

Development of Urinary System

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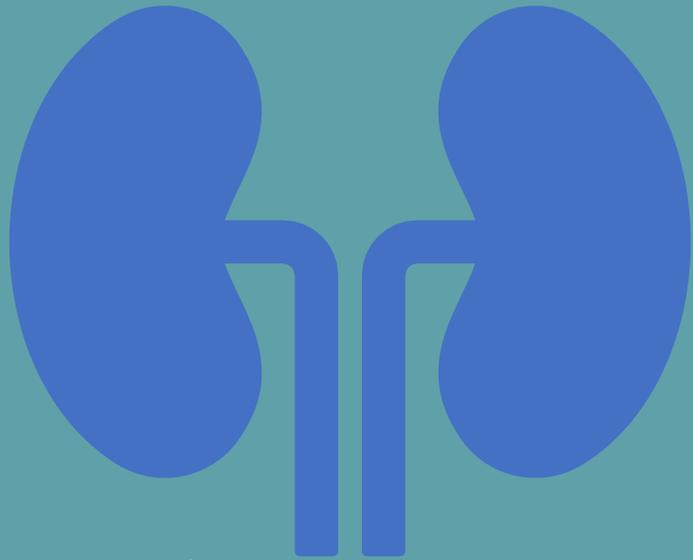
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Introduction to Urinary System Embryology

Urinary System



- With the exception of the epithelial lining of the bladder and urethra, which are of endodermal origin, the urinary system of vertebrates develops from intermediate mesoderm.
- The urinary system has a number of important functions which include elimination of metabolic waste products by filtration and excretion, regulation of electrolyte levels in the body and reabsorption of water and low molecular weight molecules, all of which are essential aspects of homeostasis. In addition, the kidney, through the production of the enzyme renin, has a role in the regulation of blood pressure.
- An important endocrine function of the kidney is the production of erythropoietin in the renal cortex, which has a regulatory role in erythrocyte production by cells of the bone marrow.

Kidney

- The primordial kidney consists of tubular units, nephrons, which function by selective filtration, reabsorption and finally excretion of waste products. As mammalian evolution progressed, functional kidney units developed from primitive structures to highly complex, efficient filtration units. Developing vertebrate nephric tubules exhibit increased complexity, as those which form in the cervical region are sequentially replaced in the thoraco-lumbar and sacral regions by more functionally competent structures. These structures are referred to as the pronephros, mesonephros and metanephros, respectively.
- As the more caudal structures develop and become functional, the pronephric and mesonephric tubules atrophy and the metanephros persists as the definitive functioning kidney.

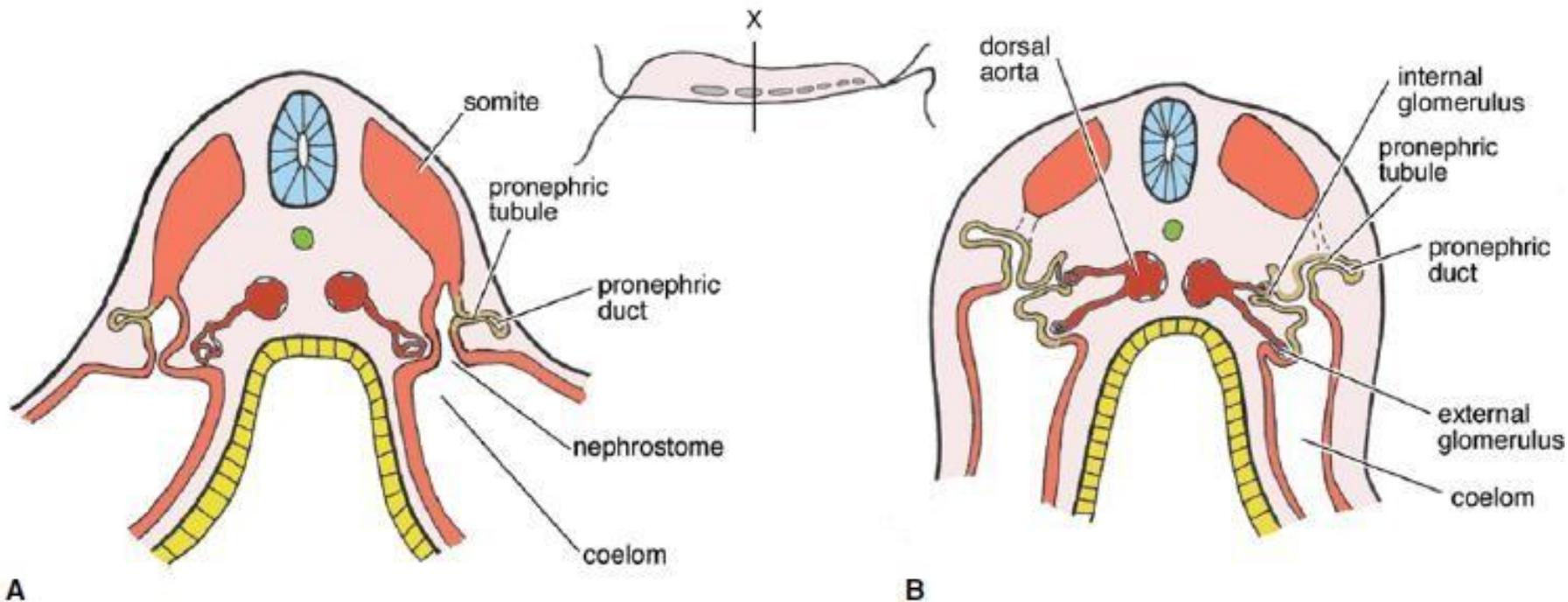


Kidney

- The evolutionary development of the kidney is illustrated by the increasing refinement of renal structure and function evident in vertebrate animals. Lower vertebrates have relatively primitive kidneys in comparison with higher vertebrates. In fish and amphibians, the mesonephros, which replaces the pronephros, becomes the functional kidney.
- In reptiles, birds and mammals, the definitive kidney is formed by the metanephros, an additional structure which succeeds the pronephros and mesonephros, both of which atrophy.

