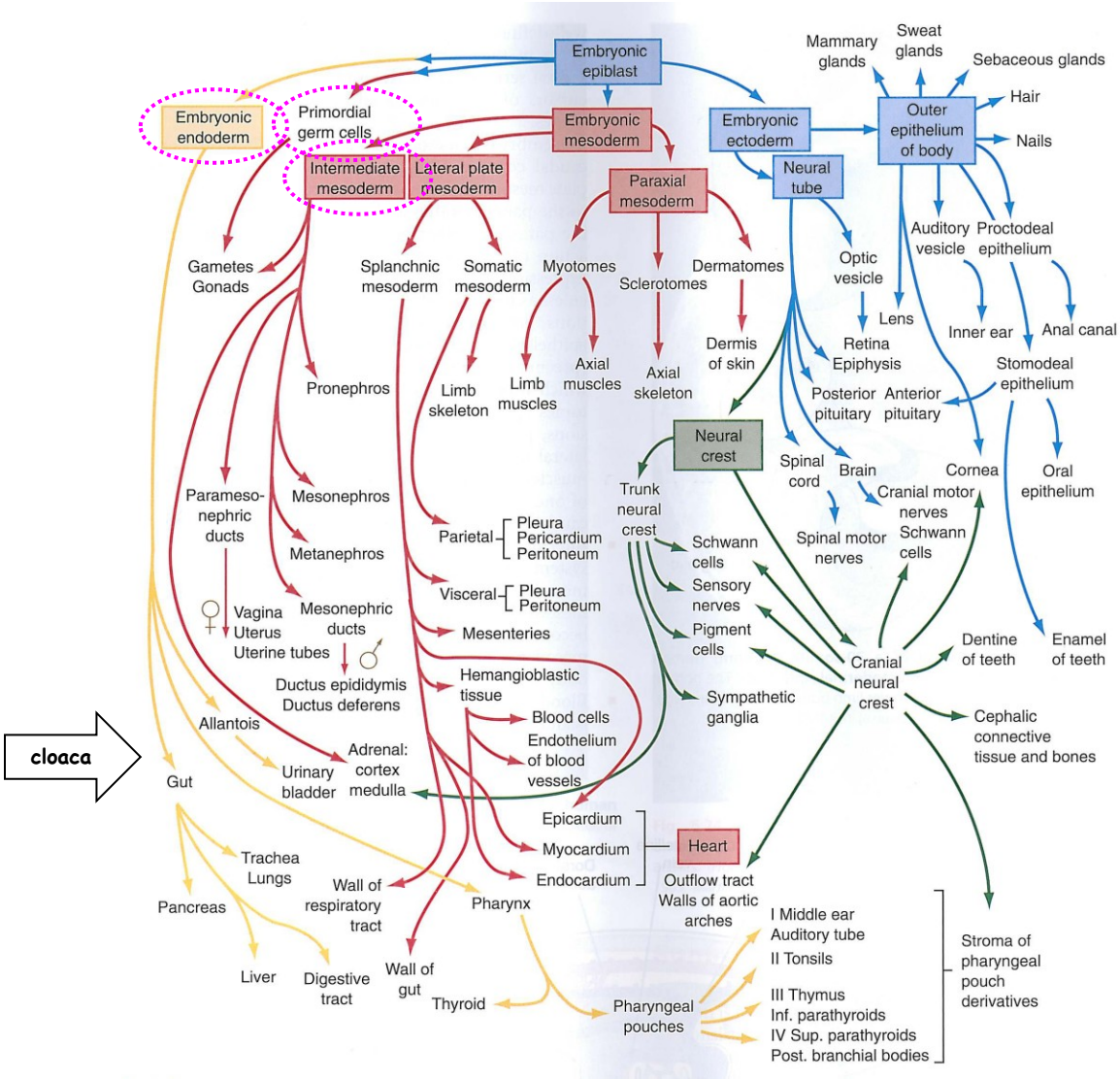
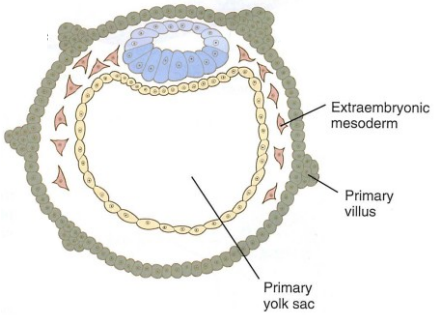
Urogenital system - Development

