3RD EDITION

current OBSTETRIC & GYNECOLOGIC DIAGNOSIS & TREATMENT

RALPH C. BENSON

1980

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By

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Preface

We are most gratified by the wide and growing acceptance of this textbook of obstetrics and gynecology in this country and abroad. Traditionally, authors and publishers have held that a medical book which has reached its third edition has achieved a certain maturity. By this time, an important content, laudable accuracy, and good balance usually will have been achieved. We trust this applies to *Current Obstetric & Gynecologic Diagnosis & Treatment*.

In this third edition, we still pursue our original objectives: to be useful without being tedious and to emphasize what is common and important as well as what is uncommon though still important. Our goal is to present the basic principles of diagnosis and treatment in sufficient detail to cover the management of the patient in clinical practice. Current sources of more detailed information are provided in the references.

Each chapter has been brought up to date. The chapters on disorders of the uterine corpus, menopause, and postmenopause have been totally rewritten. The chapter on pelvic infections has been reorganized and greatly improved. The chapters on special medical and surgical conditions in gynecology, operative delivery, and antimicrobial chemotherapy have been heavily revised.

A Spanish translation is available, and Portuguese, German, and French ones are in preparation. The book is reprinted (in English) in Singapore, Taipei, and Beirut for distribution in developing countries.

The editor's sincere thanks go to the contributing authors for their patience and expertise and to the students and physicians who have made helpful suggestions.

Ralph C. Benson, MD

Portland, Oregon
August, 1980

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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).

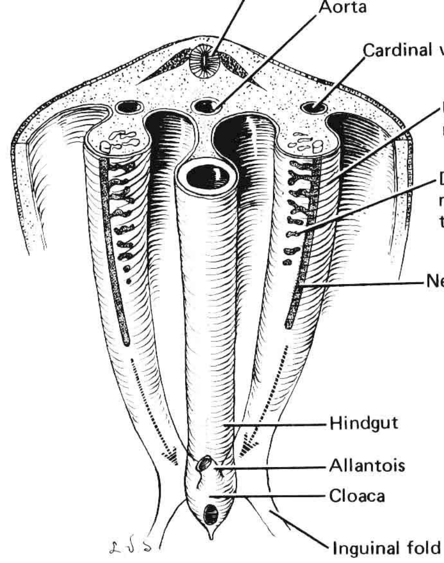

Figure 1–1. Caudad growth of the nephric duct within the urogenital ridge toward the cloaca. The tissue parallel to the duct, in which mesonephric tubules are differentiating, is the nephrogenic cord.

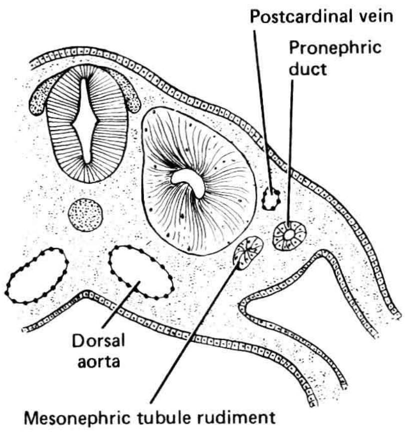

Figure 1-2. Diagrammatic section of an embryo at the level of the mesonephros in the fourth week. The rudiment of a mesonephric tubule has just developed, is still without a lumen, and is not yet connected with the nephric duct.

