SPRINGER PUBLISHING COMPANY

Carole Kenner • Leslie B. Altimier • Marina V. Boykova
EDITORS

SIXTH EDITION

COMPREHENSIVE NEONATAL NURSING CARE

Comprehensive Neonatal Nursing Care

Carole Kenner, PhD, RN, FAAN, FNAP, ANEF, is the Carol Kuser Loser Dean/Professor of the School of Nursing, Health, and Exercise Science at The College of New Jersey. Dr. Kenner received a bachelor's of science in nursing from the University of Cincinnati and her master's and doctorate in nursing from Indiana University. She specialized in neonatal/perinatal nursing for her master's and obtained a minor in higher education for her doctorate. She has authored more than 100 journal articles and 30 textbooks.

Her career is dedicated to nursing education and to the health of neonates and their families, as well as educational and professional development of healthcare practices in neonatology. Her dedication includes providing a healthcare standard for educating neonatal nurses nationally and internationally. Her passion led her to begin the journal *Newborn and Infant Nursing Reviews*, in which she served as editor and then associate editor. She worked with the National Coalition on Health Professional Education in Genetics (NCHPEG) and the American Nurses Association to develop genetic competencies. She helped develop the End-of-Life Nursing Education Consortium (ELNEC) Neonatal/Pediatric modules. She served as the co-chair of the Oklahoma Attorney General's Task Force on End of Life/Palliative Care. She also helped develop program recommendations for perinatal/neonatal palliative care as part of a family-centered/developmental care project sponsored by the National Perinatal Association. She serves on the Consensus Committee of Neonatal Intensive Care Design Standards, which sets recommendations for Neonatal Intensive Care Unit designs, and serves on the March of Dimes Nursing Advisory Committee. She is a fellow of the American Academy of Nursing (FAAN), a fellow in the National Academies of Practice, a fellow in the Academy of Nursing Education, past president of the National Association of Neonatal Nurses (NANN), and founding president of the Council of International Neonatal Nurses (COINN), the first international organization representing neonatal nursing-setting standards globally. She is the 2011 recipient of the Audrey Hepburn Award for Contributions to the Health and Welfare of Children Internationally.

Leslie B. Altimier, DNP, RNC, MSN, NE-BC, is the director for clinical innovation and research for Phillips HealthTech, where she is responsible for developing clinical analytic support algorithms and research tools for future NICU technology. She received her BSN from Kent State University, MSN from the University of North Carolina, DNP from Northeastern University in Boston, and she completed a postdoctoral fellowship in compassionate healthcare through the Northeastern University in collaboration with the Schwartz Center for Compassionate Healthcare and the Jonas Center for Nursing and Veterans Healthcare. In her 30-year nursing career, she has worked in a variety of neonatal, pediatric, and adult intensive care units, and has been a clinical director of nursing for a hospital network consisting of a 50-bed level III NICU and multiple level II NICUs.

Dr. Altimier is a renowned clinician who lectures internationally and has published over 100 articles, chapters, and books on topics related to the care of neonates and families, NICU design, and organizational leadership. She was the editor-in-chief of *Newborn and Infant Nursing Reviews (NAINR)* journal and most recently is the editor-in-chief of the *Journal of Neonatal Nursing (JNN)*, the official journal of the Neonatal Nurses Association (NNA). She is a member of NANN (the National Association of Neonatal Nurses), COINN (Council of International Neonatal Nurses, Inc.), and INANE (the International Academy of Nurse Editors). She also holds a nursing executive certification by the AANC (American Nurses Credentialing Center).

Dr. Altimier has contributed to nursing through practice, education, leadership, research, and publications. She is passionate about neuroprotective developmental care, family-integrated care, and compassionate care and has earned the Neonatal Developmental Care Specialist Designation from NANN. Her goal is to create a culture of change in healthcare worldwide.

Marina V. Boykova, PhD, RN, is an assistant professor of nursing in the School of Nursing and Allied Health Professions, Holy Family University, Philadelphia, Pennsylvania. Dr. Boykova received her Diploma in Nursing Practice from the School of Nursing #3, Saint Petersburg, Russia; a Certificate in Theory and Practice of Nurse Education, Medical College #1, Saint Petersburg, Russia; a Certificate in Theory and Practice of Nurse Education, Chester, United Kingdom; Bachelor of Science with Honours in Professional Practice (Nursing), University of Liverpool, Chester, United Kingdom; Diploma of Higher Education in Nursing, Novgorod University of Y. Mudrogo, Novgorod, Russia; Master of Science in Health Promotion (Distinction), University of Liverpool, Chester, United Kingdom; and Doctor of Philosophy in Nursing, University of Oklahoma, Oklahoma City, Oklahoma. She is a member of Sigma Theta Tau International. She serves as a nonexecutive director for the Council of International Neonatal Nurses, Inc. (COINN). Dr. Boykova's clinical background is neonatal intensive care nursing. Her research interests center on transition from hospital to home and to primary care for parents of preterm infants. She has published in this area as well as neonatal care topics. She coauthored a policy brief on Reducing Preterm Births for the American Academy of Nursing.

Comprehensive Neonatal Nursing Care

Sixth Edition

Carole Kenner, PhD, RN, FAAN, FNAP, ANEF
Leslie B. Altimier, DNP, RNC, MSN, NE-BC
Marina V. Boykova, PhD, RN

SPRINGER PUBLISHING COMPANY

Springer Publishing Company, LLC
11 West 42nd Street
New York, NY 10036
www.springerpub.com
http://connect.springerpub.com

Acquisitions Editor: Elizabeth Nieginski
Compositor: S4Carlisle Publishing Services

ISBN: 978-0-8261-3909-2
e-book ISBN: 978-0-8261-3914-6
DOI: 10.1891/9780826139146

19 20 21 22 / 5 4 3 2 1

Cataloging in Publication Data is available from the Library of Congress.
LCCN Number: 2019020459

Carole Kenner: https://orcid.org/0000-0002-1573-5240
Leslie B. Altimier: https://orcid.org/0000-0001-8558-3011
Marina V. Boykova: https://orcid.org/0000-0002-9065-3704

Printed in the United States of America.

I wish to first express my appreciation, love, and support for my dad, who died in 2017 at the age of 105½. He always got excited when a new edition published.
—Carole

I would like to thank my children, Jen, Julie, and Kevin, for their love, support, and encouragement for me as a mom and as a professional.
—Leslie

For my mom, whose love and support were endless.
—Marina

Together we would like to express our appreciation for the assistance of Margaret Zuccarini, from Springer Publishing Company, who is a longtime trusted colleague who guided this project, along with Elizabeth Nieginski, who took over from Margaret, to a successful birth. Thank you for believing in this project. A special thank-you goes to Joanne Jay from Springer for all the assistance and guidance through the development and publication. We really enjoyed working with all of you. Finally, we want to thank the professionals across the globe who take care of the babies and their families.
—Carole Kenner, Leslie Altimier, and Marina Boykova

Contents

Contributors

Leslie B. Altimier, DNP, RNC, NE-BC
Director of Clinical Innovation and Research
Phillips Research and Development
Cambridge, Massachusetts

Diane M. Anderson, PhD, RD
Associate Professor
Department of Pediatrics, Section of Neonatology
Baylor College of Medicine
Houston, Texas

Shreyas Arya, MD, MBBS
Clinical Fellow
Division of Neonatology and Pulmonary Biology
Cincinnati Children's Hospital Medical Center
Cincinnati, Ohio

Gail A. Bagwell, DNP, APRN, CNS
Clinical Nurse Specialist—Perinatal Outreach
Nationwide Children's Hospital
Columbus, Ohio

Susan Tucker Blackburn, PhD, RN, FAAN
Professor Emeritus
Department of Family and Child Nursing,
School of Nursing
University of Washington
Seattle, Washington

Mary Beth Bodin, DNP, CRNP, NNP-BC
Neonatal Consultant
Tuscaloosa, Alabama

Marina V. Boykova, PhD, RN
Assistant Professor
School of Nursing and Allied Health
Holy Family University, School of Nursing
and Allied Health
Philadelphia, Pennsylvania

Caitlin Bradley, MS, NNP-BC, RN
Neonatal Nurse Practitioner
Boston Children's Hospital
Boston, Massachusetts

Ashlea D. Cardin, OTD, OTR/L, BCP
Assistant Professor of Occupational Therapy
Missouri State University
Springfield, Missouri

Waldemar A. Carlo, MD
Edwin M. Dixon Professor of Pediatrics
Division Director, Neonatoloygy
UAB Division of Neonatology
University of Alabama at Birmingham
Birmingham, Alabama

Terri A. Cavaliere, DNP, NNP-BC, RN
Clinical Associate Professor
Stony Brook University
Stony Brook, New York
Neonatal NNP Cohen Children's Hospital at North Shore
Manhasset, New York

Robin Dawn Clark, MD
Professor of Pediatrics in Medical Genetics
Loma Linda University Health
Loma Linda, California

Amy D'Agata, PhD, MS, RN
Assistant Professor, College of Nursing
University of Rhode Island
Kingston, Rhode Island
Adjunct Assistant Professor, Department of Pediatrics
Brown University
Providence, Rhode Island

Deborah A. Discenza, MA
Founder, President
PreemieWorld, LLC
Springfield, Virginia

Georgia R. Ditzenberger, PhD, NNP-BC, APNP
Assistant Professor, CHS
Neonatology Division, Department of Pediatrics, University of Wisconsin, School of Medicine and Public Health
Madison, Wisconsin

Jenna L. Dobry, BSc (Hon)
Clinical Research Coordinator
Section of Neonatology, Department of Pediatrics
Cummings School of Medicine
University of Calgary
Calgary, Alberta, Canada

Dolores R. Dzubaty, PhD, MSN, RNC-OB
Assistant Professor, Department of Nursing
School of Nursing, Health, and Exercise Science
The College of New Jersey
Ewing, New Jersey

Taryn M. Edwards, MSN, CRNP, NNP-BC
Neonatal Nurse Practitioner
Division of General, Thoracic, and Fetal Surgery
Children's Hospital of Philadelphia (CHOP)
Philadelphia, Pennsylvania

Kelly Benham French
Parent and Professor of Practice in Journalism
The Media School
Indiana University
Bloomington, Indiana

Samuel Gentle, MD
Assistant Professor
Division of Neonatology
University of Alabama at Birmingham
Birmingham, Alabama

Donna A. Goff, MD, MS
Assistant Professor of Pediatrics
Attending Physician in Pediatric Cardiology
Loma Linda University Children's Hospital
Loma Linda, California

Kathleen Haubrich, PhD, RN
Associate Professor, Department of Nursing
Miami University
Hamilton, Ohio

Stephanie Hoe, BSN, RN
Neonatal Staff Nurse
Kapiolani Medical Center for Women & Children
Caring for Hawai'i Neonates,
Honolulu, Hawaii

Jacqueline Hoffman, DNP, APRN, NNP-BC
Assistant Professor, Department of Nursing
Department of Women, Children and Family Nursing
College of Nursing
Rush University
Chicago, Illinois

Diane Holditch-Davis, PhD, RN, FAAN
Associate Dean for Research Affairs
Duke University School of Nursing
Durham, North Carolina

Kathleen P. Juco-Purdy, BSN, RN, CNOR
Lead of Transplant Service
Seattle Children's Hospital
Seattle, Washington

Susan Kau, BSN, RNC-NIC
Neonatal Staff Nurse
Kapiolani Medical Center for Women & Children
Caring for Hawai'i Neonates
Honolulu, Hawaii

Carole Kenner, PhD, RN, FAAN, FNAP, ANEF
Carol Kuser Loser Dean/Professor
School of Nursing, Health, and Exercise Science
The College of New Jersey
Ewing, New Jersey
Founding President
Council of International Neonatal Nurses, Inc. (COINN)
Yardley, Pennsylvania

Joanne McManus Kuller, RN, MS
Neonatal Clinical Nurse Specialist
University of California at San Francisco Benioff Children's Hospital Oakland
Oakland, California

Abhay Lodha, DM, MD, MBBS, MSC
Associate Professor
Department of Pediatrics
Cumming School of Medicine,
University of Calgary
Calgary, Alberta, Canada

