ANATOMY

☑ Sheet ○ Slide ○ Handout

Number

15

Subject

Embryology 2

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Price:

- this sheet was written according to section 1 recording.

DEVELOPMENT OF MALE EXTERNAL GENITALIA

The steps of Penis formation and the penile urethra are:

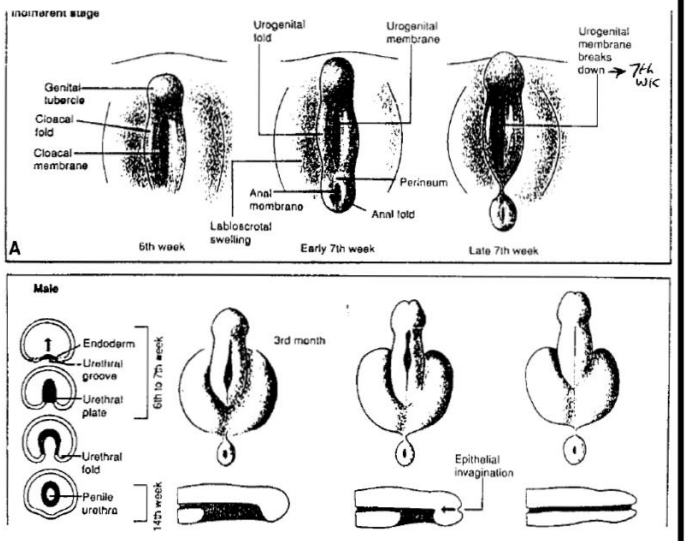
1- Rapid growth and elongation of the **genital tubercle** (phallus) forming the penis.

2- Rupture of the **urogenital membrane,** which is a groove between the two urethral folds (they lie on the sides of the genital tubercle and used to be called urogenital folds), the urogenital membrane closes the **urogenital sinus** from below. *"when it gets ruptured it will allow endodermal cells to migrate"*

3- Groove formation on the inferior surface of the penis called the urethral groove, this groove will be filled with **endodermal cells** coming from the urogenital sinus forming the urethral plate.

(*after the rupture of urogenital membrane, endodermal cells will migrate and fill the groove)*

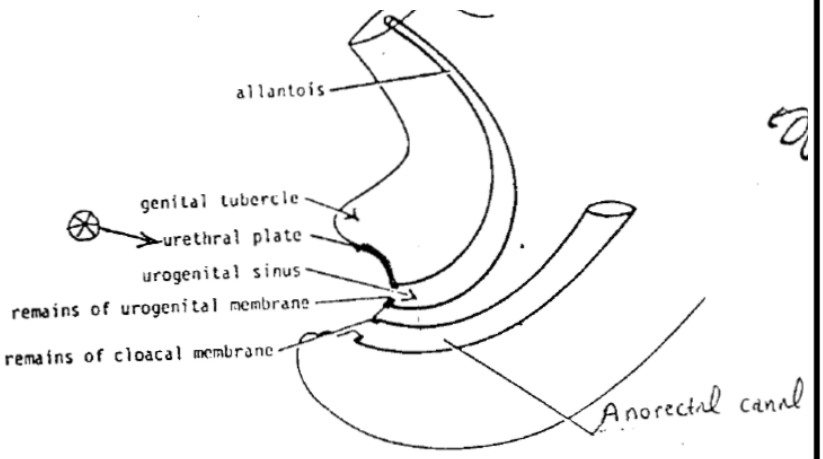
If we look at the cross section → urethral groove getting filled with endodermal cells → will form urethral plate → undergoes recanalization and becomes groove again but this time even deeper → the two urethral folds lying beside this groove will get closer to each other and eventually will close it transforming it to a tube "the urethra, penile part!".