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 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,

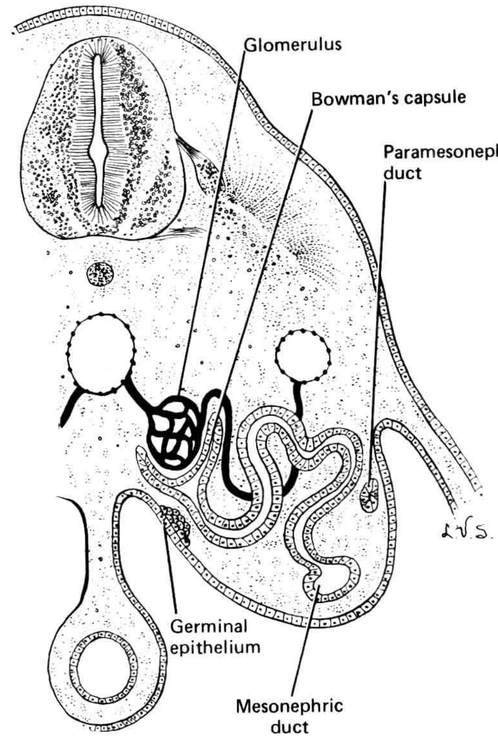

Figure 1-4. Diagrammatic section of a portion of an embryo in the sixth week. The vascular pattern is complete. The elongation and elaborate convolution of the tubule (simplified in this diagram) cause the urogenital ridge to bulge into the peritoneal cavity. The gonad will differentiate in relation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

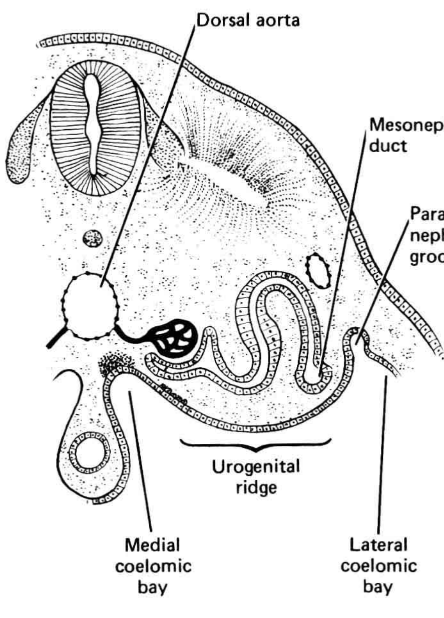

Figure 1-3. Diagrammatic section of an embryo at about 5 weeks. A glomerulus is forming, and the tubule has elongated, curved, and connected with the duct.

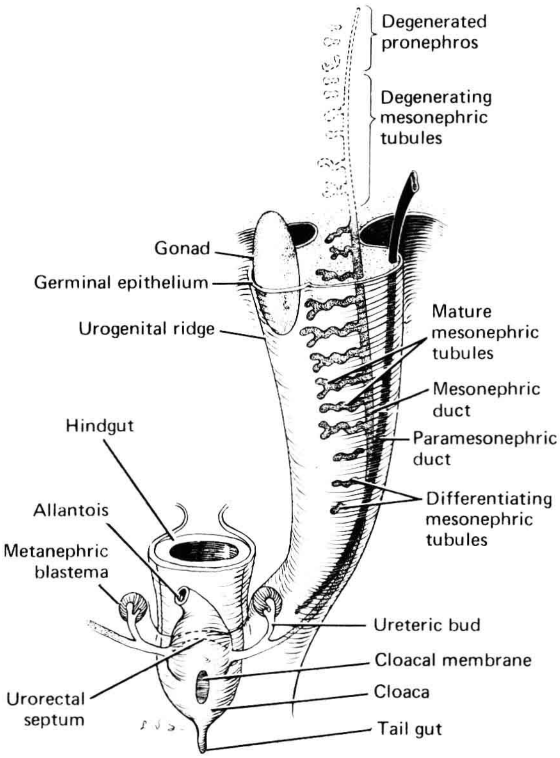

Figure 1–5. Diagram showing relations of developing gonad to mesonephric tubules and duct and relations of ureteric bud, mesonephric duct, urogenital sinus, and urorectal septum.