Carolyn Houska Lund, MS, RN, FAAN
Neonatal Clinical Nurse Specialist
University of California at San Francisco Benioff Children's Hospital Oakland
Associate Professor
University of California at San Francisco School of Nursing
Oakland, California

Christina Mahoney, BSN, RN
Staff Nurse
Neonatal Intensive Care Unit
Boston Children's Hospital
Boston, Massachusetts

Maureen F. McCourt, MS, RN, NNP-BC, PNP
Instructor, NNP Program
Northeastern University
Boston, Massachusetts
Neonatal Nurse Practitioner Supervisor
Women and Infants Hospital
Providence, Rhode Island

Jacqueline M. McGrath, PhD, RN, FNAP, FAAN
Vice Dean for Faculty Excellence
School of Nursing
University of Texas at San Antonio
San Antonio, Texas

Kathryn R. McLean, MSN, RN, NNP-BC
Neonatal Nurse Practitioner
Women and Infants Hospital
Providence, Rhode Island

Mary E. Coughlin McNeil, MS, NNP, RNC-E
President and Founder
Caring Essentials Collaborative, LLC
Boston, Massachusetts

Tamara M. Meeker, MSN, CRNP, NNP-BC
Neonatal Surgical Nurse Practitioner
Division of General, Thoracic, and Fetal Surgery
Children's Hospital of Philadelphia (CHOP) NICU
Philadelphia, Pennsylvania

Samual Mooneyham, MSN, RN
Clinical Nurse Manager
Brookline Pediatrics
Brookline, Massachusetts

Merry-K. Moos, BSN, FNP, FAAN
Research Professor (retired)
Department of Obstetrics and Gynecology
University of North Carolina at Chapel Hill,
School of Medicine
Consultant, Center for Maternal and Infant Health
Lead Nurse Planner, National March of Dimes
President, MK Moos, Inc.
Chapel Hill, North Carolina

Dorothy M. Mullaney, DNP, MHSc, ANPRN, NNP-BC, RN
Director, Associate Providers
Dartmouth Hitchcock Medical Center
Assistant Professor of Pediatrics
Geisel School of Medicine at Dartmouth
Hanover, New Hampshire

Vivek Narendran, MD, MBA, MRCP
Medical Director University of Cincinnati Medical Center NICU
Medical Director, Cincinnati Perinatal Outreach Project
Department of Pediatrics
Univerisity of Cincinnati
Cincinnati Children's Hospital Medical Center
Cincinnati, Ohio

Susan K. Newbold, PhD, RN-BC, FAAN, FHIMSS
Director, Nursing Informatics Boot Camp
Franklin, Tennessee

Khiet D. Ngo, DO, MS
Assistant Professor of Basic Sciences & Clinical Medicine
Department of Medical Education & Pediatrics
Loma Linda University School of Medicine
Loma Linda University Children's Hospital
Loma Linda, California

Debra M. Parker, MSN, APRN-NP
Lead Neonatal Nurse Practitioner
Methodist Women's Hospital
Omaha, Nebraska

Leslie A. Parker, PhD, NNP-BC, FAAN
Associate Professor
University of Florida
Gainesville, Florida

Raylene M. Phillips, MD, FAAP, FABM, IBCLC
Neonatologist
Loma Linda University Children's Hospital
Loma Linda, California

Lyn S. Prater, PhD, RN
Senior Lecturer and Undergraduate Clinical Coordinator
Baylor University, School of Nursing
Dallas, Texas

Shahirose S. Premji, PhD, MScN, BSc, BScN, RN, FAAN
Director and Professor
School of Nursing, Faculty of Health
York University
Toronto, Ontario, Canada

Jana L. Pressler, PhD, RN
Assistant Dean and Professor
University of Nebraska Medical Center College of Nursing
Lincoln Division
Lincoln, Nebraska

Geralyn Sue Prullage, DNP, APN, NNP/PNP-BC
Neonatal and Pediatric Nurse Practitioner
Optimus Hospitalist and Pediatric Subspecialists, Ltd.
Chicago, Illinois

Cheryl Riley, DNP, RN, NNP-BC
Clinical Associate Professor and NNP Program Coordinator
Baylor University, School of Nursing
Dallas, Texas

Lori Baas Rubarth, PhD, APRN, NNP-BC
Associate Professor and NNP Program Coordinator
Creighton University School of Nursing
Omaha, Nebraska

Donna J. Ryan, DNP, RN, CNE
Assistant Professor, Nurse Educator
Elmira College
Elmira, New York

Manoj Shah, MD, FAAP
Chief Pediatric Gastroenterology & Nutrition
Loma Linda University School of Medicine
Loma Linda, California

Elizabeth L. Sharpe, DNP, ARNP, NNP-BC, VA-BC, FAANP
Associate Professor of Clinical Nursing
Neonatal Nurse Practitioner Program Specialty Track Director
The Ohio State University
Columbus, Ohio

Beth Shields, PharmD
Associate Director of Operations
Pediatric Clinical Specialist
Rush University Medical Center
Chicago, Illinois

Kaye Spence, AM, RN, MN
Adjunct Associate Professor
Clinical Nurse Consultant—Neonatology
Grace Centre for Newborn Care
The Children's Hospital at Westmead
Westmead, Australia

Becky Spencer, PhD, RN, IBCLC
Assistant Professor
Texas Woman's University
College of Nursing
Denton, Texas

Carol Turnage Spruill, MSN, APRN-CNS, CPHQ, NTMNC
Clinical Nurse Specialist
Department of Women, Infants and Children
University of Texas Medical Branch
Galveston, Texas

Deborah K. Steward, PhD, RN
Faculty Emeritus
Ohio State University
College of Nursing
Columbus, OH

Valerie Boebel Toly, PhD, RN, CPNP
Assistant Professor
Frances Payne Bolton School of Nursing
Case Western Reserve University
Cleveland, Ohio

Colm Travers, MD
Neonatologist
Division of Neonatology
University of Alabama at Birmingham
Birmingham, Alabama

Dorothy Vittner, PhD, RN, CHPE
Director, Senior NIDCAP Trainer
Carolina NIDCAP Training Center
Infant and Family Specialist
WakeMed Hospital and Health Systems
Raleigh, North Carolina

Marlene Walden, PhD, RN, NNP-BC, CCNS, FAAN
Nurse Scientist Manager
Arkansas Children's Hospital
Adjunct Associate Professor
University of Arkansas for Medical Sciences
Little Rock, Arkansas

Karen Walker, PhD, RN
Clinical Associate Professor, University of Sydney
Research Manager, Grace Centre for Newborn Care
Senior Research Fellow, IMPACT for Cerebral Palsy
President, Australia College of Neonatal Nurses
Vice President, Council of International Neonatal Nurses, Inc. (COINN)
Westmead, Australia

Tami Wallace, DNP, APRN, NNP-BC
Neonatal Nurse Practitioner and Educator Nationwide Children's Hospital
Columbus, Ohio

Robert D. White, MD
Director, Regional Newborn Program
Pediatrix Medical Group
Beacon Children's Hospital
South Bend, Indiana

Parent Voices Contributors

Amy Blanchard
Graham's Foundation
Perrysburg, Ohio

Jennifer Canvasser, MSW
NEC Society
Davis, California

Katie Reginato Cascamo, MA
Courageous Steps
Stillwater, Maine

Jennifer Degl
Mahopac Falls, New York

Deborah A. Discenza
PreemieWorld, LLC
Springfield, Virginia

Jennifer M. Driscoll
Lily's Hope Foundation
Allentown, Pennsylvania

Crystal Duffy
Twin to Twin
Houston, Texas

Ali Dunn
MeTwo Books
Indianapolis, Indiana

Jimena Guild
Graham's Foundation
Perrysburg, Ohio

Yamile Jackson, PhD, PE, PMP
The Zaky—Nurtured by Design
Sugar Land, Texas

Laural Kapferer, MS
Team Grayson
Boston, Massachusetts

Gigi R. Khonyongwa-Fernandez
Families Blossoming, LLC
Vienna, Virginia

Jenny R. McCormick
PreemieWorld, LLC
Springfield, Virginia

Healther McKinnis
Graham's Foundation
Perrysburg, Ohio

Rosie Moore, DNP, RN
The Gift of Life
Boca Raton, Florida

Farrin Moreano
The University of Texas at San Antonio
San Antonio, Texas

Tracy Pella
Connected Forever
Tecumseh, Nebraska

Keira Sorrells
Preemie Parent Alliance
Madison, Mississippi

Heather Tanner
Sister Friend Up
USA

Past Contributors to the Fifth Edition

Jennifer Arnold, MD, MSc, FAAP
Assistant Professor
Division of Neonatology
Baylor College of Medicine
Houston, Texas

Beverly Bowers, PhD, APRN-CNS, ANEF
Assistant Dean for the Center for Educational Excellence and Associate Professor
University of Oklahoma College of Nursing
Oklahoma City, Oklahoma

Joyce M. Butler, MSN, NNP-BC
Instructor
Department of Pediatrics
University of Mississippi Medical Center
Jackson, Mississippi

Tony C. Carnes, PhD
Senior Technical Fellow, Integrated Patient Intelligence Group
Respiratory and Monitoring Solutions
Covidien
Mansfield, Massachusetts

Sergio DeMarini, MD
Neonatologist
IRCCS Burlo Garofolo
Trieste, Italy

Willa H. Drummond, MD, MS (Medical Informatics)
Professor of Pediatrics, Physiology and Large Animal Clinical Sciences
University of Florida
Gainesville, Florida

Wakako Eklund, MS, NNP, RN
Neonatal Nurse Practitioner
Pediatrix Medical Group, Inc.
Nashville, Tennessee

Susan Ellerbee, PhD, RNC-OB
Associate Professor
University of Oklahoma, College of Nursing
Oklahoma City, Oklahoma

Jody A. Farrell, MSN, RN
Director, Fetal Treatment Center
University of California at San Francisco Benioff Children's Hospital
San Francisco, California

Linda MacKenna Ikuta, MN, RN, CCNS, PHN
Neonatal Clinical Nurse Specialist
Packard Children's Hospital
Palo Alto, California

Jamieson E. Jones, MD
Staff Neonatologist
Desert Regional Medical Center Hospital
San Diego, California

Nadine A. Kassity-Krich, MBA, BSN, RN
Adjunct Professor
University of San Diego
San Diego, California

Judith A. Lewis, PhD, RN, WHNP-BC, FAAN
Professor Emerita
Virginia Commonwealth University, School of Nursing
Richmond, Virginia

Cindy M. Little, PhD, WHNP-BC, CNS
Assistant Clinical Professor
Drexel University
Philadelphia, Pennsylvania

Judy Wright Lott, PhD, NNP-BC, FAAN
Dean of Nursing
Wesleyan College
Macon, Georgia

Sheryl J. Montrowl, MSN, NNP-BC
Clinical Coordinator Pediatrics, Neonatal Nurse Practitioner
Division of Neonatology, Department of Pediatrics
University of Florida
Gainesville, Florida

Beth Mullins, MSN, NNP-BC
Neonatal Nurse Practitioner
Instructor, Department of Pediatrics
University of Mississippi Medical Center
Jackson, Mississippi

Linda L. Rath, PhD, RN, NNP-BC
Associate Professor
University of Texas at Tyler
Tyler, Texas

Rachel Ritter, BSN, RN
Staff Nurse
Neonatal Intensive Care Unit
Children's Hospital Boston
Boston, Massachusetts

Debra A. Sansoucie, EdD, ARNP, NNP-BC
Vice President
Advanced Practitioner Program
Pediatrix Medical Group
Sunrise, Florida

Thomas D. Soltau, MD
Assistant Professor
University of Alabama at Birmingham
Birmingham, Alabama

Kathleen R. Stevens, EdD, RN, ANEF, FAAN
Professor and Director
Academic Center for Evidence-Based Practice—
www.ACESTAR.uthscsa.edu and
Improvement Science Research Network—www.ISRN.net
University of Texas Health Science Center at San Antonio
San Antonio, Texas

Laura A. Stokowski, MS, RNC
Staff Nurse
Inova Fairfax Hospital for Children
Falls Church, Virginia

Tanya Sudia-Robinson, PhD, RN
Professor
Georgia Baptist College of Nursing of Mercer University
Atlanta, Georgia

Lynda Law Wilson, PhD, RN, FAAN
Professor and Assistant Dean for International Affairs
The University of Alabama at Birmingham School of Nursing
Birmingham, Alabama

Foreword

Comprehensive Neonatal Nursing Care has been the go-to resource for evidence-based and practical guidance for novice and expert neonatal nurses in classroom and clinical settings since 1993. As we have come to expect and rely upon, the new *sixth edition* includes the latest information on neonatal embryology, physiology, medical and surgical management, psychosocial care, emerging infections, neuroprotection, pain control, care of the late preterm infant, and much more. The textbook is organized with a focus on integrative management of the newborn and family. There is extensive use of research findings in each of the chapters to provide evidence to support practice strategies and clinical decision-making. Complete references are found at the end of each chapter.