*All of this is happening on the **Ventral** aspect of the penis

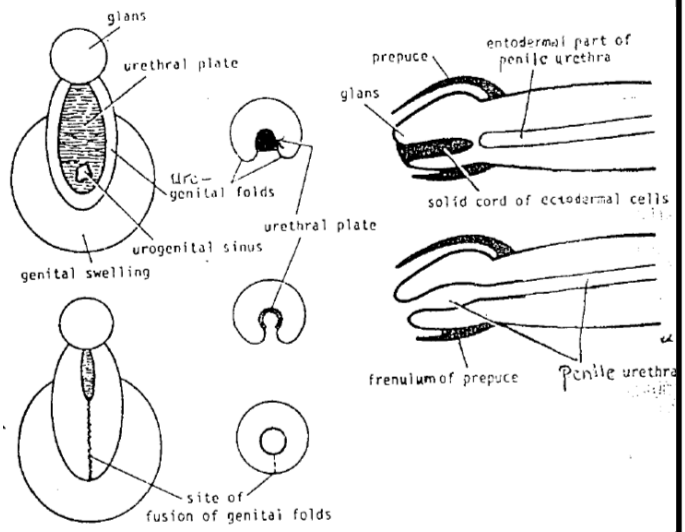
- if the urethra didn't close, the urethra will open to the inferior side "instead of opening at the tip of the penis" → *hypospadias*

❖ looking at the sagittal section → we see the genital tubercle, behind it the groove getting filled with the endodermal cells and becomes the <u>urethral plate</u>



- briefly: groove → filled with endodermal cells → urethral plate → re-canalization → deeper groove → closed by the fusion of urethral folds…

- now some details:



- Genital tubercle undergoes fast growth and elongation.

- behind it are the two urethral folds

- the area between them is a groove and gets filled with endodermal cells coming from the UG sinus then called the urethral plate

- re-canalization, then the tube is closed from the inferior side by the fusion of two urethral folds → penile urethra!

- this concept applies to the whole penile urethra except the terminal part (inside the glans penis):

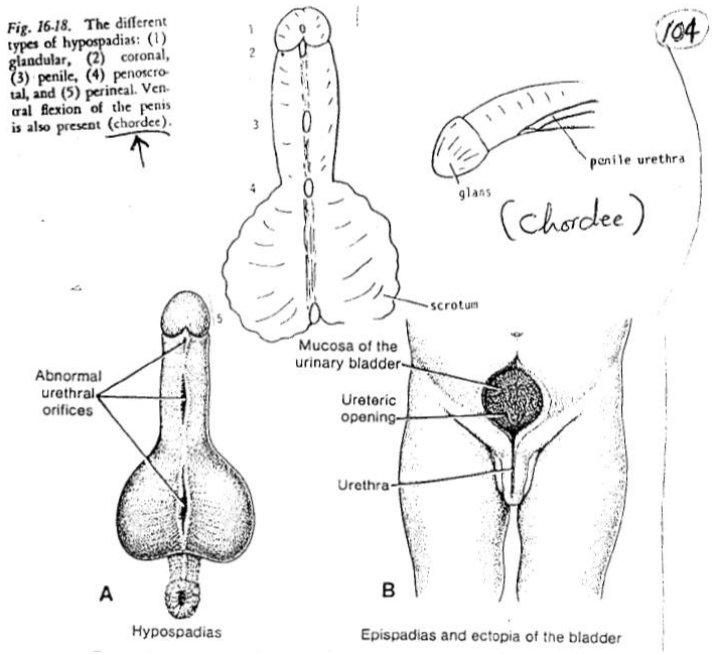
- the cells here are **<u>Ectodermal</u>** in origin (not endodermal)

- enter as a plate without undergoing canalization, and unite with the endodermal part located in the back

Congenital anomalies of the penile urethra:

❖ Hypospadias:

- The most common anomaly is the **<u>hypospadias</u>** → (opening of the urethra is on the underside of the penis), this happens if the two urethral folds fail to fuse or unite "incomplete fusion"
- Location: <u>underside</u> of the → glans penis "corona", body of penis, root of penis or perineum
- it's important to notice that in this condition the ectodermal plate doesn't form (stay closed), this means that if a baby has hypospadias we <u>can't</u> insert a <u>catheter</u> through the glans penis!
- Also the penis will be bent downward (**<u>chordee</u>**)



➢ *3 characteristics of hypospadias (<u>opened</u> urethra downward, no <u>ectodermal</u> plate formation and <u>chordee</u>)

➢ The <u>foreskin</u> is an extra skin covering the glans penis, gets removed during circumcision… → clinical correlation:

- if a baby is born with hypospadias, do we perform circumcision on him?
  - the answer is NO, because we can use that extra skin to <u>close</u> the opened urethra

❖ Epispadias: *(not mentioned in the lecture)*

- Results when the genital tubercle grows **caudally** in the region of the urorectal septum, and when the UG membrane ruptures, the UG sinus opens on the **dorsal** aspect of the penis, therefore the urethral opening is found on the dorsum of the penis.
- It is often associated with exstrophy "protrusion" of the bladder

❖ Comparison with the external genitalia of the female:

Males	Females
- the external genitalia grow under the effect of **androgen** (Testosterone & DHT) - phallus (genital tubercle) grows **rapidly** → **glans penis & shaft** (major difference) - rupture of UG membrane - fusion of urethral folds → **penile urethra & penis around it** - genital swellings (labio-scrotal) fuse and form the scrotum - the definitive UG sinus will be the source of the endodermal cells for the urethral plate	- the external genitalia grow under the effect of **estrogen** (maternal & placental estrogen) - phallus (genital tubercle) grows **slowly** & a little bit → **clitoris** (major difference) - rupture of the UG membrane (the UG membrane is **under** the **hymen**) - the urethral folds don't fuse together → forming the **labia minora** - genital swellings stay separated → forming the **labia majora** - the labia majora unite together superiorly forming the **mons pubis** - the definitive UG sinus will form the vestibule of the vagina

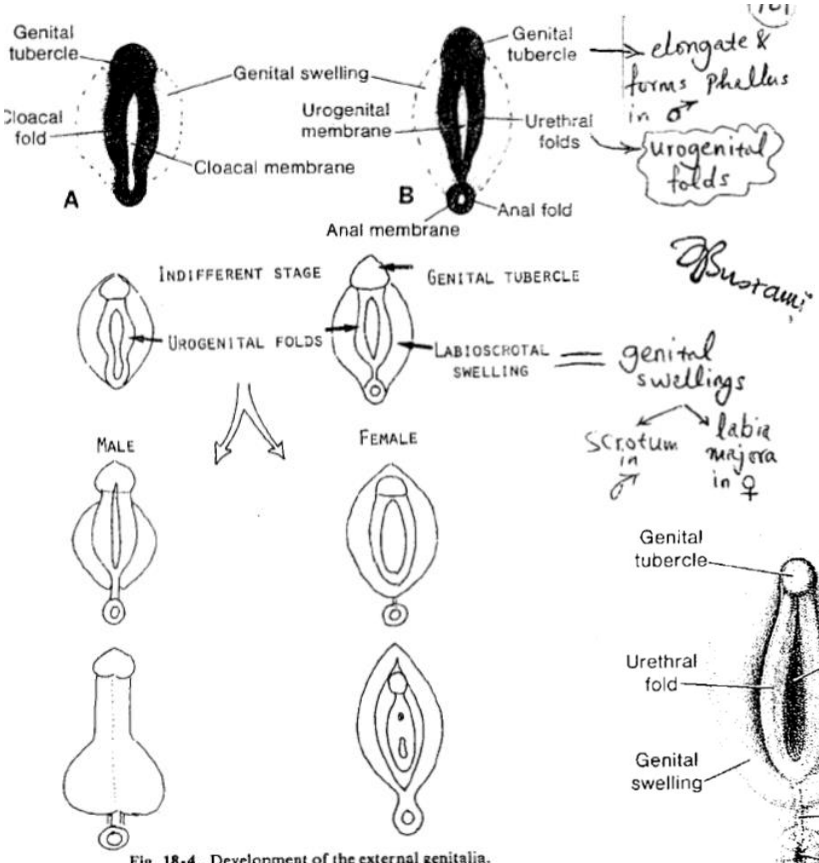


Fig. 18-4. Development of the external genitalia.

