Development of the Urinary System

Objectives:

- Describe the development and fate of the pronephric duct
- Describe the development and fate of the mesonephric kidney
- Describe the development and fate of the metanephric kidney and ureter
- Understand the ascent of the metanephric kidney and its changing blood supply
- Describe the development of the urinary bladder and the tissues that contribute to its development.

Introduction;

The urinary system develops from the intermediate mesoderm (kidneys and ureters) and the cloaca (bladder and urethra).

Kidney Development;

The intermediate mesoderm forms bilateral strips of tissue that extend through the length of the embryo lying on each side between the paraxial mesoderm and the lateral late mesoderm. Folding movements of the embryo in week 4 leave the intermediate mesoderm positioned on the posterior wall of the body cavity.
The kidney goes through 3 phases of development; pronephric, mesonephric, and metanephric. Each phase takes place in a different part of the intermediate mesoderm along the length of the embryo, and each of the phases overlap to some extent in time.

During the pronephric phase (approximately weeks 3 to 5), a duct begins to appear in the intermediate mesoderm adjacent to the cervical segments on each side of the embryo. The tips of these ducts extend caudally and connect to the cloaca. Following the separation of the cloaca into the rectoanal canal and urogenital sinus by the urorectal septum, the openings of the duct are found entering the urogenital sinus.

The intermediate mesoderm in the cervical segments of the embryo, along with the adjacent part of the duct to which they gave rise, soon degenerate. However, the rest of the duct in the intermediate mesoderm of the thoracic, lumbar and sacral segments of the embryo remains. The duct is now properly called the mesonephric duct although the former name ‘Wolffian duct’ is still sometimes used.

The mesonephric phase follows the pronephric phase and occurs in the intermediate mesoderm of the thoracic and lumbar segments. Beginning in the fourth week, mesonephric tubules resembling nephrons appear in the intermediate mesoderm in these regions. These tubules open into the mesonephric duct.

For a time these mesonephric tubules secrete urine into the mesonephric duct which conveys it to the urogenital sinus. Much of the intermediate mesoderm in this region then begins to degenerate and has mostly disappeared by the beginning of fourth month of development. Some of the tubules and part of the duct, however, are retained in male embryos and incorporated into structures in the reproductive system as the efferent ductules of the testicle and the vas deferens.
The intermediate mesoderm that lies adjacent to the sacral segments of the embryo (i.e. in the developing pelvis) is referred to as the metanephric blastema. Beginning around 5 weeks after fertilization, the metanephric blastema begins to release molecular signals, which stimulate the mesonephric duct to extend a branch tube into it. The branch tube is called the ureteric bud and it extends from the mesonephric duct at a point very close to where the duct enters the cloaca. Through a series of reciprocal inductive interactions, the metanephric blastema and the ureteric bud give rise to the adult kidney and ureter. Failure of the ureteric bud and metanephric blastema to interact leads to renal agenesis.

When renal agenesis is unilateral, the remaining kidney will undergo compensatory hypertrophy and fulfill the role of 2 kidneys for the newborn. When renal agenesis is bilateral the fetus can survive to term because the placenta removes wastes from fetal blood. However, the condition is typically fatal for the newborn.

The intermediate mesoderm throughout the cervical, thoracic, and lumbar segments of the embryo is destined to regress, and the same fate would have affected the metanephric blastema, except that the ureteric bud secretes factors that rescue and promote its further development. The metanephric blastema will form the urine-producing structures of the kidney, including the glomeruli and nephrons; the
ureteric buds form the collecting system, including collecting tubules, collecting ducts, calyces, pelvis and ureter.

Under the molecular influence of the metanephric blastema, the ureteric bud begins to branch repeatedly, first forming the major, then minor calyces, then the collecting ducts and tubules.

Sometimes the ureteric bud will divide one or more times before entering into the metanephric blastema. This results in branching duplications of the ureter. This is typically an asymptomatic condition, but a common observation in the dissecting room.

Occasionally the metanephric blastema induces the mesonephric duct to sprout 2 ureteric buds resulting in two ureters that enter the urogenital sinus separately.
Signals from the cells at the tips of the collecting tubules at the ends of the ureteric bud branches cause condensations of mesoderm cells called metanephric tissue caps to organize adjacent to them. The tissue caps develop cavities within them, forming nephric vesicles. The vesicles elongate forming nephrons. One end of the developing nephron connects with the end of the collecting tubule. The other (blind) end is invaginated by capillaries, which form a glomerulus. About 1 million of these nephrons will develop in each kidney.

Nephron formation is typically finished by the time of birth and the kidney initially has a lobulated appearance. After birth, the kidney grows in size and the lobulation of the surface disappears as the tubules elongate and the kidney accumulates interstitial connective tissue.