In the new *sixth edition*, the chapters have been thoroughly updated and refreshed with the latest research and practice tips, written by authors who are recognized experts in their fields. New features include callouts highlighting parent perspectives, quality and safety practice points, and emergency alerts. There are new chapters on trauma-informed care, neonatal abstinence, and support for families. Uniquely among neonatal textbooks, the *sixth edition* of *Comprehensive Neonatal Nursing Care* includes a focus on the neonatal care ecosystem, with chapters on emerging trends in research and care delivery, genetics and genomics, and competency-based education and support for neonatal unit managers and directors.

In today's world, neonatal nurses are faced with the constant threat of information overload and ever-present concerns about the accuracy and relevance of what appears in print, online, and in videos, blogs, podcasts, or instant messages. It is therefore reassuring—and indeed essential—to have the well-written, accessible, thoroughly researched and accurate *Comprehensive Neonatal Nursing Care* as our constant and trustworthy companion as we strive to provide high-quality care to all newborns and their families. The editors and authors are to be congratulated for maintaining such a high standard of excellence and practical application. Your dedication enables neonatal nurses everywhere to provide essential care to the more than 30 million sick and premature newborns and their families who depend on nurses to survive and thrive.

Thank you!

Linda S. Franck, PhD, RN, FRCPCH, FAAN
Professor and Jack & Elaine Koehn Endowed
Chair in Pediatric Nursing
Department of Family Health Care Nursing
University of California, San Francisco

Preface

One of the most complex issues in healthcare is the care of sick or premature infants and those with multiple, severe congenital anomalies. Despite advanced technology and knowledge, preterm delivery continues to be a significant problem in the United States. Maternal risk factors have changed over the past decade. For example, more women with congenital heart anomalies and chronic illnesses, such as diabetes or sickle cell anemia, are giving birth to infants with consequent health problems. The rise of in vitro fertilization has resulted in increased multiple births and prematurity. Many infants in neonatal intensive care units (NICUs) have been exposed to substances or are born to mothers with other risk factors such as delayed childbearing or childhood cancers.

The care of these at-risk infants requires the use of more and more complex technology. Surfactant administration, nitric oxide administration, high-frequency jet ventilators, neurally adjusted ventilatory assist (NAVA; Stein & Firestone, 2014), and new hybrid ventilators providing high-frequency and conventional modes of ventilation are being used in Europe and are likely to be brought to the United States for Food and Drug Administration (FDA) approval. New technologies now can provide continuous, noninvasive monitoring of endotracheal tube position and obstruction (Hütten et al., 2015). Servo-controlled oxygen administration, which leads to greater compliance with targeted oxygen saturation ranges, is being developed (Claure & Bancalari, 2015). Near-infrared spectroscopy (NIRS), amplitude-integrated EEGs (aEEGs), dialysis, organ transplantation, and other extraordinary measures are becoming commonplace. Better integration of technologies (both electronic medical records [EMRs] and medical devices) will be the basis for decision support and predictive analytics. However, in the midst of these high-tech interventions, neuroprotective developmentally supportive care interventions such as olfactory and gustatory support, using visible rather than audible alarms, music therapy, cycling lights, using more physiologically and developmentally appropriate positioning, and skin-to-skin contact are being recognized as evidence-based neuroprotective interventions, due to increasing evidence regarding the importance of maintaining a developmentally supportive NICU environment for improved long-term infant/child and family outcomes. Some consequences of prematurity are caused by early parent–infant separation and a lack of parents' participation in the care of their infant during traditional neonatal intensive care. The family is an essential partner in decision-making and care for their infant, and family-centered care is being expanded to family-integrated care, a paradigm shift from nurse caring to nurse coaching for parents providing the care.

Providers of neonatal care need up-to-date accurate and comprehensive information as a basis for providing care to newborns. A thorough understanding of normal physiology as well as the pathophysiology of disease processes is necessary for well-designed care practices. Knowledge about associated risk factors, genetics, critical periods of development, principles of nutrition and pharmacology, and current neonatal research findings are all essential in providing optimal care for neonates. A newer concept called de-implementation refers to the science of abandoning and unlearning practices built on the scaffolding of habit. Practices that are novel but yet not fully tested, unproven practices (those that lack supporting evidence), and practices of habit (practices that continue despite contradictory evidence) should go through the process of de-implementation. Care practices need to be based on best evidence-based practices available, rather than on tradition and habits.

A multidisciplinary approach has been replaced by an integrated interprofessional approach to care. All these elements form the foundation for assessment, planning, implementation, and evaluation of the effectiveness of neonatal care. The nurse plays a vital role in the provision of integrated healthcare to newborns. During the past decade, the nurse's role has included added responsibilities, which are recognized at both the staff and advanced practice levels. For the purposes of this book, we define the roles of the neonatal staff nurse, clinical nurse specialist (CNS), and neonatal nurse practitioner (NNP).

NEONATAL STAFF NURSE

The neonatal staff nurse role requires accurate and thorough assessment skills, excellent ability to communicate with other health professionals and patients' families, and a broad understanding of physiology and pathophysiology on which to base management decisions. It requires highly developed technical skills as well as critical decision-making skills. With healthcare delivery changes, the role also requires supervision of ancillary

personnel and an informed delegation of certain patient-oriented tasks. These changes require the staff nurse to possess even better assessment skills and sound knowledge of physiology and pathophysiology than in the past because some decision-making will be done in concert with other, less highly trained personnel. Additionally, the neonatal nurse is an essential contributor to the decision-making process surrounding the care of the critically ill neonate, including involvement in the ethical challenges that may occur regarding the level of care provided. In a recent position statement (#3067) by the National Association of Neonatal Nurses (NANN; Conway-Orgel, 2016), it was recommended that nursing be a part of the multidisciplinary team that facilitates decision-making affecting the health and well-being of the infant throughout the hospital stay.

In 2014, as the professional voice of neonatal nurses, NANN published a position statement (#3061) recommending that subspecialty NICUs (Level II, III, and IV NICUs) be staffed with a sufficient number and an appropriate mix of qualified registered nurses to attend to the emergent and complex care requirements of critically ill and convalescent infants (NANN, 2014c).

CLINICAL NURSE SPECIALIST

CNSs are advanced practice registered nurses (APRNs) who have graduate preparation (master's or doctorate) in nursing. Like other APRNs, they are trained in physiology, pharmacology, and physical assessment in addition to their particular areas of specialty. CNSs are expert clinicians with advanced education and training in a specialized area of nursing practice who work in a wide variety of healthcare settings. Regardless of specialty or setting, CNSs provide leadership in clinical expertise, nursing practice, and systems innovation. CNSs provide for the diagnosis, treatment, and ongoing management of patients. CNSs diagnose, develop plans of care for, treat, and provide ongoing management of complex patients. In many states, the CNSs can prescribe medications and offer durable medical equipment and therapies. They also provide expertise and support to nurses caring for patients at the bedside, help drive practice changes throughout the organization, and ensure the use of best practices and evidence-based care to achieve the best possible patient outcomes. Research and demonstration projects have shown that the CNS role is uniquely suited to lead implementation of evidence-based quality improvement actions that also reduce cost throughout the healthcare system (National Association of Clinical Nurse Specialists, 2016).

NEONATAL NURSE PRACTITIONER

The NNP is a registered nurse with clinical expertise in neonatal nursing who has received formal education at either the master's or doctoral level, with supervised clinical experience in the management of sick newborns and their families. The NNP manages a caseload of neonatal patients with consultation, collaboration, and general supervision from a physician; however, many state legislatures are following the Institute of Medicine's (IOM's) recommendation for autonomous NNP practice by repealing restrictive practice laws, thereby increasing healthcare access for millions of patients (American Association of Nurse Practitioners, 2018; Barton Associates, 2019). As a result, NNPs have increasing authority and responsibility. Using extensive knowledge of pathophysiology, pharmacology, and physiology, the NNP exercises independent or intradependent (in collaboration with other health professionals) judgment in the assessment, diagnosis, and initiation of certain delegated medical processes and procedures. As an advanced practice neonatal nurse, the NNP is additionally involved in education, consultation, and research at various levels.

NANN and the National Association of Neonatal Nurse Practitioners (NANNP), a division of NANN, published position paper #3059, a synthesis of previous efforts, which discusses the role, preparation, and scope of practice of the neonatal APRN (NANN, 2014b). NANN and NANNP define the educational and preparation standards for those pursuing the NNP role. NANN published a position statement in 1990, reaffirmed the definition of the NNP in 2000, and in 2009 issued another position statement that defined the NNP competencies (NANN, 2009). NANN (2014a) reaffirmed these core competencies for NNPs in its *Education Standards and Curriculum Guidelines for Neonatal Nurse Practitioner Programs* in 2014, which were further elaborated upon by NANNP in the development and revision of its *Competencies and Orientation Toolkit for Neonatal Nurse Practitioners* (NANNP, 2014). In 2017, NANN and NANNP published a document describing the minimum standards necessary for preparation of NNPs, titled *Education Standards and Curriculum Guidelines for Neonatal Nurse Practitioner Programs* (NANN, 2017).

In the current practice environment, outcome measures specific to the NNP must now be incorporated into professional requirements. To guide the process of continuous practice evaluation, individual practice standards have been provided by The Joint Commission in the form of ongoing professional practice evaluation or as focused professional practice evaluation (The Joint Commission, 2015). To accomplish this goal, NNPs must participate, direct, and develop performance metrics to evaluate their individual (direct) and collaborative (aggregate) contributions to improving patient and family care and outcomes while demonstrating decreased healthcare expenditures (Snapp, Wilson, Puchalski, & Wallace, 2016). Developing these outcome evaluation tools and processes will assist in the benchmarking and validation of care provided by NNPs.

The American Association of Colleges of Nurses (AACN) has proposed a change in the educational preparation for APRNs. The proposal recommends that the nurse practitioner be prepared at a "doctor of nursing practice" (DNP) level. This will likely affect the NNP role, as well as other APRNs, over the next few years.

PURPOSE AND CONTENT

The book's sixth edition provides a comprehensive assessment and examination of the care of neonates from a physiologic and pathophysiologic approach appropriate for any health professional concerned with neonatal care.

This text provides a complete physiologic and embryologic foundation for each neonatal body system. Additionally, it includes medical, surgical, and psychosocial care because the integrative management approach is absolutely imperative to the well-being of the newborn and family. Appropriate diagnostic tests and their interpretation are included in each organ-system chapter. There is extensive use of research findings in the chapters to provide evidence to support practice strategies and demonstrate the rationale for clinical decision-making. Complete references for more in-depth reading are found at the end of each chapter so that the reader may pursue more specific information on a topical area. Use of tables and illustrations further supports material that is presented in the narrative portions. New to this edition are special emergency alerts, quality and/or safety issues, and parent

voices, which are infused into applicable chapters. New chapters include Neonatal Abstinence Syndrome, The NICU—Through a Mother's Eyes (interview with a mother), and Touch a Life, Impact a Lifetime: Trauma-Informed Care in the NICU.