Pronephros

- During the early developmental period, when somites are present, cells of the intermediate mesoderm in the cervical region separate into an outer parietal layer and an inner visceral layer, forming a cavity, the nephrocoele, between the two layers. At the level of each somite, cords of cells referred to as nephrotomes, which grow out from the dorsal (parietal) wall of the intermediate mesoderm, later form pronephric tubules (Fig 1.).



- The distal end of each tubule proliferates and extends initially in a lateral direction and then caudally, before fusing with the corresponding proliferating cells of the tubule developing immediately caudal to it. The primordium of the excretory pronephric duct arises from fusion of the distal ends of each tubule.

Figure 1. Cross-section, at the level indicated, through an early embryo, A, and an embryo at a later stage of development, B, showing formation of a pronephric duct and an internal and external glomerulus.

Pronephros

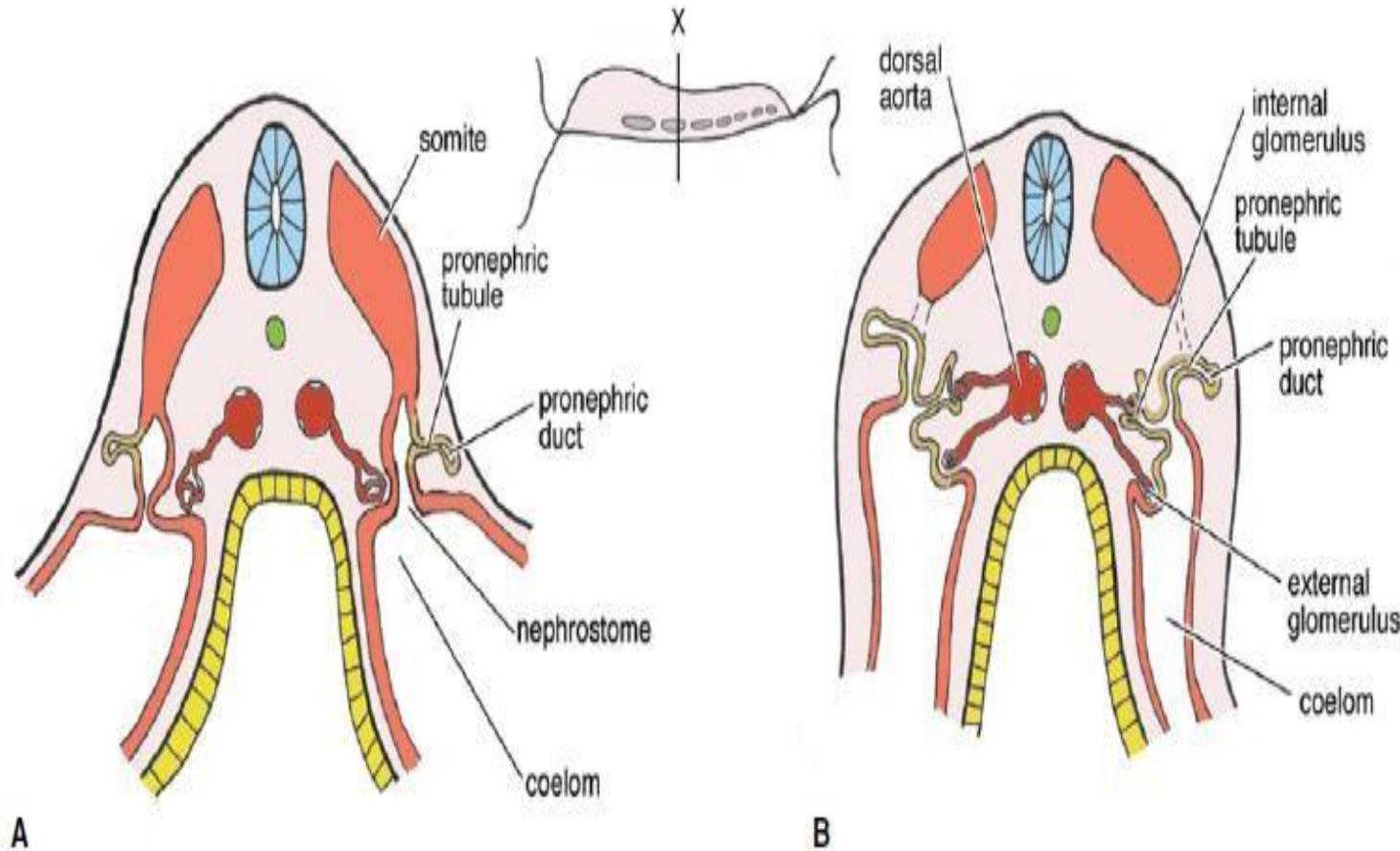


Figure 1. Cross-section, at the level indicated, through an early embryo, A, and an embryo at a later stage of development, B, showing formation of a pronephric duct and an internal and external glomerulus.

- The pronephric duct grows towards the cloaca and becomes canalised. As more caudal pronephric tubules develop, they open into the primordial pronephric duct. The lumen of each pronephric tubule becomes continuous with the nephrocoele which opens into the coelomic cavity through an aperture termed a **nephrostome**.

