

## **9. Development of urinary system. Pronephros. Mesonephros. Metanephros. Urinary passages. Cloaca.**

The development of the urinary system is intimately interwoven with the development of the genital system. Both systems originate from the intermediate mesoderm, which forms a ridge along the posterior wall of the abdominal cavity. Initially, the excretory ducts of both systems enter a common cavity named the cloaca. Three partially overlapping paired organs are formed in a cranial-to-caudal sequence from the intermediate mesoderm, which is also named the nephrogenic cord: the pronephros, mesonephros, and metanephros.

### **Pronephros**

- it serves as an excretory organs in early developmental stages of some fish and amphibians
- in human, pronephros develop between weeks 3-4 from in the cervical region of the segmented nephrogenic cord;
- 7-10 solid cell cords form vestigial excretory units (nephrotomes); the cranial nephrotomes regress before the caudal are formed
- some of the pronephric nephrotomes join the pronephric tubule, which is only partially luminized; the pronephric tubule is heading caudally towards the mesonephric tubule (see below)
- by the end of the week 4, the pronephric system has disappeared; it never serves the excretory function in human

### **Mesonephros**

- it serves as an excretory organs in adult fish and amphibians
- in human, it originates during week 4 from intermediate mesoderm from upper thoracic (C6) to upper lumbar (L3) segments
- the first mesonephric excretory tubules appear during regression of the pronephric system
- during month 2, the mesonephros and the liver are the largest organs of an embryo
- the mesonephros and the surrounding paramesonephric blastema is named the Wolffian body
- the mesonephric tubules lengthen, develop a lumen and form a Bowman's capsule, which acquires a tuft of capillaries named a glomerulus
- the glomeruli are supplied by the segmental arteries branching from the dorsal aorta
- the glomerulus and its Bowman's capsule form a unit named renal corpuscle
- the mesonephric tubules enter laterally a longitudinal collecting duct known as the mesonephric or Wolffian duct
- the mesonephric duct collect the urine that is filtrated from the glomeruli and enters the cloaca
- on the medial side of each mesonephros, gonad develops, thus bulging into the dorsal wall of the coelom body cavity as the urogenital ridge
- in month 2, cranial tubules disappear, while caudal tubules are still differentiating
- in female, the mesonephric tubules disappear (occasionally, some may persist in some individuals)

- in male, caudal mesonephric tubules persist and form the efferent ductules connecting the rete testis with the epididymis; in male, the mesonephric duct also persists, forming part of the genital ducts

### **Metanephros**

- this is the permanent kidney, the excretory organ of reptiles, birds, and mammals (including the human)
- it develops in week 5 from two primordia: the duct system (from the ureteric bud) and the metanephric mesoderm (provides nephrons as the excretory units) as follows
  - from the the mesonephric duct, close to its entrance to the cloaca, a new ureteric (metanephric) bud grows out:
    - the bud penetrates the metanephric mesoderm tissue
    - the bud dilates, forming the primitive ureter, renal pelvis branching into the major calyces
    - each calyx forms new buds penetrating the metanephric blastema and forms minor calyces
    - further branching of the minor calyces gives rise to the collecting tubules
  - the metanephric tissue (blastema) develops from the sacral portion of the nephrogenic blastema that is penetrated by the ureteric bud
    - the origin of small renal vesicles is induced within the metanephric tissue
    - the vesicles form Bowman's capsules of nephrons, into which glomerular capillaries grow
    - the vesicles elongate, thus forming the excretory units of the kidney named nephrons: the proximal convoluted tubule, loop of Henle, and distal convoluted tubule
    - the metanephric tissue gives rise to more than 1 million of kidney nephrons
    - finally, the distal convoluted tubules join the collecting tubules, thus establishing an open communication between the excretory units and the collecting system
- the kidney becomes functional near the week 12; the urine is passed into the amniotic cavity and mixes with the amniotic fluid
- the kidney is initially formed in the pelvic (sacral) region; then it shifts cranially to the level of the L3-L5 vertebrae, which is named the relative ascent of the kidney
- this is caused by the changes of the body curvature and differential growth of the lumbar and sacral regions
- originally, the pelvic metanephros receive its arterial supply from pelvic branches of the aorta; in its final lumbar position, the kidney is vascularized by renal arteries branching from the lumbar abdominal aorta

