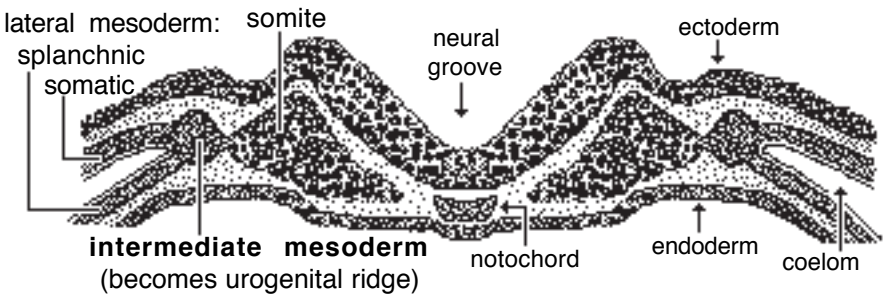
Urinary System

NOTE: Urine production requires an increased capillary surface area (glomeruli), epithelial tubules to collect plasma filtrate and extract desirable constituents, and a duct system to convey urine away from the body.

Intermediate mesoderm:



NOTE:
All mesoderm is derived from *primary mesenchyme* that migrated through the primitive streak.

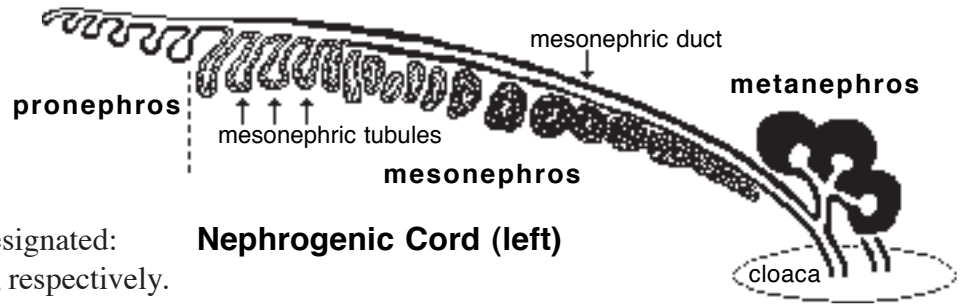
Intermediate mesoderm is situated between somites and lateral mesoderm (somatic and splanchnic mesoderm bordering the coelom).

Intermediate mesoderm (including adjacent coelom mesothelium) forms a *urogenital ridge,* consisting of a laterally-positioned *nephrogenic cord* (that becomes kidneys & ureter) and a medially-positioned *gonadal ridge* (for ovary/testis & female/male genital tract formation).

Urinary & genital systems have a common embryonic origin; also, they share common ducts.

Kidneys:

• three kidneys develop chronologically, in cranial-caudal sequence, from each bilateral *nephrogenic cord*

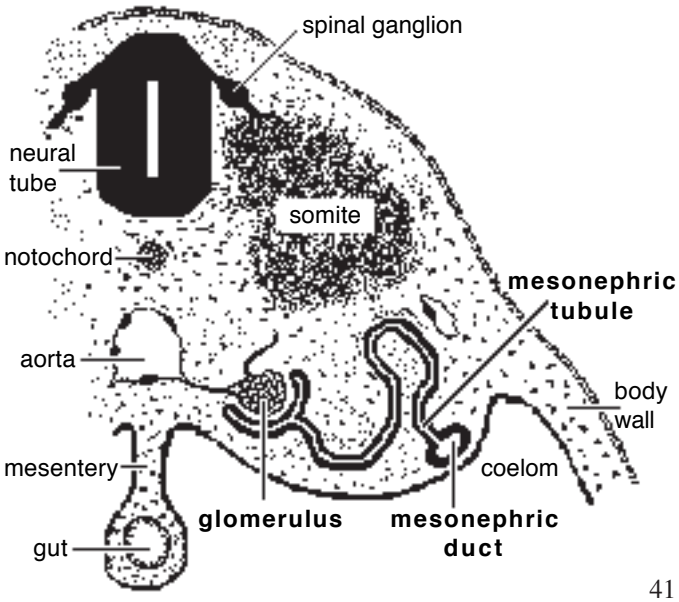


Nephrogenic Cord (left)

• the three kidneys are designated: *pro—*, *meso—*, and *meta—*, respectively.