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 calyces of the adult kidney. An additional calyx soon is added near the middle of the pelvis. Each calyx 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 calyces. Thus, the fifth generation tubules open into the minor calyces (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 calyx 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-

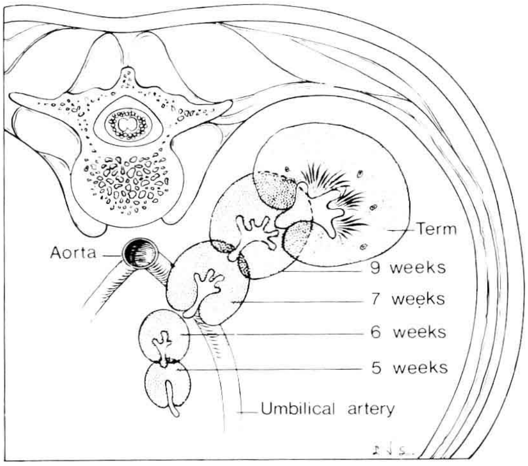

Figure 1–6. Cross-sectional diagram showing migration and rotation of the kidney. Sections of the kidney at 5 stages have been projected on one plane. (Redrawn and modified from Kelly HA, Burnam CF: *Diseases of Kidneys, Ureters and Bladder*. Appleton-Century-Crofts, 1972.)

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.

THE 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 1–8).

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.

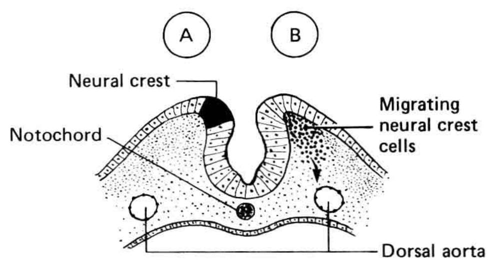

Figure 1–7. Diagrammatic section of open neural tube stage. *A:* Location of neural crest. *B:* Later stage indicating cells leaving epithelium and beginning their migration.

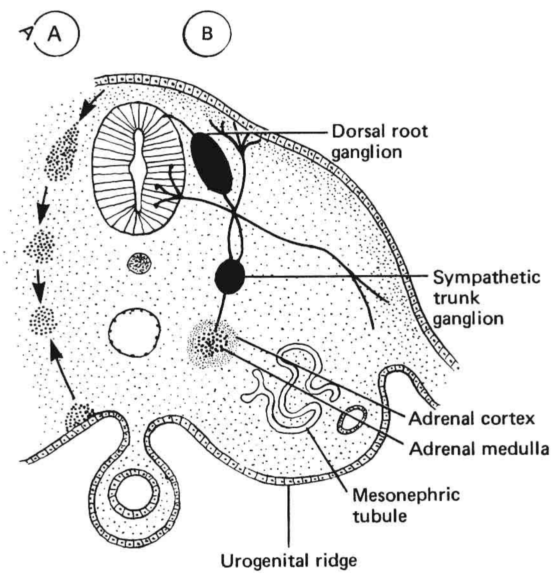

Figure 1–8. *A:* Route of migration of neural crest cells. One cluster remains near the neural tube to form the spinal ganglion; another proceeds to the location of future sympathetic trunk ganglion; and still another continues and becomes associated with cortical cells emigrating from the coelomic epithelium.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

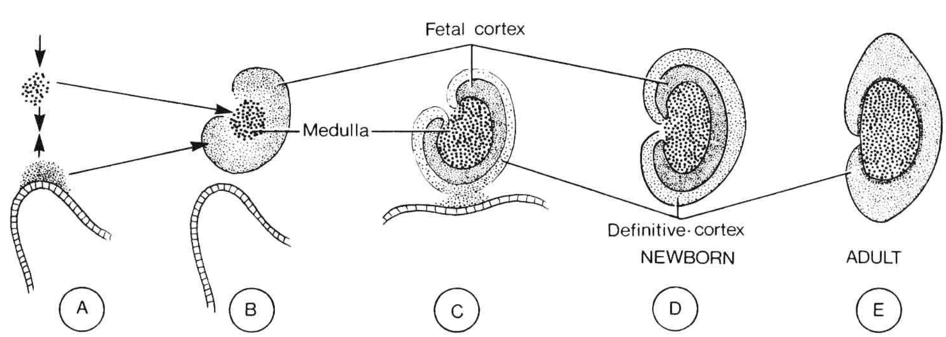

Figure 1–9. *A–E:* Stages in the migration, assembly, and differentiation of the adrenal gland.