### **Cloaca, bladder and urethra**

- the cloaca is the dilated part of the hindgut (lined by the entoderm); initially, it is closed by the cloacal membrane
- the left and right mesonephric ducts enter the cloaca
- ventrally, the allantois grows from the cloaca into the connecting stalk; (in placental mammals, the allantois is a rudimentary fetal membrane)
- during weeks 4-7, the urorectal septum divides the cloaca into the anterior part named the urogenital sinus and the posterior part named the anal canal

- the urorectal (or cloacal) septum is a frontal layer of mesoderm that proliferates caudally towards the cloacal membrane
- the tip of the urorectal septum will form the perineal body, into which several perineal muscles insert
- three portions of the urogenital sinus can be distinguished:
  - the upper part differentiates into the urinary bladder (lined with endoderm); only the trigonum of the bladder originates from the mesodermal mesonephric ducts and ureters that are incorporated into the growing bladder; initially, the bladder is continuous with the allantois, which is later on obliterated onto a thick fibrous cord, the urachus; the urachus connects the apex of the bladder with the umbilicus (becoming the median umbilical ligament)
  - the narrow middle and caudal part of the urogenital sinus gives rise to the male prostatic and membranous urethra; the male prostatic urethra forms 30-50 prostatic glands; in female, it develops into the female urethra and a vaginal bud, which luminizes into the caudal portion of vagina
  - the phallic part is pulled ventrally, forming the phallus

### **Overview of organs developing from the temporary structures of the urogenital system**

- from the urogenital sinus, following structures develop:
  - in male and female: the urinary bladder
  - in female: urethra, caudal portion of the vagina, vestibule of the vagina, major vestibular glands, urethral glands
  - in male: urethra except the navicular fossa (which originates by invagination of the ectoderm on the glans penis), prostate, bulbourethral gland
- from the mesonephric (Wolffian) duct and the mesonephric tubules, following structures develop:
  - in male and female, the mesonephric duct gives rise to the ureter, renal pelvis, major and minor calyces, papillary ducts and collecting ducts
  - in female, remnants may persist in some individuals, thus appearing Gartner canal (may form cysts between the broad ligament of the uterus and the wall of vagina), and small appendages adjacent to the ovary (a cranial epoophoron and a caudal paroophoron)
  - in male: the mesonephric tubules form the efferent ductules in the head of epididymis; the mesonephric ducts give rise to the epididymic duct, the deferent duct, ejaculatory duct, seminal vesicles; in some individuals, an appendix of the epididymis may be present
- from the paramesonephric (Müllerian) duct, following structures develop (see also development of genital organs)
  - in female: uterine tubes, uterus, cranial portion of the vagina
  - in male, some remnants may persist in some individuals: appendix of testis, the prostatic utricle

### **Developmental defects of the urinary system**

- renal dysplasia or agenesis: involution of kidneys, nephrons fail to develop and the ureteric bud fails to branch; may be unilateral or bilateral
- accessory kidney: abnormal branching of the ureteric bud and separation of metanephric mesodermal tissue

- horseshoe kidney: lower poles of the left and the right kidneys are pushed close together and fuse – its ascent is then prevented by the root of the inferior mesenteric artery
- pelvic (dystopic) kidney results from a failure of its ascent
- reniculated kidney: persistence of small kidney lobules (segments) reflecting the branching pattern of the ureteric bud
- accessory renal arteries and veins are common; these are persistent embryonic vessels induced from the aorta and from the inferior vena cava
- congenital polycystic kidney disease: cysts form when the nephrons fail to join the collecting ducts; autosomal recessive or dominant inheritance; the autosomal recessive polycystic kidney disease results in renal failure in infancy
- ectopic ureteral openings in various portions of the bladder, vagina, or urethra
- partial or complete duplication of the ureter
- epispadia is associated with the exstrophy of the bladder and the urethral opening is found on the dorsum of the penis; this results from an abnormal localization of the phallus (genital tubercle) in relation to the urogenital sinus
- hypospadias results from incomplete fusion of urethral folds and the penile urethra opens abnormally on the inferior aspects of the penis
- exstrophy of the bladder: a ventral body defect, in which the bladder mucosa is exposed below the umbilicus
- urachal fistula is caused by a persistence of the allantois, when the urachus fails to obliterate; thus, allantois drains urine from the apex of the bladder to the umbilicus
- rectovesical fistula results from an insufficient (incomplete) division of the cloaca with the urorectal septum; thus, the rectum still communicates with the urogenital sinus