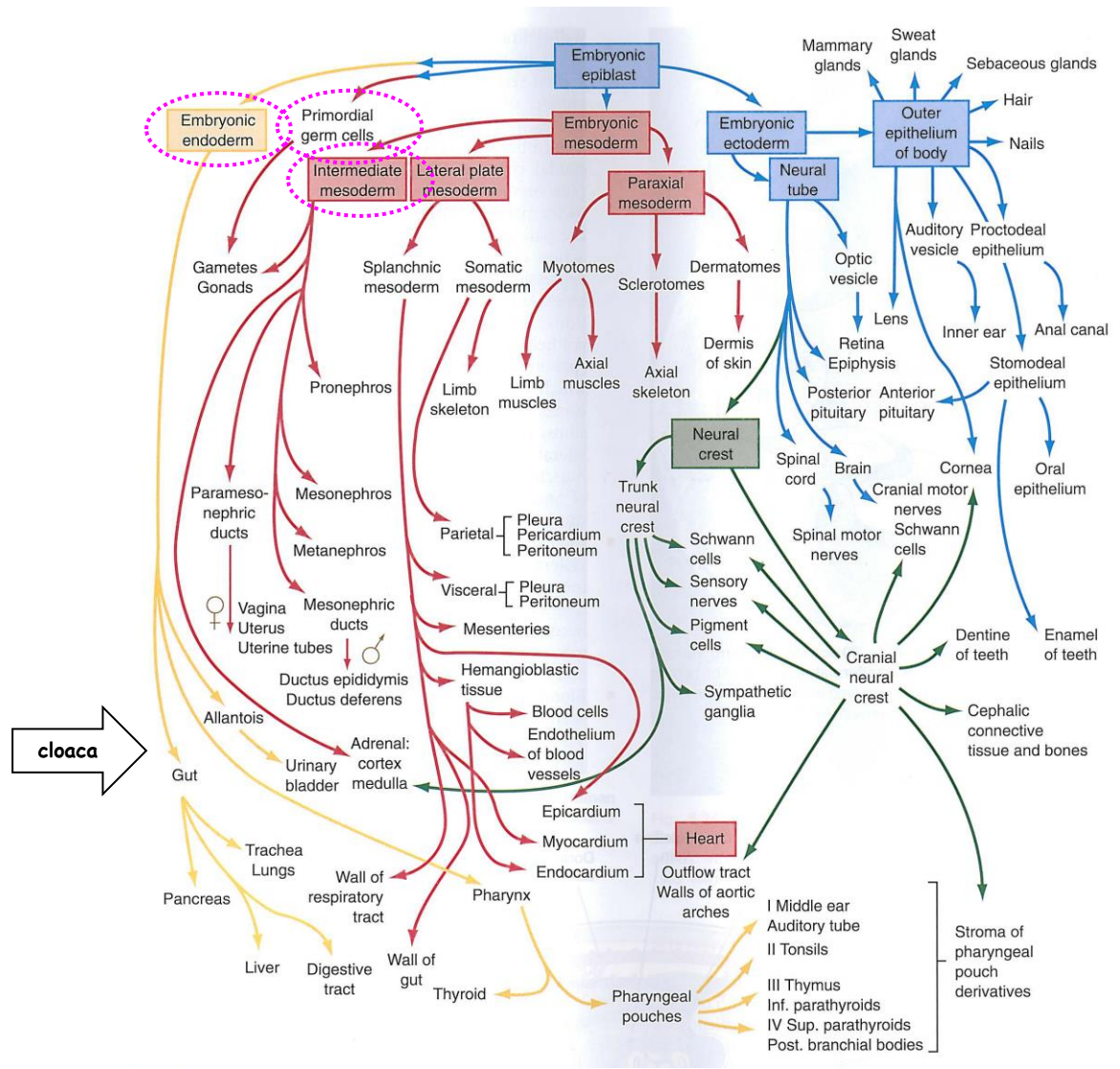


Development of Urinary and Reproductive Systems

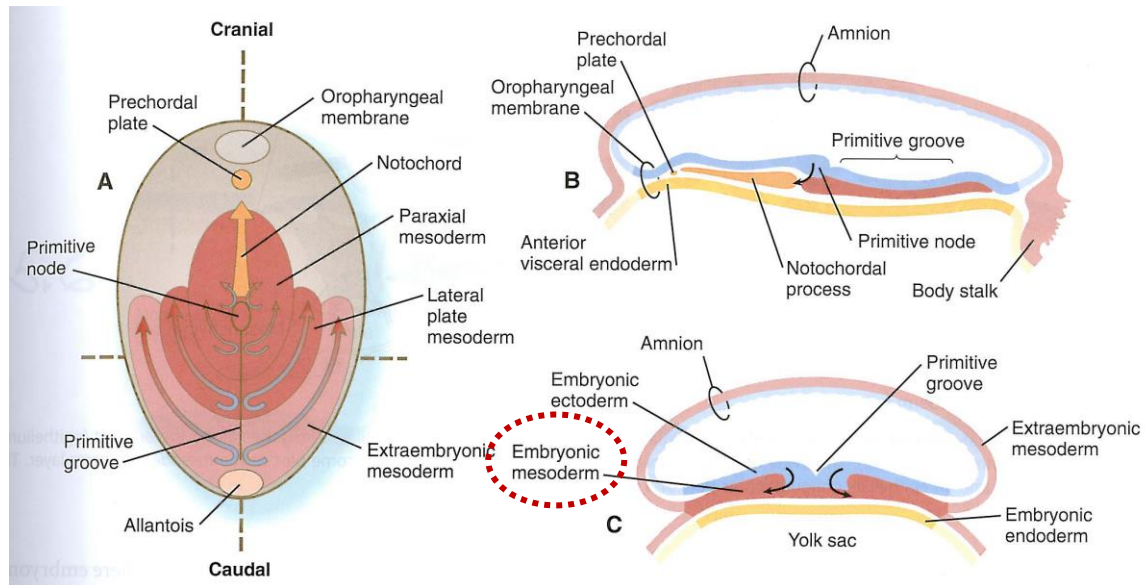
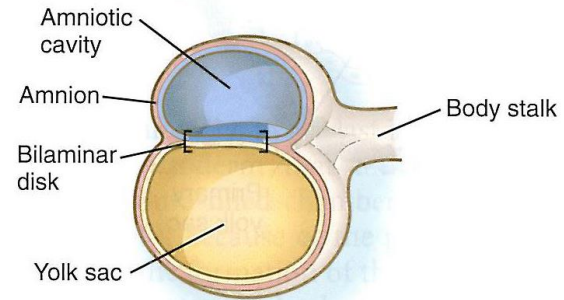
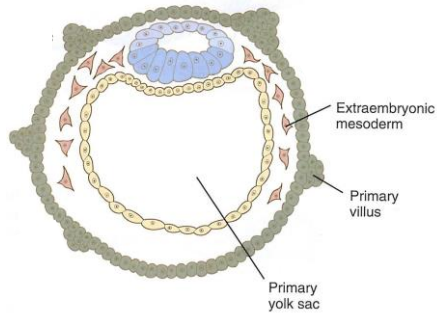
Aleš Hampl

November 2024

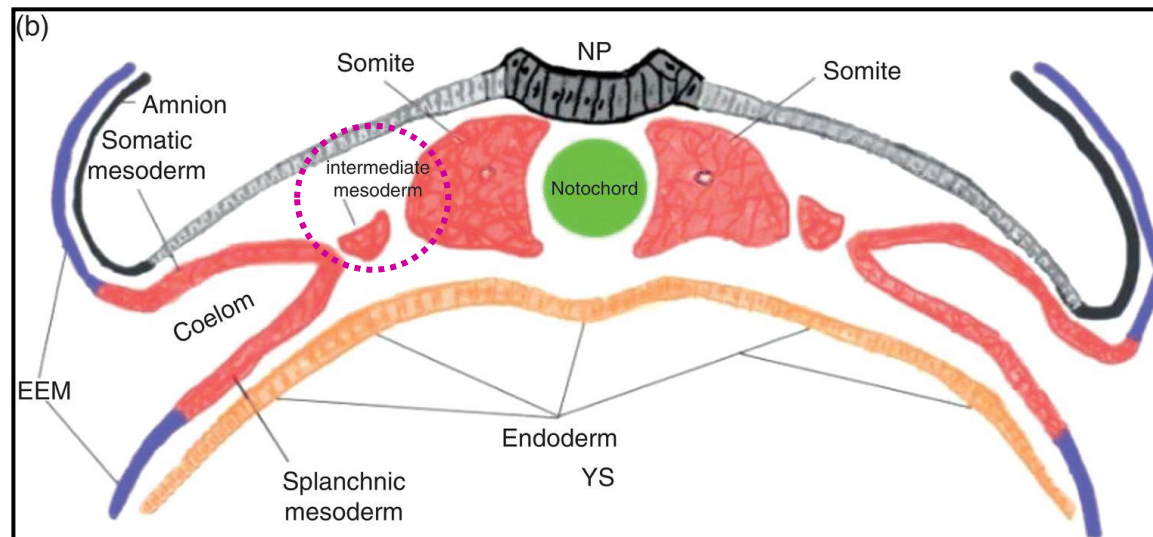
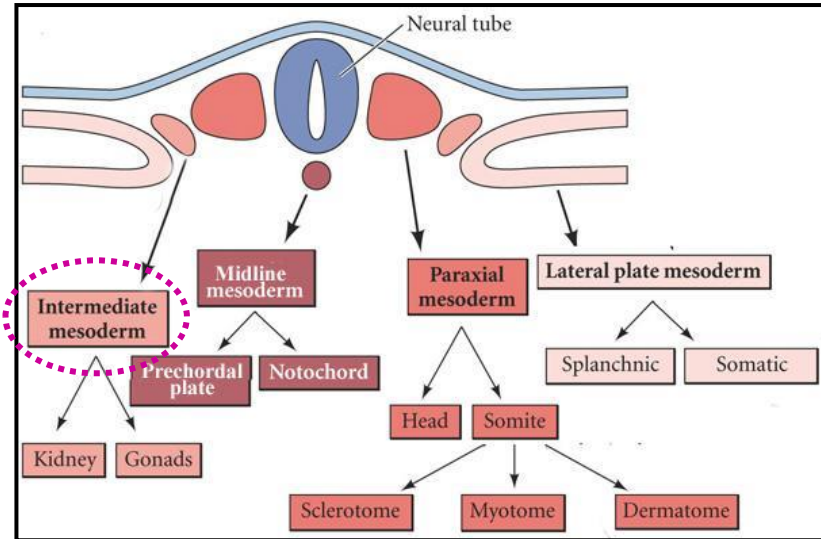
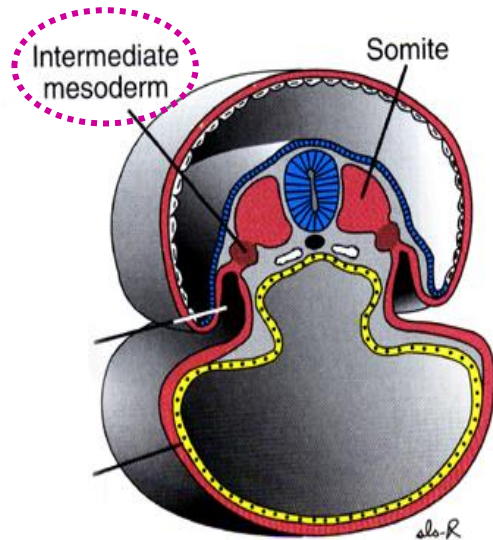
Urogenital system - Overall picture



Urogenital system - Reminder



Urogenital system - Intermediate mesoderm

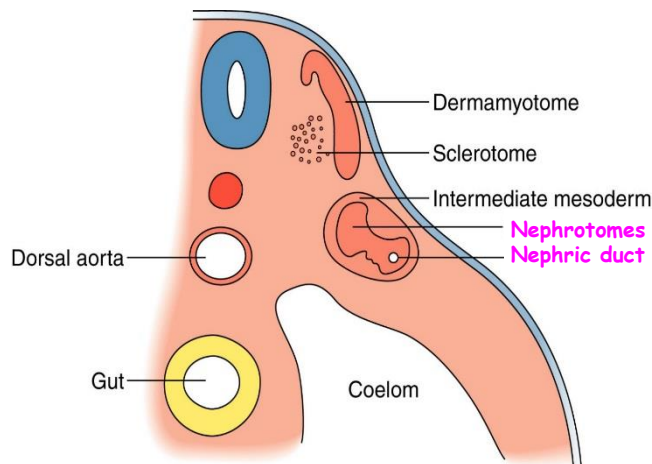


Urogenital system - Early forms of kidneys - Pronephros

Recapitulation of three stages of evolution of kidneys in a cranial to caudal sequence:

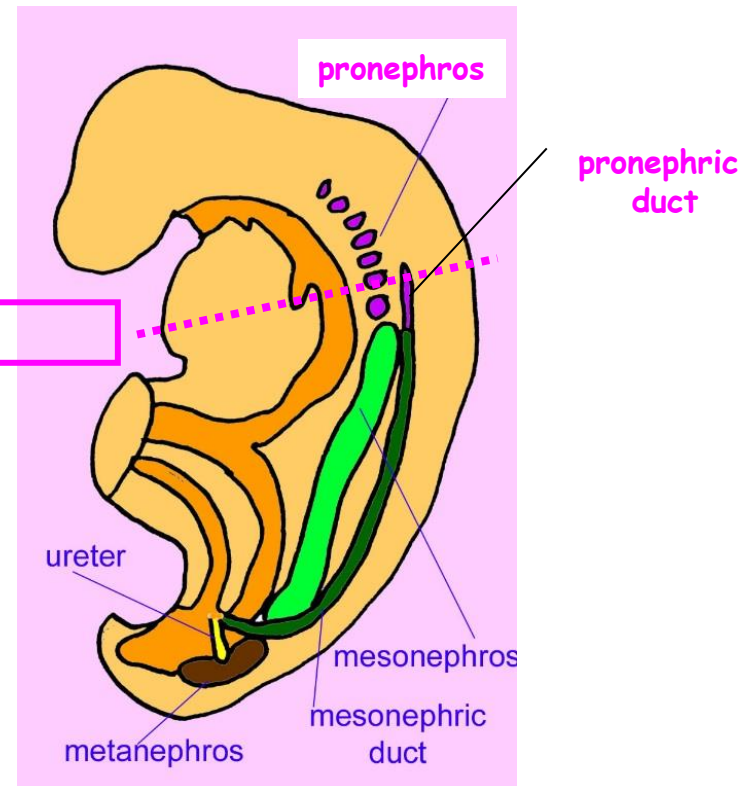
- Nephrogenic cord
- Genital ridge

- pronephros
- mesonephros
- metanephros

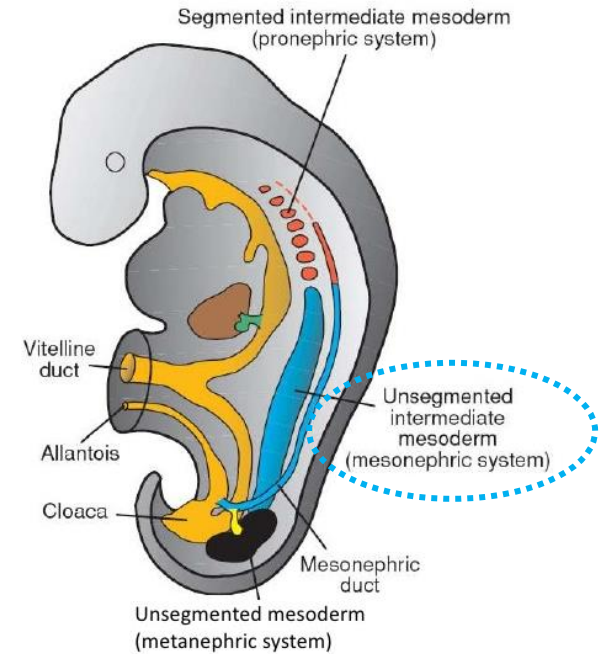
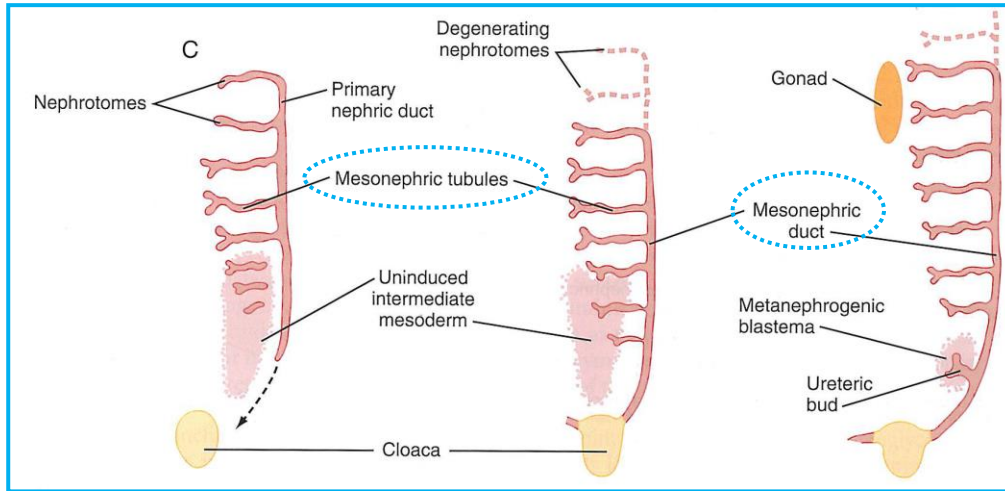