Branches from the dorsal aorta form tufts of capillaries, glomeruli, which may invaginate either into the coelomic epithelium, or alternatively into the wall of each pronephric tubule. Glomeruli which invaginate into the coelomic epithelium are referred to as **external glomeruli**; those which invaginate into the tubular wall are termed **internal glomeruli** (Fig 1.).

Pronephros

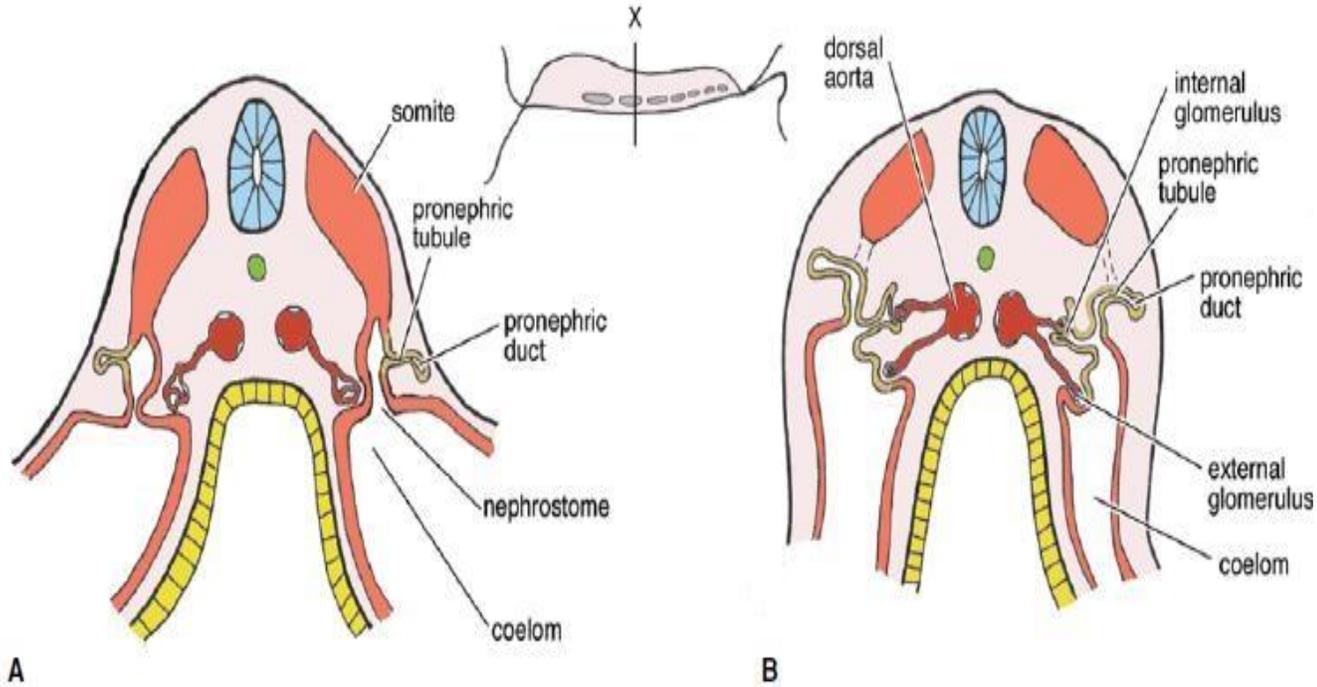


Figure 1. Cross-section, at the level indicated, through an early embryo, A, and an embryo at a later stage of development, B, showing formation of a pronephric duct and an internal and external glomerulus.

- The term 'Bowman's capsule' is used to describe the invaginated epithelium surrounding each glomerulus. Formation of external glomeruli, a feature of lower vertebrates, results in a filtration arrangement which is less efficient than internal glomerular filtration, as the filtrate has to be propelled from the coelomic cavity to the pronephric tubule by the ciliary action of cells surrounding the nephrostome.
- With the formation of internal glomeruli, a feature of higher vertebrates, the connection between the pronephric tubules and the coelomic cavity is lost. Water and some electrolytes are reabsorbed from the pronephric tubules and waste products are conveyed to the cloaca. In placental mammals, these waste products are transported from the foetus to the placenta for excretion.

Mesonephros

- Towards the end of the post-somite stage of development, a column of tissue referred to as the urogenital ridge develops from proliferating intermediate mesoderm in the thoraco-lumbar region and projects into the coelomic (peritoneal) cavity. Later, this structure divides into a medial genital ridge and a lateral urinary ridge. Lateral to the urinary ridge, the pronephric ducts, which extend caudally towards the cloaca, induce the mesonephric tissue to form S-shaped tubules within the urinary ridge (Fig 2.). Invagination of the medial end of each mesonephric tubule by a glomerular tuft induces the formation of Bowman's capsule by the mesonephric tubule epithelium.

