Benson

current Obstetric & Gynecologic Diagnosis & Treatment

5TH EDITION

current
Obstetric & Gynecologic Diagnosis & Treatment

5TH EDITION

Edited By

RALPH C. BENSON, MD

Professor of Obstetrics & Gynecology and
Emeritus Chairman, Department of Obstetrics & Gynecology
Oregon Health Sciences University
Portland, Oregon

With Associate Authors

Illustrated by Laurel V. Schaubert

Lange Medical Publications

Los Altos, California 94022

Lange Medical Publications
Drawer L, Los Altos, California 94022

Spanish Edition: *Editorial El Manual Moderno, S.A. de C.V., Av. Sonora 206, 06100-Mexico, D.F.*
Portuguese Edition: *Editora Guanabara Koogan, S.A., Travessa do Ouvidor, 11-ZC-00, 20,040 Rio de Janeiro - RJ, Brazil*

International Standard Book Number: *0-87041-214-0*
Library of Congress Catalogue Card Number: *84-81907*

Current Obstetric & Gynecologic Diagnosis & Treatment

A Concise Medical Library for Practitioner and Student

Current Medical Diagnosis & Treatment 1984 (annual revision). Edited by M.A. Krupp and M.J. Chatton. 1153 pp.	1984
Current Pediatric Diagnosis & Treatment, 8th ed. Edited by C.H. Kempe, H.K. Silver, and D. O'Brien. 1164 pp, *illus.*	1984
Current Surgical Diagnosis & Treatment, 6th ed. Edited by L.W. Way. 1221 pp, *illus.*	1983
Current Emergency Diagnosis & Treatment. Edited by J. Mills, M.T. Ho, and D.D. Trunkey. 738 pp, *illus.*	1983
Harper's Review of Biochemistry (formerly **Review of Physiological Chemistry**), 19th ed. D.W. Martin, Jr., P.A. Mayes, and V.W. Rodwell. 638 pp, *illus.*	1983
Review of Medical Physiology, 11th ed. W.F. Ganong. 643 pp, *illus.*	1983
Review of Medical Microbiology, 16th ed. E. Jawetz, J.L. Melnick, and E.A. Adelberg. 557 pp, *illus.*	1984
Basic & Clinical Endocrinology. Edited by F.S. Greenspan and P.H. Forsham. 646 pp, *illus.*	1983
Basic & Clinical Immunology, 5th ed. Edited by D.P. Stites, J.D. Stobo, H.H. Fudenberg, and J.V. Wells. 803 pp, *illus.*	1984
Basic & Clinical Pharmacology, 2nd ed. Edited by B.G. Katzung. 888 pp, *illus.*	1984
Basic Histology, 4th ed. L.C. Junqueira and J. Carneiro. 510 pp, *illus.*	1983
Clinical Cardiology, 3rd ed. M. Sokolow and M.B. McIlroy. 763 pp, *illus.*	1981
General Urology, 11th ed. D.R. Smith. 661 pp, *illus.*	1984
General Ophthalmology, 10th ed. D. Vaughan and T. Asbury. 407 pp, *illus.*	1983
Correlative Neuroanatomy & Functional Neurology, 18th ed. J.G. Chusid. 476 pp, *illus.*	1982
Principles of Clinical Electrocardiography, 11th ed. M.J. Goldman. 438 pp, *illus.*	1982
Electrocardiography: Essentials of Interpretation. N. Goldschlager and M.J. Goldman. 236 pp, *illus.*	1984
Review of General Psychiatry. Edited by H.H. Goldman. About 775 pp, *illus.*	1984
Handbook of Obstetrics & Gynecology, 8th ed. R.C. Benson. 804 pp, *illus.*	1983
Physician's Handbook, 20th ed. M.A. Krupp, L.M. Tierney, Jr., E. Jawetz, R.L. Roe, and C.A. Camargo. 774 pp, *illus.*	1982
Handbook of Pediatrics, 14th ed. H.K. Silver, C.H. Kempe, and H.B. Bruyn. 883 pp, *illus.*	1983
Handbook of Poisoning: Prevention, Diagnosis, & Treatment, 11th ed. R.H. Dreisbach. 632 pp.	1983