In the United States, the economic impact of preterm births is well over $25 billion per year (Behrman & Butler, 2007). Greater cost savings can be derived from technology that reduces labor costs, as NICU RN and respiratory therapy labor expenses account for over 60% of total neonatal care (Rhine, 2016). Now more than ever, neonatal care providers must examine patient, family, and staff outcomes to meet the demands for providing cost-effective and high-quality care. Research is critical to support both the art and science of neonatal care. Whenever possible, the contributors remind the reader of areas in need of further study. This book is not a quick reference; it provides comprehensive in-depth discussions along with detailed physiologic principles and collaborative management strategies. It provides a sound basis for safe and effective neonatal care; however, the format should make the information easier to find.

We begin the sixth edition with the impact of environmental influences and critical periods on the developing fetus. This transitions into the aspects of perinatal care, the high-risk pregnancy, the effects of labor on the fetus, and postpartal risk factors. The text then focuses on more specific neonatal topics, starting with resuscitation and stabilization of the newborn, assessment of the newborn and infant, followed by the normal term infant. Each organ system is discussed in depth, including the respiratory system, its complications and new technologies, followed by assessment of, and management strategies for, the cardiovascular, gastrointestinal, metabolic, endocrine, immunologic, integumentary, hematopoietic, musculoskeletal, neurologic, auditory, ophthalmic, and genitourinary systems. The thread of integrative management is interwoven throughout the text. Foundational topics such as fluids, electrolytes, and acid–base balance, nutrition management, pharmacology, and pain management, as well as emerging technologies and healthcare simulation are included, in addition to fetal therapy, surgical considerations, and emerging infections. Vulnerable populations cared for frequently in NICU settings are included, such as infants undergoing transplants, extremely low birth weight infants, late preterm infants, and unfortunately a growing population of infants withdrawing from opioids/neonatal abstinence syndrome. Chapters addressing environmental health and family-centered care in the NICU and beyond include neurobehavioral development, management of the NICU environment, trauma-informed care, family partnerships, palliative and end-of-life care, postdischarge care of the newborn, and, new to this section, the NICU through a mother's eyes. The final group of chapters covers neonatal care in the new millennium with topics including trends in neonatal care delivery, informatics, human genetics and genomics, trends in neonatal research and evidence-based practice, legal issues, global perspectives in neonatal care, and competency-based education and continuous competency. The sixth edition recognizes that neonatal nursing and care are global issues. The last section includes neonatal diagnostic and evidence-based care protocols pulled out separately, so they are easy to find and use. New protocols introduced in the sixth edition include neuroprotective interventions and neuroprotection of skin-to-skin contact.

To provide depth to these topical areas, physicians, nurses, infant developmental specialists, and other health professionals concerned with neonatal care from across the country and around the world have contributed in all editions. The attempt was made not only to tap the experts in the neonatal field but also to have them represent as wide a geographic area as possible. We hope that the broad geographic distribution of contributors and reviewers will help minimize the effect of regional differences in clinical practice.

We hope that you will find the text's information very useful and helpful to you in providing high-quality care to newborns and their families.

Carole Kenner
Leslie B. Altimier
Marina V. Boykova

RECOMMENDED READINGS

American Nurses Association. (2015). *Code of ethics for nurses with interpretive statements*. Silver Spring, MD: Author.

Institute of Medicine. (2011). *The future of nursing: Leading change, advancing health* (pp. 163–220). Washington, DC: National Academies Press.

National Governors Association. (2012). *Nurse practitioners have potential to improve access to primary care*. Retrieved from https://classic.nga.org/cms/home/news-room/news-releases/page_2012/col2-content/nurse-practitioners-have-potenti.html

Prasad, V., & Ioannidis, J. P. (2014). Evidence-based de-implementation for contradicted, unproven, and aspiring healthcare practices. *Implementation Science, 9*, 1. doi:10.1186/1748-5908-9-1

REFERENCES

American Association of Nurse Practitioners. (2018). *State practice environment*. Retrieved from https://www.aanp.org/legislation-regulation/state-legislation/state-practice-environment

Barton Associates. (2019). *Nurse practitioner scope of practice laws*. Retrieved from https://www.bartonassociates.com/nurse-practitioners/nurse-practitioner-scope-of-practice-laws

Behrman, R. E., & Butler, A. S. (Eds.). (2007). *Preterm birth: Causes, consequences, and prevention*. Washington, DC: National Academies Press.

Claure, N., & Bancalari, E. (2015). Oxygen saturation targeting by automatic control of inspired oxygen in premature infants. *NeoReviews, 16*, e406–e412. doi:10.1542/neo.16-7-e406

Conway-Orgel, M. (2016). *Position statement #3067: NICU nurse involvement in ethical decisions (treatment of critically ill newborns)*. Chicago, IL: National Association of Neonatal Nurses. Retrieved from http://nann.org/uploads/3067_NICU_Nurse_Involvement_in_Ethical_Decisions.pdf

Hütten, M. C., Goos, T. G., Ophelders, D., Nikiforou, M., Kuypers, E., Willems, M., . . . Kramer, B. W. (2015). Fully automated predictive intelligent control of oxygenation (PRICO) in resuscitation and ventilation of preterm lambs. *Pediatric Research, 78*, 657–663. doi:10.1038/pr.2015.158

The Joint Commission. (2015). *Standards BoosterPak™ for focused professional practice evaluation/ongoing professional practice evaluation (FPPE/OPPE)*. Oakbrook Terrace, IL: Author.

National Association of Clinical Nurse Specialists. (2016). *Key findings from the 2016 Clinical Nurse Specialists Consensus*. Retrieved from https://nacns.org/wp-content/uploads/2016/11/2016-CNS-Census-Findings.pdf

National Association of Neonatal Nurse Practitioners. (2014). *Competencies & orientation toolkit for neonatal nurse practioners* (2nd ed.). Chicago, IL: National Association of Neonatal Nurses.

National Association of Neonatal Nurses. (2009). Position statement #3042: Requirements for advanced neonatal nursing practice in neonatal intensive care units. *Advances in Neonatal Care, 9*(4), 190–194. doi:10.1097/ANC.0b013e3181b0129a

National Association of Neonatal Nurses. (2014a). *Educaton standards and curriculum guidelines for neonatal nurse practitioner programs*.

Chicago, IL: Author. Retrieved from http://nann.org/uploads/About/PositionPDFS/1.4.8_Education%20Standards%20and%20Curriculum%20Guidelines%20for%20Neonatal%20Nurse%20Practitioner%20Programs.pdf

National Association of Neonatal Nurses. (2014b). *Position statement #3059: Advanced practice registered nurse: Role, preparation, and scope of practice*. Chicago, IL: Author. Retrieved from http://nann.org/uploads/Membership/NANNP_Pubs/APRN_Role_Preparation_position_statement_FINAL.pdf

National Association of Neonatal Nurses. (2014c). *Position statement #3061: RN staffing in the neonatal intensive care unit*. Chicago, IL: Author. Retrieved from http://nann.org/uploads/About/PositionPDFS/1.4.6_RN%20Staffing%20in%20the%20NICU.pdf

National Association of Neonatal Nurses. (2017). *Educaton standards and curriculum guidelines for neonatal nurse practitioner programs*. Chicago, IL: Author. Retrieved from http://nann.org/uploads/2017_NNP_Education_Standards_completed_FINAL.pdf

Rhine, W. D. (2016). Technology—Considerations for the NICU of the future. *Newborn and Infant Nursing Reviews, 16*(4), 208–212. doi:10.1053/j.nainr.2016.09.005

Snapp, B., Wilson, J., Puchalski, M., & Wallace, T. (2016). *Position statement #3068: Quality metrics* (Approved by the NANN Board of Directors and the NANNP Council). Chicago, IL: National Association of Neonatal Nurses. Retrieved from http://nann.org/uploads/Quality_Metrics_Position_Statement_Final.pdf

Stein, H., & Firestone, K. (2014). Application of neurally adjusted ventilatory assist in neonates. *Seminars in Fetal and Neonatal Medicine, 19*, 60–69. doi:10.1016/j.siny.2013.09.005

Acknowledgments

The idea for this book was born in the basement office of the lead editor (Dr. Carole Kenner) in Cincinnati, Ohio. In 1992, we recognized there was not a comprehensive book about nursing care for neonates. The first edition of the book was created in 1993. Over the course of the next two decades, we have refined the content to reflect new trends in neonatal care. This edition has two new editors who are committed to excellence in neonatal nursing care. I am grateful to Drs. Leslie Altimier and Marina Boykova for taking this journey with me.

Carole Kenner

Share

Comprehensive Neonatal Nursing Care

CHAPTER 1

Fetal Development: Environmental Influences and Critical Periods

Carole Kenner

INTRODUCTION

In this chapter, the major events of prenatal development are described, and critical development periods for the major organ systems are identified. A brief review of the events beginning with fertilization is included, but the reader is referred to an embryology text for a more thorough account. Human genetics is discussed in Chapter 40, Human Genetics and Genomics: Impact on Neonatal Care.

EARLY FETAL DEVELOPMENT

The process of human development begins with the fertilization of an ovum (female gamete) by a spermatocyte (male gamete). The fusion of the ovum and sperm initiates a sequence of events that causes the single-celled zygote to develop into a new human being. During the 38 to 42 weeks of gestation, dramatic growth and development occur that are unequaled during any other period of life.

Fertilization

Large numbers of spermatozoa are necessary to increase the chances for conception because the spermatozoa must traverse the cervical canal, uterus, and uterine (fallopian) tubes to reach the ovum; approximately 200 to 600 million sperm are deposited in the posterior fornix of the vagina during ejaculation. The usual site of fertilization is in the ampulla, the widest portion of the uterine tubes, located near the ovaries. Sperm are propelled by the movement of the tails, aided by muscular contractions of the uterus and fallopian tubes. The spermatozoa undergo two physiologic changes to penetrate the corona radiata and zona pellucida, the barriers around the secondary oocyte. The first change is capacitation, an enzymatic reaction that removes the glycoprotein coating from the spermatozoa and plasma proteins from the seminal fluid. Capacitation generally occurs in the uterus or uterine tubes and takes about 7 hours. The second change, the acrosome reaction, occurs when a capacitated sperm passes through the corona radiata, causing structural changes that result in the fusion of the plasma membranes of the sperm and the oocyte. Progesterone released from the follicle at ovulation stimulates the acrosome reaction. Three enzymes are released from the acrosome to facilitate entry of the sperm into the ovum. Hyaluronidase allows the sperm to penetrate the corona radiata, whereas trypsin-like enzymes and zona lysin digest a pathway across the zona pellucida (Moore, Persaud, & Torchia, 2015; Sadler, 2015).

Only about 300 to 500 spermatozoa actually reach the ovum. When a spermatozoon comes into contact with the ovum, the zona pellucida and the plasma membrane fuse, preventing entry by other sperm. After penetration by a single sperm, the oocyte completes the second meiotic cell division, resulting in the haploid number of chromosomes (22,X) and the second polar body. The chromosomes are arranged to form the female pronucleus (Moore et al., 2015; Sadler, 2015).

As the spermatozoon moves close to the female pronucleus, the tail detaches, and the nucleus enlarges to form the male pronucleus. The male and female pronuclei fuse forming a diploid cell called the zygote. The zygote contains 23 autosomes and 1 sex chromosome from each parent (46,XX or 46,XY). The genetic sex of the new individual is determined at fertilization by the contribution of the father. The male parent (XY) may contribute either an X or a Y chromosome. If the spermatozoon contains an X chromosome, the offspring is female (46,XX). If the spermatozoon receives one Y chromosome, the offspring is male (46,XY). Individual variation is the result of random or independent assortment of the autosomal chromosomes (Moore et al., 2015; Sadler, 2015).

Cleavage

Mitotic cell division occurs after fertilization as the zygote passes down the uterine tube, resulting in the formation of two blastomeres (Figure 1.1). The cells continue to divide, increasing in number, although decreasing in size. The term *cleavage* is used to describe the mitotic cell division of the zygote (Figure 1.2). When the number of cells reaches approximately 16 (usually on the third day), the zygote is called a morula, because of its resemblance to a mulberry. The zygote reaches the morula stage about the time it enters the uterus. The morula consists of groups of centrally located cells called the inner cell mass and an outer cell layer. At this stage, the individual cells are called blastomeres. The outer cell layer forms the trophoblast, from which the placenta develops. The inner cell mass, called the embryoblast, gives rise to the embryo (Moore et al., 2015; Sadler, 2015).

