, and some centers do not follow this protocol.
 5. **Chronic spinal cord injuries** are discussed in Chapter 27.
 6. **Airway management** of patients with cervical spine injury is discussed in section VI.
- D.** Neuroradiologic procedures are performed in suites often remote from the main operating room. For a detailed discussion of anesthetic issues pertaining to the patient having a magnetic resonance imaging or interventional radiologic procedures, see sections IV and V in Chapter 33.

Suggested Readings

- Cottrell JE, Young WL, eds. *Cottrell and Young's Neuroanesthesia*. 5th ed. St. Louis: Mosby; 2010.
- Drummond JC, Patel PM, Neurosurgical anesthesia. In: Miller RD, 7th ed. *Miller's Anesthesia*. Philadelphia: Churchill Livingstone; 2010:2045–2088.
- Koht A, Sloan TB, Toleikis JR eds. *Monitoring the Nervous System for Anesthesiologists and Other Health Care Professionals*. New York: Springer; 2012.
- Mashour GA, Farag E, *Case Studies in Neuroanesthesia and Neurocritical Care*. New York: Cambridge; 2011.
- Newfield P, Cottrell JE. *Handbook of Neuroanesthesia*. 5th ed. Philadelphia: Lippincott; 2012.
- Patel PM, Drummond JC. Cerebral physiology and the effects of anesthetic drugs. In: Miller RD, ed. *Miller's Anesthesia*. Philadelphia: Churchill Livingstone; 2010:305–339.
- Seubert CN, Mahla ME, Neurologic monitoring. In: Miller RD, ed. *Miller's Anesthesia*. Philadelphia: Churchill Livingstone; 2010, 1477–1514.
- Koht A, Sloan TB, Toleikis JR eds. *Monitoring the Nervous System for Anesthesiologists and Other Health Care Professionals*. New York: Springer; 2012.

I. ANESTHESIA FOR OPHTHALMIC SURGERY**A. General Considerations**

1. **Intraocular pressure (IOP;** normal range 10 to 22 mm Hg) is principally determined by (1) aqueous volume (the rate of production of aqueous humor in relation to its rate of drainage) and (2) the blood volume within vessels of the eye. Due to scleral inelasticity, small volume changes result in large changes in IOP.
 - a. **Factors that may increase IOP** include hypertension, hypercarbia, hypoxia, laryngoscopy and endotracheal intubation, venous congestion, vomiting, coughing, straining, bucking, external pressure on the eye, succinylcholine, and ketamine.
 - b. **Factors that may decrease IOP** include hypocarbia, hypothermia, central nervous system depressants, ganglionic blockers, most volatile and intravenous (IV) anesthetics, nondepolarizing muscle relaxants, mannitol, diuretics, acetazolamide, and head elevation.
2. **Glaucoma**
 - a. **Open-angle glaucoma** usually arises from chronic obstruction of the aqueous humor drainage and is characterized by a progressive, insidious course that may *be painless*.
 - b. **Closed-angle glaucoma** results from acute aqueous outflow obstruction due to a narrowing of the anterior chamber. This occurs as a result of pupillary dilation or lens edema and is *painful*.
3. **Oculocardiac reflex**
 - a. The oculocardiac reflex (OCR) is mediated by afferent impulses via the ophthalmic branch (CN VI) of the trigeminal nerve to the ciliary ganglion and efferents from the vagus nerve (CN X). Increases in IOP, manipulation of the globe, or traction on the extrinsic eye muscles may result in bradycardia or asystole. Administration of ocular regional anesthesia may also elicit this response. OCR is common in patients undergoing strabismus surgery.
 - b. The OCR should be promptly treated by cessation of the stimulus. Atropine (0.01 to 0.02 mg/kg IV) may be administered if bradyarrhythmias persist. The reflex fatigues quickly with repeated stimulation. However, if the reflex persists, infiltration of local anesthetic near the extrinsic eye muscles or placement of a peribulbar or retrobulbar block is effective. Alternatively, atropine prophylaxis can be helpful in preventing the reflex.
4. **Commonly used drugs**
 - a. **Topical.** Most ophthalmic medications are highly concentrated solutions that are administered topically and may produce systemic effects.
 1. **Mydriatics**
 - a. **Phenylephrine** eye drops may cause hypertension and reflex bradycardia, especially when administered as a 10% solution.

For this reason, a 2.5% solution is commonly used. It dilates the pupil and constricts periocular blood vessels.

- b. **Cyclopentolate, atropine, and scopolamine** are anticholinergic agents that can produce central nervous system toxicity (e.g., confusion and seizures), particularly in the elderly and young. Additional effects include flushing, thirst, dry skin, and tachycardia.
- c. **Epinephrine** 2% topical solution reduces IOP in open-angle glaucoma by decreasing aqueous secretion while improving outflow. Complications can include hypertension, tachycardia, dysrhythmias, and syncope.
2. **Miotics.** Cholinergic drugs (e.g., pilocarpine 0.25% to 4% solution) may produce bradycardia, salivation, bronchorrhea, and diaphoresis.
3. **Drugs that decrease IOP**
 - a. **β -Adrenergic antagonists** (e.g., timolol or betaxolol) may cause bradycardia, hypotension, congestive heart failure, and bronchospasm.
 - b. **Anticholinesterases**, such as echothiophate, depress plasma cholinesterase activity for 2 to 4 weeks and may prolong recovery from succinylcholine and mivacurium.
 - c. **Apraclonidine**, an α_2 -adrenergic agonist, is used to reduce IOP by decreasing aqueous production and improving outflow. Systemic side effects may include sedation and drowsiness. Rebound hypertension may result from acute withdrawal after chronic therapy.
- b. **Systemic**
 1. **Acetazolamide**, a carbonic anhydrase inhibitor, is administered systemically to control aqueous humor secretion. Chronic use can lead to the development of hyponatremia, hypokalemia, and metabolic acidosis.

B. Anesthetic Management

1. **Preoperative evaluation.** Patients undergoing eye surgery are often at the extremes of age, presenting with significant concomitant diseases that may require careful evaluation (e.g., the formerly premature infant with bronchopulmonary dysplasia for retinal surgery or the elderly patient with cardiovascular disease for cataract excision). Preoperative testing should be dictated by medical comorbidities. However, recent evidence indicates that even complex patients undergoing low-risk eye surgery without routine testing have no increased risk of adverse events as compared with those who do undergo evaluation.
2. **Avoidance of coughing, sudden movement, or straining is essential.** Unexpected patient or eye movements during delicate microscopic intraocular surgery can lead to increased IOP, choroidal hemorrhage, expulsion of vitreous material, or loss of vision.
3. **Regional anesthesia**
 - a. **Ophthalmic procedures** such as cataract extraction, corneal transplant, anterior chamber irrigation, oculoplastic procedures, and even vitreoretinal procedures lasting 3 to 4 hours can be performed under regional anesthesia and light sedation.
 - b. Patient cooperation and lack of head motion are important for the success of this technique. Patients who are unable to participate due to extremes of age, impaired hearing, psychosis, or a language barrier or who are unable to maintain a relatively motionless position because of chronic cough, tremor, or arthritis may not be candidates for regional anesthesia for delicate eye surgery.

- c. The advantages of regional anesthesia include a lower incidence of coughing, straining, and emesis on emergence, reliable postoperative analgesia, and earlier discharge compared with general anesthesia.
- d. **IV sedation** may be used perioperatively. Midazolam (0.25 to 1 mg IV), fentanyl (10 to 50 μg IV), remifentanyl (0.25 to 1 $\mu\text{g}/\text{kg}$ IV), or propofol (5 to 20 μg IV) can be administered just before the regional injection. Patients should have standard ASA monitors during regional block placement and receive supplemental oxygen if indicated.
- e. **Technique.** Intraocular surgery requires adequate sensory and motor block of the eye and often the eyelids as well. Anesthesia of the eye is accomplished by injecting local anesthetic into the retrobulbar space, peribulbar space, or episcleral space, facilitating neural blockade of cranial nerves II through VI.
- f. **Retrobulbar block** is achieved by injecting 4 to 6 mL of a 50:50 mixture of 1% lidocaine and 0.375% bupivacaine (with 5 units hyaluronidase) within the muscle cone formed by the four recti muscles and the two oblique muscles. With the eye in a neutral position, a 23- or 25-gauge Atkinson 1 1/4 inch needle is inserted through the lower lid or conjunctiva at the level of the inferior orbital rim in the inferotemporal quadrant. The needle is first advanced slightly inferiorly and temporally approximately 1.5 cm; once past the equator of the eye, the needle is then directed superiorly and nasally toward the apex of the orbit to a depth of approximately 3.5 cm, while feeling for a “pop” as the needle penetrates through the muscle cone. Retrobulbar hemorrhage is a potential complication, the treatment of which is surgical decompression (Fig. 26.1).

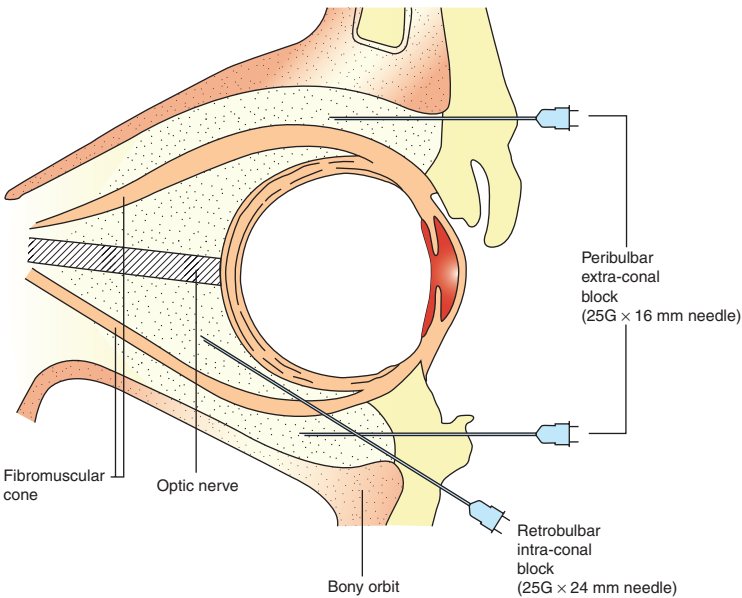


FIGURE 26.1 Retrobulbar and peribulbar blocks.

- g. **Peribulbar block.** No attempt is made to enter the muscle cone. A 25-gauge 3/4 inch Atkinson needle is advanced along the inferior orbital floor to a depth of approximately 2.5 cm. Between 8 and 10 mL of local anesthetic is required, and hyaluronidase (3.75 to 15 units/mL) is frequently added to help facilitate spread through the muscle cone. Careful aspiration before injection is required for both blocks, followed by gentle massage or orbital compression to promote spread of the anesthetic (although orbital compression should be avoided in patients with glaucoma). If desired, the facial nerve can also be blocked by infiltrating 2 to 4 mL of additional local anesthetic along the inferior and superior orbital rim to help prevent squinting. The retrobulbar block provides faster, more reliable anesthesia and akinesia but has a higher complication rate as compared to the peribulbar block.
 - h. **Episcleral block (sub-Tenon block).** Local anesthetic is injected into the episcleral space via a needle or cannula. Needle entry is into the fornix at an angle tangential to the globe, between the conjunctival semilunar fold and globe. Upon entry into the conjunctiva, the needle is shifted medially and advanced posteriorly until a “click” is felt. Local anesthetic is then injected, with volumes greater than 6 mL producing both globe analgesia and akinesia. Using the cannula technique, topicalization is performed and the bulbar conjunctiva lifted in the inferonasal quadrant with forceps. A small nick is made in the conjunctiva and Tenon capsule using blunt Westcott scissors, accessing the episcleral space. A specially designed blunt cannula is inserted, advanced into the episcleral space, and 3 to 4 mL of local anesthetic injected.
 - i. **Complications of regional anesthesia** are infrequent but include direct optic nerve trauma, transient globe compression with increased IOP, globe perforation, and stimulation of the OCR. Hyaluronidase is toxic to the eye if injected into the globe. Intravascular injection of local anesthetic may cause seizures or myocardial depression. Rarely, the local anesthetic may dissect proximally along the neural sheath of the optic nerve and a total spinal can occur; treatment is supportive.
 - j. During the procedure, fresh air at a flow rate of 10 to 15 L/min is provided to the patient under the drapes using a large face mask. This helps to remove exhaled carbon dioxide and helps offset the sense of claustrophobia some patients may experience. Oxygen may be used if indicated, but the surgeon should be notified not to use electrocautery while oxygen is flowing. Capnography is frequently used since visual inspection of respiration may be difficult while patients are draped.
4. **General anesthesia**
- a. Since the eye is highly innervated, eye surgery requires sufficient depth of general anesthesia to prevent eye motion, coughing, straining, or hypertension. General anesthesia with an inhalation agent, supplemented by a nondepolarizing muscle relaxant, is usually satisfactory.
 - b. **Ketamine** can cause blepharospasm, nystagmus, and vomiting. It may increase arterial pressure and IOP. For these reasons, ketamine usually is a poor choice for most ophthalmic surgery. Low doses of ketamine, however, do not increase IOP and may be useful as a supplement to IV sedation for retrobulbar or peribulbar block.

- c. **Smooth emergence and extubation** are particularly desirable after ophthalmic surgery. This may be facilitated by thorough posterior pharyngeal suctioning while the patient is still deeply anesthetized, administration of an opioid to reduce the cough reflex, and IV lidocaine (1 to 1.5 mg/kg) 5 minutes before planned extubation. Deep extubation is also an option but does not guarantee a smooth emergence.

C. Ophthalmic Procedures

1. **Open-eye injury.** Penetrating eye trauma may be a surgical emergency but often needs to be addressed within 24 hours of injury to minimize the risk of infection. It requires a carefully conducted anesthetic designed to prevent aspiration and favorably affect IOP (see section I.A.1). A sudden increase in IOP can result in extrusion of ocular contents and cause permanent vision loss. Trauma to the eye and orbit, long-duration and complex surgery, and a crying patient with a full stomach usually mandate general endotracheal anesthesia.
 - a. Succinylcholine administered during a rapid sequence induction causes an increase in IOP of approximately 6 to 12 mm Hg for 10 minutes. Pretreatment with nondepolarizing muscle relaxants may attenuate but does not ablate this response. Nevertheless, succinylcholine often is the drug of choice to quickly establish adequate intubating conditions in the eye surgery patient with a full stomach. Alternatively, nondepolarizing muscle relaxants in higher doses can be used, but adequate intubating conditions may not be achieved for 60 to 90 seconds.
 - b. An adequate depth of anesthesia and degree of neuromuscular blockade must be ensured before laryngoscopy and intubation to minimize increases in IOP (which may rise to 40 to 50 mm Hg) secondary to straining, coughing, and bucking.
 - c. In children, if an IV cannot be placed, an inhalation induction using cricoid pressure and nonirritating volatile anesthetics (e.g., nitrous oxide, sevoflurane) may be necessary.
2. **Strabismus repair** is a procedure to alter the lengths of the extraocular muscles.
 - a. Surgical manipulation frequently elicits the **oculocardiac reflex** (see section I.A.3).
 - b. **Postoperative nausea and vomiting (PONV)** are very common (40% to 85% incidence in untreated patients). Minimizing opioids, use of multimodal analgesia (i.e., acetaminophen and ketorolac), antiemetics given 30 minutes before surgery, and gastric decompression with an orogastric tube can help reduce PONV.
3. **Retinal surgery for detachment and vitreous hemorrhage** often is performed on patients in extremes of age and/or with multiple comorbidities. Meticulous attention to airway management, fluid status, normothermia, and postoperative transport is crucial (see Chapter 29). Premature infants, especially those less than 60 weeks postconceptional age, are at risk for postoperative central apnea. They should demonstrate a 12-hour apnea-free interval before discharge. Patients with diabetes or sickle cell anemia also may require retinal surgery (see Chapters 6 and 34, section X.C).
 - a. **Regional anesthesia** is suitable for short procedures (<3 hours) in cooperative patients, although unexpected movement during the delicate retinal repair may result in vision loss.

- b. An **intravitreal gas bubble** containing an inert, high molecular weight, low-diffusivity gas such as sodium hexafluoride (SF_6), perfluoropropane (C_3F_8), octofluorocyclobutane (C_4F_8), or air, may be injected at the conclusion of surgery to reduce intravitreal bleeding. The presence of nitrous oxide will rapidly expand the bubble and increase IOP. Hence, **nitrous oxide should be avoided** in surgeries where an intravitreal gas bubble is injected. Because these gas bubbles remain for various periods of time, readministration of nitrous oxide should be avoided for 5 days after an air injection, 10 days after SF_6 injection, and 60 days after C_3F_8 injection. *Due to pressure changes associated with air travel, patients should be instructed to avoid air travel for 3 to 4 weeks after intravitreal gas injection.*

II. ANESTHESIA FOR OTORHINOLARYNGOLOGIC PROCEDURES

A. General Considerations

1. **Airway.** The airway is often shared with the surgeon. Pathology, scarring from previous surgery or irradiation, congenital deformities, trauma, or manipulation can produce chronic or acute airway obstruction, bleeding, and a potentially difficult airway. Preoperative discussion with the surgeon and analysis of previous anesthetic records regarding perioperative airway management, endotracheal tube size and position, patient positioning, and use of nitrous oxide and muscle relaxants are essential. The patient may require awake examination of the airway under sedation and topical anesthesia or an awake fiberoptic intubation before induction of general anesthesia.
2. Patients presenting for ORL surgery may have a history of heavy smoking, alcohol abuse, obstructive sleep apnea (OSA), and chronic upper respiratory tract infections. Preoperative testing should be dictated by medical comorbidities.
3. In addition to standard monitors, intra-arterial blood pressure and urine output monitoring may be needed for lengthy cases or surgeries with significant anticipated blood loss.
4. **Extubation** after any upper airway surgery requires careful planning. Extubation is performed once the throat packs are removed, the pharynx is suctioned, and full protective laryngeal reflexes return. Excessive upper airway bleeding, edema, or pathology may preclude extubation in the operating room.

B. Ear Surgery

1. Preoperative considerations
 - a. Ear surgery often involves dissecting and preserving the **facial nerve (CN VII)**. Primary anesthetic concerns include patient positioning, facial nerve preservation, use of nitrous oxide, adequate hemostasis, smooth emergence, and prevention of PONV.
 - b. The **middle ear** communicates with the oropharynx via the eustachian tube. If eustachian tube patency is compromised by trauma, edema, inflammation, or congenital deformity, normal venting of middle ear pressure cannot occur. In this situation, a high concentration of nitrous oxide can increase middle ear pressure to 300 to 400 mm Hg in 30 minutes. Conversely, acute cessation of nitrous oxide can result in rapid resorption and a net negative pressure in the middle ear. These changes may result in alteration of middle ear anatomy, rupture of tympanic membrane, disarticulation of artificial stapes, disruption of surgical grafts, and PONV.

- c. **Positioning.** During surgery, the patient's head often is elevated and turned to the side. Extremes of head position should be assessed preoperatively to determine limits of range of motion, especially in patients with arthritis or cerebrovascular disease. Furthermore, attention to adequate venous drainage is necessary with extremes of head position.
 2. **Anesthetic technique.** Anesthesia is induced with a hypnotic and short-acting muscle relaxant or by inhalation and is maintained with a volatile anesthetic or total intravenous anesthesia (TIVA). The use of nitrous oxide should be discussed with the surgeon or avoided; nitrous oxide should be discontinued at least 30 minutes before placement of a tympanic membrane graft.
 - a. Delicate microsurgery of the ear requires adequate hemostasis. Volatile anesthetics, remifentanyl, and α - or β -adrenergic antagonists work well to maintain mean arterial pressures of 60 to 70 mm Hg. Elevation of the head of the bed to approximately 15 degrees to decrease venous congestion and local application of epinephrine for vasoconstriction usually improve operating conditions.
 - b. Myringotomy with tube placement is one of the most frequently performed outpatient pediatric surgeries. These procedures are short and can usually be performed under mask anesthesia with or without an IV placement. Deep anesthesia using volatile anesthetics alone or in combination with remifentanyl can be used. If the procedure is performed without an IV line, intranasal fentanyl (1 to 2 $\mu\text{g}/\text{kg}$) and preoperative oral acetaminophen (20 to 40 mg/kg) can be used for postoperative pain management.
- C. Nasal Surgery**
1. **Anesthetic technique.** Nasal surgery can be performed with local or general anesthesia. With either technique, the surgeon may initially apply 4% cocaine to the nasal mucosa, followed by injection of 1% to 2% lidocaine with 1:100,000 to 1:200,000 epinephrine for hemostasis. These agents may cause tachycardia, hypertension, and arrhythmias. In a healthy adult, the cocaine dose should not exceed 1.5 mg/kg (each drop of a 4% solution contains about 3 mg of cocaine). Smaller doses should be used when administered with epinephrine or in patients with cardiovascular disease. General anesthesia may be needed to provide immobility, airway protection, or amnesia.
 - a. For endoscopic sinus surgery, some providers advocate for total intravenous anesthesia (TIVA), which has been associated with decreased blood loss as compared with volatile anesthetics.
 2. After **nasal cosmetic surgery**, the nose is unstable and application of a face mask is undesirable. Smooth emergence and extubation are important to decrease postoperative bleeding and to avoid laryngospasm and the need for positive-pressure ventilation by mask.
 3. **Blood loss** during nasal surgery may be substantial and difficult to estimate. A throat pack may help decrease PONV by preventing passage of blood into the stomach. An orogastric tube may be placed to evacuate the stomach of any swallowed blood.
 4. Patients with **severe epistaxis** presenting for internal maxillary artery ligation or embolization often are anxious, hypertensive, tachycardic, and hypovolemic. They are assumed to have a full stomach containing blood and induction of anesthesia, and endotracheal intubation should be planned accordingly. Hypertension should be controlled to reduce blood loss. Posterior nasal packing, while helpful, can cause edema and

hypoventilation. Because the extent of blood loss is difficult to assess, adequate IV access (16- or 18-gauge IV) and blood for transfusion should be available. Removal of the posterior packing can be associated with substantial blood loss.

D. Upper Airway Surgery

1. Tonsillectomy and adenoidectomy

a. **Preoperative evaluation** should seek a history of bleeding disorders, recent respiratory tract infection, and OSA. The STOPBANG questionnaire for OSA is a useful screening tool.

1. Do you **snore** loudly at night?
2. Do you feel **tired** during the day?
3. Has anyone **observed** apnea?
4. Do you have or are you being treated for high blood **pressure**?
5. Is your **BMI** greater than 35?
6. Is your **age** over 50?
7. Is your **neck** circumference over 17 inches (male) or 16 inches (female)?
8. Is your **gender** male?

A score of 5 or greater is strongly predictive of OSA. Patients with OSA may be difficult to ventilate and intubate. These patients also have an increased incidence of postoperative respiratory complications and should be considered for prolonged observation in the PACU or overnight admission to monitor for respiratory compromise.

b. Most **children** receive an inhalation induction, followed by placement of an appropriately sized IV. A technique consisting of a volatile agent, supplemented with an opioid (e.g., morphine 0.05–0.1 mg/kg IV), usually is performed. Muscle relaxation facilitates intubation but is not mandatory. Inadvertent endotracheal tube obstruction, disconnection, or dislodgement can occur during head and mouth gag manipulation. Endotracheal tubes should be firmly secured at the midline of the mandible for surgical access.

c. **At the end of surgery**, the throat pack should be removed, an orogastric tube should be placed to empty the stomach of any swallowed blood, and the pharynx should be suctioned thoroughly. Administration of antiemetic agents should be considered. Extubation may be performed under deep anesthesia or when the patient is awake with intact airway reflexes. The use of an oropharyngeal airway after surgery can cause surgical wound disruption and bleeding if not carefully placed in the midline. Nasal airways are useful alternatives.

d. Auscultate for unobstructed breathing before transport to the post-anesthesia care unit (PACU) and checked for a dry pharynx before discharge.

2. Tonsillar rebleeding

a. **Rebleeding** after a pediatric tonsillectomy occurs in approximately 5% of cases. Primary bleeds occur within 24 hours after surgery. Secondary bleeding is common 7 to 10 days postoperatively as the eschar sloughs. Hematemesis, tachycardia, frequent swallowing, pallor, and airway obstruction may be seen. The extent of blood loss is often underestimated because the blood is swallowed.

b. **Posttonsillectomy hemorrhage** is a surgical emergency, and induction of anesthesia in a bleeding, hypovolemic child can result in severe hypotension or cardiac arrest. Appropriate IV access is necessary, and the patient should be adequately resuscitated (with blood

products if necessary) before reoperation. Hematocrit, coagulation studies, and availability of blood products should be ascertained. Doses of anesthetic agents may need to be reduced in the setting of hypovolemia.

- c. Because the stomach is full of blood, a **rapid-sequence induction** should be performed. Two working suctions and an additional stylet-tipped endotracheal tube one size smaller than anticipated should be available. The surgeon should be present. Extubation is safest with the patient awake.
3. **A tonsillar or parapharyngeal abscess** may present with trismus, dysphagia, and a distorted, compromised airway. The surgeon may be able to decompress the abscess with needle aspiration before the induction of anesthesia. If needed, an awake fiberoptic intubation may be performed. Anesthetic management and extubation procedures are similar to those for tonsillectomy (see section II.D.1). In Ludwig angina, a cellulitis of the submandibular and sublingual spaces may extend to the anterior compartments of the neck. Trismus, airway edema, and distorted anatomy often make visualization by direct laryngoscopy of the glottic opening difficult. General anesthesia is contraindicated if stridor occurs at rest. *Awake fiberoptic intubation is the safest approach in this scenario.* If awake fiberoptic intubation is not possible, consider tracheostomy under local anesthesia to secure the airway.
4. **Direct laryngoscopy** is indicated for diagnostic (biopsy) or therapeutic (vocal cord polyp removal) purposes and may involve potentially compromised airways. Evaluation of imaging studies (magnetic resonance imaging or computed tomography) and laboratory studies (pulmonary flow-volume loops) may help identify airway abnormalities and potential perioperative problems. Many patients have a history of smoking and cardiopulmonary disease.
 - a. **Anesthetic management** is described in Chapter 21, section IV.
 - b. **Postoperative airway edema** may develop. If anticipated, dexamethasone (4 to 10 mg IV) may be given. Additional treatment includes head elevation, humidified oxygen by mask, and nebulized racemic epinephrine. Occasionally, cessation of nebulized racemic epinephrine is associated with the return of airway edema.
5. **Laser use in ORL surgery.** **Laser** (light amplification by stimulated emission of radiation) produces a high-energy, high-density beam of coherent light that generates focused heat on contact with tissue. The emission media used to produce the monochromatic light determines the wavelength.
 - a. **Short-wavelength (1 μ m) laser** (argon gas, ruby, neodymium: yttrium aluminum garnet [Nd:YAG]) emissions in the red-green visible part of the electromagnetic spectrum are poorly absorbed by water but well absorbed by pigmented tissues such as the retina and blood vessels.
 - b. **Infrared (10 μ m) carbon dioxide laser** emissions are well absorbed by water and superficial surface cells and are commonly used to treat laryngeal lesions. They cannot be transmitted through fiberoptics.
 - c. **Eyes must be protected** from the laser beam. Operating room personnel must wear appropriate safety goggles (green tinted for argon, amber for Nd:YAG, and clear for carbon dioxide). The patient's eyes should be taped closed and covered with safety goggles.
 - d. **The most serious complication of laser airway surgery is airway fire.** The likelihood of fire depends on the gas environment of the airway,

the energy level of the laser, the manner in which the laser is used, the presence of moisture, and the type of endotracheal tube used. Oxygen and nitrous oxide both support combustion. A safe gas mixture during laser upper airway surgery is oxygen/air or oxygen/helium to achieve a fraction of inspired oxygen of 25% to 30%.

- e. **Safe laser use.** Lasers should be used intermittently, in the non-continuous mode, and at moderate power (10 to 15 W). Surgeons should not use the laser as a cautery and should share responsibility for fire prevention by limiting the energy input, allowing time for heat dispersal, packing aside nontarget tissue and endotracheal tube cuffs with moist gauze, and maintaining moisture (as a heat sink) in the field.
- f. **Airway options during laser surgery.** Specially designed, fire-resistant, impregnated or shielded endotracheal tubes (e.g., Xomed Laser-Shield II endotracheal tube) are used, and the cuff is filled with blue saline. For some procedures, intubation is not possible because the surgeon requires free access to the surgical field. Options include the following:
 1. Jet-Venturi technique. This technique eliminates the need for an endotracheal tube, but airway fire may still occur due to dry tissue igniting. All patients are at risk for barotrauma; pediatric patients, patients with emphysema, and patients with chronic obstructive pulmonary disease are at highest risk.
 2. Ventilation and apneic oxygenation. The surgeon operates during periods of apnea and stops intermittently to allow the anesthesiologist to ventilate and oxygenate the patient.
- g. **If an airway fire occurs,** stop ventilation and immediately disconnect the endotracheal tube from the breathing circuit, remove the tube, pour saline in the pharynx to absorb the heat, suction, mask ventilate, and reintubate with a new endotracheal tube. After the fire is extinguished, examine the airway by bronchoscopy. **Complications** include airway edema, inhalation injury, tracheal and laryngeal granulation tissue formation, and airway stenosis.
- h. The **anesthetic technique** for laser surgery is similar to that described above (section II.D.5.f) and Chapter 21, section IV.E. Goals include adequate surgical exposure, fire prevention, and return of protective airway reflexes before extubation. Surgeons may or may not request muscle relaxants for vocal cord examination or manipulation; therefore, communication with the surgical team is essential before proceeding with induction. Endotracheal intubation, jet ventilation, or intermittent mask ventilation may be used. Regardless of the technique, a mixture of oxygen/air is essential (<30% oxygen). Because airway edema may occur, the patient is given humidified oxygen postoperatively and is observed closely in the PACU. Corticosteroids or aerosolized racemic epinephrine may be necessary.

III. ANESTHESIA FOR PROCEDURES OF THE NECK

A. General considerations

The **primary anesthetic concerns** during neck surgery are establishing and maintaining a secure airway, tissue preservation, and nerve monitoring.

1. An **armored endotracheal tube** (e.g., Tovell) may be necessary to prevent kinking.
2. An **elective tracheostomy** under local anesthesia may be performed before induction of general anesthesia for some extensive procedures or for those with the potential for acute airway obstruction.

3. **Teflon injection of the vocal cords** must be performed during awake laryngoscopy to allow continuous assessment of voice quality. The procedure should be performed with adequate local anesthesia and light sedation.

B. Radical Neck Dissection

1. **Patient condition.** These patients are often elderly, chronically debilitated, malnourished, and frequently have a history of tobacco and alcohol use. The severity of cardiac, pulmonary, renal, and hepatic diseases will determine the extent of preoperative evaluation and choice of perioperative monitoring. Radical neck dissection in previously irradiated patients may be associated with large blood loss and a difficult airway.
2. **Anesthetic technique.** Airway management is of primary concern in this patient population, particularly if mass lesions exist. Awake fiberoptic intubation, rigid fiberoptic scopes, video laryngoscope, or awake tracheostomy may be necessary in patients with compromised airways. A volatile anesthetic without muscle relaxant is generally preferred to allow the surgeon to identify nerves with a nerve stimulator. A 15- to 30-degree head-up tilt and mild hypotension (mean arterial pressure 60 to 70 mm Hg), facilitated by a volatile anesthetic, vasodilators, or remifentanyl, may help reduce blood loss. However, prolonged, profound hypotension and anemia may increase the risk of end-organ damage.
3. Neck dissection often involves rotational flaps or free flaps. During dissection, traction or pressure on the carotid sinus can cause **dysrhythmias** such as bradycardia or asystole. Treatment is immediate cessation of the stimulus. If necessary, the surgeon can infiltrate local anesthetic near the sinus.
4. If airway compromise is anticipated postoperatively, the endotracheal tube is left in place or an elective tracheostomy is performed.
5. Maintenance of normothermia, adequate hydration with crystalloids, and minimizing the use of vasoconstrictors are desirable during reconstructive flap transfer surgery. Intraoperative predictors of free flap compromise include significant medical comorbidity, administration of greater than 7 L of crystalloid, and prolonged operative time. Postoperatively, blood pressure should be adequate to maintain perfusion to the new flap, but not so high that a hematoma develops. Consultation with the surgeon for optimal perfusion pressure can be helpful.

C. Thyroid Surgery

1. General endotracheal anesthesia is the most common technique. Approximately 40% of surgically associated recurrent laryngeal nerve palsies are related to thyroid surgery. Use of a "nerve integrity monitor" (NIM) endotracheal tube for intraoperative recurrent laryngeal nerve monitoring may be considered. Succinylcholine is the agent of choice for intubation, and additional muscle relaxants should be avoided in the setting of recurrent laryngeal nerve monitoring (Fig. 26.2).
2. Injury to one recurrent laryngeal nerve may cause unilateral vocal cord paralysis, a benign condition limited to hoarseness, and a weak voice. Bilateral vocal cord paralysis, however, usually leads to increasing upper airway obstruction and stridor, and the patient will be unable to phonate. Obstruction may be relieved by positive-pressure ventilation while preparations are being made for reintubation. The patient may require tracheostomy for long-term airway management.
3. **Anesthetic technique.** Surgical manipulation near the trachea can be very stimulating, while postoperative pain may only be mild to moderate. Inhalational anesthetics, sometimes augmented with a **remifentanyl** infusion, is commonly used to maintain an adequate plane of anesthesia and avoid the use of muscle relaxants.

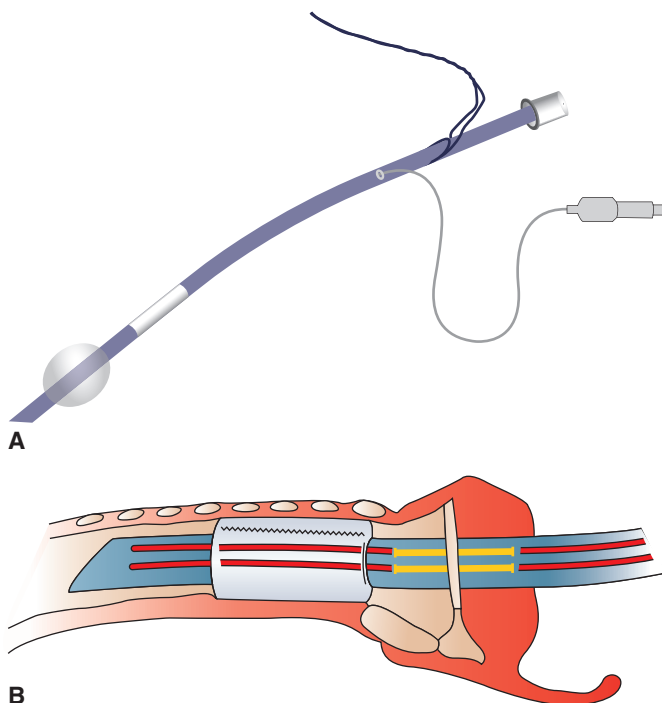


FIGURE 26.2 Intraoperative recurrent laryngeal nerve monitoring. **A:** Xomed NIM II endotracheal tube electrode (Medtronic Xomed). **B:** Proper intraluminal position of NIM II. (Redrawn from White WM, Randolph GW, Hartnick CJ, et al. Intraoperative Recurrent laryngeal nerve monitoring during thyroidectomy and related cervical procedures in the pediatric population. *Arch Otolaryngol Head Neck Surg* 2009;135(1):88–94.)

4. **Bleeding** at the operative site after thyroid or parathyroid surgery may compress the trachea and cause airway obstruction. Opening the wound by placing a sterile hemostat through the incision allows egress of trapped blood. If this maneuver fails, the obstruction may be secondary to acute lymphedema and may necessitate immediate reintubation.

D. Dentistry and Oral and Maxillofacial Surgery

1. Patients requiring general anesthesia for dentistry may be young children, adults with severe phobias, or the mentally or physically impaired; thus, they often require premedication. Oral midazolam (0.5 to 1.0 mg/kg) or rectal methohexital (25 mg/kg as a 10% solution) is suitable for children less than 5 years old. Intramuscular ketamine (3 to 5 mg/kg) with midazolam (0.05 to 0.1 mg/kg) and glycopyrrolate (0.01 mg/kg) may be necessary for the agitated or uncooperative patient.
2. **Nasal intubation** is usually preferred; care must be taken not to damage the turbinates or adenoids. Prior to intubation, topicalization of the nasal mucosa with oxymetazoline (Afrin), use of a lubricant, and

warming/softening the endotracheal tube before insertion may help to reduce epistaxis. The use of undiluted phenylephrine (1% solution) may cause profound hypertension and lead to pulmonary edema. The endotracheal tube should be securely taped, pressure on the nasal septum avoided, and eyes protected and padded.

3. Patients with maxillomandibular skeletal anomalies, temporomandibular pathology, facial fractures, intermaxillary fixation, or trismus may require fiberoptic intubation.
4. **Hypotensive anesthesia** (mean arterial pressure 60 to 70 mm Hg) for orthognathic surgery may reduce blood loss and can be facilitated by volatile anesthetics, α - and β -adrenergic blockers, nitroprusside, and head elevation. The overall medical condition of the patient may preclude the use of controlled hypotension.
5. If intermaxillary fixation with wires is present, the endotracheal tube is removed only when the patient is awake, edema has subsided, and bleeding is controlled. Administration of an antiemetic and decompression of the stomach with a nasogastric tube before extubation are recommended. Wire cutters are kept at the bedside should emergent access to the mouth be necessary. The oropharynx should be suctioned before extubation and before the jaw is wired.

Suggested Readings

- Ankicheetty SP, Ponniah M, Cherian VT, et al. Comparison of total intravenous anesthesia using propofol and inhalational anesthesia using isoflurane for controlled hypotension in functional endoscopic sinus surgery. *J Anaesthesiol Clin Pharmacol* 2011;27:328–332.
- Brimacombe J, Berry A. The laryngeal mask airway for dental surgery—a review. *Aust Dent J* 1995;40:10–14.
- Chung F, Subramanyam R, Liao P, et al. High STOP-Bang score indicates a high probability of obstructive sleep apnoea. *Br J Anaesth* 2012;108:768–775.
- Donlon JV Jr. Anesthesia for eye, ear, nose, and throat surgery. In: Miller RD, ed. *Anesthesia*. 6th ed. New York: Churchill Livingstone; 2005:2173–2198.
- Ferrari LR, Vassallo SA. Anesthesia for otorhinolaryngology procedures and anesthesia for ophthalmology. In: Coté CJ, Todres ID, Ryan JF, et al., eds. *A Practice of Anesthesia for Infants and Children*. 3rd ed. Philadelphia: WB Saunders; 2001:461–492.
- Litman RS. Anesthesia for pediatric ophthalmologic surgery. In: Litman RS, ed. *Pediatric Anesthesia the Requisite in Anesthesiology*. Philadelphia: Elsevier Mosby; 2004:267–274.
- Litman RS, Samadi DS, Tobias JD. Anesthesia for pediatric ENT surgery. In: Litman RS, ed. *Pediatric Anesthesia the Requisite in Anesthesiology*. Philadelphia: Elsevier Mosby; 2004:236–251.
- McGoldrick KE, ed. *Anesthesia for Ophthalmic and Otolaryngologic Surgery*. Philadelphia: WB Saunders; 1992.
- Pattani KM, Byrne P, Boahene K, et al. What makes a good flap go bad?: a critical analysis of the literature of intraoperative factors related to free flap failure. *Laryngoscope* 2010;120:717–723.
- Philips MB, Bendel RE, Crook JE, et al. Global health implications of preanesthesia medical examination for ophthalmic surgery. *Anesthesiology* 2013;118(5):1038–1045.
- Ragab SM, Hassanin MZ. Optimizing the surgical field in pediatric functional endoscopic sinus surgery: a new evidence-based approach. *Otolaryngol Head Neck Surg* 2010;142(1):48–54.
- Rampil IJ. Anesthesia for laser surgery. In: Miller RD, ed. *Anesthesia*. 6th ed. New York: Churchill Livingstone; 2005:2573–2587.
- Supkis DE, Dougherty TB, Nguyen DT, et al. Anesthetic management of the patient undergoing head and neck cancer surgery. *Int Anesthesiol Clin* 1998;36:21–29.
- Troll GF. Regional ophthalmic anesthesia: safe techniques and avoidance of complications. *J Clin Anesth* 1995;7:163–172.

I. INTRODUCTION

Spine surgery presents a set of challenges, including prolonged procedures, prone positioning, fluid shifts, and manipulations adjacent to nerves and blood vessels. Although most patients undergo elective procedures, a significant number present with acute injuries and neurologic compromise that require emergent interventions. Spinal conditions treated with surgical intervention include intervertebral disc disease, spinal stenosis, scoliosis, spondylosis, tumors, and trauma.

A. Spinal Cord Injury

1. Acute spinal cord injury can present with neurogenic shock, usually with lesions above T6, characterized by hemodynamic instability secondary to the resultant sympathectomy. Resulting vasodilation causes hypotension and increased heat loss. After the acute phase of spinal shock, autonomic dysreflexia predominates, with hypertension and bradycardia, myocardial ischemia, retinal/cerebral hemorrhage, and seizures.
2. Cervical spine injury is commonly associated with head trauma. Notable lesions are C5 injury presenting with deltoid, biceps, brachialis, and brachioradialis weakness, partial diaphragmatic paralysis, and C4 lesions, which necessitate artificial respiration to be survivable.
3. Prolonged immobility secondary to paraplegia/quadruplegia results in increased extrajunctional receptors at the neuromuscular junction. Succinylcholine is therefore contraindicated after 48 hours after spinal cord injury secondary to risk of hyperkalemia.

B. Airway

1. In addition to the standard concerns for securing an airway, additional caution is needed for patients with cervical spine injuries to prevent or not worsen damage to the spinal cord.
2. For severely unstable cervical spines, awake fiberoptic intubation and positioning should be considered. The process is explained to the patient in advance. A neurologic exam is done immediately before intubation. With minimal or no sedation and adequate topicalization of the airway with local anesthetic, the patient is intubated. The patient is then asked to move their fingers and toes as a method to confirm that no changes in the neurologic examination have occurred. With assistance, the patient then moves to the OR table in the desired position. Once a postposition neurologic examination is made, the patient is then anesthetized.
3. **Manual inline stabilization** is assumed to limit cervical range of motion by a second provider holding the shoulders and head to limit motion of the neck. Although this technique has traditionally been used and is a component of Advanced Trauma Life Support (1), it has been questioned since it may potentially increase craniocervical motion and worsen the laryngoscopic view (2).
4. In emergency situations where there is no evidence of facial/basal skull fractures, blind nasotracheal intubation is an acceptable option.

C. Positioning Prone

1. The physiologic changes associated with prone positioning include depressed cardiac index, inferior vena cava obstruction, increased

functional residual capacity, and pulmonary blood flow and lung ventilation redistribution to dependent areas (3).

2. The eyes, abdomen, genitalia, and breasts should be free of pressure, and the stomach and bladder should be decompressed with an orogastric tube and urinary catheter. Malpositioning of the arms can result in vascular and brachial plexus injury, specifically increased pressure within the cubital tunnel with elbow flexion greater than 130 degrees. Complications such as shoulder dislocation, facial edema, eye injuries, and peripheral nerve palsy have been reported. The greatest risk for cord compromise is when the patient is turned from supine to prone after intubation, while attempting to maintain spinal cord alignment with cervical spine injury. Intraoperative neurologic monitoring is useful for such positional changes.

D. Monitoring

1. **Intraoperative monitoring** of the integrity of the spinal cord involves electrophysiologic monitors that detect changes suggestive of ischemia. The different methods of monitoring include epidural electrodes, somatosensory-evoked potentials (SSEPs), motor-evoked potentials (MEPs), electromyography, transcranial electrodes, electrical stimulation of screws, neuromuscular junction monitoring, electrical impedance testing, stimulation of motor spinal roots, F-responses, H-reflexes, and testing specific reflexes. It is recommended to combine methods when risk of ischemia is increased (4). The use of monitoring has been demonstrated to reduce postoperative neurologic morbidity and even identify real-time compromise with surgical manipulation (i.e., retractor placement) (5).
2. **Somatosensory- (SSEPs) and motor-evoked (MEPs) potentials** are two important modalities for neural monitoring where the amplitude and latency are measured. Peripheral nerves at distal sites are stimulated to obtain SSEPs, and the blood supply for these nerves is largely the posterior spinal arteries. MEPs monitor spinal cord pathways, and the corresponding blood supply is the single anterior spinal artery.
3. The intraoperative **"wake-up test"** assesses motor function. After the patient has received appropriate narcotic analgesia and the neuromuscular blockade is reversed, the anesthetic is reduced enough for the patient to respond to the commands to move hands and feet.
4. Confounders that may artificially increase latency or decrease amplitude of transmission that may be suggestive of ischemia include non-specific physiologic changes and dose-dependent effect of inhaled anesthetics, including nitrous oxide. Desflurane and N₂O will still allow some degree of intraoperative monitoring (6,7). Propofol, remifentanyl, ketamine, midazolam, and etomidate are recommended to allow successful MEP monitoring (8). For more details on neural monitoring, see the chapter titled Neural Monitoring.

II. BLOOD LOSS

Decortication during instrumentation and fusion of the vertebral column accounts for the majority of blood loss during spinal surgery. The factors predicting increased blood loss and the need for transfusion include surgical technique, type of surgery (fusion versus laminectomy), low preoperative hemoglobin, tumor surgery, increased number of levels fused, and underlying pulmonary disease (9). Factors likely to decrease blood loss include acute normovolemic hemodilution, use of the Jackson table, hypotensive techniques, and the use of cell saver. Monitoring for development of intraoperative coagulopathy includes testing PT/INR and PTT.

III. SPINAL CORD PERFUSION

Spinal cord perfusion may be compromised by the trauma itself, surgical manipulation, and hemodynamic changes. Similar to cerebral perfusion pressure, spinal cord perfusion pressure (SCPP) is determined by mean arterial pressure (MAP) and intraspinal pressure (ISP) (or central venous pressure if it is greater than ISP) ($SCPP = MAP - ISP$). Vessel injury (decreased local blood flow delivery), hypotension (decreased MAP), and obstruction to blood flow (either segmental or elevated ISP) will decrease SCPP. Methods to maximize SCPP include setting elevated MAP goals to maximize delivery, and recent studies have demonstrated utility of intraspinal pressure monitoring and cerebrospinal fluid drainage to minimize obstruction to blood flow (10,11).

A. Complications

1. Spinal surgery carries significant risks with complication rates that are accordingly higher than many other procedures. Major complications occur in 11% of cases; minor complications in 24%. The lowest complication rates were among adolescents undergoing idiopathic scoliosis surgery and highest among patients with neuromuscular scoliosis. Combined anterior/posterior approach surgeries carried greater complication rate than staged procedures (12). Age greater than 60 years old increase the possibility of complications.
2. **Venous air embolism (VAE)** can be fatal during spinal surgery. The risk is elevated secondary to a large amount of exposed bone and the surgical site being elevated relative to the heart. Routine monitoring is with capnography and precordial Doppler. The most sensitive detection is with transesophageal echocardiography. Treatment, if VAE is suspected, includes irrigating the wound, discontinuing N_2O , starting vasopressors, turning a prone patient supine (difficult with an open surgical exposure), institution of advanced life support, and potentially initiating cardiopulmonary bypass.
3. **Bone cement embolism** is a rare complication of vertebroplasty or kyphoplasty for vertebral compression fractures, where emboli migrate to the pulmonary vasculature secondary to leakage of bone cement into the low-pressure venous drainage system of the vertebrae. Most are incidentally found, but a small fraction (<1%) present with symptoms, typically dyspnea. The diagnosis is typically made via imaging demonstrating cement emboli in a vascular distribution (by chest x-ray or CT), and treatment is typically conservative monitoring but can include systemic anticoagulation and surgical embolectomy depending on the severity of symptoms.
4. **Postoperative Visual Loss (POVL)** occurs in approximately 0.2% of cases and has been postulated to involve ischemia to the optic nerve by venous engorgement, decreased arterial perfusion pressure from hypotension, hemodilution, and increased intraocular pressure in the prone position. Risk factors include vascular disease, preoperative anemia, prolonged procedures, substantial blood loss, obesity, and tobacco use. The ASA recommends continuous blood pressure monitoring, use of colloids with crystalloids for substantial blood loss, periodic hemoglobin/hematocrit monitoring and case-by-case consideration for the use of deliberate hypotension, central venous pressure monitoring, and staging surgical procedures in high-risk patients (13).
5. **Peripheral Nerve Injury** Ulnar nerve injury is the most common peripheral nerve injury during spine surgery. Elbow flexion greater than 130 degrees results in increased internal pressure in the cubital tunnel and resulting ulnar nerve injury.

TABLE 27.1 Major Blood Vessels at Risk of Injury During Common Surgical Spine Procedures

Surgical Procedure	Vessel(s)
Anterior screw fixation of the odontoid fracture	Vertebral artery Internal carotid artery
Anterior cervical spine surgery	Vertebral artery
Posterior C1–C2 arthrodesis	Vertebral artery
Posterior cervical spine surgery	Vertebral artery
Anterolateral approach for thoracolumbar spine fracture	Aorta Inferior vena cava
Posterior thoracic spine surgery	Thoracic aorta
Scoliosis surgery	Superior mesenteric artery
Anterior lumbar interbody fusion	Inferior vena cava Iliac veins and arteries (L > R)
Lumbar disc surgery	Inferior vena cava Iliac veins
Posterior lumbar spine surgery	Epidural venous bleeding

6. **Spinal cord injury** can result in paraplegia postoperatively, and this can occur despite monitoring SSEPs and MEPs. To prevent cervical spine injury, traction has been demonstrated as an effective method to decrease movement at the occipitocervical junction. Immobilization is another method to reduce movement, while performing orotracheal intubation and positioning/turning the patient (14).

7. **Vascular Injury** can result as there are major vasculature structures adjacent to and within the spine. The major vessels at risk are summarized in Table 27.1 (15).

IV. DISPOSITION

Immediate postprocedure care is dependent upon the procedure and the comorbidities of the patient. For all patients, frequent neurologic checks are performed. Factors determining disposition to an ICU include extensive surgery, significant blood loss, large, facial and airway edema, and postoperative ventilatory support. Emphasizing optimal postoperative pulmonary care, for example, incentive spirometry, is essential to avoid complications such as atelectasis and pneumonia.

V. POSTOPERATIVE PAIN MANAGEMENT

- A. Postoperative pain management may be a significant issue for patients with chronic pain, specifically back pain, who present on high doses of chronic opioid therapy prior to surgical intervention.
- B. Continuous opioid infusions of short-acting medications during surgery, such as fentanyl or remifentanyl, have demonstrated adequate intraoperative pain control and can also facilitate a “wake-up test.” Postoperative pain is typically managed with opioids, either intravenously by patient-controlled analgesia or in the epidural space in conjunction with local anesthetics. Other techniques for postoperative pain include a double epidural—utilizing two epidural catheters simultaneously at two different spinal levels (T7/8 and T12/L1) intrathecal opioids, continuous infusion of local anesthetics at the surgical site using an automated pump.

In order to augment pain control, adjuncts that have demonstrated efficacy include preoperative celecoxib and gabapentin and intraoperative ketamine infusions. The dose of ketamine used is typically 0.15 mg/kg bolus given before surgical stimulus, followed by a low-dose infusion of 0.015 to 0.02 mg/kg/min (16–19).

Suggested Readings

1. American College of Surgeons. *Advanced Trauma Life Support: Student Course Manual*. Chicago: American College of Surgeons; 2012.
2. Manoach S, Paladino L. Manual in-line stabilization for acute airway management of suspected cervical spine injury: historical review and current questions. *Ann Emerg Med* 2007;50(3):236–245.
3. Edgcombe H, Carter K, Yarrow S. Anaesthesia in the prone position. *Br J Anaesth* 2008;100(2):165–183.
4. Lennarson PJ, Smith D, Todd MM, et al. Segmental cervical spine motion during orotracheal intubation of the intact and injured spine with and without external stabilization. *J Neurosurg Spine* 2000;92:201–206.
5. Raw DA, Beattie JK, Hunter JM. Anaesthesia for spinal surgery in adults. *Br J Anaesth* 2003;91(6):886–904.
6. Lo YL, Dan YF, Tan YE, et al. Intraoperative motor-evoked potential monitoring in scoliosis surgery: comparison of desflurane/nitrous oxide with propofol total intravenous anesthetic regimens. *J Neurosurg Anesthesiol* 2006;18(3):211–214.
7. Banoub M, Tetzlaff JE, Schubert A. Pharmacologic and Physiologic influences affecting sensory evoked potentials. *Anesthesiology* 2003;99(3):716–737.
8. Scheufler KM, Zentner J. Total intravenous anesthesia for intraoperative monitoring of the motor pathways: an integral view combining clinical and experimental data. *J Neurosurg* 2002;96:571–579.
9. Nuttall GA, Horlocker TT, Santrach PJ, et al. Predictors of blood transfusions in spinal instrumentation and fusion surgery. *Spine* 2000;25(5):596–601.
10. Werndle M, Saadoun S, Phang I, et al. Monitoring of spinal cord perfusion pressure in acute spinal cord injury: initial findings of the injured spinal cord pressure evaluation study. *Crit Care Med* 2014;42(3):646–655.
11. Kong CY, Hosseini AM, Belanger LM, et al. A prospective evaluation of hemodynamic management in acute spinal cord injury patients. *Spinal Cord* 2013;51:466–471.
12. McDonnell MF, Glassman SD, Dimar JR, et al. Perioperative complications of anterior procedures on the spine. *J Bone Joint Surg* 1996;78(6):839–847.
13. American Society of Anesthesiology. Practice advisory for perioperative visual loss associated with spine surgery: an updated report by the American Society of Anesthesiologists Task Force on Perioperative Visual Loss. *Anesthesiology* 2012;116(2):274–285.
14. Lennarson PJ, Smith DW, Sawin PD, et al. Cervical spinal motion during intubation: efficacy of stabilization maneuvers in the setting of complete segmental instability. *J Neurosurg Spine* 2001(265):270.
15. Inamasu J, Guiot BH. Vascular injury and complication in neurosurgical spine surgery. *Acta Neurochir* 2006;148(4):375–387.
16. Klatt JWB, Mickelson J, Hung M, et al. A randomized prospective evaluation of 3 techniques of postoperative pain management after posterior spinal instrumentation and fusion. *Spine* 2013;38(19):1626–1631.
17. Reynolds RA, Legakis JE, Tweedie J, et al. Postoperative pain management after spinal fusion surgery: an analysis of the efficacy of continuous infusion of local anesthetics. *Global Spine J* 2013;3(1):7–14.
18. Urban MK, Ya Deau JT, Wukovits B, et al. Ketamine as an adjunct to postoperative pain management in opioid tolerant patients after spinal fusions: a prospective randomized trial. *HSS J* 2007;4:62–65.
19. Schmid RL, Sandler AN, Katz J. Use and efficacy of low-dose ketamine in the management of acute postoperative pain: a review of current techniques and outcomes. *Pain* 1999;82(2):111–125.

I. ANESTHESIA FOR SPECIFIC UROLOGIC PROCEDURES

A. Cystoscopy and ureteroscopy are performed to diagnose and treat lesions of the lower (urethra, prostate, and bladder) and upper (ureter and kidney) urinary tracts.

1. Warmed irrigation fluids are used to improve visualization and to remove blood, tissue, and stone fragments.

a. **Electrolyte solutions** (normal saline and lactated Ringer's) are isotonic and do not cause hemolysis upon intravascular absorption. Because of ionization, they cannot safely be used for procedures involving monopolar electrocautery. However, these solutions can be used with newer, bipolar electrocautery.

b. **Sterile water** has optimal visibility and is nonconductive. However, intravascular absorption can cause hemolysis and hyponatremia/hyposmolality.

c. **Nonelectrolyte solutions** of glycine, sorbitol, and mannitol have good visibility and are nonconductive. Near isotonicity minimizes hemolysis, although large volume absorption may cause hyponatremia (see section 3.a.1).

2. Anesthesia

a. Depending on the patient and procedure, anesthesia for cystoscopy/ureteroscopy can range from topical lubrication alone to monitored anesthesia care, regional, and/or general anesthesia (GA). Placement of a rigid cystoscope (particularly in males) and distention of the bladder and ureters can be quite stimulating. Postoperative pain is minimal.

b. If regional anesthesia is used, a T6 level is required for upper tract instrumentation, whereas a T10 level is adequate for lower tract surgery.

c. GA can be effective with short-acting intravenous (IV) and inhaled anesthetics. Transient muscle relaxation may be required.

d. Lithotomy position is most common.

B. Transurethral resection of the bladder (TURB) is performed to diagnose and treat lesions of the bladder (anesthetic considerations are similar to TURP—see below). Muscle relaxation should be considered as inadvertent stimulation of the obturator nerve, deep to the lateral bladder wall, may result in leg adduction, thus risking damage to the bladder.

C. Transurethral resection of the prostate (TURP) is performed to relieve urinary obstruction due to benign prostatic hypertrophy (BPH). This procedure uses a modified cystoscope (resectoscope) with a wire loop connected to an electrocautery unit for resection of tissue and coagulation of bleeding vessels. Alternatives to TURP include medical management (α -blockers and hormonal therapies) and newer minimally invasive techniques including laser ablation, microwave thermotherapy, and prostatic stents.

1. During surgery, large prostatic venous sinuses can be opened, which allow irrigant to be absorbed. The quantity of fluid absorbed depends on the following factors:

- a. Irrigant hydrostatic pressure, proportional to the height of the irrigant above the patient.
- b. Surgical technique: duration of exposed sinuses, irrigation flow rate, and cystoscope size.
- c. Number and size of venous sinuses opened (influenced by prostate size).
- d. Peripheral venous pressure (lower pressure favors increased absorption).

2. Anesthesia

- a. If GA is used, it is essential to prevent coughing or patient movement, which can cause increased bleeding or bladder/prostatic capsule perforation. Positive-pressure ventilation may decrease irrigant absorption by raising venous pressure.
- b. Advantages of regional anesthesia may include an atonic bladder (improved surgical visualization) and elimination of bladder spasms (more rapid hemostasis postoperatively). Awake patients may report symptoms that allow earlier detection of the TURP syndrome or bladder perforation.
- c. Spinal anesthesia can be achieved with an iso- or hyperbaric solution of local anesthetic with or without opioid, providing adequate anesthesia with minimal hemodynamic effects. A T10 sensory level is recommended to counteract pain from bladder distention. Lower venous pressures associated with neuraxial blockade may reduce bleeding but increase irrigant absorption.
- d. Methods for monitoring fluid absorption intraoperatively may include volumetric fluid balance, gravimetric weighing, and measurement of exhaled ethanol when a known amount of ethanol is added to the irrigating fluid.

3. Complications

- a. **TURP syndrome** refers to a collection of neurologic and cardiovascular signs and symptoms caused by excessive irrigant absorption. It may appear early (direct intravascular absorption) or after several hours (absorption from retroperitoneal and perivesicular spaces).
 1. **Central nervous system** symptoms include nausea, agitation, confusion, visual changes, seizures, and coma. These symptoms likely are multifactorial and have been attributed to hyponatremia/hyposmolality leading to cerebral edema, hyperglycinemia, and hyperammonemia (glycine is hepatically metabolized to ammonia) associated with glycine solutions and concomitant sedating medications.
 2. **Cardiovascular** symptoms include hypertension/hypotension, bradycardia, dysrhythmias, pulmonary edema, and cardiac arrest likely secondary to pronounced fluid shifts and associated electrolyte disturbances. Hypervolemia initially occurs with fluid absorption, followed by rapid redistribution of the irrigant to the interstitium.
 3. **Treatment involves** notifying the surgeon, completing the procedure as quickly as possible, and maintaining hemodynamic stability. There is disagreement in the literature about the most appropriate therapy. Fluid restriction and diuresis with furosemide have been advocated to treat volume overload, reserving hypertonic saline for severe symptoms or hyponatremia (serum sodium <120 mmol/L). Others suggest that the diuretic strategy may exacerbate intravascular volume depletion and

hyponatremia and recommend early use of hypertonic saline (with slow correction of hyponatremia to minimize the risk of central pontine myelinolysis), reserving diuresis for acute pulmonary edema. Any therapy should be guided by regular measurements of serum sodium and osmolality.

b. Bladder perforation

1. Extraperitoneal perforation is more common and manifests as suprapubic fullness, abdominal spasm, or pain in the suprapubic, inguinal, or periumbilical regions.
2. Intraperitoneal perforation presents as upper abdominal pain or referred pain from the diaphragm to the shoulder. This may result in hypertension, tachycardia, and abdominal distention, followed by hypotension and cardiovascular collapse.

c. Bacteremia may occur due to absorption of bacteria through prostatic venous sinuses, commonly associated with indwelling urinary catheters or with subclinical or partially treated prostatitis.

d. Blood loss and coagulopathy. Assessing blood loss is extremely difficult during a TURP because of irrigant dilution. Continuous postoperative bleeding may result from surgical bleeding, dilutional thrombocytopenia, disseminated intravascular coagulation, or the release of fibrinolytic enzymes from the prostate. Hemodynamic responses to blood loss may be masked by hypervolemia from irrigant absorption.

D. Laser resection of prostate is a newer clinical approach to treating BPH with less perioperative morbidity. Hemostatic properties of laser limit tissue penetration and create a practically bloodless field. They provide an alternative for seriously ill patients (TURP morbidity 18%) and those on oral anticoagulants. Bladder irritation (transient), delayed gross hematuria, and transient dysuria are common complications. The procedure time is relatively short in duration. General, regional (subarachnoid or sacral canal block), or possibly even local anesthesia (for selected patients) may be safely performed.

1. The **Holmium** (yttrium-aluminum-garnet = YAG) laser is a 60- to 80-W high-power pulse laser with a wavelength = 2,140 nm. The high absorption by water limits tissue penetration. It is used for the enucleation of the prostate. Holmium laser preserves the histologic architecture of the prostate facilitating detection of prostate cancer.
2. The **KTP** (potassium titanyl phosphate) is a 60- to 80-W high-power laser through a crystal with a wavelength = 532 nm. It is highly absorbed by oxyhemoglobin, potentially creating a bloodless field, and is poorly absorbed by water. It is used for the enucleation of the prostate in a procedure known as "Photoselective Vaporization of Prostate" (**PVP**) that is less technically demanding than the Holmium laser is. PVP is as effective as TURPs (2- to 4-year follow-up) for relief of BPH symptoms and has less perioperative morbidity, postoperative bladder irrigation, catheterization time, incidence of sexual dysfunction, and hospital stay. A disadvantage is that it alters prostatic histology samples.

E. Radical retropubic prostatectomy (RRP) is the operative procedure for the treatment of prostate cancer. Prostatectomy is rarely done for BPH. It can be by open and laparoscopic methods.

1. Anesthesia

- a. **Open RRP** may be performed safely using general, general/epidural, epidural, or spinal anesthesia. Several small-scale prospective randomized trials compared general with epidural techniques and

found modest benefits of epidural anesthesia in reducing operative blood loss, reducing postoperative pain, and hastening recovery of bowel function. Studies using spinal anesthesia with or without sedation have shown significant improvement in these outcomes as well as decreased postanesthesia sedation, length of hospital stay, and pain scores. Regardless of these results, experienced surgeons routinely perform prostatectomies using GA with minimal blood loss, well-controlled intraoperative and postoperative pain, and short hospital stays. For radical prostatectomies, an opioid-sparing technique has been reported to reduce cancer recurrence, although such observations require further studies to clarify treatment specifics.

- b. **Laparoscopic prostatectomies (LRP)** are promoted for their minimal invasiveness and comparable clinical outcomes. Prospective, nonrandomized trials comparing LRP to RRP show no significant differences in postoperative pain score, amount of narcotics administered, length of hospital stay, readmission rates, or complication rates. Anesthetic considerations are similar to those for laparoscopic procedures in general surgery or gynecology. Retroperitoneal insufflation of carbon dioxide may be associated with increased systemic absorption compared with intraperitoneal insufflation, although reports are conflicting. In the United States, urologists have been performing an increasing number of robotic radical prostatectomies using the da Vinci system. The three-dimensional surgical visualization allows for greater surgical precision and dexterity, and enhanced comfort for the surgeon. The disadvantage is that there is no tactile feedback from the robotic arms to the surgeon. Also, prolonged lithotomy and steep reverse Trendelenburg position can have adverse consequences.
 - c. **Diagnostic dyes** may be used during the procedure to demonstrate the integrity of the reconstructed urinary tract.
 1. **Methylene blue 1% (1 mL)** bolus may lead to hypotension. It may also cause transient erroneous decreases in pulse oximetry readings (SaO_2) to as low as 65%, lasting 10 to 70 seconds.
 2. **Indigo carmine 0.8% (5 mL)** is an α -agonist and may cause hypertension.
 - d. **Complications** generally relate to blood loss, including hypothermia, anemia, and coagulopathy. Large-bore IV access is recommended. Urine output measurements are interrupted during mobilization of the prostatic urethra. Venous sinuses can be exposed during surgery, which can increase blood loss and potentially lead to air emboli.
- F. Nephrectomy** is performed for neoplasm, transplantation, chronic infection, trauma, and severe cystic or calculous disease.
1. Patients undergoing nephrectomy for renal cell carcinoma require preoperative staging. These tumors can be quite large. If the tumor extends into the inferior vena cava (IVC) or right atrium, two potential complications must be considered:
 - a. **The tumor may partially or fully occlude the IVC**, leading to poor venous return and hypotension.
 - b. **Tumor fragments may embolize** to the pulmonary circulation. Consequently, pulmonary artery catheterization and some central venous access approaches are risky if catheter placement dislodges tumor in the IVC or right atrium. Transesophageal echocardiogram

should be considered if there is high risk of tumor embolism. Cardiopulmonary bypass may be used to minimize the risk of pulmonary emboli intraoperatively.

2. Patients undergoing nephrectomy for transitional cell carcinoma likely will also undergo an associated complete ureteral resection.

3. Anesthesia

- a. The patient is positioned supine for a transabdominal approach or in the lateral decubitus position for a retroperitoneal approach. In the lateral position, kidney rest and table **flexion are often used** to improve exposure. Hypotension can be produced by the kidney rest position, likely due to IVC compression, or blood pooling in dependent extremities.
- b. A thoracoabdominal incision may be required for larger or upper pole tumors.
- c. Combined general/epidural anesthesia can maximize postoperative analgesia with an upper abdominal or thoracoabdominal incision.
- d. Large-bore IV access with or without arterial line is appropriate as blood loss can be massive because of tumor size and vascularity.

G. Cystectomy

1. **Simple and partial cystectomy** is the removal of all or part of the bladder. Adjacent organs and structures, including pelvic lymph nodes, are left intact.

2. **Radical cystectomy** is performed for invasive bladder tumors. It frequently involves removal of other pelvic organs, such as the prostate or uterus. Patients with pelvic malignancies, neurogenic bladder dysfunction, chronic lower urinary tract obstruction, or postradiation bladder dysfunction may require an ileal or colonic urinary diverting procedure.

3. Anesthesia

- a. Large-bore IV access may be indicated as substantial blood loss may occur.
- b. Arterial or central venous access may be indicated as large volume shifts occur while the ureters are disconnected.
- c. Combined general/epidural anesthesia should be considered.

H. Orchidopexy, orchiectomy, and urogenital plastic surgery procedures

are performed to treat congenital deformities, neoplasms, and impotence. Patients with torsion of the testicle may require emergency reduction and orchidopexy to prevent ischemia.

1. **Renal transplantation** is performed for patients with end-stage renal disease. The recipients commonly have hypertension and/or diabetes mellitus and are at increased risk for coronary artery disease and congestive heart failure. Patients may present with electrolyte and acid–base abnormalities, anemia, and platelet dysfunction. Preoperative dialysis, if possible, can improve potassium and acid–base abnormalities. The anesthesia provider must also make sure that the patient receives the proper perioperative immunosuppressants.

1. Anesthesia

- a. IV access may be difficult, and placement in extremities with fistulas or shunts should be avoided. The benefits of additional invasive monitors (arterial or central venous lines) should be weighed against the risks of catheter-related sepsis in immunosuppressed patients.
- b. Patients may have delayed gastric emptying from diabetes, uremia, and preoperative opioids.

- c. Recent studies show that lactated Ringer's may be preferential to normal saline as large volumes of the latter can cause hyperchloremic metabolic acidosis.
- d. Graft function depends on adequate intravascular volume before and after vascular anastomosis to maintain perfusion to the transplanted kidney. Intravascular volume expanders include crystalloid, albumin, and mannitol.
- e. Intraoperative hypotension may compromise renal perfusion and should be treated promptly by addressing mechanical factors such as IVC compression or treating hypovolemia with additional volume. If pharmacologic support is necessary, inotropes (dopamine and dobutamine) are preferred to α -agonists (phenylephrine and norepinephrine), which may raise systemic blood pressure but decrease renal blood flow via vasoconstriction. In cases of marked acidemia, sodium bicarbonate may improve hemodynamics.
- f. Urine output provides an immediate gauge of renal function, which may be affected by hypovolemia, acute rejection, or patency of the anastomoses. Both mannitol and furosemide may be requested to promote diuresis after anastomosis.

II. LITHOTRIPSY

- A. The treatment of kidney stones ranges from open surgical procedures, to less invasive approaches including cystoscopy and ureteroscopy with mechanical stone extraction and/or laser lithotripsy being two of the most common techniques.
 - 1. Anesthetic options include regional, MAC, and GA (LMA vs. ETT) and depend on both patient and surgical factors.
- B. **Extracorporeal shockwave lithotripsy (ESWL)**, a noninvasive technique, focuses acoustic shock waves at urinary stones. At interfaces between materials of differing density, such as between soft tissue and stones, reflections of these acoustic waves set up complex patterns of internal echoes resulting in stresses that cause stones to fracture. While early-generation lithotripters required patient immersion into water baths, current models allow positioning on an operating table, have smaller cutaneous "shock entry" zones, and are more precisely focused onto the stone with less energy dissipated on surrounding structures.
- C. **Anesthesia**
 - 1. The patient is generally positioned supine but may be prone depending on the precise location of the stone(s). Lithotomy position may be necessary for concurrent cystoscopy or stent placement.
 - 2. Monitored anesthesia care is usually adequate with newer lithotripters. Adequate analgesia can generally be achieved with IV short-acting opioids (i.e., remifentanyl and alfentanil) with additional sedation titrated to patient comfort. Other strategies include neuraxial blockade and GA.
 - 3. Adequate IV hydration with occasional diuretic supplementation may aid passage of stone fragments.
 - 4. Absolute contraindications are pregnancy, untreated infections or bleeding diatheses, and abdominal pacemakers. Relative contraindications are pacemakers/implantable cardioverter defibrillator, abdominal aortic or renal artery aneurysms, orthopedic prostheses, and morbid obesity.
- D. **Complications**
 - 1. Ureteral colic soon after the procedure may manifest as nausea, vomiting, or bradycardia.

2. Hematuria is common and treated with hydration and diuretics.
3. Cardiac dysrhythmias such as bradycardia, premature atrial contractions, and premature ventricular contractions can occur intraoperatively secondary to mechanical (shock wave) strains on the cardiac conduction system. If premature ventricular contractions are frequent or symptomatic, they may be minimized by synchronization of the shock waves to the cardiac cycle.
4. Hypertension can reach extreme levels in patients who have autonomic dysreflexia.
5. Renal (subcapsular) hematoma may result from collateral damage to renal vasculature, especially in hypertensive patients.
6. Severe pulmonary or intestinal damage is rare and occurs if the shock waves are inadvertently applied to the lung or intestines, as may occur with a patient movement during treatment.

III. PATIENTS WITH SPINAL CORD PATHOLOGY

- A. Spinal cord injury frequently causes urinary retention, which promotes urinary tract infections, nephrolithiasis, and vesicoureteric reflux.
- B. **Autonomic dysreflexia** is manifested by an acute onset of sympathetic hyperreactivity to certain stimuli below the level of a spinal cord lesion, generally at or above the T6–T7 level. The syndrome may appear at any time from a few months to many years after the injury.
 1. Common findings include hypertension (potentially severe), headache, diaphoresis, flushing or pallor, and bradycardia.
 2. Common precipitants include visceral stimulation, most commonly bladder distention, although urinary tract infection, fecal impaction, uterine contraction, bowel distention, and other intra-abdominal and cutaneous stimuli have been reported.
 3. Pathophysiology is thought to involve disorganized connections between afferent neurons and sympathetic neurons below the level of the injury that lead to vasoconstriction and hypertension. The parasympathetic nervous system is unable to counteract this vasoconstriction resulting from the spinal cord injury.
 4. Treatment of autonomic dysreflexia includes removal of the inciting stimulus, increasing anesthetic depth, and pharmacologic treatment of persistent hypertension with rapidly acting agents such as sublingual nifedipine, or IV nitroglycerin or nitroprusside. Neuraxial anesthesia blocks both limbs of the reflex arc and prevents dysreflexia. However, a preexisting complete sensory deficit impairs determining the level of anesthesia by cutaneous testing. For short procedures, spinal may be preferable to epidural anesthesia because of more reliable block without spared segments.

Suggested Readings

- Biki B, Mascha E, Moriarty DC, et al. Anesthetic technique for radical prostatectomy surgery affects cancer recurrence: a retrospective analysis. *Anesthesiology* 2008;109(2):180–187.
- Conacher ID, Soomro NA, Rix D, et al. Anaesthesia for laparoscopic urological surgery. *Br J Anaesth* 2004;93(6):859–864.
- Domi R, Sula H, Ohri I, et al. Anesthetic challenges of patients with cardiac comorbidities undergoing major urologic surgery. *Int Arch Med* 2014;7:17. doi:10.1186/1755-7682-7-17.
- Gravenstein D. Extracorporeal shock wave lithotripsy and percutaneous nephrolithotomy. *Anesthesiol Clin North America* 2000;18(4):953–971.
- Hahn RG. Fluid absorption in endoscopic surgery. *Br J Anaesth* 2006;96(1):8–20.

- Hambly PR, Martin B. Anaesthesia for chronic spinal cord lesions. *Anaesthesia* 1998;53:273–289.
- Hanson R, Zornow M, Coulin M, et al. Laser resection of the prostate: implications for anesthesia. *Anesth Analg* 2007;105(2):475–479.
- Hsu RL, Kaye AD, Urman RD. Anesthetic challenges in robotic-assisted urologic surgery. *Rev Urol* 2013;15(4):178–184.
- O'Malley C, Frumento R, Hardy M, et al. A randomized, double-blind comparison of lactated ringer's solution and 0.9% NaCl during renal transplantation. *Anesth Analg* 2005;100:1518–1524.
- Scavonetto F, Yeoh TY, Umbreit EC, et al. Association between neuraxial analgesia, cancer progression, and mortality after radical prostatectomy: a large, retrospective matched cohort study. *Br J Anaesth* 2014;113(Suppl 1):i95–i102.
- Schmid S, Jungwirth B. Anaesthesia for renal transplant surgery: an update. *Eur J Anaesthesiol* 2012;29(12):552–558.
- Sprung J, Scavonetto F, Yeoh TY, et al. Outcomes after radical prostatectomy for cancer: a comparison between general anesthesia and epidural anesthesia with fentanyl analgesia: a matched cohort study. *Anesth Analg* 2014;119(4):859–866.
- Whalley DG. Anesthesia for radical prostatectomy, cystectomy, nephrectomy, pheochromocytoma, and laparoscopic procedures. *Anesthesiol Clin North America* 2000; 18(4):899–917.

I. PHYSIOLOGIC CHANGES ASSOCIATED WITH AGING**A. Cardiovascular**

1. **Arteries stiffen with age**, leading to faster propagation and reflection of the pulse pressure waveform. The reflected waveform augments the pressure at the aortic root. With increasing age, the reflected energy arrives progressively earlier in the cardiac cycle, shifting from early diastole to late systole. Thus, aging causes decreased diastolic and increased systolic pressure (and pulse pressure) and leads to ventricular thickening and prolonged ejection.
2. **Slower myocardial relaxation and ventricular hypertrophy** lead to late diastolic filling and diastolic dysfunction. Atrial contraction is important to maintain late filling.
3. **Reduced venous capacitance** decreases the “vascular reserve volume” available to buffer hemorrhage.
4. **Reduced baroreceptor reflexes** result from increased sympathetic tone, decreased parasympathetic tone, decreased baroreceptor sensitivity, and decreased responsiveness to β -adrenergic stimulation. Thus, hypotension occurs frequently with changes in volume, position, anesthetic depth, and regional anesthetic-induced sympathetic blockade.
5. **Maximal heart rate decreases with age while stroke volume remains constant**, but end-diastolic volume increases and ejection fraction decreases.
6. **Maximal oxygen consumption decreases** because of reductions in arterio-venous oxygen tension difference and cardiac output.

B. Respiratory

1. **Parenchymal changes.** Approximately 30% of alveolar wall tissue is lost between ages 20 and 80, diminishing elastic recoil and parenchymal traction that maintain airway patency. The loss produces the following changes:
 - a. **Increased residual volume, closing volume, and functional residual capacity;** decreased vital capacity and forced expiratory volume in first second (FEV₁).
 - b. **Progressive mismatching of ventilation to perfusion**, with an age-dependent decrease in arterial oxygen tension.
 - c. **Increased physiologic dead space** and reduced diffusing capacity.
2. **Chest wall changes:** multiple factors lead to a stiffer chest wall and respiratory muscle mass decreases.
3. **Depressed ventilatory response** to hypoxia and hypercarbia.
4. **Decreased protective airway reflexes** increase aspiration risk.

C. Central Nervous System

1. Progressive loss of neurons and decreased neurotransmitter activity contribute to **decreased anesthetic requirements** for all agents.
2. Cerebral autoregulatory responses to blood pressure, CO₂, and O₂ are maintained.

D. Renal

1. **Serum creatinine remains stable** with advancing age because age-associated decreases of creatinine clearance are offset by reduced

creatinine production from skeletal muscle. A normal creatinine level in the elderly should not be interpreted as an absence of renal impairment. For example, a healthy 80-year-old patient is expected to have half the creatinine clearance of a 20-year-old patient, even though they may have similar serum creatinine levels.

2. Progressive atrophy of renal parenchyma and sclerosis of vascular structures lead to **diminished renal blood flow and glomerular filtration rate**.
 3. Reduced ability to correct alterations in electrolyte concentrations, intravascular volume, and free water.
 4. **Reduced glomerular filtration rate** leads to delayed renal drug excretion.
- E. Hepatic**
1. Decreased liver mass and reduced portal and hepatic blood flows result in reduced hepatic drug clearance.
 2. Cytochrome P-450 enzyme activity decreases with aging.
 3. Phase 1 (oxidation and reduction) and phase 2 (conjugation) reactions may be depressed with aging.
- F. Body Composition and Thermoregulation**
1. Basal metabolism and heat production decrease because of skeletal muscle atrophy and variable replacement with adipose tissue.
 2. The propensity for hypothermia increases because of blunted central thermoregulation and body compositional changes.
 3. Decreases in muscle mass and total body water, coupled with increases in body fat, reduce the volume of distribution of water-soluble drugs and increase it for lipid-soluble drugs.

II. PHARMACOLOGIC CHANGES ASSOCIATED WITH AGING

A. Pharmacokinetic Changes in Elderly

1. **Protein binding of anesthetic drugs is reduced** because of decreased levels of circulating serum protein—for example, albumin. Therefore, their pharmacologic effects are potentiated.
2. Reduction in blood volume, an increase in percentage of body fat, and decreases in hepatic and renal function result in prolonged elimination for drugs dependent on redistribution and/or elimination for termination of action thereby prolonging anesthetic effects.

B. Pharmacodynamic Changes in Elderly

1. The elderly brain is more sensitive to drugs. Reductions in neuronal density, cerebral blood flow, and oxygen consumption result in an **age-related reduction in inhalation and intravenous anesthetic requirements**.
2. Drug sensitivity varies with the type of drug. Responses to specific drugs are difficult to predict and may vary widely in the elderly. For example, catecholamines require higher doses for equivalent effects, and benzodiazepines exert greater effects in the elderly.
3. The rate of adverse drug reaction increases with age and with the number of drugs administered. This includes the increased occurrence of over sedation, excess respiratory depression, and altered mental status.

III. ANESTHESIA CONSIDERATIONS FOR ELDERLY PATIENTS

A. Preoperative Evaluation

1. Age-related coexisting disease is a major predictor for perioperative mortality and serious morbidity. Age-related coexisting disease increases elderly patients' risks for perioperative events such as:
 - a. Myocardial infarction
 - b. Congestive heart failure
 - c. Delirium

- d. Stroke
 - e. Aspiration and pneumonia
 - f. Sepsis
 - g. Adverse drug reactions
 - h. Falls
 - i. Pressure sores
2. Age alone is a minor predictor for perioperative complications.
 3. **Assessment of health and functional status.** A detailed history and physical examination are required, with emphasis on physical condition, ambulation, activities of daily living, preoperative living situation, and preexisting disabilities.
 4. **Preoperative testing. Testing should be based on coexisting disease and recommended guidelines (see Chapter 1). Recommended testing in elderly patients includes** electrocardiogram, chest radiograph, complete blood count, electrolyte panel that includes blood urea nitrogen, creatinine, potassium (especially if the patient is receiving a diuretic), and glucose.

B. Intraoperative Management

1. **Major risk factors** for serious adverse perioperative events in the elderly include emergency surgery, operative site within a major body cavity, vascular surgery, and the American Society of Anesthesiologists physical status classification III or IV.
2. No significant difference in perioperative complications can be attributed to any specific anesthetic agent or to regional versus general anesthesia.
3. In general, the elderly have reduced functional reserves of all organ systems and a diminished therapeutic index of anesthetic interventions. The therapeutic diminution is highly variable and unpredictable because of environmental effects, physical deconditioning, and undiagnosed diseases. Diminished functional reserves may be manifest only under severe stress, such as that of surgery. Thus, vigilance and preparation for contingencies are essential in conducting anesthesia for the elderly.

C. Postoperative Cognitive Dysfunction (POCD)

1. POCD is a subtle deterioration in memory, attention, and speed of information processing associated with anesthesia and surgery.
2. There is currently no standard methodology or criteria for the diagnosis of POCD, but it typically requires pre- and postoperative findings on psychometric tests.
3. Up to 40% and up to 10% of all patients over 60 will have POCD at hospital discharge and 3 months, respectively, after major noncardiac surgery.
4. Elderly patients have a higher rate of persistent POCD than do young and middle-aged adults.
5. Risk factors for persistent POCD include increasing age, lower educational level, history of previous cerebral vascular accident (CVA) without residual impairment, and POCD at hospital discharge.
6. POCD is associated with a decline in performance of activities of daily life, earlier retirement, and greater utilization of social financial assistance.
7. Patients with POCD at hospital discharge have a higher incidence of mortality in the first 3 months postoperatively. Patients with POCD at hospital discharge and at 3 months postoperatively have a higher incidence of mortality in the first year after anesthesia and surgery.

8. Short-term POCD can negatively affect the postdischarge functioning of patients, such as taking medications, providing self-care, and so forth, which could lead to other adverse health outcomes.
9. The pathogenesis is unclear and further research is necessary. However, findings of animal experiments suggest there may be an important role of inflammation, neuronal loss, Tau protein hyperphosphorylation, β -amyloid protein accumulation, and others.
10. It is postulated that patients with persistent POCD may have a decreased cognitive reserve and are therefore more susceptible to a perioperative insult.
11. Present clinical data comparing regional anesthesia and general anesthesia have not demonstrated significant differences in the incidence of POCD. However, some studies suggest that different anesthetics may have different roles in the POCD pathogenesis.

IV. ANESTHESIA CARE FOR PATIENTS WITH AGING-RELATED DISEASES

A. Disorders of the Central Nervous System

1. **Delirium** is a transient disorder of cognition and consciousness characterized by an acute onset and fluctuating course.
 - a. Symptoms may include agitation, somnolence, social withdrawal, and psychosis.
 - b. The Confusion Assessment Method (CAM) algorithm, developed in 1990, is widely utilized to determine the presence of delirium in human patients. CAM consists of four clinical criteria: (1) acute onset and fluctuating course, (2) inattention, (3) disorganized thinking, and (4) altered level of consciousness. For delirium to be defined by this algorithm, both the first and the second criteria have to be present, plus either the third and/or the fourth criterion.
 - c. Risk factors include advanced age, underlying dementia, use of psychoactive drugs, and perioperative hypoxia, hypercarbia, and sepsis.
 - d. Common precipitants include psychoactive drugs (anticholinergics, benzodiazepines, and barbiturates), infection, stroke, MI, electrolyte abnormalities, drug withdrawal, and urinary retention.
 - e. The focus is on treating any underlying disorder, encouraging interaction with family members, encouraging normal sleep–wake cycles, and avoiding restraints, if possible. Haloperidol (PO or IM) may be used for control of acute agitation.
2. **Dementia** is a persistent and progressive impairment of cognition that interferes with activities of daily living.
 - a. Alzheimer disease is the most common cause of dementia in the elderly and affects 30% to 50% of people by age 85.
 1. Pathogenesis is thought to be related to the aberrant production and deposition of A β peptide, the dominant component of neuritic plaques. The pathologic hallmarks of the disease include neurofibrillary tangles, neuritic plaques, neuronal thread protein, and marked cortical atrophy with ventricular enlargement.
 2. Current treatment includes cholinesterase inhibitors such as donepezil, tacrine, and rivastigmine and the NMDA antagonist memantine.
 3. Anesthetic considerations include avoiding preoperative sedation and centrally acting anticholinergic agents. Hypoxia and hypercapnia should also be avoided.
 - b. Other causes of dementia include Pick disease, vascular dementia, Parkinson disease, normal pressure hydrocephalus, and Creutzfeldt-Jakob disease.

3. **Parkinson disease** is a degenerative neurologic disorder characterized by tremor, bradykinesia, rigidity, and postural instability.
 - a. Pathogenesis is due to the degeneration of dopaminergic neurons of the substantia nigra and a reduction in striatal dopamine content.
 - b. About 10% to 15% of patients with Parkinson disease develop dementia.
 - c. Treatment is directed at controlling symptoms and includes levodopa, anticholinergics, dopamine agonists, amantadine, and type B monoamine oxidase inhibitors.
 - d. Anesthetic considerations
 1. Antiparkinsonian medications should be continued perioperatively because of the short half-life of levodopa.
 2. Phenothiazines, butyrophenones, and metoclopramide should be avoided as they may exacerbate symptoms as a consequence of their antidopaminergic activity.
 3. Anticholinergics and antihistamines may be used for acute exacerbations.
 4. Patients may have pharyngeal and laryngeal muscle dysfunction putting them at higher risk for airway obstruction, laryngospasm, and aspiration. One should consider a rapid sequence induction with cricoid pressure in these. Response to depolarizing and non-depolarizing muscle relaxants is normal.
 5. Hemodynamic instability may occur with induction of anesthesia, especially in patients receiving long-term levodopa therapy. Invasive arterial blood pressure monitoring may be warranted.
 6. Cardiac irritability may increase the risk for dysrhythmias. Ketamine and local anesthetics with epinephrine should be used cautiously.

B. Visual Impairment

1. **Cataracts** are opacities of the crystalline lens that may affect visual acuity, contrast sensitivity, and light perception.
 - a. The prevalence of cataracts approaches 100% in patients 90 years old.
 - b. Cataract surgery is the most commonly performed surgery in elderly patients and is the only effective therapy for cataracts.
 - c. Anesthesia for cataract surgery can be general or regional (retrobulbar block, see Chapter 26).
2. **Glaucoma** is an optic neuropathy with peripheral vision loss occurring before loss of central vision. It is characterized by an acute (narrow-angle) or chronic (usually open-angle) increase in intraocular pressure.
 - a. Treatments include β -blockers (decrease aqueous production by the ciliary bodies), miotic eye drops (constrict the pupils to enhance aqueous outflow), carbonic anhydrase inhibitors (decrease aqueous production from the ciliary bodies), and synthetic prostaglandin (decreases intraocular pressure).
 - b. Use of anticholinergic drugs in combination with anticholinesterases to reverse neuromuscular blockade is acceptable because these drugs do not result in significant pupil dilation.
 - c. **Scopolamine should be avoided** as it may cause a significant increase in the diameter of the pupil.
 - d. Use of succinylcholine may cause a transient increase in intraocular pressure.
3. **Retinal detachment** is separation between the photoreceptors and retinal pigment epithelium with accumulation of fluid or blood in the potential space. **Nitrous oxide should be avoided** as the gas may diffuse into any surgically introduced air bubbles within the globe (Chapter 26).

C. Orthopedic Disorders

1. Osteoarthritis

- a. The most significant anesthetic consideration in patients with osteoarthritis is **cervical spine changes**.
 1. Extension and flexion of the neck are diminished.
 2. Loss of flexibility and extensibility of the cervical spine increases the distance from the posterior portion of the cricoid ring to the anterior portion of the vertebral body. It may be difficult to apply effective cricoid pressure.
 3. Direct laryngoscopy may be more difficult in elderly patients, and fiberoptic tracheal intubation may be indicated when neck mobility is severely limited.

2. Hip fractures

- a. Background
 1. More than 300,000 hip fractures occur in adults in the United States every year.
 2. Hip fractures are associated with a substantial risk of morbidity and mortality.
 3. Approximately 1% to 6% of patients die during their hospital stay, and 4% to 10% die within 30 days of hospital admission.
- b. Anesthetic Approach
 1. Regional anesthesia may avoid airway management, decreased blood loss, reduced risk of deep venous thrombosis, and improved postoperative analgesia.
 2. General anesthesia may be associated with a more stable hemodynamic state compared to regional anesthesia.
 3. A number of studies have attempted to determine whether regional anesthesia offers benefits over general anesthesia for surgical repair of hip fractures, but there continues to be controversy and conflicting evidence.

D. Metabolic Derangements

1. Dehydration

- a. Types of dehydration
 1. Isotonic—the balanced loss of sodium and water, as in fasting, diarrhea, and vomiting.
 2. Hypertonic—water losses exceed sodium losses, as in fever.
 3. Hypotonic—sodium losses exceed water losses, as in diuretic use.
- b. Diagnosis of dehydration may be difficult because symptoms may be vague or absent in the elderly. Indicators include the following:
 1. Poor skin turgor
 2. High urine specific gravity
 3. Orthostatic hypotension or orthostatic increase in heart rate
 4. Blood urea nitrogen:creatinine ratio greater than 25
- c. Treatment of dehydration
 1. Fluid requirement in the elderly is about **30 mL/kg/d** and may be replaced orally (by sports replacement drinks or the equivalent) or parenterally.
 2. Patients should be monitored carefully for signs and symptoms of volume overload.

2. Malnutrition

- a. Incidence of malnutrition is **20% to 40%** in elderly inpatients.

- b. Predisposing factors of malnutrition are congestive heart failure, chronic obstructive pulmonary disease, and cancer.
- c. Indicators of malnutrition include weight loss, low body mass index, nutrient-related disorder (e.g., anemia), and albumin being less than 3.5 g/dL.

Suggested Readings

- Cook DJ. Geriatric anesthesia. 2004. www.americangeriatrics.org
- Gibbs J, Cull W, Henderson W, et al. Preoperative serum albumin level as a predictor of operative mortality and morbidity: results from the National VA Surgical Risk Study. *Arch Surg* 1999;134:36–42.
- Hines RL, Marschall KE. Geriatric disorders. In: *Stoelting's Anesthesia and Co-existing Disease*. 5th ed. Philadelphia: Churchill Livingstone; 2008:639–649.
- Leung JM, Sands LP. Long-term cognitive decline: is there a link to surgery and anesthesia? *Anesthesiology* 2009;111(5):931–932.
- Moller JT, Cluitmans P, Rasmussen LS, et al. Long-term postoperative cognitive dysfunction in the elderly: ISPOCD1 study. *Lancet* 1998;351:857–861.
- Monk T, et al. Predictors of cognitive dysfunction after major noncardiac surgery. *Anesthesiology* 2008;108:18–30.
- Newman MF, Kirchner JL, Phillips-Bute B, et al. Longitudinal assessment of neurocognitive dysfunction after coronary-artery bypass surgery. *N Engl J Med* 2001;344:395–402.
- O'Hara DA, Duff A, Berlin JA, et al. The effect of anesthetic technique on post-operative outcomes in hip fracture repair. *Anesthesiology* 2000;84:450–455.
- Pedersen T, Eliassen K, Henriksen E. A prospective study of mortality associated with anaesthesia and surgery: risk indicators of mortality in hospital. *Acta Anaesthesiol Scand* 1990;34:176–182.
- Williamson J, Chopin JM. Adverse reactions to prescribed drugs in the elderly: a multicentre investigation. *Age Ageing* 1980;9:73–80.
- Williams-Russo P, Sharrock NE, Mattis S, et al. Cognitive effects after epidural vs general anesthesia in older adults: a randomized trial. *JAMA* 1995;274:44–50.

Care of the Neonate

Jamie Rubin, Katherine A. Sparger, and Jesse D. Roberts Jr.

I. DEVELOPMENT

A. Organogenesis is virtually complete after the 12th gestational week.

B. Respiratory Development

1. Anatomic

- a. **The lungs** begin as a bud on the embryonic gut in the 4th week of gestation. Failure of separation of the lung bud from the gut later results in the formation of a **tracheoesophageal fistula (TEF)**.
- b. **The diaphragm** forms during the 4th through 10th week of gestation, dividing the abdominal and thoracic cavities.
 1. If the diaphragm is not completely formed when the midgut reenters the abdomen from the umbilical pouch, the abdominal contents can enter the thorax.
 2. The presence of abdominal contents within the thorax is associated with arrested lung growth.
 3. The lungs from patients with **congenital diaphragmatic hernia (CDH)** have a decreased number of arterioles in the hypoplastic lung. In addition, the pulmonary arteries of both lungs are abnormally thick and reactive, resulting in increased pulmonary vascular resistance.

2. Physiologic

- a. **Lung development** is generally insufficient for survival at less than the 23rd week of gestation, prior to the saccular stage of lung development when thinning of the pulmonary interstitium due to decreased collagen fiber deposition, increased cellular differentiation, and capillary development begins the capacity for gas exchange.
- b. Secretion of **surfactant**, which reduces alveolar wall surface tension and promotes alveolar aeration, is often inadequate until the last month of gestation.
 1. Birth before 32 weeks of gestation is associated with **respiratory distress syndrome (RDS)**.
 2. Because glucose metabolism affects lung surfactant maturation, infants of diabetic mothers are at increased risk of RDS when prematurely born at later stages of gestation.
 3. Antenatal treatment with steroids is associated with a decrease in the incidence of RDS in prematurely born infants.
- c. After birth, the onset of breathing is stimulated by hypoxemia, hypercarbia, tactile stimulation, and a decrease in plasma prostaglandin E_2 . After aeration and distension of the lung, the pulmonary vascular resistance decreases, and pulmonary blood flow increases nearly 10-fold. Failure of the reduction of pulmonary vascular resistance after birth is associated with extrapulmonary shunting of blood and severe hypoxemia and is called **persistent pulmonary hypertension of the newborn (PPHN)**.

C. Cardiovascular Development

1. Anatomic

- a. **The cardiovascular system is the first organ system to function in utero. Its formation consists of three developmental stages including tube formation, looping, and septation. Heart formation is complete by approximately 8 weeks of gestation.**
- b. The primitive **cardiac tube** consists of the sinoatrium, the ventricle, the bulbus cordis (primitive right ventricle), and the truncus (primitive main pulmonary artery). During the 2nd month of gestation, a heart with two parallel pumping systems develops out of this initially tubular system. During this process, various structures divide and migrate. Failure of structural maturation at this stage of development causes numerous cardiac malformations. For example:
 1. Failure of division of the sinoatrium into the two atria results in a single atrium. Improper closure results in an **atrial septal defect**.
 2. Failure of migration of the ventricular septum and atrioventricular valve between the primitive ventricle and the bulbus cordis results in a **double-outlet left ventricle** (single ventricle). Minor migrational defects result in **ventriculoseptal defects**.
 3. Failure of division of the truncus into the pulmonary artery and the aorta results in **truncus arteriosus**.
- c. The aortic arch system initially consists of six pairs of arches.
 1. The sixth arches produce the pulmonary arteries. The **ductus arteriosus** develops from the distal portion of the right sixth arch. Although the left proximal sixth arch usually degenerates, it can persist and form an aberrant left ductus arteriosus.
 2. Failure of regression of various portions of the aorta and arch system also can result in aberrant vessels and vascular rings. For example, failure of regression causes a **double aortic arch**. Regression of the left-sided but not the right-sided arches can result in a right-sided aortic arch.

2. Physiologic

- a. **Fetal circulation:** After the 12th week, the circulatory system is in its final form. Oxygenated blood from the placenta passes through the umbilical vein and the ductus venosus and returns to the heart. Subsequently, 85% to 95% of fetal cardiac output bypasses the pulmonary circulation by flowing right to left through the foramen ovale and the ductus arteriosus into the aorta.
- b. **At birth,** umbilical placental circulation ceases with the clamping of the umbilical cord, and blood flow through the ductus venosus ceases. However, the ductus venosus often remains patent for up to a week. Also, the interruption of umbilical blood flow at birth reduces right atrial pressure and causes functional closure of the foramen ovale. Moreover, pulmonary resistance decreases as the lungs are distended and ventilated at birth, while systemic resistance increases with removal of the high-capacitance placental circulation. Constriction of the ductus arteriosus occurs with increasing PaO_2 . Cessation of ductus arteriosus blood flow often occurs within several hours to days in term infants but may be delayed in prematurely born or sick infants.

D. Body Composition

1. **Extracellular fluid (ECF)** and total body water decrease as the fetus grows, while intracellular fluid increases with gestational age. ECF is 90% of total body weight at 28 weeks, 80% at 36 weeks, and 75% at term.

2. After birth, a physiologic diuresis occurs, with the term infant losing 5% to 10% of ECF in the first few days of life. Premature infants may lose up to 15% of ECF.
3. Before 32 weeks of gestation, the **neonatal kidney is immature** and has a relatively low glomerular filtration rate and altered tubular function. This leads to difficulties in excreting water loads and diminished capacity to reabsorb sodium and water and thereby concentrate urine. In part, this is due to incomplete glomerular development, tubule insensitivity to vasopressin, loops of Henle that have not yet penetrated into the medulla, low osmolality in the medullary interstitium, and low serum urea levels. Renal tubular function increases with postnatal age, and the concentrating ability of the kidney reaches adult levels at 6 to 12 months postnatal age.

II. GENERAL ASSESSMENT

A. History

1. In collecting the neonatal patient's medical history, it is important to include information about antenatal events. Fetal growth and development are affected by **maternal disorders**, including hypertension, diabetes, lupus, and drug, cigarette, and alcohol use. Poly- or oligohydramnios, abnormal α -fetoprotein, maternal infections, and premature labor are often associated with neonatal problems.
2. **Perinatal history** also includes gestational age, time of onset of labor and rupture of membranes, use of tocolytics and fetal monitors, signs of fetal distress, type of anesthesia used and mode of delivery (spontaneous, forceps or vacuum assisted, or cesarean), condition of the infant at delivery, and immediate resuscitation steps required (e.g., intubation for meconium, ventilatory assistance, surfactant administration, CPR, or medication administration). **The Apgar score** should be noted as it reflects the degree of intrapartum stress as well as the effectiveness of initial resuscitation (Table 30.1). Points are awarded for each of the five criteria, with the maximum score being 10. Although the Apgar score at 1 minute correlates with intrauterine conditions, the 5- and 10-minute Apgar scores correlate best with neonatal outcome. In addition, ensure that vitamin K and ocular antibiotic ointment were given after birth to prevent hemorrhagic disease of the newborn and ophthalmia neonatorum, respectively.

B. Physical Examination

1. A complete, systematic evaluation is needed. No assumptions should be made about the development, location, or function of organ systems. An abnormality in one system may be associated with abnormalities in another.

TABLE
30.1

Normal Vital Signs

Vital Sign	Term	Preterm
Pulse (beats/min)	80–120	120–160
Respiration (breaths/min)	30–40	50–70
Blood pressure (mm Hg)	60–90/40–60	40–60/20–40
Temperature (°C)	37.5 (rectal)	37.5

TABLE
30.2
Apgar Scores

Sign	Score		
	0	1	2
Heart rate	Absent	<100/min	>100/min
Respiratory effort	Absent	Irregular	Good, crying
Muscle tone	Limp	Some flexion	Active motion
Reflex irritability	Absent	Grimace	Cough or sneeze
Color	Blue	Acrocyanosis	Completely pink

- Vital signs** provide a useful physiologic screen of organ function. If a cardiac abnormality is suspected, a chest x-ray (CXR), electrocardiogram (ECG), and four extremity blood pressure measurements are required. Postductal oxygen saturation should be greater than 94%. In addition, an echocardiogram and pediatric cardiology consultation should be considered. Normal vital signs are summarized in Table 30.2.
- Gestational age** influences care, management, and survival potential of the neonate. An infant is considered preterm if the gestational age is less than 37 weeks, term if it is 37 to 41 weeks, and postterm if the gestational age is more than 42 weeks. Although the date of conception and ultrasound examination can be used to predict gestational age, a physical examination to determine gestational age should be performed. **The Dubowitz-Ballard scoring system** involves evaluation of physical characteristics of the skin, external genitalia, ears, breasts, and neuromuscular behavior to assess gestational age.
- Weight determination.** Similar to gestational age, birth weight is an important prognostic factor for premature infants. By convention, low birth weight (LBW) infants weigh less than 2,500 g, very low birth weight infants (VLBW) less than 1,500 g, and extremely low birth weight (ELBW) infants less than 1,000 g. Intrauterine growth restriction (IUGR) is defined as a rate of growth less than a fetus' predetermined genetic potential. **Small-for-gestational age (SGA) infants at birth are less than 10th percentile of the standard population-based weight.** This may be the result of chromosomal defects, maternal hypertension, chronic placental insufficiency, maternal cigarette or drug use, or congenital infection. These infants have a high incidence of hypoglycemia, hypocalcemia, and polycythemia. Infants who are **large for gestational age (LGA)** are greater than 90th percentile of standard population-based weight and may have mothers with diabetes. In the immediate postnatal period, LGA newborns should be evaluated for hypoglycemia and polycythemia. Infants of diabetic mothers and LGA infants are at risk of complications from fetal macrosomia, including shoulder dystocia and brachial plexus injuries.
- Respiratory.** Signs of respiratory distress include tachypnea, grunting, nasal flaring, intercostal and subcostal retractions, rales, rhonchi, asymmetry of breath sounds, and apnea. **Pulse oximetry** is used to screen the levels of systemic oxygenation in neonates. Blood gas tensions should be measured in patients with suspected cardiopulmonary abnormalities.
- Cardiovascular.** Central cyanosis and capillary refill should be assessed. Distal pulses should be palpated, noting whether they are bounding.

A delay between brachial and femoral pulses is suggestive of **coarctation of the aorta**. Note the character and location of murmurs and splitting of the second heart sound. During the first 48 hours after birth, murmurs may appear as intracardiac pressure gradients change and disappear as the ductus arteriosus closes.