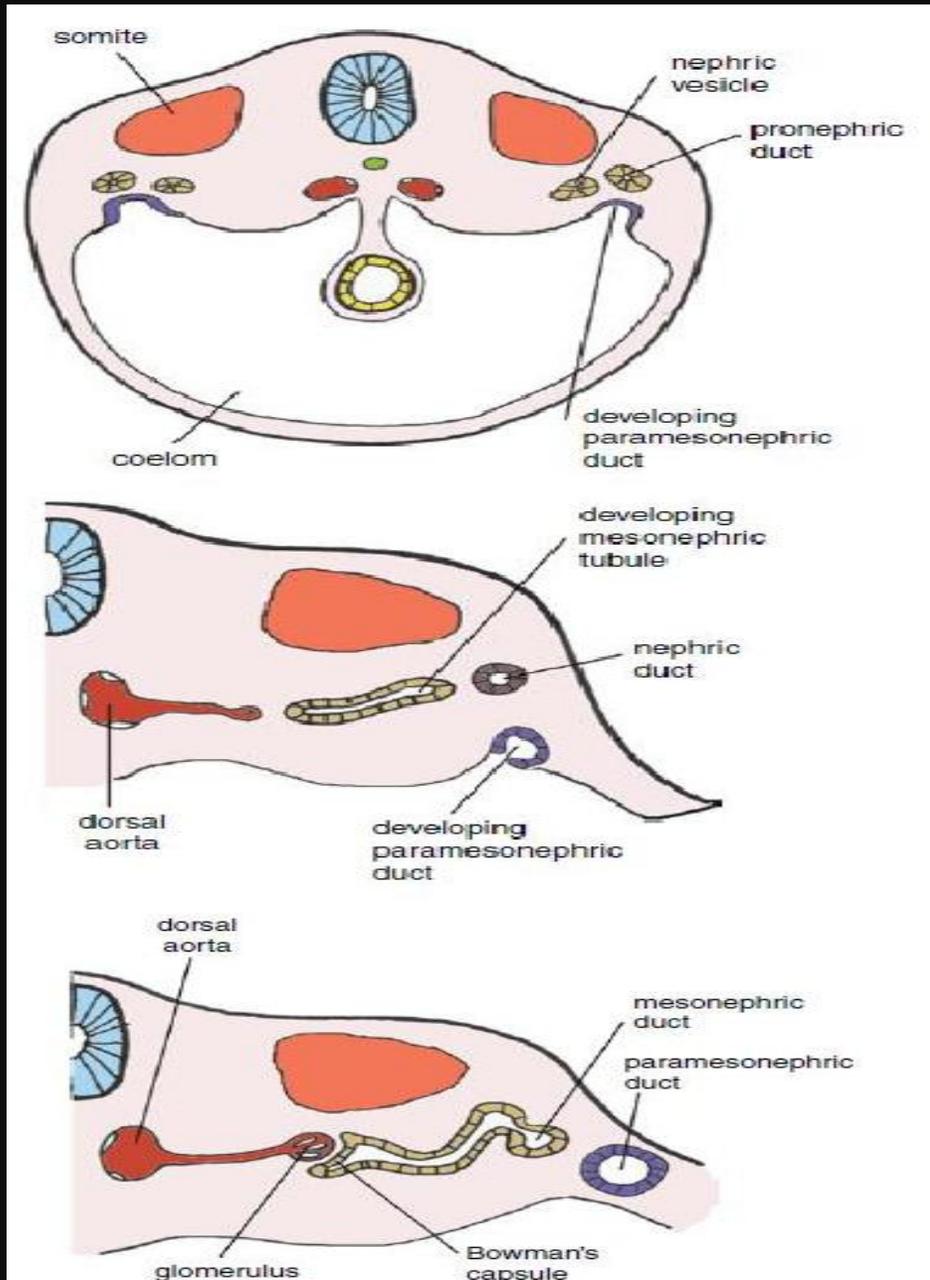


Figure 2. Cross-sections through an embryo showing successive stages in the formation of a mesonephric tubule and paramesonephric duct.

- The combination of Bowman's capsule and the glomerular tuft forms a filtration unit known as a renal corpuscle. The lateral end of each mesonephric tubule enters separately into the pre-existing pronephric duct, which at this stage is referred to as the mesonephric duct (Fig 3.).
- With the development of the mesonephric system, the pronephric tubules and the cranial portion of the pronephric duct atrophy (Fig 4. and 5.). The development of a peritubular capillary network around the mesonephric tubules assists in the reabsorption of water and electrolytes. **In contrast to the structure of the pronephros, where only one tubule develops at the level of each somite, in the mesonephros multiple tubules may develop at the level of each somite.**

