

# Development of the genitourinary system

The development of the urinary and sexual systems is closely related. They develop together from the **intermediate mesoderm** (it runs along the back wall of the abdomen) and their ducts initially open into a common cavity – the **cloaca**.

## Urinary system

During prenatal human development, 3 partially overlapping systems of excretory organs are established:

- **Pronephros** – is rudimentary and non-functional organ.
- **Mesonephros** – is functionally applied only in a short period of time, in the early fetal period
- **Metanephros** – which is the definitive kidney.

### Pronephros

The pronephros, also known as the foreskin, develops during **the 4th week**. This organ is visible at the beginning of the fourth week as **7-10 distinct groups of cells in the neck region**. These clusters of cells are considered rudimentary excretory units – **nephrotomes**. These structures are no longer visible by the end of the 4th week, with the cranially lying nephrotomes disappearing before the caudally lying ones are formed.

### Mesonephros

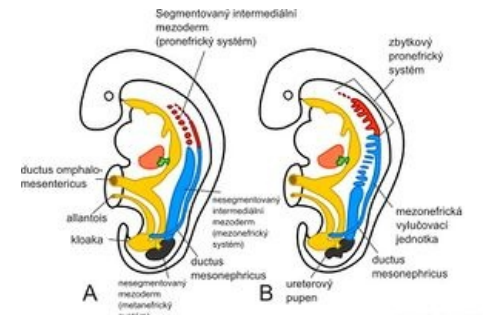
The mesonephros, also known as the primary kidney, consists of a group of excretory ducts and the ductus mesonephricus, which originate *from the intermediate mesoderm at the level from the upper thoracic to the upper lumbar region* (L3 segment). The first excretory ducts appear at the time of the disappearance of the pronephros - **at the beginning of the 4th week of development**. These tubules rapidly elongate, acquire an S-shaped loop, and make contact with a ball of capillaries that forms a **glomerulus** at their medial end. The excretory ducts form **Bowmann's capsule** around the glomerulus and together with it form a structure called the **corpusculum renale**. The excretory ducts laterally open into a longitudinal draining duct - **ductus mesonephricus**, also called **Wolffian duct**. The mesonephros is a large ovoid paired organ on the sides of the midline in the middle of the second month. Here it lies lateral to the developing gonad, and the mound formed by both of these organs forms the fold, the **plica urogenitalis**. Gradually, the canals and glomeruli of the mesonephros disappear in the craniocaudal direction, and by the **end of the 2nd month** of development, most of the mesonephros is already degenerated in this way. Only in male fetuses *do several caudal ducts and the ductus mesonephricus persist*, so that they can participate in the formation of the excretory gonads, this does not happen in female fetuses.

### Metanephros

The final excretory organ appears in the 5th week. Its excretory units develop in the same way as the mesonephros, *from the metanephrogenic blastema* – an unsegmented mass of intermediate mesoderm tissue in the lower thoracic, lumbar, and sacral regions. However, the development of the system of collection and drainage channels is different. The collecting and efferent ducts of the definitive kidney are formed **by the end of the 5th week** of development, developing **from the ureteric bud**, which arises from the mesonephric duct near its opening into the cloaca. The bud grows into the metanephros tissue, which forms a cap above it. As the bud subsequently expands, it forms a primitive **renal pelvis** and divides into cranial and caudal parts, the basis of the next **calyces majores**. Each calyx further forms 2 new buds that penetrate the tissue of the metanephros and continue dividing until a min. 12 generations of channels. However, the appearance of the ducts created in this way changes, as the ducts of the 2nd order enlarge and pull the ducts of the 3rd and 4th generation into each other, creating **calices minores**. Furthermore, the collecting and draining ducts of the 5th and higher generations lengthen considerably and at the same time converge to the calices minores to form **pyramides renales**. The ureteral bud thus gives rise to the **ureter, renal pelvis, small and large calyces, as well as collecting and draining ducts**, of which 1–3 million are established.

## Excretory system

At the periphery of each newly formed collecting duct, we find a *cap of metanephros tissue*. The collecting ducts induce the formation of small vesicles in this tissue - **vesicules renales**, which are formed by metanephros cells. S-shaped channels are gradually formed from renal vesicles, then capillaries grow around the ace-shaped channel and form balls - **glomeruli**. These channels and their glomeruli are the basis of the excretory unit – the nephron. From the peripheral end of the nephron, Bowman's capsule is formed around the glomerulus, and the glomerulus is eventually taken into it. The opposite end of the canal opens into the collecting duct, allowing passage from the Bowman's capsule into the drainage system. Subsequently, the excretory duct grows in length to form the **proximal convoluted tubule, the loop of Henle, and the distal convoluted tubule**.



