



GENITOURINARY SYSTEM

SUBJECT : Anatomy
LEC NO. : 11 & 12
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وَقُلْ رَبِّ زِدْنِي عِلْمًا

Development of Male and Female Reproductive System



Learning Objectives

- **To learn the development and congenital abnormalities of testes and the ovaries**
- **To learn the sex determination**
- **To learn the development and congenital abnormalities of genital ducts**
- **To learn the development and congenital abnormalities of external genitalia**

Development of genital system

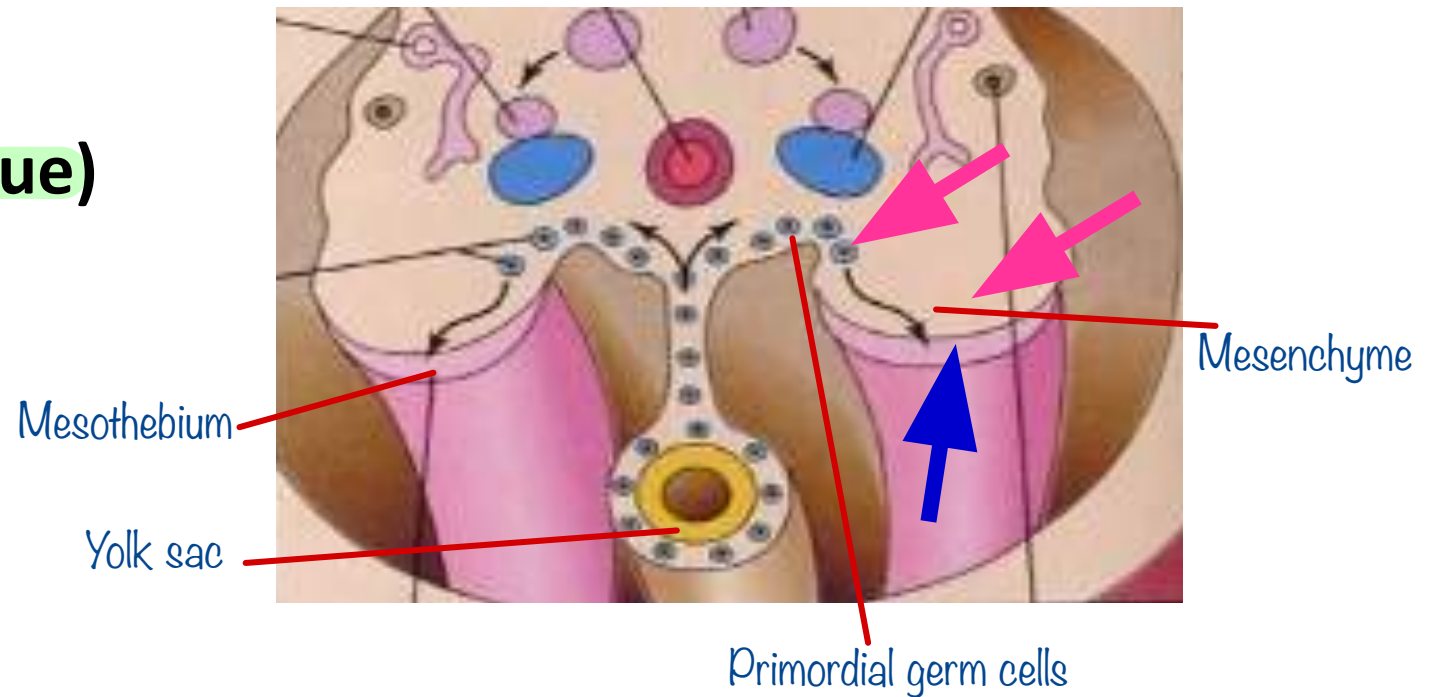
- The **sex of the fetus** is established at **fertilization by the genotype of sperm that fertilizes the ovum**
- The gonads begin to **attain sexual characteristics from the 7th week**.
- **Early genital systems** in the two sexes are **similar**; this initial period is called the **indifferent stage of sexual development**



Development of Gonads

Gonads are derived from three sources

- The mesothelium:
(mesodermal epithelium) lining the posterior abdominal wall
- The underlying mesenchyme:
(embryonic connective tissue)
- The primordial germ cells:



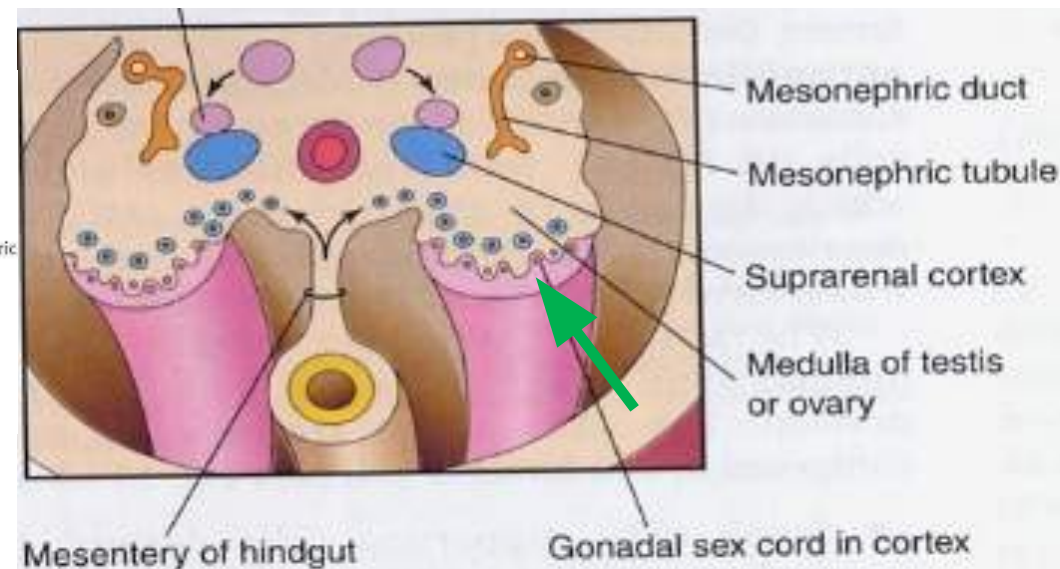
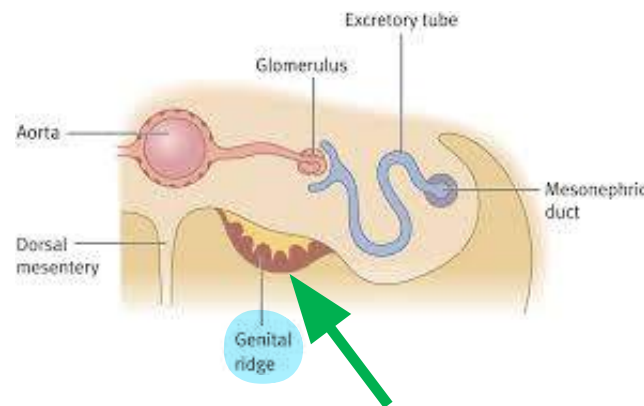
Indifferent gonads

Gonadal (genital) ridges → Lining epithelium + mesoderm

- During the 5th week, a thickened area of mesothelium develops on the medial side of the mesonephros due to the proliferation of mesothelium and underlying mesenchyme

Gonadal cords

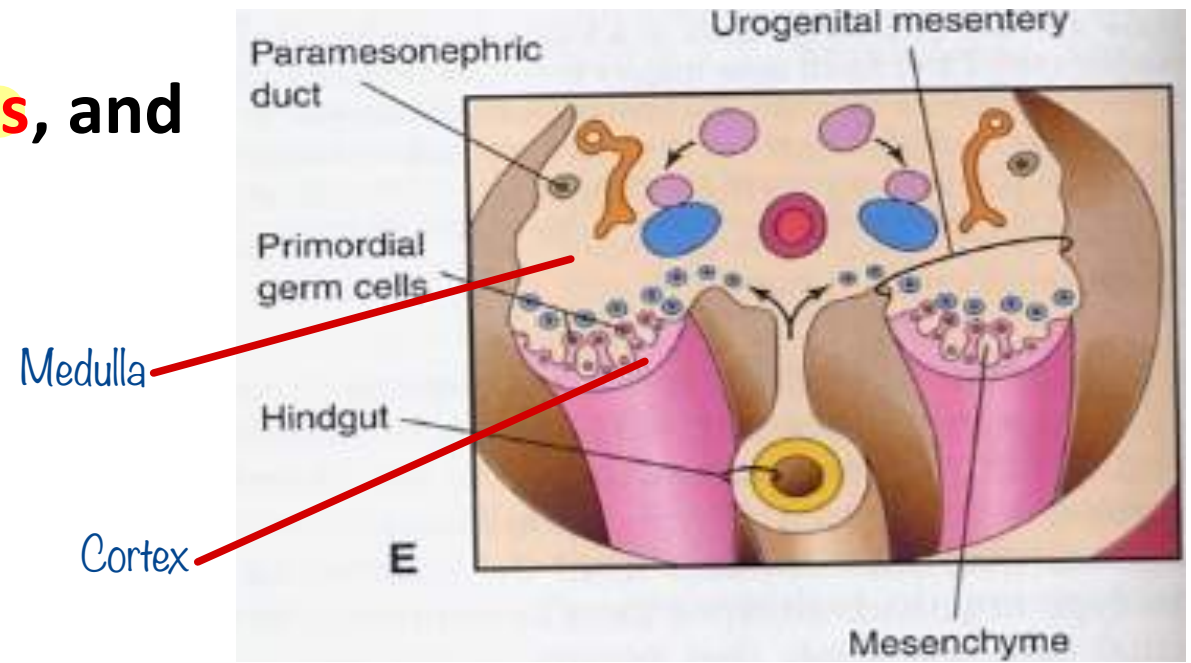
- Finger-like epithelial cords (Gonadal cords) grow into the underlying mesenchyme



Indifferent gonads Cont., 1. 2.

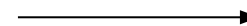
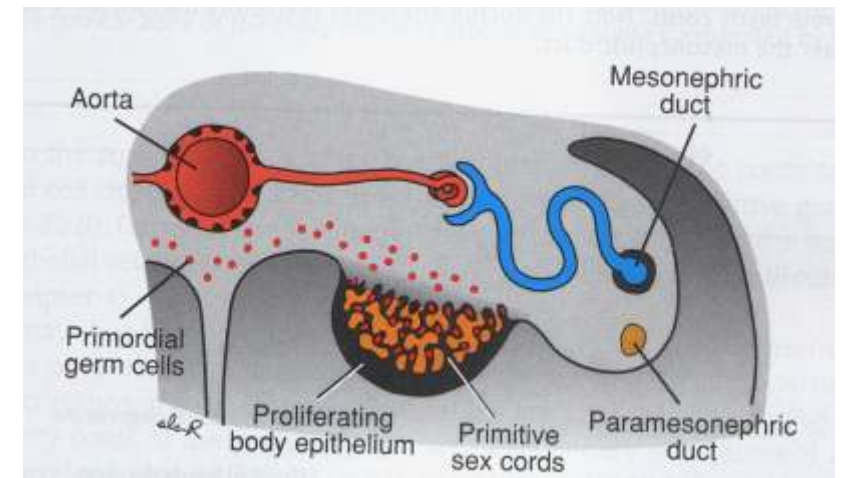
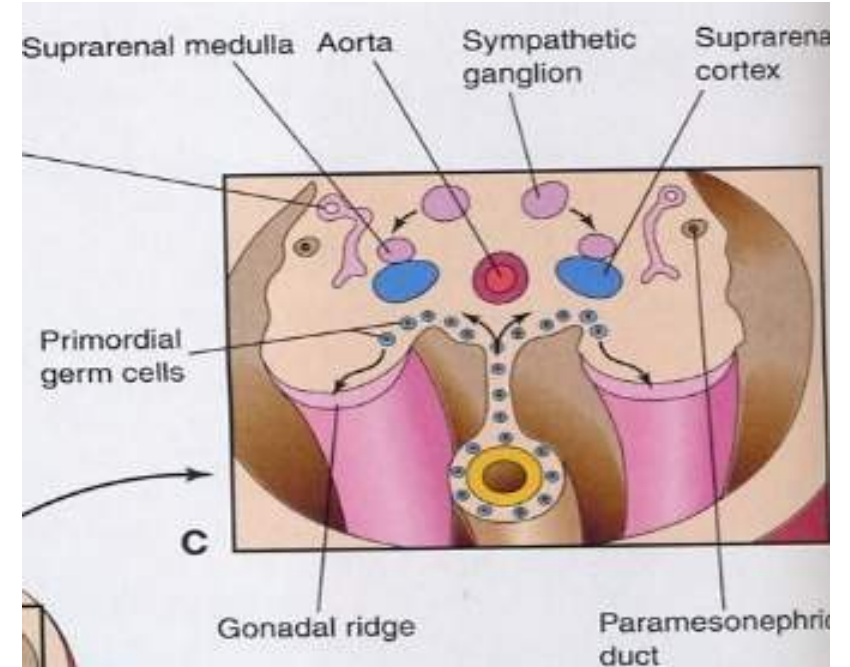
- The indifferent gonad now consists of an **external cortex** and an **internal medulla**.
- If the embryo is **XX (Female)**:
cortex will differentiate into an **ovary**, and the **medulla** will regress
- If the embryo is **XY (Male)**:
medulla differentiates into a **testis**, and the **cortex** will regress except for **vestigial remnants**