Nephrotomes

- at about day 22 in cervical part of nephrogenic cord
- 7 to 10 groups of epithelial cells
- connect to pronephric duct
- non-functional
- disappear by day 28

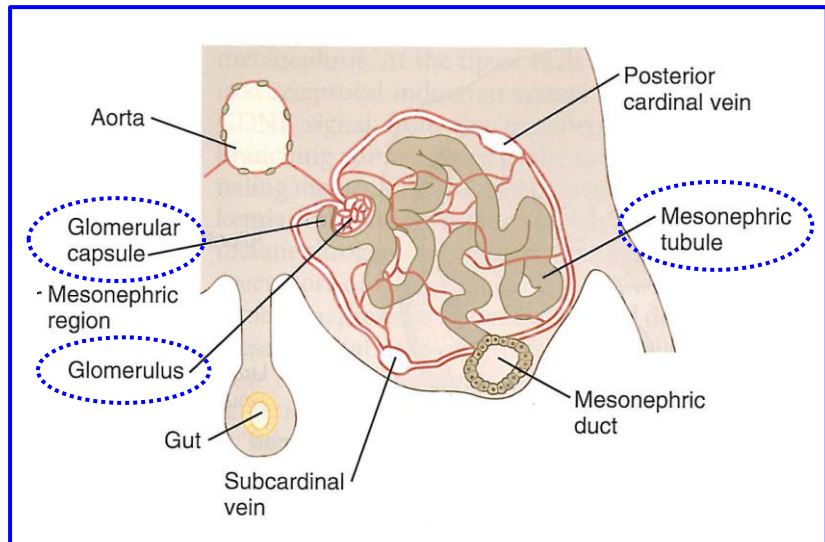


Urogenital system - Early forms of kidneys - Mesonephros

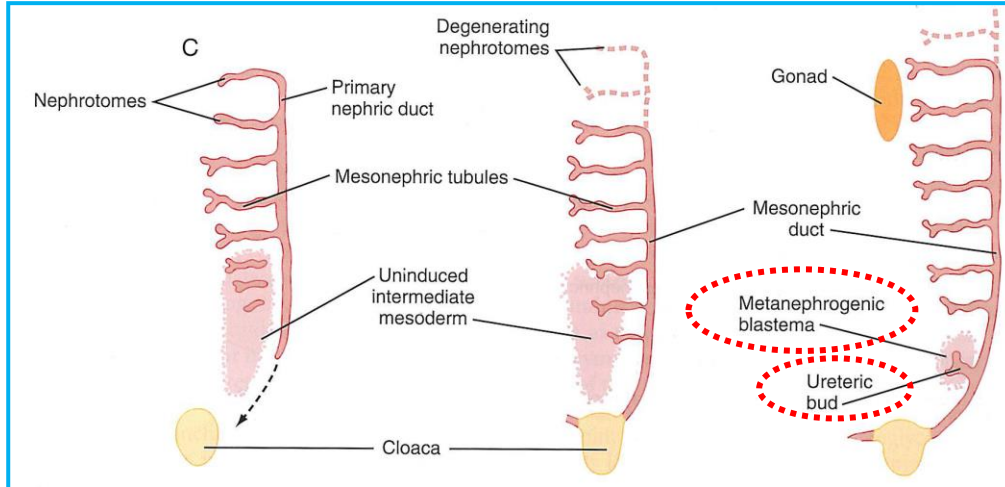


Mesonephros

- caudal continuation of nephrogenic cord
- thoracolumbar region
- unsegmented intermediate mesoderm
- mesonephric ducts (paired) - Wolffian ducts
- mesonephric tubuli - open individually into m. duct
- 36 to 40 m. tubuli in total (on one side)
- some filtration - **mesonephric unit** →
- mesonephros is most prominent when metanephros start to shape - **active since week 6 til week 10**
- then they disappear fast
- mesonephric ducts persist in males



Urogenital system - Definitive kidneys - Metanephros



Develop since week 5

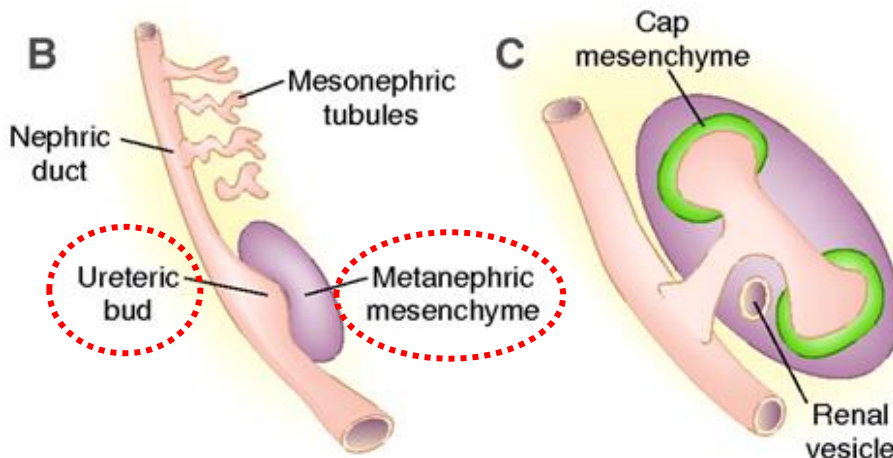
Ureteric bud = metanephric diverticulum

+

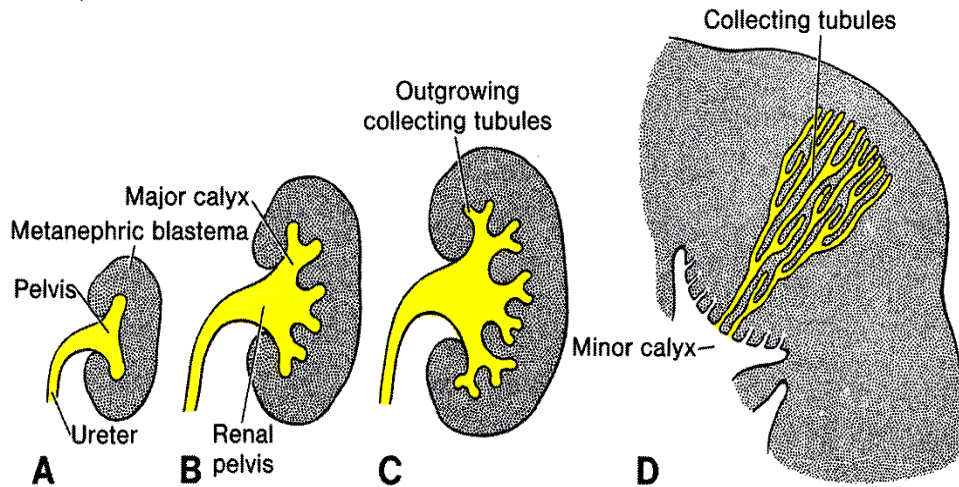
Metanephrogenic blastema
(mesenchyme)

Branching
and
Elongation

14 to 15 x



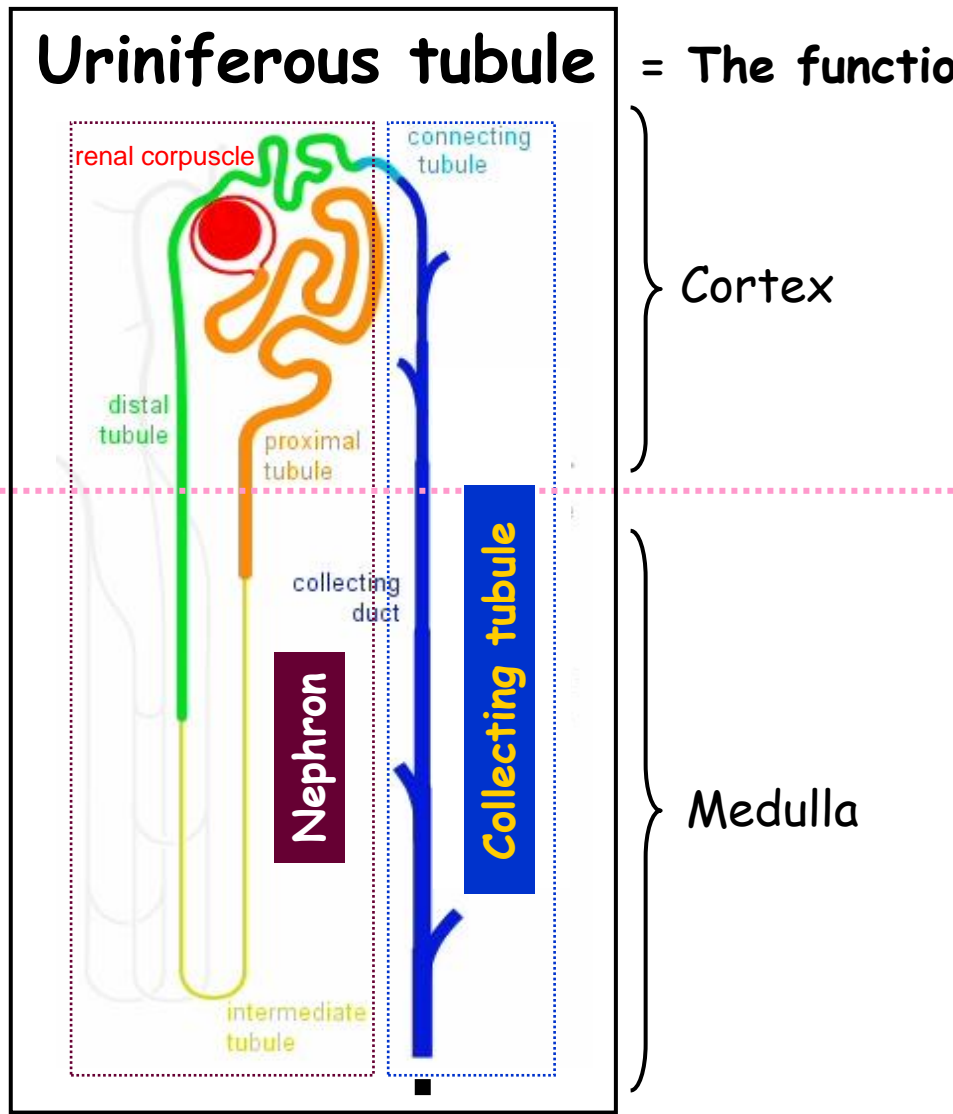
Urogenital system - Definitive kidneys - Metanephros



Repeated branching of ureteric bud produces:

- ureter
- pelvis
- calyces (major + minor)
- collecting tubuli (1 to 3 millions)

Urineriferous tubule = The functional unit of the kidney



Cortex

Medulla

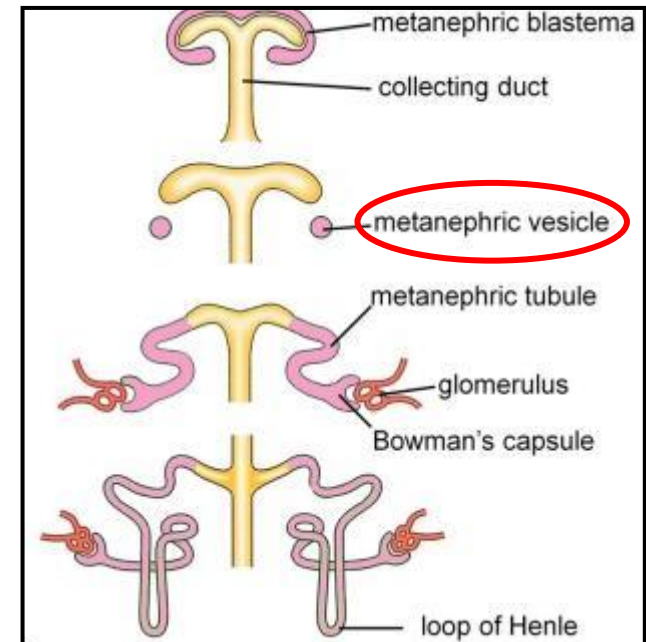
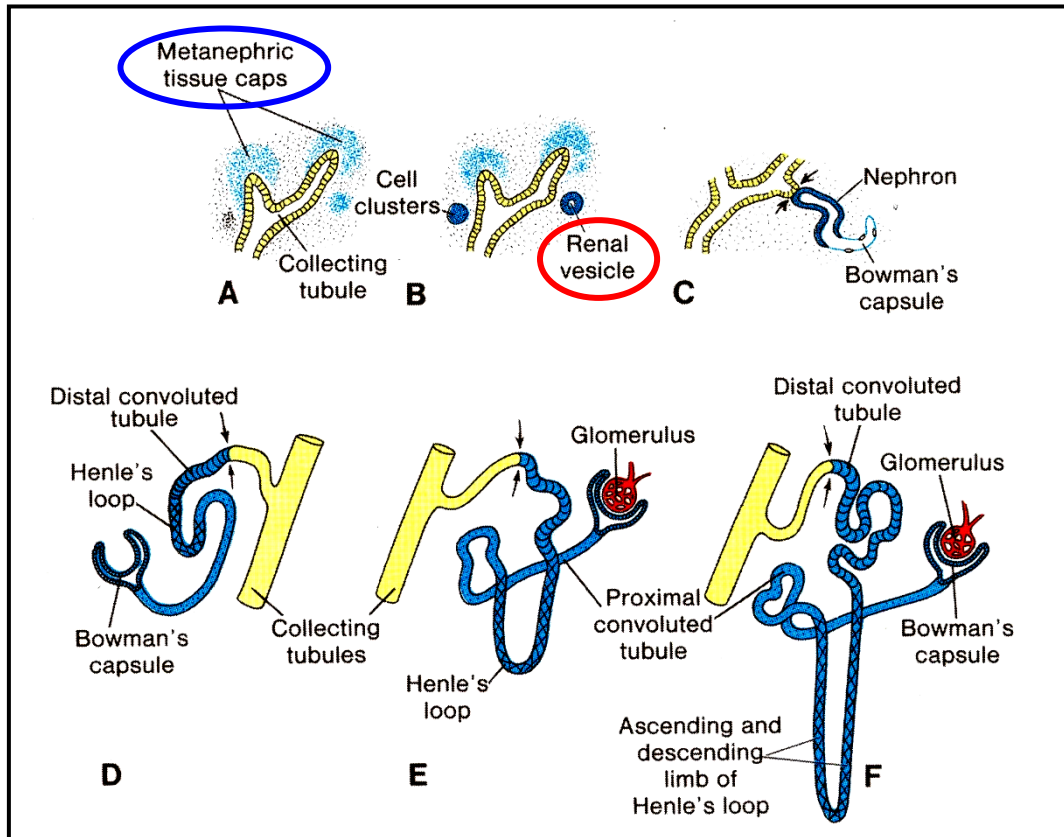
Ducts of Bellini