After the morula penetrates the uterine cavity, fluid enters through the zona pellucida into the intercellular spaces of the inner cell mass. The fluid-filled spaces fuse, forming a large cavity known as the blastocyst cavity about the fourth day after fertilization. The morula is now called the blastocyst. This outer cell layer, known

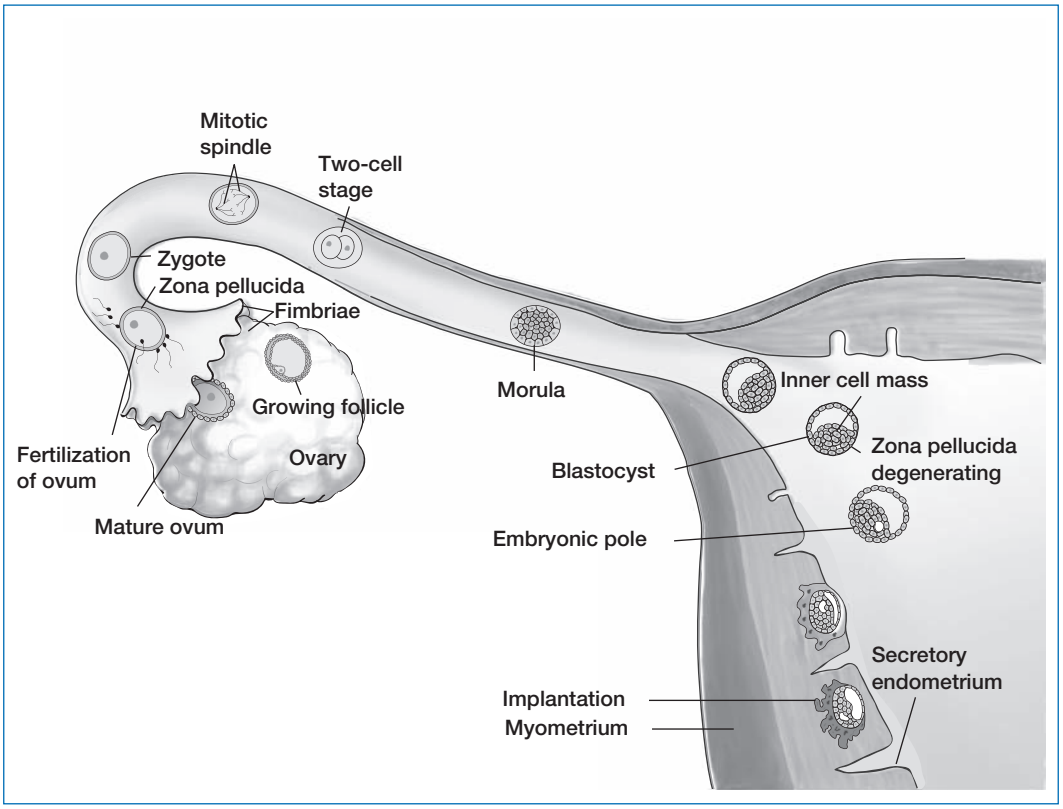

FIGURE 1.1 Fantastic voyage. From fertilization to implantation. The journey through the fallopian tubes takes approximately 4 days. During this time, mitotic cell division occurs. Implantation occurs on about day 9 through 12.

as the trophoblast, forms the wall of the blastocyst, which later becomes the placenta, and the embryoblast projects from the wall of the blastocyst into the blastocyst cavity. The uterine secretions nourish the blastocyst until implantation occurs (Moore et al., 2015; Sadler, 2015).

Implantation

Degeneration of the zona pellucida occurs on about the fifth day after fertilization, allowing the blastocyst to attach to the endothelium of the endometrium on about the sixth day. The trophoblasts then secrete proteolytic enzymes that destroy the endometrial endothelium and invade the endometrium. Two layers of trophoblasts develop; the inner layer is made up of cytotrophoblasts, and the outer layer is composed of syncytiotrophoblasts. The syncytiotrophoblast has finger-like projections that produce enzymes capable of further eroding the endometrial tissues. By the end of the seventh day, the blastocyst is superficially implanted (Figure 1.3).

Formation of the Bilaminar Disk

Implantation is completed during the second week. The syncytiotrophoblast continues to invade the endometrium and becomes embedded. Spaces in the syncytiotrophoblast, called lacunae, fill with blood from ruptured maternal capillaries and secretions from eroded endometrial glands. This fluid nourishes the embryoblast by diffusion. The lacunae give rise to the uteroplacental circulation. The lacunae fuse to form a network that then becomes the intervillous spaces of the placenta. The endometrial capillaries near the implanted embryoblast become dilated and eroded by the syncytiotrophoblast. Maternal blood enters the lacunar network and provides circulation and nutrients to the embryo. Maternal embryonic blood circulation provides the developing embryo with nutrition and oxygenation and removes waste products before the development of the placenta. Finger-like projections, primary chorionic villi, of the chorion develop into the chorionic villi of the placenta at about the same time (Moore et al., 2015; Sadler, 2015).

The inner cell mass differentiates into two layers: the hypoblast (endoderm), a layer of small cuboidal cells, and the epiblast (ectoderm), a layer of high columnar cells. The two layers form a flattened, circular bilaminar embryonic disk. The amniotic cavity is derived from spaces within the epiblast. As the amniotic cavity enlarges, a thin layer of epithelial cells covers the amniotic cavity. During the development of the amniotic cavity, other trophoblastic cells form a thin extracoelomic membrane, which encloses the primitive yolk sac. The yolk sac produces fetal red blood cells. Other trophoblastic cells form a layer of mesenchymal tissue, called the extraembryonic mesoderm, around the amnion and primitive yolk sac. Isolated coelomic spaces in the extraembryonic mesoderm fuse to form a single, large, fluid-filled cavity surrounding the amnion and yolk sac, with the exception of the area where the amnion is attached to the chorion by the connecting stalk. The primitive yolk sac decreases in size, creating a smaller secondary yolk sac (Moore et al., 2015; Sadler, 2015).

Two layers of extraembryonic mesoderm result from the formation of the extraembryonic cavity. The extraembryonic somatic mesoderm lines the trophoblast and covers the amnion, and the extraembryonic splanchnic mesoderm covers the yolk sac. The chorion is made up of the extraembryonic somatic mesoderm, the cytotrophoblast, and the syncytiotrophoblast. The chorion forms the chorionic sac, in which the embryo, the amniotic sac, and the yolk sac are located. By the end of the second week, there is a slightly thickened area near the cephalic region of the hypoblastic disk, known as the prochordal plate, which marks the location of the mouth (Moore et al., 2015; Sadler, 2015).

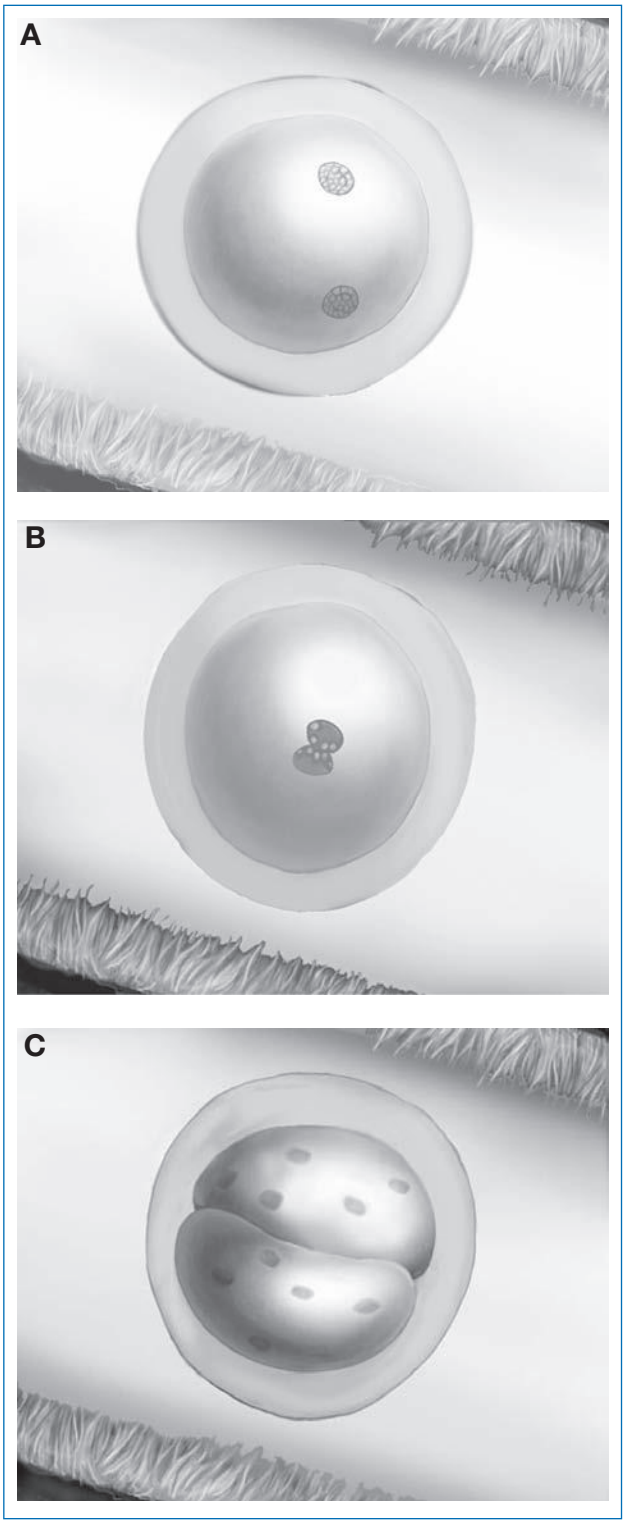

FIGURE 1.2 Stages of cell division: cleavage. (A) Zygote. (B) Zygote undergoing first cleavage. (C) Two-cell blastomere state.

Formation of the Trilaminar Embryonic Disk: The Third Week of Development

The third week of development is marked by rapid growth, the formation of the primitive streak, and the differentiation of the three germ layers, from which all fetal tissue and organs are derived (Moore et al., 2015; Sadler, 2015; Figure 1.4).

Gastrulation. Gastrulation is the process through which the bilaminar disk develops into a trilaminar embryonic disk.

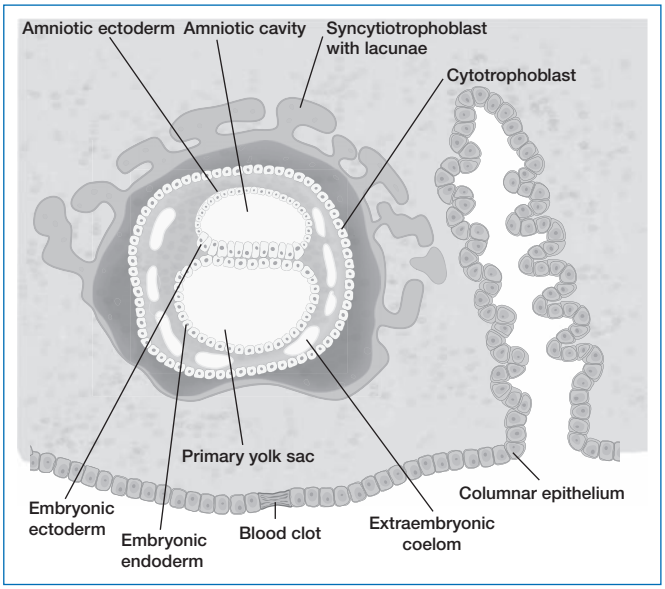

FIGURE 1.3 Cross section of a blastocyst at 11 days. Two germ layers are present. The trophoblast has differentiated into the syncytiotrophoblast and the cytotrophoblast.

