L3

Development of the male Reproductive system

MED 443
King Saud University

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Embryology
Team 443
Reproductive

Objectives

- List the causes of differentiation of genitalia into the male type.
- Describe the origin of each part of the male internal & external genitalia.
- List the causes & describe the events of descent of testis.
- List the common anomalies of male genital system & describe the causes of each of them.

This lecture was presented by : DR.Ahmed Fathallah & DR.Sanaa Al Shaarawi

Editing File

Color index :
Main text (black)
Female Slides (Pink)
Male Slides (Blue)
Important (Red)
Dr's note (Green)
Extra Info (Grey)

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Overview by Lama Alotaibi

IMPORTANT

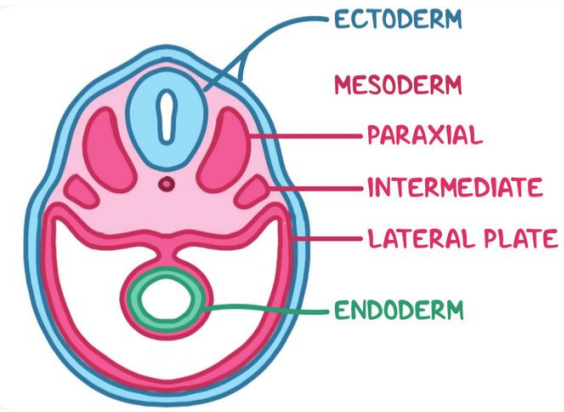
Extra

The alien from pathology took a trip to embryology to tell you a story

Step 1

Embryo Has 3 Layers

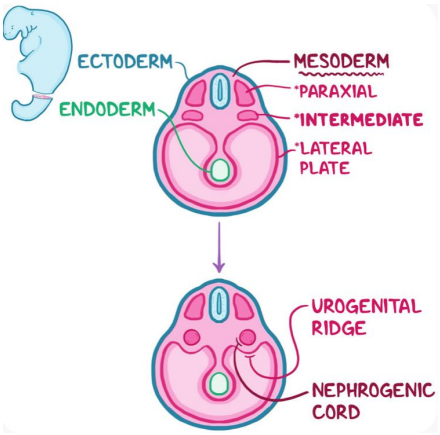
- Ectoderm
- Mesoderm
  - Paraxial
  - Intermediate
  - Lateral plate
- Endoderm



Step 2

A. Intermediate mesoderm form urogenital ridge
B. Urogenital Ridge Become nephrogenic cord
C. Nephrogenic cord gives gonadal ridge
D. Gonadal Ridge gives gonads

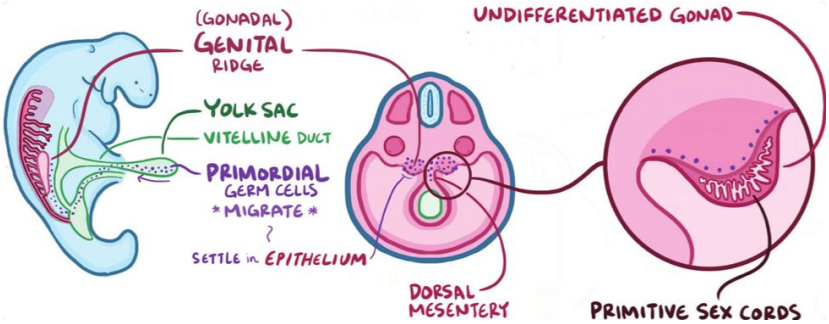
Week 5



Step 3

Gonads Development Start at yolk sac :
Primordial germ cells migrate to gonads
Note : primordial germ cell form at yolk sac in W4 & migrate in W5