7. **Abdominal exam.** A scaphoid abdomen suggests **diaphragmatic hernia**. A normal umbilical cord has two arteries and one vein. In nearly 40% of cases, the existence of a single umbilical artery is associated with renal abnormalities. The size of the liver, spleen, and kidneys and the presence of hernias or abdominal masses should be determined by inspection and palpation. The location and patency of the anus should be assessed.
 8. **Neurologic.** A thorough examination includes evaluation of motor activity, muscle strength and tone, and newborn reflexes (Moro, tonic neck, grasp, suck, and stepping reflexes). Full-term newborns should have an up-going Babinski reflex and brisk deep tendon reflexes.
 9. **Genitourinary.** The gonads may be differentiated or ambiguous, and in males, the testes should be palpable. The location of the urethra should be determined, remembering that hypospadias precludes a circumcision. A male infant with hypospadias and bilateral cryptorchidism must be evaluated for congenital adrenal hyperplasia.
 10. **Musculoskeletal.** Any deformities, unusual posturing, or asymmetric limb movement should be noted, and the hips should be examined for possible dislocation with congenital hip dysplasia, particularly in breech infants. A clavicle or humerus may be fractured during a difficult delivery.
 11. **Craniofacial.** One should determine head circumference, the location and size of the fontanelles, the presence of a cephalohematoma or caput, and ensure the palate is intact. Observing nasal gas flow despite occluding each naris or passage of a nasogastric tube will rule out choanal atresia.
- C. Laboratory Studies.** Routine initial laboratory studies may include hematocrit and serum glucose. Additional studies should be guided by the individual problem. For example, blood type and Coombs determination may be indicated in infants at risk for hyperbilirubinemia such as those whose mothers who are blood type O. In addition, a CBC and blood culture should be checked and wide spectrum antibiotic therapy initiated if there is suspicion of neonatal sepsis or maternal chorioamnionitis.
- D. Fluids**
1. **The total fluid requirement** varies with birth weight.
 - a. Less than 1.0 kg, use 100 mL/kg/d.
 - b. 1.0 to 1.5 kg, use 80 to 90 mL/kg/d.
 - c. 1.5 to 2.5 kg, use 80 mL/kg/d.
 - d. Greater than 2.5 kg, use 60 mL/kg/d.
 2. **Isosmolar solutions** should be used.
 - a. **Electrolyte supplementation** is not required within the first day of life for maintenance fluids in full-term infants. For premature infants, check the electrolytes at 8 to 12 hours of life and consider adjusting the fluid infusion rate and/or adding electrolytes as indicated.
 - b. **10% Dextrose** in water is typically used as the initial IV fluid in pre-term and term infants. Blood glucose concentrations should be monitored closely in high-risk infants and the dextrose concentration of IV fluids should be adjusted as required to maintain serum glucose levels described below.

3. Additional fluids may be required **for insensible water loss.**
 - a. Fluid requirements increase with lower birth weight and gestational age, as well as with many neonatal interventions including phototherapy, radiant warmer use, and support of infant with respiratory distress.
 - b. Insensible losses from pathologic causes (e.g., omphalocele, gastroschisis, neural tube defect, bladder exstrophy) must similarly be taken into account and replaced. The electrolyte composition of the replacement fluid should match that of what is lost.
 - c. Infants who are mechanically ventilated absorb free water through their respiratory system.
4. Several signs will determine the adequacy of fluid infusions.
 - a. Urine output at least 1 mL/kg/h.
 - b. Only a 1% loss in body weight per day for the first 10 days of life.
 - c. Stable hemodynamics and good perfusion.
- E. **Electrolytes**
 1. The usual electrolyte requirements after the first 12 to 24 hours of life are as follows:
 - a. Na^+ , 2 to 4 mEq/kg/d.
 - b. K^+ , 1 to 2 mEq/kg/d.
 - c. Ca^{+2} , 150 to 220 mEq/kg/d.
 2. The frequency of laboratory tests for serum electrolyte levels will be determined by the rate of insensible loss.
- F. **Glucose.** Supplemental glucose should be given after birth to keep blood glucose levels between 50 and 125 mg/dL.
 1. In most infants, 10% D/W at maintenance fluid rates will provide adequate glucose. This infusion rate provides the 5 to 8 mg/kg/min of glucose that is required for basal metabolism.
 2. Infants with hyperinsulinism, intrauterine growth restriction, or metabolic defects can require glucose infusion rates as high as 12 to 15 mg/kg/min.
 3. In peripheral intravenous lines, up to 12.5% D/W may be infused. In central lines, 15% to 20% D/W may be infused.
 4. **Hypoglycemia** (glucose <50 mg/dL) is treated with a bolus of glucose and increased glucose infusion rate.
 - a. Glucose at 200 mg/kg intravenously (IV) is given over a minute (e.g., 10% D/W at 2 mL/kg).
 - b. The glucose infusion rate is increased from the current level or started at 8 mg/kg/min IV.
 - c. Serial blood tests are necessary to determine the effectiveness of the increased glucose.
- G. **Nutrition.** The gastrointestinal tract is functional after 28 weeks of gestation but is of limited capacity. Requirements vary with each neonate.
 1. **Calories.** Requirements are 100 to 130 kcal/kg/d.
 2. **Protein.** Requirements are 2 to 4 g/kg/d.
 3. **Fat.** Initiate at 1 g/kg/d and increase gradually as tolerated up to 3 to 4 g/kg/d so that the fat provides 40% of the daily calories.
 4. **Vitamins** A, B, D, E, C, and K should be provided.
 5. **Iron.** Requirements are 2 to 4 mg/kg/d of elemental iron. The adequacy of iron supplementation can be assessed by measuring the hemoglobin or hematocrit and the reticulocyte count.
 6. **Minerals.** Calcium, phosphate, magnesium, zinc, copper, manganese, selenium, and iron need to be replaced. Premature infants, in particular, have increased calcium and phosphate requirements in order to prevent metabolic bone disease of prematurity.

7. **Enteral feedings.** Feedings are usually initiated with breast milk or a formula contains the whey-to-casein ratio that is contained in breast milk. For infants that exhibit lactose intolerance, non- or low-lactose containing formulas are available. Infants less than 32 weeks of gestation often have poor suck and swallow reflexes and require gavage feedings. For premature infants or ill full-term neonates, small volume enteral feedings are generally initiated once the baby is stable. Subsequently, the volumes of the feedings are gradually increased every 12 to 24 hours as they are tolerated. Once the desired goal volume of enteral feedings is reached, the breast milk or formula is supplemented with additional calories, as needed, to attain the desired weight gain.
8. **Parenteral feeding.** If enteral feeding is impossible, parenteral nutrition should be started as soon as possible to promote positive nitrogen balance and growth. The metabolic status of the infant should be assessed frequently so that the parenteral formulation can be adjusted to meet the infant's needs and to identify signs of toxicity from hyperalimentation. Usual studies include serum glucose, electrolytes, osmolality, liver function tests, blood urea nitrogen, creatinine, lipid levels, and platelet count.
- H. **Thermoregulation.** It is critical to measure the newborn's body temperature and use active measures to maintain it in a euthermic range. Babies exhibit thermal instability because of decreased epidermal and dermal thickness, minimal subcutaneous fat, immature nervous system, and increased surface area to body weight ratio with a relatively large head size. Moreover, premature newborns are particularly susceptible to hypothermia because they lack thermogenic brown fat cells. Measures to maintain the newborn's body heat include using a warm incubator during transport to and from the nursery; keeping the ambient operating room temperature at 85°F (30°C); using warming blankets, radiant warmers, and a head cover; and prewarming intravenous fluids. Neonates with significant cold stress are particularly prone to hypoglycemia.

III. COMMON NEONATAL PROBLEMS

A. Preparation for Surgery

1. Conditions that require emergent surgery in neonates are often accompanied with medical problems. As a result, the care for these critically ill newborns requires careful coordination of medical, surgical, and nursing management. In some cases, surgical procedures might occur in the neonatal intensive care unit. In these instances, before the surgical procedure is initiated, it is important to identify and integrate the key resources and care measures provided by the NICU team into the anesthetic management of the surgical procedure.
2. Routine standard monitoring for neonates undergoing surgical procedures includes blood pressure monitoring and continuous electrocardiograph, temperature, pulse oximetry, and O_2 and CO_2 gas measurements. Specialized monitoring for surgical procedures detailed below may also include postductal pulse oximetry, chest piece stethoscopes, and continuous blood pressure monitoring and intermittent blood sampling through arterial and central lines. In infants with umbilical arterial and venous catheters, it is important to confirm the precise location of the tips of the lines and their suitability for fluid and drug infusions and blood sampling.
3. Nonrebreathing circuits are effective for ventilating and for delivering gaseous anesthetic agents to newborns and infants. The system must

have provisions for humidification of the inspired gases to decrease the insensible fluid losses and thereby help maintain the patient's thermostability. If gaseous anesthetic agents are to be used in the NICU, it is important to scavenge the gases that are exiting the ventilator. In some cases, it is better to continue to use the specialized ventilators used in the NICU (e.g., high-frequency oscillator ventilator) rather than the anesthesia machine to support the patient during surgery. A warm operating room (85°F), underbody heaters, radiant warmers, head wraps, and prewarmed intravenous and surgical fluids are also critical in helping the infant maintain thermoregulation.

4. A warm neonatal transport isolette complete with monitors, adequate oxygen supply, and emergency airway and drugs is required for moving neonatal patients to and from the intensive care unit and OR.

B. Respiratory Disorders

1. **Differential diagnosis.** The following diseases present similarly as pulmonary parenchymal disease and should be considered when evaluating an infant with respiratory distress.
 - a. **Airway obstruction.** Choanal atresia, vocal cord palsy, laryngomalacia, tracheal malacia or stenosis, and compression of the trachea by external masses (e.g., cystic hygroma, hemangioma, and vascular ring).
 - b. **Developmental anomalies.** TEF, CDH, congenital lobar emphysema, pulmonary sequestration, bronchogenic cysts and congenital pulmonary airway malformations (CPAMs)/congenital cystic adenomatoid malformations (CCAMs).
 - c. **Nonpulmonary.** Cyanotic heart disease, PPHN, congestive heart failure, and metabolic disturbances.
2. **Laboratory studies** for an infant in respiratory distress should include an arterial blood gas, pre- and postductal oxygen saturation (determined by pulse oximetry), hemoglobin or hematocrit, 12-lead ECG, and CXR. If these results are abnormal, potential cardiac disease should be evaluated by assessing blood gas tensions while the neonate breathes 100% O₂ (hyperoxia test). As indicated, cardiology consultation and an echocardiogram will help evaluate potential congenital heart disease.

3. Apnea

a. Etiology and treatments

1. **Central apnea** is due to immaturity or depression of the respiratory center (e.g., narcotics). It is related to the degree of prematurity and is exacerbated by metabolic disturbances (e.g., hypoglycemia, hypocalcemia, hypothermia, hyperthermia, and sepsis). Before 34 weeks of gestational age, central apnea is often treated with **methyloxanthines** such as caffeine citrate.
2. **Obstructive apnea** is caused by inconsistent maintenance of a patent airway. It can result from incomplete maturation and poor coordination of upper airway musculature. This form of apnea may respond to changes in head position, insertion of an oral or nasal airway, or placement of the infant in a prone position. Occasionally, administration of **continuous positive airway pressure** (CPAP) or a high-flow oxygen nasal cannula may be beneficial. These therapies especially may be effective in infants with a large tongue, such as with trisomy 21 or Beckwith-Wiedemann syndrome.
3. **Mixed apnea** represents a combination of both central and obstructive apnea.

b. Postoperative apnea in the neonate

1. Apnea may be associated with anesthesia in infants that are born prematurely. Although it has been observed following general anesthesia, apnea has been reported in infants treated with local anesthesia.
2. If it is not possible to delay surgery until the patient is more mature, it is prudent to use **postoperative apnea monitoring** in neonates who undergo anesthesia at less than 60 weeks postconceptional age.

4. Respiratory distress syndrome (RDS)

- a. **Pathophysiology.** RDS results from physiologic surfactant deficiency. This causes decreased lung compliance, alveolar instability, progressive atelectasis, and hypoxemia resulting from intrapulmonary shunting of deoxygenated blood.
- b. Prematurely born infants have an increased incidence of RDS. Newborns at risk for RDS can be identified prenatally by amniocentesis and evaluation of the amniotic fluid phospholipid profile. Lung surfactant maturity in the fetus is associated with a lecithin-to-sphingomyelin ratio greater than 2, saturated phosphatidylcholine level greater than 500 $\mu\text{g}/\text{dL}$, or presence of phosphatidylglycerol in the specimen.
- c. **Glucocorticoid (betamethasone) treatment** of the mother at least 48 hours prior to delivery decreases the incidence and severity of RDS. Only one full course of a glucocorticoid treatment regimen during a pregnancy is necessary. This is accomplished by giving one dose of glucocorticoid to the pregnant woman per day for 2 days.
- d. **Clinical features** of RDS include tachypnea, nasal flaring, grunting, and retractions. Cyanosis appears shortly after birth. Because of the intrapulmonary shunt across atelectatic lung units, infants with RDS remain hypoxemic despite breathing at high FiO_2 .
- e. The **chest x-ray** will show low lung volumes. A “ground-glass” pattern of the lung fields and air bronchograms may also be evident.
- f. **Initial treatment** includes warmed, humidified oxygen administered by hood or nasal cannula. The FiO_2 should be adjusted to maintain the PaO_2 between 50 and 80 mm Hg (SaO_2 between 88% and 92%). If an FiO_2 greater than 60% is required to keep the patient oxygenated, **nasal CPAP** should be administered. With more severe disease, or if the nasal CPAP is poorly tolerated, intubation and ventilation with positive end-expiratory pressure may be required. In intubated newborns with RDS, endotracheally administered exogenous **surfactant** decreases the morbidity and mortality of the disease. In babies with severe RDS, **high frequency oscillatory ventilation (HFOV)** decreases the incidence of air leaks and chronic lung disease (CLD).
- g. **Broad-spectrum antibiotics** are often begun after appropriate cultures are obtained because the clinical signs and CXR of patients with RDS are indistinguishable from pneumonia.
- h. In more mature newborns, RDS may be self-limited. Clinical improvement often occurs after 2 to 3 days and is associated with a spontaneous diuresis. In extremely premature newborns, RDS may progress to CLD.
- i. The **morbidity and mortality** of patients with RDS are directly related to the degree of prematurity, perinatal resuscitation, and the coexistence of other complications of prematurity (e.g., patent ductus arteriosus, infection, intraventricular hemorrhage). **Pneumothoraces, pulmonary interstitial emphysema, and pulmonary hemorrhage** may complicate the recovery and can be associated with the evolution to CLD.

5. Bronchopulmonary dysplasia (BPD)

- a. **Etiology.** BPD is defined as the continued need for oxygen therapy or mechanical ventilation beyond 36 weeks postconceptual age. BPD is also referred to as CLD of prematurity and is associated with oxygen toxicity, chronic inflammation, and mechanical injury in the lung. BPD can be worsened by the presence of a patent ductus arteriosus or infection. However, in some premature infants, BPD occurs in the absence of significant lung injury. Recent studies suggest that BPD is associated with excessive transforming growth factor-beta (TGF- β) signaling in the injured developing lung. Preventive strategies include vitamin A or caffeine administration and early initiation of CPAP.
- b. **Clinical features** include retractions, rales, and areas of lung hyper- and hypoinflation. Because of nonhomogenous ventilation, an intrapulmonary shunt may produce hypoxemia and hypercarbia in patients with BPD. Hypoxia and hypercarbia may also be associated with bronchospasm in many patients with severe BPD. Many patients with severe BPD have growth failure and require high-caloric feeds.
- c. **Treatment** consists of supportive respiratory care, aggressive nutrition, and diuretic therapy. Because patients with BPD may have lung segments with long time constants, a ventilatory pattern with low respiratory rates and increased inspiratory and expiratory time may decrease gas trapping and improve gas exchange. Permissive hypercapnia is typically utilized to minimize further lung injury. In addition, **bronchodilator therapy** may be lifesaving in patients with BPD and bronchospasm. Systemic steroids sometimes are used to treat patients with CLD. However, because of adverse long-term neurodevelopmental outcomes observed in infants treated with systemic steroids, this therapy is typically reserved for the most severe cases. In some patients with severe BPD, pulmonary hypertension might be observed. In these cases, pulmonary vasodilators including inhaled NO and type 5 phosphodiesterase inhibitors have been used.
- d. **Prognosis** of BPD varies with the severity of the disease. Of severely affected infants, 20% die within the first year. Most infants are generally asymptomatic by 2 years of age but additional morbidities include recurrent respiratory infections, increased pulmonary reactivity and asthma, repeated hospitalizations, pulmonary hypertension, and neurodevelopmental abnormalities.

6. Pneumothorax

- a. **Etiology.** Pneumothorax can occur in infants requiring positive pressure or mechanically ventilation. In addition, spontaneous pneumothorax can occur in 1% to 2% of otherwise healthy full-term infants who often remain asymptomatic or mildly symptomatic and require no intervention. The incidence increases up to 5% to 10% of full-term infants with meconium staining or prematurely born infants with RDS.
- b. **Clinical features.** The diagnosis should be considered in any neonate with an acute deterioration in clinical condition (e.g., sudden cyanosis and hypotension). Occasionally, asymmetric chest movement with ventilation and asymmetric breath sounds may be appreciated; however, endobronchial intubation should be ruled out.
- c. **Laboratory studies.** Transillumination of the chest with a strong light usually will show a hyperlucent hemithorax. If the patient is stable, a CXR may be obtained to confirm the diagnosis.

d. Treatment

1. In otherwise stable and well-oxygenated term infants with minimal respiratory distress, a nitrogen washout by breathing a high concentration of oxygen has historically been used to assist with resolution of the pneumothorax. However, the data supporting this mode of therapy are minimal and should be weighed against newer ones suggesting that hyperoxia is associated with end-organ injury.
2. In the **unstable infant**, immediate aspiration of the pleural space with an IV catheter should be performed. Reaccumulation of clinically significant air after aspiration warrants placement of a chest tube.

7. Meconium aspiration syndrome

- a. **Meconium staining of amniotic fluid** occurs in 12% of all births and may be associated with fetal distress and perinatal depression.
- b. To **decrease the effects of aspiration**, it is prudent to intubate and suction the airways of infants with meconium-stained fluid who are born with depressed respirations and poor tone.
- c. **Meconium aspiration** may produce lung airspace disease by mechanical obstruction of the airways with fecal matter and chemical inflammation and surfactant inactivation causing pneumonitis. Complete obstruction of the airways by meconium results in distal atelectasis. Partial obstruction of the airways may produce overinflation of distal air spaces by a ball-valve effect, leading to pneumothorax. The bile in meconium may cause chemical pneumonitis and airway edema.
- d. **Meconium aspiration syndrome** is also associated with PPHN (see section III.B.5).
- e. Chest radiographic findings can include diffuse, patchy intraparenchymal densities with areas of hyper- and hypoinflation.
- f. **Respiratory support** for meconium aspiration is dependent on the etiology of the poor gas exchange. Obstruction of airways with meconium may require mechanical ventilation with long expiratory times to decrease gas trapping. Pneumothorax is treated by placement of a chest tube. Sometimes high-frequency oscillatory ventilation can recruit closed lung segments and improve gas exchange. Alkalosis and **inhaled nitric oxide (INO)** have been useful to decrease pulmonary vasoconstriction. Exogenous **surfactant** has also been observed to be beneficial as meconium inhibits endogenous surfactant activity.

8. Congenital diaphragmatic hernia (CDH)

- a. **CDH** is a defect of the diaphragm allowing abdominal contents to herniate into the chest. CDH occurs in 1 in 5,000 live births and has a high mortality, with 40% not surviving infancy.
- b. **Clinical features.** CDH is usually detected during a prenatal ultrasound. Eighty-five percent of defects occur in the left posterior lateral region of the diaphragm through the foramen of Bochdalek. The neonate often has a scaphoid abdomen with absent breath sounds on the involved side. Rarely, bowel sounds are heard in the affected hemithorax. The clinical spectrum of CDH may vary and is probably related to the degree of lung hypoplasia and associated pulmonary hypertension and cardiac dysfunction.
- c. The **diagnosis** is confirmed by CXR. The intestines and stomach are typically observed in the thorax. The liver, spleen, and/or kidneys may also be involved. Approximately 40% of infants with CDH have

associated anomalies including cardiac, gastrointestinal, genitourinary, or renal anomalies that significantly increase the risk of mortality.

- d. **Treatment is geared toward decreasing pulmonary vascular resistance and facilitating CO₂ elimination prior to surgical correction.** Insufflation of the stomach and intestines is minimized by intubating the patients while they are spontaneously breathing and may often take place in the delivery room. However, if necessary, ventilation with bag and mask should be accomplished with minimal airway pressures. Continuous gastric suction also decreases air insufflation. Conventional ventilation or HFOV is used. Ventilation with INO has been observed to decrease pulmonary vasoconstriction and cyanosis in some patients with CDH. The main causes of mortality are respiratory insufficiency and pulmonary hypertension. Pneumothorax in the unaffected lung can occur and is often the cause of death during resuscitation. Hypotension and shock are frequently seen secondary to prolonged systemic hypoxemia, cardiac impairment caused by shifting of the mediastinal contents by the hernia, and gastrointestinal fluid losses.
- e. **Surgical repair** involves replacing the abdominal contents and repairing the diaphragm. Current evidence supports first stabilizing the patients with medical therapy and gentle ventilation, using **extracorporeal membrane oxygenation (ECMO)** as a last resort (see section III.B.5.d.5). During the stabilization period, pulmonary artery pressures fall, and the patient is subsequently taken to the OR for repair.
- f. **Anesthetic considerations:** Decompression of the gut with continuous nasogastric suction is helpful. An arterial catheter is indicated for the frequent assessment of acid–base balance, oxygenation, and ventilation. Sodium bicarbonate and hyperventilation are used to treat metabolic and respiratory acidosis, respectively. In addition, alkalosis and INO may decrease pulmonary vasoconstriction. Although spontaneous ventilation may prevent gastric inflation and lung compression, ventilator support is often needed. Using the lowest effective inflating pressures reduces the risk of pneumothorax and ventilator-induced lung injury (VILI). Nitrous oxide is avoided because it may distend the gut and compromise lung function. Muscle relaxation, narcotics, and oxygen therapy are often used during anesthesia.
- g. Postoperative morbidities include feeding difficulty, gastroesophageal reflux, hearing loss, neurodevelopmental disability, and potential recurrence of the diaphragmatic hernia, particularly in those infants with a large defect requiring a patch repair.

C. Cardiovascular Disorders

1. **Congenital heart disease** should be suspected in the setting of persistent cyanosis, hypotension, respiratory distress, murmur, hypoxemia, poor perfusion, or shock. Congenital heart disease occurs with an overall incidence of 8 per 1,000 live births with 2 per 1,000 presenting in the first year of life. The most common congenital heart disease lesions include ventricular septal defects, pulmonary stenosis with intact ventricular septum, tetralogy of Fallot, atrial septal defects, or transposition of the great arteries.
2. **Cyanosis**
 - a. **Etiology.** There are many causes of cyanosis, including diffusion abnormalities in the lung, intracardiac and extracardiac shunts, and polycythemia. The pulmonary causes of cyanosis are described above.

- b. **Cardiac lesions** may cause systemic hypoxemia by decreasing pulmonary blood flow or by causing admixture of systemic and pulmonary venous blood via shunts.
 - c. Several factors allow the majority of fetuses to tolerate congenital heart lesions in utero. Fetal oxygenation occurs via the placenta, rather than being dependent on pulmonary blood flow. Both the left and right ventricles contribute to systemic blood flow, and mixing occurs at atrial and ductal levels. Furthermore, the fetus has greater oxygen carrying capacity because of fetal hemoglobin and an elevated hemoglobin concentration.
 - d. In the newborn, the **ductus arteriosus may initially permit pulmonary blood flow** in patients with transposition of the great arteries, pulmonary stenosis or atresia, tetralogy of Fallot, or ventricular hypoplasia. Most of these infants become symptomatic as the ductus arteriosus closes at 2 to 3 days of life. If a ductal-dependent cardiac lesion exists, prevention of ductal closure is critical to maintain pulmonary blood flow. This may be accomplished with a **prostaglandin E₁** infusion. Side effects of prostaglandin treatment include apnea, hypotension, and seizure activity.
 - e. Many patients with **septal defects** are asymptomatic during the fetal and neonatal period. However, with increased pulmonary vascular resistance, right-to-left shunting of deoxygenated blood may produce systemic hypoxemia. Later in life, the normal decrease in pulmonary vascular resistance increases blood flow to the lung and potentially causes pulmonary vascular overcirculation and pulmonary hypertension.
 - f. **Laboratory studies.** In the infant with signs and symptoms of cardiovascular disease, relevant studies include an arterial blood gas, pre- and postductal oxygen saturations, 4 extremity blood pressures, an ECG, CXR, hemoglobin or hematocrit, and determination of arterial blood gas tension during inhalation of pure oxygen ("**hyperoxia test**"). A PaO₂ that remains below 150 mm Hg while the infant breathes 100% oxygen is suggestive of an intracardiac shunt. Cardiology consultation is indicated, and echocardiography is frequently performed to detect potential structural heart lesions.
- 3. Patent ductus arteriosus (PDA)**
- a. **Clinical features.** PDA is commonly encountered in the premature infant and is characterized by a murmur at the left sternal border radiating to the back, bounding pulses, widened pulse pressure, evidence of increased pulmonary blood flow by CXR, respiratory distress, and excessive weight gain. The PDA often can be confirmed by cardiac ultrasound. In some cases, cardiac dysfunction associated with a PDA may decrease systemic blood pressure, peripheral perfusion, and urine output and may be associated with metabolic acidosis.
 - b. Although **early treatment** of a PDA consists of fluid restriction and supportive care, it is important to maintain systemic perfusion. If the degree of shunt through the ductus arteriosus is significant, and renal and platelet function are adequate, pharmacologic closure of the ductus with **indomethacin** or **ibuprofen** may be attempted.
 - c. **Surgical closure** of a PDA is indicated in symptomatic infants for whom medical therapy has either failed, is contraindicated, such as those with decreased renal or platelet function, or thought not to be effective.

d. Anesthetic considerations: Often these infants are critically ill, requiring high levels of oxygen support, ventilator support and vasopressor therapy. They may have renal dysfunction, because of decreased cardiac output caused by the PDA and fluid restriction, and platelet dysfunction because of medical therapies. Many PDA closures may take place in the NICU to avoid the risk of transporting the infant to the OR. In addition to a preductal pulse oximeter that is used to assess cerebral oxygen delivery, a postductal oximeter can be helpful during the surgical procedure for detecting inadvertent occlusion of the aorta during assessment of the anatomy of the central circulation. An opiate-based anesthetic (e.g., fentanyl) with muscle relaxation is a common technique used for infants undergoing PDA ligation. Infants should be monitored closely in the postoperative period for complications including pneumothorax, hypotension, and oliguria.

4. Dysrhythmias

- a. Supraventricular tachycardia (SVT)** is the most frequent dysrhythmia seen in fetuses and neonates. The associated heart rate greater than 250 beats/min is often self-limited and well tolerated. However, if the SVT is associated with hypotension or hemoglobin oxygen desaturation, prompt treatment is required.
- b. SVT treatment** consists of vagal maneuvers such as nasopharyngeal stimulation or placement of a cold pack glove or ice-filled glove on the infant's face. Massage of the eye should be avoided, as this may lead to disruption of the lens in neonates. **Adenosine** and **esophageal pacing** are also useful for acute management of symptomatic SVT.
- c. Synchronized electrocardioversion** is indicated if the patient is hemodynamically unstable.

5. Persistent pulmonary hypertension of the newborn (PPHN)

- a. Pathophysiology.** PPHN, previously referred to as persistent fetal circulation, is manifested by an increase in lung vascular resistance with resulting pulmonary arterial hypertension, right-to-left shunting across the foramen ovale and the ductus arteriosus, and systemic hypoxemia.
- b. Etiology.** It is suspected that many newborns with PPHN have abnormal muscularization of the distal lung vascular bed and reactivity of the pulmonary arteries. Although PPHN is associated with perinatal depression, meconium aspiration, bacterial pneumonia, or sepsis, the exact role of these in the etiology of PPHN is unknown.
- c. Clinical features.** Typically, term or near-term newborns with PPHN have severe systemic hypoxemia unrelieved by breathing at high FiO_2 . They may have shunt evidenced by higher oxygen saturations in the upper versus lower extremities. ECG may reveal right ventricular hypertrophy, and CXR may show decreased pulmonary vascular markings. Echocardiography may demonstrate shunting of blood at the level of the PDA and/or PFO.

d. Treatment of PPHN

- 1.** Specific treatments include: intubation and mechanical ventilation with high FiO_2 , induced respiratory or metabolic alkalosis, and INO administration. In nearly 50% of cases, carefully administered inhaled NO gas rapidly vasodilates the pulmonary vasculature, decreases shunt, and increases systemic oxygenation. In babies breathing NO gas, the levels of methemoglobin and inhaled NO oxides need to be measured.

2. Nonspecific and supportive treatments include aggressive blood pressure support, sedation with narcotics (e.g., fentanyl), and occasionally muscle relaxants.
3. Extracorporeal Membrane Oxygenation (**ECMO**) may be lifesaving for some patients with PPHN refractory to ventilatory and medical therapy.
 - a. The **ECMO circuit** consists of tubing, a reservoir, pump, membrane oxygenator, and heat exchanger. To prevent clotting, the patient is treated with heparin. Because of platelet consumption during ECMO, platelet infusions are often required.
 - b. **Access.** General anesthesia is required for central vascular cannulation during the initiation of ECMO. In neonates with adequate cardiac function, **venovenous (VV)** ECMO is performed with a single double-lumen catheter placed in the right ventricle via the right internal jugular vein. In neonates with compromised cardiac function and/or congenital heart disease associated with the PPHN, **venoarterial (VA)** ECMO is facilitated by cannulation of the right common carotid artery and the right internal jugular vein or the femoral artery and vein.
 - c. **Potential morbidities** are associated with ECMO. Heparin treatment can cause intracranial hemorrhage and bleeding from other sites. Right-sided cerebral injuries (focal left-sided seizures, left hemiparesis, and progressive right cerebral atrophy) are thought secondary to cannulation and ligation of the right internal carotid artery.
 - d. Because of the potential risks of ECMO, it is reserved for term and late preterm (>34 weeks) infants with a birth weight generally greater than 1,800 to 2,000 g with severe systemic hypoxemia. Prior to ECMO cannulation, a screening head ultrasound, echocardiogram, and baseline laboratory evaluation should be performed. Most infants with significant intracranial hemorrhage are excluded because of the unacceptable risk of hemorrhage extension while being treated with heparin. Also excluded are infants with multiple congenital anomalies, severe neurologic impairment, or cyanotic congenital heart disease.

D. Hematologic Disorders

1. Hemolytic disease of the newborn (erythroblastosis fetalis)

- a. **Isoimmune hemolytic anemia** in the fetus is caused by transplacental passage of maternal IgG antibodies against fetal erythrocytes.
- b. **Rh hemolytic disease** is usually caused by anti-D antibodies but can also be caused by antibodies to minor antigens including Kell, Duffy, and Kidd. The absence of D antigen makes one Rh negative. A mother can be sensitized to fetal antigens by leakage of fetal blood into the maternal circulation during pregnancy, delivery, abortion, or amniocentesis. To prevent sensitization, an unsensitized Rh-negative mother is given **anti-D immune globulin (Rhogam)** during pregnancy at 28 weeks of gestation, after any invasive procedure (e.g. amniocentesis), and at delivery. Once a mother is sensitized, immune prophylaxis is of no value. Even if treated with immune globulin, a mother can still be sensitized during pregnancy if a large fetomaternal transfusion occurs.
- c. **ABO hemolytic disease** can occur without maternal sensitization, because a mother with group O blood has naturally occurring anti-A and anti-B antibodies in her circulation. Because these are usually

IgM antibodies that cannot cross the placenta, ABO hemolytic disease tends to be milder than Rh disease, with little or no anemia, mild indirect hyperbilirubinemia, and rare need for exchange transfusion.

- d. An **indirect Coombs test** on maternal blood can detect the presence of IgG antibodies.
 - e. A **direct Coombs test** on the infant's red blood cells can detect cells already coated with antibody, thus indicating a risk for hemolysis.
 - f. **Hemolysis** occurs when antibodies cross the placenta and attach to the corresponding antigens on fetal erythrocytes. Hepatosplenomegaly results from increased hematopoiesis triggered by hemolysis.
 - g. **Clinical features.** Physical examination may reveal hepatosplenomegaly, edema, pallor, scleral icterus, or jaundice.
 - h. **Laboratory studies** often reveal anemia, thrombocytopenia, a positive direct Coombs test, indirect hyperbilirubinemia, hypoglycemia, hypoalbuminemia, and an elevated reticulocyte count that increases proportionally with the severity of the disease. Serial hematocrit and indirect bilirubin levels should be followed.
 - i. **First-line treatment** consists of **phototherapy**. IVIG administration and/or an exchange transfusion may be required if the total indirect bilirubin level is very high or the rate of rise of bilirubin exceeds 1 mg/dL/h.
- 2. Hydrops fetalis**
- a. **Hydrops fetalis** is associated with excessive accumulation of fluid in at least two body compartments of the fetus and can range from mild peripheral edema to massive anasarca with pleural and/or pericardial effusions.
 - b. **Etiologies.** Hydrops fetalis is associated with anemia (e.g., hemolytic disease, fetomaternal hemorrhage, donor twin–twin transfusion), cardiac arrhythmias (e.g., complete heart block, SVT), congenital heart disease, vascular or lymphatic malformation (e.g., hemangioma of the liver, cystic hygroma), and infection (e.g., viral, toxoplasmosis, syphilis).
 - c. **Treatment.** The main goals of therapy include prevention of intrauterine or extrauterine death from anemia and hypoxia, restoration of intravascular volume, and avoidance of neurotoxicity from hyperbilirubinemia.
 1. Survival of the unborn fetus may be improved by in utero transfusion via the umbilical vein.
 2. Care of the live born infant with hydrops may include respiratory support with intubation and mechanical ventilation, paracentesis and/or thoracentesis, echocardiogram, placement of central lines, correction of hypovolemia and acidosis, and exchange transfusion. Some of these babies require aggressive and prolonged ventilator support because of pulmonary hypoplasia.
 3. Late complications include anemia, mild graft-versus-host reactions, inspissated bile syndrome (characterized by persistent icterus with elevated direct and indirect bilirubin), and portal vein thrombosis (as a complication of umbilical vein catheterization).

E. Gastrointestinal Disorders

1. Hyperbilirubinemia

- a. **Pathophysiology.** Bilirubin is formed from the breakdown of hemoglobin. It is rapidly bound to albumin, transported to the liver

(where it is conjugated with glucuronate), and delivered to the intestine in bile. In the intestine, it is either deconjugated by intestinal bacteria and reabsorbed or converted to excretory urobilinogen.

- b. **Etiology.** Hyperbilirubinemia results from overproduction (e.g., hemolysis, absorption of sequestered blood, polycythemia), underconjugation (e.g., immature or damaged liver), or underexcretion (e.g., biliary atresia). It is often seen in sepsis, asphyxia, and metabolic disorders (e.g., hypothyroidism, hypoglycemia, galactosemia) as well as in healthy, typically breast-fed infants.
- c. **Toxic effects.** Unconjugated (indirect) bilirubin is lipid soluble and is capable of crossing the blood–brain barrier and entering the central nervous system. Toxic levels of bilirubin result in damage of neurons. This process, leads to **bilirubin encephalopathy** or **kernicterus** and may cause symptoms ranging from mild lethargy and fever to convulsions. Infants with prematurity, respiratory distress, sepsis, metabolic acidosis, hypoglycemia, hypoalbuminemia, or severe hemolytic disease are at risk for kernicterus. Later in life, kernicterus causes neurologic sequelae including diminished cognitive function, mental retardation, sensorineural hearing loss, dental dysplasia, and choreoathetoid cerebral palsy.
- d. **Physiologic jaundice** results from increased red cell turnover and an immature hepatic conjugation system. It occurs in 60% of term newborns, and peak bilirubin levels occur by day 2 to day 4 of life. Premature infants have an increased incidence (80%) and later bilirubin peak (day 5 to day 7 of life).
- e. **Breast milk jaundice** develops gradually in the 2nd or 3rd week of life. In this disease, bilirubin levels peak at 15 to 25 mg/dL, and the elevated bilirubin levels may persist for 2 to 3 months. Other causes of hyperbilirubinemia should be excluded before making this diagnosis. Interrupting nursing for a few days and supplementing with formula results in a marked decrease in serum levels, at which time nursing can be restarted. This is a benign type of jaundice without adverse sequelae.
- f. **Laboratory studies** include total and direct bilirubin, blood type and direct Coombs test, hemoglobin or hematocrit, reticulocyte count, blood smear for red cell morphology, electrolytes, blood urea nitrogen, creatinine, and appropriate cultures if sepsis is suspected. Because hyperbilirubinemia may be the presenting sign of a urinary tract infection, urinalysis and urine cultures should be considered.
- g. **Treatment**
 - 1. An elevated bilirubin level in the first 24 hours of life is pathologic and always warrants further investigation.
 - 2. Management of physiologic or mild hemolytic jaundice consists of monitoring serial bilirubin levels and starting early feeding to reduce enterohepatic cycling of bilirubin.
 - 3. **Phototherapy** is used if moderate indirect bilirubin levels or an accelerated rate of rise is noted. Light therapy of 420- to 470-nm wavelength results in photoisomerization of bilirubin, making it water soluble. Eyes must be shielded during phototherapy to prevent retinal damage.
 - 4. For severe hyperbilirubinemia, IVIG administration and/or **exchange transfusion** are indicated (e.g., indirect bilirubin >25 mg/dL in a full-term infant).

2. Esophageal atresia (EA) and tracheoesophageal fistula (TEF)

- a. EA is usually associated with TEF. The location of the fistula in patients with TEF is variable, with the most common configuration consisting of a proximal esophageal pouch and a distal TEF. EA/TEF is often accompanied by other congenital abnormalities, particularly cardiac defects.
- b. **Pathophysiology.** The proximal esophageal pouch has a small capacity, resulting in overflow aspiration. Aspiration leads to the classic clinical triad of coughing, choking, and cyanosis in patients with EA. Occasionally, copious secretions with drooling requiring frequent suctioning may be the only early symptom.
- c. The **diagnosis** is confirmed by the inability to pass a nasogastric tube into the stomach. A CXR that includes the neck with air or water-soluble contrast agent will confirm the existence of esophageal atresia.
- d. **Medical treatment** is directed at reducing aspiration. Neonates should be kept NPO. A nasogastric tube is placed on continuous low suction and the head of the bed is elevated. Aspiration pneumonia should be treated with antibiotics and oxygen as required. Endotracheal intubation and ventilation may be required for severe pneumonia. However, ventilation may be difficult when a TEF exists.
- e. **Surgical treatment** depends on the stability of the infant. In newborns with severe pneumonia, surgery may be delayed until the lungs improve. If gastric distension because of air transiting the TEF into the GI track compromises pulmonary function, a gastrostomy tube may be placed under local anesthesia. After initial stabilization, definitive repair of the esophagus and fistula may occur.
- f. **Anesthetic considerations:** It is critical, and sometimes difficult, to establish an airway in patients with a TEF. Surgeons should be readily available during the induction should emergent decompression of the stomach be required. The patient should be fully monitored; a precordial chest piece should be placed over the left thorax to aid in the assessment of ventilation. If the patient has a gastrostomy tube, it should be placed to water seal. An inhalation induction or awake intubation should be performed. To facilitate placement of the endotracheal tube so that its tip resides between the fistula and the carina, the tube may be placed first into the right mainstem bronchus. The tube then may be withdrawn slowly until breath sounds are heard over the left thorax. Decreased breath sounds and insufflation of the stomach or gas exiting from the gastrostomy tube suggest that the end of the endotracheal tube is above the fistula and that it should be advanced. Once the tube is in a good location, it must be carefully secured and monitored for dislodgement during the surgical procedure.
- g. **Intraoperative management.** Inhalation anesthesia with spontaneous ventilation should be maintained until a gastrostomy is performed. Positive pressure ventilation should be attempted before a muscle relaxant is administered.

3. Duodenal atresia

- a. **Clinical features.** Duodenal atresia usually presents with bile-stained emesis, abdominal distention, and increased volume of gastric aspirates. It is associated with trisomy 21 and may coexist with other intestinal malformations.

- b. Prenatal ultrasound or a postnatal **abdominal x-ray** often reveals a “**double bubble**,” representing air in the stomach and proximal duodenum.
- c. **Treatment** consists of avoiding oral feeds, use of nasogastric suction, ensuring adequate hydration, and managing electrolytes. Anesthesia consists of an awake or rapid sequence intubation, avoidance of nitrous oxide, and often the use of muscle relaxants.

4. Pyloric stenosis

- a. **Clinical features:** Pyloric stenosis usually presents in the 3rd to 5th week of life and is characterized by hypertrophy of the pylorus, which causes gastric outlet obstruction. The patient may present with persistent nonbilious emesis. Although the infant may exhibit hypochloremic, hypokalemic metabolic alkalosis from loss of hydrochloric acid, protracted vomiting may result in metabolic acidosis, intravascular volume depletion, and shock. An abdominal mass consisting of the hypertrophic pylorus or “olive” may be palpable.
- b. An **abdominal x-ray** usually shows gastric dilatation. The diagnosis is confirmed by abdominal ultrasound. In the past, x-ray examinations with contrast were performed to confirm this disease.
- c. **Treatment** consists of rehydration, correction of metabolic alkalosis, and nasogastric or orogastric drainage before surgical repair via pyloromyotomy.
- d. **Anesthetic considerations:** It is critical to empty the stomach before anesthetic induction. Since the patient’s nasogastric tube is often blocked with gastric secretions, it is best replaced just before induction and the patient suctioned while they are positioned supine, lateral, and prone. A rapid-sequence or awake intubation may then be performed. Inhalation anesthetics or muscle relaxants can be used as needed. Narcotics often are not necessary, and the patient may be prone to respiratory depression from narcotics due to CSF alkalosis. Rectal acetaminophen and local anesthetic infiltration of the surgical incision may be sufficient for analgesia. The neonate should be fully awake and breathing adequately before removing the endotracheal tube.

5. Omphalocele and gastroschisis

- a. **Clinical features.** An **omphalocele** is caused by failure of the migration of the intestine into the abdomen and subsequent closure of the abdominal wall at 6 to 8 weeks of gestation. The viscera remain outside the abdominal cavity and are covered with intact peritoneum. Associated defects are present in 45% to 80% of patients with an omphalocele and can include genetic abnormalities (50%), cardiac defects (28%), exstrophy of the bladder and other genitourinary abnormalities (20%), craniofacial defects (20%), and congenital diaphragmatic hernia (12%). **Gastroschisis** occurs later in fetal life (12 to 18 weeks of gestation) from interruption of the omphalomesenteric artery. The resulting paraumbilical defect allows exposure of the bowel to the intrauterine environment without peritoneal coverage. Bowel loops are often edematous and covered with an inflammatory exudate. In contrast to omphalocele, gastroschisis is associated with other congenital abnormalities in only 10% to 20% of cases but may be complicated by intestinal atresia/stenosis or midgut volvulus in up to 16% of cases.
- b. **Medical stabilization** includes nasogastric drainage, IV hydration, and protection of the viscera before surgical repair. If the peritoneal

sac is intact, the omphalocele should be covered with sterile, warm, saline-soaked gauze to decrease heat and water loss and the risk of infection. If the sac has ruptured or if the infant has gastroschisis, warm saline-soaked gauze should be used to wrap the exposed viscera or the infant can be placed in a sterile plastic bag with careful ongoing monitoring of intestinal perfusion. The infant should then be wrapped in warm sterile towels before surgical repair.

- c. **Anesthetic considerations:** In the operating room, special measures are directed at compensating for the increased insensible water and heat loss associated with the abdominal surgery. After carefully emptying the stomach, a rapid-sequence induction or awake intubation is performed. Muscle relaxation aids the surgeons in placing the organs into the abdominal wall or silo. Special attention is required to maintain ventilation and systemic blood flow after the organs are placed in the abdomen, which can be facilitated by measuring ventilatory pressures, urine output, and lower body blood pressure and oxygen saturation. These data aid in the decision of whether the lesion should be corrected in a single or staged procedure. It is essential to assess ventilation and oxygenation of the patient prior to extubation. The increased intra-abdominal pressures associated with the procedure can compromise the pulmonary function of the patient and perfusion of the abdominal contents.

6. Necrotizing enterocolitis (NEC)

- a. **NEC** is an acquired intestinal necrosis that appears in the absence of functional or anatomic lesions. It occurs predominantly in premature infants with an increased incidence at lower gestational ages and may be endemic or epidemic. It usually develops during the first few weeks of life and almost always after the institution of enteral feedings. Mortality may be as high as 40%.
- b. **Pathogenesis** is unclear but involves critical stress of an immature gut by ischemic, infectious, or immunologic insults. Enteral feedings seem to potentiate mucosal injury, though feeding with breast milk may be protective.
- c. **Clinical features** include abdominal distention, feeding intolerance with gastric aspirates or emesis, ileus, abdominal wall erythema, and bloody stool. The infant may demonstrate temperature instability, lethargy, respiratory and circulatory instability, apnea, oliguria, and DIC.
- d. **Laboratory studies** should include an abdominal x-ray (which may show **pneumatosis intestinalis**, fixed loops of bowel, portal venous air, or free intraperitoneal air), CBC (revealing leukocytosis, leukopenia, thrombocytopenia), arterial blood gases (demonstrating acidosis), electrolytes (showing hyponatremia or acidosis), stool guaiac (often showing occult blood), and stool Clinitest (showing evidence of carbohydrate malabsorption). Because the differential diagnosis includes sepsis, cultures of blood and urine should also be obtained. If the patient is stable and disseminated intravascular coagulation is not evident, cerebrospinal fluid (CSF) should be obtained by lumbar puncture for Gram stain and culture.
- e. **Treatment.** When NEC is suspected, enteral feedings are discontinued, and the stomach is decompressed with a nasogastric tube. Oral feeds are withheld for at least 10 to 14 days, and the patient is supported with parenteral nutrition. Broad-spectrum antibiotics (ampicillin, an aminoglycoside and, if perforation is suspected, metronidazole or clindamycin) are administered empirically.

f. **Surgical consultation** is indicated, although laparotomy or abdominal drain placement is usually reserved for intestinal perforation, a fixed loop on serial abdominal x-rays, or persistent metabolic acidosis. The **key anesthetic issues** are preventing aspiration of gastric contents and maintaining organ perfusion in the presence of significant third-space fluid losses.

7. Volvulus

- a. **Volvulus** may occur as a primary lesion or, more commonly, as the result of intestinal malrotation, which can rapidly compromise blood flow to the intestine causing ischemia. If present in utero, intestinal necrosis may be present at birth, and immediate resection is indicated.
- b. **Clinical features** may include abdominal distention, bilious emesis, and signs of dehydration, acidosis, sepsis, or shock.
- c. **The diagnosis** of malrotation is made by upper gastrointestinal and small bowel follow-through examination, which demonstrates an abnormally positioned ligament of Treitz.
- d. **Treatment** involves volume resuscitation, placement of a nasogastric tube, cessation of feeding, antibiotic administration, and surgical repair.
- e. **Anesthetic Considerations:** After evacuation of the stomach, a rapid sequence induction should be performed and anesthesia maintained with inhalation or IV anesthetics as tolerated. Nitrous oxide should be avoided to prevent further distention of the bowel.

F. Neurologic Disorders

1. Seizures

- a. **Seizures** may be generalized, focal, or subclinical.
- b. **Etiologies** include birth trauma, intracranial hemorrhage, hypoxic ischemic encephalopathy, metabolic disturbances (hypoglycemia or hypocalcemia), drug withdrawal, and infections.
- c. **Laboratory evaluation**
 1. Initial evaluation includes electrolytes, glucose, calcium, magnesium, and arterial blood gas and pH determination. If a metabolic disease is suspected, serum lactate and ammonia, serum/urine amino acids, and urine for organic acids should be obtained.
 2. CBC with differential, platelet count, and the appropriate cultures, including blood and CSF.
 3. To identify underlying causes of the seizures, neuroimaging is performed, which may include cranial ultrasound, computed tomography (CT) scan, and/or magnetic resonance imaging (MRI) sometimes with T2 diffusion-weighted imaging, and electroencephalograms may be obtained, sometimes during pyridoxine administration.
- d. **Treatment** includes supportive care. It is critical to ensure that the patient maintains adequate oxygenation. In addition, it is important to correct potential underlying metabolic abnormalities that cause the seizures (e.g., hypoglycemia, hypocalcemia). Anticonvulsants are started and, if indicated, a test dose of pyridoxine is administered. In newborns ≥ 36 weeks of gestational age, if a hypoxic-ischemic event at or near the time of birth is thought to be contributing to the brain injury, and clinical signs suggest that there is moderate-to-severe encephalopathy, then total body or head cooling to 33.5°C to 34.5°C is often initiated in the NICU within the first 6 hours of life and employed for 72 hours. In these cases, consultation with experts in neonatal neurology is often sought.

e. Anticonvulsants

1. Acute medical treatments include the following:
 - a. **Phenobarbital**, 20 mg/kg IV load over 10 minutes; maintenance dose of 2.5 mg/kg twice daily to maintain a serum level of 20 to 40 $\mu\text{g/mL}$.
 - b. **Benzodiazepine** (e.g., lorazepam 0.1 to 0.3 mg/kg IV).
 - c. **Fosphenytoin**, 15 to 20 mg/kg IV load over 15 minutes; maintenance dose of 2.5 mg/kg twice daily to maintain a therapeutic level of 15 to 30 $\mu\text{g/mL}$.
2. Chronic treatment for neonatal seizures is usually with phenobarbital or levetiracetam.

2. Intracranial hemorrhage

- a. **Intraventricular hemorrhage** occurs in more than 30% of infants with birth weights below 1,000 g typically within the first 7 days of life. Subdural and subarachnoid hemorrhages are much less common.
- b. **Clinical features.** Intraventricular hemorrhage is often asymptomatic, although it may present with unexplained lethargy, apnea, or seizures. On examination, the head circumference can be increased, and the fontanelle may be bulging.
- c. **Laboratory studies.** Laboratory examination may show anemia and acidosis. Screening head ultrasounds are generally performed in infants under 32 weeks of gestational age.
- d. **Grading of intraventricular hemorrhage**
 1. **Grade I.** Subependymal or choroid plexus bleeding only.
 2. **Grade II.** Intraventricular bleeding without dilatation of ventricles.
 3. **Grade III.** Intraventricular bleeding with dilatation of ventricles.
 4. **Grade IV.** Intraparenchymal bleeding.
- e. The **major complication** of intraventricular hemorrhage is CSF obstruction resulting in **hydrocephalus**. This is followed by measuring daily head circumferences and by serial cranial ultrasounds. Serial lumbar punctures or intraventricular shunting is often required.
- f. Hypertonic agents (e.g., 25% dextrose in water) that had previously been advocated in the treatment of hypoglycemia have been implicated in the etiology of intraventricular hemorrhage and should be avoided.

3. Myelodysplasia

- a. Abnormal neurulation of the embryo can result in failed closure of the posterior neural tube by the 4th week of gestation. A **meningocele** is caused when the meninges herniate through a bony abnormality in the spine (spina bifida) and form a sac filled with CSF. The spinal cord and nerve roots are generally not involved. A **myelomeningocele** is the result of spinal cord and meninges herniating through a defect in the spinal canal. Eight percent of myelomeningoceles involve the lumbar spinal region. Hydrocephalus may affect as many as 90% of newborns with myelomeningocele because the cord lesion can displace the cerebellum and interfere with cerebrospinal fluid flow.
- b. Myelomeningoceles occur with an incidence of 4 to 10 per 10,000 live births. The incidence has significantly decreased with maternal folic acid supplementation. Women with diabetes or taking certain medications (e.g., antiepileptics) are at increased risk of having a child with myelodysplasia.
- c. **Postnatal management** includes covering the defect with a warm, normal saline-soaked sterile dressing to prevent adhesion of the

dressings to the defect. The infant should be kept prone, and latex exposure should be avoided. Preoperatively, the infant should undergo assessment for additional abnormalities (e.g., scoliosis, hydrocephalus, Arnold-Chiari malformation), and neuroimaging is recommended. Early surgical repair significantly decreases the risk of infection. Postoperatively, infants must be monitored closely for seizures and hydrocephalus that may require shunt placement. Prognosis ultimately depends on the level of the lesion and the presence of other congenital anomalies.

- d. **Anesthetic considerations:** During intubation of the patient in a supine position, special care must be taken to pad the exposed neural tissue to prevent injury. In some cases, intubation of the patient in the left lateral decubitus position may be preferred to protect the lesion. Many patients with myelomeningocele may have a short trachea, creating an increased risk for endobronchial intubation. Blood loss tends to be minimal unless extensive subcutaneous tissue dissection is required to mobilize the skin so that it can cover a large lesion. If hydrocephalus is present, the neonate may have a diminished response to hypoxia causing an increased risk of apneic episodes in the postoperative period.

4. Retinopathy of prematurity (ROP)

a. Etiologies

1. **The risk of ROP** is increased in premature neonates requiring oxygen therapy. ROP is seen in infants with birth weights less than 1,500 g and gestational age less than 30 weeks. There is an 80% incidence in infants weighing less than 1,000 g. To decrease the incidence of ROP, **hyperoxia should be avoided.**
2. Factors other than hyperoxic exposure and prematurity may produce ROP, as it has been demonstrated in full-term infants, infants with cyanotic heart disease, stillborn infants, and infants without hyperoxic exposure. Factors that may increase risk include anemia, infection, intracranial hemorrhage, acidosis, and PDA.

- b. **Pathophysiology.** ROP begins in the temporal peripheral retina, which is the last part of the retina to vascularize. An elevated ridge demarcating vascularized and nonvascularized retina is initially seen. **Fibrovascular proliferation** from this border extends posteriorly, and in 90% of patients, gradual resolution occurs from this stage. These patients may develop strabismus, amblyopia, myopia, or peripheral retinal detachment in later life.

- c. In 10% of patients, fibrovascularization extends into the vitreous, resulting in vitreous hemorrhage, peripheral retinal scarring, temporal dragging of the disk and macula, and partial retinal detachment. In severe disease, extensive fibrovascular proliferation can result in a retrolental white mass (leukocoria), complete retinal detachment, and loss of vision.

- d. **Infants ≤ 32 weeks of gestational age, birth weight $\leq 1,500$ g, or with additional risk factors should undergo** indirect ophthalmoscopy at 34 weeks of corrected gestational age. If ROP is identified, the infant is reexamined at 1- to 2-week intervals until spontaneous resolution occurs. New cases of ROP do not occur after 3 months of age.

- e. **Treatment** for severe manifestations of ROP has included photocoagulation, diathermy, cryotherapy, vitrectomy, and bevacizumab injection.

G. Infectious Diseases

1. Environment

a. **Neonates are particularly vulnerable to infection.** They have decreased cellular and humoral immune defense systems and are at increased risk for colonization and nosocomial infection.

b. **Prevention.** Infectious transmission may be reduced by using separate equipment and isolettes for each infant, by hand washing before and after each contact, and by wearing cover gowns.

2. **Risk factors for infection.** Prolonged rupture of membranes is associated with a high incidence of chorioamnionitis and subsequent ascending bacterial and viral infection in the neonate. Maternal fever, maternal leukocytosis, prolonged rupture of membranes, and fetal tachycardia are also associated with neonatal infection.

3. **Laboratory studies** include complete blood count with differential and blood cultures. A lumbar puncture for culture and analysis of CSF may be indicated. If appropriate, viral cultures should be obtained.

4. Neonatal sepsis

a. Organisms responsible for infections soon after birth are usually acquired in utero or during birth. These can include group B β -hemolytic *streptococcus*, *Escherichia coli*, *Listeria monocytogenes*, and herpes simplex virus. Later-onset infections may be caused by *Staphylococcus aureus*, *Staphylococcus epidermidis*, *Enterobacter cloacae*, enterococcus, and *Pseudomonas aeruginosa*.

b. **The clinical features of sepsis** include respiratory failure, seizures, and shock. Subtle signs, including respiratory distress, apnea, irritability, and poor feeding, are often seen first and warrant evaluation.

c. **Laboratory studies** should include blood, urine, and CSF cultures; CBC with differential; blood glucose; urinalysis; and CXR.

d. **Antibiotic coverage** with ampicillin and an aminoglycoside is begun and continued for 48 to 72 hours. If cultures are positive, treatment should continue as indicated by the severity and location of infection. Aminoglycoside serum levels should be monitored and dosages adjusted to prevent toxicity.

Suggested Readings

- Anand KJS, Hickey PR. Pain and its effects in the human neonate and fetus. *N Engl J Med* 1987;317:1321–1329.
- Arant BSJ. Developmental patterns of renal functional maturation compared in the human neonate. *J Pediatr* 1978;92:705–712.
- Bahrami KR, Van Meurs KP. ECMO for neonatal respiratory failure. *Semin Perinatol* 2005;29:15–23.
- Bell EF, Warburton D, Stonestreet BS, et al. Effect of fluid administration on the development of symptomatic patent ductus arteriosus and congestive heart failure in premature infants. *N Engl J Med* 1980;302:598–604.
- Cote CJ, Lerman J, Anderson BJ. *A Practice of Anesthesia for Infants and Children, and Adolescents*. 5th ed. Philadelphia: Saunders Elsevier; 2013.
- Coté CJ, Zaslavsky A, Downes JJ, et al. Postoperative apnea in former preterm infants after inguinal herniorrhaphy. A combined analysis. *Anesthesiology* 1995;82:809–822.
- Fanaroff AA, Wald M, Gruber HS, et al. Insensible water loss in low birth weight infants. *Pediatrics* 1972;50:236–245.
- Fluge G. Clinical aspects of neonatal hypoglycaemia. *Acta Paediatr Scand* 1974;63:826–832.
- Gallagher TM, Crean PM. Spinal anaesthesia for infants born prematurely. *Anaesthesia* 1989;44:434–436.

- Gersony WM, Peckham GJ, Ellison RC, et al. Effects of indomethacin in premature infants with patent ductus arteriosus: results of a national collaborative study. *J Pediatr* 1983;102:895–906.
- Hall BD. Choanal atresia and associated multiple anomalies. *J Pediatr* 1979;95:395–398.
- Keith CG, Doyle LW. Retinopathy of prematurity in extremely low birth weight infants. *Pediatrics* 1995;95:42–45.
- Koehtop DE, Rodman JH, Brundage DM, et al. Pharmacokinetics of fentanyl in neonates. *Anesth Analg* 1986;65:227–232.
- Krane EJ, Haberkern CM, Jacobson LE. Postoperative apnea, bradycardia, and oxygen desaturation in formerly premature infants: prospective comparison of spinal and general anesthesia. *Anesth Analg* 1995;80:7–13.
- Kurth CD, Spitzer AR, Broennle AM, et al. Postoperative apnea in preterm infants. *Anesthesiology* 1987;66:483–488.
- Marks KH, Devenyi AG, Bello ME, et al. Thermal head wrap for infants. *J Pediatr* 1985;107:956–959.
- Motoyama, EK, Brinkmeyer, SD, Mutich, RL, et al. Reduced FRC in anesthetized infants: effect of low PEEP. *Anesthesiology* 1982;57:A418.
- Moya FR, Lally KP. Evidence-based management of infants with congenital diaphragmatic hernia. *Semin Perinatol* 2005;29:112–117.
- Philippart AI, Canty TG, Filler RM. Acute fluid volume requirements in infants with anterior abdominal wall defects. *J Pediatr Surg* 1972;7:553–558.
- Roberts JD Jr, Fineman JR, Morin FC III, et al. Inhaled nitric oxide and persistent pulmonary hypertension of the newborn. The Inhaled Nitric Oxide Study Group. *N Engl J Med* 1997;336:605–610.
- Roberts JD Jr, Polaner DM, Lang P, et al. Inhaled nitric oxide (NO): a selective pulmonary vasodilator for the treatment of persistent pulmonary hypertension of the newborn (PPHN). *Circulation* 1991;84:A1279.
- Roberts JD, Polaner DM, Lang P, et al. Inhaled nitric oxide in persistent pulmonary hypertension of the newborn. *Lancet* 1992;340:818–821.
- Sola A. Oxygen in neonatal anesthesia: friend or foe? *Curr Opin Anaesthesiol* 2008;21:332–339.
- Srinivasan G, Jain R, Pildes RS, et al. Glucose homeostasis during anesthesia and surgery in infants. *J Pediatr Surg* 1986;21:718–721.
- Touloukian RJ, Higgins E. The spectrum of serum electrolytes in hypertrophic pyloric stenosis. *J Pediatr Surg* 1983;18:394–397.
- Tyszczyk L, Meek J, Elwell C, et al. Cerebral blood flow is independent of mean arterial blood pressure in preterm infants undergoing intensive care. *Pediatrics* 1998;102:337–341.
- Wessel DL, Keane JF, Parness I, et al. Outpatient closure of the patent ductus arteriosus. *Circulation* 1988;77:1068–1071.
- Wright TE, Orr RJ, Haberkern CM, et al. Complications during spinal anesthesia in infants: high spinal blockade. *Anesthesiology* 1990;73:1290–1292.
- Yaster M, Buck JR, Dudgeon DL, et al. Hemodynamic effects of primary closure of omphalocele/gastroschisis in human newborns. *Anesthesiology* 1988;69:84–88.

I. ANATOMY AND PHYSIOLOGY

A. Upper Airway

1. **Neonates are obligate nose breathers** due to weak oropharyngeal muscles and increased compliance of the pharynx, larynx, and bronchial tree. Their nares are relatively narrow, and a significant fraction of the work of breathing is needed to overcome nasal resistance. Occlusion of the nares by bilateral choanal atresia or tenacious secretions can cause complete airway obstruction; however, some infants will convert to mouth breathing. Placement of an oral airway, a laryngeal mask airway, or an endotracheal tube may be necessary to reestablish airway patency during sedation or anesthesia.
2. **Infants have relatively large tongues**, which can make mask ventilation and laryngoscopy challenging. A recent study called tongue size into question and found the tongue to be proportional in children aged 1 to 12. Clinically, the tongue can easily obstruct the airway if excessive submandibular pressure is applied during mask ventilation.
3. **Infants and children have a more cephalad glottis** (C3 vertebral level in premature infants, C4 in infants, and C5 in adults) and a **narrow, long, angulated epiglottis**, which can make laryngoscopy difficult.
4. In infants and young children, **the narrowest part of the airway is at the cricoid cartilage** (recent studies have questioned this; see suggested readings), rather than at the glottis (as in adults). An endotracheal tube that passes through the cords may still be too large distally.
5. **Deciduous teeth** erupt within the first year and are shed between ages 6 and 13 years. To avoid dislodging a loose tooth, it is safest to open the mandible directly, without introducing a finger or appliance into the oral cavity. Loose teeth should be documented on the preoperative evaluation. In some instances, unstable teeth should be removed before laryngoscopy. Parents and patients should be informed of this possibility in advance.
6. **Airway resistance** in infants and children can be increased dramatically by subtle changes in an already small-caliber system. Even a small amount of edema can significantly increase airway resistance and cause airway compromise.

B. Pulmonary System

1. Neonates have **higher metabolic rates**, resulting in an elevated oxygen consumption (6 mL/kg/min) when compared with adults (3 mL/kg/min).
2. **Neonatal lungs have high closing volumes**, which fall within the lower range of their normal tidal volume. Below closing volume, alveolar collapse and shunting occur.
3. To meet the higher oxygen demand, infants have a **higher respiratory rate and minute ventilation**. An infant's functional residual capacity (FRC) is nearly equivalent to that of an adult (FRC of an infant, 25 mL/kg; adult, 35 mL/kg). Their higher minute ventilation to FRC ratio results in rapid

inhalational induction. The tidal volume for infants and adults is equivalent (6 to 7 mL/kg).

4. **Anatomic shunts** including patent ductus arteriosus and patent foramen ovale may develop significant right-to-left flow with increases in pulmonary artery pressure (e.g., hypoxia, acidosis, or high positive airway pressure). This may predispose to air emboli if care is not taken to remove it from the IV tubing.
 5. The characteristics of the infant's pulmonary system contribute to **rapid desaturation during apnea**. Profound desaturation can occur when an infant coughs or strains and alveoli collapse. Treatment may require deepening anesthesia, using neuromuscular relaxants, as well as alveolar recruitment.
 6. The **diaphragm** is the infant's major muscle of ventilation. Compared with the adult diaphragm, the newborn has only half the number of Type I, slow-twitch, high-oxidative muscle fibers essential for sustained increased respiratory effort. Thus, the infant's diaphragm fatigues earlier than the adult's. By 2 years of age, the child's diaphragm would have attained mature levels of Type I fibers.
 7. The **pliable rib cage** (compliant chest wall) of an infant cannot maintain negative intrathoracic pressure easily. This diminishes the efficacy of the infant's attempts to increase ventilation.
 8. An infant's **dead space** is 2 to 2.5 mL/kg, equivalent to an adult's.
 9. Infants' high baseline minute ventilation limits their ability to increase their ventilatory effort further. End-tidal CO₂ concentrations should be followed if spontaneous ventilation is permitted under anesthesia; assisted or controlled ventilation may be necessary.
 10. **Alveolar maturation** occurs by 8 to 10 years of age when alveoli number and size reach adult ranges.
 11. **Retinopathy of prematurity** (see Chapter 30).
 12. **Apnea and bradycardia** after general anesthesia occur with increased frequency in infants who are premature and in infants who have anemia, sepsis, hypothermia, central nervous system disease, hypoglycemia, hypothermia, or other metabolic derangements. These patients should have cardiorespiratory monitoring for a minimum of 24 hours postoperatively. Such infants are not candidates for ambulatory day surgery. The guidelines for discharge vary among institutions. Most hospitals agree that infants who are less than 45 to 60 weeks of postconceptual age are monitored postoperatively. Any full-term infant who displays apnea after general anesthesia should also be monitored.
- C. Cardiovascular System**
1. **Heart rate and blood pressure** vary with age and should be maintained at age-appropriate levels perioperatively (Tables 31.1 and 31.2).
 2. **Cardiac output** is 180 to 240 mL/kg/min in newborns, which is two to three times that of adults. This higher cardiac output is necessary to meet the higher metabolic oxygen consumption demands.
 3. The **ventricles** are less compliant and have a relatively smaller contractile muscle mass in newborns and infants. The ability to increase contractility is limited; increases in cardiac output occur by increasing heart rate rather than stroke volume. Bradycardia is the most deleterious dysrhythmia in infants, and hypoxemia is a frequent cause of bradycardia in infants and children.
 4. Neonates have immature calcium signaling and handling in the sarcoplasmic reticulum and myocardium and are more dependent on ionized calcium concentrations for myocardial function.

TABLE 31.1
Age Dependence of Typical Respiratory Parameters

Variable	Newborn	1 Year	3 Years	5 Years	Adult
Respirations (breaths/min)	40–60	20–30	Gradual decrease to 18–25	18–25	12–20
Tidal volume (mL)	15	80	110	250	500
FRC (mL/kg)	25		35		40
Minute ventilation (L/min)	1	1.8	2.5	5.5	6.5
Hemoglobin(g/dL)	14–20	10–11	—	—	13–17
Hematocrit (%)	47–60	33–42			38–50
Arterial pH	7.30–7.40	7.35–7.45	—	—	—
Paco ₂ (mm Hg)	30–35	30–40	—	—	—
Pao ₂ (mm Hg)	60–90	80–100	—	—	—

D. Fluid and Electrolyte Balance

1. The **glomerular filtration rate** at birth is 15% to 30% of the normal adult value. Adult value is reached by 1 year of age. Renal clearance of drugs and their metabolites is diminished during the first year of life.
2. Neonates have an intact renin–angiotensin–aldosterone pathway, but the distal tubules resorb less sodium in response to aldosterone. Thus, newborns are “obligate sodium losers,” and IV fluids should contain sodium.
3. The **total body water** in the preterm infant is 90% of body weight. In term infants, it is 80%; at 6 to 12 months, it is 60%. This increased percentage of total body water affects drug volumes of distribution. The dosages of some drugs (e.g., propofol, succinylcholine, pancuronium, and rocuronium) are 20% to 30% greater than are the equally effective dose for adults.

E. Hematologic System

1. Normal values for hemoglobin and hematocrit are listed in Table 31.1. The nadir of physiologic anemia is at 3 months of age, and the hemoglobin may reach 10 to 11 g/dL in an otherwise healthy infant. Premature infants may demonstrate a decrease in hemoglobin concentration as early as 4 to 6 weeks of age.
2. At birth, **fetal hemoglobin** (HbF) predominates, but β -chain synthesis shifts to the adult type (HbA) by 3 to 4 months of age. HbF has a higher

TABLE 31.2
Cardiovascular Variables

Age	Blood Pressure (mm Hg)		
	Heart Rate (beats/min)	Systolic	Diastolic
Preterm neonate	120–180	45–60	30
Term neonate	100–180	55–70	40
1 Year	100–140	70–100	60
3 Years	84–115	75–110	70
5 Years	84–100	80–120	70

affinity for oxygen; that is, the oxyhemoglobin dissociation curve is shifted to the left, but debate exists regarding the clinical relevance.

3. See section IX.B for calculations of blood volume and red cell mass.

F. Hepatobiliary System

1. **Liver enzyme systems**, particularly those involved in phase-II (conjugation) reactions, are immature in the infant. Drugs metabolized by the P-450 system may have prolonged elimination times.
2. **Jaundice** is common in neonates and can be physiologic or have pathologic causes.
3. **Hyperbilirubinemia** and displacement of bilirubin from albumin by drugs can result in kernicterus. Premature infants develop kernicterus at lower levels of bilirubin than do term infants (see Chapter 30).
4. **Plasma levels of albumin** are lower at birth and as a result, drugs that are protein bound may have a higher free fraction and higher effective concentration.

G. Endocrine System

1. **Newborns**, particularly premature babies and those small for gestational age, have decreased glycogen stores and are more susceptible to **hypoglycemia**. Infants of diabetic mothers have high insulin levels because of prolonged exposure to elevated maternal serum glucose levels and are prone to hypoglycemia. Infants who fall into these groups may have dextrose requirements as high as 5 to 15 mg/kg/min. Normal glucose concentrations in the full-term infant are ≥ 45 mg/dL (2.5 mmol/L).
2. **Hypocalcemia** is common in infants who are premature, are small for gestational age, have a history of asphyxia, are offspring of diabetic mothers, or have received transfusions with citrated blood or fresh-frozen plasma. Serum calcium concentration should be monitored in these patients and calcium administered if the ionized calcium is less than 4.0 mg/dL (1.0 mmol/L).

H. Temperature Regulation

1. Compared with adults, infants and children have a greater surface area to body weight ratio, which increases loss of body heat.
2. Infants have significantly less muscle mass and cannot compensate for cold by shivering or adjusting their behavior to avoid the cold.
3. Infants respond to cold stress by increasing norepinephrine production, which enhances metabolism in brown fat. Norepinephrine also produces pulmonary and peripheral vasoconstriction, which can lead to right-to-left shunting, hypoxemia, and metabolic acidosis. Sick and preterm infants have limited stores of brown fat and therefore are more susceptible to cold. Strategies to prevent cold stress are discussed in section IV.C.

II. THE PREANESTHETIC VISIT

General principles of the preanesthetic visit are discussed in Chapter 1. The preoperative visit is an excellent opportunity to address the concerns of the child and parents.

A. History should include the following:

1. Maternal health during gestation, including alcohol or drug use, smoking, diabetes, and viral infections
2. Prenatal tests (e.g., ultrasound and amniocentesis)
3. Gestational age and weight
4. Events during labor and delivery, including Apgar scores and length of hospital stay
5. Hospitalizations/emergency room visits

6. Congenital, chromosomal, metabolic anomalies or syndromes
7. Recent upper respiratory infections, tracheobronchitis, “croup,” reactive airway disease (asthma), exposure to communicable diseases, cyanotic episodes, or history of snoring
8. Sleeping position (prone, side, or supine)
9. Respiratory quality and pattern (i.e., noisy breathing that increase with sleep; periods of apnea with sleep)
10. Growth history
11. Vomiting and gastroesophageal reflux
12. Siblings’ health
13. Parents who smoke
14. Past surgical and anesthetic history
15. Allergies (environmental, drugs, food, and latex)
16. Bleeding tendencies
- B. Physical examination** should include the following:
 1. General appearance, alertness, color, tone, congenital anomalies, head size and shape, activity level, and social interaction
 2. Vital signs, height, and weight
 3. Loose teeth, craniofacial anomalies, or large tonsils that could complicate airway management
 4. Respiratory pattern and quality. Signs of upper respiratory infection and/or reactive airways disease (excessive secretions may predispose patients to laryngospasm and bronchospasm during induction and emergence of anesthesia).
 5. Cardiac exam including age-appropriate heart rate, rhythm, and heart murmurs (which may indicate flow through anatomic shunts)
 6. Potential vascular access sites
 7. Strength, developmental milestones, activity level, and motor and verbal skills
 8. Additional exam(s) pertinent to specific anesthetic/surgical condition
- C. Laboratory data** appropriate for the child’s illness and proposed surgery should be obtained. Most centers agree that a “routine hemoglobin” is unnecessary for healthy children. If indicated, laboratory tests can often be obtained after induction of general anesthesia (e.g., blood bank sample).

III. PERIPROCEDURAL CONSIDERATIONS AND FASTING GUIDELINES

A. Perioperative Considerations

1. Children face a multiple stressors in the perioperative period. They may not understand the specific disease; the concept of anesthesia, or the procedure itself. Honesty about the procedure(s), associated pain, and the sequence of events is essential in maintaining the trust of children regardless of their level of development.
 - a. Approaches to optimize the perioperative experience include the use of nonpharmacologic techniques. Examples of these strategies include distraction, humor, sharing control (e.g., would you like to sit up or lie down for induction?), and medical reinterpretation of equipment. The use of a child life specialist, tablet, and/or a teaching module may decrease the need for preprocedure pharmacologic therapy and improve a child’s experience.
2. Infants less than 8 months old generally tolerate short periods of separation from parents and usually do not require premedication.
3. Children 8 months to 5 years of age likely have developed separation anxiety and may require sedation before the induction of anesthesia (see section V.B).

TABLE
31.3 Fasting Guidelines

Type of Food	Fasting Guidelines (hours)
Clear fluids	2
Breast milk	4
Nonhuman milk	6
Solid food	8

- Older children generally respond well to information and reassurance. Parental and patient anxiety may be reduced by having parents accompany their children to the operating room. An especially anxious child may benefit from premedication.
- Premedication with intramuscular (IM) **anticholinergics** generally is not recommended. If vagolytic drugs are indicated, they are usually administered intravenously (IV) at the time of induction of anesthesia.
- In the presence of **gastroesophageal reflux**, **ranitidine** (2 to 4 mg/kg PO, 2 mg/kg IV) along with **metoclopramide** (0.1 mg/kg) can be administered 2 hours before surgery to increase gastric pH and reduce gastric volume.
- Children receiving medications for medical problems such as reactive airways disease, seizures, or hypertension should continue to take these medications preoperatively.

B. Fasting Guidelines

- Milk, breast milk, formula, and solid foods should be restricted as outlined in Table 31.3.
- The **last feeding** should consist of clear fluids or sugar water. Studies document that there is no increased risk of aspiration if clear fluids are offered up to 2 hours preoperatively. This policy minimizes preoperative dehydration and hypoglycemia and contributes to a smooth induction and stable operative course. We recommend that patients receive clear fluids until 2 hours before surgery is scheduled. Oral intake is then restricted (see Table 31.3).
- If schedule delays occur, clear fluids may be given. Some patients may require IV placement for hydration and/or glucose administration.

IV. PREPARATION OF THE OPERATING ROOM

- Perioperative/procedure huddle is a useful meeting to confirm procedure details, anesthetic requirements, special concerns, patient-specific factors, and nonroutine steps.
- Anesthetic Circuit**
 - The **semiclosed circuit** normally used in adults has some disadvantages if used in very small infants:
 - The inspiratory and expiratory valves increase resistance during spontaneous ventilation: This can be overcome by closing the APL valve to 3 to 5 cm of water and providing adequate gas flow rates to maintain pressure, or the use of pressure support).
 - The large volume of the absorber system acts as a reservoir for anesthetic agents.
 - The breathing circuit tubing has a large compression volume; however, neonatal and pediatric tubing are available that help compensate for this, as well as decrease the circuit dead space volume.

2. The **nonrebreathing, open circuit (Mapleson D)** solves these problems (see Chapter 9). **Rebreathing** is prevented by using fresh gas flows 2.0 to 2.5 times the minute ventilation to wash out carbon dioxide. Capnography is essential in recognizing rebreathing (inspired $\text{CO}_2 > 0$) and avoiding excessive hyperventilation. This circuit is useful for very small infants who are allowed to breathe spontaneously and during transport.
3. A passive heat and moisture exchanger may be used with either circuit.
4. The **reservoir bag volume** should be at least as large as the child's vital capacity but small enough so that a comfortable squeeze does not overinflate the chest. General guidelines for bag volumes are as follows: newborns, 500-mL bag; 1 to 3 years, 1,000-mL bag; and more than 3 years, 2,000-mL bag.
5. For **most infants and children**, the semiclosed-circuit-absorber system can be used with a smaller reservoir bag and a pediatric breathing circuit with small-caliber tubing (i.e., circle system).

C. Airway Equipment

1. A **mask** with minimal dead space should be chosen. A clear plastic type is preferred because the lips (for color) and mouth (for secretions and vomitus) can be visualized.
2. The appropriate size of **oral airway** can be estimated by holding the airway in position next to the child's face. The tip of the oral airway should reach to the angle of the mandible with the base at the lips.
3. **Laryngoscopy**
 - a. A **narrow handle** is often preferred because it has a more natural feel when using a smaller blade.
 - b. **Straight blade** (Miller or Wis-Hipple) is recommended for children less than 2 years old. The smaller flange and long tapered tip of the straight blade provide better visualization of the larynx and manipulation of the epiglottis in the confined spaces of a small oral cavity (see section Endotracheal Intubation, Oral Approach)
 - c. **Curved blades** are generally used for patients more than 5 years old.
 - d. **Guidelines for laryngoscope blade sizes** (Table 31.4)
4. **Endotracheal tubes.** Traditionally, uncuffed tubes were used for children under 6 to 7 years of age (5.5-mm inner diameter endotracheal tube or smaller). The risk of tracheal stenosis is minimal with modern

TABLE 31.4 Guidelines for Choice of Laryngoscope Blades

Age	Blade
Premature and neonate	Miller 0
Infant up to 6–8 mo	Miller 0–1
9 mo to 2 y	Miller 1
	Wis-Hipple 1.5
2–5 y	Macintosh 1
	Miller 1–1.5
	Wis-Hipple 1.5
Child over 5 y	Macintosh 2
	Miller 2
Adolescent to adult	Macintosh 3
	Miller 2

TABLE
31.5

Guidelines for Endotracheal Tube Sizes

Age	Size (mm Internal Diameter)
Premature newborn	2.5–3.0
Full-term newborn	3.0
6–12 mo	3.5
12–20 mo	4.0
2 y	4.5
Over 2 y	4+ (age [years]/4)
6 y	5.5
10 y	6.5

Note: Tube length at mouth (cm) = (10 + age [years])/2.

low-pressure cuffs, and cuffed tubes may be used when indicated (e.g., tonsillectomy or proximal bowel obstruction) and may even provide additional benefit against aspiration. Concern for tracheal injury (including postintubation stridor) in extremely small infants with microcuff endotracheal tubes has been reported.

5. Care must be taken not to overinflate the cuff and to realize that N₂O can diffuse into the cuff. At the time of intubation, endotracheal tubes that are one size larger and smaller than the estimated size should be available. Special techniques of endotracheal intubation are discussed in section VI. Table 31.5 provides guidelines for endotracheal tube sizes.

D. Temperature Control

1. The **operating room should be warmed** to 80°F to 90°F before the child's arrival and an underbody warmer placed on the operating room table. Infants should be kept covered with a blanket and a hat.
2. A **servocontrolled radiant warmer** will keep infants warm during the induction of anesthesia and positioning. Skin temperature should be measured and should not exceed 39°C.
3. **Passive heat and moisture exchangers** can be used for most routine cases. Some practitioners prefer to actively heat and humidify inspired gases during prolonged surgery.
4. Fluids, blood products, and irrigation solutions should be warmed.

E. Monitoring

1. In addition to standard monitoring (Chapter 10), a **precordial or esophageal stethoscope** provides information about heart and respiratory function.
2. **Blood pressure**
 - a. A blood pressure cuff should cover at least two thirds of the upper arm but not encroach on the axilla or antecubital space.
 - b. The cuff can be placed on the leg if the arms are inaccessible (e.g., cast present).
 - c. Several manufacturers of oscillometric blood pressure cuffs have different preset initial pressure settings and cycle durations, for neonate, pediatric, and adult sized cuffs. Care should be taken to choose the appropriate size/setting to avoid inadvertent injury.
3. **Pulse oximetry** is one of the best indicators for the early detection of desaturation. It can also provide plethysmographic data on perfusion and respiratory variation.

4. Observed **end-tidal carbon dioxide measurements** usually will be lower than expected when a nonrebreathing circuit is used, because exhaled gas will be diluted with high flows of fresh gases.
5. **Temperature** should routinely be monitored. In small infants esophageal, rectal, or axillary probes are acceptable. Once the drapes are placed, the warming blanket and room temperature should be adjusted so that children (especially small infants) do not become hyperthermic.
6. **Urine output** can provide a good reflection of volume status in children. In newborns, 0.5 mL/kg/h is adequate; for infants over 1 month of age, 1.0 mL/kg/h usually indicates adequate renal perfusion.
7. **Noninvasive cardiac output monitoring** is a developing technology that may provide earlier identification of hemodynamic changes in the pediatric patient when compared to the current monitoring methods. When this monitor was compared with transthoracic echocardiography, it was shown to have variability with absolute cardiac output; however, it has been shown to accurately predict volume responsiveness.
8. **EEG** utilization and density spectral array data (see Chapter 11) to determine depth of anesthesia can be a useful tool(s) to monitor the cortical biorhythm in the pediatric patient and prevent anesthetic overdose. Caution is advised in children under 2 years of age due to developmental changes in the EEG signal.

F. IV Setup and Supplies

1. For children less than 10 kg, a control chamber (burette) should be used to prevent inadvertent fluid administration and to quantify the fluid volume given.
2. Extension tubing (low volume) used as a drug push-line connected proximally to the patient facilitates drug administered as close to the IV insertion site as possible and prevents excessive flush fluid administration.
3. For older children, a pediatric infusion set is used where 60 drops equal 1 mL.
4. Extra care should be taken to purge IV tubing of air because right to left shunting of blood (and possibly air) can occur in infants with a patent foramen ovale. An air filter should be used in infants and children with known or suspected intracardiac shunts (some drugs are not compatible with these filters; i.e., propofol).

V. INDUCTION TECHNIQUES

- A. **Infants less than 8 months old** can often be transported to the operating room without sedation; anesthesia can then be induced by an inhalation technique (see section V.C). The vessel-rich organs are proportionately larger, and the muscle and fat groups are smaller in neonates than in adults, affecting uptake and distribution of inhalation agents (see Chapter 11).
- B. **Sedation options for children 8 months to 5 years old** (without established IV access) include the following:
 1. Often children who are older than 5 to 6 years old are able to proceed to the procedure without sedation (see section Perioperative/Procedure Considerations); however, these techniques are useful in special circumstances where sedation in an older child are required (i.e., developmental delay, extreme anxiety, etc.)
 2. **Oral midazolam**, 0.5 to 0.75 mg/kg, dissolved in sweet syrup, usually produces sedation within 20 minute, although the time to onset of action can be quite variable. Patients often remain awake but sedated, and, generally, they will have no recall of leaving their parents or of induction of anesthesia.

3. **Ketamine**, 5 mg/kg given orally, produces sedation within 10 to 15 minutes and is synergistic with midazolam. Emergence time may be prolonged. This may be partially avoided by inserting an orogastric tube and emptying the stomach after induction, but generally not recommended.
 4. **Intranasal dexmedetomidine (0.5 to 2 μ g/kg)** is an effective sedative given 30 to 75 minutes prior to induction with relatively preserved respiratory function. It has also been used to reduce emergence delirium, an adjunct to postoperative pain management, and opioid withdrawal. Side effects can include decreased sympathetic activity, including bradycardia and hypotension.
 5. **Oral clonidine** (4 μ g/kg) is an effective sedative medication given approximately 45 minutes prior to induction. Its mechanism is similar to that of dexmedetomidine (α_2 -agonist) and has been shown to have good sedating qualities with relatively preserved respiratory function, with side effects including impaired insulin release, bradycardia, and possible hypotension. It has been used to reduce emergence delirium, an adjunct to postoperative pain, and has been added to regional and neuraxial anesthesia techniques for synergistic pain management.
 6. **Chloral hydrate** (25 to 50 mg/kg orally or rectally) is a drug used by pediatricians and radiologists for sedation during procedures. It causes minimal respiratory depression but may need to be repeated.
 7. **Pulse oximetry** is used routinely once a patient is sedated.
- C. Inhalation Induction**
1. This is the most common approach for pediatric patients, except when a rapid sequence IV induction is indicated.
 2. An “**excitement stage**” of anesthesia is often encountered during inhalation induction. Therefore, noise and activity in the operating room should be minimized. This stage should be explained to parents if they will be present during induction.
- 3. Techniques**
- a. **Children 8 months to 5 years old** may be anesthetized after premedication. The face mask is held near the child’s face, and low total flow rates (approximately 3 L/min) of oxygen and nitrous oxide are begun. The concentration of sevoflurane is gradually increased in 0.5% to 1% increments. When the eyelid reflex disappears, the mask can be applied to the child’s face and the jaw gently lifted.
 - b. A **slow inhalation induction** may be used in cooperative toddlers and older children who have not received premedication. Children are shown how to breathe through a clear anesthetic mask. O_2 and N_2O are delivered via facemask, and sevoflurane is gradually added to the mixture. An engaging story incorporating breathing instructions can be very useful.
 - c. A “**single-breath induction**” may be accomplished with a mixture of a volatile anesthetic with nitrous oxide.
 1. Loss of consciousness can be achieved with a single vital capacity breath of 8% sevoflurane and 70% N_2O in O_2 . Desflurane, a very pungent volatile anesthetic, is not recommended for inhalation induction.
 2. The circuit is primed with 70% N_2O – O_2 and 7% to 8% sevoflurane. The end of the circuit should be occluded with a plug or another reservoir bag. Care should be taken to avoid environmental exposure of anesthetic gas to personnel in the room.

3. Painting the mask with flavor extracts or flavored lip balm may increase acceptance by children.
 4. The child is instructed to take a deep breath approaching vital capacity of room air, blow it all out as a forced expiration, and then hold his or her breath. At this point, the anesthetist gently places the mask on the patient's face. The child then takes a deep inspiration of the anesthetic mixture and again holds his or her breath. This sequence is repeated for four or five breaths.
 5. Most children will be anesthetized within 60 seconds; a few children will need longer.
 - d. Children can become frightened, uncooperative, and even combative during an inhalation induction. Should this occur, it is imperative to have a backup plan, such as an IM injection of a sedative or hypnotic medication.
- D. Intramuscular Induction.** For the extremely uncooperative or developmentally delayed child, anesthesia may be induced with ketamine (4 to 8 mg/kg IM), which takes effect in 3 to 5 minutes. Atropine (0.02 mg/kg IM) or glycopyrrolate (0.01 mg/kg IM) should be mixed with the ketamine to prevent excessive salivation. Midazolam, 0.2 to 0.5 mg/kg IM, may also be given to reduce the chance of emergence delirium.
- E. IV Induction**
1. **For children more than 8 years old:** Often, older children may prefer an IV technique rather than a mask. Anesthesia can be induced with propofol (3 to 4 mg/kg). Ketamine (1 to 2 mg/kg) is a useful inductive agent in patients requiring hemodynamic stability upon induction. Etomidate (0.2 to 0.3 mg/kg) can be used in children with major trauma associated with hemodynamic instability or children with cardiomyopathy.
 2. IV induction at this age is often preferable to a mask induction because many older children do not like the smell of volatile anesthetics. Local anesthesia before IV placement can be achieved with subcutaneous injection of lidocaine 1%. Alternatively **EMLA cream** (a eutectic mixture of 2.5% lidocaine and 2.5% prilocaine), **LMX cream** (lidocaine 4%), or Synera (a heated topical patch with a eutectic mixture of lidocaine and tetracaine) can be applied to the skin approximately 45 minutes before IV placement. EMLA cream is also useful to reduce the pain of accessing a Portacath. The use of the jet injection lidocaine applicator is another method for achieving analgesia for IV placement.
- F. Children with "Full Stomachs"**
1. **For rapid sequence induction,** in general, the same principles apply to infants and children as for adults.
 - a. **Atropine** (0.02 mg/kg) may be given IV to prevent bradycardia, especially if succinylcholine will be given.
 - b. Children often require larger doses propofol (3 to 4 mg/kg) and succinylcholine (1 to 2.0 mg/kg) because of a larger volume of distribution for these drugs.
 - c. Infants with gastric distention (e.g., pyloric stenosis) should have their stomachs decompressed with an orogastric tube before induction of anesthesia. This gastric tube should be suctioned again before the trachea is extubated.
 - d. **Ranitidine** (2 to 4 mg/kg) can be given to decrease gastric volume and increase gastric pH. **Ondansetron** (0.1 mg/kg) can be given for postoperative nausea and vomiting prophylaxis.
 - e. **Metoclopramide** should not be given if gastric outlet or bowel obstruction is suspected.

2. **An awake laryngoscopy and intubation** is an option for the moribund infant or an infant with a grossly abnormal airway (e.g., severe craniofacial anomaly) and a “full stomach.”
3. **A cuffed endotracheal tube** should be considered for a child with a full stomach. This option minimizes the need for replacing an uncuffed tube that proves too small. The cuff volume can be adjusted to ensure an appropriate air leak.

VI. ENDOTRACHEAL INTUBATION

A. Oral Approach

1. Older children are placed in the “sniffing” position using a blanket. Infants and small children have large occiputs, and a small rolled towel placed under the scapulae can be helpful.
2. During laryngoscopy, the tip of the blade is used to elevate the epiglottis. If this technique does not provide a good view of the glottis, the laryngoscope blade can be placed in the vallecula even with a straight blade.
3. The distance from the glottis to the carina is about 4 cm in a term neonate. Pediatric endotracheal tubes have a single black line located 2 cm from the tip and a double black line at 3 cm; these markings should be observed while the tube is passed beyond the vocal cords.
4. If resistance is met during intubation, a half-size smaller tube should be tried.
5. After intubation, the chest should be examined for bilateral equal expansion, end tidal CO_2 , and the lungs auscultated for equal breath sounds. There should be a leak around an uncuffed tube when 15 to 20 cm H_2O positive pressure is applied. If the leak is present at less than 10 cm H_2O pressure, the endotracheal tube should be exchanged for the next larger size.
6. The chest should be auscultated after every change in head or body position to verify equal bilateral breath sounds. Extension of the head can result in extubation, while flexion can result in tube advancement into either mainstem bronchus.
7. Endotracheal tubes should be securely taped and the numerical marking on the tube closest to the gingiva noted; migration of the endotracheal tube will be apparent from any change in this relation.

B. Nasal Approach

1. This method is generally similar to that for adults (see Chapter 14).
2. The cephalad position of the infant larynx makes unaided intubation difficult; Magill forceps or a fiberoptic scope are frequently needed to guide the tip of the tube through the vocal cords.
3. Nasal intubation should be performed only when specifically indicated (e.g., oral surgery) because of the risk of epistaxis from enlarged adenoids.

C. Muscle Relaxants

1. **Muscle relaxants** often are used to facilitate endotracheal intubation. Muscle relaxants may be contraindicated in infants and children with abnormal airway anatomy.
2. **Succinylcholine** can cause bradycardia and may be exaggerated with repeated doses. Atropine (0.02 mg/kg) may be given before administration of succinylcholine in infants or children with immature respiratory and autonomic nervous systems. The use of succinylcholine in children with occult myopathies may result in life-threatening hyperkalemia, manifesting as wide complex bradycardia, ventricular tachycardia,

ventricular fibrillation, or asystole. A history of mild muscle weakness or failure to attain age-appropriate physical milestones may be absent, as the Duchenne and Becker types of muscular dystrophy may not be apparent until the child is 4 years of age. Any suspicion of muscle weakness, particularly in male infants, should warrant a preoperative creatine kinase level. The FDA “black box” warns that “succinylcholine in children should be reserved for emergency intubation or instances where immediate securing of the airway is necessary, for example, laryngospasm, difficult airway, full stomach.” Succinylcholine should be avoided in children with a close family history of malignant hyperthermia (see Chapter 19).

3. **Rocuronium** (0.6 to 1.2 mg/kg) has a quick onset of action (40 to 90 seconds), and in most cases; this drug has replaced succinylcholine when a rapid sequence induction is mandated. Reduced dosing (0.25 to 0.5 mg/kg) is recommended in infants due to pharmacokinetic/dynamic properties.
4. Routine neuromuscular relaxation can be achieved with **cisatracurium** (0.1 to 0.2 mg/kg).
5. For very long cases (e.g., craniotomy and cardiac surgery), **pancuronium** (0.1 mg/kg) is an option.
6. Reversal of neuromuscular blockade with **neostigmine** (0.05 to 0.06 mg/kg) and an anticholinergic drug (e.g., atropine or glycopyrrolate) should occur if the twitch monitor (train of 4 ratio is less than 0.9) or clinical examination suggests weakness.
- D. The **laryngeal mask airway** (see Chapter 14) has revolutionized pediatric anesthesia. It has replaced the mask airway for simple cases (e.g., herniorrhaphy) and the endotracheal tube for many procedures (e.g., magnetic resonance imaging or computed tomography scan).

VII. ANALGESIA

Perioperative/periprocedural pediatric pain evaluation, treatment, and monitoring are essential to mitigate biologic and psychological stresses and improve long-term outcomes. Multiple methods are used for treatment of pediatric pain and include nonpharmacologic and pharmacologic techniques. These include neuraxial, regional, nonopioid, and opioid pharmacotherapy.

VIII. PHARMACOTHERAPY

- A. Nonopioid pharmacotherapeutic agents can be used as sole or adjuvant therapy for the treatment of pain. Common medications include the following:
 1. **Acetaminophen** 10 to 15 mg/kg PO (IV administration is also 10 to 15 mg/kg) and 30 to 45 mg PR. Daily dosing should not exceed 75 mg/kg for children, 60 mg/kg for neonates, and 45 mg/kg for preterm infants.
 2. **Ketorolac** given 0.5 mg/kg IV or IM (given q6h). Caution is used in patients less than 2 years old.
 3. Additional agents include ketamine, gabapentin, dexmedetomidine, clonidine, and magnesium.
- B. Opioid therapy is summarized in Table 31.6. There are multiple PO and IV agents to achieve analgesia. Codeine received a black box warning by the FDA in 2013 and warning in 2012 for tonsillectomy and adenoidectomy and caution in postsurgical pediatric for rare but adverse events (rapid metabolism to morphine), respectively. Controversy exists surrounding the use of remifentanyl and the induction of rapid tolerance and hyperalgesia. It should also be noted that clearance is higher in neonatal patients.

TABLE
31.6

Guidelines for Opioid Administration in Pediatric Patients

Drug	Starting IV Dose and Interval	Parenteral: Oral Dose Ratio	Starting Oral Dose and Interval
Codeine	—	—	0.5–1 mg/kg q 3–4 h
Morphine	0.05–0.1 mg/kg q2–4h	1:3	0.3 mg/kg q 3–4 h
Oxycodone	—	—	0.1–0.2 mg/kg every 3–4 h
Methadone	0.1 mg/kg every 4–8 h	1:2	0.1 mg/kg every 4–8 h
Fentanyl	0.5–1.0 μ g/kg every 1–2 h Infusion: 0.5–2.0 μ g/kg/h	—	—
Hydromorphone	0.02 mg/kg every 2–4 h	1:4	0.04–0.08 mg/kg every 3–4 h
Meperidine	0.8–1.0 mg/kg every 2–3 h	1:4	2–3 mg/kg every 3–4 h
Remifentanyl	0.1–0.25 μ g/kg 1–4 μ g/kg for intubation Infusion 0.05–0.15 μ g/kg/min	—	—

As previously discussed, remifentanyl can be used to facilitate endotracheal intubation; caution should be taken due to the side effects of hypotension and bradycardia, especially with elevated dosing.

- C. Regional and neuraxial anesthesia** for pediatric patients has gained acceptance because of a better understanding of the pharmacokinetics and pharmacodynamics of local anesthetics in infants and children and the availability of specifically designed equipment. In addition, regional anesthesia has been demonstrated to be safe when performed during general anesthesia, and complication rates are comparable under general anesthesia versus sedated or awake children.

D. Pharmacology of Local Anesthetics

- 1. Protein binding** of local anesthetics is decreased in neonates because of decreased levels of serum albumin. Free drug concentration may be increased, especially for bupivacaine.
- 2. Plasma cholinesterase activity** may be decreased in infants less than 6 months old, which theoretically diminishes clearance of amino esters.
- 3. Hepatic microsomal enzyme systems** are immature in the neonate, and this will decrease the clearance of amino amides.
- 4. The increased volume of distribution** in the infant and child acts to decrease free local anesthetic concentrations in the blood.
- 5. Systemic toxicity** is the most frequent complication of regional anesthetics, and doses should be carefully calculated on a weight basis. The risk of accumulation of free drug after repeated doses of local anesthetics is increased in infants and children.

E. Brachial Plexus Block and Additional Regional Blocks

Brachial plexus blocks (for upper extremity surgery), **penile blocks** (for circumcision), and **ilioinguinal blocks** (for inguinal herniorrhaphy) are particularly useful and common regional techniques in the pediatric population. In addition, regional techniques as performed in pediatric patients as in the adult population have yielded great postoperative analgesia and are discussed in Chapter 18.

F. Spinal Anesthesia

1. Indications

- Premature infants less than 60 weeks postconceptual age and infants with a history of apnea and bradycardia, bronchopulmonary dysplasia, or need for long-term ventilatory support are at increased risk for apnea and cardiovascular instability after general anesthesia. Spinal anesthesia may decrease the likelihood of these postoperative anesthetic complications. These infants still require a minimum of 24 hours of cardiorespiratory monitoring postoperatively, regardless of the anesthetic technique. Sedation during spinal anesthesia may negate the potential benefits.
 - Children at risk for malignant hyperthermia.
 - Children with chronic airways disease such as reactive airway disease or cystic fibrosis.
 - Cooperative older children and adolescents with full stomachs undergoing peripheral emergency surgery (e.g., fractured ankle).
- 2. Anatomy.** The spinal cord in an infant terminates at approximately L3 and does assume the adult L1–L2 termination until approximately 12 months.

3. Technique

- The procedure may be performed with the patient in the lateral decubitus or sitting position. Premature infants and neonates are positioned in the sitting position to limit rostral spread of drug. The head is supported upright to prevent upper airway obstruction. A 22-gauge 1.5-inch spinal needle is used for infants, because cerebrospinal fluid flow can be very slow especially with a smaller needle. In children older than 2 years, a 25-gauge needle is acceptable.
- An IV should be started before spinal anesthesia, and the patient should be monitored throughout the procedure. Maintaining normothermia is essential, especially for premature infants and neonates. The infant should remain supine after placement of the spinal anesthetic; the Trendelenburg position should be avoided because of possible cephalad migration in the subarachnoid space.

4. Drugs and dosage

- Hyperbaric solutions of bupivacaine or tetracaine are used most frequently.
- The dosage requirements are increased, and the duration of action is decreased in infants.
- Recommended dosages** for infants, for a T6 level of anesthesia.
 - Bupivacaine** 0.5% (isobaric solution): 0.5 to 1 mg/kg
 - Bupivacaine** 0.75% in 8.25% dextrose: 0.5 to 1 mg/kg
 - Tetracaine**, 1% in 5% dextrose: 0.8 to 1.0 mg/kg in an infant and 0.25 to 0.5 mg/kg in a child. This dose is large compared with adult dosage, but it is necessary in infants.
- Duration of surgical anesthesia** averages 90 minutes with both tetracaine and bupivacaine. Multiple agents have been added to the local anesthetic in attempts to prolong the block. **Epinephrine** 2 to 5 $\mu\text{g/kg}$ and **clonidine** 1 $\mu\text{g/kg}$ have been shown to prolong duration of spinal block.

5. Complications and contraindications

- The anesthetic level** recedes more quickly in children than in adults. If the block subsides, supplemental sedation must be used cautiously, especially in premature infants and neonates. If subarachnoid anesthesia is inadequate, it is best to initiate general anesthesia before positioning.

- b. **Hypotension** is rare in children less than 7 to 10 years old, perhaps because resting sympathetic vascular tone is lower than in adults. A high spinal anesthetic may be heralded only by mottled skin or apnea and bradycardia.
- c. **Contraindications** are similar to those in adults, with particular attention to congenital anatomic defects of the central nervous system and a history of intraventricular hemorrhage.

G. Caudal and Epidural Anesthesia

1. **Indications.** These techniques are useful in combination with general anesthesia for minor and major procedures of the thorax, abdomen, pelvis, bladder, and lower extremities, particularly when significant postoperative pain is anticipated (e.g., orthopedic surgery).
2. **Anatomy** is outlined in Chapter 17. Note that the dural sac ends at the level of the S3 vertebra in the neonate; care is required to avoid dural puncture during placement of the caudal needle.
3. **Technique** is outlined in Chapter 17.
 - a. Most caudal and lumbar epidural anesthetics are placed after induction of general anesthesia.
 - b. **Caudal anesthesia** may be administered as a single injection of local anesthetic through a 1.5-inch, short-bevel stylet needle placed into the caudal epidural space. This technique is ideally suited for short procedures with mild-to-moderate postoperative pain such as inguinal herniorrhaphy, orchiopexy, and circumcision. For longer procedures or prolonged postoperative analgesia, a catheter may be advanced from the sacral epidural space. Intermittent boluses or a continuous infusion of local anesthetic with or without an opioid may be used. In infants, 22-gauge caudal catheters are placed through 20-gauge, 40- to 50-mm Tuohy needles; older children require 20-gauge catheters placed through 17- or 18-gauge, 90- to 100-mm Tuohy needles.
 - c. **Caudal catheters** can be advanced to lumbar or thoracic levels in young children because the epidural space is not yet extensively vascularized. The recommended levels are T6–T9 vertebral level for thoracic surgery (e.g., pectus excavatum repair), T10–T12 vertebral level for abdominal surgery (e.g., Nissen fundoplication or bowel resections), and L3–L4 vertebral level for pelvic procedures. Usually, these catheters advance easily; resistance may indicate malpositioning. If necessary, confirmation of catheter placement can be done with contrast dye, stimulation, ECG, and fluoroscopy techniques. While easy to place when compared with a lumbar catheter, the caudal catheter has a greater potential to become contaminated from stool. Also, the catheter may become dislodged postoperatively.
 - d. **Epidural catheters** may be placed via lumbar or thoracic approaches. The distance from the skin to the epidural space is short (1 to 2 cm) in children, and, again, care must be taken to avoid dural puncture. Loss of resistance is usually accomplished with saline. In older children, 18-gauge Tuohy needles and 20-gauge catheters are used. Thoracic catheters are useful for pectus excavation repair or thoracotomy.
4. **Drugs and doses**
 - a. In **single-dose caudal anesthesia**, a long duration of sensory blockade with minimal motor blockade is desirable. Bupivacaine, 0.125% to 0.25% with epinephrine, is administered according to the formula of

0.06 mL of local anesthetic per kg per segment, where the number of segments is counted from the S5 spinal level to the desired level of analgesia. A simple alternative dosing scheme is to administer 0.125% bupivacaine with epinephrine at a dose of 1 to 1.25 mL/kg. Increasing the concentration of bupivacaine above 0.25% does not appear to improve analgesia. Dosages of bupivacaine 2.5 mg/kg without epinephrine and 3 mg/kg with epinephrine result in plasma levels in infants and children below the toxic range determined for adults. Ropivacaine 2% has been successfully used in caudal anesthesia at doses of 1 mL/kg for minor elective surgery.

- b. The addition of **clonidine** 0.5 to 2 $\mu\text{g/kg}$ to bupivacaine prolongs the duration of analgesia by 2 to 3 hours. It may cause increased sedation postoperatively and should be avoided in babies at risk of apnea (neonates and ex-preterm infants).
- c. **Continuous infusion:** Bupivacaine 0.05% to 0.1% or ropivacaine 0.2% can be infused epidurally at a dose of 0.2 to 0.3 mg/kg/h in infants and 0.2 to 0.4 mg/kg/h in children. Opioids may be added in μg to the local anesthetic solution: fentanyl (1 to 3 $\mu\text{g/mL}$), infused at 0.3 to 1 $\mu\text{g/kg/h}$; morphine 5 to 10 $\mu\text{g/mL}$, infused at 1 to 5 $\mu\text{g/kg/h}$; or hydromorphone 3 to 7 $\mu\text{g/mL}$, infused at 1 to 2.5 $\mu\text{g/kg/h}$. Infants younger than 6 to 12 months generally do not receive opioids in the epidural infusion, unless they are in a closely monitored setting.
- d. **Postoperative analgesia** may be provided by infusion through the caudal or epidural catheter. Generally, an infusion of 0.1% bupivacaine with fentanyl, 1 to 3 $\mu\text{g/mL}$ at 0.3 to 1 $\mu\text{g/kg/h}$, will provide good analgesia without motor blockade. However, some patients benefit from omission of local anesthetic from the infusion, and fentanyl, 0.5 to 1 $\mu\text{g/kg/h}$, can be used in these patients. Because of concern about postoperative respiratory depression, infants younger than 6 to 12 months generally do not receive epidural opioids unless they are in a closely monitored setting. These infants receive an infusion of 0.1% bupivacaine, 0.2 to 0.4 mL/kg/h.
5. **Contraindications** are the same as for spinal anesthesia (see section XII.B.5).
Chlorhexidine use in infants less than 2 months old or with skin breakdown is controversial due to systemic absorption and risk of burn injury.
6. **Complications** of epidural and caudal anesthesia are discussed in Chapter 17.