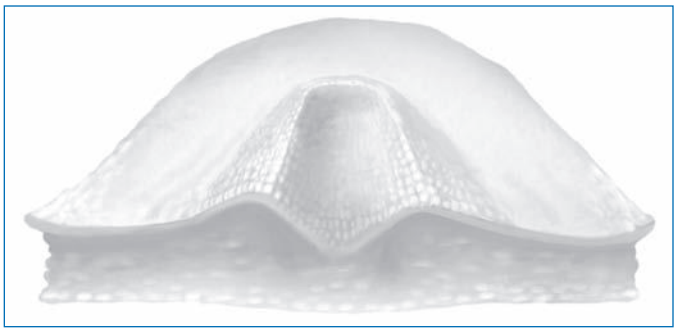

FIGURE 1.4 Formation of the trilaminar embryonic disk: gastrulation. During gastrulation, the bilaminar embryonic disk changes to a trilaminar embryonic disk, consisting of the epiblast (ectoderm), hypoblast (endoderm), and mesoblast (mesoderm).

Gastrulation is the most important event of early fetal formation; it affects all of the rest of embryologic development. During the third week, epiblast cells separate from their original location and migrate inward, forming the mesoblast, which spreads cranially and laterally to form a layer between the ectoderm and the endoderm called the intraembryonic mesoderm. Other mesoblastic cells invade the endoderm, displacing the endodermal cells laterally, forming a new layer, the embryonic ectoderm. Thus, the hypoblastic ectoderm produces the embryonic ectoderm, embryonic mesoderm, and the majority of the embryonic endoderm. These three germ layers are the source of the tissue and organs of the embryo (Moore et al., 2015; Sadler, 2015).

Primitive Streak. Over days 14 and 15, a groove and thickening of the ectoderm (epiblast), called the primitive streak, appears caudally in the center of the dorsum of the embryonic disk. The primitive streak results from the migration of ectodermal cells toward the midline in the posterior portion of the embryonic disk. The primitive groove develops in the primitive streak. When the primitive streak begins to produce mesoblastic cells that become intraembryonic mesoderm, the epiblast is referred to as the embryonic ectoderm and the hypoblast is referred to as the embryonic mesoderm (Moore et al., 2015; Sadler, 2015).

Notochordal Process. Cells from the primitive knot migrate cranially and form the midline cellular notochordal process. This process grows cranially between the ectoderm and the endoderm until it reaches the prochordal plate, which is attached to the overlying ectoderm, thus forming the oropharyngeal membrane. The cloacal membrane, caudal to the primitive streak, develops into the anus (Moore et al., 2015; Sadler, 2015).

The primitive streak produces mesenchyme (mesoblasts) until the end of the fourth week. The primitive streak does not grow as rapidly as the other cells, making it relatively insignificant in size when compared with the other structures that continue to grow. Persistence of the primitive streak or remnants is the cause of sacrococcygeal teratomas (Moore et al., 2015; Sadler, 2015).

The notochord, a cellular rod that develops from the notochordal process, is the structure around which the vertebral column is formed. It forms the nucleus pulposus of the intervertebral bodies of the spinal column (Figure 1.5; Moore et al., 2015; Sadler, 2015).

Neurulation. Neurulation is the process through which the neural plate, neural folds, and neural tube are formed. The developing notochord stimulates the embryonic ectoderm to thicken, forming the neural plate. The neuroectoderm of the neural plate gives rise to the central nervous system (CNS). The neural plate develops cranial to the primitive knot. As the neural plate elongates, it gets wider and extends cranially to the oropharyngeal membrane. The neural plate invaginates along the central axis to form a neural groove with neural folds on each side. The neural folds move together and fuse, forming the neural tube showing the first indication of brain development (Figure 1.6). The neural tube detaches from the surface ectoderm, and the free edges of the ectoderm fuse, covering the posterior portion of the embryo. With formation of the neural tube, nearby ectodermal cells lying along the crest of each neural fold migrate inward, invading the mesoblast on each side of the neural tube. These irregular, flattened masses are called the neural crest. This structure's cells give rise to the spinal ganglia, the ganglia of the autonomic nervous system, and cranial nerves V, VII, IX, and X. Neural crest cells also form the meningeal covering of the brain and spinal cord and the sheaves that protect nerves. The neural crest cells contribute to the formation of pigment-producing cells, the adrenal medulla, and skeletal and muscular development in the head (Moore et al., 2015; Sadler, 2015).

Development of Somites. Another important event of the third week is the development of somites, which give rise to most of the skeleton and associated musculature and much of the dermis of the skin. During formation of the neural tube, the intraembryonic mesoderm on each side thickens, forming longitudinal columns of paraxial mesoderm. At about 20 days, the paraxial mesoderm begins to divide into paired cuboidal bodies known as somites. In all, 42 to 44 somites develop, in a craniocaudal sequence, although only 38 develop during the "somite" period. These somite pairs can be counted and give an estimate of fetal age before a crown-rump (C-R) measurement is possible (Moore et al., 2015; Sadler, 2015).

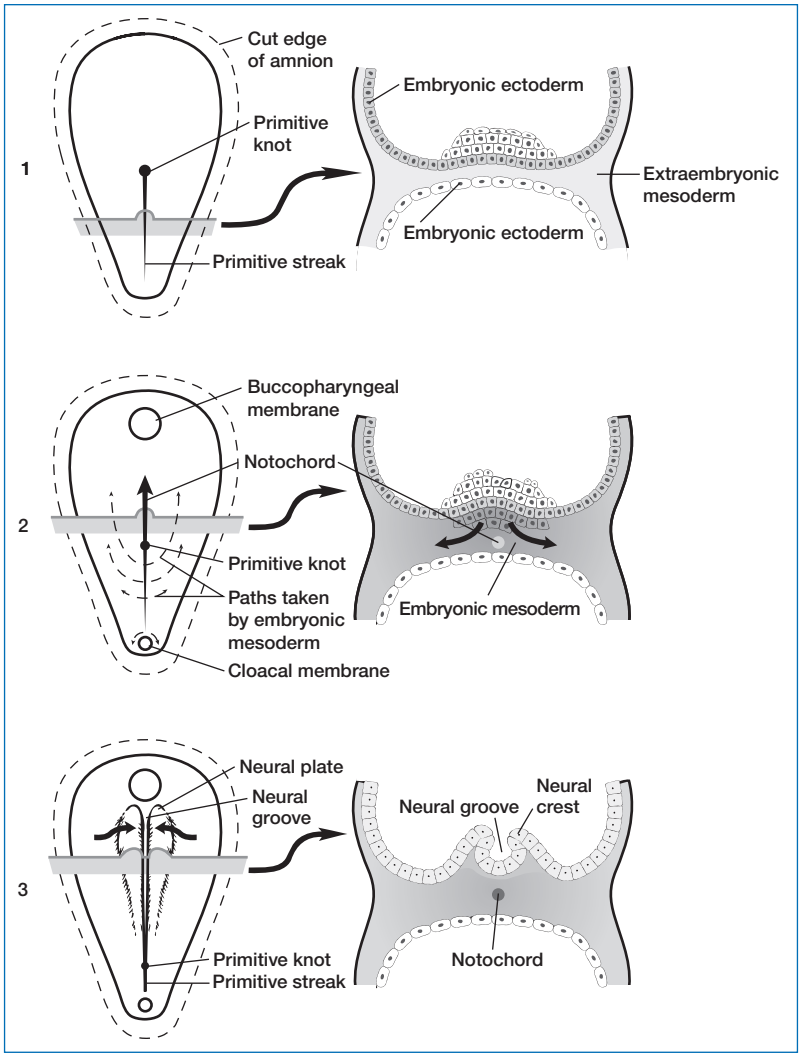

FIGURE 1.5 Formation of primitive streak, primitive knot, notochord, and neural groove.

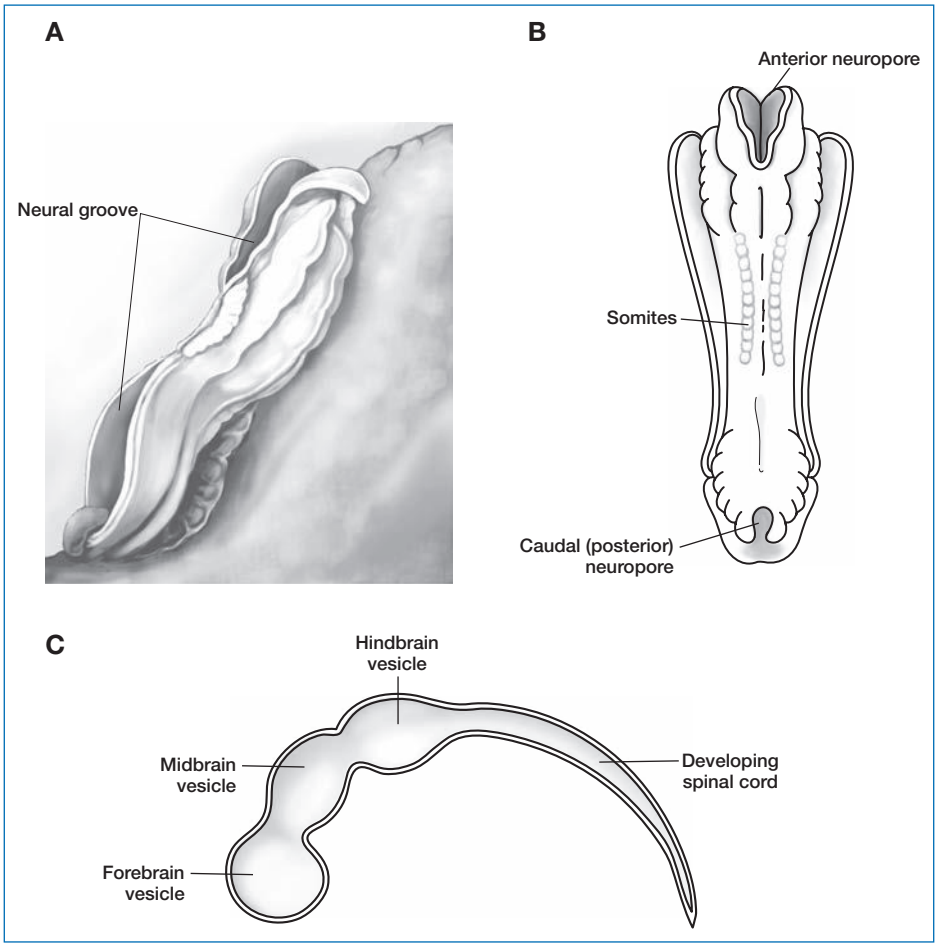

FIGURE 1.6 Formation of the neural tube. (A) Neural groove. (B) Closure of the neural tube almost completed. (C) Dilation of the neural tube forms the forebrain, midbrain, and hindbrain.

Intraembryonic Cavity. Another significant process is the formation of the intraembryonic cavity. This structure first appears as a number of small spaces within the lateral mesoderm and the cardiogenic mesoderm. These spaces combine to form the intraembryonic cavity; it is horseshoe-shaped and lined with flattened epithelial cells that eventually line the peritoneal cavity. The intraembryonic cavity divides the lateral mesoderm into the parietal (somatic) and visceral (splanchnic) layers. It gives rise to the pericardial cavity, the pleural cavity, and the peritoneal cavity (Moore et al., 2015; Sadler, 2015).

PLACENTAL DEVELOPMENT AND FUNCTION

The rudimentary maternal fetal circulation is intact by the fourth week of gestation. Growth of the trophoblast results in numerous primary and secondary chorionic villi, covering the surface of the chorionic sac until about the eighth week of gestation. At about the eighth week, the villi overlying the conceptus (decidua capsularis) degenerate, leaving a smooth area (smooth chorion). The villi underlying the conceptus (decidua basalis) remain and increase in size, producing the chorion frondosum, or fetal side of the placenta. The maternal side of the placenta is made up of the chorion and the chorionic villi. On implantation of the conceptus, maternal capillaries of the decidua basalis rupture, causing maternal blood to circulate through the developing fetal placenta (chorion frondosum). As growth and differentiation progress, extensions from the cytotrophoblast invade the syncytial layer and form a cytotrophoblastic shell, surrounding the conceptus and chorionic villi. This shell is continuous, but has communications between maternal blood vessels in the decidua basalis and the intervillous spaces of the chorion frondosum. The latter is attached to the maternal side of the placenta (decidua basalis) by the cytotrophoblastic shell and anchoring villi. The placenta is mature and completely functional by 16 weeks of development (Figure 1.7). If the corpus luteum begins to regress prior to the 16th week and fails to produce enough progesterone (the hormone responsible for readying the uterine cavity for the pregnancy), the pregnancy is aborted because the placenta is not capable of supporting the pregnancy on its own until about this time (Moore et al., 2015; Sadler, 2015).