1 to 1.4 millions
of nephrons
in one kidney

Area cribrosa
Minor calyx

Nephrons X Collecting tubules
Different embryological origin

Urogenital system - Metanephros - Nephrons



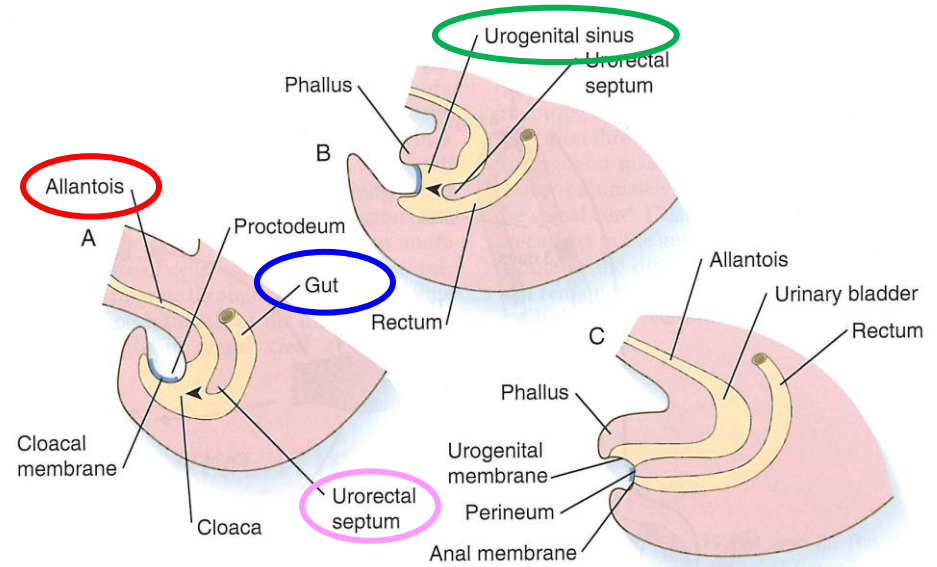
- arched ampulous endings of ureteric ducts (collecting tubuli) - **capping** by condensed mesenchyme
- part of the cap cells differentiate into **nephrogenic vesicle**
- vesicles elongate
- vesicles open to the collecting tubulus on one end
- distal from the ducts, the cells of elongating vesicles polarize and form **lumen and basal lamina**
- precursors of endothelia grow into this area - **glomerulus**
- endothelia connect to branches of dorsal aorta - **glomerular circulation**
- production of urine since week 10

Urinary system - Bladder

Cloaca

=

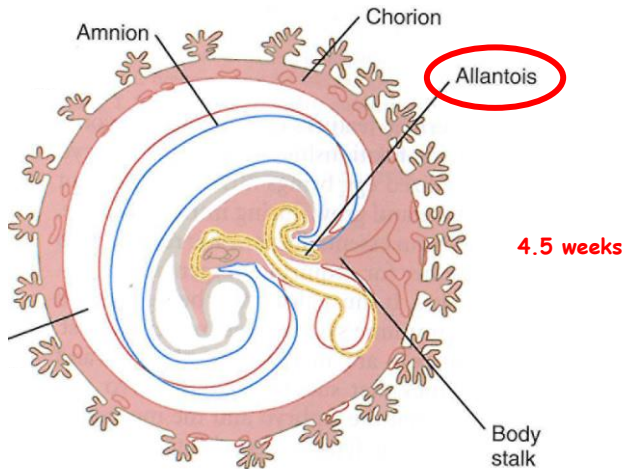
terminal part of the hindgut + allantois



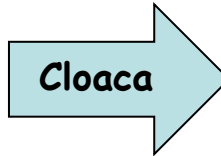
5 weeks

6 weeks

8 weeks



4.5 weeks

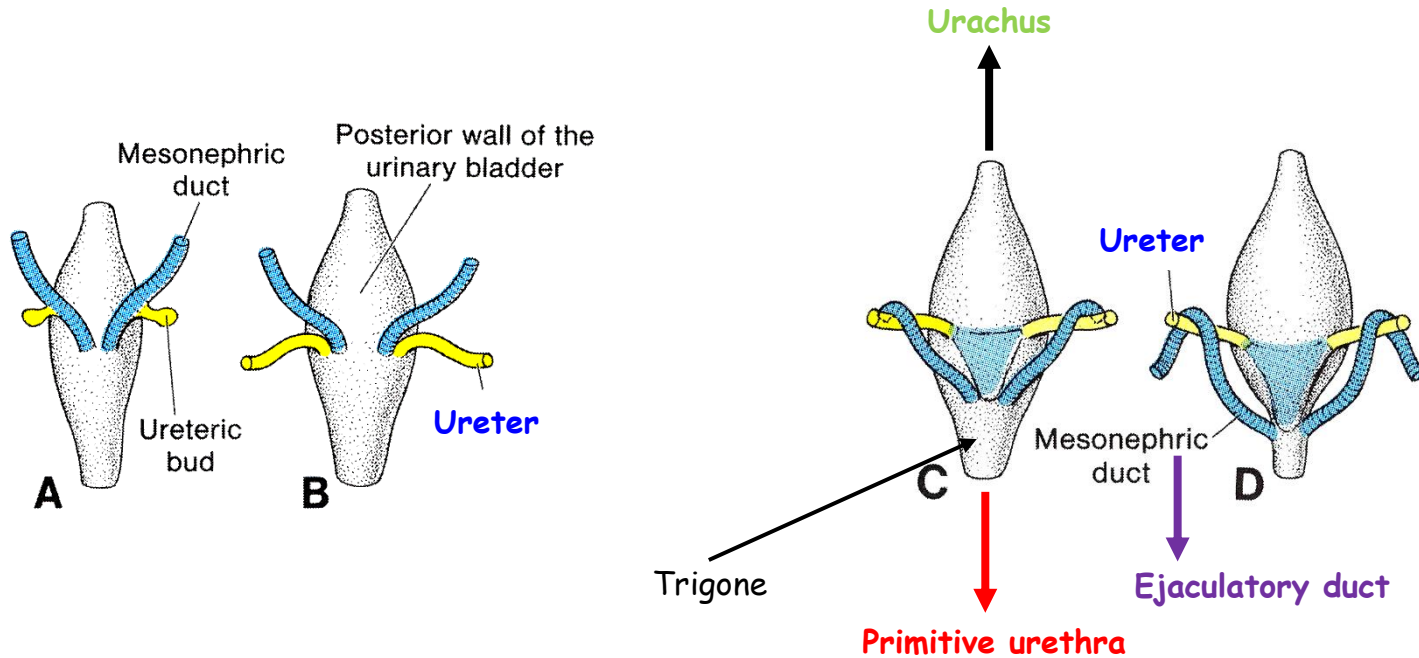


Urogenital sinus	Urogenital membrane
Urorectal septum	Perineum
Primitive rectum	Anal membrane

- ventral outpocketing of the hindgut
- sac-like structure (respiration)
- in umbilical cord
- proximal part - URACHUS - continuous with bladder
- URACHUS - transforms to Median umbilical ligament

Urinary system - Bladder + Ureters + Urethra

Posterior view



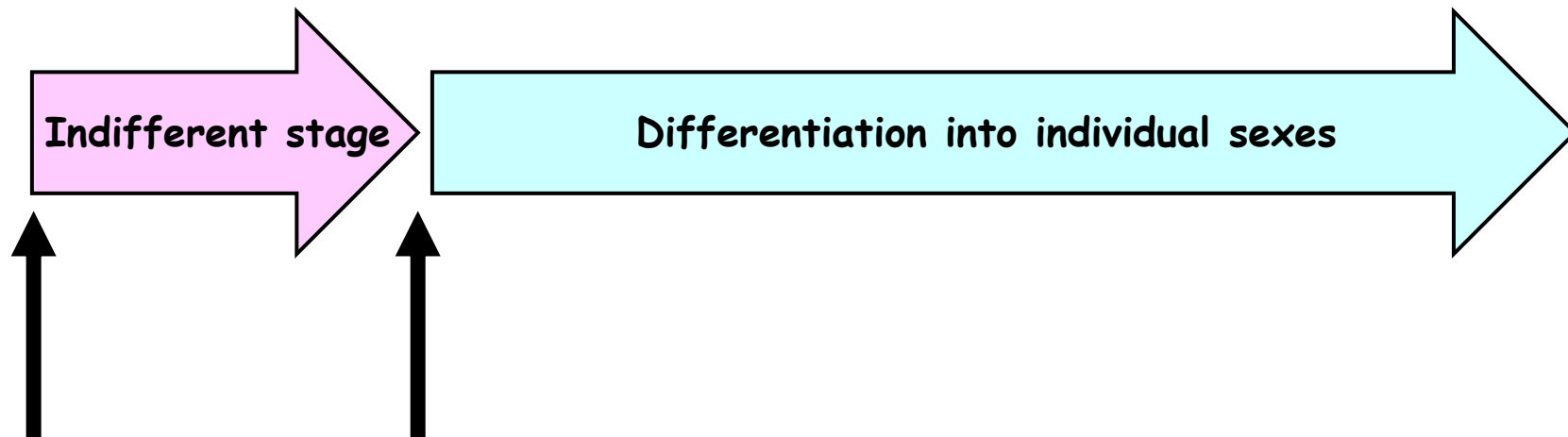
- alantosis expands - urinary bladder
- initially bladder is continuous with alantosis - then obliteration - **urachus** - **median umbilical ligament**
- caudal portions of mesonephric ducts become absorbed by the bladder wall - separation - **ureters** + **ejaculatory ducts**

Genital system

Sexual dimorfism - individual can only have one type of genital organs

Genetic determination:

- Heterogametic (XY) - male
- Homogametic (XX) - female



Fertilization

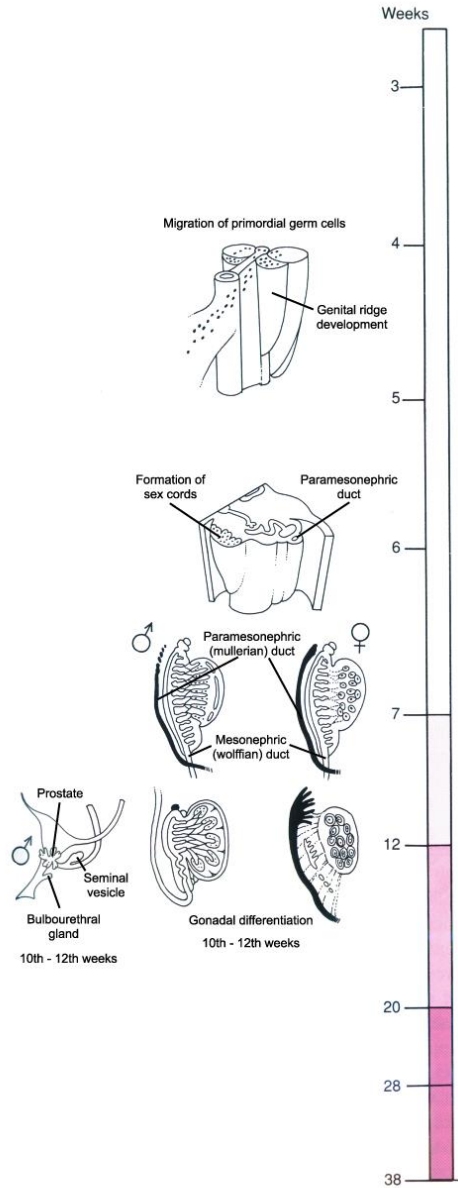
7th week

=

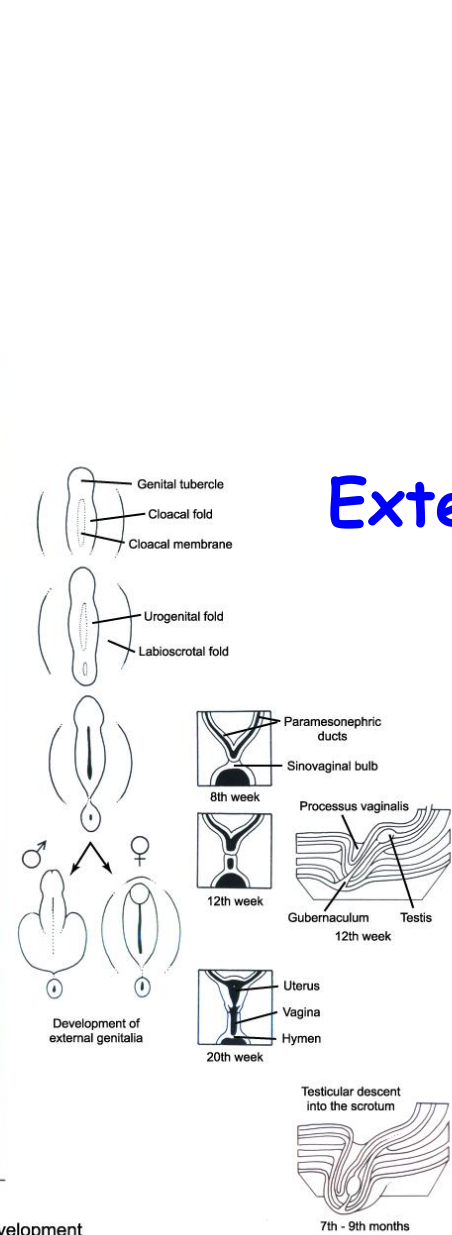
genetic gender established
(Barr body)