IX. FLUID MANAGEMENT

The following calculations may be used to estimate fluid requirements for infants and children. Other reflections of volume status, including clinical exam, blood pressure, heart rate, urine output, central venous pressure, pulse pressure variation, straight leg raise, noninvasive cardiac output monitoring, fluid challenge, and osmolarity may guide further adjustments.

A. Maintenance Fluid Requirements

1. Administer 4 mL/kg/h for the first 10 kg of body weight (100 mL/kg/d), 2 mL/kg/h for the second 10 kg (50 mL/kg/d), and then add 1 mL/kg/h for more than 20 kg (25 mL/kg/d). For example, maintenance fluids for a 25-kg child would be $([4 \text{ mL/kg} \times 10 \text{ kg}] + [2 \text{ mL/kg} \times 10 \text{ kg}] + [1 \text{ mL/kg} \times 5 \text{ kg}]) = 65 \text{ mL/hour}$.
2. The usual solution for replacement of fluid deficits and ongoing losses in the healthy child is **lactated Ringer solution**. A second solution of 5%

dextrose is frequently used in the perioperative period for premature infants, septic neonates, infants of diabetic mothers, and those receiving total parenteral nutrition. These patients should have their blood glucose levels measured periodically.

B. Estimated Blood Volume (EBV) and Blood Losses

1. **EBV** is 95 mL/kg in premature neonates, 80 to 90 mL/kg in full-term neonates, 75 to 80 mL/kg in infants up to 1 year old, and 70 mL/kg thereafter.
2. **Acceptable blood loss (ABL).** ABL can be estimated with a simple formula. This should be used with caution if fluid redistribution/equilibration has not occurred.

$$ABL = EBV \times \left(\text{Hct}_{\text{initial}} - \text{Hct}_{\text{acceptable}} \right) / \text{Hct}_{\text{initial}}$$

General guidelines are as follows:

- a. If the amount of the blood loss is less than one third of the ABL, it can be replaced with lactated Ringer solution.
 - b. If the amount of blood loss is greater than ABL, replace with packed red blood cells (leukoreduced, CMV negative, and irradiated). Fresh frozen plasma and platelet transfusions should be guided by the results of coagulation tests, estimates of the present and anticipated blood losses, and adequacy of clot formation in the wound.
 - c. For infants and young children, blood loss should be measured using small suction containers and by weighing sponges. Because it is sometimes difficult to measure small-volume blood losses precisely in young children, monitoring of hemoglobin and hematocrit will help avoid unnecessary transfusions and also alert the anesthetist to the need for blood transfusion.
 - d. The **"acceptable hemoglobin and hematocrit"** is no longer considered to be 10 g/dL and 30%. Each patient is evaluated with regard to the need for red blood cell transfusion. A healthy child with normal cardiac function can compensate for acute anemia by increasing cardiac output. A premature infant, a debilitated child, a child with sepsis, a child receiving chemotherapy, or one facing massive surgery may require a higher hemoglobin.
- C. **Estimated fluid deficit** = (maintenance fluid per hour) $\times$ hours since the last oral intake. The entire estimated fluid deficit replaced during all major cases; the first half is administered during the first hour, and the remaining deficit is infused over the next 1 to 2 hours.
- D. **Third-space losses** may require up to an additional 10 mL/kg/h of lactated Ringer solution or normal saline if there is extensive exposure of the intestine or a significant ileus.

X. EMERGENCE AND POSTANESTHESIA CARE

A. Extubation

1. **Laryngospasm** may occur during emergence, especially during the critical period of excitement.
2. In most cases, the trachea is extubated after emergence from anesthesia. Coughing is not a sign that the child is ready for extubation. Instead, children should demonstrate purposeful activity (e.g., reaching for the endotracheal tube) or eye opening before extubation. In the infant, hip flexion and strong grimaces are useful indications of awakening.
3. Alternatively, the trachea may be extubated while the patient is in a deep plane of anesthesia with spontaneous ventilation. This can be

done in operations such as inguinal herniorrhaphy where coughing on emergence is undesirable or in patients with reactive airways disease. Extubation under deep anesthesia is not appropriate for the child with a full stomach; a child whose trachea was difficult to intubate or the child who had oral or laryngeal surgery. Clinical judgment is essential.

4. **Emergence delirium** is a relatively common postanesthetic event and can be difficult to differentiate from pain. Common risk factors include; age (1 to 5 years old), surgery type (ENT/ophthalmic procedures), preoperative anxiety, preoperative medication, rapid emergence, and pain. Treatment options after treating pain include early reunion with parents, fentanyl ($1\text{ }\mu\text{g/kg}$), propofol (1 mg/kg), and dexmedetomidine ($0.5\text{ }\mu\text{g/kg}$).
- B. **During transport** to the postanesthesia care unit (PACU), the child's color and ventilatory pattern should be continuously monitored. Supplemental oxygen may be administered if indicated (e.g., the child with anemia or pulmonary disease).
- C. **In the PACU**, early reunion of the child and parents is desirable. Discharge criteria often follow the Aldrete Scoring system (motor function, breathing, blood pressure, consciousness, and oxygenation) as well as pain control. In addition, extended postoperative/procedural monitoring of infants and children should be considered on a case-by-case basis (obstructive sleep apnea, prematurity, children less than 3 years who underwent airway surgery including tonsillectomy, etc.)

XI. SPECIFIC PEDIATRIC ANESTHESIA PROBLEMS

A. The Compromised Airway

1. Etiologies

- a. Congenital abnormalities (e.g., choanal atresia, Pierre Robin syndrome, tracheal stenosis, or laryngeal web).
- b. Inflammation (e.g., tracheobronchitis or "croup," epiglottitis, and pharyngeal abscess).
- c. Foreign bodies (FBs) in the trachea or esophagus.
- d. Neoplasms (e.g., congenital hemangioma, cystic hygroma, or thoracic lymphadenopathy).
- e. Trauma.

2. Initial management

- a. Administer 100% oxygen by face mask (continually assess oxygenation and ventilation).
- b. Keep the child as calm as possible. Evaluation should be efficient, because it may increase agitation and cause further airway compromise. Parents are invaluable in their ability to pacify their children and should remain with them as long as feasible.
- c. An anesthetist must be present during transport to the operating room. Oxygen, a resuscitation bag and mask, laryngoscope, atropine, succinylcholine, drugs suitable for sedation and hypnosis, appropriate endotracheal tubes and laryngeal mask airways, oral airways, and pulse oximetry must be available.

3. Induction of anesthesia with a compromised airway

- a. **Minimize manipulation of the patient.** A precordial stethoscope and pulse oximeter are adequate monitors during the initial induction of anesthesia.
- b. The child may remain in a **semisitting position**, with the parents present if indicated. A **gradual inhalation induction** with sevoflurane is the next step (see section V.C.3). Airway obstruction and poor air exchange will prolong induction.

- c. Parents are asked to leave when the child becomes unconscious, and an IV is started. If indicated, atropine may be given at this time. Alternatively a preinduction IV may be started if there is concern for acute decompensation and proceed with IV or inhalational induction.
 - d. **Patients with croup** may benefit from gentle application of continuous positive airway pressure, but any positive pressure can cause acute airway obstruction in patients with epiglottitis or an FB.
 - e. The **oral endotracheal tube** should have a stylet and be at least one size smaller than the predicted size. If postoperative ventilation is anticipated (e.g., epiglottitis), a cuffed endotracheal tube may be indicated.
 - f. At this point, patients usually are hypercarbic (ETCO₂ between 50 and 60 mm Hg), but generally, this is well tolerated. Bradycardia is an indication of hypoxemia and requires immediate establishment of a patent airway.
 - g. Perform laryngoscopy only when the child is deeply anesthetized. The decision to give a muscle relaxant depends on the situation. A muscle relaxant facilitates intubation and obviates the need for deep anesthesia in certain circumstances. In other cases, muscle relaxation may further compromise the airway. In general, orotracheal intubation should be accomplished before any further airway procedures are attempted. **Bronchoscopy** is indicated before intubation in cases of large upper airway FBs or friable subglottic tumors (e.g., hemangioma).
 - h. **A nasal tube** may be more appropriate for illnesses that require several days of intubation (e.g., epiglottitis). An orotracheal tube may be changed to a nasotracheal tube at the end of the procedure, provided the oral intubation was easily accomplished. Never jeopardize a secure oral endotracheal tube for the sake of changing it to a nasal endotracheal tube.
 - i. Children should be sedated during transport to the intensive care unit. A combination of a narcotic and a benzodiazepine, propofol infusion, or dexmedetomidine infusion or bolus can be effective. Breathing may be spontaneous or assisted during the immediate postoperative period. Propofol is not approved by the FDA for sedation of pediatric intensive care patients due to the risk of propofol infusion syndrome and its associated metabolic derangements.
4. **Management of the inhaled Foreign Body (FB)**
- a. FB aspiration usually occurs between 7 months and 4 years of age. About 75% of FBs lodge in the proximal airway (larynx, trachea, and right/left mainstem bronchus). Most deaths occur at the time of aspiration, and the mortality in most series is zero if the child reaches the hospital alive.
 - b. Choking and wheezing following a witnessed aspiration event is the most common **presentation**. The triad of coughing, wheezing, and reduced breath sounds is present in only 50% of cases. Chest x-ray may show radiopaque objects, postobstructive emphysema, or a localized pneumonia but has a false-negative rate of 40%.
 - c. **Management** is prompt rigid bronchoscopy regardless of chest x-ray findings. It is vital to communicate with the bronchoscopist before and during the procedure. An emergency tracheotomy and thoracotomy kit should be prepared. There are two approaches to the anesthetic: spontaneous ventilation and controlled ventilation.

- d. **Spontaneous ventilation:** After preoxygenation and IV atropine or glycopyrrolate, a sevoflurane/100% oxygen induction is performed. Sevoflurane is preferred for inhalational induction, and spontaneous ventilation is maintained. Once an adequate depth is achieved, the vocal cords and subglottic space are sprayed with topical lidocaine (2% for school age children and 1% for small infants). The trachea is then intubated with a ventilating bronchoscope. A sufficient depth of anesthesia is required to prevent moving and coughing. Consider a small dose of muscle relaxant just before removal of the FB through the vocal cords. The stomach is then suctioned, and the patient is allowed to emerge breathing through either a mask or an endotracheal tube placed after FB removal. Advantages of this technique are better air flow distribution and ventilation-perfusion matching, uninterrupted ventilation, and the ability to immediately assess ventilatory mechanics after FB removal. Disadvantages are the risks of patient movement, coughing, laryngospasm, and prolonged emergence.
 - e. **Controlled ventilation:** Anesthesia is commenced with a rapid sequence induction using propofol and a muscle relaxant. Maintenance anesthesia can be provided with propofol and remifentanyl infusions and muscle relaxant. The trachea is intubated with a ventilating bronchoscope, and ventilation is performed in concert with the bronchoscopist's interventions. When the bronchoscope is in place, ventilation is achieved with high inspiratory pressures, and long expiratory times are necessary to prevent barotrauma. Emergence is achieved in a manner similar to the spontaneous ventilation technique. The advantages of controlled ventilation are rapid control of the airway, no patient movement, and lower anesthetic requirements. However, ventilation is intermittently interrupted, and there are risks of displacing the FB distally and causing barotrauma with ball-valve hyperinflation.
 - f. A large retrospective study showed that **ventilatory technique** did not affect the success of FB removal or influence adverse outcomes (hypoxia, hypercarbia, bradycardia, and hypotension).
 - g. Subglottic edema resulting in postextubation croup can be treated with humidified oxygen. If symptoms are severe, then racemic epinephrine (0.5 mL of a 2% solution in 2 to 4 mL of volume) can be given. In addition dexamethasone (0.25 to 0.5 mg/kg up to 8 mg) should be considered.
- B. Recent Upper Respiratory Infection.** Infants and children can have 6 to 10 upper respiratory infections each year. It is important to balance the severity of symptoms with the urgency of surgery. Wheezing, fever, and cough are signs of lower respiratory inflammation and are associated with an increased risk of perioperative airway complications. Conversely, myringotomy and ear tube placement may relieve the rhinorrhea associated with chronic otitis media.
- C. Intra-abdominal malformations** include pyloric stenosis, gastroschisis, omphalocele, atresia of the small intestine, and volvulus (see Chapter 30).
1. **Gastrointestinal emergencies** frequently produce marked dehydration and electrolyte abnormalities. Repair of pyloric stenosis should be delayed until intravascular volume is restored and the hypokalemic, hypochloremic, and metabolic alkalosis is corrected. The situation is more urgent with other diagnoses (e.g., duodenal atresia), and rehydration can be continued intraoperatively.

2. **Abdominal distention** in infants and young children rapidly causes respiratory compromise, so nasogastric drainage is mandatory. Even so, a few moribund infants may require endotracheal intubation before the induction of anesthesia.
 3. Children with less severe physiologic disturbances and only mild or moderate distention can undergo a rapid sequence induction of anesthesia.
 4. A severely dehydrated and septic child may require additional monitoring (e.g., arterial line, central venous line, and urinary catheter).
 5. Volatile anesthetics are appropriate for the previously healthy infant undergoing a simple operation (such as pyloromyotomy). In the case of an extremely ill child (e.g., perforated viscous), the anesthetic management should include an O_2 -air mixture and drugs causing minimal myocardial depression. Opioids, benzodiazepines, and neuromuscular relaxants are usually better tolerated than volatile anesthetics. Nitrous oxide should be avoided because it may add to abdominal distention.
 6. **Fluid and heat losses.** When the bowel is exposed and manipulated, third-space losses may be excessive, and remarkable fluid volumes may be necessary. Even when using all possible warming strategies, heat loss may be unavoidable.
 7. Postoperative ventilatory support is often indicated until abdominal distention is diminished, hypothermia resolves, and fluid requirements decrease.
- D. Thoracic Emergencies**
1. **Tracheoesophageal fistula.** See Chapter 30.
 2. **Congenital diaphragmatic hernia.** See Chapter 30.
- E. Congenital Heart Disease.** See Chapters 2, 23, and 30.
- F. Head and Neck Procedures**
1. Strabismus repair. See Chapter 26.
 2. Tonsillectomy, adenoidectomy, and emergency surgery in the child with bleeding tonsils. See Chapter 26.
- G. Neurotoxicity**
1. There is a growing concern regarding the long-term developmental effects of general anesthesia on our pediatric patients. The data regarding the long-term outcomes of pediatric patients exposed to general anesthesia early in development are mixed and have several limitations (i.e., study design, anesthetic used, surgical exposure, comorbidities, etc.). The first prospective randomized control trial (GAS; NCT00756600) investigating the effects of general versus regional anesthesia on neurodevelopmental outcomes in infants undergoing inguinal hernia repair is currently under way and should provide early results in 2017.
 2. In vivo and in vitro animal models of neuronal cell death have been demonstrated with almost all of the commonly used anesthetic agents (i.e., propofol, ketamine, desflurane, halothane, isoflurane, sevoflurane, xenon, diazepam, midazolam, chloral hydrate, pentobarbital). However, the long-term outcomes regarding neurodevelopmental effects and tests of memory and cognitive processing in animal studies are mixed and call into question the effects of anesthetic drugs. Furthermore, significant limitations in animal studies (i.e., developmental equivalence, dosing/duration of exposure controlled for life span, study design, etc.) preclude extrapolation to our pediatric patient.

3. In advising a parent or caregiver concerned about the neurodevelopmental effects of general anesthesia, it may be helpful to discuss several points below:
 - a. Alternatives if possible to general anesthesia
 - b. Necessity of surgical/procedural intervention
 - c. Not exceeding the required amount of anesthesia for the indicated procedure to accomplish procedural and patient comfort goals
 - d. Uncertainty regarding the human and animal data

Suggested Readings

- Berde CB, Sethna NF. Analgesics for the treatment of pain in children. *N Engl J Med* 2002;347(14):1094–1103.
- Cloherly JP, Eichenwald EC, Hansen AR, Stark AR. *Manual of Neonatal Care*. 7th ed. Philadelphia: Lippincott Williams & Wilkins; 2011.
- Constant I, Sabourdin N. The EEG signal: a window on the cortical brain activity. *Paediatr Anaesth* 2012;22(6):539–552.
- Coté CJ, Lerman J, Anderson BJ. *A Practice of Anesthesia for Infants and Children*. 5th ed. Philadelphia: Saunders Elsevier; 2013.
- Coté CJ, Sui J, Anderson TA, et al. Continuous noninvasive cardiac output in children: is this the next generation of operating room monitors? Initial experience in 402 pediatric patients. *Paediatr Anaesth* 2015;25(2):150–159.
- Dalal PG, Murray D, Messner AH, et al. Pediatric laryngeal dimensions: An age-based analysis. *Anesth Analg* 2009;108(5):1475–1479.
- Dalens B, Khandwala R. *Regional Anesthesia in Infants, Children, and Adolescents*. Baltimore: Williams & Wilkins; 1995.
- Dorsch JA, Dorsch SE. *Understanding Anesthesia Equipment*. 5th ed. Philadelphia: Wolters Kluwer Health, Lippincott Williams & Wilkins; 2008.
- Greeley WJ. *Pediatric Anesthesia*. New York: Churchill Livingstone; 1999.
- Gregory GA. *Pediatric Anesthesia*. 4th ed. New York: Churchill Livingstone; 2001.
- Johns Hopkins Hospital, Custer JW, Rau RE, Lee CK. *The Harriett Lane Handbook*. 18th ed. Philadelphia: Elsevier Health Sciences; 2008.
- Kliegman RM, Behrman RE, Jenson HB, et al. *Nelson Textbook of Pediatrics*. 18th ed. Philadelphia: WB Saunders Elsevier; 2007.
- Lin EP, Soriano SG, Loepke AW. Anesthetic neurotoxicity. *Anesthesiol Clin* 2014;32(1):133–155.
- Miller RD, ed. *Anesthesia*. 8th ed. Philadelphia: Elsevier-Churchill Livingstone; 2009.
- Motoyama EK, Davis PJ. *Smith's Anesthesia for Infants and Children*. 8th ed. Philadelphia: St. Elsevier Mosby–Saunders; 2007.
- O'Neill JA, Rowe MI, Grosfeld J, et al. *Pediatric Surgery*. 5th ed. Mosby–Year Book; 1998.
- Vergnaud E, Vidal C, Montmayeur Verchere J, et al. Noninvasive cardiac output measurement using bioreactance in postoperative pediatric patients. *Paediatr Anaesth* 2015;25(2):160–166.

I. MATERNAL PHYSIOLOGY IN PREGNANCY (TABLE 32.1)**A. Respiratory System**

- 1. Capillary engorgement of the mucosa** may occur throughout the respiratory tract, beginning early in the first trimester and increasing throughout pregnancy. Historically, a 6.0- to 6.5-mm (inner diameter) endotracheal tube has been recommended for intubation to decrease the possibility of airway trauma. However, the use of larger tubes may be possible in most patients should it be required. Fluid retention may lead to an enlarged tongue that may explain the increased prevalence of Mallampati class 3 and 4 airways in term parturients compared to the general population. Additionally, the airway exam may change during the course of labor resulting in a further increase in the airway class. Lastly, because of mucosal engorgement, nasotracheal intubation may cause epistaxis and is best avoided in pregnant women.
- 2. Minute ventilation increases by 45%** to support the higher oxygen requirements of the mother and fetus and is driven by a proportional increase in tidal volume. As the pregnancy progresses, elevation of the diaphragm from the gravid uterus leads to 20% decrease in maternal **functional residual capacity**. The resultant decrease in oxygen reserve mandates adequate preoxygenation prior to induction of general anesthesia.

B. Cardiovascular System

- 1. Cardiac output increases** progressively up to 50% from the end of the second trimester to term primarily due to increased stroke volume with a small contribution of increased heart rate. During labor, contractions of the engorged uterus provide a 300- to 500-mL autotransfusion into the maternal circulation, further increasing cardiac output. Cardiac output becomes highest immediately postpartum and may increase 80% to 100% above prelabor values due to further autotransfusion and loss of inferior vena cava (IVC) compression by the fetus. Despite the significant increase in cardiac output, blood pressure is not elevated at term from prepregnancy levels due to decreased peripheral vascular resistance.
- 2. Supine hypotension** usually occurs after 20 weeks of gestation when the gravid uterus compresses the aorta and IVC of the patient in the supine position. Aortocaval compression decreases venous return and results in maternal hypotension and decreased uteroplacental blood flow. Providing left uterine displacement of 15 degrees when the patient is supine will mitigate this problem, with the potential for further increases in blood pressure and cardiac output at angles greater than 15 degrees.

C. Hematology

- 1. Blood volume increases** markedly throughout the course of pregnancy. Because the plasma volume increases more than does red cell mass, a relative **dilutional anemia** occurs.

TABLE
32.1
Physiologic Changes Associated with Pregnancy

System	Parameters	Changes
Respiratory	<i>Capacities/volume</i>	
	Total lung capacity	−5%
	Vital capacity	No change
	Functional residual capacity	−20%
	Inspiratory reserve volume	+5%
	Expiratory reserve volume	−20%
	Residual volume	−15
	Closing capacity	No change
	Tidal volume	+45%
	<i>Mechanics</i>	
	FEV ₁	No change
	FEV ₁ /FVC	No change
	Minute ventilation	+45%
	Alveolar ventilation	+45%
	<i>Blood gases</i>	
	PaCO ₂	−10%
	PaO ₂	+5%–10%
	pH	No change
	HCO ₃	Decrease
Cardiovascular	<i>Oxygen consumption</i>	+20%
	P50 at term	30 mm Hg
	Cardiac output	+50%
	Stroke volume	+25%
	Heart rate	+20%–25%
Hematology	Systematic vascular resistance	−20%
	Blood volume	+45%
	Plasma volume	+55%
	Red blood cell volume	+25%
	<i>Coagulation factors</i>	
	Factors VII, VIII, IX, X, XII, fibrinogen	Increase
	Prothrombin	No change
	Factors XI, XIII	Decrease
	Platelet count	No change or decrease
	Total protein (albumin, globulin)	Decrease
Central nervous system	MAC	Decrease
	Local anesthetic requirement	Decrease
Gastrointestinal	<i>Gastric emptying</i>	
	First trimester	No change
	Second trimester	No change
	Third trimester	No change
	Labor	Decrease
	Postpartum (18 h)	No change
	<i>Barrier pressure</i>	
Hepatic	First, second, third trimesters, labor	Decrease
	AST, ALT, LDH, bilirubin	Increase
	Alkaline phosphatase	Increase
Renal	Glomerular filtration rate	+50%
	Renal plasma flow	+75%

2. The pregnant patient is **hypercoagulable** throughout gestation. The concentration of most coagulation factors increases in pregnancy as does platelet production, activation, and consumption. This hypercoagulable state helps to limit blood loss at delivery although it also increases the risk for thrombotic complications.

D. Nervous System

1. The **minimum alveolar concentration (MAC)** for inhalational anesthetics is decreased by 30% during pregnancy. The etiology is unclear but may be related to alterations of hormone and endorphin concentrations during pregnancy, which result in an increased pain threshold or pregnancy-induced analgesia. However, this increased sensitivity to volatiles may not translate to enhanced effect in the brain; therefore low MAC should be used with caution to avoid an increase in the incidence of awareness under anesthesia.
2. The **local anesthetic** dose required for regional anesthesia is reduced in the parturient compared to the patient who is not pregnant. Reasons for this include the following:
 - a. **A decrease in cerebrospinal fluid (CSF) protein** results in a greater proportion of free and active drug.
 - b. **Elevated CSF pH** increases the un-ionized fraction of the local anesthetic.
 - c. **Distension of epidural veins** during pregnancy results in a decrease in lumbar CSF volume with enhancement of local anesthetic spread and reduction of the segmental dose requirement for **spinal anesthesia**.
3. **Sympathetic nervous system (SNS) activity increases** from as early as 6 weeks of gestation despite decreases in diastolic pressure and total peripheral resistance. The parturient is highly dependent on the SNS for hemodynamic control, which is reflected by the significant decrease in blood pressure seen after regional anesthesia. SNS activity may return to normal by 36 to 48 hours postpartum.
4. The apex of **lumbar lordosis is shifted cephalad** with reduced thoracic kyphosis in the supine position. This may contribute to the increased cephalad spread of spinal anesthesia during pregnancy.

E. Gastrointestinal System. Because of the **relaxation of the lower esophageal sphincter** and mechanical **displacement of the stomach** by the gravid uterus, gastric reflux and heartburn are present in many pregnant patients. It is not clear when during the pregnancy the risk for aspiration increases, although the difference between intragastric pressure and lower esophageal sphincter tone is decreased as early as the first trimester. Gastric emptying is not delayed during pregnancy, but it is slowed during labor particularly following the administration of opioids. When a general anesthetic is planned, a nonparticulate antacid should be given routinely; a histamine (H_2) blocker and metoclopramide should be considered. Patients in the second and third trimester should have a rapid sequence induction for general anesthesia.

F. Renal System. Renal plasma flow and glomerular filtration increases by up to 50%, leading to increased creatinine clearance and decreased blood urea nitrogen and serum creatinine levels.

G. Musculoskeletal. Increased lumbar lordosis and intra-abdominal pressure secondary to the enlarging uterus can stretch and compress the lateral femoral cutaneous nerve and produce a sensory loss over the anterolateral thigh ("meralgia paresthetica"). Carpal tunnel syndrome is common with a possible multifactorial etiology. Widening of the pubic symphysis is likely secondary to an increase in the hormone relaxin during pregnancy.

II. LABOR AND DELIVERY

A. Labor is defined as the onset of painful uterine contractions that lead to cervical change, and it may be divided into three stages.

1. The **first stage** begins with the onset of regular contractions and ends with full cervical dilation. It is divided into a slow latent phase and a rapidly progressive active phase characterized by accelerated cervical dilation. Patients with body mass index greater than 30 kg/m² and male fetuses may experience prolonged first stage of labor. Such factors highlight the limitations of widespread use of a single labor curve for all patients.
2. The **second stage** extends from full cervical dilation until delivery of the infant.
3. The **third stage** begins after delivery of the infant, ending with delivery of the placenta.

B. Pain during the early first part of labor is primarily caused by uterine contractions and cervical dilation. Pain during the first portion of labor is mediated by the T10 to L1 segments of the spinal cord. In the active phase of the first stage of labor and in early second-stage labor, there is an additional component of pain due to perineal stretching that travels via the pudendal nerve to enter the spinal cord between the S2 and S4 segments.

C. Intrapartum fetal evaluation is most commonly accomplished with **fetal heart rate (FHR) monitoring**—either continuous or intermittent. Continuous FHR monitoring is used in up to 85% of laboring patients in the United States. The normal FHR ranges from 110 to 160 beats per minute (bpm) over 10 minutes. Fetal tachycardia may signify fetal asphyxia, maternal fever, and/or chorioamnionitis or may be the result of maternally administered drugs. Persistent fetal bradycardia is most commonly due to hypoxia, but other etiologies include congenital heart block, maternally administered β -blockers, or hypothermia. FHR baseline variability is defined as the fluctuation in FHR of at least 2 bpm over an observed 10-minute period. Minimal variability refers to less than 5 bpm fluctuation, moderate ranges from 6 to 25 bpm, and marked greater than 25 bpm. It is modulated by fetal vagal tone and is a sign of underlying fetal health. Lack of variability must be interpreted in the context of FHR decelerations (decreases in FHR of 15 seconds or more from baseline to nadir). Recurrent concerning decelerations (late or deep variables), especially in the setting of minimal or absent variability, should prompt further evaluation to detect fetal compromise. Decelerations have been categorized (Fig. 32.1) as follows:

1. **Early decelerations** are gradual FHR decelerations that occur concomitantly with uterine contractions providing a mirror image of the uterine contraction, with the nadir of the deceleration occurring at the peak of the contraction. They are caused by an increase in fetal vagal tone, likely from mild hypoxia and compression of the fetal head, and do not require intervention.
2. By definition, **variable decelerations** are variable in both duration and appearance, and can occur spontaneously. Variable decelerations are associated with umbilical cord compression and decreased umbilical blood flow. They may indicate fetal compromise when severe and/or repetitive. Amnioinfusion (the instillation of amniotic fluid through a transcervical catheter after rupture of the fetal membranes) has been demonstrated to decrease the need for emergent cesarean delivery by improving or eliminating them.
3. **Late decelerations** are gradual decelerations that begin after the onset of a uterine contraction with a return of the FHR to the baseline only

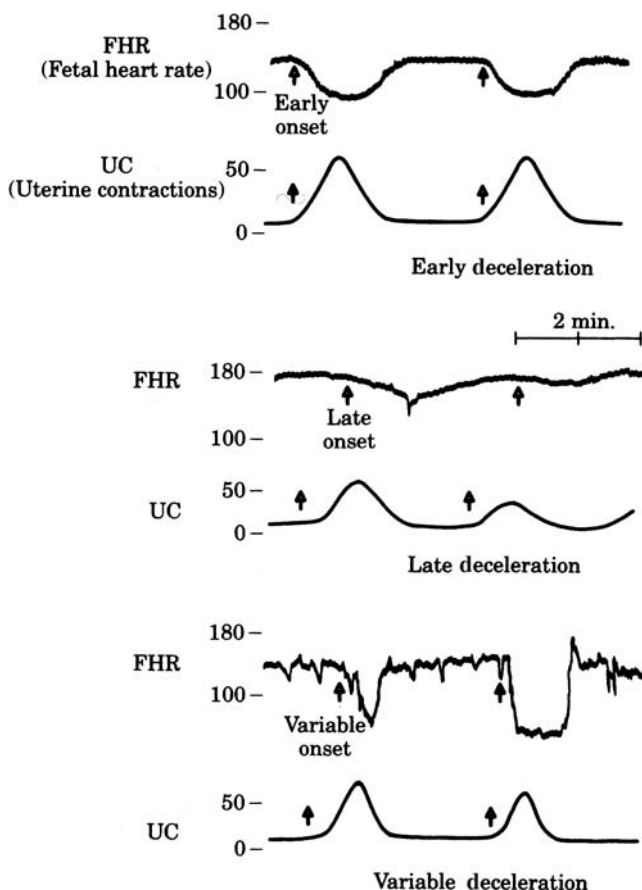


FIGURE 32.1 Patterns of periodic FHR decelerations in relation to uterine contractions.

after the contraction has ended. Late decelerations suggest impaired maternal–fetal oxygen exchange and are triggered in susceptible fetuses by the decrease in fetal reserve with resulting intolerance of transient hypoxia. Medical interventions are tailored to improve placental oxygen delivery, among them left uterine displacement, correction of maternal hypotension, reconsideration of oxytocin dosing, and oxygen by face mask to the mother. A persistent late deceleration pattern might require delivery of the fetus.

4. Electronic FHR monitoring has several significant limitations including a high rate of false positives and significant variability in its interpretation. Lastly, the use of electronic fetal monitoring has been associated with an increase in operative deliveries but has not resulted in a decrease in cerebral palsy rates. To minimize intervention based on false positives, additional ancillary tests may be considered:

- a. **Fetal scalp stimulation.** A FHR acceleration in response to digital or instrumental stimulation of the fetal head is associated with a healthy nonacidotic fetus.
- b. **Fetal scalp blood pH determination** is another method employed to evaluate the presence of fetal acidosis when abnormal FHR patterns cannot be corrected or their significance is unclear. In general, a pH above 7.25 is acceptable, and the labor may continue. A pH below 7.20 suggests that the fetus is acidotic and should be promptly delivered. If the pH is in the range of 7.20 to 7.25, close FHR monitoring and repeated scalp blood sampling are recommended.
- c. **Fetal pulse oximetry** was designed to improve the assessment of the fetal status by continuously measuring fetal oxygen saturation in the setting of a nonreassuring FHR tracing. Unfortunately, studies have shown that the technology is not associated with a decrease in cesarean delivery rates or improvement in neonatal outcomes.

III. MEDICATIONS COMMONLY USED FOR LABOR AND DELIVERY

- A. **Vasopressors.** Symptoms of maternal hypotension include light-headedness, nausea, difficulty breathing, and diaphoresis. Maternal hypotension may lead to decreased placental perfusion and fetal distress. Sympathetic blockade from regional anesthesia and decreased systemic vascular resistance may cause symptomatic maternal hypotension. An ideal vasopressor for obstetric anesthesia is one that increases both maternal blood pressure and placental blood flow.
 - 1. **Ephedrine** is an indirect agonist of α - and β -adrenergic receptors. Its inotropic and chronotropic effects increase peripheral and uterine blood flow. Historically, ephedrine was the drug of choice for treatment of maternal hypotension.
 - 2. Pure α -adrenergic agents such as **phenylephrine** were previously believed to increase maternal blood pressure but decrease uteroplacental blood flow. Recent evidence indicates that judicious and precise dosing of phenylephrine is not associated with an increased incidence of fetal acidemia or decreased Apgar scores. Phenylephrine infusions have become increasingly common to prevent and treat maternal hypotension.
 - 3. The more potent vasoconstrictors and inotropes such as **norepinephrine** and **epinephrine** are indicated for severe maternal hypotension resistant to volume resuscitation and traditional vasopressors.
- B. **Oxytocics** or **ecbolics** are agents that stimulate uterine contractions.
 - 1. **Indications**
 - a. To induce or augment labor
 - b. To control postpartum uterine atony and bleeding
 - c. To induce therapeutic abortion
 - 2. The most frequently used drugs include the synthetic posterior pituitary hormone, **oxytocin** (Pitocin); the ergot alkaloids, **ergonovine** (Ergotrate) and **methylergonovine** (Methergine); and the prostaglandins, **prostaglandin 15-methyl F₂** (Hemabate) and **prostaglandin E₁** (misoprostol).
 - a. **Oxytocin** acts on the uterine smooth muscle to stimulate the frequency and force of contractions. Cardiovascular side effects of oxytocin include vasodilation, hypotension, tachycardia, and arrhythmias. In high doses, oxytocin may have an antidiuretic effect and produce hyponatremia, cerebral edema, and subsequent seizures. Recent evidence has suggested a possible association

between oxytocin therapy and neurodevelopmental disorders. Oxytocin is routinely diluted and given by continuous intravenous (IV) infusion.

- b. **Ergot alkaloids** control postpartum bleeding following the third stage of labor. Side effects include systemic vasoconstriction and hypertension, which may be amplified in the presence of vasopressors. IV injection has been associated with severe hypertension, seizures, stroke, myocardial infarction, and pulmonary edema. Intramuscular (IM) administration is therefore highly recommended. Ergot alkaloids should be used with caution or avoided in patients with peripheral vascular disease, preeclampsia, hypertension, or coronary artery disease.
 - c. **Prostaglandin 15-methyl $F_{2\alpha}$** is a treatment for uterine atony. The usual dose is 250 μ g IM or intramyometrially, not more frequently than every 15 minutes, with a total maximum dose of 2 mg. Transient hypertension, severe bronchoconstriction, and increased pulmonary vascular resistance have been reported, contraindicating its use in patients with a history of asthma. Fever, nausea, vomiting, and diarrhea are additional side effects.
 - d. **Prostaglandin E_1** increases myometrial intracellular free calcium concentrations and improves uterine tone. It is available in 200- μ g tablets that are placed rectally or vaginally for the treatment of postpartum hemorrhage. Side effects are less common but are similar to those of prostaglandin 15-methyl $F_{2\alpha}$.
- C. Tocolytics** are used to delay or stop premature labor in patients with viable fetuses less than or equal to 34 weeks of gestation. Cervical dilation of less than 4 cm and cervical effacement of less than 80% are associated with a greater likelihood of success in terminating premature labor.

1. Indications

- a. To stop preterm contractions
- b. To slow or arrest labor while initiating other therapeutic measures (e.g., betamethasone to accelerate fetal lung maturation)
- c. To allow transfer from a community hospital to a tertiary care center with a neonatal intensive care unit

2. Contraindications

- a. Chorioamnionitis
- b. Fetal distress
- c. Intrauterine fetal demise
- d. Severe hemorrhage

3. Specific drugs

- a. **β_2 -Adrenergic agonists** such as **terbutaline** produce myometrial relaxation, maternal bronchodilation, vasodilation, and tachycardia. In addition, they cause hyperglycemia, hypokalemia, hyperinsulinemia, and metabolic acidosis. Pulmonary edema and chest pain are rare in the setting of less than 24 hours of therapy. Preexisting hyperglycemia should be corrected, and a baseline electrocardiogram should be considered for patients with preexisting cardiac disease.
- b. **Magnesium sulfate** is used for the prevention of preeclamptic seizures and as a tocolytic agent. It antagonizes intracellular calcium and inhibits myometrial contraction. Side effects include hyporeflexia, lethargy, and nausea; at higher serum concentrations, peripheral respiratory depression, electrocardiogram changes, and pulmonary edema are possible.

- c. **Cyclooxygenase inhibitors** such as **indomethacin** inhibit arachidonic acid conversion to prostaglandins critical in parturition. Maternal side effects are uncommon. This class of medications can lead to premature closure of the fetal ductus arteriosus and decreased fetal urine output. They should therefore be used with caution after 32 weeks of gestation and in oligohydramnios.
- d. **Calcium channel blockers** block the release of calcium from smooth muscle sarcoplasmic reticulum thus inhibiting uterine contractions. Calcium channel blockers are effective tocolytic agents and are well tolerated. Hypotension is an expected side effect.

IV. PLACENTAL TRANSFER OF DRUGS

- A. **Placental transport of anesthetics** occurs primarily by passive diffusion. Drugs with higher diffusion constants more readily cross placental membranes. Factors that promote rapid diffusion include the following:
 - 1. Low molecular weight (<600 Da)
 - 2. High lipid solubility
 - 3. Low degree of ionization
 - 4. Low protein binding
- B. Most of the inhalational and IV anesthetics readily cross the placenta because they have a low molecular weight, have high lipid solubility, are relatively nonionized, and are minimally protein bound.
- C. **Muscle relaxants** are water-soluble, ionized molecules, with high molecular weights, and therefore do not readily cross the placenta.
- D. **Vasoactive medications**—antihypertensive, antiarrhythmic medications, and vasopressors—cross the placenta and do exert some effect on the fetus.
- E. Fetal acidosis, exacerbated in fetal distress, favors placental transfer and subsequent “ion trapping” of basic drugs (e.g., amide local anesthetics). Following placental transfer, the drug becomes ionized and accumulates in the acidic fetal environment; however, in normal circumstances, these concentrations rarely result in clinical toxicity.

V. ANALGESIA FOR LABOR AND VAGINAL DELIVERY

- A. **Natural Childbirth.** Some women favor a delivery plan with minimal medical intervention. Nonetheless, it is important to evaluate each patient's medical history and physical findings to provide informed and expedient emergency care.
- B. **Systemic Analgesia**
 - 1. **Mixed opioid agonist–antagonists.** Nalbuphine or butorphanol are often the initial choice for systemic analgesia due to their efficacy combined with a ceiling effect on maternal ventilatory depression.
 - 2. **Opioids.** Meperidine, morphine, and fentanyl are commonly used opioids. Maternal side effects, including dose-dependent respiratory depression, sedation, and rapid placental diffusion, limit their use. These drugs may also cause decreased FHR variability, a need for active neonatal resuscitation, and possible neurobehavioral effects in the neonate.
 - 3. **Inhalational analgesia.** Nitrous oxide is used in different parts of the world, most commonly in a 50% mixture with oxygen. Its analgesic efficacy is limited. Environmental pollution is a concern, and hypoxemia is possible in combination with systemic opioids. Neonatal depression is rare. Preliminary experience with sevoflurane suggests a possible role for intermittent inhalation during contractions.

C. Epidural provides the most effective labor analgesia and eases the transition to effective neuraxial anesthesia if a cesarean delivery becomes necessary. Existing evidence does not show an increased rate of cesarean delivery when compared to systemic analgesia. The duration of the second stage of labor is about 15 minutes longer, and the instrumental delivery rate is increased with epidurals.

1. Technique

- a. Initial IV access should be established. Prehydration with 500 to 1,000 mL of crystalloid may minimize hypotension as analgesia is initiated.
- b. Vital signs and FHR should be monitored according to institutional protocol.
- c. It is customary to administer a 30-mL oral dose of nonparticulate antacid.
- d. Specific physiologic and anatomic features of term pregnancy—for example, epidural venous distention, increased abdominal size, and intermittent uterine contractions—must be taken into account.

2. Advantages

- a. Epidurals offer continuous analgesia for the duration of labor and cesarean section if necessary.
- b. Drug dose and delivery mode (e.g., patient controlled analgesia) may be individualized.
- c. The hyper/hypoventilation cycle and associated decrease in PaO_2 or O_2 saturation are favorably modified.
- d. Memory, alertness, and emotional perception are preserved.

3. Disadvantages

- a. Patient cooperation is necessary.
- b. Providers skilled in neuraxial technique in pregnant women are required.
- c. Vital signs must be regularly monitored and systemic hypotension corrected.
- d. Accidental dural puncture complicates approximately 1% to 2% of placements.

4. Contraindications

- a. Patient refusal
- b. Coagulation disorder or significant thrombocytopenia—either acquired or inherited
- c. Infection at the site of catheter placement
- d. Severe hypovolemia
- e. Space-occupying lesion with increased intracranial pressure predisposing the patient to herniation after accidental dural puncture and CSF loss

5. Anesthetics

- a. **A test dose** of 3 mL of 1.5% lidocaine (45 mg) with 1:200,000 epinephrine (15 μg) aids in detection of intrathecal or intravascular placement. Concurrent hypertension or preeclampsia might contraindicate addition of epinephrine to the test dose.
- b. The ideal analgesia in labor provides adequate pain relief and minimizes motor block. The combination of a local anesthetic and an opioid helps to achieve this goal. Our current practice is to administer an epidural mix of 0.08% (0.8 mg/mL) bupivacaine with 2 μg /mL of fentanyl. The patient-controlled epidural analgesia (PCEA) delivers a continuous infusion of 5 mL/h and allows patient boluses of 10 mL every 20 minutes with a maximum hourly infusion of 25 mL.

Additional clinical boluses are typically between 5 and 10 mL. In the course of labor, it is not uncommon to administer concentrated local anesthetics—that is, 1% to 2% lidocaine and 0.125% to 0.25% bupivacaine—to meet analgesic requirements. Malfunction and malposition of the epidural catheter must be considered when the observed analgesic effect is lower than expected.

- c. Blood pressure monitoring must be more frequent at the onset of epidural analgesia and after local anesthetic boluses since hypotension may become symptomatic and cause impaired placental perfusion. The usual treatment of the hypotension is crystalloid volume expansion, ephedrine 5 to 10 mg, and/or phenylephrine 80 μ g IV repeated as necessary.
- d. **Continuous infusion for labor** is also possible but not common practice in our hospital.

6. Complications

- a. **Dural penetration** complicates 1.5% of labor epidural placements. Increased depth of the epidural space and number of attempts correlate with increased frequency of this complication. Conversely, practitioners' skill and experience as well as loss of resistance to saline might decrease the incidence of inadvertent dural puncture. Accidental intrathecal catheters can be kept and dosed accordingly in particularly difficult epidural placements.
 - b. **Postdural puncture headache (PDPH)**. Up to 80% of inadvertent dural punctures will cause frontal or occipital headache of variable intensity with possible radiation to the neck. Exacerbation of symptoms within 15 minutes of assuming an upright position characterizes PDPH. Risk factors for PDPH include young age, female gender, low BMI, and vaginal delivery. In mild PDPH, hydration, analgesics, and avoidance of heavy lifting are indicated. Severe PDPH may warrant an **epidural blood patch (EBP)** (see Chapter 17). Immediate symptomatic relief occurs in up to 75% of cases. A second EBP might be considered in refractory cases. Atypical cases should be evaluated for other etiologies.
 - c. **Intravascular injection**. Total dose and rate of intravascular injection are correlated with signs and symptoms of local anesthetic toxicity. When intravascular injection is suspected, infusion should be discontinued and appropriate therapy immediately instituted. Cardiovascular collapse must be treated with cardiopulmonary resuscitation (CPR), left uterine displacement, and emergent cesarean delivery. **Intralipid** therapy and cardiopulmonary bypass have been described in the literature.
 - d. **Intrathecal injection**. Aspiration before each epidural dose helps to detect intrathecal catheters. Large epidural doses inadvertently injected into the intrathecal space may produce high or total spinal anesthesia. Nausea, hypotension, and loss of consciousness may precede cardiopulmonary arrest. Critical interventions include IV crystalloid, pressors, inotropes, left uterine displacement and management of the airway. Cardiac and respiratory arrest associated with a total spinal must be emergently treated in accordance with the advanced cardiac life support (ACLS) protocol for pregnancy.
- D. Spinal Anesthesia.** A small intrathecal dose of 0.25% bupivacaine (2.5 to 3 mg) provides prompt analgesia lasting up to 90 to 120 minutes. When delivery is not imminent, better positioning for successful epidural is

facilitated by the existing spinal analgesia. Alternatively, the spinal might be repeated.

- E. **Combined spinal-epidural analgesia (CSE)** offers both a rapid onset of sacral analgesia for advanced labor and the benefit of continuous epidural infusion. CSE might improve the success of the epidural, but it prevents immediate verification of epidural function and therefore might not be a preferred option when cesarean section is likely.

VI. ANESTHESIA FOR CESAREAN SECTION

The anesthetic technique for cesarean section must be planned according to the urgency of the delivery. Common elective cesarean section indications are breech presentation, prior cesarean section or uterine surgery, and maternal request. Urgent and emergent cesarean sections are required for vaginal hemorrhage, fetal distress, and failure to progress,

A. Regional Anesthesia

1. **Spinal anesthesia** provides rapid onset of surgical anesthesia and is the common choice for cesarean sections expected to be completed in less than 2 hours. Our practice is to prehydrate the patient with 500 to 1,000 mL of IV crystalloid and to administer 30 mL of oral sodium citrate. A standard dose of 12 mg of 0.75% hyperbaric bupivacaine (equivalent to 1.6 mL) is mixed with preservative-free 10 to 25 μ g of fentanyl and 0.1 mg to 0.25 mg morphine to attain a T4 sensory level. Intrathecal opioids improve intraoperative anesthesia and postoperative analgesia. Postoperatively, patients should be monitored and assessed for delayed respiratory depression and pruritus.
2. **Conversion from epidural labor analgesia to surgical anesthesia** is likely to be successful when the preexisting analgesia has been satisfactory. Titration of up to 25 mL of 2% lidocaine with epinephrine mixed with 2 mL of 8.4% sodium bicarbonate administered via epidural usually produces a T4 surgical level within 5 to 10 minutes. Twenty milliliter of 3% 2-chloroprocaine (with or without sodium bicarbonate) has a faster onset of T4 surgical level for emergent cesarean sections. When necessary, the duration of epidural anesthesia can be extended. If lidocaine was chosen, 50% of the initial dose may be readministered at 40 to 45 minutes; the shorter duration of chloroprocaine necessitates redosing of 50% of the initial dose at 20 to 25 minutes. Postoperative analgesia is improved by epidural administration of 3 mg morphine. Monitoring for postoperative respiratory depression and pruritus is indicated.
3. The onset of anesthesia is slower when an **epidural is placed de novo** for elective cesarean section, and dose titration over at least 20 minutes is essential to achieve a surgical level.
4. **Combined spinal-epidural analgesia** offers the advantage of rapid onset and the option to prolong the duration of the anesthetic. Although the function of the epidural catheter is not tested at the start, recent literature has shown that positioning of the epidural catheter is usually correct with this technique.

B. General Anesthesia

1. Indications
 - a. Failure of neuraxial technique
 - b. Insufficient time to implement neuraxial anesthesia
 - c. Maternal preference
 - d. Lack of patient cooperation for neuraxial placement
 - e. Medical contraindication to regional anesthesia

2. The potential for a difficult airway and increased risk of aspiration in the pregnant patient mandate careful preparation and discussion of alternative airway plans and immediate availability of advanced airway equipment. Preoxygenation followed by rapid sequence induction with endotracheal intubation is the technique of choice. Preadministration of a nonparticulate antacid should also be included.
3. To minimize fetal exposure to anesthetics, the cesarean section should begin immediately upon securing the airway. Halogenated agents antagonize uterine contracture; therefore, it is customary to decrease their inhaled concentration to 0.75 to 0.5 MAC and increase the N_2O fraction immediately after delivery. Administration of 1 to 2 mg of midazolam may reduce the risk of intraoperative awareness in the setting of decreased volatile anesthetic concentrations.
4. Oxytocin should be administered following delivery of the placenta to stimulate uterine contraction and minimize blood loss.

VII. PREECLAMPSIA

Preeclampsia is a common diagnosis occurring in approximately 5% of pregnancies, particularly in nulliparous, diabetic, hypertensive patients or those with chronic disease. Persistent hypertension after 20 weeks of gestational age should prompt a diagnostic workup for preeclampsia (Table 32.2). Recent changes in the diagnostic criteria do not require the presence of proteinuria for the diagnosis, and since fetal growth restriction is similarly managed in the absence of preeclampsia, it has been eliminated as a finding of severe preeclampsia. Although the etiology is incompletely understood, anomalous placentation with failure of trophoblastic invasion and up-regulation of placental factor sFlt-1 (a soluble tyrosine kinase that inhibits blood vessel growth) leads to diffuse maternal endothelial damage.

A. Two additional diagnoses, **HELLP syndrome** and **eclampsia**, are also part of this spectrum of disease.

1. **Eclampsia** describes the new onset of seizures in a parturient with preeclampsia due to central nervous system involvement. It is observed in approximately 50% of maternal deaths associated with preeclampsia.

TABLE
32.2 Diagnostic Criteria for Preeclampsia

	Preeclampsia	Preeclampsia with Severe Features
Blood pressure	>140/90 but <160/110 mm Hg	>160/110 mm Hg
Proteinuria	>0.3 g in 24 h urine collection, Pr:Cr >0.3 1–2+ on urine dip	>5 g in 24 h urine collection, or 3–4+ on urine dip
Additional signs or symptoms	None Absence of proteinuria does not preclude diagnosis of preeclampsia	New-onset cerebral or visual disturbances Impaired liver function (>2× nl LFTs) Severe, persistent epigastric or RUQ pain Thrombocytopenia <100,000 Pulmonary edema Cr >1.1 or 2× baseline

2. **HELLP syndrome** (Hemolysis, Elevated Liver enzymes and Low Platelets) involves a constellation of laboratory abnormalities and is generally regarded as a subset of severe preeclampsia. The diagnosis of HELLP syndrome is also associated with an increased risk of adverse outcomes including placental abruption, renal failure, hepatic subcapsular hematoma formation and liver rupture, and fetal and maternal death.

B. Management

1. **Delivery.** Delivery of the placenta is the accepted treatment for preeclampsia. Maturity of the fetus weighed against the severity of the disease influence the decision for optimal timing of delivery.
2. **Pharmacologic Therapy**
 - a. **Magnesium sulfate** is beneficial to prevent recurrence of eclamptic seizures. Its use for seizure prophylaxis in mild preeclampsia should be assessed on a case-by-case basis. Magnesium is administered during labor and delivery and for 24 to 48 hours postpartum via an IV loading dose of 4 g given over 30 minutes, followed by an infusion of 2 g/h. Due to its relaxant effect on smooth muscle, magnesium therapy may decrease maternal blood pressure and predispose the patient to postpartum uterine atony and hemorrhage.
 - b. **Antihypertensive medications** such as **labetalol**, **hydralazine**, and **calcium channel blockers** are frequently administered for blood pressure control. The goal of therapy is not to normalize blood pressure but to prevent progression to hypertensive crisis, encephalopathy, or stroke. It is important to remember that the placenta has minimal ability to autoregulate flow. A sudden drop in maternal blood pressure may decrease placental perfusion and result in significant fetal compromise.
 - c. **Fluid management.** Volume assessment is challenging. Intravascular depletion should be corrected with judicious administration of crystalloid, as preeclamptic patients are at increased risk for the development of pulmonary edema.
 - d. **Coagulation abnormalities.** A platelet count less than 100,000/ μ L is the most common coagulation abnormality and is diagnostic of severe preeclampsia. The threshold for neuraxial placement for most providers is a platelet count greater than 75,000/ μ L. Vigilance for the risk of epidural hematoma and availability of neurosurgical consultation are essential. The coexistence of other hemostatic abnormalities (e.g., prolonged prothrombin time or partial thromboplastin time, low fibrinogen) should be taken into account. Repeated coagulation testing at regular intervals may be advisable.

C. Anesthesia

1. **Epidural anesthesia.** Early epidural placement offers possible improved uteroplacental perfusion, reduction in circulating maternal catecholamines, and assessment of the function of the epidural catheter prior to the development of fetal intolerance to labor and urgent cesarean section. Documentation of the platelet count prior to epidural catheter removal may be advisable.
2. **Spinal anesthesia.** Growing evidence in the literature shows that spinal anesthesia is not associated with more severe hypotension in preeclamptic patients, supporting the safe use of this technique.
3. **General anesthesia** is usually reserved for emergent cesarean sections or for patients with coagulopathy or other contraindications to regional techniques. The disadvantages of general anesthesia include autonomic

stimulation and hypertension that may occur with intubation and extubation. The hypertensive response to laryngoscopy can be blunted by the use of remifentanyl on induction instead of or in addition to succinylcholine. Diffuse, severe interstitial edema of the airway may also increase the likelihood of a difficult intubation. The interaction of magnesium with nondepolarizing muscle relaxants might prolong their duration of action in preeclamptic patients.

VIII. PERIPARTUM HEMORRHAGE

Peripartum hemorrhage is the leading cause of maternal mortality worldwide.

A. Antepartum hemorrhage threatens oxygen transfer to the fetus since it is most commonly due to hemorrhage originating along the uteroplacental interface.

1. **Placenta previa** occurs when the placenta implants in advance of the fetal presenting part. The position of the cervical os relative to the placenta further classifies placenta previa into total (os completely covered), partial (os partially covered), and marginal (close to but not covering the os). The hallmark presentation is painless vaginal bleeding in the second or third trimester. The first hemorrhage is usually self-limiting and does not compromise the fetus. Patients with a previous cesarean section and placenta previa have a higher incidence of **placenta accreta** with a subsequent need for a gravid hysterectomy. Any degree of placenta previa is an indication for cesarean section. The amount and rate of blood loss and severity of associated signs and symptoms are the primary considerations in the anesthetic choice.
2. **Placental abruption** is the premature separation of a normally implanted placenta. Classically, an abruption is painful and associated with either vaginal bleeding or hemorrhage concealed behind the placenta. Hypertension, preeclampsia, and advanced maternal age are associated with an increased risk for abruption. Patients may deliver vaginally or via cesarean section depending on the degree of compromise. Anesthetic management is similar to the management of placenta previa. Coagulopathy occurs in 10% of abruptions, increasing the risk for fetal mortality and disseminated intravascular coagulation (DIC).
3. **Vasa previa** is a condition in which the fetal vessels are in front of the presenting part of the fetus and are not protected by the umbilical cord. Trauma during vaginal examination, artificial rupture of membranes, or descent of the presenting part might tear the vessels causing fetal hemorrhage. Immediate cesarean section is warranted.
4. **Vaginal birth after cesarean (VBAC) section.** Patients with a singleton fetus in vertex presentation and a history of a single low transverse uterine incision might be candidates for a trial of labor and VBAC. Although induction with prostaglandins is contraindicated, oxytocin augmentation may be administered to patients attempting a VBAC. Regional anesthesia techniques might encourage more women to attempt a trial of labor. Uterine scar dehiscence occurs in 0.7% of VBAC and does not compromise the fetus nor cause excessive hemorrhage. Uterine rupture (0.65% of VBAC) *does* result in fetal compromise, maternal hemorrhage, or both, necessitating cesarean section or postpartum exploratory laparotomy. If uterine rupture occurs, the presence of a functioning epidural may provide a means for establishing a quick, safe anesthetic for cesarean section. If uterine rupture causes massive hemorrhage, anesthetic management is the same as for any actively bleeding patient.

B. Postpartum Hemorrhage

1. **Uterine atony**, defined as the inadequate contractile response of the uterus after delivery, is the most common cause of postpartum hemorrhage. **Oxytocin** is given to all patients after delivery for prophylaxis and is also the first-line treatment of uterine atony. Bolus administration is generally avoided due to resultant hypotension. As a second-line agent, 0.2 mg intramuscular **methylergonovine** is probably more effective than are prostaglandins. Patients should receive adequate resuscitation with crystalloid, colloid, and blood products as clinically indicated. If conservative measures fail, surgical management or arterial embolization may be necessary.
2. **Retained placenta** occurs in up to 3.3% of all vaginal deliveries and often requires manual exploration of the uterine cavity facilitated by epidural or spinal block. When additional uterine relaxation is needed, nitroglycerin in 50 to 100 μg IV boluses can be used. For analgesia, small doses of ketamine or an inhalation anesthetic may be used if a regional anesthetic is not in place. If there has been significant bleeding and the patient is hypovolemic, general endotracheal anesthesia with a volatile agent may be necessary. When the retained placenta has been removed, the volatile anesthetic must be discontinued to reverse uterine relaxation. Many patients require additional uterotonics to improve uterine tone.
3. **Retained products of conception** may cause significant postpartum bleeding. Uterine relaxation is usually not necessary for uterine curettage to remove remaining placental fragments. Anesthetic options are augmentation of an existing labor epidural, spinal, or general anesthesia.
4. **Laceration of the vagina, cervix, or perineum** is a common cause of postpartum hemorrhage. Bleeding may be insidious and difficult to estimate. Patients require adequate analgesia to facilitate repair that may involve augmentation or placement of regional blocks, infiltration of local anesthetics, or a general anesthetic.
5. **Uterine inversion** is a rare cause of postpartum hemorrhage (1 in 3,000 to 1 in 5,000 births) that represents a true obstetric emergency. Nitroglycerin in small IV boluses may produce adequate uterine relaxation and may avoid the need for general anesthesia. Atony commonly follows the replacement of the uterus after inversion, and uterotonic medications are indicated.
6. **Placenta accreta** refers to an abnormally adherent placenta complicating up to 1 in 530 pregnancies, with increasing incidence in patients with prior cesarean sections or placenta previa. The condition may be divided into three types: accreta vera (abnormal placental attachment to the myometrium), increta (invasion into the myometrium), and percreta (invasion through the myometrium into the serosa and adjacent organs). Placenta accreta generally necessitates peripartum hysterectomy with antenatal diagnosis improving the chance of favorable outcomes. Anesthetic management should include close interdisciplinary communication and planning as well as preparation for major hemorrhage.

IX. AMNIOTIC FLUID EMBOLISM

- A. **Amniotic fluid embolism (AFE)** is a rare and catastrophic condition unique to pregnancy. The true incidence of AFE is unknown since it is a diagnosis of exclusion, often made postmortem. U.S. estimates range from 4 to 6 per 100,000 live births with mortality rates as high as 80%, usually occurring within the first hours of onset. Permanent neurologic dysfunction affects up to 75% of survivors.

- B. Pathophysiology.** The pathophysiology of AFE is poorly understood and likely does not arise from an embolic event in the classical sense. AFE seems to involve an initial breach in the barrier between the maternal and fetal compartments resulting in an abnormal maternal systemic response to the fetal tissue, activation of proinflammatory mediators, and a resulting syndrome similar to the Systemic Inflammatory Response Syndrome (SIRS).
- C. Clinical Presentation.** Universal diagnostic criteria for AFE do not exist, and consistent risk factors have yet to be identified. The diagnosis is made based on clinical features of acute peripartum hypoxia and hypotension, with rapidly deterioration to cardiovascular collapse, coagulopathy, and death.
- D. Manifestations.** AFE affects multiple organ systems, and the presentation may vary.
- 1. Cardiovascular.** Hypotension is a key feature of the disease, present in 100% of patients with severe disease. A biphasic model of shock has been proposed with an initial transient pulmonary hypertension—likely from the release of vasoactive substances—resulting in hypoxia and right heart failure. The patients who survive the initial insult develop a left heart failure and pulmonary edema due to left ventricular ischemic injury or direct myocardial depression.
 - 2. Respiratory.** Hypoxia is an early manifestation of AFE, thought to arise from acute pulmonary hypertension, decreased cardiac output, and ventilation–perfusion mismatch. Later, pulmonary edema develops in association with left ventricular failure. Many patients will also manifest noncardiogenic pulmonary edema when the left ventricular function improves.
 - 3. Coagulation.** Disruption of the normal clotting cascade occurs in up to two thirds of patients. It remains unclear whether the coagulopathy is the result of a consumptive process or massive fibrinolysis.
- E. Management** of AFE involves aggressive resuscitation. Early recognition and treatment may result in improved outcomes. Therapy includes supportive care with maintenance of oxygenation and airway management, circulatory support with fluid and pressor resuscitation, and correction of the coagulopathy with blood products as needed. Cardiopulmonary bypass, extracorporeal membrane oxygenation (ECMO), and intra-aortic balloon counterpulsation have been described in the literature as successful options for the treatment of refractory AFE. The decision for immediate delivery of the fetus should be made by the obstetrician to maximize chances of fetal survival and aid maternal resuscitation.

X. ANESTHESIA FOR NONOBSTETRIC SURGERY DURING PREGNANCY

- A.** Approximately 1% to 2% of women undergo nonobstetric surgery during pregnancy. Purely elective surgical procedures are relatively contraindicated in pregnancy and should be postponed until 6 weeks postpartum. If a surgical procedure must be performed, the second trimester is the preferred time. The objectives in the anesthetic management include the following:
- 1. Maternal safety.** Induction and emergence from general anesthesia are more rapid in pregnant patients due to the increase in minute ventilation and decrease in FRC. Uterine displacement to minimize aortocaval compression should be considered as early as the second trimester. Local anesthetic potency is also increased in these patients. The dose should be reduced because lower plasma concentrations are associated with toxicity. During any anesthetic, oxygen transport to the placenta must be maintained.

2. **Teratogenicity.** Some practitioners avoid the use of N_2O in the first and second trimesters because of its interference with DNA synthesis. Recent studies show an increase in neuronal apoptosis in animals exposed to volatile anesthetics. This effect has not been confirmed in humans. The teratogenic effect of all other anesthetics has not been demonstrated in humans. Organogenesis in the first trimester contraindicates all but emergency surgery. When feasible, surgery should be delayed until at least 2 to 6 weeks postpartum.
 3. **Reversal of residual neuromuscular block.** The use of the combination of neostigmine and glycopyrrolate might expose the fetus to unopposed neostigmine and cause fetal bradycardia, as placental permeability to glycopyrrolate is lower than to neostigmine.
- B. Procedures Directly Related to Pregnancy**
1. **Ruptured ectopic pregnancy** is the leading cause of maternal death in the first trimester. It is a surgical emergency requiring laparoscopy or laparotomy. Intra-abdominal hemorrhage is common, and it is prudent to have blood available in the room even without hemodynamic instability.
 2. **Abortion or miscarriage.** Spontaneous abortion refers to the loss of pregnancy before 20 weeks or at a fetal weight of less than 500 g (Table 32.3). A dilatation and evacuation is often indicated for incomplete abortions and missed abortions.
 3. Monitored anesthesia care, spinal, epidural, or general anesthesia can be used after careful assessment of the patient to evaluate PO status, volume status, and presence of DIC or sepsis.
 4. **Incompetent cervix** might lead to early pregnancy loss and is treated with cerclage. Regional block is the preferred anesthetic choice for cerclage except when the myometrial relaxation associated with inhalational agents is necessary.
 5. **Anesthesia for postpartum sterilization.** Elective postpartum tubal ligation is performed through a small infraumbilical incision typically within the first 48 hours after delivery. The labor epidural may be appropriately dosed to achieve a T4 sensory level, although the function of the epidural becomes less likely the longer the interval after delivery. Alternatively, spinal anesthesia is a frequent choice. Our practice is to use an intrathecal dose of 15 mg of 0.75% hyperbaric bupivacaine with 10 to 15 μ g fentanyl. General anesthesia is reserved for rescue of intraoperative neuraxial failure.

TABLE 32.3 Spontaneous Abortion Classification

Type	Vaginal Bleeding	Cervix	Products of Conception	Management
Threatened	Y	Closed	In utero	Observation
Inevitable	Y	Dilated	In utero	Await spontaneous passage or induce labor
Missed	N	Closed	In utero	Await spontaneous passage, induce labor or D&C
Incomplete	Y	Dilated	Partial expulsion	Emergent D&C
Complete	Y	Dilated	Complete expulsion	Observation

C. Procedures Incidental to Pregnancy

1. When a nonemergent procedure must be performed, the second trimester is the preferred time since organogenesis is complete and the risk of preterm labor is minimized.
2. **Consultation with an obstetrician** preoperatively improves the assessment of risks and benefits to the patients and guides the choice of perioperative monitoring. Most commonly, FHR is measured before and after surgery. In certain cases, continuous intraoperative FHR monitoring and uterine tocometry might be indicated.
3. **Use regional techniques when possible.**

XI. CARDIOPULMONARY RESUSCITATION DURING PREGNANCY

A. Cardiac arrest during pregnancy occurs in 1 per 20,000 pregnancies with a survival rate of only 6.9% despite the relative health of this population. CPR is more difficult and less successful than in individuals who are not pregnant. The following modifications to ACLS guidelines for adults are recommended for pregnant women by the American Heart Association and the Society for Obstetric Anesthesia and Perinatology:

1. Standard **basic life support** (Chapter 38) and activation of the maternal cardiac arrest team (if present in the institution) should be initiated immediately upon discovery of a pregnant patient in cardiac arrest.
2. **Compressions should occur 2 to 3 cm higher** on the sternum in third trimester patients.
3. **Left uterine displacement** should be used for all patients with a palpable or visible uterus at or above the umbilicus. Manual uterine displacement is likely preferable to left table tilt to prevent spinal hypotension and maximize mechanics for effective chest compressions.
4. CPR should continue while an automated external defibrillator is prepared. All fetal monitors may be removed prior to defibrillation but should not delay the delivery of a shock. Pads are preferred to paddles when available.
5. **Airway management.** In the nonintubated patient, two breaths of tidal volumes between 500 to 750 mL should be delivered alternating with 30 compressions. Nasal airways and repeated nasal manipulations should be avoided due to the risk for airway trauma and bleeding. Oxygenation and ventilation should be prioritized over risk for aspiration; cricoid pressure may not be effective and is not recommended.
6. IV or intraosseous access is essential and must be obtained above the diaphragm in a timely fashion.
7. Resuscitation drugs should be administered as per ACLS guidelines.
8. Neonatal survival may be optimized when the fetus is delivered within the first 5 minutes of cardiac arrest.
9. The mnemonic **BEAUCHOPS** may aid in considering causes of maternal cardiac arrest (**B**leeding/DIC, **E**mbolism, **A**nesthetic complications, **U**terine atony, **C**ardiac disease, **H**ypertension, **O**ther (common etiologies as in standard ACLS guidelines), **P**lacenta previa or placental abruption, **S**epsis).

XII. ANESTHESIA FOR GYNECOLOGIC SURGERY (SEE ALSO CHAPTER 21)

A. Abdominal Procedures

Pelvic surgery can be performed under regional anesthesia. Duration of the procedure, intraoperative blood loss, fluid shifts, and Trendelenburg positioning might require control of the airway and general anesthesia. Laparoscopic procedures are performed under general anesthesia.

Rescue IV and radial artery access may be limited by draping and position of the patient.

B. Vaginal procedures

Vaginal and intrauterine surgeries. may be performed using regional or general anesthesia. A T10 level is sufficient for these procedures, while a T4 to T6 level is necessary for vaginal hysterectomy.

XIII. ANESTHESIA FOR OOCYTE RETRIEVAL

A. Oocytes are retrieved with a transvaginal needle under ultrasound guidance. Immobility during the procedure minimizes risks and improves the quality of retrieval.

B. General Anesthesia. There is no conclusive evidence that the commonly used inhalational anesthetics adversely affect pregnancy and live birth rates for in vitro fertilization procedures. However, nitrous oxide might be avoided due to its interference with DNA synthesis. Both total IV anesthesia (TIVA) or inhalational agents are acceptable with airway management as indicated by individual patient characteristics.

C. Spinal anesthesia can provide excellent surgical conditions and provides the advantage of minimizing oocyte exposure to anesthetic agents. Mepivacaine 1.5% or 0.75% bupivacaine are commonly used. Postoperative recovery is often longer than with general anesthesia.

Suggested Readings

- Aranake A, Mashour GA, Avidan MS. Minimum alveolar concentration: ongoing relevance and clinical utility. *Anaesthesia* 2013;68:512–522.
- Briggs GG, Freeman RK, Yaffe SJ. *Drugs in Pregnancy and Lactation*. 8th ed. Philadelphia: Lippincott Williams & Wilkins; 2008.
- Chestnut DH. *Obstetric Anesthesia: Principles and Practice*. 5th ed. Philadelphia, Elsevier Saunders; 2014.
- Chin KJ, Yeo SW. Bispectral index values at sevoflurane concentrations of 1% and 1.5% in lower segment cesarean delivery. *Anesth Analg* 2004;98:1140–1144.
- Gabbe SG, Niebuhl JR, Simpson JL, et al. *Obstetrics: Normal and Problem Pregnancies*. 5th ed. Philadelphia: Churchill Livingstone; 2007.
- Goldszmidt E. Principles and practices of obstetric airway management. *Anesthesiol Clin* 2008;26:109–135.
- Hirabayashi Y, Shimizu R, Fukuda H, et al. Anatomical configuration of the spinal column in the supine position. II. Comparison of pregnant and non-pregnant women. *Br J Anaesth* 1995;75:6–8.
- Jarvis SS, Shibata S, Bivens TB, et al. Sympathetic activation during early pregnancy in humans. *J Physiol* 2012;590:3535–3543.
- Kodali BS, Chandrasekhar S, Bulich LN, et al. Airway changes during labor and delivery. *Anesthesiology* 2008;108:357–362.
- Lee SW, Khaw KS, Ngan Kee WD, et al. Haemodynamic effects from aortocaval compression at different angles of lateral tilt in non-labouring term pregnant women. *Br J Anaesth* 2012;109:950–956.
- Lipman S, Cohen S, Einav S, et al. The Society for Obstetric Anesthesia and Perinatology consensus statement on the management of cardiac arrest in pregnancy. *Anesth Analg* 2014;118:1003–1016.
- Macones GA, Hankins GDV, Spong CY, et al. The 2008 National Institute of Child Health and Human Development workshop report on electronic fetal monitoring: update on definitions, interpretation and research guidelines. *Obstet Gynecol* 2008;112:661–666.
- Palanisamy A. What's new in Obstetric Anesthesia? The 2013 Gerard W. Ostheimer lecture. *Anesth Analg* 2014;118:360–366.
- Pian-Smith MCM, Leffert L, eds. *Obstetric Anesthesia*. New York: PocketMedicine.com, Inc.; 2005.

- Silver RM, Landon MB, Rouse DJ, et al. Maternal morbidity associated with repeat cesarean deliveries. *Obstet Gynecol* 2006;107:1226–1232.
- Simhan HN, Caritis SN. Prevention of preterm delivery. *N Engl J Med* 2007;357:477–487.
- Vanden Hoek TL, Morrison LJ, Shuster M, et al. Part 12: cardiac arrest in special situations: 2010 American Heart Association Guidelines for Cardiopulmonary Resuscitation and Emergency Cardiovascular Care. *Circulation* 2010;122:S829-S861.
- Wu S, Kocherginsky M, Hibbard JU. Abnormal placentation: twenty-year analysis. *Am J Obstet Gynecol* 2005;192:1458–1461.

Anesthesia Outside of the Operating Room

Alexander Y. B. Lee and John J. A. Marota

I. GENERAL CONSIDERATIONS

For all patients requiring general anesthesia or monitored anesthesia care (MAC) in locations remote from the operating room, the same principles and requirements for anesthesia equipment, monitoring standards, patient preparation, and postanesthetic care outlined in Chapters 1, 9, 10, and 36, respectively, should be met.

A. Required Equipment in Remote Locations

1. The anesthetist must determine that all standards are met before initiation of an anesthetic.
2. **A central supply of oxygen and suction** is a minimum requirement: two independent supplies of oxygen and suction (**patient use and waste gas scavenging**) are required at an anesthetizing location. In addition, a **full reserve tank of oxygen** must be available for each case. For locations that do not have a central supply of nitrous oxide, a reserve tank is available on the machine. Adequate **lighting and electrical power outlets** connected to the emergency power supply are required. A source of medical grade compressed air is desirable but not mandatory.
3. **Functioning anesthesia machine** appropriate for the anesthetic. Extra-long gas supply hoses may be necessary; anesthesia breathing circuit tubing may require extensions to reach the patient.
4. **Anesthesia supply cart** should be readily available, containing appropriate supplies and drugs necessary for provision of anesthesia.
5. **Resuscitation equipment** must be immediately available: defibrillator, medications, and self-inflating hand resuscitator bag for transport.

B. Workspace Area and Patient Access

1. Adequate space for the anesthesia machine, equipment, and access to the patient is required.
2. Areas outside the operating room where anesthesia is performed regularly should be designated as “approved anesthetizing locations” by the hospital.
3. A direct means of communication is necessary in case of emergency.
4. Monitoring must be adapted if the anesthetist cannot remain in the room (e.g., during irradiation); viewing the patient by window or closed circuit television may be necessary. Anticipate and provide necessary monitoring during patient transport.
5. Patient positioning may be difficult in confined spaces of magnetic resonance imaging (MRI) and computed tomography (CT) scanners. Additional padding may be necessary to prevent injury from compression of soft tissues during prolonged procedures.
6. Imaging often requires that the patient repeatedly moves a significant distance during the scan. Adequate lengths of ventilation, intravenous (IV), and monitoring cables are necessary; a “test move” of full excursion of patient movement is helpful before the procedure begins.
7. Anesthetists should take appropriate precautions to minimize radiation exposure to themselves during procedures.

C. Procedural Sedation Versus MAC

1. Specially trained nurses provide sedation for most patients requiring invasive procedures outside of the operating room. **Procedural sedation** is defined as a medically controlled state of depressed consciousness that allows protective reflexes to be maintained and retains the patient's ability to maintain a patent airway and to respond appropriately to physical and verbal stimulation. American Society of Anesthesiologists (ASA), Joint Commission on Accreditation of Healthcare Organizations, and state agencies (licensing boards) have set guidelines for provision of conscious sedation by nonanesthesiologists and nonphysicians.
2. **MAC** is a physician-directed service that may include the provision of sedatives and analgesics. It requires constant assessment and management of the patient's medical problems and physiologic derangements with the ability to convert to general anesthesia if needed. When available, capnography should be used as an aid to detect apnea, especially during pediatric cases. Postprocedural patient management is required until adequate recovery from the procedure and sedation/anesthesia. An anesthesiologist is required to provide sedation for any patient in which **airway management** is considered complex (i.e., mask ventilation anticipated as difficult or impossible or potentially difficult intubation) or if **significant comorbid pathology** exists (i.e., ASA physical status classes III and IV) that require medical management by a physician.

II. CONTRAST MEDIA

- A. Contrast Media.** Ionic and nonionic contrast media are administered intravenously and intra-arterially to supplement imaging; complexed gadolinium may be administered for both MRI and x-ray-based imaging. Hypo- and isoosmolar iodinated media are used instead of hyperosmolar because they are considered less nephrotoxic. Contrast material can produce a brisk diuresis, and bladder catheterization may be necessary.
- B. Acute Contrast Media Reactions.** Serious or fatal reactions are rare but unpredictable and are not dose related. They are considered anaphylactoid because they possess features of anaphylaxis but are not IgE mediated.
 1. Risk factors include history of previous adverse reaction, asthma, hay fever allergy requiring medical therapy, and concurrent use of β -blockers or interleukin-2.
 2. Symptoms develop within 5 to 30 minutes of exposure and present as generalized skin reactions, airway obstruction, angioedema, or cardiovascular collapse.
 3. Treatment of acute reactions is supportive. Generalized anaphylactoid reactions should be treated with immediate administration of corticosteroids and H_1 and H_2 blockers. Oxygen, epinephrine, β_2 -agonists, and intubation may be necessary to treat bronchospasm and laryngeal edema; circulation is supported with IV fluids and vasopressors.
 4. Routine prophylaxis of all patients is not supported by all authors. Strategies commonly used include prednisone 50 mg PO given 13, 7, and 1 hour prior to imaging with 50 mg diphenhydramine 1 hour prior to contrast administration. Hydrocortisone 200 mg IV can be substituted for oral prednisone in patients who cannot take oral medications. Alternatively, methylprednisolone 32 mg is given orally 12 and 2 hours prior to contrast administration with or without antihistamine. For emergency procedures, treatment with 50 mg of diphenhydramine IV and 200 mg of hydrocortisone IV or 40 mg of methylprednisolone every 4 hours until the procedure is completed has been used successfully.

Patients with methylprednisolone, aspirin, or NSAID allergies, especially if they have a coexisting diagnosis of asthma, should be pretreated with 7.5 mg of dexamethasone or 6 mg of betamethasone every 4 hours until the study has been completed.

C. Patients with Compromised Renal Function

1. **N-acetylcysteine** is often administered before and after the procedures to reduce the incidence of **contrast-induced nephropathy**. Data supporting this practice continue to be controversial. Periprocedural hydration is generally recommended with crystalloid, though no optimal dosing regimen is supported. Data to support hydration with sodium bicarbonate rather than sodium chloride continue to be equivocal.
2. **Gadolinium**. Nephrogenic systemic fibrosis is a sclerosing skin condition that occurs in patients with advanced or end-stage renal disease, with or without dialysis. This typically occurs days or months following a gadolinium exposure.

III. ANESTHESIA FOR CT

- A. **CT scans** are usually performed without general anesthesia. Children and uncooperative adults (e.g., head-injured patients) may require sedation or general anesthesia to minimize motion artifacts; if so, standard monitors as outlined in Chapter 10 are required. Capnography is useful to provide evidence of ventilation during sedation; fitting a sidestream sampling tube to nasal cannula or oxygen facemask provides qualitative assessment of ventilation.
- B. **Adults**. Small IV doses of benzodiazepines, narcotics, or short-acting hypnotics (e.g., propofol or dexmedetomidine) are useful for sedation; continuous infusions should be titrated to effect.
- C. **Infants and children** less than 3 months of age may not need sedation; most children, however, will require some level of sedation or general anesthesia. Children provide specific challenges to the anesthetist as outlined in Chapter 31.
 1. **Sedation**
 - a. Small IV doses of benzodiazepines, narcotics, or short-acting hypnotics (e.g., propofol) may be used for sedation as either bolus or continuous infusions titrated to effect.
 - b. **Chloral hydrate** (30 to 50 mg/kg orally or per rectum [PR] administered 30 to 60 minutes before the procedure) is an adequate mild sedative for children.
 - c. **Methohexital, PR** (25 to 30 mg/kg), has more rapid onset (5 to 10 minutes) than does chloral hydrate and lasts approximately 30 minutes. It is useful for the induction of general anesthesia; however, effects may vary because absorption is unpredictable. Because deep sedation or general anesthesia may occur, only an anesthetist should administer methohexital with appropriate monitoring and provisions to secure the airway. The drug is not appropriate in patients at risk of reflux of gastric contents.
 2. **General anesthesia** maintained with either IV or inhalational agents may be required. The airway may be maintained naturally, with laryngeal mask airway (LMA) or endotracheal intubation as necessary.

IV. ANESTHESIA FOR MRI

- A. The physical environment of the MRI suite presents several challenges for anesthetizing patients.
 1. The long, narrow bore of the magnet in which the patient reclines does not allow ready access to or viewing of the patient during imaging.

Scanners are located in shielded rooms that contain the magnetic field and shield against radiofrequency noise that would produce image artifact.

2. The static **magnetic field** is present at all times and exerts a force on all ferromagnetic materials (e.g., steel gas tanks, batteries, and standard stethoscopes). **Ferromagnetic objects brought near the magnetic field can be forcibly pulled toward the magnet, potentially injuring people or equipment in their path.** The static field and magnetic gradients generated during scanning can interfere with mechanical components (solenoids) in automated noninvasive blood pressure monitors, ventilators, and infusion pumps; specialized compatible equipment is necessary. Only plastic stethoscopes and commercially available magnet-compatible laryngoscopes should be used in the magnet area. Credit cards, watches, and pagers must be left outside the scanning room.
3. **Radiofrequency signals and shifting magnetic fields** generated during scanning may lead artifacts on the ECG and pulse oximeter.
4. **Metallic implants (e.g., joint prostheses, aneurysm clips, and cochlear implants) or implanted devices (e.g., pacemakers, implantable cardioverter defibrillators [ICDs], insulin infusion pumps, intrathecal pumps, or spinal cord stimulators)** may potentially be dislodged, dysfunction, or suffer permanent damage by the magnetic field, and scanning or heating may occur from radiofrequency signals generated during scanning. Some specific pacemakers, ICDs, or pulmonary artery catheters are considered "MRI safe," and patients with these devices may undergo MRI scanning. Imaging of patients with these devices should not be considered routine, and individual cases should be carefully reviewed for medical necessity. Imaging may require that the pacemaker be turned off while the patient is in the magnetic field; the device is turned on after scanning. Cerebral aneurysm clips are not considered an absolute contraindication to MRI; it is important, however, to identify the type of clip present to determine MR compatibility. Not all clips are compatible. Each MRI site carries a list of medical devices designated MRI compatible by the U.S. Food and Drug Administration (FDA). Because medical devices may be upgraded or altered by a manufacturer without notifying the FDA, MRI centers should, in addition, contact the manufacturer if questions arise about specific devices.
- B. **Monitors** must be safe for the patient, function within the magnetic field, and have a minimal effect on imaging. Specialized compatible monitoring equipment is available that can remain in the magnetic field and communicate to a "slave" monitor outside the shielded magnet area.
 1. The standard ECG is subject to interference during scanning.
 2. Scanning interferes with standard **pulse oximeters**, which may also interfere with image acquisition. Specialized "MRI-compatible" monitoring systems utilizing fiberoptic cables are available.
 3. A large amount of noise can be generated during imaging.
 4. Temperature probes are not used because of the potential for thermal burns.
 5. Visualization of patients during scanning is imperative and may occur via a shielded window or closed circuit video.
 6. Electrical currents induced in coiled cables during scanning can burn patients; cables should be kept as straight as possible to minimize this risk.

C. General Issues. The duration of an MRI scan varies. Immobility is required only during the actual scanning, 3 to 12 minutes at a time. General anesthesia is necessary for most infants and children, usually utilizing an LMA or endotracheal tube. General anesthesia can be induced in the magnet area. Alternatively, induction can be performed in an area out of the static magnetic field and the anesthetized patient moved into the scanner. Maintenance of anesthesia is provided with specially modified anesthesia machines that contain only nonferrous metals. The patient *must* be removed from the magnetic field if cardiopulmonary resuscitation is required.

V. ANESTHESIA FOR NEURORADIOLOGIC PROCEDURES

Anesthetic management may be necessary for both diagnostic (angiography, balloon test, and occlusion) and therapeutic (embolization and cerebral vasospasm) procedures. Patient access after start of the procedure may be limited to the left arm and leg.

A. Endovascular embolization is performed to treat ruptured as well as unruptured cerebral aneurysms, to interrupt blood supply to intracranial and extracranial arteriovenous fistulas and malformations, vascular tumors, and bleeding vessels in the nose or pharynx.

- 1. Embolization** requires access to the vascular tree, commonly via the femoral artery, and advancement of a small catheter into the aneurysm or blood vessels supplying the area of pathology. Once position is confirmed by angiography, the vascular occlusive material (detachable metal coils, glue, or small particles) is deployed via the catheter.
- 2. Anesthetic goals** include provision of a still field during placement of the microcatheter and deployment of the occlusive material, stable hemodynamics, and rapid recovery after the procedure to test neurologic function. This often necessitates general anesthesia to provide amnesia in addition to paralysis. Anesthesia can be accomplished with IV medications (propofol, muscle relaxant, and narcotics) and/or volatile anesthetics. Nitrous oxide is avoided to minimize consequences of inadvertent arterial air emboli. These procedures are relatively painless with little stimulation from the procedure.
- 3. Hypertonic contrast agents** may produce diuresis; bladder catheterization and fluid replacement may be necessary.
- 4. Invasive arterial blood pressure monitoring** via a radial artery is often necessary for control of hemodynamics; alternatively, blood pressure may be transduced from the femoral artery sheath placed during the procedure.
- 5. Hypertension** should be avoided, because it may increase the risk of hemorrhage or aneurysm rupture. Vasoactive drugs such as phenylephrine should be used with great caution in patients with unprotected cerebral aneurysms. β -Blockers, calcium channel blockers, hydralazine, nitroglycerin, and sodium nitroprusside may be useful to treat hypertension.
- 6. Procedures may be lengthy** and place the patient at risk for untoward embolic events. Patients often require **anticoagulation** (heparin or argatroban) during the procedure to minimize propagation of thrombus from the embolization coils or microcatheters; anticoagulation is monitored by activated clotting time. Platelet inhibitors such as eptifibatide (Integrilin) may be administered by bolus and/or continuous infusion to minimize platelet aggregation. For some procedures, patients may receive aspirin and/or clopidogrel before the procedure. Aspirin can be given by suppository during procedures if necessary.

7. Intraoperative complications include rupture of the aneurysm, arteriovenous fistula or malformation, dissection or rupture of a blood vessel, and inadvertent occlusion of a blood vessel. If intracranial hemorrhage is suspected, immediate placement of a ventriculostomy may be necessary to drain cerebrospinal fluid (CSF) emergently to reduce intracranial pressure (ICP). Unlike intraoperative aneurysm rupture in open procedures (Chapter 25), there is no significant blood loss because the cranium is closed. Elevation of ICP may require hyperventilation, diuresis, or barbiturate coma. Immediate CT scan may be necessary to determine the extent of hemorrhage and need for emergency surgery to decompress the brain.
- B. **Embolization for control of epistaxis and extracranial vascular lesions** presents potential problems of hemorrhage, hemodynamic instability, large amounts of blood in the airway, and aspiration. Typed and cross-matched blood should be available; large-bore IV access may be necessary if acute hemorrhage is a potential threat. Endotracheal intubation may be required for airway control, though it could be difficult if the pathology involves the airway and/or face. The nose and nasal pharynx may be packed to prevent further bleeding.
 - C. **Embolization for Gastrointestinal Bleeding and Hemoptysis**
Transcatheter arterial embolization can be used to treat acute nonvariceal gastrointestinal hemorrhages of the upper or lower GI tracts that are not amenable to endoscopic treatment. Bronchial artery embolization is an effective treatment for massive hemoptysis. Both procedures are performed under angiographic guidance, through arterial access that allows delivery of embolic agents such as gelatin sponges, beads, microcoils, or glues, to selected arteries through microcatheters. These procedures are typically performed under general anesthesia with the patient intubated for airway control. Muscle relaxants are helpful to minimize motion artifacts if digital subtraction angiography is used.
 - D. **Balloon test occlusion** of the carotid artery is performed to determine whether permanent obstruction of the vessel will lead to neurologic deficit. Occlusion is performed endovascularly by temporarily obstructing blood flow with inflation of a balloon in the vessel; if no deficit is apparent on neurologic examination, hypotension is induced and maintained for 20 to 30 minutes to elicit signs of ischemia. Often, cerebral blood flow is evaluated during the hypotensive period by IV injection of a positron emission tomography (PET) isotope; PET scan is obtained after the procedure after the vessel is open and blood pressure returns to normal. If there is any deterioration in neurologic function, the balloon is immediately deflated, and blood pressure is returned to normal. While sedation is appropriate during initial angiography and placement of the balloon, **a completely awake, nonsedated patient is necessary for neurologic testing during occlusion**; short-acting agents are preferred. **Hypotension is induced with rapidly reversible agents** (nitroprusside or nitroglycerine). These agents may cause tachycardia, which can be offset by administering β -blockers. Emergency airway management including endotracheal intubation may be required if seizures or loss of the airway occurs during test occlusion.
 - E. **Cerebral angiography and spinal angiography** are generally painless diagnostic procedures. Only children or uncooperative adults usually require general anesthesia for angiography, though they may receive general anesthesia for comfort because of the potentially long duration. Adult patients requiring general anesthesia for intracranial angiography may have depressed mental status because of elevated ICP, encephalopathy,

recent stroke, or intracerebral hemorrhage; meticulous attention to hemodynamics may require invasive blood pressure monitoring. Spinal angiography requires several hours for each vessel supplying the spinal cord to be identified and the angiogram to be performed. The duration of the procedure may need to be limited because the upper limit of contrast agent dosing may be reached. Patients are anesthetized for their comfort; invasive hemodynamic monitoring is not necessary unless dictated by comorbidity.

- F. Vertebroplasty and kyphoplasty** are performed to treat painful vertebral body fractures that occur most commonly from osteoporosis in kyphotic, elderly women. Patients with metastatic cancers that are destructive to bone also undergo this procedure. The procedures are performed in the prone position. In vertebroplasty, a stylet is driven percutaneously through the pedicle into the fractured vertebral body. Bone cement is then deposited under pressure via the stylet. Multiple levels can be performed at one sitting, and often stylets are placed bilaterally at each level. In kyphoplasty, a balloon is inflated with contrast agent in the vertebral body to reform height lost from fracture; cement is then deposited. Either MAC or general anesthesia is appropriate. Sedation can be accomplished with diphenhydramine (25 to 50 mg IV), promethazine (5 to 25 mg IV), benzodiazepines (midazolam 1 to 2 mg IV), or other agents. Injection of cement can be painful, and analgesics may be necessary. Patients remain supine for several hours afterward to permit the cement to harden completely.
- G. Thrombolysis of acute stroke** is an emergency procedure performed to restore blood flow to cerebral vessels occluded by thrombus in patients with symptoms of acute ischemic stroke. Currently, IV thrombolytic therapy with tissue plasminogen activator (tPA) is recommended in patients for up to 6 hours after onset of symptoms. Intra-arterial infusion of tPA directly at the site of thrombus requires angiography and is recommended in patients with symptoms up to 8 hours after onset of symptoms. Similarly, endovascular mechanical disruption or retrieval of thrombus is recommended in patients for up to 8 hours after onset of symptoms. The concern is that reperfusion and anticoagulation after prolonged ischemia may predispose to hemorrhage into the site of infarction. Angioplasty of atherosclerotic plaque or placement of an intra-arterial stent may be used to supplement thrombolytic therapy to maintain patency of the occluded vessel.
- H.** Recent retrospective studies suggest that patients undergoing general anesthesia for thrombolysis and mechanical clot disruption may have a higher rate of mortality after acute ischemic strokes. These studies do not effectively account for severity of stroke symptoms and postprocedural care in this perceived higher mortality. Currently, sedation with MAC is preferred for angiography and therapeutic interventions as long as the patient can tolerate lying still and flat for the duration of the procedure. MAC has the additional benefit of permitting assessment of the neurologic exam throughout the procedure. While sedation can be accomplished with a variety of medications (ketamine, propofol, midazolam, fentanyl), dexmedetomidine infusion is most commonly used for sedation at our institution. However, if the patient is agitated, has a depressed level of consciousness, cannot protect and maintain the airway, has respiratory compromise, or cannot tolerate lying still and flat, general anesthesia with endotracheal intubation is required. History and physical examination may be limited because of time constraints; often consent is obtained by a neurologist or interventional radiologist. Arterial catheterization for

hemodynamic monitoring may be delayed until after start of the procedure to expedite therapy; invasive monitoring of arterial blood pressure can be performed from the side port of the femoral sheath until another site of arterial access is obtained. Patients may require anticoagulation after recannulization; antiplatelet aggregation therapy may be necessary with IV eptifibatide (Integrilin).

- I. **Cerebral vasospasm** is a common and potentially devastating late complication of subarachnoid hemorrhage. Patients may require angiography and local **intra-arterial infusion** of vasodilating drugs (**papavarine, nicardipine, or milrinone**) or even angioplasty to increase the diameter of segments of cerebral blood vessels that are critically constricted. Medical management includes **hypervolemia, hemodilution, and hypertension** to increase blood flow through stenotic segments of feeding vessels; patients are often on large doses of vasopressors (phenylephrine, norepinephrine, or vasopressin) to induce hypertension. ICP may be elevated from brain edema secondary to initial injury or evolving ischemic strokes.
1. **ICP monitoring** may be helpful during the procedure because intracranial hypertension is common, and ICP may increase with therapy. Intraventricular catheter is preferable because it permits drainage of CSF to treat increased ICP; "Camino" bolt is adequate for monitoring, but CSF cannot be withdrawn.
2. Anesthetic goals are to optimize cerebral perfusion by **maintaining systemic hypertension and intracranial normotension**, maintain a hyperdynamic cardiovascular state, and provide a rapidly reversible general anesthetic so that neurologic examination can be assessed immediately after intervention. Patients may require postprocedure mechanical ventilation for control of ICP. Paralysis and mechanical ventilation may be necessary to control partial pressure of carbon dioxide. If ICP is not increased, general anesthesia may be accomplished with a low concentration of volatile anesthetic supplemented by narcotics and paralysis. Alternatively, propofol infusion may be necessary to control ICP.
3. ICP may rise, and blood pressure may fall dramatically with intra-arterial infusions of **papavarine, nicardipine, or milrinone**. High doses of vasopressors such as phenylephrine or norepinephrine may be necessary. Supplementation with cardiac inotropes may be required to maintain blood pressure.
4. Because hyperglycemia may worsen consequences of cerebral ischemia, patients may be receiving an insulin infusion in conjunction with 5% dextrose in normal saline to maintain tight control of glucose.
5. Patients are often febrile. Normothermia can be maintained with surface cooling; hyperthermia may worsen consequences of cerebral ischemia.
- J. **Trigeminal Neuralgia**. Percutaneous neurolysis of trigeminal ganglion and/or terminal nerves is effective therapy for management of chronic pain. Patients frequently also suffer from multiple sclerosis. Placement of a lesioning electrode is performed in the awake patient to best define areas for ablation; neurologic examination and evaluation require an awake and fully cooperative patient. Opioid analgesics are avoided because pain is the symptom evaluated; opioid analgesics can blunt sensory neurologic examination to distinguish painful from nonpainful stimulation. Brief periods of general anesthesia are necessary for placement of the electrode in the trigeminal ganglion via foramen ovale and actual ablation because this may be excruciatingly painful. Standard monitoring is used, and unconsciousness is produced with methohexital (0.5 to 1.0 mg/kg IV)

or propofol (1 to 2 mg/kg IV). Proper position of the needle is confirmed by fluoroscopy and brief electrical stimulation to reproduce the sensory distribution of the patient's area of pain. Neurolytic techniques include injection of alcohol or, most commonly, radiofrequency lesion ablation. Hypertension is common during lesioning and may require invasive blood pressure monitoring in some patients and treatment with esmolol, labetalol, nitroglycerin, or nitroprusside. Bradycardia and asystole may occur by stimulation of the oculocardiac reflex; hemodynamically significant reactions may require treatment with atropine, glycopyrrolate, dopamine, isoproterenol, esophageal or transcutaneous pacing, or chest compressions. Mask ventilation may be difficult when the electrode is in place.

VI. ANESTHESIA FOR VASCULAR, THORACIC, AND GASTROINTESTINAL/GENITOURINARY RADIOLOGY PROCEDURES

- A. Transjugular intrahepatic portosystemic shunt (TIPS)** decompresses the portal system in patients with decompensated portal hypertension. It is a less invasive technique that may replace open portocaval and splenorenal shunts. Patients may have advanced liver disease, actively bleeding esophageal varices, massive recurrent ascites, severely compromised liver function, or hypoxemia. Oliguria from hepatorenal syndrome is common.
 1. After cannulation of the right internal jugular, a trochar is directed into a hepatic vein and passed through liver parenchyma to enter a portal vein and create a connection for egress of portal blood into systemic circulation; the conduit is dilated, and patency is maintained with a stent. Portal vein may be visualized fluoroscopically with retrograde insufflation of carbon dioxide gas via the hepatic vein.
 2. Sedation under MAC with standard monitors may be sufficient in some patients, but general anesthesia is common because of the procedure length and discomfort.
 3. Patients with bleeding or ascites should be considered to have full stomachs and receive a rapid sequence induction. It is preferable to perform paracentesis to drain ascites before induction of general anesthesia to avoid consequences of sympathectomy on rapid decompression of the portal system.
 4. Liver failure patients are often hyperdynamic with low systemic vascular resistance due to arteriovenous fistulas in the liver and lung. Preprocedural hypoxemia may be multifactorial from $\dot{V}/\dot{Q}$ mismatch or hepatopulmonary syndrome with associated intrapulmonary vascular dilations.
 5. Patients with actively bleeding varices may be treated with continuous infusion of octreotide to reduce mesenteric blood flow.
- B. Balloon-Occluded Retrograde Transvenous Obliteration (BRTO)** is a method to treat gastric varices in patients that are not candidates for TIPS procedure. Balloon-occluded sclerotherapy of gastric varices is achieved through either a transjugular or transfemoral venous approach, using 3% sodium tetradecyl sulfate as the sclerosing agent. While it is an effective treatment for gastric varices, BRTO can increase the risk of esophageal varices and ascites. This procedure can be performed under MAC or general anesthesia.
- C. Arterial Stents.** Carotid stents can be placed under sedation with MAC or general anesthesia. Tight hemodynamic control is important; stroke and bradycardia may occur during the procedure.
- D. Percutaneous lung biopsy** under CT guidance is a relatively painless procedure amenable to procedural sedation or MAC. The pleura is well

innervated, and penetration with a needle may be painful. Standard monitoring usually is sufficient. The patient may be prone or supine and must remain immobile during needle placement and biopsy. **Percutaneous radiofrequency ablation of lung tumors** is similar to the biopsy, but a larger puncture device is used to insert a probe for lesioning into the tumor; the actual ablation may be painful. Several ablations may be necessary for one tumor with repositioning of the probe. At conclusion of the procedure, the probe is removed and the wound immediately covered to prevent a sucking chest wound and pneumothorax. This necessitates turning the patient prone or supine, depending upon the insertion site, immediately after removal of the electrode. If general anesthesia is performed, ventilation should be adjusted to minimize chest movement. **Pneumothorax and tension pneumothorax** in an ever-present concern even after completion of all procedures involving penetration through the chest wall. All patients receive a chest x-ray after recovery to identify significant pneumothorax. Hemoptysis is also a concern with vascular lesions adjacent to large airways. Placement of a double lumen endotracheal tube or bronchial blocker to preserve ventilation may be necessary in the event of active bleeding.

- E. **Percutaneous insertion of gastrostomy, nephrostomy, cholecystostomy, or choledochostomy tubes** rarely require general anesthesia. Comorbid conditions may require aggressive medical management during procedures necessitating the presence of an anesthesiologist. Procedures are performed under fluoroscopy or CT guidance.

VII. ANESTHESIA FOR PROTON BEAM THERAPY AND RADIATION THERAPY

A. **Proton beam radiation therapy** is used to treat arteriovenous malformations, pituitary tumors, retinoblastomas, and an expanding number of other tumors. Irradiation is painless, but planning sessions and creation of molds may take many hours, while each individual therapy session is much shorter. During irradiation, the target area must remain in a fixed position using a stereotactic frame locked to a positioning device.

1. **In adults**, placement of small pins or screws in the skull can be performed under local anesthesia with 2% lidocaine with epinephrine. If “ear bars” are used, a satisfactory ear block can be performed by subcutaneous injection of 3 mL of 2% lidocaine with epinephrine in the outer ear canal. Sedation is usually not recommended because patient cooperation is required.

2. **For children**, a general anesthetic is usually administered. The procedure typically is performed daily for about 4 weeks; a propofol induction (2 to 4 mg/kg IV) and maintenance infusion (~75 to 300 µg/kg/min) through an implanted Broviac or Hickman catheter is a suitable technique. Spontaneous ventilation should be permitted whenever possible. The patient's head is placed in a sniffing position, and a plaster mold is formed that maintains the head in the correct position for treatment. Nasal prongs or a facemask can provide supplemental oxygen; a sidestream sampling line will provide qualitative assessment of ventilation. LMA is considered if a natural airway cannot be maintained. Standard monitoring is used, and patients are monitored and viewed via closed-circuit television because the anesthesiologist must leave the room during the brief period of radiation.

B. **Anesthesia for Radiation Therapy.** Children receiving radiation therapy often require general anesthesia.

1. Typical treatment course is three or four times a week for 4 weeks. It is desirable to choose an anesthetic that allows rapid recovery with minimal risk of nausea and vomiting.

2. The first radiation procedure may be time consuming (1 to several hours) because measurements must be performed and molds made of the patient. Subsequent treatments are typically less than 30 minutes.
3. Many patients have indwelling venous access for chemotherapy. An IV induction and maintenance with propofol infusion is a suitable technique. Intramuscular injection of a combination of midazolam, glycopyrrolate, and ketamine may be useful in children with difficult venous access.

VIII. ELECTROCONVULSIVE THERAPY

Electroconvulsive therapy (ECT) is used to treat major depression, catatonia, and mania along with other second-line indications such as in patients who have not responded to medications, are debilitated by serious side effects, or are acutely suicidal. Patients who suffer from delusions, hallucinations, or profound psychomotor retardation are less responsive to medication, and thus, early ECT is preferred for them as well. Usually, a series of 6 to 12 treatments over 2 to 4 weeks is required for a clinical response.

A. Physiologic Effects of ECT

1. The electrical stimulus produces a generalized tonic-clonic seizure consisting of a tonic phase lasting 10 to 15 seconds, followed by a clonic phase lasting 30 to 50 seconds.
2. An initial vagal discharge may result in severe bradycardia and mild hypotension. Subsequent sympathetic nervous system activation produces hypertension and tachycardia, which can persist for 5 to 10 minutes. ECG changes are common and may include pulse-rate interval prolongation, increased QT interval, T wave inversions, and atrial or ventricular arrhythmias.
3. Increased cerebral blood flow and metabolic rate lead to increased ICP. Increased intraocular and intragastric pressure may occur.

B. Anesthetic Goals. Provide amnesia and a rapid return to consciousness, prevent damage from tonic-clonic contractions (e.g., long bone fractures), control hemodynamic response, and avoid interference with initiation and duration of induced seizure.

C. The one absolute contraindication to ECT is **intracranial hypertension** (elevated ICP). **Relative contraindications** include presence of an intracranial mass lesion (with normal ICP), intracranial aneurysm, recent myocardial infarction, angina, congestive heart failure, untreated glaucoma, major bone fractures, thrombophlebitis, pregnancy, and retinal detachment. Patients on maintenance treatment with benzodiazepines or lithium should discontinue these treatments before ECT; benzodiazepines are anticonvulsants that may abolish or attenuate the seizure; lithium is associated with post-ECT confusion and delirium.

D. Anesthetic Management

1. Sedative premedication is not indicated and may prolong emergence. Anticholinergic drugs may be used to reduce secretions and to minimize bradycardia. Ondansetron may be useful in patients with a history of nausea and vomiting.
2. A small-gauge IV cannula is placed for drug administration, and standard monitors are applied.
3. The patient is preoxygenated with 100% oxygen; anesthesia is induced with methohexital (1.5 mg/kg IV) or propofol (1 mg/kg IV) and succinylcholine (1.0 mg/kg IV). Patients are ventilated with 100% oxygen via mask and Ambu bag. Small doses of short-acting nondepolarizing muscle relaxant can be used in patients with contraindications to

succinylcholine. Pretreatment with labetalol (10 to 50 mg IV) or esmolol (40 to 80 mg IV) blunts the hypertensive response and may be useful in patients with hypertension or coronary artery disease.