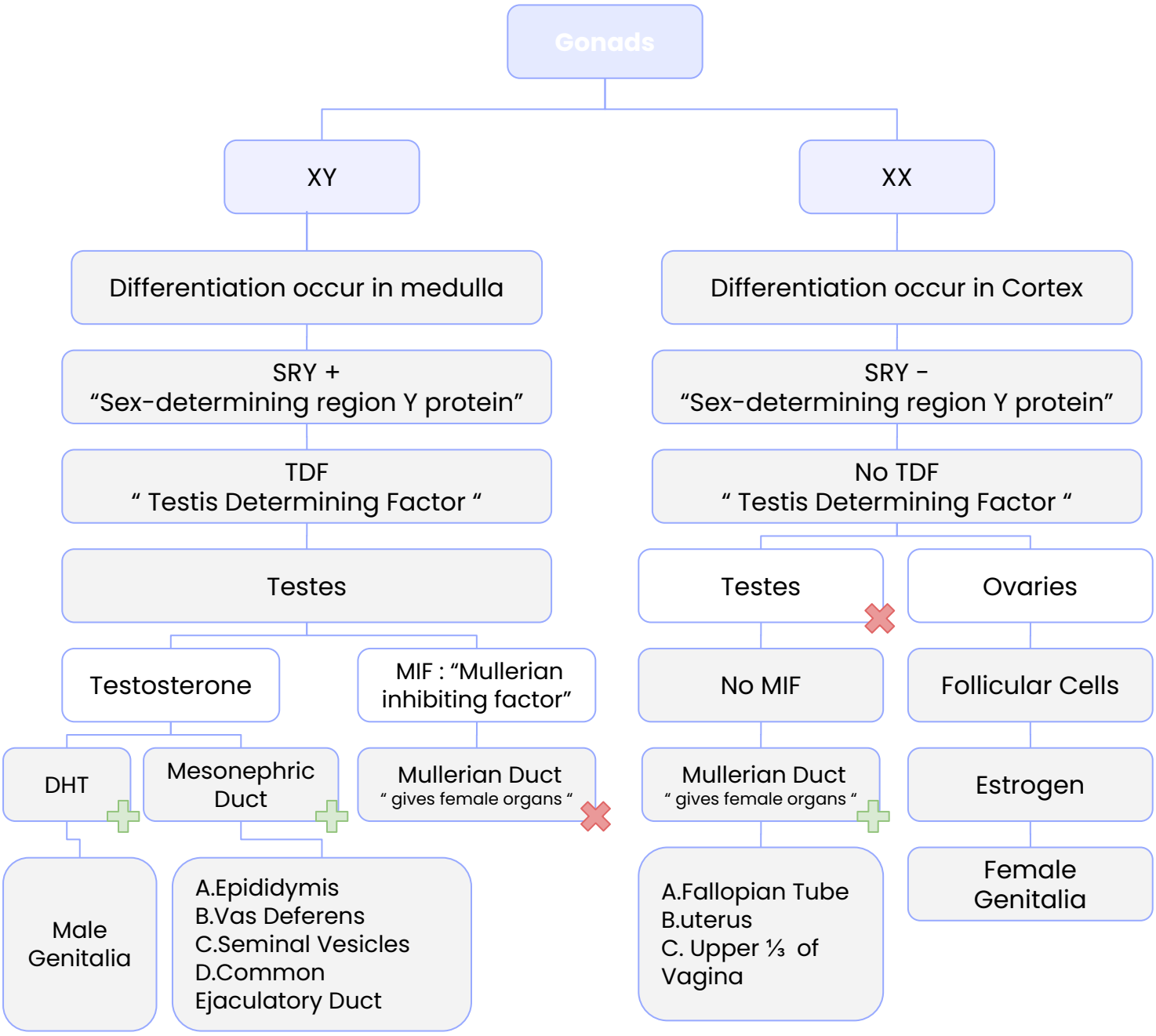
Week 5



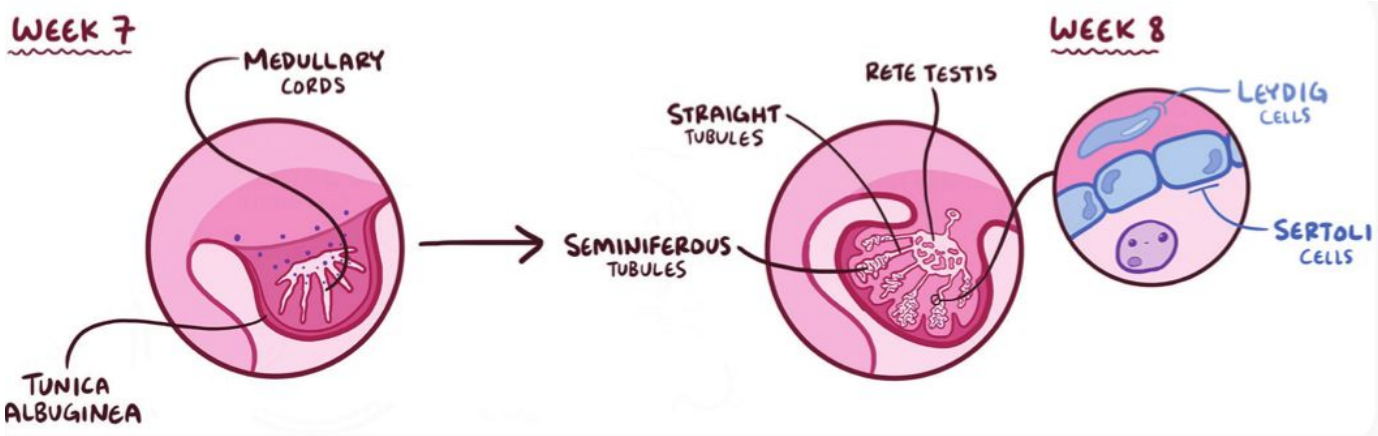
Step 4

Sex chromosomes express genes determine gonadal differentiation

Overview


Gonads
XY
XX
Differentiation occur in medulla
Differentiation occur in Cortex
SRY +
"Sex-determining region Y protein"
SRY -
"Sex-determining region Y protein"
TDF
" Testis Determining Factor "
No TDF
" Testis Determining Factor "
Testes
Testes
Ovaries
Testosterone
MIF : "Mullerian inhibiting factor"
No MIF
Follicular Cells
DHT
Mesonephric Duct
Mullerian Duct
" gives female organs "
Mullerian Duct
" gives female organs "
Estrogen
Male Genitalia
A.Epididymis
B.Vas Deferens
C.Seminal Vesicles
D.Common Ejaculatory Duct
A.Fallopian Tube
B.uterus
C. Upper ⅓ of Vagina
Female Genitalia

Step 5



A. Embryo genetically male → gene expression in Sex-determining Region in Y chromosome (SRY) promoted
B. SRY-region genes promote testis- determining factor production → testis-determining factor acts on undifferentiated gonads → gonadal transformation into testes