• the *pronephros* and *mesonephros* have a similar development:
— nephrogenic cord mesoderm undergoes segmentation,
— segments become tubules that drain into a duct
— eventually the tubules disintegrate.

1] **Pronephros**—consists of (7-8) primitive tubules and a *pronephric duct* that grows caudally and terminates in the cloaca. The tubules soon degenerate, but the pronephric duct persists as the *mesonephric duct*.



NOTE

• The *pronephros* is not functional, except in sheep.
• The *mesonephros* is functional in only some mammals (related to placental layers). However, the *mesonephros* becomes the functional kidney of adult fish & amphibians.
• The *metanephros* becomes the functional kidney of adult reptiles, birds, & mammals.
• Although kidneys may be functional *in-utero*, they are not essential because the placenta is able to remove toxic agents from fetal blood.

2] **Mesonephros:**

— consists of (70-80) tubules induced to form by the *mesonephric duct* (former pronephric duct)
— one end of each *tubule* surrounds a glomerulus (vascular proliferation produced by a branch of the dorsal aorta)
— the other end of the tubule communicates with the mesonephric duct
— eventually, the mesonephros degenerates, but the *mesonephric duct* becomes ***epididymis*** & ***ductus deferens*** and some tubules that become incorporated within the testis.

3] **Metanephros:**

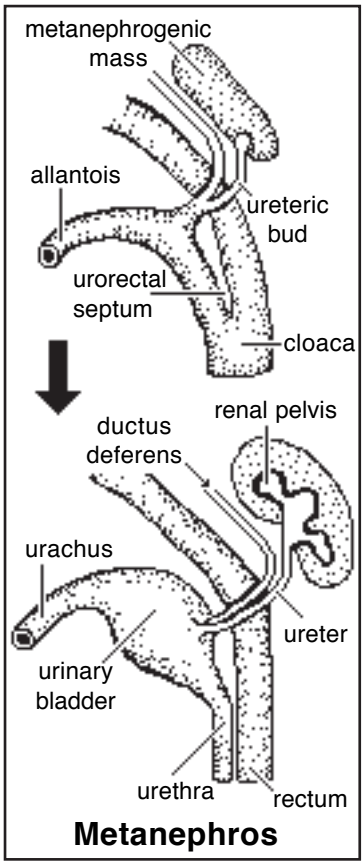
— becomes adult kidney & ureter of mammals, birds, and reptiles
— originates in the pelvic region and moves cranially into the abdomen during embryonic differential growth
— lobulated initially but becomes smooth in most species.

The *metanephros* originates from two sources:

1] a *ureteric bud*, which grows out of the mesonephric duct near the cloaca; the bud develops into the ***ureter***, ***renal pelvis***, and numerous ***collecting ducts***;

2] *metanephrogenic mass,* which is the caudal region of the nephrogenic cord; the mass forms ***nephrons***.

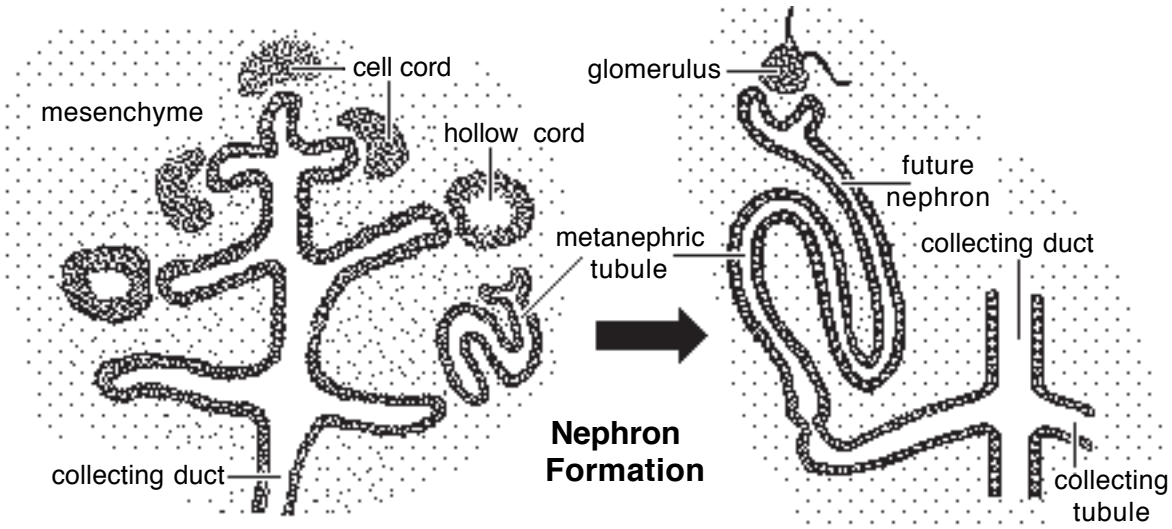
Note: The *neural tube* induces the *ureteric bud* to grow into the *metanephrogenic mass*. The bud induces development of metanephrogenic mesoderm; in turn, the mass induces the cranial end of the ureteric bud to differentiate into renal pelvis and collecting tubules—the tubules induce the metanephrogenic mass cells to form nephrons.