↗ Regress to connective tissue



Encodermal in origin ← **Primordial germ cells**
Gametes ←

- Primordial germ cells originate in the wall of the yolk sac
- The sex cells are visible early in the 4th week among the endodermal cells of the yolk sac
- The primordial germ cells migrate along the dorsal mesentery of the hindgut to the gonadal ridges
- During 6th week primordial germ cells enter the underlying mesenchyme and are incorporated in the gonadal cords.
- Eventually, they differentiate into oocytes and sperms
↳ By 7th week



Sex determination

- Chromosomal and genetic sex is established at fertilization and it depends on the type of sperm (X,Y) that fertilizes the X-bearing Oocyte
- The type of gonads that develop is determined by the sex chromosome complex of the embryo (XX or XY)
- Before 7th week gonads of both sexes are identical (indifferent gonads)
- Male phenotype requires Y- chromosome, while female phenotype requires two X chromosomes *Phenotype = الشكل الخارجي
- SRY-gene on the short arm of the Y chromosome is needed for the expression of the Testis Determining Factor (TDF).

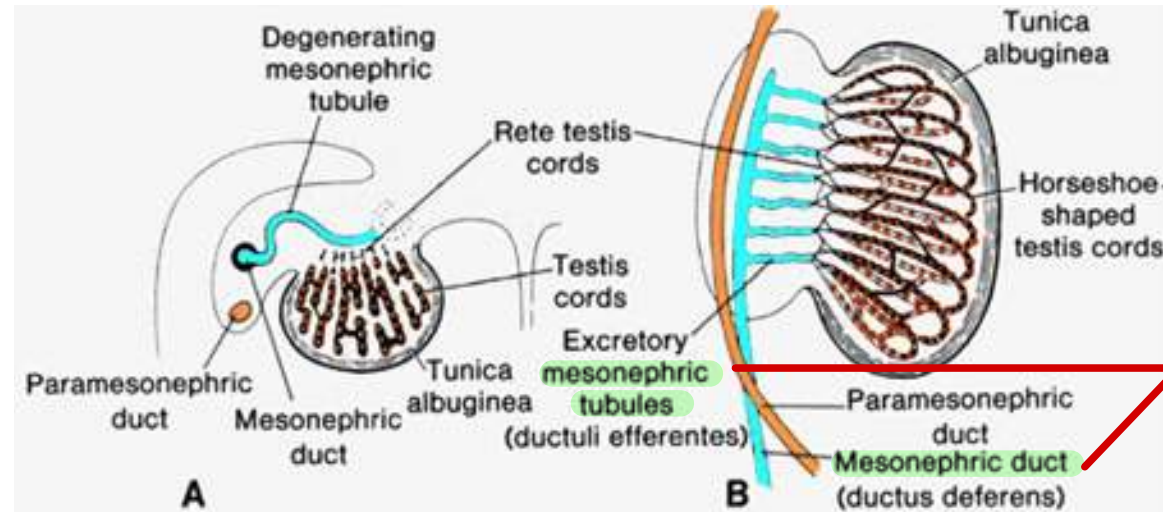
↳ Protein without it the testis will not develop

Sex determination Cont.,

- The **Y chromosome** has a testis determining effect on the **medulla** of **indifferent cords**. TDF (regulated by Y chromosome) differentiate the gonadal cords into **seminiferous cords**
- **Absence of a Y chromosome** (XX sex chromosome) results in the **formation of the ovary**
- **Types of present gonads determine the type of sexual differentiation of the genital ducts and external genitalia.**
- **Testosterone** produced by the fetal testes determines maleness.
- **Primary female sexual differentiation does not depend on hormones; occurs even if the ovaries are absent (depending possibly on an autosomal gene)**

*Testosterone important for external genitalia of the male to appear and for the secondary sexual characteristics to appear

Development of testis



حکمی تذکروا انه هدول من ال
development of kidney

- **SRY** gene on the short arm of Y-chromosome influences the expression of **Testis Determining Factor (TDF)**.
- **TDF** induces the gonadal cords (**seminiferous cords**) to condense and extend into the medulla of the indifferent gonad; where they branch and anastomose to form the **rete testis**.
- A dense layer of fibrous CT (**tunica albuginea**) separates the testis cords from the surface epithelium
- Mesenchyme between seminiferous tubules gives rise to **interstitial cells of Leydig**

Enlarge

Development of testis Cont.,

- Gradually the testis separates from degenerating mesonephros and becomes suspended by its mesentery (Mesorchium).

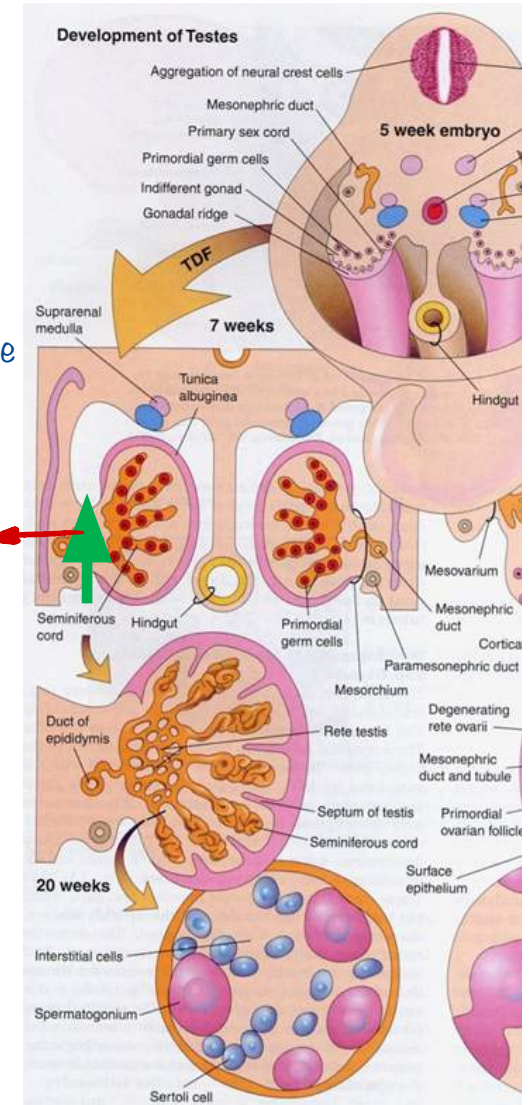
- Testis cords are now composed of primitive germ cells and Sertoli derived from the surface epithelium of the gonad

- They proliferate by mitosis and will give number of cells that will give sertoli cells less in number

- By the 8th week, interstitial cells of Leydig secrete androgenic hormones under the effect of human chorionic gonadotropin which induces masculine differentiation of mesonephric ducts and external genitalia

- Anti-Mullerian hormone by Sertoli cell inhibits differentiation of paramesonephric duct into uterus and uterine tubes

* A certain constriction will happen here by the generation of mesenchym, degeneration of mesodermal cells (mesorchium) will happen from both sides leaving the area very narrow that's what separates the testis from the mesonephrous



Development of Male Genital Ducts

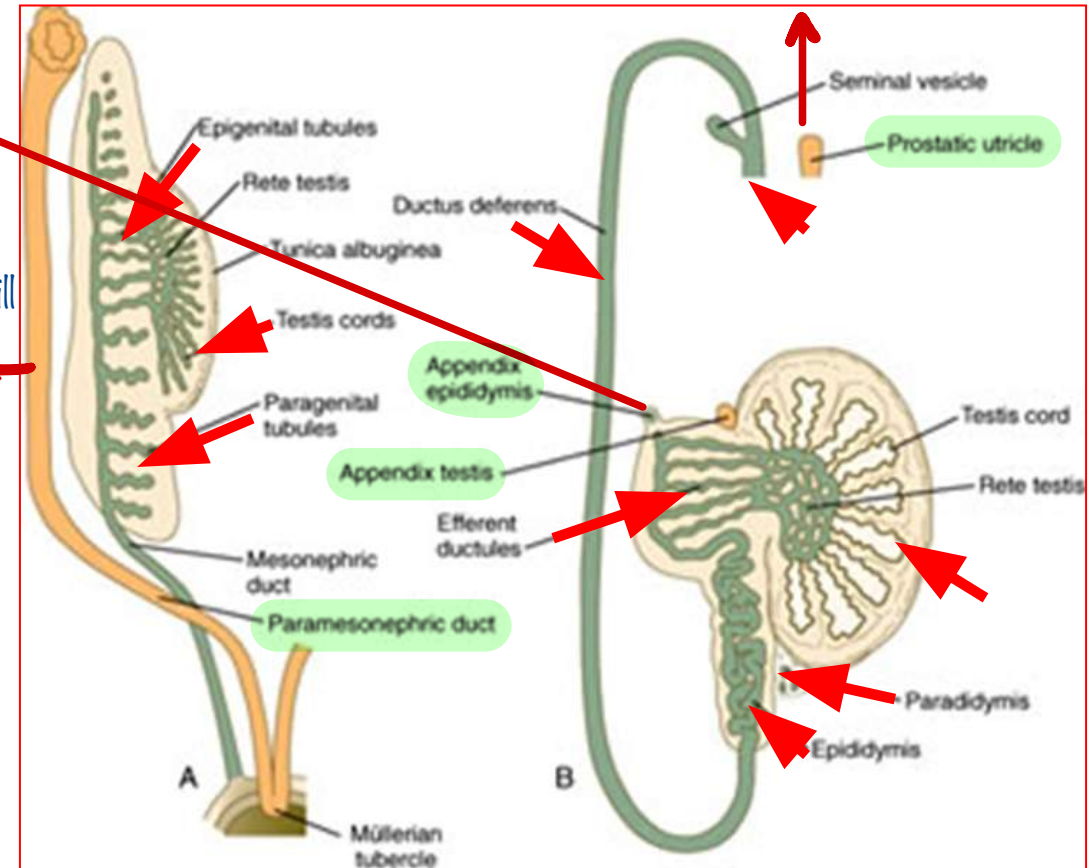
- Part of it will give prostatic utricle (part of urethra)

In the fetal testis:

- Mesonephric duct will degenerate leaving only a small part the appendix of epididymis