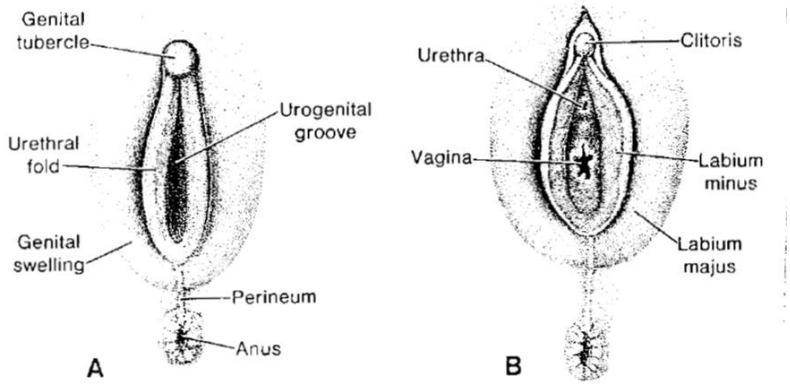
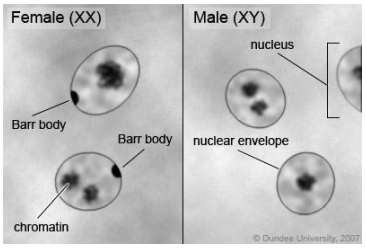


Figure 15-31. Development of the external genitalia in the female at 5 months (**A**), and in the newborn (**B**).

❖ Anomalies related to the genital system



first let's talk about the **Barr body**

Barr body:

- It is a sex chromatin body, one of the **X** chromosomes of the female, inactive and condensed
- it is seen as a dot in the inner surface of the nuclear membrane
- in the neutrophils, the Barr body has drumstick appearance

- whenever the Barr body is seen then we can say that this person has **2X** chromosomes
- yet that doesn't always mean that the person is a normal female, because that person may have **XXY** pattern

note: if the individual possesses an extra X i.e. XXX → there will be two Barr bodies in some nuclei.

- if Barr body isn't present, then the person is usually a male "having one X chromosome (XY)
- Or he could be XO, means he only have one X → incomplete female (Turner syndrome)

- Barr body can be easily seen clinically by looking at mucosal cells in the mouth (i.e. mouth swab)

Example:

in a female new born, if the clitoris was bigger than normal, and the labia majora fused together and became similar to the scrotum, we might mistakenly consider her a male baby due to her genitalia appearance,
but we can do a Barr body test to be sure about the sex if there was any suspicion

❖Congenital UG anomalies:

a. true hermaphrodite
b. pseudo-hermaphrodite (very important)

A. **True hermaphrodite**

- Means a person is born with both ovaries and testes & external genitalia of both males and females
- This case is not reported in humans!
- We may only see ovarian or testicular tissue in the opposite sexes

B. Pseudo-hermaphrodite

- female pseudo hermaphrodite (more common & more important): there's ovaries yet the external genitalia is similar to that of males, how?
  - the clitoris is penis like (very big) & the labia majora is scrotum like (fused)

- chromosomal pattern: XX
- why does the external genitalia is that of males?
  - due to the effect of the androgen secreted by the Adrenal cortex (due to adrenal cortex hyperplasia in the fetus) → Adrenogenital syndrome
- the adrenal cortex normally secretes mineralocorticoids (aldosterone), glucocorticoids (cortisol) and little amounts of androgen

- yet this baby has a deficiency in an enzyme called **(21 beta hydroxylase),** due to this deficiency no mineralocorticoids nor glucocorticoids will be synthesized, and all steroids will be converted to androgen → that will change the external genitalia of the fetus from female to male

- more than half of the babies born with ambiguous genitalia (unclear sex) are female pseudo-hermaphrodite
- it is more important to take care of the enzyme deficiency rather than trying to correct the external genitalia, because aldosterone is essential for life

- Male pseudo hermaphrodite (less common): there's testes yet the external genitalia is that of a female
- Because although there's testes but the amount of androgen is low, and the external genitalia of males depends on androgen for its development, so variable forms can be seen according to the level of androgen

(good question):
Q/ half of ambiguous genitalia cases are? → female pseudohermaphrodite →
- there's ovaries but the estrogen coming from the ovaries is overcame by the androgen secreted from the adrenal cortex

*Main androgen source in males is the testes not the adrenal gland (normally)

❖Other sex abnormalities

Turner syndrome:

- occurs in **females**, chromosomal pattern is **44 + 1X (XO)**
- in another word: she is a female with an absent Barr body

- major characteristic of this syndrome is gonadal dysgenesis
- we said before, in order for the gonads to develop, primordial germ cells must migrate from the yolk sac
- the problem here is that these cells either **didn't migrate or died** (after migration the cells degenerate)

➢ so again, this person has:
1. absent Barr body
2. no gonads (no testes nor ovaries)
3. and the absence of **Y** chromosome will make the genitalia develop in a female pattern, How?