pronephros, the primordial germ cells appear to constitute embryonic inductors. Although it has not been possible to determine this with certainty, it is currently believed that these primordial cells are the direct ancestors of the spermatozoa and ova in the adult.

This period of development of the gonad is known as the indifferent stage, because male or female gonads cannot be identified until the proliferation of the tunica albuginea, which separates the sex cords from the coelomic epithelium in the seventh week, indicates testicular development. At this time, the sex cords of the male become isolated from the coelomic epithelium, while those of the female remain in contact and continue to grow extensively.

If the gonad is to become a testis, further ingrowth and development of cortical tissue ceases, and during the eighth week the tunica albuginea isolates the 2 components. The primitive sex cords continue to grow within the medulla of the gonad and soon become less diffuse and more clearly defined as the testis cords. After its isolation from the subjacent cords by the tunica albuginea, the original germinal epithelium regresses to the typical flat squamous mesothelium. The lateral ends of the sex cords, which persist in the medulla, develop interconnecting epithelial strands in close proximity to the mesonephric tubules, where the mesonephric glomeruli are regressing. This anastomosing network will become the rete testis, but canalization does not occur until later (in the 12th to 16th weeks). The testis cords are composed of cells probably derived from 2 origins: primordial germ cells from the allantois, and epithelial cells from the coelomic surface of the gonad. Presumably, the epithelial cells eventually become the Sertoli cells of the adult, and the primitive germ cells differentiate into the spermatogonia of the adult.

If the gonad is to become an ovary, the sex cords become subdivided and broken down into irregular groups associated with some of the primordial germ cells. These cell clusters gradually disappear, and the ovarian medulla of the newborn is essentially free of these tissues. The surface epithelium is not at this stage isolated by a highly developed tunica albuginea, however, and cords continue to be produced and to penetrate the underlying mesenchyme but not the medulla. These persistent so-called secondary or cortical cords also break down eventually, and their component cells form clusters associated with primordial germ cells