- Anti-müllerian hormone will lead to degeneration of paramesonephric duct

- Part of it will remain as the appendix of testis

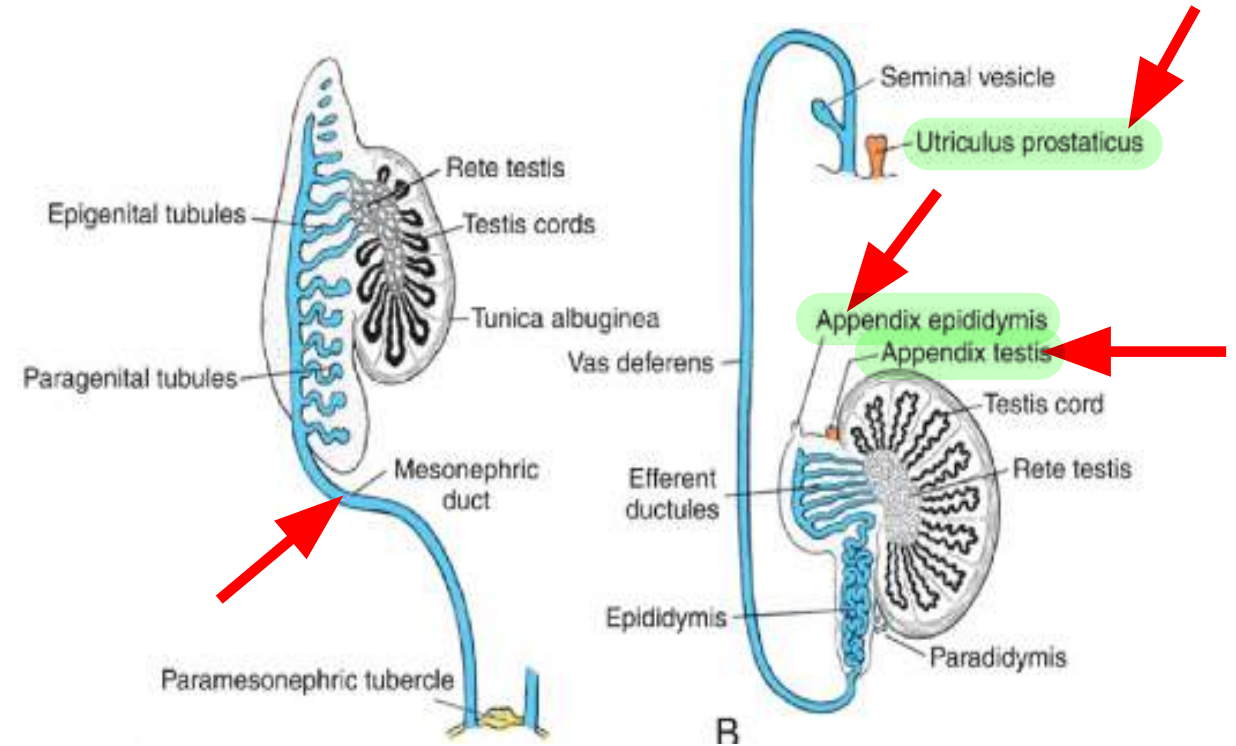


- Testis cords remain solid until puberty; when they become canalized forming seminiferous tubules
- Sertoli cells form most of the seminiferous tubules before puberty
- Rete testes become continuous with 15-20 mesonephric tubule (Epigenital tubules) that become efferent tubules

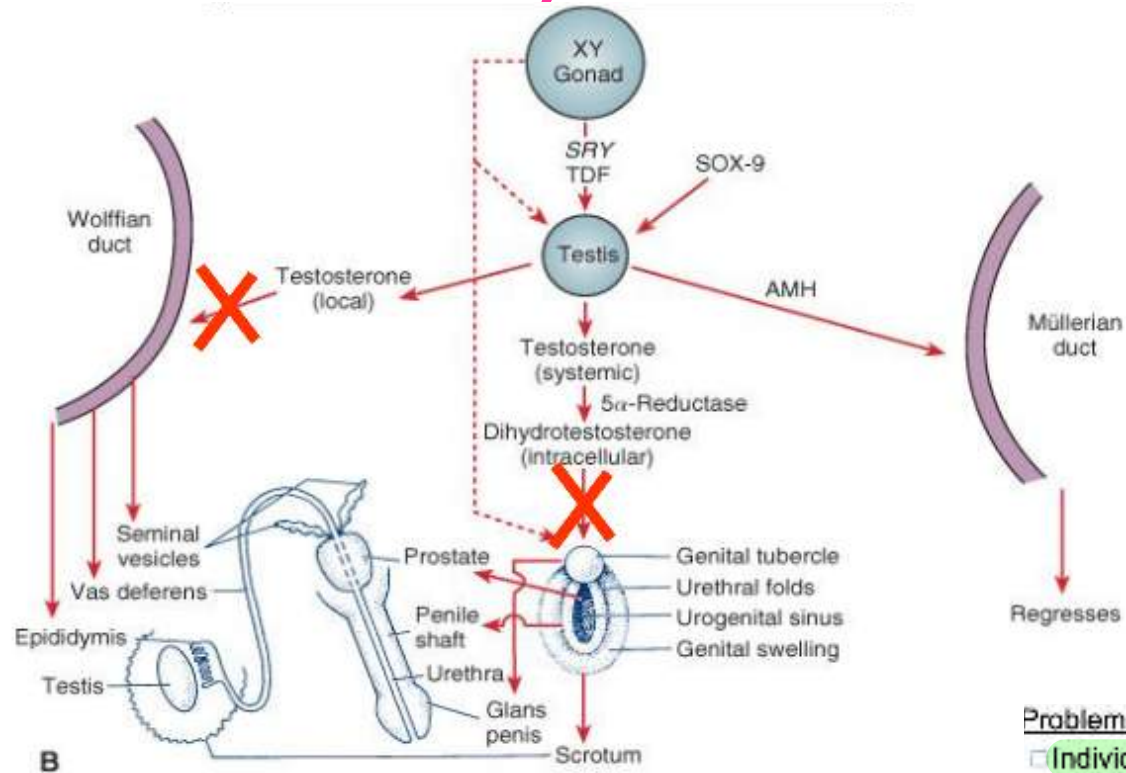
- The mesonephric duct becomes the ductus epididymis and ductus deferens
- The region of the ducts beyond the seminal vesicles is the ejaculatory duct.
- Caudal excretory (para genital tubules) do not join the cords of the rete testis; their remnants become paradiidymis.

Genital duct development in male

- Remnant of mesonephric duct gives appendix of epididymis
- Remnant of paramesonephric duct gives appendix of testis cranially, and prostatic utricle, caudally.



Androgen Insensitivity Syndrome (testicular feminization): 46XY




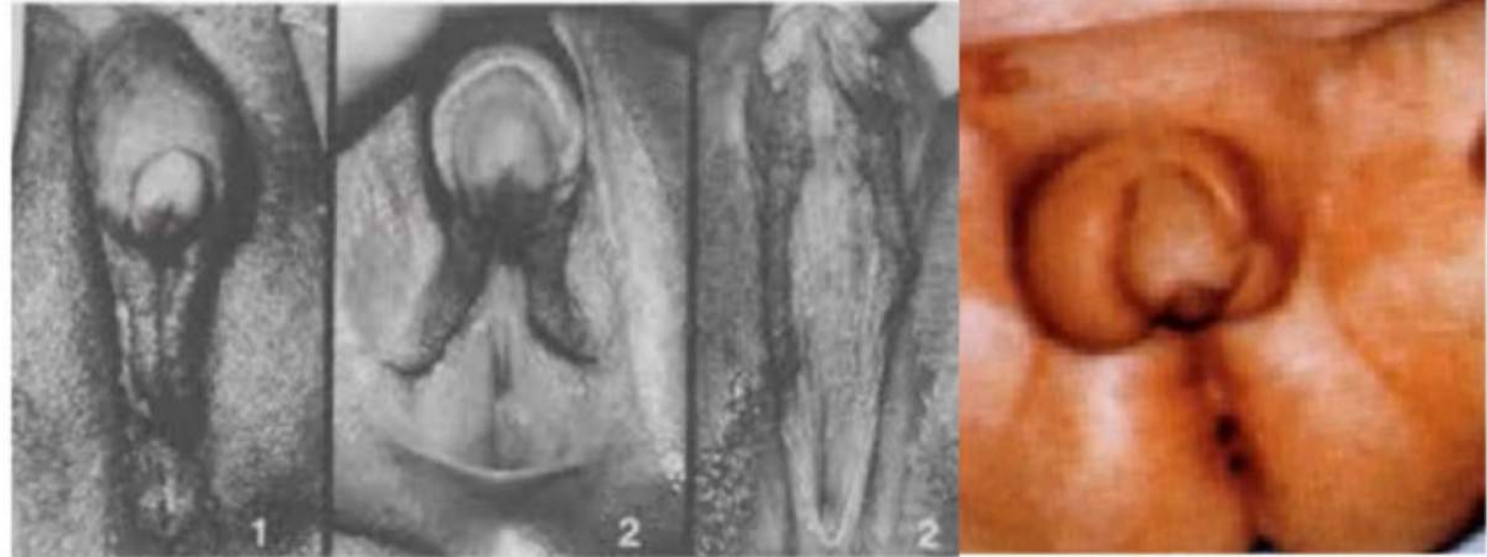
Problem: No functional androgen receptor

- Individuals are XY
- Testes develop
 - Secrete AMH & testosterone
 - Both Wolffian and Müllerian ducts regress
- Female external genitalia develop, but have blind-ended vagina
- Infertile
- Classified as a girl at birth
- Diagnosed at puberty because of primary amenorrhea

* ال zygote هون XY معناها راح يصير male و بوجود ال SRY gene gonads will differentiate into testis and will start ال and TDF anti- testosterone و الثاني- المullerian ducts regression العمل راح يعمل المullerian hormone الي بتعطي female genital tracts، التستوستيرون راح يروح لل external genitalia و راح يخليها تاخذ ال male appearance و يتكون penis, scrotum, penile urethra و بروح على wolfian duct (mesonephric duct) epididymis, vas deferens, seminal vesicles .. و لكن لسبب معين طلع testosterone على ال external genitalia ما كان في receptors و راح على wolfian ducts و ما كان في receptors برضه و هاد يعني it can't work on either of them و هاد بنتج عنه fetus عنده androgen insensitivity syndrome ال androgen فيها ما بتعرف على receptors تعونه و بنتج testicular feminization بطلع male عنده testis افرز male hormone ما اشتغل معناها راح يصير عنده female external genitalia