Lithographed in USA

current Obstetric & Gynecologic Diagnosis & Treatment

Preface

This fifth edition of *Current Obstetric & Gynecologic Diagnosis & Treatment,* like its predecessors, presents in concise form the basic information and most recent developments in the field of obstetrics and gynecology. The book is intended for use by medical students and residents and by practicing physicians as well as by nurses and other health professionals. Much new material has been added, and even those sections that did not require extensive revision have been made current by appropriate updating of the reference lists. Chapters that have been rewritten or substantially revised and expanded—or in a few cases shortened—for the new edition are as follows: Chapter 3 (physiology), Chapter 4 (placenta and fetus), Chapter 5 (history, examination, diagnosis), Chapter 9 (vulva and vagina, especially sexually transmitted diseases), Chapter 15 (pelvic infections), Chapter 17 (medical and surgical conditions), Chapter 23 (contraception and family planning), Chapter 34 (preeclampsia-eclampsia), Chapter 36 (the newborn infant), Chapter 38 (medical and surgical complications during pregnancy), Chapter 39 (dystocia), Chapter 41 (infertility management), Chapter 42 (emotional aspects of pregnancy), and the Appendix (antimicrobial therapy).

Current Obstetric & Gynecologic Diagnosis & Treatment is available in Spanish and Portuguese editions; and French, German, and Italian translations are in preparation.

The present editor of this book would like to join the publisher in extending to all of our contributors our gratitude for the time and effort expended every even-numbered year in preparing this book for publication. It is unfortunate that chapter contributors to scientific texts do not receive greater recognition for their undeniable achievements. Yet without their help, there would be no good textbooks, and not only our students but our patients and society at large would suffer for it.

We wish to thank also the many students and physicians whose suggestions and criticism are received with interest and profit and unfailingly pondered when we prepare succeeding editions.

Ralph C. Benson, MD

Portland, Oregon
October, 1984

Authors

Robert L. Bacon, PhD
Professor Emeritus of Anatomy, School of Medicine, Oregon Health Sciences University (Portland).

David L. Barclay, MD
Clinical Professor of Obstetrics and Gynecology, University of Arkansas for Medical Sciences (Little Rock, Arkansas).

David E. Barnard, MD
Assistant Professor of Obstetrics and Gynecology, Tulane University School of Medicine (New Orleans).

Ralph C. Benson, MD
Professor and Chairman Emeritus of Department of Obstetrics and Gynecology, Oregon Health Sciences University (Portland).

Hugh B. Collins, JD
Attorney at Law (Medford, Oregon).

F. Gary Cunningham, MD
Professor and Chairman of Department of Obstetrics and Gynecology, University of Texas Health Science Center (Dallas).

David N. Danforth, PhD, MD
Thomas J. Watkins Professor Emeritus of Obstetrics and Gynecology, Northwestern University Medical School (Chicago).

Russell Ramon de Alvarez, MD
Professor and Chairman Emeritus of Department of Obstetrics and Gynecology, Temple University Health Sciences Center (Philadelphia).

Albert W. Diddle, MD
Clinical Professor and Chairman Emeritus of Department of Obstetrics and Gynecology, Memorial Research Center and Hospital, University of Tennessee (Knoxville).

Raphael B. Durfee, MD
Professor of Reproductive Medicine, University of California School of Medicine (San Diego).

William F. Ganong, MD
Professor and Chairman of Department of Physiology, University of California School of Medicine (San Francisco).

Armando E. Giuliano, MD
Associate Professor of Surgery-Oncology, University of California School of Medicine (Los Angeles).

Robert C. Goodlin, MD
Department of Obstetrics and Gynecology, University of Nebraska School of Medicine (Omaha).

Ralph W. Hale, MD
Professor and Chairman of Department of Obstetrics and Gynecology, John A. Burns School of Medicine, University of Hawaii (Honolulu).

David L. Hemsell, MD
Associate Professor of Obstetrics and Gynecology and Director of Division of Gynecology, University of Texas Health Science Center (Dallas).

Lester T. Hibbard, MD
Professor of Obstetrics and Gynecology, Los Angeles County-University of Southern California Medical Center (Los Angeles).

Edward C. Hill, MD
Professor and Director of Gynecology-Oncology, University of California School of Medicine (San Francisco).

John W. Huffman, MD
Professor Emeritus of Obstetrics and Gynecology, Northwestern University Medical School (Chicago).

James M. Ingram, MD
Professor and Chairman of Department of Obstetrics and Gynecology, University of South Florida College of Medicine (Tampa).

Ernest Jawetz, MD, PhD
Professor of Microbiology and Medicine and Lecturer in Pediatrics, University of California School of Medicine (San Francisco).

Howard W. Jones, Jr., MD
Professor Emeritus of Gynecology and Obstetrics, Johns Hopkins University School of Medicine (Baltimore) and Professor of Obstetrics and Gynecology, Eastern Virginia Medical School (Norfolk).

Howard L. Judd, MD
Professor of Obstetrics and Gynecology and Director of Division of Reproductive Endocrinology, University of California School of Medicine (Los Angeles).