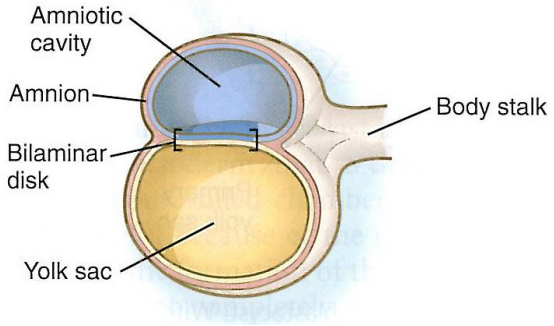
Aleš Hampl

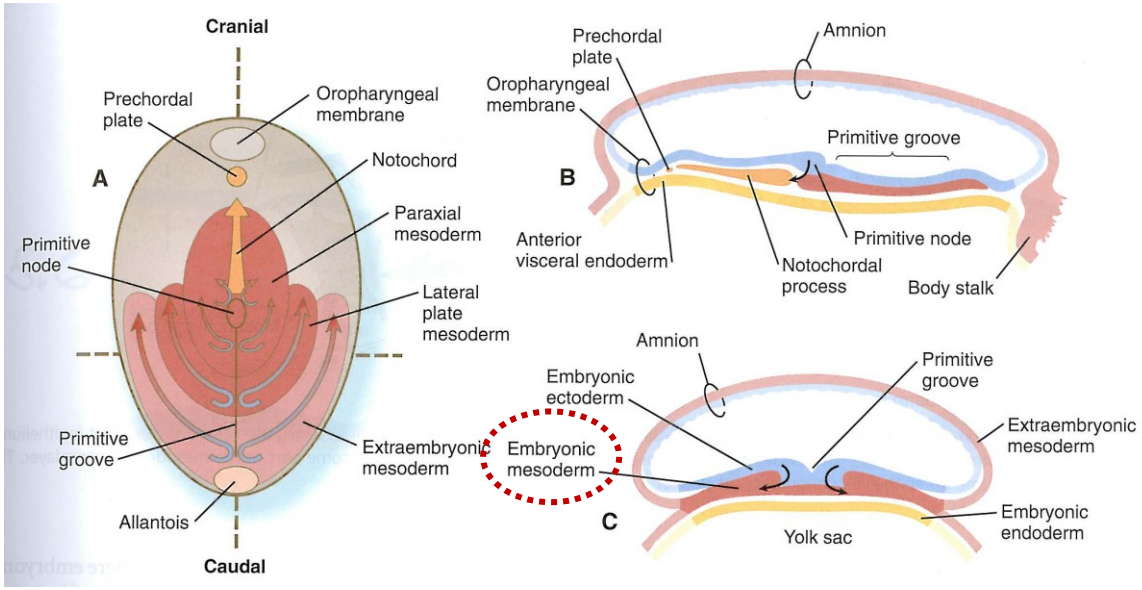
Urogenital system – Overall picture



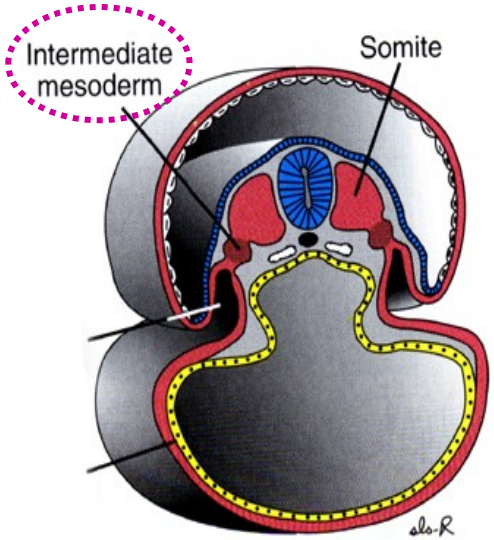
Urogenital system – Reminder

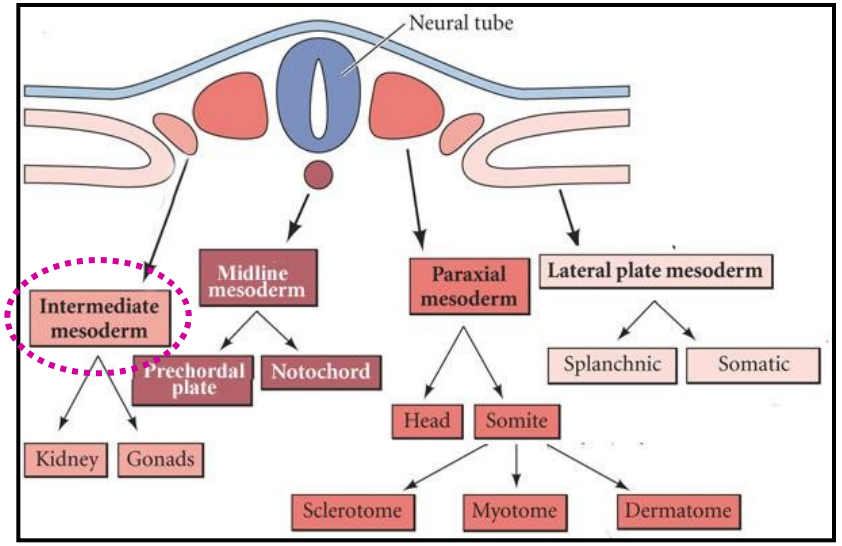


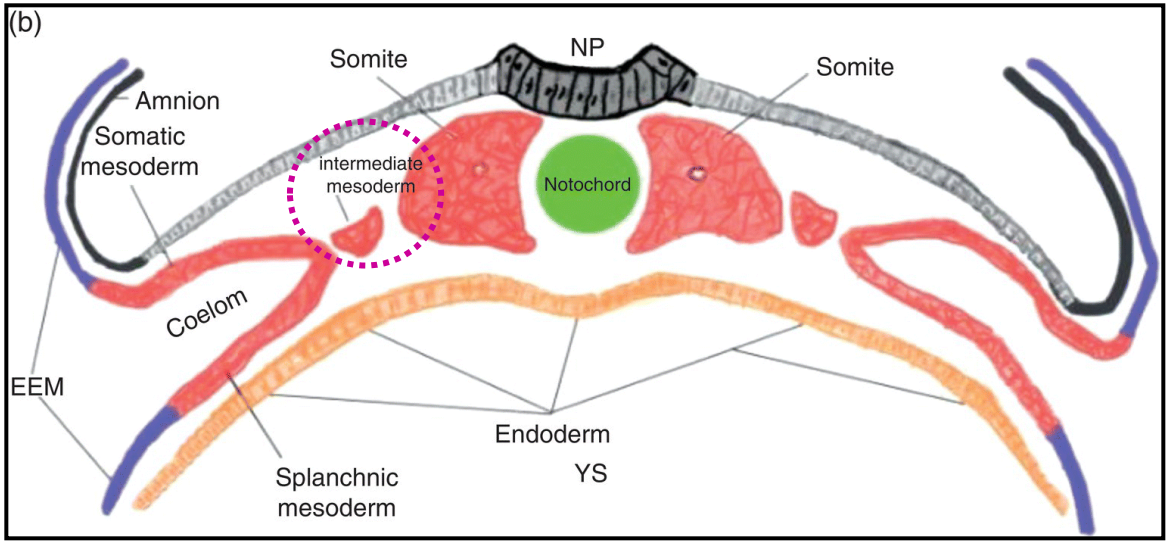




Urogenital system – Intermediate mesoderm



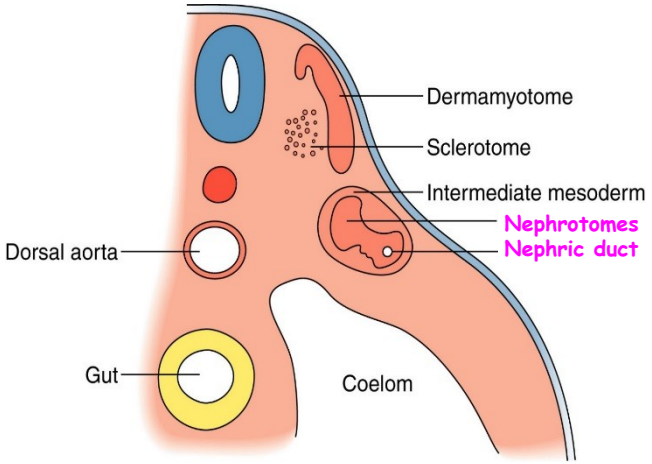


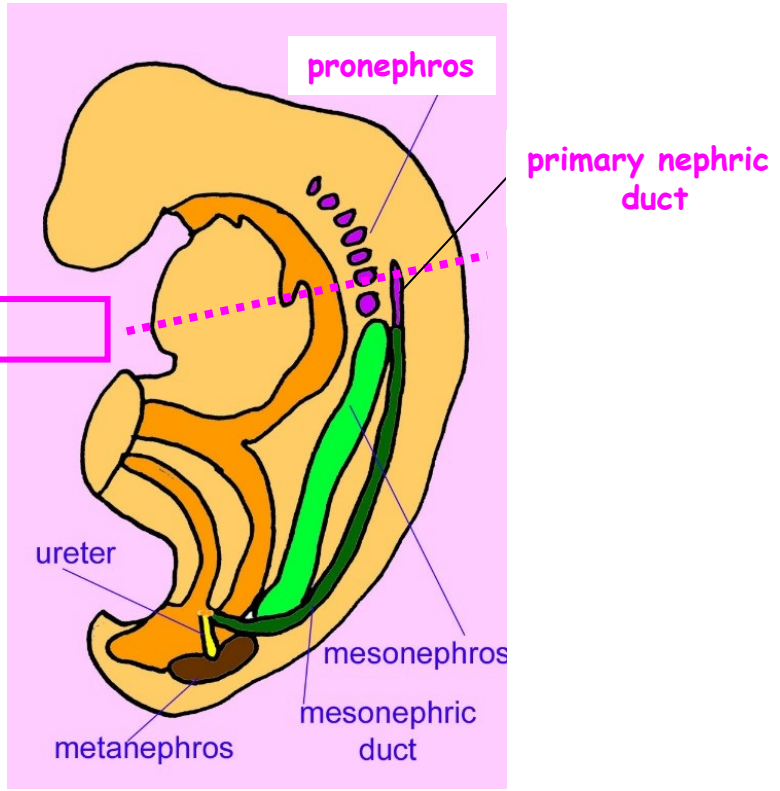


Urogenital system – Early forms of kidneys - Pronephros

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

- **pronephros**
- **mesonephros**
- **metanephros**



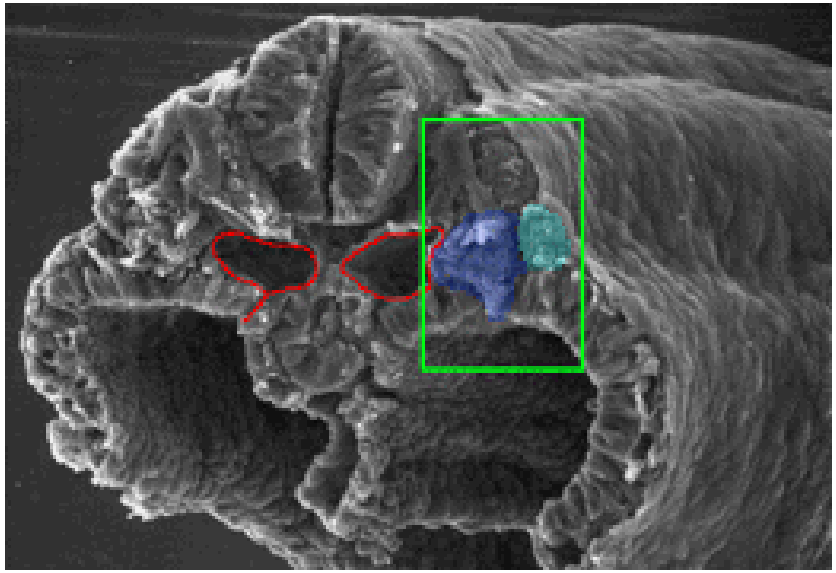


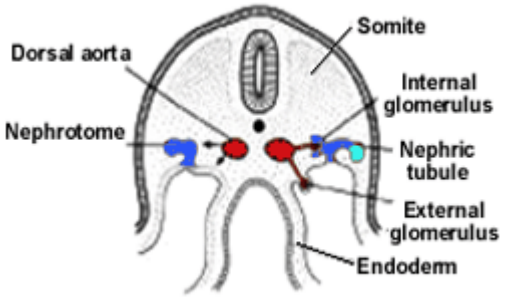
Nephrotomes

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

Urogenital system – Early forms of kidneys - Pronephros

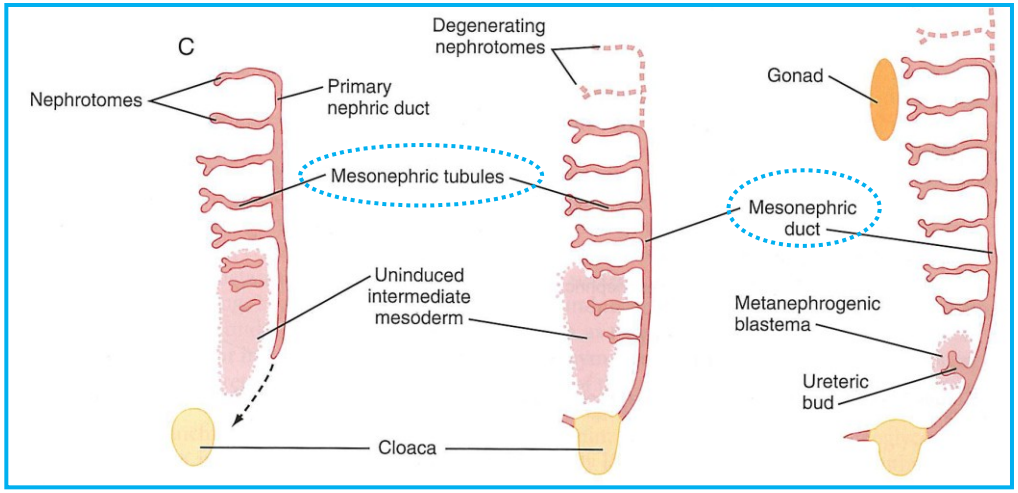
Mouse D9 – equivalent to human D27

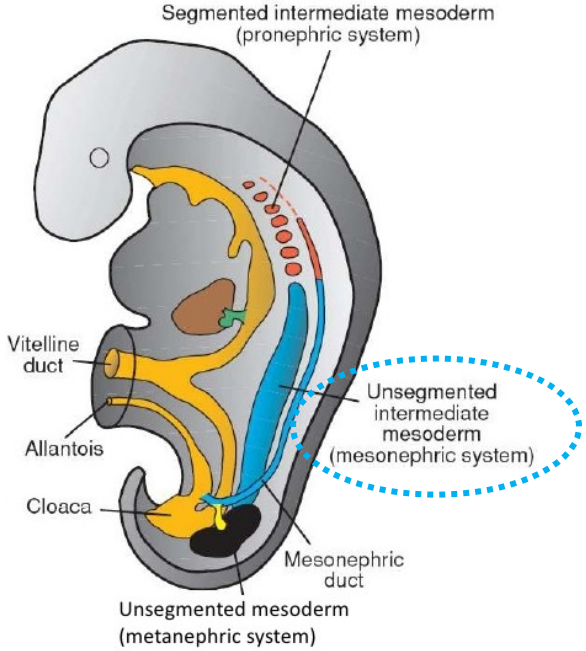




The lumen of each nephrotome opens into the primary nephric duct as well as into the body cavity. Glomeruli form as small vessels extend from the dorsal aortae.

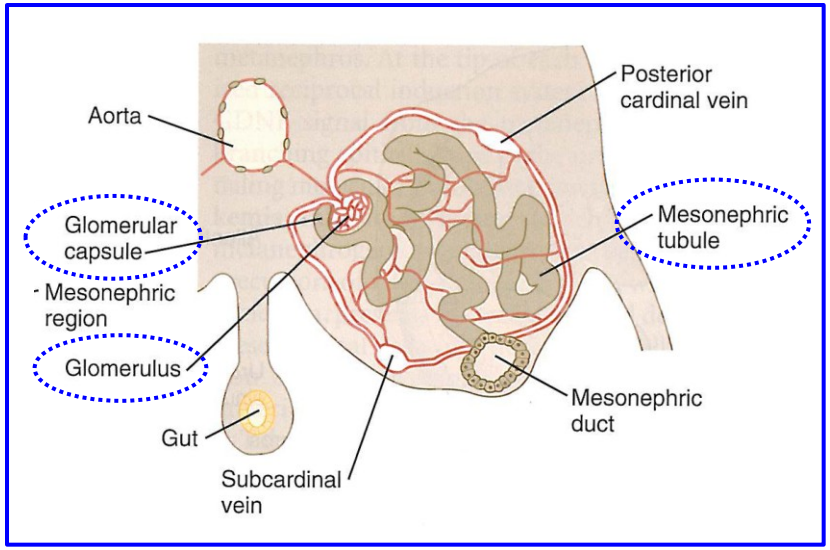
Urogenital system – Early forms of kidneys - Mesonephros



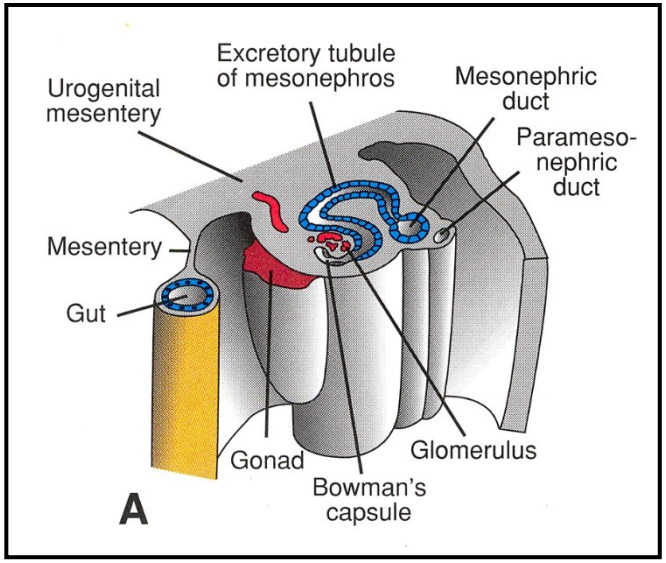


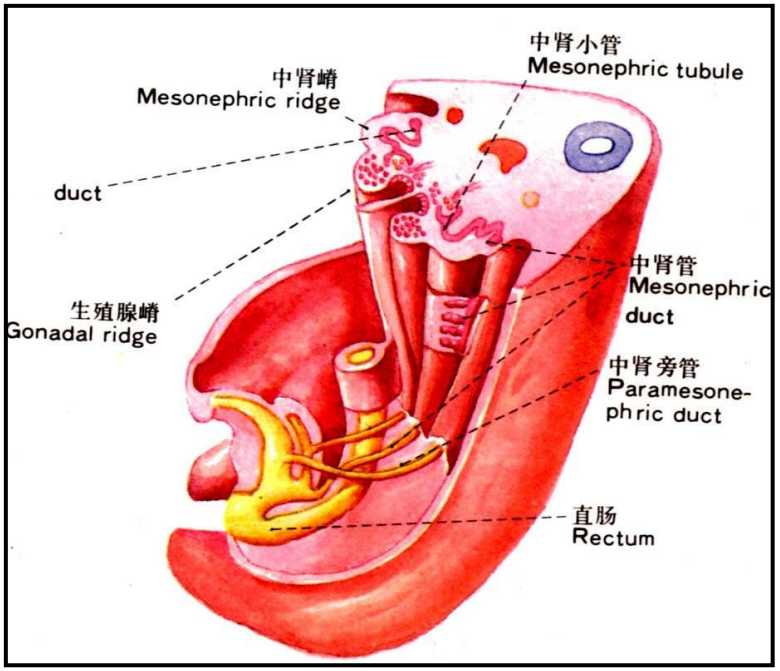
Mesonephros

- 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
- then they diasappear fast
- mesonephric ducts persist in males

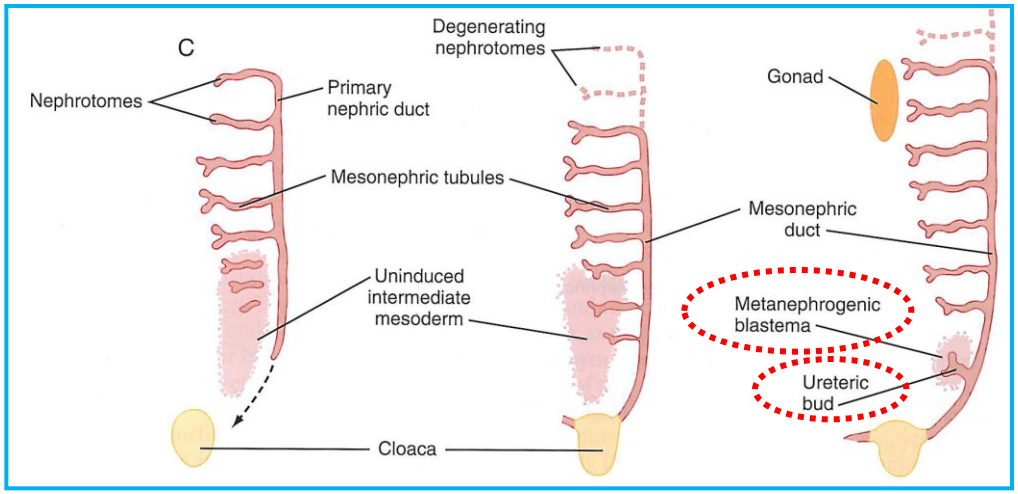


Urogenital system – Mesonephros - Another view





Urogenital system – Definitive kidneys - Metanephros

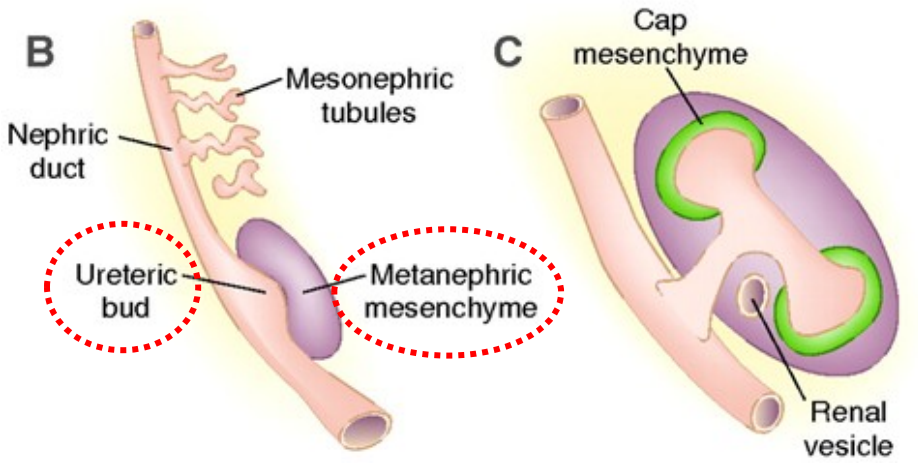


Develop since week 5

Ureteric bud = metanefric diverticulum

+

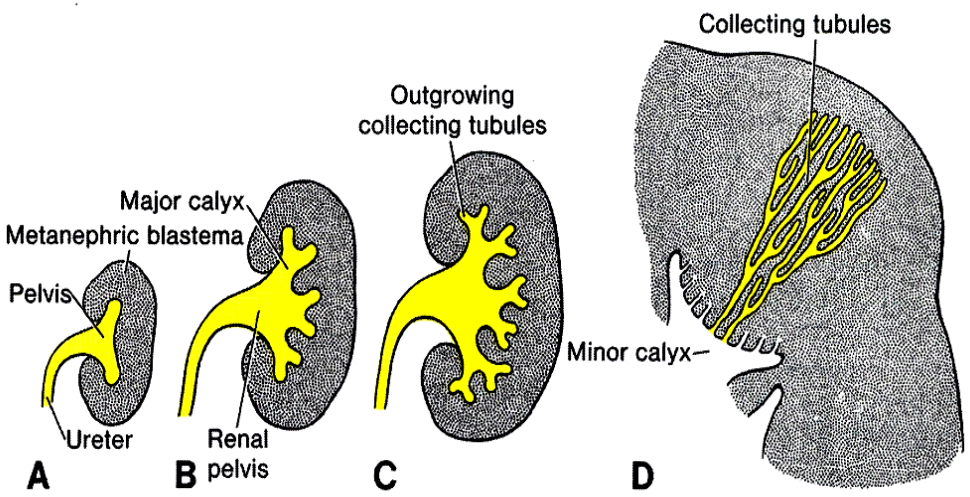
Metanephrogenic blastema (mesenchyme)



Branching and Elongation

14 to 15 x

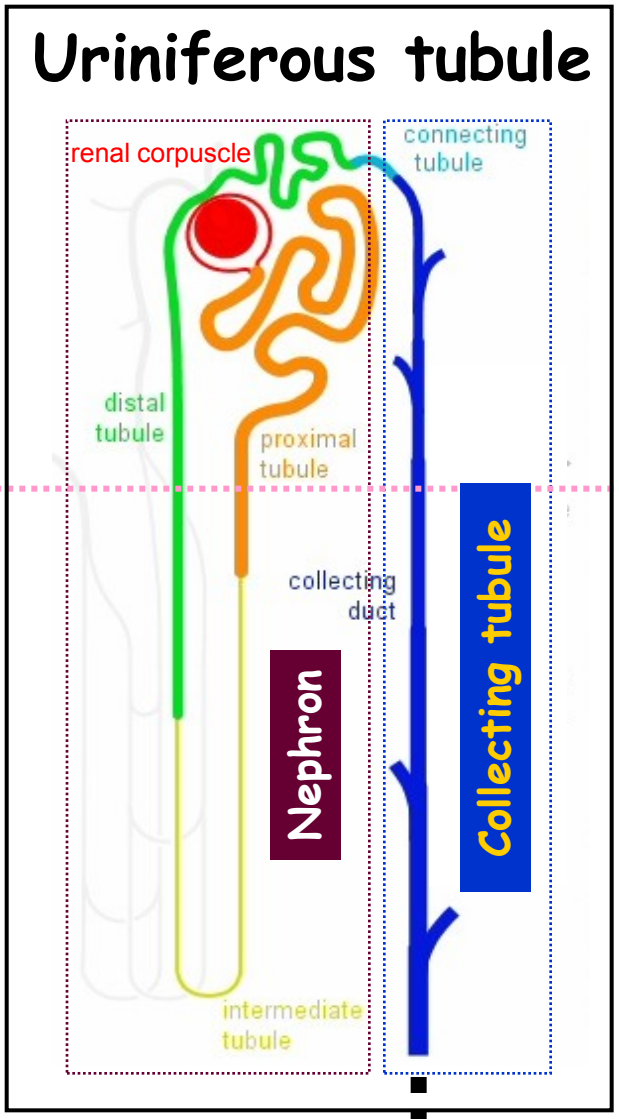
Urogenital system – Definitive kidneys - Metanephros



Repeated branching of ureteric bud produces:

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

Uriniferous tubule = The functional unit of the kidney



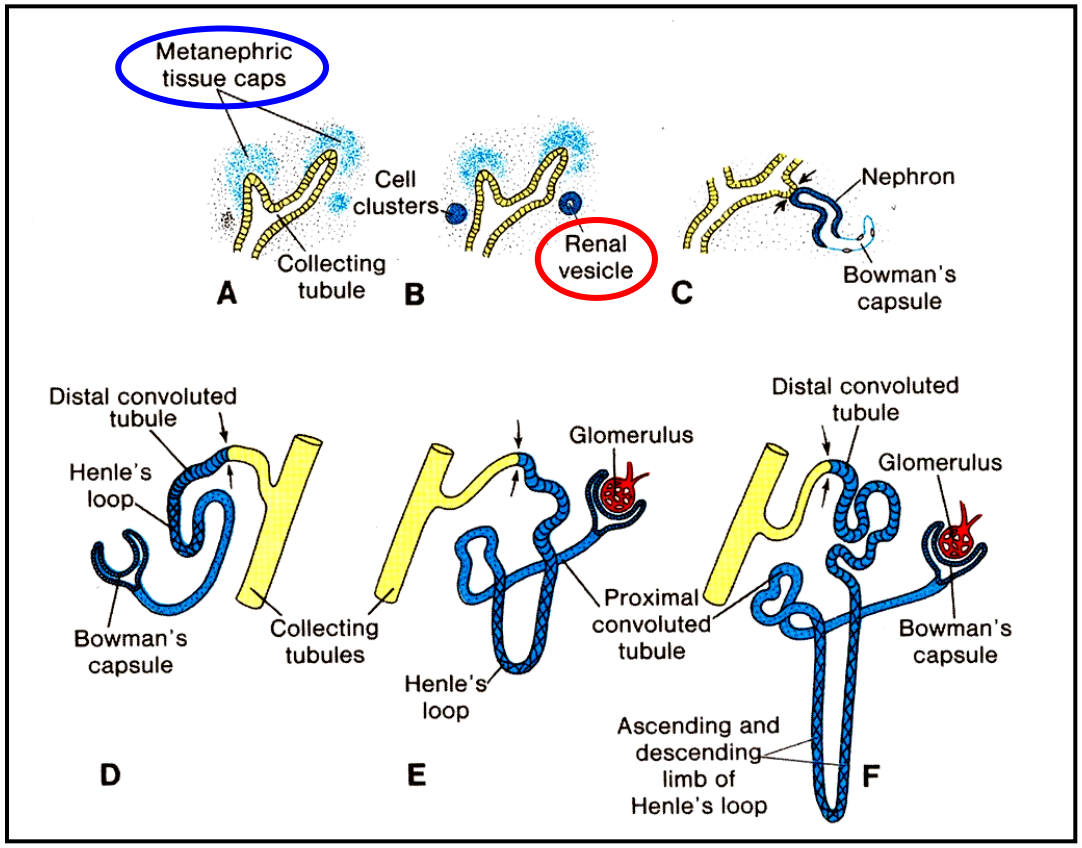
1 to 1.4 milllions of nephrons in one kidney