Metanephros

Nephron formation...

• adjacent to collecting tubules, mesodermal cells of the metanephrogenic mass proliferate and form cell cords
• the cords canalize and elongate, becoming S-shaped metanephric tubules that eventually become nephrons
• one end of each metanephric tubule expands to surround a capillary glomerulus (forming a glomerular capsule)
• the other end of the tubule must establish communication with a collecting tubule
• between the two ends, each metanephric tubule differentiates into regions characteristic of a ***nephron*** (proximal segment, thin loop, distal segment).



Nephron Formation

NOTE: Nephrons develop from deep to superficial in the kidney. Many of the early nephrons subsequently degenerate as a normal occurrence. Nephrons continue to form and mature postnatally (except in the bovine); thereafter, nephrons cannot be replaced if they are damaged.

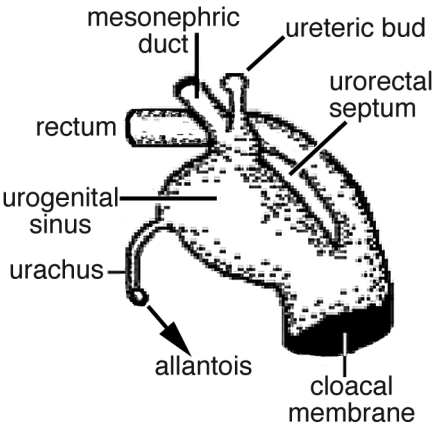
Urinary Bladder and Urethra

A *urorectal septum* divides the *cloaca* into:

- dorsally, a ***rectum***, ***anal canal*** & *anal membrane*, and
- ventrally, a *urogenital sinus* and *urogenital membrane*

The membranes subsequently degenerate, resulting in an ***anus*** and a *urogenital orifice*, respectively.

Cranially, the *urogenital sinus* connects with the *urachus*, the intra-embryonic stalk of the allantois.



Urinary bladder...

- develops from the cranial end of the *urogenital sinus* and the adjacent region of *urachus*
- growth expansion results in separate openings of the *mesonephric duct* and *ureter* into the dorsal wall of the urogenital sinus
- differential growth of the dorsal wall results in mesonephric duct and ureter openings being switched cranio-caudally, creating a **trigone region** (that anchors ureters to the bladder & urethra)

Urethra...

- develops from the urogenital sinus, caudal to the urinary bladder
- urethra development is gender specific:

females: the mid region of the urogenital sinus becomes ***urethra***. (The caudal region of the urogenital sinus become vestibule and the vagina growths out of the vestibule wall.)

males: the ***pelvic urethra*** develops from the mid region of the urogenital sinus and the ***penile urethra*** develops from elongation of the caudal end of the urogenital sinus.

NOTE: In the fetus, urine is discharged into the allantoic cavity through the urachus and into the amniotic cavity through the urogenital orifice.

Abnormalities of urinary development include:

• Hydronephrosis (cystic/polycystic kidneys) may result from ureteric atresia or from failure of nephrons to communicate with collecting tubules.

• Patent urachus (urachal fistula) results from a failure of the allantoic stalk to close at birth; & vesicourachal diverticulum (urachus persists as a bladder pouch, predisposing to chronic cystitis).