D. Frank Kaltreider, MD
Associate Professor of Gynecology and Obstetrics, Johns Hopkins University School of Medicine (Baltimore).

John L. Kitzmiller, MD
Associate Professor of Obstetrics, Gynecology, and Reproductive Sciences, University of California School of Medicine (San Francisco), and Chief of Perinatal Service, Children's Hospital of San Francisco.

Beverly L. Koops, MD
Associate Professor of Pediatrics, Texas A&M School of Medicine (Temple, Texas).

Kermit E. Krantz, MD, LittD
Professor and Chairman of Department of Gynecology and Obstetrics and Professor of Anatomy, University of Kansas Medical Center (Kansas City).

Daniel H. Labby, MD
Professor of Psychiatry and Medicine, Oregon Health Sciences University (Portland).

Conley G. Lacey, MD
Associate Professor and Co-Director of Gynecologic Oncology, University of California School of Medicine (San Francisco).

John M. Levinson, MD
Associate Professor of Obstetrics and Gynecology, Jefferson Medical College (Philadelphia).

Albert E. Long, MD
Clinical Associate, Stanford University School of Medicine (Stanford).

John R. Marshall, MD
Professor of Obstetrics and Gynecology, University of California School of Medicine (Los Angeles).

John S. McDonald, MD
Professor and Chairman of Department of Anesthesiology and Professor of Obstetrics and Gynecology, Ohio State University (Columbus).

Abe Mickal, MD
Clinical Professor and Emeritus Head of Department of Obstetrics and Gynecology, Louisiana State University Medical Center (New Orleans).

Kenneth R. Niswander, MD
Professor of Obstetrics and Gynecology, University of California School of Medicine (Davis).

Miles J. Novy, MD
Professor of Obstetrics and Gynecology, Oregon Health Sciences University (Portland).

April Gale O'Quinn, MD
Associate Professor, Department of Obstetrics and Gynecology, Tulane University School of Medicine (New Orleans).

Jack W. Pearson, MD
Professor of Obstetrics and Gynecology and Director of Division of Gynecology, University of Arizona School of Medicine (Tucson, Arizona).

Dorothee Perloff, MD
Clinical Professor of Medicine, University of California School of Medicine (San Francisco).

Martin L. Pernoll, MD
C.J. Miller Professor and Head of Department of Obstetrics and Gynecology, Tulane University School of Medicine (New Orleans).

Keith P. Russell, MD, FACOG, FACS
Clinical Professor of Obstetrics and Gynecology, University of Southern California School of Medicine (Los Angeles).

Leon Speroff, MD
Professor and Chairman of Department of Reproductive Biology, Case Western Reserve University (Cleveland).

Morton A. Stenchever, MD
Professor and Chairman of Department of Obstetrics and Gynecology, University of Washington School of Medicine (Seattle).

Richard E. Symmonds, MD
Professor and Chairman of Department of Gynecologic Surgery, The Mayo Medical School and Clinic (Rochester, Minnesota).

Howard J. Tatum, MD, PhD
Professor of Gynecology and Obstetrics, Emory University School of Medicine, and Director of Research, Family Planning Program, Emory University and Grady Memorial Hospital (Atlanta).

Randall B. Wilkening, MD
Assistant Professor of Pediatrics, University of Colorado Health Sciences Center (Denver).

J. Donald Woodruff, MD
Richard W. TeLinde Professor of Gynecologic Pathology and Professor of Gynecology and Obstetrics, Emeritus, Johns Hopkins University School of Medicine (Baltimore).

NOTICE

The authors and editors have been careful to recommend drug dosages that are in agreement with current official pharmacologic standards and the medical literature. Because all drugs may evoke idiosyncratic or toxic reactions, because drugs may interact with other drugs in ways that modify therapeutic effectiveness and toxicity, and because some drugs are teratogenic or are absorbed into breast milk and may affect a nursing infant, it is recommended that all clinicians review drug manufacturers' product information (eg, package inserts), especially in the case of new or infrequently prescribed medications. The physiologic and pathologic status of the patient must be considered, including age, sex, physical health, and activities. Furthermore, one must be thoroughly conversant with any drugs used in order to advise the patient about signs and symptoms of potential adverse reactions and incompatibilities.

The Editors

Table of Contents

Embryology of Structures Significant to Obstetrics & Gynecology

1

Robert L. Bacon, PhD

The human genitourinary system is an organ complex in which some structures that arise in close association in embryonic development assume diverse functions, and other structures that originate in widely separated areas must eventually make effective functional and structural contact. Failure particularly of the latter results in disastrous malformations in one or several portions of the system. Because of the complexity of these synchronously occurring events, the various components of the system will be described separately in the following categories: the nephroi and their ducts, the adrenal (suprarenal) glands, the gonads and their ducts, the cloaca, the urogenital sinus, and the external genitalia.