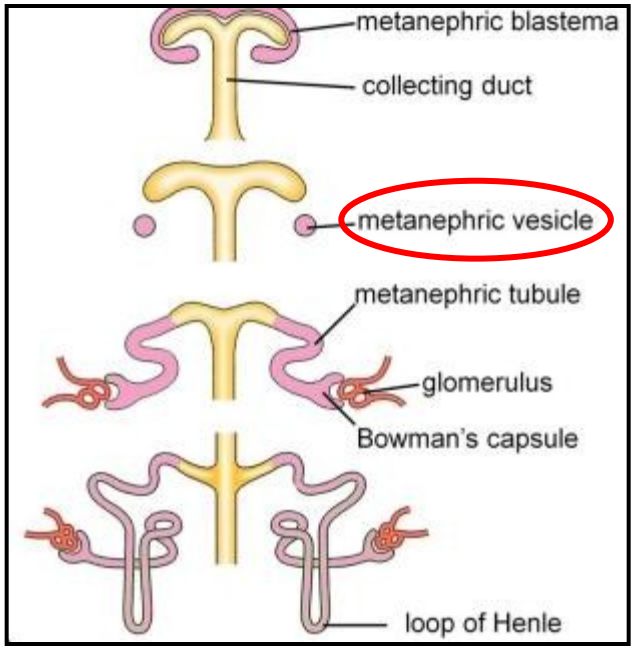
Area cribrosa

Minor calyx

Nephrons X Collecting tubules
Different embryological origin

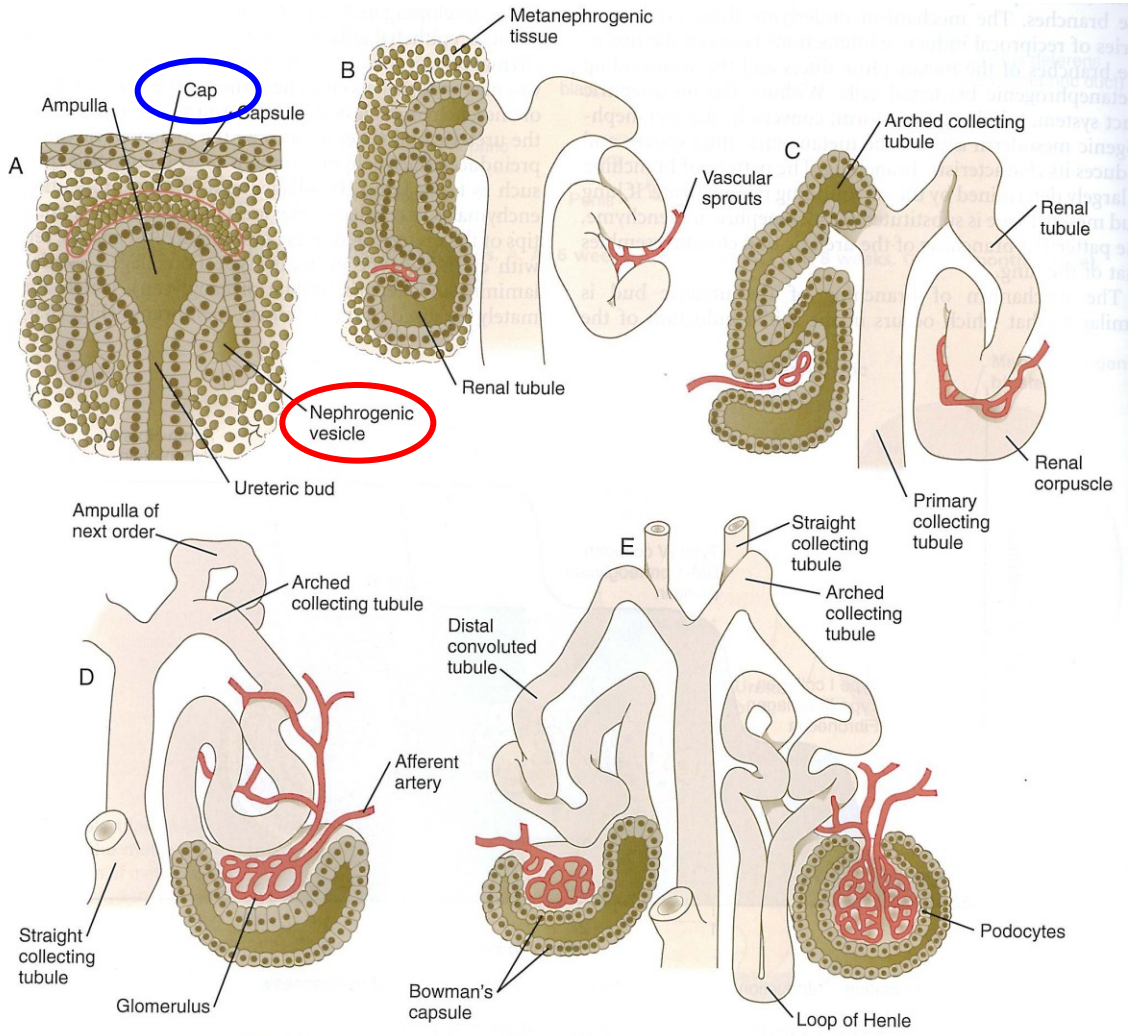
Urogenital system – Metanephros - Nephrons



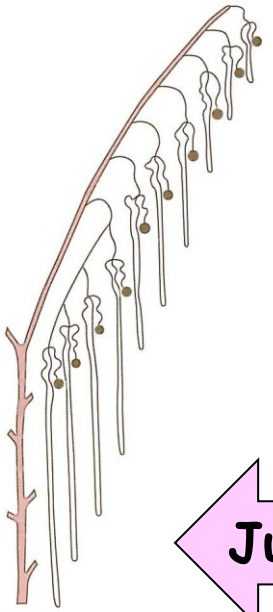


- arched ampulous endings of ureteric ducts (collecting tubuli) – **capping** by condensed mesenchyme
- part of the cap cells differentiate into **nephrogenic vesicle**
- vesicles elongate
- vesicles open to the collecting tubulus on one end
- distal from the ducts, the cells of elongating vesicles polarize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

Urogenital system – Metanephros - Nephrons



Urogenital system – Metanephros - Nephrons



Cortical nephrons

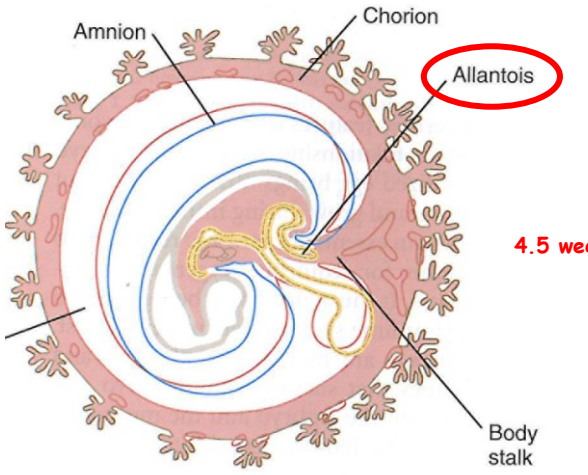
Juxtamedulary nephrons

- about **15 successive generations of nephrons** in peripheral zone of kidney
- outermost nephrons are **less mature**

Urogenital system – Definitive kidneys - Metanephros

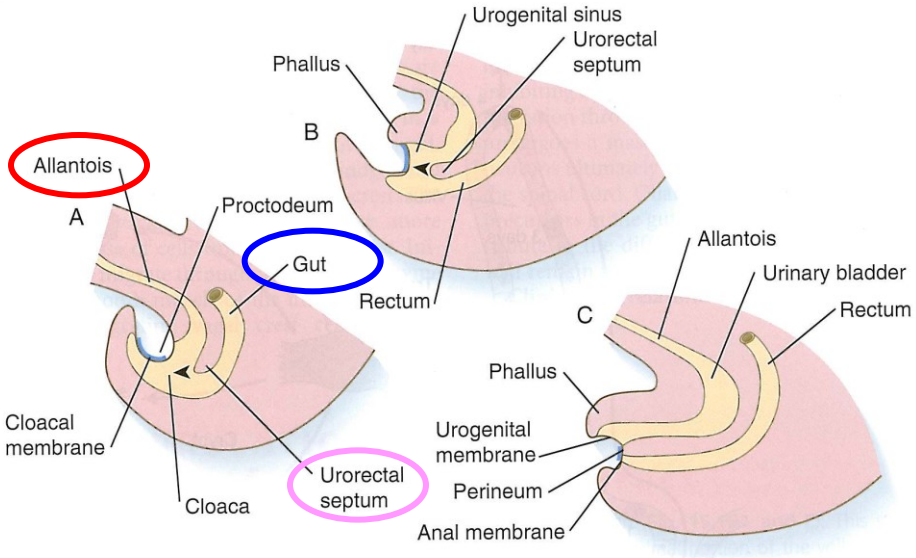
Urinary system - Bladder

Cloaca
=
terminal part of the hindgut + allantois



4.5 weeks

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



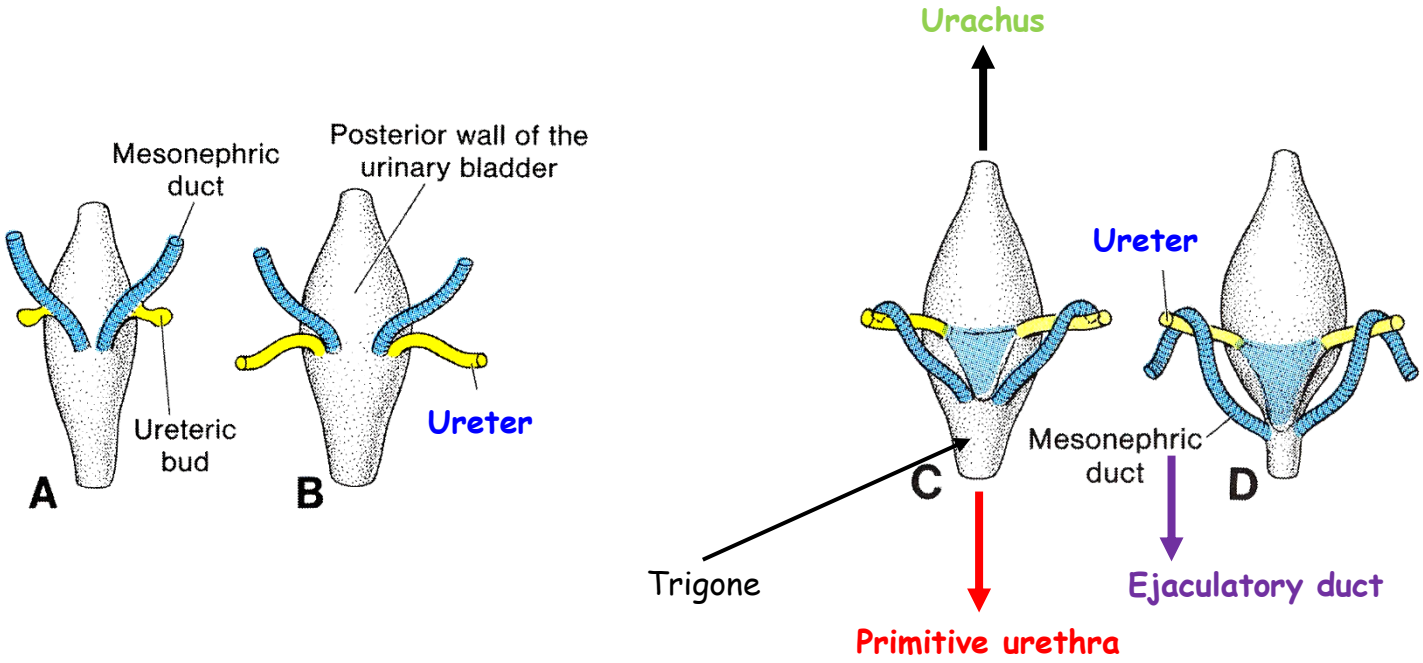
5 weeks **6 weeks** **8 weeks**

Cloaca

Urogenital simus	Urogenital membrane
Urogenital septum	Perineum
Primitive rectum	Anal membrane

Urinary system – Bladder + Ureters + Urethra

Posterior view



- alantois expands - urinary bladder
- initially bladder is continuos with alanotois – then obliteration – urachus – median umbilical ligament
- caudal portions of mesonepric ducts become absorbed by the bladder wall – separation – ureters + ejaculatory ducts