4. Ketorolac may decrease muscle pains after ECT.
5. Rolled gauze pads placed bilaterally as bite blocks protect gums and lips from biting from electrical stimulus and subsequent seizure.
6. Nature and duration of induced seizures can be monitored by electroencephalogram or by "isolated arm" technique. With the latter, inflation of a blood pressure cuff interrupts blood supply to one arm before injecting muscle relaxant; seizure activity is apparent in the isolated arm.
7. Patients are ventilated with oxygen by facemask until spontaneous ventilation resumes. They are then placed in a lateral decubitus position and monitored in a recovery area until awake and alert. Agitated delirium from tardive seizures may occur after ECT and can be treated with small doses of propofol or benzodiazepine.
8. Patients with underlying medical conditions may require special attention:
 - a. Patients with gastroesophageal reflux may require aspiration prophylaxis and rapid sequence intubation.
 - b. Patients with severe cardiac dysfunction may require invasive monitoring.
 - c. Patients with intracranial mass lesions may require invasive blood pressure monitoring for tight hemodynamic control; hyperventilation before inducing a seizure may reduce the ICP response.
 - d. Pregnant patients may require endotracheal intubation, fetal monitoring, and left uterine displacement.
9. Rarely, an induced seizure will not spontaneously terminate. Ventilation with 100% oxygen is continued, and seizure is terminated within 3 minutes with propofol (20 to 50 mg IV) or benzodiazepines.
- E. **Psychiatric Drug Interactions.** Patients requiring ECT may be treated with psychotropic drugs that have potent side effects and interactions with anesthetic drugs.
 1. **Tricyclic antidepressants** (e.g., amitriptyline, nortriptyline, desipramine, imipramine, and doxepin) potentiate effects of norepinephrine and serotonin by preventing reuptake. Untoward effects include postural hypotension, sedation, dry mouth, urinary retention, and tachycardia.
 2. **Monoamine oxidase inhibitors (MAOIs)** (e.g., phenelzine and isocarboxazid) increase availability of norepinephrine at postsynaptic receptors; orthostatic hypotension and severe hypertension may occur. Tyramine, present in certain foods, may produce a hypertensive crisis in patients taking MAOIs. Although it has been recommended previously that MAOI therapy be discontinued at least 10 days before elective surgery, the risk of severe depression outweighs the risks of discontinuing the drug. **Important interactions** between MAOIs and anesthetics include exaggerated hypotension during spinal anesthesia and severe hypertension with indirectly acting vasopressors (ephedrine). Administration of **meperidine** (and meperidine derivatives) to patients receiving MAOIs has been associated with a syndrome of serotonin excess characterized by severe hemodynamic instability, respiratory depression, malignant hyperpyrexia, seizures, coma, and death.
 3. **Selective serotonin reuptake inhibitors** (e.g., fluoxetine, sertraline, fluvoxamine, and paroxetine) are associated with only mild adverse effects. There are no known significant interactions with anesthetic drugs.

F. Upper and lower endoscopy can frequently be performed with sedation but may require general anesthesia and intubation. Interventional procedures including endoscopic retrograde cholangiopancreatography (ERCP) and percutaneous endoscopically guided gastrostomy (PEG) tube placement can be performed successfully in adults with minimal sedation; uncooperative patients or those with significant comorbid pathology may require the care of an anesthesiologist. Children often require general anesthesia. Endoscopy is not painful, and stimulation is limited to the procedure. Upper endoscopy, ERCP, and PEG require sharing the airway with the endoscopist; endotracheal intubation may be necessary for airway management. Colonoscopy is performed in the decubitus position and may be accomplished with a natural airway or LMA if appropriate. Insufflated air should be removed prior to removal of the endoscope during upper endoscopic procedures. Patients often have active reflux necessitating rapid-sequence induction and intubation.

G. Gastrostomy or Jejunostomy Tube Placement.

Patients with dysphagia or an inability to swallow often require gastrostomy and/or jejunostomy tube placement for nutritional support. This patient population often present with depressed mental status, such as coma, marginally interactive, or dementia, as well as **head and neck cancers** or **amyotrophic lateral sclerosis (ALS)**. Patients with gastric outlet obstruction from abdominal cancer may require a jejunostomy tube for nutritional support and a gastrostomy tube as a vent for stomach contents; such patients must be treated with full stomach precautions. Gastrostomy tubes may be placed endoscopically with a gastroscope. Alternatively, gastrostomy and jejunostomy tubes may be placed fluoroscopically or with CT guidance. Comorbidities associated with tobacco and alcohol use include COPD, coronary artery disease, hypertension, hepatic dysfunction, and alcohol withdrawal are common in oropharyngeal cancer patients. Airway exam is particularly important in this patient population as tumors, prior surgeries, and radiation can make mask ventilation and intubation potentially difficult. ALS is a degenerative neurologic disease with progressive profound muscle weakness that can affect respiratory function and swallowing. These patients often require CPAP or BiPAP for respiratory support and may require support postprocedure. Muscle relaxants are contraindicated in ALS because of uncertain duration of effect. Succinylcholine is contraindicated due to potential lethal hyperkalemia.

Suggested Readings

- Albers GW, Amarenco P, Easton JD, et al. Antithrombotic and thrombolytic therapy for ischemic stroke: American College of Chest Physicians Evidence-Based Clinical Practice Guidelines (8th edition). *Chest* 2008;133(6 Suppl):630S–669S.
- American College of Radiology. *Manual on Contrast Media*. 2013. <http://www.acr.org/Quality-Safety/Resources/Contrast-Manual>
- American Society of Anesthesiology. *Distinguishing Monitored Anesthesia Care ("MAC") from Moderate Sedation/Analgesia (Conscious Sedation)*. <http://www.asahq.org/publicationsAndServices/standards/35.pdf>
- American Society of Anesthesiology. *Statement on Nonoperating Room Anesthetizing Locations*. <https://www.asahq.org/For-Members/Standards-Guidelines-and-Statements.aspx>
- Barrett BJ, Parfrey PS. Preventing nephropathy induced by contrast medium. *N Engl J Med* 2006;354:379–386.
- Chun JY, Morgan R, Belli AM. Radiological management of hemoptysis: a comprehensive review of diagnostic imaging and bronchial arterial embolization. *Cardiovasc Intervent Radiol* 2010;33:240–250.

- Coté CJ. Anesthesia outside the operating room. In: Coté CJ, Todres ID, Goudsouzian NG, et al., eds. *A Practice of Anesthesia for Infants and Children*. 3rd ed. Philadelphia: WB Saunders; 2001:571–583.
- Ding Z, White PF. Anesthesia for electroconvulsive therapy. *Anesth Analg* 2002;94:1351–1364.
- Dolenc TJ, Hahl SS, Barnes RD, et al. Electroconvulsive therapy in patients taking monoamine oxidase inhibitors. *J ECT* 2004;20:258–261.
- Dougherty TB, Nguyen DT. Anesthetic management of the patient scheduled for head and neck cancer surgery. *J Clin Anesth* 1994;6:74–82.
- Gilbertson LI, ed. Conscious sedation. *Int Anesthesiol Clin* 1999;37:1–129.
- Janne d'Othée B, Walker TG, Marota JJ, et al. Splenic venous congestion after balloon-occluded retrograde transvenous obliteration of gastric varices. *Cardiovasc Intervent Radiol* 2012;35:434–438.
- Jorgensen NH, Messick JM, Gray J, et al. ASA monitoring standards and magnetic resonance imaging. *Anesth Analg* 1994;79:1141–1147.
- Kawa C, Stewart J, Hilden K, et al. A retrospective study of nurse-assisted propofol sedation in patients with amyotrophic lateral sclerosis undergoing percutaneous endoscopic gastrostomy. *Nutr Clin Pract* 2012;27:540–544.
- Marckmann P, Skov L, Rossen K, et al. Nephrogenic systemic fibrosis: suspected causative role of gadodiamide used for contrast-enhanced magnetic resonance imaging. *J Am Soc Nephrol* 2006;17:2359–2362.
- Merten GJ, Burgess WP, Gray LV, et al. Prevention of contrast-induced nephropathy with sodium bicarbonate: a randomized controlled trial. *JAMA* 2004;19:2328–2334.
- Morcos SK. Acute serious and fatal reactions to contrast media: our current understanding. *Br J Radiol* 2005;78:686–693.
- Oudemans-van Straaten HM. Strategies to prevent contrast nephropathy. *Minerva Cardioangiol* 2005;53:445–463.
- Pino RM. The nature of anesthesia and procedural sedation outside of the operating room. *Curr Opin Anaesthesiol* 2007;20:347–351.
- Prabhakar A, Owen CP, Kaye AD. Anesthetic management of the patient with amyotrophic lateral sclerosis. *J Anesth* 2013;27:909–918.
- Russell, GB. Alternate-site anesthesia: the expanding world of anesthesia outside the operating room. *Curr Opin Anaesthesiol* 1998;11:411.
- Saad WE, Khaja MS, Hirota S. Balloon-occluded retrograde transvenous obliteration of gastric varices: conception, evolution, and history. *Tech Vasc Interv Radiol* 2012;15:160–164.
- Schubert A, Deogaonkar A, Lotto M, et al. Anesthesia for minimally invasive cranial and spinal surgery. *J Neurosurg Anesthesiol* 2006;18:47–56.
- Talke PO, Sharma D, Heyer EJ, et al. Society for Neuroscience in Anesthesiology and Critical Care Expert consensus statement: anesthetic management of endovascular treatment for acute ischemic stroke. *J Neurosurg Anesthesiol* 2014;26:95–108.
- Tramèr MR, von Elm E, Loubeyre P, et al. Pharmacological prevention of serious anaphylactic reactions due to iodinated contrast media: systematic review. *BMJ* 2006;333:675.
- Walker TG, Salazar GM, Waltman AC. Angiographic evaluation and management of acute gastrointestinal hemorrhage. *World J Gastroenterol* 2012;18:1191–1201.
- Xiao P, Zhang XS. Adult laryngotracheal surgery. *Anesthesiol Clin* 2010;28:529–540.
- Young WL, Pile-Spellman J. Anesthetic considerations for interventional neuroradiology. *Anesthesiology* 1994;80:427–456.

I. INITIAL EVALUATION OF THE TRAUMA PATIENT

Rapid assessment of injuries and institution of resuscitative measures are particularly important in trauma patients. Life-threatening injuries should be identified immediately based on **Airway, Breathing, Circulation, Disability/** neurologic function, and **Environmental** priorities with treatment measures initiated simultaneously. Assume that all patients have a cervical spine injury, a full stomach, and hypovolemia until proven otherwise.

A. Airway

1. Airway assessment should include inspection for foreign bodies, facial and laryngeal fractures (palpable fracture and subcutaneous emphysema), and expanding cervical hematomas. Dyspnea, hemoptysis, dysphonia, stridor, and air leaking through the neck wound may also be signs of airway injury. Remove all secretions, blood, vomitus, and any existing foreign bodies (e.g., dentures or teeth).
2. **Minimize movement of the cervical spine during airway manipulation.** If immobilizing devices must be removed temporarily, an assistant should keep the head in a neutral position with manual in-line immobilization.
3. **Establish** a definitive airway if there is any doubt about the patient's ability to maintain airway integrity. With blunt or penetrating injuries to the neck, endotracheal intubation may worsen a laryngeal or bronchial injury. Functional suction equipment should always be immediately available to prevent aspiration if the trauma patient with a full stomach vomits.
 - a. **The awake patient.** Depending on the patient's injuries, the ability to cooperate, and cardiopulmonary stability, several options are available. Choice of technique for securing the airway should be individualized based on operator preference and patient circumstances since there are few data to support one approach over another.
 1. **Intubations after a rapid sequence induction** is our most common approach to the airway. Video laryngoscopy may be helpful in patients with suspected cervical spine injury.
 2. **Awake nasal or orotracheal intubation** with the use of a laryngoscope or fiberoptic bronchoscope is an alternative.
 3. **Blind nasal intubation** may be performed on the spontaneously breathing patient.
 4. **Awake cricothyroidotomy or tracheostomy** may be necessary for patients with severe facial trauma that might be contraindications to other methods of intubation.
 - b. **The combative patient.** A rapid sequence orotracheal intubation is often the most expedient approach provided there are no problems precluding neuromuscular blockade. Hypoxemia must always be excluded in an agitated patient.
 - c. **The unconscious patient.** Ororacheal intubation is usually the safest and most expeditious approach.
 - d. If the patient arrives with an esophageal obturator airway or esophageal gastric tube airway, perform **endotracheal intubation before removing these devices** because vomiting frequently occurs with their removal.

4. **The intubated patient.** Verify the position of an endotracheal tube by auscultating for breath sounds bilaterally and by detecting end-tidal CO_2 . Secure the endotracheal tube, and ensure adequate ventilation and oxygenation.
- B. **Breathing.** Adequate function of the lungs, diaphragm, and chest wall should be evaluated rapidly. Supplemental oxygen should be provided to all trauma patients, either by mask or by endotracheal tube.
 1. Assess the chest wall excursion, and auscultate the lungs to ensure adequate gas exchange. Visual inspection and palpation may rapidly detect injuries such as a pneumothorax.
 2. Tension pneumothorax, massive hemothorax, and pulmonary contusion are three common conditions that may acutely impair ventilation and should always be identified. Positive-pressure ventilation may worsen a tension pneumothorax (and cardiac tamponade) and can rapidly lead to cardiovascular collapse.
 3. The trauma patient's breathing and gas exchange should be reevaluated after intubation or initiation of positive-pressure ventilation and periodically after the initial assessment.
- C. **Circulation**
 1. In the severely injured trauma patient, rapid initiation of resuscitation measures is important to prevent and control hypothermia, acidosis, and coagulopathy.
 2. **Hemodynamics** is initially assessed by palpating pulses and measuring the blood pressure.
 3. **Intravenous (IV) access.** Check IV lines already in place to ensure proper function. At least two large (preferably 14 gauge) catheters should be placed. These lines should be placed above the level of the diaphragm in patients with injuries of the abdomen (where there is a potential for major venous disruption). IV access below the level of the diaphragm is helpful when obstruction or disruption of the superior vena cava, innominate, or subclavian vein is suspected.
 4. **Peripheral venous cannulation failure.** In this event, percutaneous subclavian or femoral vein cannulation should be carried out. Although the internal and external jugular veins remain options, access to these structures is frequently hindered by immobilization of the head and neck for a suspected cervical spine injury. If these approaches prove unsuccessful, **surgical cutdowns** can be performed. The saphenous vein at the ankle and the antecubital venous system are acceptable options. Intraosseous access to the vasculature is also an option for personnel trained in this technique.
 5. Volume resuscitation should be individualized. The concept of "damage control" emphasizes multiple approaches to control and prevent tissue hypoperfusion, acidosis, coagulopathy, and hypothermia.
 - a. **Damage control resuscitation (DCR)** refers to the strategy of limiting crystalloid use, early resuscitation with packed red blood cells and clotting factors, and maintenance of a systolic blood pressure around 85 to 90 mm Hg. The disadvantages to crystalloid infusion include dilution of coagulation factors, hemodilution, and clot disruption. Early administration of blood and clotting factors serves to treat trauma-induced coagulopathy that can occur early after injury. In a patient in whom hemorrhage has not been definitely controlled, elevation in blood pressure and cardiac output can cause dislodgement of a clot and further bleeding. Hypotensive resuscitation should not be used in certain subsets of patients such as patients with head trauma.
 - b. Type-specific non-cross-matched blood or type O-negative blood may be given before cross-matched blood becomes available. Fresh frozen plasma and platelets should be ordered early if a patient

requires ongoing blood transfusion. The ratio of fresh frozen plasma and platelets to packed red blood cells should be closely monitored with hemoglobin levels, prothrombin times, and platelet counts. Even the administration of components in a 1:1 ratio is inferior to the administration of fresh whole blood when clotting activity and platelet counts are compared, but whole blood resuscitation is not an option in most clinical settings except the battlefield. Aggressive resuscitation with blood products can lead to hypothermia, hyperkalemia, and hypocalcemia. Empiric treatment is often indicated as the laboratory results may lag behind the clinical scenario when massive fluid resuscitation is undertaken.

- c. Severely injured trauma patients do not tolerate prolonged surgical procedures. **Damage control surgery** refers to the concept of employing initial short surgical procedures immediately after injury with the goals of controlling hemorrhage and preventing contamination through temporary measures. Patients then undergo definitive corrective surgery at a later date after they have been stabilized.
6. **Vasopressor infusions** should not substitute for adequate volume replacement during initial resuscitation. Vasopressors may be necessary as a temporizing measure if perfusion pressure is clearly inadequate during ongoing volume resuscitation.
7. **Antifibrinolytics**, such as tranexamic and ϵ -aminocaproic acid can reduce mortality in bleeding trauma patient when started as soon as possible within 3 hours of injury. The safety of antifibrinolytics after 3 hours or in certain patient subsets such as isolated traumatic brain injury has yet to fully elucidated and may be associated with increased adverse events.
- D. **Disability/Neurologic Evaluation.** A brief neurologic examination yields useful information in assessing cerebral perfusion or oxygenation and can provide a simple and quick means of predicting a patient's outcome.
 1. The level of consciousness can be described by the AVPU method (A = alert, V = responds to verbal stimuli, P = responds only to painful stimuli, and U = unresponsive to all stimuli). A more detailed and quantitative assessment of neurologic function is with the Glasgow coma score (GCS; Table 34.1) that is the sum of the best eye opening, verbal, and motor responses.
 2. An altered level of consciousness dictates immediate reevaluation of the patient's oxygenation and circulation, even though it can be of central nervous system origin (trauma or intoxication).
 3. Neurologic deterioration can rapidly occur in trauma patients and necessitates frequent neurologic reevaluation.
- E. **Environmental Control.** Trauma patients are often hypothermic upon arrival at the hospital and require aggressive efforts to maintain body heat. Hypothermia can exacerbate coagulopathy.
 1. External warming devices should be applied, IV fluids warmed before infusion, and a warm environment maintained.
 2. If there is any suspicion of exposure to chemical agents, decontamination of the victim must be carried out before entrance to the hospital. This terminates exposure, protects the health care provider, and allows the hospital to function effectively.
- F. **Diagnostic Studies**
 1. **Laboratory studies** include blood type and cross-match, complete blood count, platelet count, prothrombin time, activated partial thromboplastin time, electrolytes, glucose, blood urea nitrogen, creatinine, urinalysis, and, if indicated, toxicologic screening.

TABLE
34.1
Glasgow Coma Score

Eye Opening	Score
Spontaneous	4
To speech	3
To pain	2
No response	1
Best Verbal Response	
Oriented	5
Confused conversation	4
Inappropriate words	3
Incomprehensible sounds	2
None	1
Best Motor Response	
Obeys commands	6
Localizes pain	5
Normal flexion (withdrawal)	4
Abnormal flexion (decorticate)	3
Extension (decerebrate)	2
None (flaccid)	1

2. **Radiographic studies** should include a lateral cervical spine film, a chest radiograph (CXR), and an anteroposterior view of the pelvis on all patients with blunt trauma. At a minimum, a CXR is obtained in all patients with penetrating injuries of the trunk. Additional studies include thoracic, lumbar, and sacral spine films and chest and abdominal computed tomography (CT) studies.

a. **Lateral radiographs of the cervical spine** must include the C7–T1 interface and must be of sufficient quality to delineate the structures of interest (i.e., soft tissues and bones).

b. If the patient's clinical condition allows time for additional studies, **open-mouth odontoid and anteroposterior views of the neck** (standard trauma cervical spine series) may be obtained.

c. If the clinical evaluation demonstrates a patient with significant neck pain and tenderness but no evidence of fracture or dislocation on the plain radiographs, CT and magnetic resonance imaging may help delineate an occult injury.

3. A **12-lead electrocardiogram (ECG)** should be performed on all major trauma patients to help evaluate the presence of myocardial injury (e.g., contusion, tamponade, ischemia, and arrhythmia).

4. Ultrasonic examination of the abdomen (called **FAST** for **F**ocused **A**bdominal **S**onography in **T**rauma) specifically focusing on free fluid within the perihaptic, perisplenic, perivesical, and pericardium is very helpful to exclude significant intraperitoneal bleeding in patients with blunt abdominal trauma.

G. **Monitoring** is dictated by the severity of the patient's injuries and preexisting medical problems.

1. **An arterial line** is useful in patients with hemodynamic instability or respiratory failure.

2. **A central venous pressure line** may be required to assess volume status and administer vasoactive drugs.

3. A **pulmonary artery catheter** may be helpful in patients with ventricular dysfunction, severe coronary artery disease, valvular heart disease, multiple organ system involvement, or hemodynamics that seem disproportionate to their trauma burden. Placement is planned according to the time available and the clinical status of the patient.

II. SPECIFIC INJURIES

A. Intracranial and Spinal Cord Trauma (see Chapter 25)

B. Facial Trauma. Considerable force is required to produce facial fractures. Accordingly, these injuries often are associated with other injuries such as intracranial and spinal cord trauma, thoracic injury, myocardial contusion, and intra-abdominal bleeding. Brisk oral or nasal bleeding, broken teeth, vomitus, or tongue or pharyngeal injury may occlude the airway and complicate airway management. Trismus may be associated with these injuries and should be assessed before the induction of anesthesia. Emergency cricothyroidotomy or tracheostomy done under local anesthesia may be lifesaving.

1. Maxillary fractures are grouped by the LeFort classification (Fig. 34.1).

- a. **Type I (transverse or horizontal).** The body of the maxilla is separated from the base of the skull above the level of the palate and below the level of the zygomatic process.

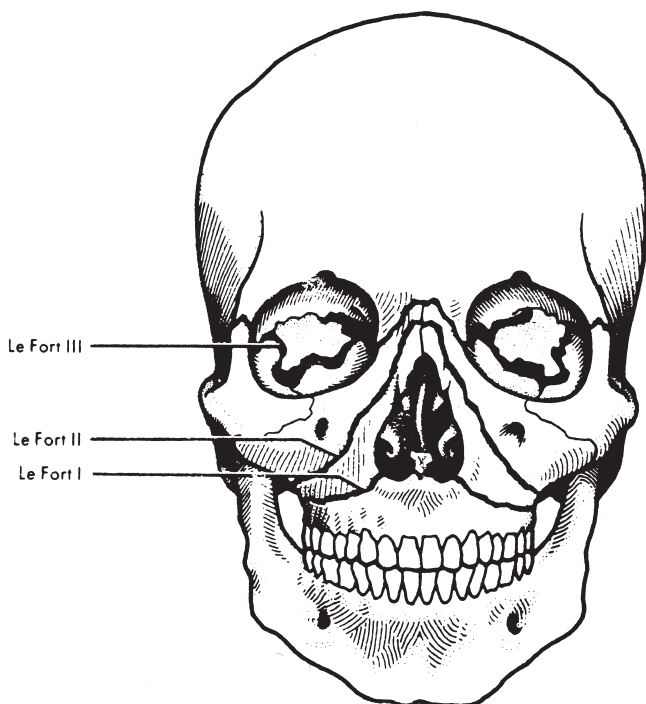


FIGURE 34.1 The LeFort classification. (From Rosen P, Baker FJ, Barkin RM, et al., eds. *Emergency Medicine: Concepts and Clinical Practice*. 2nd ed. St. Louis: Mosby; 1988.)

- b. **Type II (pyramidal).** Vertical fractures through the facial aspects of the maxilla extend upward through the nasal and ethmoid bones.
 - c. **Type III (craniofacial dysjunction).** Fractures extend through the frontozygomatic suture lines bilaterally, across the orbits, and through the base of the nose and the ethmoid region.
 - d. **Le Fort and related fractures** are frequently associated with skull fractures and **cerebrospinal fluid rhinorrhea**. Nasotracheal intubation and placement of nasogastric tubes are relatively contraindicated under these circumstances. Elective nasal intubation (or tracheostomy) may be necessary, however, before operative repair. A fiberoptic bronchoscope may be used in these cases to guide endotracheal tube into the trachea.
 - e. In the presence of rhinorrhea, positive-pressure mask ventilation can potentially cause pneumocephalus.
- 2. Mandibular fractures**
- a. Malocclusion, limitation of mandibular movement, loose or missing teeth, sublingual hematoma, and swelling at the fracture site complicate airway management.
 - b. **Posterior displacement of the tongue** producing airway obstruction is associated with bilateral condylar or parasymphysal fractures of the mandible. Simple forward traction on the tongue often provides relief.
 - c. Reestablishment of normal occlusion may necessitate intermaxillary fixation, which can also be combined with rigid fixation. Awake nasotracheal intubation is recommended if the nose has not been severely traumatized.
- 3. Ocular trauma** usually requires general anesthesia for repair. Special considerations for open-eye injuries are discussed in Chapter 26, section I.C.1.
- 4. Anesthetic management.** Most displaced facial fractures require general anesthesia for repair. Although children usually require general anesthesia, many soft tissue injuries can be treated with local anesthesia. Maintenance of a patent airway is the principal concern, and induction may require awake nasotracheal intubation, fiberoptic laryngoscopy, or tracheostomy under local anesthesia.
- C. Neck trauma** may cause cervical spine injury, esophageal tears, major vascular injuries, and airway injuries. Airway injuries may present with obstruction, subcutaneous emphysema, hemoptysis, dysphonia, or hypoxemia.
- 1. **"Clothesline"** injuries occur from direct trauma to the upper airway and can result in separation of the larynx from the trachea or separation between the cricoid cartilage and the first tracheal ring. These injuries do not always present with an open neck wound. Additional injuries include laryngotracheal transection, laryngeal fractures, and vascular injury.
 - 2. Blunt injury over the carotid arteries may result in intimal disruption and dissection, even in the absence of initial symptoms. Angiography or ultrasonography may be required to exclude these injuries.
 - 3. Initial management of **penetrating trauma** includes direct compression of involved vessels to control hemorrhage and prevent air embolism.
 - 4. Associated **thoracic injuries**, such as pneumothorax and hemorrhage from injury to the great vessels, may occur with lower neck injuries.

5. Anesthetic management

- a. **Securing the airway** is the central issue in these patients. A coordinated approach among members of the trauma team is necessary. A surgical airway or direct intubation of an open airway defect can be lifesaving. Anesthesia induction via spontaneous ventilation of a potent inhalational agent can be useful in the presence of airway disruption with the caveat that the patient likely has a full stomach and is a high risk for aspiration. Preparations should be made for fiberoptic intubation, rigid bronchoscopy, and a surgical airway.
 - b. **Great vessel injuries** in the neck may necessitate lower extremity IV access.
- D. Chest trauma** can involve injuries to the trachea or larynx, heart, great vessels, thoracic duct, esophagus, lung, or diaphragm.
1. **Rib fractures** are a common feature of major thoracic trauma and mandate assessment for pneumothorax by CXR. First-rib fractures should alert the clinician to the potential for associated internal injuries due to severe forces needed to fracture the first rib. Multiple rib fractures most commonly involve ribs 7 to 10 and often accompany lacerations of the spleen or liver.
 2. The hypoxemia and respiratory failure that accompany **flail chest** and other major chest injuries are indicative of underlying pulmonary contusion. IV fluids should be administered judiciously because the injured lung is sensitive to fluid overload.
 3. The presence of **subcutaneous emphysema** may indicate the presence of a pneumothorax or laryngeal, tracheobronchial, or esophageal trauma. Pneumothorax and hemothorax may lead to respiratory and cardiovascular collapse. If these conditions are present or highly suspected, chest tubes should be placed before the induction of general anesthesia. Avoid central line insertion (particularly by the subclavian route) on the side opposite an injury because of the potential consequence of bilateral pneumothorax. Avoid the ipsilateral side if a concomitant major venous injury is suspected.
 4. **Traumatic diaphragmatic injury** can present as an elevated diaphragm, gastric dilatation, loculated pneumothorax, or subpulmonic hematoma. An upper gastrointestinal contrast study should be considered if the diagnosis is not clear.
- 5. Anesthetic management**
- a. Patients with significant chest injuries almost always require general anesthesia.
 - b. The necessity for mechanical ventilation may extend into the postoperative period.
 - c. Avoid nitrous oxide when a pneumothorax is suspected and a chest tube has not yet been placed. Airway pressures must be closely monitored during positive-pressure ventilation.
 - d. Pulmonary hemorrhage into the main conducting airways calls for isolation of the uninjured side before it is flooded with blood. Double-lumen endotracheal tube placement, mainstem intubation, or endobronchial blockade may be needed to prevent blood from spilling into the noninjured side (see Chapter 22).
 - e. Regional anesthesia (i.e., intercostal nerve blockade, thoracic epidural anesthesia, or paravertebral blocks) may provide analgesia for multiple painful rib fractures. Adequate pain relief can reduce chest wall splinting, regional hypoventilation, and progressive hypoxemia.

E. Cardiac and Major Vascular Trauma

1. **Blunt cardiac injury** can result in myocardial muscle contusion, chamber rupture, valvular disruption, tamponade, or dysrhythmias.
2. **Cardiac trauma** may be associated with a fractured sternum, hemothorax, pericardial tamponade, myocardial dysfunction, valvular dysfunction, and ECG changes (persistent sinus tachycardia, multiple premature ventricular contractions and other dysrhythmias, bundle branch block, nonspecific ST-segment and T-wave changes, and overt ischemia).
 - a. **Beck triad** of distended neck veins, muffled heart sounds, and hypotension is present in only 30% of patients with pericardial tamponade, and pulsus paradoxus is even less reliable. The diagnostic test of choice is cardiac ultrasound.
 - b. **Pericardiocentesis** may be used to stabilize the patient until surgical repair can be performed. A subxiphoid pericardial window is ideally performed in the operating room.
3. A widened mediastinal profile, lack of clarity of the aortic knob, rightward tracheal shift, or widening of left paraspinal line without associated fracture on the CXR mandate further workup to rule out traumatic aortic injury. Helical CT is the diagnostic test of choice and is more sensitive than is angiography. Potentially salvageable patients with aortic rupture often have an incomplete laceration near the ligamentum arteriosum. An intact adventitial layer or contained hematoma prevents immediate death. An arterial line should be placed in the right arm since the compromised aorta may not transmit a normal pulse distal to the left subclavian and the flow through the left subclavian may be occluded during the course of surgical repair.
4. **The subclavian artery** is subject to injury with hyperextension of the neck and shoulder.
5. **Anesthetic management**
 - a. These patients are often **severely hypovolemic** and may have compromised cardiac function. Cardiopulmonary bypass may be required for certain repairs.
 - b. Etomidate and ketamine are good choices for induction, but use of the latter must be weighed against its risk in patients with concomitant head injury and those with cocaine abuse.
 - c. Cross-matched type-specific blood or O-negative blood should be available before induction. Inotropic and vasopressor agents should be immediately available to treat severe hypotension.

F. Peripheral Vascular Trauma

1. Check **peripheral pulses** in all extremities during the evaluation of trauma patients. Arteriography can be used to further define injuries.
2. **Anesthetic management** should focus on the recognition of hypovolemia secondary to uncontrolled hemorrhage. Regional anesthetic techniques may be considered in stable patients.

G. Abdominal Trauma

1. In stable patients without peritonitis, **penetrating abdominal wounds** (with the exception of gunshot wounds) are initially evaluated by local wound exploration. If the exploration is equivocal, diagnostic peritoneal lavage, abdominal ultrasound, or an abdominal CT scan may be performed.
2. All patients with **gunshot wounds of the abdomen** are surgically explored.
3. With **impalement injuries** (e.g., stab wounds or falls onto sharp objects), the penetrating object, if still present in the wound, will usually be removed in the operating room after anesthesia has been induced and the patient stabilized. Removal may result in exsanguination.

4. **Blunt trauma** may result in intra-abdominal or retroperitoneal bleeding.
 - a. The **spleen** is the most frequently injured abdominal organ in blunt trauma. Signs and symptoms include abdominal or referred shoulder pain, abdominal rigidity, a falling hematocrit, or hypotension. Minor splenic hematomas are often managed nonoperatively, but grade IV (active bleeding) and V (shattered/avulsed spleen) injuries require splenectomy.
 - b. The **liver** frequently fractures with blunt abdominal trauma. Minor injuries are managed nonoperatively unless other injuries mandate laparotomy. Thus, liver injuries that require operation are often complex with large blood loss and high mortality. Manual compression can temporarily control bleeding and allow time for volume resuscitation. Perihepatic packing ("**damage control surgery**") with later reexploration is sometimes considered for patients with severe injuries.
 5. **Abdominal compartment syndrome** can occur in setting of direct injury as well as after massive fluid resuscitation.
 - a. Abdominal compartment often presents with clinical triad of
 1. tense, distended abdomen
 2. respiratory distress or high peak pressure if the patient is intubated and
 3. oliguria. Hypotension is common because of a decrease in preload by compression of the inferior vena cava. IAP greater than 12 mm Hg is indicative of abdominal hypertension, and IAP 20 to 25 mm Hg warrants immediate decompression.
 - b. Retroperitoneal hematomas and aortic rupture may present with abdominal compartment syndrome. Bowel reperfusion can occur from ischemia, and peritonitis can lead to further tissue edema. Electrolyte disorders, myoglobinuria, and renal failure can occur.
 - c. Surgical decompression may be necessary. These patients are often **intravascularly depleted** and may **become severely hypotensive** after decompression due to increase in capacitance of bleeding from uncompressed vasculature. Cross-matched type-specific blood or O-negative blood should be available before induction. Inotropic and vasopressor agents should be immediately available to treat severe hypotension.
- H. Genitourinary Trauma**
1. All multiple trauma patients should have a **Foley catheter** placed. If pelvic or perineal injury has occurred, as evidenced by blood at the urethral meatus, a perineal hematoma, or a high-riding prostate, retrograde urethrography should be performed before urethral catheterization.
 2. All patients with penetrating abdominal or back injuries and those with significant hematuria after blunt trauma should have a radiographic **kidney-ureter-bladder** examination and undergo **IV pyelography** or contrast-enhanced CT.
 3. Eighty-five percent of renal injuries can be managed nonoperatively, but patients with refractory hypotension should go directly to the operating room for exploration.
 - a. **Ureteral laceration** is managed by surgical intervention after locating the disruption by retrograde urography.
 - b. **Bladder** contusions may be treated nonoperatively, but rupture usually requires exploration.
 - c. The inability of the patient to void or clinical signs of injury indicate **injury to the urethra** (see section II.G.1). Diagnostic urethrography should precede treatment with suprapubic cystostomy for urinary diversion and control of hemorrhage. Most disruptions can undergo delayed repair.

I. Orthopedic Trauma

1. All **fractures or dislocations** that compromise nerve or vascular function may constitute surgical emergencies (e.g., radial nerve injury with humeral shaft fractures and aseptic necrosis of the femoral head with hip dislocation) and must be reduced immediately. It is important to document the neurovascular examination immediately before anesthesia and upon awakening. Regional anesthesia may delay diagnosis of compartment syndrome and is relatively contraindicated if compartment syndrome is anticipated.
2. **Upper extremity**
 - a. Severe **depression or hyperabduction of the shoulder girdle** can stretch or tear the brachial plexus. Horner syndrome may present with damaged cervical sympathetic chain.
 - b. When the shoulder is struck hard from the side, the medial end of the clavicle may be dislocated upward or retrosternally. Pressure on the trachea in a retrosternal dislocation may cause life-threatening airway compromise.
 - c. Dislocation of the glenohumeral joint can cause axillary nerve injury.
 - d. **Fractures of the humeral shaft**, especially the middle or distal part, are frequently associated with radial nerve injury.
 - e. Neurovascular compromise of the forearm can occur with **fracture or dislocation of the elbow**. Peripheral ischemia is often complicated by edema of the anterior compartment with risk for nerve and muscle necrosis. Fasciotomy may be indicated.
 - f. Median nerve compression is possible with **fractures at the wrist** or with carpal dislocation and may require division of the transverse carpal ligament.
3. **Pelvis**
 - a. Patients who have sustained pelvic injuries can be divided into three major categories:
 1. **Exsanguinating hemorrhage** from external bleeding in open fractures or from retroperitoneal hematoma in closed fractures (0.5% to 1.0%). These patients almost always present with severe hypotension or cardiac arrest and rarely respond to resuscitative measures.
 2. **Hemodynamically stable** with a relatively uncomplicated course (75%). Urgent or elective surgery for repair of bony and ligamentous pelvic disruptions may be required.
 3. An **intermediate group** in critical condition with various degrees of overall injury, hemorrhage, and hemodynamic instability (25%).
 - b. **Initial management** for these injuries may include the application of a compressive binder for "open-book" fractures, pelvic angiography (with or without therapeutic embolization to control hemorrhage), and external pelvic fixation.
 - c. Pelvic fractures without major disruption, such as type I anterior posterior compression (APC) injury or type I lateral compression injury, can be treated with bed rest and delayed open reduction and internal fixation (ORIF). More complex injuries such as APC II (widened sacroiliac joint with hemorrhagic and vascular consequences) require acute external fixation with delayed conversion to internal fixation, acute ORIF, or arterial embolization.
 - d. **Fat embolism** can occur with pelvic and major long-bone fractures (see Chapter 19).
 - e. **Crush injuries** may be associated with **myoglobinuria**. Aggressive and early hydration may help prevent acute renal failure.

4. Lower extremity

- a. Fractures of the **tibia and fibula**, the most common major skeletal injuries, can be associated with neurovascular trauma and attendant compartment syndrome.
- b. With a fracture of the **femur**, blood loss can be much greater than is evident from superficial inspection.
- c. **Hip fractures** are common in the elderly, whose clinical picture is often dominated by other complicating medical illnesses. Traction is used initially for pain relief, but most fractures require ORIF to ensure adequate healing and function and to avoid the complications of prolonged immobilization.
- d. Regional, general anesthesia, and combined techniques can be considered for patients with isolated lower-extremity injuries.

5. Extremity reimplantation

- a. **Indications.** In general, these procedures are performed on the upper extremities and only in patients who are otherwise stable. An amputated arm, hand, or digit will not be reimplanted if it has sustained a severe crush injury or has been raggedly torn from major nerves and blood vessels. Reimplantations may be extremely lengthy procedures, occasionally in excess of 24 hours.
- b. **Anesthetic management**
 1. General anesthesia is usually chosen because of the long duration of these procedures. A combined technique will reduce anesthetic requirements and provide for postoperative analgesia (especially with catheter placements, rather than single-dose brachial plexus blocks). Regional anesthesia may improve blood flow via the induced sympathectomy.
 2. During general anesthesia, the head and pressure points must be evaluated every 1 to 2 hours to avoid pressure-induced injury (e.g., scalp ulceration and hair loss). Low-pressure mattresses and padded sponge blocks should be used to minimize pressure on susceptible peripheral nerves (e.g., ulnar, sciatic, peroneal, or sural). The endotracheal tube cuff pressure should be periodically assessed because nitrous oxide will diffuse into the cuff and increase the pressure on the tracheal mucosa.
 3. Patients should be kept warm and adequately hydrated. Avoid hyperventilation or the use of vasoconstrictors.
 4. Consider invasive hemodynamic monitoring for optimization of the perfusion pressure and for prolonged cases. If a noninvasive blood pressure cuff is used, it should be rotated among multiple sites. The need for anticoagulation is determined intraoperatively.
 5. Blood loss can be vastly underestimated. Blood samples should be sent periodically to assess hemoglobin levels.

III. THE PEDIATRIC TRAUMA PATIENT

A. General Considerations

1. A clear understanding of the salient anatomic and physiologic differences among adults, children, and infants as well as a working knowledge of the specific anesthetic considerations for this patient population is required (see Chapters 30 and 31).
2. **Blunt trauma**, usually from falls or motor vehicle accidents, predominates in children. Multiple injuries are the rule rather than the exception, but diagnosis is often more difficult because of the child's inability to provide an accurate history.

B. Specific Considerations

1. Although the pediatric trauma patient frequently presents with significant blood loss, initially, the **vital signs** may be minimally altered. **Reliance on vital signs alone may seriously underestimate the severity of the injury.**
2. Orotracheal intubation with protection of the cervical spine is the preferred method of obtaining airway control. Nasotracheal intubation is **not** recommended in children under the age of 12 years. **Surgical cricothyroidotomy** is rarely performed in an infant or a small child because of technical difficulties. If airway control and ventilation cannot be accomplished, needle cricothyroidotomy is an appropriate temporary approach for oxygenation.
3. **Intraosseous infusion** is an acceptable procedure for critically injured pediatric patients in whom venous access cannot be established. An initial bolus of 20 mL of crystalloid per kg of child is recommended for initial resuscitation.
4. The small child who is **hypothermic** may be refractory to therapy for shock. During initial evaluation and management, overhead heaters or thermal blankets will be needed to maintain body temperature.
5. Avoidance of hypoxemia is pertinent in pediatric population. Due to high metabolic rate and oxygen consumption, desaturation can occur rapidly, followed by severe bradycardia. **Atropine IV 10 to 20 $\mu\text{g/kg}$ or IM 20 to 30 $\mu\text{g/kg}$** should be prepared to treat bradycardia.

IV. THE PREGNANT TRAUMA PATIENT

A. General Considerations

1. Pregnancy must always be suspected in any female trauma patient of childbearing age (see Chapter 32 for management of the pregnant patient). All pregnant women greater than 24 weeks of gestation should have cardiotocographic monitoring for a minimum of 4 to 6 hours. Kleihauer-Betke analysis helps in determining the amount of fetomaternal hemorrhage and should be performed. Fetomaternal hemorrhage in an Rh-negative patient warrants Rh immunoglobulin therapy.
2. Because the fetus depends on its mother for oxygen, an **uninterrupted supply of oxygenated blood** must be provided to the fetus at all times. The resuscitation of the fetus thus depends on the optimum resuscitation of the mother. The uterus remains an intrapelvic organ until the 12th week of gestation and reaches the umbilicus by 20 weeks. **Compression of the vena cava by the gravid uterus** after 20 weeks of gestation reduces venous return to the heart, thereby decreasing cardiac output and exacerbating shock. The pregnant patient should be transported and evaluated with **left uterine displacement**.
3. Although diagnostic irradiation poses a risk to the fetus, necessary radiographic studies should always be obtained. Consultation with a radiologist may be obtained for estimation of the total radiation dose to the fetus if multiple diagnostic imaging studies with ionizing radiation have been obtained.
4. If the amniotic fluid gains access to the intravascular space, it can be a source of amniotic fluid embolism and resultant disseminated intravascular coagulation.

B. Treatment

1. If the mother's condition is stable, the status of the fetus and the extent of uterine injury will determine further management. Consultation with the patient's obstetrician is advisable.

2. A potentially viable fetus that shows no signs of distress should be monitored by external ultrasound. Premature labor is always a possibility in these patients, and tocolytic therapy should be initiated in consultation with the obstetrics team if premature labor develops.
3. When a viable fetus shows signs of distress despite successful resuscitative measures, a cesarean delivery must be performed expeditiously. A nonviable fetus may be managed conservatively in utero to optimize maternal oxygenation and circulation.
4. Primary repair of all maternal wounds should be attempted in a critically injured mother carrying a viable gestation, even at the expense of fetal distress.
5. Perimortem cesarean section should be considered in any moribund pregnant patient at greater than or equal to 24 weeks of gestation.

V. MAJOR BURN INJURIES

A. Physiologic Implications of Burn Injury

1. **Deep thermal injury** destroys skin, the body's barrier to the external environment. Skin plays a vital role in thermal regulation, fluid and electrolyte homeostasis, and protection against bacterial infection. Significant heat and protein loss, massive fluid shifts, and infections all commonly occur in patients with severe thermal injuries. In major burns, circulating mediators trigger systemic inflammation, hypermetabolism, and immune suppression. There is also diffuse alteration in the permeability of cell membranes to sodium, resulting in generalized cellular swelling. Microvascular injury results from local damage by heat and from the release of vasoactive substances from the burned tissue. Therefore, edema occurs in both burned and unburned tissues.
 - a. **Cardiovascular effects**
 1. Alterations in microvascular permeability result in a transcapillary fluid flux and significant tissue edema 12 to 24 hours after a thermal injury. Large amounts of water, electrolytes, and proteins are lost into the extravascular space leading to intravascular fluid depletion and hypovolemic shock (burn shock).
 2. Immediately after a burn injury, the cardiac output is frequently reduced due to decreased preload and myocardial depression, possibly due to circulating humoral factors. Blood pressure may be normal due to increased systemic vascular resistance (SVR). The magnitude of these pathophysiologic changes depends on the size and the depth of the burn injury.
 3. The cardiovascular response 24 to 48 hours after successful resuscitation of a major burn is characterized by an *increase* in cardiac output and *reduced* SVR, consistent with the pathophysiology of the systemic inflammatory response syndrome.
 - b. A **hypermetabolic state** develops 3 to 5 days after the burn injury. For major burn injuries, the estimated caloric need is 1.5 to 1.7 times the calculated basal metabolic rate, and the protein need is near 2.5 g/kg/d. Early initiation of enteral feeding may decrease muscle catabolism and reduce bacterial translocation through the intestinal mucosa. Ambient temperature should be kept within the thermoneutral range to avoid cooling and a further increase in the metabolic rate.
 - c. Capillary leakage results in **hemoconcentration** immediately after injury. Despite apparent adequate fluid resuscitation, the hematocrit level often remains increased during the first 48 hours after injury.

Bleeding from wounds and a shortened erythrocyte half-life, however, can result in anemia.

- d. **Microaggregation of the platelets in the skin and smoke-damaged lung and aggressive volume resuscitation** result in early **thrombocytopenia** after major burns. Thrombotic and fibrinolytic mechanisms are activated, and disseminated intravascular coagulation may complicate the course of a massive burn injury. A decrease in antithrombin III, protein C, and protein S levels can increase the thrombogenicity of these patients later in their clinical course and theoretically can cause venous thrombosis and pulmonary embolism.
 - e. **Acute renal failure** is not uncommon in patients with major burn injury and is associated with high mortality. Decreased renal blood flow secondary to hypovolemia and decreased cardiac output, as well as increased levels of catecholamines, aldosterone, and vasopressin, can contribute to renal failure. Other mechanisms include nephrotoxic effects of drugs, rhabdomyolysis, hemolysis, and sepsis (see Chapter 4).
 - f. **Gastrointestinal function** is diminished immediately after burn injury, secondary to the development of gastric and intestinal ileus. The stomach should be adequately vented with a nasogastric tube.
 1. **Curling ulcers (mucosal erosion)** will occur at variable times after major burns and may lead to gastric hemorrhage or perforation. These ulcers seem to be more common in children than in adults. Therapy consists of antacids, histamine (H_2) receptor antagonists, and proton pump inhibitors.
 2. **Other gastrointestinal complications of burns** include esophagitis, tracheoesophageal fistula (from prolonged intubation and the presence of a nasogastric tube), hepatic dysfunction, pancreatitis, acalculous cholecystitis, and mesenteric artery thrombosis.
 - g. **Infection** of burned areas delays healing and prevents successful skin grafting. Bacterial invasion of underlying tissue may result in septicemia. Common organisms involved are staphylococci, β -hemolytic streptococci, and gram-negative rods such as *Pseudomonas* and *Klebsiella* species. Local treatment with topical antimicrobials and early skin grafting are important measures to reduce risk of infection.
 2. In **electrical burns**, current creates thermal energy that destroys tissue, particularly tissues with high resistance such as skin and bone. Exposure to high voltage can result in compartment syndromes, fractures of long bones and the axial spine, myocardial injury, and rhabdomyolysis with subsequent renal injury.
 3. In **chemical burns**, the degree of injury depends on the chemical, its concentration, duration of contact, and the penetrability and resistance of the tissues involved. Some substances producing chemical burns, such as phosphorus, are absorbed systemically, producing significant and often life-threatening injury. Hydrofluoric acid exposure will cause severe hypocalcemia and requires close monitoring of serum calcium levels. Subeschar injection of calcium gluconate and emergent wound excision may be indicated.
- B. Classification of Burn Injury**
1. Burns are classified according to the total body surface area (TBSA) burned, depth of burn, and the presence or absence of inhalational injury.
 2. **The extent of a burn (TBSA)** is calculated by using a Lund-Browder or other burn diagram.
 - a. The **rule of nines** guides estimation (Fig. 34.2).

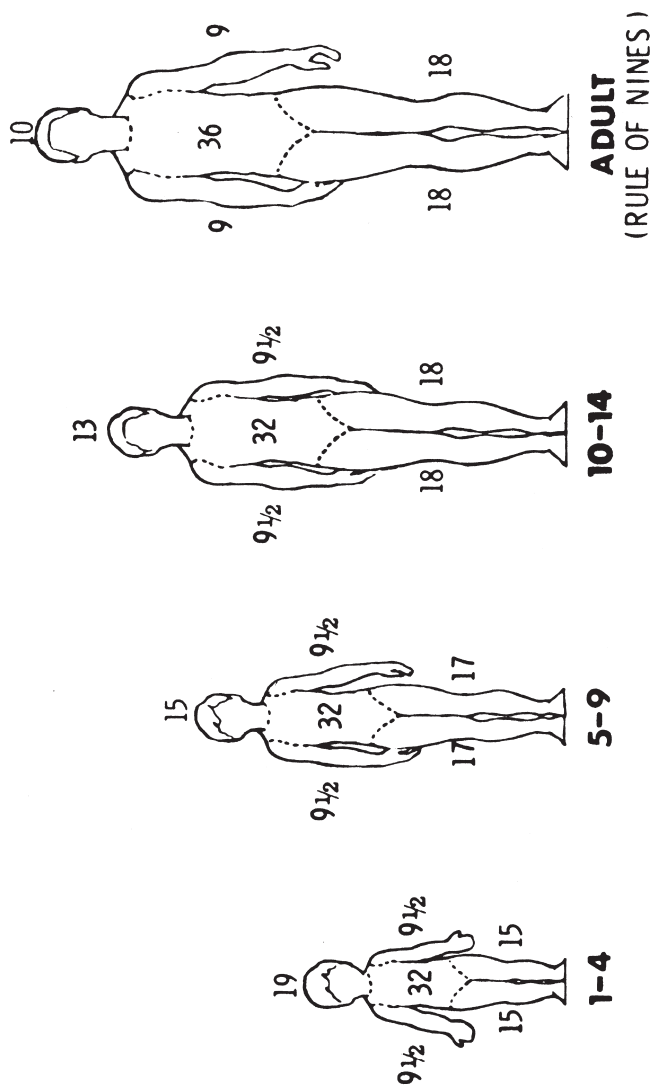


FIGURE 34.2 Rule of nines (Lung and Browder chart). (Modified from Ryan JF, Todres ID, Cote CJ et al., eds. *A Practice of Anesthesia for Infants and Children*. Philadelphia: WB Saunders; 1986:230.)

1. **Adults:** The head and each upper extremity each represent 9% TBSA. The anterior trunk, posterior trunk, and each lower extremity each represent 18% TBSA.
 2. **Infants and children:** Because of the different proportions of body surface area relative to patient age, reference must be made to the proper burn chart when calculating percent TBSA to avoid significant errors (Fig. 34.2).
 - b. Another practical method to estimate percent TBSA is that the area of the patient's hand will cover about 1% TBSA.
 3. The **depth of the burn** determines therapy (i.e., conservative management versus excision and grafting). Burn depth is difficult to determine visually; however, there are some useful guidelines:
 - a. The area under a **partial-thickness burn** should have normal or increased sensitivity to pain and temperature and should blanch with pressure.
 - b. A **full-thickness burn** will be anesthetic and will not blanch with pressure.
- C. Initial Evaluation of the Burn Patient**
1. **Airway and breathing**
 - a. Brief exposure of the epiglottis or larynx to either dry air at 300°C or steam at 100°C leads to massive edema and rapid airway obstruction. Chemical products of combustion such as ammonia, sulfur oxide, and chlorine dissolve in the tracheobronchial tree, forming acids and irritating the mucous membrane of the respiratory tract.
 - b. In general, it is better to tracheally intubate the burn patient early rather than late. Intubation should always be performed before airway edema occurs. Continued swelling and distortion of the soft tissues may progress at a rapid rate, rendering intubation difficult if not impossible.
 - c. **Circumferential full-thickness burns** of the thorax will decrease chest wall compliance, which can lead to hypoxemia and respiratory failure. Emergency escharotomies may be required.
 - d. **Ventilation strategies** involve avoidance of further respiratory compromise from barotrauma caused by increased alveolar distention and shearing forces. Low tidal volume ventilation is recommended. Bronchospasm is frequently present, and bronchodilator therapy with β_2 -agonists is warranted. Intraoperatively, minimize retained secretions and cellular debris by attention to body positioning and frequent suctioning.
 - e. **Smoke inhalation injury** may occur during a fire within a closed space or when heated noxious vapors are inhaled.
 1. An inhalation injury should be suspected in the presence of burns of the head or neck; singed nasal hairs; swelling of the mucosa of the nose, mouth, lips, or throat; a brassy cough; or carbonaceous sputum. Both the upper airway and pulmonary parenchyma may be affected.
 2. **Chemical products** of combustion combine with water in the respiratory tract to form strong acids and alkali, causing bronchospasm, edema, and mucous membrane ulceration. Inhalation of gases such as phosgene and sulfuric acid can damage the alveolar membrane and cause partial or complete airway obstruction. Aldehydes such as acrolein impair ciliary function and damage mucosal surfaces.

3. Combustion of polyurethane-containing products (e.g., insulation and wall paneling) releases **hydrogen cyanide**, which causes tissue asphyxia by inhibiting cytochrome oxidase activity. Patients may present with an anion gap metabolic acidosis and an elevated mixed venous PO_2 . Plasma lactate levels correlate with the cyanide levels. Treatment is supportive but can include administration of sodium nitrite (300 mg IV over more than 5 minutes in a volume of 100 mL of 5% dextrose) followed by sodium thiosulfate (12.5 g) and, in severe cases, inhaled amyl nitrite.
 4. **Carbon monoxide** binds hemoglobin, displacing oxygen and shifting the oxyhemoglobin curve to the left. Tissue hypoxia ensues.
 - a. All burned patients, especially those burned within a closed space, may have sustained some degree of tissue hypoxia with their thermal injury. Oxygen administration should begin at the scene.
 - b. Because oxyhemoglobin and carboxyhemoglobin (CO) absorb light at the same wavelength, conventional pulse oximetry cannot be used as an indicator of CO poisoning. Diagnosis is made on clinical suspicion and the level of arterial or venous CO, measured spectrophotometrically with a CO oximeter.
 - c. The half-life of CO is inversely related to the inspired oxygen concentration (FiO_2); it is 5 to 6 hours when breathing room air but 30 to 60 minutes when breathing 100% oxygen.
 - d. Treatment is supportive and consists of supplemental oxygen until the carbon monoxide is eliminated. Hyperbaric oxygen should be considered in comatose patients and in those with severe carbon monoxide poisoning.
 - e. **Indirect respiratory injury** and pulmonary edema may occur in burn patients without an inhalational injury. Mechanisms involved include the effect of burn wound mediators on the lung, decreased plasma oncotic pressure, and complications of burn therapy.
2. **Cardiovascular resuscitation**
- a. **Fluid replacement** consists of crystalloid, usually Ringer lactate, with or without the addition of colloid. Standard protocols for fluid replacement use body weight in kilograms and percent TBSA burned.
 1. **Parkland formula** (most commonly used at the Massachusetts General Hospital): 4.0 mL of Ringer lactate per kg per % TBSA burn per 24 hours (see section V.C.2.b below).
 2. **Brooke formula**: 1.5 mL of crystalloid per kg per % TBSA burn per 24 hours plus 0.5 mL of colloid per kg per % TBSA burn per 24 hours plus 2,000 mL of 5% dextrose in water per 24 hours (see section V.C.2.b. below).
 - b. Half the calculated fluid deficit is administered during the first 8 hours postburn, and the remainder is administered over the next 16 hours. The patient's daily maintenance fluid requirements are given concurrently.
 - c. The end points of fluid therapy are hemodynamic stability and maintenance of an adequate urine output. In extensive burns, fluid management is adjusted according to appropriate invasive monitors and laboratory studies.

D. Management of the Burn Wound

1. **Early excision and grafting of burned areas** is a widely accepted procedure and appears to decrease mortality. Patients may be brought to the operating room in the acute phase of injury, with hemodynamic instability and respiratory dysfunction. Special emphasis should be placed on correcting acid–base and electrolyte disturbances and coagulopathy. Blood loss during wound excision and grafting can be massive. Adequate colloid and blood products should be ordered in advance. IV access should be adequate for resuscitation.
2. Topical agents are used to minimize the colonization of healing wounds. Common topical agents include the following:
 - a. **Silver nitrate** may cause serum hyponatremia or, rarely, methemoglobinemia.
 - b. **Mafenide acetate**, a carbonic anhydrase inhibitor, may cause metabolic acidosis if absorbed.
 - c. **Silver sulfadiazine** may cause leukopenia, which is reversible upon discontinuing the drug.
3. The incidence of **sepsis** may be reduced by using temporary biologic dressings, either allografts (cadaver skin or amnion) or xenografts (porcine). Artificial skin (e.g., Integra) bioengineered from collagen and cultured epidermis can be used when a conventional autograft is not available.
4. The use of **systemic antibiotics** is limited to treatment of documented systemic infection (as opposed to colonization), and they are also used as prophylaxis before surgical procedures.

E. Anesthetic Considerations

1. **Burns are a form of trauma**; thus, the same A, B, C, D, and E as previously described (see sections I.A to I.E) for trauma should be initially assessed. The patient's age, preexisting disease, and the extent of burn injury provide an index of the patient's likely physiologic condition. Altered pharmacokinetics, drug tolerance, difficult IV access, and anatomic derangements of the airway (neck scar or mouth contracture) are main considerations.
2. **Airway.** Obtaining an adequate mask fit may be difficult because of edema in the early phases of burn injury or because of scars and contractures later on. The same processes can render endotracheal intubation extremely difficult in burn patients.
3. **Monitoring and IV access (Table 34.2)**
 - a. Often IV access will still be in place from the initial resuscitation. Large-bore IVs are mandatory to allow for massive fluid replacement.
 - b. In massive burns, ECG electrodes may be placed directly on debrided tissue. Alternatively, needle electrodes can be used.
 - c. **Arterial lines** are indispensable for continuous blood pressure monitoring and frequent blood sampling. The cannulation site will depend on the availability of unburned areas. If all appropriate sites are burned, the line may have to be placed through the burn wound after the area has been prepared in a sterile fashion.
 - d. **Central venous pressure lines** are useful both for monitoring central pressures and for central access for drug infusions.
 - e. A **pulmonary artery catheter** may be required for management of patients with myocardial dysfunction, persistent oliguria or hypotension, or sepsis.
4. **Muscle relaxants.** **Extrajunctional nicotinic receptors** proliferate in muscle at the burn site and at sites distant from the burn injury. Succinylcholine

TABLE 34.2 Intraoperative Monitoring Challenges in Patients with Major Burn Injury

Monitor	Possible Challenges of Burn Injury	Possible Solutions
Electrocardiography (ECG)	ECG electrodes may not adhere	Consider needle electrodes or stapling of electrodes
Noninvasive blood pressure monitor	Edema or extensive burns in the extremities may limit use of cuff	Consider alternative location, use dressing or gauze under cuff
Invasive blood pressure monitor	Hypothermia, hypovolemia, initial decreased cardiac output, vasoconstriction	Consider invasive monitoring, trend values, confirm with noninvasive blood pressure
Pulse oximetry	Extensive burn injury may limit placement. Carboxyhemoglobin will falsely elevate oxygen saturation reading	Consider alternative location, trend values, assess partial pressure of oxygen by ABG

is only safe in the immediate 12 to 24 hours after thermal injury. An increase in acetylcholine receptors is usually associated with resistance to nondepolarizing neuromuscular-blocking agents, increased sensitivity to depolarizing muscle relaxants, and life-threatening hyperkalemia when succinylcholine is used.

5. Anesthetics

a. There is no single preferred agent or combination of agents; however, **ketamine** and **etomidate** may have advantages in patients with a tenuous hemodynamic status.

b. These patients may have **greatly increased opioid requirements** due to tolerance and an increase in the apparent volume of distribution for drugs. It is important to provide adequate analgesia, which may necessitate massive doses of opiates.

6. **Temperature regulation.** The most comfortable body temperature for a burn patient is about 100°F (38°C). In the burn intensive care unit, patients are cared for in warmed, humidified rooms. Every effort should be made to maintain normothermia during transport and surgery. The operating room, IV fluids, and blood products should be warmed and inspired gases heated and humidified. Pediatric patients should be placed under a radiant heat source and on a warming blanket whenever possible.

7. **Immunosuppression.** The immune system is suppressed for weeks to months after burn injury, and the wound itself serves as an excellent medium for bacterial growth. Every attempt should be made to practice aseptic technique when handling patients, suctioning airways, and inserting intravascular lines.

8. **Postanesthetic care.** It is important to maintain normothermia while transporting patients back to the intensive care unit because shivering results in vasoconstriction and could contribute to graft loss. Supplemental oxygen should be given until patients are fully recovered from anesthesia. Severe pain is common, and patient responses vary, necessitating individual titration of analgesics and frequent reassessment of the effect.

Suggested Readings

- American College of Surgeons. *Advanced Trauma Life Support (ATLS) Student Manual*. 9th ed. Chicago: American College of Surgeons; 2012.
- Bickell WH, Wall MJ Jr, Pepe PE, et al. Immediate versus delayed fluid resuscitation for hypotensive patients with penetrating torso injuries. *N Engl J Med* 1994;331:1105–1109.
- Duchesne JC, Barbeau JM, Islam TM, et al. Damage control resuscitation: from emergency department to the operating room. *Am Surg* 2011;77(2):201–206.
- Kaiser HE, Kim CM, Sharar SR, et al. Advances in perioperative and critical care of the burn patient. *Adv Anesth* 2013;31(1):137–161.
- Martyn JA, Richtsfeld M. Succinylcholine-induced hyperkalemia in acquired pathologic states: etiologic factors and molecular mechanisms. *Anesthesiology* 2006;104:158–169.
- Neschis DG, Scalea TM, Flinn WR, et al. Blunt aortic injury. *N Engl J Med* 2008;359(16):1708–1716.
- Roberts I, Shakur H, Ker K, et al.; CRASH-2 Trial collaborators. Antifibrinolytic drugs for acute traumatic injury. *Cochrane Database Syst Rev* 2012;12:CD004896.
- Theusinger OM, Madjdpour C, Spahn DR. Resuscitation and transfusion management in trauma patients: emerging concepts. *Curr Opin Crit Care* 2012;18(6):661–670.
- Watson D. ABC of major trauma. Management of the upper airway. *BMJ* 1990;300:1388–1391.

I. THE DECISION TO INITIATE TRANSFUSION THERAPY

The decision to transfuse is complicated. There are many risks to transfusion (see section VIII), and transfusion is ultimately indicated when the potential benefits outweigh these risks. In most civilian settings, transfusion therapy utilized blood components rather than whole blood. The benefits of blood component transfusion stem from the correction of conditions that result in decreased production; increased utilization, destruction, or loss; or dysfunction of a specific blood component (red cells, platelets, or coagulation factors). Although many attempts at creating universal transfusion protocols have been introduced, few have successfully demonstrated definitive thresholds or clear superiority. Our aim in this chapter is to provide the background to help make these decisions on an individual basis.

A. Assessing Red Cell Mass and Oxygen-Carrying Ability

1. **The decision to transfuse.** Most evidence suggests that higher red cell transfusion thresholds (e.g., 10 to 12 g/dL) do not confer a mortality benefit and may even be harmful. Nonetheless, maintaining adequate red cell mass is essential for adequate oxygen-carrying capacity to the tissues. The decision to transfuse, therefore, must be based on a variety of patient and situational factors rather than rigid guidelines.
2. **Patient factors.** The main reason for transfusing red cells is to maintain oxygen-carrying capacity to the tissues, a primary determinant of which is the hemoglobin (Hb) level.
 - a. **Healthy individuals or individuals with chronic anemia** can usually tolerate Hb levels of 6.5 to 8 g/dL, assuming normal intravascular volume. The use of a "restrictive transfusion practice," aiming for Hb of 7 to 9 g/dL, is generally safe and may reduce the risk of death compared with transfusing toward a higher (10 to 12 g/dL) Hb goal. The reason for reduced mortality in the restrictively transfused group has not been clearly delineated, but the effects of allogeneic transfusion on diminished immune function have been substantiated in animal and human studies (see section VIII.D).
 - b. For **patients with coronary artery disease**, the risk of myocardial ischemia due to anemia has resulted in most practitioners transfusing to a higher (9 to 10 g/dL) Hb level. As the incidence of coronary artery disease rises substantially with age, many practitioners opt to use higher transfusion threshold in the elderly. Studies to support this practice, however, are lacking, and those that exist have produced contradictory results. A study of medical patients with acute coronary syndromes also found a higher mortality rate attributable to red cell transfusion in otherwise stable patients with a hematocrit (Hct) greater than 25%.
3. **Situational factors**
 - a. **Intraoperative blood transfusion** depends on red cell loss. This can be roughly estimated by measuring blood in suction canisters, weighing sponges, and checking blood loss in the drapes. In the perioperative period, the most common indication for transfusion is hemorrhage. During ongoing blood loss, it may be indicated to

transfuse even with a Hb greater than 10 g/dL if bleeding is brisk enough that the practitioner expects a substantial drop in the Hb in the absence of treatment.

- b. If a patient is anemic preoperatively, the etiology should be clarified. It may be secondary to decreased production (marrow suppression or nutritional deficiencies), increased loss (hemorrhage), or destruction (hemolysis).

4. Estimating blood volumes (BVs)

- a. **Estimated allowable blood loss (EABL)** can be calculated as follows, using either Hcts (as shown) or Hbs:

$$\text{EABL} = [(\text{Hct}_{\text{starting}} - \text{Hct}_{\text{allowable}}) \times \text{BV}] / [(\text{Hct}_{\text{starting}} + \text{Hct}_{\text{allowable}}) / 2]$$

BV in an adult is approximately 7% of lean body mass. This may be calculated as approximately 70 mL/kg of body weight in a normal adult man and approximately 65 mL/kg of body weight in a normal adult woman (see Chapter 31, for pediatric considerations). Obese patients have a lower percentage of body weight as blood, and the greater the degree of obesity, the lower the BV estimate on a per-kilo basis. With a body mass index (BMI) of 40, 53 mL/kg has been suggested. BV in patients with a BMI of 70 is estimated using 40 mL/kg of actual body weight.

- b. **Estimating the volume of blood to transfuse** can be calculated as follows:

$$\text{Volume to transfuse} = [(\text{Hct}_{\text{desired}} - \text{Hct}_{\text{present}}) \times \text{BV}] / \text{Hct}_{\text{transfused blood}}$$

A unit of packed red blood cells (PRBCs) has a Hct of 70% to 85% using the Adsol preservative.

- B. Thrombocytopenia** is due to either decreased bone marrow production (e.g., chemotherapy, tumor infiltration, or alcoholism) or increased utilization or destruction (e.g., trauma or surgery creating a large wound, hypersplenism, idiopathic thrombocytopenia purpura [ITP], disseminated intravascular coagulation [DIC], or drug effects). It is also seen with the dilution and loss associated with massive blood transfusion (see section IX.A.1). Spontaneous bleeding is unusual with platelet counts above 20,000/mm³. Platelet counts above 50,000/mm³ are preferable for surgical hemostasis, with the caveat that, much like with RBCs, the decision to transfuse must be made based upon clinical factors rather than merely the platelet count. For example, patients with ITP maintain high platelet turnover and will often have normal coagulation despite a low platelet count. In addition, as the process lowering the platelet count is destructive, they will not respond well to platelet transfusion.
- C. Coagulopathy.** Bleeding associated with documented factor deficiencies or prolonged clotting studies (prothrombin time [PT] and partial thromboplastin time [PTT]) mandates replacement therapy to maintain normal coagulation function. See sections II and IX for a discussion of coagulopathy.

II. COAGULATION STUDIES

The most important clue to a clinically significant bleeding disorder in an otherwise healthy patient remains in the history. A history of anemia requiring iron replacement may suggest a bleeding tendency. Prior surgical bleeding, gingival bleeding, easy bruising, epistaxis, or menorrhagia should raise concern. Many tests are available to assess the coagulation system. However, the clinician must remember that the coagulation system is a complex interplay of platelets and coagulation factors.

- A. Activated partial thromboplastin time (aPTT)** is performed by adding particulate matter to a blood sample to activate the intrinsic coagulation system. Normal values for the PTT are 22 to 34 seconds, varying according to the reagent and instruments used by the specific laboratory. The aPTT assesses factors in the intrinsic (XI, XII, VIII, IX, and contact factors) and the common (II, V, X, and fibrinogen) coagulation pathways. The test is sensitive to decreased amounts of coagulation factors and is elevated in patients on heparin therapy. The aPTT will be abnormal in patients who have hemophilia or a circulating anticoagulant (e.g., lupus anticoagulant or antibodies to factor VIII). The clinician should remember that an abnormal aPTT does not necessarily correlate with clinical bleeding. Aggressive correction of an abnormal aPTT in surgical patients is not always indicated, unless the patient is actively bleeding.
- B. Prothrombin time** is a measure of factors of the extrinsic (VII and tissue factor) and common (see above) coagulation pathways and is measured by adding tissue factor to a blood sample. While both PT and aPTT are affected by levels of factors V and X, prothrombin, and fibrinogen, the PT is specifically sensitive to deficiencies of factor VII. The PT is normal in deficiencies of factors VIII, IX, XI, XII, prekallikrein, and high molecular weight kininogen.
- C. The international normalized ratio (INR)** is a means of standardizing PT values to allow comparisons among different laboratories or at different times. It is the ratio of the patient's PT to the control PT value that would be obtained if international reference reagents had been used to perform the test. Oral warfarin anticoagulation therapy may therefore be guided by a target INR value that is independent of the laboratory variability of the PT. For example, an INR of 2.0 to 3.0 is recommended for prophylaxis against thromboembolism in atrial fibrillation.
- D. Activated clotting time (ACT)** is a modified whole blood clotting time in which diatomaceous earth (celite) or clay (kaolin) is added to a blood sample to activate the intrinsic clotting system. The ACT is the time until clot formation. A normal ACT is 90 to 130 seconds, depending on the instrument used. The ACT is a relatively easy and expedient test to perform and is useful in monitoring heparin therapy in the operating room (see Chapter 24). Because the ACT is relatively insensitive to lower levels of heparin anticoagulation, it is typically reserved for settings that require full anticoagulation such as cardiopulmonary bypass and extracorporeal membrane oxygenation (ECMO).
- E. Fibrinogen** is the precursor protein that is dimerized to form the strong fibrin components of clots. Assaying fibrinogen levels can be helpful when coagulopathy is present or suspected. While the diagnostic specificity of the fibrinogen level is low, it can be helpful to guide further transfusion support (i.e., the administration of FFP or cryoprecipitate).
- F. Thromboelastography (TEG)** is available in some centers for clinical use, often as a point-of-care test. TEG is performed by placing a small aliquot of blood into a heated oscillating cup into which is suspended a pin on a torsion wire. Clot formation in the oscillating cup generates torque on the pin, and the torque is measured and converted to an electrical signal. The signal is recorded by a computer, creating a characteristic trace (Fig. 35.1) that may be analyzed for abnormalities of clot formation. By measuring clot formation and viscoelastic clot strength, TEG provides information about the adequacy of clotting factors, fibrin levels, and platelets.

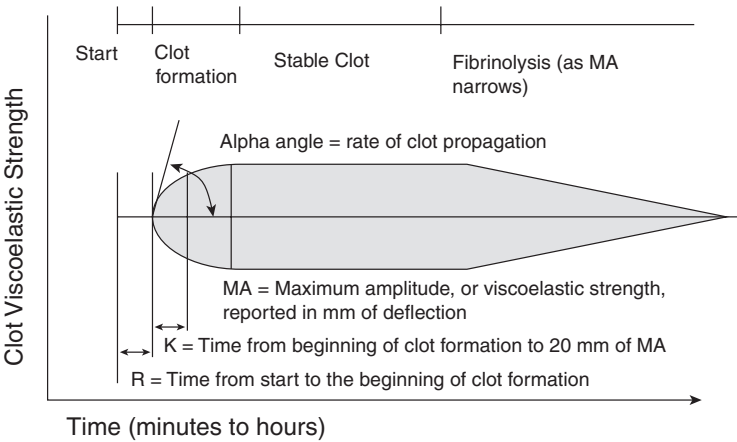


FIGURE 35.1 Thromboelastography.

In general, R represents the activity of coagulation factors, maximum amplitude the platelet function/number, and the alpha angle the acceleration of fibrin formation. Thromboelastometry or ROTEM uses a similar technology, with similarly measured parameters.

III. BLOOD TYPING AND CROSS-MATCHING

A. Donor blood and recipient blood are typed using the red cell surface **ABO and Rh systems** and screened for antibodies to other cell antigens. “Direct” cross-matching involves directly mixing the patient’s plasma with the donor’s red cells to establish that hemolysis does not occur from any undetected antibodies. An individual’s red cells have A, B, AB, or no surface antigens, which is then designated type O. If the patient’s red cells are lacking either surface antigen A or surface antigen B, then antibodies will be produced against it. A person who is type B will have anti-A antibodies in the serum, and a type O individual will have circulating anti-A and anti-B antibodies. Consequently, a person who is type AB will not have antibodies to either A or B and can receive red blood cells (RBCs) from any blood type. Type O blood has neither A nor B surface antigens and can donate blood cells to any other type (universal red cell donor; Table 35.1).

TABLE 35.1 Transfusion Compatibility		
Recipient Blood Type	RBC Donor	FFP Donor
AB	AB, A, B, or O	AB
A	A or O	A or AB
B	B or O	B or AB
O	O	A, B, AB, or O
Rh+	Rh+ or Rh−	Rh+ or Rh−
Rh−	Rh−	Rh+ or Rh−

The universal FFP donor, conversely, is AB because it will contain neither anti-A nor anti-B antibodies. Whole blood donors and recipients must be exact ABO matches because whole blood contains both RBCs and serum. For example, a unit of type O whole blood will contain serum with anti-A and anti-B antibodies and therefore cannot be used to transfuse patients who are A, B, or AB blood types.

- B. Rh surface antigens** are either present (Rh-positive) or absent (Rh-negative). Individuals who are Rh negative will develop antibodies to the Rh factor when exposed to Rh-positive blood. This is not a problem with the initial exposure, but with subsequent exposures, hemolysis will occur due to the circulating antibodies. This can be a particular problem during pregnancy. The anti-Rh antibodies are IgG and freely cross the placenta. Rh-negative mothers who have developed Rh antibodies will transmit these antibodies to the fetus. If the fetus is Rh positive, massive hemolysis will occur. **RHO immune globulin**, an Rh-blocking antibody, prevents the Rh-negative patient from developing anti-Rh antibodies. It should be administered to Rh-negative individuals who receive Rh-positive blood and to Rh-negative mothers delivering Rh-positive babies (some fetal maternal blood mixing occurs at delivery). The recommended dose is 300 μ g intramuscularly for every 15 mL of Rh-positive blood transfused.
- C. Recipient antibodies** against other donor RBC antigens (most frequently those from the Kell, Kid, Duffy, or Lewis groups) can cause hemolytic transfusion reactions. When a patient's blood sample is screened and found to have antibodies against antigens found on donor RBCs, it complicates cross-matching and can delay the availability of blood products. When a patient's antibody screen is positive, it is advisable to discuss the anticipated transfusion needs with the blood bank.
- D. If an emergency blood transfusion is needed**, type-specific (ABO) red cells usually can be obtained within minutes if the patient's blood type is known. If type-specific blood is unavailable, type O Rh-negative red cells should be transfused (type O-positive blood can be used emergently in males). Type-specific blood should be substituted as soon as possible to minimize the amount of type O plasma (containing anti-A and anti-B antibodies) transfused.

IV. BLOOD COMPONENT THERAPY

A. General Considerations

1. One unit of **PRBCs** (Hct about 70% and volume about 250 mL) usually will increase the Hct by 2% to 3% or the Hb by 1 g/dL in an euvolemic adult once equilibration has taken place. PRBCs must be ABO compatible to the recipient.
2. One unit of **platelets** increases the platelet count by 5,000 to 10,000/ mm^3 . A usual platelet transfusion is 1 unit per 10 kg of body weight. If thrombocytopenia is caused by increased destruction (due to development of antiplatelet antibodies) or if platelets are dysfunctional, platelet transfusions will be less efficacious. Transfusion of ABO-compatible platelets is not obligatory, although they may provide a better posttransfusion platelet count. Single-donor or HLA-matched platelets may be required for patients with a refractory response to platelet transfusion. A unit of single-donor platelets provides the equivalent of approximately six random donor units of platelets. **Platelets should never be stored in a cooler.**
3. **Fresh frozen plasma** (FFP, about 250 to 300 mL per unit), in a dose of 10 to 15 mL/kg, generally will increase plasma coagulation factors to 30% of normal, the minimal level necessary for hemostasis (excepting fibrinogen where 50% of the normal 200 to 400 mg/dL is required).

Fibrinogen levels increase by 1 mg/dL/mL of plasma transfused. Acute reversal of warfarin is often achieved with only 5 to 8 mL/kg of FFP, although the PT may remain modestly prolonged. FFP transfusions must be ABO compatible, but Rh compatibility and cross-matching are not required (Table 35.1).

4. **Cryoprecipitate** is prepared from FFP and contains concentrated factor VIII, factor XIII, fibrinogen, von Willebrand factor (vWF), and fibrinectin. Indications for cryoprecipitate include hypofibrinogenemia, von Willebrand disease, hemophilia A (when factor VIII is unavailable), and preparation of fibrin glue. Dosage is 1 unit per 7 to 10 kg, which will raise the plasma fibrinogen by about 50 mg/dL in a patient without massive bleeding. ABO compatibility is not mandatory for cryoprecipitate transfusion.

B. Technical Considerations

1. **Compatible infusions.** Blood products should not be infused with 5% dextrose solutions, because they cause hemolysis. Recent studies have suggested that coinfusion with lactated Ringer's, which contains calcium may not induce clot formation, but concern persists. Coadministration of blood products with Plasmalyte solutions is probably safe. Normal saline (0.9%) solution, albumin (5%), and FFP are compatible with RBCs.
2. **Blood filters.** Standard blood filters (170 to 200 μ m) remove debris and should be used for all blood components.
 - a. **Leukocyte reduction is achieved by filtration, either in the blood bank or at the bedside.** Microaggregate filters (20 to 50 μ m), which should not be used for platelets, remove 70% to 90% of leukocytes. Third-generation or adhesion filters remove more than 99.9% of leukocytes via a combination of filtration and adhesion of white blood cells. These filters are recommended for use in patients with a history of febrile, nonhemolytic transfusion reactions; for prevention of alloimmunization to foreign leukocyte antigens (e.g., in the oncologic patient expected to require multiple platelet transfusions); or to prevent cytomegalovirus (CMV) transmission in organ transplant recipients. Other potential but as yet unproved benefits of leukocyte reduction include a diminished immunomodulatory effect of allogeneic transfusion; reduced transmission of bacterial, viral, or prion diseases; prevention of transfusion-related acute lung injury (TRALI); and decreased incidence of graft versus host disease (GVHD). Several countries have implemented universal leukoreduction of transfused cellular blood products. The proposed benefits and cost-efficiency of universal leukoreduction are a matter of significant controversy within transfusion medicine and are not mandatory in the United States at this time.
 - b. Manufacturer recommendations for specific bedside blood filters should be followed with respect to the component to be filtered and the number of units administered per filter.
 - c. Severe **hypotensive reactions** associated with the use of bedside leukocyte reduction filters have been reported. The pathophysiology may involve activation of bradykinin by the leukocyte filter, and the hypotensive effect may be exaggerated in patients taking ACE inhibitors. When this reaction occurs, the transfusion should be stopped and the blood pressure supported. These interventions usually result in rapid resolution of hypotension. Products that are leukoreduced in the blood bank may carry a lower risk of this hypotensive reaction as bradykinin is rapidly metabolized in stored blood.

- C. Massive Transfusion.** Transfusion of 10 or more units of PRBCs, or one BV, in a 24-hour period can be considered massive transfusion. During episodes of massive transfusion, coordination with the blood bank is important. Initial management should be aimed at correcting causes of the hemorrhage, for example, giving several units of FFP to correct a greatly elevated INR, prior to following any formal ratio. A ratio of two units of PRBCs to one unit of FFP (2:1) with a judicious amount of a crystalloid or colloid volume expander is a time-honored approach to replacement of red cells and clotting factors during massive transfusion. Several authors suggest other ratios (like 1:1), but this approach has not proved to be beneficial. Platelet counts may be expected to fall by half for each BV that is hemorrhaged. Early transfusion of platelets and consideration of antifibrinolytics may be beneficial.
- D. Blood Substitutes.** Despite years of research intent upon finding a blood substitute capable of oxygen transport, none provides general clinical usefulness at this time. Hemoglobin-based blood substitutes continue to be an area of research.

V. PLASMA SUBSTITUTES

Various colloid products are available commercially. Their main limitations are their cost, potential allergic reactions, and their effects on coagulation.

- A. Albumin** is available as either an isotonic 5% or a hypertonic 20% or 25% solution. Albumin has an intravascular half-life of 10 to 15 days. Although frequently used to avoid high volumes of crystalloid infusion, evidence supporting its routine use over crystalloids is lacking, and its cost is substantially higher than crystalloids. For these reasons, many authors argue against the routine use of albumin.
- B. Hydroxyethyl starch** (hetastarch, Voluven [R]) is manufactured from amylopectin. Hetastarch's effects on coagulation include decreased fibrinogen, vWf, and factor VIII levels as well as decreased platelet function. It has also been shown to increase rates of renal failure and mortality in patients with severe sepsis and is now rarely used.

VI. PHARMACOLOGIC THERAPY

- A. Erythropoietin** increases RBC mass by stimulating proliferation and development of the erythroid precursor cells. It can be used before elective surgery to increase RBC production. Its role in the perioperative period is unclear. Concern remains that its use will increase the incidence of venous and arterial thrombotic events.
- B. Desmopressin.** DDAVP is an antidiuretic hormone that is known to be helpful in patients with mild hemophilia A and in some patients with von Willebrand disease. Desmopressin increases endothelial cell release, but not production, of vWf, factor VIII, and plasminogen activator. Desmopressin is also useful for patients with platelet defects associated with uremia. The dosage of desmopressin is 0.3 $\mu\text{g}/\text{kg}$ diluted in normal saline and administered over 30 minutes. Tachyphylaxis is possible if dosing is greater than every 48 hours. The intravenous (IV) dose should be given slowly, because hypotension or hypertension may occur.
- C. The lysine analogues,** aminocaproic acid and tranexamic acid, inhibit fibrinolysis, the endogenous process by which fibrin clot is broken down. They act by displacing plasminogen from fibrin, diminishing plasminogen conversion to plasmin, and preventing plasmin from binding to fibrinogen or fibrin monomers. Trials have shown that tranexamic acid may be useful in the early treatment of trauma victims to reduce bleeding and mortality.

The uses of aminocaproic acid include prophylaxis for dental surgery in hemophiliacs, reduction of bleeding in prostatic surgery, and reduction of hemorrhage in cases of excessive fibrinolysis. Because cardiopulmonary bypass has been shown to initiate fibrinolysis, aminocaproic acid has been used during cardiac surgery to decrease postoperative chest tube drainage. The drug's efficacy at diminishing blood transfusion has been demonstrated only when the transfusion trigger was low (Hb approximately 7 g/dL). Theoretic risks of thrombosis with aminocaproic acid have not been demonstrated clinically; nevertheless, the drug is contraindicated in DIC. Dosage in adults is 5 g IV load over 1 hour followed by 1 to 2 g/h IV infusion.

VII. CONSERVATION AND SALVAGE TECHNIQUES

- A. Autologous donation** usually begins 6 weeks before surgery and can reduce greatly the amount of homologous blood transfused. The length of the predonation period is limited by the length of time that blood can be stored, currently 42 days unless the blood is frozen. Current blood bank guidelines require a predonation Hb of at least 11 g/dL, donations no more frequently than every 3 days, and no donations in the 72 hours before surgery. Most patients tolerate autologous donation without complication. Patients with severe aortic stenosis or unstable angina are not candidates for autologous donation. Patients donating autologous blood should receive supplemental iron because depleted iron stores frequently limit RBC recovery. Recombinant erythropoietin treatment (see section VI.A) also may be considered. Because a risk of transfusion reaction exists due to clerical error, autologous blood should not be transfused unless a transfusion is clinically indicated.
- B. Normovolemic Hemodilution.** Preoperative or intraoperative hemodilution entails phlebotomizing a patient of one or more units of fresh whole blood while replacing the lost volume with either colloid or crystalloid. By using normovolemic hemodilution before intraoperative blood loss, fresh autologous blood is available for later reinfusion after surgical blood loss is complete. Also, any blood shed after hemodilution will constitute more plasma loss and less red cell loss. Hemodilution may also be helpful in situations in which platelet function is altered intraoperatively (e.g., cardiopulmonary bypass), because the phlebotomized blood has normal platelets and clotting factors when reinfused. Obviously, if surgical blood loss is extreme, the fresh autologous blood should be transfused before any homologous blood. It should also be remembered that the autologous blood has a Hct similar to the patient's preoperative Hct, as opposed to a unit of PRBCs, which has a Hct of approximately 70%. While hemodilution alone may not eliminate the need for homologous transfusion, when used in combination with preoperative autologous donation, it may decrease the need for homologous units. Unless the preoperative Hct is high, the patient can tolerate a low target Hct, and the expected blood loss is large; normovolemic hemodilution will only modestly diminish the need for homologous transfusion.
- C. Intraoperative autotransfusion** (cell saver) utilizes blood collected from the surgical field by a double-lumen suction device. As the shed blood is suctioned from the surgical field into one lumen, it is mixed with an anticoagulant (citrate-phosphate-dextrose or heparin) solution from the other lumen to prevent clotting of the blood in the filtered collecting reservoir. The blood then undergoes a series of steps of filtering, centrifuging, and washing designed to remove debris, plasma, free Hb, and anticoagulant.

The final product is a collection bag of RBCs having a Hct of 50% to 70%, which is ready for reinfusion immediately after about 3 minutes of processing time. Blood collected via intraoperative autotransfusion is deficient in plasma, clotting factors, and platelets. The technique is generally restricted to clean surgical fields and nononcologic procedures because of risks of reinfusing bacteria or tumor cells into patients.

VIII. COMPLICATIONS OF BLOOD TRANSFUSION THERAPY

A. Transfusion Reactions

1. **Acute hemolytic transfusion reactions** occur when ABO-incompatible blood is transfused, resulting in recipient antibodies attaching to donor RBC antigens and forming an antigen–antibody complex. This antigen–antibody complex activates complement, resulting in intravascular RBC lysis with release of RBC stroma and free Hb. Immune system activation also results in bradykinin release (leading to hypotension) and mast cell activation (causing serotonin and histamine release). The net result may be shock, renal failure due to Hb precipitation in renal tubules, and DIC (see section IX.B). Many signs and symptoms of an acute hemolytic transfusion reaction appear immediately and include fever, chest pain, anxiety, back pain, and dyspnea. Many are masked by general anesthesia, but clues to the diagnosis include fever, hypotension, hemoglobinuria, unexplained bleeding, or failure of Hct to increase after transfusion. Table 35.2 indicates steps to take if a transfusion reaction is suspected. The incidence of fatal hemolytic transfusion reaction in the United States is approximately 1 of every 250,000 to 1,000,000 units transfused. Most reactions occur because of administrative errors, with most due to improper identification of the blood unit or patient. The importance of adhering to strict policies of checking blood and matching to the correct patient in the operating room cannot be overemphasized.
2. **Delayed hemolytic transfusion reactions** occur because of incompatibility of minor antigens (e.g., Kidd) and are characterized by extravascular hemolysis. They present 2 days to months after transfusion. Patients complain of no or minimal symptoms but may display signs of anemia and jaundice. Laboratory studies reveal a positive direct antiglobulin test, hyperbilirubinemia, decreased haptoglobin levels, and hemosiderin in the urine. Treatment is aimed at correcting the anemia.

TABLE 35.2	Approach to Suspected Acute Hemolytic Transfusion Reaction

1. *Stop the transfusion.*
2. Quickly check for error in patient identity or donor unit.
3. Send donor unit and newly obtained blood sample to blood bank for recross match.
4. Treat hypotension with fluids and vasopressors as necessary.
5. If transfusion is required, use type O-negative PRBC and type AB FFP as necessary.
6. Support renal function: first, administer fluids to correct hypovolemia and second, administer diuretics (furosemide $\pm$ mannitol) to maintain brisk urine output.
7. Monitor for signs of DIC clinically and with appropriate laboratory studies; treat supportively (see section IX.B).
8. Send patient blood sample for direct antiglobulin (Coombs) test, free Hb, and haptoglobin; send urine for Hb

DIC, disseminated intravascular coagulation; FFP, fresh frozen plasma; PRBC, packed red blood cells.

3. **Febrile nonhemolytic transfusion reactions (FNHTR)** are the most common transfusion reactions, occurring in approximately 1% of RBC transfusions and up to 30% of platelet transfusions. They occur when antileukocyte antibodies in a recipient react with white blood cells in a transfused blood product. Signs and symptoms include fever, chills, tachycardia, discomfort, nausea, and vomiting. Approach to treatment involves first stopping the transfusion and excluding an acute hemolytic transfusion reaction or bacterial contamination of the donor unit. Acetaminophen and meperidine may diminish fever and rigors. Once the diagnosis of FNHTR has been made, future reactions may be avoided or diminished by administering leukocyte-reduced blood products (see section IV.B.2), premedicating at-risk patients with acetaminophen and hydrocortisone (50 to 100 mg IV), and administering the transfusion slowly.
4. **Allergic transfusion reactions** are common, occurring in 1% to 3% of transfusions. They arise from recipient antibody response to donor plasma proteins. Urticaria with pruritus and erythema is the most common manifestation, but rarely bronchospasm or anaphylaxis presents. Many patients also have a fever. Patients with IgA deficiency may be at increased risk of allergic transfusion reaction because of the presence of anti-IgA antibodies that react with transfused IgA. Treatment involves stopping the transfusion, excluding a more severe reaction (see above), and administering antihistamines (diphenhydramine 50 mg IV and ranitidine 50 mg IV). A significant reaction may warrant treating with a corticosteroid (methylprednisolone 80 mg IV). Bronchospasm and anaphylaxis should be treated as described in Chapter 19.
5. **Transfusion-Related Acute Lung Injury (TRALI)** is a condition of severe pulmonary insufficiency following blood, FFP, cryoprecipitate, or platelet transfusion. Signs and symptoms include fever, dyspnea, hypoxemia, hypotension, and pulmonary edema developing within 4 hours of transfusion. TRALI happens when anti-HLA antibodies and antileukocyte antibodies present in donor plasma cause the recipient leukocytes to injure their own tissues. Most cases are tracked to women donors who have previously been pregnant and developed anti-HLA antibodies and measures to prevent plasma donation by women who have been pregnant may reduce TRALI-related episodes.
6. **TACO** (transfusion-associated circulatory overload) is a condition of circulatory congestion secondary to the fluid volumes administered as transfusions. The symptoms are similar to congestive heart failure and include dyspnea, pulmonary edema, tachycardia, and increased jugular venous distention. While TRALI also produces pulmonary edema, signs of circulatory overload are seen in TACO that helps differentiate the two. TACO often affects patients at risk for congestive heart failure and occurs in less than 1% of transfusions. If a patient is at risk for fluid overload, diuretics can be administered with transfusion as a preventive measure.
7. **Graft-Versus-Host Disease (GVHD)** is a rare and almost always fatal complication of blood transfusions resulting from an attack of immunocompetent donor lymphocytes on the host's various tissues. After majority of transfusions, the donor lymphocytes are destroyed by the recipient's immune system preventing GVHD. However, if the host is immunodeficient or if there is a specific type of partial HLA matching between the donor and recipient, GVHD is more

likely to occur. It can develop 4 to 30 days after transfusion with patients typically presenting with fever and erythematous maculopapular rash that may become generalized. Other symptoms include anorexia, vomiting, abdominal pain, and cough. The diagnosis is made by a skin biopsy and confirmed by demonstrating circulating lymphocytes that have a different HLA phenotype verifying their origin from the donor. GVHD is poorly responsive to available treatments. Therefore, prevention is of utmost importance, which is achieved by irradiating all lymphocyte containing components with gamma radiation, thereby inactivating them. In addition to immunocompromised hosts, recipients of family donors or those receiving HLA-matched platelets are all candidates for receiving irradiated blood components.

B. Metabolic Complications of Blood Transfusions

1. **Potassium (K^+)** concentration changes are common with rapid blood transfusion but usually are clinically important only in massive transfusion or renal failure. With storage, red cells leak K^+ into the extracellular storage fluid and levels may reach greater than 20 mEq after 2 weeks. However, with transfusion and replenishment of cellular energy stores, this is rapidly corrected.
 2. **Calcium.** Citrate, which binds calcium, is used as an anticoagulant in stored blood products. Consequently, rapid transfusion may cause a decreased ionized calcium level. Hypocalcemia is usually not significant because the liver rapidly metabolizes the infused citrate, but it may become an important problem in patients with impaired liver function, during the anhepatic phase of liver transplantation, in hypothermic patients, or in patients with decreased hepatic blood flow. Ionized calcium levels should be followed, because total serum calcium measures the citrate-bound calcium and may not accurately reflect free serum calcium.
 3. **Acid–base status.** Banked blood is acidic because of accumulated red cell metabolites, with pH decreasing linearly to approximately 6.6 after 2 weeks. However, the actual acid load to the patient is minimal. Acidosis associated in the face of severe blood loss is more likely due to hypoperfusion and will improve with volume resuscitation. Alkalosis is frequent following massive blood transfusion because citrate is metabolized in the liver to bicarbonate.
 4. **Stored blood.** A study demonstrated increased rates of complications and mortality following cardiac surgery in patients who received blood that was stored for more than 2 weeks. It is known that stored blood undergoes progressive structural and functional alterations that decrease the functionality and viability of red cells following their transfusion. Prolonged storage may diminish microvascular flow as the red cells are less deformable. There is also decreased oxygen delivery secondary to depletion of 2,3-diphosphoglycerate with a resultant left shift of the oxy-Hb curve with increased adhesion and aggregation of red cells. Additionally, there is accumulation of proinflammatory substances and priming of the nicotinamide adenine dinucleotide phosphate system with reduction in concentrations of nitric oxide and adenosine triphosphate.
- C. Infectious complications of blood transfusions** have decreased with improved laboratory testing for transmissible diseases. Exposure to pooled products (e.g., cryoprecipitate) increases the risk in proportion to the number of donors.

1. Hepatitis

- a. **Hepatitis B** (see Chapter 7, for all infectious diseases transmitted by blood transfusion). The risk of hepatitis B infection from a blood transfusion has decreased since testing donated blood for hepatitis B antigen became routine in 1971. The current risk is estimated to be 1:60,000 to 1:120,000 units transfused.
- b. **Hepatitis C** Institution of routine testing for antibody to hepatitis C virus (HCV) in 1990 (and recently nucleic acid testing) has reduced the risk of transfusion-related HCV to approximately 1:800,000 to 1:1.6 million units.

2. **Human immunodeficiency virus (HIV)**. Because of improved screening and testing, the risk of transfusion-associated HIV has been estimated to be about 1:1.4 to 1:2.4 million units transfused in the United States.

3. **Cytomegalovirus (CMV)**. The prevalence of antibodies to CMV in the general adult population is approximately 70%. The incidence of transfusion-associated CMV infection in previously noninfected patients is quite high. Usually, the infection is asymptomatic, but because immunosuppressed patients and neonates can have severe reactions, CMV-negative blood or leukocyte-reduced blood may be recommended.

4. **West Nile virus (WNV)**. Following the 2002 epidemic of WNV in the United States, it was found that transfusion of red cells, platelets, and FFP can transmit WNV. Following universal screening, the risk of WNV from transfusion fell to less than 1:1 million.

5. **Bacterial sepsis** caused by transfused blood products is rare. Donors with evidence of infectious disease are excluded, and the storage of PRBCs at 4°C minimizes infectious risk. Nonetheless, PRBCs may become infected, most commonly with *Yersinia enterocolitica*. Platelets, which are stored at room temperature, are more problematic, with an estimated infection rate of 1:1,000 to 1:2,000 units. Organisms associated with platelet contamination are usually *Staphylococcus (aureus and epidermidis)* and diphtheroids. The risk of infection is directly related to the storage time of the product with 15% to 25% of infected transfused units causing severe sepsis. The signs usually are apparent during transfusion and should trigger immediate halt of the transfusion and testing of the unit for contamination. The impact on the individual patient depends on the size of the bacterial inoculum and the immunocompetence of the recipient, but overall mortality from transfusion-acquired sepsis is approximately 60%.

- D. **Immunomodulation by Blood Transfusion**. Transfusion of allogeneic blood is known to suppress the immune system. Although the exact mechanism is unknown, theories suggest that transfusion of donor leukocytes may induce an immune-"tolerant" state in the recipient. Thus, allogeneic blood transfusion has been used preoperatively and intraoperatively in renal transplant recipients to improve graft viability. Less clear and more controversial are the potential detrimental effects of intraoperative allogeneic blood transfusion on cancer recurrence rates, postoperative infections, activation of latent viral infections, and postoperative mortality. Some experts contend that many of the adverse immunomodulatory effects of allogeneic blood transfusion may be diminished by universal blood product leukoreduction.

IX. PERIOPERATIVE COAGULOPATHY THAT MAY ALTER MANAGEMENT

- A. **Coagulopathy of massive transfusion** is unusual with transfusions less than 1 to 1.5 blood volumes, assuming the patient had a normal coagulation profile, platelet count, and platelet function initially.

1. **Thrombocytopenia.** Diffuse oozing and failure to form clots after massive transfusion are often at least in part due to thrombocytopenia. The decreased platelet count is due to the transfusion of platelet-poor blood products. Clinical bleeding is unlikely with platelet counts above 50,000 cells/mm³. If loss of one BV or more is expected, platelets should be available and transfused to maintain a count of more than 50,000 cells/mm³ or greater if ongoing blood loss is expected.
2. **Clotting factors.** The normal human body has tremendous reserves of clotting factors. In addition, the patient receives small amounts of the stable clotting factors in the plasma of each unit of red cells. Bleeding from factor deficiency in the face of massive transfusion is usually due to decreased levels of fibrinogen and labile factors (V, VIII, or IX). Bleeding from hypofibrinogenemia is unusual unless the fibrinogen level is below 75 mg/dL. In some patients, factor VIII levels increase with massive transfusion because of increased release from endothelial cells. Labile clotting factors are administered in the form of FFP. Six units of platelets contain the equivalent of 1 unit of FFP. Cryoprecipitate provides a source of concentrated fibrinogen for the patient who cannot tolerate FFP due to volume overload.
- B. **Disseminated intravascular coagulation (DIC)** refers to the abnormal, diffuse systemic activation of the clotting system. The pathophysiology involves excessive formation of thrombin, resulting in fibrin formation throughout the vasculature accompanied by platelet activation, fibrinolysis, and consumption of coagulation factors. The profound consumptive coagulopathy produced by DIC often results in hemorrhage.
 1. **Causes of DIC** include infection, shock, trauma, complications of pregnancy (e.g., amniotic fluid embolism, placental abruption, or septic abortion), burns, and fat or cholesterol embolism. DIC is common in extensive head injury because of the high content of thromboplastin in brain tissue. A chronic form of DIC may accompany cirrhotic liver disease, aortic dissection, and malignancy.
 2. **Clinical features** include petechiae, ecchymoses, bleeding from venipuncture sites, and frank hemorrhage from operative incisions. The bleeding manifestations of DIC are most obvious, but the diffuse microvascular and macrovascular thromboses are usually more common, more difficult to treat, and more frequently life threatening because of ischemia to vital organs. Bradykinin release in DIC may also cause hypotension.
 3. **Laboratory features** of DIC include an elevated D-dimer, indicating fibrin degradation by plasmin, in all cases. Fibrinogen degradation products (FDPs) are increased, but this is not specific to DIC because FDPs may be present from the formation of fibrin by fibrinogen or from the degradation of fibrinogen by plasmin. The PT and PTT typically are prolonged and serial measurements reveal falling fibrinogen levels and platelet counts. After acquisition of the PTT, the waveform that is used to generate the PTT result can be reviewed for an early negative slope that is suggestive of DIC.
 4. **Treatment of DIC** involves treating the precipitating cause and transfusion of appropriate blood products (e.g., FFP, platelets, and cryoprecipitate) to correct bleeding. Inhibitors of fibrinolysis (e.g., aminocaproic acid and tranexamic acid) are contraindicated in DIC.
- C. **Chronic Liver Disease.** With the exception of factor VIII and vWf, which are manufactured by the endothelium, the liver synthesizes all coagulation factors. Patients with hepatic dysfunction may have decreased production of coagulation factors and decreased clearance of activated factors.

Patients may have an ongoing consumptive coagulopathy, similar to DIC, if circulating activated clotting factors are increased. Because the liver is also instrumental in removing the by-products of fibrinolysis, circulating fibrin degradation products may be elevated.

- D. Vitamin K Deficiency.** Vitamin K is required by the liver for production of factors II, VII, IX, and X and proteins C and S. Because vitamin K cannot be synthesized by humans, interference with vitamin K absorption will cause a coagulopathy (see Chapter 5) and a prolonged PT. Because we rely on GI flora for the production of vitamin K, vitamin K deficiency is commonly found in patients receiving broad-spectrum antibiotics, neonates who lack GI flora, and patients with short bowel syndrome. These patients can be treated with vitamin K, 10 mg SC daily for 3 days. IV administration of vitamin K may result in a slightly faster correction of the PT but is accompanied by a rare risk of anaphylaxis. If used, IV vitamin K should be administered very slowly. If faster correction of PT than vitamin K is required, FFP (5 to 8 mL/kg) can be used.

E. Pharmacologic Intervention

- 1. Heparin** acts by accelerating the effect of antithrombin III. It prolongs the PTT and has a short half-life so that its anticoagulant effect is usually fully reversed approximately 4 hours after discontinuation of the infusion. If faster reversal is required, protamine, a natural antagonist, may be administered.
- 2. Low molecular weight heparins** are commercially prepared by fractionating heparin into molecules of 2,000 to 10,000 Da. They exert their anticoagulant effect primarily by inhibiting factor X and usually do not prolong the PTT. These drugs have a longer half-life than heparin and are incompletely reversed by protamine, yet protamine reversal is indicated in the setting of a major bleeding episode. Fast reversal may require FFP transfusion.
- 3. Warfarin (Coumadin)** inhibits vitamin K epoxide reductase. This causes a deficiency of vitamin K, preventing the hepatic carboxylation of factors II, VII, IX, and X and proteins C and S to the active form. The PT and the INR are prolonged in patients taking warfarin. The drug's half-life is approximately 35 hours, requiring days for reversal. If quick reversal of warfarin is required, active factors can be given in the form of FFP (5 to 15 mL/kg). Vitamin K (2.5 to 10 mg IV or SC) can also be given for warfarin reversal, but its effect requires 6 or more hours.
- 4. Platelet inhibitors.** Aspirin and **nonsteroidal anti-inflammatory drugs (NSAIDs)** inhibit platelet aggregation by interfering with the cyclooxygenase pathway. Aspirin permanently inhibits the pathway for the 10-day life span of the platelet. The other NSAIDs reversibly inhibit the cyclooxygenase pathway; their effects are reversed within 3 days of discontinuing the drug. **Dipyridamole** is a phosphodiesterase inhibitor that increases platelet cAMP, thereby inhibiting platelet aggregation. **Ticlopidine, clopidogrel, prasugrel, and ticagrelor** are antiplatelet agents that inhibit ADP-mediated platelet aggregation. **Abciximab** is an IV monoclonal antibody against the platelet glycoprotein IIb/IIIa receptor. It causes profound platelet inhibition and produces thrombocytopenia. Although the drug's plasma half-life is short, impairment of platelet function may last for days and reversal of the effect may require multiple platelet transfusions due to adsorption of the antibody to donor platelets. Immediate reversal of platelet inhibitors may require platelet transfusion and may not be effective if the inhibitor is still present in the plasma.

