Objectives
- To identify the three stages of kidney development and give characteristics of each of the stages
- To list the adult derivatives of the embryonic structures of each of the early kidney stages
- To describe the ascent of the kidneys including changes to arterial blood supply
- To list the three components of the uro-genital sinus and describe their adult derivatives
- To explain the formation of the urinary bladder proper

Urogenital System:

- can be divided into two entirely different components:
  - the urinary system
  - the genital system.

Embryologically and anatomically, they are intimately interwoven

- Both systems develop from intermediate mesoderm (urogenital ridge): a common mesodermal ridge along the posterior wall of the abdominal cavity, and
- initially the excretory ducts of both systems enter a common cavity, the cloaca.

Kidney Systems

Three slightly overlapping kidney systems are formed in a cranial to caudal sequence during intrauterine life in humans:

(a) pronephros: rudimentary and nonfunctional

(b) mesonephros: may function for a short time during the early fetal period

(c) metanephros: forms the permanent kidney.

Pronephros

At the beginning of the 4th week, the pronephros is represented by 7 to 10 solid cell groups in the cervical region. These groups form vestigial excretory units, nephrotomes, that regress before more caudal ones are formed. The pronephric ducts run caudally and open into the cloaca.

By the end of the 4th week, the pronephroi soon degenerate; however, most of the length of the pronephric ducts persists and is used by the next set of kidneys.

Mesonephros

The mesonephros and mesonephric ducts are derived from intermediate mesoderm from upper thoracic to upper lumbar (L3) segments.

In the middle of the second month the mesonephros forms a large ovoid organ on each side of the midline.
Since the developing gonad is on its medial side, the ridge formed by both organs is known as the Urogenital ridge.

During regression of the pronephric system, the first excretory tubules of the mesonephros appear. They lengthen rapidly, form an S-shaped loop, and acquire a tuft of capillaries that will form a glomerulus at their medial extremity.

Around the glomerulus the tubules form Bowman's capsule, and together these structures constitute a renal corpuscle.

Laterally, the tubule enters the longitudinal collecting duct known as the mesonephric or wolffian duct.

While caudal tubules are still differentiating, cranial tubules and glomeruli show degenerative changes, and by the end of the second month, the majority have disappeared.

In the male, a few of the caudal tubules and the mesonephric duct persist and participate in formation of the conduit for sperm from the testes to the urethra. In the female, these ducts regress.

Metanephros: The Definitive Kidney

It appears in the fifth week. Metanephric mesoderm develops from the lower lumbar and sacral portions of the nephrogenic cord.

- Its excretory units develop from metanephric mesoderm in the same manner as in the mesonephric system.
- The development of the duct system differs from that of the other kidney systems.

Collecting System

Collecting ducts of the permanent kidney develop from the ureteric bud (an outgrowth of the mesonephric duct close to its entrance to the cloaca). The bud penetrates the metanephric tissue, which is molded over its distal end as a cap. Subsequently the bud dilates, forming the primitive renal pelvis, and splits into cranial and caudal portions, the future major calyces.

Each calyx forms two new buds while penetrating the metanephric tissue. These buds continue to subdivide until 12 or more generations of tubules have formed.

The tubules of the second order enlarge and absorb those of the third and fourth generations, forming the minor calyces of the renal pelvis.

During further development, collecting tubules of the fifth and successive generations elongate considerably and converge on the minor calyx, forming the renal pyramid.

The ureteric bud gives rise to the ureter, the renal pelvis, the major and minor calyces, and approximately 1 to 3 million collecting tubules.

Excretory System

Each newly formed collecting tubule is covered at its distal end by a metanephric tissue cap. Under the inductive influence of the tubule, cells of the tissue cap form small vesicles, the renal vesicles, which in turn give rise to small S-shaped tubules.

Capillaries grow into the pocket at one end of the S and differentiate into glomeruli. The proximal end of each nephron forms Bowman's capsule, which is deeply indented by a glomerulus. The distal end forms an open connection with one of the collecting tubules.
Continuous lengthening of the excretory tubule results in formation of the proximal convoluted tubule, loop of Henle, and distal convoluted tubule.

**Hence, the kidney develops from two sources:**

(a) metanephric mesoderm, which provides excretory units; and
(b) the ureteric bud, which gives rise to the collecting system.

There are approximately **1 million nephrons in each kidney**. They are formed until birth.

**Urine production** begins early in gestation, soon after differentiation of the glomerular capillaries, which start to form by the **10th week**.

At birth, the **kidneys have a lobulated appearance**, but the lobulation disappears during infancy as a result of further growth of the nephrons, although there is no increase in their number.

**Clinical Correlates**

**Renal agenesis**

may arise if the interaction between the metanephric mesoderm and the ureteric bud fails to occur.

**Unilateral renal agenesis** often causes no symptoms and is usually not discovered during infancy because the other kidney usually undergoes compensatory hypertrophy and performs the function of the missing kidney. Unilateral renal agenesis should be suspected in infants with a **single umbilical artery**.

**Bilateral renal agenesis** is associated with **oligohydramnios** (small amount of amniotic fluid) because little or no urine is excreted into the amniotic cavity. Most infants with bilateral renal agenesis die shortly after birth or during the first months of life.

**Congenital polycystic kidney disease**

numerous cysts form.

**Autosomal recessive polycystic kidney disease** is a progressive disorder in which **cysts form from collecting ducts**. The kidneys become very large, and renal failure occurs in infancy or childhood.