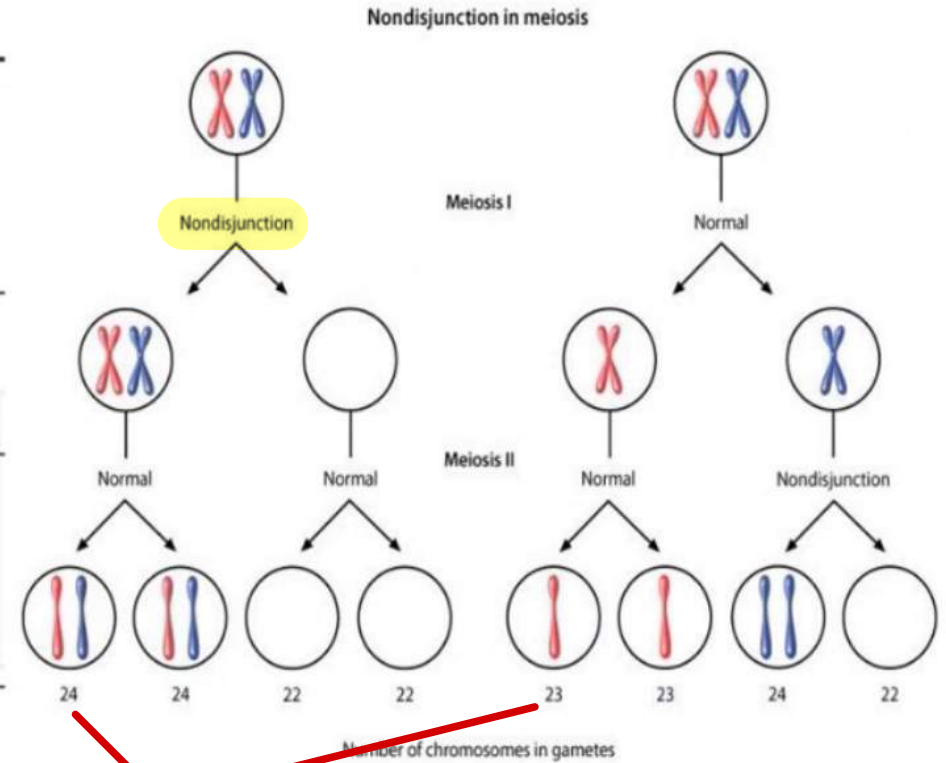
Male Pseudohermaphroditism

- Normal male genotype (46, XY)
- Chromatin -ve nuclei  Not complete effect
- Due to the decreased amount of Androgen and Anti-Mullerian factor
- Features include variable development of external and internal genitalia
- Testis may be normal or rudimentary



Non-disjunction of sex chromosomes

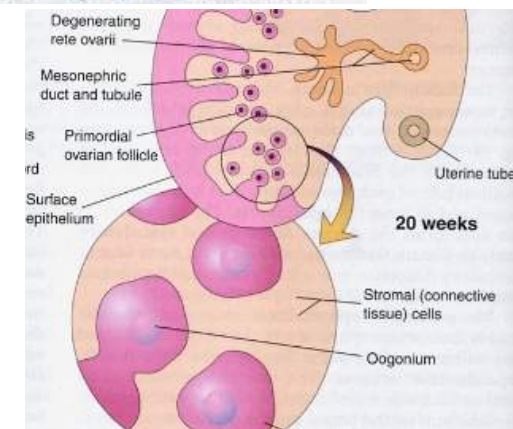
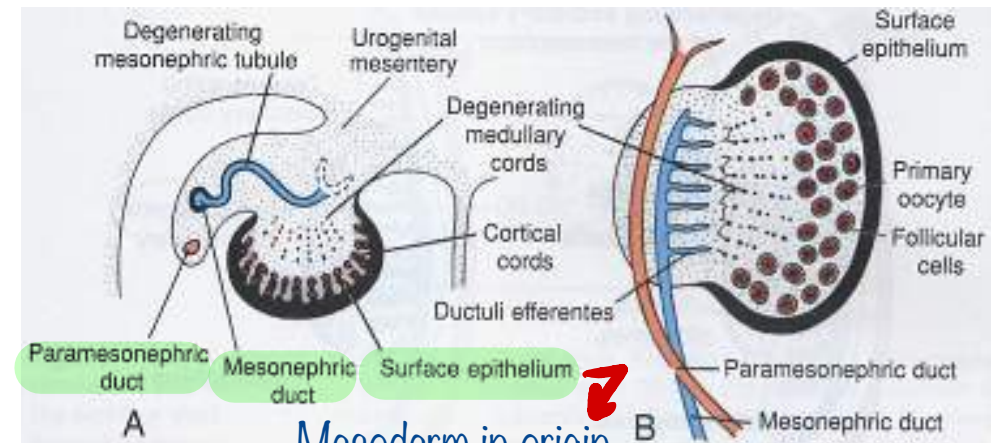
Mutation	The most common clinical features	Effects on fertility
<u>X monosomy</u> Turner syndrome 45	Usually normal external genitalia; abnormal oestrus or no clinical signs of oestrus; small or hypoplastic ovaries	<u>Sterility</u>
<u>XXX trisomy</u> 47	Normal external genitalia; usually lack of clinical signs, sometimes irregular oestrus	<u>Infertility</u>
<u>XXY trisomy</u> Klinefelter syndrome 47	Small and hypoplastic testes; abnormal spermatogenesis (oligospermia or azoospermia)	<u>Sterility</u>
<u>XYY trisomy</u> 47	Usually normal phenotype; small testes	<u>Infertility</u>



لو يصير بينهم تلقيح راح يطلع
عندي خلية عندها زيادة كروموسوم

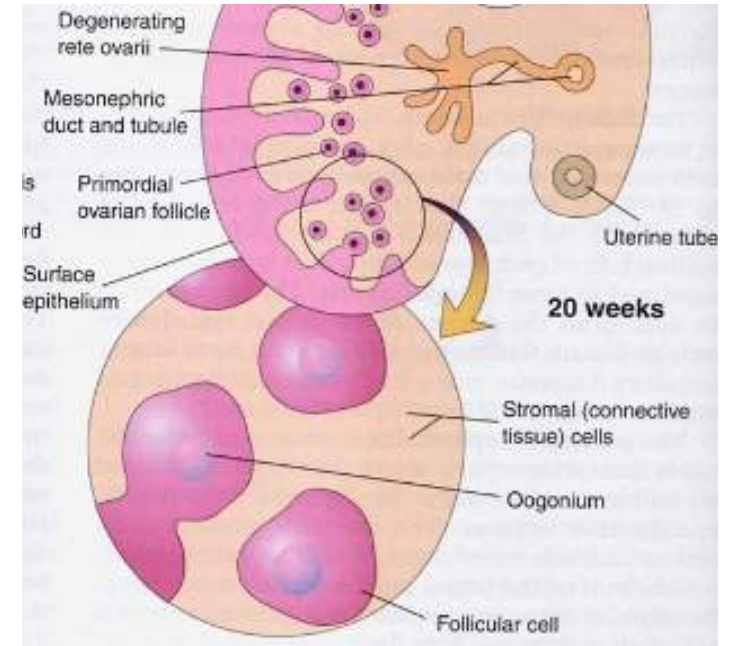
Development of the Ovary

- Genes in X chromosome and some autosomal genes play a role in ovarian development
- Gonadal cords extend into the medulla of the ovary to form a rudimentary rete ovarii that degenerate and are replaced by a vascular stroma that forms the ovarian medulla
- Gonadal cords in the cortex extend from surface epithelium underlying mesenchyme of developing ovary
- As cortical cords increase in size, primordial germ cells are incorporated into them.



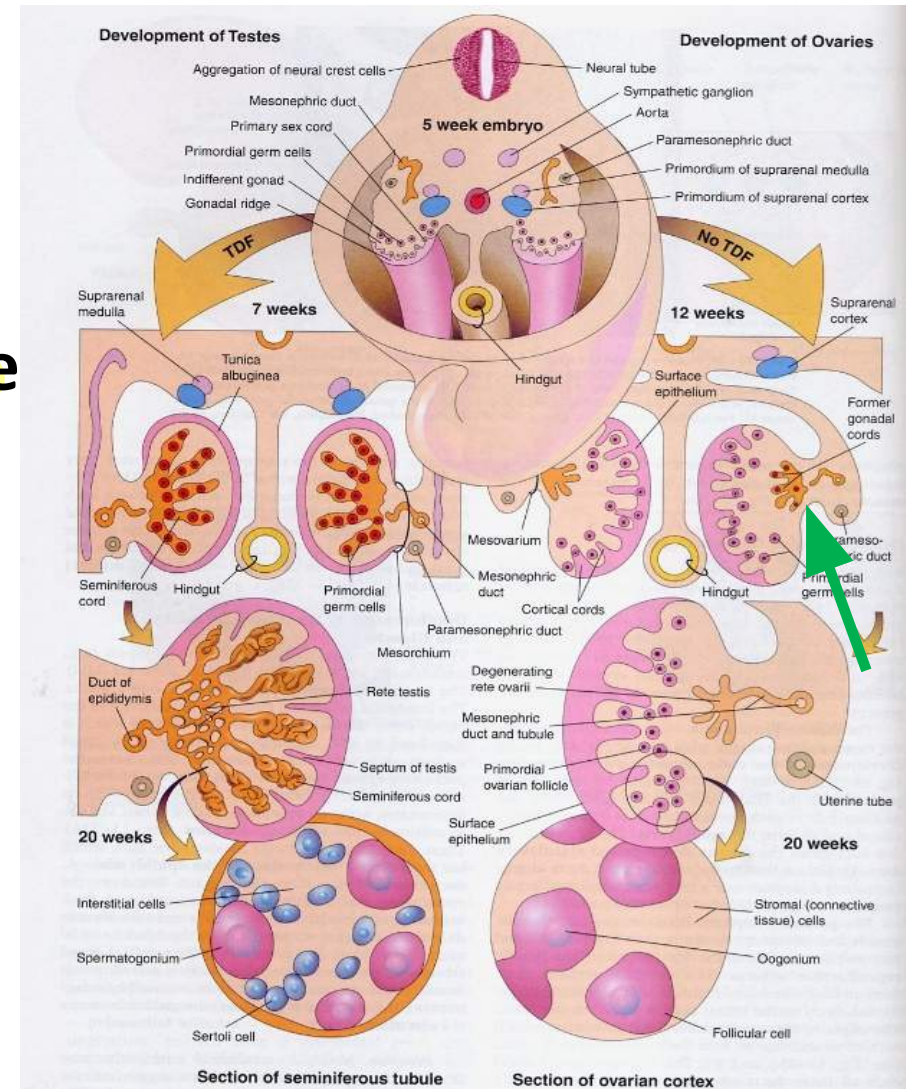
Development of the Ovary Cont.,

- At the **16th week**, **cortical cords break up into isolated cell clusters** (**Primordial follicles**).
- Each follicle consists of **Oogonium** surrounded by a single layer of **flattened follicular cells** derived from surface epithelium



Development of Ovary

- After birth, the surface epithelium covering the ovary becomes flattened to a single layer continuous with the peritoneal covering of the posterior abdominal wall (germinal epithelium)
- Surface epithelium becomes separated from the follicles by a thin fibrous capsule (Tunica Albugenia)
- Ovary become suspended by mesentery (mesovarium) after separation from regressing mesonephros



Development of Female Genital ducts

- At the beginning, both male and female embryos have 2 pairs of genital ducts:

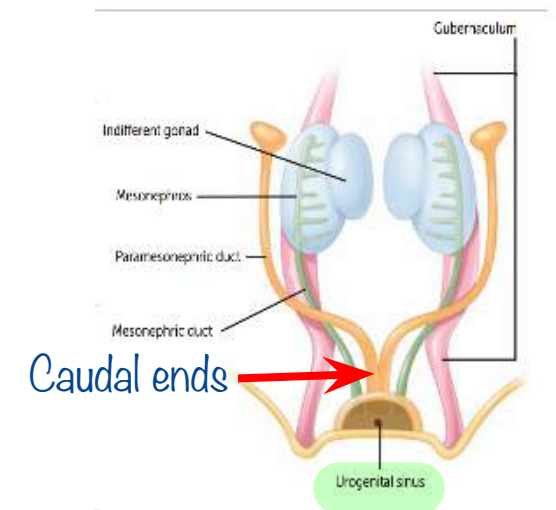
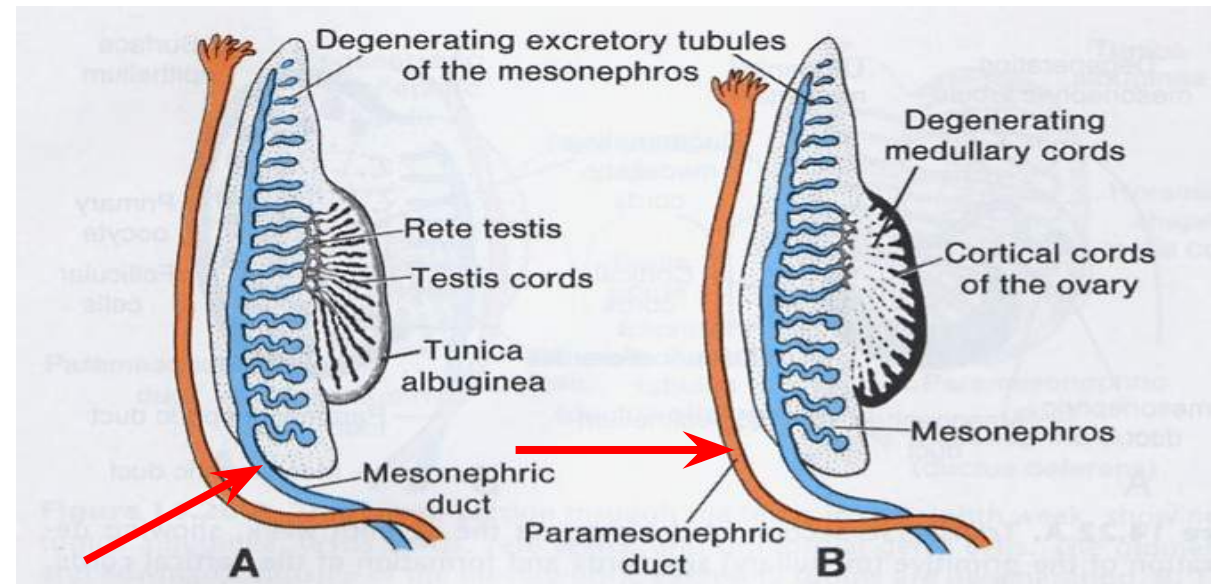
Mesonephric (Wolffian) ducts

Paramesonephric (müllerian) ducts

- The caudal tip of the combined ducts projects into the posterior wall of the urogenital sinus causing a swelling

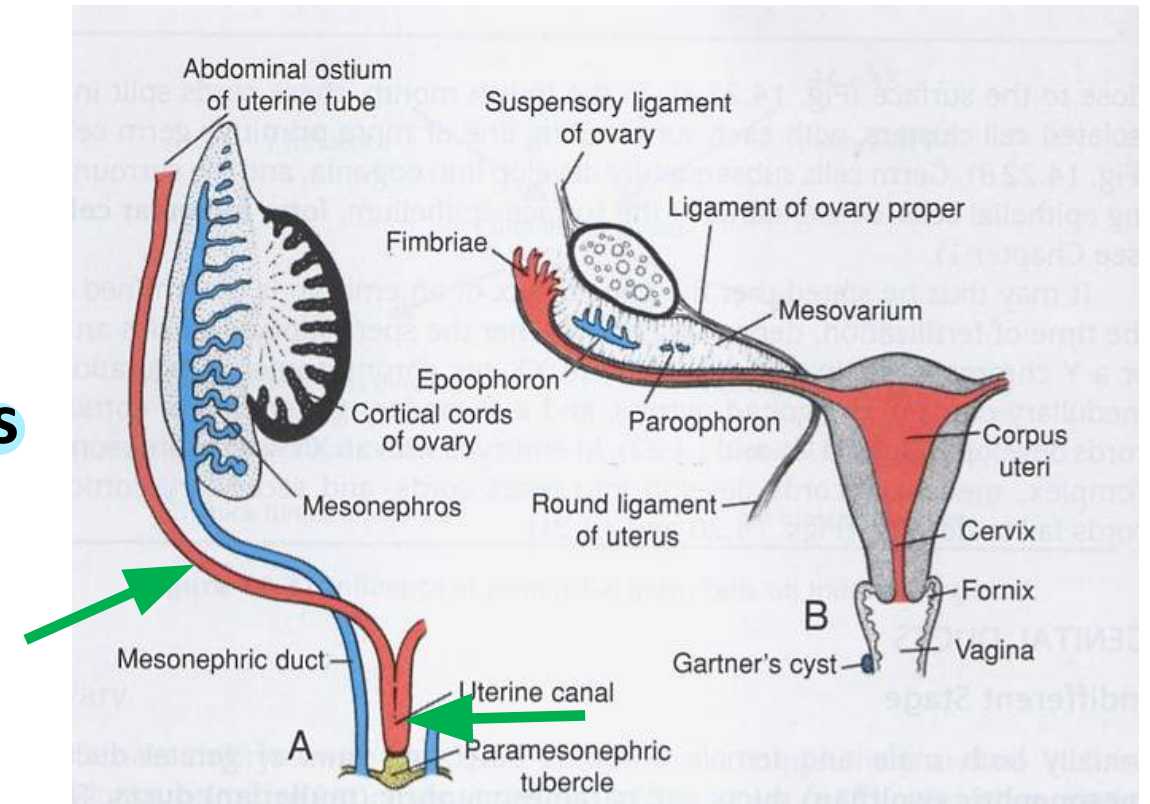
(paramesonephric/müllerian tubercle)

- The mesonephric ducts open into the urogenital sinus on either side of the müllerian tubercle



Genital duct development in female

- Paramesonephric ducts develop into the main genital ducts
- Initially, **3** parts can be recognized in each duct:
- The cranial vertical portion that opens into the abdominal cavity develops into the lateral part of the uterine tube
- The horizontal part that crosses the mesonephric duct develops to the medial part uterine tube
- The caudal vertical part that fuses with its partner from the opposite side to form a uterine canal

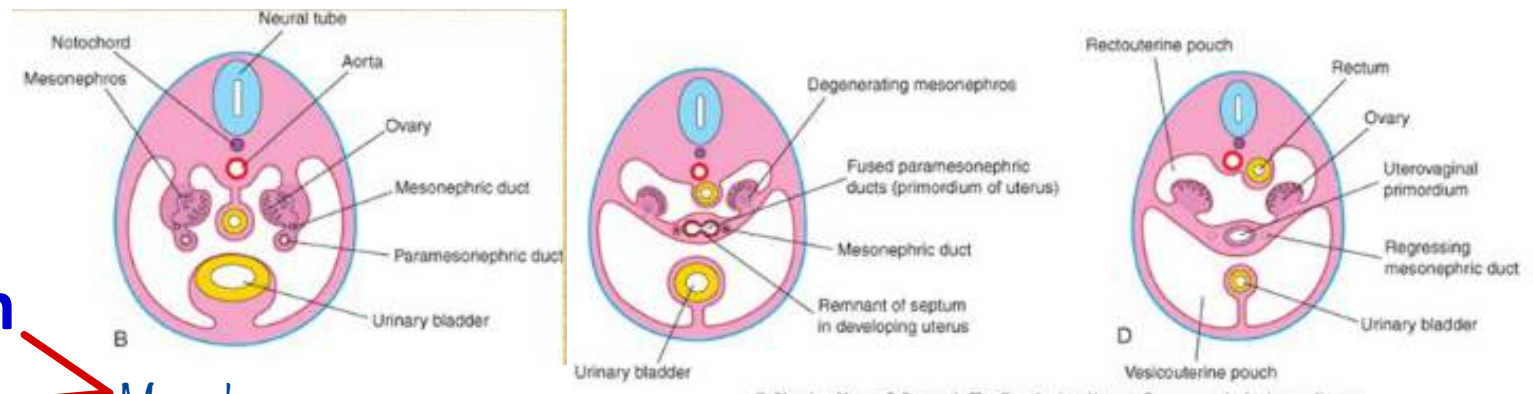


↪ Later on gives uterine cavity

Genital duct development in female

- The second part of the paramesonephric ducts move medio-caudally; from urogenital ridges gradually come to lie in a transverse plane
- As the ducts fuse in the midline; a broad transverse pelvic fold (broad ligament of the uterus) is established. The uterine tube lies in its upper border and the ovary lies on its posterior surface
- The uterus and broad ligament divide the pelvic cavity into uterorectal and ureterovesical pouches → Uterus and rectum
→ Uterus and urinary bladder
- Fused paramesonephric ducts differentiate into the corpus and cervix of the uterus.

- They are surrounded by a layer of mesenchyme that forms the myometrium and the perimetrium



Female Pseudohermaphroditism

- Normal female genotype (46,XX)
- Chromatin +ve nuclei
- Is due to exposure of females to excessive androgen which affects the development of external genitalia
- The common cause is congenital adrenal hyperplasia
- Features include masculinization of external genitalia

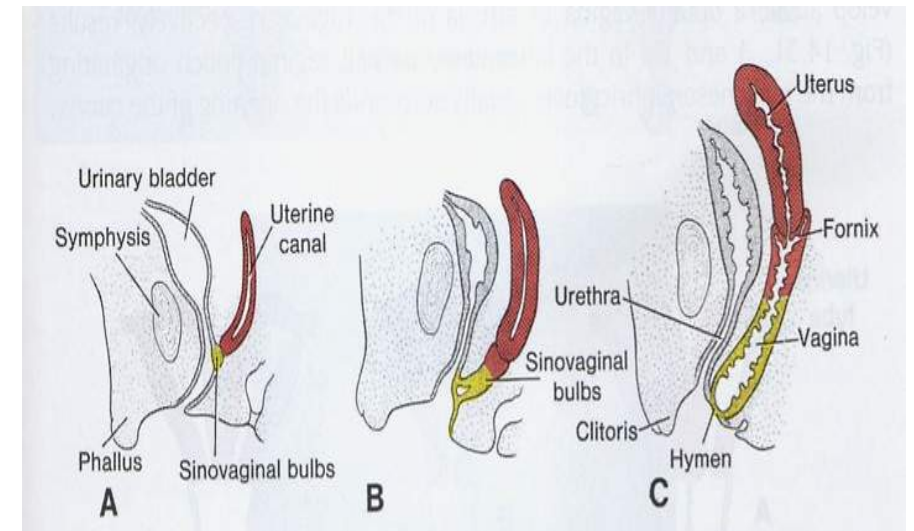
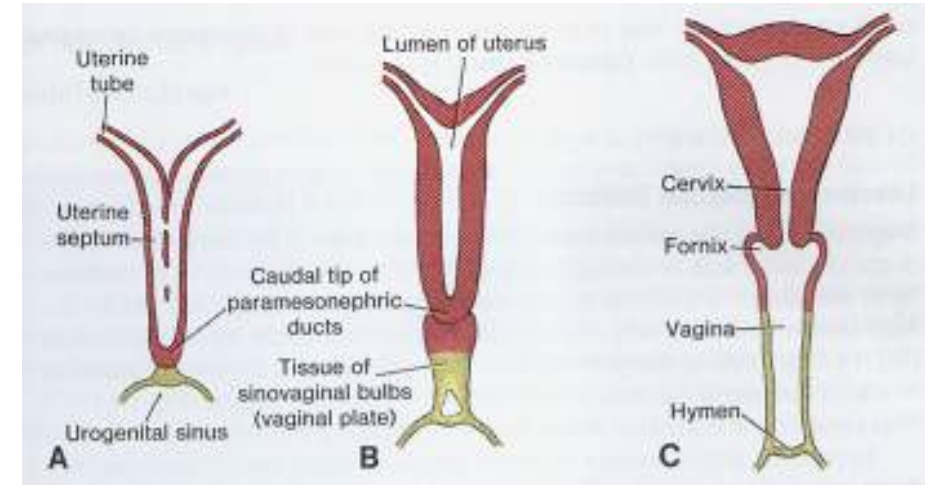
↳ False male appearance