5. **Thrombolytic agents** act by dissolving thrombi via conversion of plasminogen to plasmin, which lyses fibrin clot. They are intended to reverse thrombosis and recanalize blood vessels. Two thrombolytic agents, **tissue plasminogen activator** and **streptokinase**, are commonly used in clinical practice, each with slightly different pharmacodynamic and side effect profiles. Each of these drugs results in a hypofibrinogenemic state and carries a substantial risk of bleeding. They are generally contraindicated perioperatively. If emergent surgery is required after thrombolytic therapy, the effect may be antagonized by administration of aminocaproic or tranexamic acid. The fibrinogen level may be restored by transfusion of cryoprecipitate or FFP.
6. **Direct thrombin inhibitors (DTIs)**. **Dabigatran** and **argatroban** are among the increasingly popular DTIs, which inhibit thrombin (factor II). Dabigatran is an oral DTI often used for stroke prevention in atrial fibrillation and, unlike warfarin, does not require frequent INR monitoring. Argatroban is an IV medication used for anticoagulation in patients with heparin-induced thrombocytopenia. At this time, DTIs lack a specific reversal agent and can thus cause life-threatening bleeding if taken incorrectly.
7. **Direct factor Xa inhibitors**, such as **apixaban** and **rivaroxaban**, directly inhibit factor Xa (as opposed to LMWHs that inhibit factor Xa via antithrombin III). Like DTIs, these drugs are also typically used for the prevention and treatment of thromboembolic events. They also lack a specific reversal agent.

F. Reversal of Perioperative Coagulopathy

1. Reversal of perioperative coagulopathy can often be achieved with cryoprecipitate, platelets, and FFP depending on the cause of coagulopathy. In addition, specific clotting factors are available for patients who require rapid reversal of coagulopathy and may not tolerate the large volumes or other risks associated with transfusion of large amounts of blood products.
2. **Recombinant factor VIIa (rFVIIa)** is FDA approved for the treatment of hemophiliacs with antibody inhibitors that prevent factor VIII or IX from normalizing their coagulation. The apparent efficacy of the drug in massive surgical or traumatic bleeding from case studies had generated intense interest for a wider applicability of the drug. In addition, one major trial demonstrated reduced expansion of intracerebral hematoma in cases of nontraumatic, hemorrhagic stroke, which has created enthusiastic support for the use of rFVIIa in these patients by some neurointensivists. However, a follow-up prospective randomized controlled study by the same group showed no improvement in mortality or functional outcome after intracerebral hemorrhage although they confirmed a reduction in the size of the hematoma. There is currently no clearly defined role for rFVIIa except for treating hemophiliacs with inhibitors.
3. **Prothrombin Complex Concentrates (PCC, also by various brand names)** are preparations of factors II, V, VII, IX, X, and proteins C and S that are derived from FFP. They are useful for the urgent reversal of warfarin or other serious coagulopathy resulting from factor deficiency. They are extremely expensive, and their use is currently limited to patients who require immediate reversal of anticoagulation, such as those with life-threatening intracerebral hemorrhage.

X. SPECIAL CONSIDERATIONS

A. Hemophilia A and B are rare, sex-linked diseases affecting males almost exclusively. **Hemophilia A** is due to an abnormality in factor VIII, while **hemophilia B (Christmas disease)** is due to a factor IX abnormality. The incidence in the United States is 1:10,000 males for hemophilia A and 1:100,000 males for hemophilia.

1. Clinical features. Patients usually present early in childhood with hemarthroses and soft tissue hematomas after minor trauma. Laboratory tests demonstrate a markedly prolonged PTT with normal PT and platelet count.

2. Treatment with the appropriate factor (of either recombinant or lyophilized concentrate source) should be coordinated with the patient's hematologist. Hemophilia A is treated with factor VIII to achieve preoperative activity levels of 25% to 100%, depending on the extent of the procedure. Some patients with mild hemophilia A may respond to DDAVP therapy. In an emergency, if factor VIII is unavailable, cryoprecipitate transfusion can provide the deficient factor. Hemophilia B is treated with factor IX to achieve at least 30% to 50% activity before surgery.

B. von Willebrand disease is caused by a deficiency or abnormality in vWf, a protein involved in anchoring platelets to injured subendothelium and stabilizing factor VIII. It is the most common inherited bleeding disorder, affecting 1% to 2% of the population. It is autosomally dominant and affects both sexes equally. The disease is classified into three main phenotypes: type 1 characterized by mild-to-moderate quantitative deficiencies of vWf and factor VIII, type 2 characterized by a qualitative abnormality of vWf, and type 3 characterized by very low or undetectable levels of vWf in plasma with low but detectable levels of factor VIII.

1. Clinical presentation. The phenotypic expression is variable so that clinical manifestations may range from very mild-to-severe bleeding. Usually, patients have a history of easy bruising and bleeding from mucosal surfaces, but some patients are not diagnosed with a bleeding disorder until suffering a major trauma or surgery complicated by bleeding. Laboratory tests usually reveal a prolonged bleeding time.

2. Treatment of von Willebrand disease depends on the subtype. Many patients respond to DDAVP treatment (type 1), but others (types 2 and 3) may require cryoprecipitate or a purified, lyophilized complex of vWf and factor VIII derived from pooled human plasma (Humate-P). The lysine analogue antifibrinolytics also have been used in some patients to reduce surgical bleeding. Preoperative consultation with the patient's hematologist is recommended.

C. Sickle cell anemia affects 1:600 African Americans. The disease is caused by the substitution of valine for glutamic acid at the sixth position on the β -chain of Hb. Homozygotes for this substitution (as well as double heterozygotes SC or β -thalassemia) have clinical sickle cell disease.

1. Clinical features. The abnormal Hb polymerizes and causes a sickling deformity of the red cell under certain conditions (e.g., hypoxia, hypothermia, acidosis, and dehydration). Sickled cells cause microvascular occlusion with tissue ischemia and infarction. A sickle cell crisis typically presents with excruciating chest or abdominal pain, fever, tachycardia, leukocytosis, and hematuria. Signs and symptoms may be masked by anesthesia. The RBCs have a shortened survival time of 12 days, leading to anemia and extramedullary hematopoiesis.

2. **The anesthetic management** of these patients includes avoiding conditions that promote sickling (e.g., hypoxia, hypovolemia, acidemia, and hypothermia). Conservative transfusion management to a preoperative Hct of approximately 30% prevents postoperative complications as effectively as the traditional “exchange transfusions” that sought to reduce the amount of hemoglobin S to 30% of total Hb.
- D. **Jehovah's Witness** patients generally may refuse to receive blood or blood products because of their religious beliefs, even if such refusal results in death. Special considerations apply if the patient is a minor, is incompetent, or has responsibilities for dependents as well as in certain emergency circumstances (see also Chapter 40, section I.F). However, under elective conditions, a physician is not required to agree to treat a patient who refuses a transfusion if doing so is contrary to the physician's ethical beliefs. Blood conservation measures are crucial in these patients (see section VII). Jehovah's Witnesses may allow transfusion of intraoperatively phlebotomized blood (see section VII.B) as long as the blood remains in continuity with the body (i.e., the blood tubing must always remain connected to the patient). Erythropoietin is sometimes used to increase red cell mass perioperatively. It is incumbent on the anesthesiologist to fully discuss the patient's beliefs and decisions concerning transfusion and document these decisions clearly in the medical record as well as on operative consent forms.

Suggested Readings

- American Society of Anesthesiologists Task Force on Perioperative Blood Transfusion and Adjuvant Therapies. Practice guidelines for perioperative blood transfusion and adjuvant therapies. Approved October 22, 1995, last amended July 2006. Available at <http://www.asahq.org/publicationsAndServices/practiceparam.htm>. Accessed June 29, 2014.
- Carson JL, Carless PA, Hebert PC. Transfusion thresholds and other strategies for guiding allogeneic red blood cell transfusion. *Cochrane Database Syst Rev* 2012;4:CD002042.
- Crash-2 trial Collaborators. Effects of tranexamic acid on death, vascular occlusive events, and blood transfusion in patients with significant haemorrhage (CRASH-2): a randomised, placebo-controlled trial. *Lancet* 2010;376:23–32.
- Goodnough LT, Brecher ME, Kanter MH, et al. Transfusion medicine. I Blood transfusion. *N Engl J Med* 1999;340:438–447.
- Goodnough LT, Brecher ME, Kanter MH, et al. Transfusion medicine: II. Blood conservation. *N Engl J Med* 1999;340:525–533.
- Goodnough LT. Risks of blood transfusion. *Crit Care Med* 2003;31(12 Suppl):S678–S686.
- Hebert PC, Wells G, Blajchman MA, et al. A multicenter, randomized controlled clinical trial of transfusion requirements in critical care. *N Engl J Med* 1999;340:409–417.
- Kopko PM, Holland PV. Transfusion-related acute lung injury. *Br J Haematol* 1999;105:322–329.
- Lake CL, Moore RA, eds. *Blood: Hemostasis, Transfusion, and Alternatives in the Perioperative Period*. New York: Raven Press; 1995.
- O'Connell NM, Perry DJ, Hodgson AJ, et al. Recombinant FVIIa in the management of uncontrolled hemorrhage. *Transfusion* 2003;43:1711–1716.
- Rao SV, Jollis JG, Harrington RA, et al. Relationship of blood transfusion and clinical outcomes in patients with acute coronary syndromes. *JAMA* 2004;292:1555–1562.
- Tanaka KA, Bader SO, Görlinger K. Novel approaches in management of perioperative coagulopathy. *Curr Opin Anaesthesiol* 2014;27:72–80.

36

The Postanesthesia Care Unit

Matthew J. Meyer and Edward E. George

I. GENERAL CONSIDERATIONS

For most patients, recovery from anesthesia is uneventful. Nevertheless, when postoperative complications occur, they may be sudden and life threatening. The **postanesthesia care unit (PACU)** is designed to provide close monitoring and care to patients recovering from anesthesia and sedation. The PACU is staffed by a dedicated team of anesthesiologists, nurses, and aides. Medical oversight may range from anesthesia providers in close proximity to the PACU to a team consisting of intensivists, residents, and other clinicians with critical care experience. It is ideally located in immediate proximity to the operating room (OR), with access to radiology and the laboratory. Medications and equipment for routine care and advanced support must be readily available.

II. ADMISSION TO THE PACU

- A. **Transport** from the OR should only be considered once a patent and stable airway is confirmed. The patient should be transported under direct supervision of the anesthetist, preferably with the head of the bed elevated or with the patient in the lateral decubitus position to maximize airway patency. Oxygen delivered via face mask is indicated in most patients to prevent hypoxemia due to hypoventilation or diffusion hypoxia (see section VA). Unstable patients, such as patients receiving vasoactive medications, usually require monitoring of oxygenation and hemodynamics during transport. The anesthetist may opt to bring rescue medications and airway management tools as the clinical situation dictates.
- B. A complete **report** should be provided to the PACU team upon arrival. The anesthetist remains in charge of the care of the patient until the PACU team is prepared to assume responsibility.
- C. As clinically indicated, the anesthetist may speak directly to the anesthesiologist in charge of the PACU, the surgeon, or a consultant about issues of particular importance for the patient. The report from the anesthetist to the PACU team is often the only formal account of the intraoperative events between the OR team and the personnel who will manage the immediate postoperative care. The report should include the following:
 1. **Clinical history:** patient identification, age, surgical procedure, diagnosis, medical history (including hearing and visual impairments, psychiatric conditions, and precautions for infection control), medications, allergies, preoperative vital signs, and language preference.

2. **Intravascular access:** location and size of catheters.
3. **Intraoperative pharmacology:** premedication, antibiotics, anesthesia induction and maintenance agents, opioids, muscle relaxants, reversal agents, vasoactive drugs, bronchodilators, and other clinically relevant agents administered.
4. **Surgical procedure:** exact nature of the surgery and relevant surgical issues (e.g., adequacy of hemostasis, care of drains, restrictions on positioning, etc.); the surgeon may present these details to the PACU team.
5. **Anesthetic course:** emphasis on problems that may affect the immediate postoperative period including laboratory values, difficult intravenous (IV) access, airway management issues, intraoperative hemodynamic instability, and electrocardiographic (ECG) changes.
6. **Fluid balance:** amount, type, and reason for fluid replacement, urine output, and estimated fluid and blood losses.

III. MONITORING

Close observation of the patient's level of consciousness, breathing pattern, oxygen saturation, and hemodynamics is of utmost importance. The nurse-to-patient ratio for routine cases is one nurse to two or three patients and increases to single coverage for high-acuity patients, such as those with significant comorbidities, intraoperative complications or particularly complex procedures. Vital signs are monitored and recorded at regular intervals according to clinical necessity. Standard monitoring includes **respiratory rate** measurement, continuous **electrocardiogram**, noninvasive **blood pressure**, and **pulse oximetry**. **Temperature** should be monitored and recorded.

A. Invasive monitoring such as arterial catheters, central venous catheters, and pulmonary artery catheters can be instituted if necessary. Arterial catheters provide continuous measurement of the systemic blood pressure and provide access for blood sampling. Central venous and pulmonary artery catheters should be considered when the etiology of hemodynamic instability is unclear (see Chapter 10) or when there is a requirement for vasopressors that can be administered only in the central venous system. Bedside transthoracic echocardiography may provide a less invasive alternative to assessing cardiac function and intravascular volume status. If monitoring and care requirements are escalating and a prolonged or complicated recovery is expected, plans should be made to transfer the patient to an intensive care unit (ICU).

IV. GENERAL COMPLICATIONS

The incidence of PACU complications varies with patient population and likely dependent upon a patient's medical history as well as the anesthesia and procedure performed. The most frequent issues encountered in the PACU setting include the following:

- A. **Respiratory and airway complications**
- B. **Hemodynamic perturbations**
- C. **Postoperative nausea and vomiting**
- D. **Renal complications**
- E. **Neurologic compromise**

V. RESPIRATORY AND AIRWAY COMPLICATIONS

Respiratory complications occur in 2% to 19% of postoperative patients, and many of these are initiated by events in the PACU such as hypoxia, hypoventilation, upper airway obstruction, laryngospasm, bronchospasm, and aspiration.

- A. Hypoxemia.** General anesthesia is associated with inhibition of hypoxic and hypercapnic ventilatory drive and a reduction in the lung's functional residual capacity (FRC). These changes may persist for a variable period of time postoperatively and predispose the patient to hypoventilation and hypoxemia. Supplemental oxygen can delay the detection of hypoventilation by pulse oximetry; however, it also reduces the incidence of hypoxia in the postoperative period. The decision to administer supplemental oxygen should be clinically determined for each patient but should generally be applied when transporting the patient from the OR to the PACU. Signs of hypoxemia include dyspnea, cyanosis, altered mental status, agitation, obtundation, tachycardia, hypertension, and arrhythmias. Hypoxemia should be diagnostically ruled out before undertaking specific treatment for these symptoms.
- B. Causes of hypoxemia include the following:**
- 1. Atelectasis** is a predictable effect of the reduction in the FRC during general anesthesia and can lead to increased intrapulmonary shunting. Obese patients and those undergoing thoracic or upper abdominal procedures are more susceptible to atelectasis. Epidural anesthesia without general anesthesia is associated with little or no atelectasis formation. Deep breathing, intermittent positive-pressure breathing, and incentive spirometry are effective in rapidly reexpanding small areas of alveolar collapse, although their ability to reduce respiratory complications is uncertain. Noninvasive ventilation (NIV) has been shown to decrease atelectasis and improve oxygenation in postoperative patients. Occasionally, hypoxemia may persist and a chest radiograph may reveal a segmental or lobar collapse. Chest physiotherapy or fiberoptic bronchoscopy may help with reinflating the collapsed segment.
 - 2. Hypoventilation** causes hypoxemia by promoting alveolar collapse and increasing the partial pressure of CO_2 in the alveolar air.
 - 3. Diffusion hypoxia** may occur during washout of nitrous oxide upon emergence from general anesthesia. High-inspired O_2 fraction (FiO_2) by face mask can prevent hypoxemia.
 - 4. Upper airway obstruction** is most often caused by inadequate recovery of the airway reflexes and tone and is seen commonly in patients with obesity, preexisting obstructive sleep apnea (OSA) (see section V.C) or residual neuromuscular blockade (see Chapter 13).
 - 5. Bronchospasm** may cause hypoventilation, CO_2 retention, and hypoxemia.
 - 6. Aspiration of gastric contents** can lead to aspiration pneumonitis and pneumonia (see Chapter 37).
 - 7. Pulmonary edema** may occur from cardiac failure, increased pulmonary capillary permeability or persistent exposure to negative pressure. Cardiogenic edema occurs mostly in individuals with preexisting cardiac disease and is characterized by hypoxemia, dyspnea, orthopnea, jugular venous distention, wheezing, and an S_3 gallop. It may be precipitated by fluid overload, dysrhythmias, and myocardial ischemia. A chest radiograph, arterial blood gas, a 12-lead ECG, and troponin level should be obtained. Evaluation by a cardiologist may be indicated, particularly when aggressive management of conditions such as unstable angina or acute valvular disease is being considered. Inotropic agents, diuretics, and vasodilators are the mainstay of treatment. The use of NIV can obviate the need for intubation in patients with severe hypoxia, pending the response to the medical treatment. Noncardiogenic pulmonary edema secondary to sepsis, head injury, aspiration, transfusion

reaction, anaphylaxis, negative pressure pulmonary edema, or upper airway obstruction is characterized by hypoxemia without the signs of left ventricular overload. Negative pressure pulmonary edema happens secondary to persistent upper airway collapse such as laryngospasm, biting down on the endotracheal tube or hypopharyngeal collapse, with continued diaphragmatic activity. Treatment for pulmonary edema generally needs to be continued in an ICU (see Chapter 37).

8. **Pneumothorax** may cause hypoventilation, hypoxemia, and hemodynamic instability (see section V.B.2.e).
 9. **Pulmonary embolism** seldom occurs in the immediate postoperative period. However, it must be considered in the differential diagnosis of hypoxemia in patients with deep venous thrombosis, cancer, multiple trauma, or with extended periods of immobility.
- C. **Hypoventilation** is characterized by inadequate minute ventilation resulting in hypercarbia and acute respiratory acidosis. When severe, hypoventilation can result in hypoxemia, mental status changes, and ultimately apnea. Supplemental oxygen may mask early detection of hypoventilation through pulse oximetry. Therefore, monitoring the ventilatory status of postoperative patients should not rely entirely on pulse oximetry. Etiologies of postoperative hypoventilation may be divided into two groups:

1. **Decreased ventilatory drive**

a. All inhaled **halogenated agents** depress ventilatory drive (see Chapter 12) and may produce hypoventilation in the postoperative period. **Opioids** are also potent respiratory depressants. All μ -receptor agonists increase the apneic threshold. Overnarcotized patients typically appear pain free, with a slow respiratory rate and a tendency to become apneic if left unstimulated. Large doses of **benzodiazepines** may also inhibit ventilatory drive. The safest treatment of anesthetic-related hypoventilation is to continue mechanical ventilation until breathing is adequate. Alternatively, pharmacologic reversal may be considered.

1. Opioid-induced hypoventilation can be reversed by **naloxone**, an opioid antagonist with greatest affinity for the μ -receptor. Doses of 20 to 80 μ g IV are titrated to effect. Reversal occurs within 1 to 2 minutes and lasts for 30 to 60 minutes. Naloxone treatment may induce significant side effects such as pain, tachycardia, hypertension, and pulmonary edema. The respiratory depressant effects of the opioids may outlast a single dose of naloxone. Thus, the patient should be monitored for recurrence of opioid-induced hypoventilation. Naloxone should be used cautiously in patients with known or suspected history of chronic opioid use because it may precipitate acute withdrawal.
 2. Hypoventilation secondary to benzodiazepines can be reversed by **flumazenil** (increments of 0.2 to 1 mg IV over 5 minutes, up to a maximum of 5 mg). The onset of reversal occurs within 1 to 2 minutes with peak effect at 6 to 10 minutes. The patients should be followed closely after administration of flumazenil because re sedation may occur due to its short 7 to 15 minute half-life. Flumazenil should be used cautiously in patients with chronic benzodiazepine use because it may precipitate seizures.
- b. Less common, but potentially life-threatening, causes of decreased ventilatory drive include complications of **intracranial** and **carotid artery** surgery, **head injuries**, and intraoperative **stroke** (see section VIII).

2. Pulmonary and respiratory muscle insufficiency

- a. **Preexisting respiratory disease** is the most important risk factor for postoperative respiratory complications. **Chronic obstructive pulmonary disease (COPD)** alters the match of ventilation and perfusion, resulting in hypoxemia and hypercapnia. Impaired gas exchange and expiratory flow limitation cause a high ventilatory workload under normal circumstances. **Restrictive disease** (e.g., pulmonary fibrosis, pleural effusions, obesity, scoliosis, massive ascites, and pregnancy) is associated with fewer complications than COPD, particularly when respiratory muscle strength is preserved and the restrictive defect is extrapulmonary. NIV can be beneficial in COPD and in restrictive pulmonary disease by decreasing the work of breathing, augmenting the ventilatory parameters, and avoiding intubation.
- b. **Residual neuromuscular blockade** is defined as a train-of-four ratio less than 0.9 and suggested by the clinical observations of spasmodic twitching, generalized weakness, upper airway obstruction, or by more subtle signs such as hypoxemia or shallow breathing. Even with modern non-depolarizing neuromuscular blocking agents, approximately 30% of patients are admitted to the PACU with residual neuromuscular blockade. Adequacy of muscle strength can only be definitively assessed with the aid of a **quantitative neuromuscular transmission monitor** (see Chapter 13). If muscle weakness persists after adequate pharmacologic reversal (e.g., **neostigmine** 20 to 60 $\mu\text{g}/\text{kg}$ up to 5 mg, and **glycopyrrolate** 0.2 mg per 1 mg of neostigmine administered), it is best to institute or continue mechanical ventilation, administer adequate anxiolysis, and wait for the muscle strength to recover. At this point, special situations such as myasthenia gravis and myasthenic syndromes, pseudocholinesterase deficiency, succinylcholine-induced phase II block, hypothermia, acid-base and electrolyte imbalance, and anticholinesterase inhibitor-induced weakness should be considered.
- c. **Inadequate analgesia** after thoracic or upper abdominal surgery may cause splinting and decreased minute ventilation, resulting in alveolar collapse, hypercapnia, and hypoxemia. This is preventable with early analgesia and encouragement of deep breathing and coughing. Compared with systemic opioids, epidural analgesia may reduce the incidence of respiratory complications (atelectasis, pulmonary infections, or hypoxia).
- d. **Bronchospasm** is common in the pediatric population as well as patients with COPD, asthma, or a recent respiratory tract infection. It is often precipitated by manipulation of the airway, particularly tracheal intubation. Wheezing may also be heard upon chest examination of patients with pulmonary edema, endobronchial intubation, aspiration pneumonitis, and pneumothorax. Treatment is discussed in Chapter 37.
- e. **Pneumothorax** may complicate certain procedures such as thoracotomy, mediastinoscopy, bronchoscopy, high retroperitoneal dissection for nephrectomy or adrenalectomy, laparoscopic surgery, and spinal fusion. Insertion of central venous lines and nerve blocks of the upper extremities are other possible iatrogenic etiologies. Diagnosis is made with a chest radiograph (CXR) in the upright position. In the presence of hemodynamic instability (tension pneumothorax), a needle decompression or tube thoracostomy must be performed emergently even without CXR diagnosis (see Chapter 37).

D. Upper airway obstruction may occur during recovery from anesthesia. Principal signs are the lack of adequate air movement, intercostal and suprasternal retractions, and paradoxical abdominal and chest wall motion during inspiration. Complete upper airway obstruction is silent. Partial obstruction is accompanied by either snoring (if the obstruction is above the larynx) or stridor (if perilaryngeal). Obstruction is more commonly seen in patients with OSA, obesity, tonsillar or adenoidal hypertrophy, or craniofacial abnormalities. Often times, airway obstruction may be relieved with a chin lift or jaw thrust (see Chapter 37). Patients with OSA may benefit from the use of continuous positive airway pressure. Common etiologies for upper airway obstruction include the following:

1. **Incomplete recovery** from general anesthesia and/or neuromuscular blockade (see section V.B). Decreased strength and coordination of the intrinsic and extrinsic airway musculature causes the tongue to fall backward and occlude the airway. Patency is reestablished by inserting a nasal or oral airway, by manually assisting ventilation, or by intubating the trachea.
2. **Laryngospasm** may be precipitated by light anesthesia and irritation of the glottis by secretions, blood, or a foreign body (see Chapter 37).
3. **Airway edema** may be caused by laryngoscopy, bronchoscopy, nasogastric tube insertion, esophagoscopy, or surgery on the head and neck. It may also follow a traumatic intubation, allergic reaction, the administration of large amounts of IV fluids, or prolonged prone position. Children are particularly susceptible to airway obstruction from edema because of the small diameter of their upper airway. The cuff leak test is neither sensitive nor specific and should not be used as the sole determinant for extubation of a patient with suspected airway edema. Treatment of upper airway edema includes the following:
 - a. Administration of warmed, humidified **100% O₂** by face mask.
 - b. **Head elevation, fluid restriction**, and possible **diuresis**.
 - c. Nebulization of racemic **epinephrine** 2.25% solution, 0.5 to 1.0 mL in normal saline, or L-epinephrine, 2 mL of a 1:1,000 solution, which may be repeated in 20 minutes if needed.
 - d. **Dexamethasone**, 4 to 8 mg IV every 6 hours for 24 hours.
 - e. Administration of **Heliox** (helium:oxygen, 80:20) can dramatically improve gas exchange and the work of breathing by establishing laminar airflow and improving gas exchange at distal alveoli.
 - f. **Reintubation** of the trachea must be considered early in the course of suspected airway obstruction as distortion of airway anatomy may occur rapidly, particularly in the setting of allergic reactions.
4. **Wound hematoma** caused by bleeding at the surgical site may complicate thyroid and parathyroid surgery, neck dissections, and carotid endarterectomy. The pressure caused by an expanding hematoma within the neck tissue planes causes obstruction of venous and lymphatic drainage and massive edema. Patients complain of local pain and pressure, dysphagia, and variable degrees of respiratory distress and may have drainage from the surgical site. Neck wound hematomas must be treated immediately by emergency reexploration and evacuation in the OR. The surgeon should be notified immediately and an OR prepared. The anesthesiologist must support the airway by mask ventilation with 100% O₂, followed by intubation of the trachea under direct vision. If tracheal intubation cannot be rapidly accomplished, opening the wound at the bedside can relieve soft tissue compression of the airway and improve airway patency.

5. **Vocal cord (VC) paralysis** may occur after thyroid, parathyroid, thoracic, tracheal, and neck surgery or a traumatic endotracheal intubation. VC paralysis may be transient, resulting from manipulation of the recurrent laryngeal nerve, or permanent, from severing the nerve. Unilateral transient VC paralysis is relatively common, and the primary concern is potential aspiration of gastric contents. Permanent unilateral VC paralysis can occur without clinical symptoms as compensatory action of the contralateral VC minimizes the occurrence of aspiration. Bilateral VC paralysis can occur after radical surgery for thyroid or tracheal cancer when neoplastic infiltration makes identification of the recurrent laryngeal nerves difficult. Bilateral VC injury is a rare and serious complication that can lead to complete upper airway obstruction after extubation in the immediate postoperative period. It requires emergency endotracheal intubation (which may be more difficult due to disrupted airway anatomy) and possibly a tracheostomy.
- E. **The intubated patient** presents special considerations. The anesthesiologist in the PACU should establish a plan regarding weaning and extubation or, alternatively, transfer to an ICU. Conditions that could delay the extubation at the end of the surgery include the following:
 1. **Delayed emergence** from general anesthesia due to volatile or IV agents. Reversal may be facilitated pharmacologically for some agents, but generally it is prudent to support ventilation and allow the respiratory depression to resolve spontaneously. The presence of a full stomach mandates additional vigilance in ensuring the recovery of consciousness and pharyngeal reflexes before extubation.
 2. **Deep intraoperative neuromuscular blockade** is not appropriate to pharmacologically reverse, and the patient should remain intubated until the patient can be safely, and permanently, reversed. Additionally, if muscle weakness persists after adequate pharmacologic reversal, the patient needs mechanical ventilation until full recovery is achieved.
 3. **Inadequate O₂ and CO₂ exchange** often resolve as the effects of anesthesia, surgery, and positioning fade. While supporting ventilation, possible etiologies, discussed in sections VI.A and VI.B, must be considered.
 4. **Potential for airway obstruction** exists after any extubation but especially when the patient has had a head and neck procedure, drainage of pharyngeal abscesses, mandibular wiring, large fluid resuscitation, or a prolonged surgery in the prone position. These patients should not be extubated until fully awake. If airway edema is suspected, the patient should be treated as outlined in section V.C.3.
 5. **Hemodynamic instability**, when severe, may be associated with a variable degree of impaired gas exchange and/or consciousness that mandate continuation of mechanical ventilation. Transfer to an ICU should be arranged for patients who fail to improve.
 6. **Hypothermia** has numerous adverse effects that may make extubation undesirable immediately after surgery (see section XI.A).
- F. **Guidelines for Extubation.** There is no single value or ventilatory parameter that will predict a successful extubation with certainty. The following criteria may be used when assessing the readiness to resume unassisted ventilation in a postoperative patient:
 1. Adequate **arterial oxygen pressure** (PaO₂) or oxygen saturation (SpO₂) on minimal ventilatory support.
 2. Adequate **breathing pattern**. Patients should be able to sustain spontaneous, unlabored breathing at a slow rate (<30 breaths/min) and adequate tidal volume (>6 mL per kg), as can be tested in a trial of unsupported breathing.

3. Adequate **level of consciousness** for cooperation and airway protection.
4. Full **recovery of muscle strength** that can be identified through neuro-muscular transmission monitoring.
5. Before proceeding with **extubation**, the PACU anesthesiologist should be aware of any preexisting airway problems in the event that reintubation is necessary. Supplemental O_2 is administered; the endotracheal tube, mouth, and pharynx are suctioned; and the tube is removed after a positive-pressure breath. Oxygen is then supplied by face mask as indicated, SpO_2 is monitored, and the patient is assessed for signs of airway obstruction or ventilatory insufficiency.

VI. HEMODYNAMIC AND CARDIOVASCULAR COMPLICATIONS

Hemodynamic and cardiovascular complications occur in approximately 5% of PACU admissions, with hypotension, arrhythmias, myocardial ischemia, and pulmonary edema being the most common complications recorded.

A. Hypotension should prompt a review of the patient's history and the intra-operative management to generate a differential diagnosis. The anesthetist who performed the case can be contacted to help interpret the current events. Hemorrhage must remain a primary consideration in the evaluation of hypotension in the postoperative patient.

1. **Hypovolemia** is the most common cause of hypotension in the PACU, and administration of a fluid bolus during the initial assessment is generally appropriate. Ongoing hemorrhage, inadequate fluid replacement, osmotic polyuria, and fluid sequestration (e.g., intestinal obstruction, and ascites) are among the causes of hypovolemia in the PACU. Nonspecific signs include tachycardia, dry mucous membranes, oliguria, and thirst. A meaningful volume challenge (250 to 1,000 mL of crystalloid or an equivalent volume of synthetic colloid, blood products, or both) should be considered for specific indications. Persistent hypotension after a seemingly adequate volume replacement mandates further assessment, starting with placement of a urinary catheter and consideration of ongoing surgical bleeding. Additional diagnostics may include transthoracic echocardiogram, a pulmonary artery catheter, or noninvasive cardiac output monitoring.
2. **Impaired venous return** occurs when mechanical forces decrease the venous return to the heart in the absence of a reduction of circulating blood volume. Common causes include **positive-pressure ventilation**, dynamic hyperinflation of the lungs resulting in **autopositive end-expiratory pressure**, **pneumothorax**, and **pericardial tamponade**. Signs of obstruction to venous return are similar to those of true hypovolemia except for the presence of jugular vein distention, an elevated central venous pressure, and possibly decreased breath sounds and heart tones. Volume administration is the mainstay of symptomatic therapy, but treatment of the underlying cause is the definitive intervention.
3. **Vasodilation** leading to hypotension can be caused by neuroaxial anesthesia, residual inhalation agents, rewarming after hypothermia, transfusion reactions, adrenal insufficiency, anaphylaxis, systemic inflammation, sepsis, recent use of pharmacologic renin–angiotensin–aldosterone pathway modifiers, and the administration of vasodilating drugs. Hypovolemia accentuates the hypotension due to vasodilatation, but volume replacement alone cannot fully restore the blood pressure. Pharmacologic treatment includes α -adrenergic receptor agonists such as **phenylephrine**, **norepinephrine**, and even **epinephrine**. Diagnosis and treatment of the specific etiology should be concurrent with symptomatic treatment.

4. **Decreased cardiac output** can be caused by myocardial ischemia and infarction, dysrhythmias, congestive heart failure, administration of negative inotropic drugs (anesthetics, β -adrenergic blockers, calcium channel blockers, and antidysrhythmics), sepsis, and hypothyroidism (see Chapters 2, 6, 19, and 37). Symptoms include dyspnea, diaphoresis, cyanosis, jugular vein distention, oliguria, rhythm disturbances, wheezing, dependent crackles, and an S_3 gallop on auscultation. A CXR, 12-lead ECG, and basic laboratory tests may help with diagnosis. Invasive monitoring may be necessary to guide pharmacologic therapies, including:
 - a. **Inotropic agents** such as dopamine, dobutamine, epinephrine, nor-epinephrine, and milrinone
 - b. **Afterload reduction** with nitrates, calcium channel blockers, or angiotensin-converting enzyme inhibitors
 - c. **Diuresis** with loop diuretics for fluid overload
 - d. **Antiarrhythmics or electrical cardioversion** for arrhythmias
- B. **Hypertension** is most commonly observed in patients with preexisting hypertensive disease, particularly if antihypertensive medications were held preoperatively. Certain types of surgery such as carotid, vascular, endocrine, and intrathoracic procedures are more likely to be followed by hypertensive events. Other postoperative etiologies for hypertension may include pain, bladder distention, fluid overload, hypoxemia, hypercarbia, hypothermia, increased intracranial pressure (ICP), and administration of vasoconstrictive agents. Hypertension is usually asymptomatic, but patients with malignant hypertension may have headache, visual disturbances, dyspnea, restlessness, and even chest pain. In the initial assessment, one should verify the accuracy of blood pressure measurement by checking cuff size and placement, review the patient's history and operative course, and rule out correctable etiologies. The management of hypertension is aimed at restoring blood pressure close to the patient's baseline. Tight blood pressure control is extremely important after surgery for intracranial aneurysm, creation of vascularized muscular flaps, microvascular surgery, and in patients with severe vascular disease. If possible, resumption of chronic antihypertensive oral therapy is ideal. If needed, this can be supplemented or substituted with a fast-onset, short-acting IV medication.
 1. **β -Adrenergic blockers:** labetalol (an α -blocker and a β -blocker), 5 to 20 mg IV bolus or up to 2 mg/min IV infusion, and esmolol (β_1 -blocker), 20 to 100 mg IV bolus or 25 to 300 μ g/kg/min IV infusion, are first-line agents.
 2. **Calcium channel blockers:** verapamil, 2.5 to 5 mg IV bolus, or nifedipine initiated at 5 to 15 mg/h. Sublingual nifedipine is not recommended because it may cause an unpredictable, and at times severe, drop in blood pressure that may induce myocardial ischemia.
 3. **Hydralazine:** 5 to 20 mg IV bolus, vasodilator and may induce reflex tachycardia.
 4. **Nitrates:** nitroglycerin, starting at 25 μ g/min IV infusion, is preferentially a venodilator and useful for coexisting myocardial ischemia. Sodium nitroprusside, starting at 0.5 μ g/kg/min IV infusion, is a potent arterial and venodilator and requires invasive blood pressure monitoring.
 5. **Fenoldopam:** 0.1 to 1.5 μ g/kg/min IV infusion, a selective peripheral dopaminergic receptor agonist; side effects include tachycardia, headache, and increased intraocular pressure.
 6. **Enalaprilat:** 0.625 to 1.25 mg IV bolus, is useful as an alternative in patients receiving long-term angiotensin-converting enzyme inhibitors or angiotensin receptor blockers when they cannot take oral medication.

C. Dysrhythmias in the perioperative period can be caused by increased sympathetic outflow, hypoxemia, hypercarbia, electrolyte and acid-base imbalance, myocardial ischemia, increased ICP, drug toxicity, thyrotoxicosis, and malignant hyperthermia. Premature atrial contractions and unifocal premature ventricular contractions (PVCs) generally do not require treatment. In the presence of more worrisome rhythm disturbances, supplemental O₂ and supportive management should be administered while the etiology is investigated.

1. Common supraventricular dysrhythmias

- a. **Sinus tachycardia** may be secondary to pain, agitation, hypovolemia, fever, hyperthermia, hypoxemia, hypercarbia, congestive heart failure, and pulmonary embolism. Symptomatic treatment with β -blockers should be instituted only after its etiology is addressed, unless the patient is at risk of myocardial ischemia.
- b. **Sinus bradycardia** may result from a high neuroaxial anesthetic block, opioid administration (with the exception of meperidine), vagal stimulation, β -adrenergic blockade, and increased ICP. Symptomatic treatment with anticholinergic muscarinic agents, **atropine**, 0.4 mg IV, or **glycopyrrolate**, 0.2 mg IV, is indicated when hypotension is present or for severe bradycardia (see Chapter 38).
- c. **Paroxysmal supraventricular tachydysrhythmias** occur with a higher incidence in patients over 70 years of age, after abdominal, thoracic, or major vascular procedures, and in patients with preoperative premature atrial contractions. They include paroxysmal atrial tachycardia, multifocal atrial tachycardia, junctional tachycardia, atrial fibrillation, and flutter. These rhythms may cause significant hypotension, and treatment may include the following:
 1. **Synchronized cardioversion** should be used if the patient is hemodynamically unstable, as per the ACLS protocol (see Chapter 38).
 2. **Adenosine**: 6 mg followed by 12 mg IV, administered rapidly has a high success rate in converting paroxysmal atrial tachycardia to sinus rhythm.
 3. **Verapamil** (2.5 to 5 mg IV bolus) or **diltiazem** (5 to 20 mg IV bolus, or as an infusion with an initial 0.25 to 0.35 mg/kg IV bolus followed by an infusion rate of 5 to 15 mg/h IV) will slow the ventricular response.
 4. **Amiodarone** is the antiarrhythmic of choice for rate control of atrial dysrhythmias in the setting of a decreased myocardial function.
 5. **β -Blockers (metoprolol, esmolol, and atenolol)** (see section VI.B.1) also decrease the ventricular response to supraventricular tachydysrhythmias.

2. **Stable ventricular dysrhythmias** such as PVCs and stable nonsustained ventricular tachycardia generally do not require treatment; however, a search for reversible causes (hypoxemia, myocardial ischemia, acidosis, hypokalemia, hypomagnesemia, and irritation due to a central venous catheter) should be conducted. Stable sustained ventricular tachycardia can be treated with synchronized cardioversion or pharmacologic modalities. PVCs that are multifocal and occur in runs, or are close to the preceding T wave, should be treated, especially in patients with structural heart disease, due to the risk of developing an unstable ventricular rhythm.

- a. **β -Blockers**: esmolol, 20 to 100 mg IV bolus, or 25 to 300 μ g/kg/min IV infusion, metoprolol, 2.5 to 10 mg IV, and propranolol, 0.5 to 2.0 mg IV increments, may be used

- b. **Amiodarone:** 150 mg IV bolus over 10 minutes followed by 1 mg/min IV infusion for 6 hours and then 0.5 mg/min IV infusion is indicated in patients with a decreased myocardial function
- c. **Lidocaine:** 1.5 mg/kg IV bolus, followed by 1 to 4 mg/min IV infusion
- 3. Management for **unstable ventricular tachycardia** and **ventricular fibrillation** are described in the ACLS protocol (see Chapter 38).

D. Myocardial Ischemia and Infarction

1. **T-wave changes** (inversion, flattening, and pseudonormalization) may be associated with myocardial ischemia and infarction, electrolyte changes, hypothermia, surgical manipulation of the mediastinum, or incorrect lead placement. Isolated T-wave changes must be considered within the clinical context because they are common postoperatively and do not always indicate myocardial ischemia.
 2. **ST segment changes** including depressions and elevations are generally indicative of myocardial ischemia and infarction, respectively. ST segment elevation can be a normal variant or can occur in other conditions such as left ventricular hypertrophy, left bundle branch block, and hyperkalemia. Unlike myocardial infarctions in the nonsurgical setting, in the postoperative period, most myocardial infarctions are associated with ST depression and have a non-Q-wave pattern. As supplemental O₂ is administered and a 12-lead ECG and cardiac enzymes are obtained, possible precipitating factors for the ST segment changes must be reviewed and corrected. Common etiologies include hypoxemia, anemia, tachycardia, hypotension, and hypertension. If ischemia, patients should be rate controlled with a β -blocker. Aspirin and statins may decrease the mortality of patients with acute coronary syndrome in the perioperative period. IV nitroglycerin is a good option for cases with ST segment elevations. Cardiology consultation and transfer to an ICU should be considered.
 3. In patients at high risk for cardiac events (patients with a history of ischemic heart disease, congestive heart disease, cerebrovascular disease, renal insufficiency, diabetes mellitus, and patients undergoing intrathoracic, intraperitoneal, or suprainguinal vascular procedures), continuation, and in some settings initiation, of β -blockade may decrease the risk of adverse cardiac events perioperatively.
- E. **The patient with a permanent pacemaker (PPM) or an intracardiac defibrillator (ICD)** requires special care in the PACU. Information about the patient's pacemaker dependency state and the features of the device must be obtained from the OR team. Continuous EKG monitoring with special attention to the patient's rhythm, rate, and hemodynamic status is indicated. Electrocautery used during the surgery can potentially trigger arrhythmia responses in PPM and ICD. Modern devices are less likely to be affected by intraoperative electromagnetic interference. Placing a magnet over the PPM or ICD should not be standard practice without precise knowledge of its effects. Communication with the electrophysiology service before and after surgery is highly recommended for interrogation of the device. Interrogation and reprogramming of the device to the original parameters may be required in the PACU after the operation.

VII. RENAL COMPLICATIONS

Acute renal failure in the postoperative period significantly increases the morbidity and mortality of the surgical patient. The physiology, diagnosis, and treatment of renal abnormalities are described in Chapter 4. Three common conditions encountered in the PACU that can indicate renal malfunction are discussed here.

- A. Oliguria** is defined as a urine output of less than 0.5 mL/kg/h over 6 or more hours; however, reduced urine output in the PACU often precedes the official diagnosis. **Hypovolemia** is the most frequent cause of postoperative oliguria. Administration of a fluid bolus (250 to 500 mL of crystalloid or a synthetic colloid), even when other etiologies are not yet excluded, is acceptable, as well as placement of a urinary catheter. Further diagnostic tests (e.g., plasma and urine electrolytes) and invasive monitoring should be considered when oliguria persists. **Diuretics** (see Chapter 4) should be used only when deemed necessary, such as in congestive heart failure and chronic renal insufficiency. Categorizing urinary pathology into pre-renal, intrarenal, and postrenal is helpful in diagnosing the postoperative patient with oliguria.
- 1. Prerenal** oliguria includes conditions that decrease renal perfusion pressure. Besides **hypovolemia**, other causes of decreased cardiac output must be considered (see section VI.A.4). Abdominal compartment syndrome from high intra-abdominal pressures (i.e., intraperitoneal hemorrhage and massive ascites) can also reduce renal perfusion. Analysis of urine electrolytes (see Chapter 4) will reveal a low fractional excretion of sodium (<1%).
 - 2. Intrarenal** causes of postoperative oliguria include acute tubular necrosis secondary to hypoperfusion (e.g., hypotension, hypovolemia, and sepsis), toxins (e.g., nephrotoxic drugs and myoglobinuria), and trauma. Urinalysis may show granular casts.
 - 3. Postrenal** causes include urinary catheter obstruction, trauma, and iatrogenic damage to the ureters.
- B. Polyuria**, defined as a urine output disproportionately high for a given fluid intake, occurs less frequently. Symptomatic treatment is based on volume replacement to maintain hemodynamic stability and adequate fluid balance. Electrolyte and acid–base equilibrium may be perturbed secondary to the etiology or to large volume loss. The differential diagnosis includes the following:
- 1. Excessive volume** administration requiring simple observation in healthy subjects.
 - 2. Pharmacologic** diuresis.
 - 3. Osmotic diuresis** may be caused by hyperglycemia, hypercalcemia, alcohol intoxication, and administration of hypertonic saline, mannitol, or parenteral nutrition.
 - 4. Postobstructive diuresis** after resolution of urinary obstruction.
 - 5. Acute tubular necrosis** may cause transient polyuria due to the loss of concentrating function of the tubules.
 - 6. Diabetes insipidus** secondary to the lack of antidiuretic hormone may follow head injury, infection, or hypothalamic-based intracranial surgery.
- C. Electrolyte disturbances** such as **hyperkalemia** and acidemia can develop within hours and need to be corrected emergently to avoid ventricular dysrhythmias and death (see Chapter 4). Polyuria may cause profound dehydration, with massive potassium losses and resulting alkalemia. **Hypokalemia**, often associated with **hypomagnesemia**, may also trigger atrial and ventricular dysrhythmias, although not as severe as those associated with hyperkalemia. Potassium should be replaced cautiously to avoid overdose. Magnesium replacement may effectively treat atrial and ventricular dysrhythmias, especially if the latter are in the form of torsade de pointes.

VIII. NEUROLOGIC COMPLICATIONS

A. Delayed Awakening

1. The most frequent cause of delayed awakening is **persistent effects of anesthetics** (see section VI.B). Less common but possibly life-threatening causes include the organic cerebral events described below.
2. **Decreased cerebral perfusion** of sufficient duration, during or after surgery, may cause diffuse or localized cerebral damage responsible for obtundation and delayed awakening. In patients with cerebrovascular disease, short periods of hypotension may cause a critical reduction of cerebral perfusion resulting in brain damage. If such an event is suspected, a neurologic consultation should be obtained as soon as possible, and specific tests (e.g., computed tomography [CT], magnetic resonance imaging [MRI], or angiography) should be considered. If cerebral edema is suspected, treatment should be started immediately (see Chapter 24).
3. **Metabolic causes** of delayed awakening include hypothermia, sepsis, preexisting encephalopathies, hypoglycemia, and electrolyte or acid-base derangements.

B. Neurologic damage may be the result of a **stroke** or may be due to peripheral nerve injury (see section VIII.D). Strokes in the perioperative period have an incidence of 0.1% to 2.2% and may be ischemic or hemorrhagic. Early diagnosis of a stroke may be difficult because symptoms such as slurred speech, visual changes, dizziness, agitation, confusion, psychosis, numbness, muscular weakness, and paralysis may overlap with the manifestations of residual anesthetics. **Ischemic strokes** are more common in patients with cerebrovascular disease, hypercoagulable states, and atrial fibrillation, and they may be associated with intraoperative hypotension. Fat emboli secondary to long bone fractures can also lead to strokes. **Hemorrhagic strokes** are more common in patients with coagulopathies, uncontrolled hypertension, cerebral aneurysms, arteriovenous malformations, and head trauma. Strokes are more frequent after intracranial surgery, carotid endarterectomy, cardiac surgery, and trauma. Neurologic consultation followed by brain CT or MRI is mandatory to guide immediate, and possibly brain-saving, treatment options.

C. Emergence delirium occurs in 5% to 20% of patients and is characterized by excitement alternating with lethargy, disorientation, and inappropriate behavior. Delirium may occur in any patient but specific risk factors include age (<5 years old and >64 years old), preexisting anxiety or psychiatric diagnosis, type of surgery (breast, abdominal, ENT and ophthalmic procedures), severe postoperative pain, and benzodiazepine premedication. Many drugs used perioperatively may precipitate delirium: ketamine, opioids, benzodiazepines, large doses of metoclopramide, and anticholinergics (atropine or scopolamine). Delirium may be a symptom of ongoing pathology such as hypoxemia, acidemia, hyponatremia, hypoglycemia, intracranial injury, sepsis, severe pain, and alcohol withdrawal. Along with addressing the underlying causes, treatment is symptomatic: supplemental O₂, fluid and electrolyte replacement, and adequate analgesia. Antipsychotic medications such as **haloperidol** (2.5 to 5 mg IV increments every 20 to 30 minutes) may be indicated. Benzodiazepines (**diazepam**, 2.5 to 5 mg IV and **lorazepam**, 1 to 2 mg IV) may be added if agitation is severe. **Physostigmine** (0.5 to 2.0 mg IV) may reverse delirium due to anticholinergic agents.

TABLE
36.1 Modified Brice Protocol

What is the last thing you remember before going to sleep for the operation?
 What is the first thing you remember on waking after the operation?
 Do you remember anything between going to sleep and waking up?
 Did you have any dreams?
 What was the most unpleasant thing you remember from the operation and anesthesia?

D. Peripheral neurologic lesions may follow improper intraoperative positioning, direct surgical damage, or may be a complication of regional anesthetic techniques. In the American Society of Anesthesiologists (ASA) closed-claim analysis, ulnar nerve injury accounted for about one third of the cases of nerve injury, followed by damage of the brachial plexus and the common fibular nerve. The risk factors for nerve injury after surgery include thin body habitus, previous history of neuropathy, smoking, and diabetes. Other sites of possible nerve damage are the wrist (median and ulnar nerve), internal aspect of the arm (radial nerve), and the points of emergence of the main branches of the VII cranial nerve, which can be compressed during mask-airway cases. Lithotomy position, especially when prolonged, may result in sciatic, femoral, common peroneal, and saphenous nerve injury. Improper positioning leads to compression or stretching of the nerve with demyelination. Remyelination often occurs in 6 to 8 weeks and results in complete recovery. Nevertheless, recovery may be more prolonged and, in some instances, the deficits are permanent. Early neurologic consultation for diagnosis and rehabilitation is crucial for a full recovery.

E. Intraoperative awareness and recall are rare complications of general anesthesia (0.13% in a large multicenter trial) that can be first detected in the PACU. These are often the consequences of light anesthetic techniques and occur especially after trauma, cardiac, and obstetric surgery. Risk factors include genetic or acquired (history of substance abuse or prescribed medications) resistance, ASA physical status III to V, and the use of muscular relaxants. The long-term effects of awareness under general anesthesia range from mild anxiety to overt posttraumatic stress disorder. A short interview such as the modified Brice protocol can be conducted in the PACU to identify patients with recall (Table 36.1). Patients with recall should receive reassurance and close inpatient and outpatient follow-up. Referral for psychological counseling should be offered.

IX. PRINCIPLES OF PAIN MANAGEMENT

Principles of pain management are described in Chapter 39. Adequate analgesia begins preoperatively and continues in the OR and in the PACU.

A. Opioids (IV or epidural) are the most common form of postoperative analgesia.

- 1. Fentanyl**, a potent synthetic opioid with a rapid onset of action, is commonly limited to the operative setting. Occasionally, however, small IV doses (25 to 50 μg IV bolus) can be titrated postoperatively to establish rapid analgesia.
- 2. Morphine** (2 to 4 mg IV bolus) may be repeated every 10 to 20 minutes until adequate analgesia is achieved. In children above 1 year of age, 15 to 20 $\mu\text{g}/\text{kg}$ IV or IM can be safely administered at 30- to 60-minute intervals.

3. **Hydromorphone** (0.2 to 0.5 mg IV bolus) may also be repeated every 10 to 20 minutes until adequate analgesia is achieved. It is a synthetic opioid approximately eight times more potent than morphine and associated with significantly less histamine release.
4. **Meperidine** (25 to 50 mg IV bolus) is similarly effective. It lacks the vagotonic effect of other opiates and is frequently used to reduce postanesthetic shivering. **Meperidine must be avoided in patients taking monoamine oxidase inhibitors** (serotonin syndrome) and must be administered cautiously in patients with renal insufficiency (toxic metabolite normeperidine associated with seizures).
- B. **Nonsteroidal** anti-inflammatory drugs (NSAIDs) and **acetaminophen** are effective complements to opioids. **Ketorolac** (30 mg IV bolus followed by 15 mg IV bolus every 6 to 8 hours in the perioperative period) provides potent postoperative analgesia. Other nonselective NSAIDs (**ibuprofen**, **naproxen**, and **indomethacin**) are also effective. Potential toxicities of all NSAIDs include decreased platelet aggregation resulting in increased bleeding risk and nephrotoxicity.
- C. **Adjuvant analgesics** include spasmolytics (**cyclobenzaprine**) and small doses of benzodiazepines.
- D. **Regional sensory blocks** can be very effective postoperatively (see Chapter 18).
- E. **IV patient-controlled analgesia** has been shown to be superior in patient satisfaction compared with intermittent analgesia administered by the medical staff.
- F. **Continuous epidural analgesia** should be continued postoperatively or promptly initiated in the PACU if not used in the OR.

X. POSTOPERATIVE NAUSEA AND VOMITING

Postoperative nausea and vomiting (PONV) is a common complication of general anesthesia and less often of regional anesthesia. An algorithm for managing PONV is presented in Figure 36.1. Patients should be stratified preoperatively with regard to their risk of PONV. The incidence of PONV is higher in women, nonsmokers, and patients with a history of PONV or motion sickness and when nitrous oxide and volatile anesthetics are used under general anesthesia. Certain types of surgery (cholecystectomy, laparoscopy, and gynecologic) may also increase the risk for PONV.

- A. PONV prophylaxis is not recommended in individuals believed to be at low risk. If appropriate, patients with higher risk for PONV should be offered a regional anesthetic technique. If higher-risk patients undergo general anesthesia, they should receive antiemetic prophylaxis before or during the surgery. Monotherapy or a combination of two or three antiemetic drugs from different classes is recommended along with measures aimed to diminish the baseline risk factors for PONV: preoperative anxiolysis, use of propofol for induction and maintenance of anesthesia, total IV anesthesia, adequate hydration, and minimization of perioperative opioids. If PONV occurs in a patient who has not received prophylaxis, therapy should be initiated with a serotonin antagonist and supplemented, if necessary, with medications from other classes. In patients who have received prophylaxis, rescue therapy should consist of drugs from classes other than the ones already administered. Administration of drugs from the same class within the first 6 hours after surgery has not been found to be effective in treating PONV. Common antiemetic classes and agents include the following:
 - B. **Serotonin antagonists** (**ondansetron** 4 mg IV bolus, **granisetron** 0.35 to 3 mg IV bolus, **dolasetron** 12.5 mg IV bolus) are well studied as prophylactic antiemetics when administered at the end of surgery, and rescue antiemetics

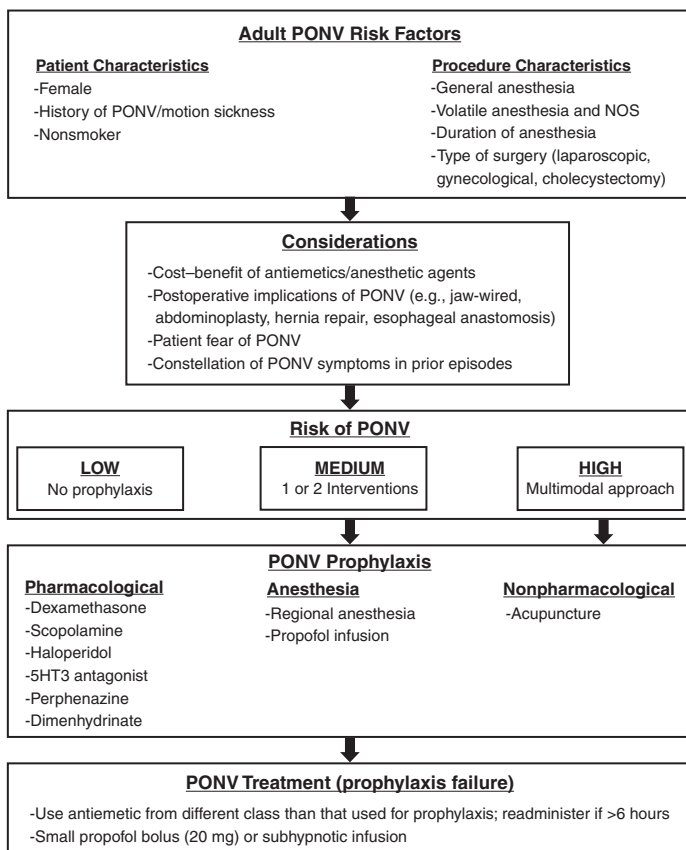


FIGURE 36.1 Algorithm for management of PONV.

when nausea and emesis have occurred postoperatively. However, if a serotonin antagonist has already been given prophylactically, there is no observed benefit of readministration as a rescue agent within 6 hours of the prophylactic dose.

- C. Corticosteroids** are commonly used for the prevention of PONV. **Dexamethasone** (4 to 8 mg IV bolus) is the best studied. It is most effective for prophylaxis if administered at induction of anesthesia and can be applied as a rescue drug for established PONV. Methylprednisolone (40 mg IV bolus) can also be used for PONV prevention.
- D. Butyrophenones** include haloperidol and droperidol. **Haloperidol** (0.5 to 2 mg IV bolus) is likely as effective as ondansetron (4 mg IV bolus) in preventing PONV. **Droperidol** (0.625 to 1.25 mg IV bolus) is no longer used as a first-line agent due to a 2001 FDA boxed warning associating it with QT segment prolongation and torsade de pointes. A normal QT segment should be documented before droperidol administration and continuous ECG monitoring for a few hours subsequent to the dose. Droperidol is still recommended as an alternative treatment for established PONV.

- E. **Transdermal scopolamine** (1.5 mg) is effective in prophylaxis if applied 2 hours before the start of the surgery. It may cause visual changes and sedation.
- F. **Phenothiazines** include **promethazine** (6.25 to 12.5 mg IV bolus) and **perphenazine** (2.5 to 5 mg IV bolus) that have been used for the prevention and treatment of PONV. Promethazine should be injected carefully as extravasation, or subcutaneous injection could result in tissue necrosis.
- G. **Antihistamines** include **dimenhydrinate** (1 mg/kg IV bolus), and **meclizine** (50 mg PO) can be used for PONV prophylaxis. The major side effect is sedation.
- H. **Propofol** (20 mg IV bolus) can be used as a rescue agent in the PACU.
- I. **NK-1 receptor antagonists** are a newer class of antiemetic agents. The only one currently available for PONV prophylaxis is **aprepitant** (40 to 80 mg PO), and it should be taken within 3 hours prior to induction. While there are limited clinical data, initial studies are promising.

XI. BODY TEMPERATURE CHANGES

- A. Postoperative **hypothermia** causes vasoconstriction with secondary elevation of blood pressure, increased myocardial contractility, and tissue hypoperfusion; it impairs platelet function and clot formation and may increase the risk of bleeding. Changes in cardiac repolarization such as prolongation of the QT interval may induce dysrhythmias. In addition, the metabolism of various drugs is slowed and may result in prolonged recovery from the neuromuscular blockade. During rewarming, shivering significantly increases O_2 consumption and CO_2 production, which may be undesirable in patients with limited cardiopulmonary reserve. Hypothermia in the perioperative period can increase length of stay in PACU, wound infection rates, and cardiac morbidity. Heated blankets, forced warm air blankets, and warm IV solutions should be used to correct hypothermia (see Chapter 19).
- B. Etiologies of **hyperthermia** include infection, transfusion reaction, hyperthyroidism, **malignant hyperthermia**, serotonin syndrome, and neuroleptic malignant syndrome. Symptomatic treatment should be limited to situations in which hyperthermia is potentially dangerous, such as in young children or patients with compromised respiratory or cardiac reserve. **Acetaminophen** (suppositories 650 to 1,300 mg or 10 mg/kg in children) and cooling blankets are commonly used. Hyperthermia can cause sinus tachycardia.

XII. RECOVERY FROM REGIONAL AND NEURAXIAL ANESTHESIA

- A. **Uncomplicated regional blocks** may not require recovery in the PACU. Postoperative monitoring is indicated when heavy sedation was administered, when a complication from the block occurred (e.g., intravascular injection of a local anesthetic and pneumothorax), or when required by the nature of the surgery (e.g., carotid endarterectomy).
- B. **Recovery from spinal and epidural anesthesia** occurs gradually. Patients should show signs of regression of both sensory and motor blockade before discharge. If recovery seems delayed, a neurologic exam should be performed to investigate the possibility of epidural hematoma or nerve injury.

XIII. CRITERIA FOR DISCHARGE

At the Massachusetts General Hospital, all patients who undergo general anesthesia are observed until ready for discharge, with no mandatory minimum recovery time. At least 30 minutes of observation after the last dose of opioids (or other respiratory depressant medication) is required to ensure the adequacy of ventilation and oxygenation.

- A. To be discharged from the PACU, patients must meet several criteria. They should be easily arousable and oriented, or at their baseline. Vital signs should be stable and within normal limits. Pain and nausea should be under control. The requirement for urination or ability to tolerate clear liquids before discharge may be required in selected patients. There should be no obvious surgical complications (e.g., active bleeding) present. Patients who have received neuroaxial anesthesia should show signs of regression of both sensory and motor block before discharge. Effective communication with both the surgical team and the ward to which the patient is to be transferred can expedite the discharge of patients from the PACU. Outpatients should be discharged to a responsible adult with written instructions regarding postoperative diet, medications, etc., and with a phone number to call in case of emergency.
- B. **Fast-track recovery** may be utilized for patients meeting certain criteria upon leaving the OR and are deemed ready to bypass the traditional PACU at the discretion of the anesthesia provider. These patients may be transferred directly to a second-stage recovery unit if they are ambulatory patients or to the floor if they are to be admitted as inpatients. Fast-track recovery criteria include the following:
 - 1. The patient should be awake, alert, and oriented (or at the baseline state).
 - 2. Vital signs should be stable (unlikely to require pharmacologic intervention).
 - 3. Oxygen saturation should be 94% or higher on room air (3 minutes or longer) or at baseline.
 - 4. If a muscular relaxant has been used, the patient should show no clinical signs of muscle weakness and/or the quantitative train-of-four monitoring should be greater than 0.9.
 - 5. Nausea and pain should be minimal (unlikely to require parenteral medications).
 - 6. There should be no active bleeding.
- C. The intraoperative use of short-acting pharmacologic agents (midazolam, propofol, dexmedetomidine, remifentanyl, succinylcholine, desflurane, and sevoflurane) and certain surgeries (orthopedic or simple gynecologic procedures) may make the fast-track recovery more likely.

XIV. ENHANCED RECOVERY AFTER SURGERY

Enhanced Recovery After Surgery (ERAS) Society promotes a series of evidenced-based interventions and treatments encompassing the entire perioperative period. When these recommendations are applied, they lead to better clinical outcomes including reduced mortality and shorter hospital lengths of stay. The foundational efforts were performed in patients who had elective colonic surgery, but additional guidelines have been presented for pancreaticoduodenectomies, rectal and pelvic surgeries, and radical cystectomies. In the PACU, specific attention can be given toward minimizing PONV, applying multimodal analgesia strategies, reducing opioid administration while maintaining adequate pain control, and judicious application of balanced crystalloids for resuscitation.

XV. CONSIDERATIONS FOR PEDIATRIC RECOVERY

- A. **PONV** is more common in the pediatric surgery population than in adults; however, children under the age of 2 years old are exceptions and have a reduced incidence relative to adults. Certain operations (adenotonsillectomy, strabismus repair, hernia repair, orchidopexy, and penile surgery) are associated with increased incidence for PONV. Risk factors, as well as

the general principles for prevention and treatment, are similar to those described in adults (see section X). There is reasonable evidence to suggest **ondansetron** (100 $\mu\text{g/kg}$ IV bolus for <6 months old; 150 $\mu\text{g/kg}$ IV bolus >6 months old up to 4 mg) and **dexamethasone** (62.5 to 500 $\mu\text{g/kg}$ up to 8 mg) are superior to other drugs in the prevention of PONV in children.

- B. Airway Obstruction** results from similar etiologies and responds to similar treatments in children as in adults (section VI.C). Active or recent upper respiratory infections increase the risk of postoperative laryngospasm, especially in children with a history of prematurity or reactive airway disease. Subglottic edema after extubation (postextubation croup) is associated with concurrent upper respiratory infections, traumatic, repeated or prolonged intubations, tight-fitting endotracheal tubes, and surgeries of the head and neck. The treatment is outlined in section VI.C. Placement of the children in the lateral decubitus position after emergence from anesthesia improves the patency of the upper airway and efficacy of chin lift and jaw thrust maneuvers, and it also minimizes the risk of aspiration of gastric contents should vomiting occur.
- C. Agitation** in children may be a normal response upon emergence from anesthesia in a strange, unfamiliar environment and in the absence of their parents. Intraoperative use of volatile anesthetics, ketamine, and atropine as well as inadequately treated pain may increase the incidence of agitation and anxiety. Other causes such as hypoxemia, hypercarbia, hypothermia, hypotension, metabolic disorders, and central nervous system pathology should be considered, investigated, and treated appropriately. Adequate pain control, reassurance, cuddling, and the presence of the parents at the bedside may mitigate the symptoms in most children.

XVI. CRITICAL CARE IN THE POSTANESTHESIA RECOVERY UNIT

Increasingly, patients are admitted to the postanesthesia recovery unit for short-term delivery of ICU level of care. Patients undergoing uncomplicated thoracic (e.g., thoracotomies, lobectomies, and wedge resections) and vascular procedures (e.g., infrarenal abdominal aortic aneurysm repairs, carotid endarterectomies), as well as other procedures involving large volume shifts, require a closer level of postoperative care. Care issues range from aggressive blood pressure management with IV medications to continued mechanical ventilation and hemodynamic resuscitation. It is important for the PACU care providers to establish a plan for continued monitoring and care. If longer-than-expected critical care needs arise, or respiratory and/or hemodynamic perturbations continue, transfer to the ICU should occur.

Suggested Readings

- Apfelbaum JL, Walawander CA, Grasela TH, et al. Eliminating intensive postoperative care in same-day surgery patients using short-acting anesthetics. *Anesthesiology* 2002;97:66–74.
- Apfelbaum JL, Silverstein JH, Chung FF, et al. Practice guidelines for postanesthetic care: an updated report by the American Society of Anesthesiologists Task Force on Postanesthetic Care. *Anesthesiology* 2013;118:291–307.
- Bartels K, Karhausen J, Clambey ET, et al. Perioperative organ injury. *Anesthesiology* 2013;119:1474–1489.
- Chenitz KB, Lane-Fall MB. Decreased urine output and acute kidney injury in the postanesthesia care unit. *Anesthesiol Clin* 2012;30:513–526.
- Fu ES, Downs JB, Schweiger JW, et al. Supplemental oxygen impairs detection of hypoventilation by pulse oximetry. *Chest* 2004;126:1552–1558.

- Gan TJ, Diemunsch P, Habib AS, et al. Consensus guidelines for the management of postoperative nausea and vomiting. *Anesth Analg* 2014;118(1):85–113.
- Gustafsson UO, Scott MJ, Schwenk W, et al. Guidelines for perioperative care in elective colonic surgery: Enhanced Recovery After Surgery (ERAS) Society recommendations. *World J Surg* 2013;37:259–284.
- Kluger MT, Bullock FM. Recovery room incidence: a review of 419 reports from the Anaesthetic Incident Monitoring Study (AIMS). *Anaesthesia* 2002;57:1060–1066.
- Lindenauer PK, Pekow P, Wang K. Perioperative beta-blocker therapy and mortality after major non cardiac surgery. *N Engl J Med* 2005;353:349–361.
- Mashour GA, Orser BA, Avidan MS. Intraoperative awareness: from neurobiology to clinical practice. *Anesthesiology* 2011;114:1218–1233.
- Munk L, Andersen LP, Gögenur I. Emergence delirium. *J Perioper Pract* 2013;23(11):251–254.
- Priebe HJ. Perioperative myocardial infarction-aetiology and prevention. *Br J Anaesth* 2005;95:3–19.
- Sebel PS, Bowdle TA, Ghoneim MM, et al. The incidence of awareness during anesthesia: a multicenter United States study. *Anesth Analg* 2004;99:833–839.
- Thompson A, Balser JR. Perioperative cardiac arrhythmias. *Br J Anaesth* 2004;93:86–94.
- Wang K, Asinger RW, Marriott HJL. ST-segment elevations in conditions other than acute myocardial infarction. *N Engl J Med* 2003;349:2128–2135.

Postoperative Pulmonary Complications

Milad Sharifpour and Edward A. Bittner

Patients undergoing general anesthesia (GA) are at risk for developing postoperative pulmonary complications (PPCs). PPCs commonly include atelectasis, hypoxemia, pneumothorax, pleural effusion, pneumonia, acute respiratory distress syndrome, and postoperative respiratory failure (PRF). The incidence of PPCs is 2% to 19%, depending on the patient population, the surgical procedure, and the type of respiratory complications studied and is comparable to that of postoperative cardiovascular complications. These complications are associated with increased mortality, intensive care unit (ICU) admissions, and increased length of stay.

I. POSTOPERATIVE RESPIRATORY FAILURE

Postoperative respiratory failure is defined as failure to wean from mechanical ventilation within 48 to 72 hours or the need for unplanned postoperative intubation. It occurs in up to 3% of the patients undergoing noncardiac surgery and is associated with increased mortality and the development of further complications such as myocardial infarction, pneumonia, renal failure, deep venous thrombosis, and pulmonary embolism. Despite advances in perioperative care, the incidence of PRF and its associated mortality have remained largely unchanged.

A. The pathophysiology of PPCs can be broadly categorized into three categories: Anesthetic related, surgical factors, and coexisting patient comorbidities.

1. **Effects of anesthetics and sedatives.** GA affects the respiratory system by altering respiratory drive and mechanics via the following mechanisms:

a. **Reduction in respiratory drive.** Volatile anesthetics, sedatives, and opioids are respiratory depressants. They exert their effects by blunting central and peripheral chemoresponsiveness to hypoxemia and hypercapnia, suppressing normal reflexive responses to negative upper airway pressure, and decreasing wakefulness.

1. **Opioids**, the most commonly prescribed analgesics for postoperative pain control, are potent inhibitors of the hypercapnic ventilatory drive. Respiratory failure secondary to postoperative opioid use peaks during the first 24 hours. Patients treated with opioids have a decreased respiratory rate and may become apneic if not stimulated. **Benzodiazepines** also inhibit ventilatory drive, but to a lesser extent than opioids. The effects of these drugs are dose dependent and influenced by age and comorbidities such as intracranial pathology, obstructive sleep apnea (OSA), or chronic obstructive pulmonary disease (COPD).

b. **Residual neuromuscular blockade** often persists despite reversal of muscle relaxants. The upper airway dilator muscles are particularly sensitive to the effects of muscle relaxants, increasing the risk of upper airway obstruction, aspiration, and reintubation when not fully reversed. Neuromuscular blocking agents should be avoided

or administered judiciously in patients with neuromuscular disorders such as Guillain-Barré, myasthenia gravis, and muscular dystrophies.

- c. **Modified respiratory mechanics.** GA alters lung and chest wall mechanics, causing reductions in lung volume and compliance, and chest wall compliance. Immediately after induction of GA functional residual capacity (FRC) decreases by as much as 20%, resulting in atelectasis in dependent regions of the lung. Atelectasis formation is further exacerbated by supine positioning of patients, as well as absorption of alveolar gas (absorption atelectasis) caused by high concentrations of oxygen. Reduced FRC and atelectasis cause ventilation perfusion mismatch, shunting, and hypoxemia.
 - d. **Intraoperative mechanical ventilation.** Ventilator induced lung injury (VILI) results from repetitive overdistention and collapse of dependent lung tissue. Lung protective ventilation with low tidal volumes, low plateau pressures, and the administration of positive end-expiratory pressure (PEEP) is the cornerstone of mechanical ventilation in ICU patients with ARDS. Patients undergoing surgery under GA may also benefit from low tidal volumes, low plateau pressures, higher levels of PEEP, and intraoperative recruitment maneuvers.
2. **Impact of surgery:** A number of surgery-related factors are associated with the development of PPCs:
 - a. **Location.** Upper abdominal and intrathoracic surgical procedures have the strongest association with PPCs.
 - b. **Degree of invasiveness.** Surgical trauma to respiratory muscles (diaphragm and/or intercostals) and phrenic nerve can directly cause respiratory muscle impairment. Postoperative pain can cause splinting and result in atelectasis and hypoxemia.
 - c. **Duration of surgery.** Longer duration is associated with higher risk of PPC.
 - d. **Urgency.** Emergent operations are associated with higher risk of PPC compared to elective cases.
 - e. **Intraoperative fluids.** Large volume intraoperative fluid resuscitation and postoperative fluid shifts can increase intra-abdominal pressure, resulting in reduced diaphragmatic excursion, decreased chest wall compliance, atelectasis, and increased work of breathing.
 3. **Patient comorbidities:** A number of patient-related comorbidities have been identified as predictors of PPC.
 - a. **Aging** is associated with reduced lung elasticity and chest wall compliance, increased dead space, decreased respiratory muscle strength, and blunted response to hypoxemia and hypercapnia. The combination of these factors leads to increased work of breathing, impaired gas exchange, and increased risk of airway obstruction.
 1. Elderly patients have increased sensitivity to the respiratory depressant effects of opioids, benzodiazepines, VAs, and muscle relaxants and decreased drug clearance secondary to impaired liver and kidney functions.
 - b. **Low preoperative oxygen saturation (SaO_2)** as measured by peripheral pulse oximetry is associated with increased risk of PPC. Low SaO_2 may reflect presence of other comorbidities such as congestive heart failure, COPD, or other respiratory diseases.
 - c. **Obesity** is associated with increased risk of unplanned tracheal intubation. Excess chest and abdominal fat decrease chest wall compliance, FRC, and respiratory muscle function, and increase work of

breathing; therefore, obese patients are at increased risk of hypoxia. Adipose tissue deposition within the pharyngeal airway increases the risk of upper airway collapse. Obesity is strongly associated with **obstructive sleep apnea (OSA)** and other cardiovascular comorbidities that place patients at increased risk for PRF.

- d. **Obstructive sleep apnea** is an independent predictor of PPC. OSA has a known prevalence of 5% in women and 14% in men in general population, but its prevalence is likely much higher in the patients undergoing elective surgery due to being undiagnosed. Patients with OSA have increased susceptibility to the respiratory depressant effects of benzodiazepines, opioids, and VAs. They are at increased risk for upper airway obstruction, hypoventilation, and hypoxemic and hypercapnic respiratory failure.
 1. Neuraxial anesthesia, peripheral nerve blocks, and local anesthetic infiltration should be considered as alternatives to GA when possible to reduce the risk of PPCs.
 2. **Short-acting anesthetics** and opioids such as propofol, desflurane, and remifentanyl should be used intraoperatively to minimize postoperative airway-related complications. **Opioid-sparing analgesics** such as acetaminophen, NSAIDs, COX-2 inhibitors, and gabapentinoids can be used to limit postoperative opioid use.
 3. Extubation should only be performed after the patient is fully awake and following commands. Postoperatively, patients with OSA who use continuous positive airway pressure (CPAP) at home should be treated with the same levels of CPAP to prevent airway collapse and hypoxemia.
- e. **Chronic obstructive pulmonary disease** is another independent risk factor for PRF. This increased risk could be attributed to blunted ventilatory responses to hypoxia and hypercapnia and respiratory muscle failure.
 1. Gas exchange may be impaired due to reduced alveolar surface area, increased sensitivity to opioids and benzodiazepines, and abnormal ventilatory control. Hyperinflation of the lungs in patients with COPD flattens the diaphragm, resulting in a mechanical disadvantage that further increases these patients' risk of PRF.
 2. When possible, patients with COPD should undergo respiratory optimization with nebulized bronchodilators, steroids, and antibiotics as appropriate prior to undergoing elective surgery under GA.
 3. Neuraxial and regional anesthesia should be considered as alternatives to GA.
 4. Brachial plexus nerve blocks such as the interscalene block should be used with caution since they are associated with high risk of phrenic nerve blockade and a potential risk of pneumothorax, which can worsen a patient's respiratory function.
- f. **Respiratory tract infection** in the month prior to surgery is associated with increased airway reactivity. When possible, delay of the surgery should be considered if a recent respiratory tract infection is identified.
- g. **Smoking** increases airway irritability and mucus production, impairs respiratory system's immune defenses, and increases the risk of pneumonia, bronchospasm, and PRF. Smoking cessation 4 to 8 weeks prior to elective surgery is associated with improved pulmonary outcomes.

II. UPPER AIRWAY OBSTRUCTION

Upper airway obstruction may occur during recovery from anesthesia. Principal signs are the lack of adequate air movement, intercostal and supra-sternal retractions, and paradoxical abdominal and chest wall motion during inspiration. It can occur immediately after extubation in the operating room or can be delayed and occur in the PACU, on the general care floor, or in the ICU.

A. Common causes of upper airway obstruction include the following:

1. **Residual neuromuscular blockade** secondary to incomplete reversal seen in the immediate postoperative period.
2. **Residual effects of opioids, benzodiazepines, and intravenous- and volatile anesthetics** in the immediate postoperative period.
3. **Laryngeal edema** is a frequent cause of postoperative upper airway obstruction.
 - a. Factors that increase the risk of laryngeal edema include the following:
 1. Multiple intubation attempts or traumatic endotracheal intubation
 2. Prone or Trendelenburg intraoperative position
 3. Large volume fluid resuscitation
 4. Upper airway or neck surgery
 - b. External signs such as facial or scleral edema may indicate the presence of laryngeal edema. However, lack of these signs does not reliably exclude edema.
 - c. Direct-, flexible-, or video laryngoscopy can help clinicians visualize pharynx and larynx and assess the degree and distribution of edema.
 - d. Reverse Trendelenburg or head up position, IV steroids, and nebulized epinephrine may reduce laryngeal edema.
4. **Laryngospasm**, a “protective reflex,” is an involuntary contraction of the vocal cords after stimulation of the superior laryngeal nerve by noxious stimuli such as blood and airway secretions. It is characterized by stridor or the absence of breath sounds and air movement. Children, smokers, and obese patients are at increased risk for laryngospasm.
5. **Negative pressure pulmonary edema (NPPE)** results when inhalation against a closed upper airway generates high negative intrathoracic pressures, disrupts alveolar epithelium and pulmonary vascular endothelium, and results in noncardiogenic pulmonary edema. Young, healthy, athletic patients with good muscle strength are at increased risk for NPPE, which commonly develops immediately after airway obstruction is relieved. It is characterized by hypoxemia, pink frothy sputum, and bilateral infiltrates on chest x-ray that usually resolve within 24 to 48 hours.
6. **Vocal cord paralysis** may be due to direct trauma (traumatic intubation or surgical trauma) or injury to the nerves that innervate the larynx. **Injury to the recurrent laryngeal nerve** leads to adduction of the ipsilateral vocal cord by unopposed action of cricothyroid muscle, which may presents with hoarseness but is often asymptomatic. Bilateral vocal cord paralysis presents as stridor and airway obstruction.
7. **Bleeding and hematoma formation from surgery of the neck** (thyroidectomy, parathyroidectomy, carotid endarterectomy, anterior cervical spine surgery, etc.) may lead to laryngeal edema and tracheal deviation, which can compromise the airway, requiring emergent reintubation or the need for a surgical airway.

III. PREVENTION OF POSTOPERATIVE PULMONARY COMPLICATIONS

Identifying patients at high risk for PPCs allows for preoperative optimization, tailoring of the anesthetic plan and selection of an appropriate setting for postoperative monitoring with the goal of reducing the risk of PPCs.

- A. Risk prediction models based on patient- and surgery-related risk factors may be helpful in identifying individuals at high risk of PPCs.

IV. POSTOPERATIVE MONITORING

- A. Appropriate monitoring is necessary for early detection of respiratory impairment and reducing the risk of PRF.
 1. Patients undergoing surgery are at the highest risk for PPCs during the first 72 hours after surgery. One half of unanticipated endotracheal intubations occur during the first 3 postoperative days.
 2. The risk of respiratory failure due to opioid use is the highest during the first 24 hours after surgery.
 3. The incidence of significant hypoxemia and sleep-disordered breathing peaks on postoperative day 3.
- B. Postoperative respiratory monitoring options include the following:
 1. Acoustic respiratory rate monitors
 2. Pulse oximetry
 3. Capnography appears to be more effective than pulse oximetry in detecting early signs of respiratory depression in patients receiving supplemental oxygen.

V. MANAGEMENT OF POSTOPERATIVE RESPIRATORY INSUFFICIENCY

- A. The immediate goal of managing a patient with respiratory insufficiency is to ensure adequate oxygenation and ventilation. As this is being accomplished, attention should focus on diagnosing and reversing the underlying process(es).
- B. Therapeutic options to achieve adequate oxygenation and ventilation include the following:
 1. **Supplemental oxygen** can be provided through the following mechanisms:
 - a. **Nasal cannula:** A low flow open system. The FiO_2 is increased by approximately 0.03 to 0.04 (3% to 4%) per L/min of O_2 flow. Flows above 4 L/min dry the nasal mucosa and may produce nasal irritation and bleeding. Maximal FiO_2 does not exceed 40% to 50%.
 - b. **Face mask (FM):** Increase the FiO_2 to 0.55 or 0.60 by virtue of higher O_2 flow rates and reservoir space.
 - c. **Masks with reservoir bag (nonrebreather):** High flow, high oxygen, open devices designed to minimize entrainment of air in patients with high inspiratory flow demands. The reservoir bag fills with 100% oxygen so if the patient makes an inspiratory effort generating a flow higher than the wall circuit can deliver, the reservoir of oxygen will be emptied to minimize entrainment of room air.
 - d. **Venturi masks:** Provide variable oxygen concentration at low-to-moderate flows and deliver a more precise FiO_2 in the range of 0.24 to 0.50, by entraining a set ratio of room air to oxygen. As the FiO_2 increases above 0.40, higher oxygen flow rates are required because of the higher O_2 /air entrainment ratio, and the actual FiO_2 may be lower than what the dial would indicate. These masks are useful in patients with COPD in whom precise titration of oxygen concentration may be desirable in order to minimize an increase in PaCO_2 .

- e. **High-flow systems** provide gas flows at 30 to 120 L/min to meet the patient's peak inspiratory flow rate. The maximum FiO_2 depends on the mask fit and can approach 1.0. High-flow systems can cause excessive drying of the airway mucosa if not humidified.
- f. **Resuscitation bag-mask-valve** is a high flow device that requires oxygen flow of approximately 15 L/min. Establishing a tight seal between the mask and the patient's face can minimize room air entrainment. The bag should be squeezed periodically to open the one-way valve in between the high FiO_2 mixture in the reservoir and the patient and provide the patient with higher oxygen concentration.
2. **Clearance of airway secretions:** Secretions can reduce airway diameter and increase airway resistance. Mucous plugs can cause alveolar/lobar collapse and cause significant hypoxemia. Clearance of airway secretions can be facilitated by the following:
 - a. **Suctioning:** Oropharyngeal secretions can be cleared using a Yankauer suction tip, while soft suction catheters can be utilized to effectively remove secretions from the larynx and upper airways.
 - b. **Chest physiotherapy:** percussion and postural drainage can mobilize airway secretions and mucus plugs.
3. **Maneuvers to reestablish airway patency:**
 - a. Simple bedside maneuvers such as chin lift and jaw thrust can reestablish airway patency.
 - b. Oropharyngeal and/or nasopharyngeal airways can also be utilized to maintain airway patency. Careful insertion of these devices is necessary, however, as they can cause airway trauma and bleeding.
4. **Noninvasive positive pressure ventilation (NPPV):** Can be used in the postoperative setting to prevent or treat acute respiratory failure secondary to hypoxemia from atelectasis or pulmonary edema, acute congestive heart failure, and acute hypercarbia from hypoventilation. Noninvasive ventilation can be provided as follows:
 - a. **Continuous positive airway pressure (CPAP)** provides pressure support breaths, as well as positive airway pressure throughout the respiratory cycle. It is mainly used to improve oxygenation in case of hypoxemia secondary to atelectasis and shunting.
 - b. **Bilevel positive airway pressure:** Which applies different levels of positive airway pressure at inspiration and expiration, improving ventilation, oxygenation, and alveolar recruitment.
 1. Gastric distention from air insufflation is a common side effect of NIV and may predispose patients to vomiting and aspiration. The use of NIV immediately after abdominal surgery should be discussed with the surgeon.
5. **Reintubation:** Efforts to reestablish airway patency and provide oxygenation and ventilation may be inadequate and reintubation becomes necessary. Immediate access to airway equipment and skilled personnel is essential. If the airway is anticipated to be difficult, then surgical backup should be available should a surgical airway be needed.
- C. Diagnostic maneuvers to find and treat reversible causes of ARF should be performed while airway patency and adequate oxygenation and ventilation are being established. The diagnostic approach includes the following:
 1. **Review of the anesthetic record:** Can provide information about preexisting comorbidities, baseline and intraoperative vital signs, timing and dosage of anesthetics, opioids, benzodiazepines, neuromuscular blocking agents, and the amount of intraoperative fluids and blood products received, and details regarding airway management and extubation.

2. **Physical examination:** Lung auscultation can provide information about the underlying cause of respiratory insufficiency.
 - a. Stridor, wheezing, rhonchi, crackles, and absent breath sounds can point to the site of airway obstruction (upper versus lower airway), as well as specific etiologies such as laryngospasm, bronchospasm, mucus plugging, or pneumothorax.
 - b. Presence of an irregular heart sounds can indicate an underlying cardiac etiology for respiratory failure.
 - c. Neck swelling may indicate bleeding and hematoma formation, and facial, scleral, or tongue edema may indicate airway edema.
3. **Chest x-ray:** A portable chest x-ray can identify atelectasis, pneumothorax, lobar collapse, or pulmonary edema. **High-resolution chest CT** with contrast can identify pulmonary emboli.
4. **Portable ultrasound** can identify pneumothorax, pulmonary edema, cardiac wall motion abnormalities, valvular abnormalities, or volume overload.
5. **Arterial blood gas analysis:** Can provide information on the severity of the respiratory failure and can help differentiate between hypoxemic and hypercapnic respiratory failure.
6. **Other studies:**
 - a. 12-lead electrocardiogram (ECG) and echocardiography can help with diagnosing myocardial infarction, arrhythmias, heart failure, pulmonary embolism, and cardiac tamponade as potential cause(s) of respiratory failure.
 - b. Direct- or video laryngoscopy may be useful in the diagnosis airway edema.
 - c. Fiberoptic bronchoscopy can be performed to diagnose and remove excessive airway secretions and mucus plugs.
 - d. A nerve stimulator ("twitch monitor") can provide information on the presence of residual neuromuscular blockade.
- D. **Therapies Directed at Reversible Causes of Respiratory Distress:**
 1. Benzodiazepines and opioids may be reversed by careful titration of small doses of flumazenil and naloxone, respectively.
 2. Residual neuromuscular blockade may be reversed with small doses of neostigmine (accompanied by glycopyrrolate to prevent bradycardia).
 - a. Sugammadex is approved in Europe for reversal of aminosteroid nondepolarizing muscle relaxants but is not currently available for clinical use in the United States.
 3. Reverse Trendelenburg or head-up position, administration of intravenous steroids, nebulized epinephrine, diuretics, and inhaled helium-oxygen mixture may be beneficial for patients with postextubation laryngeal edema.
 - a. Early reintubation should be performed if there is no improvement in response to these maneuvers.
 4. Laryngospasm is treated with application of 100% oxygen, jaw thrust, and PEEP. If it does not respond to these interventions, administration of a small amounts of propofol or succinylcholine may be required to break the laryngospasm.
 5. Treatment of NPPE is supportive care with supplemental oxygen and diuretics. Patients with NPPE may require NPPV or reintubation.
 6. Bilateral vocal cord paralysis is a surgical emergency and often requires a surgical airway.
 7. Patients with neck hematoma should be closely monitored for signs of airway obstruction.

- a. A rapidly expanding hematoma should be evacuated emergently, as this may lead to laryngeal edema and tracheal deviation and make endotracheal intubation extremely difficult.
8. A tension pneumothorax should be immediately decompressed with needle thoracostomy or chest tube insertion.
9. Hemodynamically significant pulmonary emboli may present as sudden cardiac arrest and require intravenous or intraarterial thrombolytic therapy or surgical embolectomy.

Suggested Readings

- Bruckmann B, Villa-Urbe J, Bateman BT, et al. Development and validation of a score for prediction of postoperative respiratory complications. *Anesthesiology* 2013;118:1276–1285.
- Canet J, Gallart L. Postoperative respiratory failure: pathogenesis, predication, and prevention. *Curr Opin Crit Care* 2014;20:56–62.
- Canet J, Gallart L. Predicting postoperative pulmonary complications in the general population. *Curr Opin Crit Care* 2013;26:107–115.
- Canet J, Gallart L, Gomar C, et al. Prediction of postoperative pulmonary complications in a population-based surgical cohort. *Anesthesiology* 2010;113:1338–1350.
- Hemmes SNT, Neto AS, Schultz MJ. Intraoperative ventilatory strategies to prevent postoperative pulmonary complications: a meta-analysis. *Curr Opin Anaesthesiol* 2013;26:126–133.
- Ramachandran SK, Nafiu OO, Ghaferi A, et al. Independent predictors and outcomes of unanticipated early postoperative tracheal intubation after nonemergent, noncardiac surgery. *Anesthesiology* 2011;115:44–53.
- Shander A, Fleisher LA, Barie PS, et al. Clinical and economic burden of postoperative pulmonary complications: patient safety summit on definition, risk-reducing interventions, and preventive strategies. *Crit Care Med* 2011; 39: 2163–2172.
- Weingarten TN, Kor DJ, Gali B, et al. Predicting postoperative pulmonary complications in high-risk populations. *Curr Opin Anaesthesiol* 2013;26:116–125.

Adult, Pediatric, and Newborn Resuscitation

Peter L. Bekker, Somalettha Bhattacharya,
and Richard M. Pino

I. OVERVIEW

Cardiopulmonary resuscitation (CPR) in the operating room (OR) is the responsibility of the anesthesiologist who knows the location and function of resuscitation equipment, delegates tasks, and instills calmness in assisting personnel. The algorithms described below have been modified as appropriate for the anesthesiologist in a hospital setting but closely follow the evidenced-based *2010 American Heart Association Guidelines for Cardiopulmonary Resuscitation and Emergency Cardiovascular Care* that includes basic life support (BLS), advanced cardiac life support (ACLS), and pediatric advanced life support (PALS). Essential to the swift return of spontaneous circulation (ROSC) after a sudden cardiac arrest (SCA) is defibrillation for ventricular fibrillation (VF) or pulseless ventricular tachycardia (VT), the prompt delivery of effective, minimally interrupted chest compressions to maintain cerebral and cardiac perfusion, and the avoidance of hyperventilation that may cause continued hypotension through a decrease venous return to the heart. Effective compressions deliver oxygen and energy substrates to the myocardium and increase the likelihood that a perfusing rhythm will return after defibrillation. It is important that CPR be resumed immediately after defibrillation without pause for pulse or rhythm checks. When defibrillation terminates VF and ROSC occurs, continuation of chest compressions is often required, since the myocardium has been depleted of oxygen and metabolic substrates and is “stunned.” Table 38.1 lists the classifications for the quality of evidence used to support most of the protocol interventions presented in this chapter.

II. CARDIAC ARREST

- A. Diagnosis.** The absence of a palpable pulse in a major peripheral artery (carotid, radial, or femoral) in an unconscious, unmonitored patient is diagnostic. An electrocardiogram (ECG) may reveal a nonperfusing rhythm (asystole, VF, VT) or an organized rhythm (as for PEA).
- B. Etiologies.** Common causes of cardiac arrest are
 1. Hypoxemia
 2. Acid–base disturbances
 3. Derangements of potassium, calcium, and magnesium
 4. Hypovolemia
 5. Adverse drug effects
 6. Pericardial tamponade
 7. Tension pneumothorax
 8. Pulmonary embolus
 9. Hypothermia
 10. Myocardial infarction

TABLE
38.1 Evidence Classification for Interventions

Class	Evidence	Clinical Use
I	Excellent	Definitely recommended
IIa	Good/very good	Acceptable, safe, and useful
IIb	Fair/good	Acceptable, safe, and useful
Indeterminate	Preliminary research stage	May be used
III	Positive evidence absent or strongly suggests or confirms harm	None

C. Pathophysiology. If CPR is not immediately started after a cardiac arrest, the cessation of blood flow causes tissue hypoxia, anaerobic metabolism, accumulation of cellular wastes, and permanent organ damage. Acidosis from anaerobic metabolism may cause systemic vasodilation, pulmonary vasoconstriction, and decreased responsiveness to the actions of catecholamines.

III. ADULT RESUSCITATION

A. Basic life support (BLS) includes those fundamental principles that are taught to the general public but applies equally to OR situations. A cardiac arrest should be suspected in any person unexpectedly found unconscious. If the subject cannot be aroused, the 2010 AHA guidelines for CPR and ECC stress immediate activation of the emergency response system and initiation of chest compressions to provide **Circulation** prior to **Airway** management and **Breathing (C-A-B)**. The vast majority of cardiac arrest in adults is due to VF or pulseless VT, etiologies in which early chest compressions and defibrillation are most critical. The C-A-B sequence minimizes delay associated with opening the airway and associated positioning, obtaining a seal for mouth-to-mouth breathing, or obtaining bag-mask equipment. Beginning with chest compressions may also increase likelihood that bystanders will perform CPR on persons who have suffered from SCA, since laypersons and some health care providers may find airway management a challenging first step and therefore be hesitant to initiate CPR. For lone rescuers, the lay public is taught the “phone first/phone fast” rule (evidence class indeterminate). For adults, children aged 8 years and older, and all children known to be at high risk for arrhythmias, the emergency medical system (911; EMS) should be activated (phone first) before attempts at resuscitation by a lone rescuer. An initial resuscitation attempt followed by the activation of EMS (“phone fast”) is indicated for children less than 8 years old and for all ages in cases of submersion or near drowning, arrest secondary to trauma, and drug overdose.

1. Circulation. The patient should be on a firm surface (e.g., backboard) with the head on the same level as the thorax. The rescuer (surgeon in the OR) compresses the sternum between the nipples with the heel of one hand, the other hand on top of the first so that the hands are overlapped and parallel (evidence class IIa), shoulders positioned directly over the patient, and elbows locked to depress the chest to a depth of 1.5 inches (infants) and of at least 2.0 inches in children and a normal-sized adult. The chest compression rate is 100/minute at a compression–relaxation ratio of 1:1. For a single rescuer, the compression–ventilation ratio is 30:2.

Unlike adults, in children, the compression–ventilation ratio becomes 15:2 if there are 2 rescuers. For a prone patient in the OR who cannot be quickly turned supine for CPR, one rescuer can place a clenched fist between the subxiphoid area and the OR table while compressions are administered over the corresponding region of the back. If an advanced airway (i.e., endotracheal tube or laryngeal mask airway) is in place during two-rescuer CPR, ventilations should be given at a rate of 8 to 10 breaths/min, chest compressions at a rate of 100/min without pauses for ventilation, and compressions are not synchronized between breaths.

2. **Airway and breathing.** Spontaneous ventilation is evaluated by observation and auscultation and is aided by repositioning (chin lift and jaw thrust) or insertion of an oropharyngeal or nasopharyngeal airway. If the patient is apneic or has ineffective spontaneous breaths (e.g., gasping only), rescue breathing or ventilation by bag-valve-mask with 100% O₂ is started. Two slow breaths at low airway pressures (to limit gastric distention) are first given, followed by ventilation with a respiratory rate of 8 to 10 breaths/min. If ventilation is not possible after these maneuvers, efforts to clear the airway of a suspected foreign body (e.g., Heimlich maneuver, chest compressions, or manual removal) should be attempted.
3. **Defibrillation** within 3 minutes in the hospital (evidence class I) and 5 minutes after calling the EMS (along with immediate high-quality CPR) is the major determinant of a successful resuscitation, since VF is the most likely etiology of a cardiac arrest in adults. Public access defibrillation programs have enabled “level I” responders (e.g., fire personnel, police, security guards, and airline attendants) to employ readily accessible automated external defibrillators (AEDs). AEDs are small, lightweight devices that use adhesive electrode pads for both sensing and delivering shocks. Visual and voice prompts are provided to assist the operators. The AED, after analysis of the frequency, amplitude, and slope of the ECG signal, *advises* either “shock indicated” or “no shock indicated.” The AED is manually triggered and does not automatically defibrillate the patient. AEDs are now also equipped with pediatric pad-cable systems that attenuate the adult dose to smaller dose appropriate for children. The dose attenuators should be used in children less than 8 years of age and less than 25 kg in weight. For infants, manual defibrillator is recommended but if unavailable AED with or without an attenuator can be used.
4. **Reassessment.** CPR should be resumed immediately after defibrillation (without checking for a pulse or rhythm) and continued for five cycles (or about 2 minutes if an advanced airway is in place) after which time the rhythm should be checked. For health care providers, if there is evidence for a perfusing rhythm, the pulse should be checked to determine if there is ROSC. If a nonshockable rhythm or no pulse is detected, CPR should be resumed, with rhythm checks every five cycles.
- B. **Advanced cardiac life support**, including endotracheal intubation, electrical defibrillation, and pharmacologic intervention, is the definitive treatment for cardiac arrest.
 1. **Intubation.** Swift control of the airway optimizes oxygenation and the removal of carbon dioxide during resuscitation. Endotracheal intubation by the most experienced person present should minimally disrupt other resuscitative measures. Quantitative waveform capnography should be used to confirm and monitor endotracheal tube placement. The endotracheal tube may be used to deliver certain drugs like naloxone, atropine, vasopressin, epinephrine, or lidocaine (NAVEL) if

intravenous (IV) access has not been established. Higher doses (two to three times) of these drugs diluted in 10 mL of sterile saline should be used, since peak drug concentrations are lower with the endotracheal route compared to IV administration.

2. **Defibrillation.** Pulseless VT and VF are the most common dysrhythmias associated with a cardiac arrest (Fig. 38.1). As the duration of an SCA increases, cardiac function worsens and it becomes more difficult to convert to ROSC. Defibrillation is the priority and can often be administered by the anesthetist without compromising the surgical field. It is the responsibility of the person operating the defibrillator to ensure that members of the resuscitation team are not in contact with the patient during defibrillation.

- a. **Defibrillators** deliver energy in a **biphasic** pulse that flows in a positive direction for specified milliseconds followed by reversal of current flow in the negative direction. The optimal dose determined to terminate VF is 150 to 200 J and is indicated on the front of the

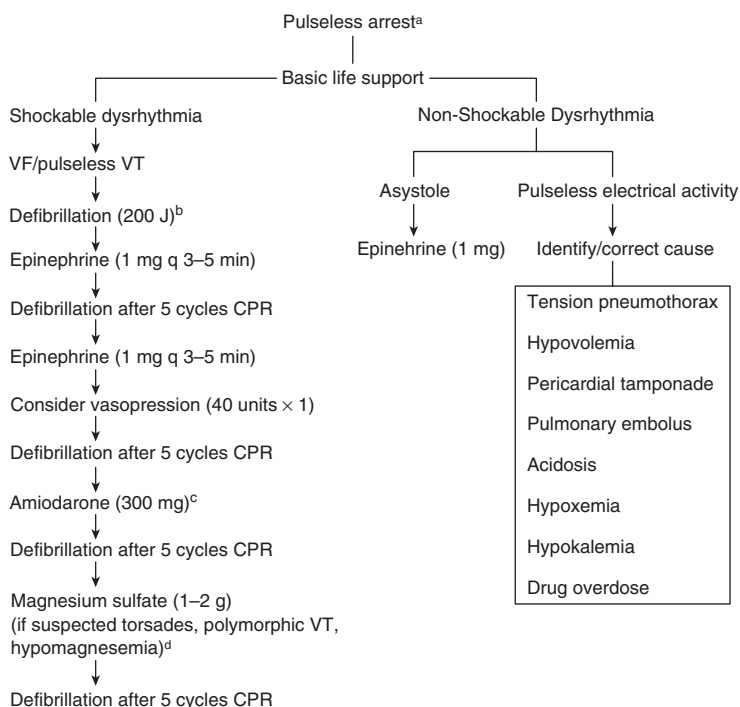


FIGURE 38.1 Algorithm for pulseless arrest. VF, ventricular fibrillation; VT, ventricular tachycardia.

^aWhen rhythm is unclear and could be VF, treat as shockable rhythm. ^bBiphasic. One cycle of CPR should follow any successful defibrillation. ^cAmiodarone bolus should be administered in 20 to 30 mL saline or D₅W. This is followed by an infusion of 1 mg/min for 6 hours and then 0.5 mg/min thereafter. An additional dose of 150 mg IV can be readministered for recurrence of VF or VT. ^dConsider earlier in the algorithm in addition to the other interventions if these are suspected.

defibrillator. In children, an initial dose of 2 to 4 J/kg is advised, and the dose can be increased with successive shocks. The dose should not exceed 10 J/kg or the maximum adult dose. The large adult paddles (8 to 13 cm) are recommended in children above 1 year of age and at least 10 kg in weight. Infant paddles (4.5 cm) are used in children less than 10 kg in weight.

- b. **Cardioversion** using synchronized biphasic shocks of 50 to 100 J is used for supraventricular arrhythmias such as paroxysmal supraventricular tachycardia (PSVT). The recommended initial biphasic energy dose for cardioversion of atrial fibrillation is 120 to 200 J, depending on the manufacturer of the device; dosing can be increased in stepwise fashion if initial shock is ineffective. Hemodynamically stable VT can be cardioverted using 100 J as the starting point. The initial dose for cardioversion in children is 0.5 to 1 J/kg followed by subsequent doses of 2 J/kg.
3. **Pacing.** High-grade heart block with profound bradycardia is one etiology of cardiac arrest. Temporary pacing should be used when the heart rate does not increase with pharmacologic therapy. Transcutaneous pacing is the easiest method to increase the ventricular rate. Transesophageal atrial pacing is efficacious for sinus bradycardia with maintained atrioventricular (AV) conduction and is useful intraoperatively for bradycardia-related hypotension in otherwise stable patients. Transvenous pacing via a temporary wire into the right heart is a third option to increase heart rate while CPR continues. Special pacing pulmonary artery catheters are capable of AV pacing.
4. **IV access** is imperative for a successful resuscitation, though establishment of venous access should not delay chest compressions or defibrillation (when appropriate). The most desirable route is into the central circulation. The insertion site (internal jugular, external jugular, subclavian, or femoral vein) is predicated based on the anatomy of the patient, experience of the physician, and what is the least disruptive to the resuscitation. Peripheral IV catheters in antecubital veins are adequate when an appropriate volume is used to flush medications toward the central circulation. If peripheral vascular access is not easily established, intraosseous (IO) cannulation should be attempted. IO access can be done in less than a minute in children. All drugs and fluids can be given through an IO route till good IV access is obtained.
5. **Drugs.** The drugs described below are used in ACLS protocols for the treatment of hemodynamic instability, myocardial ischemia and infarction, and arrhythmias. The doses of drugs used for **Pediatric Advanced Life Support (PALS)** are in parentheses following discussion of adult doses.
 - a. **Adenosine**, an endogenous purine nucleoside with a half-life of 5 seconds, slows AV nodal conduction and interrupts AV node reentry pathways to convert a PSVT to a sinus rhythm. It also assists in the differential diagnosis of supraventricular tachycardia (e.g., atrial flutter with a rapid ventricular response versus PSVT). Adenosine can also be considered in the diagnosis and treatment of stable, regular wide complex monomorphic tachycardia. The initial dose is a 6 mg rapid IV bolus. A brief asystole ensues, followed by P waves, flutter waves, or fibrillation waves that are initially without ventricular responses. PSVT is sometimes converted to a sinus rhythm by the 6 mg dose. A second injection of 12 mg may terminate PSVT if the first dose is unsuccessful. Recurrent PSVT, AF, and atrial flutter will require longer-acting drugs for definitive treatment. The dose of adenosine should be increased in the presence of methylxanthines

(competitive inhibition) and decreased if dipyridamole (potential via blockage of nucleoside transport) has been administered (PALS: 0.1 mg/kg; repeat dose 0.2 mg/kg; maximum dose 12 mg).

