

ANATOMY

Sheet

Slide

Handout

Number

14

Subject

Genital Embryology -1

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Price:





Genotype VS Phenotype: when can be the sex of the embryo determined?

Genotype (genetic sex) of the embryo can be determined at the time of fertilization.

if the sperm carry (Y) chromosome >> MALE (XY)

if the sperm carry (X) chromosome >> Female (XX)

The Phenotype: (determined by the external genitalia)

Until the 12th week, it is difficult to tell if the embryo is male or female.

as both female and male developing embryos have the same early stages
(indifferent stage)

The Sequence of Genital development

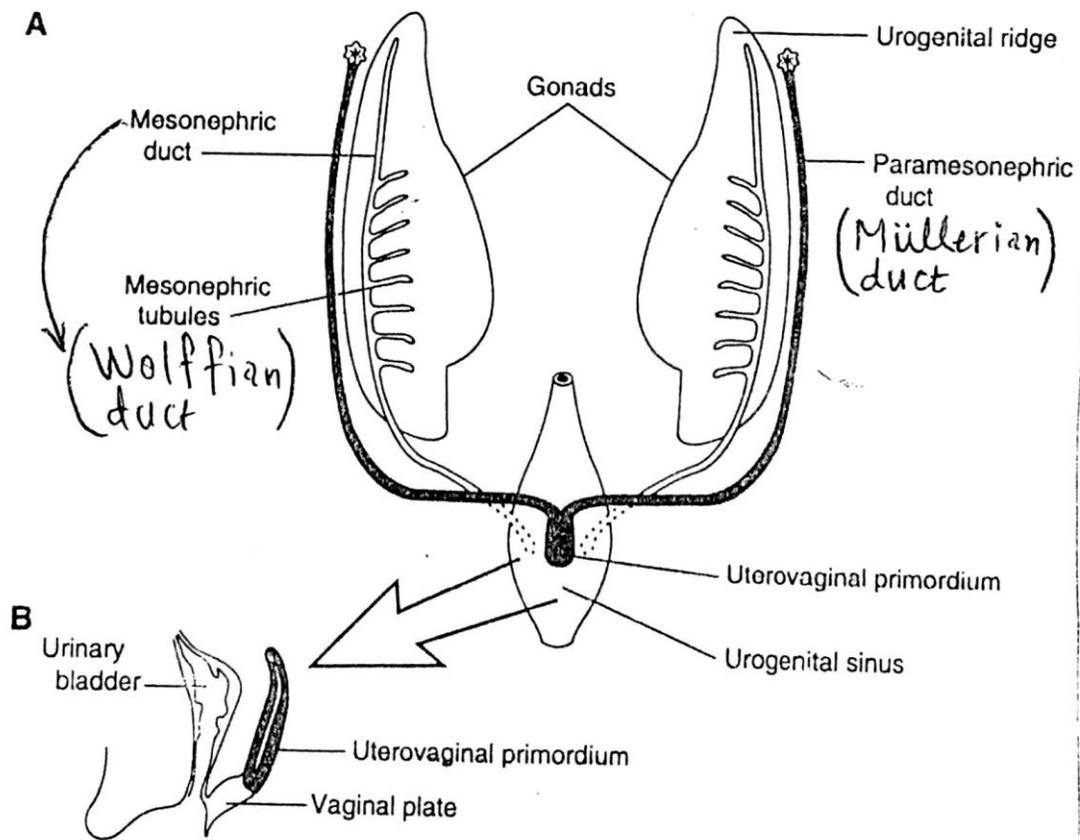
First the gonads (Ovaries or Testis) will develop.

then the internal genital organs → then the external genitalia.

Why gonads first?

- the gonads will secrete hormones that affect the development of the internal and the external genitalia.
- the internal genitalia are simply the **genital ducts**.
- in the Male, the genital ducts are: epididymis, vas deference, seminal vesicle & ejaculatory duct.
- In Female, the genital ducts are: uterine tube, uterus & upper third of vagina.

- at early stages whether the embryo is male or female, the embryo will have 2 genital ducts:
 - ✓ Meso-nephric duct and tubule (AKA **Wolffian** duct)
 - ✓ Para-Meso-nephric duct (AKA **Mullerian** duct)



you can recognize 2 different ducts here:

- ✓ Meso-nephric duct and tubule (AKA Wolffian duct)
 - The main function of this duct is to form the kidney
 - In males, it forms all the genital ducts
- ✓ Para-Meso-nephric duct (AKA Mullerian duct)
 - From its cranial part (upper vertical part) forms the uterine tube.
 - Its lower horizontal part the **uterovaginal primordium** which will form the uterus & upper 1/3 of vagina.

We said before that both of these ducts are initially there, but we cannot keep both of them in the fetus.

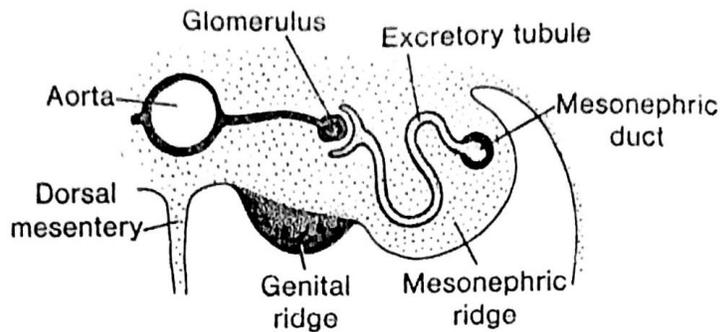
- ✓ The mesonephric duct will remain in the male.
- ✓ The para-mesonephric duct will remain in the female.

(but keep in mind that the kidney is developed from the mesonephric duct in both sexes)

Gonads Development

The Gonads (ovaries or testis) develop from the **urogenital ridge** (recall this ridge from the previous lec.).

The urogenital ridge consists of the mesonephric ridge (uro-part) and Genital ridge (genital-part)



The gonads will develop from the genital ridge , HOW?

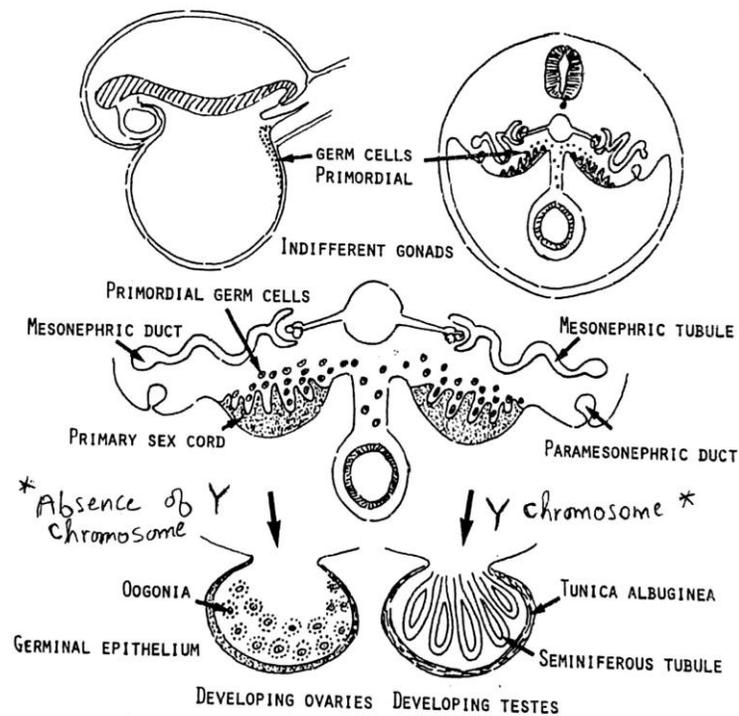


Fig. 18-1. Development of gonads.