Development of vagina

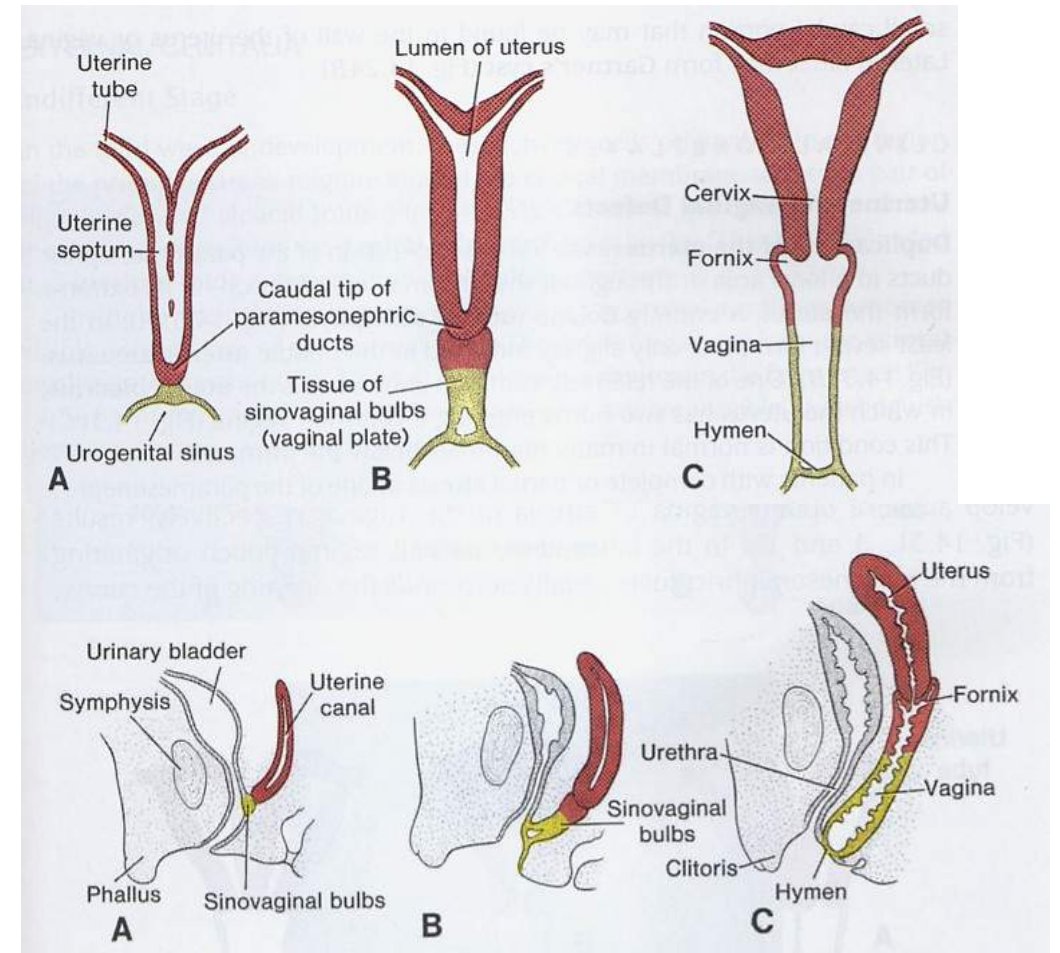
Elongates downward

- After the **solid tip** of the mesonephric ducts reaches the **urogenital sinus**; two solid evaginations (**sinovaginal bulbs**) grow out from the pelvic part of the sinus.
- Sinovaginal bulbs proliferate and form a **solid vaginal plate** → Before canalization
- Proliferation continues at the cranial end of the plate; increasing the distance between the uterus and the urogenital sinus.
- By the **5th month** vaginal outgrowth is entirely canalized. **Vaginal fornices** (wing-like expansions of the vagina around the end of uterus) are of paramesonephric origin



Development of vagina

- The vagina has two origins:
 - upper portion derived from the uterine canal
 - lower portion derived from the urogenital sinus
- Lumen of the vagina remains separated from that of the urogenital sinus by a thin tissue plate; the hymen
- Hymen consists of the epithelial lining of the sinus and a thin layer of vaginal cells. It usually develops an opening during perinatal life

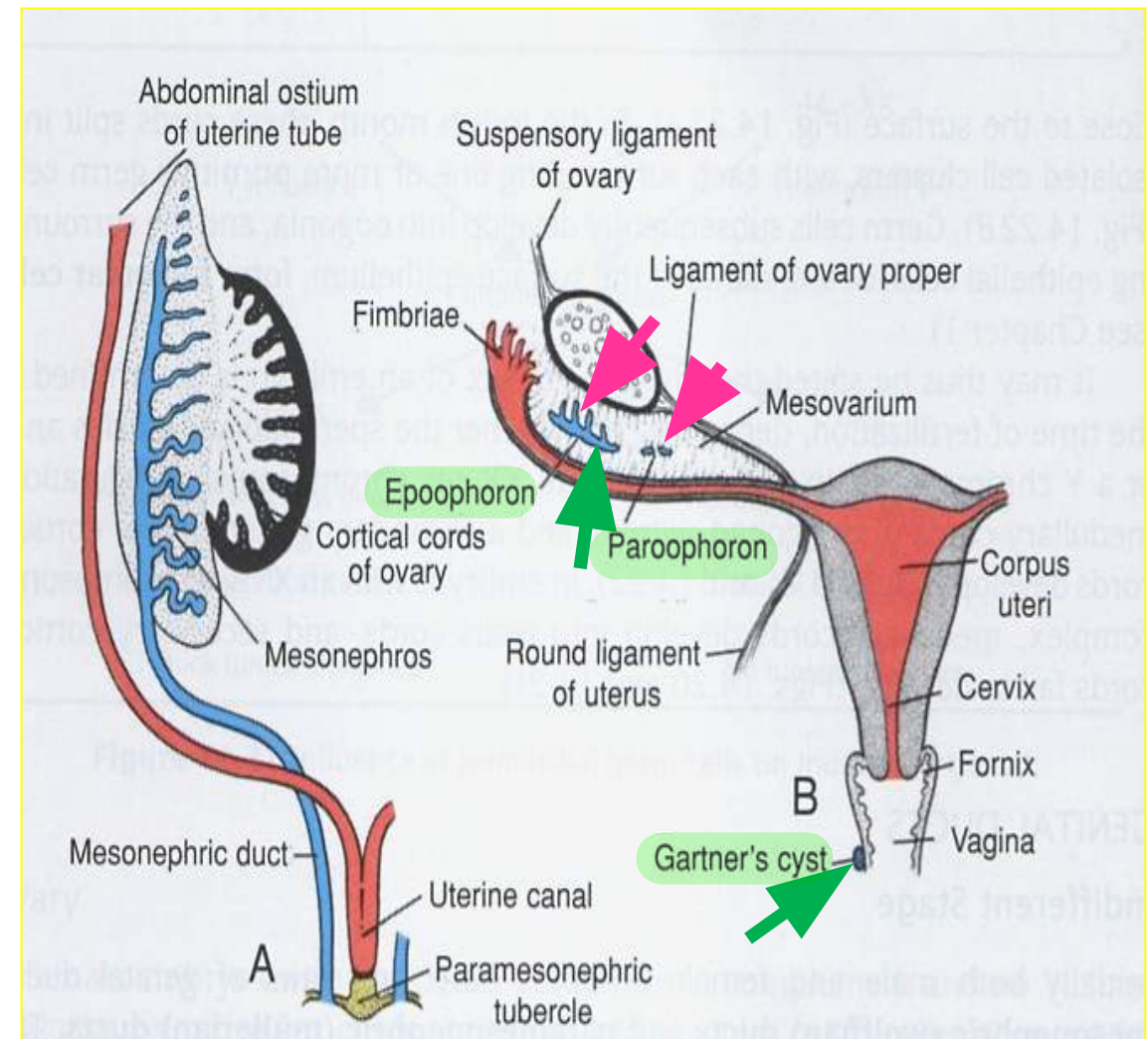


Remnants of the ducts in female

- Remnants of the cranial and caudal excretory mesonephric tubules in the mesovarium disappear except for small portions that remain as epoophoron and paroophoron respectively.
- Mesonephric duct disappears except for a small cranial portion found in epoophoron and a small caudal portion in the wall of the uterus or vagina (Gartner's cyst).

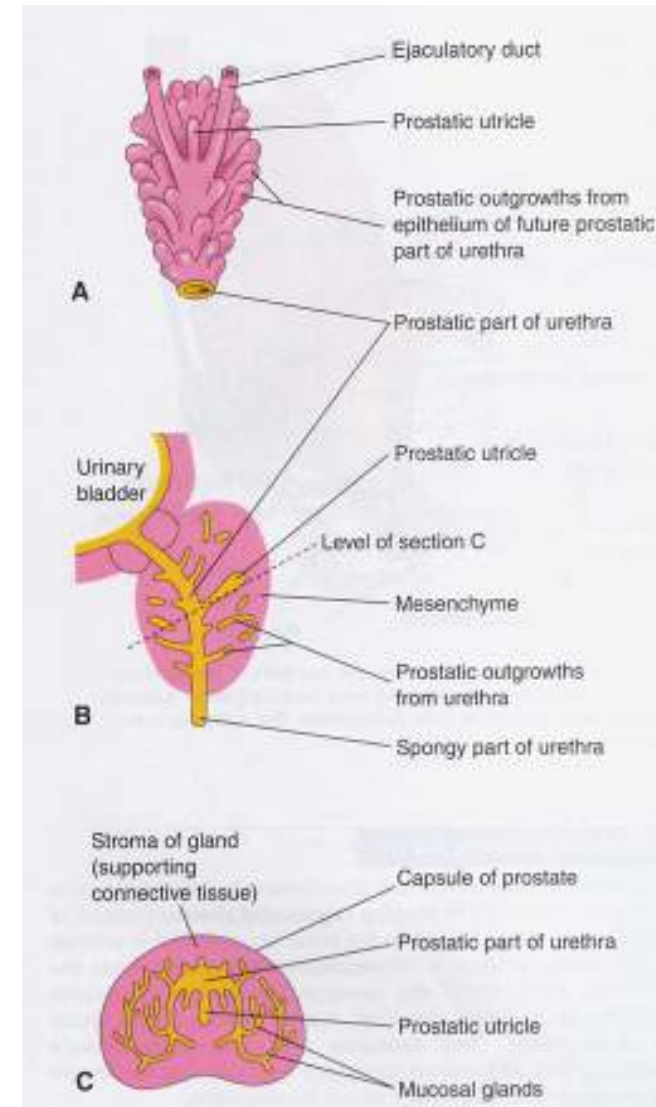
↳, If it was located in an upper part it will be a duct

- Part of paramesonephric duct will remain as hydatid of morgagni



Development of male genital glands

- A lateral outgrowth from the caudal end of each mesonephric duct gives rise to seminal vesicle/gland
- Multiple endodermal outgrowths arising from the prostatic part of the urethra grow into the surrounding mesenchyme and differentiate into prostate glandular epithelium; mesenchyme differentiates into prostatic stroma
- Bulbourethral glands develop from paired outgrowths from the spongy part of the urethra



Congenital anomalies of vagina

- **Absence of vagina:**
Results from the failure of sinovaginal bulbs to develop.
- **Vaginal atresia:**
Failure of the recanalization of the vaginal plate.
- **Imperforate hymen:**
Failure of perforation of the inferior end of the vaginal plate