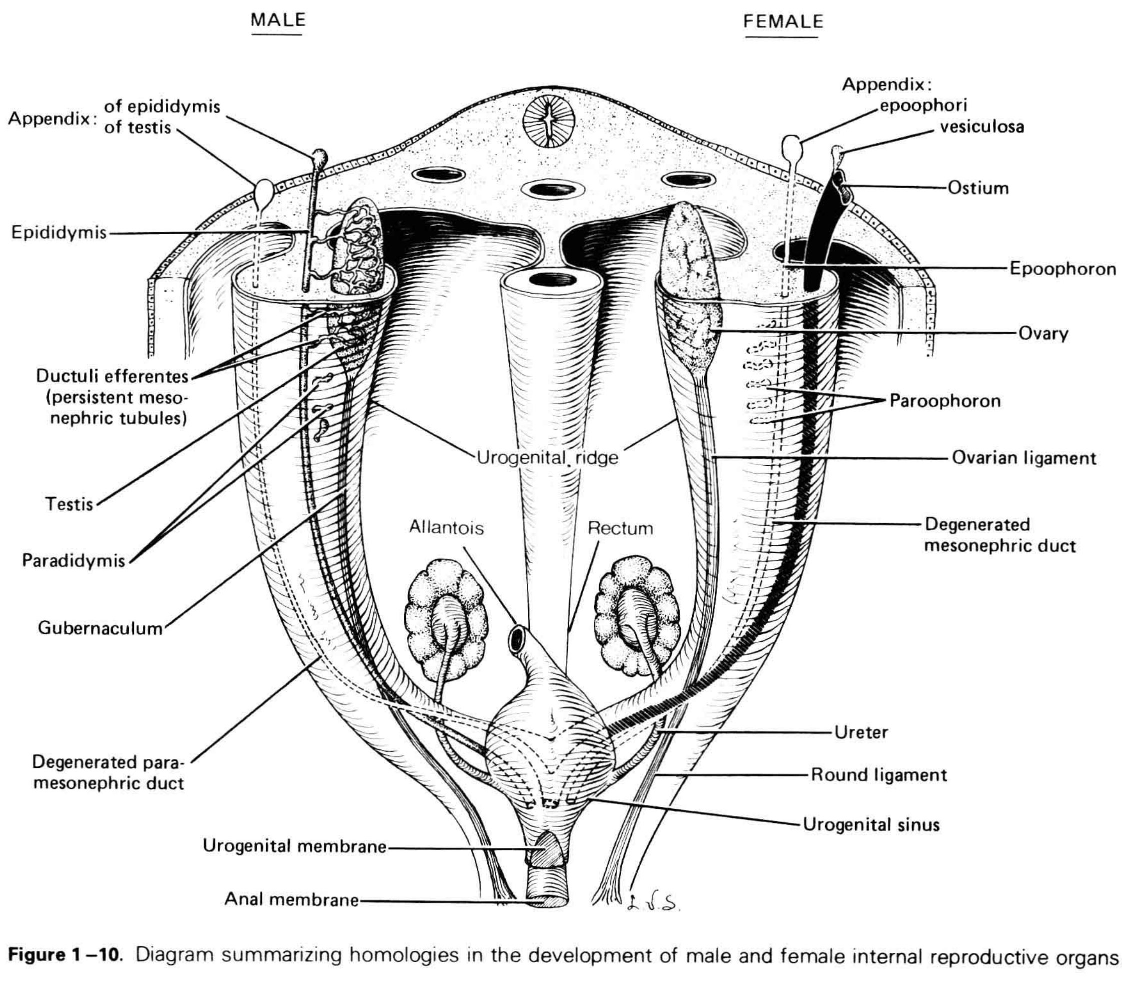

Figure 1–10. Diagram summarizing homologies in the development of male and female internal reproductive organs.

that probably become the oogonia, with the former epithelial cells making up the primordial follicles. Although a presumptive ovarian rete appears in the lateral portion of the ovary and several mesonephric tubules are present, the rete does not become patent and the mesonephric tubules are nonfunctional. They may persist, however, along with a small segment of the mesonephric duct, to become the vestigial epoophoron.

The mesenchymal substance of the genital ridge inferior to the gonad terminates caudally in the region of the future external genitalia. This strand of tissue differentiates into the gubernaculum (Fig 1–10), a structure that apparently does not grow at the same rate as the surrounding structures. The gubernaculum is thereby relatively shortened and perhaps actually contracts. The gubernaculum is involved in the process by which the gonad descends from its original high position in the abdominal cavity into the scrotum. The male gonad may carry with it remnants of the mesonephric and paramesonephric systems. Since the lower portion of the gubernaculum is made up of several strands that terminate in other areas, the male gonad occasionally may be guided to an anomalous position such as the upper thigh or prepubic region.

In the female, however, the relatively massive lateral expansions of the fused portions of the paramesonephric ducts—which are to become the uterus—attach to the gubernaculum in the angle where the paramesonephric ducts swing medially to join each other (Fig 1–10). This angle becomes the junction of the oviduct with the uterus. Thus, in the female, although the gonad descends a considerable distance, the gubernaculum is anchored at the tubouterine junction, and further descent of the gonad ordinarily does not occur (Fig 1–11). That portion of the gubernaculum between the ovary and the uterus is the ovarian ligament; the remainder, from the uterine attachment to the inguinal region, is the round ligament of the uterus. The course of the descent of the gonad in each sex is