Genital system - 7 weeks at indifferent stage

Gonads



External genitalia

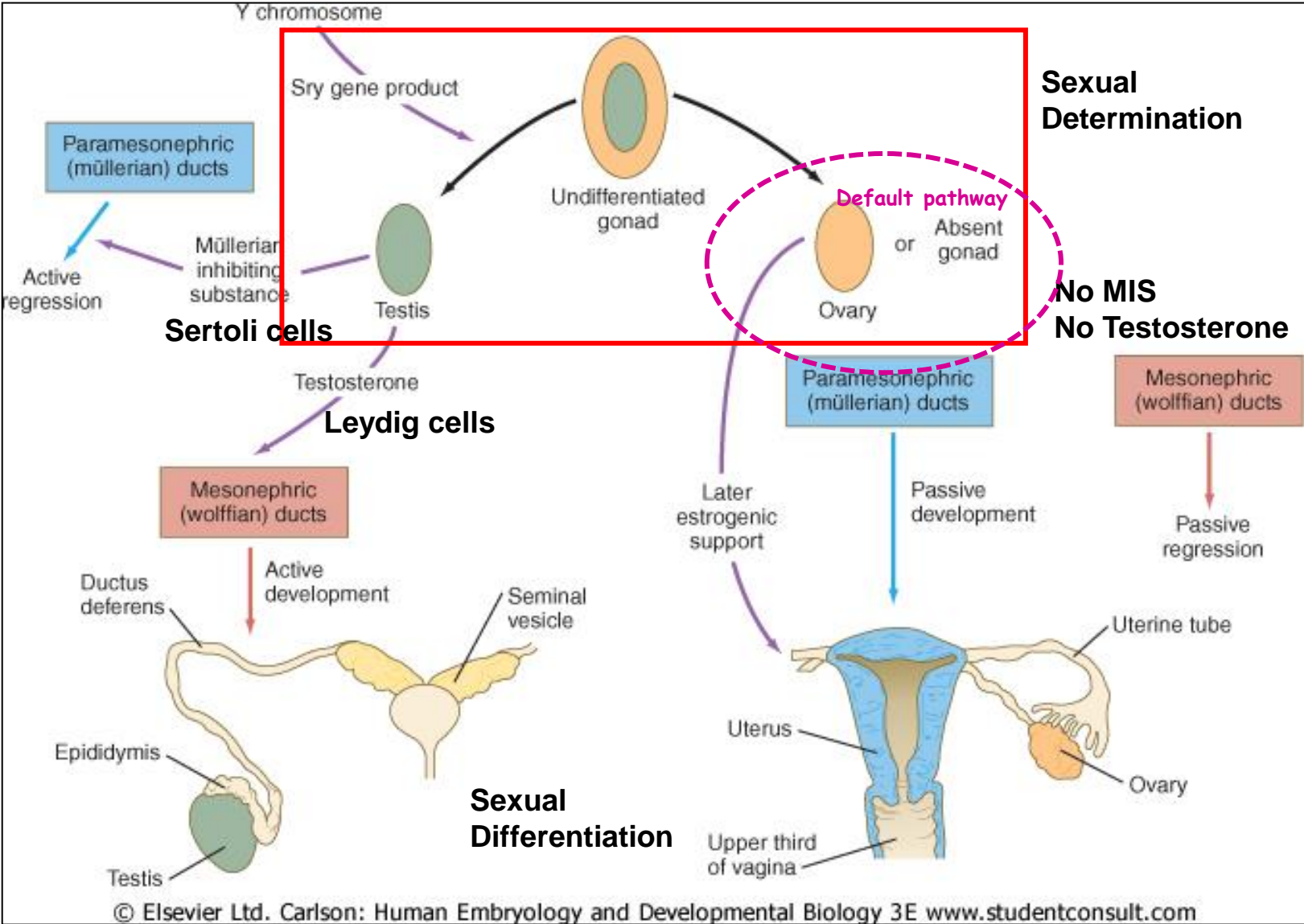


C. Genital development

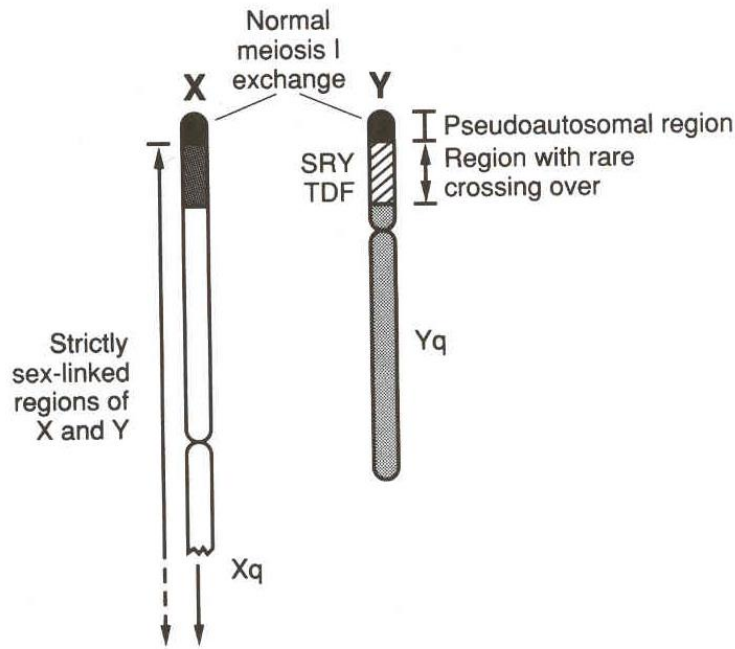
Genital system - Sry gene

Y chromosome decides
 XXY - male
 XO - female

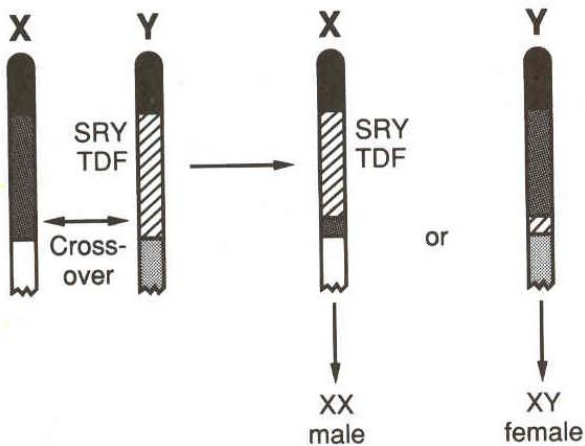
Sry gene - Sox family TF - on short arm of Y chromosome



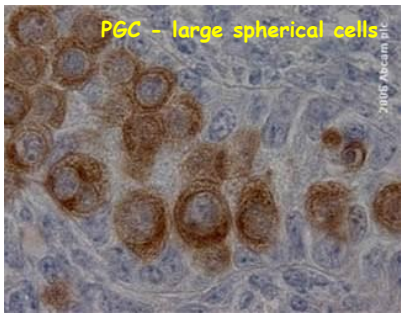
Genital system - Sry gene



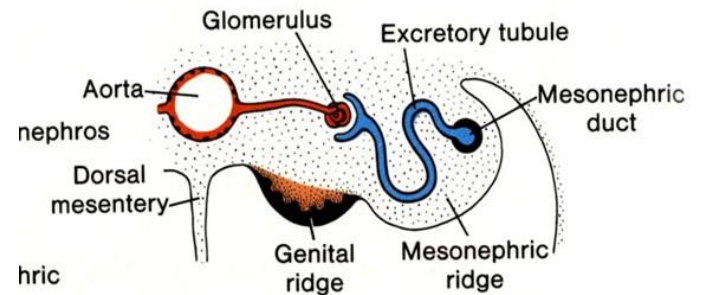
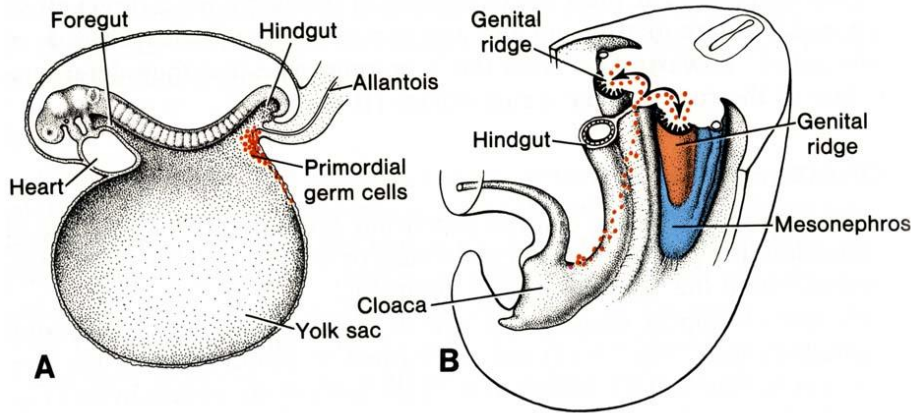
Pairing of X and Y chromosomes in pseudoautosomal region during meiosis



Rare crossing-over causes translocation of SRY to X chromosome: XY females or XX males

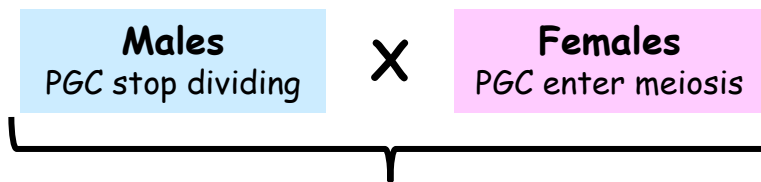


Genital system - Primordial germ cells



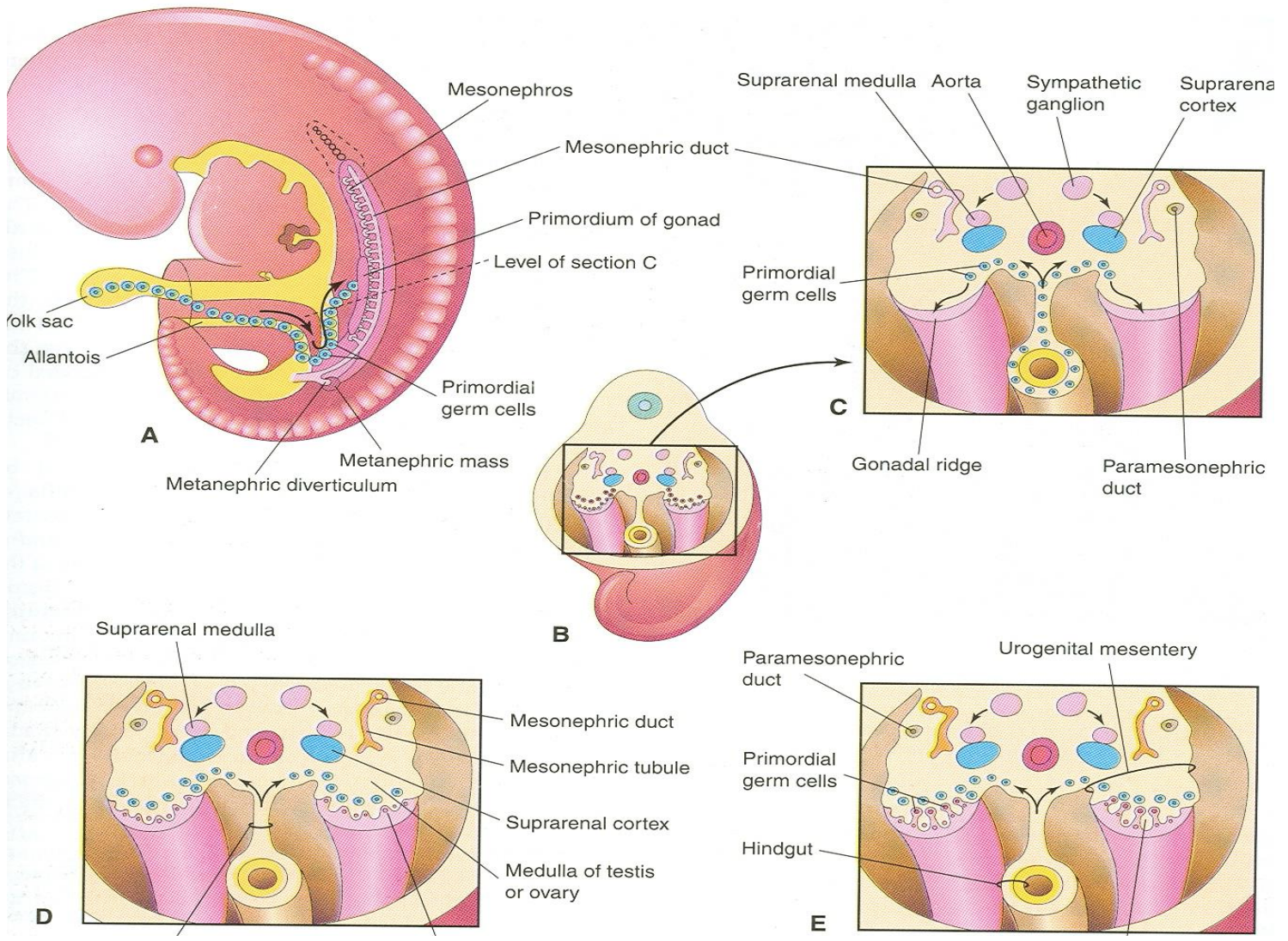
Primordial germ cells (PGC)

- first recognizable at day 24
- from epiblast-derived extraembryonic mesoderm
- few cells among endodermal cells of the yolk sac
- they migrate through the dorsal mesentery of the hindgut
- migrate towards genital ridges (plicae genitales)
- proliferate during migration
- reach genital ridges on week 6 of gestation