- b. **Amiodarone** is the most versatile drug in the ACLS algorithms. It has the properties of all four classes of antiarrhythmics (lengthening of action potential, sodium channel blockade at high frequencies of stimulation, noncompetitive antisynaptic actions, and negative chronotropism). Because of its high efficacy and low incidence of proarrhythmic effects, it is the preferred antiarrhythmic for patients with severely impaired cardiac function. For pulseless VT and VF, 300 mg diluted in 20 to 30 mL of saline or 5% dextrose in water (D5W) is administered rapidly. To treat stable dysrhythmias (e.g., hemodynamically stable AF), 150 mg is administered over 10 minutes, followed by an infusion of 1 mg/min for 6 hours, and then 0.5 mg/min. The maximum daily dose is 2 g. Immediate side effects can be bradycardia and hypotension (PALS: loading dose, 5 mg/kg; maximum dose, 15 mg/kg/day). Amiodarone is indicated in the following arrhythmia situations.
 1. Unstable VT (evidence class IIb)
 2. VF or pulseless VT after failed electrical defibrillation and epinephrine treatment (evidence class IIb)
 3. Attempted rate control during stable monomorphic VT, polymorphic VT (evidence class IIb), or AF (evidence class IIa)
 4. Attempted ventricular rate control of rapid atrial arrhythmias when digitalis is ineffective (evidence class IIb) or when the tachycardia is secondary to accessory pathways (evidence class IIb)
 5. Need for an adjunct to electrical cardioversion of refractory PSVT (evidence class IIa) or atrial tachycardia (evidence class IIb)
- c. **Atropine** is useful in the treatment of hemodynamically significant bradycardia (evidence class I) or AV block occurring at the nodal level (evidence class IIa). It increases the rate of sinus node discharge and enhances AV node conduction by its vagolytic activity. The dose of atropine for bradycardia or AV block is 0.5 mg repeated every 3 to 5 minutes to a total dose of 0.04 mg/kg. Atropine is not indicated for asystole but should be considered for treatment of a profound bradycardia that may appear as asystole. Full vagal blockade is obtained at a cumulative dose of 3 mg (PALS: 0.02 mg/kg; minimum dose, 0.1 mg; maximum single dose, 0.5 mg in child, maximum dose for adolescent 3 mg).
- d. **β -Adrenergic-blocking drugs** (atenolol, metoprolol, and propranolol) have established utility (evidence class I) for patients with unstable angina or myocardial infarction. These drugs reduce the rate of recurrent ischemia, nonfatal reinfarction, and postinfarction VF. In contrast to calcium channel blockers, β -blockers are not direct negative inotropes. β -Blockers are useful for the acute treatment of PSVT, AF, atrial flutter (evidence class I), and ectopic atrial tachycardia (evidence class IIb). Initial and subsequent IV doses, if tolerated, are atenolol, 5 mg over 5 minutes, repeated once at 10 minutes; metoprolol, three doses of 5 mg every 5 minutes; propranolol, 0.1 mg/kg divided into three doses given every 2 to 3 minutes; esmolol, 0.5 mg/kg over 1 minute followed by an infusion starting at 50 μ g/min and titrated as needed up to 200 μ g/min. Contraindications include second- or third-degree heart block, hypotension, and severe congestive heart failure. Although β -blockers may trigger

bronchospasm in a small number of patients, they are tolerated by most patients with chronic lung disease.

- e. **Calcium** is indicated during cardiac arrest only when hyperkalemia, hypomagnesemia, hypocalcemia, or toxicity from calcium channel blockers is suspected. Calcium chloride, 5 to 10 mg/kg IV, can be repeated as necessary (PALS: calcium chloride 10%: 20 mg/kg = 0.2 ml/kg).
- f. **Dopamine** has dopaminergic ($<2 \mu\text{g/kg/min}$), β -adrenergic (2 to 5 $\mu\text{g/kg/min}$), and α -adrenergic (5 to 10 $\mu\text{g/kg/min}$) activities. Although the above are “traditional” doses, the dose responses are not reliable (e.g., tachycardia may occur with the lowest doses). Dopamine should be started at a low dose (e.g., 150 $\mu\text{g/min}$) and titrated until the desired effect (e.g., increased urine output, increased heart rate/inotropy, or increased blood pressure) is seen or undesired side effects (e.g., tachyarrhythmia) limit further increases.
- g. **Epinephrine** continues to be the mainstay of pharmacologic therapy for cardiac arrest. Its α -adrenergic vasoconstriction of noncerebral and noncoronary vascular beds produces compensatory shunting of blood toward the brain and the heart. High doses may contribute to myocardial dysfunction. The recommended dose is 1.0 mg IV, repeated every 3 to 5 minutes. Epinephrine used for symptomatic bradycardia is evident as class IIb (PALS: bradycardia, 0.01 mg/kg; pulseless arrest, 0.01 mg/kg).
- h. **Ibutilide** is used for the acute conversion of AF, either alone or with electrical cardioversion. It prolongs the duration of the action potential and increases the refractory period. The dose is 1 mg given over 10 minutes and can be repeated in 10 minutes. The dose for patients weighing less than 60 kg is 0.01 mg/kg. Continuous monitoring of the patient is required during its administration and for at least 6 hours thereafter, since the major side effect of ibutilide is polymorphic VT (including torsade de pointes).
- i. **Isoproterenol** is a β_1 -adrenergic and β_2 -adrenergic agonist. It is a second-line drug used to treat hemodynamically significant bradycardia that is unresponsive to atropine and dobutamine in the event that a temporarily pacemaker is not available (evidence class IIb). Its β_2 activity can cause hypotension. Isoproterenol is administered by IV infusion at 2 to 10 $\mu\text{g/min}$, titrated to achieve the desired heart rate.
- j. **Lidocaine** may be useful for the control (not prophylaxis) of ventricular ectopy during an acute myocardial infarction. The initial dose is 1.0 to 1.5 mg/kg IV that may be repeated as a 0.5- to 0.75-mg/kg bolus every 3 to 5 minutes to a total dose of 3 mg/kg followed by a continuous infusion at 2 to 4 mg/min. The lidocaine dose should be decreased for patients with reduced cardiac output, hepatic dysfunction, or advanced age (PALS: 1 mg/kg; infusion, 20 to 50 $\mu\text{g/kg/min}$).
- k. **Magnesium** is a cofactor in a variety of enzyme reactions including that of the Na^+ , K^+ -ATPase. Hypomagnesemia can precipitate refractory VF as well as exacerbate hypokalemia. Magnesium replacement is effective for the treatment of drug-induced torsade de pointes. The dose for emergent administration is 1 to 2 g in 10 mL D5W over 1 to 2 minutes. Hypotension and bradycardia are the side effects of rapid administration (PALS: 25 to 50 mg/kg; maximum dose, 2 g).
- l. **Oxygen** (100%) should be administered to all cardiac arrest victims by bag-valve-mask or endotracheal ventilation and to hemodynamically stable, breathing patients by unpressurized face mask.

- m. **Procainamide** can convert AF and atrial flutter to sinus rhythm (evidence class IIa), can control the ventricular response to supraventricular tachycardia secondary to accessory pathways (evidence class IIb), and is useful during cardioversion of wide complex tachycardias of unknown origin (evidence class IIb). It has essentially been replaced by amiodarone. The loading dose is a continuous infusion of 20 to 30 mg/min that is terminated when the arrhythmia is suppressed, hypotension occurs, the QRS complex is widened by 50% of its original size, or a total dose of 17 mg/kg is reached. When the arrhythmia is suppressed, a maintenance infusion of 1 to 4 mg/min should be initiated, with reduced dose considered in the presence of renal failure. An ECG should be examined for QRS widening at least daily (PALS: 15 mg/kg over 30 to 60 minutes).
 - n. **Sodium bicarbonate** administration is detrimental in most cardiac arrests because it creates a paradoxical intracellular acidosis (evidence class III). It can be considered when the standard ACLS protocol has failed in the presence of severe preexisting metabolic acidosis and for the treatment of hyperkalemia or tricyclic antidepressant overdose. The initial dose of bicarbonate is 1 mEq/kg IV, with subsequent doses of 0.5 mEq/kg given every 10 minutes (as guided by arterial blood pH and partial pressure of carbon dioxide [PaCO_2]) (PALS: 1 mEq/kg).
 - o. **Vasopressin**, a hormone from the neurohypophysis, has pressor (V_1) and antidiuretic (V_2) activities. Endogenous levels of vasopressin are increased in patients undergoing CPR who eventually have ROSC. It is more effective than epinephrine in maintaining the coronary perfusion pressure, has a longer half-life of 10 to 20 minutes, and may be substituted for either the first or second dose of epinephrine in the treatment of pulseless arrest (40 units IV). However, although it may have some advantage in the treatment of asystole, the evidence for its effectiveness in a cardiac arrest is limited (PALS: 0.4 to 1 unit/kg bolus with a maximum dose of 40 units for cardiac arrest and 0.0002 to 0.002 units/kg/min for catecholamine-resistant hypotension).
 - p. **Verapamil** and **diltiazem**, calcium channel blockers that depress AV nodal conduction, are used to treat hemodynamically stable, narrow complex PSVT unresponsive to vagal maneuvers or adenosine. The initial verapamil dose is 2.5 to 5.0 mg IV, with subsequent doses of 5 to 10 mg IV administered every 15 to 30 minutes. Diltiazem is given as an initial bolus of 20 mg. An additional dose of 25 mg and an infusion of 5 to 15 mg/h can be administered if needed. Their vasodilator and negative inotrope properties can cause hypotension, exacerbation of congestive heart failure, bradycardia, and enhancement of accessory conduction in patients with Wolff-Parkinson-White syndrome. The hypotension can often be reversed with calcium chloride, 0.5 to 1.0 g IV.
6. **Specific ACLS protocols** are shown in Figures 38.1 to 38.3.
 - a. Pulseless arrest (Fig. 38.1)
 - b. Bradycardia (Fig. 38.2)
 - c. Tachycardia with pulse (Fig. 38.3)
 7. **Open-chest direct cardiac compression** is an intervention used at institutions with appropriate resources to manage penetrating chest trauma, abdominal trauma with cardiac arrest, pericardial tamponade, hypothermia, or pulmonary embolism. Direct cardiac compressions also are indicated for individuals with anatomic deformities of the chest that prevent adequate closed-chest compression.

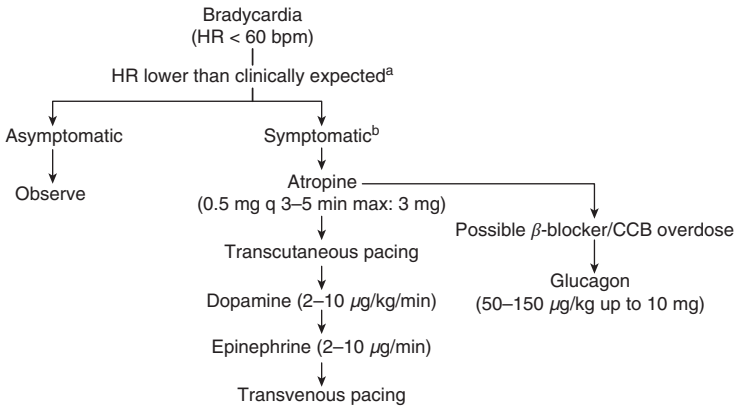


FIGURE 38.2 Algorithm for bradycardia HR, heart rate; bpm, beats per minute; CCB, calcium channel blocker. ^aNormal heart rate goal may be <60 bpm for patients receiving therapeutic nodal agents (e.g., β -blocker). ^bSymptoms may include altered mental status, hypotension, pulmonary edema, congestive heart failure, and myocardial infarction.

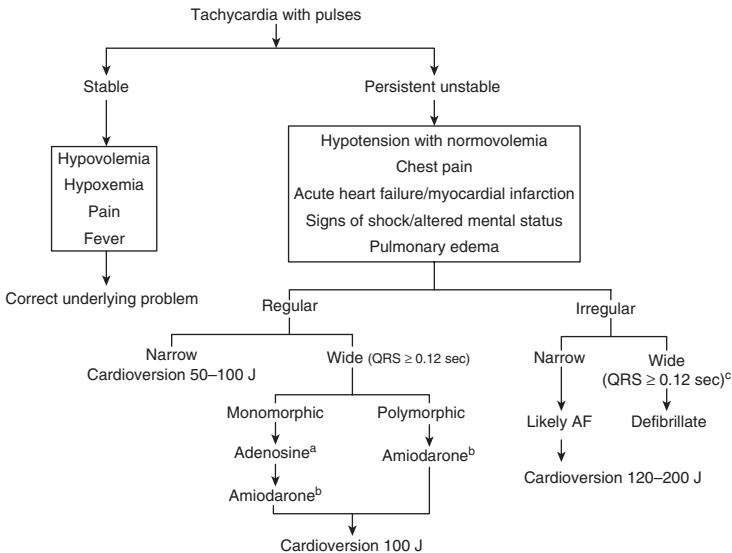


FIGURE 38.3 Algorithm for tachycardia with pulse ^aAdenosine: rapid peripheral IV push, 6 to 12 mg if second dose is needed; central access: initial dose 3 mg, second dose 6 mg. ^bAmiodarone bolus should be administered in 20 to 30 mL saline or D₅W. This is followed by an infusion of 1 mg/min for 6 hours and then 0.5 mg/min thereafter. ^cWhen rhythm is unclear and could be VF, treat as shockable rhythm (Fig. 38-1).

8. **Termination of CPR.** There are no absolute guidelines to determine when to stop an unsuccessful resuscitation, but there is a very low probability of survival after 30 minutes. It is at the discretion of the physician in charge to determine when the failure of the cardiovascular system to respond to adequately applied BLS and ACLS indicates that the patient has died. There should be a meticulous documentation of the resuscitation, including the reasons for terminating the effort.
9. The advanced directive **"Do not resuscitate" (DNR)** places the anesthesiologist in a key position with respect to intraoperative and postoperative care. It is often incorrectly *assumed* that a DNR order is suspended in the perioperative period. Each institution's written guidelines should be reviewed. In advance of a procedure, physicians and the patient with the DNR status or the patient's health care proxy should clarify any resuscitative measures that would be compatible with the patient's wishes. For example, the use of a pressor to control hypotension following induction of general anesthesia might be permitted while defibrillation and CPR for spontaneous VF might be prohibited. When asked to perform an emergent intubation outside of the OR, the anesthesiologist should ask about the patient's code status and is ethically and legally bound to a known decision to limit treatment.

IV. PEDIATRIC RESUSCITATION

- A. **Basic Life Support.** The need for CPR in the pediatric age group is rare after the neonatal period. Pediatric cardiac arrests usually result from hypoxemia linked to respiratory failure or airway obstruction. Initial efforts should be directed toward the establishment of a secure airway and adequate ventilation. The pediatric guidelines apply to infants between the ages of about 1 month and 1 year and to children more than 1 year of age. For newborns, see section V below. The definition of "children" for health care providers is patients between the ages of 1 year and the start of puberty; for the lay public, a child is defined as aged 1 to 8 years. In contrast to the guideline of "phone first" for adult CPR, one should "phone fast" for infants and children. That is, the lone rescuer should perform five cycles (about 2 minutes) of CPR before phoning 911. The "phone fast" rule also applies to resuscitation from drowning, traumatic arrest, or drug overdose. Exceptions include witnessed and sudden arrests (e.g., an athlete who collapses on the playing field) or situations in which a child is known to be at high risk for a sudden arrhythmia. Modifications of the rate and magnitude of compressions and ventilations, as well as of the hand position for compressions, are necessary because of anatomic and physiologic differences (Table 38.2). Differences between pediatric and adult resuscitation techniques are detailed below.
 1. **Airway and breathing.** Maneuvers to establish an airway are the same as in the adult, with a few caveats. For children less than 1 year of age, abdominal thrusts are not used, since the gastrointestinal tract can be damaged easily. Hyperextension of an infant's neck for the head tilt/chin lift may lead to airway obstruction because of the small diameter and ease of compression of the immature airway. Submental compression while performing the chin lift can also lead to airway obstruction by pushing the tongue into the pharynx. Ventilations should be given slowly with low airway pressures to avoid gastric distention and should be of sufficient volume to cause the chest to rise and fall.
 2. **Circulation.** The brachial or femoral artery is used for pulse assessment in infants (patients <1 year old) because the carotid artery is difficult to palpate. Upon determination that a pulse is absent, chest compressions

TABLE
38.2 Adult and Pediatric Cardiopulmonary Resuscitation

Age	Ventilations/ Minute	Compressions/ Minute	Ventilation: Compression Ratio	Depth of Compressions
Neonate	30	90	3:1 ^{a,b}	1/3 depth of chest
Infant (<1 y)	12–20	100	30:2 ^a /15:2 ^b	1/3–1/2 depth of chest
Child (1–8 y)	12–20	100	30:2 ^a /15:2 ^b	1/3–1/2 depth of chest
Adult and child >8 y	10–12	100	30:2 ^{a,b}	1.5–2 inches

^a One-person rescue.

^b Two-person rescue.

should be initiated. Chest compressions in infants are delivered using two fingertips applied to the sternum or by encircling the chest with both hands and using the thumbs to depress the sternum one fingerbreadth below the intermammary line. In older children, the correct hand position is determined as for adults, but with only one hand depressing the sternum. The chest should be compressed about one third to one half of its anterior–posterior depth. The compression/ventilation ratio is 30:2 for one-rescuer CPR of infants and children, and 15:2 when 2 rescuers are available. If an advanced airway is in place during two-person CPR, there is no need to synchronize breaths between compressions. Ventilations should be given at a rate of approximately 8 to 10 breaths/min, and chest compressions should be given at a rate of 100/min without pauses for ventilation.

B. Pediatric Advanced Life Support (PALS). Most pediatric cardiac arrests present as asystole and bradycardia, rather than ventricular arrhythmias. In infants less than 1 year old, respiratory and idiopathic (sudden infant death syndrome) etiologies predominate. Anatomic and physiologic differences from the adult require defibrillator settings and drug doses to be weight based.

- 1. Intubation.** Introduction of low-pressure high-volume cuffed endotracheal (ET) tubes have shifted the choice toward the use of cuffed ET tubes in children. The cuff pressure should be monitored and maintained between 20 and 30 cm of water. The internal diameter (ID) of ET tube required in children less than 1 year of age is 3.5 mm uncuffed or 3 mm cuffed and 1 to 2 years of age, the size is 4 mm uncuffed or 3.5 mm cuffed. The formula for size of ET tube (ID in mm) in children above 2 years of age is as follows: age in years/4 + 4 for uncuffed tubes and age in years/4 + 3.5 for cuffed tubes. Correct positioning is confirmed with capnography. Auscultation and radiographic confirmation is required to rule out endobronchial intubation. If an intubated patient's condition deteriorates, rule out displacement or obstruction of ET tube, pneumothorax, and equipment failure (mnemonic DOPE).
- 2. Defibrillation.** Defibrillator paddles used for infants are 4.5 cm in diameter, and those used for older children are 8 cm in diameter (adult paddles). The energy level is 2 J/kg for the initial biphasic shock and 4 J/kg or the lowest level that was previously successful for any subsequent shocks. Hypoxemia, acidosis, or hypothermia should be considered as treatable causes of an arrest if the defibrillation attempts are

unsuccessful. For cardioversion, the starting energy is 0.2 J/kg, with escalation to 1.0 J/kg if needed. The configuration for pediatric paddles varies among defibrillators.

3. **IV access.** During resuscitation, peripheral IV access is preferred over central venous access as its placement may require interruption in chest compressions. If a central access is in place that is the preferred route for delivery of drugs and fluids. All drugs by peripheral route should be flushed with saline to the central circulation. IO route can be used in all age groups if initial venous access is an issue.
4. **Medications.** Many of the drugs described in the adult ACLS section (section III.B.5) apply to PALS, with doses adjusted to the child's weight. Weight estimations are obtained using body length tape with precalculated weights (Broselow tape) or formulas like the European pediatric life support (EPLS) formula [(age in years + 4) × 2 kg]. Extracorporeal life support should be considered.
5. Specific PALS algorithms are shown in Figures 38.4 to 38.6.
 - a. Pediatric cardiac arrest (Fig. 38.4)
 - b. Pediatric bradycardia (Fig. 38.5)
 - c. Pediatric tachycardia with pulses (Fig. 38.6)

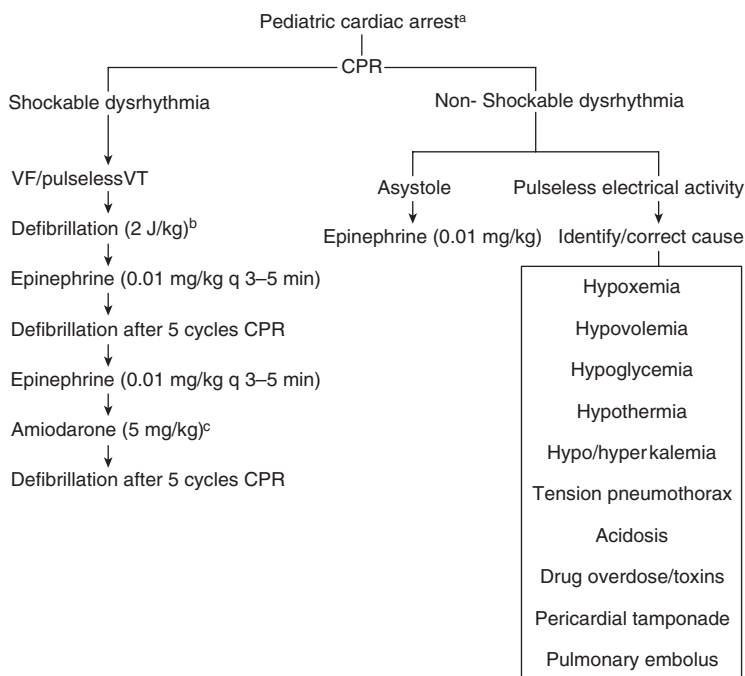


FIGURE 38.4 Algorithm for pediatric cardiac arrest CPR, cardiopulmonary resuscitation; VF, ventricular fibrillation; VT, ventricular tachycardia. ^aProvide oxygen, establish intravenous or intraosseous access. ^bFirst shock, 2 Joules (J)/kg, second shock 4 J/kg, subsequent shocks ≥ 4 up to 10 J/kg or adult dose (200 J). ^cMay repeat up to two times for VF or refractory VT.

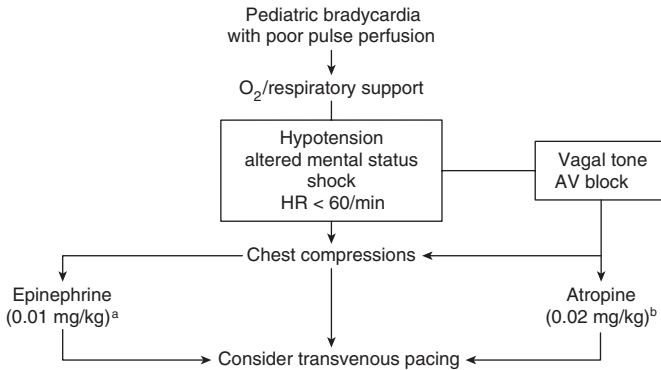


FIGURE 38.5 Algorithm for pediatric bradycardia. HR, heart rate; AV, atrioventricular. ^aMay repeat every 3 to 5 minutes. If vascular access is not available, may give 0.1 mg/kg via endotracheal tube. ^bMay repeat once. Minimum atropine dose is 0.1 mg; maximum 0.5 mg.

6. Family Presence. Family presence during pediatric resuscitation is becoming the norm in most institutions. Studies have shown that this is beneficial to family members, and parents should be offered the opportunity to observe the resuscitative efforts. One person should be assigned to stay with the family to explain and answer questions and also to provide comfort and support during the resuscitative process. Parents can be requested to leave if they are disruptive. The team should be aware of the presence of the family.

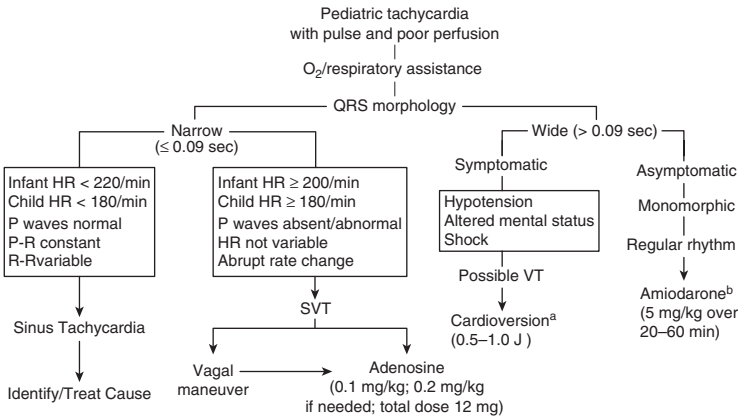


FIGURE 38.6 Algorithm for pediatric tachycardia with pulse and poor perfusion. HR, heart rate; SVT, supraventricular tachycardia; VT, ventricular tachycardia. ^aIf not effective, increase to 2 J/kg. ^bAlternative to amiodarone is procainamide, 15 mg/kg over 30 to 60 minutes.

V. NEONATAL RESUSCITATION (FIG. 38.7)

The neonatal period extends through the first 28 days of life. About 10% of newborn require assistance with respiration at birth but only 1% require active resuscitation. At least one person who is skilled in resuscitation of

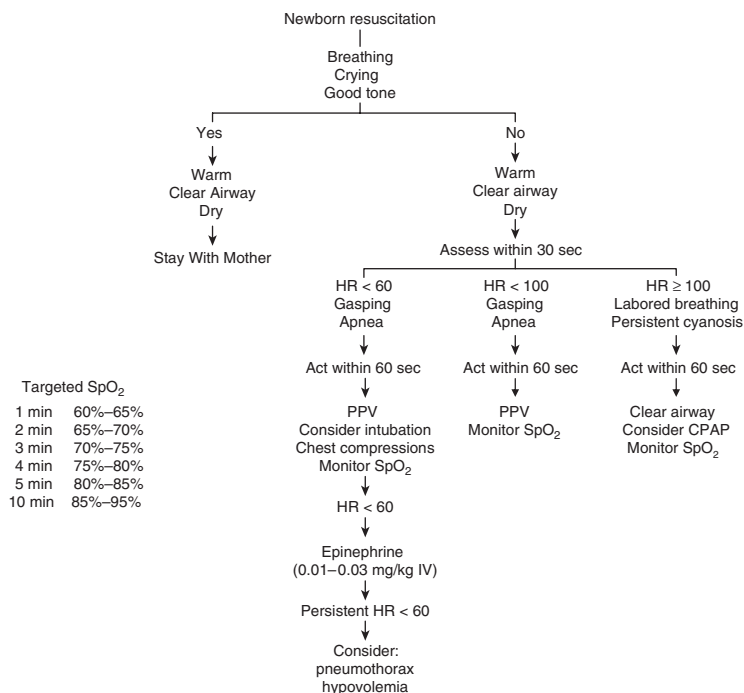


FIGURE 38.7 Algorithm for newborn resuscitation. HR, heart rate; PPV, positive pressure ventilation.

newborns should be present at every delivery. Rapid assessment regarding term gestation, respiration/crying, and muscle tone helps in identifying the babies who require resuscitation. Resuscitation is often needed during an emergent cesarean section for fetal distress. In the event that the anesthesiologist is the only one available to treat the newborn, the neonatal warmer should be brought to the head of the OR table to facilitate the treatment and monitoring the mother and child until the pediatrician arrives.

A. Assessment. Immediate neonatal resuscitation is crucial, since profound hypoxemia occurs rapidly and will be exacerbated by respiratory acidosis, which contributes to the persistence of fetal circulation and right-to-left shunting. A neonate who requires resuscitation will likely have a significant right-to-left shunt.

1. The **Apgar score** is an objective assessment of the physiologic well-being of the child and is done at 1 and 5 minutes after birth (Table 38.2).
2. An Apgar score of 0 to 2 mandates immediate CPR. Neonates with scores of 3 to 4 will need bag and mask ventilation and may require more extensive resuscitation. Supplemental oxygen and stimulation are normally sufficient for newborns with Apgar scores of 5 to 7. Respiratory activity should be evaluated by watching chest excursions and by auscultation. The heart rate is assessed by auscultation or by palpation of the umbilical pulse.
3. If rapid assessment at birth regarding term gestation, crying/breathing and good muscle tone is “yes,” then in most cases what is required

is drying the baby and providing warmth (mother/wrapping). If the answer is "no," the following four categories should be followed in sequence. Initial steps in stabilization (dry, provide warmth, position, clear airway, stimulate to breathe).

4. Ventilation.
 5. Chest Compressions.
 6. Medications/volume expansion.
- B.** The "Golden Minute" (first 60 seconds) is the time allotted for the initial steps and evaluation to decide if the baby requires ventilation. The decision to progress is on simultaneous assessment of two vital characteristics: respiration and heart rate. Once ventilation is required, assessment is based on three vital characteristics: heart rate, respiration, and oxygenation (pulse oximetry is used to avoid hyperoxia, and hence color is not recommended). Most sensitive indicator to a successful response is an increase in heart rate.
1. **Initial steps.** The cold-intolerant neonate should be dried thoroughly after birth and warmth provided by placing the baby under a radiant heat source. Hypothermia and iatrogenic hyperthermia should be avoided. Placement in the lateral Trendelenburg position with the head in a "sniffing" position helps to open the airway. Routine intrapartum suctioning of the oro- or nasopharyngeal area is not recommended. Clear the airway if required with a bulb syringe or suction catheter. Drying and suctioning usually provide adequate respiratory stimulation. Nonvigorous babies with meconium aspiration are intubated and suctioned (evidence class IIb), but if intubation attempts are prolonged, bag-mask ventilation needed. Pulse oximetry is recommended during resuscitation to avoid hyperoxia which has been proved to be detrimental. Pulse oximetry (SpO_2) and heart rate are reliably measured 90 seconds after birth with a neonatal probe. Preductal values (right upper limb) are higher than post ductal. Oximetry should be used in conjunction and should not replace clinical assessment of heart rate.
 2. **Ventilation.** Positive-pressure ventilation is initiated if the baby is apneic/gasping and if heart rate is less than 100 beats/min with shorter or longer inspiratory times. The initial peak inspiratory pressure required for chest movement and increase in heart rate are variable. If pressure is monitored, an initial peak pressure of 20 cm of water may be required in preterm babies and higher pressures of 30 to 40 cm of water in term babies. If pressures are not monitored, the minimal pressure required to increase heart rate and minimal chest rise should be used. In a preterm baby, excessive chest expansion could create lung injury. Assisted ventilation should be delivered at 40 to 60 breaths/min. PEEP has been shown to be beneficial and should be used if proper equipment is available for delivery. CPAP is recommended for preterm babies breathing spontaneously with difficulty, thus avoiding intubation and ventilation. Endotracheal intubation is indicated in prolonged or ineffective bag-mask ventilation, during chest compression, suctioning of meconium and in special circumstances like diaphragmatic hernia. Exhaled CO_2 monitoring is used for confirmation of correct ET tube placement. Based on studies comparing air and 100% oxygen for newborn resuscitation, air has been shown to have higher survival rate. Resuscitation based on 2010 guidelines should be initiated using air or blended oxygen and adjusting the oxygen concentration to achieve the targeted range of preductal oxygen saturation (table in figure). If blended oxygen is unavailable, resuscitation should be started with air and if no improvement in 90 seconds, 100% oxygen should be used.

3. **Chest compressions are indicated if the heart rate is less than 60 beats/min in spite of adequate ventilation with oxygen for 30 seconds.** They should be delivered on the lower third of the sternum, and the chest should be compressed approximately one third of its anterior–posterior depth. Compressions and ventilations should be coordinated to avoid simultaneous delivery and delivered at a 3:1 ratio, with 90 compressions and 30 breaths to achieve approximately 120 events/min. The two thumb-encircling hands technique is recommended. Frequent interruption of compression should be avoided. Periodic assessment of ventilation, heart rate, and oxygenation should be done, and compressions are stopped when the spontaneous heart rate is greater than 60 beats/min.
4. **Delivery of resuscitation drugs and fluids.** Resuscitation drugs should be administered when the heart rate remains below 60 beats/min despite adequate ventilation with 100% oxygen and chest compressions. The umbilical vein, the largest and thinnest of the three umbilical vessels, provides the best vascular access for resuscitation of the newborn. It is cannulated with a 3.5- to 5.0-French umbilical catheter after the umbilical cord stump has been prepped with an antiseptic and trimmed. Sterile umbilical tape placed at the base of the cord will prevent bleeding. The catheter should be placed below the skin level with blood aspirated freely, and care must be taken not to permit air into the system. If vascular access is unavailable, the endotracheal tube can be used to administer drugs. An alternative is IO route.
5. **Medications and volume expansion**
 - a. **Epinephrine.** The β -adrenergic effect of epinephrine increases the intrinsic heart rate during neonatal resuscitation. Epinephrine should be used for asystole and for heart rates less than 60 despite adequate oxygenation and chest compressions. The dose is 0.01 to 0.03 mg/kg per dose of a 1:10,000 solution is recommended intravenously (evidence class IIb). Higher IV doses are not recommended. If the drug is given via the endotracheal route, a dose of 0.05 to 0.1 mg/kg of 1:10,000 (0.1 mg/mL) should be considered (class IIb).
 - b. **Naloxone** is a specific opiate antagonist used for neonatal respiratory depression secondary to narcotics administered to the mother. The initial dose is 0.1 mg/kg. Naloxone is not recommended as part of the initial resuscitative efforts in newborn in the 2010 guidelines. Depressed respiration due to narcotics should be treated with assisted ventilation. Studies have shown misuse of naloxone in newborn and association of seizures following administration.
 - c. The use of **sodium bicarbonate** is not recommended for newborn resuscitation unless specifically considered during prolonged arrests in an attempt to relieve depression of myocardial function and reduced action of catecholamines induced by marked acidosis. Intraventricular hemorrhage in premature infants has been associated with the osmolar load occurring with bicarbonate administration. A neonatal preparation of sodium bicarbonate (4.2% or 0.5 mEq/mL) should be used to prevent this from occurring. The initial dose is 1 mEq/kg IV given over 2 minutes. Subsequent doses of 0.5 mEq/kg may be given every 10 minutes and should be guided by arterial blood pH and PaCO_2 .
 - d. **Atropine, calcium, and glucose** are not recommended for use in neonatal resuscitation unless specifically indicated.
 - e. **Fluids.** Hypovolemia should be considered in the setting of peripartum hemorrhage, hypotension, weak pulses, and persistent pallor,

despite adequate oxygenation and chest compressions. The fluid of choice for volume expansion in the delivery room is an isotonic crystalloid rather than albumin (class IIb). The volume infused should be 10 mL/kg and repeated as necessary. The administration of volume expanders too rapidly to premature infants has been associated with intraventricular hemorrhage.

6. **Postresuscitation care.** After resuscitation, the baby should be in an environment where continuous monitoring and anticipatory care are provided. Maintenance of normothermia and normoglycemia is important in preventing any further injury to the brain. Therapeutic hypothermia should be offered to near-term babies with evolving moderate-to-severe hypoxic–ischemic encephalopathy. It should be conducted and initiated under clearly defined protocols in centers with facilities and capabilities of a multidisciplinary team (evidence class IIa).
7. **Guidelines for withholding and discontinuing resuscitation**
 - a. It is considered reasonable to withhold resuscitative efforts when the conditions are known to be associated with high mortality and poor outcome especially with parental consent.
 - b. The following guideline must be interpreted with the regional outcome.
 1. Gestation (<23 weeks), birth weight (<400 g), and congenital anomalies (anencephaly, trisomy 13) associated with high mortality (evidence class IIb).
 2. High rate of survival and acceptable morbidity. Resuscitation is usually indicated. Gestational age approximately 25 weeks and most congenital malformations (evidence class IIb).
 3. Condition with uncertain prognosis and survival is borderline. Morbidity rate is high and anticipated burden to child is high (evidence class IIb).
 - c. Discontinuation of resuscitation is appropriate if no heart beat is detectable after 10 minutes of efficient resuscitation. Decision to continue after 10 minutes is influenced by presumed etiology of arrest, gestational age, potential reversibility of the situation, and parents' request.

Suggested Readings

- Kattwinkel J, Perlman JM, Aziz K, et al. 2010 American Heart Association guidelines for cardiopulmonary resuscitation and emergency cardiovascular care. Part 15: newborn resuscitation *Circulation* 2010;122(Suppl 3):S909–S919.
- Kleinman ME, Chameides L, Schexnayder SM, et al. 2010 American Heart Association guidelines for cardiopulmonary resuscitation and emergency cardiovascular care. Part 14: pediatric advanced life support. *Circulation* 2010;122(Suppl 3):S876–S908.
- Neumar RW, Otto CW, Link MS, et al. 2010 American Heart Association guidelines for cardiopulmonary resuscitation and emergency cardiovascular care. Part 8: adult advanced cardiovascular life support. *Circulation* 2010;122(Suppl 3):S729–S767.

I. DEFINITION AND TERMINOLOGY

A. Pain is an unpleasant sensory and emotional experience that is associated with actual or potential tissue damage or described in terms of such damage (The International Association for the Study of Pain). Different categories of pain can be defined according to the duration, etiology, or perception of the painful experience.

1. **Acute pain** is pain that is secondary to physical injury to body tissues and usually resolves as the wound heals. Improved control of acute pain following surgery has become a focus for practice improvement measures leading to a more timely and diversified approach to pain therapy. Studies demonstrate that techniques that effectively reduce acute pain are associated with a lower incidence of subsequent chronic pain.
2. **Chronic pain** is pain that continues for months or longer and is often defined as pain persisting beyond 3 to 6 months. Common chronic pain conditions include low back pain, complex regional pain syndrome, postherpetic neuralgia, cancer pain, and myofascial pain.
3. **Neuropathic pain** results from pathologic function of the somatosensory system, either in peripheral elements (receptor or peripheral nerves) or in the central nervous system. The abnormal somatosensory function of neuropathic pain is the direct result of injury to the nervous system, and this type of pain persists even after tissue healing appears to be complete. It is most frequently described as burning, radiating, lancinating, or shooting in nature. Neuropathic pain can result in *allodynia*, which is the perception of pain from a normally innocuous stimulus, for example, light touch perceived as pain.
4. **Nociceptive pain** results from injury that activates peripheral nociceptors, which can be somatic or visceral in origin, and is the well-localized pain associated with most acute injuries. **Visceral pain** arises from distention or injury to the viscera and is usually less well localized than somatic pain, owing to the less dense innervation of the organs as compared to other tissues.
5. **Inflammatory pain** categorized as nociceptive pain in the presence of acute inflammation, but chronic inflammatory states can play mechanistic roles in neuropathic pain states (Loeser & Treede, Kyoto). Inflammation resulting from tissue damage can lead to *hyperalgesia*, which is the exaggerated painful perception of a known noxious stimulus.

II. TREATMENT OF ACUTE PAIN IN THE PERIOPERATIVE SETTING

A. Pharmacologic Treatment of Pain

1. **Nonsteroidal anti-inflammatory drugs (NSAIDs)**, Table 39.1) can effectively treat mild-to-moderate pain, particularly pain associated with inflammatory conditions. Drugs classified as NSAIDs have diverse chemical structures, but all share the ability to inhibit the enzyme cyclooxygenase (COX) and thereby inhibit the formation of prostaglandins from arachidonic acid.
 - a. **Mechanism of action** and COX selectivity. The apparent mechanism for analgesia produced by the NSAIDs is the prevention of neuronal

TABLE 39.1 Classification of Common NSAIDs Based on COX Inhibition and Selectivity

Aspirin	Irreversible inhibition of both COX-1 and COX-2
Ibuprofen, naproxen	Reversible, competitive inhibition of both COX-1 and COX-2
Indomethacin	Slower, time-dependent, but reversible inhibition of both COX-1 and COX-2
Celecoxib	Slow, time-dependent, and highly selective COX-2 inhibition

sensitization by diminishing prostaglandin production. Type I cyclooxygenase (COX-1) is a constitutively expressed enzyme that is present in varying amounts in most cells at a fairly constant level. COX-1 serves a key role in cellular homeostasis and is the primary form of the enzyme present in platelets, the kidney, stomach, and vascular smooth muscle. COX-2-selective inhibitors were developed with the goal to reduce side effects such as gastrointestinal (GI) bleeding associated with NSAIDs, and they were successful in doing so, but they have also been associated with a slight increase in the risk of adverse cardiovascular effects (e.g., myocardial infarction and stroke). COX-2 inhibitors should be used with *caution* when cardiovascular risk factors are present and are contraindicated during coronary artery bypass graft surgery. Celecoxib is now the only available COX-2 inhibitor in the United States. For an overview of the NSAIDs according to their inhibition of COX and their selectivity for the COX-2 isoenzyme, see Table 39.1.

b. Toxicity from NSAIDs impacts primarily the GI, renal, hematologic, and hepatic systems.

1. GI. Dyspepsia is the most common side effect, and nonselective NSAIDs lead to asymptomatic ulcers in 20% to 25% of users within 1 week of administration. Complicated ulcers, including perforated ulcers, upper GI bleeding, and obstruction occur in a significant number of long-term NSAID users. Factors that increase the risk of NSAID-induced GI toxicity are shown in Table 39.2.
2. Renal impairment occurs in some patients taking NSAIDs and results from reduction in renal perfusion due to inhibition of prostaglandin synthesis. In patients with contraction of their intravascular volume (e.g., congestive heart failure, acute blood loss, and hepatic cirrhosis), renal perfusion is maintained through the vasodilatory effects of prostaglandins. Renal toxicity may manifest as acute interstitial nephritis or nephrotic syndrome. Acute renal failure occurs in as many as 5% of patients using NSAIDs; renal impairment typically resolves with the discontinuation of

TABLE 39.2 Risk Factors That Increase the Risk of NSAID-Induced GI Toxicity

Age over 60 y
Prior history of peptic ulcer disease
Steroid use
Alcohol use
Use of multiple NSAIDs
The first 3 mo of use

TABLE
39.3

Factors That Increase the Risk of NSAID-Induced Renal Toxicity

Hypovolemia
– Acute blood loss
– Chronic diuretic use
Low cardiac output (congestive heart failure)
Hepatic cirrhosis
Preexisting renal insufficiency

NSAID therapy but, rarely, progresses to end-stage renal disease. Factors that increase the risk of NSAID-induced renal toxicity are shown in Table 39.3.

3. Hematologic toxicity associated with NSAIDs takes the form of inhibition of normal platelet function. Platelet activation is blocked by the inhibitory effects of NSAIDs on cyclooxygenase and the secondary decrease of prostaglandin conversion to thromboxane A_2 (a platelet activator). Aspirin irreversibly acetylates cyclooxygenase, and thus, the platelet inhibition resulting from aspirin use persists for the 7 to 10 days required for new platelet formation. Nonaspirin NSAIDs induce reversible platelet inhibition that resolves when most of the drug has been eliminated.
4. Hepatic toxicity may also result from NSAID use. Minor elevations in hepatic enzyme levels appear in 1% to 3% of patients. The mechanism appears to be immunologic or metabolic-mediated direct hepatocellular injury, with dose-related toxicity occurring with both acetaminophen and aspirin. Periodic assessment of liver function is recommended in those on long-term NSAID therapy.
5. Inhibition of normal bone formation has been reported in both clinical and animal models. The clinical relevance to NSAID use in the immediate postorthopedic surgery period and following acute fractures requires further study; despite the frequent use of NSAIDs to provide analgesia after orthopedic surgery and injury, there is little evidence that they dramatically affect healing.
- c. **Clinical uses.** NSAIDs are used most widely to treat the pain and inflammation associated with rheumatic and degenerative arthritides. They also serve as a useful adjunct to opioids for providing control of acute pain. Addition of an NSAID can often reduce opioid requirements and related side effects in the postoperative period. Numerous agents are available for oral administration, and several are available without prescription. Thus, they are among the most common first-line analgesics.
- d. **Available formulations.** Ketorolac and diclofenac are currently the only parenteral NSAIDs approved for clinical use in the United States. Both are potent analgesics and antipyretics, and several studies have demonstrated its usefulness in treating moderate postoperative pain. Ketorolac and diclofenac are nonselective NSAIDs, and despite a parenteral form, intravenous administration is still associated with GI toxicity similar to other orally administered NSAIDs. Familiarity with the dosing and administration of several oral NSAIDs as well as the parenteral formulations is an important tool for those treating acute pain. For a summary of comparative efficacy and dosages of commonly used nonopioid analgesics, see Table 39.4. Combination therapy with the addition of opioids to

Selected Nonopioid Analgesics and Comparative Efficiency

Special Nonopioid Analgesic Dosage and Comparative Efficiency to Standards

Drug	Common Brand Names	Average Analgesic Dose (mg)	Dose Interval (hours)	Maximum Daily Dose (mg)	Analgesic Efficacy Compared with Standards	Plasma Half-life (hours)	Comments
Acetaminophen	Tylenol numerous	500–1,000 PO	4–6	4,000	Comparable to aspirin 650 mg	2–3	Use with caution in presence of alcoholism or liver disease
Aspirin (<i>Salicylate</i>)	Numerous	500–1,000 PO	4–6	4,000		0.25	Rectal suppository available Because of risk of Reye syndrome, do not use in children under 12 y with possible viral illness
Ibuprofen (<i>Propionic acid</i>)	Advil numerous	200–400 PO	4–6	2,400	Superior at 200 mg to aspirin 650 mg	2–2.5	Rectal suppository available
Naproxen	Naprosyn	500 PO initial 250 PO	6–8	1,250		12–15	
Indomethacin	Indocin	25 PO	8–12	100	Comparable to aspirin 650 mg	2	Not routinely used because of high incidence of side effects
Ketorolac (<i>Pyrrolacetic acid</i>)	Toradol	15–30 IV or IM	6	150 first day, 120 thereafter	Comparable to 6–12 mg morphine	6	Do not take >5 d
Diclofenac (<i>Phenyl acetic acid</i>)	Dyloject	75–150 IV or IM	24	150 daily		1–2 h	Do not take >2 d
Celecoxib (<i>COX-2 inhibitor</i>)	Celebrex	100–200 PO	12	400			Not to be taken if allergic to sulfa

NSAID therapy during the perioperative period can often provide synergistic analgesia and reduce opioid-related side effects. While it is important to avoid NSAIDs in patient populations at significant risk for toxicity, many patients having surgery can benefit from their addition.

2. **Acetaminophen** is a para-aminophenol derivative with analgesic and antipyretic properties similar to the NSAIDs. Acetaminophen does not produce any significant peripheral inhibition of prostaglandin production. Acetaminophen causes no significant GI toxicity or platelet dysfunction, and there are few side effects within the normal dose range. Acetaminophen is entirely metabolized by the liver, and minor metabolites are responsible for the hepatotoxicity associated with overdose. The most common oral analgesics used to treat moderate-to-severe pain incorporate acetaminophen in combination with one of the opioids. Standing per os or rectum dosing of 1 g of acetaminophen every 6 hours can be a very useful adjunct in the postoperative setting and can significantly improve pain and reduce opioid requirement. An intravenous formulation of acetaminophen was recently approved in the United States for treating mild-to-moderate pain.
3. **Ketamine** is an atypical anesthetic and potent analgesic that is an NMDA receptor antagonist. In contrast to opioids, spontaneous respiration and airway reflexes are relatively well maintained. Hypersalivation is a common side effect that can be eased by coadministration of an antisialogogue such as glycopyrrolate. Ketamine causes indirect stimulation of the sympathetic nervous system by inducing a catecholamine release. In high doses, ketamine causes a “dissociative” state and is associated with unpleasant side effects such as nightmares, which may be attenuated by concomitant administration of benzodiazepines. A low-dose ketamine infusion (5 to 10 $\mu\text{g/kg/min}$) can be used as an intraoperative anesthetic adjunct. A Cochrane review of perioperative ketamine demonstrated both reduced pain and opioid consumption, increased time to first analgesic, and decreased postoperative nausea and vomiting, at the consequence of increased dysphoric side effects (hallucinations, unpleasant dreams, nystagmus). Ketamine bolus can also be used in the immediate postoperative period as a rescue analgesic, especially after opioid rescue has failed. Patients should be premedicated with a benzodiazepine to mitigate dysphoria and be monitored on telemetry (bolus 10 to 30 mg). A Cochrane review reported that 27 of 37 studies demonstrated a significant reduction in postoperative pain with the use of ketamine. Use of ketamine as an adjuvant anesthetic has been shown to result in decreased opioid requirements in the immediate postoperative period in the majority of studies without significant increase in adverse outcomes. Ketamine is especially useful in the management of perioperative pain in patients on chronic opioid therapy.
4. **Opiates and opioids.** **Opiates** are among the most universally effective agents available for treating acute pain. Morphine, the prototypical opiate, is derived from the milk of the scored seed pod of the Oriental poppy, *Papaver somniferum*. Several other compounds can be derived directly through the chemical modification of morphine. Those drugs derived directly from morphine are termed the opiates. Other synthetic compounds have been produced that act via opiate receptors—all compounds that act via opiate receptors are termed the **opioids**. While opioids form the cornerstone of effective acute pain management, they have significant side effects, and their long-term effectiveness is limited

by tolerance, physical dependence, and the possibility of addiction. Common prescribing practices in the United States have led to an epidemic of prescription opioid misuse and abuse. In 2013, more overdose deaths in the United States were attributed to prescription opioids than heroin and cocaine overdoses combined. Significant reform in physicians' prescribing patterns likely represent the first step in addressing this public health issue. Opioids are extremely useful for treating acute pain; although they are in widespread clinical use, their long-term effectiveness for treating chronic, noncancer pain is less clear.

a. Metabolism. Following injection, morphine rapidly undergoes hepatic conjugation with glucuronic acid; morphine remains largely in the ionized form at physiologic pH and is highly protein bound. The plasma concentration attained after an identical dose of morphine increases progressively with increasing age of patients (Fig. 39.1). Plasma concentration of morphine correlates poorly with its pharmacologic effect. Analgesia and depressed ventilation correlate more closely with cerebrospinal fluid (CSF) concentration. After intravenous injection of morphine, a metabolite, morphine glucuronide can be detected within 1 minute. While morphine-6-glucuronide (M-6-G) is produced in smaller amounts to morphine-3-glucuronide (1:9), M-6-G is pharmacologically active producing both analgesia and respiratory depression via interaction with μ -opioid receptors. M-6-G elimination is significantly impaired in patients with renal failure (Fig. 39.2) and can lead to prolonged depression of ventilation. Histamine release follows IV morphine administration but not fentanyl (Rosow et al., 1982), resulting decrease in SVR and BP following morphine administration (Fig. 39.3).

b. Side effects associated with opioid analgesics

1. Respiratory depression. Opioids cause a dose-dependent reduction in responsiveness of the brain stem respiratory centers to increases in arterial carbon dioxide tension (PaCO_2) that manifests as reduction in breathing rate and at high doses, apnea.

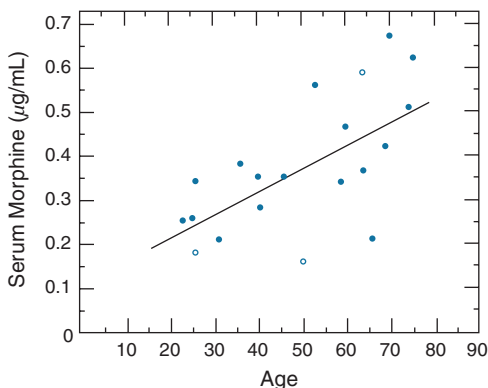


FIGURE 39.1 The plasma (serum) concentration of morphine increases progressively increases with advancing age. (From Berkowitz BA, Ngai SH, Yang JC, et al. The disposition of morphine in surgical patients. *Clin Pharmacol Ther* 1975;17:629–635, with permission.)

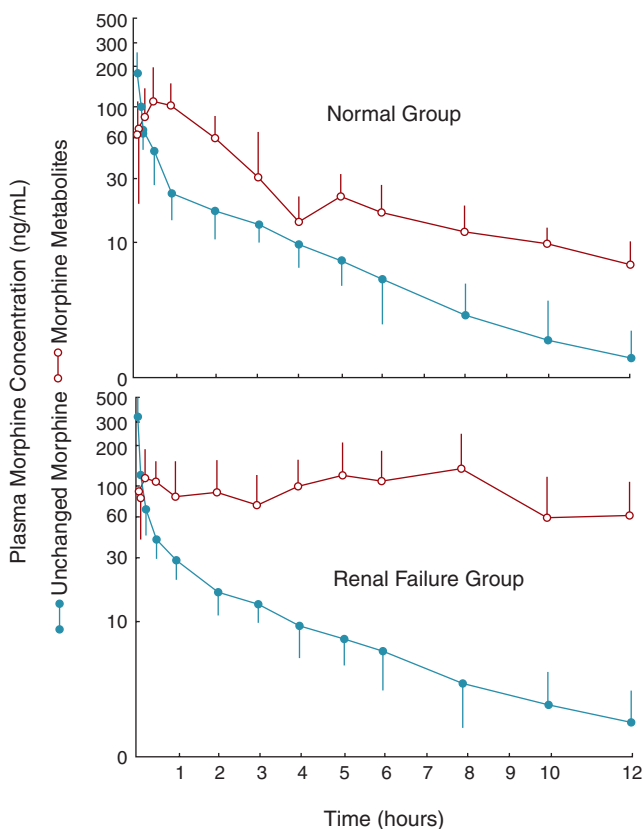


FIGURE 39.2 Plasma concentration of unchanged morphine (closed circles) and morphine metabolites in normal and renal failure patients. (From Chauvin M, Sandouk P, Scherman JM, et al. Morphine pharmacokinetics in renal failure. *Anesthesiology* 1987;66:327–331, with permission.)

2. Sedation. Mediated through the limbic system.
3. Pupillary constriction. Excitatory action on the autonomic segment of the Edinger-Westphal nucleus of the oculomotor nerve.
4. Nausea and vomiting. Direct stimulation of the chemoreceptor trigger zone within the area postrema in the medulla.
5. Constipation. Reduction in the propulsive peristaltic contractions of the small and large intestines.
6. Bradycardia. Central stimulation of the vagal nucleus within the medulla.
- c. **Tolerance.** With continued use of substantial amounts of opioids, larger doses of the drug are required over time to produce the same physiologic effects. This phenomenon is called tolerance and is characteristic of the entire class of opioids.

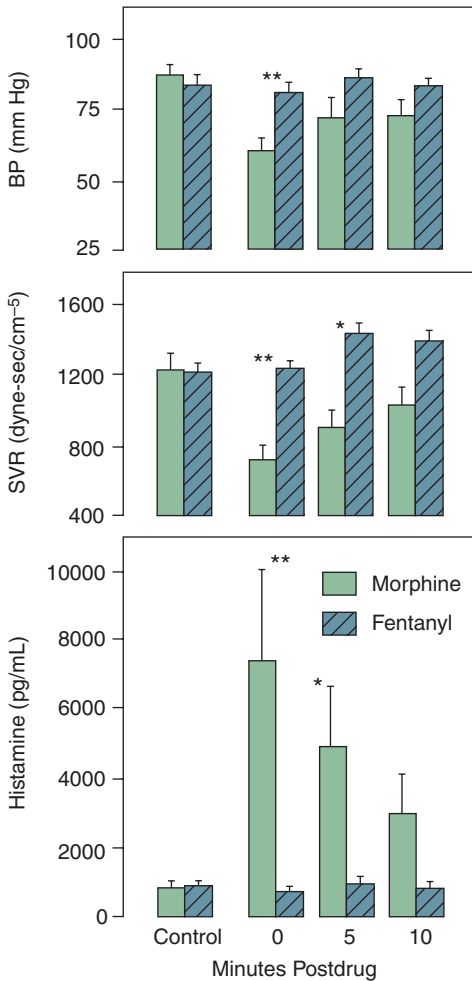


FIGURE 39.3 Morphine-induced decreases in systemic blood pressure (BP) and systemic vascular resistance (SVR) are accompanied by increases in the plasma concentration of histamine. Similar changes do not accompany the intravenous administration of fentanyl. (From Rosow CE, Moss J, Philbin DM et al. Histamine release during morphine and fentanyl anesthesia. *Anesthesiology* 1982;56:93–96, with permission.)

- d. Physical dependence.** The precipitation of a distinct withdrawal (abstinence) syndrome when the opioid is discontinued. Manifestations of opioid withdrawal include diaphoresis, hypertension, tachycardia, abdominal cramping, and nausea and vomiting. Physical dependence occurs in any individual given a large enough dose of opioid for a long enough period of time, and it is *not* synonymous with addiction.

- e. **Addiction.** Addiction is popularly conceived as a compulsion or overpowering drive to obtain a drug in order to experience its psychological effects. Opioid addiction is rarely induced iatrogenically, and fears of addiction should not lead to limiting opioid dosing during attempts to control pain acutely.
- f. **Forms of Opioids**
1. **Oral opioids** are common agents used for the control of mild-to-moderate pain in those who are able to continue oral intake. Many agents are available as combination preparations containing an opioid along with acetaminophen. The duration of analgesic action for the orally administered opioids is similar and in the range of 3 to 4 hours. Commonly used oral opioids are listed in Table 39.5. In those with opioid tolerance or greater than average opioid requirements, oral opioid alone (without acetaminophen) should be used to avoid hepatic toxicity
 2. **Intravenous (IV) opioids.** Control of moderate-to-severe pain or treatment of those who are unable to tolerate oral intake often requires the use of IV opioids. The pharmacokinetic profiles of opioid analgesics administered intramuscularly are similar but somewhat more erratic due to variations in the muscle blood flow compared to that seen with IV administration; however, there is significant discomfort with IM administration. There is no maximum dose for any of the pure opioid agonists (either orally or parenterally), and the dose can be increased until acceptable analgesia is produced or intolerable side effects ensue. Patients who require large doses of opioids should be closely monitored during initial dose titration as marked respiratory depression and apnea may occur unexpectedly.
- g. **Morphine first initiative.** Common clinical practice at MGH moved from use of morphine as the first-line agent to near universal use of hydromorphone. Reasons for this shift were multifactorial and included anecdotal reports of better analgesia with fewer side effects using hydromorphone (PONV, sedation, and hypotension).

TABLE
39.5

Common Oral Opioid and Opioid/Acetaminophen Combinations Used to Treat Mild-to-Moderate Pain

Drug	Equianalgesic Oral Dose (mg)	How Supplied
Acetaminophen	—	325-, 500-, 625-mg tabs; 500-mg/15-mL elixir
Codeine	60	15-, 30-, 60-mg tabs; 15-mg/5-mL elixir
Acetaminophen with codeine	—	300–15-, 300–30-, 300–60-mg tabs; 120–12/5-mL elixir
Hydrocodone	60	(Available only in combination with acetaminophen)
Acetaminophen with hydrocodone	—	500–2.5-, 500–5-, 500–7.5-, 660–10-mg tabs; 500–7.5/15-mL elixir
Oxycodone	10	5-mg tabs; 5-mg/5-mL elixir
Acetaminophen with oxycodone	—	325–5-, 500–5-mg tabs; 325–5/5-mL elixir
Morphine	10	15-, 30-mg tabs; 10-, 20-mg/5-mL elixir
Hydromorphone	2	2-, 4-, 8-mg tabs; 5-mg/5-mL elixir

Yet, as we examined MGH-specific data, we noted a 41% longer stay with a higher occurrence of drug-related adverse effects in patients who received hydromorphone when compared to patients who received morphine. This recently led us to launch the Morphine First Initiative, a hospital-wide initiative aimed at using morphine as the first-line analgesic for treating severe pain in hospitalized patients requiring parenteral opioids.

B. Adjuncts Used with Opioids

1. **Gabapentin:** Meta-analyses of preoperative use of gabapentin (250 to 500 mg) has shown decrease opioid use for 24 hours (by 35%), decreased pain at rest and with movement, decreased pruritus, nausea, and vomiting, but increased dizziness and mild sedation.
2. **α_2 -Agonists:** α_2 -Agonists have been shown to decrease risks of nausea and morphine use (IV clonidine (4 mg) or IV dexmedetomidine (14.5 mg)) in the first 24 hours postoperatively without increased recovery times, but increased risk of bradycardia and hypotension.
3. **Lidocaine (IV):** Meta-analyses of IV lidocaine infusion demonstrate decreased morphine consumption in both open and laparoscopic abdominal surgery. Additionally, this review found moderate decreases in pain at both rest and with movement, time to first flatus and bowel movement (7 and 12 hours, respectively), as well as hospital stay.

C. Specific Pain Treatment Modalities Used in the Postoperative Setting

1. **Patient-controlled analgesia (PCA)** utilizes patient self-administration of opioid analgesia via a patient-activated infusion device. This method for delivering analgesics has evolved with the introduction of computer-controlled, programmable infusion pumps. The PCA paradigm holds that the timely administration of small intermittent doses of analgesics will allow maintenance of optimal plasma drug concentration while minimizing side effects and periods of poor analgesia associated with intermittent IV or IM administration. Typical PCA devices can be programmed to deliver a specified dose of opioid and then “lock-out” further administration for a specified interval; most devices can also be programmed to administer a continuous basal infusion suitable for meeting the background requirements of those with opioid tolerance. Guidelines for PCA administration of common opioid analgesics are shown in Table 39.6. PCA provides superior analgesia in many settings where hospitalized patients experience acute pain. Patients are very accepting of this technology and are typically quite satisfied with the close degree of control of pain that PCA allows. The addition of a basal infusion to the PCA dosing regimen should be reserved for those

TABLE
39.6

Guidelines for Opioid Administration via IV PCA

Drug (Concentration)	Typical Demand Dose (Range)	Typical Lockout Interval (Range)
Morphine (1 mg/mL)	1 mg (0.5–3 mg)	10 min (5–12 min)
Meperidine ^a (10 mg/mL)	10 mg (5–30 mg)	10 min (5–12 min)
Fentanyl (10 μ g/mL)	10 μ g (10–20 μ g)	10 min (5–10 min)
Hydromorphone (0.2 mg/mL)	0.2 mg (0.1–0.5 mg)	10 min (5–10 min)

^a Use of meperidine has diminished, as this agent has an active metabolite, normeperidine, which can accumulate and lead to central nervous system excitation and seizures at very high doses.

patients with opioid tolerance—routinely including a basal infusion does not improve analgesia, but simply increases the total opioid dose used and the frequency of opioid-related side effects.

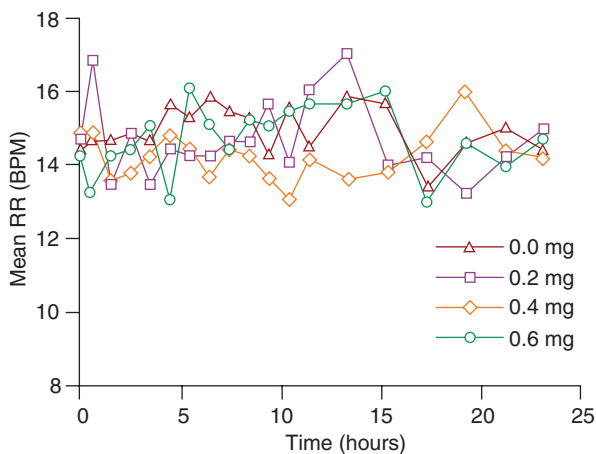
- a. **Advantages** of PCA: PCA allows each patient to control their own pain relief, provides for rapid administration of analgesic immediately on patient request, has a high degree of patient acceptance and satisfaction, and reduces total opioid dose and related side effects.
- b. **Disadvantages** of PCA: PCA requires the patient's ability to understand and follow directions, requires availability of specific PCA infusion pumps, and is subject to programming errors that can cause overdosing or underdosing.

2. **Neuraxial analgesia.** The pharmacology and clinical use of intrathecal and epidural opioids and local anesthetics has been covered extensively in Chapter 17. In this section, we will focus on the practical aspects for using neuraxial techniques to provide postoperative analgesia. The combined use of thoracic epidural analgesia with general anesthesia (when compared to GA with IV opioids) has demonstrated many advantages for abdominal and thoracic surgery including decreased length of hospitalization, improved postoperative pain control with less sedation, improved respiratory function, accelerated recovery of bowel function, improved lower-extremity blood flow, and reduced stress response.

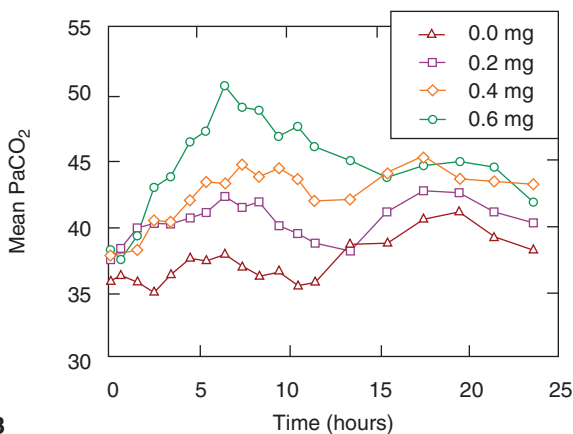
- a. Intrathecal opioids can provide prolonged analgesia after a single injection. When a surgical procedure is to be carried out using spinal anesthesia, the addition of an opioid to the local anesthetic serves as a practical and effective means for improving postoperative analgesia. The technique is limited by the frequency of side effects at higher doses and the inability to provide complete analgesia for more extensive and painful procedures. There are two general classes of opioids used for spinal analgesia: those that are hydrophilic (e.g., morphine) and those that are lipophilic (e.g., fentanyl and sufentanil).

1. Hydrophilic opioids are slower in onset (peak analgesic effect occurs between 20 and 60 minutes) but persist at significant levels within the CSF for prolonged periods of time. The prototypic hydrophilic agent is morphine. While it produces prolonged analgesia, it has also been associated with a small incidence of delayed respiratory depression occurring as late as 18 to 20 hours after administration. This is believed to be due to the persistence of significant levels of the drug within the CSF for up to 24 hours and the rostral spread of drug within the CSF. Morphine 0.1 to 0.3 mg can provide analgesia for up to 8 to 24 hours; however, patients should remain hospitalized and observed periodically to detect and promptly treat delayed respiratory depression with this agent. The depression of ventilation can be difficult to detect because patients may demonstrate a relatively normal respiratory rate, however, hypoxemia detected by pulse oximetry, PaCO_2 (with bimodal peak of approximately 6 and 18 hours) detected by blood gas, and clinically depressed level of consciousness (Fig. 39.4).

2. Lipophilic opioids have a rapid onset (peak analgesic effect within 5 to 10 minutes) and a short duration of analgesic action (2 to 4 hours). Delayed respiratory depression has not been observed



A



B

FIGURE 39.4 (A) Mean respiratory rate (RR) versus time before (time 0) and after three different doses of intrathecal morphine; **(B)** mean arterial carbon dioxide partial pressure (mm Hg) versus times before (time 0) and after three different doses of intrathecal morphine. (From Bailey PL, Phondeau S, Schafer PG, et al. Dose-response pharmacology of intrathecal morphine in human volunteers. *Anesthesiology* 1993;79:49E–59E, with permission.)

with the lipophilic opioids. Fentanyl 10 to 25 μg or sufentanil 2.5 to 10 μg is often combined with small doses of local anesthetic to provide surgical anesthesia and postoperative analgesia for outpatient surgery.

- b. Epidural opioids. Opioid analgesics also provide effective analgesia when administered into the epidural space. They can be administered as single bolus injections, but it is far more common to place a

catheter and administer combinations of opioid and low-dose local anesthetic to provide for continuous analgesia following surgery. It is imperative to understand the dermatomal extent of analgesia that can be expected from each agent and to place the injection at or near the midpoint of the dermatomal location of the surgical incision.

1. Hydrophilic agents such as morphine can be placed in the lumbar region and still provide analgesia for incisions that extend to the thoracic region, while fentanyl will not spread to the same extent. However, if the epidural injection or infusion is administered outside of the dermatomal distribution of the incision, addition of local anesthetic will not provide additional analgesia.
 2. Local anesthetics provide analgesia only within the dermatomes adjacent to the site of injection.
 3. Regional analgesic effects are observed when epidural opioids are administered by bolus, but less so when administered by infusion. Infusion of epidural opioids increases analgesia in parallel to plasma concentration with little regional effect, just as seen by subcutaneous or intravenous route.
 4. Analgesic effects from infusions requires larger total doses (three times larger) than effective bolus dosing. The analgesia following bolus dosing is likely mediated by a subset of spinal opioid receptors. The systemic analgesia observed with infusion is more likely mediated by supratentorial receptors. When administering combined opioid and local anesthetic infusions via an epidural catheter, it is important to begin with an initial bolus to establish analgesia, prior to starting the infusion.
- c. **Continuous epidural infusion and patient-controlled epidural analgesia (PCEA).** Continuous epidural infusions of opioids or opioid–local anesthetic combinations result in fewer fluctuations in the concentration of the analgesic drug and allows for patient-controlled supplementation via PCEA using programmable infusion pumps identical to those used for IV PCA. As discussed above, IV PCA relies on the patient-administered intermittent bolus doses to provide analgesia, and continuous infusions are seldom needed. In contrast, when using PCEA, the continuous infusion provides the majority of the analgesia, and small intermittent patient-administered doses are used to supplement analgesia. There is ample evidence that patients can safely receive epidural opioids while on the regular hospital ward, provided that an anesthesiology-based acute pain service is responsible for all adjustments of analgesic and sedative medications.
- d. **Adverse effects** associated with neuraxial opioid administration include sedation, pruritus, nausea, and vomiting, and urinary retention are common in patients receiving epidural or intrathecal opioids. Standing orders should be in place for addressing these common, minor side effects. Suggested standing orders for management of common side effects associated with neuraxial opioid administration are shown in Table 39.7.
- e. Treatment of **inadequate analgesia** in patients receiving continuous epidural infusions requires a systematic approach. A member of the acute pain service should be immediately available to assess the patient and determine the cause for inadequate analgesia. A common algorithm for responding to inadequate analgesia in patients

TABLE
39.7

Pharmacologic Management of Common Side Effects Associated with Neuraxial Opioid Administration

Adverse Effect	Standing Orders for Treatment
Nausea	• Ondansetron 1–4 mg IV or dolasetron 12.5 mg IV • Nalbuphine 1–3 mg IV or butorphanol 0.25–0.5 mg IV every 4 h as needed
Pruritus	• Diphenhydramine 25–50 mg IV every 4 h as needed • Nalbuphine 1–3 mg IV or butorphanol 0.25–0.5 mg IV every 4 h as needed
Urinary retention	• Keep indwelling urinary catheter in place until discontinuation of the epidural analgesia
Sedation or respiratory depression	• Notify acute pain service immediately, for respiratory rate less than 6/min • Place supplemental oxygen 4 L/min via nasal cannula • Administer naloxone 0.4 mg IV

receiving epidural analgesia is shown in Table 39.8. Daily management of the patient receiving epidural analgesia requires a systematic approach aimed at assuring safe and effective pain treatment. A suggested daily checklist that will guide patient management is shown in Table 39.9.

TABLE
39.8

Suggested Management of Inadequate Analgesia in Patients Receiving Continuous Epidural Analgesia

1. Assess the patient directly at the bedside to determine the cause for inadequate analgesia. If unable to respond in a timely fashion, consider alternate means for providing analgesia (e.g., order a one-time IV dose of opioid by telephone; consider discontinuing epidural infusion and beginning IV PCA).
2. Examine the patient for signs of a unilateral block or a dislodged or disconnected epidural catheter.
3. Administer a bolus dose of the opioid or opioid–local anesthetic combination in use for continuous infusion. Choose the dose based on the severity of pain and use between $\frac{1}{2}$ and 1 hour's worth of the medication (e.g., 4–8 mL bolus of fentanyl 4 μ g/mL/bupivacaine 0.0625% in a patient receiving 8 mL/h).
4. If there is no improvement in pain relief within 20–30 min, consider test dosing the epidural catheter with 10 mL of 2% lidocaine. *Do not* administer a test dose unless the patient can be attended continuously and monitored with blood pressure checks at least every 5 min for 20 min after the bolus is given. Means for treating hypotension must be readily available (IV access and ready availability of a vasopressor such as ephedrine or phenylephrine).
5. If no sensory or motor block appears within 20 min, replace or discontinue epidural catheter and begin an alternate means for providing analgesia (e.g., IV PCA).
6. If a unilateral sensory block develops, withdraw the epidural catheter slightly and readminister an epidural bolus of the medication in use for continuous infusion.
7. If a bilateral sensory or motor block develops, readminister an epidural bolus of the medication in use for continuous infusion and increase the epidural infusion rate. Be alert for causes of inadequate analgesia (e.g., a lumbar epidural catheter in use for pain following thoracotomy). Consider changing the opioid in use if the catheter location is suboptimal or there is an extensive incision

TABLE
39.9
Suggested Daily Checklist for Daily Management of Patients Receiving Epidural Analgesia

1. Examine the nursing record for adjustments and supplemental analgesics as well as medications for side effects. Check vital signs for evidence of persistent fever or hypotension
2. Assess for adequate analgesia and side effects by directly questioning the patient. Be alert for sedation, pruritus, nausea and vomiting, and urinary retention
3. Examine the patient to detect signs of unilateral block or excessive sensory or motor block
4. Examine the epidural catheter site for signs of infection and the presence of an intact occlusive dressing
5. Interrogate the infusion pump to assess the patient's use of supplemental doses, assure that it is properly programmed. Examine the infusion bag directly to be certain the medication ordered is what the patient is receiving
6. Document your interaction in detail in the patient's chart and order any changes needed. Include when you anticipate changing or discontinuing therapy

f. Complications associated with epidural analgesia. Although the goal of epidural analgesia is to provide pain relief and minimize side effects, there are several serious complications associated with its use.

1. Subarachnoid catheter migration can lead to increasing levels of sensory block and total spinal anesthesia.
 2. Indwelling epidural catheters can become infected directly at the skin entry site or through hematogenous seeding of the catheter tip within the epidural space. Superficial site infection is common and rarely needs treatment beyond the removal of the catheter. Extension of a superficial infection or direct seeding of the catheter tip to produce an epidural abscess is rare.
 3. Epidural hematoma formation is also uncommon but may follow epidural placement in a patient receiving systemic anticoagulants. Both epidural abscess and hematoma present with worsening back pain and neurologic deficit (urinary retention and sensory and motor loss in the lower extremities). The recognition and management of these complications are discussed in detail in Chapter 17. Some institutions limit the use of epidural infusions to the intensive care and postanesthesia care units.
- 3. Continuous peripheral nerve blocks** using catheters are continuing to gain popularity in the inpatient as well as the ambulatory setting. The focus in this chapter is to outline a strategy for management of continuous nerve catheters in the postoperative period. For placement of peripheral nerve blocks, see Chapter 18. The availability of lightweight and sophisticated infusion pumps has greatly facilitated the use of continuous perineural infusions of local anesthetics. The development of catheters incorporating an insulated electrode at the catheter tip enables physicians to elicit a motor response to confirm the proximity of the catheter to the nerve. Ultrasound is now commonly used to guide catheter placement. Advances in technology and the emergence of literature supporting continuous perineural infusions for improved postoperative analgesia and recovery have led to more wide spread use of continuous perineural infusions of local anesthetics.

- a. **Specific indications** for continuous peripheral nerve blocks. Continuous femoral nerve block following total knee arthroplasty provides good analgesia and reduces the need for supplemental analgesics. Because the posterior aspect of the knee joint is innervated by contributions from the obturator and sciatic nerves, femoral nerve block usually must be supplemented with IV analgesics. Brachial plexus block using continuous infusion has also proven effective for surgery on the shoulder and upper extremity.
 - b. **Choice of drug, concentration, and infusion rate** will depend on the target nerve or plexus, the surgical procedure, as well as the individual patient's response. Infusion rates can be fixed or variable including the possibility of a bolus (patient-controlled regional anesthesia—PCRA). Continuous peripheral nerve blocks are carried out by infusing local anesthetic alone (e.g., 0.125% bupivacaine, or 0.2% ropivacaine) at a rate of 5 to 10 mL/h.
 - c. **Management of continuous peripheral nerve catheters.** Since the extremity will have decreased sensitivity for the duration of the block, care should be taken to prevent injury to exposed nerves. A properly fitted sling, brace, and thorough patient education are paramount to provide adequate protection. Given the high cumulative dose of local anesthetic, patients with hepatic or renal insufficiency should not receive continuous perineural infusions. Daily follow-up of hospitalized patients with a perineural catheter should include close attention to specific aspects shown in Table 39.10.
 - d. **Use of perineural catheters in ambulatory patients.** Perineural catheters have been successfully employed in the ambulatory care setting. This requires careful patient selection, comprehensive patient education, and the implementation of a protocol for patient follow-up. Patient education should include instructions on how to operate the pump, signs of catheter-related complications (such as infection, migration, and leak), and signs of local anesthetic toxicity. Patients should be aware of the expected time for resolution of the block and should understand the necessity to abstain from driving or operating machinery. A plan for breakthrough pain management should be in place. Patient education should include the patient's caregiver. Daily follow-up should be arranged, and provisions for immediate contact with an anesthesiologist should be available.
- D. Acute pain management in patients with opioid tolerance or addiction.**
1. Patients with opioid tolerance or a history of opioid addiction represent a unique challenge to the anesthesiologist in the perioperative period.

TABLE
39.10

Checklist for Daily Follow-Up of Patients with Perineural Catheters

1. Inspect the catheter insertion site to assess for signs of infection, leaks, and catheter dislocation.
2. Assure that ongoing analgesia is adequate.
3. Assess the patient for signs of excessive motor and/or sensory block.
4. Assess the patient for signs or symptoms of local anesthetic toxicity (local anesthetic toxicity is rare in the context of continuous perineural infusion, but the daily dose and any associated side effects should be assessed daily).

Addiction is defined by the WHO as a psychic and sometimes physical state resulting from the interactions between a living organism and other responses that always include a compulsion to take the drug on a continuous or periodic basis in order to experience its psychic effects and sometimes to avoid the discomfort of its absence. Tolerance may or may not be present.

- a. **Perioperative management of patients with opioid tolerance or a history of opioid dependence.** Concepts to consider when managing patients who have been taking large doses of opioids for chronic pain and those with current or previous addiction are shown in Table 39.11.
- b. **Managing acute pain in patients on buprenorphine maintenance therapy.** Buprenorphine has been introduced for ambulatory treatment of patients with opioid addiction. Treating acute pain in these patients is becoming a more common challenge to the anesthesiologist. Buprenorphine is a semisynthetic, long-acting opioid that is 20 to 50 times more potent than morphine. It is a partial agonist at the μ receptor that, at higher doses, acts as an antagonist leading to decreased level of respiratory depression and decreased analgesia. When prescribed in the outpatient setting, buprenorphine is mixed with naloxone (Suboxone) to be taken sublingually. Naloxone has poor bioavailability after oral and sublingual administration; however, if the drug combination is administered intravenously, i. e. if the drug is abused in this way, the naloxone is bioavailable in high concentrations, and IV use of the combination drug will cause acute withdrawal symptoms in opioid-dependent patients. The addition of naloxone aims at limiting both abuse and diversion of the drug. Buprenorphine alone (Subutex) is used for initial testing prior to initiating a buprenorphine therapy-based

TABLE 39.11 Managing Patients with Opioid Tolerance or with Current or Previous Addiction

Consider use of regional anesthesia (spinal opioids and epidural infusions) can improve analgesia and minimize systemic opioid effects. Higher than usual doses of neuraxial opioid may be required in those with significant tolerance.

Use adjunctive analgesics whenever possible to reduce total opioid requirements (e.g., NSAIDs).

Administer opioids liberally to control pain in the immediate postoperative period. *Do not* attempt to limit opioid dose or wean opioid analgesics in the immediate postoperative period. Those with significant tolerance will probably require higher than average doses to control acute pain.

Use preoperative opioid doses as a baseline requirement and administer additional doses beyond this to control acute pain. This baseline requirement can be administered as a continuous IV infusion or by continuing the preoperative long-acting opioid in addition to the use of a PCA.

Consider consultation with a substance abuse specialist during hospitalization for those with ongoing opioid abuse or a history of addiction.

Closely coordinate (communicate) the pain management with the patient's primary care provider before hospital discharge. While acute escalation in the opioid requirement is often necessary in the perioperative period, a plan for weaning the opioids to their previous levels should be established *before* the patient is discharged from the hospital.

TABLE
39.12
Perioperative Considerations for the Patient Receiving Long-term Buprenorphine Treatment

For patients undergoing elective surgery, buprenorphine therapy can be discontinued and replaced with a full opioid agonist (e.g., morphine and hydromorphone) during the week prior to the scheduled surgery. The opioid dose can then be adjusted as needed to treat acute pain in the perioperative period. Once the acute pain has resolved, buprenorphine maintenance therapy can be reinstated using an induction protocol. It should be noted that on reinstituting buprenorphine therapy, the initial dose of buprenorphine can precipitate withdrawal symptoms. This approach should be closely coordinated with the physician primarily responsible for the opioid agonist therapy to ensure safety and supervision of the necessary changes in the therapeutic regimen. Note that continuation of buprenorphine therapy, even in those scheduled for elective surgery who are likely to require parenteral opioid therapy, is becoming more the norm than the exception.

For patient requiring urgent or emergent surgery or when prior conversion to a full agonist is not feasible, a short-acting full agonist such as fentanyl can be titrated to effect. As is the case for patients maintained with other opioid agonists, higher than usual doses to achieve adequate analgesia are likely to be required. The appropriate dose of fentanyl in a patient taking buprenorphine might also be higher because of the strong affinity of buprenorphine for the μ receptor. After buprenorphine therapy is discontinued, the effects of a full agonist will become more pronounced; once the buprenorphine has been cleared from the body, the dose of the full agonist will need to be reduced over time. Close monitoring of the patient's response to therapy is required.

maintenance regimen in the opioid-addicted patient. Subutex has also gained some popularity for use in the treatment of chronic pain, owing to its limited abuse potential and significant efficacy as an analgesic agent.

2. There is a paucity of data for the management of patients receiving buprenorphine who present for surgery. In addition to the general principles for managing patients with opioid tolerance or addiction discussed above, specific considerations for the patient receiving buprenorphine are shown in Table 39.12.

Suggested Readings

- Alford DP, Compton P, Samet JH. Acute pain management for patients receiving maintenance methadone or buprenorphine therapy. *Ann Intern Med* 2006;144:127–134.
- Benzon TB, Rathmell JP, Wu CL, et al. *Raj's Practical Management of Pain*. 4th ed. Philadelphia: Mosby Elsevier; 2008.
- Blaudszun G, Lysakowski C, Elia N, et al. Effect of perioperative systemic α_2 agonists on postoperative morphine consumption and pain intensity: systematic review and meta-analysis of randomized controlled trials. *Anesthesiology* 2012;116:1312–1322.
- Boezaart AP. Perineural infusion of local anesthetics. *Anesthesiology* 2006;104:872–880.
- Ilfeld BM, Enneking FK. Continuous peripheral nerve blocks at home: a review. *Anesth Analg* 2005;100(6):1822–1833.
- Joshi GP, Gertler R, Fricker R. Cardiovascular thromboembolic adverse effects associated with cyclooxygenase-2 selective inhibitors and nonselective antiinflammatory drugs. *Anesth Analg* 2007;105:1793–1804.
- Mitra S, Sinatra RS. Perioperative management of acute pain in the opioid-dependent patient. *Anesthesiology* 2004;101:212–227.

- Rathmell JP, Lair TR, Nauman B. The role of intrathecal drugs in the treatment of acute pain. *Anesth Analg* 2005;101(5 Suppl):S30–S43.
- Rathmell JP, Neal JM, Viscomi CM. *Regional Anesthesia. The Requisites in Anesthesiology*. Philadelphia: Elsevier Mosby; 2004.
- Straube S, Derry S, Moore RA, et al. Single dose oral gabapentin for established acute post-operative pain in adults. *Cochrane Database Syst Rev* 2010;(5):CD008183.
- Sun Y, Li T, Wang N, et al. Perioperative systemic lidocaine for postoperative analgesia and recovery after abdominal surgery: a meta-analysis of randomized controlled trials. *Dis Colon Rectum* 2012;55:1183–1194.

Complementary and Alternative Medicine

Dan Drzymalski, Margaret Gargarian, and
P. Grace Harrell

I. COMPLEMENTARY AND ALTERNATIVE MEDICINE (CAM)

Complementary and alternative therapies encompass a broad range of therapeutic modalities that can be integrated into Western medicine. CAM offers patients treatment options, especially when dealing with chronic illness and symptom alleviation. As physicians, the more comfortable and informed we are about CAM, the more effectively we can help our patients make safe and intelligent decisions. As anesthesiologists, we should ask about CAM use during our standard history taking, especially the use of herbs. Knowledge of CAM use can help prevent potential hazards during surgery and can assist with the management of pain, anxiety, and nausea and vomiting.

A. Definitions of CAM

1. Practices that are not accepted as correct or in conformity with the beliefs of the dominant group of medical practitioners in a society
2. Interventions neither taught widely in medical schools nor generally available in hospitals

B. Categories of CAM Practices. The National Center for Complementary and Alternative Medicine, a subdivision of the National Institutes of Health, has grouped CAM practices into five major subdivisions:

1. **Alternative medical systems** are complete systems of theory and practice that have evolved in various cultures, mostly before the inception of conventional medicine. An example is traditional oriental medicine, which uses acupuncture, herbal medicine, massage, and qi gong.
 - a. **Acupuncture** involves the insertion of fine, solid needles into specific points on the body to produce a therapeutic result. Acupuncture influences the nervous system at multiple levels and causes release of endorphins, serotonin, norepinephrine, and cortisol. Many of these substances reduce inflammation and pain sensation.
2. **Mind–body interventions** use techniques to facilitate the mind's ability to affect bodily functions. Examples include hypnosis, meditation, prayer, art therapy, music medicine and therapy, and mental healing.
3. **Biologically based treatments** overlap with conventional medicine's use of dietary supplements. They include herbal therapy (see section III), special diets, shark cartilage to treat cancer, and bee pollen to treat autoimmune diseases.
4. **Manipulative and body-based methods** use movement or manipulation of the body to restore health. Examples include chiropractic medicine, massage therapy, and osteopathic manipulation.
5. **Energy therapies** focus on energy fields originating within the body (bio-fields) or from other sources (electromagnetic fields). Examples include qi gong, reiki, and therapeutic touch.

C. Prevalence of CAM

1. Information released by the National Center for Complementary and Alternative Medicine and the National Center for Health Statistics has

estimated that 38.3% of adults and 11.8% of children have used some form of complementary or alternative medicine. The most commonly used modalities include the use of natural products, deep breathing, meditation, and chiropractic/osteopathic manipulation. Total out-of-pocket expense for CAM represents billions of dollars and compares with the money spent on traditional physicians.

2. Most CAM therapies are used for chronic conditions, especially back and neck pain, depression, anxiety, and insomnia. Symptom relief is the main benefit reported. The vast majority of people use CAM in conjunction with conventional therapies.
3. **Disclosure rates.** Although disclosure rates have been increasing, there are still many patients who do not tell their doctors about the CAM therapies they are using. This places the burden on physicians to elicit this information from their patients, and effectively discussing CAM can be challenging. A physician informed about alternative medicine can help patients avoid dangerous side effects and also help them make safe and intelligent choices.

II. HERBAL THERAPY AND ANESTHESIA

- A. **Herbal medicines and phytopharmaceuticals** are plants or parts of plants that contain biologically active components. There is tremendous variability in the purity and potency of herbal preparations. The amount of active component can vary widely within the same species depending on growing conditions. Herbal products are sometimes adulterated with foreign substances, including pharmaceuticals, bacteria, and toxic metals. **Dietary supplements** contain “concentrate, metabolite, constituent, extract, or combination of any ingredient of a vitamin, mineral, amino acid, enzyme or herb.” Vitamins are supplements that contain essential organic compounds or nutrients that are required in small amounts to maintain bodily functions. **Homeopathic medications** are derived from plant, animal, or mineral sources. It is thought that they stimulate natural defenses in very diluted doses.
- B. Herbal medicines are regulated by the U.S. Food and Drug Administration in the category of “dietary supplements” along with compounds such as vitamins and amino acids. The manufacturer does not have to prove efficacy or safety of a compound before it is marketed, and products are not scrutinized via the same stringent testing placed on drugs. Some companies are now using techniques such as chromatography to identify and standardize herbal preparations.
- C. **The American Society of Anesthesiologists recommends discontinuing herbal remedies 2 weeks before elective surgery.** Herbal medications may be dangerous when used in combination with prescription or over-the-counter drugs. They can alter the metabolism of drugs and have been associated with arrhythmias and bleeding. The sale of Ephedra (Ma Huang) was banned by the federal government in 2004 after a review of adverse events including heart attack, stroke, and death. However, ephedra is still available online in a modified form that removes certain alkaloids that technically makes it still legal. There is little evidence in the form of prospective studies or randomized clinical trials documenting the adverse effects of herbal medications used in the perioperative period. Case reports provide most of the evidence for the deleterious effects of herbal medications. For example, four cases of spontaneous intracranial bleeding have been caused by the use of ginkgo biloba. The mechanism could be related to platelet inhibition.

D. It has been estimated that one in five Americans taking prescription drugs is also taking vitamins or herbal supplements. The most frequently used herbs are echinacea, ginkgo biloba, St. John's wort, garlic, and ginseng.

E. Commonly used herbs/supplements and possible anesthetic interactions

1. Echinacea (*Echinacea purpurea*, purple cone flower)

- a. Uses: for common colds, wounds and burns, urinary tract infections, coughs, and bronchitis (immunostimulation via enhanced phagocytosis and nonspecific T-cell stimulation).
- b. Problems and interactions: may cause hepatotoxicity or potentiate hepatotoxic effects of anabolic steroids, amiodarone, ketoconazole, and methotrexate. By inhibiting microsomal enzymes, can precipitate the toxicity of drugs dependent on hepatic metabolism (e.g., phenytoin, rifampin, and phenobarbital). May decrease effectiveness of corticosteroids and cyclosporine.

2. Ephedra (*Ephedra sinica*, Ma Huang) not approved by FDA

- a. Uses: in over-the-counter diet aids; for bacteriostatic, antitussive actions (sympathomimetic with positive inotropic/chronotropic effects; α - and β -adrenergic agonist)
- b. Problems and interactions: potential interactions with cardiac glycosides and halothane (arrhythmias); guanethidine (enhanced sympathomimetic effects); monoamine oxidase inhibitors (MAOIs; enhanced sympathomimetic effects); oxytocin (hypertension); intraoperative hypotension better treated with phenylephrine than ephedrine

3. Feverfew (*Tanacetum parthenium*)

- a. Uses: as migraine prophylactic and antipyretic (inhibits serotonin release from aggregating platelets via inhibition of arachidonic acid release).
- b. Problems and interactions: can inhibit platelet activity (potentiate anticoagulants); rebound headache with sudden cessation; 5% to 15% develop aphthous ulcers or gastrointestinal irritation. Like other tannin-containing herbs, feverfew can interact with iron preparations and decrease bioavailability.

4. GBL, BD, and GHB (γ -butyrolactone; butyrolactone γ ; 1,4-butanediol; γ -hydroxybutyrate) not approved by FDA.

- a. Uses: bodybuilding, weight loss aid, sleep aid
- b. Problems and interactions: death, seizures, unconsciousness, bradycardia, slowed respirations

5. Garlic (*Allium sativum*)

- a. Uses: lipid lowering, vasodilatory, antihypertensive, antiplatelet, antioxidant, and antithrombotic/fibrinolytic qualities.
- b. Problems and interactions: may potentiate effects of warfarin. A case of spontaneous epidural hematoma has been reported. Of note, cooked garlic does not exhibit these anticoagulant effects.

6. Ginger (*Zingiber officinalis*)

- a. Uses: for antiemetic, antvertigo, and antispasmodic effects
- b. Problems and interactions: potent inhibitor of thromboxane synthetase; can potentiate anticoagulant effects of other medications

7. Ginkgo (*Ginkgo biloba*, maidenhair tree)

- a. Uses: as a circulatory stimulant; antioxidant; for intermittent claudication, tinnitus, vertigo, memory loss, dementia, and sexual dysfunction (inhibits platelet-activating factor, modulates nitric oxide, has anti-inflammatory effects).

- b. Problems and interactions: may enhance bleeding in patients already on anticoagulant or antithrombotic therapy (e.g., aspirin, nonsteroidal anti-inflammatory drugs, warfarin, heparin). Cases of spontaneous subarachnoid hemorrhage and subdural hematomas have been reported. May decrease effectiveness of anticonvulsant drugs (e.g., carbamazepine, phenytoin, and phenobarbital).
- 8. **Ginseng** (*Panax ginseng*)
 - a. Uses: to enhance energy level, and for antioxidant and reported aphrodisiac effects (thought to augment adrenal steroidogenesis via a centrally mediated mechanism).
 - b. Problems and interactions: "ginseng abuse syndrome" (more than 15 g/d) characterized by sleepiness, hypertonia, and edema. May see tachycardia or hypertension with other stimulants, hypotension intraoperatively, mastalgia, postmenopausal bleeding, mania in patients on MAOIs (phenelzine), and decreased effectiveness of warfarin. Hypoglycemic effect may necessitate monitoring in diabetics or neurosurgical patients receiving steroids.
- 9. **Goldenseal** (*Hydrastis canadensis*, turmeric root)
 - a. Uses: as diuretic, anti-inflammatory, laxative
 - b. Problems and interactions: functions as an oxytocic; overdose may cause paralysis (amount not known); free water diuresis (no sodium excreted, just free water); electrolyte abnormalities; hypertension
- 10. **Kava-kava** (*Piper methysticum*)
 - a. Uses: as anxiolytic, treatment for gonorrhea, skin diseases.
 - b. Problems and interactions: thought to inhibit norepinephrine; potentiates sedating effects of barbiturates, benzodiazepines; can potentiate ethanol effects. Increased suicide risk in patients with endogenous depression.
- 11. **Licorice** (*Glycyrrhiza glabra*)
 - a. Uses: for gastritis, gastric and duodenal ulcers, cough, and bronchitis.
 - b. Problems and interactions: glycyrrhizic acid in licorice may cause hypertension, hypokalemia, and edema. Contraindicated in many chronic liver conditions, renal insufficiency, hypertonia, hypokalemia.
- 12. **Saw palmetto** (*Serenoa repens*, cabbage palm)
 - a. Uses: for treatment of benign prostatic hypertrophy; has an antiandrogenic effect
 - b. Problems and interactions: may see additive effects with other hormone therapies (including oral contraceptives and estrogen replacement therapy)
- 13. **St. John's wort** (*Hypericum perforatum*, goat weed)
 - a. Uses: for depression, anxiety, sleep disorders, vitiligo (may inhibit monoamine oxidase, γ -aminobutyric acid, and serotonin receptors).
 - b. Problems and interactions: possible interaction with MAOIs, may prolong effects of anesthesia, and may photosensitize. Potential serotonergic syndrome (tremors, hypertonicity, autonomic dysfunction, and hyperthermia) with concomitant use of β -sympathomimetic amines or selective serotonin reuptake inhibitors, including fluoxetine, paroxetine.
- 14. **Valerian** (*Valeriana officinalis*, all-heal, vandal root)
 - a. Uses: has mild sedative and anxiolytic properties
 - b. Problems and interactions: potentiates effects of barbiturates, may decrease symptoms of benzodiazepine withdrawal, and prolong anesthetic actions

15. Vitamin E (Vitamin E)

- a. Uses: to slow aging process, prevention of stroke and pulmonary emboli, prevention of atherosclerosis, promotion of wound healing, effective against fibrocystic breast syndrome
- b. Problems and interactions: May increase bleeding

III. PERIOPERATIVE ACUPUNCTURE

- A. Preoperative Use.** Numerous studies using preoperative acupuncture, including ear points, show significant relaxation. In two double-blinded studies, preoperative auricular acupuncture reduced anxiety up to 48 hours compared with sham acupuncture. This reduction in anxiety correlates with less pain and analgesic consumption postoperatively. Acupuncture may complement the use of anxiolytics preoperatively.
- B. Intraoperative Use.** acupuncture creates analgesia and sedation but does not provide muscle relaxation, suppress autonomic reflexes, or provide unconsciousness. Available data show that acupuncture has little or no effect on anesthetic requirements. A recent study monitoring neuro-muscular blockade at the P6 point significantly reduced the incidence of PONV for 24 hours.
- C. Postoperative Use**
 - 1. Pain control:** although the findings are controversial, several good studies reveal substantial reduction in postoperative pain with acupuncture. This probably requires a well-trained practitioner who can design a complex treatment plan that treats varieties of pain, such as visceral and dermatomal pain.
 - 2. Postoperative nausea and vomiting:** The use of acupuncture to treat PONV has been well studied and is very effective, even in children. Laser stimulation of PC6 (Fig. 40.1) after induction of general anesthesia in children will still effectively reduce PONV. Acupuncture may be used with or without conventional antiemetics.

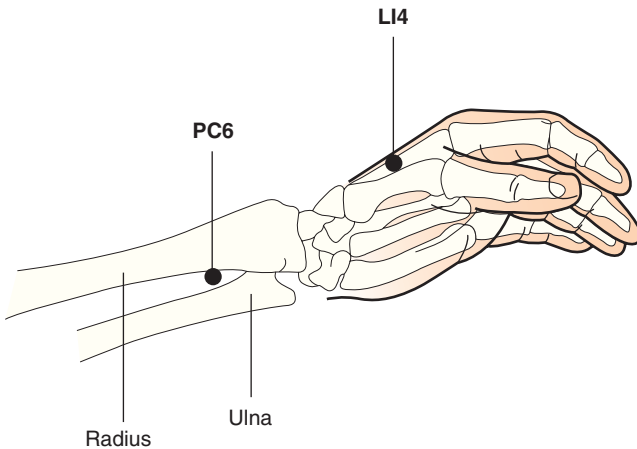


FIGURE 40.1 PC6 helps relieve anxiety, nausea, and travel sickness. LI4 is good for headaches, toothache, sinusitis, colds, and pain in the upper body. (From Kuhn MA. *Complementary Therapies for Health Care Providers*. Philadelphia: Lippincott Williams & Wilkins; 1999:296.)

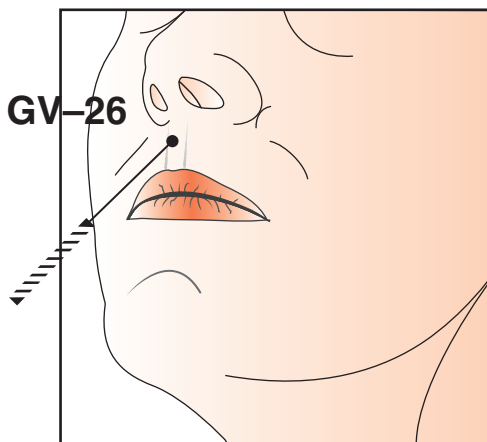


FIGURE 40.2 GV 26. (From Helms JM. *Acupuncture Energetics, a Clinical Approach for Physicians*. New York: Medical Acupuncture Publishers; 1995:296.)

3. Other applications: Studies in dogs have shown the successful use of acupuncture for cardiovascular resuscitation. GV26 (Fig. 40.2) has been shown to improve cardiac output and SV and is suggested to treat cardiovascular collapse in humans. A small study in humans has shown a beneficial effect of postoperative acupuncture in restoring intestinal function after abdominal surgery.

IV. HYPNOSIS

- A. **Definition.** hypnosis involves the induction of a state of mind, allowing for heightened receptivity to suggestions. It is generally a state of relaxation in which critical thought is bypassed.
- B. **Mechanism.** hypnosis influences the affective (cognitive/evaluative) component of pain. FMRI and PET scans show that this affective processing of pain occurs in the medial thalamus with projections to the anterior cingulate gyrus. Hypnosis also reduces the activity in the frontal cortex and may influence descending pathways that inhibit pain perception.
- C. **Possible Applications.** Many studies focus on the use of hypnosis to alleviate perioperative pain, anxiety, and nausea. Although findings vary, the use of preoperative hypnotic suggestion has often been found to reduce emesis and narcotic requirements postoperatively. Children are often receptive to hypnosis-guided imagery. Hypnoanalgesia has emerged as a combination of hypnotic techniques with pharmacologic analgesics and sedation. It has been used effectively for dressing changes in burn patients, with the concurrent suggestions of improved appetite and nutrition. Positive suggestions to anesthetized patients may also promote fewer postoperative complications.

V. MUSIC MEDICINE AND MUSIC THERAPY

- A. **Definitions:** **Music Medicine** is the practice of passive listening to prerecorded music; it is generally administered by physicians and nurses. **Music Therapy** is the application of an individualized music intervention

and therapeutic process based on music preferences. It is administered by a trained music therapist.

- B. Preoperative Use:** Music interventions offer a safe, inexpensive, and effective nonpharmacologic intervention for reduction of preoperative stress and anxiety that avoids the side effects of benzodiazepines.
- C. Intraoperative Use:** Music interventions in patients undergoing neuraxial anesthesia significantly decrease the need for sedatives and opiates intraoperatively. Patients also experience reduced cardiovascular and endocrine stress responses.
- D. Postoperative Use:** Music interventions decrease pain intensity scores and result in lower use of opiates in the PACU. Patients also report better interactions with their caretakers and a more positive overall stay in the PACU. Music interventions also result in earlier mobilization of patients.

Suggested Readings

- Amberger M, Stadelmann K, et al. Monitoring of neuromuscular blockade at the P6 acupuncture point reduces the incidence of postoperative nausea and vomiting. *Anesthesiology* 2007;107(6):903–908.
- American Society of Anesthesiologists. What you should know about your patient's use of herbal medicines. Accessed June 2014, <http://www.asahq.org>
- Astin JA. Why patients use alternative medicine: results of a national study. *JAMA* 1998;279:1548–1553.
- Ben-Arye E, Halabi I, et al. Asking patients the right questions about herbal and dietary supplements: cross cultural perspectives. *Complement Ther Med* 2014;22(2):304–310.
- Chernyak GV, Sessler D. Perioperative acupuncture and related techniques. *Anesthesiology* 2005;102(5):1031–1049.
- Chin S, Cristofaro J, Aston S. Perioperative management of antidepressants and herbal medications in elective plastic surgery. *Plast Reconstr Surg* 2009;377–385.
- Jonas W, Levin J, eds. *Essentials of Complementary and Alternative Medicine*. Philadelphia: Williams & Wilkins; 1999.
- Kaye AD, Kucera I, Sabar R. Perioperative anesthesia clinical considerations of alternative medicines. *Anesthesiol Clin North America* 2004;22:125–139.
- Matsota P, Christodouloupoulou T, et al. Music's use for anesthesia and analgesia. *J Altern Complement Med* 2013;19(4):298–307.
- Micozzi M. *Fundamentals of Complementary and Alternative Medicine*. Philadelphia: Saunders; 2010.
- National Center for Complementary and Alternative Medicine. The use of complementary and alternative medicine in the United States. Accessed June 2014, <http://www.nccam.nih.gov>
- Stewart JH. Hypnosis in contemporary medicine (review). *Mayo Clin Proc* 2005;80(4):511–524.
- Tsen LC, Segal S, Pothier M, et al. Alternative medicine use in presurgical patients. *Anesthesiology* 2000;93:148–151.
- Wobst AH. Hypnosis and surgery: past, present, and future. *Anesth Analg* 2007;104(5):1199–1208.
- Zhang Y, Peck K, et al. Discrepancy between patients' use of and health providers' familiarity with CAM. *Patient Educ Couns* 2012;89(3):399–404.

This chapter explores ethical issues that frequently arise in anesthetic practice. Customs, laws, ethical beliefs, and religious practices vary among cultures and societies. This chapter describes the prevailing practice at the Massachusetts General Hospital in Boston, Massachusetts.

I. DECISIONS CONCERNING TREATMENT

A. Patient autonomy is a highly valued guiding ethical principle in U.S. medicine. Adult patients with decision-making capacity can and may choose to accept or refuse medical therapies. If a patient's decision-making capacity is questionable, a psychiatrist should evaluate the patient. Decision-making capacity contains four essential elements; understanding, appreciation, reasoning, choice. Competence is a legal term and thus should be limited in use.

B. Autonomy is best preserved by involving the patient in medical decision making whenever possible. Obtaining **informed consent** for procedures and therapies is an ethical responsibility of the treating physician (see Chapter 1). Rarely, a patient's condition and emergent circumstances may prevent the discussion involved in the informed consent process. Many critically ill patients cannot make medical decisions because of the gravity of their illness or because of sedative/analgesic medications used to diminish suffering. In these circumstances, an advance directive and/or surrogate may be helpful.

1. An advance directive, commonly called a living will, is a legal document specifying the types of treatment that the patient wishes to receive or reject should future need arise and often includes a designated surrogate. Most hospitals require documentation upon admission that clarifies the wishes for limitations of life-sustaining treatment. For example, a patient with terminal cancer may desire placement of a central venous access for chemotherapy but will refuse resuscitation in the event of a cardiac or respiratory arrest. The limitation of life-sustaining treatment orders especially with respect to do not resuscitate (DNR) and do not intubate (DNI) must be considered prior to each anesthetic.