1. At the surface, there are coelomic epithelium (remember: the body cavities rise from the coelom) this epithelium will proliferate.
2. The underlying mesenchyme will condensate → forming together with the proliferative epithelium → the genital ridge.
3. This ridge will receive primordial germ cells from the yolk sac.
[if the germ cells did not come from the yolk sac the gonads won't form => Gonadal-dys-gensis "main cause"]
4. The early stages of gonads development are called **Indifferent stage**. the indifferent gonads will become differentiated by the effect of (Y-chromosome), HOW?
 - a. The indifferent gonads have cortex and medulla.
in the differentiated gonads we shall have the cortex or the medulla.
 - b. If the Y chromosome is there, the indifferent gonads will become testis as under the effect of Y chromosome the cortex will disappear and the medulla will remain forming the testis → MALE
 - c. If the Y chromosome is absent, the indifferent gonads will become ovaries as the medulla will disappear and the cortex remains forming the ovaries → FEMALE.

We can also notice from the figure how the celomic epithelium sends finger like projections interiorly into the mesenchyme → called **Primary sex cords**. These will surround the primordial germ cells."بتحضانهم"

In a male these primary sex cord will form the seminiferous tubules eventually, but first it will only form the seminiferous cords. (cords will become tubules at puberty)

(remember: the seminiferous tubules will unite posteriorly forming straight tubules → rete testes → efferent ductules → head of epididymis → duct of epididymis → body + tail of epididymis)

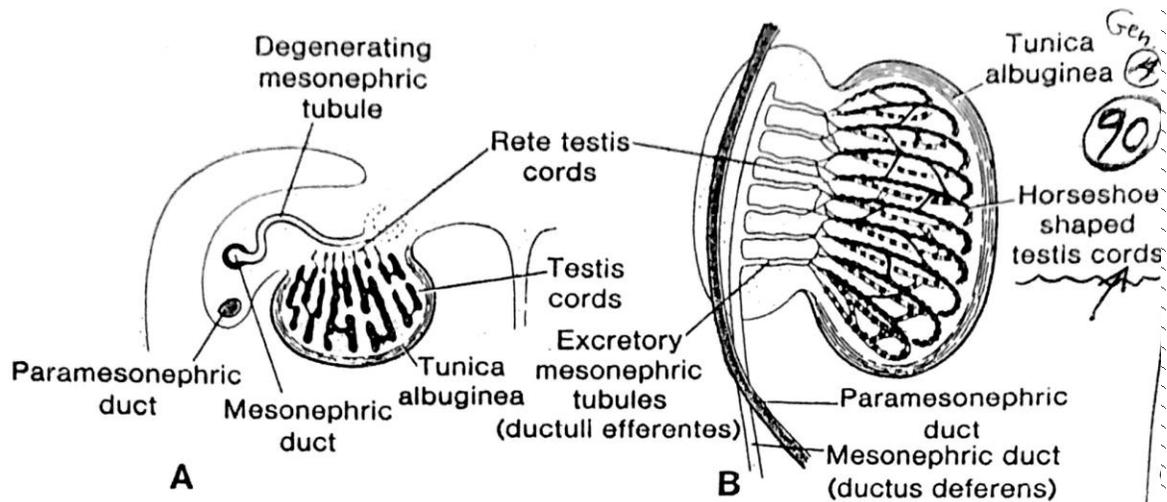


Figure 15.17 A. T

The testis is connected with the epididymis via the efferent ductules.

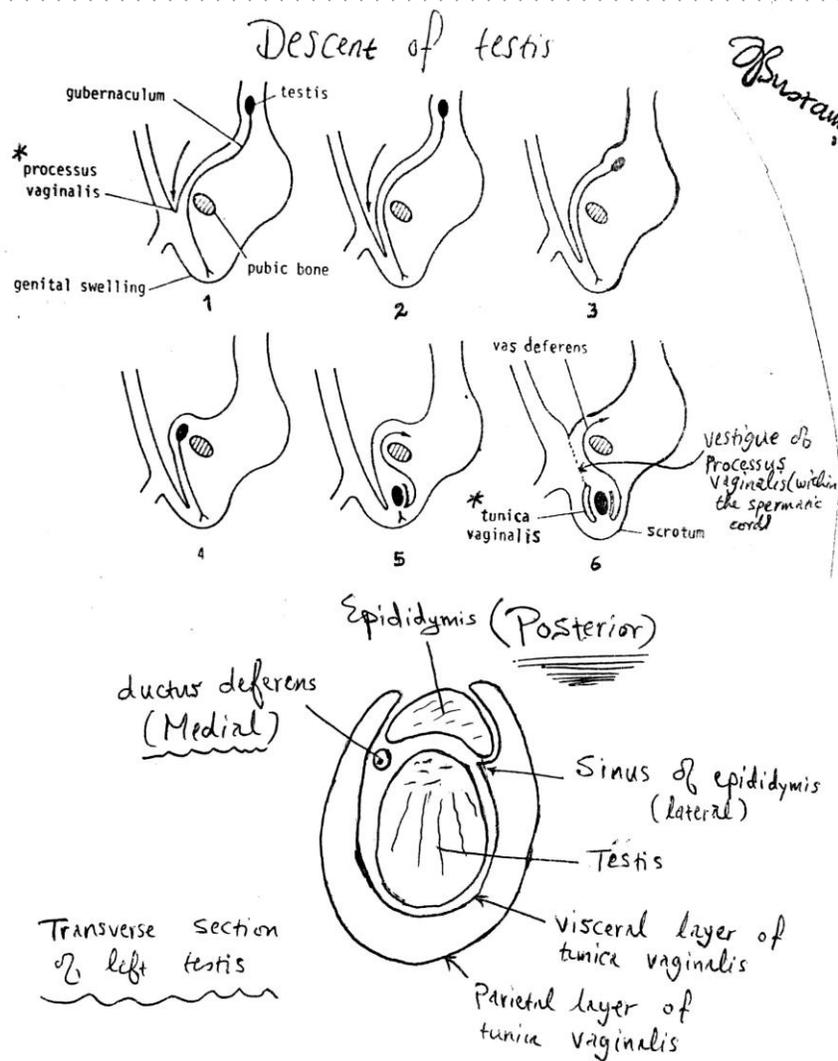
these efferent ductules rise from mesonephric tubules.

at figure B , notice:

- ✓ The paramesonephric duct will degenerate.
- ✓ The mesonephric duct will remain → follow it and notice how the mesonephric tubules arise from the duct into the testis.
- ✓ These tubules are obviously going to make the efferent ductules. (as they are between the testis and the epididymis)
 Note : there are mesonephric tubules in other sites but they will degenerate.
- ✓ The rest of the mesonephric duct will form the rest of the genital ducts in male (epididymis , Vas deferens)

Descent of Testis :

The testis develop inside the abdomen then descend to the scrotum .