decided by somatic cells in the genital ridges

Genital system - migration of PGC into gonadal anlagen



Genital system - gonadal anlagen

Steroidogenic mesoderm
along the ventromedial border of the mesonephros

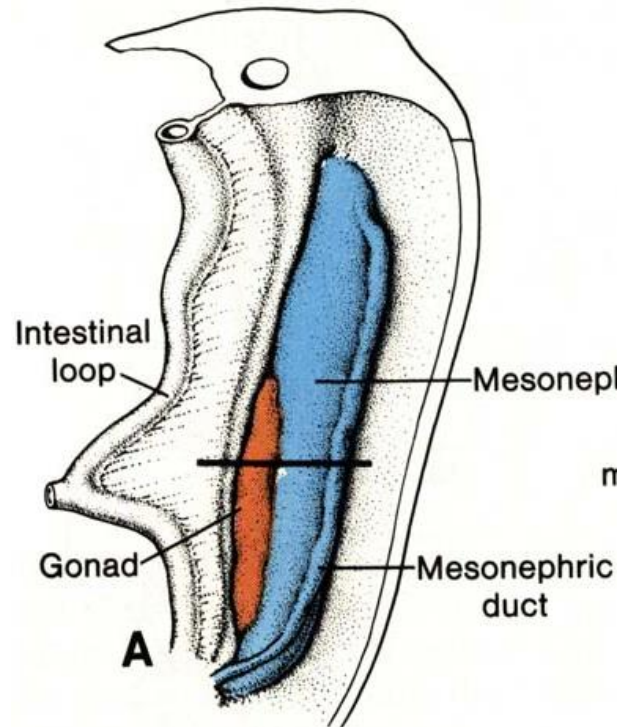
cranial region
Adrenocortical primordia

caudal region
=
Genital ridges

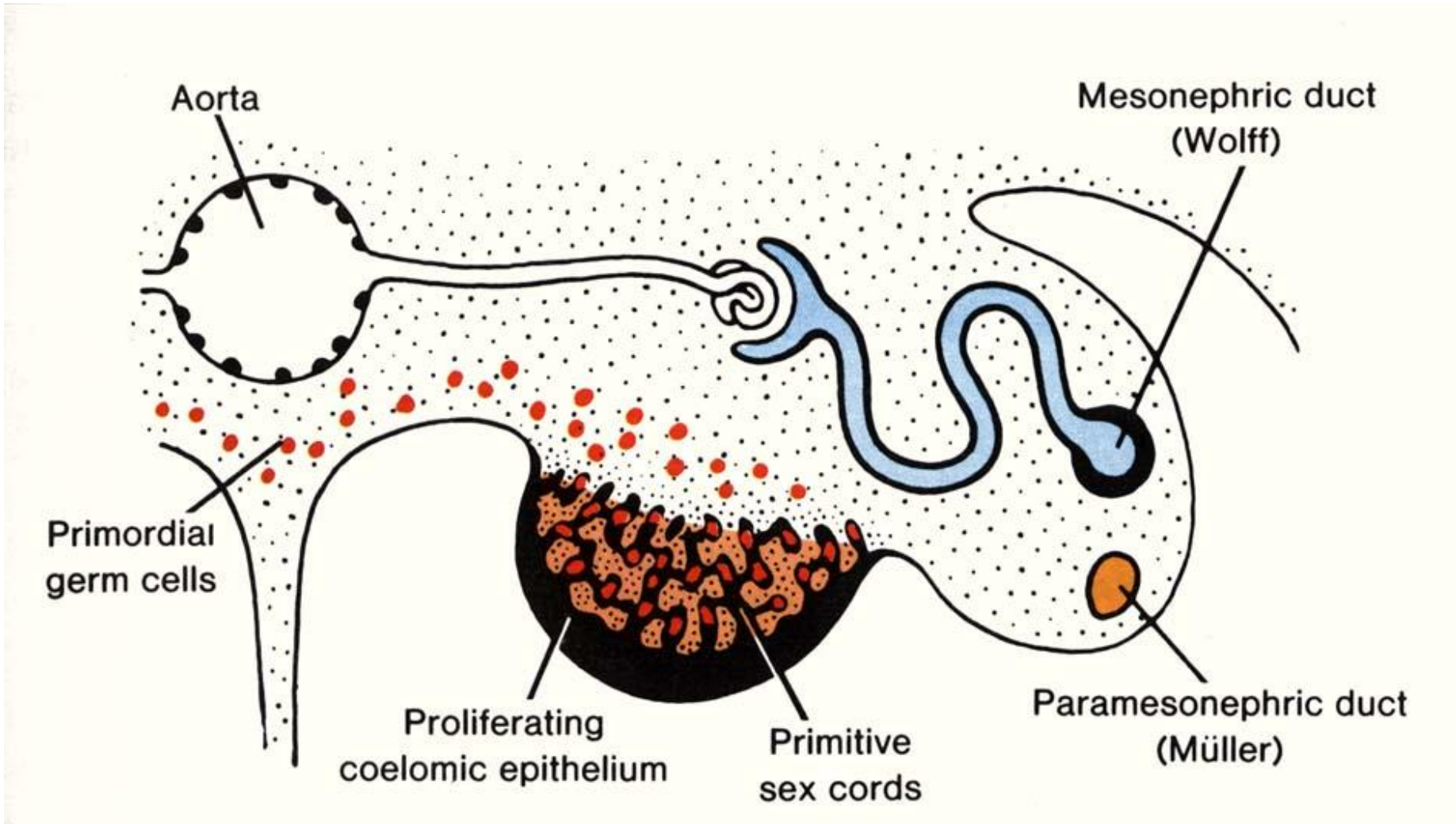
cells of **coelomic epithelium**
+
cells from **mesonephric ridge**

Week 4 - Th6 to S2
cranial + caudal parts involute
Week 6 - L3 to L5

become populated by PGC at week 6



Genital system - indifferent gonade (week 6)



Gonadal cords

Genital system - Differentiation of the testes

Late 6th week

Cord cells differentiate to Sertoli cells

(meiosis-inhibiting factor, anti-mullerian substance, androgen binding factor)

Tunica albuginea develops

(sets barrier between coelomic epithelium and testis cords)

Cord cells form seminiferous tubuli, tubuli recti, and rete testis

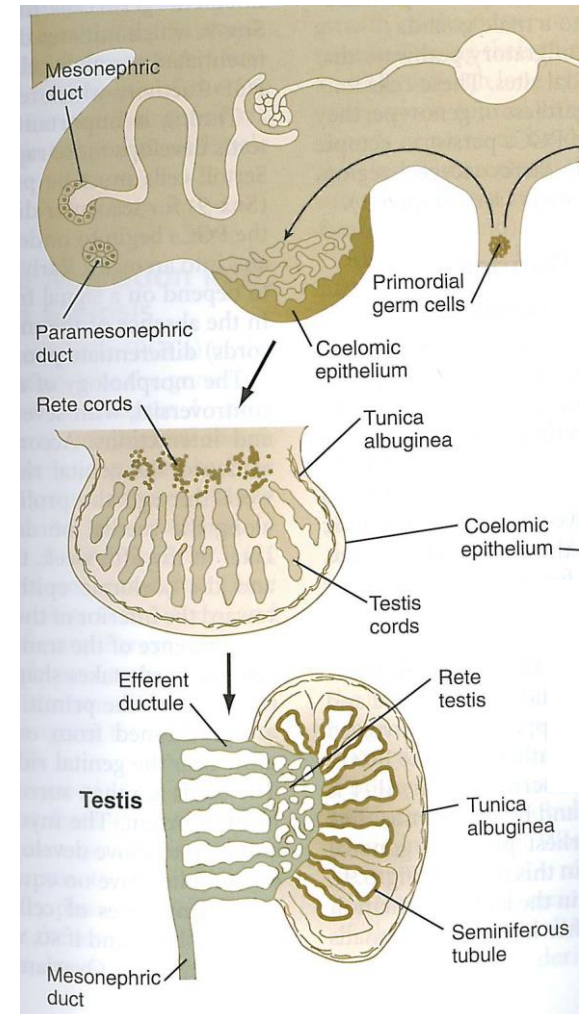
Rete testis joins ductuli efferentes that are derived from mesonephric ducts

(5th to 12th)

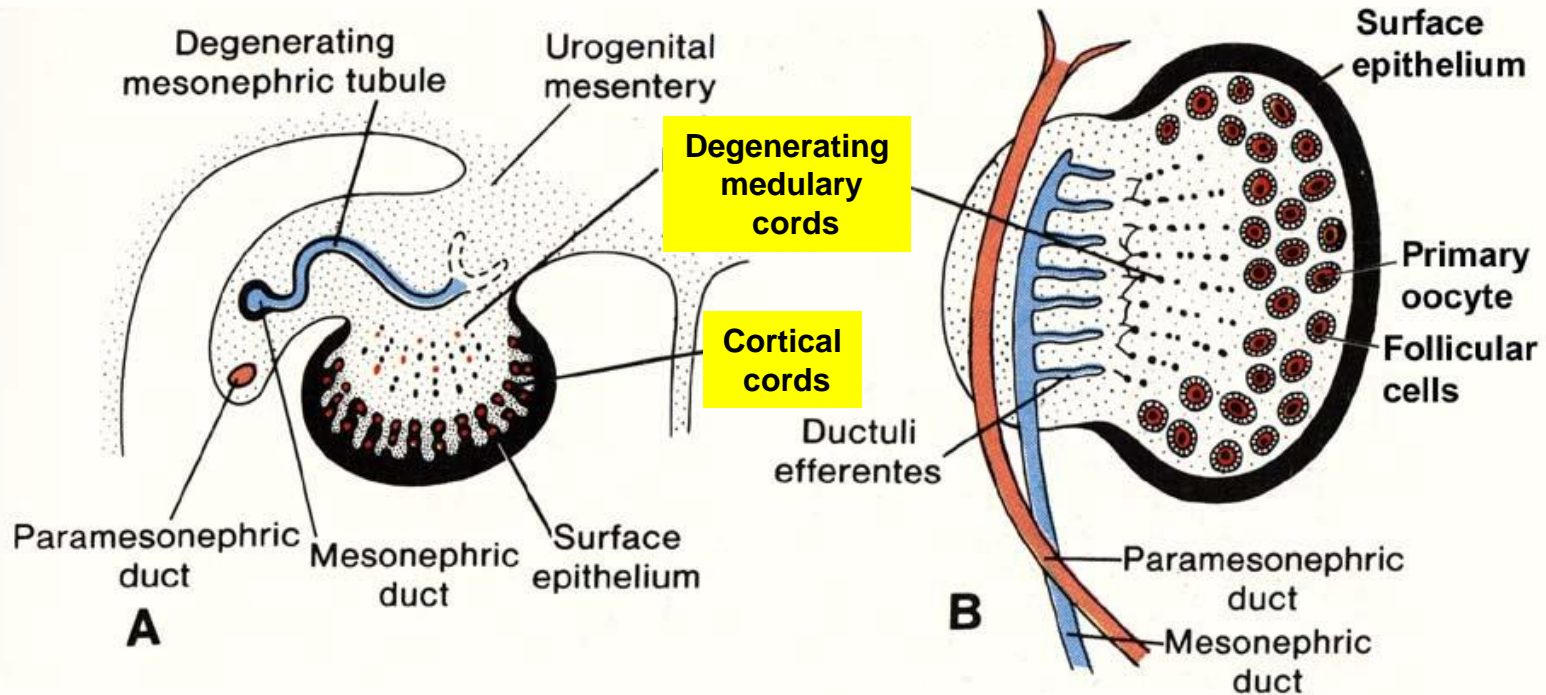
Week 8 to 18

Leydig cells develop and function in developing testis

- from coelomic epithelia and mesonephros
- produce testosterone
- support development of Wolfian (mesonephric) duct
- support development of external genitalia



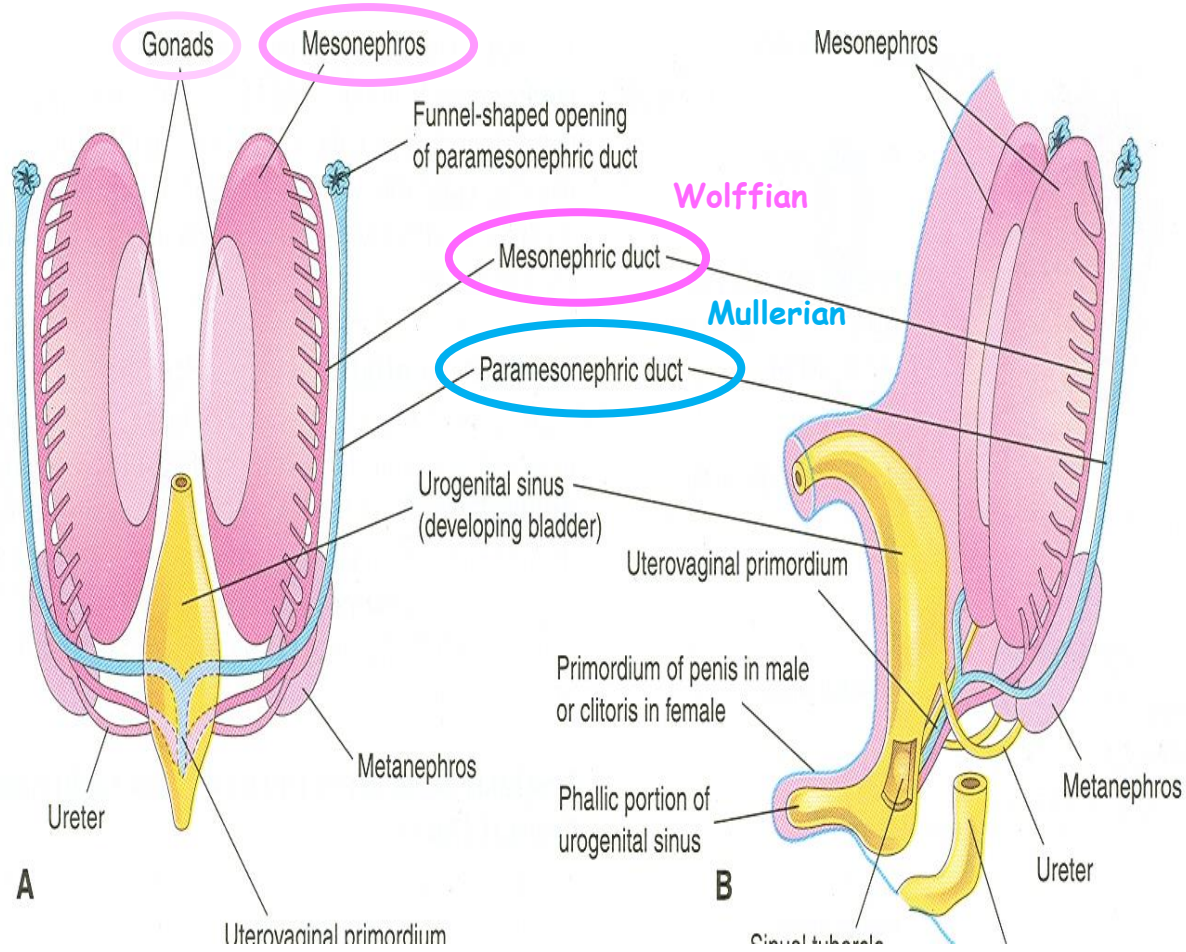
Genital system - Differentiation of the ovaries



- PGC concentrate in the cortical region
- PGC proliferate (max until week 22) and then enter meiosis - arrest in prophase
- Ovarian follicles develop
(somatic cell contribution is not understood)
- Transient rete ovarii develops in medullary region
- Medulla contains connective tissue and vasculature derived from mesonephros

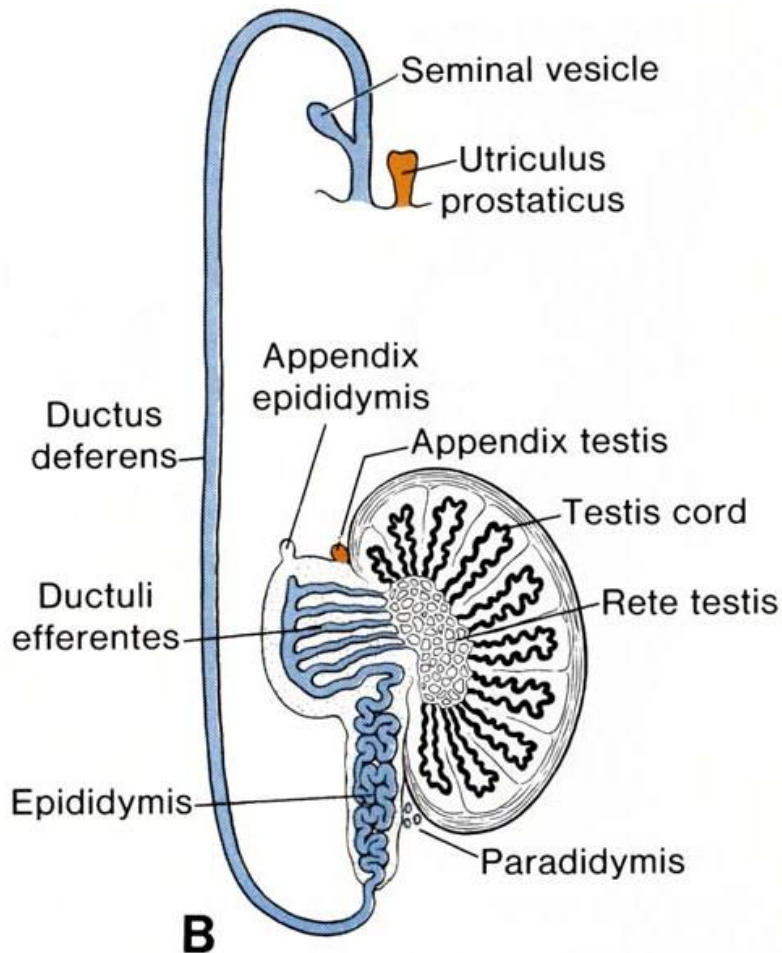
Genital system - Sexual duct system - Indifferent stage

Week 7



Paramesonephric duct
Develops at days 44 to 48
Cranially opens to coelomic cavity

Genital system - Sexual duct system - Male



Mesonephric ducts (Wolffian)

- Ductus epididymis
- Ductus deferens
- Ductus ejaculatorius
- Seminal vesicle

Paramesonephric ducts (Mullerian)

regresses in week 8 (anti-M hormone)

- Appendix testis (cranial part)
- Utriculus prostaticus (caudal part)

Mesonephros

- Ductuli efferentes
- Paradiidymis (under the testis, nonfunctional)

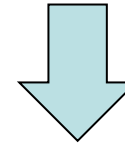
Genital system - Descent of the testes

„Prerequisites + driving forces“ for the descent of testes:

- testes enlargement
- atrophy of mesonphros - allows for caudal movement
- tension of gubernaculum
- atrophy of paramesonephric ducts - move to unquinal canal
- enlargement of processus vaginalis peritonei (6th month)
- increased intraabdominal pressure ?