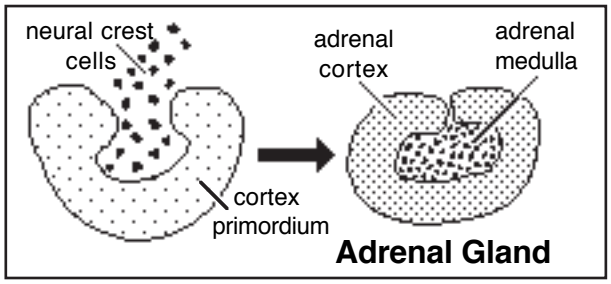
• Ectopic ureter, where the ureter opens into the urethra or vagina instead of the bladder; a source of incontinence because urine is delivered beyond urinary sphincters.

Adrenal Cortex

NOTE: The adrenal gland consists of an **adrenal medulla** and an **adrenal cortex** that are embryologically, histologically, and functionally different, even though they are combined anatomically.

The ***adrenal medulla*** is derived from *neural crest* (ectoderm).

The ***adrenal cortex*** arises from cells of *mesonephric tubules* that dissociate and migrate to the location of the adrenal gland after the mesonephros degenerates.



Genital System

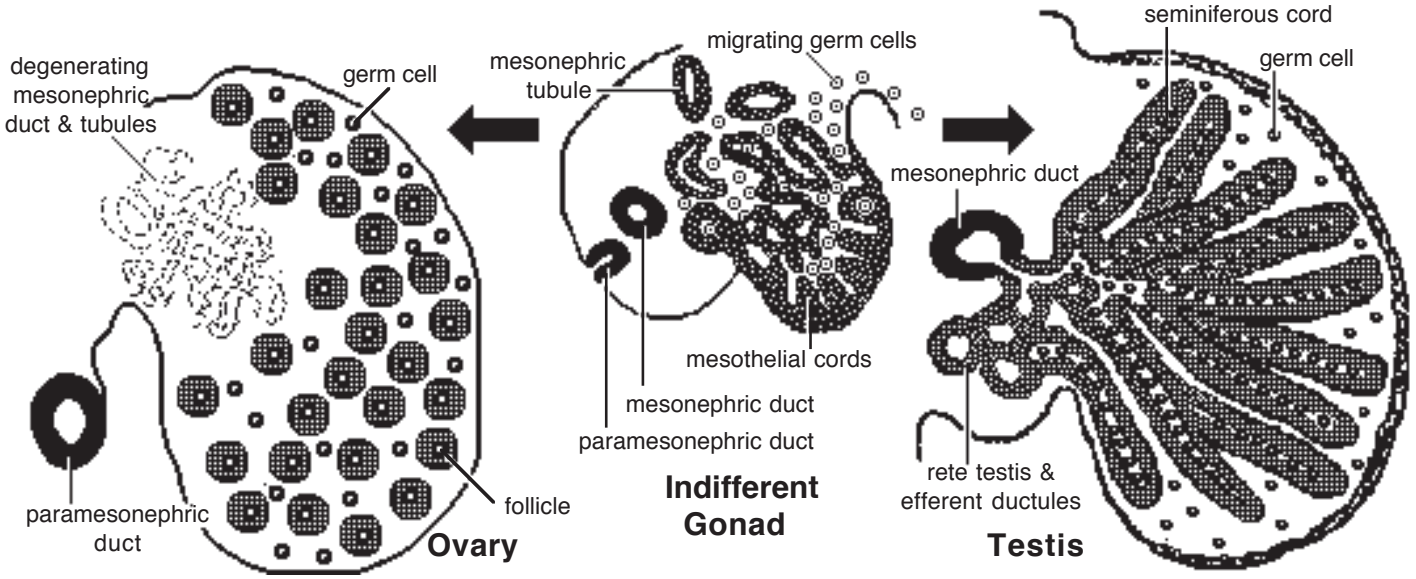
Gender **genotype** is inherited, but gender **phenotype** is a consequence of hormones released during embryonic development, by the gonad determined by genotype.

Genital development involves transition through an *indifferent stage* in which gonads, genital ducts and external features are the same in both sexes. Thus, many genital anomalies involve some combination of intersex development and appearance.