Urinary system – Congenital anomalies

1. Agenesis
2. Duplication
3. Anomalies of shape
4. Abnormal of position
5. Congenital polycystic kidney

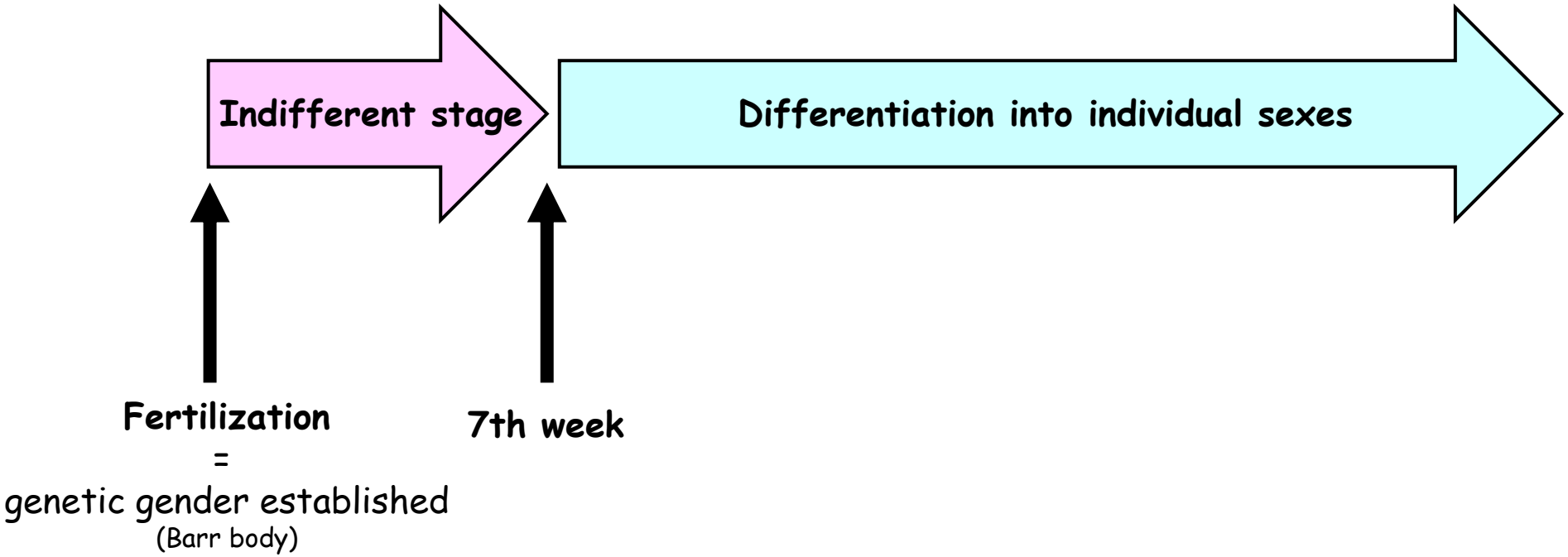
Horseshoe kidney

Genital system

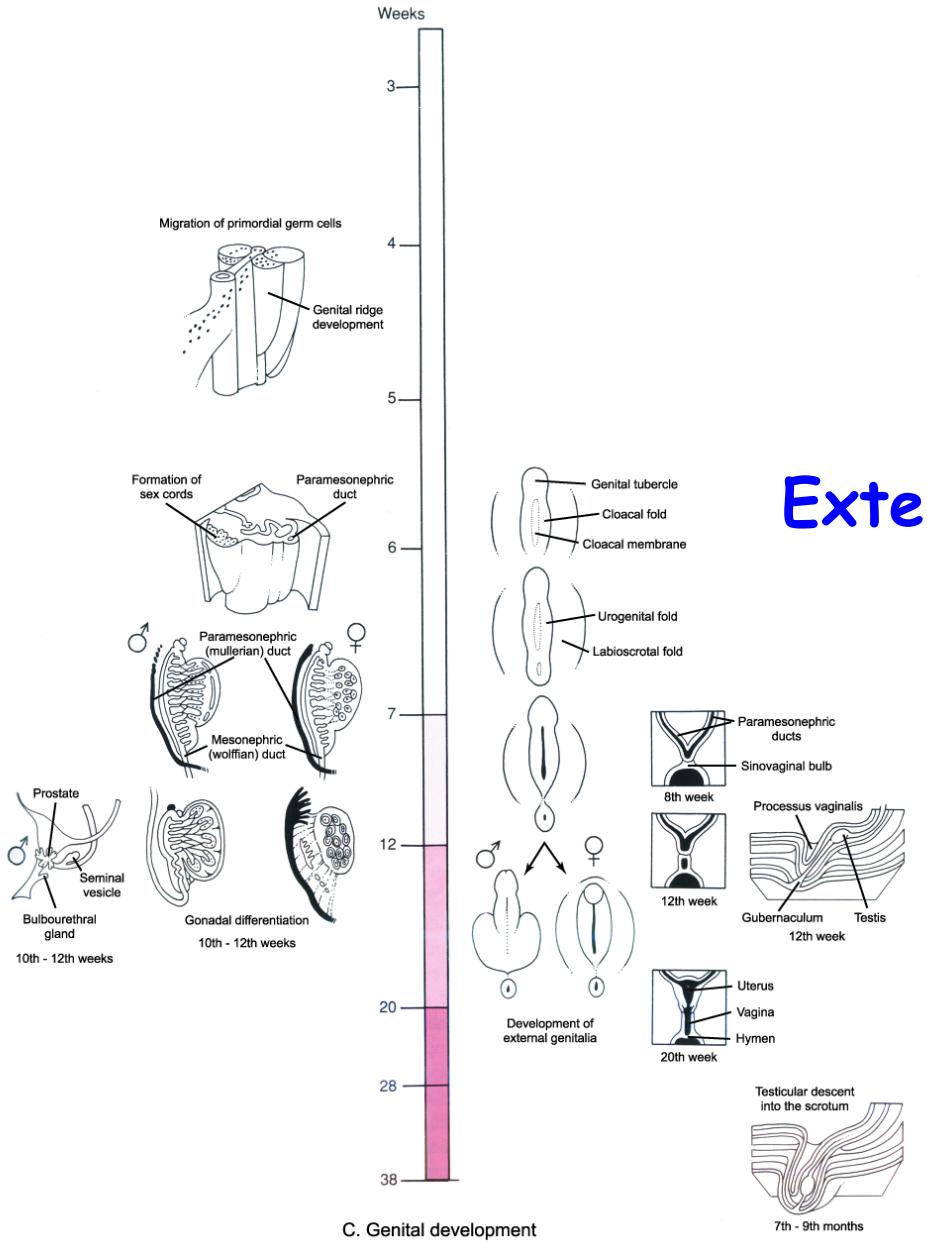
Sexual dimorfism – individual can only have one type of genital organs

Genetic determination:

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



Genital system – 7 weeks at indifferent stage



C. Genital development

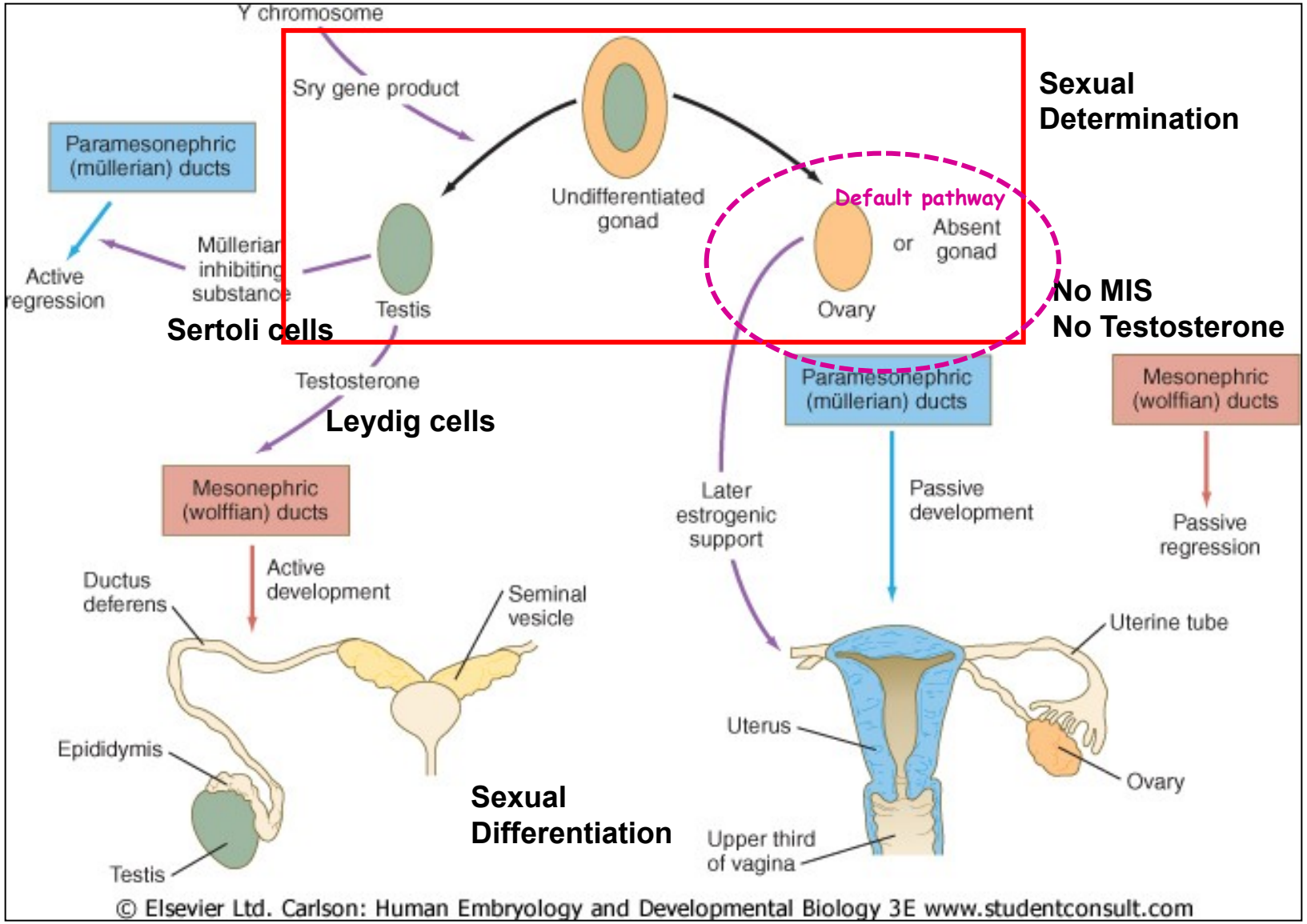
Gonads

External genitalia

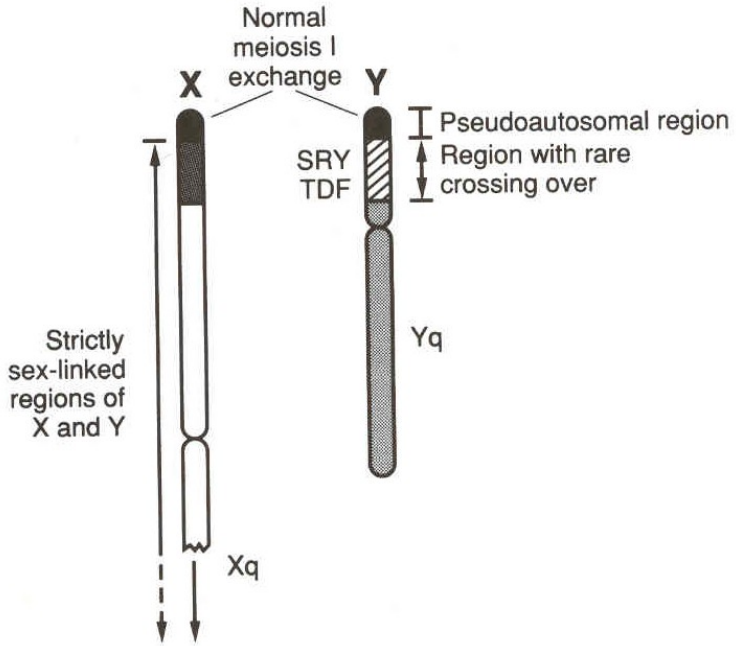
Genital system – Sry gene

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

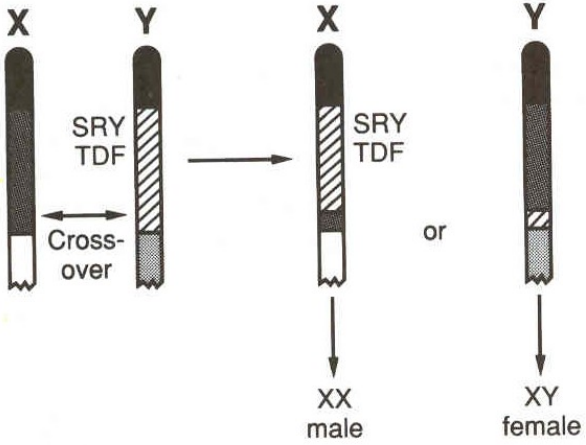
Y chromosome decides
XXY – male
XO – female



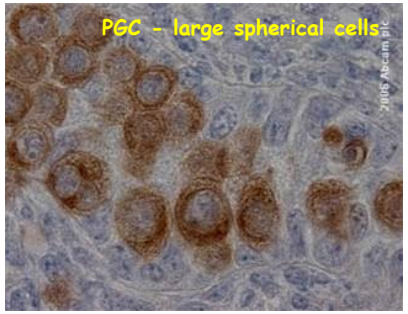
Genital system – Sry gene



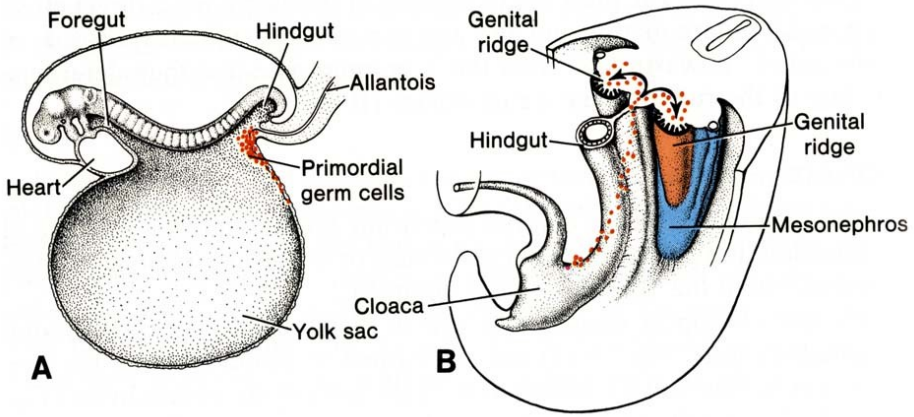
Pairing of X and Y chromosomes in pseudoautosomal region during meiosis

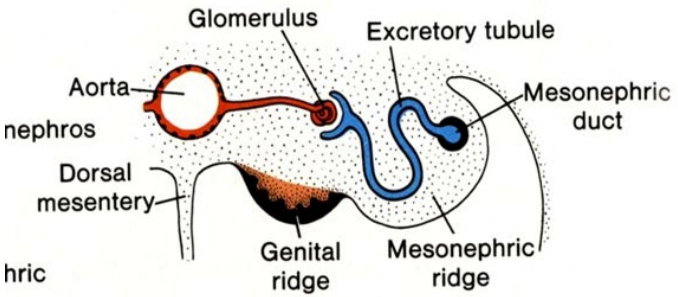


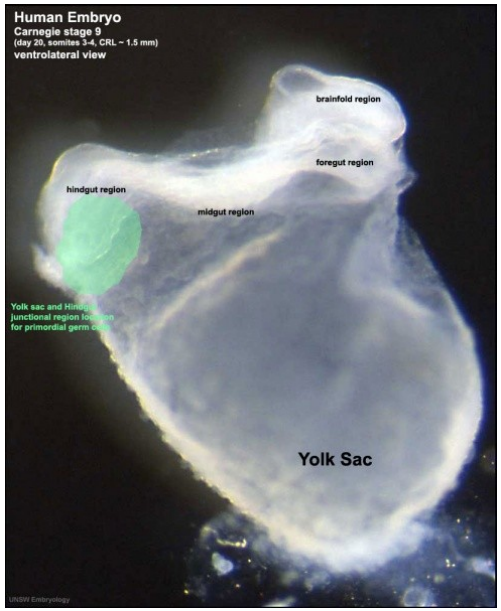
Rare crossing-over causes translocation of SRY to X chromosome:
XY females or XX males



Genital system – Primordial germ cells







Primordial germ cells (PGC)

- first recognizable at day 24
- from epiblast-derived extraembryonic msoderm
- few cells among endodermal cells of the yolk sac
- they migrate through the dorsal mesentery of the hindgut
- migrate towards genital rigdes (plicae genitales)
- proliferate during migration
- reach (1-2 thousands) genital ridges on week 6 of gestation

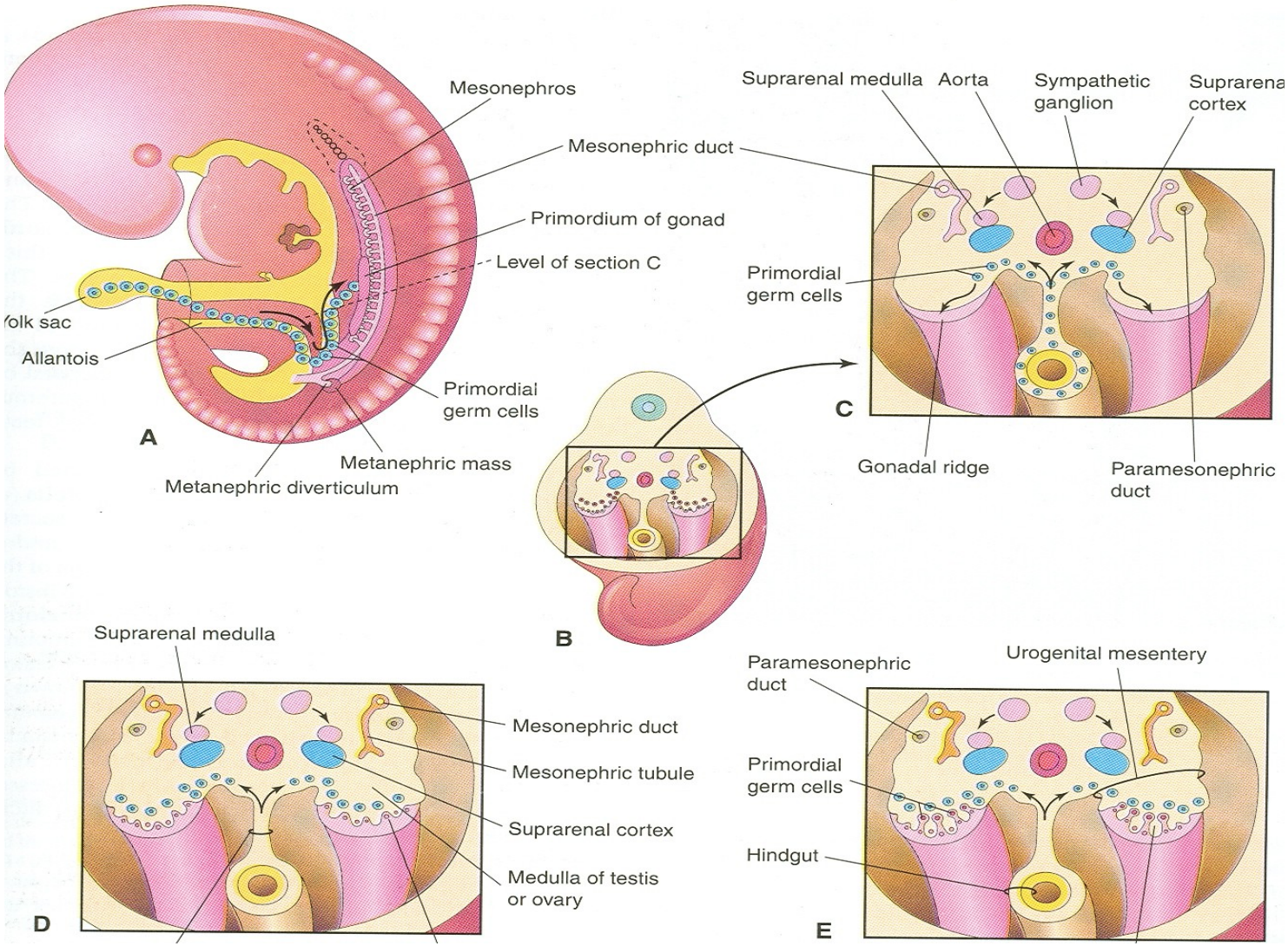
Males
PGC stop dividing

X

Females
PGC enter meiosis

decided by somatic cells in the genital ridges

Genital system – migration of PGC into gonadal anlagen



Genital system – gonadal anlagen

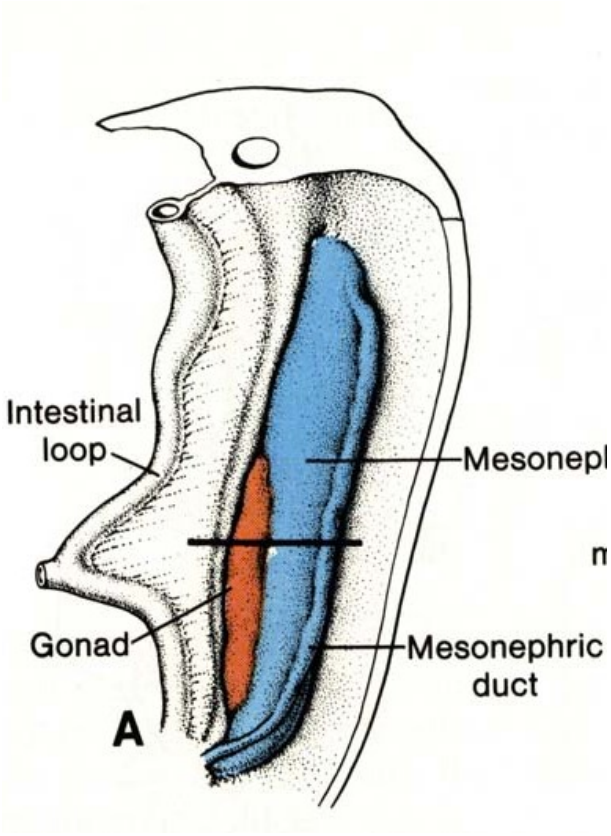
Steroidogenic mesoderm
along the ventromedial border of the mesonephros