THE NEPHROI & THEIR DUCTS

The human embryo develops 3 successive sets of organs designed to remove wastes and control electrolyte balance. The **pronephros** is a system for transporting coelomic fluids; the **mesonephros** removes wastes from coelomic fluid and blood; and the **metanephros** is the definitive kidney, which excretes wastes from the circulating blood.

Pronephros

The pronephros is a functional system in embryos of many species and in a very limited number of primitive vertebrates. In humans, it is never completed either structurally or functionally, even in the embryo. This persistent vestigial structure appears to be necessary for the subsequent 2 stages of development of the excretory system. Only enough pronephros develops to set in motion the process by which the nephric duct is constructed. Approximately 7 or 8 pairs (in segments 7–14) of incompletely differentiated tubules appear in the intermediate mesoderm (between the somites and the lateral plate mesoderm), with the cephalic tubules already beginning to undergo degeneration before the caudal ones appear. The pronephros exists for about 1 week; it appears first in the third week and has degenerated by the fourth week. The duct established by fusion of the ends of these very transitory tubules persists, however, and continues to grow caudad from the future cervical (neck) region, where it originates, until it eventually fuses with the cloaca (Figs 1–1 and 1–5).

Mesonephros

The mesonephros may be a functional organ in the embryo and is structurally and functionally equivalent to the permanent excretory organ of most fish and amphibians. As the growing pronephric duct extends caudally, it apparently induces the differentiation of excretory mesonephric tubules in the tissue through which it passes. In response to this stimulus, tissue of the nephrogenic cord condenses in each segment to a cell cluster that soon becomes a hollow vesicle (Fig 1–2). The vesicle elongates and bends into an S-shaped tubule whose lateral end joins with a short outpouching of the nephric duct (Figs 1–1 and 1–3).

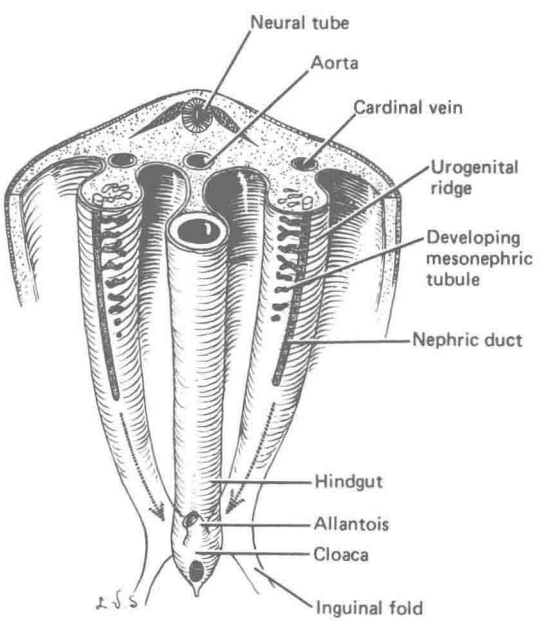

Figure 1–1. Caudad growth of the nephric duct within the urogenital ridge toward the cloaca. The tissue parallel to the duct, in which mesonephric tubules are differentiating, is the nephrogenic cord.

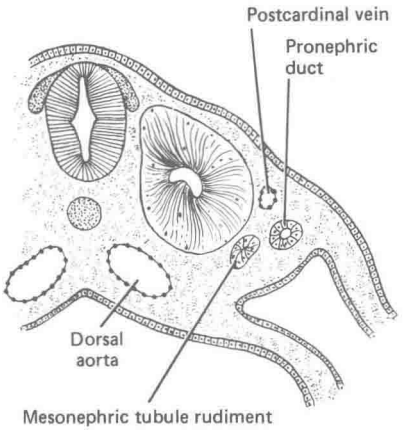

Figure 1–2. Diagrammatic section of an embryo at the level of the mesonephros in the fourth week. The rudiment of a mesonephric tubule has just developed, is still without a lumen, and is not yet connected with the nephric duct.

