Urogenital System
Genital System

Sex differentiation is a complex process that involves many genes, including some that are autosomal. The key to sexual dimorphism is the Y chromosome, which contains the ***SRY* (sex-determining region on Y) gene** on its short arm (Yp11). The protein product of this gene is a transcription factor initiating a cascade of downstream genes that determine the fate of rudimentary sexual organs. The SRY protein is the **testis determining factor;** under its influence male development occurs; in its absence female development is established.

GONADS

Although the sex of the embryo is determined genetically at the time of fertilization, the gonads do not acquire male or female morphological characteristics until the seventh week of development.

Gonads appear initially as a pair of longitudinal ridges, the **genital** or **gonadal ridges**. They are formed by proliferation of the epithelium and a condensation of underlying mesenchyme. **Germ cells** do not appear in the genital ridges until the sixth week of development. Primordial germ cells first appear at an early stage of development among endoderm cells in the wall of the yolk sac close to the allantois. They migrate by ameboid movement along the dorsal mesentery of the hindgut, arriving at the primitive gonads at the beginning of the fifth week and invading the genital ridges in the sixth week. If they fail to reach the ridges, the gonads do not develop. Hence the primordial germ cells have an inductive influence on development of the gonad into ovary or testis. Shortly before and during arrival of primordial germ cells, the epithelium of the genital ridge proliferates, and epithelial cells penetrate the underlying mesenchyme. Here they form a number of irregularly shaped cords, the **primitive sex cords**. In both male and female embryos, these cords are connected to surface epithelium, and it is impossible to differentiate between the male and female gonad. Hence, the gonad is known as the **indifferent gonad.**

Testis

If the embryo is genetically male, the primordial germ cells carry an XY sex chromosome complex. Under influence of the *SRY* gene on the Y chromosome, which encodes the testis-determining factor, the primitive sex cords continue to proliferate and penetrate deep into the medulla to form the **testis** or **medullary cords**. Toward the hilum of the gland the cords break up into a network of tiny cell strands that later give rise to tubules of the **rete testis**. During further development, a dense layer of fibrous connective tissue, the **tunica albuginea,** separates the testis cords from the surface epithelium. In the

fourth month, the testis cords become horseshoe shaped, and their extremities are continuous with those of the rete testis. Testis cords are now composed of primitive germ cells and **sustentacular cells of Sertoli** derived from the surface epithelium of the gland.

Interstitial cells of Leydig, derived from the original mesenchyme of the gonadal ridge, lie between the testis cords. They begin development shortly after onset of differentiation of these cords. By the eighth week of gestation, Leydig cells begin production of **testosterone,** and the testis is able to influence sexual differentiation of the genital ducts and external genitalia. Testis cords remain solid until puberty, when they acquire a lumen, thus forming the **seminiferous tubules.** Once the seminiferous tubules are canalized, they join the rete testis tubules, which in turn enter the **ductuli efferentes.** These efferent ductules are the remaining parts of the excretory tubules of the mesonephric system. They link the rete testis and the mesonephric or wolffian duct, which becomes the **ductus deferens**.

Ovary

In female embryos with an XX sex chromosome complement and no Y chromosome, primitive sex cords dissociate into irregular cell clusters. These clusters, containing groups of primitive germ cells, occupy the medullary part of the ovary. Later they disappear and are replaced by a vascular stroma that forms the **ovarian medulla**. The surface epithelium of the female gonad, unlike that of the male, continues to proliferate. In the seventh week, it gives rise to a second generation of cords, **cortical cords,** which penetrate the underlying mesenchyme but remain close to the surface. In the fourth month, these cords split into isolated cell clusters, with each surrounding one or more primitive germ cells. Germ cells subsequently develop into oogonia, and the surrounding epithelial cells, descendants of the surface epithelium, form **follicular cells**. It may thus be stated that the genetic sex of an embryo is determined at the time of fertilization, depending on whether the spermatocyte carries an X or a Y chromosome. In embryos with an XX sex chromosome configuration, medullary cords of the gonad regress, and a secondary generation of cortical cords develops. In embryoswith an XY sex chromosome complex, medullary cords develop into testis cords, and secondary cortical cords fail to develop.