C. Gonadal ridge becomes seminiferous tubules, rete testis, straight tubules
D. The testes contain :

- germ cells that will produce spermatogonia (endodermal)
- Sertoli cells that was derived from surface epithelium of testis (mesothelial)
- Leydig cells : From mesenchyme surrounding the tubules (W8)

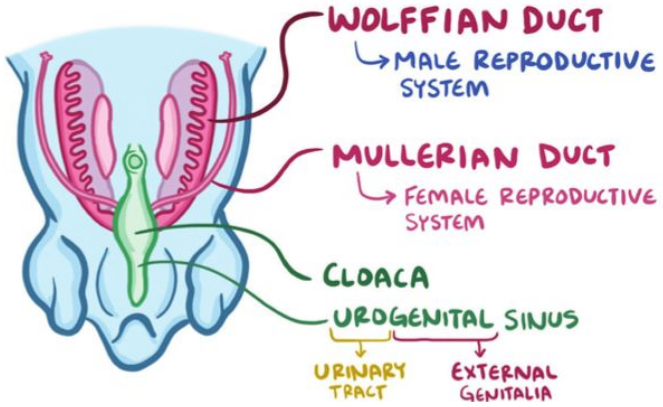
1. In Female : cortex gives ovaries & medulla regress
2. In males : medulla gives Testes & cortex regress

Remember **M**edulla = **M**ale

Week 7

Step 6

A.Sertoli cells: synthesize, secrete anti- Müllerian hormone; AKA Müllerian inhibiting substance :
Promotes Müllerian/paramesonephric duct atrophy
(Remember that Müllerian duct was the one to give female system : uterus, fallopians tubes , vagina)
B.Leydig cells: synthesize, secrete testosterone → become internal male genitalia
Promote Wolffian / mesonephric duct growth & differentiation



Week 7

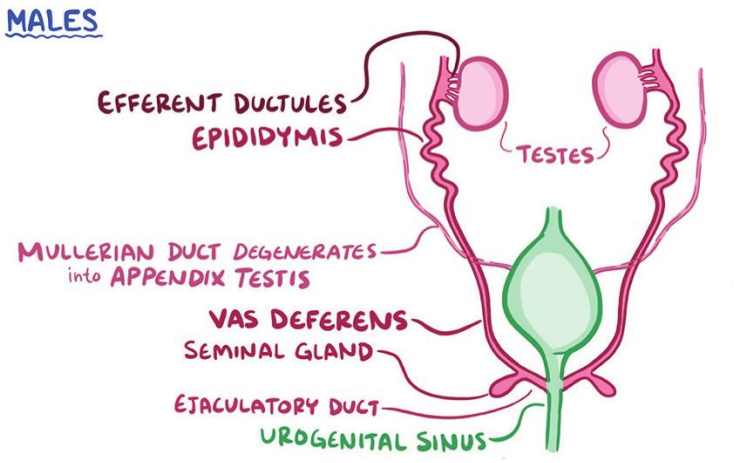
Extra

Step 7

A.wolffian duct (mesonephric duct)
Gives :