The medial end of each tubule thins out and surrounds a tuft of capillaries (the glomerulus) that develops at the end of a small lateral branch of the aorta (Fig 1–3). The efferent vessels from these glomeruli, after developing intimate association with the convolutions of the mesonephric tubule, empty into the cardinal system of veins (Fig 1–4). Thus is formed a simplified version of the far more complex nephron that will develop later in the metanephros or permanent kidney. Mesonephric tubules begin to be formed in the middle of the fourth week, before all the pronephric tubules

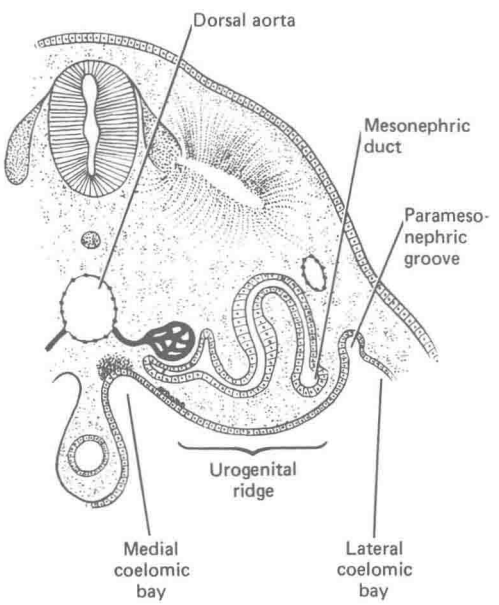

Figure 1–3. Diagrammatic section of an embryo at about 5 weeks. A glomerulus is forming, and the tubule has elongated, curved, and connected with the duct.

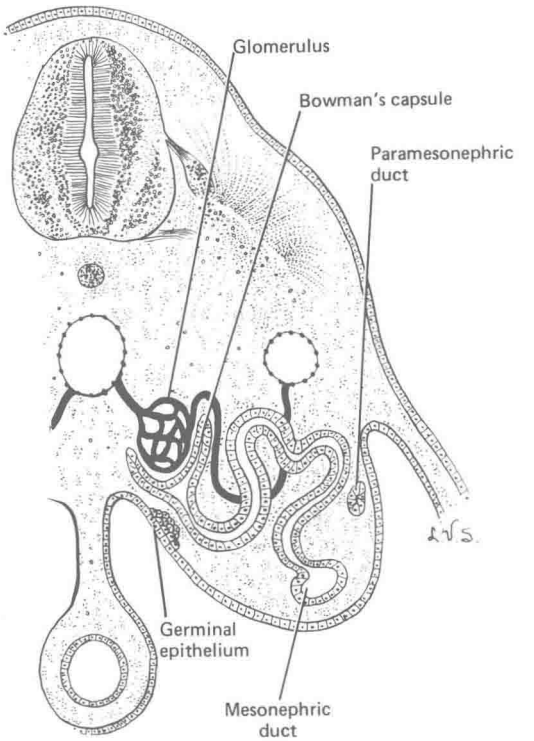

Figure 1–4. Diagrammatic section of a portion of an embryo in the sixth week. The vascular pattern is complete. The elongation and elaborate convolution of the tubule (simplified in this diagram) cause the urogenital ridge to bulge into the peritoneal cavity. The gonad will differentiate in relation to germinal epithelium facing the medial coelomic bay.

have degenerated, and first appear at about the level of T1. Thus, they overlap the pronephros both in space and in time. As with the pronephros, the processes of differentiation and regression both occur in a craniocaudal sequence. By the time most caudal tubules have developed at about somite 26, the more cephalic tubules have degenerated completely (Fig 1–5). These 2 processes occur at approximately equal rates, so that the number of mesonephric tubules remains roughly constant (30–34) and the entire organ appears to shift caudally in the embryo. Although the pronephros was segmental, with one pronephric tubule for each of the segments involved, only the most cephalic of the mesonephric tubules are segmentally arranged. Those in the lower thoracic and lumbar segments, which develop later, have 2–4 tubules with several glomeruli. At its maximum length, the mesonephros extends from the level of the heart to the future second or third lumbar segments. Shortly after the eighth week, relatively few intact mesonephric tubules still exist.

While it has been shown that the mesonephroi of the embryos of a number of mammals have the ability to eliminate phenolsulfonphthalein and ferrocyanide,