HOW THE TESTIS DESCENDS: (from the abdomen to the scrotum)

The testis is hanged from the spermatic cord.

the **gubernaculum** pulls the testis down,

the gubernaculum is a remnant of mesonephros (descend from up -down-ward):

it is a ligament that is attached to the lower pole of the testis on one side and to the scrotum on the other, passing through the inguinal canal.

HOW it pulls the testis down?

Under the effect of androgens this ligament will grow slowly → and relative to its surroundings it appears as if it is shortening → when it gets shorter it pulls the testis down to the scrotum.

the descent of testis occur sequentially → first it reach the deep inguinal ring under the "pulling-down- effect " of the gubernaculum.

It's now at the level of the lower abdominal wall → it faces the peritoneum
“و تأخذه في طريقها” → it descend through the peritoneum thus a sac of peritoneum will cover the testis , this sac is called **processus vaginalis**.

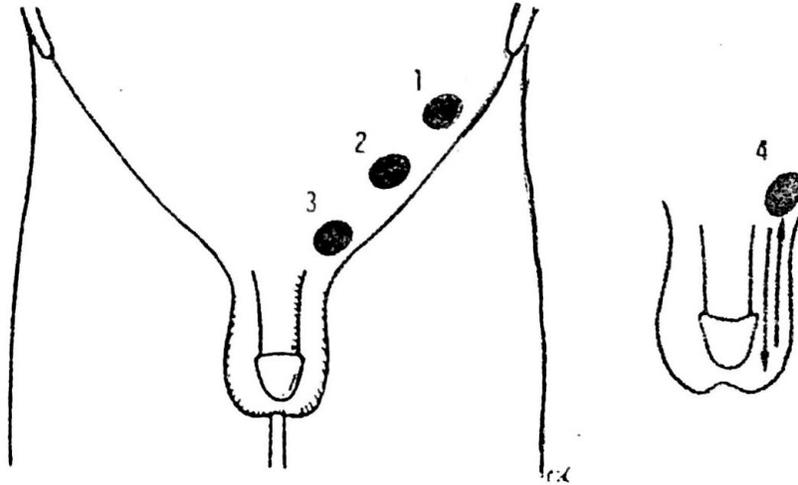
this process will give a cover to the testis called tunica vaginalis ,of two layers : visceral and peritoneal.

What is the difference between the processus vaginalis and tunica vaginalis?

- The processus vaginalis represent an earlier stage and consists of both the covering of the testis and the route that the testis descends via it through the peritoneum.
- The **tunica vaginalis** is a later stage and represent only the covering, this part is what persist after the testis enter the scrotum, it is the distal part of the process (the proximal part degenerate → a thin thread of it may persist forming vestige of processus vaginalis.
- this the normal state, but if the proximal part of the process didn't obliterate it will form a “canal” or a “preformed sac” that “invite” the intestines into the scrotum → forming congenital indirect inguinal hernia. (there is also an acquired form associated with conditions of increased intra-abdominal pressure like persistent cough → persistent cough invite the intestines into persistent processus vaginalis)

Some of the anomalies with regard to the descent of testis :

- ✓ **Incomplete descent**
- ✓ **Retractile testis**
- ✓ **Mal descent of testis**



Un-descended testis :

There are common sites that the testis remain stuck there : -indicated in the figure as #1- #3-

- ✓ Deep inguinal ring
- ✓ Inside the inguinal canal
- ✓ At the superficial inguinal canal

this anomaly accompanied with two side effects:

- ✓ This testis is liable to develop malignancy
 - ✓ Defective spermatogenesis.
- Surgical intervention is acquired in such cases to fix the testis inside the scrotum.
- Another anomaly is retractile testis indicated in the figure as #4 here the testis moves up and down through the scrotum >> it also needs to be surgically fixed.

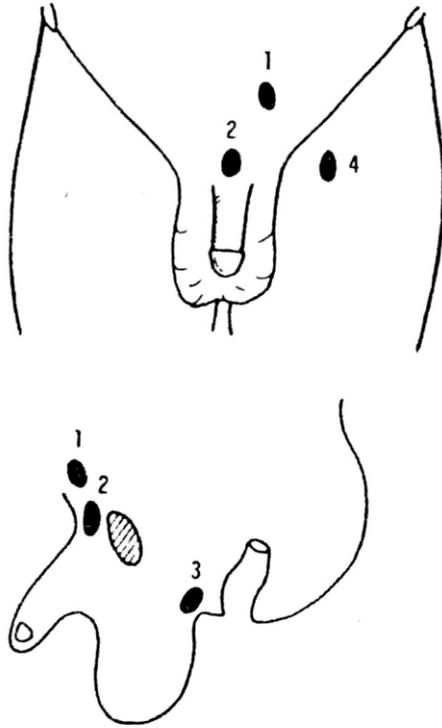


Fig. 16-12. The common sites of maldescent of the testis: (1) abdominal, (2) root of penis, (3) perineum, and (4) femoral triangle.

Mal-descent of the testis :
Here the testis descends but in abnormal route,
the testis end at the root of the penis, abdomen, femoral triangle...
“look at the indications at the figure”

to correct this case, we also perform a surgery.