- Epididymis
- vas deferens
- seminal gland
- ejaculatory duct

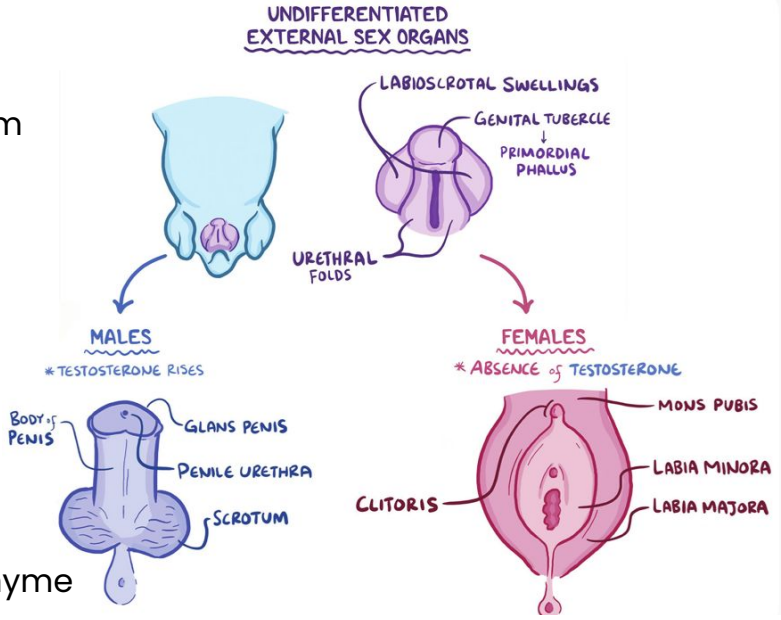
Remember Wolffian (mesonephric) duct gives male system not the Müllerian duct (paramesonephric) How ?
Wolffian = wolf = ذِيبان !



Week 7

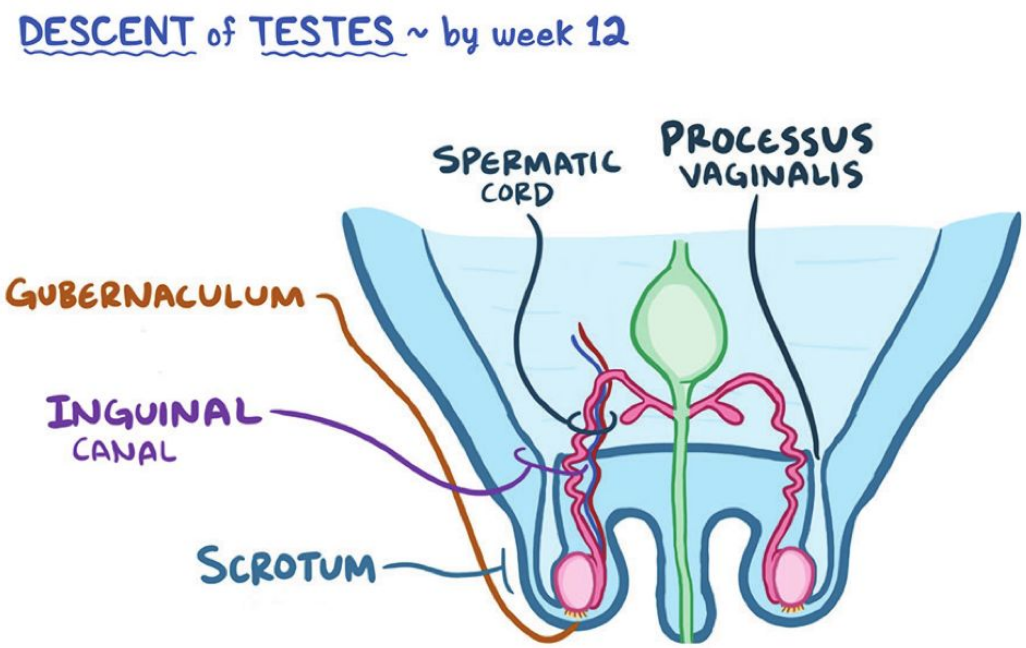
Step 8

A.Male external genitalia differentiation from urogenital sinus depends on testosterone presence
-5 alpha reductase in target tissues converts testosterone more potent dihydrotestosterone
-Dihydrotestosterone: responsible for masculinizing external genitalia
B. Differentiation as :
■Urethral folds → urethra (both)
■ urogenital folds →
Labioscrotal swellings → scrotum
■ Genital tubercle Produced from mesenchyme at the cranial end of cloacal membrane → elongates to form a
primordial phallus → penis