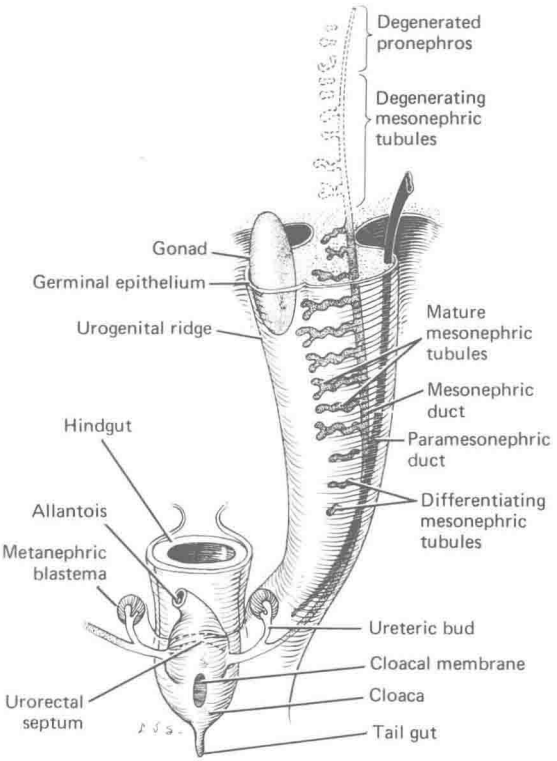

Figure 1–5. Diagram showing relations of developing gonad to mesonephric tubules and duct and relations of ureteric bud, mesonephric duct, urogenital sinus, and urorectal septum.

it is not known what functions the human mesonephros may have. Cytologic examination of the mesonephric tubules with their brush borders and readily demonstrable alkaline phosphatase, together with the remarkable electron microscopic similarities between mesonephric and metanephric tubules, suggests that the mesonephros probably is functional in the embryo.

The mesonephros itself contributes no functioning structures to the anatomy of the adult female. The degenerative process involved in removing the mesonephros includes extrusion of the glomerulus from Bowman's capsule. Most of the tubules that remain after this process is completed disappear entirely. As will be shown later, some do persist and are taken over, in the male, as efferent ductules connecting the rete testis to the epididymis. Various aberrant and vestigial vesicles, tubules, or cysts in both the male and the female may result from the persistence of mesonephric tubules at other levels. In the male, the mesonephric duct becomes the epididymis and vas deferens; in the female, a portion of the duct may persist as Gartner's duct.

Metanephros

For purposes of description and discussion, the development of the definitive kidney will be subdivided into collecting duct systems, excretory units, and migration.

A. Collecting Duct Systems: Shortly after attachment of the mesonephric duct to the cloaca, the metanephric diverticulum (ureteric bud) appears as a dorsal outgrowth of the duct very close to its connection to the cloaca opposite the level of the 28th somite (L4). The bud grows dorsally and cranially into the caudal end of the nephrogenic cord at the level of the 26th somite (Figs 1–5 and 1–12). The cord tissue responds to the growing tip by condensing and proliferating around it to form the metanephric blastema, which provides the cells that will form the major part of each nephron. The ureteric bud dilates to become the primitive renal pelvis and produces cranial and caudal expansions that are destined to become major calices of the adult kidney. An additional calix soon is added near the middle of the pelvis. Each calix expands into 2 buds (secondary collecting tubules). Divisions continue for 12–13 generations until the fetus is 6 months old. The later generations of branching generally are dichotomous, but the third, fourth, and fifth generations may produce 3–4 buds instead of 2. While tubular divisions are continuing near the cortical surface of the metanephros, the secondary tubules enlarge and absorb the third and fourth generations of tubules, to form the minor calices. Thus, the fifth-generation tubules open into the minor calices (expanded third- and fourth-generation ducts), and in view of the fact that the previous 2 generations have produced several branches instead of the usual 2, the number of collecting ducts entering a minor calix varies widely from about 10 to about twice that number. One to 3 million collecting tubules are produced by these several generations of division.

B. Excretory Units: The excretory portion of each nephron differentiates from the blastema of nephrogenic cord tissue under the inductive action of the growing collecting duct system and passes through the same series of basic morphologic changes that characterized the development of the mesonephric tubules. An S-shaped tubule forms in the tissue cap over the end of each collecting tubule. The elongated vesicle expands, and one end thins out into a cuplike arrangement that comes to enclose a tuft of glomerular capillaries. At the other end, the vesicle joins with its collecting duct. A departure from the mesonephroslike configuration occurs when the mid portion of the S begins to grow extensively into what will be Henle's loop, which extends into the medulla of the organ. Subsequently, the 2 ends of the originally simple S elongate and become tortuous, to form the proximal and distal convoluted tubules of the adult nephron. The glomerulus and capsule remain essentially unchanged; at 2500 g (36 weeks), the glomeruli are fully developed.