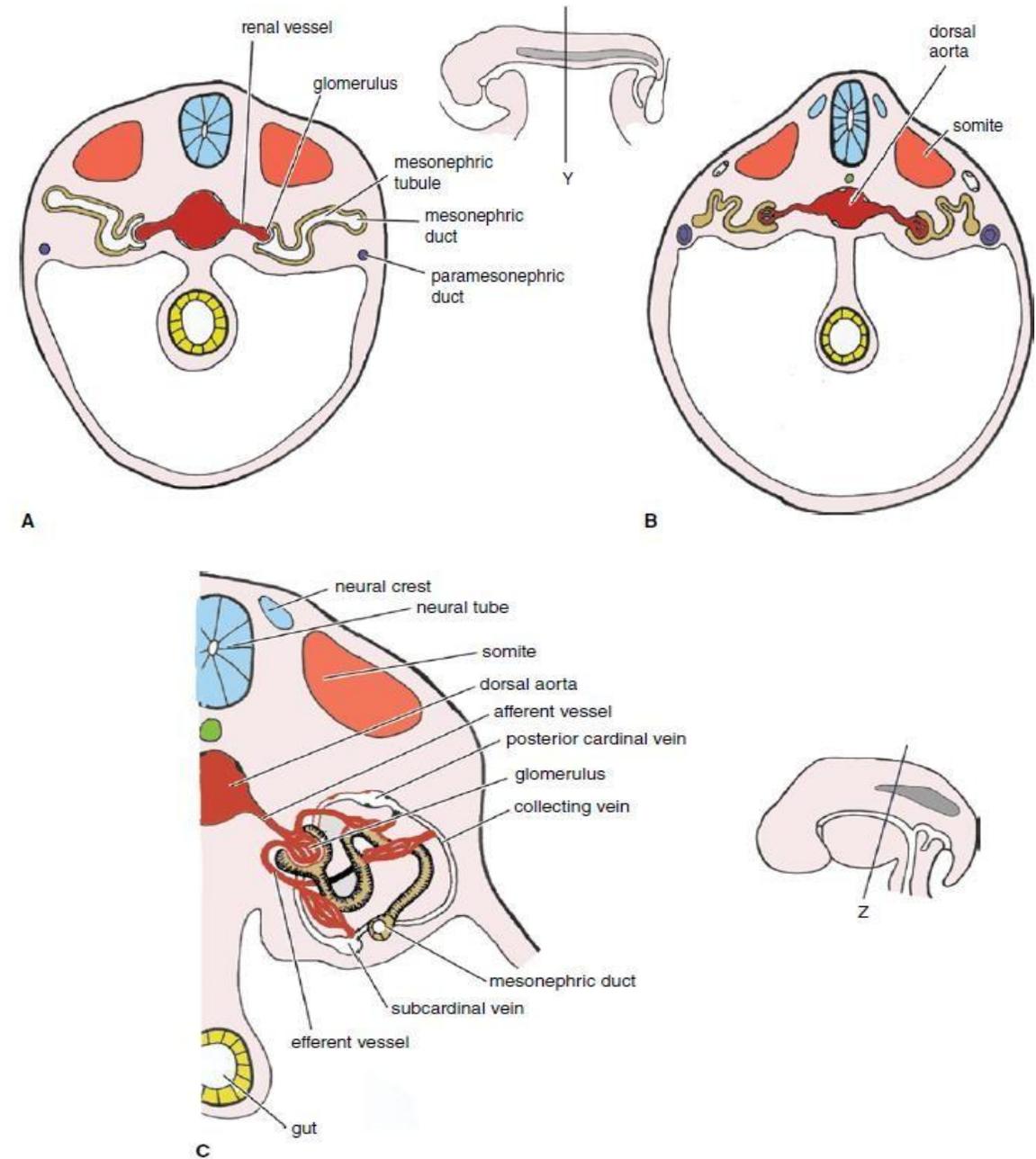


Figure 3. Cross-sections through embryos at the levels indicated, showing the formation of a mesonephric tubule and duct (A to C).