cranial region
Adrenocortical primordia

caudal region
=
Genital ridges

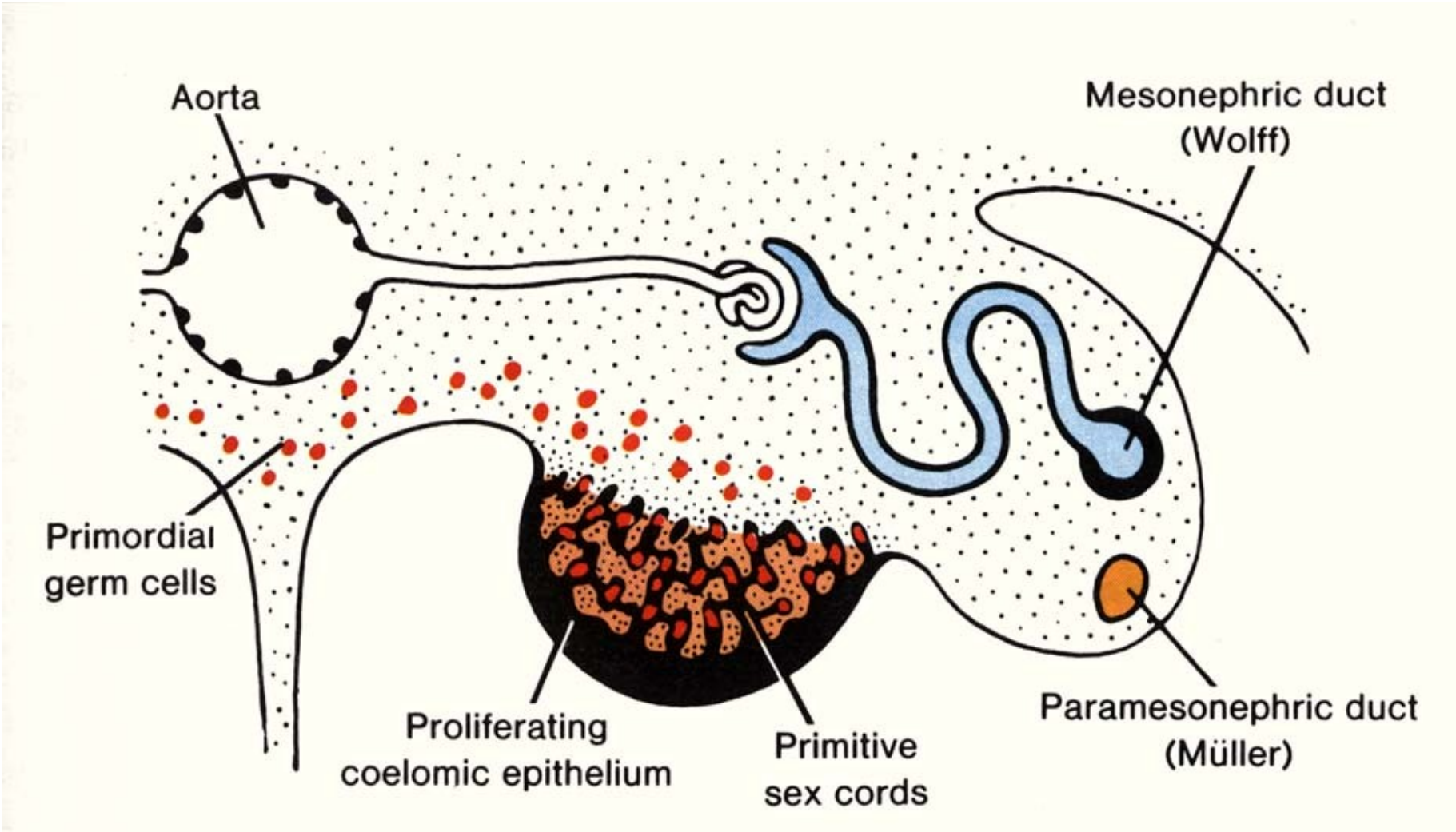
cells of **coelomic epithelium**
+
cells from **mesonephric ridge**

Week 4 – Th6 to S2
ranial + caudal parts involute
Week 6 – L3 to L5



become populated by PGC at week 6

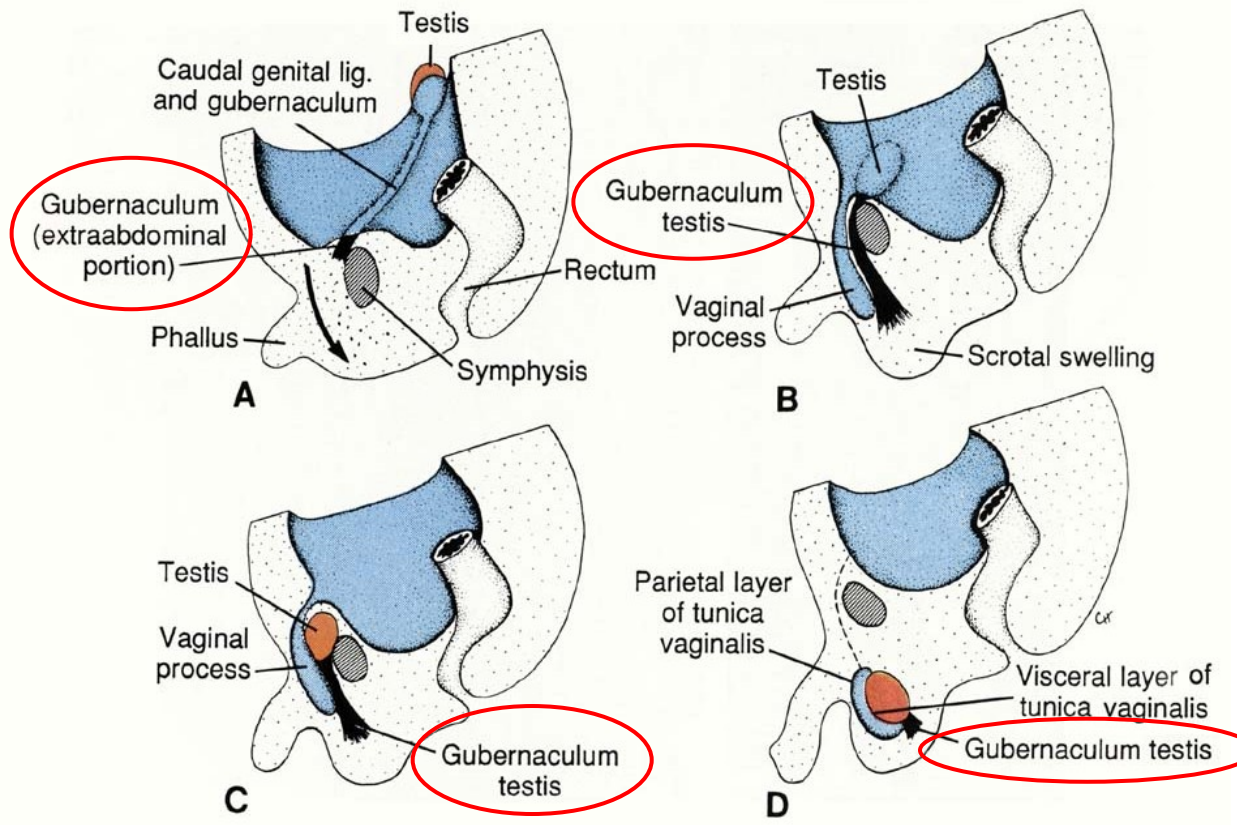
Genital system – indifferent gonade (week 6)



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

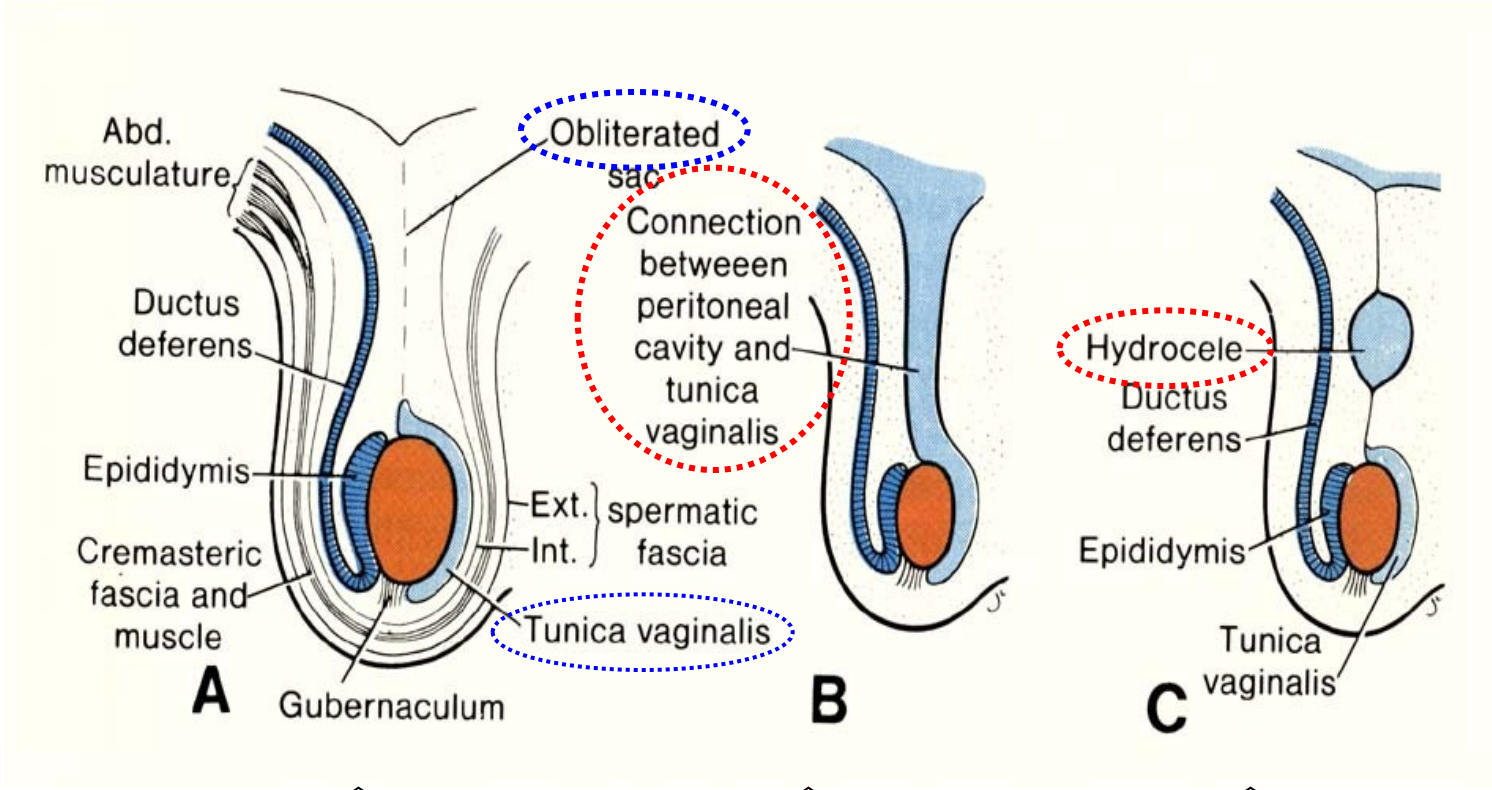
More than 97% of full-term newborn males have both testes in the scrotum

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

Remanining connection

ABNORMAL

Remaing cyst = Hydrocele

ABNORMAL

Genital system – Differentiation of the testes

Late 6th week

Cord cells differentiate to Sertoli cells
(meiosis-inhibiting factor, anti-mullerian substance, androgen binding factor)

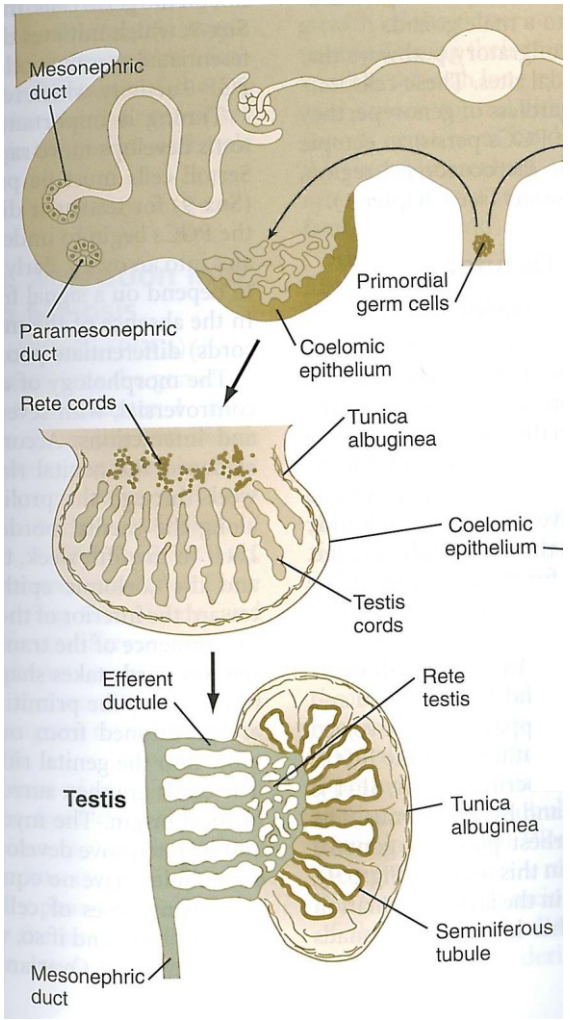
Tunica albuginea develops
(sets barrier between coelomic epithelium and testis cords)