C. Migration: The migration of the metanephros out of the pelvis and into the abdomen to its ultimate position (Fig 1–6) is important because deviations from the normal course of this process account for clinically significant abnormalities. Some of this mi-

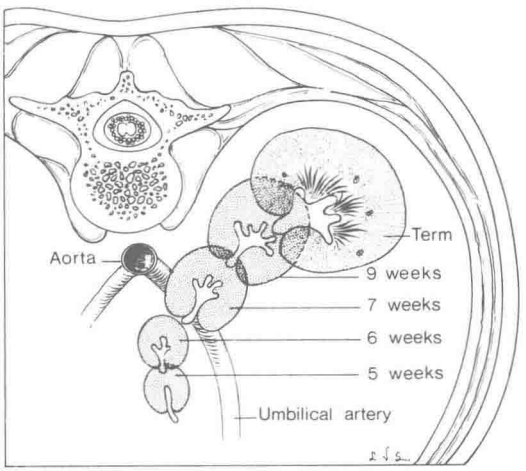

Figure 1–6. Cross-sectional diagram showing migration and rotation of the kidney. Sections of the kidney at 5 stages have been projected on one plane. (Redrawn and modified from Kelly HA, Burnam CF: *Diseases of Kidneys, Ureters and Bladder*. Appleton-Century-Crofts, 1972.)

gration is more apparent than real and is due to rapid expansion of the body wall caudal to the site of metanephric development. By the end of the 12th week, the kidney lies adjacent to the second or third lumbar vertebra. Some of this positional change is due to migration. The metanephroi, as they shift cranially, are brought close together near the midline in the angle of the aortic bifurcation. It is at this point during the seventh week, before the metanephroi have slid over the umbilical arteries out of the narrow pelvis into the more capacious abdomen, that horseshoe kidney may result if fusion occurs. Similarly, it is probable that these large vessels may act as barriers, occasionally blocking further upward migration of the metanephros. This results in pelvic kidney, with one or both organs located near the level of origin. As the normally developing kidney slides out of the pelvis over the artery, it is guided laterally by the larger developing vertebrae and muscle masses at these levels and is rotated on its long axis approximately 90 degrees, with the convex border facing laterally instead of dorsally.

Relation of Nephric Ducts to Urogenital Sinus

Enlargement of the urogenital sinus is accompanied by absorption of mesonephric ducts into its wall (Figs 1–12 to 1–15). Thus, the metanephric diverticulum—originally an outgrowth of the mesonephric duct—eventually comes to have a separate opening into the sinus. That portion of the sinus wall between the mesonephric and metanephric openings is composed of tissue derived from the ducts (trigone).

The termination of the mesonephric duct at first is superior to that of the metanephric duct (ureter). The mesonephric ducts have the same stromal investment as the fused paramesonephric ducts, which have reached this level in the midline at about the time the urogenital sinus is rapidly expanding rostrally and laterally. The ureters, not anchored to the mesonephric ducts, are carried rostrally and laterally as the tissue of the sinus wall in this area grows and the organ expands. In contrast, mesonephric ducts are anchored near the midline to a portion of the sinus that will remain narrow as the prostatic urethra in the male or be carried even further caudally as vestiges associated with the lateral wall of the upper portion of the vagina in the female.

ADRENAL (SUPRARENAL) GLANDS

The adrenal (suprarenal) glands are formed by the intimate association of cell populations derived from 2 widely different origins. The medulla is derived from ectodermal cells that migrate from the crest of the neural folds (Fig 1–7). These cells follow a complex migratory pathway to arrive at their final position above the kidneys (Fig 1–8A). The adrenal cortex is derived from mesodermal cells of the coelomic mesothelium of the medial coelomic bay between the root of the mesentery and the urogenital ridge (Fig 1–8B).

In the fifth week, columnar mesothelial cells proliferate and leave the coelomic epithelium to lie in the subjacent mesenchyme and differentiate into enlarged acidophilic cells (Fig 1–9A). At about the same time, clusters of future medullary cells arrive and assemble in groups closely associated with the first wave of cortical cells (Fig 1–9A). At first they are scattered on the surface or are partially within the cortical mass; they do not become truly medullary in position until later (Fig 1–9B). The initial proliferation of large acidophilic cortical cells constitutes the fetal or provisional cortex that is destined to disappear after birth. In the sixth week, a second wave of smaller, less well differentiated mesothelial cells spreads over the surface of the previously assembled glandular mass (Fig 1–9C). This second wave is destined to form the definitive cortex of the adult.

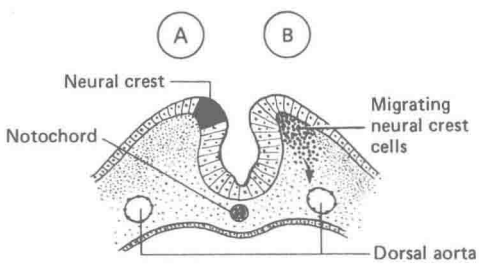

Figure 1–7. Diagrammatic section of open neural tube stage. *A:* Location of neural crest. *B:* Later stage indicating cells leaving epithelium and beginning their migration.