2. In addition to or in the absence of an advance directive, a patient may designate a **surrogate** (health care proxy or durable power of attorney for health care) who has the legal charge to execute the patient's wishes should he or she become unable to do so. The surrogate offers **substituted judgment** for the patient, providing decisions that the patient would make if capable. If the patient has not designated a surrogate before becoming unable to make medical decisions, the next of kin may become the de facto surrogate. In some circumstances where no family is living or available, a trusted friend may act as the patient's surrogate. The durable power of attorney for health care may **or may not be responsible** for financial decisions based upon the wishes of the patient.

3. In emergency situations, physicians may need to act in the **best interest of the patient** until the patient's wishes, either directly from the patient or from an advance directive, can be elucidated.

4. A court-appointed legal **guardian** may be necessary in rare instances in which no family member or friend is able to make decisions in the best interest of the patient.
- C. **Conflict** is best resolved via ongoing discussion with the individuals involved. The anesthetist must recognize and respect cultural differences that influence a patient's decisions. Irresolvable conflict among family members, health care team members, or between the family and the medical care team often is best addressed by the institutional ethics committee (see below).
- D. **The institutional ethics committee** is generally composed of a group of health care professionals trained in medical ethics.
 1. **The purpose** of the ethics committee is to provide education, advice, and consultation to promote resolution of ethical conflicts. The ethics committee offers an objective analysis of the patient's case and uses basic ethical principles to guide the health care team, patient, and family to a consensus about the therapeutic course.
 2. An ethics consult may be requested by physicians, nurses, other health care professionals or staff members, patients, and patients' families/friends, and the ethics committee should be easily accessible to all those involved in the case. This diminishes inequalities of power present in the hospital environment and promotes a climate of respect for all viewpoints.
 3. When the ethics committee is requested to consult on a case, the question to be answered or the nature of the conflict should be clearly stated. The patient's condition and prognosis should be documented. Members of the ethics committee may help organize and/or attend a family meeting to facilitate decision making.
 4. In rare situations in which irreconcilable differences exist between the physician and the patient and/or family, care of the patient may be transferred to another accepting attending physician. It is even more extraordinary for ethical conflicts to reach resolution by judicial intervention.
- E. **The pediatric patient** deserves special consideration when ethical issues are confronted. Legally, such decisions are deferred to the parents. Ethically, the child may participate in these decisions depending on his or her developmental level and decision-making capacity. If the child is too immature to participate in decisions, parents are relied upon to make decisions in the best interest of the child, incorporating family values as well as weighing the benefit versus burden of the planned therapy. Pediatric anesthetists must be sensitive to individual family dynamics and parenting styles when approaching such discussions.
- F. **Jehovah's Witness'** belief is that the bible prohibits consumption of blood and that blood that has been removed is unclean. Patients who are Jehovah's Witnesses generally do not accept transfusions of blood products. However, each Jehovah's witnesses must be assessed individually. Some patients will accept blood subfractions or products made from recombinant DNA. Similarly, some individuals will accept autotransfused blood, chest tube-salvaged autologous blood, dialysis or cardiopulmonary bypass return as it is possible for blood to remain in contiguous circulation with the vasculature by allowing a constant connection of the tubing withdrawing the blood from the patient with the transfusion tubing. Special considerations regarding homologous transfusion may apply if the patient is a minor, is incompetent, or has responsibilities for dependents,

and in certain emergency circumstances when the patient's wishes are not yet known. Law and judicial practices vary from state to state, requiring that health care practitioners be familiar with their particular state's statutes or seek advice from hospital legal counsel. Careful documentation of preoperative discussions, informed consent, and agreement of the entire operating room team to honor the patient's wishes and not transfuse even in the event of an unexpected blood loss are mandatory. Legal precedent generally supports patient autonomy regarding the acceptance of transfusion.

Recently, Jehovah's witnesses have accepted organ transplants. An ethical dilemma presents as human organs are in short supply and their donation is an incredible gift. Although there have been hearts, lungs, kidneys, liver, and pancreas transplants performed in Jehovah's Witness patients without blood, the question remains if it is ethical to transplant these organs into patients who will not take optimal care of the organ by accepting a needed transfusion. Although some have argued for transfusion contracts in the setting of organ transplants, there are ethical questions regarding the appropriateness of pressuring a patient to accept blood.

- G. **"Do not resuscitate (DNR)" orders** should not be automatically suspended when a patient enters the operating room. Rather, the institution's written policy regarding this situation should be followed. The American Society of Anesthesiologists recognizes a patient's right to self-determination and recommends that preexisting advance directives be discussed with the patient (or surrogate) and other involved parties (e.g., surgeon and primary physician) before initiating anesthetic care. Specific aspects of the anesthetic that might be considered resuscitation in another setting (e.g., endotracheal intubation) may be necessary to provide successful anesthesia intraoperatively. All communications regarding DNR orders should be documented in a chart and used to guide the anesthetic care. Three general courses of action may usually be agreed upon:
1. A full resuscitation status is implemented for the anesthetic and perioperative period, suspending the "DNR" status.
 2. A limited, procedure-directed resuscitation is implemented for the anesthetic and perioperative period. For example, a patient may accept endotracheal intubation, which may be necessary for the surgical procedure, but he or she may reject chest compressions in the event of cardiac arrest.
 3. A limited, goal-directed resuscitation, based on the patient's values, is followed for the perioperative period. For example, the patient may allow resuscitation for events that are deemed to be reversible and known complications of the anesthetic (e.g., hypotension) but not allow resuscitation for events that in the judgment of the anesthesiologist are likely irreversible (e.g., ventricular fibrillation due to myocardial ischemia). Similarly, a patient may define a priori based on his or her values circumstances what would result in an unacceptable quality of life and may request a limitation of life-sustaining therapies in those circumstances.
 - a. Importantly, the duration of the perioperative period should be defined and well documented. This, however, may be a difficult time period to distinctly define, especially if the patient receives postoperative care in an intensive care unit (ICU) or has a prolonged PACU stay. Communication regarding the patient's wishes should be documented in the patient's chart.

H. Ethical Issues for the Anesthetist

The ethical and moral beliefs of the anesthetist must be taken into consideration for elective procedures. It is within the right of the individual to refuse to participate in the care of, for example, a Jehovah's Witness, a therapeutic abortion or a patient who is DNR, without the need to justify this decision.

II. DETERMINATION OF DEATH USING BRAIN CRITERIA

A. "Brain death" is a legal definition by the Uniform Determination of Death act (UDDA) and can be defined as an irreversible loss of all functions of the brain, including the brain stem. The three pivotal findings for brain death are **coma**, **absent brain stem reflexes**, and **apnea**. A patient who is determined to be brain dead is legally and clinically dead. Several states have adopted amendments regarding physician qualifications and confirmation by second physician for diagnoses of brain death and religious exemption for the diagnosis of brain death. Brain death must be understood to be no different from a diagnosis of death made by cardiac criteria. Practically, the diagnosis of brain death means that a patient can potentially become an organ donor on the conditions of consent and medical acceptability. Locally accepted guidelines are used to establish the diagnosis of brain death. Diagnostic criteria for the clinical diagnosis of brain death in adults, adapted from those used at the Massachusetts General Hospital (MGH), are summarized below. Other institutions may have different criteria. At MGH, brain death may be declared only by an **attending neurologist or attending neurosurgeon**.

B. Clinical Diagnosis of Brain Death

C. Prerequisites include the following:

1. Irreversible and proximate cause of the brain injury must be known. Clinical or neuroimaging evidence of a central nervous system (CNS) catastrophe must exist to explain the findings.
2. Exclusion of complicating medical conditions that may confound clinical assessment (e.g., severe electrolyte, acid-base, or endocrine disturbance).
3. Absent evidence of drug intoxication or poisoning. In cases where CNS depressants are known to have been administered, ancillary brain testing may be recommended.
4. Absent evidence of neuromuscular blockade if the patient has had recent or prolonged use of muscle relaxants.
5. Core temperature greater than 36.5°C (96.8°F).
6. In the presence of confounding variables, brain death may still be determined with the aid of ancillary testing (see below). A period of observation of at least 24 hours without clinical neurologic change is necessary if the cause of the coma is unknown.

D. Although a complete clinical exam is acceptable and the preferred method for determination of diagnostic testing, there are instances in which a clinical exam cannot be applied. **Confirmatory ancillary tests** may support the diagnosis of brain death and include angiography, electroencephalography, transcranial Doppler ultrasonography, and technetium-99m hexamethylpropyleneamine oxime brain scanning. MRA and CT angiography are currently considered investigational as ancillary tests for brain death but may be acceptable in the future. The accuracy of somatosensory-evoked potentials in determining brain death have been called into question and are not used at MGH as a sole ancillary test.

III. ORGAN DONATION

In the United States, the United Network for Organ Sharing (UNOS) maintains the national Organ Procurement and Transplantation Network (OPTN) contract. UNOS is responsible for creating and maintaining an organ sharing system to maximize the use of the scarce organ supply and maintain data regarding transplants. In the United States, most organs are retrieved from donors who are declared brain dead; however, an increasing number of organs are being harvested from living donors and from donation after cardiac death (DCD). DCD organ donors are critically ill patients who are expected to die imminently upon withdrawal of life-sustaining treatments. Importantly, data to date suggest that outcomes of organs from DCD donors are not significantly different from those of brain-dead donors, despite a known warm ischemia time.

- A. Conversations with the family** regarding organ donation should not be conducted by the physician caring for the patient due to a potential conflict of interest. Rather, federal regulations require that these discussions be conducted by trained personnel from the regional organ procurement agency. Studies support that families are more likely to agree to organ donation when they are approached by a trained professional from the organ procurement agency. The topic is often introduced by asking the family if the deceased had ever expressed an opinion regarding the use of his or her organs after death. Many families are consoled by the thought that their loved ones body parts may be lifesaving to another individual and may in some sense carry on the life that has been lost.
- B. Early contact** with the organ procurement agency is critical in cases of potential organ donors. Organ procurement agencies generally have specific protocols regarding medications (e.g., vasopressors and hormonal support), mechanical ventilator settings, and laboratory blood work to be performed.
- C. Care of the brain-dead patient** for organ donation is challenging (see Chapter 21). Frequently encountered problems include hypotension, dysrhythmias, hypoxemia, and diabetes insipidus. If a successful donation is to occur, attendance of a vigilant anesthesiologist and/or ICU team, in concert with direction from the organ procurement agency, is necessary.
- D. DCD organ procurement** demands adherence to guiding ethical principles. The institutional policy for DCD procurement should be reviewed and followed when DCD organ procurement is planned. Care of the dying patient, including provision of analgesic and amnestic medications by the ICU team caring for the patient, supersedes the goal of organ procurement. The institutional policy should clearly define the following:
 - 1. The nonoverlapping roles of caregivers to the donor and the recipient to avoid a conflict of interest.
 - 2. The physician (usually the intensivist) responsible for pronouncing cardiac death.
 - 3. The time interval after asystole at which death is cleared. Currently, at the Massachusetts General Hospital (MGH), this time interval is 5 minutes.
 - 4. The process for obtaining consent for and administering medications or treatments necessary for organ procurement but not of benefit (and potentially harmful) to the patient. Examples include heparin administration or femoral arterial cannula placement.
 - 5. The process for allowing family presence at the time of death (in the ICU or operating room).

6. The time interval after which organ procurement will not be attempted in the case of unexpected patient survival after the withdrawal of life-sustaining therapies and the process of return to the ICU. Currently, this time interval is 2 hours after extubation at the MGH.
If the institutional transplant team will participate in harvesting or transplanting organs, it is prudent to establish contact with the team and immediately apprise them of any change in the donor's condition that might warrant expedited harvest.

IV. CARING FOR SURVIVORS

- A. **Support** of the patient's survivors after a death begins with honest, frequent, and compassionate communication from the medical team.
- B. **Cultural background and individual values** will affect each conversation. The medical team should strive for flexibility when presented with each situation.
 1. A social worker may be an important source for understanding the families' religious and cultural background.
 2. Clergy support may be helpful and should be offered to the family.
 3. Follow-up with the family may be beneficial both to survivors and to the medical team. It is routinely performed by the organ procurement agency in cases where organ donation has occurred.

V. LEGAL CONSIDERATIONS

Physicians who engage in honest, open communication with patients and their families about ethical and end-of-life issues should rarely find themselves resolving such issues in a court of law. Nevertheless, several recent judicial rulings have implications that may prove useful to the clinician when confronted with ethical issues.

- A. **Patient autonomy is primary in decision making.** Legal precedent is clear that patients may refuse life-sustaining or other therapies.
- B. **Human life has qualification beyond mere biologic existence.** A surrogate may decide to withdraw care based on the potential for meaningful existence ("quality of life").
- C. **Care once rendered may be withdrawn.** Although life-sustaining therapy such as intubation has been implemented, it can be discontinued, and terminal extubation is acceptable.
- D. **End-of-life decisions are best addressed by the physician and the patient and/or family** with help from institutional facilitators (e.g., ethics committee) as needed. In most states, permission to withdraw or withhold a therapy does not require a "court order."
- E. **Withdrawal of hydration or nutritional support is not legally different from withdrawal of other life support.** In addition to legal decisions, this stance has been supported by numerous medical societies, including the American Medical Association and the American Academy of Neurology.
- F. **Physicians are not bound to provide care that they deem futile.** However, determination of "futility" may be problematic and, in circumstances of conflict with the patient or family, it is advisable for the physician to pursue every avenue of conflict resolution, including removing himself or herself from the care of a patient, before exercising this dictum against a family's wishes.
- G. **For unusual or questionable cases,** it is appropriate to seek the advice of the institutional legal counsel before acting on decisions.

Suggested Readings

- American Society of Anesthesiologists. Ethical guidelines for the anesthesia care of patients with do-not-resuscitate orders or other directives that limit treatment. Approved October 17, 2001, last affirmed October 22, 2008.
- Bernat JL. The boundaries of organ donation after circulatory death. *N Engl J Med* 2008;359:669–671.
- Jenkins K, Baker AB. Consent and anaesthetic risk. *Anaesthesia* 2003;58:962–984.
- Steinbroock R. Organ donation after cardiac death. *N Engl J Med* 2007;357:209–213.
- Truog RD, Miller F. The dead donor rule and organ transplantation. *N Engl J Med* 2008;359:674–675.
- Truog RD, Waisel DB, Burns JP. DNR in the OR: a goal-directed approach. *Anesthesiology* 1999;90:289–295.
- Van Norman, GA. Another matter of life and death: what every anesthesiologist should know about the ethical, legal, and policy implications of the non-heart-beating cadaver organ donor. *Anesthesiology* 2003;98:763–773.

This page intentionally left blank.

Drugs with Narrow Therapeutic Ranges and Potential for Harm

Richard M. Pino

Anesthetists frequently administer intravenous medications with narrow therapeutic windows and the potential for critical events. The drugs described in this section list agents that are not routinely administered by anesthetists but may be requested by others. It does not include agents that fall within the scope of the training and practice of anesthetists, for example, neuromuscular blockers.

A. ABCIXIMAB (REOPRO): Glycoprotein IIb/IIIa inhibitor preventing platelet adhesion and aggregation.

Indications: Prevent thrombus formation peri-PTCA and poststent placement.

Administration guidelines

- a. Standard concentration: 9 mg/250 mL 0.9% sodium chloride.
- b. The IV tubing must have a filter on it (0.2- or 0.22- μ m low-protein-binding filter) and no other medications should be piggybacked through this line.
- c. Loading dose (straight drug): 0.25 mg/kg administered 10 to 60 minutes prior to PCI. Withdraw through the 0.2- or 0.22- μ m low-protein-binding filter the appropriate amount of abciximab for the patient's weight. Hypotension may occur with bolus dose.
- d. Maintenance at a rate of 0.125 μ g/kg/min to a max of 10 μ g/min (17 mL/h) for 12 hours. To prepare, withdraw 4.5 mL (9 mg) of abciximab through 0.2- or 0.22- μ m low-protein-binding filter and inject into 250-mL bag of 0.9% sodium chloride.

B. ALPROSTADIL (PGE₁): Vasodilator; decreases peripheral resistance, which causes reflexive increase in cardiac output and heart rate.

Indications:

- a. Primary nonfunctional liver transplant characterized by rising transaminases, minimal bile production, and coagulopathy within 4 to 34 hours after transplantation.
- b. Pulmonary hypertension.
- c. Distal ischemia (limb or digit) refractory to conventional revascularization or drug therapy.
- d. Vasospastic disorders (Raynaud's), vasculitis, Buerger's, atheroembolic diseases.
- e. Protection against tacrolimus nephrotoxicity.

Administration guidelines:

- a. Standard concentration: 500 μ g of alprostadil in 1,000 mL NS (1 μ g = 1,000 ng).
- b. Infusion rates should be titrated to patient response.
 1. Remove rings/tight-fitting jewelry during the infusion since most experience extremity swelling. Patients often experience a "flushing" feeling during the initiation that is not necessarily an indication to stop the infusion, unless there is a drop in BP.
 2. Start the infusion at 1 ng/kg/min. If the patient becomes hypotensive, wean back to the previous dose. A starting dose of 0.4 ng/kg/min is recommended for patient with borderline low blood pressure and/or poor LV function.
 3. The infusion rate (dose) may be doubled every 30 minutes as tolerated to a peak dose of 16 ng/kg/min.

C. ALTEPLASE (ACTIVASE): Tissue Plasminogen Activator (tPA)**Indications:**

- a. Acute myocardial infarction.
- b. Pulmonary embolism.
- c. Peripheral arterial or venous thrombosis.
- d. Catheter occlusion.

Administration guidelines:**a. Acute myocardial infarction**

1. Standard concentration: 100 mg/100 mL.
2. Patient weight less than 67 kg: 15-mg bolus, then 0.75 mg/kg (max 50 mg) over 30 minutes. Initiate **heparin** therapy with a bolus, then 0.5 mg/kg (max 35 mg) over the next hour.
3. Patient weight greater than 67 kg: 15-mg bolus, then 50 mg over the next 30 minutes. Institute heparin therapy with a bolus. Infuse remaining 35 mg of TPA over the next hour (total dose of TPA = 100 mg).

b. Pulmonary embolus:

1. Standard concentration: 100 mg/100 mL.
2. Maintenance infusion: 100 mg continuous infusion over 2 hours.

c. Peripheral arterial or venous thrombosis

1. Standard concentration: 50 mg/500 mL, 25 mg/250 mL.
2. Loading dose: none.
3. Maintenance infusion: 0.5 to 4 mg/h for 24 hours (recommended max 50 mg/24 hours). Heparin (no loading dose) should be started after alteplase infusion is completed to maintain aPTT in a therapeutic range.

d. Venous and arterial thrombosis catheter-directed thrombolysis

1. Standard concentration: 50 mg/500 mL, 25 mg/250 mL.
2. Loading dose: 4 to 10 mg.
3. Maintenance infusion: 0.5 to 4 mg/h for 4 to 24 hours IV. Recommended cumulative maximum of 50 mg (load plus infusion). Heparin should be used at a low non-weight-adjusted dose (e.g., 250 units/h) keeping aPTT less than 1.5 times baseline during alteplase infusion.

D. ARGATROBAN: Direct Thrombin Inhibitor**Indications:**

- a. Anticoagulation in patients with suspected or confirmed heparin-induced thrombocytopenia (HIT type II).
- b. Anticoagulation during and immediately following percutaneous coronary interventions (PCI).

Administration guidelines

- a. Standard concentration (1 mg/mL): 50 mg/50 mL premixed vial in NaCl for large volume infusion pump.
- b. Low concentration (0.05 mg/mL): 2.5 mg/50 mL bag.
- c. Microinfusion: 2.5 mg/50 mL syringe.
- d. **Bolus: none.**
- e. Maintenance:
 1. Start 0.5 to 2 μ g/kg/min as a continuous infusion.
 2. Reduce initial dose to 0.5 μ g/kg/min for hepatic and/or renal dysfunction, and critically ill.
 3. Check the PTT 2 hours after the start of the infusion and after any rate change until stable (i.e., two consecutive values within the goal range). Goal: aPTT 1.5 to 3 $\times$ baseline not to exceed a PTT of 100 seconds.
 4. When ACT greater than 450 seconds, reduce maintenance to 15 μ g/kg/min and recheck in 5 to 10 minutes.

E. BIVALIRUDIN (ANGIOMAX): Direct Thrombin Inhibitor

Indication: Anticoagulation in patients with strongly suspected or confirmed heparin-induced thrombocytopenia (type II).

Administration guidelines

- a. Standard concentration (5 mg/ mL): 250 mg/50 mL bag.
- b. Low concentration (1 mg/mL): 100 mg/100 mL bag (low concentration).
- c. Microinfusion: 250 mg/50 mL syringe.
- d. **Bolus: None.**
- e. Maintenance
 1. Starting dose: 0.15 mg/kg/h (CrCl >60 mL/min).
 2. If CrCl 30 to 60 mL/min: 0.05 mg/kg/h.
 3. If CrCl less than 30 mL/min or renal replacement therapy: 0.025 mg/kg/h.
 4. Goal aPTT: 1.5 to 2.5 times baseline. Check the PTT 2 hours after the start of the infusion and after any rate change until two consecutive PTT values are within the goal range.

F. EPOPROSTENOL SODIUM (FLOLAN): Potent vasodilator that also inhibits platelet aggregation.

Indication: Pulmonary hypertension.

Administration guidelines

- a. Do not give with other parenteral medications or carriers.
- b. A dedicated central venous catheter is required for administration with an air-eliminating filter.
- c. **Do not flush catheter with epoprostenol in-line.**
- d. **Bolus: None.**
- e. Maintenance infusion:
 1. Initial dose: 1 to 2 ng/kg/min IV.
 2. Titrate in 1 to 2 ng/kg/min increments every 15 to 30 minutes.
- f. If catheter needs to be flushed, withdraw 3 mL of fluid/blood from the catheter into a syringe and discard. The line should be primed with epoprostenol-specific diluent only.
- g. Avoid abrupt withdrawal that may cause rebound pulmonary artery hypertension.
- h. Syringe is only stable for 8 hours at room temperature.

G. EPTIFIBATIDE (INTEGRILIN)

Indication: Prevention of thrombus formation after PCI.

Dosage: Bolus (180 µg/kg), then 2 µg/kg/min continuous infusion.

Effect: Inhibits glycoprotein IIb/IIIa; prevents platelet adhesion and aggregation.

Comments: Bleeding complications and thrombocytopenia are common side effects.

H. INSULIN, REGULAR (HUMAN): Humulin R, Novolin R

Indications: Hyperglycemia, hyperkalemia, diabetic ketoacidosis.

Administration guidelines:

- a. Regular insulin is the only insulin that can be administered intravenously.
- b. Insert infusion into y-site below any in-line filters.
- c. Standard concentration for microinfusion: 50 units/50 mL normal saline.
- d. Loading dose: 5 to 20 units IVP or bolus (usually given prior to starting maintenance).
- e. Maintenance infusion: 2 to 25 units/h IV titrated according to blood glucose level.
- f. Once under control, blood glucose should be monitored at a minimum of every 2 hours and more often as needed.

I. POTASSIUM CHLORIDE (KCl)

Indication: Correction of hypokalemia.

a. Caution: Hypokalemia is not usually treated in the OR.

b. The decision to administer KCl requires **anesthesia attending approval** in advance of administration.

Administration guidelines:

a. Bolus dose: None. **May cause cardiac arrest.**

b. Peripheral concentration: 80 mEq/1,000 mL.

c. Central concentration: 20 mEq/100 mL; 40 mEq/100 mL.

d. Rate: Not to exceed 20 mEq/h.

Commonly Used Drugs

The drugs listed in this section are those that are commonly used or encountered by anesthesiologists during perioperative patient care. Anesthetics and muscle relaxants are not included and are covered in respective chapters.

ABCIXIMAB (REOPRO) (SEE APPENDIX I)

ADENOSINE

Indications: Paroxysmal supraventricular tachycardia.

Dosage: Adult: 6 to 12 mg peripheral IV bolus followed by rapid 20 mL saline IV flush. Central line: initial dose, 3 mg. Pediatric: 50 μ g/kg IV.

Effect: Slows or temporarily blocks AV node conduction and conduction through reentrant pathways (especially those involving the AV node).

Comments:

- Contraindicated in patients with second- or third-degree heart block or sick sinus syndrome.
- Not effective in terminating atrial flutter or fibrillation but may aid in diagnosis by slowing ventricular response.
- Asystole for 3 to 6 seconds after administration is common and resolves spontaneously.
- May cause bronchospasm or hypotension.
- Use with caution in patients with preexcitation syndromes (e.g., Wolff-Parkinson-White).

ALBUTEROL

Indications: Bronchospasm.

Dosage: Aerosolized: 2.5 mg in 3 mL saline via nebulizer; 180 or 200 μ g (two puffs) via MDI. PO: 2.5 mg. Pediatric: 0.1 mg/kg (syrup 2 mg/5 mL).

Effect: β_2 -Receptor agonist, causing bronchial smooth muscle relaxation.

Comments: Possible β -adrenergic overload, tachydysrhythmias. Increased dose required when using MDI for intubated patients (four to six puffs).

ALPROSTADIL (SEE APPENDIX I)

ALTEPLASE (SEE APPENDIX I)

AMINOCAPROIC ACID (AMICAR)

Indications: Prevention of bleeding due to fibrinolysis.

Dosage: 5 g/100 to 250 mL of NS IV to load, followed by 1 g/h infusion.

Effect: Stabilizes formed clot by inhibiting plasminogen activators and plasmin.

Comments: Contraindicated in disseminated intravascular coagulation.

AMIODARONE

Indications: Refractory or recurrent atrial and ventricular tachydysrhythmias.

Dosage: 150 mg (ACLS 300 mg) IVP, then 1 mg/min for 6 hours (360 mg), then 0.5 mg/min for 18 hours (540 mg).

Effect: Depresses the sinoatrial node and prolongs the PR, QRS, and QT intervals; produces α - and β -adrenergic blockade.

Comments:

- May cause severe sinus bradycardia, ventricular arrhythmias, AV block, liver and thyroid function test abnormalities, hepatitis, and cirrhosis.
- Pulmonary fibrosis can result from long-term use.
- Increases serum levels of digoxin, oral anticoagulants, diltiazem, quinidine, procainamide, and phenytoin.

ARGATROBAN (SEE APPENDIX I)

ATENOLOL

Indications: Hypertension, angina, and postmyocardial infarction (post-MI).

Dosage: PO: 50 to 100 mg/d. IV: 5 mg prn.

Effect: β_1 -Selective adrenergic receptor blockade.

Comments:

- Relatively contraindicated in acute congestive heart failure and heart block.
- Caution in patients on calcium channel blockers and other agents prolonging AV conduction.

ATROPINE

Indications: Antisialagogue; bradycardia; cardiac arrest (ACLS protocol).

Dosage:

a. Antisialagogue, adult, 0.2 to 0.4 mg IV. 0.4 to 1.0 mg IV; pediatric, 0.01 mg/kg/dose IV/IM (<0.4 mg).

b. Bradycardia, adult, 0.2 to 0.4 mg IV; pediatric, 0.02 mg/kg/dose IV (<0.4 mg).

c. Cardiac arrest, adult, 1 mg IV; pediatric, 0.01 to 0.02 mg/kg/dose IV.

Effect: Competitive blockade of acetylcholine at muscarinic receptors.

Comments:

- Low doses may cause paradoxical bradycardia.
- May cause tachydysrhythmias, AV dissociation, premature ventricular contractions, dry mouth, or urinary retention.
- CNS effects occur at high doses.

BICARBONATE, SODIUM (NaHCO_3)

Indications: Metabolic acidosis; urinary alkalinization.

Dosage: IV dose in mEq NaHCO_3 = (base deficit $\times$ weight [kg] $\times$ 0.3) (subsequent doses titrated against patient's pH).

Effect: H^+ neutralization.

Comments:

- Not compatible with many IV medications.
- May cause metabolic alkalosis, hypercarbia, and hyperosmolality.
- In neonates, can cause intraventricular hemorrhage.
- Crosses placenta.
- An 8.4% solution is approximately 1.0 mEq/mL; a 4.2% solution is approximately 0.5 mEq/mL.

BIVALIRUDIN (SEE APPENDIX I)**CALCIUM CHLORIDE; CALCIUM GLUCONATE**

Indications: hypocalcemia, hyperkalemia, and hypermagnesemia.

Dosage:

- a. Calcium chloride: 5 to 10 mg/kg IV prn ($10\% \text{CaCl}_2 = 1.36 \text{ mEq Ca}^{2+}/\text{mL}$).
- b. Calcium gluconate: 15 to 30 mg/kg IV prn ($10\% \text{calcium gluconate} = 0.45 \text{ mEq Ca}^{2+}/\text{mL}$).

Effect: Maintains cell membrane integrity, muscular excitation–contraction coupling, glandular stimulation–secretion coupling, and enzyme function. Increases blood pressure.

Comments:

- a. May cause bradycardia or arrhythmia (especially with digitalis).
- b. Irritating to veins. Ca^{2+} less available with calcium gluconate than with calcium chloride due to binding of gluconate.
- c. Rapid infusion may cause coronary vasoconstriction.

CARBOPROST (PROSTAGLANDIN $\text{F}_{2\alpha}$; HEMABATE)

Indications: Refractory postpartum hemorrhage.

Dosage: 250 μg IM; may repeat q15–90 min, maximum total dose 2 mg.

Effect: Causes uterine muscle contraction.

Comments: May cause significant bronchospasm, especially in patients with reactive airways, or hypertension.

CLEVIDIPINE (CLEVIPREX)

Indications: Treatment of acute hypertension when oral therapy is undesirable/unavailable.

Dosage: IV infusion: 1 to 2 mg/h; double the dose q90s until approaching goal, then adjust q5–10 min. Maximum dose 32 mg/h.

Effect:

- a. Dihydropyridine calcium channel blocker; causes blood pressure reduction $\pm$ reflex tachycardia via decreased systemic vascular resistance (SVR).
- b. May have negative inotropic effects. Does not affect preload.
- c. No dose adjustments for hepatic/renal dysfunction.

Effect: Lasts 5 to 15 minutes after discontinuation.

Comments:

- a. Rapidly titratable. In lipid emulsion.
- b. Discard unused portion after 4 hours.
- c. Contraindicated in soy/egg allergic patients, defective lipid metabolism, or severe aortic stenosis.
- d. Risk of rebound hypertension with prolonged infusion; risk of atrial fibrillation.

CLOPIDOGREL (PLAVIX)

Indications: Antiplatelet agent.

- a. Acute coronary syndrome.
- b. PCI.
- c. Recent MI, recent thromboembolic stroke, or established arterial disease.
- d. Coronary stent stenosis prophylaxis.

Dosage: Load, 300 to 600 mg PO; maintenance, 75 mg qd.

Effect: Irreversible platelet ADP receptor blockade.

Comments:

- a. Major side effect is bleeding.
- b. Reduce dose in hepatic insufficiency.
- c. Proton pump inhibitors may reduce clopidogrel efficacy.
- d. Recommend discontinuing 7 days prior to neuraxial anesthesia.

DALTEPARIN (FRAGMIN)

Indications: Prophylaxis of deep venous thrombosis, acute coronary syndromes (ACS), deep venous thrombosis (DVT).

Dosage:

- a. DVT prophylaxis, 2,500 to 5,000 units SC qd.
- b. ACS, 120 units/kg (maximum dose 10,000 units) SC q12h $\times$ 5 to 8 days with concurrent aspirin therapy.
- c. DVT, 100 units/kg SC bid or 200 units/kg SC qd.

Effect: Anticoagulant; inhibits both factor Xa and factor IIa. See Heparin.

Comments:

- a. Reduce dose for Cr clearance less than 30 mL/min.
- b. Equally effective as unfractionated heparin; more predictable dose-response characteristics.
- c. Spinal and epidural hematomas have been associated with spinals/lumbar punctures, or epidural catheter placement or removal. Use with caution when placing or removing neuraxial blockade in patients on Fragmin.
- d. Only partially reversed by protamine.

DANTROLENE

Indications: Malignant hyperthermia (MH); neuroleptic malignant syndrome.

Dosage: Mix 20 mg in 60 mL of sterile water. At first signs of MH, 2.5 mg/kg IV bolus; repeat dose, up to 10 mg/kg. Prophylactic IV treatment is not recommended.

Effect: Reduces Ca^{2+} release from sarcoplasmic reticulum; relaxes skeletal muscles.

Comments: Dissolves slowly into solution. Avoid extravasation as it is a tissue irritant.

DESMOPRESSIN ACETATE (DDAVP)**Indications:**

- a. Treatment of coagulopathy in von Willebrand disease, hemophilia A (but contraindicated if factor VIII $>5\%$ activity), renal failure.
- b. Central diabetes insipidus.

Dosage: Coagulopathy, 0.3 $\mu\text{g/kg}$ IV (diluted 50 mL NS), infused over 15 to 30 minutes. Central DI, 5 to 20 μg intranasally qd/bid.

Effect: Increases plasma levels of factor VIII activity by causing release of von Willebrand factor from endothelial cells; increases renal water reabsorption (ADH effect).

Comments: Chlorpropamide, carbamazepine, and clofibrate potentiate the antidiuretic effect. Repeat doses q12–24h will have diminished effect compared with initial dose. Has no vasopressor effect.

DEXAMETHASONE (DECADRON)

Indications: Cerebral edema; airway edema; prophylaxis of postoperative nausea and vomiting.

Dosage:

- a. Edema: 10 mg IV, 4 mg IV q6h (tapered over 6 days).
- b. N/V: 4 mg IV.

Effect: See Hydrocortisone. Has 20 to 25 times the glucocorticoid potency of hydrocortisone. Minimal mineralocorticoid effect.

Comments: See Hydrocortisone.

DEXTRAN 40 (RHEOMACRODEX)

Indications: Inhibition of platelet aggregation and improvement of blood flow in low-flow states (e.g., vascular surgery).

Dosage: 15 to 30 mL/h IV (10% solution); a load of 30 to 50 mL IV over 30 minutes is optional.

Effect: Immediate, short-lived (1.5 hours) plasma volume expansion; decreases platelet adhesion.

Comments: May cause volume overload, anaphylaxis, bleeding tendency, thrombocytopenia, interference with blood cross-matching, or false elevation of blood sugar.

DILTIAZEM (CARDIZEM)

Indications: Angina pectoris, variant angina from coronary artery spasm, atrial fibrillation/flutter, paroxysmal supraventricular tachycardia, hypertension.

Dosage: 20 mg IV bolus then 10 mg/h infusion; PO 30 to 60 mg q6h.

Effect: Calcium channel antagonist that slows conduction through sinoatrial and AV nodes, dilates coronary and peripheral arterioles, and reduces myocardial contractility.

Comments:

- May cause bradycardia and heart block.
- Possible impairment of contractility by interaction with β -blockers and digoxin.
- Causes transiently elevated liver function tests.
- Avoid use in patients with accessory conduction tracts, AV block, IV β -blockers, or ventricular tachycardia.

DOBUTAMINE

Indications: Inotropy for heart failure.

Dosage: Begin infusion at 2 $\mu\text{g/kg/min}$ and titrate to effect.

Effect: β_1 -Adrenergic agonist.

Comments: May cause hypotension, arrhythmias, or myocardial ischemia. Can increase ventricular rate in atrial fibrillation.

DOPAMINE

Indications: Hypotension, heart failure.

Dosage: 5 to 20 $\mu\text{g/kg/min}$ IV titrate to effect.

Effect: dopaminergic; α - and β -adrenergic agonist.

Comments:

- May cause hypertension, dysrhythmias, or myocardial ischemia.
- Primarily dopaminergic effects (increased renal blood flow) at 1 to 5 $\mu\text{g/kg/min}$.
- Primarily α - and β -adrenergic effects at greater than or equal to 10 $\mu\text{g/kg/min}$.

ENOXAPARIN (LOVENOX)

Indications:

- Prophylaxis of deep venous thrombosis.
- Treatment of deep venous thrombosis.
- Acute coronary syndromes.

Dosage:

- a. DVT prophylaxis, 30 mg SC bid or 40 mg SC qd.
- b. DVT treatment, 1 mg/kg SC q12h or 1.5 mg/kg SC qd.
- c. ACS, 1 mg/kg SC bid for a minimum of 2 days, in conjunction with aspirin therapy.

Effect: Anticoagulant; inhibits both factor Xa and factor IIa. See Heparin.

Comments:

- a. Equally effective as unfractionated heparin with more predictable dose-response characteristics.
- b. Spinal and epidural hematomas have been associated with spinals/lumbar punctures, or epidural catheter placement or removal.
- c. Only partially reversed by protamine.

EPHEDRINE

Indication: Treatment of hypotension.

Dosage: 5 to 10 mg IV.

Effect: α - and β -adrenergic stimulation; norepinephrine release at sympathetic nerve endings.

Comments:

- a. May cause hypertension, dysrhythmias, myocardial ischemia, CNS stimulation, decrease in uterine activity, and mild bronchodilation.
- b. Minimal effect on uterine blood flow. Crosses the placenta.
- c. Avoid in patients taking MAO inhibitors.
- d. Tachyphylaxis with repeated dosing.

EPINEPHRINE**Indications:**

- a. Heart failure.
- b. Cardiac arrest (ACLS).
- c. Bronchospasm, anaphylaxis.
- d. Airway edema.

Dosage:

- a. Heart failure, 1 to 12 μ g/min titrated to effect.
- b. ACLS, 0.1 to 1 mg IV or 1 mg intratracheal q5min prn. Pediatric, 0.01 mg/kg IV up to 0.5 mg, 0.01 mg/kg SC q15min $\times$ 2 doses up to 1 mg/dose.
- c. Bronchospasm, anaphylaxis, 0.1 to 0.5 mg SC, 0.1 to 0.25 mg IV, or 0.25 to 1.5 μ g/min IV infusion.
- d. Airway edema, nebulized: 0.5 mL of 2.25% solution in 2.5 to 3.5 mL of NS q1–4h prn.

Effect: α - and β -adrenergic agonist.

Comments: May cause hypertension, arrhythmias, or myocardial ischemia. Topical or local injection (1:80,000–1:500,000) causes vasoconstriction. Crosses the placenta.

EPOPROSTENOL (FLOLAN) (SEE APPENDIX I)**EPITIFIBATIDE (INTEGRILIN) (SEE APPENDIX I)****ERGONOVINE (ERGOTRATE, SEE ALSO METHYLERGONOVINE)**

Indication: Postpartum hemorrhage due to uterine atony.

Dosage: For postpartum hemorrhage: IV (emergency only), 0.2 mg in 5 mL of NS greater than or equal to 1 minutes; IM, 0.2 mg q2–4h prn for less than or equal to 5 doses, then PO: 0.2 to 0.4 mg q6–12h for 2 days or prn.

Effect: Constriction of uterine and vascular smooth muscle.

Comments: May cause hypertension from systemic vasoconstriction (especially in eclampsia and hypertension), dysrhythmias, coronary spasm, uterine tetany, or GI upset. Overdosage may cause convulsions or stroke.

ESMOLOL (BREVIBLOC)

Indications: Supraventricular tachydysrhythmias and myocardial ischemia.

Dosage: Start with 5 to 10 mg IV bolus and increase q3min prn to total 100 to 300 mg; infusion 1 to 15 mg/min.

Effect: Selective β_1 -adrenergic blockade.

Comments: May cause bradycardia, AV conduction delay, hypotension, congestive heart failure; β_2 activity at high doses.

FENOLDOPAM

Indications: Hypertension.

Dosage: 0.03 to 0.1 $\mu\text{g}/\text{kg}/\text{min}$ (most common dose); increase to 0.05 to 0.1 $\mu\text{g}/\text{kg}/\text{min}$ every 15 minutes.

Effect: Selective postsynaptic dopamine-1 receptor agonist.

Comments:

- Evidence does not indicate that it will prevent contrast-induced nephropathy.
- May cause hyperkalemia.
- Tachycardia possible at higher doses.
- May increase intraocular pressure.

FLUMAZENIL (MAZICON)

Indications: Reversal of benzodiazepine overdose.

Dosage: 3 to 5 mg IV at 0.5 mg/min.

Effect: Competitive antagonism of CNS benzodiazepine receptor.

Comments:

- Duration of action shorter than midazolam and other agonists.
- May induce CNS excitation including seizures, acute withdrawal, nausea, dizziness, and agitation.
- Only partial reversal of midazolam-induced ventilatory depression.

FOSPHENYTOIN

Indication: Seizure prophylaxis, treatment of seizures (see Phenytoin).

Dosage:

- It is a prodrug; active metabolite is phenytoin.
- 1.5 mg fosphenytoin is equivalent to 1 mg phenytoin and is referred to as 1 mg phenytoin equivalent (PE).
- Dilute fosphenytoin in 5% dextrose or 0.9% saline solution for injection to a concentration ranging from 1.5 to 25 mg PE/mL.
- The loading dose of fosphenytoin is 10 to 20 mg PE/kg given IV.
- Maximum rate, 150 mg PE/min.

Effect: Anticonvulsant.

Comments:

- Intravenous bolus may cause bradycardia, hypotension, respiratory arrest, cardiac arrest, or CNS depression.
- Determination of unbound phenytoin levels may be helpful in patients with renal failure or hypoalbuminemia 2 hours after infusion has been completed.
- Multiple drug interactions that may change effective concentration of phenytoin.

FUROSEMIDE (LASIX)

Indications: Edema, hypertension, intracranial hypertension, renal failure, and hypercalcemia.

Dosage: 2 to 40 mg IV (initial dose, dosage individualized).

Effect: Increases excretion of Na^+ , Cl^- , K^+ , PO_4^{3-} , Ca^{2+} , and H_2O by inhibiting reabsorption in loop of Henle.

Comments: May cause electrolyte imbalance, dehydration, transient hypotension, deafness, hyperglycemia, or hyperuricemia. Sulfa-allergic patients may exhibit hypersensitivity to furosemide.

GLUCAGON

Indications:

- Duodenal or choledochal relaxation.
- Refractory β -adrenergic blocker toxicity.

Dosage:

- GI effects, 0.25 to 0.5 mg IV q20min prn.
- β -Blocker toxicity, 5 mg IV bolus, with 1 to 10 mg/h titrated to patient response.

Effect: Catecholamine release. Positive inotrope and chronotrope.

Comments:

- May cause anaphylaxis, nausea, vomiting, hyperglycemia, or positive inotropic and chronotropic effects.
- High doses potentiate oral anticoagulants.
- Use with caution in the presence of insulinoma or pheochromocytoma.

GLYCOPYRROLATE

Indications: Decrease GI motility, antisialagogue. Bradycardia.

Dosage: 0.1 to 0.2 mg IV/IM/SC

Effect: Competitive blockade of acetylcholine at muscarinic receptors.

Comments: Longer duration, possibly less chronotropic effect than atropine. Does not cross blood-brain barrier or placenta.

HALOPERIDOL (HALDOL)

Indications: Psychosis, delirium, agitation, and postoperative nausea and vomiting.

Dosage: 0.5 to 10 mg IM/IV prn (dosage individualized); antiemetic, 1 mg IV.

Effect: Antipsychotic effects due to dopamine (D_2) receptor antagonism. CNS depression.

Comments:

- May cause mild α -adrenergic antagonism.
- Can prolong QT interval and produce ventricular arrhythmias, notably torsade de pointes, and lower seizure threshold.
- May precipitate neuroleptic malignant syndrome.
- Contraindicated in Parkinson disease.

HEPARIN—UNFRACTIONATED

Indications: Anticoagulation for:

- Thrombosis, thromboembolism.
- Cardiopulmonary bypass.
- Disseminated intravascular coagulation.
- Thromboembolism prophylaxis.

Dosage:

- a. Thrombosis, LOAD: 50 to 150 units/kg IV; MAINT: 15 to 25 units/kg/h IV; titrate dosage with aPTT.
 - b. CPBP, LOAD: 300 units/kg IV; MAINT: 100 units/kg/h IV; titrate with ACT.
 - c. DIC, LOAD: 50 to 100 units/kg IV; MAINT: 15 to 25 units/kg/h IV; titrate with coagulation tests.
 - d. DVT prophylaxis, 5,000 units q8–12h SC.
- Effect:** Potentiates action of antithrombin III; blocks conversion of prothrombin and activation of other coagulation factors.

Comments:

- a. May cause thrombocytopenia, allergic reactions.
- b. Half-life increased in renal failure and decreased in thromboembolism and liver disease.
- c. Does not cross the placenta.
- d. Reversed by protamine.
- e. Spinal and epidural hematomas have been associated with neuraxial anesthesia (single-shot, or catheter placement or removal) and lumbar punctures in patients on heparin infusions.

HYDRALAZINE

Indication: Hypertension.

Dosage: 2.5 to 5 mg IV. Repeat as needed up to total dose of 20 mg.

Effect: Reduces arterial smooth muscle tone; diastolic more effected than systolic.

Comments: May cause reflex tachycardia, systemic lupus erythematosus syndrome. Increases coronary, splanchnic, cerebral, and renal blood flows.

HYDROCORTISONE (SOLU-CORTEF)**Indications:**

- a. Adrenal insufficiency.
- b. Inflammation and allergic reaction.
- c. Cerebral edema from CNS tumors.
- d. Asthma.

Dosage: 10 to 100 mg IV q8h. Physiologic replacement: IV: 0.25 to 0.35 mg/kg/d; PO: 0.5 to 0.75 mg/kg/d.

Effect:

- a. Anti-inflammatory.
- b. Mineralocorticoid effect.
- c. Stimulates gluconeogenesis.
- d. Inhibits peripheral protein synthesis.
- e. Has membrane stabilizing effect.

Comments:

- a. May cause adrenocortical insufficiency (addisonian crisis) with abrupt withdrawal.
- b. Delayed wound healing.
- c. CNS disturbances, osteoporosis, or electrolyte disturbances.

INDIGO CARMINE

Indications: Evaluation of urine output. Localization of ureteral orifices during cystoscopy.

Dosage: 40 mg IV slowly (5 mL of 0.8% solution).

Effect: Rapid glomerular filtration produces blue urine.

Comments: Hypertension from α -adrenergic stimulation with rapid administration, lasts 15 to 30 minutes after IV dose. Dye color may interfere with pulse oximetry.

ISOPROTERENOL

Indications: Heart failure; bradycardia.

Dosage: 2 $\mu\text{g}/\text{min}$ titrated up to 20 $\mu\text{g}/\text{min}$.

Effect: β -Adrenergic agonist; positive chronotrope and inotrope.

Comments: May cause dysrhythmias, myocardial ischemia, hypertension, or CNS excitation.

KETOROLAC (TORADOL)

Indications: Nonsteroidal anti-inflammatory drug (NSAID) for moderate pain. Useful adjunct for severe pain when used with parenteral or epidural opioids.

Dosage: 30 to 60 mg, then 15 to 30 mg q6h.

Effect: Limits prostaglandin synthesis by cyclooxygenase inhibition.

Comments:

- Adverse effects are similar to those with other NSAIDs: peptic ulceration, bleeding, decreased renal blood flow.
- Duration of treatment not to exceed 5 days.
- Caution when used in the elderly or in patients with preexisting renal dysfunction or significant hypovolemia.

LABETALOL

Indications: Hypertension, controlled hypotension.

Dosage: 5 to 10 mg IV increments at 5-minute intervals, to 40 to 80 mg/dose.

Infusion: titrate to desired response, 10 to 180 mg/h.

Effect: Selective α_1 -adrenergic blockade with nonselective β -adrenergic blockade. Ratio of α/β -blockade = 1:7.

Comments: May cause bradycardia, AV conduction delays, and postural hypotension. Crosses the placenta.

LEVETIRACETAM (KEPPRA)

Indication: Seizure prophylaxis; treatment of seizures.

Dosage: 500 to 1,000 mg IV.

Effect: Suppression of seizure activity.

Comments: Adjustment for renal insufficiency.

LIDOCAINE (XYLOCAINE)

Indications:

- Ventricular dysrhythmias.
- Cough suppression.
- Local anesthesia.

Dosage:

- Dysrhythmias, 1 mg/kg IV $\times$ 2 (second dose 20 to 30 minutes after first dose) followed by 15 to 50 $\mu\text{g}/\text{kg}/\text{min}$ IV (1 to 4 mg/min).
- Cough 1 mg/kg IV.

Effect: Decreases conductance of sodium channels. Antiarrhythmic effect, sedation, neural blockade.

Comments:

- May cause dizziness, seizures, disorientation, heart block (with myocardial conduction defect), or hypotension.
- Crosses the placenta.
- Caution in patients with Wolff-Parkinson-White syndrome.

LOW MOLECULAR WEIGHT HEPARIN

Please see individual entries for dalteparin (Fragmin) and enoxaparin (Lovenox).

MAGNESIUM SULFATE

Indications:

- Preeclampsia/eclampsia.
- Hypomagnesemia.
- Polymorphic ventricular tachycardia (torsade de pointes).

Dosage:

- OB, 1 to 8 g IV, then 1 to 4 g/h.
- Hypomagnesemia, 1 to 2 g q6–8h, prn
- VT, 1 to 2 g in 10 mL D5W over 1 to 2 minutes; 5 to 10 g may be administered for refractory arrhythmias.

Effect: Treatment and prevention of hypomagnesemia; prevents and treats seizures or hyperreflexia associated with preeclampsia/eclampsia.

Comments:

- Potentiates neuromuscular blockade.
- Potentiates CNS effects of anesthetics, hypnotics, and opioids.
- Toxicity occurs with serum concentration greater than or equal to 10 mEq/L.
- May alter cardiac conduction in digitalized patients. Avoid in patients with heart block.
- Caution in patients with renal failure.

MANNITOL

Indications:

- Increased intracranial pressure.
- Oliguria or anuria associated with acute renal injury.

Dosage:

- ICP, 0.25 to 1.0 g/kg IV as 20% solution over 30 to 60 minutes (in acute situation, can give bolus of 1.25 to 25.0 g over 5 to 10 minutes).
- Renal, 0.2 g/kg test dose over 3 to 5 minutes, then 50 to 100 g IV over 30 minutes if adequate response.

Effect: Increases serum osmolality, which reduces cerebral edema and lowers intracranial and intraocular pressure; also causes osmotic diuresis and transient expansion of intravascular volume.

Comments:

- Rapid administration may cause vasodilation and hypotension.
- May worsen or cause pulmonary edema, intracranial hemorrhage, systemic hypertension, or rebound intracranial hypertension.

METHYLENE BLUE

Indications:

- Surgical marker for genitourinary surgery.
- Methemoglobinemia.
- Vasoplegic syndrome.

Dosage:

- GU, 100 mg (10 mL of 1% solution) IV.
- Methemoglobinemia, 1 to 2 mg/kg IV of 1% solution over 10 minutes; repeat q1h, prn.
- Vasoplegia, 2 mg/kg IV.

Effect: Low dose promotes conversion of methemoglobin to hemoglobin. High dose promotes conversion of hemoglobin to methemoglobin.

Comments:

- a. May cause RBC destruction (prolonged use), hypertension, bladder irritation, nausea, diaphoresis.
- b. May inhibit nitrate-induced coronary artery relaxation.
- c. Interferes with pulse oximetry for 1 to 2 minutes.
- d. Can cause hemolysis in patients with glucose-6-phosphate dehydrogenase deficiency.

METHYLERGONOVINE (METHERGINE)

Indication: Postpartum hemorrhage due to uterine atony.

Dosage:

- a. IV (*emergency only*, after delivery of placenta): 0.2 mg in 5 mL of NS, dose over greater than or equal to 1 minute.
- b. IM: 0.2 mg q2–4h, prn (<5 doses).

Comments: See Ergonovine. Caution in patients with hypertension although hypertensive response less marked than with ergonovine.

METHYLPREDNISOLONE (SOLU-MEDROL)

Indications: See Hydrocortisone. Spinal cord injury; status asthmaticus.

Dosage:

- a. 40 to 60 mg IV q6h. Higher doses in transplant patients.
- b. Status asthmaticus, 2 mg/kg; then 0.5 to 1 mg/kg q6h.
- c. Spinal cord injury, 30 mg/kg IV over 15 minutes; after 45 minutes begin 5.4 mg/kg/h $\times$ 23 or 47 hours.

Effect: See Hydrocortisone; has five times the glucocorticoid potency of hydrocortisone with almost no mineralocorticoid activity.

Comments: See Hydrocortisone.

METOCLOPRAMIDE (REGLAN)

Indications: Gastroesophageal reflux, diabetic gastroparesis, pulmonary aspiration prophylaxis, and antiemetic.

Dosage: 10 mg IV q6–8h.

Effect:

- a. Facilitates gastric emptying by increasing gastric motility; relaxes pyloric sphincter and increases peristalsis in the duodenum and jejunum.
- b. Increases resting tone of the lower esophageal sphincter.
- c. Weak antiemetic effects appear secondary to antagonism of central and peripheral dopamine receptors.
- d. Case causes neuroleptic malignant syndrome.

Comments:

- a. Avoid in patients with GI obstruction, pheochromocytoma, or Parkinson disease.
- b. Extrapyramidal reactions occur in 0.2% to 1% of patients.

METOPROLOL (LOPRESSOR)

Indications: Hypertension, angina pectoris, dysrhythmia, hypertrophic cardiomyopathy, MI, and pheochromocytoma.

Dosage: 2.5 to 5 mg IV q2min, prn, up to 15 mg.

Effect: β_1 -Adrenergic blockade (β_2 -adrenergic antagonism at high doses).

Comments:

- a. May cause symptomatic bradycardia.
- b. Can increase risk of heart block.

MILRINONE

Indication: Myocardial depressing requiring inotropy.

Dosage: 50 $\mu\text{g}/\text{kg}$ IV over 10 minutes, then titrate 0.375 to 0.75 $\mu\text{g}/\text{kg}/\text{min}$ to effect.

Effect: Phosphodiesterase inhibition causing positive inotropy and vasodilation.

Comments:

- May increase ventricular ectopy.
- Possible worsening of outflow tract obstruction in HOCM.
- Hypotension is common.

NALOXONE (NARCAN)

Indication: Reversal of systemic opioid effects.

Dosage: Adult: 0.04- to 0.4-mg doses IV, titrated q2–3min. Pediatric: 1 to 10 $\mu\text{g}/\text{kg}$ IV (in increments) q2–3min (up to 0.4 mg).

Effect: Antagonizes effects of opioids by competitive inhibition.

Comments:

- May cause hypertension, dysrhythmias, rare pulmonary edema, and delirium usually if given in high doses.
- Reversal of analgesia.
- Withdrawal syndrome in opioid-dependent patients.
- Renarcotization may occur because antagonist has shorter duration than opiates.

NITROGLYCERIN

Indications:

- Angina, myocardial ischemia, or infarction.
- Hypertension.
- Congestive heart failure.
- Controlled hypotension.
- Esophageal spasm.

Dosage:

- Initial IV infusion at 50 $\mu\text{g}/\text{min}$, then titrate to effect.
- SL: 0.15 to 0.6 mg/dose.
- Topical: 2% ointment, 0.5 to 2.5 in q6–8h.

Effect:

- Produces smooth muscle relaxation by enzymatic release of NO, causing systemic, coronary, and pulmonary vasodilatation (veins more than arteries).
- Bronchodilation, biliary, GI, and genitourinary tract relaxation.

Comments:

- May cause reflex tachycardia, hypotension, or headache.
- Tolerance with chronic use may be avoided with a 10- to 12-hour nitrate-free period.
- May be adsorbed by plastic in IV tubing.

NITROPRUSSIDE (NIPRIDE)

Indications: Hypertension, controlled hypotension, and congestive heart failure.

Dosage: IV infusion initially at 0.1 $\mu\text{g}/\text{kg}/\text{min}$, then titrated to patient response to maximum 10 $\mu\text{g}/\text{kg}/\text{min}$.

Effect: Direct NO donor causing smooth muscle relaxation in both arterioles and veins.

Comments:

- May cause excessive hypotension if not titrated slowly.
- Reflex tachycardia.

- c. Accumulation of cyanide with liver dysfunction; thiocyanate with kidney dysfunction. Cyanide/thiocyanate buildup with prolonged infusion.
- d. Avoid with Leber hereditary optic atrophy, hypothyroidism, or vitamin B₁₂ deficiency.
- e. Solution and powder are light sensitive and must be wrapped in opaque material.

NOREPINEPHRINE (LEVOPHED)

Indication: Hypotension, myocardial depression.

Dosage:

- a. 1 to 30 $\mu\text{g}/\text{min}$ IV, titrated to desired effect.
- b. Administered through central venous catheter.

Effect: Both α - and β -adrenergic activity, with α -adrenergic activity predominating.

Comments:

- a. May cause tachycardia and dysrhythmias in some patients.
- b. Increased uterine contractility.
- c. Constricted microcirculation.

OCTREOTIDE (SANDOSTATIN)

Indications:

- a. Upper GI tract bleeding and acute variceal hemorrhage.
- b. Treatment of symptomatic carcinoid.

Dosage: 25–50 μg IV bolus followed by continuous IV infusion of 25 to 50 $\mu\text{g}/\text{h}$.

Effect: Somatostatin analogue that suppresses release of serotonin, gastrin, vasoactive intestinal peptide, insulin, glucagon, and secretin.

Comments: May cause nausea, decreased GI motility, and transient hyperglycemia.

ONDANSETRON (ZOFRAN)

Indications: Prophylaxis and treatment of perioperative nausea and vomiting.

Dosage: Adult: 4 mg IV over greater than 30 seconds or 8 mg PO. Pediatric: 4 mg PO.

Effect: Selective 5-HT₃ receptor antagonist.

Comments: Used in much higher doses for chemotherapy-induced nausea. Mild side effects include headache and reversible transaminase elevation.

OXYTOCIN (PITOCIN)

Indications: Postpartum hemorrhage, uterine atony, and augmentation of labor.

Dosage:

- a. Hemorrhage, 10 units IM or 10 to 40 units in 1,000 mL of crystalloid-infused IV at rate necessary to control atony (e.g., 0.02 to 0.04 units/min).
- b. Labor induction: 0.0005 to 0.002 units/min, increasing until contraction pattern established or maximum dose of 20 milliunits/min reached.

Effect: Reduces postpartum blood loss by contraction of uterine smooth muscle. Renal, coronary, and cerebral vasodilation.

Comments:

- a. May cause uterine tetany and rupture, fetal distress, or anaphylaxis.
- b. Intravenous bolus can cause hypotension, tachycardia, and dysrhythmia.

PHENOBARBITAL

Indication: Seizure suppression.

Dosage: 10 to 20 mg/kg IV, additional 5 mg/kg doses q15–30min for control of status epilepticus, then 3 to 5 mg/kg/d PO or IV in divided doses.

Comments:

- a. May cause hypotension.
- b. Multiple drug interactions through induction of hepatic enzyme systems.
- c. Therapeutic anticonvulsant concentration 15 to 40 $\mu\text{g/mL}$ at trough (just before next dose).

PHENOXYBENZAMINE

Indication: Preoperative preparation for pheochromocytoma resection.

Dosage: 10 to 40 mg/d PO (start at 10 mg/d and increase dosage by 10 mg/d every 4 days prn).

Effect: Nonselective and noncompetitive α -adrenergic antagonist.

Comments: May cause orthostatic hypotension (which may be refractory to norepinephrine) and reflex tachycardia.

PHENYLEPHRINE (NEOSYNEPRINE)

Indication: Hypotension.

Dosage: 10 $\mu\text{g/min}$ IV initially, then titrated to response; IV bolus 40 to 100 $\mu\text{g/dose}$. Customary mix: 10 to 30 mg in 250 mL of D5W or NS.

Effect: α -Adrenergic agonist.

Clearance: Hepatic metabolism; renal elimination.

Comments: May cause hypertension, reflex bradycardia, microcirculatory constriction, uterine contraction, or uterine vasoconstriction.

PHENYTOIN (DILANTIN)

Indications: Seizure prophylaxis, treatment of seizures.

Dosage: 10 to 15 mg/kg IV at less than 50 mg/min (up to 1,000 mg cautiously, with ECG monitoring); for neurosurgical prophylaxis, then 100 to 200 mg IV q4h (at <50 mg/min).

Effect:

- a. Anticonvulsant effect via membrane stabilization.
- b. Antidysrhythmic effect similar to those of quinidine or procainamide.

Comments:

- a. Intravenous bolus may cause bradycardia, hypotension, respiratory arrest, cardiac arrest, or CNS depression.
- b. Nystagmus, diplopia, ataxia, drowsiness, gingival hyperplasia, GI upset, hyperglycemia, or hepatic microsomal enzyme induction.
- c. Crosses the placenta.
- d. Significant interpatient variation in dose needed to achieve therapeutic concentration of 7.5 to 20.0 $\mu\text{g/mL}$.
- e. Determination of unbound phenytoin levels may be helpful in patients with renal failure or hypoalbuminemia.

PHOSPHORUS (SODIUM PHOSPHATE)**Indications:**

- a. Treatment and prevention of hypophosphatemia.

Dosage: 0.15 to 0.25 mmol/kg IV over 6 to 12 hours.

Effect: Electrolyte replacement.

Comments:

- a. Infuse doses of IV phosphate over a 4- to 6-hour period since risks of rapid IV infusion include hypocalcemia, hypotension, muscular irritability, calcium deposition, renal function deterioration, and hyperkalemia.
- b. Use with caution in patients with cardiac disease and renal insufficiency.

PHYSOSTIGMINE (ANTILIRIUM)

Indications: Postoperative delirium, tricyclic antidepressant overdose, and reversal of CNS effects of anticholinergic drugs.

Dosage: 0.5 to 2.0 mg IV q15min prn.

Effect: Central and peripheral cholinergic effects; inhibits cholinesterase.

Comments: Rarely may cause bradycardia, tremor, convulsions, hallucinations, CNS depression, mild ganglionic blockade, or cholinergic crisis.

POTASSIUM (KCL) (SEE APPENDIX I)**PROCHLORPERAZINE (COMPazine)**

Indications: Nausea and vomiting.

Dosage: 5 to 10 mg IV (≤ 40 mg/d); 5 to 10 mg IM q2–4h prn; 25 mg PR q12h prn.

Effect: Central dopamine (D_2) antagonist with neuroleptic and antiemetic effects with antimuscarinic and antihistaminic (H_1) actions.

Comments: May cause hypotension (especially when given IV), extrapyramidal reactions, neuroleptic malignant syndrome, leukopenia, and cholestatic jaundice.

PROMETHAZINE (PHENERGAN)

Indications: Nausea and vomiting.

Dosage: Adult: 12.5 to 25 mg IV q4–6h prn. Pediatric: 0.1 to 1 mg/kg IV, IM, PO, PR q4–6h prn.

Effect: Antagonist of H_1 and muscarinic receptors.

Comments: Lower doses (3 to 6 mg) may be effective in immediate postoperative period for nausea and vomiting. May cause mild hypotension or mild anticholinergic effects.

PROPRANOLOL (INDERAL)

Indications:

- a. Hypertension, atrial and ventricular dysrhythmias, myocardial ischemia, or infarction.
- b. Junctional rhythm.
- c. Hypertrophic cardiomyopathy.
- d. Thyrotoxicosis.
- e. Migraine headache.

Dosage: 0.5 to 1 mg IV, then titrate to effect; 0.5 mg IV for junctional rhythm.

Effect: Nonspecific β -adrenergic blockade.

Comments: May cause bradycardia, AV dissociation.

PROSTAGLANDIN E_1 (ALPROSTADIL) (SEE APPENDIX I)**PROTAMINE**

Indication: Reversal of the effects of heparin.

Dosage: 1 mg/100 units of heparin activity IV at less than or equal to 5 mg/min.

Effect: Polybasic compound forms complex with polyacidic heparin.

Comments:

- a. May cause myocardial depression and peripheral vasodilation with sudden hypotension or bradycardia.
- b. May cause severe pulmonary hypertension, particularly in the setting of cardiopulmonary bypass.

- c. Concern for allergic reaction/anaphylaxis for patients taking NPH insulin.
- d. Transient reversal of heparin may be followed by rebound heparinization.
- e. Monitor response with a PTT or ACT.

SCOPOLAMINE

Indications: Sedation, nausea/vomiting, motion sickness, amnesia.

Dosage: 0.3 to 0.6 mg IV/IM, 1.5-mg transdermal patch.

Effect: Peripheral and central cholinergic (muscarinic) antagonism.

Comments:

- a. Excessive CNS depression can be reversed by physostigmine.
- b. May cause excitement, delirium, transient tachycardia, hyperthermia, or urinary retention.
- c. Care when handling patch because contact with eyes may cause long-lasting mydriasis and cycloplegia.
- d. Crosses the blood-brain barrier and placenta.

VASOPRESSIN (ANTIDIURETIC HORMONE, PITRESSIN)

Indications:

- a. Diabetes insipidus.
- b. Upper GI hemorrhage.
- c. Pulseless ventricular tachycardia or ventricular fibrillation.
- d. Shock refractory to fluid and vasopressor therapy.

Dosage:

- a. DI, 5 to 10 units IM/SC q8–12h.
- b. GI, 0.1 to 0.4 units/min IV infusion.
- c. ACLS, 40 units IV bolus (single dose).
- d. Shock, 0.04 units/min IV infusion titrated as required.

Effect:

- a. Increases urine osmolality and decreases urine volume.
- b. Smooth muscle constriction; vasoconstriction of splanchnic, coronary, muscular, and cutaneous vasculature.

Comments:

- a. May cause oliguria, water intoxication, pulmonary edema; hypertension, arrhythmias, myocardial ischemia; abdominal cramps (from increased peristalsis); contraction of gallbladder, urinary bladder, or uterus; vertigo or nausea.
- b. Patients with coronary artery disease are often treated with concurrent nitroglycerin.
- c. Useful in shock states as effect of drug is not pH dependent.

VERAPAMIL

Indications: Supraventricular tachycardia, atrial fibrillation or flutter, Wolff-Parkinson-White syndrome.

Dosage: 2.5 to 10 mg IV over ≥ 2 minutes, repeat once if no response in 30 minutes.

Effect: Blocks slow calcium channels in the heart. Prolongs PR interval. Negative inotrope and chronotrope; systemic and coronary vasodilator.

Comments:

- a. May cause severe bradycardia, AV block (especially with concomitant β -adrenergic blockade), excessive hypotension, or congestive heart failure.
- b. May increase ventricular response to atrial fibrillation or flutter in patients with accessory tracts.
- c. Active metabolite has 20% of the antihypertensive effect of the parent compound.

VITAMIN K

Indications: Deficiency of vitamin K–dependent clotting factors, reversal of warfarin anticoagulation.

Dosage: 2.5 to 10 mg IM/SC/PO or 1 to 10 mg IV at less than or equal to 1 mg/min (with caution). If prothrombin time is not improved 8 hours after initial dose, repeat prn.

Effect: Increases levels of clotting factors II, VII, IX, and X by regeneration of vitamin K–dependent epoxide reductase blocked by warfarin.

Comments:

- a. Excessive doses can make patient refractory to further oral anticoagulation.
- b. Rapid IV bolus can cause profound hypotension, fever, diaphoresis, bronchospasm, anaphylaxis, and pain at injection site.

WARFARIN (COUMADIN)

Indication: Anticoagulation.

Dosage: 5 mg PO $\times$ 2 to 5 days, then 2 to 10 mg PO, titrated to INR (international normalized ratio should be 2 to 3, based on indication).

Effect: Inhibits vitamin K epoxide reductase effectively lowering vitamin K levels to inhibit synthesis of factors II, VII, IX, and X, and proteins C, S, and Z.

Comments:

- a. May be potentiated by ethanol, antibiotics, dextran, thyroxine, diazoxide, ethacrynic acid, glucagon, methyldopa, monoamine oxidase inhibitors, phenytoin, prolonged use of narcotics, quinidine, sulfonamides, congestive heart failure, hyperthermia, liver disease, and malabsorption.
- b. May be antagonized by barbiturates, chlorthalidopoxide, haloperidol, oral contraceptives, hypothyroidism, and hyperlipidemia.

Common Intravenous Antibiotics

The antibiotics listed in this appendix are those usually given in the perioperative period. Doses marked by (+) are those that are recommended by the MGH Infectious Disease service for standard surgical procedure antibiotic prophylaxis. These should be administered within 1 hour of incision unless indicated.

Drug	Dose: ≤80 kg	Dose: >80 kg	Dosing Interval (h) ^a	Comments
Ampicillin– sulbactam (Unasyn) (+)	3 g	3 g	q2h × 3 doses, then q6h	Not effective against <i>Pseudomonas</i> spp.
Aztreonam (+)	2g	2 g	q4h	
Cefoxitin	2 g	2 g	q2h	
Cefazolin (Ancef) (+)	2 g	2g 3 g if >120 kg	q4h	5%–10% of penicillin- allergic patients will react to cephalosporins.
Ceftazidime	2 g	2 g	q4h	Preferred for <i>Pseudomonas aeruginosa</i> infections and neutropenic patients with fever.
Ceftriaxone (+)	2 g	2 g		Preferred for empiric coverage for bacterial meningitis.
Cefuroxime (+)	1.5 g	1.5 g	q4h	Preferred for community- acquired pneumonia.
Ciprofloxacin (+)	400 g	400 g	q6h	Administer within 2 h of incision
Clindamycin (+)	900 g	900 g	q6h	Associated with <i>Clostridium difficile</i> colitis. May prolong neuromuscular blockade.
Doxycycline	100 g	100 g		
Fluconazole	200–400 mg	200–400 mg	q24h	
Gentamicin (+)	5 mg/kg	5 mg/kg	q24	Use adjusted body weight for high BMI. Initial dose unchanged for renal failure. Renal toxicity and ototoxicity. Precipitates with heparin. May cause/prolong neuromuscular blockade.

(continued)

Drug	Dose: ≤80 kg	Dose: >80 kg	Dosing Interval (h) ^a	Comments
Imipenem– cilastatin	500 mg	500 mg	q2h × 3 doses, then q6h	Preferred for multiple- drug resistant. Gram-negative bacterial infections. Renal adjustment to prevent seizures.
Levofloxacin	500 mg	500 mg	qd	Treatment of VRE. >7–10 d use may cause myelosuppression MAO inhibitor: Do not give meperidine.
Linezolid	600 mg	600 mg	q12h	
Meropenem	0.5–1 g	0.5–1 g	q2h × 3 doses, then q6h	Adjust for renal insufficiency.
Metronidazole (Flagyl) (+)	500 mg	500 mg	q12 h	Preferred for antistaphylococcal coverage.
Nafcillin	1–2	1–2 g	q2h × 3 doses, then q6h	
Penicillin G	500,000– 2,000,000 U	500,000– 2,000,000 U	q4h	Hypersensitivity is common. May induce seizures at high doses and induce interstitial nephritis.
Piperacillin– tazobactam (Zosyn)	3.375 g	3.375 g	q2h × 3 doses, then q6h	Tazobactam expands activity of piperacillin to include β-lactamase- producing strains of <i>Staphylococcus aureus</i> , <i>Haemophilus influenzae</i> , <i>Enterobacteriaceae</i> , <i>Pseudomonas</i> , <i>Klebsiella</i> , <i>Citrobacter</i> , <i>Serratia</i> , <i>Bacteroides</i> , and other gram- negative anaerobes.
Vancomycin (+)	1 g over 30–60 min	2 g over 30–60 min	q24h	Preferred for MRSA patients. Increase dose interval in renal disease. Histamine release (“red man syndrome”). May precipitate with other medications.

^aConsider more frequent dosing during procedures with rapid blood loss.

Index

Note: Page numbers followed by “f” indicate figure; those followed by “t” indicate table.

A

AAA. *See* Abdominal aortic aneurysm

Abciximab (Reopro), 590

administration guidelines, 673

indications, 673

Abdomen

gunshot wounds, 564

physical examination, 6

Abdominal aortic aneurysm (AAA),
380–381

Abdominal aortic repair

emergency in

hemodynamically stable patients,
380–381

hemodynamically unstable patients,
380–381

EVAR, 375–377, 377f

open abdominal aortic surgery,
378–379

Abdominal surgery

anesthesia management

ERAS, 334

fluid losses, 332

fluid replacement, 331

induction, 331

intraoperative problems, 333–334

maintenance, 331–334

muscle relaxation, 332–333

NG tubes, 333

nitrous oxide, use of, 333

protocol-based strategy, 331

anesthetic considerations

after brain death, recovery of organs

for transplantation, 343–345

biliary tract procedures, 338

esophageal surgery, 336

gastric surgery, 336

hepatic surgery, 337

heterotopic pancreatic

transplantation, 343

intestinal and peritoneal surgery,
336–337

intraoperative radiation therapy,
338–339

laparoscopic surgery, 334–336

orthotopic liver transplantation,
342–343

pancreatic surgery, 338

splenectomy, 338

surgery for obese, 339–342

anesthetic techniques

GA, 329

regional anesthetic techniques,
329–331

preanesthetic considerations

anticipated postoperative course,
329

emergency abdominal procedures,
329

hematologic derangements, 329

hypovolemia, etiology of, 328–329

length of surgery, 329

metabolic derangements, 329

preoperative fluid status, 328

ABG. *See* Arterial blood gas

Abiomed BVS 5000, 416

ABO hemolytic disease, 489–490

Abortion, 539

Acceleromyography, 187

Acetaminophen, 608, 610, 643

Acetazolamide, 443

Acetylcholine (ACh), 177

Acetylcholine receptor (AChR), 177

Acetylcholinesterase (AChE), 177

ACh. *See* Acetylcholine

AChE. *See* Acetylcholinesterase

Achondroplasia, 194

AChR. *See* Acetylcholine receptor

Acid–base management, 400

ACM. *See* Alcoholic cardiomyopathy

Acromegaly, airways, 194

ACS. *See* Acute coronary syndrome

ACT. *See* Activated clotting time

ACTH. *See* Adrenocorticotrophic
hormone

Activated clotting time (ACT), 373–396,
579

Activated partial thromboplastin time
(aPTT), 579

Acute airway obstruction, 375

Acute coronary syndrome (ACS), 17–18

Acute interstitial nephritis, 53–54

Acute kidney injury

classification system, 49, 50t

diagnosis, 49, 51t

epidemiology, 49

etiology, 49

- Acute kidney injury (*Continued*)
 prevention, 49
 treatment
 CRRT, 51–52
 hemodialysis, 51
 medications, 49
- Acute pain
 pharmacologic treatment
 acetaminophen, 643
 definitions, 639
 ketamine, 643
 NSAIDs, 639–643, 640t
 opiates and opioids, 643–644
 treatment modalities
 acute pain management, 654–656
 continuous peripheral nerve blocks, 653–654
 neuraxial analgesia, 646–653
 patient-controlled analgesia, 648–649, 648t
- Acute tubular necrosis (ATN), 45, 49, 53
- Addison disease, 93
- Adductor canal block, 279–280
- Adenosine, 488
 comments, 677
 dosage, 677
 effect, 677
 hemodynamic control, perioperative, 325
 indications, 677
- Adrenal cortical disease
 glucocorticoid excess
 anesthetic considerations, 93
 clinical features, 93
 etiologies, 92–93
 pharmacology, 92, 92t
 physiology
 androgens, 92
 glucocorticoids, 91–92, 92t
 mineralocorticoids, 92, 92t
 primary hyperaldosteronism, 92
 (*see also* Conn syndrome)
- Adrenal cortical hypofunction
 anesthetic considerations, 94
 clinical features
 acute adrenal insufficiency, 93
 primary adrenal insufficiency, 93
 secondary adrenal insufficiency, 93
 etiologies, 93
 treatment, 93–94
- Adrenal medullary disease
 pheochromocytoma
 anesthetic considerations, 95–96
 clinical features, 94–95
 epidemiology, 94
 preoperative evaluation and preparation, 95
 physiology, 94
- Adrenergic(s)
 β -antagonists, 320, 321t, 322
 drug dosage calculations, 326
 induced hypotension, 325–326
 pharmacology
 α -agonists, 314, 317
 β -agonists, 317
 mixed agonists, 317–318
 nonadrenergic agents, 319–320
 receptors, perioperative hemodynamic control
 α_1 receptors, 312
 α_2 receptors, 312, 314
 β_1 receptors, 314
 β_2 receptors, 314
 β_3 receptors, 314
 dopaminergic receptors, 314
 receptor regulation, 314
 vasodilators, 322–325, 322t
- Adrenergic agonists, 425–426
- β -Adrenergic antagonists, 443
 esmolol, 320, 321t
 labetalol, 321t, 322
 metoprolol, 320, 321t
 propranolol, 320, 321t
- β -Adrenergic blockers, 602
- α -Adrenergic receptors, 312, 314
- β -Adrenergic receptors, 314
- Adrenocorticotrophic hormone (ACTH), 91
- Adult resuscitation
 advanced cardiac life support
 defibrillation, 625–626
 drugs, 626–629, 630f, 631
 intubation, 624–625
 IV access, 626
 pacing, 626
 basic life support
 airway and breathing, 624
 circulation, 623–624
 defibrillation, 624
 reassessment, 624
- Advanced cardiac life support, adult
 resuscitation
 defibrillation
 cardioversion, 626
 defibrillators, 625–626
 ventricular fibrillation, 625f
 drugs
 adenosine, 626–627
 algorithm, 630f
 amiodarone, 627
 atropine, 627
 β -Adrenergic-blocking drugs, 627–628
 calcium, 628
 CPR termination, 631
 diltiazem, 629

- do not resuscitate, 631
- dopamine, 628
- epinephrine, 628
- ibutilide, 628
- isoproterenol, 628
- lidocaine, 628
- magnesium, 628
- open-chest direct cardiac compression, 629
- oxygen, 628
- procainamide, 629
- sodium bicarbonate, 629
- vasopressin, 629
- verapamil, 629
- intubation, 624–625
- IV access, 626
- pacing, 626
- Adverse anesthesia event, guidelines
 - anesthesiologist, 121
 - objectives, 120, 120f
- Adverse reactions and side effects, anesthesia, 1–2
- Agitation, 612
- AI. *See* Aortic insufficiency
- Air cylinders, 122
- Airway(s)
 - anesthesia for otorhinolaryngologic procedures, 447
 - applied anatomy of, 192–193
 - awake intubation
 - complications, 209
 - indications, 208
 - techniques, 208–209
 - difficult, 205–206, 206f
 - emergency airway techniques
 - cricothyroidotomy, 207
 - percutaneous needle cricothyroidotomy, 207
 - rigid bronchoscopy, 207
 - tracheostomy, 207
 - endotracheal intubation of
 - alternative intubation techniques, 204–205
 - fiberoptic, 203–204
 - nasotracheal, 203
 - orotracheal, 200, 202–203
- ETT changes, 209
- evaluation
 - achondroplasia, 194
 - acromegaly, 194
 - arterial blood gas tensions, 196
 - arthritis, 193
 - body mass index, 193
 - burns/radiation/surgery, 194
 - cervical disk disease, 193
 - cervical spine mobility, 195
 - chest/cervical imaging, 195–196
 - congenital anomalies, 194
 - dwarfism, 194
 - head/neck, 194–195
 - history, 193–194
 - infections, 193
 - laryngoscopy, 195
 - Mallampati classification, 195, 195f
 - physical examination, 194–195
 - pulmonary function tests, 196
 - scleroderma, 194
 - tracheal tomograms, 196
 - trauma, 194
 - trisomy 21 patients, 194
 - tumors, 193
- laryngeal mask airway, thyroid surgery, 88
- LMA
 - adverse effects, 200
 - contraindications, 197
 - Fastrach, 198, 200, 200f
 - indications, 197
 - intubating, 198, 200
 - use of, 198, 198t, 199f
- management, 214, 339–340
- mask
 - complications, 197
 - indications, 196
 - techniques, 196–197
 - ventilation, 197, 218
- obesity, 84
- obstruction, 196
- patency, 197, 619
- patient evaluation, 3, 10
- protection, respiratory system, 69
- rapid sequence induction
 - equipment/technique, 207–208
 - indications, 207
- secretion clearance, 619
- sleep apnea, 4, 84
- Stiff joint disease, 84
- Albumin, 64
- Albuterol
 - comments, 677
 - dosage, 677
 - effect, 677
 - indications, 677
- Alcoholic cardiomyopathy (ACM), 68–69
- Aldosterone, 45
- Allergies
 - and drug reactions, anesthesia, 1–2
 - local anesthetics and, 2, 227
 - medication errors, 114
 - toxicity of, 227
 - transfusion reactions, 586
 - true reactions, 2
- α_1 -Acid glycoprotein, 64

- Alprostadil (PGE₁)
 - administration guidelines, 673
 - indications, 673
- Alteplase (Activase)
 - administration guidelines
 - acute myocardial infarction, 674
 - peripheral arterial, 674
 - pulmonary embolus, 674
 - venous and arterial thrombosis
 - catheter-directed thrombolysis, 674
 - venous thrombosis, 674
 - indications, 674
- American College of Cardiology and American Heart Association (ACC/AHA), 17
- American Society of Anesthesiologists (ASA), 350, 659
 - algorithm, diffi cult airway, 206f
- Amides, 222
- Aminocaproic acid (Amicar), 398
 - comments, 677
 - dosage, 677
 - effect, 677
 - indications, 677
- Aminoglycosides, 108
- Amiodarone (Cordarone), 296
 - comments, 678
 - dosage, 677
 - effect, 677
 - indications, 677
- Analgesia
 - labor and vaginal delivery, 530–533
 - pediatric pain evaluation, 512
 - postoperative, 359
- Anaphylactic and anaphylactoid reactions, 309
- Anaphylaxis, 309
- Anemia, 577
- Anesthesia
 - for abdominal surgery
 - after brain death, recovery of organs
 - for transplantation, 343–345
 - anesthetic techniques, 329–331
 - biliary tract procedures, 338
 - esophageal surgery, 336
 - gastric surgery, 336
 - hepatic surgery, 337
 - heterotopic pancreatic transplantation, 343
 - intestinal and peritoneal surgery, 336–337
 - intraoperative radiation therapy, 338–339
 - laparoscopic surgery, 334–336
 - management, 331–334
 - orthotopic liver transplantation, 341–343
 - pancreatic surgery, 338
 - preanesthetic considerations, 328–329
 - splenectomy, 338
 - surgery for obese, 339–341
 - assessment and plan, 10
 - for cardiac surgery
 - anesthetic management, 393–395
 - cardiac tamponade, 414
 - cardiac transplantation, 414–415
 - cardiopulmonary bypass (CBP), 388–389
 - constrictive pericarditis, 414
 - deep hypothermic circulatory arrest (DHCA), 415–416
 - extracorporeal membrane oxygenation (ECMO), 417–418
 - induction, 395–405, 398t, 401t, 404t
 - off-bypass CABG, 413–414
 - “off-site” cardiac procedures, 418–420
 - pediatric cardiac anesthesia, 406–409, 410t–412t, 413
 - postoperative care, 405–406
 - preoperative assessment, 389–393, 390t–393t
 - “redo” cardiac surgery, 414
 - ventricular assist devices (VAD), 416–417
 - chest radiography before, 7
 - documentation, 12–13
 - effects on kidney
 - direct effects, 54, 56
 - indirect effects, 54
 - electrocardiogram before, 7
 - general, 152
 - anesthetic plan, 211
 - emergence from, 218–220
 - induction of, 213–215, 214t
 - maintenance of, 215–218
 - monitoring, 213
 - postoperative visit after, 220, 220t
 - preoperative medications, 212–213
 - preoperative preparation, 211–213
 - primary goals, 211
 - secondary goals, 211
 - stages of, 214t
 - transport of, 220
 - for geriatric patients
 - anesthesia considerations, 469–471
 - central nervous system, 471–472
 - metabolic derangements, 473
 - orthopedic disorders, 472
 - pharmacologic changes associated with aging, 469
 - physiologic changes associated with aging, 468–469
 - visual impairment, 472

- gynecologic surgery, 540–541
- for head and neck surgery
 - ophthalmic surgery, 442–447, 444f
 - otorhinolaryngologic procedures, 447–451
 - procedures of neck, 451–454
- hematological studies before, 6–7
- history
 - allergies and drug reactions, 1–2
 - anesthetic records, 2–3
 - family history, 3
 - medications, 1
 - presenting illness, 1
 - social history and habits, 3
- informed consent, 11–12
- laboratory studies before, 6–8
- liver disease, 72–74
- neuraxial anesthesia, 231
- neurologic examination before, 6
- for neurosurgery
 - electrophysiologic monitoring, 427–428
 - intraoperative management, 429–433
 - pharmacology, 425–427, 425t
 - physiology, 422–424, 423f, 424f
 - preoperative considerations, 429
 - specific neurosurgical procedures, 433–439
 - spine and spinal cord, 440–441
- NPO status, 11t
- for oocyte retrieval, 541
- outside operating room
 - contrast media, 544–545
 - for CT, 545
 - for ECT, 553–555
 - for gastrointestinal procedures, 551–552
 - genitourinary procedures, 551–552
 - for MRI, 545–547
 - for neuroradiologic procedures, 547–551
 - for proton beam therapy and radiation therapy, 552–553
 - thoracic procedures, 551–552
 - for upper/lower endoscopy, 555
 - vascular procedures, 551–552
- physical examination for
 - abdomen, 6
 - extremities, 6
 - head and neck, 6
 - height and weight measurement, 6
 - lungs, 6
 - precordium, 6
 - vital signs, 5–6
- preexisting medical conditions
 - anticoagulation therapy, 8
 - asthma, 9
 - CAD, 8
 - diabetes mellitus, 9
 - HTN, 8
 - NSAID, 8–9
 - opioids, 9
 - pulmonary aspiration, risk of, 9–10
- premedication
 - antiemetic agents, 13, 14t
 - glycopyrrolate, 13
 - sedatives and analgesics, 13
- pulmonary function tests, 7
- review of systems
 - cardiovascular, 4
 - endocrine, 4–5
 - gastrointestinal, 5
 - hematology, 5
 - musculoskeletal, 5
 - obstetric/gynecologic, 5
 - respiratory, 4
- safety in
 - adverse anesthesia event, guidelines, 120–121, 120f
 - cognitive errors, 115–116, 115t–116t
 - communication errors, 117–118
 - crisis prepare, 119
 - documentation, 120
 - handoff errors, 116–117, 117f
 - human factors errors, 116
 - learn from close calls, 119
 - medication errors, 114
 - observations, verify, 119
 - preoperative plan prepare, 118
 - procedure errors, 114–115
 - quality assurance, 119–121
 - risks, 113
 - safety training, 119–120
 - situational awareness, 118
 - standards and guidelines, 119
 - stressors compensate, 118–119
 - teamwork enhances, 118
 - time and economic constraints, 119
 - transition errors, 116–117, 117f
- segmental level/surgery and, 231, 232f, 232t
- serum chemistry studies before, 7
- for spine surgery
 - airway, 455
 - blood loss, 456
 - disposition, 458
 - monitoring, 456
 - positioning prone, 455–456
 - postoperative pain management, 458–459
 - spinal cord injury, 455
 - spinal cord perfusion, 457–458, 458t
 - surgical procedures, delay, 14–15

Anesthesia (*Continued*)

- for thoracic surgery
 - bronchopleural fistula, 362–363
 - endoscopic procedures, 349–352
 - esophageal surgery, 363–365
 - intrapulmonary hemorrhage, 362
 - lung transplantation, 365–366
 - lung volume reduction surgery, 366
 - mediastinal operations, 352–353
 - monitoring, 349
 - preoperative evaluation, 348
 - preoperative preparation, 348–349
 - pulmonary resection, 353–359
 - tracheal resection and reconstruction, 359–362
 - for urologic surgery
 - cystectomy, 464
 - cystoscopy and ureteroscopy, 460
 - laser resection of prostate, 462
 - lithotripsy, 465–466
 - nephrectomy, 463–464
 - orchidopexy, 464
 - orchiectomy, 464
 - radical retropubic prostatectomy (RRP), 462–463
 - renal transplantation, 464–465
 - spinal cord injury, 466
 - TURB, 460
 - TURP, 460–462
 - urogenital plastic surgery
 - procedures, 464
 - for vascular surgery
 - abdominal aortic repair, 375–381
 - amputations, 385
 - carotid revascularization, 372–375
 - peripheral arterial surgery, 370–372
 - preoperative assessment and management, 368–370
 - thoracoabdominal aortic aneurysm repair, 381–385, 382f, 384t
- Anesthesia machines
- accessories for, 130
 - breathing systems
 - circle system, 124, 125f, 126
 - T-piece systems, 126–127, 127f
 - checkout recommendations for, 131–132
 - gas analysis
 - infrared analysis, 129–130
 - mass spectrometry, 129
 - oxygen analyzers, 130
 - gas delivery system, 123f
 - flow control valves and flowmeters, 124
 - gas outlet, 124
 - gas supplies, 122, 124
 - oxygen flush valve, 124
 - vaporizers, 124
 - next-generation, 131
 - safety features of, 128
 - scavenging systems, 129
 - ventilators, 127–128
- Anesthetic plan, 211
- Anesthetics
- inhalation, 425, 425t
 - inhalational, induction of, 213–214
 - local anesthetics, 513
- Anesthetists, 10–11
- infection control, 101
 - responsibilities, 101
- Angiography
- cerebral, 548–549
 - spinal, 548–549
- Angiotensin-converting enzyme (ACE)
- inhibitors, 45, 47, 391
- Angiotensin II, 45
- Ankle block, 284–285, 285f
- Antacids, 10
- Anterior pituitary gland, 96–97
- Anterior spinal artery syndrome, 383
- Antiarrhythmics, 391
- Antibiotic resistant bacteria, 110
- Antibiotics
- intravenous, 695–696
 - in operating room
 - aminoglycosides, 108
 - β -lactams, 107
 - clindamycin, 107
 - endocarditis, 106–107
 - fluoroquinolones, 108
 - indications for, 105
 - metronidazole, 108
 - prophylaxis principles, 105
 - SCIP, 105, 106t
 - surgical wounds, 107
 - vancomycin, 107–108
- Anticholinergics, 13, 41
- Anticholinesterases, 443
- Anticoagulation, 389
- neuraxial anesthesia, 253–254
- Anticoagulation therapy, 8
- Antiemetic agents, 13, 14t
- Antihistamines, 610
- Antimicrobial preservatives, 224
- Antioxidants, 224
- Antiplatelet drugs, 253
- Antiplatelet therapy, 368–369
- Anxiolytics, 21
- Aortic cross-clamping, 378–379, 384
- Aortic dissection, 396
- Aortic insufficiency (AI), 395
- Aortic regurgitation, 24
- Aortic stenosis

- anesthetic considerations, 24, 395
- cardiac pacing, 24
- etiology, 23
- ischemia treatment, 24
- nitrates and peripheral vasodilators, 24
- normal sinus rhythm, 24
- pathophysiology, 23
- symptoms, 23
- ventricle, 23
- Aortic unclamping, 379
- APCs. *See* Atrial premature contractions
- Apgar scores, 477, 477t
 - neonatal resuscitation, 632t, 635
- Apixaban, 591
- Apnea, 243
- Appendectomy, 336
- Apraclonidine, 443
- Aprepitant, 610
- Aprotinin, 342
- APTT. *See* activated partial thromboplastin time
- Aqueous vasopressin, 432
- Argatroban, 591
 - administration guidelines, 674
 - indications, 674
- Arginine vasopressin (AVP), 45
 - hemodynamic control, perioperative and, 319
- Arndt blocker, 356
- Arterial blood gas (ABG), 36–37, 348
- Arterial blood pressure, cardiovascular system
 - arterial cannulation, 135–136
 - automated noninvasive blood pressure, 134
 - invasive blood pressure, 134–135
 - mean, 134
- Arterial cannulation
 - complications, 136
 - considerations for placement, 136
 - locations, 135
 - procedure, 135–136, 135f
- Arterial carbon dioxide tension, 357
- Arterial catheter, 73, 373
- Arterial stents, 551
- Arteriovenous malformation (AVM), 434
- Artery of Adamkiewicz, 383
- Arthritis, airways, 193
- AS. *See* Aortic stenosis
- ASA. *See* American Society of Anesthesiologists
- Ascending nociceptive (pain) pathway, 152
- Aspiration, 302–303
- Aspirin, 21, 368–369, 590
- Asthma, 4, 9, 34
- Atenolol
 - comments, 678
 - dosage, 678
 - effect, 678
 - indications, 678
- Atherosclerotic aneurysm, 381
- ATN. *See* Acute tubular necrosis
- Atracurium, 67, 184
- Atrial fibrillation, 295
- Atrial flutter, 295
- Atrial natriuretic peptide, 45
- Atrial premature contractions (APCs), 294
- Atrial-to-left-femoral-artery bypass shunt, 384–385
- Atropine, 443
 - comments, 678
 - dosage, 678
 - effect, 678
 - indications, 678
- Atropine sulfate, 39
- Audible oxygen alarm, 128
- Autonomic dysreflexia, 466
- AVM. *See* Arteriovenous malformation
- AVP. *See* Arginine vasopressin
- Awake craniotomy, 436
- Axillary block, 257
- Axillofemoral bypass grafting, 372

B

- Backpain, spinal anesthesia, 239
- Backup atrial pacing, 414
- Bacteria
 - antibiotic resistant, 110
 - contamination of anesthesia machine, 103
 - mycobacterium tuberculosis, 110
 - sepsis, 588
- Bain circuit, 126
- Balloon
 - angioplasty and stenting, 370–371
 - test occlusion, 548
- Balloon-occluded retrograde transvenous obliteration (BRTO), 551–552
- BAMH. *See* Bilateral adrenal micronodular hyperplasia
- Baralyme, 126
- Barbiturates, 13, 58, 67, 425, 426
 - as inhalation anesthetic, 172–176, 172t
 - as intravenous (IV) anesthetics
 - action mode of, 164
 - adverse effects, 165
 - cardiovascular system, 164
 - CNS, 164
 - dosage and administration, 163t, 165
 - pharmacodynamics of, 164–165
 - pharmacokinetics of, 164
 - respiratory system, 164–165

- Bare metal coronary stents (BMS), 22
- Bariatric surgery, 340
- Basic life support (BLS)
- adult resuscitation, 623–624
 - pediatric resuscitation, 631–632
- Basilic vein, 141
- Benzodiazepines, 13, 41, 57–58, 67, 425, 614
- as inhalation anesthetic, 172–176, 172t
 - as intravenous (IV) anesthetics
 - action mode of, 165
 - adverse effects, 166
 - cardiovascular system, 166
 - CNS, 166
 - dosage and administration, 163t, 166
 - pharmacodynamics of, 166
 - pharmacokinetics of, 165
 - respiratory system, 166
- β_1 - and β_2 -adrenergic effects, 39
- β -blockers, 21
- β -lactams, 107
- Bicarbonate, sodium (NaHCO_3)
- comments, 678
 - dosage, 678
 - effect, 678
 - indications, 678
- Bilateral adrenal micronodular hyperplasia (BAMH), 93
- Bilevel positive airway pressure, 619
- Biliary drainage procedures, 338
- Biliary tract procedures, abdominal surgery, 338
- Bispectral index (BSI), 153–154
- Bivalirudin (Angiomax)
- administration guidelines, 675
 - indication, 675
- Bladder, spinal anesthesia, 235
- Bleeding
- abdominal surgery, 329
 - vascular surgery, 376
- β -Blocker therapy, 368
- Blood
- component therapy, 581–583
 - flow regulation, 44
 - pressure, 312
 - substitutes, 583
 - typing and cross-matching, 580–581
 - 580t
 - volumes (BVs), estimating, 578
- Blood–brain barrier, 431
- Blood pressure
- arterial cannulation, 135–136
 - invasive, 134–135
 - mean, 134
 - noninvasive, automated, 134
- Bloody tap
- epidural anesthesia, 248
 - spinal anesthesia, 239
- BLS. *See* Basic life support
- BMI. *See* Body mass index
- BMS. *See* Bare metal coronary stents
- Body mass index (BMI), 193, 339
- Bone cement embolism, 457
- Bowel, manipulation, 378
- BPD. *See* Bronchopulmonary dysplasia
- Brachial plexus, blockade, 264–265
- Bradycardia, 243
- Brain death, 345, 668
- Brainstem–auditory evoked potentials (BAEPs), 428
- Breathing systems
- circle system, 124, 125f, 126
 - T-piece systems, 126–127, 127f
- Bronchopulmonary dysplasia (BPD), 484
- Bronchoscopy
- aspiration, 303
 - flexible, 350
 - GA, 350
 - rigid, 350–351
- Bronchospasm
- histamine-releasing drugs, 302
 - reflex bronchiolar constriction, 301–302
 - treatment, 302
 - wheezing, 302
- Brooke formula, 573
- BRTO. *See* Balloon-occluded retrograde transvenous obliteration
- BSI. *See* Bispectral index
- Burn(s)
- anesthetic considerations, 574–575
 - chemical burns, 570
 - classification of, 570, 571f, 572
 - deep thermal injury
 - acute renal failure, 570
 - cardiovascular effects, 569
 - gastrointestinal function, 570
 - hemoconcentration, 569–570
 - hypermetabolic state, 569
 - infection, 570
 - thrombocytopenia, 570 - electrical burns, 570
 - ESU, 310
 - initial evaluation
 - airway and breathing, 572–573
 - cardiovascular resuscitation, 573
 - management of, 574
- Butyrophonones, 57–58, 609

C

- CABG. *See* Coronary artery bypass grafting
- CAD. *See* Coronary artery disease

- Calcium
 - channel antagonists, 324
 - channel blockers, 602
 - channel blockers, 530
- Calcium chloride (calcium gluconate)
 - comments, 679
 - dosage, 678
 - effect, 679
 - indications, 678
- Calcium metabolism and parathyroid disease
 - hypercalcemia
 - anesthetic considerations, 90
 - bisphosphonates, 89–90
 - clinical features of, 89, 89t
 - etiologies of, 88–89
 - gallium nitrate, 90
 - glucocorticoid therapy, 90
 - hydration, 89
 - salmon calcitonin, 90
 - treatment of, 89–90
 - hypocalcemia
 - anesthetic considerations, 91
 - clinical features of, 90
 - etiologies of, 90
 - treatment of, 91
 - physiology, 88
 - serum calcium, 88
- CAM. *See* Complementary and alternative medicine; Confusion Assessment Method algorithm
- Carbon dioxide, partial pressure of (PaCO_2), 37
- Carbonic anhydrase inhibitors, 55t
- Carbon monoxide, 573
- Carboprost (prostaglandin $\text{F}_{2\alpha}$; hemabate)
 - comments, 679
 - dosage, 679
 - effect, 679
 - indications, 679
- Carcinoid
 - anesthetic considerations, 99
 - clinical features, 99
 - syndrome, 98–99
 - treatment, 99
 - tumors, 98
- Cardiac arrest, 622–623
- Cardiac catheterization, 389, 408
- Cardiac disease
 - cardiac transplant
 - anesthetic considerations, 28
 - monitoring, 28
 - physiology, 27–28
 - CHD, 26–27
 - congestive heart failure
 - anesthetic considerations, 26
 - etiologies, 25–26
 - pathophysiology, 26
 - hypertrophic cardiomyopathy, 26
 - ischemic heart disease
 - myocardial oxygen consumption, 22–23
 - oxygen supply-demand balance, 22
 - pacemakers
 - five-letter code, 28–29
 - ICD, 30–31
 - indications, 29
 - intraoperative management, 30
 - pacing options, perioperative, 30
 - permanent, preoperative evaluation, 29
 - preanesthetic considerations, 21–22
 - preoperative cardiovascular evaluation, noncardiac surgery
 - ACC/AHA guidelines, 17
 - cardiac catheterization and consultation, 20–21
 - echocardiography, 20
 - functional capacity, 18, 19
 - initial screening, 17–18
 - 12-lead ECG, 20
 - MACE risk, 18–19
 - PCI, 21–22
 - stress testing, 20
 - supplemental cardiac evaluation, 20–21
 - valvular heart disease
 - aortic regurgitation, 24
 - aortic stenosis, 23–24
 - mitral regurgitation, 25
 - mitral stenosis, 24–25
- Cardiac dysrhythmias, 180
- Cardiac evaluation, 389–390, 390t, 391t
- Cardiac ischemia, 223
- Cardiac medications, 389–391, 392t, 393
- Cardiac output, 312, 602. *See also* Central venous pressure
 - dilution techniques, 146–147
 - esophageal doppler, 147
 - modified fick technique, 147
 - pulse contour analysis, 146
 - thermodilution, 146
 - thoracic bioimpedance, 147
 - thoracic bioreactance, 147
- Cardiac surgery
 - anesthetic management
 - monitoring, 393–394
 - preinduction, 394–395
 - cardiac tamponade and constrictive pericarditis, 414
 - cardiac transplantation, 414–415
 - cardiopulmonary bypass (CPB)
 - components of circuit, 388–389
 - pathophysiology, 388–389
 - pharmacokinetics, 389

Cardiac surgery (*Continued*)

- deep hypothermic circulatory arrest (DHCA), 415–416
- extracorporeal membrane oxygenation (ECMO), 417–418
- induction
 - actual separation from CPB, 403, 404t
 - anesthetic management of patient, 395–396
 - cardiopulmonary bypass, 399–401, 401t
 - discontinuing CPB, 401–403
 - postbypass period, 403–405
 - prebypass period, 396–399, 398t
 - transfer to ICU, 405
- off-bypass CABG, 413–414
- off-site cardiac procedures
 - ASD, patent foramen ovale (PFO), 418
 - ASD, percutaneous device closure, 418
 - cardioversion, 419
 - IABP, 418
 - implantable cardioverter defibrillator (ICD), 418–419
 - percutaneous aortic valve replacement, 419–420
 - percutaneous mitral valve repair, 420
- pediatric cardiac anesthesia
 - anesthetic management, 408–409
 - cardiopulmonary bypass, 409
 - CHD, 406–407
 - CHD lesions, management of, 409, 410t–412t, 413
 - neonatal *vs.* adult cardiac physiology, 406
 - PDA ligation, 409
 - transition from fetal to adult circulation, 406
- postoperative care
 - complications, 405–406
 - warming, 405
- preoperative assessment
 - cardiac evaluation, 389–390, 390t
 - cardiac medications, 390–391, 391t, 392t, 393
 - laboratory studies, 390
 - pertinent to cardiac procedure, 389
- “redo” cardiac surgery, 414
- VAD, 416–417
- Cardiac tamponade, 306
- Cardiopulmonary bypass (CBP)
 - cardiac surgery
 - components of circuit, 388–389
 - induction, 399–401, 401t
 - pathophysiology, 388–389
 - pharmacokinetics, 389
 - pediatric cardiac anesthesia, 409
- Cardiopulmonary resuscitation (CPR), 622, 623t
- Cardiovascular instability, 435
- Cardiovascular system (CVS)
 - anesthesia, 4
 - liver disease, 68
 - local anesthetics and, 228
 - monitoring
 - arterial blood pressure, 134–136
 - ECG, 133–134
 - ischemia detection, 134
 - mechanism of, 133–134
 - rhythm detection, 134
 - signs/symptoms of perfusion abnormalities, 133
- Cardioverter-defibrillator device, 4
- Carotid endarterectomy (CEA), 369
- Carotid sinus, 374
- CARP trial. *See* Coronary Artery Revascularization Prophylaxis trial
- Catecholamines, 58
- Catheter, Foley, 565
- Caudal anesthesia
 - anatomy, 251
 - complications, 251
 - physiology, 251
 - technique, 251, 252f
- CBF. *See* Cerebral blood flow
- CDH. *See* Congenital diaphragmatic hernia
- CEA. *See* Carotid endarterectomy
- Central line-associated blood stream infection (CLABSI), 103–104
- Central nervous system (CNS)
 - local anesthetics and, 228
 - vascular surgery, preoperative assessment, 370
- Central venous catheters (CVCs), 103–104
- Central venous pressure (CVP), 73–74, 422
 - analysis for, 137
- cardiac output
 - dilution techniques, 146–147
 - esophageal doppler, 147
 - modified fick technique, 147
 - pulse contour analysis, 146
 - thermodilution, 146
 - thoracic bioimpedance, 147
 - thoracic bioreactance, 147
- echocardiography, 147–148
- indications of, 136–137
- pathology and, 137
- positive-pressure ventilation, 137–138