**Cysts form from all segments of the nephron** and usually do not cause renal failure until adulthood. The autosomal dominant disease is more common but less progressive than the autosomal recessive disease.

(A) Surface view of a fetal kidney with multiple cysts

(B) Section of the kidney in A, showing multiple cysts.

**Duplication of the ureter**

results from:

**Early splitting of the ureteric bud**. Splitting may be partial or complete, and metanephric tissue may be divided into two parts, each with its own renal pelvis and ureter.

In rare cases, **one ureter opens into the bladder, and the other is ectopic**, entering the vagina, urethra, or vestibule. This abnormality results from development of two ureteric buds. One of the buds usually has a normal position, whereas the abnormal bud moves down together with the mesonephric duct. Thus it has a low, abnormal entrance in the bladder, urethra, vagina, or epididymal region.

**Position of the Kidney**
The kidney, initially in the pelvic region, later shifts to a more cranial position in the abdomen. This ascent of the kidney is caused by:

- diminution of body curvature and
- growth of the body in the lumbar and sacral regions

The position of the kidneys becomes fixed once they come into contact with the suprarenal glands in the ninth week where they attain their adult position.

In the pelvis, the metanephros receives its arterial supply from a pelvic branch of the aorta. During its ascent to the abdominal level, it is vascularized by arteries that originate from the aorta at continuously higher levels.

The lower vessels usually degenerate, but some may remain.

Initially the hilum of the kidney, where vessels and nerves enter and leave, faces ventrally; however, as the kidney relocates (ascends), it rotates medially almost 90 degrees. By the ninth week, the hilum is directed anteromedially.

**Abnormal Location of the Kidneys**

During their ascent, the kidneys pass through the arterial fork formed by the umbilical arteries, but occasionally one of them fails to do so. Remaining in the pelvis close to the common iliac artery, it is known as a **pelvic kidney**.

Sometimes the kidneys are pushed so close together during their passage through the arterial fork that the lower poles fuse, forming a **horsehoe kidney**. The horseshoe kidney is usually at the level of the lower lumbar vertebrae, since its ascent is prevented by the root of the inferior mesenteric artery.

**Accessory renal arteries**

are common. They derive from the persistence of embryonic vessels that formed during ascent of the kidneys. These arteries usually arise from the aorta and enter the superior or inferior poles of the kidneys.

**Function of the Kidney**

The definitive kidney becomes **functional near the 12th week**.

Urine is passed into the amniotic cavity and mixes with the amniotic fluid. The fluid is swallowed by the fetus and recycles through the kidneys.

During fetal life, the kidneys are not responsible for excretion of waste products, since the placenta serves this function.

**Bladder and Urethra**

During the fourth to seventh weeks of development, the Cloaca divides into the urogenital sinus anteriorly and the anal canal posteriorly.

The Urorectal septum is a layer of mesoderm between the primitive anal canal and the urogenital sinus. The tip of the septum will form the perineal body.

Three portions of the urogenital sinus can be distinguished:

- the upper part (the urinary bladder) is the largest part. Initially, the bladder is continuous with the allantois when the lumen of the allantois is obliterated, a thick fibrous cord, the Urachus, remains and connects the apex of the bladder with the umbilicus. In the adult, it is known as the median umbilical ligament.
- The next part is the pelvic part of the urogenital sinus is a rather narrow canal, in the male, it gives rise to the prostatic and membranous parts of the urethra.
- The last part is the phallic part of the urogenital sinus
It is flattened from side to side, and as the genital tubercle grows, this part of the sinus will be pulled ventrally.

Development of the phallic part of the urogenital sinus differs greatly between the two sexes.

During differentiation of the cloaca, the caudal portions of the mesonephric ducts are absorbed into the wall of the urinary bladder. As a result of ascent of the kidneys, the orifices of the ureters move farther cranially; those of the mesonephric ducts move close together to enter the prostatic urethra and in the male become the ejaculatory ducts.

**Trigone of the bladder**

Since both the mesonephric ducts and ureters originate in the mesoderm, the mucosa of the bladder is also trigone the bladder formed by incorporation of the ducts (the mesodermal. With time, the mesodermal lining of the trigone is replaced by endodermal epithelium, so that finally the inside of the bladder is completely lined with endodermal epithelium. In infants and children, the urinary bladder, even when empty, is in the abdomen. It begins to enter the greater pelvis at approximately 6 years of age, but it does not enter the lesser pelvis and become a pelvic organ until after puberty.

**Urethra**

The epithelium of the urethra in both sexes originates in the endoderm; the surrounding connective and smooth muscle tissue is derived from splanchnic mesoderm.

At the end of the third month, epithelium of the prostatic urethra begins to proliferate and forms a number of outgrowths that penetrate the surrounding mesenchyme.

In the male, these buds form the prostate gland.

In the female, the cranial part of the urethra gives rise to the urethral and para-urethral glands.

**Clinical Correlates**

**Bladder Defects**

A: When the lumen of the intraembryonic portion of the allantois persists, a urachal fistula may cause urine to drain from the umbilicus.

B: If only a local area of the allantois persists, secretory activity of its lining results in a cystic dilation, a urachal cyst.

C: When the lumen in the upper part persists, it forms a urachal sinus. This sinus is usually continuous with the urinary bladder.

**Exstrophy of the bladder**

is a ventral body wall defect in which the bladder mucosa is exposed. Epispadias is a constant feature. Exstrophy of the bladder may be caused by a lack of mesodermal migration into the region between the umbilicus and genital tubercle, followed by rupture of the thin layer of ectoderm.

**Thank you**

**Next lecture: Genital System**