Gonads

Indifferent stage:

- the gonad originates from the *gonadal ridge,* a thickening of intermediate mesoderm plus coelomic mesothelium that develops medial to the mesonephric kidney.
- the gonad is composed of germ cells and supporting cells:
  - *supporting cells* form cellular cords (*gonadal cords*) that radiate into the gonadal ridge, the cells arise from invading mesothelium and disintegrating mesonephric tubules
  - *germ cells* arise from yolk sac endoderm, they migrate along the gut wall and mesentery to reach the gonadal ridge. Their arrival induces further gonadal development.
- germ cells proliferate and must migrate inside gonadal cords so they are surrounded by supporting cells (germ cells that fail to enter gonadal cords suffer degeneration).



Testis:

- gonadal cords hypertrophy and are called *seminiferous cords*
- germ cells within seminiferous cords differentiate into *spermatogonia* and become dormant.
- at puberty, seminiferous cords become canalized, forming ***seminiferous tubules***, and spermatogonia initiate ***spermatogenesis*** (deep cords that lack germ cells become tubules of the *rete testis*, located centrally in the testis).
- supporting cells differentiate into *sustentacular (Sertoli) cells* and *interstitial cells*:
  - *sustentacular cells*, located in walls of seminiferous tubules, secrete inhibitory factors that suppress both spermatogenesis and female duct development (paramesonephric duct)
  - *interstitial cells*, located outside seminiferous tubules, become two populations: one produces androgen hormones immediately, the other population delays androgen production until sexual maturity (androgens stimulate male genitalia development)
- mesothelium covering the testis becomes visceral peritoneum; mesenchyme deep to the mesothelium becomes the tunica albuginea of the testis.

Ovary:

- *gonadal cords* undergo reorganization such that individual germ cells become surrounded by a sphere of flat supporting cells, thus ***primordial follicles*** are formed
- germ cells (oogonia) differentiate into primary oocytes that commence meiosis, but remain stuck in prophase of Meiosis I (meiosis is not continued until ovulation occurs, as an adult)
- follicle and germ cell proliferation is completed *in utero*, the lifetime allotment of primary oocytes is already present in the neonatal ovary.

NOTE: Because they fail to become incorporated within follicles, 90% of the germ cells complete meiosis and then degenerate (to reduce degeneration, meiosis onset is delayed in the embryos of species having longer gestations).

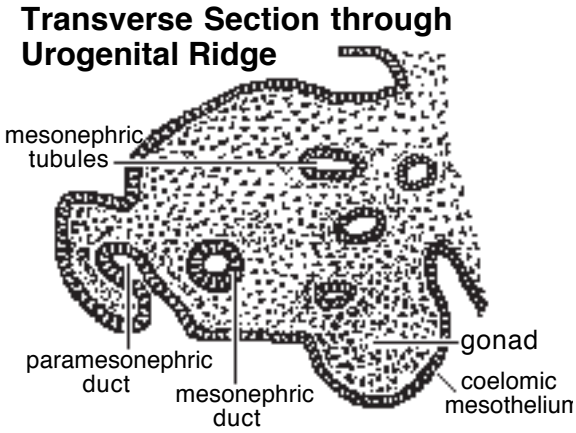
Genital Ducts | Accessory Glands | Ligaments

Indifferent stage:

- both sexes have male (*mesonephric*) and female (*paramesonephric*) genital ducts and a *urogenital sinus*
- the *mesonephric* (Wolffian) *duct* persists after the mesopnephros disintegrates
- a *paramesonephric* (Mullerian) *duct* develops along the ventrolateral coelomic surface of the mesonephros (it begins as a groove, then becomes a core of cells, and subsequently it canalizes and elongates)
- testicular hormones determine which duct system develops:

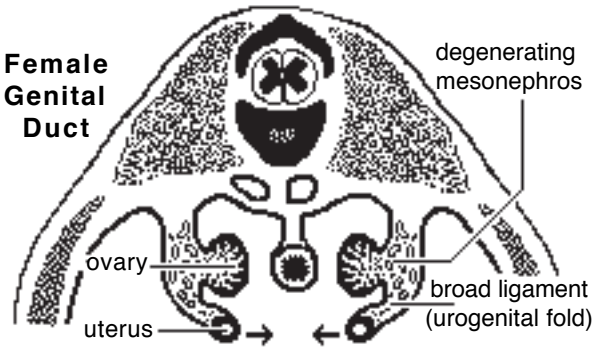
male duct development requires testosterone, produced by interstitial cells;