In the past they used to wait before doing the surgery because:

As the testis descend under the effect of the slow shortening of the gubernaculum testis, which do shorten under the effect of androgens, in the past they used to wait until the baby (born with a testis-descent-anomaly) grows, hoping that the androgen level is the problem and it will become higher through life but nowadays they do a corrective surgery directly as early as possible

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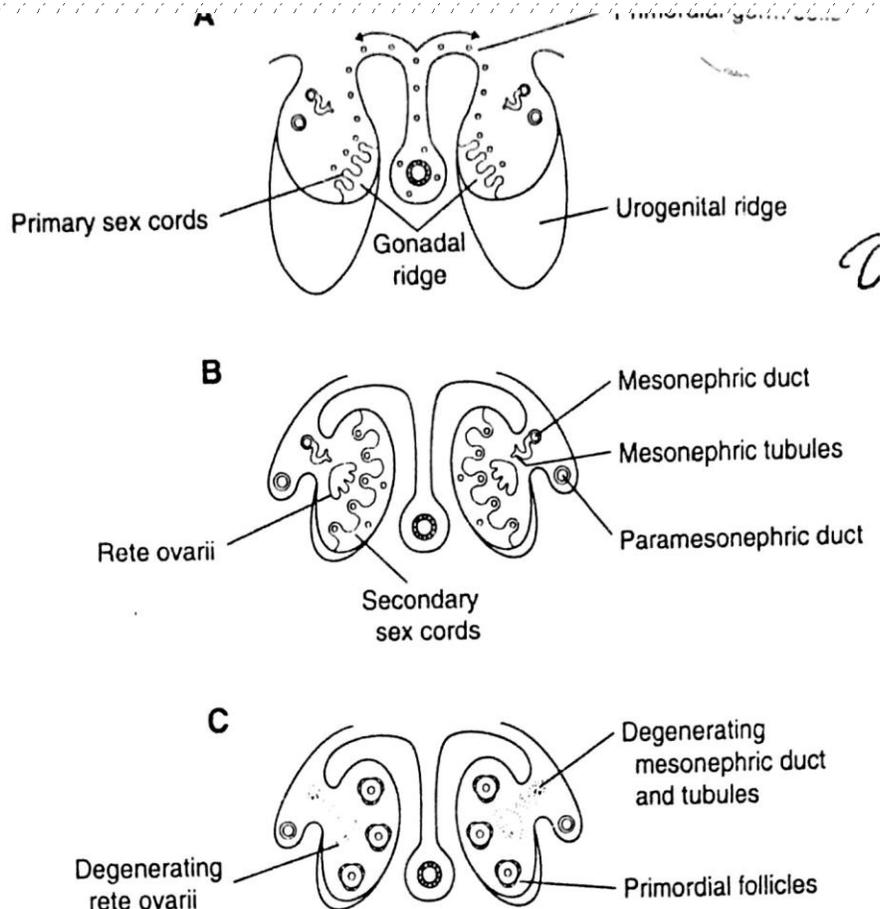
to avoid the side effects of these anomalies like malignancies of the testis.

بدناش إياها تخرب لذا ما بنستنى

Development of the ovaries

The ovaries (which are gonads) also develop from the gonadal ridge (part of the urogenital ridge)

This implies that the ovaries are **mesodermal** in origin.



(figure A) in the female the **primary sex cords** that surround the primordial germ cells will “disappear”.

They won't really disappear → they will become **Rete ovarii** (these are indicated in figure B) that will eventually themselves disappear.

however, **secondary sex cords** (B) will arise, these will invaginate inside → then they will form **primordial follicles**. (C)

each follicle surround an ovum = 1ry oocyte suspended in prophase of 1st meiotic division.

Descent of Ovaries:

The ovaries develop in the abdomen (upper lumbar region), the gubernaculum ovarii will pull the ovaries down-ward.

this ligament is attached to the ovaries pass through the inguinal canal and attach itself to labia majora (it is the round ligament in adults Female)

BUT!

Why won't the ovaries descend all the way to the external genitalia "like the testis"?

- Because the function of the ovaries CAN be accomplished inside the body, they do not have to get out in the scrotum to a lower Temperature.
- So, "and as the function defines the structure" the gubernaculum ovarii is different structurally from the gubernaculum testis; the gubernaculum ovarii is attached also to the lateral angle of the uterus this limits its (pulling downward) effect upon the ovaries → the ovaries will just reach the pelvis (i.e. pelvic structures)

actually, this ligament will be divided into 2 ligaments -inside the broad ligament- :

- ✓ Ovarian ligament: between the ovary and the uterus (posteriorly)
 - ✓ Round ligament of uterus : between the uterus and the external genitalia (anteriorly)
-

❖ Differentiation of the Duct system

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We said before that regardless of the sex of the fetus, 2 ducts will form (mesonephric and paramesonephric)

the differentiation of these ducts is guided by the gonads (remember : we said that the gonads is formed first then the internal genitalia then the external genitalia)

In a male fetus:

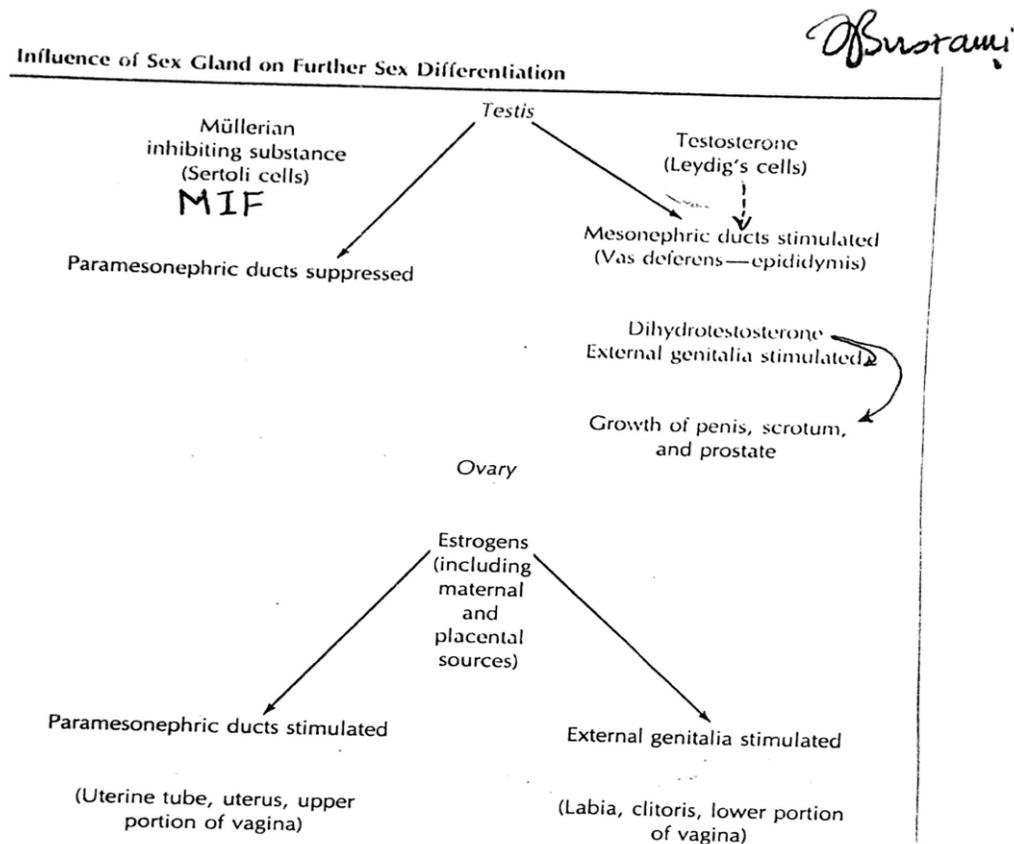
- ✓ The testis of a male fetus have sertoli cells.
- ✓ Sertoli cells secrete Mullerian inhibiting factor (MIF) which will inhibit the Mullerian duct (i.e. the paramesonephric duct) → so no uterine tube + no uterus + no upper third of vagina.
- ✓ The testis have Leydig's cells → which will secrete testosterone (which can be converted into dihydrotestosterone DHT)
- ✓ The testosterone will help in growth of genital duct in the male: the epididymis , vas deference , ejaculatory duct & seminal vesicle.