Developmental types of excretory organs

## The kidney therefore arises from 2 foundations:

- from mesoderm metanephros - excretory unit;
- from the ureteral bud - collection and drainage system.

Nephrons are formed only in the prenatal period and there are approximately 1 million of them at birth. urine begins to form from the 10th week of development not long after glomerular capillaries have begun to differentiate.

## Molecular mechanisms of kidney development

Kidney differentiation is conditioned by the interaction of epithelium (ureteral bud epithelium) and mesenchyme (mesenchyme of metanephrogenic blastema). The mesenchyme expresses the transcription factor WT 1, which is responsible for the ability of the metanephrogenic blastema to respond to the inductive influence of the ureteric bud. The mesenchyme also produces a number of other growth factors that mediate the interaction between the epithelium and the mesenchyme.

See Molecular Mechanisms of Kidney Development for more details

## Bladder and urethra

During the 4th-7th week of development divides the septum urorectale of the **cloaca** into *sinus urogenitalis* (in front) and **canalis analis** (back). The septum urorectale is a layer of mesoderm between the primitive anal canal and the sinus urogenitalis.

There are 3 parts to the urogenital sinus.

- *The upper and largest part is the base of the **urinary bladder**. The latter is initially related to the allantois duct, which represents the **urachus**. After the lumen of the allantois is obliterated, a fibrous band from the top of the bladder to the navel remains - **ligamentum umbilicale medianum**.*
- Another part of the urogenital sinus is its *pelvic section*, from which the **prostatic and membranous part of the urethra** originates in males and **the entire** urethra in females.
- The last part of the urogenital sinus is its *spongy part*. From that in the male sex, the **spongy part of the urethra** arises except for its pars glandis, which arises from the ectoderm epithelial plug. In female fetuses, the *vestibulum vaginae* arises from this part.
- During cloacal differentiation, the caudal sections of the ductus mesonephricus are retracted into the bladder wall, so that *the ureters now empty into the bladder separately*. As the kidneys rise, their *mouths move cranially*, while *the mouths of the ductus mesonephricus come closer to each other*, and in males they open into the prostatic part of the urethra as the **ductus ejaculatorii**. In females, the *mesonephric duct disappears above the ureteral bud gap*.

### Urethra

The epithelium of the urethra originates from the **endoderm** in both sexes. *The ligament and smooth muscle tissue* that surrounds the urethra is derived **from the mesoderm of the splanchnopleura**. Towards *the end of the 3rd month*, the epithelium of the prostatic part of the urethra begins to *proliferate* to lay the foundations for the *prostate* in male fetuses and the **urethral and paraurethral glands** in female fetuses.

## Genital system

Sex differentiation is a complex process in which many genes are involved. The key to sexual dimorphism is the Y chromosome, which contains a testis-determining gene called SRY (sex region on Y). The protein product of this gene is a transcription factor that initiates a gene cascade that causes the reduction or even the disappearance of the genital tract of the opposite sex. Protein SRY – determines the formation of the testicle, i.e. the male sex.

### Gonads

They develop their characters in the 7th week of development. Initially, they are established as elongated paired slats - plicae genitales, medially from the base of the kidneys (mesonephros).

#### 3 basics

- Intermediate mesoderm.
- Proliferation of the surface epithelium (coeloma) - a derivative of the somatopleura.
- Primordial cells – in the 5th week they migrate through the dorsal mesentery, in the 6th week they travel to the gonadal bar, where they come into contact with the cords of epithelial cells that are from the coelomic epithelium, forming a series of solid cell bands (medullary cords) = this stage is called Indifferent stage of the gonad. **!!If the cells do not travel, the gonads will not develop!!**

### Testis (=varle)

An embryo is genetically male if it carries XY gonosomes. Under the influence of the Y chromosome and the SRY gene, the following occurs:

- developing medullary cords,
- tunica albuginea – separates the medullary cords from the surface coelom,
- cortical cords are not formed.

4th month –horseshoe-shaped cords contain primordial cells and supporting Sertoli cells, which are from cells of the surface, coelomic epithelium of the gland.

Week 8 – Leydig cells, which are derivatives of the original mesenchyme of the plica genitalis and lie between the medullary cords of the testis, produce testosterone, which affects the differentiation of the ejaculatory ducts and external genitalia.