- due to the effect of maternal & placental estrogen the external & the internal genitalia develop in a female pattern, yet after birth the source of estrogen is lost so the genitalia stays small in size (**infantile**)
- small uterus will make this person have primary amenorrhea when reaching puberty

another condition similar to Turner syndrome is:

Pure gonadal dysgenesis

- Called pure because there's no chromosomal abnormality (normal **XX** or **XY**)
- the same story about dysgenesis occurs here, the primordial cells either didn't migrate or died (after migration the cells degenerate)
- and the external genitalia will also grow to a female genitalia due to the influence of maternal & placental estrogen

* the doctor may ask a "beautiful comparison question" about these abnormalities (Turner & Pure gonadal dysgenesis), so pay attention to the similarities and differences!

- other symptoms of **Turner Syndrome**: (that are not seen in Pure gonadal dysgenesis)

I. Short stature
II. Webbed neck
III. Wide chest and the nipple widely separated
IV. Born with an edema in the leg (obstruction of lymphatics)

Androgen insensitivity syndrome (testicular feminization syndrome)

- The patient has **44 + XY** (normal male pattern)
- Yet the external genitalia is that of female, but why?
  - That's because external genitalia is **insensitive** to androgen

- So, the patient do have testes and they are producing androgen → the genitalia is insensitive to it → as if there's no androgen → female genitalia due to estrogen influence
- but the genitalia will also be **infantile**, yet keep in mind that:

- the testes will also produce **MIF** → suppression to paramesonephric duct → no uterus nor uterine tube → only small part of the vagina will develop

- this person will be given estrogen in order to live normally as a female and develops breasts or even he/she might have breast augmentation

notes:

- Since the MIF is produced, the paramesonephric duct system is suppressed and the uterine tube and uterus don't develop → the vagina is short and ends blindly
- The testes are found in the inguinal or labial region, but spermatogenesis does not occur

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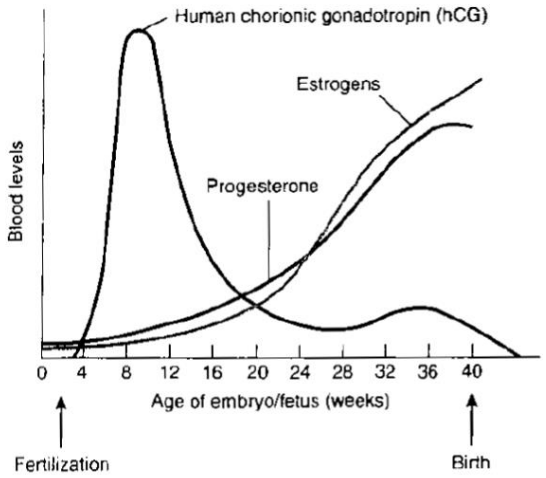
∞ THE PLACENTA

- the placenta produces **hCG**, which replaces the LH (analog)
- keeps the corpus Luteum growing until the third month of pregnancy
- hCG is also used in pregnancy test (by measuring its level), we can know if the female is pregnant as early as the 23rd day of the cycle (even before ending the current cycle)
- hCG is responsible for the **morning sickness** in pregnant women