- procedure
 - basilic vein, 141
 - complications, 138
 - external jugular vein, 141
 - femoral vein, 141
 - internal jugular Seldinger technique, 138–140, 139f
 - locations, 138
 - materials, 138
 - SCV, 141
- pulmonary artery catheter procedure
 - and
 - indications, 142
 - materials/catheter types, 142, 144
 - mechanism, 141–142
 - PA and PAOP, 142, 143f
 - pathology, 142
 - procedure, 144–145
 - securing, 145
 - waveform and, 137, 137f
- Cerebral angiography, 548–549
- Cerebral blood flow (CBF), 422, 423f
- Cerebral hyperperfusion syndrome (CHS), 375
- Cerebral metabolic rate (CMRO₂), 422–423
- Cerebral perfusion pressure (CPP), 167, 422, 457
- Cerebral protection, 426–427
- Cerebral salt wasting syndrome, 432
- Cerebral vasospasm, 550
- Cerebrospinal fluid (CSF), 422
 - spinal anesthesia, 234
- Cervical disk disease, airways, 193
- Cervical plexus block
 - deep, 261–262
 - regional anesthesia, for neck, 260–262, 260f
 - superficial, 261
- Cervical spinal cord injury, 438
- Cervical spine, 195, 557, 560
- CF. *See* Cystic fibrosis
- Chamberlain procedure, 352
- Chassaignac tubercle, 261
- CHD. *See* Congenital heart disease
- Chest wall deformity, 34
- Child-Turcotte-Pugh (CTP), 71, 71t
- Chloral hydrate, 545
- Cholecystectomy, 338
- Cholecystojejunostomy, 338
- Choledochojejunostomy, 338
- Cholestasis, 68, 70
- Cholinergic receptors, 177–178
- Cholinesterase
 - activity, reduced, 223
 - atypical, 223
- Cholinesterase inhibitors, 58
- Christmas disease (hemophilia B), 592
- Chronic bronchitis, 33–34
- Chronic hypoxemia, respiratory system, 69
- Chronic interstitial nephritis, 54
- Chronic kidney disease (CKD)
 - anesthetic management, 61–62
 - clinical features, 52
 - epidemiology, 52, 52t
 - etiology, 52
 - treatment, 53
- Chronic obstructive pulmonary disease (COPD), 33–34, 598, 616
- CHS. *See* Cerebral hyperperfusion syndrome
- Cimetidine (Tagamet), 9
- CIN. *See* Contrast-induced nephropathy
- Cisatracurium, 67, 184
- CKD. *See* Chronic kidney disease
- CLABSI. *See* Central line-associated blood stream infection
- Clevidipine (Cleviprex)
 - comments, 679
 - dosage, 679
 - effect, 679
 - indications, 679
- Clindamycin, 107
- Clonidine, 509
- Clonidine (Catapres), 314
- Clopidogrel (Plavix), 369, 590
 - comments, 679
 - dosage, 679
 - effect, 679
 - indications, 679
- Clopidogrel therapy, 369
- Closed-loop communication, errors, 118
- Clothesline injury, 562
- Clotting factors, 65, 589
- CMV. *See* Cytomegalovirus
- CNS. *See* Central nervous system
- Coagulopathy, 14, 578
- Colectomy, 337
- Colectomy/hemicolectomy, 337
- Colloids, 332
 - IV fluids and, 217
- Comorbid pathology, 544
- Complementary and alternative medicine (CAM)
 - categories, 658
 - definitions, 658
 - herbal therapies as, anesthesia, 659–662
 - hypnosis, 663
 - music medicine and music therapy, 663–664
 - perioperative acupuncture, 662–663, 662f–663f
 - prevalence, 658–659

- Complete global ischemia, 426
 - Computed tomography (CT), 545
 - Confusion Assessment Method (CAM) algorithm, 471
 - Congenital anomalies, airways, 194
 - Congenital diaphragmatic hernia (CDH), 485–486
 - Congenital heart disease (CHD), 26–27, 406–407
 - Congestive heart failure
 - anesthetic considerations, 26
 - etiologies, 25–26
 - pathophysiology, 26
 - Conn syndrome
 - clinical features, 92
 - etiologies, 92
 - treatment, 92
 - Contamination, bacteria in anesthesia machine, 103
 - Context-sensitive half-time (CSHT), 162
 - Continuous positive airway pressure (CPAP), 619
 - Continuous renal replacement therapy (CRRT), 51–52
 - Contrast-induced nephropathy (CIN), 369
 - COPD. *See* Chronic obstructive pulmonary disease
 - Coronary artery bypass grafting (CABG), 106t
 - Coronary artery disease (CAD), 4, 8
 - Coronary Artery Revascularization Prophylaxis (CARP) trial, 368
 - Corticosteroids, 40, 609
 - CPAP. *See* Continuous positive airway pressure
 - CPP. *See* Cerebral perfusion pressure
 - Crawford classification, thoracoabdominal aneurysms, 381, 382f
 - Creutzfeldt-Jakob disease, 110–111
 - Cricoid cartilage, of larynx, 192
 - Cricothyroid membrane, of larynx, 192
 - Cricothyroidotomy, 207
 - Cromolyn, 40
 - CRRT. *See* Continuous renal replacement therapy
 - Cryoprecipitate, 582
 - Crystalloid solutions, IV fluids and, 217
 - CSF. *See* Cerebrospinal fluid
 - CSF shunts, 439
 - CSHT. *See* Context-sensitive half-time
 - CTP. *See* Child-Turcotte-Pugh
 - Cushing syndrome, 92–93
 - CVCs. *See* Central venous catheters
 - CVP. *See* Central venous pressure
 - CVS. *See* Cardiovascular system
 - Cyanide toxicity, 323
 - Cyclobenzaprime, 608
 - Cyclopentolate, 443
 - Cystectomy, 464
 - Cystic fibrosis (CF), 34, 365
 - Cystoscopy, 460
 - Cytokines, 61
 - Cytomegalovirus (CMV), 110, 588
- D**
- Dabigatran, 591
 - Dalteparin (Fragmin)
 - comments, 680
 - dosage, 680
 - effect, 680
 - indications, 679
 - Dantrolene
 - comments, 680
 - dosage, 680
 - effect, 680
 - indications, 680
 - DCD. *See* Donation after cardiac death
 - Deep brain stimulators, 437
 - Deep peroneal nerve, 284–285
 - Defibrillation, 402
 - Dehydration, 473
 - Delirium, 471
 - Dementia, 471
 - Dentistry and oral and maxillofacial surgery, 453–454
 - DES. *See* Drug-eluting stents
 - Desflurane, 56
 - Desflurane effects, on brain, 158
 - Desmopressin, 432, 583
 - Desmopressin acetate (DDAVP)
 - comments, 680
 - dosage, 680
 - effect, 680
 - indications, 680
 - Dexamethasone, 599, 609, 612
 - Dexamethasone (Decadron)
 - comments, 680
 - dosage, 680
 - effect, 680
 - indications, 680
 - Dexmedetomidine
 - as inhalation anesthetic, 172–176, 172t
 - as intravenous (IV) anesthetics
 - action mode of, 169
 - adverse effects, 169
 - cardiovascular system, 169
 - CNS, 169
 - dosage and administration, 163t, 169
 - endocrine system, 169
 - pharmacodynamics of, 169

- pharmacokinetics of, 169
- respiratory system, 169
- Dexmedetomidine (Precedex)
 - hemodynamic control, perioperative and, 314, 317
- Dexmedetomidine effects, on brain, 158–159, 160f
- Dextran 40 (Rheomacrodex)
 - comments, 681
 - dosage, 680
 - effect, 681
 - indications, 680
- DI. *See* Diabetes insipidus
- Diabetes insipidus (DI), 97–98, 432, 605
- Diabetes mellitus (DM), 4–5, 9, 60
 - acute complications
 - DKA, 79–80
 - HHS, 80–81
 - anesthetic considerations
 - airway management, 84
 - DKA, HHS, and metabolic abnormalities, 81
 - fixed ratio insulin combinations, 83
 - glycemic management, 81–83
 - insulin infusions, 82t, 83
 - insulin-treated type 2 diabetics, 82
 - neuropathy, 83–84
 - oral hypoglycemic agents, 81–82
 - protamine, 84
 - vascular disease, 83
 - outpatient therapy
 - injectable agents, 78–79, 79t
 - oral hypoglycemic agents, 76–78, 77t
 - physiology of, 76
 - types of
 - gestational, 76
 - secondary, 76
 - type 1, 76
 - type 2, 76
- Diabetic ketoacidosis (DKA), 79–80
- Diabetic neuropathy, 53
- Diaphoresis, 301
- Diaphragmatic compression, 34
- Diazepam, 606
- DIC. *See* Disseminated intravascular coagulation
- Digoxin (Lanoxin), 58
- Diltiazem (Cardizem)
 - comments, 681
 - dosage, 681
 - effect, 681
 - indications, 681
- Dimenhydrinate, 610
- Dipeptidyl peptidase IV (DPP-IV)
 - inhibitors, 78
- Dipyridamole, 590
- Direct factor Xa inhibitors, 591
- Direct laryngoscopy, 450
- Direct thrombin inhibitors (DTIs), 591
- Disseminated intravascular coagulation (DIC), 589
- Diuretics, 54, 55t
- DKA. *See* Diabetic ketoacidosis
- DM. *See* Diabetes mellitus
- DNR. *See* Do not resuscitate
- Dobutamine
 - comments, 681
 - dosage, 681
 - effect, 681
 - hemodynamic control, perioperative and, 318
 - indications, 681
- DOE. *See* Dyspnea on exertion
- Dolasetron, 608
- Donation after cardiac death (DCD), 344, 669–670
- Do not resuscitate (DNR), 667
- Dopamine (Intropin), 54
 - comments, 681
 - dosage, 681
 - effect, 681
 - hemodynamic control, perioperative and, 318
 - indications, 681
- Dopaminergic, 312
- Droperidol, 609
- Drug(s)
 - for gastric acid/volume, 212–213
- Drug-eluting stents (DES), 22
- 3D spectrogram, 156, 157f
- DTIs. *See* Direct thrombin inhibitors
- Duchene muscular dystrophy, 190
- Dwarfism, 194
- Dyspnea, 243
- Dyspnea on exertion (DOE), 4
- Dysrhythmias, 27, 345
 - delaying surgical procedures, 14
 - heart block, 294
 - hemodynamic complications, PACU
 - stable ventricular dysrhythmias, 603–604
 - supraventricular dysrhythmias, 603
 - unstable ventricular tachycardia and ventricular fibrillation, 604
 - sinus bradycardia, 293
 - sinus tachycardia, 293–294
 - supraventricular tachycardias, 294–295
 - ventricular dysrhythmias, 295–296

E

- EABL. *See* Estimated allowable blood loss
- Ear surgery, 447–448
- Echinacea, 660

- Echocardiography, 20, 147–148, 389
- ECT. *See* Electroconvulsive therapy
- Edentulous patients, 196
- Edrophonium, 187
- EEG. *See* Electroencephalogram
- Electrical hazards, 310
- Electroconvulsive therapy (ECT)
 - anesthetic goals, 553
 - anesthetic management, 553–554
 - gastrostomy/jejunostomy tube placement, 555
 - physiologic effects of, 553
 - psychiatric drug interactions during, 554
- Electroencephalogram (EEG), 373
 - biophysics of, 153, 153f, 154f
 - bispectral index, 153–154
 - level of consciousness, 152
 - narcotrend, 155
 - patient safety index, 154–155
 - spectral analysis of, 155–156, 156f
- Electrolyte balance, 45–48
- Electromyography (EMG), 187, 428
- Embolization
 - for control of epistaxis/extracranial vascular lesions, 548
 - endovascular, 547–548
- Emergency airway techniques
 - cricothyroidotomy, 207
 - difficult airway
 - LMA, 205–206
 - regional anesthesia, 205
 - percutaneous needle cricothyroidotomy, 207
 - rigid bronchoscopy, 207
 - tracheostomy, 207
- Emesis, 328
- EMG. *See* Electromyography
- EMLA. *See* Eutectic mixture of local anesthetics
- Empysema, 33
- Enalaprilat, 602
 - hemodynamic control, perioperative, 324–325
- Endobronchial tubes, 353–355
- Endocarditis, 106–107
- Endocrine disease
 - adrenal cortical disease
 - glucocorticoid excess, 92–93
 - pharmacology, 92, 92t
 - physiology, 91–92
 - primary hyperaldosteronism, 92 (*see also* Conn syndrome)
 - adrenal cortical hypofunction, 93–94
 - adrenal medullary disease, 94–96
 - calcium metabolism and parathyroid disease, 88–91, 89t
 - carcinoid, 98–99
 - diabetes mellitus
 - acute complications, 79–81
 - anesthetic considerations, 81–84, 82t
 - outpatient therapy, 76–79, 77t, 79t
 - physiology of, 76
 - types of, 76
 - hypoglycemia, 84
 - parathyroid disease (*see* Parathyroid disease)
 - pituitary disease
 - anterior pituitary gland, 96–97
 - posterior pituitary gland, 97–98
 - thyroid disease
 - evaluation and laboratory studies, 85
 - hypothyroidism, 87–88
 - physiology, 84
 - thyroid surgery, 88
 - thyrotoxicosis, 85–86, 86t
 - vascular surgery, preoperative assessment, 370
- End-of-life issues
 - determination of death as, 668
 - legal considerations of, 670
 - organ donation, 669–670
 - regarding treatments
 - conflict, 666
 - do not resuscitate orders, 667
 - informed consent, 665
 - institutional ethics committee, 666
 - Jehovah's witness, 666–667
 - patient autonomy, 665
 - pediatric patient, 666
 - supporting survivors, 670
- Endoscopic procedures
 - flexible bronchoscopy, 350
 - flexible esophagoscopy, 351–352
 - laser surgery, 352
 - rigid bronchoscopy, 350–351
 - rigid esophagoscopy, 352
- Endoscopic retrograde
 - cholangiopancreatography (ERCP), 555
- Endoscopy, upper/lower anesthesia, 555
- Endotracheal intubation, 438
 - alternative intubation techniques
 - gum elastic bougie, 204
 - laryngoscope, 204
 - light wand, 205
 - retrograde tracheal intubation, 205
 - fiberoptic, 203–204
 - nasotracheal, 203
 - orotracheal, 200, 202–203
- Endotracheal tubes (ETTs), 202–203, 214, 216, 217, 219
- End-tidal anesthetic criterion, 155

- Enhanced recovery after surgery (ERAS)
 - abdominal surgery, 334
- Enoxaparin (Lovenox)
 - comments, 681
 - dosage, 681
 - effect, 681
 - indications, 681
- Ephedra (Ma Huang), 660
- Ephedrine
 - comments, 682
 - dosage, 682
 - effect, 682
 - hemodynamic control, perioperative
 - and, 318
 - indications, 682
- Epidural analgesia, 358, 359
- Epidural anesthesia
 - anatomy, 243–244
 - combined spinal, 250–251
- epidural blockade
 - bloody tap, 248
 - catheter complications, 248–249
 - direct spinal cord injury, 250
 - dural puncture, 248
 - epidural abscess, 250
 - epidural hematoma, 250
 - Horner syndrome, 250
 - intravascular injection, 249
 - levels of, 247
 - local anesthetic overdose, 249
 - onset and duration of, 248
 - postdural puncture headache, 250
 - unintentional subarachnoid
 - injection, 249
- physiology of, 244
- techniques
 - catheter placement, 246–247
 - epidural needles, 244
 - injection of, 247
 - lumbar, 245–246
 - monitoring, 245
 - patient position, 244
 - test dose, 247
 - thoracic, 246
- Epidural hematoma, 250
- Epilepsy surgery, 437–438
- Epinephrine (Adrenalin), 443
 - comments, 682
 - dosage, 682
 - effect, 682
 - hemodynamic control, perioperative
 - and, 317
 - indications, 682
 - local anesthetics and, 224
- Episcleral block, 445
- Epoprostenol sodium (Flolan)
 - administration guidelines, 675
 - indication, 675
- Eptifibatide (Integrilin)
 - comments, 675
 - dosage, 675
 - effect, 675
 - indication, 675
- ERCP. *See* Endoscopic retrograde cholangiopancreatography
- Ergonovine (Ergotrate). *See also* Methylergonovine
 - comments, 682
 - dosage, 682
 - effect, 682
 - indications, 682
- Errors, anesthesia safety
 - cognitive, 115–116, 115t–116t
 - handoff, 116–117, 117f
 - human factors in, 116
 - medication (*see* Medication errors)
 - procedure type, 114–115
 - teamwork and communication type, 117–118
- Erythropoietin, 48, 583
- Esmolol (Brevibloc)
 - comments, 682
 - dosage, 682
 - effect, 682
 - hemodynamic control, perioperative
 - and, 320, 321t
 - indications, 682
- Esophageal bougie, 336
- Esophageal doppler, 147
- Esophageal surgery
 - anesthetic considerations for
 - abdominal procedures, 336
 - general considerations, 363
 - operative approach and anesthesia, 363–365
- Esters, 222
- Estimated allowable blood loss (EABL), 578
- Ether-derived anesthetics, on brain, 158, 159f
- Ethical issues
 - determination of death as, 668
 - legal considerations of, 670
 - organ donation, 669–670
 - regarding treatments
 - conflict, 666
 - do not resuscitate orders, 667
 - informed consent, 665
 - institutional ethics committee, 666
 - Jehovah's witness, 666–667
 - patient autonomy, 665
 - pediatric patient, 666
 - supporting survivors, 670

- Etomidate, 58, 67, 425
 as inhalation anesthetic, 172–176, 172t
 as intravenous (IV) anesthetics
 action mode of, 167
 adverse effects, 167
 cardiovascular system, 167
 CNS, 167
 dosage and administration, 163t, 167
 pharmacodynamics of, 167
 pharmacokinetics of, 167
 respiratory system, 167
- ETTs. *See* Endotracheal tubes
- Eutectic mixture of local anesthetics (EMLA), 224
- Evoked potential monitoring
 neurosurgery, 427–428
- Exercise stress testing, cardiac
 evaluation, 20
- Extracorporeal cooling, 301
- Extubation
 awake
 criteria, 219
 removal of, 219
 techniques, 219
 deep
 criteria, 219
 techniques, 219
- F**
- Face mask (FM), 618
- Fascia iliaca compartment block, 278
- Febrile nonhemolytic transfusion
 reactions (FNHTR), 586
- Femoral-femoral bypass grafting, 371
- Femoral herniorrhaphies, 337
- Femoral nerve block, 278–279, 279f
- Femoral pseudoaneurysm, 372
- Fenoldopam, 54, 325, 602
 comments, 683
 dosage, 683
 effect, 683
 indications, 683
- Fentanyl, 444, 607
- Ferromagnetic objects, 546
- Fetal acidosis, 223
- Feverfew, 660
- FFP. *See* Fresh frozen plasma
- Fiberoptic bronchoscopy, 209
- Fiberoptic bronchoscopy, 362
- Fiberoptic intubation
 alternative intubation techniques
 gum elastic bougie, 204
 laryngoscopes, 204
 light wand, 205
 retrograde tracheal intubation, 205
 indications, 204
 standard equipment, 203
 techniques, 204
- Fibrinogen, 579
- Fibrinolytic and thrombolytic agents, 253
- Fire hazards, 309–310
- Flexible bronchoscopy, 350
- Flow generators, 127–128
- Fluid deficit, 212
- Fluid management, 378
- Flumazenil (Mazicon), 166
 comments, 683
 dosage, 683
 effect, 683
 indications, 683
- FM. *See* Face mask
- FNHTR. *See* Febrile nonhemolytic
 transfusion reactions
- Focal ischemia, 426
- Foley catheter, 378
- Fosphenytoin
 comments, 683
 dosage, 683
 effect, 683
 indications, 683
- FRC. *See* Functional residual capacity
- Fresh frozen plasma (FFP), 70, 581
- Functional residual capacity (FRC),
 35, 37
- Fundoplication, 364–365
- Furosemide (Lasix)
 comments, 683
 dosage, 683
 effect, 683
 indications, 683
- G**
- GA. *See* General anesthesia
- Gadolinium, 545
- Garlic (*Allium sativum*), 660
- Gas delivery system, 123f
 flow control valves and flowmeters,
 124
 gas outlet, 124
 gas supplies, 122, 124
 oxygen flush valve, 124
 vaporizers, 124
- Gastric surgery, 336
- Gastroesophageal reflux disease, 5
- General anesthesia (GA), 152
 abdominal surgery, 329
 administration of
 anesthetic plan, 211
 monitoring, 213
 preoperative medications, 212–213
 preoperative preparation, 211–213

- primary goals, 211
 - secondary goals, 211
 - emergence from
 - agitation and delayed awakening, 219–220
 - extubation, 218–219
 - goals and technique, 218
 - patient positioning and ventilation, 218
 - induction of
 - airway management, 214
 - environment, 213
 - patient position, 213
 - techniques, 213–214, 214t
 - maintenance of
 - intraoperative, 215
 - intraoperative IV fluid, 217–218
 - methods, 216
 - ventilation, 216–217
 - postoperative visit after, 220, 220t
 - stages of, 214t
 - transport of, 220
 - Geriatric patients
 - anesthesia considerations
 - intraoperative management, 470
 - postoperative cognitive dysfunction (POCD), 470–471
 - preoperative evaluation, 469–470
 - body composition, 469
 - cardiovascular, 468
 - central nervous system, 468, 471–472
 - hepatic, 469
 - metabolic derangements, 473–474
 - orthopedic disorders, 473
 - pharmacodynamic changes, 469
 - pharmacokinetic changes, 469
 - renal, 468–469
 - respiratory, 468
 - thermoregulation, 469
 - visual impairment, 472
 - GH. *See* Growth hormone
 - Ginger (*Zingiber offi cinalis*), 660
 - Ginkgo, 660–661
 - Ginseng (*Panax ginseng*), 661
 - Glaucoma, 442
 - Glossopharyngeal nerve, 192
 - Glottis, 193
 - Glucagon
 - comments, 684
 - dosage, 684
 - effect, 684
 - indications, 684
 - Gluconeogenesis, 70
 - Glyburide, 76–77, 77t
 - Glycopyrrolate
 - comments, 684
 - dosage, 684
 - effect, 684
 - indications, 684
 - Glycopyrrolate (Robinul), 39, 349, 373
 - Goldenseal, 661
 - Graft *vs.* host disease (GVHD), 582, 586–587
 - Granisetron, 608
 - Growth hormone (GH), 96–97
 - Gum elastic bougie, 204
- ## H
- Haloperidol (Haldol), 606, 609
 - comments, 684
 - dosage, 684
 - effect, 684
 - indications, 684
 - Halothane hepatitis, 74
 - Handoff checklist, 117, 117f
 - HBV. *See* Hepatitis B virus
 - HCV. *See* Hepatitis C virus
 - Head and neck surgery
 - airways, 194–195
 - ophthalmic surgery
 - anesthetic management, 443–446, 444f
 - general considerations, 442–443
 - procedures, 446–447
 - otorhinolaryngologic procedures
 - ear surgery, 447–448
 - general considerations, 447
 - nasal surgery, 448–449
 - upper airway surgery, 449–451
 - procedures of neck
 - dentistry and oral, 453–454
 - general considerations, 451–452
 - maxillofacial surgery, 453–454
 - radical neck dissection, 452
 - thyroid surgery, 452–453, 453f
 - Head trauma, 438–439
 - Heart block, 294
 - Heart transplant. *See also* Cardiac disease
 - anesthetic considerations, 28
 - monitoring, 28
 - physiology of, 27–28
 - Heliox, 599
 - Hematologic system, 5
 - vascular surgery, preoperative assessment, 370
 - Hemicolectomy, 337
 - Hemodilution, 550
 - Hemodynamic(s)
 - anesthetic considerations, 335
 - cardiac catheterization, 390
 - complications, 601–604

- Hemodynamic(s) (*Continued*)
 control, perioperative
 β -adrenergic antagonists, 320, 321t, 322
 adrenergic pharmacology, 314, 315t–316t, 317–320
 adrenergic receptor physiology, 312, 313t, 314
 autoregulation, 312
 blood pressure, 312
 drug dosage calculations, 326
 induced hypotension, 325–326
 instability, 600
 mitral stenosis (MS), 396
 monitoring, 399–400
 stability, 403
 vasodilators, 322–325, 322t
- Hemophilia, 592
- Hemorrhage, 342
- Hemorrhoidectomy, 337
- Hemostasis, 403–405
- Heparin, 373, 378
 perioperative coagulopathy, 590
- Heparin-induced thrombocytopenia (HIT), 370, 389
- Heparin–unfractionated
 comments, 684–685
 dosage, 684
 effect, 684
 indications, 684
- Hepatic drug elimination, 66
- Hepatic function
 degradation
 heme and bile, 66
 proteins, 65
 steroid hormones, 65
 drug metabolism
 enzyme induction/cytochrome P450, 66
 hepatic clearance, 66
 hepatic drug elimination, 66
 hepatic extraction ratio, 66
 protein binding, 66
 synthesis and storage
 carbohydrates, 65
 heme and bile, 65
 lipids, 65
 proteins, 64–65
- Hepatic surgery, 337
- Hepatitis, 588
- Hepatitis B virus (HBV), 109
- Hepatitis C virus (HCV), 109
- Hepatorenal syndrome, 70
- Herbal medications, 254
- Herpes simplex viruses (HSV) I and II, 109–110
- HFJV. *See* High-frequency jet ventilation
- HHS. *See* Hyperglycemic hyperosmolar syndrome
- High-frequency jet ventilation (HFJV), 363
- Histamine (H_2) antagonists, 9, 41
- HIT. *See* Heparin-induced thrombocytopenia
- HIT type 2, 397–398, 398t
- HIV. *See* Human immunodeficiency virus
- Homeostasis, disorders of
 potassium, 47–48
 sodium, 45–47
- Hormonal therapy, 344
- Horner syndrome, 250
- HTN. *See* Hypertension
- Human immunodeficiency virus (HIV), 108–109, 588
- Hydralazine, 324, 602
 comments, 685
 dosage, 685
 effect, 685
 indications, 685
- Hydrochloride salts, 224
- Hydrocortisone (solu-cortef)
 comments, 685
 dosage, 685
 effect, 685
 indications, 685
- Hydrophilic opioids, 239
- Hygiene standards, operating room, 103
- Hypercalcemia, 88–90, 89t
- Hypercarbia, 297–298
- Hypercholesterolemia, 339
- Hyperglycemia, 426
- Hyperglycemic hyperosmolar syndrome (HHS), 80–81
- Hyperkalemia, 7, 47–48, 180–181, 605
- Hypernatremia, 46–47
- Hypertension (HTN), 4, 8, 345, 378–379, 550
 etiologies, 292
 treatment of, 292–293
- Hyperthermia, 300–301, 426, 610
- Hypertrophic cardiomyopathy, 26
- Hypervolemia, 550
- Hypocalcemia, 90–91
- Hypoglycemia, 70, 84
- Hypoglycemic agents, 76–78, 77t
- Hypokalemia, 7, 47, 605
- Hypomagnesemia, 605
- Hyponatremia, 45–46
- Hypotension, 234, 240, 243, 345, 379
 contractility, 290
 decreased SVR, 290
 dysrhythmias, 291

- hemodynamic complications, PACU
 - cardiac output, 602
 - hypovolemia, 601
 - impaired venous return, 601
 - vasodilation, 601
- inadequate venous return, 291
- myocardial ischemia, 304
- treatment of, 292
- Hypotensive anesthesia, 454
- Hypotensive reactions, 582
- Hypothermia, 399, 426, 600, 610
 - anesthetic effects, 299
 - heat loss, 299
 - prevention and treatment of, 299–300
 - severe, physiologic changes caused by, 299
- Hypovolemia, 291, 328–329, 605
- Hypoxemia, 344, 358
 - intraoperative etiologies, 296–297
 - treatment of, 297
- Hypoxia, 342
 - delaying surgical procedures, 14
- I**
- Ibuprofen, 608
- ICD. *See* Implantable cardioverter-defibrillator; Intracardiac defibrillator
- ICP. *See* Intracranial pressure
- ICU. *See* Intensive care unit
- Ilioinguinal–iliohypogastric block, 277
- Immunomodulation, blood transfusions, 588
- Immunosuppression, 575
- Implantable cardioverter-defibrillator (ICD), 30–31
- Implantable devices, 546
- Inamrinone, 319
- Indigo carmine
 - comments, 685
 - dosage, 685
 - effect, 685
 - indications, 685
- Indomethacin, 608
- Induced hypotension, 325–326
- Induction
 - of GA
 - airway management, 214
 - environment, 213
 - patient position, 213
 - techniques, 213–214, 214t
 - of inhalational anesthetics, 213–214
- Infectious complications, blood transfusions, 587–588
- Infectious diseases and infection control
 - air exchanges, 103
 - anesthetist responsibilities in OR, 101
 - antibiotics, in OR
 - aminoglycosides, 108
 - β -lactams, 107
 - clindamycin, 107
 - endocarditis, 106–107
 - fluoroquinolones, 108
 - indications for, 105
 - metronidazole, 108
 - prophylaxis principles, 105
 - SCIP, 105, 106t
 - surgical wounds, 107
 - vancomycin, 107–108
 - aspiration pneumonia, 104
 - bacteria
 - antibiotic resistant bacteria, 110
 - contamination of anesthesia machine, 103
 - mycobacterium tuberculosis., 110
 - bactericidal cleaning agents, 103
 - clean workstation standards, 103
 - CVC, 103–104
 - exposure
 - management, 111
 - prevent, 111
 - methods, infection spread, 101
 - peripheral intravenous lines, 103
 - prevention, infection spread, 101
 - prior diseases, 110–111
 - standard precautions, 101–102
 - sterilization
 - of reusable equipment, 103
 - techniques of, 103
 - transfusion-related infections, 104, 105t
 - transmission-based precautions
 - airborne precautions, 103
 - contact precautions, 102
 - droplet precautions, 102
 - virus exposure, in OR
 - CMV, 110
 - HBV, 109
 - HCV, 109
 - HIV, 108–109
 - HSV I and II, 109–110
 - influenza virus, 110
 - VZV, 110
- Inferior laryngeal nerve, 192
- Influenza virus, 110
- Informed consent
 - anesthesia, 11–12
- Infrared analysis, 129–130
- Inguinal herniorrhaphies, 337
- Inhalational anesthetics, 213–214
- Inhalation anesthetic(s)
 - action mode of, 172t, 173
 - desflurane, problems associated with, 176

- Inhalation anesthetic(s) (*Continued*)
 diffusion hypoxia, 176
 MAC and, 172
 nitrous oxide as
 cardiovascular system, 175
 CNS, 174–175
 respiratory system, 175
 pharmacodynamics of, 174–175
 pharmacokinetics of, 173–174, 173f
 sevoflurane, problems associated with, 176
 volatile anesthetics
 cardiovascular system, 175
 CNS, 175
 hepatic system, 175
 neuromuscular system, 175
 renal system, 175
 respiratory system, 175
 Inhalation anesthetics, 425
 Inotropes, 304
 INR. *See* International normalized ratio
 Institutional ethics committee, 666
 Insulin, 78, 79t
 Insulin (Humulin R, Novolin R)
 administration guidelines, 675
 indications, 675
 Intensive care unit (ICU), 189
 Internal jugular Seldinger technique, 138–140, 139f
 International normalized ratio (INR), 579
 Intestinal and peritoneal surgery, 336–337
 Intestine, spinal anesthesia, 235
 Intra-anesthetic problems
 anaphylactic and anaphylactoid reactions, 309
 aspiration, 302–303
 bronchospasm, 301–302
 cardiac tamponade, 306
 diaphoresis (sweating), 301
 dysrhythmias
 heart block, 294
 sinus bradycardia, 293
 sinus tachycardia, 293–294
 supraventricular tachycardias, 294–295
 ventricular dysrhythmias, 295–296
 electrical hazards in, 310
 fire hazards in, 310
 hypercarbia, 297–298
 hypertension, 292–293
 hyperthermia, 300–301
 hypotension, 290–292
 hypothermia, 299–300
 hypoxemia, 296–297
 laryngospasm, 301
 malignant hyperthermia, 306–308
 myocardial ischemia, 304
 pneumothorax, 303
 pulmonary embolism, 305–306
 urine output, abnormal, 298
 Intra-arterial infusion, 550
 Intracardiac defibrillator (ICD), 604
 Intracranial compliance, 425, 425f
 Intracranial normotension, 550
 Intracranial pressure (ICP), 181, 292–293, 422, 423–424, 424f
 Intraocular pressure (IOP), 181, 442
 Intraoperative blood transfusion, 577–578
 Intraoperative radiation therapy, 338–339
 Intrapulmonary hemorrhage, 362
 Intravenous (IV) anesthetics, 425
 barbiturates
 action mode of, 164
 adverse effects, 165
 cardiovascular system, 164
 CNS, 164
 dosage and administration, 163t, 165
 pharmacodynamics of, 164–165
 pharmacokinetics of, 164
 respiratory system, 164–165
 benzodiazepines
 action mode of, 165
 adverse effects, 166
 cardiovascular system, 166
 CNS, 166
 dosage and administration, 163t, 166
 pharmacodynamics of, 166
 pharmacokinetics of, 165
 respiratory system, 166
 dexmedetomidine, 163t, 169
 etomidate, 163t, 167
 ketamine
 action mode of, 167
 adverse effects, 168–169
 cardiovascular system, 168
 CNS, 168
 dosage and administration, 163t, 168
 pharmacodynamics of, 168
 pharmacokinetics of, 168
 respiratory system, 168
 opioids
 action mode of, 170
 adverse effects, 171–172
 cardiovascular system, 171
 CNS, 170–171
 dosage and administration, 170, 171

- gastrointestinal system, 171
 - pharmacodynamics of, 170–171
 - pharmacokinetics of, 170, 170t
 - respiratory system, 171
 - propofol
 - action mode of, 162
 - adverse effects, 163–164
 - cardiovascular system, 163
 - CNS, 162–163
 - dosage and administration, 163, 163t
 - pharmacodynamics of, 162–163
 - pharmacokinetics of, 162
 - respiratory system, 163
 - Intravenous antibiotics, 695–696
 - Intravenous (IV) fluids
 - administration of, 217–218
 - assessment of, 218
 - colloid solutions and, 217
 - crystalloid solutions and, 217
 - intraoperative requirements, 217–218
 - Intravenous (IV) regional anesthesia (Bier block), 274
 - Intubation
 - alternative
 - gum elastic bougie, 204
 - laryngoscope, 204
 - light wand, 205
 - retrograde tracheal intubation, 205
 - fiberoptic, 203–204
 - nasotracheal, 203
 - orotracheal, 200, 202–203
 - IOP. *See* Intraocular pressure
 - Ipratropium bromide, 39
 - Ischemic heart disease
 - myocardial oxygen consumption, 22–23
 - oxygen supply-demand balance, 22–23
 - Isoflurane, 56, 158
 - Isoproterenol (Isuprel)
 - comments, 685
 - dosage, 685
 - effect, 685
 - hemodynamic control, perioperative and, 317
 - indications, 685
 - Isotonic salt solution, 332
 - Ivacaftor, 41
 - Ivor Lewis esophagectomy, 364
- J**
- Jehovah's Witness, 593, 666–667
 - Joint disease, stiff, 84
 - Just culture, anesthesia safety, 119
- K**
- Kava kava (*Piper methysticum*), 661
 - Ketamine, 41, 67, 425, 445, 643
 - effects on brain, 159–160, 160f
 - as inhalation anesthetic, 172–176, 172t
 - as intravenous (IV) anesthetics
 - action mode of, 167
 - adverse effects, 168–169
 - cardiovascular system, 168
 - CNS, 168
 - dosage and administration, 163t, 168
 - pharmacodynamics of, 168
 - pharmacokinetics of, 168
 - respiratory system, 168
 - Ketorolac (Toradol), 512, 608
 - comments, 686
 - dosage, 685
 - effect, 685
 - indications, 685
 - Kidney disease(s)
 - anesthetic management
 - blood urea nitrogen, 59
 - chest radiographs, 60
 - CKD, 61–62
 - fluid replacement, 61
 - history, 58–59
 - induction agents, 61
 - intraoperative management, 61–62
 - laboratory studies, 59–60
 - narcotics and volatile anesthetics, 61
 - optimization, 60
 - physical examination, 59
 - positioning, 61
 - postoperative management, 62
 - premedication, 61
 - preoperative assessment, 58–60
 - renal transplantation, 62
 - risk assessment, 60
 - urinalysis, 59
 - urine electrolytes, 59
 - blood flow regulation, 44
 - electrolyte balance
 - potassium homeostasis disorders, 47–48
 - sodium homeostasis disorders, 45–47
 - extrarenal regulatory and metabolic functions, 48
 - fluid regulation
 - daily adult water intake, 45
 - hypervolemia, 45

Kidney disease(s) (*Continued*)

- hypovolemia, 44–45
- macula densa, 44
- osmotic equilibrium, 45
- TBW, 44
- pharmacology
 - kidney, 54, 54t, 55
 - renal failure, 56–58, 56t, 57t
- renal failure
 - acute kidney injury, 49–52
 - causes of, 53–54
 - chronic kidney disease, 52–53

Kidney failure

- acute kidney injury
 - classification system, 49, 50t
 - diagnosis, 49, 51t
 - epidemiology, 49
 - etiology, 49
 - prevention, 49
 - treatment, 49, 51–52
- causes of
 - ATN, 53
 - diabetic nephropathy, 53
 - glomerulonephropathies, 53
 - hypertensive nephrosclerosis, 53
 - obesity, 54
 - polycystic kidney diseases, 54
 - tubulointerstitial diseases, 53–54
- chronic kidney disease
 - clinical features, 52
 - epidemiology, 52, 52t
 - etiology, 52
 - treatment, 53
- pharmacology
 - drug class, 56t–57t
 - ionized drugs, 58
 - lipid-soluble drugs, 57–58
 - vasoactive agents, 58
- transplantation, anesthetic management, 62

King–Denborough syndrome, 308

Kinins, 45

Kuru disease, 110–111

Kyphoplasty, 549

L

Labetalol

- comments, 686
- dosage, 686
- effect, 686
- hemodynamic control, perioperative and, 321t, 322
- indications, 686

Labor

- definition, 526
- intrapartum fetal evaluation, 526–528, 527f

medications, 528–530

- pain, 526
- placental transfer of drugs, 530 and vaginal delivery, 530–533
- Laparoscopic prostatectomies (LRP), 463

Laparoscopy

- anesthetic considerations, 335
- anesthetic management, 335–336
- operative technique, 334

Laryngeal mask airway (LMA), 214

- adverse effects, 200
- classic, 197
- contraindications, 197
- Fastrach, 198, 200, 200f
- indications, 197
- intubating, 198, 200
- removal of, 198
- use of, 198, 198t, 199f

Laryngeal muscles, 192

Laryngoscope

- intubation and, 214

Laryngospasm, 301, 599, 617

Larynx, 192–193

LAST. *See* Local anesthetic systemic toxicity

Lefort classification, 561–562, 561f

Leukotriene (LT) modifying drugs, 40

Levetiracetam (Keppra)

- comments, 686
- dosage, 686
- effect, 686
- indications, 686

Levosimendan, 319

Licorice (*Glycyrrhiza glabra*), 661

Lidocaine (Xylocaine), 350, 425, 426, 430

- comments, 686
- dosage, 686
- effect, 686
- indications, 686

Light wand, 205

Line isolation monitors, 310

Lipophilic opioids, 239

Lithium dilution (LiDCO) technique, 147

Lithotomy/subgluteal approach, 281

Lithotripsy

- anesthesia, 465
- anesthetic options, 465
- complications, 465–466
- extracorporeal shockwave lithotripsy (ESWL), 465

Liver

- anatomy
 - blood supply, 64
 - structure, 64
- function (*see* Hepatic function)

- Liver disease
 - anesthesia, 72–74
 - anesthetics metabolism, intravenous barbiturates, 67
 - benzodiazepines and opioids, 67
 - etomidate, 67
 - induction agents, 66–67
 - ketamine, 67
 - neuromuscular blocking agents, 67
 - propofol, 66
 - cardiovascular system manifestations
 - ACM, 68–69
 - hyperdynamic circulatory state, 68
 - total body fluid volume, 68
 - central nervous system, 68
 - cholestasis, 68
 - coagulopathy, 70
 - gastrointestinal system manifestations, 69
 - glycemic control, 70
 - nutritional deficiency, 70
 - parenchymal
 - acute hepatocellular injury, 67–68
 - chronic parenchymal disease, 68
 - postoperative liver dysfunction
 - halothane hepatitis, 74
 - nonsurgical, 74
 - surgical causes, 74
 - renal system manifestations
 - hepatorenal syndrome, 70
 - prerenal azotemia, 69
 - water and electrolyte balance, 70
 - respiratory system manifestations
 - airway protection, 69
 - chronic hypoxemia, 69
 - surgical risk
 - mortality, 71
 - preoperative assessment, 71–72
 - risk assessment, 71, 71t, 72t
- Liver dysfunction, 389
- LMWH. *See* Low molecular weight heparin
- Local anesthetics
 - clinical uses of, 225t–226t
 - combinations of, 224
 - epinephrine, 224
 - meperidine, 227
 - opioids, 226
 - phenylephrine, 226
 - principles
 - chemistry, 222
 - commercial preparations of, 224
 - mechanism of action, 222–223, 223t
 - regional anesthesia, 256, 256f
 - sodium bicarbonate, 226–227
 - toxicity of
 - allergic reactions, 227
 - CNS, 228
 - CVS, 228
 - intravascular injection, 227–228
- Local anesthetic systemic toxicity (LAST), 227–229
- Lorazepam (Ativan), 13, 433, 606
- Lower airway, 193
- Lower-extremity bypass grafting, 371
- Lower extremity, regional anesthesia
 - anatomy, 274–276, 275f
 - complications, 277
 - indications, 276–277
 - techniques
 - adductor canal block, 279–280
 - ankle block, 284–285, 285f
 - fascia iliaca compartment block, 278
 - femoral nerve block, 278–279, 279f
 - ilioinguinal–iliohypogastric block, 277
 - LFC nerve block, 278, 278f
 - lumbar plexus block (psoas block), 277
 - obturator nerve block, 278f, 280
 - saphenous nerve block, 283–284
 - sciatic nerve block, 280–283, 281f, 283f, 284f
- Low molecular weight heparin (LMWH), 253, 686. *See also* Dalteparin (Fragmin); Enoxaparin (Lovenox)
- Lumbar, epidural anesthesia and hanging drop technique, 246
- loss-of-resistance techniques, 245–246
- Lumbar plexus, 274–275, 275f
- Lung transplantation
 - anesthetic technique, 365–366
 - bronchoscopies and biopsies, 366
 - following surgery, 366
 - monitors and equipment, 365
- Lung volume reduction surgery, 366
- Lysine analogues, 583–584

M

- Macintosh blade, 200, 202
- Macroshock, 310
- Mafenide acetate, 574
- Magnesium, 426
- Magnesium sulfate
 - comments, 687
 - dosage, 686
 - effect, 687
 - indications, 686
- Magnetic resonance imaging (MRI), 348, 545–547
- Major adverse cardiac event (MACE) risk, 18–19

- Malignant hyperthermia, 610
 anesthesia for, 308
 clinical features, 307
 etiology, 306
 neuroleptic malignant syndrome, 308
 syndromes, 308
 treatment, 307
- Malignant hyperthermia (MH), 181
- Mallampati classification, of airways, 195, 195f
- Malnutrition, 473–474
- Mannitol
 comments, 687
 dosage, 687
 effect, 687
 indications, 687
- MAOIs. *See* Monoamine oxidase inhibitors
- MAP. *See* Mean arterial pressure
- Mapleson D and F circuit, 126–127
- Mask, airway
 complications, 197
 indications, 196
 techniques, 196–197
 ventilation, 197
 ventilation and, 218
- Massive transfusion, 583
- Mass spectrometry, 129
- Mean arterial pressure (MAP), 422
- Mechanomyography, 187
- Meconium aspiration syndrome, 485
- Median minimal alveolar concentration (MAC) value, 155
- Median nerve block, 271–272, 273f
- Median sternotomy, 353
- Mediastinal surgery, 353
- Mediastinoscopy, 352
- Medication errors
 handoff errors, 116–117
 modification strategies, 114
- Medications, patient evaluation, 1
- MELD. *See* Model for end-stage liver disease
- Mental status, 373
- Meperidine, local anesthetics, 227
- MEPs. *See* Motor-evoked potentials
- Metabolic acidosis, 400, 401
- Metabolic complications, blood transfusions
 acid-base status, 587
 calcium, 587
 potassium (K⁺), 587
 stored blood, 587
- Metallic implants, 546
- Metformin, 370
- Methemoglobinemia, 229–230
- Methohexital, 545
- Methylene blue
 comments, 687
 dosage, 687
 effect, 687
 hemodynamic control, perioperative and, 319
 indications, 687
- Methylergonovine (methergine)
 comments, 688
 dosage, 687
 effect, 687
 indications, 687
- Methylprednisolone (Solu-medrol)
 comments, 688
 dosage, 688
 effect, 688
 indications, 688
- Methylxanthines, 39
- Metoclopramide (Reglan), 10
 comments, 688
 dosage, 688
 effect, 688
 indications, 688
- Metoprolol (Lopressor)
 comments, 688
 dosage, 688
 effect, 688
 hemodynamic control, perioperative and, 320, 321t
 indications, 688
- Metronidazole, 108
- MG. *See* Myasthenia gravis
- MH. *See* Malignant hyperthermia
- MI. *See* Myocardial infarction
- Microshock, 310
- Midazolam, 13, 444
- Miller blade, 202
- Milrinone, 550
 comments, 688
 dosage, 688
 effect, 688
 indications, 688
- Miotics, 443
- Mitral regurgitation (MR), 25, 396
- Mitral stenosis (MS), 396
 anesthetic considerations, 25
 etiology, 24
 pathophysiology, 24
- Mivacurium, 183–184
- Model for end-stage liver disease (MELD), 71
- Monitoring
 cardiovascular system
 arterial blood pressure, 134–136
 ECG, 133–134
 ischemia detection, 134
 mechanism of, 133–134

- rhythm detection, 134
 - signs/symptoms of perfusion abnormalities, 133
 - of CVP
 - analysis for, 137
 - cardiac output, 146–147
 - echocardiography, 147–148
 - indications of, 136–137
 - pathology and, 137
 - positive-pressure ventilation, 137–138
 - procedure, 138–141
 - pulmonary artery catheter procedure and, 141–145, 143f, 144f
 - waveform and, 137, 137f
 - of respiratory system
 - mandatory respiratory monitors, 148
 - oxygenation, 148
 - ventilation, 149–150, 149f
 - standard monitoring, 133
 - temperature monitoring, 150–151
 - Monoamine oxidase inhibitors (MAOIs), 554
 - Morphine, 607
 - Motor-evoked potentials (MEPs), 383, 456
 - Mouth, airways, 194
 - Mucolytics, 40
 - Muscle
 - laryngeal, 192
 - relaxants, 574–575
 - abdominal surgery, 333
 - Muscular dystrophies, 190
 - Musculocutaneous nerve block, 273
 - Myalgia, 180
 - Myasthenia gravis (MG), 189–190
 - Mydriatics, 442–443
 - Myocardial dysfunction, 27
 - Myocardial infarction (MI), 368
 - Myocardial ischemia, 304
 - and infarction, 604
 - Myocardial protection, 399
 - Myotonic dystrophy, 190–191
 - Myotonic syndromes, NMBDs, 190–191
 - Myxedema coma, 87
- N**
- N-acetylcysteine (NAC), 60, 369
 - Naloxone (Narcan)
 - action mode of, 172
 - adverse effects, 172
 - comments, 689
 - dosage, 688
 - dosage and administration, 172
 - effect, 689
 - indications, 688
 - pharmacodynamics of, 172
 - pharmacokinetics of, 172
 - Naproxen, 608
 - Narcotics, 61
 - Narcotrend, 155
 - Nasal cosmetic surgery, 448
 - Nasal surgery
 - anesthetic technique, 448
 - blood loss, 448
 - nasal cosmetic surgery, 448
 - severe epistaxis, 448–449
 - Nasotracheal intubation, 203
 - NASPE. *See* North American Society of Pacing and Electrophysiology
 - Nausea and vomiting, 243
 - Neck, airways, 194–195
 - Negative pressure pulmonary edema (NPPE), 617
 - Neonate
 - body composition, 476–477
 - cardiovascular development
 - anatomic, 476–477
 - fetal circulation, 477
 - cardiovascular disorders
 - congenital heart disease, 486
 - cyanosis, 486–487
 - dysrhythmias, 488
 - PDA, 487–488
 - PPHN, 488–489
 - electrolytes, 480
 - fluids, 479–480
 - gastrointestinal disorders
 - anesthetic considerations, 494
 - duodenal atresia, 492–493
 - EA, 492
 - gastroschisis, 493–494
 - hyperbilirubinemia, 490–491
 - NEC, 494–495
 - omphalocele, 493–494
 - pyloric stenosis, 493
 - TEF, 492
 - volvulus, 495
 - glucose, 480
 - hematologic disorders
 - hemolytic disease of the newborn, 489–490
 - hydrops fetalis, 490
 - laboratory studies, 479
 - maternal disorders, 477
 - neurologic disorders
 - infectious diseases, 498
 - intracranial hemorrhage, 496
 - myelodysplasia, 496–497
 - ROP, 497
 - seizures, 495–496
 - nutrition, 480–481

- Neonate (*Continued*)
 organogenesis, 475
 perinatal history, 477
 physical examination, 477–479
 preparation for surgery, 481–482
 respiratory development
 anatomic, 475
 PPHN, 475
 RDS, 475
 respiratory disorders
 apnea, 482–483
 BPD, 484
 CDH, 485–486
 differential diagnosis, 482
 laboratory studies, 482
 meconium aspiration syndrome, 485
 pneumothorax, 484–485
 RDS, 483
 resuscitation
 assessment, 635–636
 chest compressions, 637
 drugs and fluids, 637–638
 postresuscitation care, 638
 ventilation, 636
 thermoregulation, 481
 vital signs, 477, 477t
 Neostigmine, 187
 Nephrectomy, 463–464
 Nephrogenic diabetes insipidus, 98
 Nephropathy, contrast-induced, 545
 Nerve(s)
 fibers, local anesthetics and, 222–223, 223t
 localization techniques, in regional anesthesia, 257–260
 Neuraxial analgesia
 acute pain management
 buprenorphine maintenance therapy, 655–656, 656t
 perioperative management, 655, 655t
 continuous peripheral nerve blocks, 653–654, 654t
 epidural opioids, 650–651
 algorithm, 651–652, 652t
 checklist, 652, 653t
 complications, 653
 PCEA, 651
 pharmacologic management of, 651, 652t
 intrathecal opioids
 hydrophilic, 649
 lipophilic, 650–651
 Neuroleptic malignant syndrome (NMS), 308
 Neurologic deficits, 375
 Neuromuscular blockade, 614–615, 617
 clinical choice of, 185, 186t
 depolarizing, 180–183, 182f
 disorders, 188–191
 monitoring, 182f
 acceleromyography, 187
 clinical assessment, 186t
 double-burst stimulation, 187
 electromyography, 187
 mechanomyography, 187
 peripheral nerve stimulators, 185
 posttetanic count, 187
 posttetanic single twitch, 186
 single twitch, 186
 tetanic stimulus, 186
 TOF, 186–187
 NMJ, 177–178, 178f, 179t, 180t
 nondepolarizing, 179t, 180t, 183f
 atracurium, 184
 cardiovascular side effects, 185
 cisatracurium, 184
 clinical pharmacology, 179t, 183
 mivacurium, 183–184
 pancuronium, 184–185
 rocuronium, 184
 vecuronium, 184
 reversal of, 187–188
 succinylcholine, 180–183
 Neuromuscular blocking drugs, 177–191
 Neuromuscular junction (NMJ), 177–178, 178f, 179t, 180t
 Neuroradiologic procedures, anesthesia, 547–551
 Neurosurgery
 AVM, 433–435
 awake craniotomy, 436
 deep brain stimulators, 437
 electrophysiologic monitoring
 EEG, 427
 evoked potential monitoring, 427–428
 epilepsy surgery, 437–438
 head trauma, 438–439
 intracranial aneurysms, 433–434, 433t
 intraoperative management
 emergence, 430–431
 immediate postoperative care, 432–433
 induction of anesthesia, 429–430
 maintenance, 430
 perioperative fluid management, 431–432
 pharmacology
 cerebral protection, 426–427
 inhalation anesthetics, 425, 425t
 IV anesthetics, 425

- muscle relaxants, 425
 - vasoactive drugs, 425–426
 - physiology
 - CBF, 422, 423f
 - CMRO₂, 422–423
 - ICP, 423–424, 424f
 - pituitary gland, transsphenoidal resection of, 436–437
 - posterior fossa surgery, 435–436
 - preoperative considerations, 429
 - spine and spinal cord, 440–441
 - stereotactic surgery, 437
 - Neurotoxicity, 237
 - Nicardipine, 550
 - Nimodipine, 426
 - Nissen fundoplication, 336
 - Nitroglycerin, 304, 323–324, 384
 - comments, 689
 - dosage, 689
 - effect, 689
 - indications, 689
 - Nitroprusside (Nipride), 384
 - comments, 689
 - dosage, 689
 - effect, 689
 - indications, 689
 - Nitrous oxide (N₂O), 333, 425
 - Nitrous oxide effects, on brain, 160–161, 161f
 - NK-1 receptor antagonists, 610
 - NMJ. *See* Neuromuscular junction
 - NMS. *See* Neuroleptic malignant syndrome
 - Nociceptive–medullary–autonomic (NMA) circuit, 152
 - Non–heart-beating organ donation, 344
 - Noninvasive positive pressure ventilation (NPPV), 619
 - Nonosmotic loop, 55t
 - Nonsteroidal anti-inflammatory drugs (NSAIDs), 8–9, 590, 608
 - clinical uses, 641
 - COX inhibition, 640t
 - diclofenac, 641
 - GI toxicity, 640t
 - ketorolac, 641
 - mechanism, 639–640
 - nonopioid analgesics, 641, 642t
 - renal toxicity, 641t
 - toxicity, 640–641
 - Norepinephrine (Levophed), 384
 - comments, 690
 - dosage, 689
 - effect, 689
 - hemodynamic control, perioperative and, 317–318
 - indications, 689
 - Normovolemic hemodilution, 584
 - North American Society of Pacing and Electrophysiology (NASPE), 29
 - Nose, airways, 194–195
 - NPPE. *See* Negative pressure pulmonary edema
 - NPPV. *See* Noninvasive positive pressure ventilation
 - NSAIDs. *See* Nonsteroidal anti-inflammatory drugs
 - Nutritional deficiency, 70
- O**
- Obesity, 615–616
 - diabetes mellitus, 76, 84
 - renal disease risk, 54
 - Obstetrics and gynecology, 5. *See also* Labor; Pregnancy
 - Obstructive airway diseases, 33–34
 - Obstructive sleep apnea (OSA), 4, 616
 - Obturator nerve block, 278f, 280
 - OCR. *See* Oculocardiac reflex
 - Octreotide (Sandostatin)
 - comments, 690
 - dosage, 690
 - effect, 690
 - indications, 690
 - Oculocardiac reflex (OCR), 442
 - Ohm's law, 312
 - Oliguria, 345, 400, 605
 - Omalizumab, 40
 - Ondansetron (Zofran), 612
 - comments, 690
 - dosage, 690
 - effect, 690
 - indications, 690
 - One-lung ventilation
 - anesthetic management, 357
 - oxygenation, 356–357
 - difficulties, 357–358
 - ventilation, 357
 - Open-eye injury, 446
 - Operating room (OR)
 - anesthesia outside, 543–555
 - anesthetist, infection control, 101
 - antibiotics
 - aminoglycosides, 108
 - β-lactams, 107
 - clindamycin, 107
 - endocarditis, 106–107
 - fluoroquinolones, 108
 - indications for, 105
 - metronidazole, 108
 - prophylaxis principles, 105
 - SCIP, 105, 106t

- Operating room (OR) (*Continued*)
 surgical wounds, 107
 vancomycin, 107–108
 infection control
 aspiration pneumonia, 104
 CVC, 103–104
 hygiene standards, 103
 infection spread methods, 101
 infection spread prevention, 101
 standard precautions, 101–102
 transfusion-related infections, 104, 105t
 transmission-based precautions, 102–103
- Opioid(s), 13, 41, 58, 425, 614
 α_2 -Agonists, 648
 gabapentin, 648
 as inhalation anesthetic, 172–176, 172t
 as intravenous (IV) anesthetics
 action mode of, 170
 adverse effects, 171–172
 cardiovascular system, 171
 CNS, 170–171
 dosage and administration, 170, 171
 gastrointestinal system, 171
 pharmacodynamics of, 170–171
 pharmacokinetics of, 170, 170t
 respiratory system, 171
 as IV anesthetics, 647
 lidocaine, 648
 local anesthetics and, 226
 metabolism, 644, 644f–646f
 neuraxial analgesia
 epidural, 650–653, 652t, 653t
 intrathecal, 649–651
 oral, 647, 647t
 side effects, 644–645
- OR. *See* Operating room
- Oral anticoagulants, 253
- Orotacheal intubation
 complications of, 203
 indications, 200
 techniques, 200, 201f, 202–203
- Orthopedic disorders, 473
- Orthotopic liver transplantation, 342–343
- OSA. *See* Obstructive sleep apnea
- Osmotic diuresis, 605
- Osteoarthritis, 473
- Oxygen
 analyzers, 130
 audible alarm, 128
 supply-demand balance, 22
- Oxygenation, 356–357
- Oxytocin (Pitocin)
 comments, 690
 dosage, 690
 effect, 690
 indications, 690
- ## P
- Pacemakers
 five-letter code, 28–29
 ICD, 30–31
 indications, 29
 intraoperative management, 30
 pacing options, perioperative, 30
 permanent, preoperative evaluation, 29
- PACU. *See* Postanesthesia care unit
- Pain
 acute (*see* Acute pain)
 chronic, 639
 definitions, 639
 inflammatory, 639
 neuropathic, 639
 nociceptive, 639
 visceral, 639
- PALS. *See* Pediatric advanced life support
- Pancreatic surgery, 338
- Pancreatojejunostomy, 338
- Pancuronium, 67, 184–185
- Panhypopituitarism, 93
- PAOP. *See* Pulmonary artery occlusion pressure
- PAP. *See* Pulmonary artery pressure
- Papavarine, 550
- Papillary muscle rupture after
 myocardial infarction, 396
- Parathyroid disease
 hypercalcemia
 anesthetic considerations, 90
 bisphosphonates, 89–90
 clinical features of, 89, 89t
 etiologies of, 88–89
 gallium nitrate, 90
 glucocorticoid therapy, 90
 hydration, 89
 salmon calcitonin, 90
 treatment of, 89–90
 hypocalcemia
 anesthetic considerations, 91
 clinical features of, 90
 etiologies of, 90
 treatment of, 91
 physiology, 88
 serum calcium, 88
- Parathyroid hormone, 48
- Paravertebral nerve blocks, 359
- Parkinson disease, 472
- Parkland formula, 573

- Paroxysmal supraventricular tachycardia, 295
- Partial hepatectomy, 337
- Partial pressure of carbon dioxide (PaCO_2), 37
- Partial pressure of oxygen (PaO_2), 36–37
- Patent ductus arteriosus (PDA), 487–488
- Patient-controlled epidural analgesia (PCEA), 651
- Patient safety index (PSI), 154–155
- PCEA. *See* Patient-controlled epidural analgesia
- PCI. *See* Percutaneous coronary intervention
- PDA. *See* Patent ductus arteriosus
- PDPH. *See* Postdural puncture headache
- Pediatric advanced life support (PALS), 632–634
- Pediatric resuscitation
 - airway and breathing, 631
 - bradycardia algorithm, 634f
 - circulation, 631–632
 - PALS, 632–634
- Pediatric surgery
 - analgesia, 512
 - anatomy and physiology
 - cardiovascular system, 501, 502t
 - endocrine system, 503
 - fluid and electrolyte balance, 502
 - hematologic system, 502–503
 - hepatobiliary system, 503
 - pulmonary system, 500–501
 - temperature regulation, 503
 - upper airway, 500
 - compromised airway, 518–520
 - emergence and postanesthesia care
 - extubation, 517–518
 - PACU, 518
 - during transport, 518
 - endotracheal intubation
 - laryngeal mask airway, 512
 - muscle relaxants, 511–512
 - nasal approach, 511
 - oral approach, 511
 - fluid management
 - blood losses, 517
 - estimated blood volume (EBV), 517
 - estimated fluid deficit, 517
 - maintenance fluid requirements, 516–517
 - third-space losses, 517
 - induction techniques
 - full stomachs, 510–511
 - inhalation induction, 509–510
 - intramuscular induction, 510
 - IV induction, 510
 - sedation options, 508–509
- intra-abdominal malformations, 520–521
- neurotoxicity, 521–522
- operating room preparation
 - airway equipment, 506–507, 506t, 507t
 - anesthetic circuit, 505–506
 - IV setup and supplies, 508
 - monitoring, 507–508
 - perioperative/procedure huddle, 505
 - temperature control, 507
- periprocedural considerations and fasting guidelines
 - fasting guidelines, 505, 505t
- periprocedural considerations, 504–505
- pharmacotherapy
 - additional regional blocks, 513
 - brachial plexus block, 513
 - caudal and epidural anesthesia, 515–516
 - local anesthetics, pharmacology of, 513
 - nonopioid pharmacotherapeutic agents, 512
 - opioid therapy, 512–513
 - regional and neuraxial anesthesia, 513
 - spinal anesthesia, 514–515
- preanesthetic visit
 - history, 503–504
 - laboratory data, 504
 - physical examination, 504
 - upper respiratory infection, 520
- PEEP. *See* Positive end-expiratory pressure
- Pelvis trauma, 566
- PEP. *See* Post-exposure prophylaxis
- Percutaneous coronary intervention (PCI), 21–22
- Percutaneous lung biopsy, 551–552
- Percutaneous radiofrequency ablation, 552
- Peribulbar block, 444f, 445
- Pericardial tamponade, 396
- Pericardiocentesis, 564
- Perioperative coagulopathy
 - chronic liver disease, 589–590
 - disseminated intravascular coagulopathy
 - causes of, 589
 - clinical features, 589
 - laboratory features, 589
 - treatment of, 589
- massive transfusion
 - clotting factors, 589
 - thrombocytopenia, 589

- Perioperative coagulopathy (*Continued*)
 pharmacologic intervention
 direct factor Xa inhibitors, 591
 direct thrombin inhibitors, 591
 heparin, 590
 low molecular weight heparins, 590
 platelet inhibitors, 590
 thrombolytic agents, 591
 warfarin (coumadin), 590
 vitamin K deficiency, 590
 Perioperative hemodynamic control
 adrenergic pharmacology
 α -agonists, 314, 317
 β -agonists, 317
 mixed agonists, 317–318
 nonadrenergic agents, 319–320
 adrenergic receptor physiology
 α_1 receptors, 312
 α_2 receptors, 312, 314
 β_1 receptors, 314
 β_2 receptors, 314
 β_3 receptors, 314
 dopaminergic receptors, 314
 receptor regulation, 314
 autoregulation, 312
 β -adrenergic antagonists, 320, 321t, 322
 blood pressure, 312
 drug dosage calculations, 326
 induced hypotension, 325–326
 vasodilators
 adenosine, 325
 calcium channel antagonists, 324
 enalaprilat, 324–325
 fenoldopam, 325
 hydralazine, 324
 nitroglycerin, 323–324
 phenolamine, 325
 prostaglandin E_1 , 325
 sildenafil, 325
 sodium nitroprusside, 322–323
 Peripheral aneurysms, 372
 Peripheral embolectomy, 372
 Peripheral nerves, 222–223
 injury, 457
 stimulators, 185
 Peripheral neurological lesions, 607
 Perirectal abscess, 337
 Perirectal abscess drainage, 337
 Permanent pacemaker (PPM), 604
 Perphenazine, 610
 PFTs. *See* Pulmonary function tests
 Phantom limb pain (PLP), 386
 Pharmacologic stress testing, cardiac
 evaluation, 20
 Pharynx, 192
 Phenobarbital
 comments, 690
 dosage, 690
 effect, 690
 indications, 690
 Phenothiazines, 610
 Phenoxybenzamine
 comments, 690
 dosage, 690
 effect, 690
 indications, 690
 Phentolamine, 325
 Phenylephrine (Neosynephrine), 384, 442–443
 comments, 691
 dosage, 691
 effect, 691
 indications, 691
 local anesthetics and, 226
 Phenytoin (Dilantin)
 comments, 691
 dosage, 691
 effect, 691
 indications, 691
 Phosphorus (sodium phosphate)
 comments, 691
 dosage, 691
 effect, 691
 indications, 691
 Physostigmine (Antilirium), 606
 comments, 691
 dosage, 691
 effect, 691
 indications, 691
 Phytopharmaceuticals, 659
 Pilocarpine, 443
 Pilonidal cystectomy, 337
 Pituitary adenomas, 436
 Pituitary disease
 anterior pituitary gland
 hyperfunction, 96–97
 hypofunction, 97
 physiology, 96
 posterior pituitary gland
 diabetes insipidus, 97–98
 physiology, 97
 SIADH, 98
 Plasma substitutes
 albumin, 583
 hydroxyethyl starch, 583
 Pleural disease, 34
 PM. *See* Pringle maneuver
 Pneumomediastinum, 362
 Pneumopericardium, 335
 Pneumothorax, 303, 484–485, 552
 Poikilothermia, 344
 Polycystic kidney diseases, 54

- Polyuria, 345, 605
- PONV. *See* Postoperative nausea and vomiting
- Porphyria, 165
- Portal-systemic shunting, 66
- Portal vein flow (PVF), 64
- Positive end-expiratory pressure (PEEP), 333
- Postanesthesia care unit (PACU), 220, 449
 - admission, 594–595
 - body temperature changes, 610
 - definition, 594
 - discharge criteria, 610–611
 - fast-track recovery, 611
 - enhanced recovery after surgery, 612
 - extubation guidelines, 600–601
 - general complications, 595
 - hemodynamic complications
 - dysrhythmias, 603–604
 - hypertension, 602
 - hypotension, 601–602
 - intracardiac defibrillator, 604
 - myocardial ischemia and infarction, 604
 - permanent pacemaker, 604
- hypoventilation
 - pulmonary and respiratory muscle insufficiency, 598
 - ventilatory drive, decreased, 597
- hypoxemia
 - atelectasis, 596
 - bronchospasm, 596
 - diffusion hypoxia, 596
 - hypoventilation, 596
 - pneumothorax, 597
 - pulmonary edema, 596–597
 - pulmonary embolism, 597
 - upper airway obstruction, 596
- intubated patient, 600
- monitoring, 595
- neurological complications
 - delayed awakening, 606
 - emergence delirium, 606
 - intraoperative awareness and recall, 607, 607t
 - neurological damage, 606
 - peripheral neurological lesions, 607
- pain management principles
 - adjuvant analgesics, 608
 - continuous epidural analgesia, 608
 - IV patient-controlled analgesia, 608
 - nonsteroidal, 608
 - opioids, 607–608
 - regional sensory blocks, 608
- pediatric recovery considerations
 - agitation, 612
 - airway obstruction, 612
- PONV, 611–612
- postanesthesia recovery unit, critical care, 612
- postoperative nausea and vomiting, 608, 609f
 - antihistamines, 610
 - butyrophenones, 609
 - corticosteroids, 609
 - dexamethasone, 609
 - NK-1 receptor antagonists, 610
 - phenothiazines, 610
 - propofol, 610
 - serotonin antagonists, 608–609
 - transdermal scopolamine, 610
- regional and neuraxial anesthesia, recovery from, 610
- renal complications
 - electrolyte disturbances, 605
 - oliguria, 605
 - polyuria, 605
- respiratory and airway complications, 595–601
 - upper airway obstruction, 599–600
- Post-CPB pulmonary dysfunction, 389
- Postdural puncture headache (PDPH), 240
- Posterior fossa tumors, 435
- Posterior pituitary gland, 97–98
- Posterior tibial nerve, 285
- Post-exposure prophylaxis (PEP), 108–109
- Postobstructive diuresis, 605
- Postoperative analgesia, 359
- Postoperative nausea and vomiting (PONV), 446, 608–610, 609f, 662
- Postoperative pulmonary complications (POPCs), 33. *See also* Pulmonary disease
 - insufficiency, management
 - airway patency, 619
 - diagnostic approach, 619–620
 - noninvasive positive pressure ventilation, 619
 - reintubation, 619
 - respiratory distress causes, 620–621
 - secretion clearance, 619
 - supplemental oxygen, 618–619
 - monitoring, 618
 - prevention, 618
 - respiratory failure
 - anesthetics and sedatives effects, 614–615
 - definition, 614
 - patient-related comorbidities, 615–616
 - surgery-related factors, 615
 - upper airway obstruction, 617

- Postoperative respiratory failure (PRF)
 anesthetics effects
 intraoperative mechanical ventilation, 615
 residual neuromuscular blockade, 614
 respiratory drive, 614
 respiratory mechanics modification, 615
 definition, 614
 patient-related comorbidities
 aging, 615
 chronic obstructive pulmonary disease, 616
 low preoperative oxygen saturation, 615
 obesity, 615–616
 obstructive sleep apnea, 616
 respiratory tract infection, 616
 smoking, 616
 surgery-related factors, 615
 Postoperative visual loss (POVL), 457
 Post spinal pain syndrome (PSPS), 227
 Posttetanic potentiation (PTP), 186
 Posttonsillectomy hemorrhage, 449–450
 Potassium chloride (KCl)
 administration guidelines, 676
 indication, 676
 Potassium homeostasis disorders, 47–48
 POVL. *See* Postoperative visual loss
 PPCs. *See* Postoperative pulmonary complications
 Preanesthetic considerations, abdominal surgery
 full stomachs as, 329
 hematologic derangements, 329
 hypovolemia, 328–329
 length of surgery, 329
 metabolic derangements, 329
 preoperative fluid status, 328
 Preanesthetic evaluation, 1
 Precedex effects, on brain, 158–159
 Pregnancy
 amniotic fluid embolism (AFE), 537–538
 cardiopulmonary resuscitation, 540
 cardiovascular system, 523
 cesarean section, 533–534
 gastrointestinal system, 525
 gynecologic surgery, 540–541
 hematology, 523, 524
 labor and delivery
 definition, 526
 intrapartum fetal evaluation, 526–528, 527f
 medications, 528–530
 pain, 526
 placental transfer of drugs, 530
 and vaginal delivery, 530–533
 musculoskeletal, 525
 nervous system, 525
 nonobstetric surgery, 538, 540, 540t
 oocyte retrieval, 541
 peripartum hemorrhage, 536–537
 physiologic changes, 524t
 preeclampsia, 534–536, 534t
 renal system, 525
 respiratory system, 523
 Premedication(s), 408
 anesthesia
 antiemetic agents, 13, 14t
 glycopyrrolate, 13
 sedatives and analgesics, 13
 pulmonary disease, 41
 renal disease, 61
 Prerenal azotemia, 69
 Pressure alarms, 128
 Pressure regulators, 122, 124
 PRF. *See* Postoperative respiratory failure
 Pringle maneuver (PM), 73
 Prion diseases, 110–111
 Prochlorperazine (Compazine)
 comments, 692
 dosage, 691
 effect, 692
 indications, 691
 Promethazine (Phenergan), 610
 comments, 692
 dosage, 692
 effect, 692
 indications, 692
 Propofol, 58, 66, 425, 426, 444, 610
 as inhalation anesthetic, 172–176, 172t
 as intravenous (IV) anesthetics
 action mode of, 162
 adverse effects, 163–164
 cardiovascular system, 163
 CNS, 162–163
 dosage and administration, 163, 163t
 pharmacodynamics of, 162–163
 pharmacokinetics of, 162
 respiratory system, 163
 Propofol effects, on brain, 156, 158
 Propofol infusion syndrome, 164
 Propranolol (Inderal), 320, 321t
 comments, 692
 dosage, 692
 effect, 692
 indications, 692
 Prostaglandin E₁, 325
 Protamine
 comments, 692
 dosage, 692

- effect, 692
 - indications, 692
 - Prothrombin time, 579
 - Proton beam radiation therapy, 552
 - Proton pump inhibitors, 9
 - Proximal saphenous vein graft
 - anastomoses, 398
 - Pruritis, 243
 - Pseudocholinesterase, 64–65
 - PSI. *See* Patient safety index
 - PSPS. *See* Post spinal pain syndrome
 - PTP. *See* Posttetanic potentiation
 - Pulmonary artery catheters, 73
 - indications, 142
 - materials/catheter types, 142, 144
 - mechanism, 141–142
 - PA and PAOP, 142, 143f
 - pathology, 142
 - procedure, 144–145, 144f
 - securing, 145
 - Pulmonary artery occlusion pressure (PAOP), 141, 142, 143f
 - Pulmonary artery pressure (PAP), 141, 142
 - Pulmonary disease
 - anesthesia and surgery
 - breathing regulation, 37–38
 - ciliary function effect, 38
 - respiratory mechanics and gas exchange, 37
 - surgery effect, 38
 - anesthetic technique, 41–42
 - diagnostic studies
 - arterial blood gas tensions, 36–37
 - chest radiograph, 36
 - electrocardiogram, 36
 - pulmonary function tests, 37
 - history, 34–35
 - obstructive airway diseases
 - asthma, 34
 - COPD, 33–34
 - cystic fibrosis, 34
 - perioperative treatment, 38
 - anti-IgE antibody, 40
 - COPD/asthma, 38
 - corticosteroids, 40
 - cromolyn, 40
 - intraoperative management, 38
 - ivacaftor, 41
 - ketamine, 41
 - LT modifying drugs, 40
 - lung expansion maneuvers, 38
 - methylxanthines, 39
 - mucolytics, 40
 - parasympatholytics, 39
 - PDE4 inhibitor, 40
 - perioperative thromboembolism, 38
 - sleep apnea, 38
 - smoking cessation, 38
 - sympathomimetics, 39
 - physical findings
 - body habitus, 35
 - cardiovascular signs, 36
 - respiratory signs, 35–36
 - postoperative management, 42
 - premedication, 41
 - pulmonary hypertension, 34
 - restrictive pulmonary disease
 - extrinsic, 34
 - intrinsic, 34
 - Pulmonary edema, 34, 596–597
 - Pulmonary embolism
 - air embolism, 305
 - fat embolism, 305–306
 - thromboemboli, 305
 - Pulmonary embolus, 396
 - Pulmonary function tests (PFTs), 37, 348, 390
 - before anesthesia, 7
 - Pulmonary hypertension, 34
 - Pulmonary interstitial disease, 34
 - Pulmonary resection
 - anesthetic technique, 358
 - bronchial blockers, 355–356
 - emergence and extubation, 358–359
 - endobronchial tubes
 - double-lumen tubes range, 353
 - insertion, 354–355
 - right-and left-sided double-lumen tubes, 354
 - lung isolation techniques, 356
 - one-lung ventilation, 356–358
 - positioning, 356
 - postoperative analgesia, 359
 - surgical techniques, 353
 - univent tubes, 355
 - Pulmonary vascular resistance (PVR), 318
 - Pulse oximeters, 546
 - PVF. *See* Portal vein flow
 - PVR. *See* Pulmonary vascular resistance
- ## Q
- Quincke needle, 235
- ## R
- Radial nerve block, 272–273, 273f
 - Radiation therapy, anesthesia, 552–553
 - Radical neck dissection, 452
 - Radical retropubic prostatectomy (RRP), 462–463
 - Radiofrequency signals, 546
 - Ranitidine (Zantac), 9

- RAP. *See* Retrograde autologous priming
- Rapid sequence induction, 73
- airways
 - equipment/technique, 207–208
 - indications, 207
- Recombinant deoxyribonuclease, 40
- Recombinant factor VIIa (rFVIIa), 591
- Rectus sheath block, abdomen, 288–289
- Red cell mass, 577–578
- Regional anesthesia, 12, 72, 205
- abdomen
 - rectus sheath block, 288–289
 - thoracic paravertebral block, 286–287
 - transversus abdominis plane block, 287–288
 - for abdominal surgery, 329–330
 - complications
 - hematomas, 256–257
 - local anesthetics, 256, 256f
 - nerve damage, 256
 - consent for, 255
 - continuous catheter techniques, 257
 - equipment, 257, 258f
 - for head and neck surgery, 443–445
 - of lower extremity
 - anatomy, 274–276, 275f
 - complications, 277
 - indications, 276–277
 - techniques, 277–285, 278f, 279f, 281f, 283f–285f
 - for neck, cervical plexus block
 - anatomy, 260–261, 260f
 - complications, 261
 - indications, 261
 - techniques, 261–262
 - needles for
 - block, 257
 - nerve stimulators, 257, 258f
 - short bevel, 257
 - nerve localization techniques, 257–260
 - peripheral nerve blockade, 255
 - postoperative follow-up, 255
 - preoperative anxiety, 255
 - preoperative assessment, 255
 - thorax and abdomen, thoracic
 - paravertebral block for
 - anatomy, 286, 286f
 - complications, 286
 - contraindications, 286
 - indications, 286
 - techniques, 286–287
 - upper extremity
 - anatomy, 262, 263f, 264, 264f
 - axillary approach, 270–274, 270f, 272f–273f
 - complications, 265–274, 267f–270f, 272f, 273f
 - indications, 264–265
 - infraclavicular technique, 268–270, 269f
 - intrascalene technique, 265–266, 265f, 267f
 - median nerve block, 271–272, 273f
 - musculocutaneous nerve block, 273
 - radial nerve block, 272–273, 273f
 - supraclavicular technique, 266–268, 268f
 - techniques, 265–274, 267f–270f, 272f, 273f
 - ulnar nerve block, 271
- Remifentanyl, 444
- Renal blood flow, 44
- Renal insufficiency, 389
- Renal protection, 383
- Renal system
 - diseases of (*see* Kidney disease(s))
 - failure (*see* Kidney failure)
 - liver disease manifestations
 - hepatorenal syndrome, 70
 - prerenal azotemia, 69
 - water and electrolyte balance, 70
 - transplantation, anesthetic
 - management, 62
 - vascular surgery, preoperative
 - assessment, 369
- Renin-angiotensin-aldosterone system, 45
- Respiratory system, 4, 339
- liver disease, 69
 - monitoring
 - end-tidal carbon dioxide, 149–150
 - mandatory respiratory monitors, 148
 - oxygenation, 148
 - ventilation, 149–150
 - vascular surgery, preoperative
 - assessment, 369
- Restrictive pulmonary disease, 34
- Resuscitation
- adult
 - advanced cardiac life support, 624–629, 630f, 631
 - basic life support, 623–624
 - neonatal
 - assessment, 635–636
 - chest compressions, 637
 - drugs and fluids, 637–638
 - postresuscitation care, 638
 - ventilation, 636
 - pediatric, advanced life support, 632–634
 - pediatric, basic life support
 - airway and breathing, 631

bradycardia algorithm, 634f
 circulation, 631–632
 PALS, 632–634
 Retrobulbar block, 444, 444f
 Retrograde autologous priming (RAP), 398
 Retrograde tracheal intubation, 205
 Retroperitoneal (RP) approach, 378
 RHO immune globulin, 581
 Rh surface antigens, 581
 Rigid bronchoscopy, 207
 Rima glottidis, 193
 Rivaroxaban, 591
 Rocuronium, 67, 184
 Roflumilast, 40
 Roux-en-Y gastric bypass, 340
 RRP. *See* Radical retropubic prostatectomy
 Rule of nines, 570, 571f

S

Sacral plexus, 275–276
 Sacrococcygeal membrane, 251
 Saphenous nerve, 285
 Saphenous nerve block, 283–284
 Saw palmetto, 661
 SBP. *See* Systemic blood pressure
 Sch. *See* Succinylcholine
 Sciatic nerve block
 anterior approach, 282
 classic posterior/gluteal approach, 280–281, 281f
 foot and ankle, 280
 knee surgery, 280
 lithotomy/subgluteal approach, 281
 popliteal approach, 282–283, 283f
 subgluteal approach, 281–282
 thigh surgery, 280
 ultrasound guidance, 281–283, 281f
 283f
 SCIP. *See* Surgical Care Improvement Project
 Scleroderma, airways, 194
 Scopolamine, 443
 comments, 692
 dosage, 692
 effect, 692
 indications, 692
 SCV. *See* Subclavian vein
 Second gas effect, 174
 Sedation
 procedural, 544
 Sedatives, 13
 Seizures, 432–433
 Seldinger technique, internal jugular, 138–140, 139f

Selective serotonin reuptake inhibitors (SSRIs), 554
 Sellick maneuver, 208
 Sensory-evoked potentials (SEPs), 427–428
 Sepsis, 223
 Serotonin antagonists, 608–609
 Serum
 creatinine kinase, 190
 Serum osmolality, 432
 Severe hepatic disease, 223
 Sevoflurane, 56
 Sevoflurane effects, on brain, 158, 159f
 Shivering, 243
 Shunting
 hypoxemia, 297
 Shunting, portal-systemic, 66
 Shunts
 transjugular intrahepatic portosystemic, 551
 SIADH. *See* Syndrome of inappropriate antidiuretic hormone secretion
 Sickle cell anemia
 anesthetic management, 593
 clinical features, 592
 Sildenafil, 325
 Silver nitrate, 574
 Silver sulfadiazine, 574
 Sinus bradycardia, 293
 Sinus rhythms, normal, 24
 Sinus tachycardia, 293–294
 Sleep apnea, obstructive, 339
 Smoking cessation, 38
 Sniffing position, 202
 Sodium bicarbonate (NaHCO₃)
 local anesthetics and, 226–227
 vascular surgery, preoperative assessment, 369
 Sodium bicarbonate infusion (SBI), 60
 Sodium-glucose cotransporter 2 (SGLT2) inhibitors, 78
 Sodium homeostasis disorders, 45–47
 Sodium nitroprusside, 58, 322–323
 Somatosensory-evoked potentials (SSEPs), 383, 428, 456
 Spectral analysis, of EEG, 155–156
 Spinal and epidural anesthesia recovery, 610
 Spinal anesthesia
 anatomy
 CSF, 234
 interlaminar ligaments, 233
 interspinous ligament, 233
 ligamentum flavum, 233
 meninges, 234
 spinal canal in, 233, 233f
 spinal cord, 233
 subarachnoid space, 234

- Spinal anesthesia (*Continued*)
- complications and side effects
 - cardiovascular system, 240, 243
 - infections, 243
 - neurological, 239–240, 241t–242t
 - pruritis, 243
 - respiratory system, 243
 - shivering, 243
 - visceral, 243
 - determinants of spinal blockade
 - CSF turbulence, 238
 - CSF volume, 238
 - drug dose, 238
 - drug volume, 238
 - hyperbaric solutions, 238, 238t
 - hypobaric solutions, 238
 - intra-abdominal pressure, 238
 - isobaric solutions, 238
 - spinal curvatures, 238, 239f
 - durational determinants of spinal blockade in
 - drugs and dose, 239
 - vasoconstrictors, 239
 - physiological changes
 - cardiovascular system, 234
 - CNS, 235
 - neural blockade, 234
 - neuroendocrine, 235
 - respiratory system, 234
 - thermoregulation, 235
 - visceral effects, 235
 - techniques
 - patient position, 235–236
 - procedural, 236–237, 236f
 - spinal needle, 235
- Spinal angiography, 548–549
- Spinal blockade
- determinants of
 - CSF turbulence, 238
 - CSF volume, 238
 - drug dose, 238
 - drugs and dose, 239
 - drug volume, 238
 - hyperbaric solutions, 238, 238t
 - hypobaric solutions, 238
 - intra-abdominal pressure, 238
 - isobaric solutions, 238
 - spinal curvatures, 238, 239f
 - vasoconstrictors, 239
- Spinal cord injury, 458
- Spinal cord pathology, 466
- Spinal cord perfusion pressure (SCPP), 383, 457
- Spinal curvatures, 238, 239f
- Spinal hematoma, 240
- Spine surgery
- airway, 455
 - blood loss, 456
 - disposition, 458
 - monitoring, 456
 - positioning prone, 455–456
 - postoperative pain management, 458–459
- spinal cord injury, 455
- spinal cord perfusion
- bone cement embolism, 457
 - complications, 457–458
 - peripheral nerve injury, 457
 - POVL, 457
 - spinal cord injury, 458
 - VAE, 457
 - vascular injury, 458, 458t
- Splenectomy, 338
- Sprotte needle, 235
- SSRIs. *See* Selective serotonin reuptake inhibitors
- Stereotactic surgery, 437
- Sterilization, infectious diseases
- of reusable equipment, 103
 - techniques of, 103
- Steroids, 426
- St. John's wort, 661
- Stomach, full
- abdominal surgery, 329–330
- Strabismus repair, 446
- Streptokinase, 591
- Stress testing, cardiac disease, 20
- Strokes
- hemorrhagic, 606
 - ischemic, 606
- Subarachnoid injection, 249
- Subarachnoid space, in spinal anesthesia, 234
- Subclavian vein (SCV), 141
- Succinylcholine (SCh), 425
- laryngospasm, 301
 - neuromuscular blockade, 180–183
- Succinylcholine allergy, 2
- Sugammadex, 188
- Sulfonylureas, 76–77, 77t
- Superficial peroneal nerve, 285
- Superior laryngeal nerve, 192, 208
- Supplemental drug information, 673–676
- Supraventricular tachycardias (SVT)
- APCs, 294
 - atrial fibrillation, 295
 - atrial flutter, 295
 - junctional/AV nodal rhythms, 294–295
 - paroxysmal supraventricular tachycardia, 295
- Sural nerve, 285
- Surgery
- esophageal, 336
 - gastric, 336

- hepatic, 337
 - intestinal and peritoneal, 336–337
 - for obese
 - anesthetic management, 340–341
 - preanesthetic considerations, 339–340
 - surgical techniques, 340
 - pancreatic, 338
 - positioning of, 215
 - pulmonary function, effects of
 - breathing regulation, 37–38
 - ciliary function effect, 38
 - respiratory mechanics and gas exchange, 37
 - Surgical Care Improvement Project (SCIP), 105, 106t
 - Surrogate, 665
 - SVR. *See* Systemic vascular resistance
 - SVT. *See* Supraventricular tachycardias
 - Sympathetic blockade, 234
 - Sympathomimetics, for pulmonary disease, 39
 - Synaptic vesicles, 177
 - Synchronized cardioversion, 603
 - Syndrome of inappropriate antidiuretic hormone secretion (SIADH), 87, 98
 - Systemic acidosis, 385
 - Systemic air emboli, 27
 - Systemic blood pressure (SBP), 312, 646
 - Systemic vascular resistance (SVR), 646
 - caval compression, 291
 - decreased
 - allergic reactions, 290
 - sepsis, 290
 - sympathetic blockade, 290
 - vasoactive metabolites, 290
 - hypovolemia, 291
 - inadequate venous return, 291
 - intrathoracic pressure, 291
 - venous capacitance, 291
- T**
- Tachycardias
 - sinus, 293–294
 - supraventricular
 - APCs, 294
 - atrial fibrillation, 295
 - atrial flutter, 295
 - junctional/AV nodal rhythms, 294–295
 - paroxysmal supraventricular tachycardia, 295
 - ventricular, 295–296, 604
 - Tachydysrhythmias, 291, 603
 - Tachypnea, 35
 - TACO. *See* Transfusion-associated circulatory overload
 - TBSA. *See* Total body surface area
 - TBW. *See* Total body water
 - TEG. *See* Thromboelastography
 - Temperature
 - body, 610
 - monitoring, 150–151
 - Tension pneumocephalus, 433
 - Tension pneumothorax, 552
 - Terlipressin hemodynamic control, perioperative, 319
 - Tetanic stimulus, neuromuscular function and, 186
 - Tetracaine (Pontocaine), 225t
 - Tetralogy of Fallot, 409
 - TEVAR. *See* Thoracoabdominal aortic aneurysm repair
 - Thermal injuries, 189, 569–570
 - Thermomodulation, 146
 - Thermoregulation, 235
 - Thiazides (chlorothiazide, dyazide, and metolazone), 55t
 - Thiazolidinediones, 77t, 78
 - Thigh
 - anterior, 276
 - operations of, 276
 - Thiocyanate, 323
 - Thoracic aortic disease, etiology of, 381
 - Thoracic epidural anesthesia, 246
 - Thoracic paravertebral block, thorax and abdomen
 - anatomy, 286, 286f
 - complications, 286
 - contraindications, 286
 - indications, 286
 - techniques, 286–287
 - Thoracic surgery
 - bronchopleural fistula
 - anesthetic management, 363
 - general considerations, 362–363
 - endoscopic procedures
 - flexible bronchoscopy, 350
 - flexible esophagoscopy, 351–352
 - laser surgery, 352
 - rigid bronchoscopy, 350–351
 - rigid esophagoscopy, 352
 - esophageal surgery
 - anesthesia, 363–365
 - general considerations, 363
 - operative approach, 363–365
 - intrapulmonary hemorrhage, 362
 - lung transplantation, 365–366
 - lung volume reduction surgery, 366
 - mediastinal operations
 - chamberlain procedure, 352
 - mediastinal surgery, 353
 - mediastinoscopy, 352
 - monitoring, 349

Thoracic surgery (*Continued*)

- preoperative evaluation
 - ABG, 348
 - cardiac function, 348
 - chest radiography, 348
 - computed tomography (CT), 348
 - magnetic resonance imaging (MRI), 348
 - patients schedule, 348
 - pulmonary function tests, 348
 - three-dimensional reconstruction, 348
- preoperative preparation
 - airway obstruction, 349
 - glycopyrrolate, 349
 - heavy sedation, 348
 - preoperative sedation, 348–349
- pulmonary resection
 - anesthetic technique, 358
 - bronchial blockers, 355–356
 - emergence and extubation, 358–359
 - endobronchial tubes, 353–355
 - lung isolation techniques, 356
 - one-lung ventilation, 356–358
 - positioning, 356
 - postoperative analgesia, 359
 - surgical techniques, 353
 - univent tubes, 355
- tracheal resection and reconstruction
 - emergence and extubation, 361
 - general considerations, 359–360
 - intraoperative management, 360–361
 - tracheal disruption, 362
- Thoracoabdominal aortic aneurysm repair (TEVAR)
 - associated findings, 381–382
 - Crawford classification, 381, 382f
 - endovascular thoracic, 385
 - open thoracic aortic aneurysm repair, 382–385, 385t
 - thoracic aortic disease, etiology of, 381
- Thoracotomies, 356
- Thrombocytopenia, 570, 578, 589
- Thromboelastography (TEG), 579–580, 580f
- Thromboembolism, 38
 - pulmonary embolism, 305
- Thrombolysis of acute stroke, 549
- Thrombolytic agents, 253, 591
- Thrombophlebitis, superficial, 166
- Thymectomy, 353
- Thyroid disease
 - anesthesia, 5
 - cartilage of larynx, 192
 - evaluation and laboratory studies, 85
 - hypothyroidism
 - anesthetic considerations, 87–88
 - clinical features, 87
 - etiologies of, 87
 - myxedema coma, treatment, 87
 - treatment, 87
 - physiology, 84
 - thyroid surgery, 88
 - thyrotoxicosis
 - anesthetic considerations, 85–86
 - etiologies of, 85
 - hypermetabolic state, 85
 - thyroid storm, treatment, 85, 86t
 - treatment, 85
- Thyroid-stimulating hormone (TSH), 84
- Thyroid storm treatment, 85, 86t
- Thyroid surgery, 88, 452–453, 453f
- Thyromental distance, 194
- Thyrototoxicosis
 - anesthetic considerations, 85–86
 - etiologies of, 85
 - hypermetabolic state, 85
 - thyroid storm, treatment, 85, 86t
 - treatment, 85
- Ticlopidine, 590
- Timolol (Blocadren), hemodynamic control, perioperative, 321t
- Tiotropium (Spiriva), 39
- TIPS. *See* Transjugular intrahepatic portosystemic shunts
- Tissue plasminogen activator, 591
- TIVA. *See* Total intravenous anesthesia
- TNS. *See* Transient neurologic syndrome
- TOF. *See* Train-of-four
- Tonsillar or parapharyngeal abscess, 450
- Total body fluid volume, 68
- Total body surface area (TBSA), 570, 572
- Total body water (TBW), 44
- Total hepatic vascular exclusion (TVE), 73
- Total intravenous anesthesia (TIVA), 216, 358, 384, 448
- Tourniquet pain, 276
- T-piece systems, 126–127, 127f
- Trachea, 193
- Tracheal disruption, 362
- Tracheal stenosis, 348
- Tracheostomy, 195, 207
- Train-of-four (TOF), 186–187
- TRALI. *See* Transfusion-related acute lung injury
- Transabdominal approach, 378
- Transdermal scopolamine, 610
- Transduodenal sphincteroplasty, 338
- Transfusion-associated circulatory overload (TACO), 586

- Transfusion compatibility, 580, 580t
- Transfusion reactions
 - acute hemolytic transfusion reactions, 585, 585t
 - allergic transfusion reactions, 586
 - delayed hemolytic transfusion reactions, 585
 - FNHTR, 586
 - GVHD, 586–587
 - TACO, 586
 - TRALI, 586
- Transfusion-related acute lung injury (TRALI), 582, 586
- Transfusion therapy
 - blood component therapy
 - cryoprecipitate, 582
 - fresh frozen plasma, 581
 - massive transfusion, 583
 - substitutes, 583
 - technical considerations, 582
- blood typing and cross-matching
 - donor blood and recipient blood, 580–581, 580t
 - emergency, transfusion, 581
 - recipient antibodies, 581
 - Rh surface antigens, 581
- coagulation studies
 - ACT, 579
 - aPTT, 579
 - fibrinogen, 579
 - international normalized ratio, 579
 - prothrombin time, 579
 - TEG, 579–580, 580f
- coagulopathy, 578
- complications, blood
 - immunomodulation by, 588
 - infectious complications, 587–588
 - metabolic complications, 587
 - reactions, 585–587, 585t
- conservation and salvage techniques
- autologous donation, 584
- intraoperative autotransfusion, 584–585
- normovolemic hemodilution, 584
- hemophilia, 592
- Jehovah's witness, 593
- oxygen-carrying ability, 577–578
- perioperative coagulopathy
 - chronic liver disease, 589–590
 - disseminated intravascular coagulopathy, 589
 - massive transfusion, 588–589
 - pharmacologic intervention, 590–591
 - reversal of, 591
 - vitamin K deficiency, 590
- pharmacologic therapy
 - desmopressin, 583
 - erythropoietin, 583
 - lysine analogues, 583–584
- plasma substitutes
 - albumin, 583
 - hydroxyethyl starch, 583
- recombinant factor VIIa, 591
- red cell mass, 577–578
- sickle cell anemia, 592–593
- thrombocytopenia, 578
- von Willebrand disease, 592
- Transient neurologic syndrome (TNS), 239
- Transient paresthesias, 239
- Transjugular intrahepatic portosystemic shunts (TIPS), 337, 551
- Transplantation
 - cardiac, 414–415
 - heterotopic pancreatic, 343
 - liver, 342–343
 - lung
 - anesthetic technique, 365–366
 - bronchoscopies and biopsies, 366
 - following surgery, 366
 - monitors and equipment, 365
 - organ recovery for, 343–345
 - renal, 464–465
- Transpulmonary thermodilation, 146–147
- Transurethral resection of the prostate (TURP)
 - anesthesia, 461
 - complications, 461–462
 - cystectomy, 464
 - laser resection of prostate, 462
 - nephrectomy, 463–464
 - orchidopexy, 464
 - orchiectomy, 464
 - prostatic venous sinuses, 460–461
 - renal transplantation, 464–465
 - RRP, 462–463
 - urogenital plastic surgery procedures, 464
- Transversus abdominis plane (TAP)
 - block, abdomen
 - anatomy, 287
 - complications, 288
 - indications, 287–288
 - techniques, 288
- Trauma
 - abdominal, 564–565
 - airway, 194, 557–558
 - anesthetic management, 563
 - blunt, 567
 - breathing, 558
 - cardiac and major vascular trauma, 564
 - chest, 563

- Trauma (*Continued*)
 circulation, 558–559
 diagnostic studies, 559–560
 disability/neurologic evaluation, 559
 environmental control, 559
 facial
 anesthetic management, 562
 mandibular fractures, 562
 maxillary fractures, 561–562, 561f
 ocular, 562
 genitourinary, 565
 intracranial and spinal cord, 561
 maxillary fractures, 561–562, 561f
 monitoring, 560–561
 neck, 562–563
 orthopedic
 extremity reimplantation, 567
 fractures/dislocations, 566
 lower extremity, 567
 pelvis, 566
 upper extremity, 566
 in pediatrics, 567–568
 peripheral vascular, 564
 pregnant, 568–569
 Traumatic disruption, 381
 Tricuspid regurgitation, 146
 Tricyclic antidepressants, 554
 Trigeminal neuralgia, 550–551
 Trisomy 21 patients, 194
 True allergic reactions, anesthesia, 2
 TSH. *See* Thyroid-stimulating hormone
 Tubulointerstitial diseases, 53–54
 Tumors
 airway, 193
 carcinoid, 98
 Tuohy/Weiss needle, 244
 TURP. *See* Transurethral resection of the prostate
 TVE. *See* Total hepatic vascular exclusion
- U**
- Ulnar nerve block, 271
 Ultrasound
 equipment, regional anesthesia, 257
 guidance, regional anesthesia and, 259–260, 281–283, 281f, 283f, 285
 Unfractionated heparin, 253
 Univent tubes, 355
 Upper airway obstruction, 617
 Upper airway surgery
 direct laryngoscopy, 450
 laser, 450–451
 tonsillar or parapharyngeal abscess, 450
 tonsillar rebleeding, 449–450
 tonsillectomy and adenoidectomy, 449
 Upper extremity
 regional anesthesia
 anatomy, 262, 263f, 264, 264f
 complications, 265–274, 267f–270f, 272f, 273f
 indications, 264–265
 techniques, 265–274, 267f–270f, 272f, 273f (*see also* Regional anesthesia)
 vascular surgery of, 372
 Upper respiratory infection (URI), 4
 Ureter, 565
 Ureteroscopy, 460
 Urethra, 565
 URI. *See* Upper respiratory infection
 Urinalysis, 59
 Urinary retention, 172, 243
 Urine
 electrolytes, 59
 output
 abnormal, 298
 anuria, 298
 high, 298
 oliguria, 298
 Urologic surgery
 cystectomy, 464
 cystoscopy and ureteroscopy, 460
 laser resection of prostate, 462
 lithotripsy, 465–466
 nephrectomy, 463–464
 orchidopexy, 464
 orchiectomy, 464
 radical retropubic prostatectomy (RRP), 462–463
 renal transplantation, 464–465
 spinal cord injury, 466
 transurethral resection of the bladder (TURB), 460
 transurethral resection of the prostate (TURP), 460–462
 urogenital plastic surgery procedures, 464
- V**
- VAD. *See* Ventricular assist devices
 Vagal nerve stimulators (VNS), 438
 Vagal tone, dysrhythmias and, 293
 Valerian, 661
 Valvular heart disease, 368
 aortic regurgitation, 24
 aortic stenosis
 anesthetic considerations, 24
 cardiac pacing, 24
 etiology, 23

- ischemia treatment, 24
- nitrates and peripheral vasodilators, 24
- normal sinus rhythm, 24
- pathophysiology, 23
- symptoms, 23
- ventricle, 24
- mitral regurgitation, 25
- mitral stenosis
 - anesthetic considerations, 25
 - etiology, 24
 - pathophysiology, 24
- Valvular lesions, 396
- Vancomycin, 107–108
- Vaporizers, 124
- Varicella-Zoster virus (VZV), 110
- Vascular cannulation, 12
- Vascular diseases, DM and, 83
- Vascular injuries, 335
- Vascular injury, 458, 458t
- Vascular occlusion catheters, 355
- Vascular surgery
 - abdominal aortic repair
 - EVAR, 375–377
 - open abdominal aortic surgery, 378–379
 - ruptured abdominal aortic
 - aneurysm, emergent repair of, 380–381
- amputations
 - general considerations, 385–386
 - phantom limb pain (PLP), 386
- carotid revascularization
 - carotid artery stenting, 373
 - carotid endarterectomy, 373–375
 - general considerations, 372–373
- peripheral arterial surgery
 - axillofemoral bypass grafting, 372
 - femoral pseudoaneurysm, 372
 - general considerations, 370
 - lower-extremity bypass grafting, 371
 - percutaneous balloon angioplasty
 - and stenting, 370–371
 - peripheral aneurysms, 372
 - peripheral embolectomy, 372
 - upper extremity, 372
- preoperative assessment and management
 - cardiovascular system, 368–369
 - central nervous system, 370
 - endocrine system, 370
 - hematologic system, 370
 - renal system, 369
 - respiratory system, 369
- TEVAR
 - associated findings, 381–382
 - Crawford classification, 381, 382f
 - endovascular thoracic, 385
 - open thoracic aortic aneurysm
 - repair, 382–385, 385t
 - thoracic aortic disease, etiology of, 381
- Vasoactive agents, 58
- Vasoactive drugs, 425–426
- Vasoconstrictors, spinal anesthesia, 239
- Vasodilation, 601
- Vasodilators, 384, 426
 - perioperative hemodynamic control
 - adenosine, 325
 - calcium channel antagonists, 324
 - enalaprilat, 324–325
 - fenoldopam, 325
 - hydralazine, 324
 - nitroglycerin, 323–324
 - phenolamine, 325
 - prostaglandin E₁, 325
 - sildenafil, 325
 - sodium nitroprusside, 322–323
- Vasopressin (antidiuretic hormone, pitressin)
 - comments, 693
 - dosage, 693
 - effect, 693
 - indications, 693
- Vasopressors, 384
- Vecuronium, 67, 184
- Venous air embolism, 435
- Venous capacitance, increased, 291
- Venous gas embolism, 335
- Venous return, inadequate, 291
- Ventilation
 - airway mask, 197, 218
 - alveolar, 173, 173f
 - assessment of, 217
 - controlled, 216–217
 - during general anesthesia, 216–217
 - hypercarbia, 297–298
 - spontaneous/assisted, 216
- Ventilation, positive-pressure, 37
- Ventilators
 - anesthesia machines, 127–128
 - microprocessor-controlled, 128
- Ventral herniorrhaphies, 337
- Ventricular assist devices (VAD), 416–417
- Ventricular dysrhythmias
 - ventricular fibrillation, 296
 - ventricular preexcitation, 296
 - ventricular premature contractions, 295–296
 - ventricular tachycardia, 296
- Ventricular fibrillation, ventricular dysrhythmias, 296

- ventricular preexcitation, ventricular dysrhythmias, 296
 - Ventricular septal defect (VSD), 396
 - Venturi masks, 618
 - Verapamil, 603
 - comments, 693
 - dosage, 693
 - effect, 693
 - hemodynamic control, perioperative, 324
 - indications, 693
 - Vertebral artery injections, 261
 - Vertebroplasty, 549
 - Viruses, infection control in OR
 - CMV, 110
 - HBV, 109
 - HCV, 109
 - HIV, 108–109
 - HSV I and II, 109–110
 - influenza virus, 110
 - VZV, 110
 - Vital signs, 5–6
 - Vitamin D, 48, 88
 - Vitamin E, 662
 - Vitamin K, 70
 - comments, 693
 - deficiency, 590
 - dosage, 693
 - effect, 693
 - indications, 693
 - VNS. *See* Vagal nerve stimulators
 - Vocal cords
 - laryngospasm, 301
 - paralysis, 600, 617
 - Volatile anesthetics
 - inhalation anesthetics and, 173
 - cardiovascular system, 175
 - CNS, 175
 - hepatic system, 175
 - neuromuscular system, 175
 - renal system, 175
 - respiratory system, 175
 - narcotics and, 61
 - Vomiting
 - aspiration, 302
 - postoperative, 608–610, 609f
 - von Willebrand disease, 592
 - VSD. *See* Ventricular septal defect
 - VZV. *See* Varicella-Zoster virus
- W**
- Wake-up test, 456
 - Warfarin (Coumadin), 369, 590
 - comments, 694
 - dosage, 694
 - effect, 694
 - indications, 694
 - Waste gas scavenging, 543
 - Water
 - electrolyte balance and, 70
 - intake, daily, 45
 - Weiss needles, 244
 - West nile virus (WNV), 588
 - Wheezing, 302
 - Whitacre needle, 235
 - WNV. *See* West nile virus
 - Wolff–Parkinson–White syndrome, 296
 - Wound, infection control in OR, 107
 - Wrists, 271–273, 273f
- Z**
- Zenker diverticulum, 363
 - Zingiber officinalis*, 660

This page intentionally left blank.