UROGENITAL SYSTEM develops from intermediate mesoderm.

- URINARY SYSTEM
- MALE REPRODUCTIVE SYSTEM
- FEMALE REPRODUCTIVE SYSTEM

After lateral folding intermediate mesoderm is carried ventrally.
On each side of dorsal aorta is formed ▲longitudinal elevation of the mesenchyme = the urogenital ridge
Paramesonephric duct forms as invagination of coelomic epithelium (surface of urogenital ridge)

Urogenital ridge differentiates into:
- **medial** genital ridge (1) – it gives rise to genital system
- **lateral** nephrogenic ridge/cord (2) – it gives rise to the urinary system.

Urinary system develops before genital system.
DEVELOPMENT OF URINARY SYSTEM

Nephrogenic cord develops into three sets of nephric structures:

1. **Pronephros**: is the most cranial structure; transitory (disappears by week 5th), forms pronephric tubules and duct, no function in human
2. **Mesonephros**: is the middle nephric structure; is partially transitory, forms mesonephric tubules that open laterally to mesonephric duct (Wolffian duct, WD). WD opens to cloaca.
   - function like kidney
   - temporary structure; : week 4 – 12, than degenerates.
   (Some of the tubules and WD participate in the male genital system development)
3. **Metanephros**: is the most caudal (L4 – L5) mesoderm. PRIMORDIUM OF PERMANENT KIDNEYS. Begins to form in the 5th week and is functional in fetus at 10th week.
The permanent kidneys develop from two sources of mesoderm:

1. ureteric bud
2. metanephrogenic blastema
1. The ureteric bud is an outgrowth from the mesonephric duct (Wolfian duct - WD), near its entrance into the cloaca, and is the primordium for development of ureter, renal pelvis, calices, and collecting tubules.
2. **metanephrogenic blastema** is a mass of cells derived from the nephrogenic cord that forms the NEPHRONS (renal corpuscle, proximal tubule, Henle’s loop, distal tubule).

Sequence of changes in metanephrogenic blastema:

a. formation of **metanephric vesicles**;

b. **metanephric tubules** (S-shaped, later coiled),
   - distal end is in contact with collecting duct
   - proximal end forms Bowmann capsule

New nephrones develop only during fetal life.
CHANGES IN POSITION OF KIDNEYS

„ASCEND“ of kidneys = change of position:

1. Fetal metanefros is located in the pelvis, at vertebral level S1- S2

   During ascend, the kidneys:
   a) rotate at 90° angle - hilum medially
   b) come into contact with suprarenal gland
DEVELOPMENT OF URINARY BLADDER

Division of the cloaca by the urorectal septum into:

a) ventral, urogenital sinus
b) dorsal, rectum

The urogenital sinus is divided into three parts

1. cranial vesical part that forms most of the urinary bladder and is continuous with the allantois (becomes urachus)
2. middle pelvic part that becomes the urethra in the neck of the bladder,
   - the prostatic part of the urethra in males,
   - the entire urethra in females
3. caudal phallic part that grows toward the genital tubercle - the primordium of the penis or the clitoris (female).
DEVELOPMENT of GENITAL SYSTEM

A. The genotype of an embryo is determined at fertilization:
   Female 46, XX chromosomes
   Male 46, XY

B. During weeks 1–6, the embryo remains in an indifferent stage:
   genetically female embryos and genetically male embryos are phenotypically indistinguishable
   = indifferent stage

C. During week 7, the indifferent embryo begins phenotypic sexual differentiation.

D. By week 12, female or male characteristics of the external genitalia can be recognized.

E. By week 20, phenotypic differentiation is complete.
Genital system develops from intermediate mesoderm

In embryo, on each side of dorsal aorta is longitudinal ridge of mesoderm = urogenital ridge (▲)

Surface of the ridge is covered by coelomic epithelium.