GENITAL DUCTS

Indifferent Stage Initially both male and female embryos have two pairs of genital ducts: **mesonephric (wolffian) ducts** and **paramesonephric (m¨ullerian) ducts.** The paramesonephric duct arises as a longitudinal invagination of the epithelium on the anterolateral surface of the urogenital ridge. Cranially the duct opens into the abdominal

cavity with a funnel-like structure. Caudally it first runs lateral to the mesonephric duct, then crosses it ventrally to grow caudomedially. In the midline it comes in close contact with the paramesonephric duct from the opposite side. The two ducts are initially separated by a septum but later fuse to form the **uterine canal**. The caudal tip of the combined ducts projects into the posterior wall of the urogenital sinus, where it causes a small swelling, the paramesonephric or m¨ullerian tubercle. The mesonephric ducts open into the urogenital sinus on either side of the m¨ullerian tubercle.

Genital Ducts in the Male

As the mesonephros regresses, a few excretory tubules, the **epigenital tubules,** establish contact with cords of the rete testis and finally form the **efferent ductules** of the testis. Excretory tubules along the caudal pole of the testis, the **paragenital tubules,** do not join the cords of the rete testis. Their vestiges are collectively known as the **paradidymis.** Except for the most cranial portion, the **appendix epididymis,** the mesonephric ducts persist and form the main genital ducts. Immediately below the entrance of the efferent ductules, the mesonephric ducts elongate and become highly convoluted, forming the **(ductus) epididymis.** From the tail of the epididymis to the outbudding of the **seminal vesicle,** the mesonephric ducts obtain a thick muscular coat and form the **ductus deferens.** The region of the ducts beyond the seminal vesicles is the **ejaculatory duct.** The paramesonephric ducts in the male degenerate except for a small portion at their cranial ends, the **appendix testis**.

Genital Ducts in the Female

The paramesonephric ducts develop into the main genital ducts of the female. Initially, three parts can be recognized in each duct:
(*a*) a cranial vertical portion that opens into the abdominal cavity,
(*b*) a horizontal part that crosses the mesonephric duct, and
(*c*) a caudal vertical part that fuses with its partner from the opposite side.

With descent of the ovary, the first two parts develop into the **uterine tube** and the caudal parts fuse to form the **uterine canal.**

When the second part of the paramesonephric ducts moves mediocaudally, the urogenital ridges gradually come to lie in a transverse plane. After the ducts fuse in the midline, a broad transverse pelvic fold is established. This fold, which extends from the lateral sides of the fused paramesonephric ducts toward the wall of the pelvis, is **the broad ligament of the uterus.** The uterine tube lies in its upper border, and the ovary lies on its posterior surface. The uterus and broad ligaments divide the pelvic cavity into the **uterorectal pouch** and the **uterovesical pouch.** The fused paramesonephric ducts give rise to the **corpus** and **cervix** of the uterus. They are surrounded by a layer of

mesenchyme that forms the muscular coat of the uterus, the **myometrium,** and its peritoneal covering, the **perimetrium.**

VAGINA

Shortly after the solid tip of the paramesonephric ducts reaches the urogenital sinus, two solid evaginations grow out from the pelvic part of the sinus. These evaginations, the **sinovaginal bulbs,** proliferate and form a solid **vaginal plate.** Proliferation continues at the cranial end of the plate, increasing the distance between the uterus and the urogenital sinus. By the fifth month, the vaginal outgrowth is entirely canalized. The winglike expansions of the vagina around the end of the uterus, the **vaginal fornices,** are of paramesonephric origin. Thus, the vagina has a dual origin, with the upper portion derived from the uterine canal and the lower portion derived from the urogenital sinus. The lumen of the vagina remains separated from that of the urogenital sinus by a thin tissue plate, the **hymen**, which consists of the epithelial lining of the sinus and a thin layer of vaginal cells. It usually develops a small opening during perinatal life.

The female may retain some remnants of the cranial and caudal excretory tubules in the mesovarium, where they form the **epoophoron** and **paroophoron,** respectively. The mesonephric duct disappears except for a small cranial portion found in the epoophoron and occasionally a small caudal portion that may be found in the wall of the uterus or vagina. Later in life it may form **Gartner's cyst**.

EXTERNAL GENITALIA

Indifferent Stage, In the third week of development, mesenchyme cells originating in the region of the primitive streak migrate around the cloacal membrane to form a pair of slightly elevated **cloacal folds**. Cranial to the cloacal membrane the folds unite to form the **genital tubercle.** Caudally the folds are subdivided into **urethral folds** anteriorly and **anal folds** posteriorly. In the meantime, another pair of elevations, the **genital swellings,** becomes visible on each side of the urethral folds. These swellings later form the **scrotal swellings** in the male and the **labia majora** in the female. At the end of the sixth week, however, it is impossible to distinguish between the two sexes.