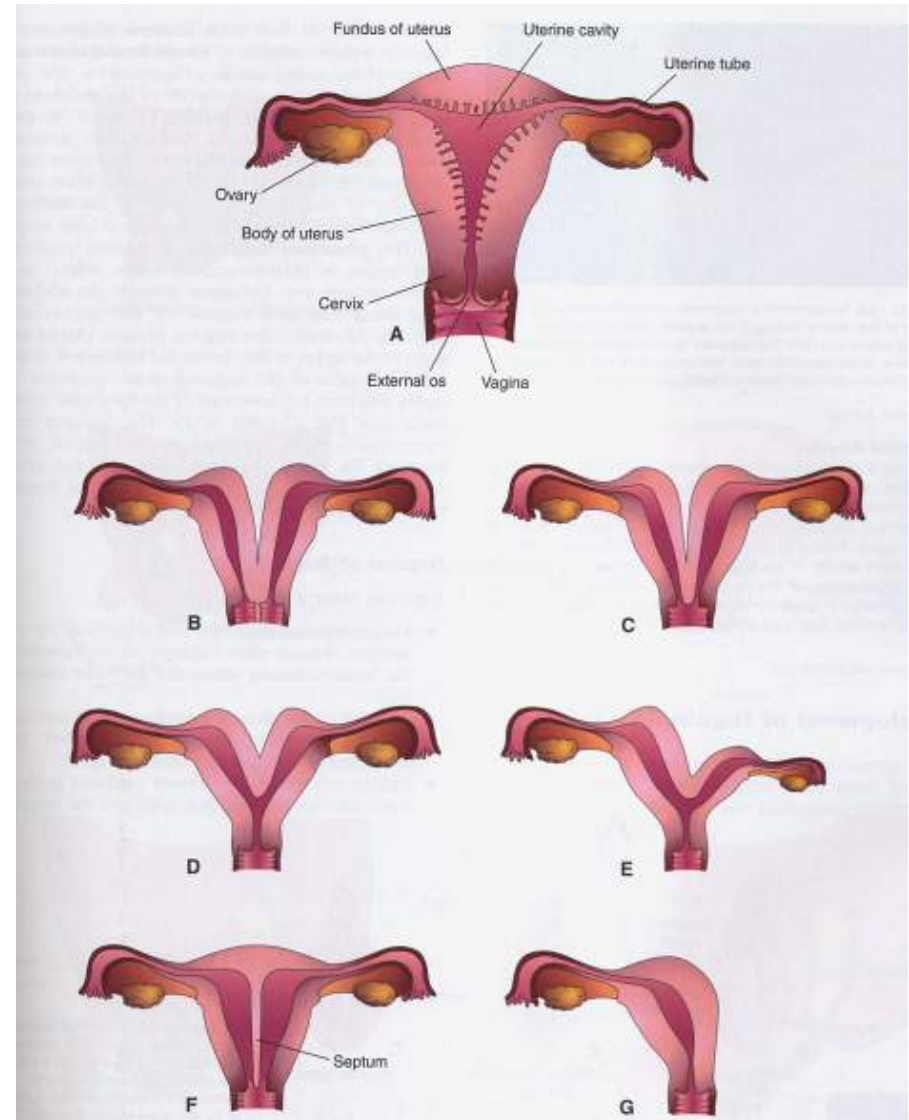
↳ Discovered after puberty ↴

بتكون المريضة تشكي انه ما عندها period و هو الدم بكون يتجمع جواها ما بتنزل ف بنعمل perforation surgically

↪ Abnormal fusion of uterine ducts

Uterine anomalies

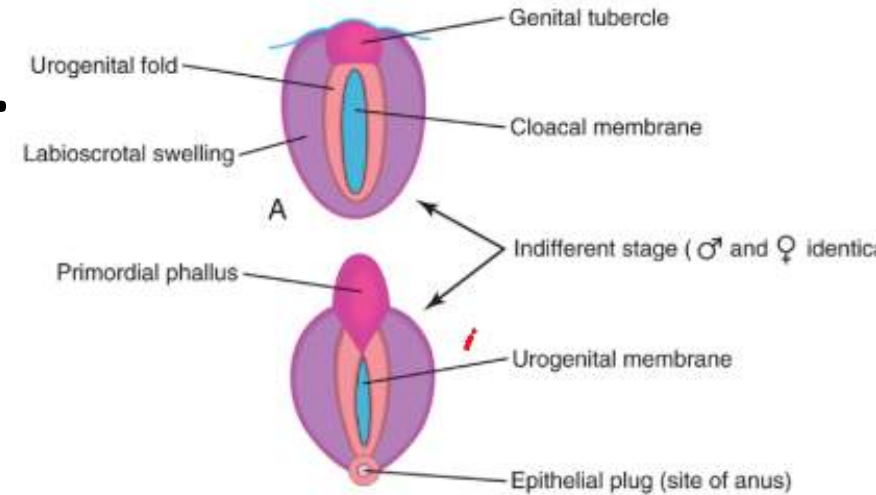
- A. Normal uterus and vagina
- B. Double uterus
- C. Double uterus with single vagina
- D. Bicornuate uterus
- E. Bicornuate uterus with a rudimentary left horn
- F. Septate uterus
- G. Unicornuate uterus



Development of External Genitalia

Indifferent Stage

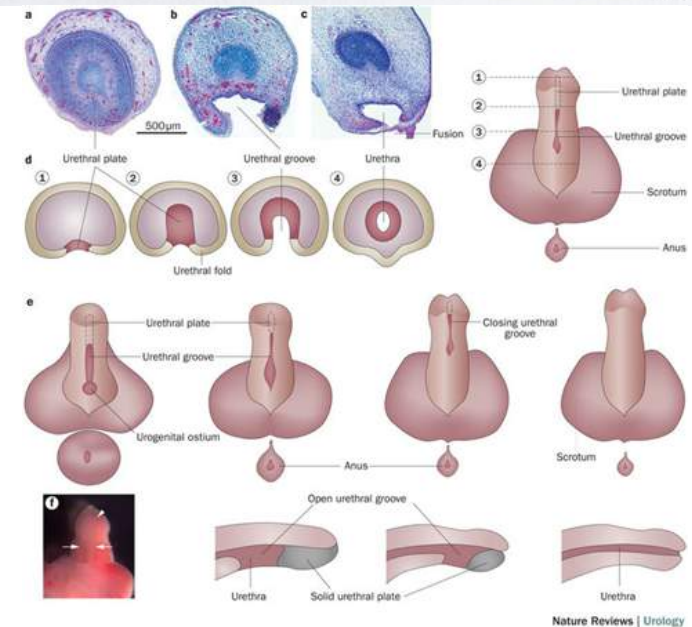
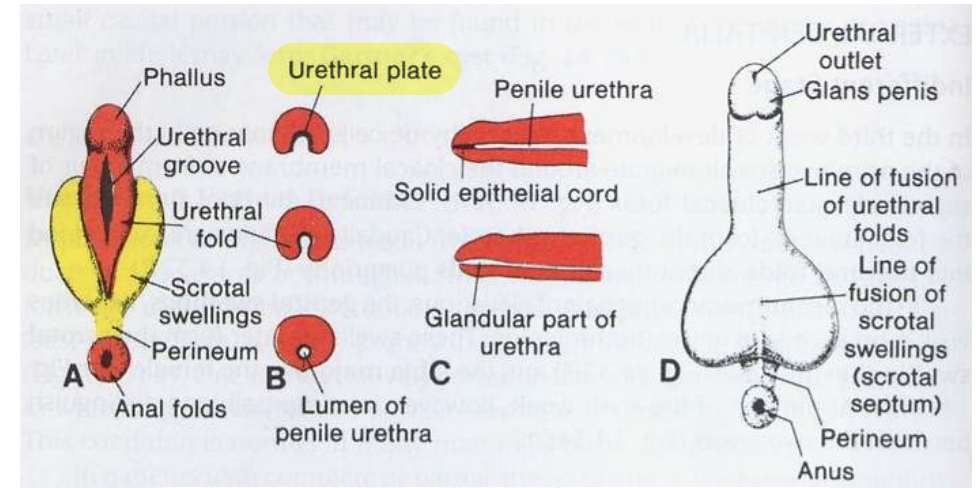
- In the **3rd week**, mesenchyme cells originating in the region of the primitive streak migrate around the **cloacal membrane** to make a pair of slightly elevated **urogenital folds**.
- Cranial to the **cloacal membrane**, the folds unite to form the **genital tubercle**
- Caudally, the folds are subdivided into **urogenital folds** anteriorly and **anal folds** posteriorly
- Another pair of elevations (**Labioscrotal folds**) becomes visible on each side of the urogenital folds
- Later these swellings from the **scrotal swellings** in males, **labia majora** in females



Development of external genitalia in male

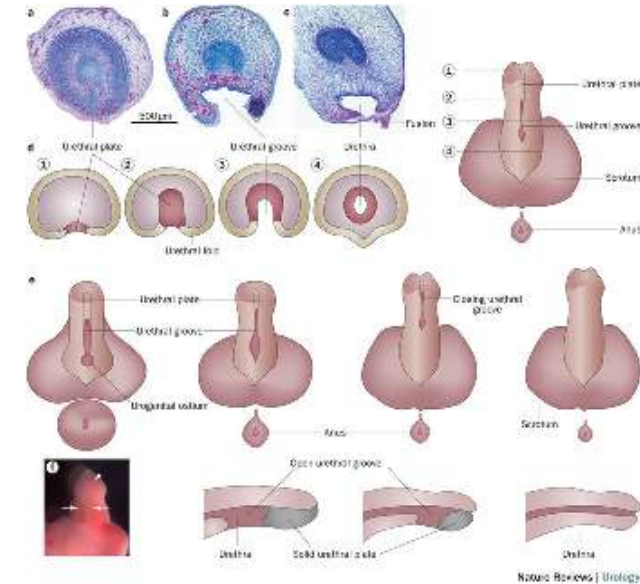
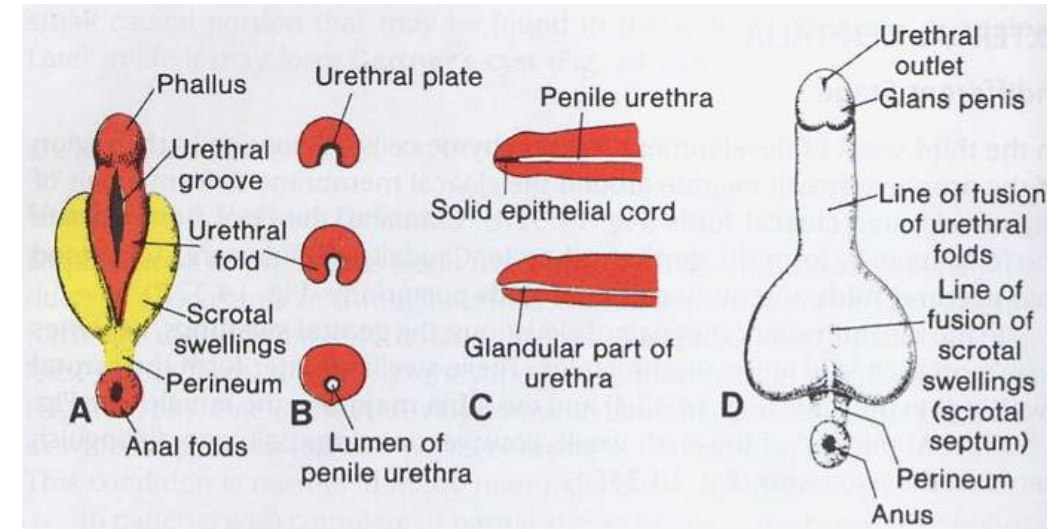
- Is under the influence of androgens from the fetal testes
- Characterized by rapid elongation of the genital tubercle (phallus); during which the phallus pulls the urethral folds forward so that they form the lateral walls of the urethral groove
- The urethral groove does not reach the most distal part (glans)
- The epithelial lining of the groove which originates from the endoderm, proliferates to form the urethral plate