(b) Blood levels of hormones during pregnancy

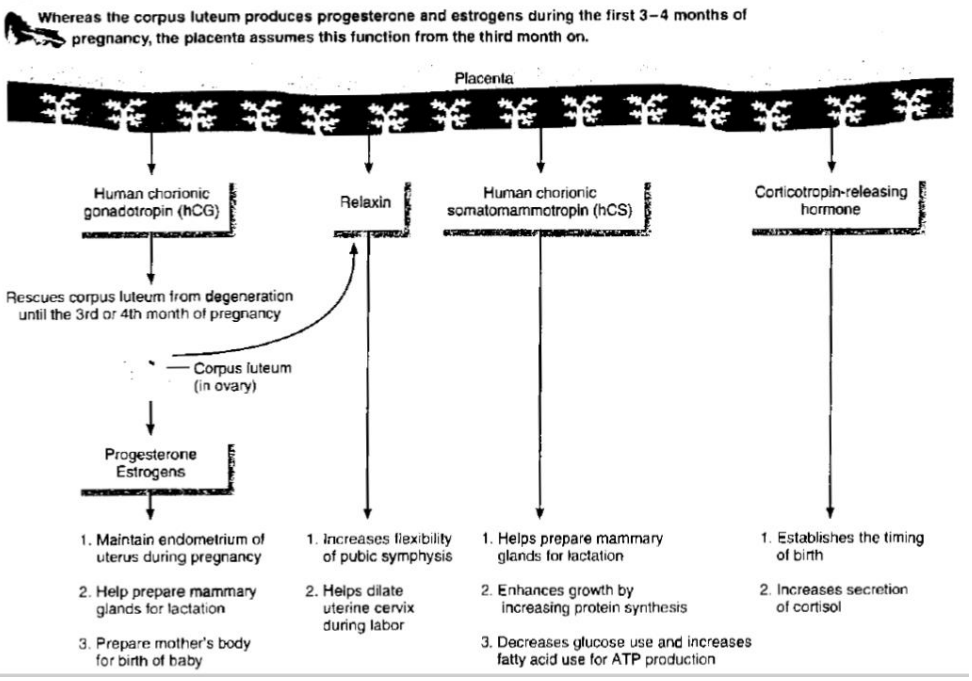
Which hormone is detected by early pregnancy tests?

➢ Hormones secreted from the placenta:

1. **hCG** (human chorionic gonadotropin)
2. **Relaxin**: increases the flexibility of the joints around the pelvic area, and also helps in the dilation of the cervix
3. **human chorionic somatomammotropin**: its function is similar to the Growth Hormone by sparing the glucose and using the fatty acids as the source of energy, increasing the availability of glucose for the fetus.
4. **CRH** (corticotropin releasing hormone): establish timing of birth!

- The **CRH** is normally secreted from the hypothalamus to the pituitary inducing it to secrete ACTH which works on the adrenal cortex to secrete cortisol
- What will the cortisol do to the fetus?
    - it will induce the synthesis of **Surfactant** which critical to the fetus and thus establish timing of birth

- If CRH was high → high cortisol → surfactant is produced rapidly → premature delivery (about 2-3 weeks earlier)
- If CRH was low → low cortisol → surfactant is produced slowly → delayed delivery (more than 40 week)



❖ Placenta previa:

- *The placenta in the beginning of pregnancy is lying low in the uterus above the internal os,*
- It moves up as the pregnancy progresses and attaches to the <u>posterior wall of the uterus</u>
- now if the placenta <u>stayed</u> in the <u>lower uterine segment</u> above the internal os, during the time of delivery the cervix will be dilated gradually, and as it dilates the placenta will have some ruptures and bleeding will occur in the mother (vaginal bleeding)

- if a female came to the hospital or clinic with vaginal bleeding and she was in the 7th month of pregnancy or more, it's mostly likely to be placenta previa

- that was the case in the old days before the **Ultrasound**

  ✓ Nowadays the doctor can easily see that the placenta is in the lower uterine segment during the first weeks of pregnancy (using Ultrasound)
  ✓ Also, the doctor should be aware not to perform **PV** (per vagina), if placenta previa was suspected

  ✓ medical intervention for the Placenta previa is **C-section**

Le Fin.

This is really the end of Dr. Faraj Legacy

It is really sad to realize that our mentor has left us to face the clinical life all alone

Thanks a lot Dr. Faraj Bustami

You will always be remembered

And I'm honored to be one of & that last person to write sheets after you

Good luck to you all ♡

Done by: *Omar Saffar*

Thank you Abdullah Sulaiman
for being a true friend