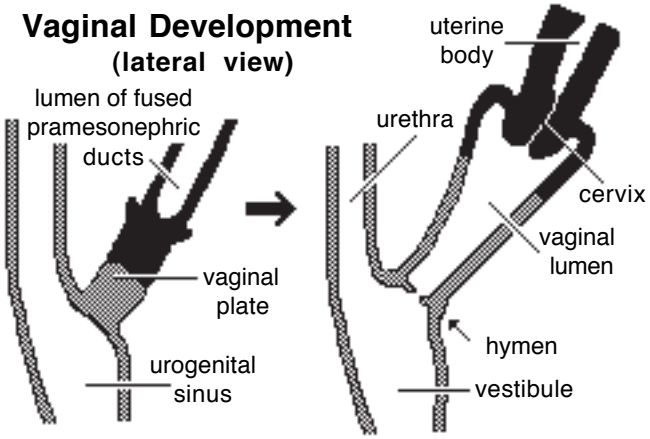
female duct development is suppressed by an inhibitory hormone released by sustentacular cells.



Females:

- in the absence of testosterone, mesonephric ducts fails to develop (remnants may be found in the wall of the vestibule).
- the cranial region of each paramesonephric duct remains open and forms the future *uterine tube*
- caudal to the level of the inguinal fold (gubernaculum), each paramesonephric duct becomes a *uterine horn*.





- further caudally, bilateral paramesonephric ducts shift medially and fuse into a single tube that ends blindly in contact with the urogenital sinus. The fused ducts become: ***uterine body***, ***uterine cervix***, and the cranial third of the ***vagina***.

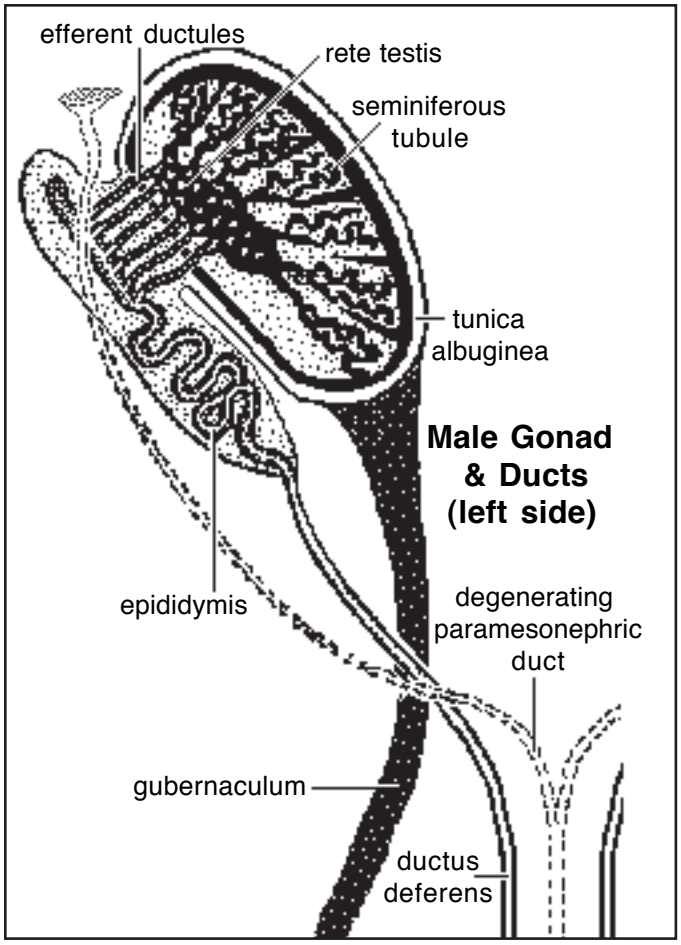
NOTE: The degree of paramesonephric duct fusion is species dependent. Among domestic mammals, fusion is greatest in the horse and least in carnivores. In primates (women) fusion normally produces a uterine body without horns. In contrast, rodents and the rabbit have a double uterus (two cervices enter a single vagina). Monotremes and many marsupials have a double vagina (no fusion at all).

The ***vagina*** has a dual origin:

- the cranial one-third comes from fused *paramesonephric* ducts.
- the caudal two-thirds comes from an outgrowth of the future *vestibule*, as follows:
  - — at the site where the fused paramesonephric ducts contact the urogenital sinus, a solid tubercle, the *vaginal plate*, grows outward from the future vestibule
  - — degeneration of the center of the solid tubercle creates the vaginal lumen.
  - — a hymen may persist where the vagina joins urogenital sinus.