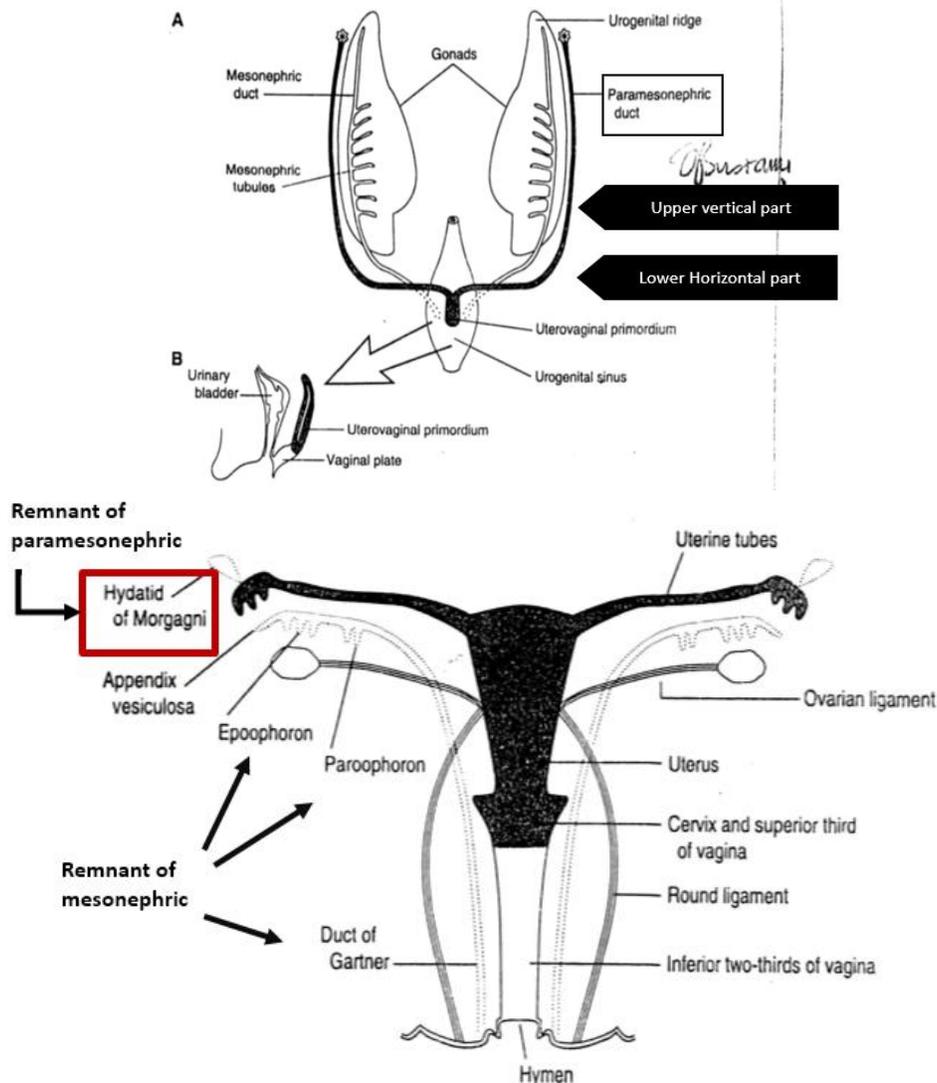
- ✓ The DHT will help in growth of the penis , scrotum & prostate.

In Female fetus:

- ✓ The ovaries have no MIF or testosterone so the mesonephric duct is not stimulated
- ✓ Under the effect of estrogen from the fetus ovaries or -mostly- maternal or **placental** estrogen → the paramesonephric duct will grow and differentiate.
- ✓ The paramesonephric duct will give rise to the uterine duct , the uterus & upper third of vagina.
- ✓ Also the external genitalia formation is stimulated (labia majora + minora + clitoris + lower 2/3 of vagina)

Check this diagram it summaries it all





What is the fate of paramesonephric duct in a female?

(remember: it is composed from upper/cranial vertical part + lower/ caudal horizontal part)

The upper vertical part will differentiate into uterine tube (on each side)

Note : a small undifferentiated sac might be found at the end of the uterine tube → this represent remnants of the paramesonephric duct and is called

Hydatid of Morgagni (Hydatid = sac filled with watery fluid) the significance of this sac is that : it can be enlarged in some cases and might be misdiagnosed initially as a tumor .

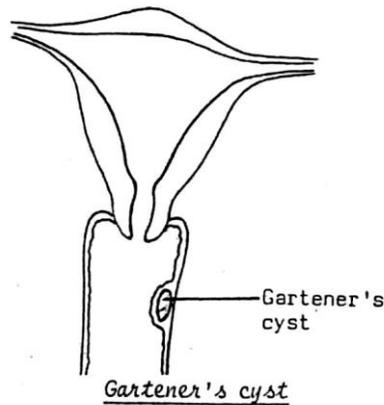
The two lower horizontal parts of the paramesonephric duct will come close to each other making the utero-vaginal primordium, which will develop into the uterus -including the cervix- and the upper third of vagina.

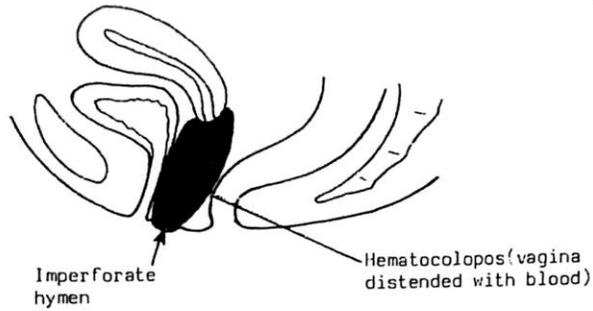
› The fate of the mesonephric duct in female :

It will regress due to the absence of the testosterone.