Ascent of the Kidney

The metanephric blastema and the ureteric buds are located deep within the pelvis of the embryo and so must change position to reach their normal location in the upper abdomen. This is accomplished as a result of the straightening of the curvature of the early embryonic body, and through the elongation of the pelvis, which virtually grows out from underneath the kidneys.

As the kidneys first develop in the pelvis, the kidney hilus (where the renal pelvis enters the kidney) faces anteriorly, and blood supply comes from the local vessels in the pelvis. As the kidneys ascend, they pass between umbilical arteries (later to become the common iliacs), they begin to rotate medially, their ureters lengthen, and blood supply changes to successively more superior branches of the aorta.
Sequence of kidney ascent, passing between the umbilical (common iliac) arteries. Note the lobulated appearance of the fetal kidney and the medial rotation of the hilus as the kidney ascends.

Sequence of kidney ascent showing the changing blood supply from arterial branches of the aorta at successively higher levels. When one of the vessels from which the kidney formerly received its blood supply is retained, it forms an accessory renal artery, arising from the aorta, inferior to the normal renal artery.

Kidneys that have failed to ascend completely (ectopic kidneys) will have ectopic vascular supply, will not have completed their full rotation medially, and will have a ureter that is an appropriate length for their ectopic position. This helps in distinguishing a congenitally ectopic kidney from one that has reached, but then slipped out from its normal position (renal ptosis/dropped kidney).

Occasionally, the kidneys may become fused into a single organ while still in the pelvis. The most common form is the horseshoe kidney, examples of which can be seen in the JCB Grant Anatomy Museum. Fused kidneys are typically ectopic because the inferior mesenteric artery will prevent their normal ascent.
The metanephric kidney begins to function at around 9 weeks of fetal development. Fetal urine is excreted into the amniotic cavity where it makes a major contribution to the volume of amniotic fluid.

Fetal swallowing is essential for controlling the volume of fluid in the amniotic cavity, and the amniotic fluid also contains growth factors that are important in stimulating the development of the fetal digestive system. The amniotic fluid that the fetus swallows is absorbed by the intestine into the fetal circulation. The placenta then removes toxins and excess volume into the maternal circulation.

Development of the Bladder

The bladder develops from the endoderm of the urogenital sinus (the anterior of the 2 chambers created when the urorectal septum divides the cloaca), and the splanchnic mesoderm surrounding it. Opening into the cloaca are the two mesonephric ducts and the allantois. The allantois is a blind-ended diverticulum that extends from the superior surface of the urogenital sinus up to the connecting stalk (and later the umbilical cord which organizes around the connecting stalk).

The urogenital sinus viewed from behind

The upper part of the urogenital sinus begins to dilate as it fills with urine. Part of this expansion is through incorporation of the caudal ends of the mesonephric ducts and the inferior part of the allantois.
As a result of this expansion, the ureters and the mesonephric ducts come to open separately into the urogenital sinus. The ascent of the kidneys draws the ureteric buds cranially into the dilating part of the urogenital sinus, which becomes the bladder. The openings of the mesonephric ducts remain in the lower part of the urogenital sinus, which does not expand as much. The lower part of the urogenital sinus develops into the urethra. Each mesonephric duct will develop into a vas deferens in the male. They will degenerate in females.

The upper part of the allantois narrows forming a tubular structure called the urachus, which then involutes to become a fibrous cord-like structure called the median umbilical ligament, which can be found passing from the fundus of the bladder to the umbilicus.

Failure of the urachus to involute completely can result in patent remnants such as those shown in the following diagrams.
References


Summary

- The kidneys and ureters develop from the intermediate mesoderm.

- Three successive types of kidney develop in the embryo. The pronephric kidney develops first, located in the cervical region. It is transient and non-functional. Before it degenerates, it gives rise to the pronephric duct, which enters the part of the cloaca that will become the urogenital sinus. The mesonephric kidney follows next and develops in the thoracic and lumbar regions. It takes over the remains of the pronephric duct as the mesonephric duct. Excretory tubules form in the mesonephric kidney and empty into the mesonephric duct. The mesonephric kidney functions transiently but has degenerated by the fourth month. The final kidney that develops is the metanephric kidney. It develops in the pelvis from intermediate mesoderm called the metanephric blastema, and from an outgrowth of the mesonephric duct called the ureteric bud.

- Through a series of reciprocal interactions between the metanephric blastema and the ureteric bud, the ureteric bud forms the collecting system, including the ureter, renal pelvis, major and minor calyces, collecting ducts and collecting tubules. The metanephric blastema forms the nephrons.

- The metanephric kidneys are initially located in the pelvis and must gradually shift position, ascending into the abdomen.

- The urinary bladder and urethra develop from the urogenital sinus, which was created by division of the cloaca.