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

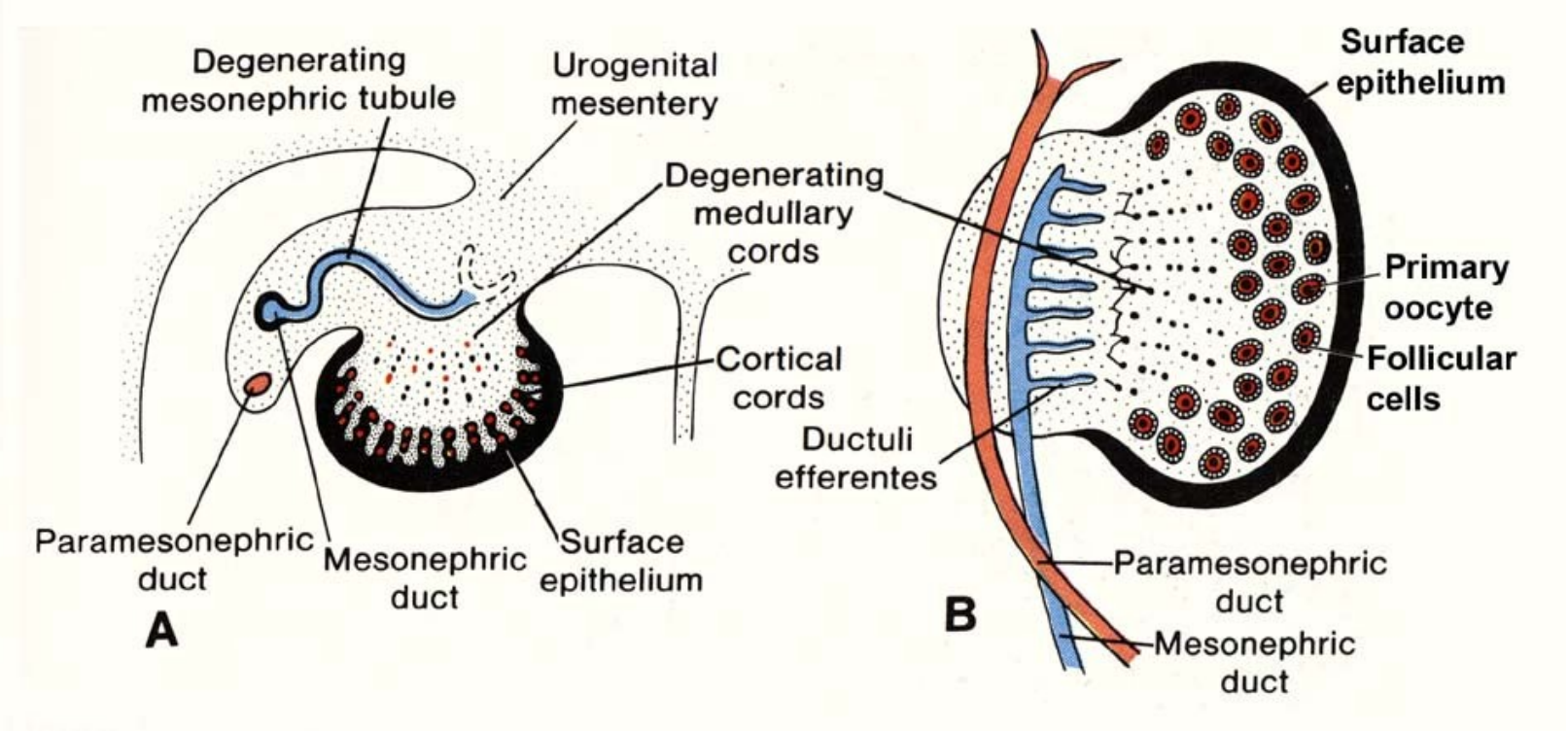
Rete testis joints ductli efferentes that are derived from mesonephric ducts
(5th to 12th)

Week 8 to 18

Leydig cells develop and function in developing testis
- from coelomic epithelia and mesonphros
- produce testosteron
- support development of Wolfian (mesonephric) duct
- support development of external genitalia



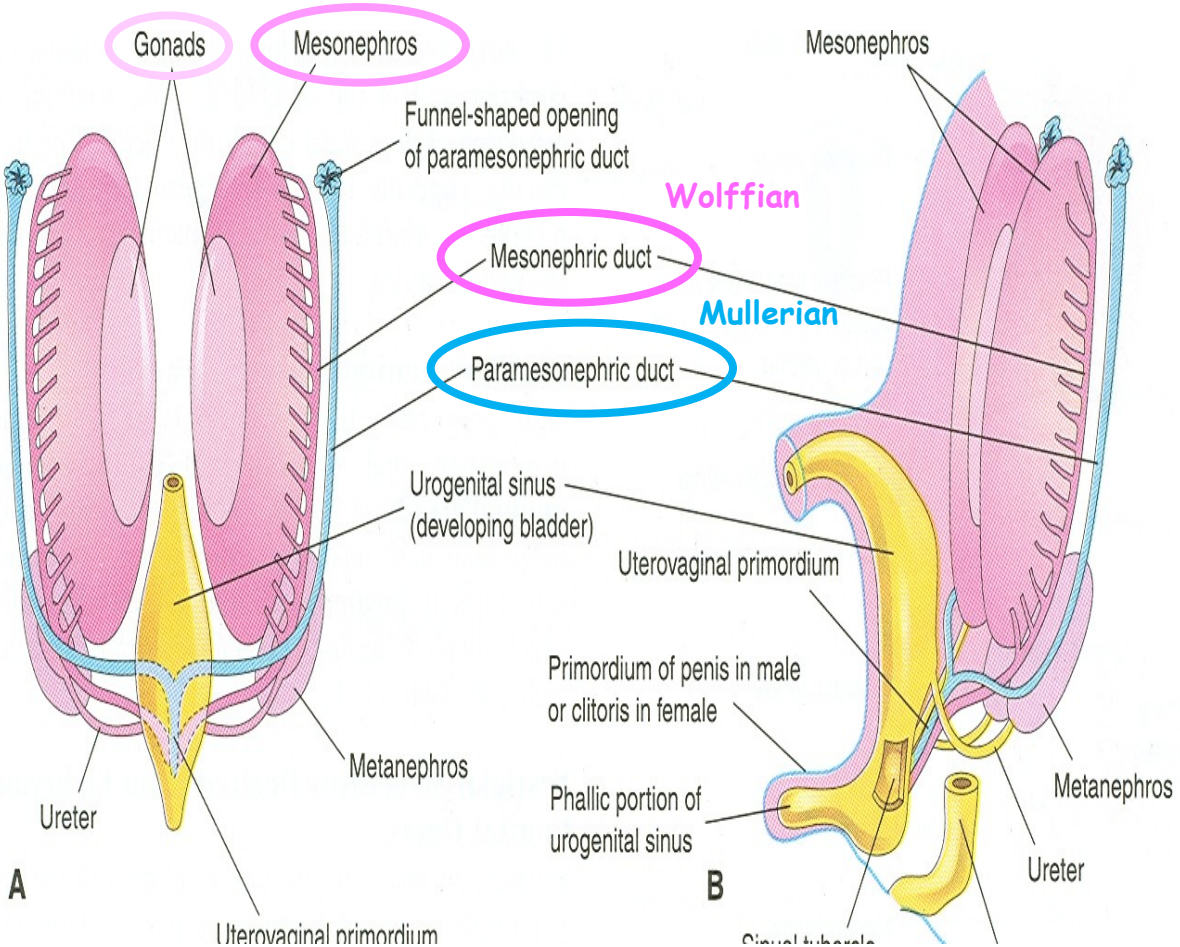
Genital system – Differentiation of the ovaries



- 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 connetive tissue and vasculature derived from mesonephros

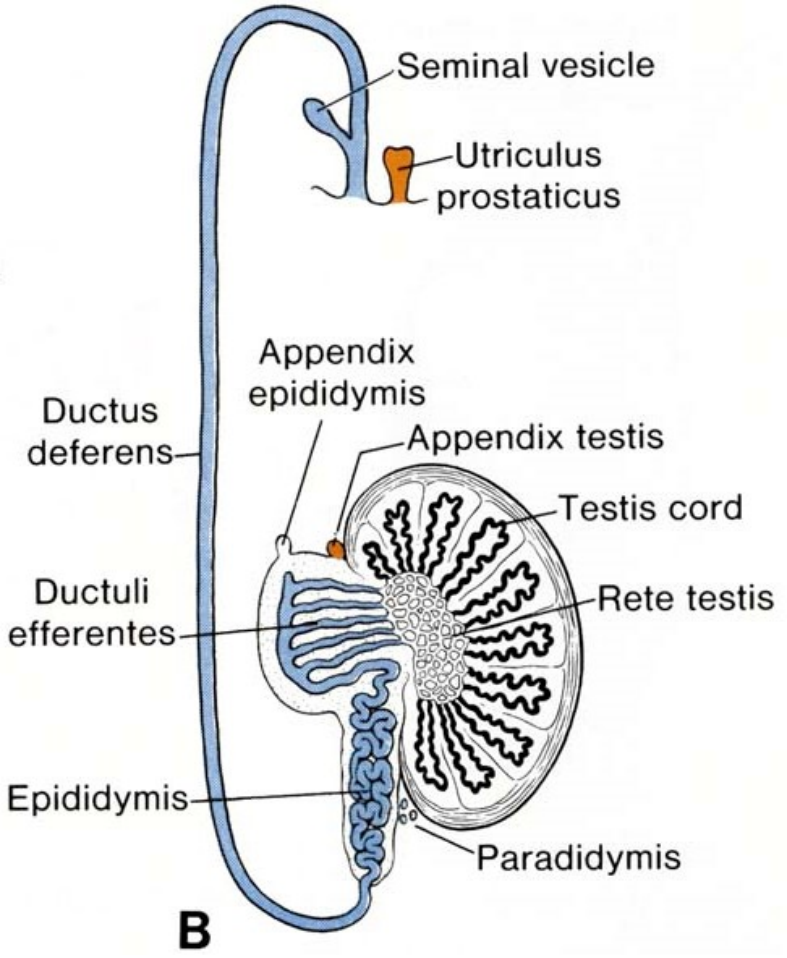
Genital system – Sexual duct system – Indifferent stage

Week 7



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

Genital system – Sexual duct system – Male

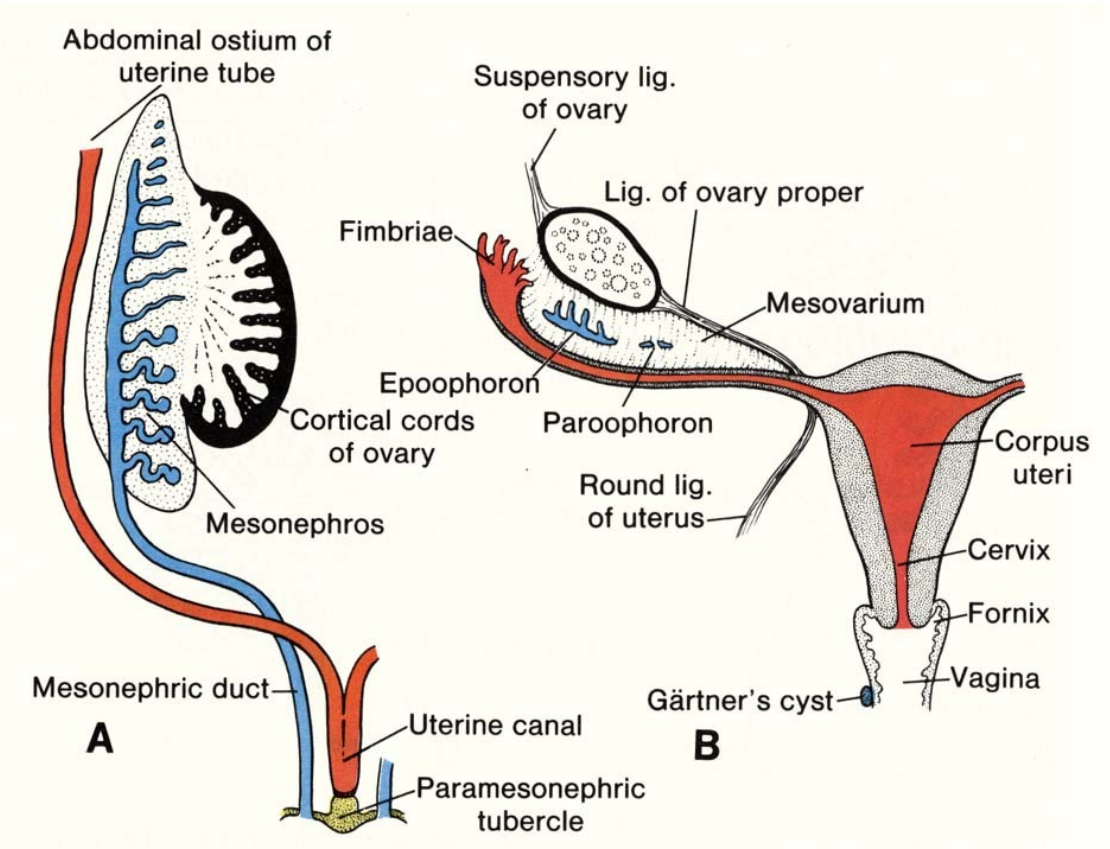


Mesonephric ducts (Wolffian)
- **Ductus epididymis**
- **Ductus deferens**
- **Ductus ejaculatorius**
- **Seminal vesicle**

Paramesonephric ducts (Mullerian)
regresses in week 8 (anti-M hormone)
- **Appendix testis** (cranial part)
- **Utriculus prostaticus** (caudal part)

Mesonephros
- **Ductuli efferentes**
- **Paradidymis** (under the testis, nonfunctional)

Genital system – Sexual duct system – Female



Mesonephric ducts (Wolffian)
regresses (absence of testosterone)
- **Gartners cyst** (caudal part)

Paramesonephric ducts (Mullerian)
involutes in week 8
- **Uterine tubes (falopian t.)**
- **Uterus**
- **Vagina**

Mesonephros (+Mesonephric duct)
- **Epoophoron** (appendix of ovary)
- **Paraophaoron**

Genital system – Sexual duct system – Uterus

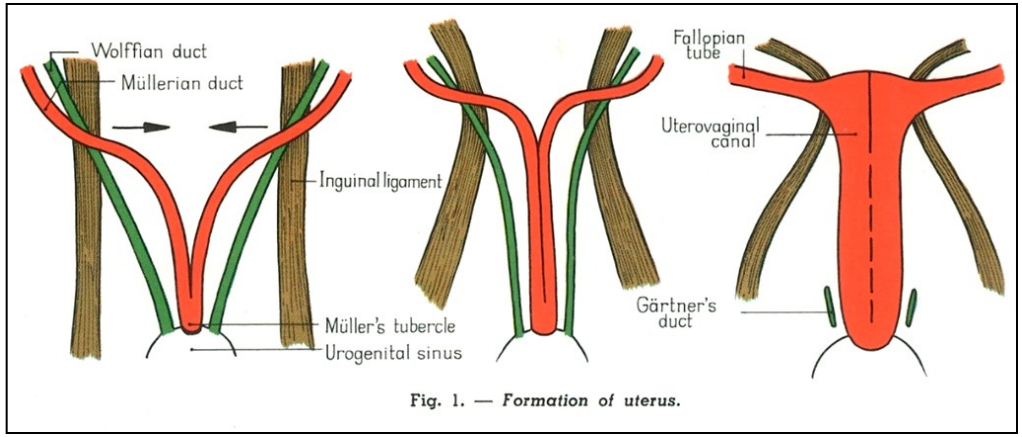
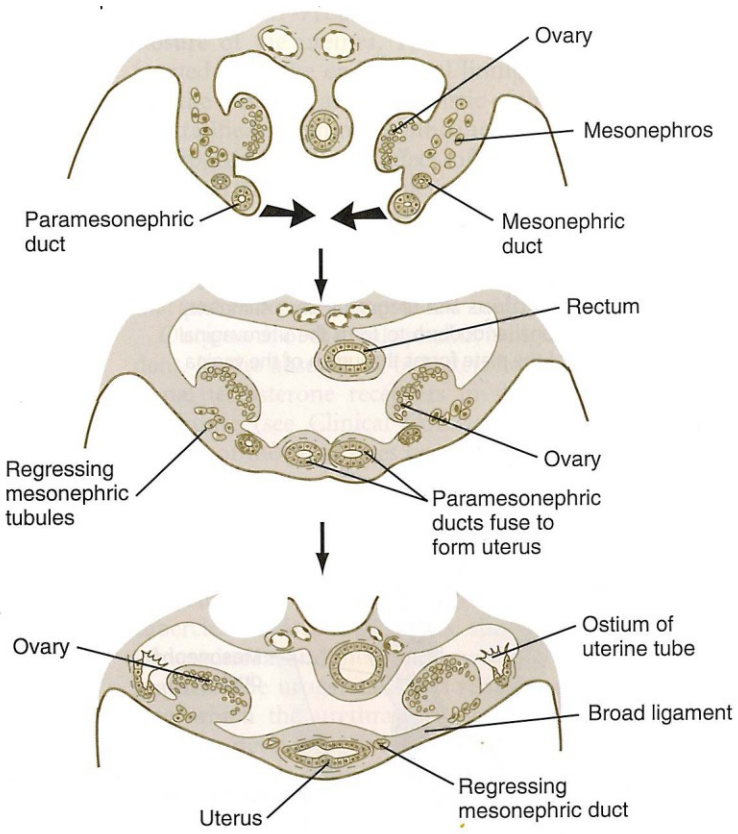
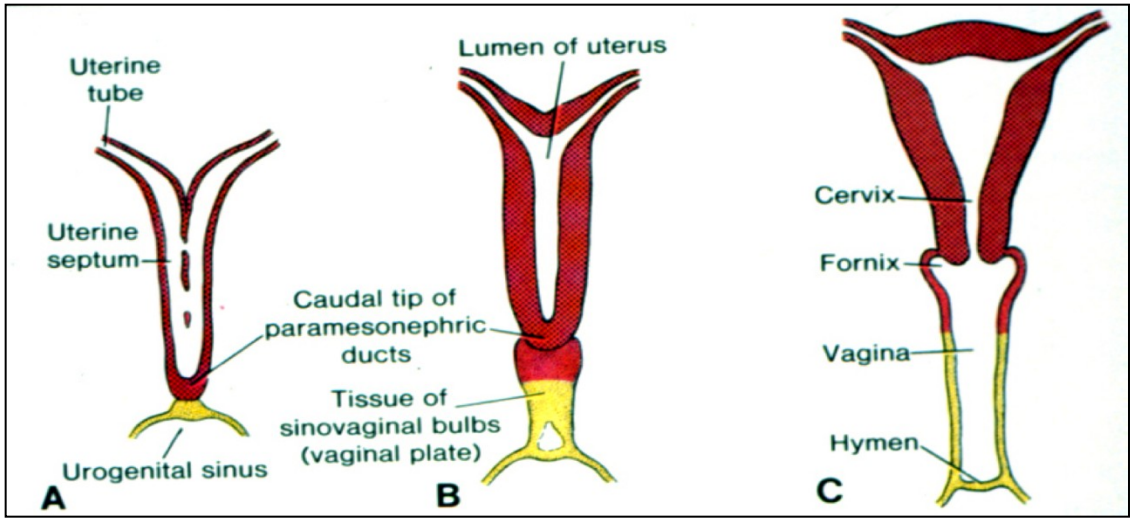