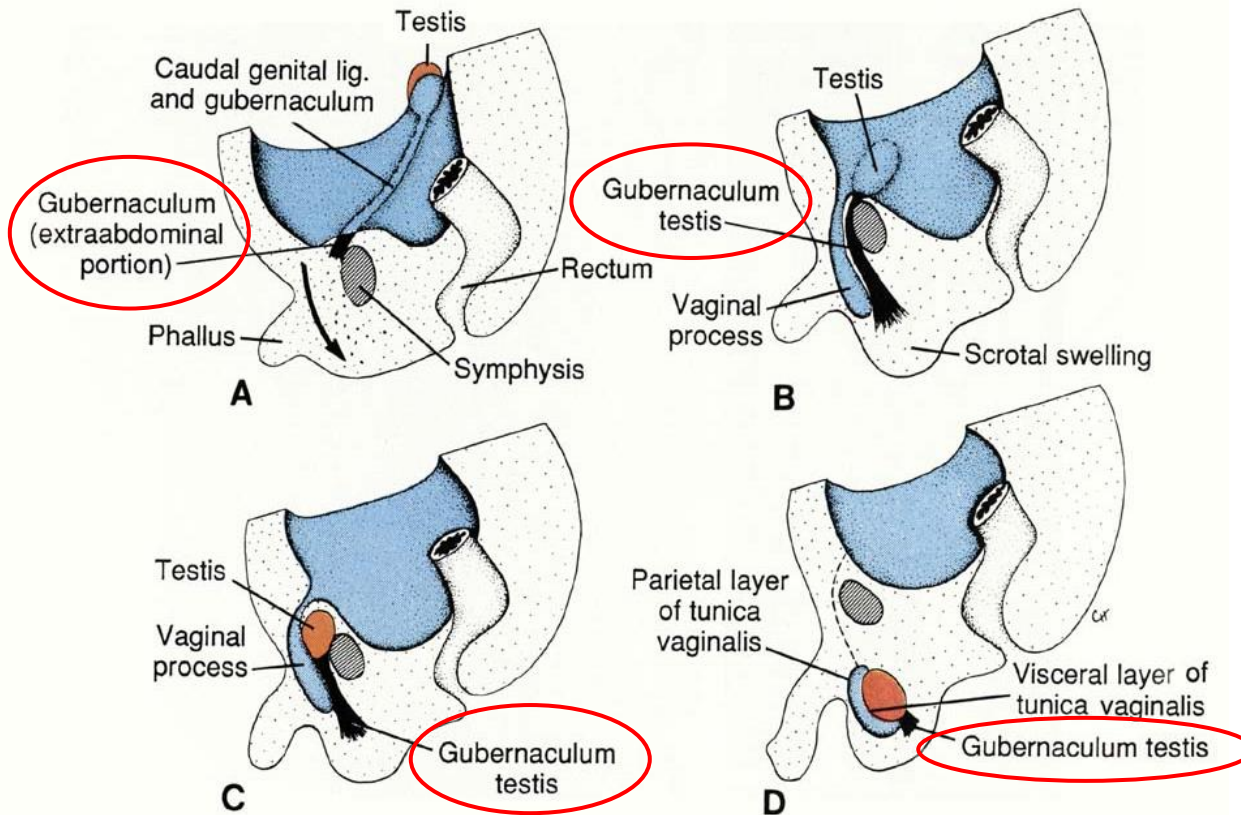
By 26 weeks

- the testes have descended retroperitoneally to the deep **inguinal rings**



During 26th week

- final descent through the **inguinal canals** into the scrotum - 2 to 3 days



NOTES

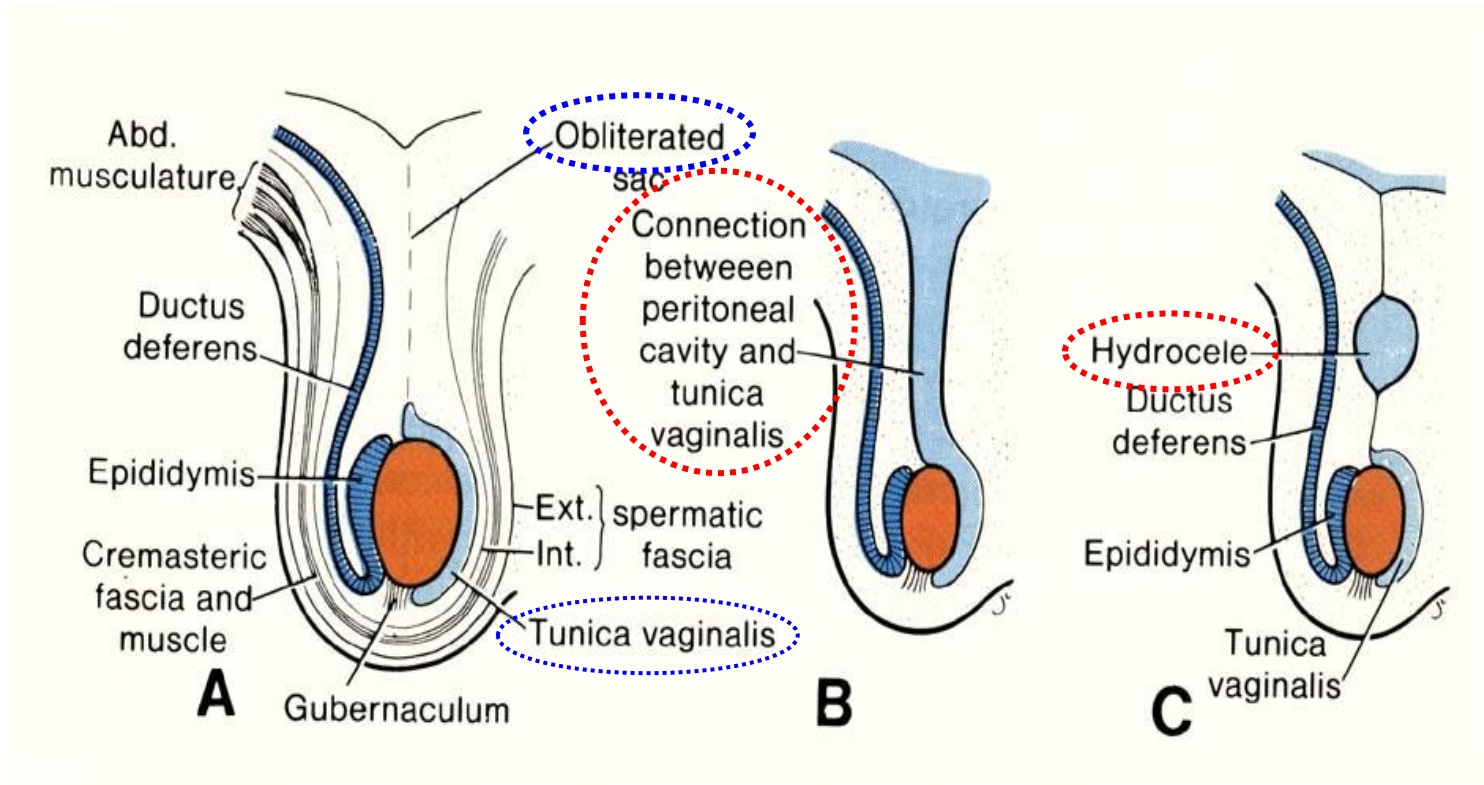
More than 97% of full-term newborn males have both testes in the scrotum

During the first 3 months after birth, most undescended testes descend into the scrotum

Spontaneous testicular descent does not occur after the age of one year

Gubernaculum - originates from caudal portion of genital ridge

Genital system - Descent of the testes

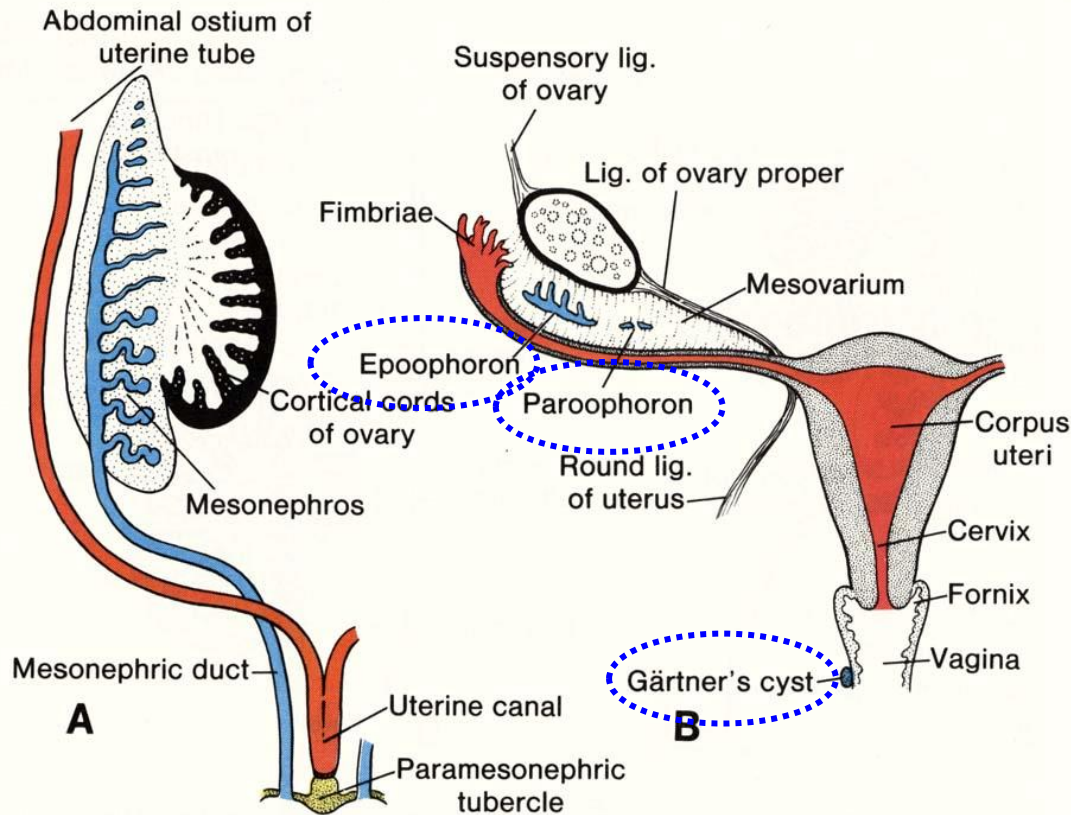


Processus vaginalis obliterated
NORMAL

Remaning connection = Risk of hernia
ABNORMAL

Remaing cyst = Hydrocele
ABNORMAL

Genital system - Sexual duct system - Female



Mesonephric ducts (Wolffian)

regresses (absence of testosterone)

- Gartner's cyst (caudal part)

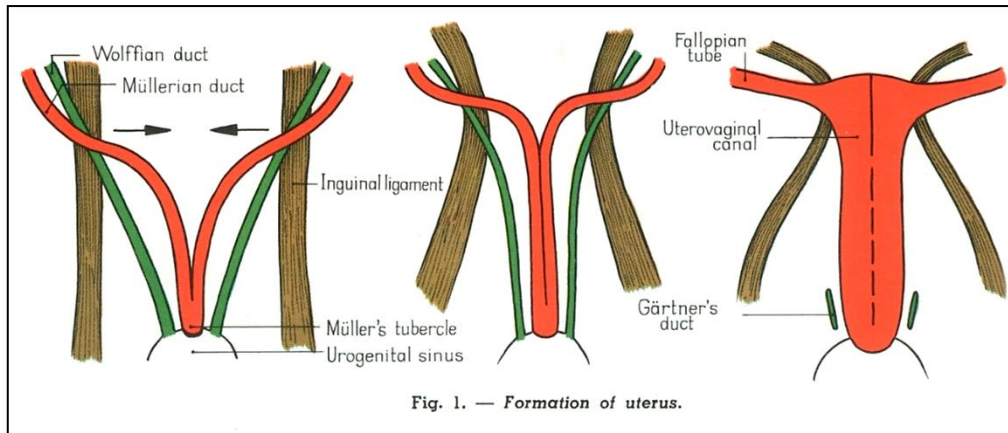
Paramesonephric ducts (Mullerian)

- Uterine tubes (oviducts, falopian t.)
- Uterus
- Vagina

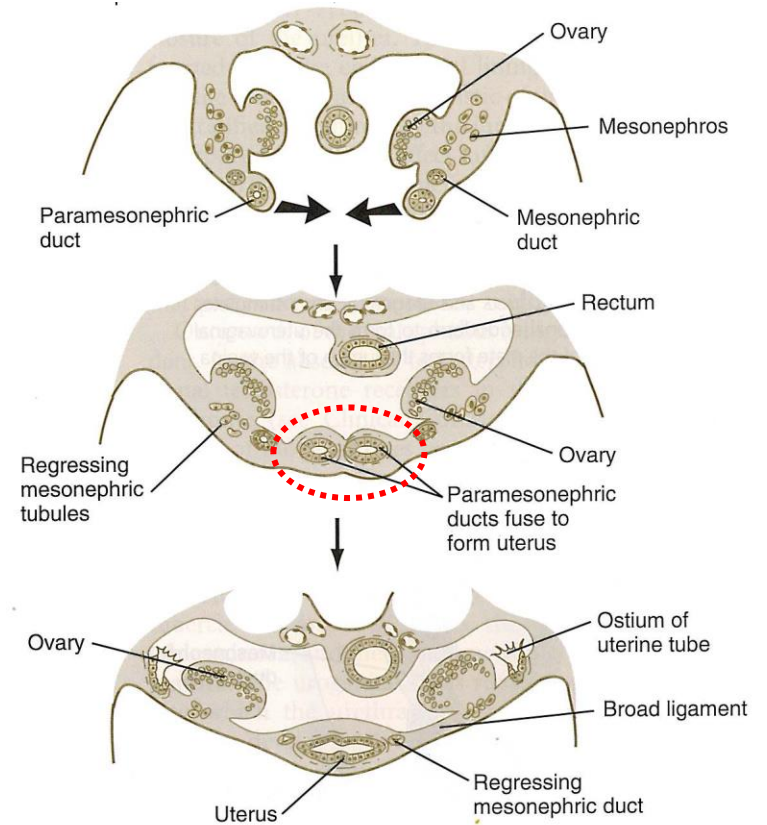
Mesonephros (+Mesonephric duct)