Begin at Week 9 end at 12

Step 9



Phase 1 (Internal) : 12th W
Descent of testis from posterior abdominal wall to deep inguinal ring.
Because of resulting from elongation of cranial part of abdomen away from its caudal part
Phase 2 (External) : 7th month and takes 2 to 3 days
Descent of testis from deep inguinal ring, to scrotum.
Guided by gubernaculum & Facilitated by processus vaginalis.
Controlled by androgens thus lack of androgens during fetal life causes Cryptorchidism

Development of gonads

Male genital system is made of :

Gonad: Testis.
Genital Duct: Epididymis, Vas deferens and Urethra.
Genital glands: Seminal vesicle , Prostate and Bulbourethral glands.

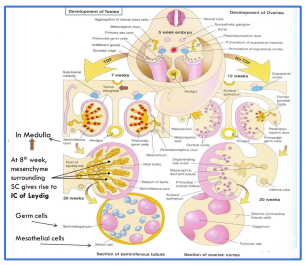
Development of Gonads:

During **5th week**: gonadal development occurs. IMPORTANT

Until 7th week gonads are similar in both sexes and called **indifferent gonads .** (Neither male or female)

Gonads are derived from 3 sources:
1)Primordial germ cells
2)underlying mesenchyme
3)Mesothelium(mesodermal epithelium lining the coelomic cavity)

كيس mesothelium من برا ، و mesenchyme من جوا
primordial germ cells are from the yolk sac (endodermal in origin)



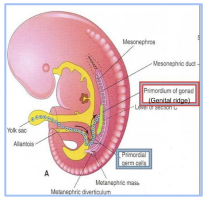
Indifferent Gonads

IMPORTANT

Gonadal ridges

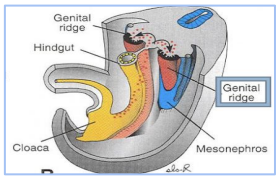
A bulge on the medial side of mesonephros produced by

- Proliferation of mesothelium (cortex)
- Proliferation of mesenchyme (medulla)



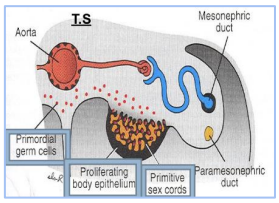
Gonadal (primary sex) cords

The proliferating mesothelial cells fuse and penetrate the underlying mesenchyme the medulla to form primitive sex cords.



Primordial germ cells

Endodermal cells of the yolk sac migrate along dorsal mesentery of hind gut to gonadal ridges and become incorporated into gonadal cords.



gonadal cords is made up of mesothelium proliferation (the layer in black)

Development of Testis

At Fertilization — the **Y** chromosome has a **testis-determining factor** (TDF) that differentiates primitive gonad into testis.

At 7th week :

regression of cortex and differentiation of medulla (of primitive gonads) into **testis**. "Medulla the important part in males because it gives rise to the testis"

Gonadal cords condense and extend into all the **medulla** (medullary cords) to form **seminiferous cords.** later it'll become seminiferous tubules .

IMPORTANT

The characteristic feature is the development of a thick **fibrous capsule** (**tunica albuginea**) that separate the enlarging testis mesonephros .

seminiferous cords develop into -> seminiferous tubules. seminiferous tubules remain **solid** until puberty and its walls are composed of :

A. Sertoli cells -> derived from surface epithelium of testis (mesothelial cells)

B. Spermatogonia -> derived from primordial germ cells (endodermal in origin)

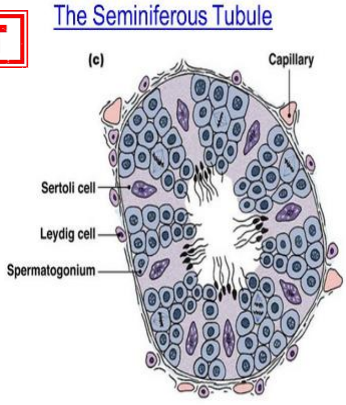
At 8th week:

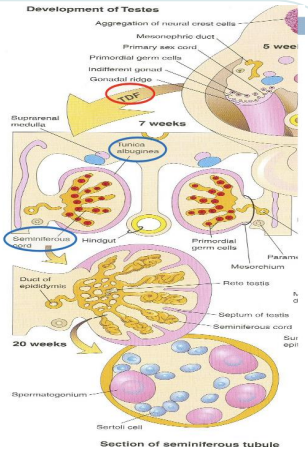
Mesenchyme

Which is surrounding seminiferous cords mesothelial cells will give rise to **interstitial cells (of leydig)** secreting testosterone.