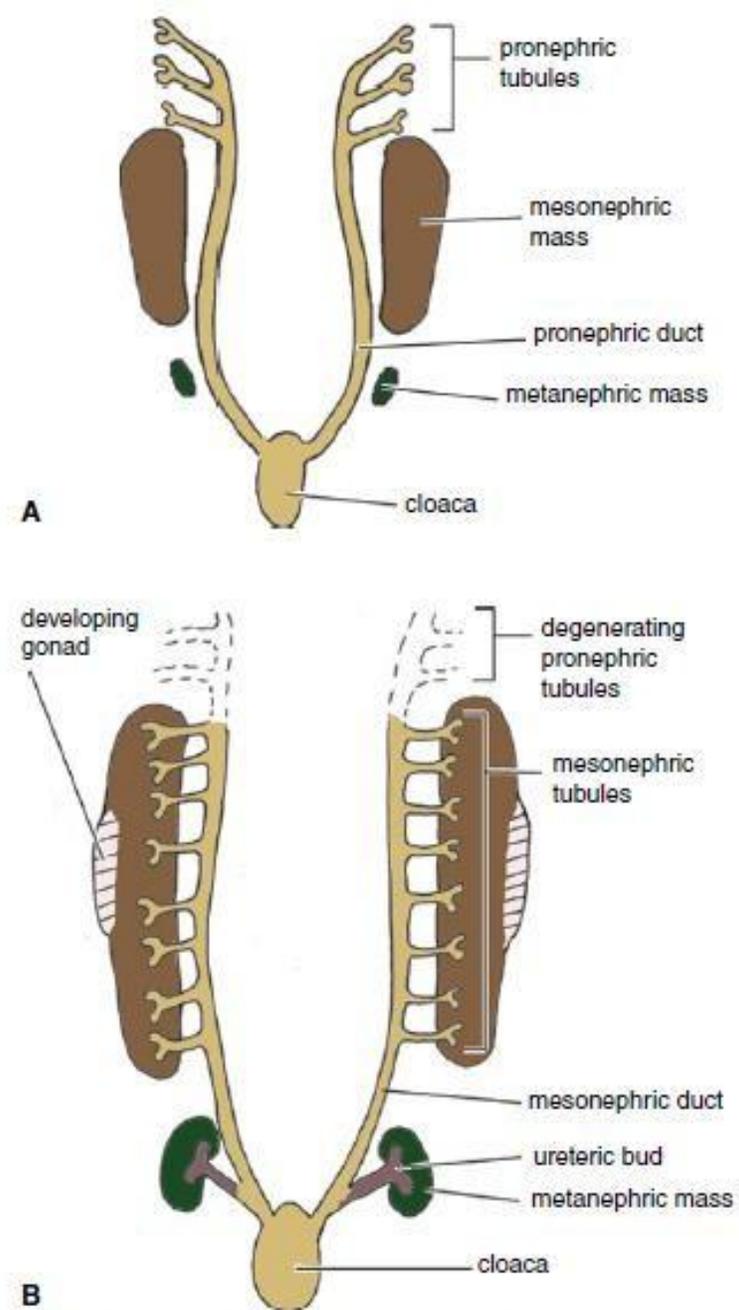
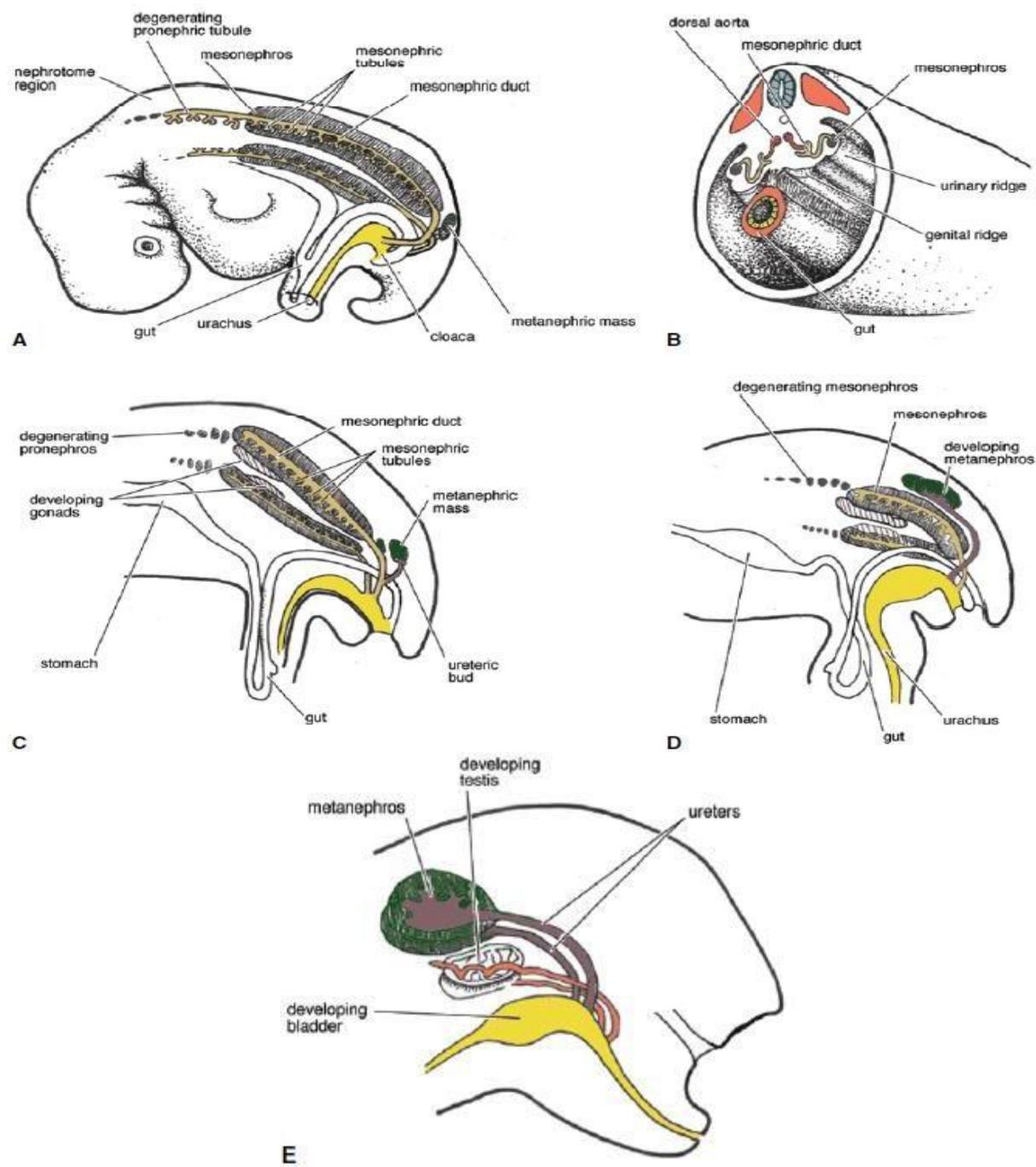


Figure 5. Dorsal views of the developing pronephros, mesonephros and metanephros (A and B).

Figure 4. Changes in the formation of the pronephros, mesonephros and metanephros and their relationships to other developing structures (A to E).

Mesonephros

- The developing left mesonephros and right mesonephros project into the abdominal cavity as distinct anatomical structures in the developing embryo and are especially prominent in porcine embryos up to 35 days of gestation (Fig 4.). **These structures are less prominent in horses, ruminants, dogs and cats than in pigs; in rodents and humans they are poorly developed.**
- The mesonephros regresses in horses around the 65th day of gestation, in cattle at approximately 58 days, in pigs at around 50 days and in dogs at approximately 36 days. **A unique feature of the mesonephric tubules of ruminant embryos is the presence of giant glomeruli associated with the more cranial tubules. The significance of these giant glomeruli is unclear. It has been suggested that they may be related to the large allantoic cavity and the associated high volume of allantoic fluid in ruminants.**