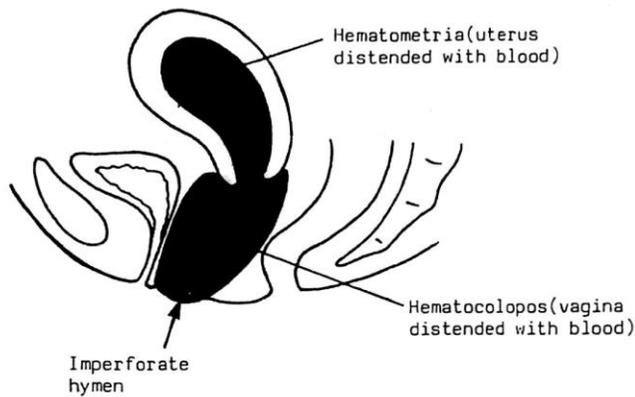
however it will leave some remnants , these are: (indicated at the figure)

- ✓ **Epoophoron** : Inside the broad ligament , above the ovary (hence the name) you can see small tubules that opens into the mesonephric duct. These tubules are opened superiorly and closed inferiorly. these are just remnants of the mesonephric tubules.
- ✓ **Paroophoron**: similar to the previous, but with different location, medial to the ovary (para not epi) and they are closed superiorly and inferiorly.
- ✓ **Duct of Gartner**: the whole duct remains as a thread, lateral to the uterus, cervix and the vagina
significance of this: it may become Gartner cyst around the uterus, vagina and cervix.
>> it must be distinguished from a malignant tumor.
in fact all of these remnants may become cystic.





Hematocolpos



the vagina and urethra should open into the vaginal vestibule (the interval between two labia minora)

the opening of the vagina is closed by the hymen which must be perforated so that the blood can pass out when the female menstruate.

one of the anomalies is **imperforate hymen**

- ✓ this will cause the blood to accumulate in the vagina , described as **Hematocolpos** = vagina distended with blood.
- ✓ If the blood continue to accumulate it will start to accumulate in the uterus , described as **Hematometria** = uterus distended with blood.

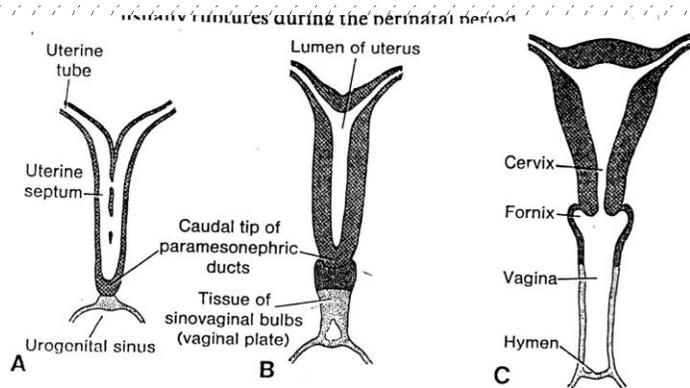
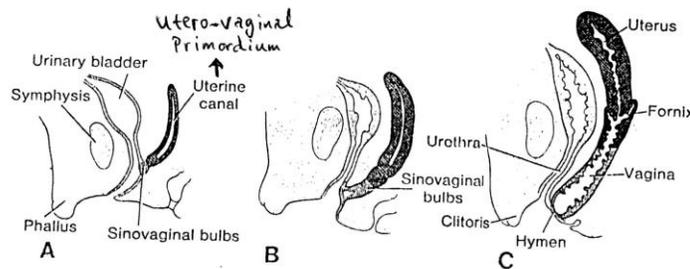


Figure 15-24. Schematic drawing showing the formation of the uterus and vagina. **A**, At 9 weeks. Note the disappearance of the uterine septum. **B**, At the end of the 3rd month. Note the tissue of the sinovaginal bulbs. **C**, Newborn. The upper portion of the vagina and the fornices are formed by vacuolization of the paramesonephric tissue and the lower portion by vacuolization of the sinovaginal bulbs.



How the lower 2/3 of vagina is formed :

We said that the lower horizontal part of the paramesonephric duct give arise to the **utero-vaginal primordium** this will grow inside the wall of the **urogenital sinus** (remember: this is derivative of the endodermal hindgut = the cloaca that give arise to the bladder and the urethra)

- ✓ The growth of the uterovaginal primordium inside the wall of the urogenital sinus → will stimulate it → inducing growth of the **sino-vaginal bulb** from the wall of the urogenital sinus.
- ✓ Two sino-vaginal bulbs on each sides will fuse together forming **vaginal plate**, which will be canalized (تفرغ من الداخل) → forming the lower 2/3 of vagina

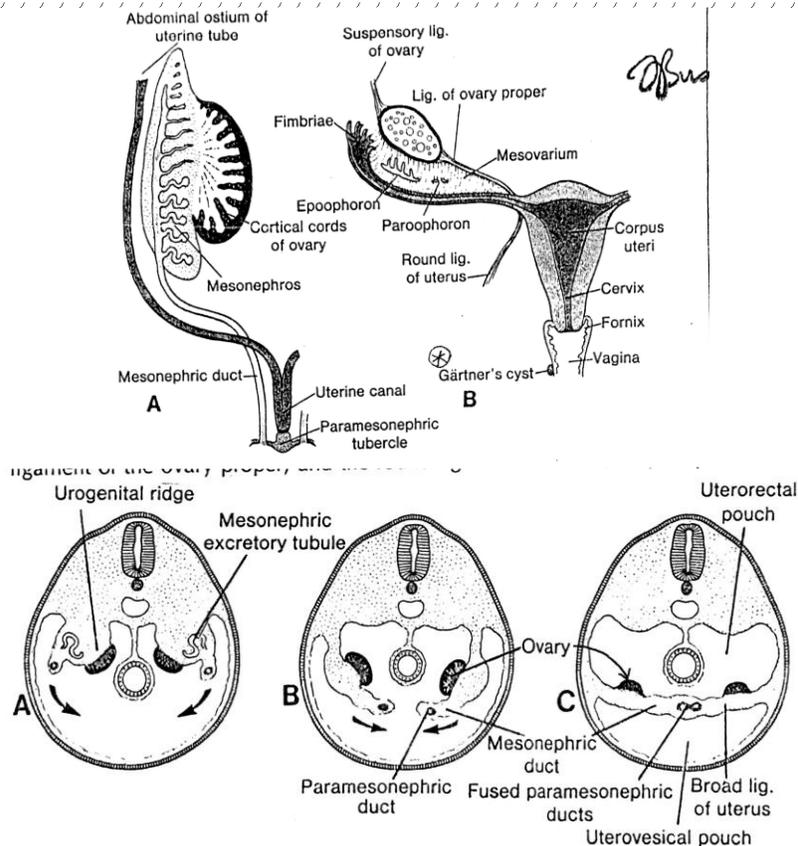
It is so important to emphasis on the fact that the two sino-vaginal bulbs will fuse together → if not, double vagina (anomaly) will occur
 And if these bulbs did not develop → no lower 2/3 of vagina.

To sum up:

From The paramesonephric duct (mesoderm) : the uterus , uterine tube & upper third of vagina.

The urogenital sinus (endoderm) : the lower two third of vagina.