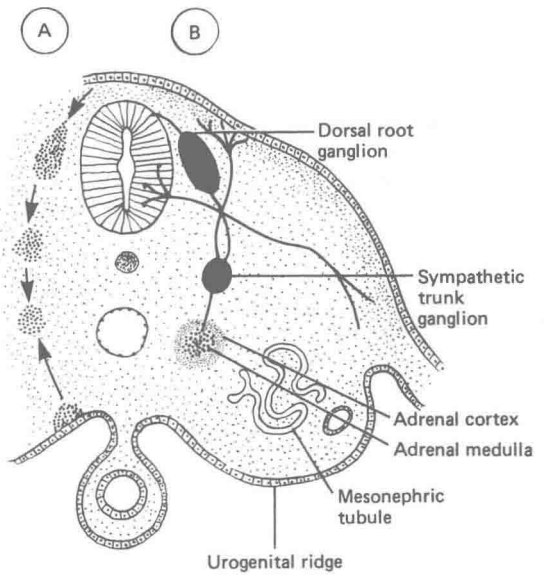

Figure 1–8. *A:* Route of migration of neural crest cells. One cluster remains near the neural tube to form the spinal ganglion; another proceeds to the location of future sympathetic trunk ganglion; and still another continues and becomes associated with cortical cells emigrating from the coelomic epithelium. *B:* Diagram of structures formed by these groups of neural crest cells.

The fetal adrenals are relatively large organs owing to the considerable size of the fetal cortex. At term they constitute about 0.2% of the body weight and are 20 times the size of those in the adult relative to body weight. Differentiation of the permanent cortex is not completed until about 3 years after birth, and it does not keep up with degeneration of the fetal cortex. As a result of this discrepancy between regression and differentiation, there is an absolute decrease in size of the adrenal glands after birth.

There is evidence that both components of the adrenal glands are functional in the fetus. The fetal cortex appears to be dependent on pituitary function during fetal life. Tumors of the fetal cortex apparently produce considerable quantities of androgens and therefore may cause pseudohermaphroditic changes in female fetuses. The medullary cells show cytochemical evidence of catecholamines, and, after the tenth week, norepinephrine and, later, epinephrine may be found in these cells.

As might be expected from what has just been said about the complex development of these structures, accessory medullary or cortical tissue may be found in a variety of locations. The development of this large organ in the limited space between the aorta and the urogenital ridge might lead one to predict that accessory adrenal tissue would be found near the gonads, which develop in the urogenital ridge. Accessory adrenal tissue occasionally is found in areas where it may have been carried by the migrating testis or ovary, eg, in the broad ligament of the female (accessory adrenal of Marchand) or in the scrotum of the male.

THE GONADS & THEIR DUCTS

The first indication of the developing gonad is a thickening in the coelomic epithelium on the inner surface of the urogenital ridge facing the medial coelomic bay (Figs 1–4 and 1–5). This becomes noticeable late in the fourth week. At the same time, the underlying mesenchyme condenses and the basement membrane between the epithelium and the mesenchyme disappears. The 2 cellular components become intimately mixed. Condensation of cells gives rise to the anastomosing primitive sex cords that extend from the epithelium deep into the substance of the urogenital ridge. Meanwhile, during the sixth week, the important primordial germ cells arrive after their long migration from the wall of the yolk sac near the allantois, where they first appear. They have migrated through the mesentery from the region of the hindgut to the dorsal body wall and then laterally into the developing gonad on each side. In experimental animals, if the primordial cells are removed or prevented from reaching their destination, the gonad undergoes only minimal differentiation. Thus, as with the developing

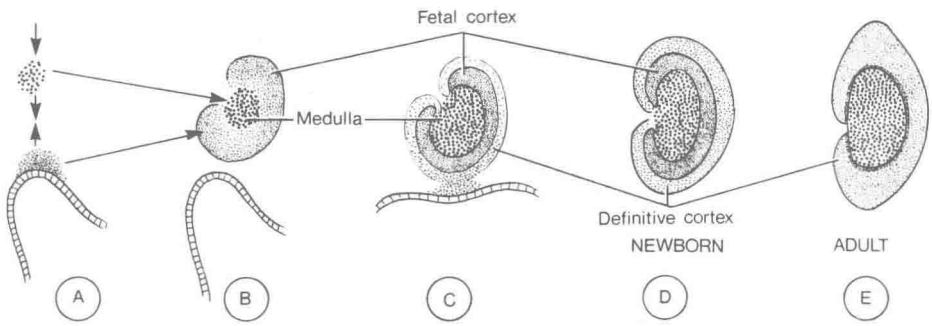

Figure 1–9. *A–E:* Stages in the migration, assembly, and differentiation of the adrenal gland.