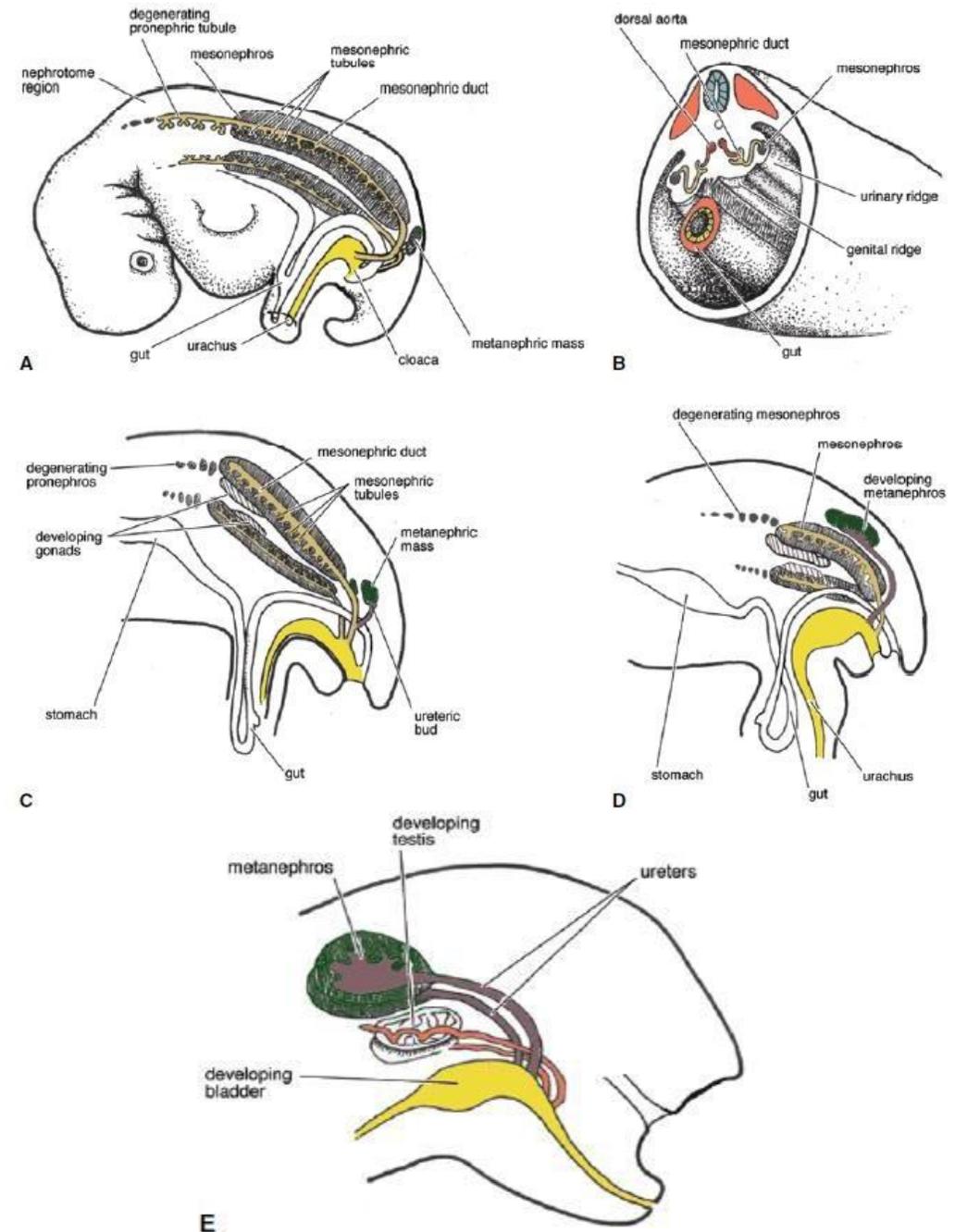


Figure 4. Stages in the formation of the pronephros, mesonephros and metanephros and their relationships to other developing structures (A to E)

Metanephros

The metanephros is formed from two primordial structures:

- The ureteric bud, which is an outgrowth of the mesonephric duct
- The metanephric blastema located in the sacral region, which forms from the caudal end of the nephric ridge (Fig 4. and 5.).