Conclusion : the vagina has double embryological origin. (like the kidney and the male urethrae)

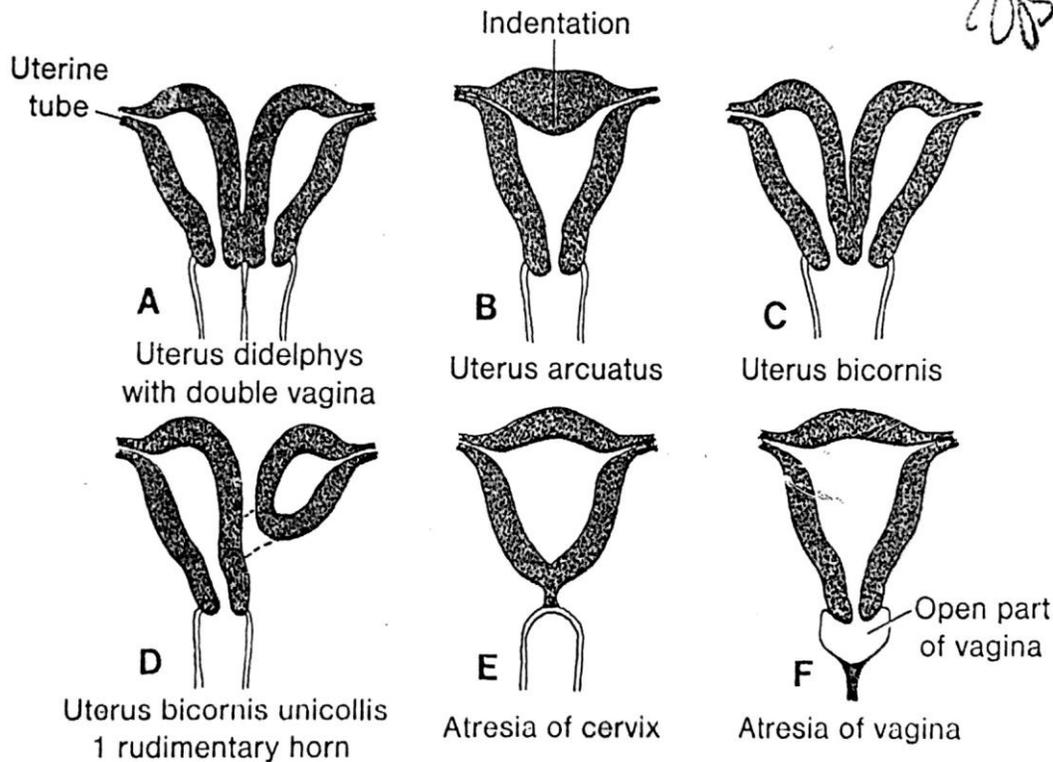


We said that the two horizontal parts of the paramesonephric duct will form the uterovaginal primordium by MOVING medially.

when they do MOVE they will pull with them fold of peritoneum , these will form the broad ligament in the future – when fused together in each sides - when the broad ligament is formed it will separate the pelvic cavity into :

- ✓ a posterior pouch, Rectovaginal pouch or Douglas's pouch
- ✓ an anterior pouch, Uterovesical pouch.

During this MOVEMENT the ovary is Sticking into the posterior aspect of the broad ligament.



Congenital anomalies related to the uterus:

1. **Agensis of the uterus**, if the paramesonephric duct didn't form the uterus won't form.
2. **Rudimentary uterus**, if the paramesonephric duct is small (a girl who reached puberty and didn't menstruate or menstruated with minimal blood → diagnosed with Rudimentary uterus "ultrasound is used for diagnosis" → such a girl will never menstruate normally or get pregnant)
3. **Duplication of the uterus**, as the uterus is formed from the fusion of the uterovaginal primordium if these two didn't fuse properly → i.e. the barrier between them did not fade → double uterus.
 - a. the most extreme case of doubling is called **Uterus didelphys with double vagina** (both uterus and vagina are duplicated)
 - b. **Uterus Arcuate**, this is the least sever case of doubling → a minor doubling occurs at the level of the fundus of the uterus → you can see it how it is slightly indented inside.
 - c. **Uterus Bicornis**, double uterus with single vagina, **most common** case. This condition is normal in some lower animals هسا جماعة التطور بكيفوا 🤪🤪🤪
4. **Atresia of the uterus** , (atresia = no canalization)

a. Uterus bicornis unicollis with rudimentary horn

(bicornis = two uterine cavities , unicollis = single vagina)

if one of the paramesonephric ducts that form the uterus did not go canalization and did not form lumen → one of the uterus cavities won't open into the vagina → its horn is rudimentary.

- when such a girl with such a condition menstruate the blood of the atretic uterus will collect in the peritoneal cavity causing lower abdominal pain.

b. Atresia of cervix, remember; as the uterus + cervix + upper 1/3 of vagina are formed from the same horizontal part of the paramesonephric duct they are liable to form related anomalies.

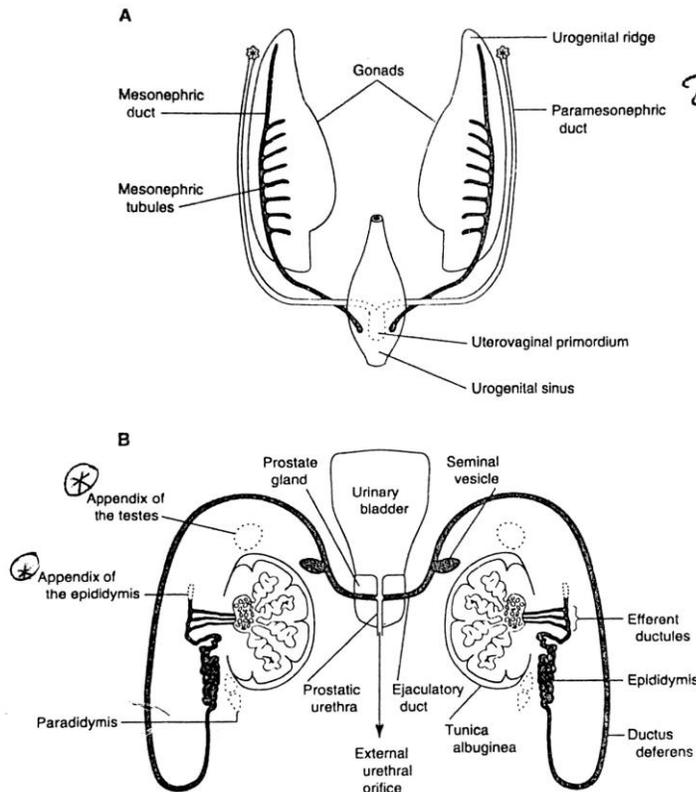
c. Atresia of vagina, here we are not talking about a paramesonephric duct problem as the upper 1/3 of vagina is canalized and normal.

the lower 2/3 of vagina do not go canalization (the vaginal plate do not undergo canalization)

GENTIL DUCTS IN THE MALE:

As said before both ducts (paramesonephric – mesonephric duct) develop in male & The paramesonephric duct will regress as the testis secrete **MIF**.

the testosterone -secreted from the gonads of the fetus- will help in the growth of mesonephric duct in its differentiation into genital ducts (epididymis , ejaculatory duct, Vas deference, seminal vesicle) .