IMPORTANT

"So now we have 3 kinds of cells : 1) Spermatogonium 2)Sertoli cells 3)Leydig cells"





Development of internal genitalia

VERY IMPORTANT

1. Leydig cells

Secretes

Testosterone (8th week)

IMPORTANT Function:

1. Masculine differentiation of **mesonephric duct**(Wolffian ducts): epididymis, vas deferens, seminal glands, ejaculatory duct.

3 ducts, 1 gland

2. Masculine differentiation of external genitalia

"In female the mesonephric duct will turn into ureter only"

2. Sertoli cells

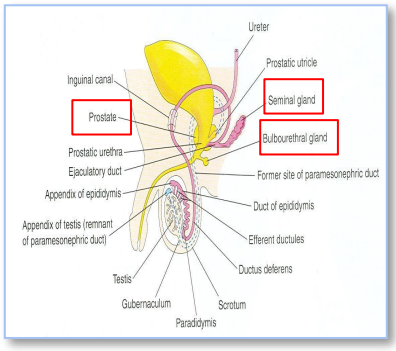
Secretes

Müllerian inhibiting substance (Anti-Müllerian hormone) (7th week)

Function:

-Suppression of development of paramesonephric (Müllerian) duct

-"Paramesonephric duct is the main duct in female that give rise to their reproductive organs, that's why it needs to be suppressed"

Glands	Origin	
1-Seminal	Mesodermal outgrowth from mesonephric duct	
2-Prostate	Endodermal outgrowth from prostatic urethra.	
3-Bulbourethral	Endodermal outgrowth from spongy(penile) urethra	
Stroma & smooth muscles in 2 & 3 are derived from surrounding mesenchyme		

Summary of Development of male genitalia

male slides

Testis

1. Regression of cortex +differentiation of medulla
2. Gonadal cords extend to medulla → form medullary (seminiferous) cords
3. Appearance of Tunica Albuginea

- Seminiferous cords give rise → Seminiferous tubules
  - Germ cells →Spermatogonia
  - Mesothelial cells →Sertoli cells
- Mesenchyme surrounding tubules gives rise → Interstitial cells of Leydig

Internal Genitalia

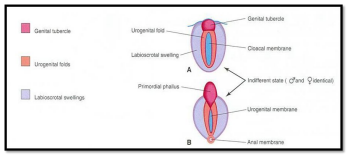
	Structure	Origin
Mesodermal structure	Testis	From medulla of genital ridge
	Seminiferous tubules	From medullary cords of ridge
	Sertoli cells	From mesothelial cells of ridge
	Leydig cells	From mesenchyme surrounding the tubules
	Epididymis, vas deferens, seminal glands, ejaculatory duct	From mesonephric duct
Endodermal structure	Spermotogonia:	from primordial germ cells of yolk sac
	Prostate gland	from prostatic urethra
	Bulbourethral gland	from spongy urethra

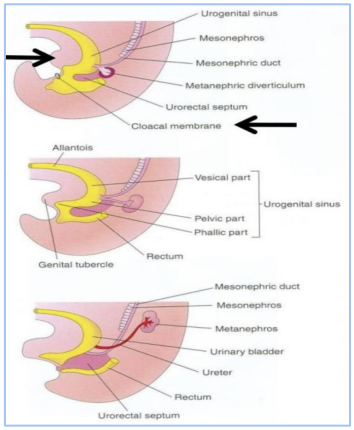
Development of External Genitalia

(from **4th to 7th** week)

IMPORTANT **Indifferent Stage**

Genital tubercle	Produced from mesenchyme at the cranial end of cloacal membrane. It elongates to form a **primordial phallus.** which will later form the penis.
Urogenital folds	Develop on each side of cloacal membrane.
Labioscrotal swellings	Develop on each side of urogenital folds.which will later form the scrotum.
Note	"The yellow tube is the hind gut , its last part enlarge and gives us CLOACA, then the cloaca will close, and gets separated from the middle by URORECTAL SEPTUM. the urorectal septum divides the cloaca into two parts , ventral and dorsal parts. the dorsal part will give rise to the anorectal canal, and the ventral part will give rise to urogenital sinus (which contains urinary bladder and urethra). Just above the cloaca, a small protrusion will happen which is called Genital tubercle."