- Epooophoron (appendix of ovary)
- Paraophaoron

Genital system - Sexual duct system - Uterus

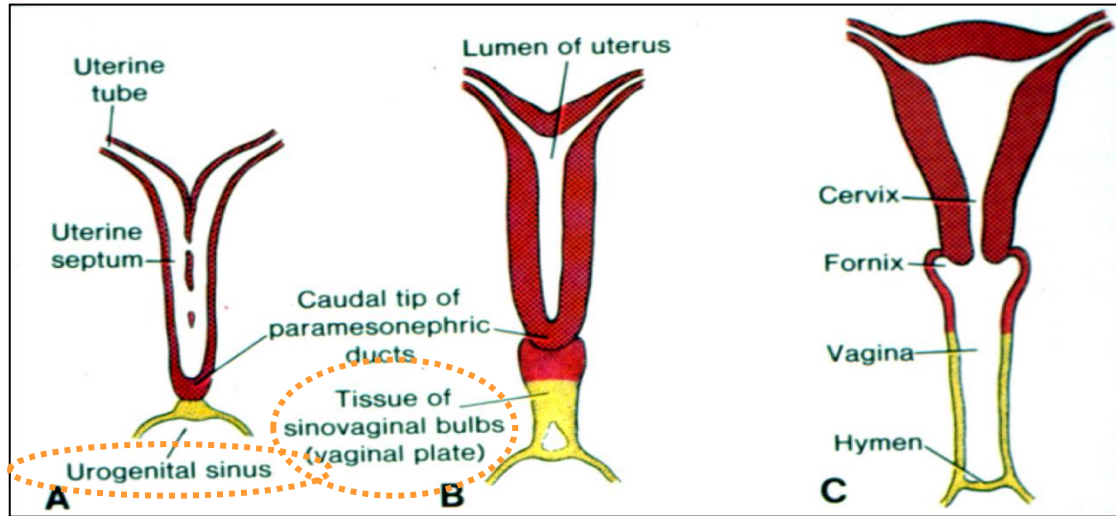


Uterovaginal canal

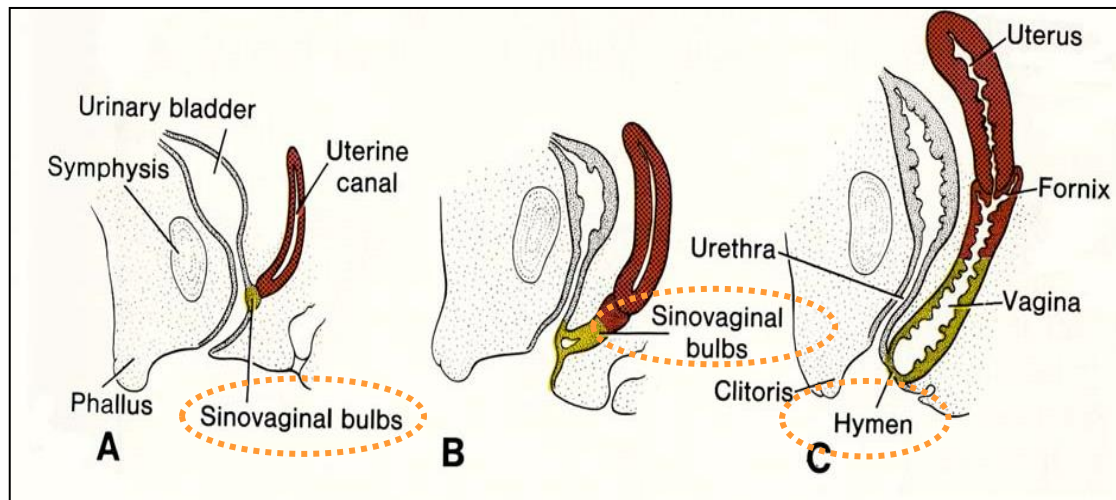


Genital system - Duct system - Uterovaginal channel

Dorsal view

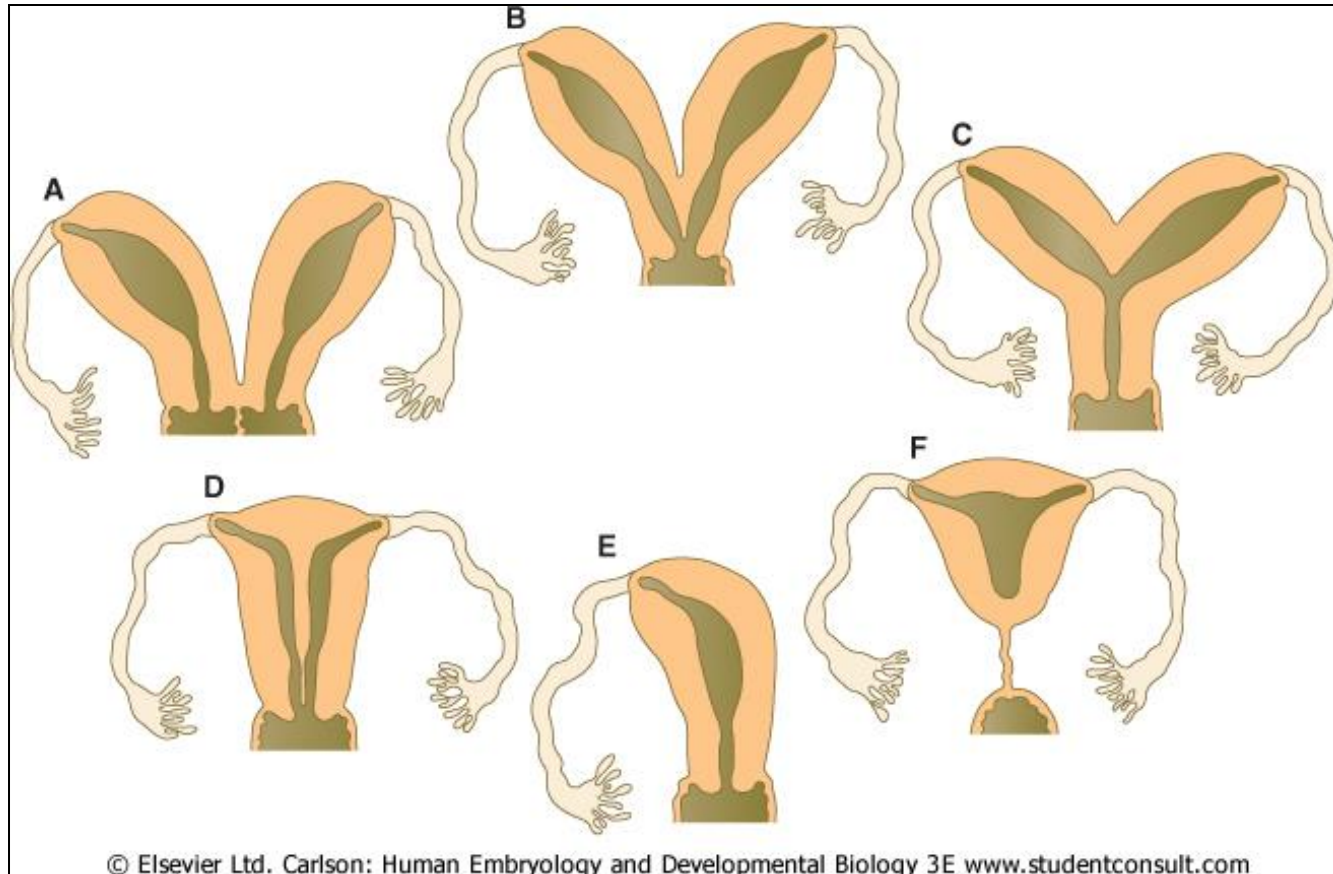


Lateral view



Paramesonephric (Mullerian) ducts fuse to form uterus and upper 1/3 of vagina

Genital system - Uterovaginal channel - Anomalies

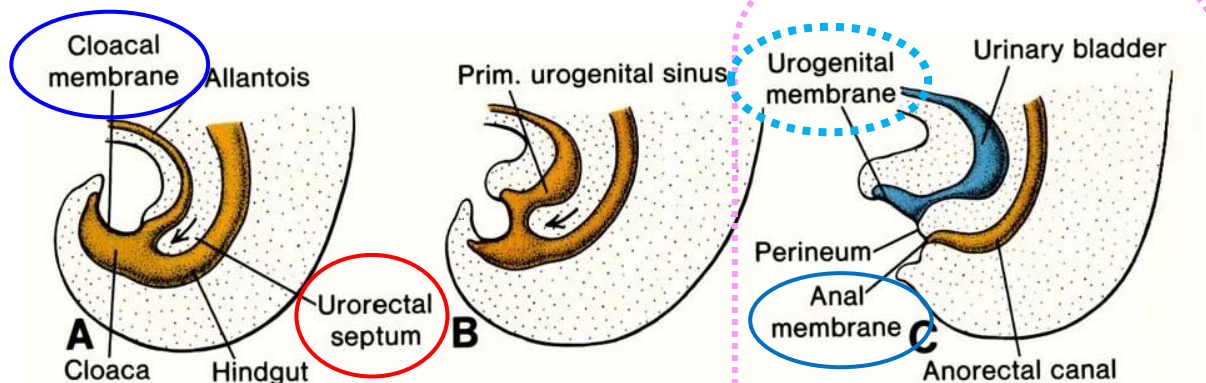


Genital system - External genitalia - Indifferent stage

They are derived from a complex mesodermal tissue located around cloaca.

HORMONE-INDEPENDENT

Week 6 to 8

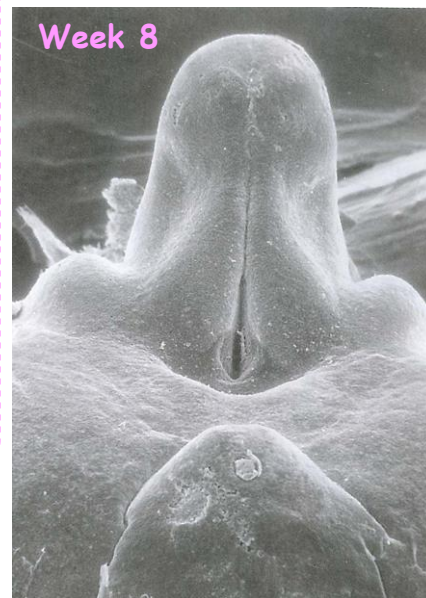
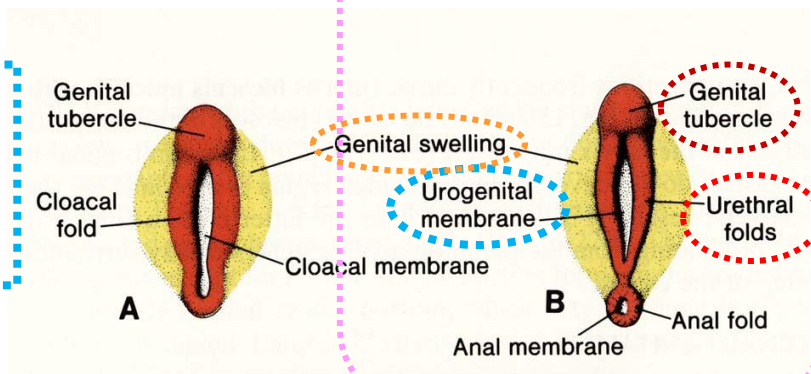


Orificium urogenitale primitivum demarcated by:

Genital tubercle - Phallus

Urethral (genital) folds - Plicae urogenitales

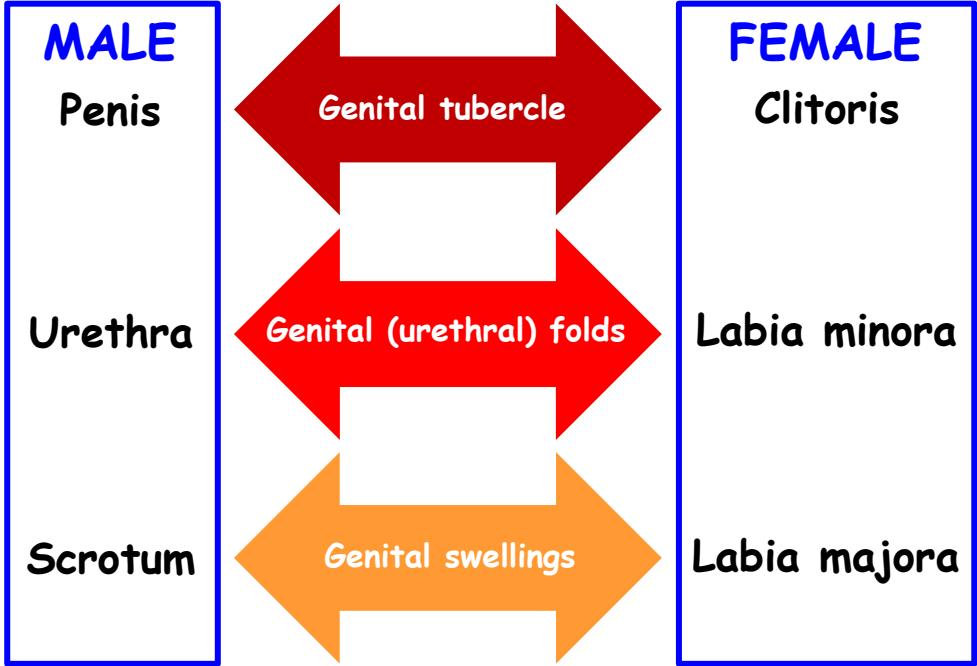
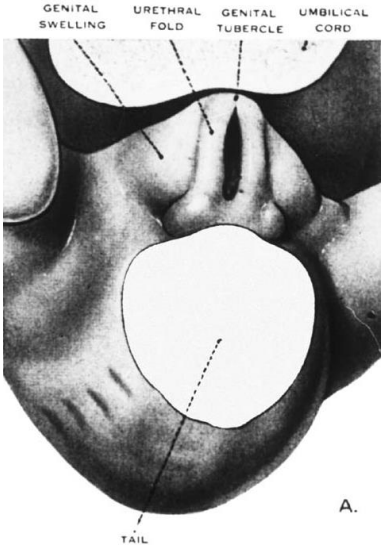
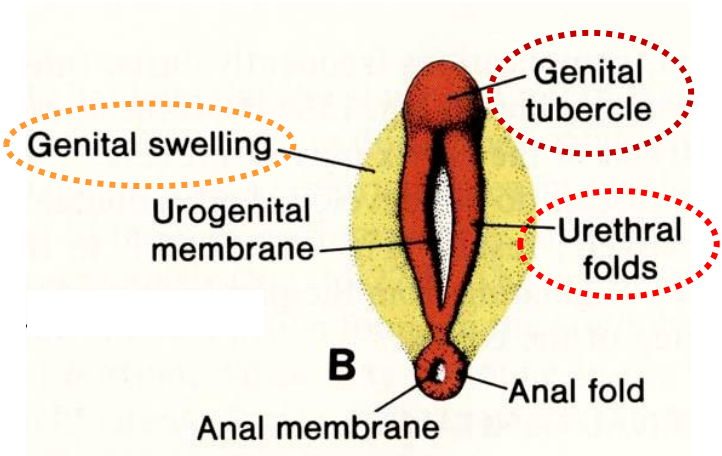
Genital swellings - Tori genitales