Fig. 1. — *Formation of uterus.*

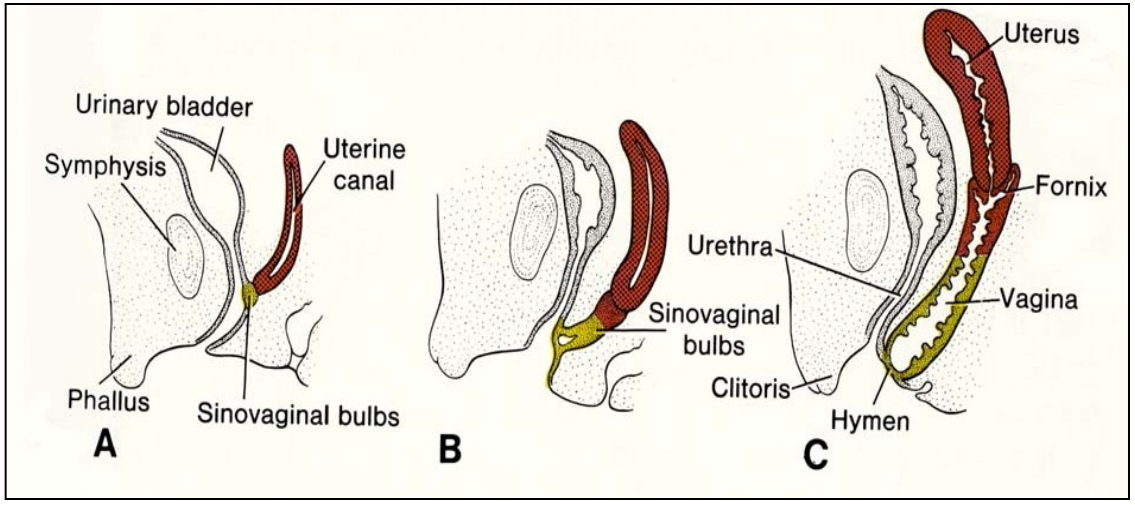


Genital system – Duct system – Uterovaginal channel

Dorsal view

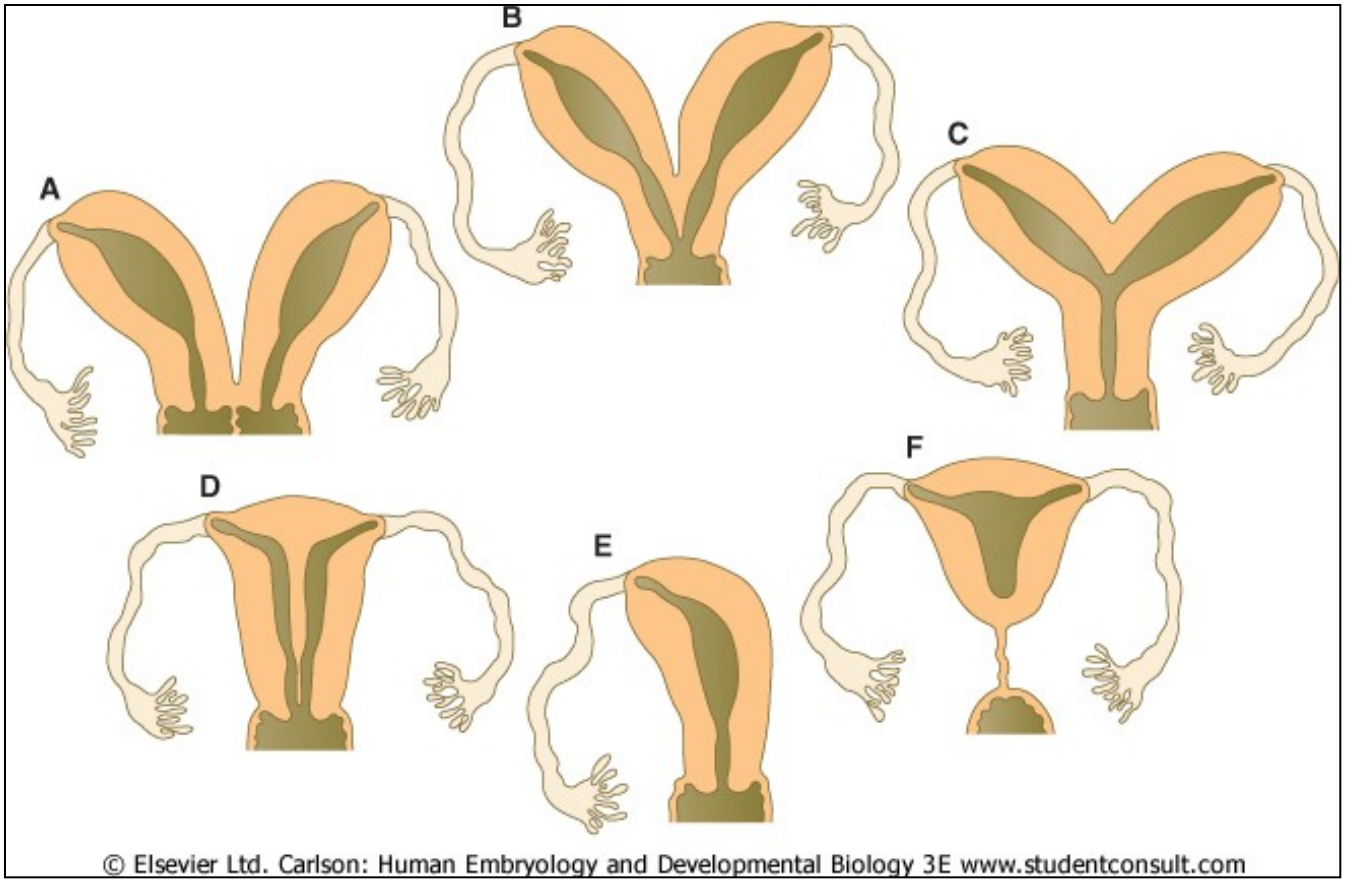


Lateral view



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

Genital system – Uterovaginal channel - Anomalies

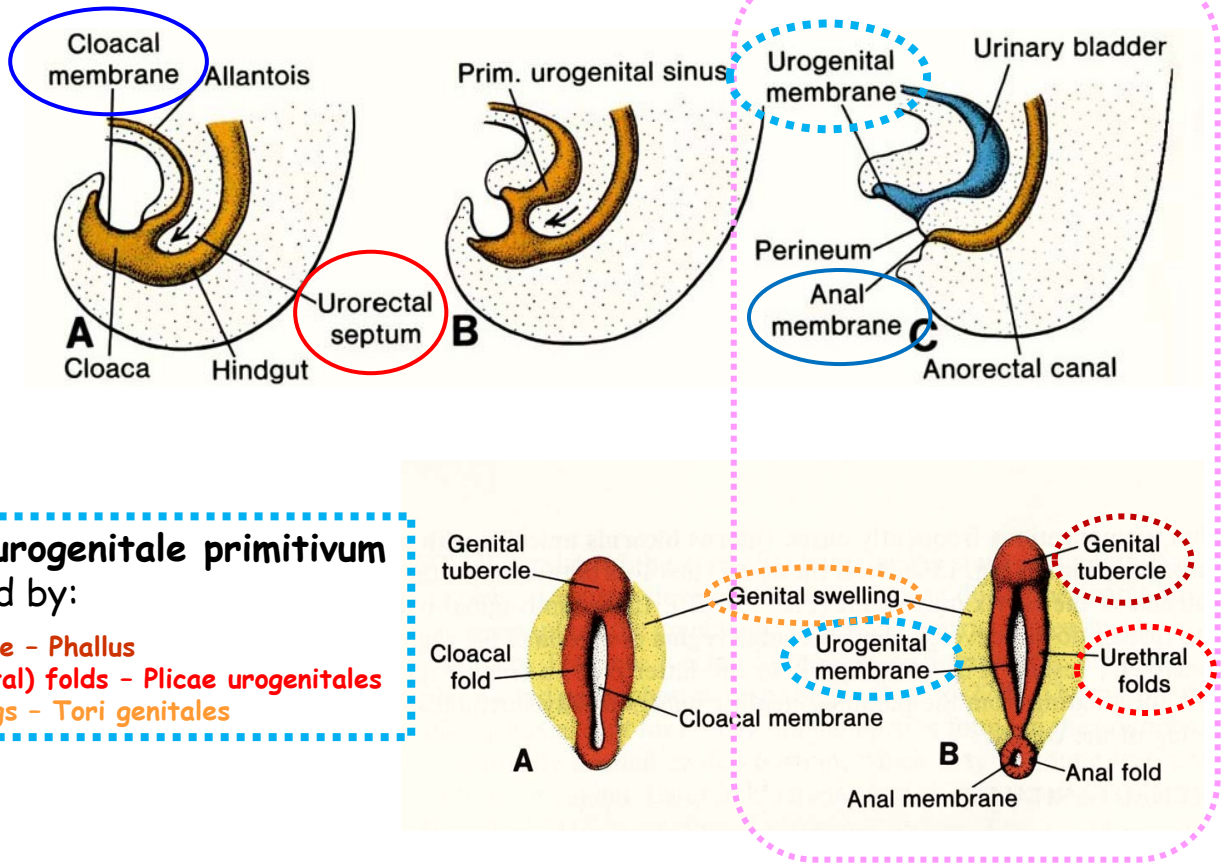


Genital system – External genitalia - Indifferent stage

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

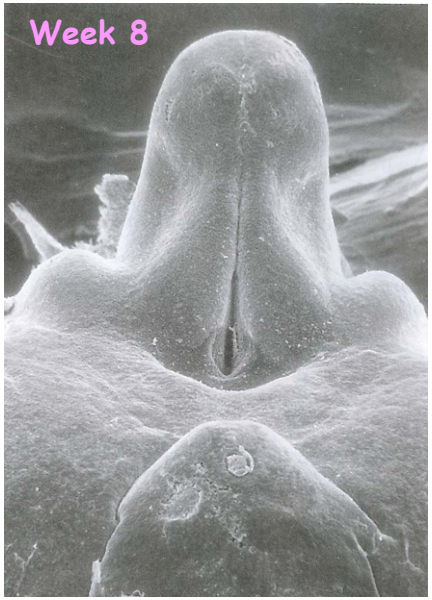
HORMONE-INDEPENDENT

Week 6 to 8

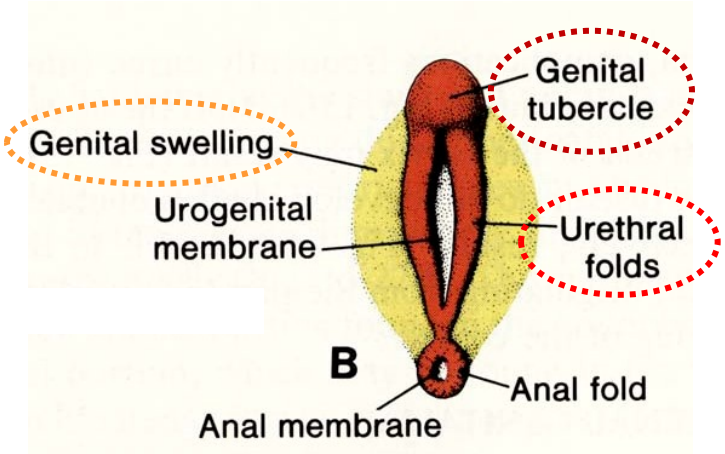


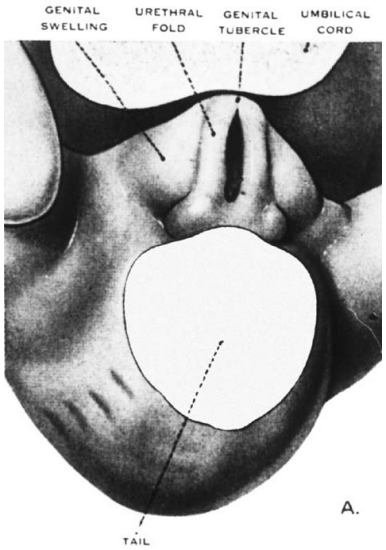
Orificium urogenitale primitivum demarcated by:

Genital tubercle – Phallus
Urethral (genital) folds – Plicae urogenitales
Genital swellings – Tori genitales



Genital system – External genitalia - Dimorphism





Week 9 to 13

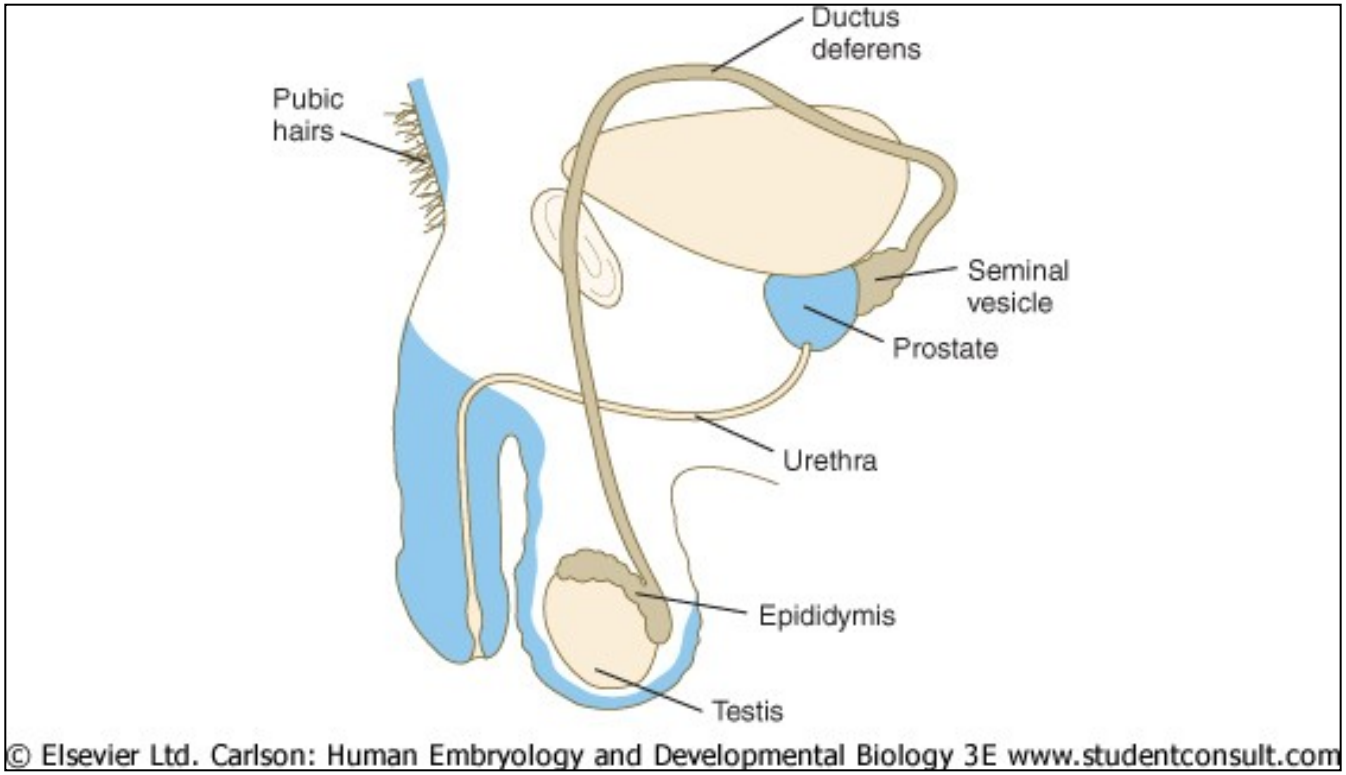
Weeks 12 + 13 are particularly critical
=
fusing of urethral folds

MALE		FEMALE
Penis	Genital tubercle	Clitoris
Urethra	Genital (urethral) folds	Labia minora
Scrotum	Genital swellings	Labia majora

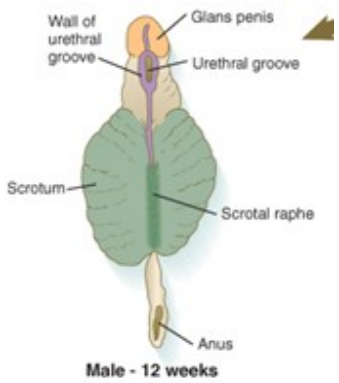
Genital system – External genitalia - Male