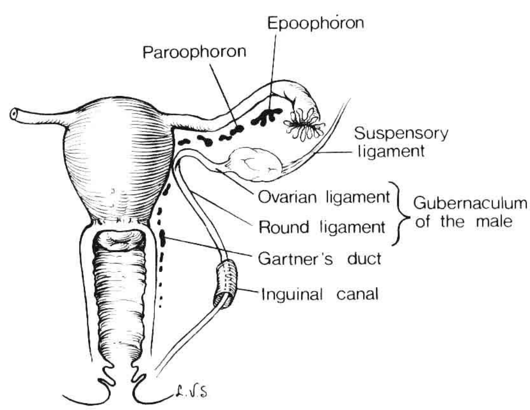

Figure 1–11. Diagram of female reproductive tract showing vestigial mesonephric structures and components of the gubernaculum.

marked by the blood vessels. The arteries arise from the aorta not far below the origin of the renal arteries; the right gonadal vein enters the vena cava at the same high level, and the left enters the left renal vein.

In the indifferent stage of sexual development, a complete set of genital duct systems is established for both sexes. That of the male is derived from the mesonephric duct, which has been discussed above. The first indication of the female duct system is the appearance in the sixth week of a groove toward the superior end of the genital ridge lateral to and parallel with the mesonephric duct (Fig 1–3). This groove becomes deeper and closes over to form a tube. The lower end of the tube grows caudally, much as the old pronephric duct did, and eventually fuses with the wall of the portion of the cloaca that is destined to become the urogenital sinus (Figs 1–5 and 1–13). The opening of the paramesonephric duct persists as the ostium of the uterine tube. The lower end of the paramesonephric duct, normally late in reaching the urogenital sinus, probably arrives at this position late in the eighth or early in the ninth week of development.

Throughout much of its length, the genital ridge is parallel to the paramesonephric duct (Fig 1–10). As these ridges are followed caudally, however, they must first swing ventrally and then medially if the lower ends of the ducts that they contain are to fuse with the portion of the cloaca that later separates from the rectum to form the urogenital sinus. As these ducts are followed caudally, they swing medially, and the originally more laterally placed paramesonephric duct finally comes to lie closest to the midline, in intimate proximity to its neighbor from the opposite side (Figs 1–10 and 1–14). Thus, the fused ends of the paramesonephric ducts are joined to the urogenital sinus in the midline dorsally. Immediately lateral to this junction are the terminations of the mesonephric duct in the wall of the same chamber.

Mesonephric Ducts

The mesonephric ducts undergo different development in the 2 sexes. If the individual is to become a male, the mesonephric duct persists and begins its typical histogenesis in the seventh week. Most of the duct is involved in the formation of the epididymis and vas deferens. From its lower portion, a new outgrowth appears that becomes a seminal vesicle (Fig 1–14), while its upper portion becomes very tortuous and does not develop an extensive muscular investment but remains as a thin-walled, highly convoluted tubule, the epididymis. The prostatic buds develop from that portion of the urogenital sinus which is to become the prostatic urethra. These buds surround and enclose the terminal portion of the mesonephric duct (Fig 1–14), which then becomes the ejaculatory duct. The most cranial portion of the mesonephric duct, superior to that part into which the efferent ductules open, persists in most instances as a small cystic structure, the appendix epididymis. From 5 to 15 mesonephric tubules persist after the degeneration of the glomeruli to connect the rete testis (which has developed from the deep