Placental Fetal Circulation

A simple ebb-and-flow circulation is present in the embryo, yolk sac, connecting stalk, and chorion by 21 days of gestation. By 28 days, unidirectional circulation is established. Deoxygenated fetal blood leaves the fetus via the umbilical arteries and enters the capillaries in the chorionic villi, where gaseous and nutrient exchanges take place. Oxygenated blood returns to the fetus through the umbilical veins. At first, there are two arteries and two veins, but one vein gradually degenerates, leaving two arteries and one vein. If only one artery is present, a congenital anomaly, especially a renal one, should be suspected (Moore et al., 2015; Sadler, 2015).

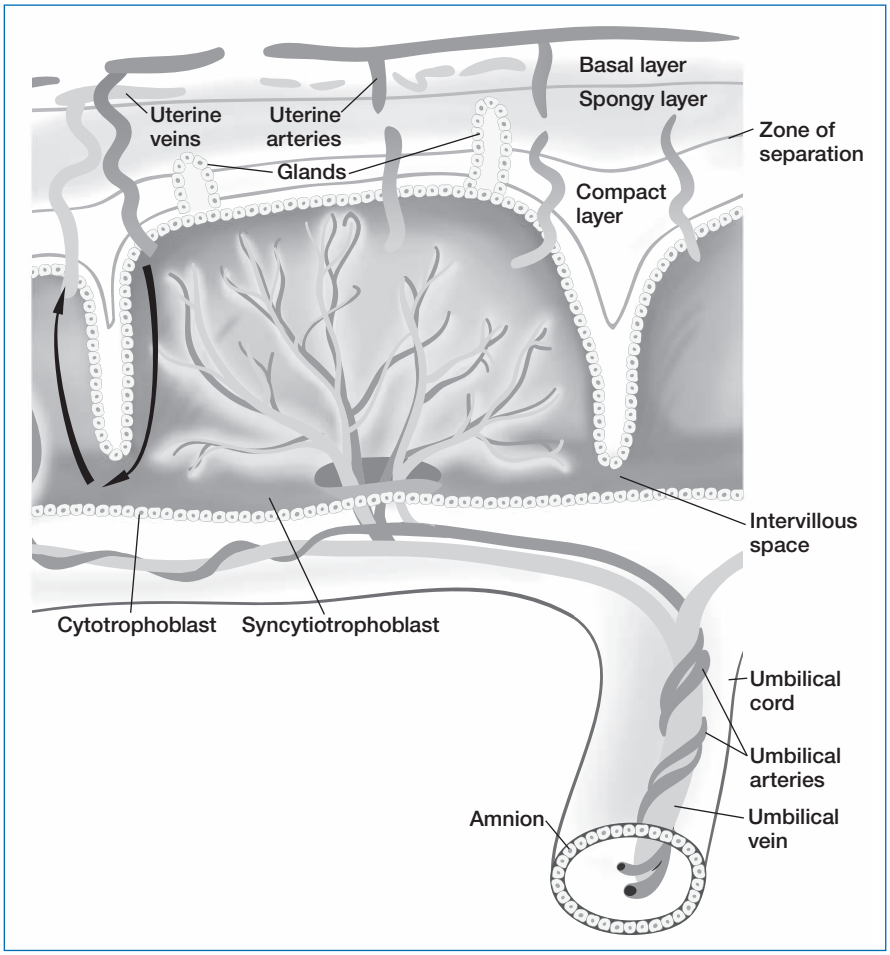

FIGURE 1.7 Formation of the placenta. The fetal and maternal sides of the placenta. Separation of the placenta from the uterus occurs at the site indicated by the gray line labeled zone of separation.

Placental Function

Normal growth and development of the embryo depend on adequate placental function. The placenta is responsible for oxygenation, nutrition, elimination of wastes, production of hormones essential for maintenance of the pregnancy, and transport of substances. In addition, the placenta synthesizes glycogen, cholesterol, and fatty acids, which provide nutrients and energy for early fetal development. Transport across the placental membrane occurs primarily through simple and facilitated diffusion, active transport, and pinocytosis. Oxygen, carbon dioxide, and carbon monoxide cross the placenta through simple diffusion. The fetus depends on a continuous supply of oxygenated blood flowing from the placenta (Moore et al., 2015; Sadler, 2015).

Water and electrolytes cross the placenta freely in both directions. Glucose is converted to glycogen in the placenta as a carbohydrate source for the fetus. Amino acids move readily across the placental membranes for protein synthesis in the fetus. Free fatty acids are transferred across the placenta by pinocytosis. There is limited or no transfer of maternal cholesterol, triglycerides, and phospholipids. Water- and fat-soluble vitamins cross the placenta and are essential for normal development (Moore et al., 2015; Sadler, 2015).

The placenta produces and transports hormones that maintain the pregnancy and promote growth and development of the fetus. Chorionic gonadotropin, a protein hormone produced by the syncytiotrophoblast, is excreted in maternal serum and urine. The presence of human chorionic gonadotropin is used as a test for pregnancy. Human placental lactogen, also a protein hormone produced by the placenta, acts as a fetal growth–promoting hormone by giving the fetus priority for receiving maternal glucose (Moore et al., 2015; Sadler, 2015).

The placenta also produces steroid hormones. Progesterone, produced by the placenta throughout gestation, is responsible for maintaining the pregnancy. Estrogen production by the placenta depends on stimulation by the fetal adrenal cortex and liver. Placental transport of maternal antibodies provides the fetus with passive immunity to certain viruses. IgG antibodies are actively transported across the placental barrier, providing humoral immunity for the fetus. IgA and IgM antibodies do not cross the placental barrier, placing the neonate at risk for neonatal sepsis. However, failure of IgM antibodies to cross the placental membrane explains the lower incidence of a severe hemolytic process in ABO blood type incompatibilities when compared with Rh incompatibilities. The latter result when an Rh-negative mother has an Rh-positive fetus. If the mother is sensitized to the Rh-positive fetal blood cells, the mother produces IgG antibodies. IgG is transferred from the maternal to fetal circulation, and hemolysis of fetal red blood cells occurs (Moore et al., 2015; Sadler, 2015).

The placenta is selective in the transfer of substances across the placenta; however, this selectivity does not screen out all potentially harmful substances. Viral, bacterial, and protozoal organisms can be transferred to the fetus through the placenta. Toxic substances such as drugs and alcohol can also be transferred to the fetus. The effects of these substances depend on the stage of gestation and type and duration of exposure, as well as the interaction of these and other factors, such as nutrition.

EMBRYONIC PERIOD: WEEKS 4 THROUGH 8

The embryonic period lasts from the beginning of gestational week 4 through the end of week 8. Organogenesis, which is the formation of all major organs, occurs during this period. The shape of the embryo changes as the organs develop, taking a more human shape by the end of the eighth week. The major events of the embryonic period are the folding of the embryo and organogenesis.

Folding of the Embryo

In the trilaminar embryonic disk, the growth rate of the central region exceeds that of the periphery so that the slower growing areas fold under the faster growing areas, forming body folds. The head fold appears first as a result of craniocaudal elongation of the notochord and growth of the brain, which projects into the amniotic cavity. The folding downward of the cranial end of the embryo forces the septum transversum (primitive heart), the pericardial cavity, and the oropharyngeal membrane to turn under onto the ventral surface. After the embryo has folded, the mass of mesoderm cranial to the pericardial cavity, the septum transversum, lies caudal to the heart. The septum transversum later develops into a portion of the diaphragm. Part of the yolk sac is incorporated as the foregut, lying between the heart and the brain. The foregut ends blindly at the oropharyngeal membrane, which separates the foregut from the primitive mouth cavity (stomodeum; Moore et al., 2015; Sadler, 2015).

The tail fold occurs after the head fold as a result of craniocaudal growth progression. Growth of the embryo causes the caudal area to project over the cloacal membrane. During the tail folding, part of the yolk sac is incorporated into the embryo as the hindgut. After completion of the head and tail folding, the connecting stalk is attached to the ventral surface of the embryo, forming the umbilical cord. Folding also occurs laterally, producing right and left lateral folds. The lateral body wall on each side folds toward the median plane, causing the embryo to assume a cylindrical shape. During the lateral body folding, a portion of the yolk sac is incorporated as the midgut. The attachment of the midgut to the yolk sac is minimal after this fold develops. After folding, the amnion is attached to the embryo in a narrow area in which the umbilical cord attaches to the ventral surface (Moore et al., 2015; Sadler, 2015).

Organogenesis: Germ Cell Derivatives

The three germ cell layers (ectoderm, mesoderm, and endoderm) give rise to all tissues and organs of the embryo. The germ cells follow specific patterns during the process of organogenesis. The main germ cell derivatives are listed in Box 1.1. The development of each major organ system is discussed separately. The embryonic period is the most critical period of development because of the formation of internal and external structures. The critical periods of development for the organs are also discussed in the section on specific organ development.

Box 1.1

GERM CELL DERIVATIVES

Ectoderm

- CNS (brain, spinal cord)
- Peripheral nervous system
- Sensory epithelia of eye, ear, and nose
- Epidermis and its appendages (hair and nails)
- Mammary glands
- Subcutaneous glands
- Teeth enamel
- Neural crest cells
- Spinal, cranial, and autonomic ganglia cells
- Nerve sheaths of peripheral nervous system
- Pigment cells
- Muscle, connective tissue, and bone of branchial arch origin
- Adrenal medulla
- Meninges

Mesoderm

- Cartilage
- Bone
- Connective tissue
- Striated and smooth muscle
- Heart, blood, and lymph vessels and cells
- Gonads
- Genital ducts
- Pericardial, pleural, and peritoneal lining
- Spleen
- Cortex of adrenal gland

Endoderm

- Epithelial lining of respiratory and gastrointestinal tracts
- Parenchyma of tonsils, thyroid, parathyroid, liver, thymus, and pancreas
- Epithelial lining of bladder and urethra
- Epithelial lining of tympanic cavity, tympanic antrum, and auditory tube

CNS, central nervous system

DEVELOPMENT OF SPECIFIC ORGANS AND STRUCTURES

Nervous System

The origin of the nervous system is the neural plate, which arises as a thickening of the ectodermal tissue about the middle of the third week of gestation. The neural plate further differentiates into the neural tube and the neural crest. The neural tube gives rise to the CNS. The neural crest cells give rise to the peripheral nervous system (Figure 1.8; Moore et al., 2015; Sadler, 2015).

The cranial end of the neural tube forms the three divisions of the brain: the forebrain, the midbrain, and the hindbrain. The

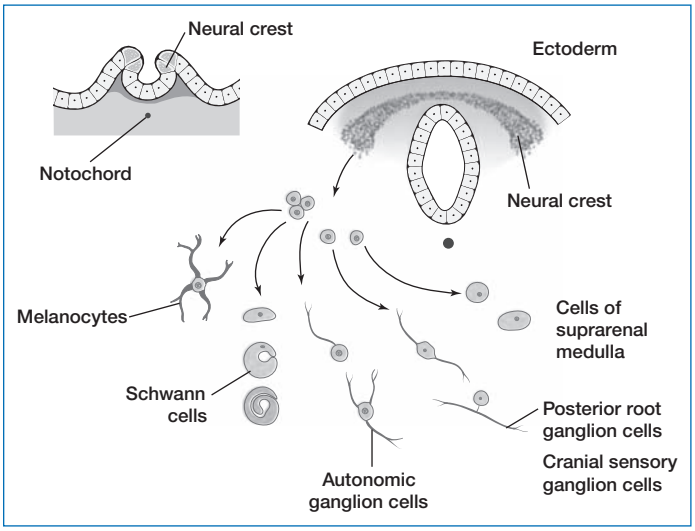

FIGURE 1.8 Differentiation of the nervous system. The cells of the neural crest differentiate into the cells of the ganglia, Schwann cells, and the cells of the suprarenal medulla and melanocytes.