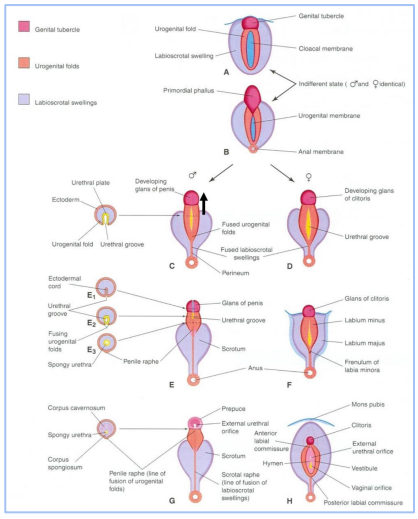




(Begins at **9th** week)

IMPORTANT **Different Stage**

Stimulated by:	**testosterone** secreted by leydig cells.
Complete differentiation	**at 12th week**: 1. The **phallus** enlarges to form the glans **penis** & pulls forward the urogenital folds. 2.The urogenital folds fuse to enclose the **spongy** (penile) **urethra** & form the shaft of the penis. 3. The **labioscrotal folds** (swellings) fuse to form the **scrotum**.



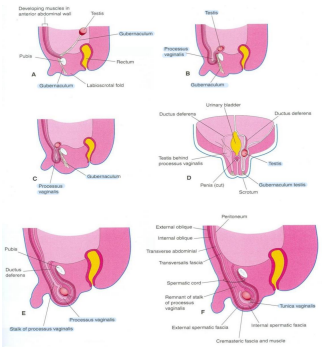
Descent of Testis

The testes are initially located on the posterior abdominal wall, to descend it needs 3 things:

Gubernaculum: a mesenchymal band extending from inferior pole of gonad to labioscrotal fold. a fibrous cord that connects the fetal testis with the bottom of the scrotum and by failing to elongate in proportion to the rest of the fetus causes the descent of the testis.

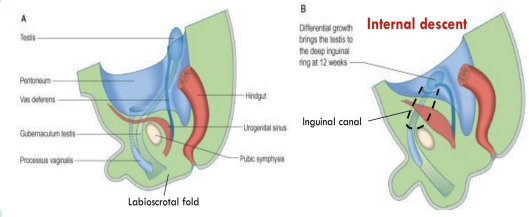
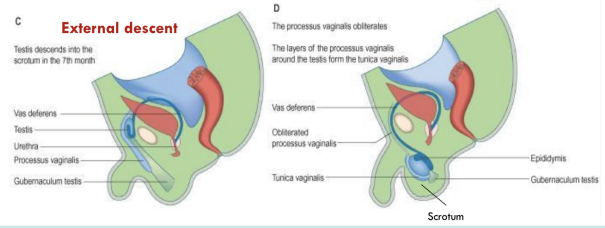
Inguinal canal: a pathway formed by gubernaculum passing through layers of anterior abdominal wall.

Processus vaginalis: a peritoneal fold passing through inguinal canal before testis, to facilitate its descent.(it's very smooth)



Descent of testis occurs in 2 steps:

IMPORTANT

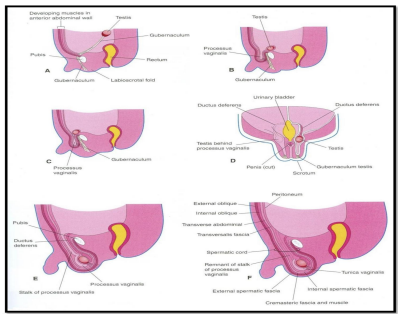
Types	1. Internal	2. External
Definition	Descent of testis from posterior abdominal wall to deep inguinal ring.	Descent of testis from deep inguinal ring, through inguinal canal, to scrotum.
Time	During **12th week**	Begins in 7th month and takes **2 to 3 days**
Causes	A relative movement (حركة نسبية)resulting from elongation of cranial part of abdomen away from its caudal part (future pelvic cavity). no hormones or anything.	1. Controlled by androgens. (Testosterone) 2. Guided by **gubernaculum.** 3. Facilitated by **processus vaginalis.** after descending processus vaginalis form Tunica vaginalis. 4. Helped by increased intra-abdominal pressure resulting from growth of abdominal viscera.
Pictures		

External Descent of Testis

1. More than 97% of full-term newborn males have both testes in scrotum.
2. During first **3** months after birth, most undescended testes descend into scrotum.
3. No spontaneous descent occurs after the age of 1 year.