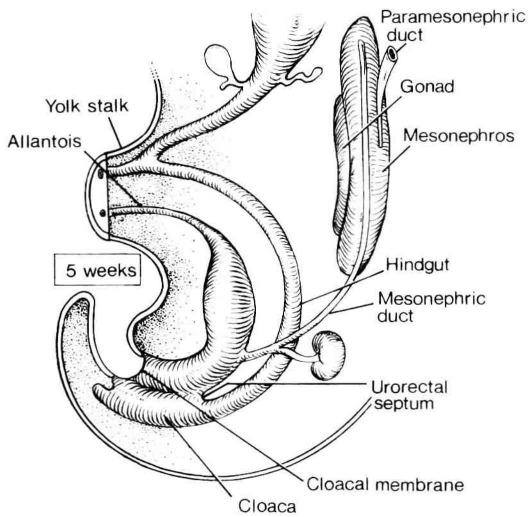

Figure 1–12. Diagrammatic left lateral view of urogenital system in relation to the hindgut at about 5 weeks. The paramesonephric duct does not appear until the sixth week but is shown here to indicate its position and downgrowth.

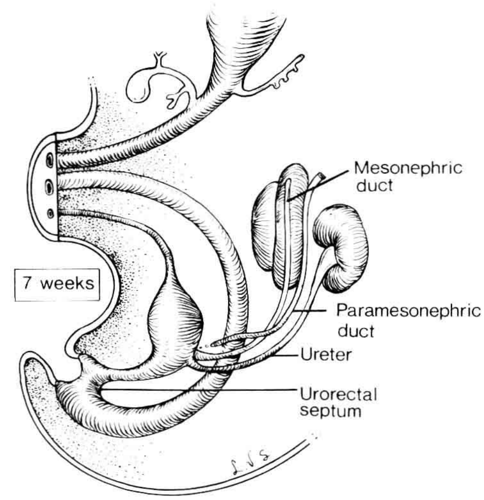

Figure 1–13. Diagrammatic left lateral view of the urogenital system in relation to gut at about 7 weeks. The paramesonephric duct is shown at a more advanced stage to demonstrate its approach to the urogenital sinus. No sexual differentiation has yet occurred.

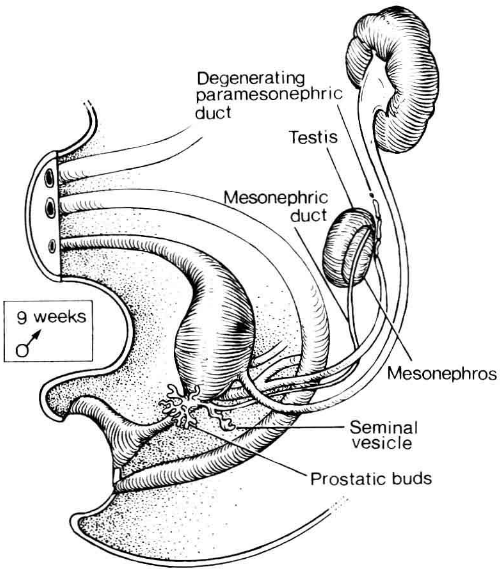

Figure 1–14. Diagram of male reproductive tract at an early stage of sexual differentiation (about 9 weeks). Although prostatic buds are shown here for emphasis, they do not reach this degree of development for several weeks.

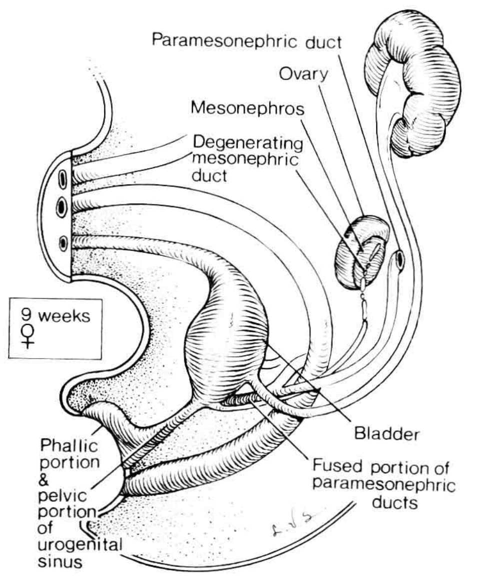

Figure 1–15. Diagram of female reproductive tract at an early stage of sexual differentiation (about 9 weeks).