Males:

- paramesonephric ducts regress due to an inhibitory hormone produced by sustentacular cells of the testis (duct remnants are often evident in the adult male horse as a uterus masculinus).
- several *mesonephric tubules* become ***efferent ductules*** (they already communicate with the mesonephric duct but must establish communication with the rete testis tubules)
- the cranial region of the *mesonephric duct* undergoes extensive elongation and coiling to become the ***epididymis***; the remainder of the duct enlarges and becomes ***ductus deferens***
- the mesonephric duct (ductus deferens) empties into the region of urogenital sinus that becomes ***pelvic urethra***.



Glands. ***Prostate*** and ***bulbourethral glands*** develop in typical gland fashion by outgrowths of *urogenital sinus endoderm*. (Vestibular glands are female homologues of male bulbourethral glands.) Vesicular glands (seminal vesicles) arises as an epithelial outgrowth from the caudal region of the mesonephric duct (mesoderm). Gland smooth muscle comes from surrounding mesenchyme.

Descent of the testis:

- a *gubernaculum* is produced by condensation of mesenchyme within the inguinal fold, which runs along the body wall linking the gonad to the inguinal region
- the gubernaculum accumulates fluid and become a gel mass as large in diameter as a testis (under the influence of gonadotropins and testicular androgens)
- the swollen gubernaculum preclude closure of the body wall, and is responsible for formation of the inguinal canal and vaginal process (coelom evagination)
- subsequent outgrowth of the scrotal wall and dehydration of the gubernaculum passively pulls the testis to the inguinal canal
- a sudden increase in intra-abdominal pressure can pop it through the canal into the scrotum.

NOTE: In both genders, there is some caudal shift of the gonad from its original position, due to elongation of the body and a variable degree of retention by inguinal fold derivatives that pull on the gonad.

In females, the ovary remains intra-abdominal and the extent of caudal shift is species dependent (e.g., slight in the bitch vs. descent into the pelvis in the cow).

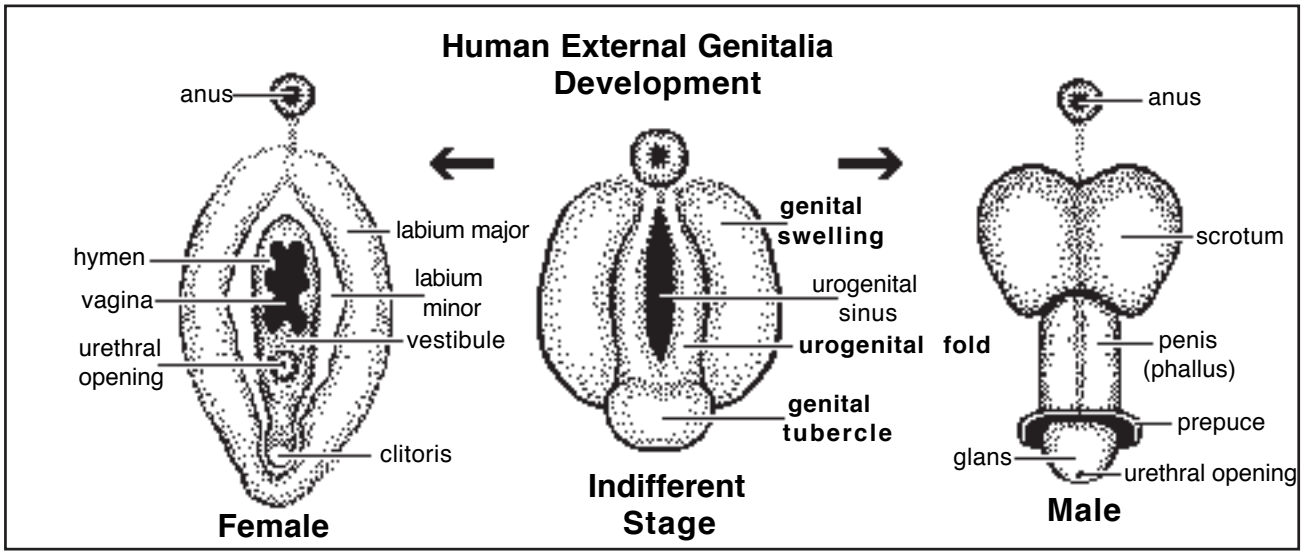
In males, each testis descends to the inguinal region (scrotum).