External Genitalia in the Male

Development of the external genitalia in the male is under the influence of androgens secreted by the fetal testes and is characterized by rapid elongation of the genital tubercle, which is now called the **phallus**. During this elongation, the phallus pulls the urethral folds forward so that they form the lateral walls of the **urethral groove**. This groove extends along the caudal aspect of the elongated phallus but does not reach

the most distal part, the glans. The epithelial lining of the groove, which originates in the endoderm, forms the **urethral plate**.
At the end of the third month the two urethral folds close over the urethral plate, forming the **penile urethra**. This canal does not extend to the tip of the phallus. This most distal portion of the urethra is formed during the fourth month, when ectodermal cells from the tip of the glans penetrate inward and form a short epithelial cord. This cord later obtains a lumen, thus forming the **external urethral meatus**. The genital swellings, known in the male as the scrotal swellings, arise in the inguinal region. With further development they move caudally, and each swelling then makes up half of the scrotum. The two are separated by the **scrotal septum**.

External Genitalia in the Female

Estrogens stimulate development of the external genitalia of the female. The genital tubercle elongates only slightly and forms the **clitoris**; urethral folds do not fuse, as in the male, but develop into the **labia minora.** Genital swellings enlarge and form the **labia majora.** The urogenital groove is open and forms the **vestibule**. Although the genital tubercle does not elongate extensively in the female, it is larger than in the male during the early stages of development. In fact, using tubercle length as a criterion (as monitored by ultrasound) has resulted in mistakes in identification of the sexes during the third and fourth months of gestation.

DESCENT OF THE TESTES

Toward the end of the second month, the **urogenital mesentery** attaches the testis and mesonephros to the posterior abdominal wall. With degeneration of the mesonephros the attachment serves as a mesentery for the gonad. Caudally it becomes ligamentous and is known as the **caudal genital ligament**. Also extending from the caudal pole of the testis is a mesenchymal condensation rich in extracellular matrices, the **gubernaculum**. Prior to descent of the testis, this band of mesenchyme terminates in the inguinal region between the differentiating internal and external abdominal oblique muscles. Later, as the testis begins to descend toward the inguinal ring, an extra-abdominal portion of the gubernaculum forms and grows from the inguinal region toward the scrotal swellings. When the testis passes through the inguinal canal, this extra-abdominal portion contacts the scrotal floor (the gubernaculum forms in females also, but in normal cases it remains rudimentary).
Factors controlling descent of the testis are not entirely clear. It appears, however, that outgrowth of the extra-abdominal portion of the gubernaculum produces intra-abdominal migration, that an increase in intra-abdominal pressure due to organ growth produces passage through the inguinal canal, and that regression of the extra-abdominal portion of the gubernaculum completes movement of the testis into the scrotum. Normally, the

testes reach the inguinal region by approximately 12weeks gestation, migrate through the inguinal canal by 28 weeks, and reach the scrotum by 33 weeks. The process is influenced by hormones, including androgens and MIS. During descent, blood supply to the testis from the aorta is retained, and testicular vessels extend from their original lumbar position to the testis in the scrotum. Independently from descent of the testis, the peritoneum of the abdominal cavity forms an evagination on each side of themidline into the ventral abdominal wall. This evagination, the **processus vaginalis,** follows the course of the gubernaculum testis into the scrotal swellings. Hence the processus vaginalis, accompanied by the muscular and fascial layers of the body wall, evaginates into the scrotal swelling, forming the **inguinal canal**. The testis descends through the inguinal ring and over the rim of the pubic bone and is present in the scrotum at birth. The testis is then covered by a reflected fold of the processus vaginalis. The peritoneal layer covering the testis is the **visceral layer of the tunica vaginalis;** the remainder of the peritoneal sac forms the **parietal layer of the tunica vaginalis**. The narrow canal connecting the lumen of the vaginal process with the peritoneal cavity is obliterated at birth or shortly thereafter. In addition to being covered by peritoneal layers derived from the processus vaginalis, the testis becomes ensheathed in layers derived from the anterior abdominalwall through which it passes. Thus, the **transversalis fascia** forms the **internal spermatic fascia,** the **internal abdominal oblique muscle** gives riseto the **cremasteric fascia and muscle,** and the **external abdominal oblique muscle** forms the **external spermatic fascia**. The transversus abdominis muscle does not contribute a layer, since it arches over this region and does not cover the path of migration.

DESCENT OF THE OVARIES

Descent of the gonads is considerably less in the female than in the male, and the ovaries finally settle just below the rim of the true pelvis. The cranial genital ligament forms the **suspensory ligament** of the ovary, whereas the caudal genital ligament forms the **ligament of the ovary proper** and the **round ligament of the uterus**. the latter extends into the labia majora.