The mesonephric tubules are adjacent to the mesonephric duct which as we said earlier connect the testis and the epididymis.

These tubules will become efferent ductules. (the rest of mesonephric tubules regress)

In both males and females, the mesonephric duct will give rise to the kidney (via ureteric bud)

The paramesonephric duct will regress but will leave some remnants :

- ✓ **Appendix testis** ,of the size of a Lentil grain above the testis
- ✓ **Appendix epididymis** , of the size of the Lentil grain above the epididymis.

*Significance of these structures: they may enlarge and they are liable to form cysts → when forming cysts they are liable to undergo torsion → ischemia and pain.

in fact, when a patient present to you with severe pain in his scrotum without trauma:

- ✓ Torsion of the testis on the spermatic cord >> which will cause ischemia of the testis >> quick interference is a must to save the testis.
- ✓ Cysts of the appendix testis or epididymis.

Development of the External genitalia:

We said previously that the cloaca (part of the hindgut / endoderm) will divide into anorectal canal posteriorly & urogenital sinus anteriorly.

the urogenital sinus will give the urinary bladder in both sexes, parts of the urethra and lower 2/3 of vagina.

The cloaca used to be covered by a membrane called cloacal membrane. and like the buccopharyngeal membrane, it will rupture → as any membrane formed only from ectoderm or/and endoderm will rupture.

as the rule says:

ANY PART OF THE EMBRYO DEVOID OF MESODERM SHOULD RUPTURE AT ONE TIME.

*NOTES:

- ✓ The mesoderm comes from the primitive streak
- ✓ The cloacal membrane is ectodermal + endodermal.

more details :

1. At the 3rd week, some mesoderm will invaginate into two parts of the cloacal membrane → so these parts won't rupture → called **cloacal folds**.
إذن حشي الغشاء بالميزوديوم أنتج هذه الثنيتين
2. The two cloacal folds will fuse together anteriorly forming **Genital tubercle** (AKA : Phallus = related to penis)
3. At the time that the cloacae divide into anorectal canal posteriorly & urogenital sinus anteriorly → the cloacal folds will also divide similarly into
 - a. **Urethral or urogenital fold**
 - b. **Anal fold.** (around the anus – GI ملناش دخل)
4. At the middle of the urethral fold , there's **urogenital membrane** → which at certain stage will rupture as it is a part of the cloacal membrane without mesodermal invagination → giving an opening to the urogenital sinus

5. Outside the urethral folds, there are other two called genital swellings or labio-scrotal swellings → will differentiate into scrotum in male and will remain as labia majora in females.

From the figure, you can notice the indifferent stage at early genesis of external genitalia in both sexes.

because of that it is hard to define the sex of the fetus in the 2nd or 3rd month. (many mixes may occur)

Indifferent stage = urethral folds fuse anteriorly forming genital tubercle/ phallus + outside two genital swellings/ labioscrotal swellings.

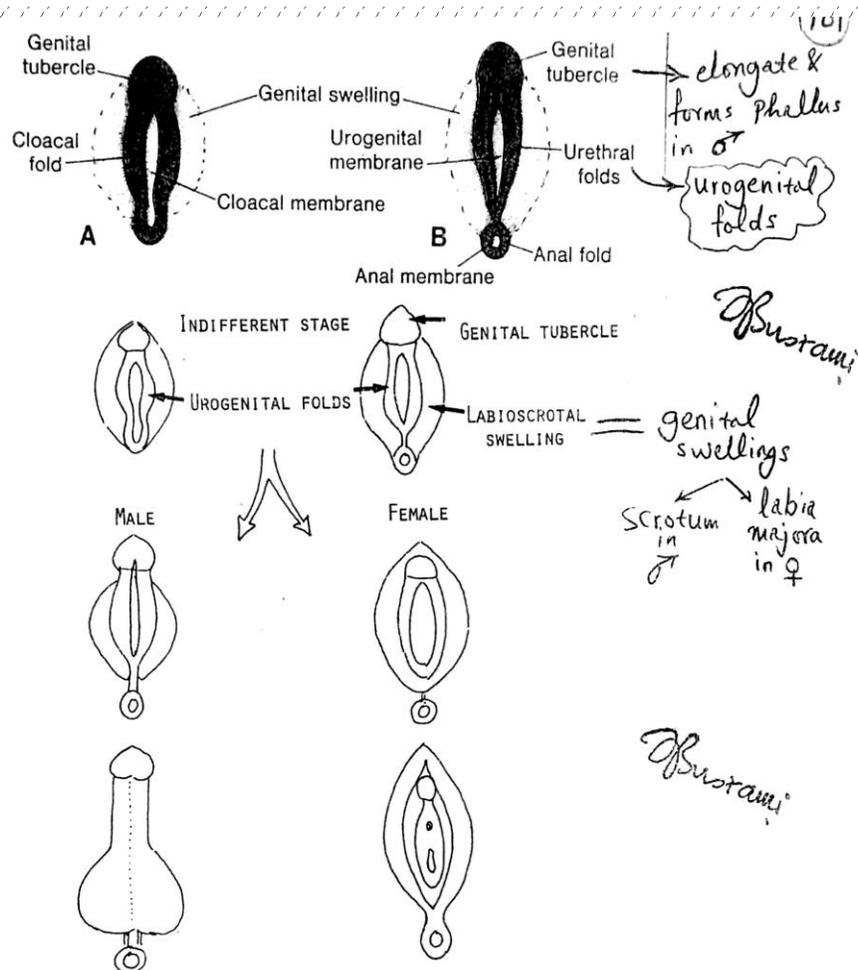


Fig. 18-4. Development of the external genitalia.

In Male:

- ✓ The genital tubercle or the phallus will grow fast forming the penis.
- ✓ The urethral folds will fuse together surrounding the urethrae.
- ✓ The genital swelling will grow inferiorly forming the scrotum.

In Female:

- ✓ The genital tubercle remains small forming the clitoris
- ✓ The urethral folds won't fuse around the urethra they remain separate forming labia minora.
- ✓ The genital swellings will remain separate forming labia majora.

END OF TEXT

في نهاية هذا الشيت أود أن أعتذر عن أي خطأ وردَ فيها أو في أي شيت سبق أن كتبته؛ هو حقاً تقصيرٌ مني، و ما كان فيهن من خير فهو من توفيق ربي.
و نتمنى لكم الخير - جميعاً.

Le Fin.

Revised by: *Omar Saffar*