Genital ridge with coelomic epithelium

Urogenital ridge differentiates into:

- **medial** genital ridge (1) – it gives rise to genital system
- **lateral** nephrogenic ridge/cord (2)
INDIFFERENT GONADS

Gonads develop from 3 sources:

1. **Primordial germ cells** (future oogonia, spermatogonia)
2. **Coelomic epithelium** (future follicular cells – ovary; or Sertoli cells - testis)
3. **Mesenchyma** of genital ridge (future stroma: interstitial CT, tunica albuginea; thecal cells – ovary; or Leydig cells – testis)

Week 5,

- **migration of primordial germ cells** from the wall of yolk sac into genital ridge
Sex determination is influenced by TESTIS DETERMINING FACTOR (TDF)

- **In the presence of TDF**, indifferent embryo become **male phenotype**.
- As the indifferent gonad develops into the testis, **Leydig cells** differentiate and produce testosterone and **Sertoli cells** produce Müllerian-inhibiting factor (MIF)
- **In the absence of TDF**, testosterone, and MIF, the indifferent embryo will be directed to the **female phenotype**.

**TESTES** start to differentiate at week 7 – 8;
**OVARIES** later, week 12!
DEVELOPMENT of TESTES
week 7 – 8,

- Germ cells (XY genotype) inhabit spaces between primary sex cords
- Development of seminiferous epithelium: Sertolli cells and spermatogonia
  The germ cells divide mitotically,
  Meiosis begins only with puberty!

- Mesenchyma forms interstitial CT, contain Leydig cells
- F: differentiation of genital ducts and external genitalia
- Sertolli cells produce Müllerian inhibiting factor (MIF) = supresses development of Müllerian duct in male genital system

SUMMARY
Seminiferous tubules, tubuli recti, and rete testis develop from primary sex cords (coelomic epithelium).
Efferent ductules develop from mesonephric tubules.
Epididymis duct, ductus deferens, seminal vesicle, and ejaculatory duct develop from mesonephric duct.

Week 28, DESCEND OF TESTIS from abdominal cavity into the scrotum through inguinal canal, with help of inguinal ligament (remnant - gubernaculum testis).
DEVELOPMENT of OVARIES

In female, gonads starts to develop in week 12

- **Primary sex cords** develop from the gonadal ridge and incorporate **primordial germ cells** (XX genotype)
- Primary sex cords extend into the medulla and develop into the **rete ovarii** = temporary structure, later degenerates

Month 4, formation of ovarian cortex

- Coelomic epithelium proliferates and forms **secondary sex cords** = cortical cords, that surround primordial germ cells = **oogonia**.

  - **Oogonia** undergo:
    - **mitotic division** (6 milion) in the first half of pregnancy
    - **meiotic division** starts prenatally, but is finished in puberty and in adult life!

- **Coelomic epithelium**: remains on the surface like germinal epithelium; is a primordium for follicular cells
- **Mesenchyma** – CT stroma and thecal cells
Summary

Mesonephric (Wolffian) ducts – paired. Important for development of intra- and extra-testicular ducts (epididymis, ductus deferens, seminal vesicle, and ejaculatory duct). A few mesonephric tubules form the efferent ductules of the testes.

Paramesonephric (Müllerian) ducts – paired. Important for development of uterine tubes, uterus and upper part of vagina. (In male degenerate, influenced by MIF)
FEMALE GENITAL SYSTEM – DEVELOPMENT OF UTERINE TUBES, UTERUS, VAGINA

1. the PARAMESONEPHRIC DUCTS (paraMD) develop as invaginations of the lateral surface of the urogenital ridge

2. the cranial unfused portions of the paraMD develop into: uterine tubes

3. the caudal portions of the paraMD fuse in the midline and develops into: uterus, cervix, and superior one third of the vagina

4. inferior two thirds of the vagina develop from vaginal plate

5. epithelium of vagina - endodermal origin; connective tissue and muscles intermediate mesoderm
Indifferent stage, week 4 – 7

Development of swellings around the cloacal membrane:
1. **genital tubercle**
2. **urogenital folds**
3. **labioscrotal folds**

Differentiation of external genitalia, week 9 – 12

**Male**
1. **urogenital folds** fuse and form **spongy urethra**
2. **Scrotal folds** increase, grow medially and form **scrotum**
3. **Genital tubercle** elongates and gives rise to **phalus**

**Female**
1. **urogenital folds** don’t fuse, later develop to **labia minora**
2. most parts of the **labioscrotal folds** remain unfused and form **labia majora.**
3. **genital tubercle** gives rise to **clitoris**