Genital system - External genitalia - Dimorphism

Week 9 to 13

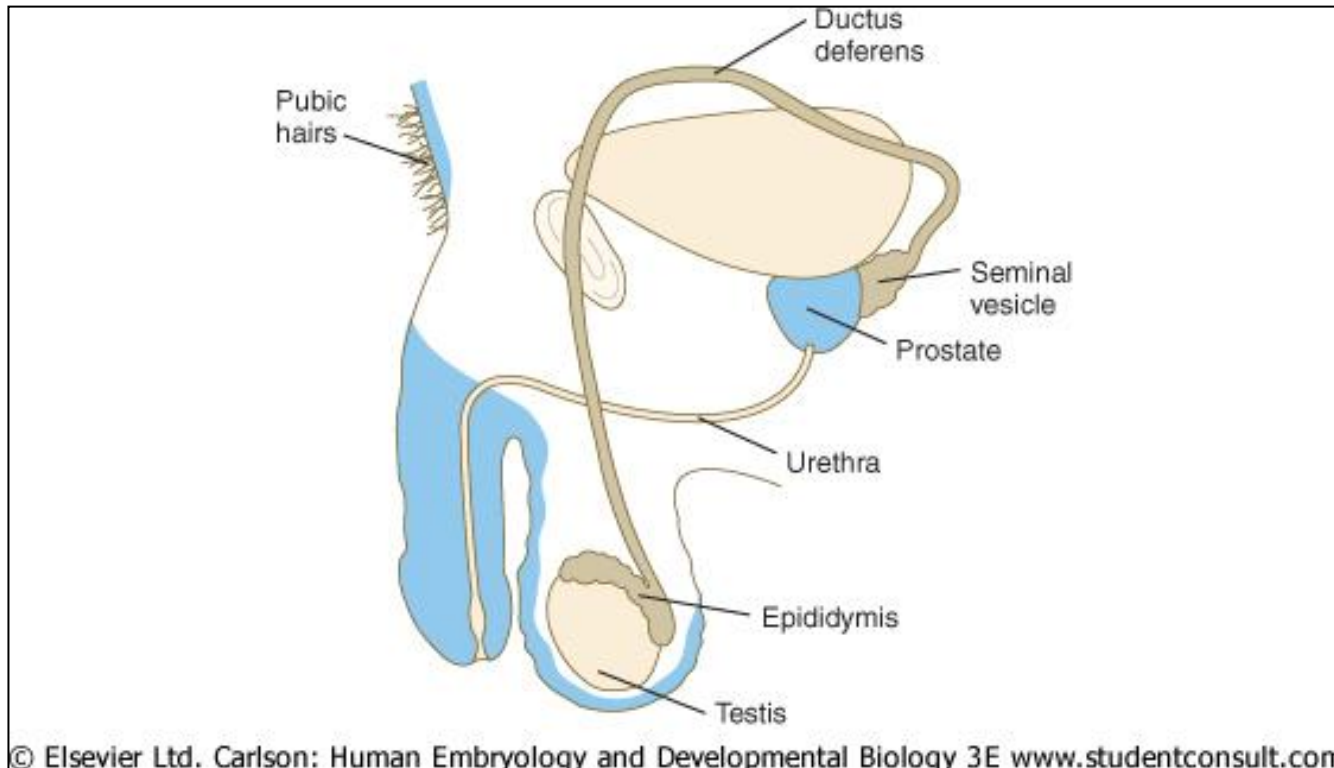
Weeks 12 + 13 are particularly critical
= fusing of urethral folds



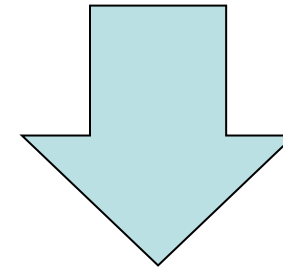
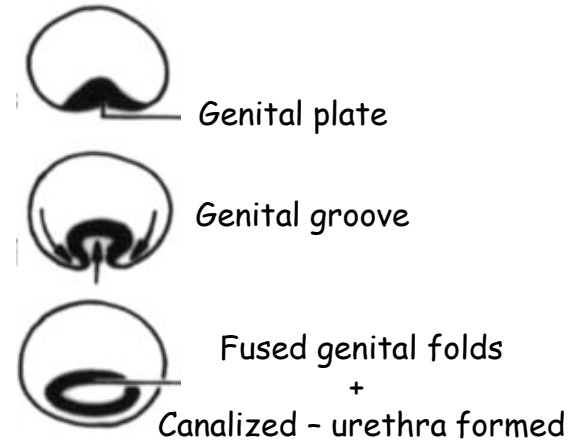
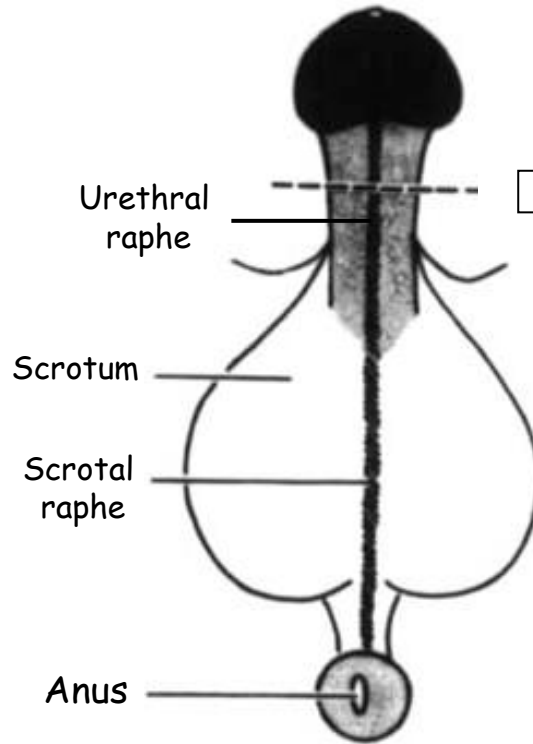
Genital system - External genitalia - Male

Influenced by dihydrotestosterone

Influenced by testosterone



Genital system - External genitalia - Male



Genital tubercle elongates - penis (phallus)

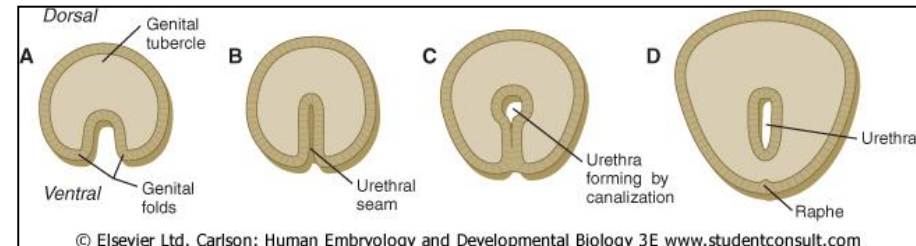
Genital swellings enlarge - scrotum

Genital folds form the lateral walls of the urethral groove

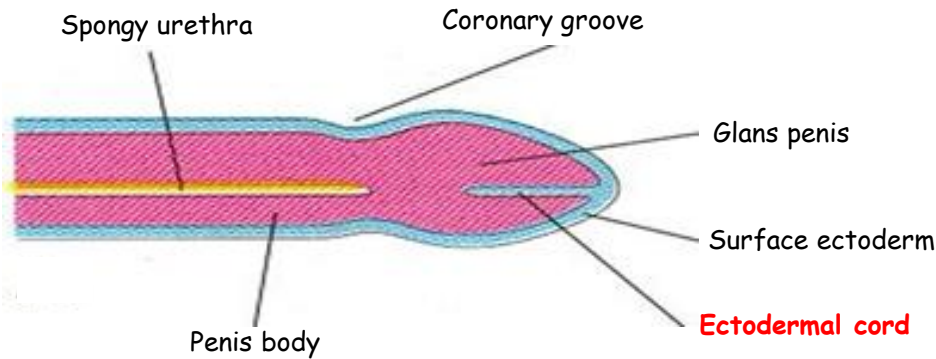
Genital folds form the spongy urethra

Ventral epithelium of genital folds - urethra proper

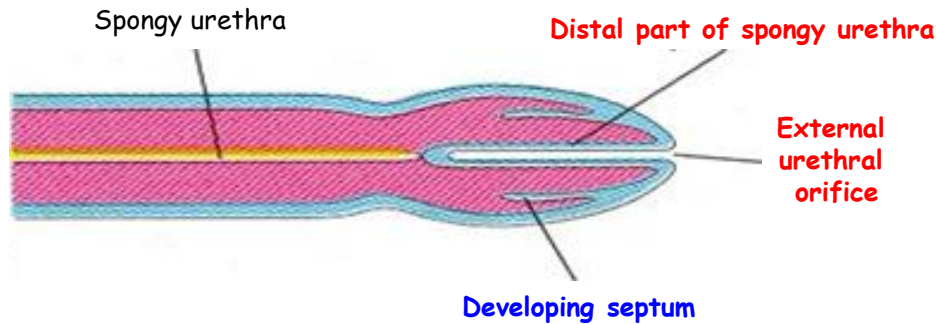
Corpora cavernosa develop from mesenchyme



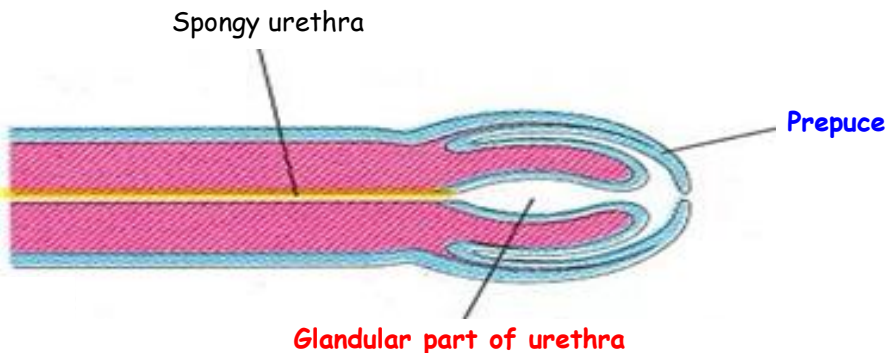
Genital system - External genitalia - Urethral orifice



- ectodermal ingrowth forms a cellular **ectodermal cord**

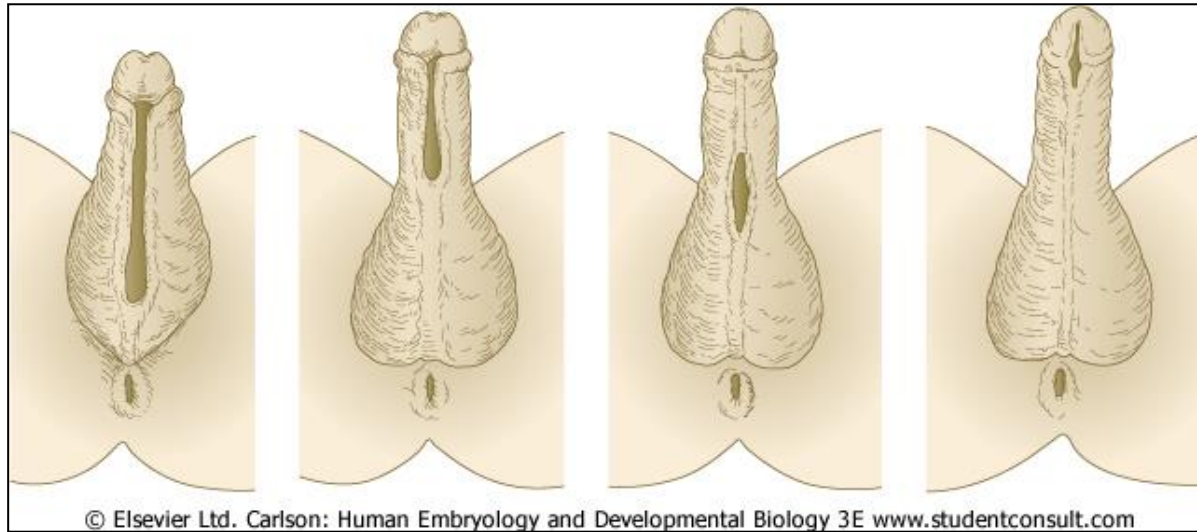


- the **cord** grows towards the root of the penis to meet the spongy urethra
- the **cord** canalizes
- **circular ingrowth** of ectoderm occurs at the periphery of the glans penis (week 12)



- **circular ingrowth** breaks down forming **prepuce** (for some time adherent to the glans penis, hard to retract at birth)

Genital system - External genitalia - Male hypospadias

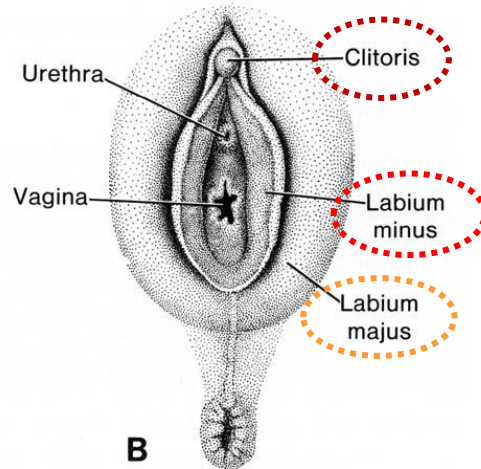
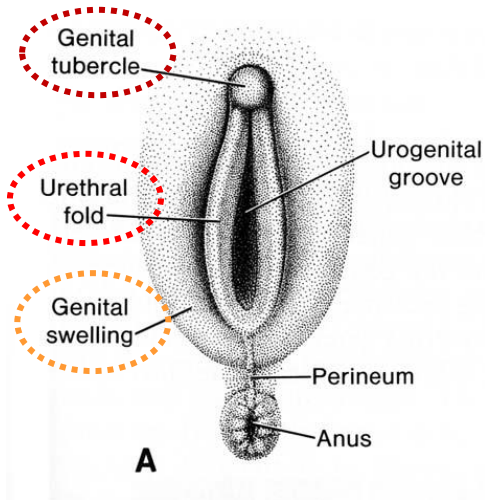


Normal midline raphe



Raphe off center

Genital system - External genitalia - Female



urethra and vagina open into **vestibule** = from urogenital sinus

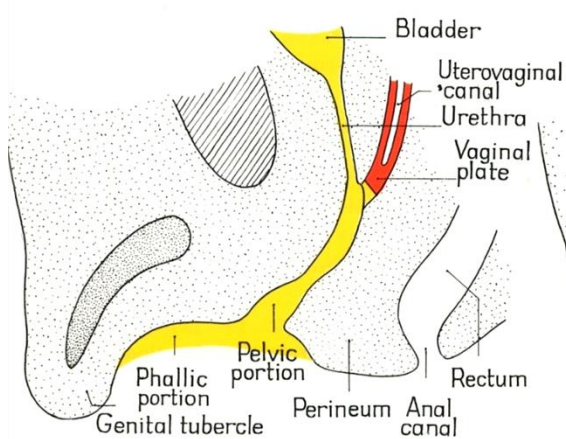


Fig. 2. — Opening of urogenital membrane.

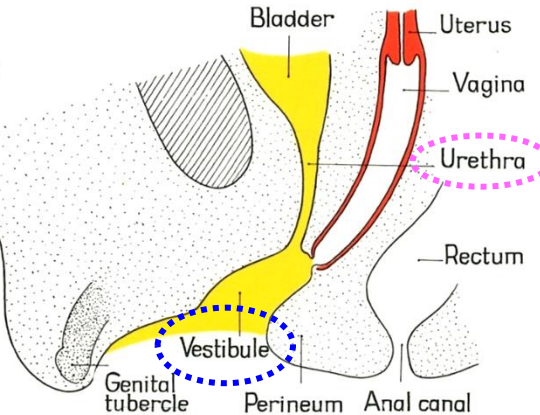


Fig. 3. — The definitive vestibule.

urethra develops from the more cranial part of urogenital sinus - equivalent to prostatic urethra

Thank you for your attention !

Questions and comments at:
ahampl@med.muni.cz