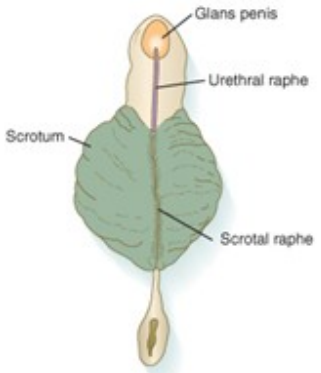
Influenced by dihydrotestosterone

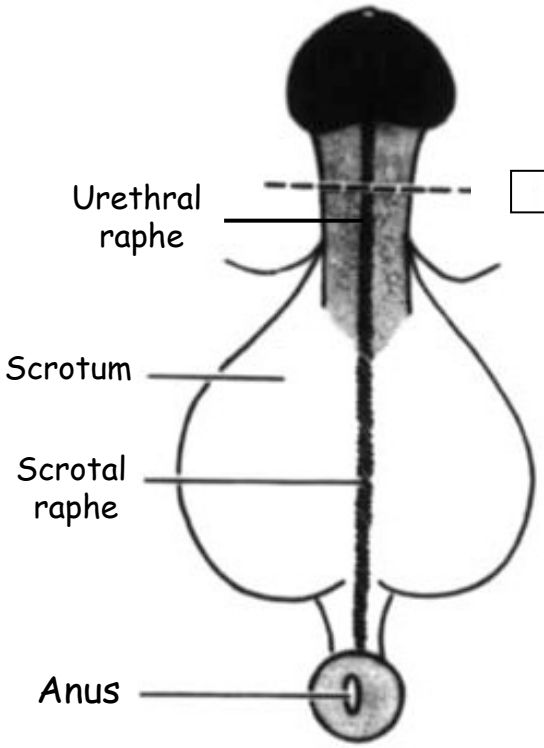
Influenced by testosterone

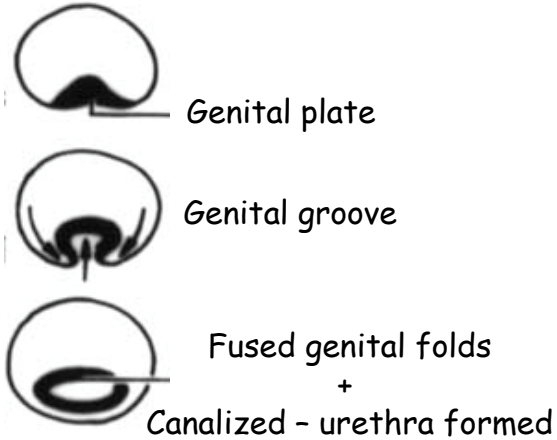


Genital system – External genitalia - Male









Genital tubercle elongates – penis (phallus)

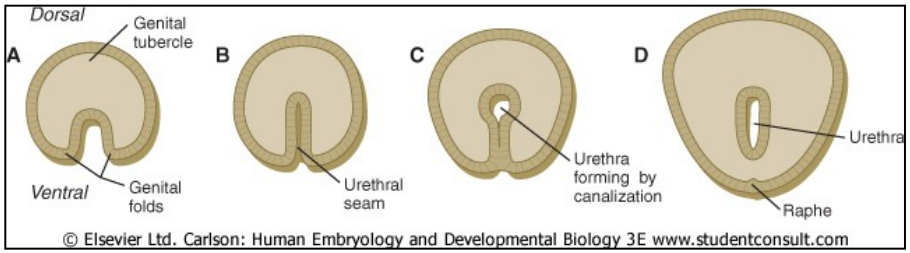
Genital swellings enlarge – scrotum

Genital folds form the lateral walls of the urethral groove

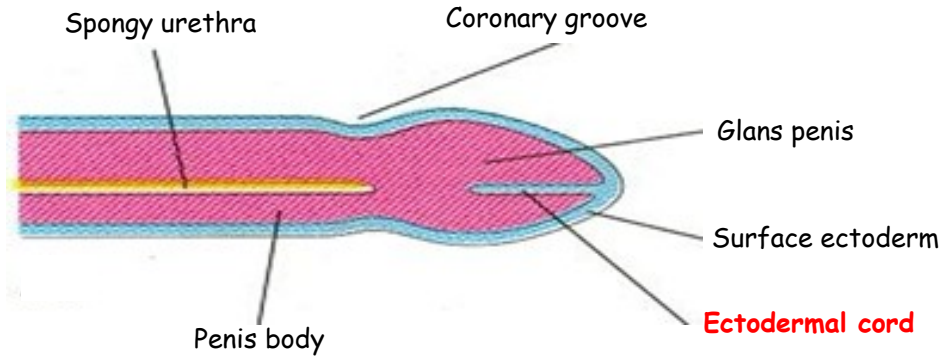
Genital folds form the spongy urethra

Ventral epithelium of genital folds – urethra proper

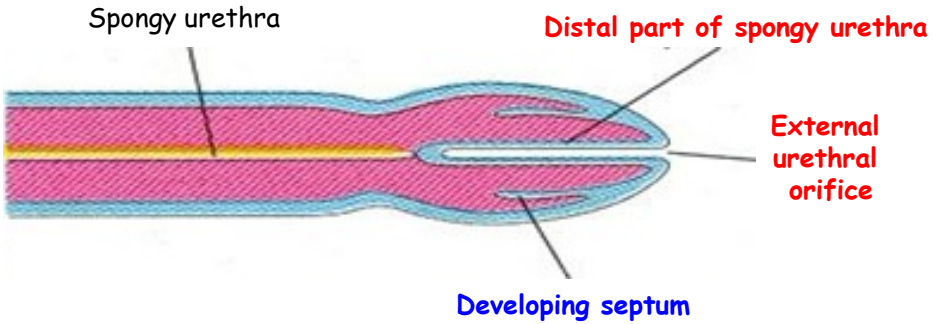
Corpora cavernosa develop from mesenchyme



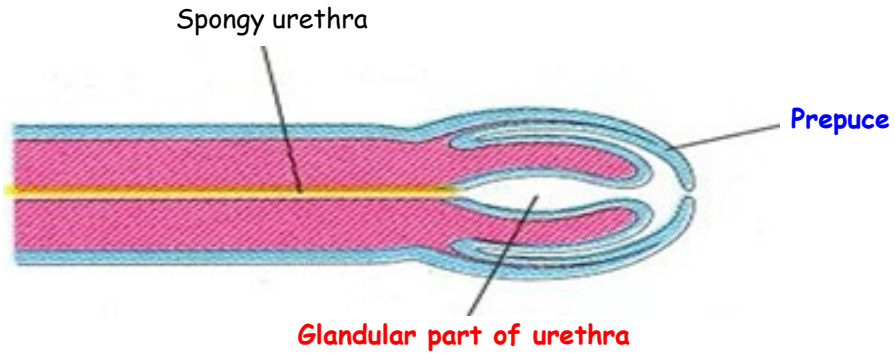
Genital system – External genitalia – Urethral orifice



- ectodermal ingrowth forms a cellular ectodermal cord

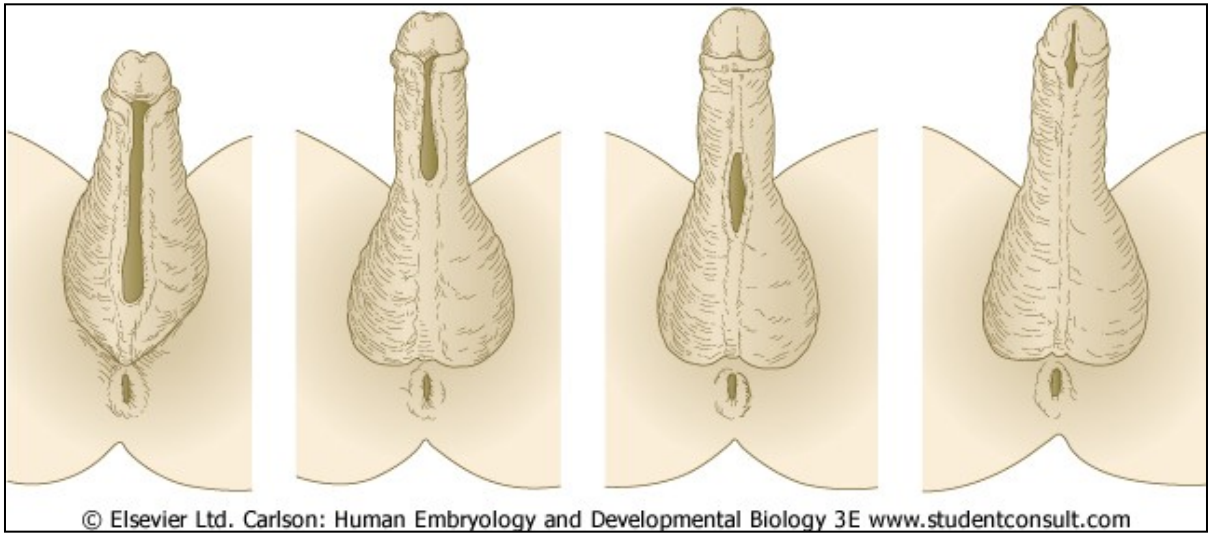


- the cord grows towards the root of the penis to meet the spongy urethra
- the cord canalizes
- circular ingrowth of ectoderm occurs at the periphery of the glans penis (week 12)



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

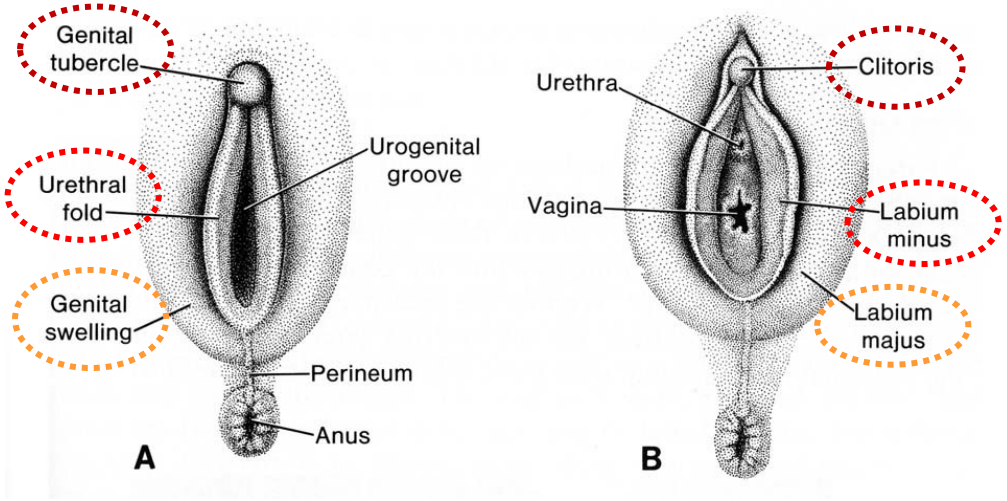
Genital system – External genitalia – Male hypospadia



Normal midline raphe

Raphe off center

Genital system – External genitalia - Female



urethra and vagina open into
vestibule = from urogenital sinus

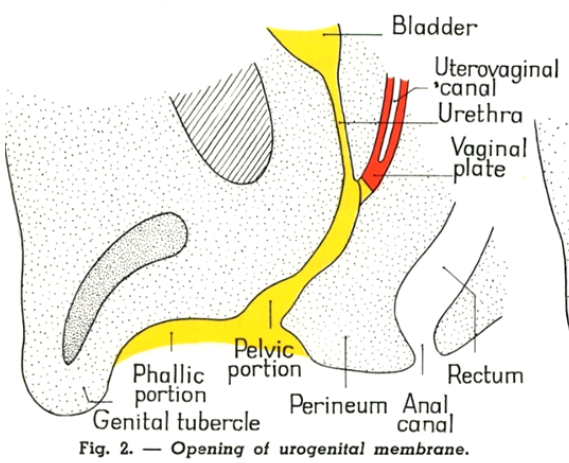


Fig. 2. — *Opening of urogenital membrane.*

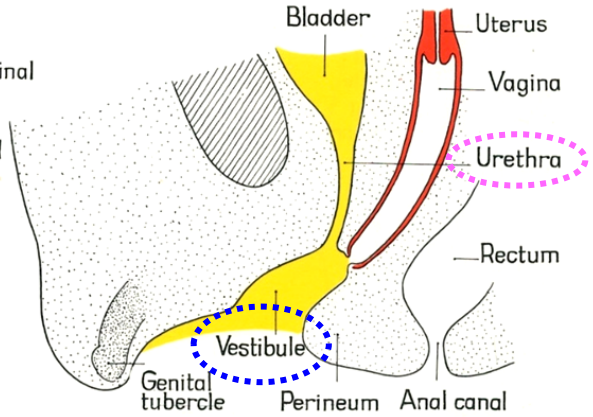
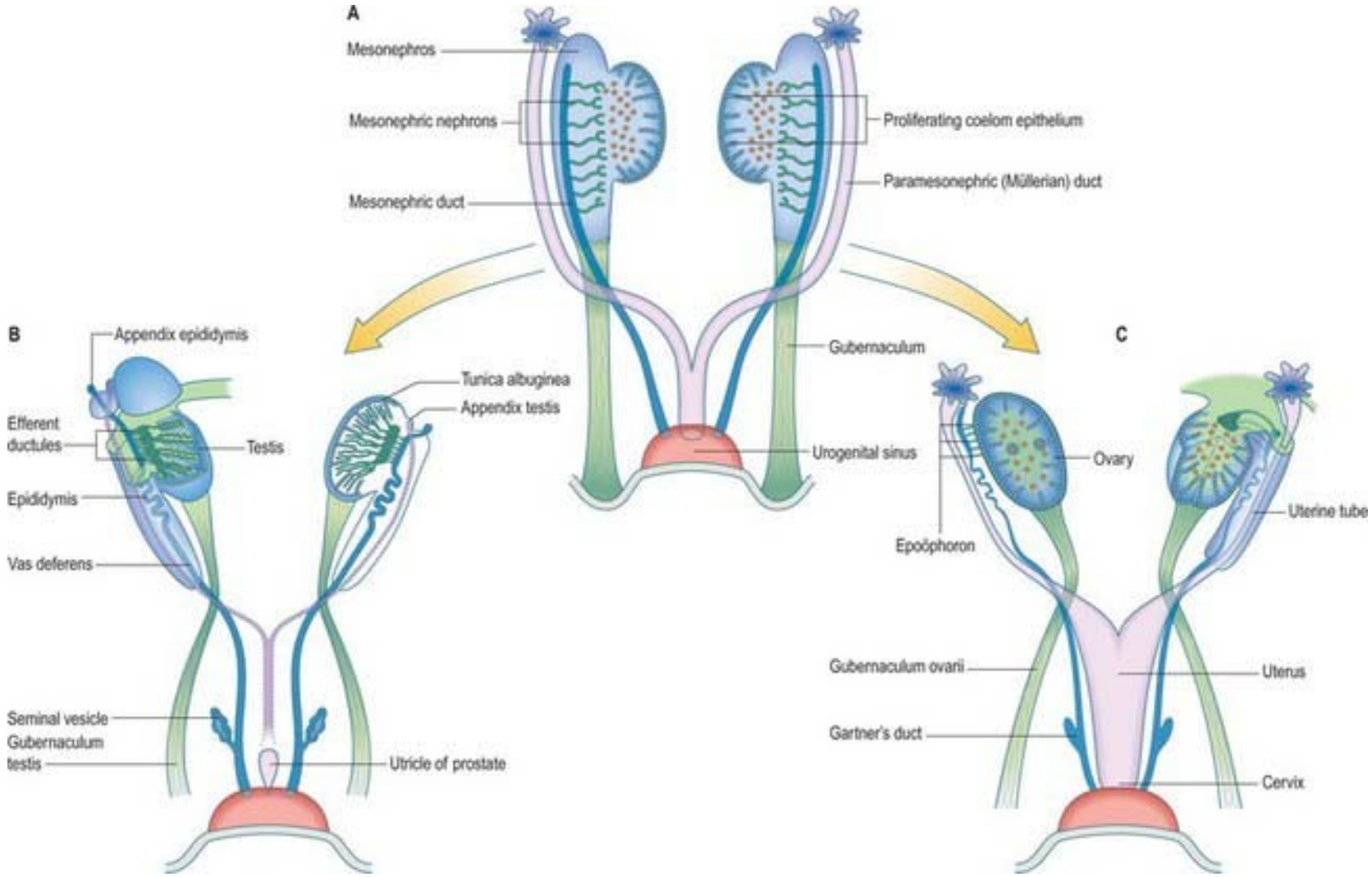


Fig. 3. — *The definitive vestibule.*

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


A
Mesonephros
Mesonephric nephrons
Mesonephric duct
Proliferating coelom epithelium
Paramesonephric (Müllerian) duct
Gubernaculum
Urogenital sinus
B
Appendix epididymis
Efferent ductules
Testis
Epididymis
Vas deferens
Tunica albuginea
Appendix testis
Seminal vesicle
Gubernaculum testis
Utricle of prostate
C
Ovary
Epoöphoron
Uterine tube
Gubernaculum ovarii
Uterus
Gartner's duct
Cervix