The medullary cords of the testis remain compact until puberty, after which they develop a lumen and differentiate into tubules seminiferi contorti. These connect to the **rete testis**. The rete testis opens into the **ductuli efferentes testis**, which are the remainder of the excretory tubules of the mesonephros. They connect the rete testis with the **ductus mesonephricus Wolffii**, from which it develops bringing **leadership**.

### Ovarium (=ovary)

Chromosome equipment of gonosome XX. The absence of a Y chromosome causes that

- medullary cords degenerate,
- cortical cords develop,
- tunica albuginea does not develop.

In the 4th month, the cortical cords disintegrate into isolated islands of cells and each of them surrounds one or more primordial cells. Primordial cells proliferate mitotically, surround themselves with a single layer of cells, and form primary follicles. The surface cells that arose from the cells of the surface epithelium are called follicular cells and the primordial cells are called oogonia.

## Genital ducts

### Indifferent stage

Originally, both male and female embryos have both pairs of ducts (mesonephric, Wolffian duct and paramesonephric, Müllerian duct).

**Paramesonephric duct** it arises as an elongated invagination of the coelomic epithelium on the anterolateral surface of the urogenital bar. At the cranial end, it has a funnel-shaped opening through which it opens into the abdominal cavity. Caudally, it first runs laterally from the mesonephric duct, then crosses it ventrally and continues to grow caudally and medially. In the midline, it comes into contact with the bilateral paramesonephric duct. The two ducts are first separated by the septum, but then merge to form the uterovaginal canal. The common lower tip of the ducts continues to grow caudally to the back wall of the urogenital sinus, where it forms a small elevation – the paramesonephric Müller's tubercle. On the sides of this bump, the mesonephric duct opens to the right and left. Původně mají embrya mužského i ženského pohlaví oba páry vývodných cest (mezonefrický, Wolffův vývod a paramezonefrický, Müllerův vývod).

### Male genital tract

When the mesonephros dies, some of its ducts join the rete testis and subsequently differentiate into the testis efferent ductuli. The ducts in the region of the caudal pole of the testis do not connect with the rete testis and the remnants persist as the paradidymis. The ductus mesonephricus persists in the appendix epididymidis (the most cranial part) and in the main part of the male ejaculatory ducts – ductus epididymidis (epididymis), ductus deferens and ductus ejaculatorius. Müller's duct in males degenerates with the exception of a short section, the appendix testis.

### Female genital tract

The female ducts develop from the ductus paramesonephrici Mülleri. The paramesonephric ducts are contained in the edge of the urogenital bar, which gradually curves into the transverse plane until they join in the midline to form the plica lata uteri. The Müllerian ducts give rise to the tubae uterinae and, after joining the two canals, the canalis uterovaginalis. Canalis uterovaginalis gives the base of the uterus and the upper third of the vagina. The lower two thirds arise from two buds in the wall of the sinus urogenitalis – sinovaginal bulbs. From them, the vaginal plate is formed through gradual development, which differentiates in the vagina.

## External genitalia

### Indifferent stage

The external genitalia develop from paired cloacal cilia formed around the cloacal membrane. These join in the anterior part at the tuberculum genitale. At week 6, the cloacal cilia divide into anterior urethral and posterior anal cilia. Meanwhile, raised mounds, tori genitales, form on the outer edge of the urethral folds.

### Male external genitalia

They arise under the influence of androgenic hormones, which are produced in the fetal testicles. Development is characterized by rapid growth of the tuberculum genitale, which is the basis for the corpus penis and glans penis. Together with it, the urethral cilia grow, which are the basis of the corpus spongiosum penis and the raphae penis, and which subsequently delimit the urethral groove. This groove elongates along with the base of the penis. In the third month, the urethral cilia fuse in the midline and form the corpus spongiosum penis, but do not reach the pars glandis penis. The glandular part of the urethra is formed from an epithelial plug, which is formed from the ectoderm on the surface of the glans penis. The cord luminates and forms the pars glandis urethrae and ostium externum. The tori genitales merge, move caudally, and differentiate into the scrotum.

### **Female external genitalia**

The development of this part of the female reproductive system is stimulated by estrogens. The tuberculum genitale elongates minimally to form the clitoris. The urethral cilia do not fuse to form the labia minora. The tori genitales form the labia majora. The urogenital groove remains open and forms the vestibulum vaginae.

## **Links**

### **Related articles**

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### **References**

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- MOORE, Keith L and TVN PERSAUD. *Human birth: Embryology with a clinical focus*. 1st edition. 2000. 564 pp. ISBN 80-85866-94-3 .