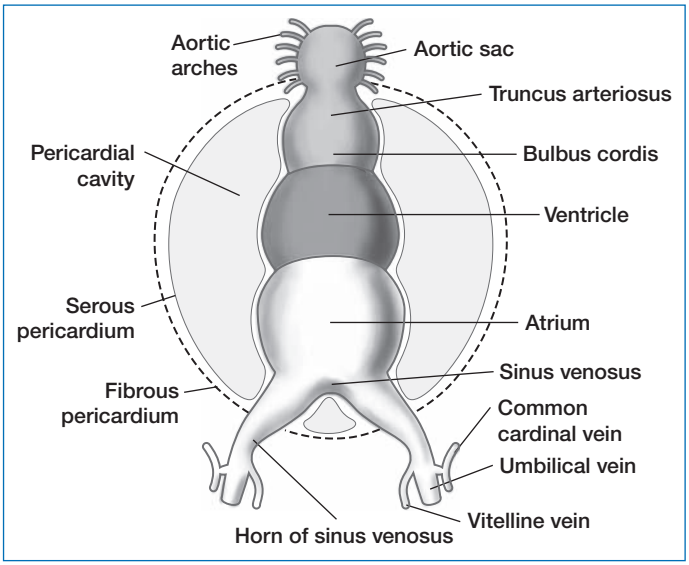

FIGURE 1.9 Formation of the single heart tube. The appearance of the single heart tube inside the pericardial cavity. Note that the atrium and sinus venosus are outside the pericardial cavity.

cerebral hemispheres and diencephalon arise from the forebrain; the pons, cerebellum, and medulla oblongata arise from the hindbrain. The midbrain makes up the adult midbrain (Moore et al., 2015; Sadler, 2015).

The cavity of the neural tube develops into the ventricles of the brain and the central canal of the spinal column. The neuroepithelial cells lining the neural tube give rise to nerves and glial cells of the CNS. The peripheral nervous system consists of the cranial, spinal, and visceral nerves and the ganglia. The somatic and visceral sensory cells of the peripheral nervous system arise from neural crest cells. Cells that form the myelin sheaths of the axons, called Schwann cells, also arise from the neural crest cells (Moore et al., 2015; Sadler, 2015).

Cardiovascular System

The fetal cardiac system appears at about 18 to 19 days of gestation, and circulation is present by about 21 days. The cardiovascular system is the first organ system to function in utero. The heart starts to beat at the beginning of the fourth week. The heart and blood develop from the middle layer (mesoderm) of the trilaminar embryonic disk. Tissue from the lateral mesoderm migrates up the sides of the embryonic disk, forming a horseshoe-shaped structure that arches and meets above the oropharyngeal membrane. With further development, paired heart tubes form, which then fuse into a single heart tube (Figure 1.9). The vessels that make up the vascular system throughout the body develop from mesodermal cells that connect to each other, with the developing heart tube and the placenta. Thus, by the end of the third week of gestation, there is a functional cardiovascular system (Moore et al., 2015; Sadler, 2015).

As the heart tube grows, the folding of the embryonic disk results in the movement of the heart tube into the chest cavity. The heart tube differentiates into three layers: the endocardial layer, which becomes the endothelium; the cardiac jelly, which is a loose tissue layer; and the myoepicardial mantle, which becomes the myocardium and pericardium. The single heart tube is attached at its cephalic end by the aortic arches and at the caudal end by the septum transversum. The attachments limit the length of the heart tube. Continued growth results in dilated areas and bulges, which become specific components of the heart. The atrium, ventricle, and bulbus cordis can be identified first, followed by the sinus venosus and truncus arteriosus. To accommodate continued growth, two separate bends in the heart occur. It first bends to the right to form a U shape, and the next bend results in an S-shaped heart. The bending of the heart is responsible for the typical location of cardiac structures (Figure 1.10; Moore et al., 2015; Sadler, 2015).

Initially, the heart is a single chamber; partitioning of the heart into four chambers occurs from the fourth to sixth weeks of gestation. The changes that cause the partitioning of the heart occur simultaneously. The atrium is separated from the ventricle by endocardial cushions, which are thickened areas of endothelium that develop on the dorsal and ventral walls of the open area between the atrium and ventricle. The endocardial cushions fuse with each other to divide the atrioventricular canals into right and left atrioventricular canals. Partitioning of the atrium occurs through invagination of tissue toward the endocardial cushions, forming the septum primum. As the septum primum grows toward the endocardial cushions, it becomes very thin and perforates, becoming the foramen ovale. The septum primum does not fuse completely with the endocardial cushions; it has a lower portion that lies beside the endocardial cushions. Overlapping of the septum primum and the septum secundum forms a wall if the pressure in both atria is equal. In utero, the pressure on the right side is increased, allowing blood to flow across the foramen ovale from the right side of the heart to the left side (Figure 1.11; Moore et al., 2015; Sadler, 2015).

The ventricle is also partitioned by a membranous and muscular septum. The muscular portion of the septum develops from the fold of the floor of the ventricle. With blood flowing through the atrioventricular canal, ventricular dilation occurs on either side of the fold or ridge, causing it to become a septum. The membranous septum arises from ridges inside the bulbus cordis. These ridges, continuous into the bulbus cordis, form the wall that divides the bulbus cordis into the pulmonary artery and the aorta. The bulbar ridges fuse with the endocardial cushions to form the membranous septum. The membranous and muscular septa fuse to close the intraventricular foramen, resulting in two parallel circuits of blood flow. The pulmonary artery is continuous with the right ventricle, and the aorta is continuous with the left ventricle (Figure 1.12; Moore et al., 2015; Sadler, 2015).

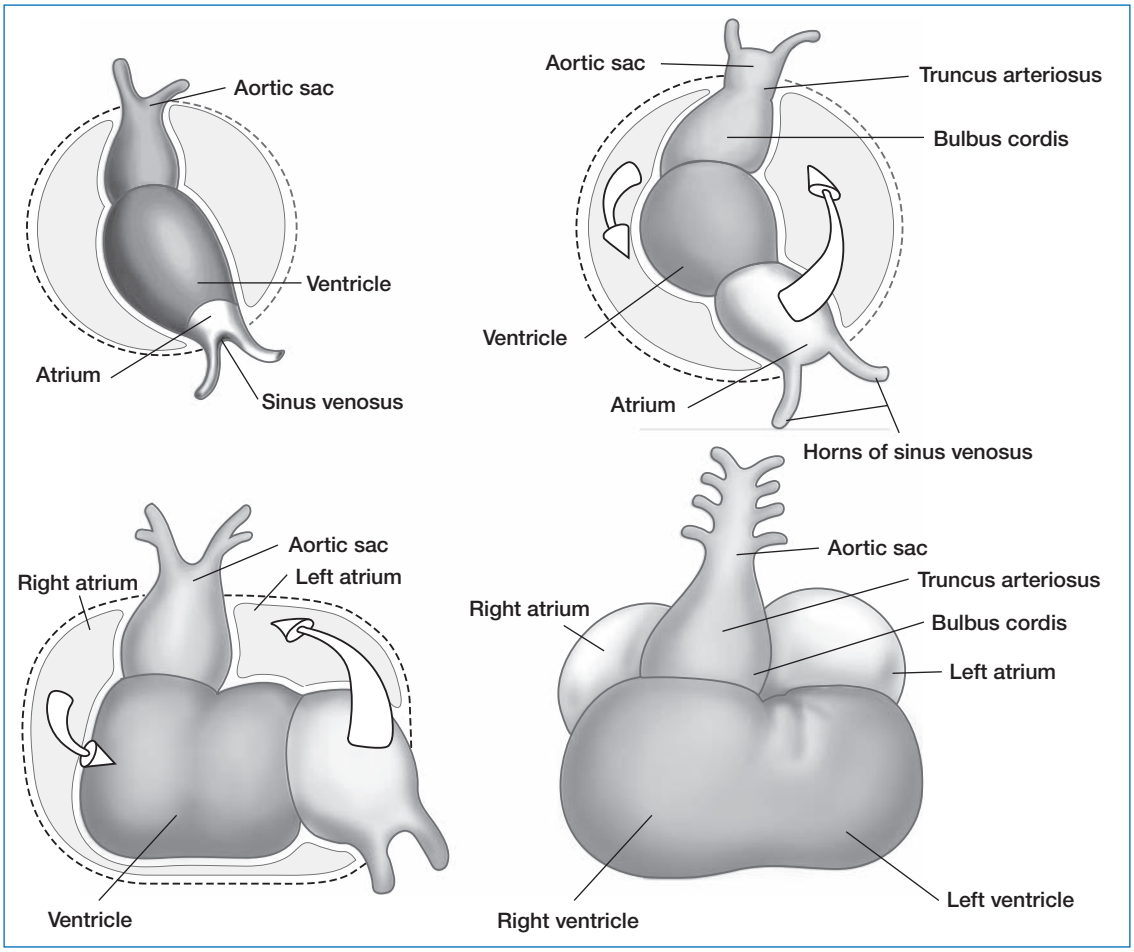

FIGURE 1.10 Bending of the heart tube inside the pericardial cavity. The bending of the heart tube brings the atrium into the pericardial cavity. The sinus venosus is taken into the right atrium and the coronary sinus.

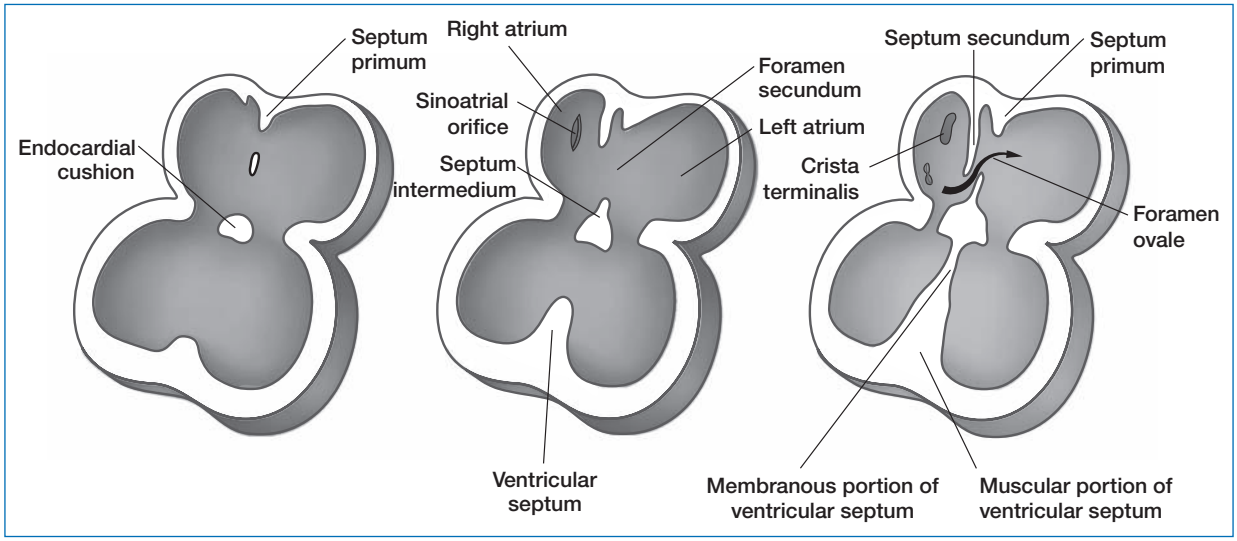

FIGURE 1.11 Partitioning of the atrium. The partitioning of the atrium into the right and left atria through septation.

The blood flowing through the bulbus cordis and truncus arteriosus in a spiral causes the formation of ridges. The ridges fuse to form two separate vessels that twist around each other once. Thus, the pulmonary artery exits the right side of the heart and is in the left upper chest; the aorta exits the left side of the heart and is located close to the sternum (Moore et al., 2015; Sadler, 2015).

The pulmonary veins grow from the lungs to a cardinal vein plexus. Concurrently, a vessel develops from the smooth wall of the left atrium. As the atrium grows, the pulmonary vein is incorporated into the atrial wall. The atrium and its branches give rise to four pulmonary veins that enter the left atrium. These pulmonary vessels, connected to the plexus of the cardinal vein, provide