Complete descent of testis is associated by:

1. Degeneration of gubernaculum.
   "To prevent herniation"
2. Obliteration of stalk of processus vaginalis.
   Obliteration=total destruction, gets fibrosed
3. Persistence of part of processus vaginalis surrounding the testis in the scrotum to form **"tunica vaginalis"**

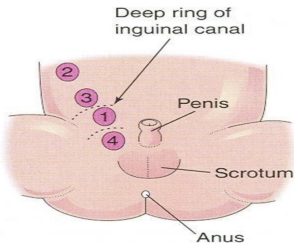
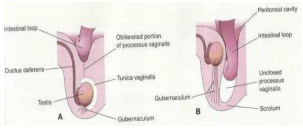
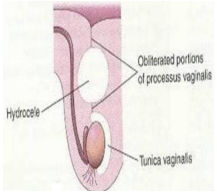
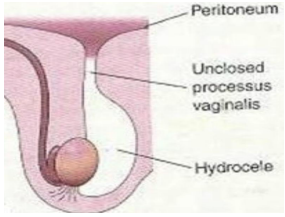


Dates to Remember:

male slides

At 5th week	Appearance of gonads.
At 7th week	Beginning of differentiation of gonads into testes, suppression of paramesonephric (Müllerian) ducts.
At 8th week	Leydig's cells secretes testosterone.
At 9th week	Beginning of differentiation of male external genitalia.
At 12th week	Completion of differentiation of male external genitalia, internal descent of testis.
At 7th month	External descent of testis.
At puberty	Canalization of seminiferous tubules.

Congenital Deformities

IMPORTANT **Cryptorchidism (Undescended testis)**	• Incidence: is up to 30% of premature & 3-4% of full term males. **Most common congenital anomaly of the male reproductive system.** • Cause: **deficiency of androgens.** testosterone • Common sites: look at the figure. Dr. Sanaa verbally mentioned **DEEP INGUINAL RING.** • Complications: 1. Sterility, if bilateral. العقم 2. Testicular cancer (20-44%).	
Congenital inguinal hernia Check this video for better understanding	Definition: Herniation of a loop of intestine through a non-obliterated processus vaginalis. A: incomplete B: complete (in scrotum) Cause: The processus vaginalis does not obliterate & remains in open communication with the peritoneal cavity.	
Hydrocele of spermatic cord	Accumulation of fluid in spermatic cord due to a non-obliterated **portion of stalk** of processus vaginalis.	
IMPORTANT **Hydrocele of testis**	Accumulation of fluid in tunica vaginalis (in scrotum surrounding the testis) due to non-obliteration of the **whole** stalk of Processus vaginalis.	

MCQ

1

Which one of the following structure is a derivative of male urethra? -Male dr

A Seminal gland

B Prostate gland

C Vas deferens

D Ejaculatory duct

2

Which one of the following cells are responsible for masculine differentiation of external genitalia?-Male dr

A Sertoli cells

B Leydig's cells

C Mesothelial cells

D Primordial germ cells

3

At which one of the following age periods gonads begin to differentiate into testes?-Male dr

A At 5th week.

B At 7th week.

C At 8th week.

D At 9th week.

4

The gubernaculum is a fibrous cord that helps in the descent of the testes. It is derived from which embryonic structure?

A paramesonephric duct

B urogenital sinus

C mesonephric duct

D ectoderm

5

The vas deferens is derived from which embryonic structure?

A urogenital sinus

B ectoderm

C paramesonephric duct

D mesonephric duct

Answer key : 1-B 2-B 3- B 4- C 5- D

MCQ

1

interstitial cells (of Leydig) secreting testosterone. happen...? -Female dr

A During 5th week

C During 6th week

B At 7th week

D By 8th week

2

Deficiency of androgens cause? - Female dr

A Inguinal hernia

C Cryptorchidism

B Hydrocele of spermatic cord

D Hydrocele Of Testis

3

Accumulation of fluid in tunica vaginalis cause: -Female dr

A Inguinal hernia

C Cryptorchidism

B Hydrocele of spermatic cord

D Hydrocele Of Testis

4

Complete descent of testis is associated by: -Female dr

A Formation of gubernaculum

C Obliteration of stalk of processus vaginalis

B Degradation of tunica vaginalis

D All of above

5

At which of the following does full differentiation of male external genitalia occur?

A 5th week

C 9th week

B 7th week

D 12th week

Answer key : 1-D 2-C 3-D 4-C 5-D

Embryology Team

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زياد العتيبي

لمى العتيبي

فيصل الشويعر

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