Genital Ligaments:

- when the *mesonephros* degenerates, it leaves behind a *genital fold* that persists to suspend the gonad and genital duct system
- the caudal extension of the genital fold that runs along the body wall and into the inguinal region is called the *inguinal fold* and it gives rise to the *gubernaculum* of the fetus
- the genital and inguinal folds becomes male & female genital ligaments:

  females: the *genital fold* becomes the ***broad ligament*** (*suspensory ligament of the ovary, mesovarium, mesosalpinx,* and *mesometrium)*; the *inguinal fold* becomes the ***proper ligament of the ovary*** and ***round ligament of the uterus***

  males: the *genital fold* becomes ***mesorchium*** and ***mesoductus deferens***; the *inguinal fold* becomes the *gubernaculum* and the adult ***proper ligament of the testis*** and ***ligament of the tail of the epididymis***.



External Genitalia

Indifferent stage:

- external genitalia are derived from three different perineal swellings:
  - — bilateral *urogenital folds* border the *urogenital orifice* and elongate ventrally (Urogenital folds are the caudal end of the urogenital sinus.)
  - — a *genital tubercle*, develops at the ventral commissure of the urogenital folds
  - —bilateral *genital* (labioscrotal) *swellings* are located lateral to the urogenital swellings (in domestic mammals these persist only in males, unlike primates, where the swellings develop in both sexes, forming major labia in females and scrotum in males).

Males:

- growth at the base of the *genital tubercle* generates an elongate ***phallus*** with the original genital tubercle becoming ***glans*** at the tip of the phallus
- the *urogenital orifice* and *urogenital folds* elongate ventrally along with the attached phallus; the folds form a urogenital groove and the ***penile urethra*** is created when the groove closes by medial merger of urogenital folds in proximal to distal sequence.
- the opening at the distal end of the penile urethra, within the original *genital tubercle*, is created by ectoderm invasion and canalization which establishes communication between the ectoderm exterior and the endoderm interior of the penile urethra
- genital tubercle mesenchyme gives rise to penile erectile tissue, tunica albuginea, smooth muscle, and bone (carnivores).

• ***prepuce*** is formed when a ring of surface ectoderm invades into the mesenchyme of the free end of the phallus, dividing tissue into a penis encircled by preputial skin. (Except in the cat, the phallus of domestic mammals elongates deep to the skin of the ventral body wall.)

• *genital swellings* enlarge and merge at the midline to form a single ***scrotum*** (with two compartments). The scrotum initially overlies the gubernaculum and vaginal process in the inguinal region, and then it generally shifts cranially (except that it remains caudal in the cat and pig).

Females:

• *urogenital orifice* becomes the ***vulval cleft***, which opens into the ***vestibule*** (*urogenital sinus*)

• the *genital tubercle* becomes the ***clitoris***

• *urogenital folds* elongate, overgrow the genital tubercle, and become ***labia*** of the vulva

• *genital swellings* disappear in female domestic mammals (but become major labia in primates).

Mammary Glands

In both genders, a mammary ridge (line) of thickened ectoderm forms bilaterally from the axillary region to the inguinal region.

Mammary buds develop periodically along the ridge; elsewhere, mammary ridge ectoderm regresses. Buds determine the number and locations of mammary glands, since each bud develops into a *mammary gland* (2, sheep, goat, mare; 4 cow; 8, queen; 10, bitch; 14; sow).

At each mammary bud, ectoderm induces proliferation of underlying mesoderm and mesoderm induces epithelial cell proliferation (teat formation).

Epithelial cell solid cords invade underlying mesoderm and eventually canalize to form epithelial lined lactiferous ducts. The number of cell cord invasions and subsequent lactiferous duct systems per teat is species dependent (approximately: 1, sheep, goat, cow ; 2 mare sow; 6, queen; 12, bitch).

In some cases, multiple lactiferous ducts open into a pit (inverted nipple) that becomes a nipple following proliferation of underlaying mesoderm.

It is common for extra buds develop and degenerate, failure to degenerate results in supernumerary teats.