↪ Enlargement



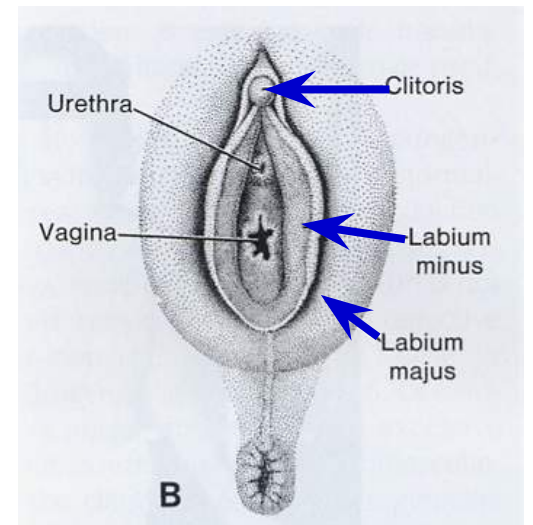
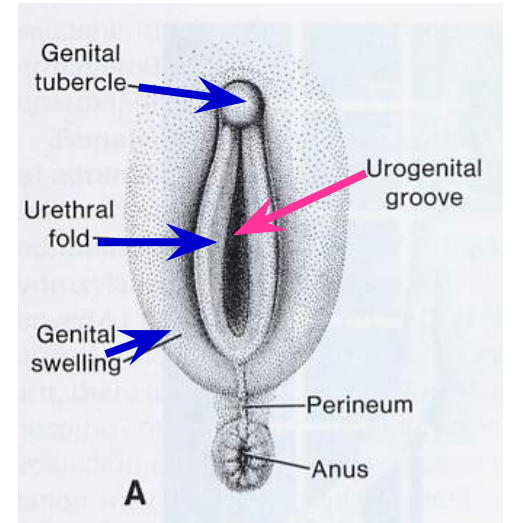
Development of external genitalia in male

- At the end of 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
- The most distal urethra is formed during 4th month when ectodermal cells from the tip of the glans penetrate inward and form an epithelial cord.
- Recanalization of epithelial cord forms the external urethral meatus
- The genital/scrotal swellings arise in the inguinal region; move caudally and each one makes up half of the scrotum, separated by scrotal septum.



Development of external genitalia in female

- Under the effect of estrogens, the genital tubercle elongates only slightly forming the clitoris
- Urethral folds do not fuse; develop into 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 females, it is larger than in males during the early stages; resulting in mistakes in identification of the sex by US examination.



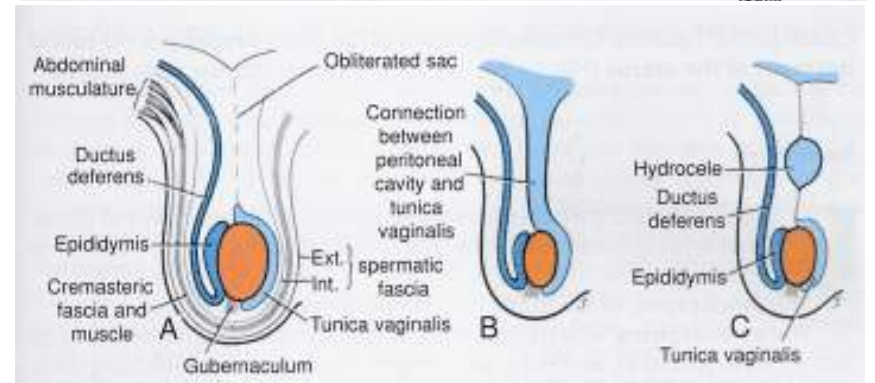
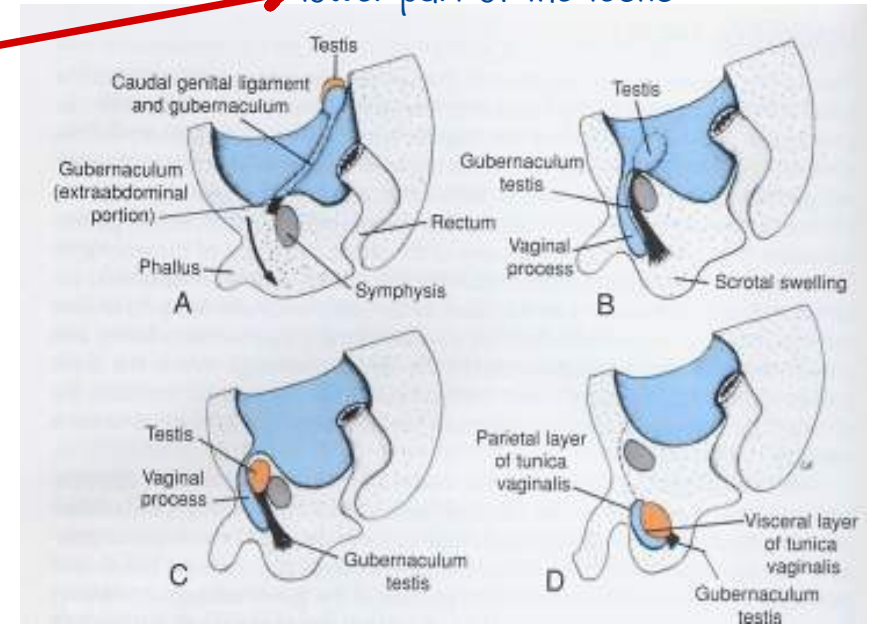
Congenital anomalies of penis

- **Hypospadias**: most common anomaly of the penis. The external urethral orifice is on the ventral surface of the glans penis (**penile hypospadias**). Resulting from inadequate production of androgens by the fetal testes/ or inadequate receptor sites for the hormone
- **Epispadias**: The urethra opens on the dorsal surface of the penis; often associated with exstrophy of the bladder; resulting from inadequate ectodermal-mesodermal interactions during the development of genital tubercle
- **Agensis of external genitalia**: Absence of penis or clitoris; resulting from the failure of development of genital tubercle.
- **Bifid penis and double penis**: vary rare, often associated with exstrophy of the bladder or urinary anomalies; results when two genital tubercles develop.
- **Micropenis**: The penis is so small that it is almost hidden by the suprapubic pad of fat. It results from a fetal testicular failure.

Descent of the testes

- By 26 weeks have descended retroperitoneally from the posterior abdominal wall to the deep inguinal rings
- Androgens, gubernaculum (a mesenchymal condensation) may guide the descent
- Descent may take 2-3 days and the inguinal canal contracts after they enter the scrotum
- As the testis and the ductus deferens descend, they are ensheathed by the facial extensions of the abdominal wall

Between scrotum and lower part of the testis



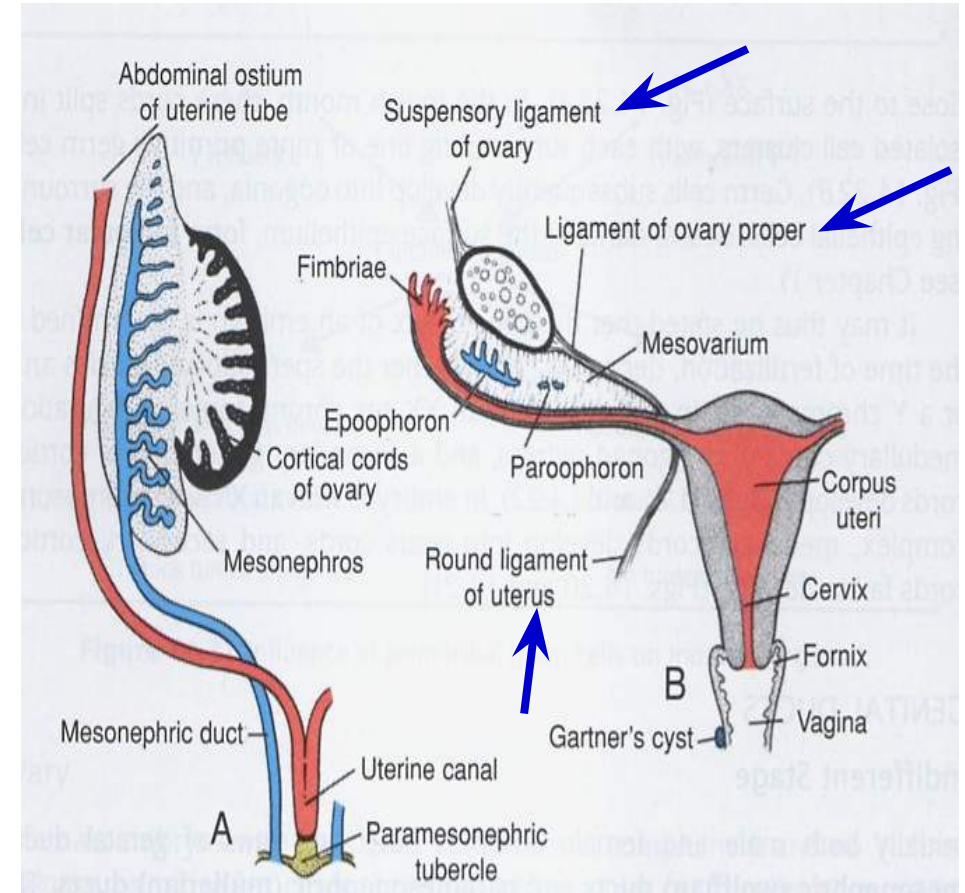
حکای مومووم نغز

Congenital anomalies of descent of the testes

- **Cryptorchidism or undescended testis**: occurs in 30 % of premature, 3-4% of full-term males. It may be uni or bilateral. Failure of descent in the first year causes atrophy of the testes. It may be in the abdominal cavity or anywhere along the descent path, usually in the inguinal canal. It may be caused by the deficiency of androgen production in the testes.
- **Ectopic testes**: After traversing the inguinal canal, the testis may deviate from its usual path of descent and lodge in various abnormal locations.

Descent of the ovaries

- Descent is considerably less in female
- The ovaries settle below the rim of the true pelvis
- The cranial genital ligament forms 1. the suspensory ligament of the ovary
- The caudal genital ligament forms 2. the ligament of the ovary proper and 3. the round ligament of the uterus



احفظوه
بصبر

MALE	EMBRYONIC STRUCTURE	FEMALE
<i>Testis</i>	Indifferent gonad	Ovary
<i>Seminiferous tubules</i>	Cortex	<i>Ovarian follicles</i>
<i>Rete testis</i>	Medulla	<i>Rete ovarii</i>
Gubernaculum testis	Gubernaculum	<i>Ovarian ligament</i>
<i>Efferent ductules of testis</i>	Mesonephric tubules	<i>Round ligament of uterus</i>
Paradidymis		Epoophoron
Appendix of epididymis	Mesonephric duct	Paroophoron
<i>Duct of epididymis</i>		Appendix vesiculosa
<i>Ductus deferens</i>		Duct of epoophoron
<i>Ureter, pelvis, calices, and collecting tubules</i>		Longitudinal duct; Gartner duct
<i>Ejaculatory duct and seminal gland</i>		<i>Ureter, pelvis, calices, and collecting tubules</i>
Appendix of testis	Paramesonephric duct	Hydatid (of Morgagni)
		<i>Uterine tube</i>
		<i>Uterus</i>
<i>Urinary bladder</i>	Urogenital sinus	<i>Urinary bladder</i>
<i>Urethra (except navicular fossa)</i>		<i>Urethra</i>
Prostatic utricle		<i>Vagina</i>
<i>Prostate gland</i>		<i>Urethral and paraurethral glands</i>
<i>Bulbourethral glands</i>		<i>Greater vestibular glands</i>
Seminal colliculus	Sinus tubercle	Hymen
<i>Penis</i>	Phallus	<i>Clitoris</i>
<i>Glans penis</i>		<i>Glans of clitoris</i>
<i>Corpora cavernosa of penis</i>		<i>Corpora cavernosa of clitoris</i>
<i>Corpus spongiosum of penis</i>		<i>Bulb of vestibule</i>
<i>Ventral aspect of penis</i>	Urogenital folds	<i>Labia minora</i>
<i>Scrotum</i>	Labioscrotal swellings	<i>Labia majora</i>