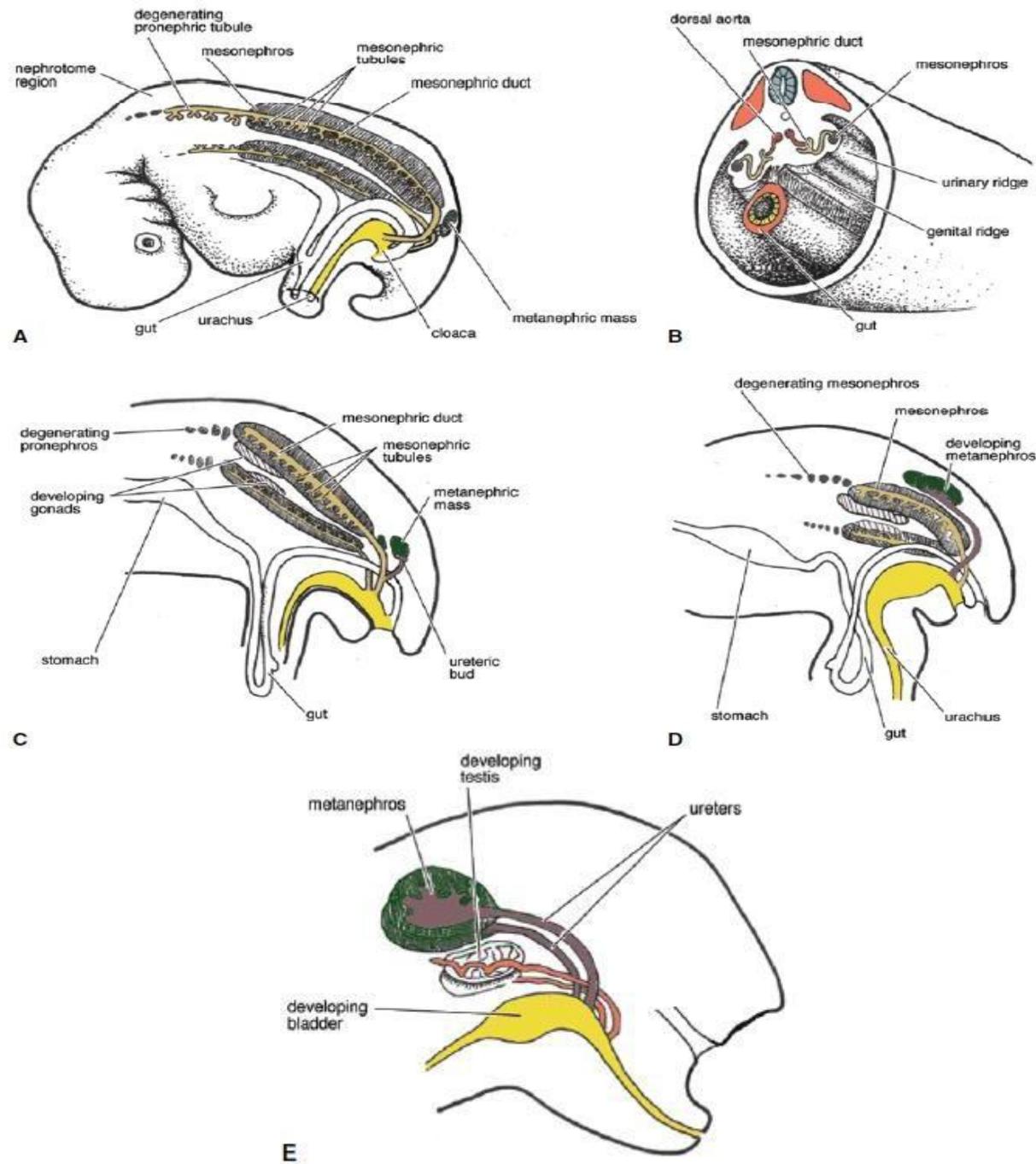


Figure 4. Stages in the formation of the pronephros, mesonephros and metanephros and their relationships to other developing structures (A to E).

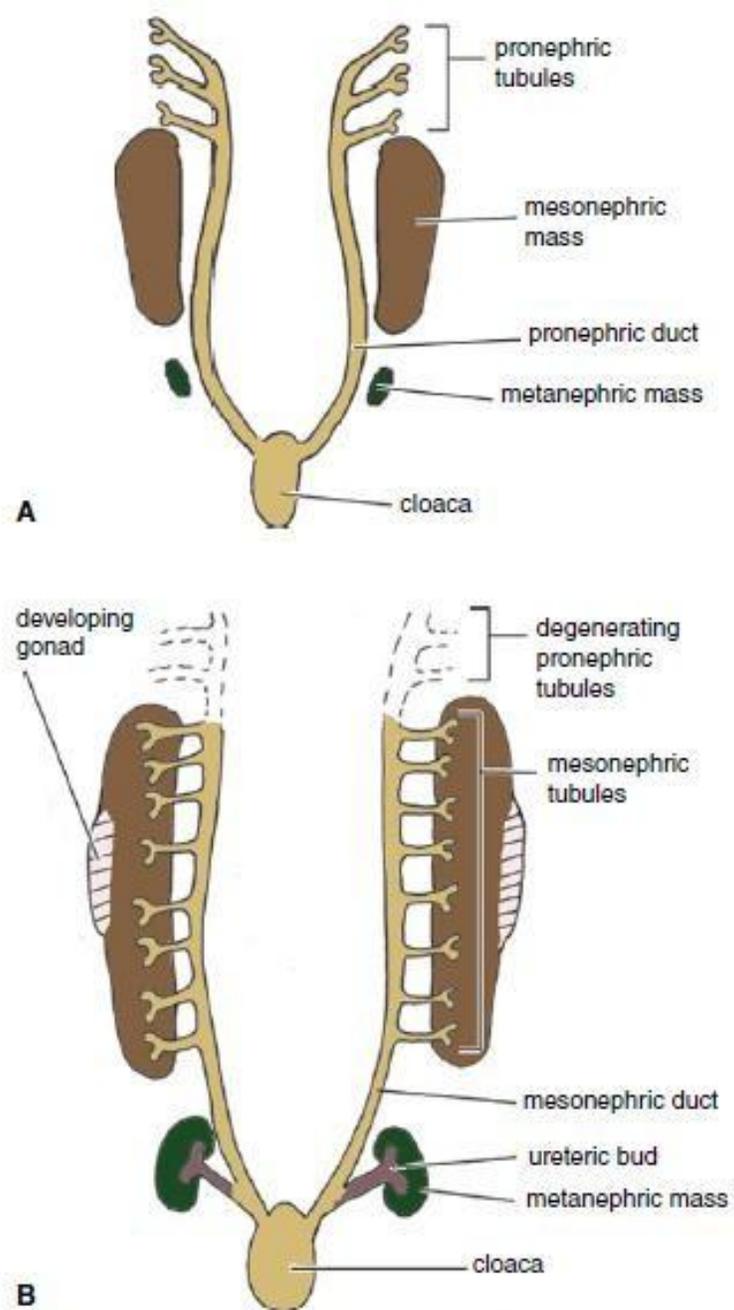


Figure 5. Dorsal views of the developing pronephros, mesonephros and metanephros (A and B).

Metanephros

- The ureteric bud extends cranially towards the metanephric blastema and dilates at its cranial end where it becomes almost completely surrounded by metanephric tissue. The dilated portion of the ureteric bud gives rise to the pelvis and the collecting ducts of the definitive kidney. The formation of the collecting ducts induces the metanephric tissue to give rise to metanephric tubules (Fig 6.).
- The manner in which the dilated end of the ureteric bud differentiates, influences the final anatomical arrangement of the fully developed kidney in mammals. Accordingly, the anatomical form of mammalian kidneys ranges from unilobar to distinct multilobar structures, with intermediate gradations of partial and complete lobar fusion.

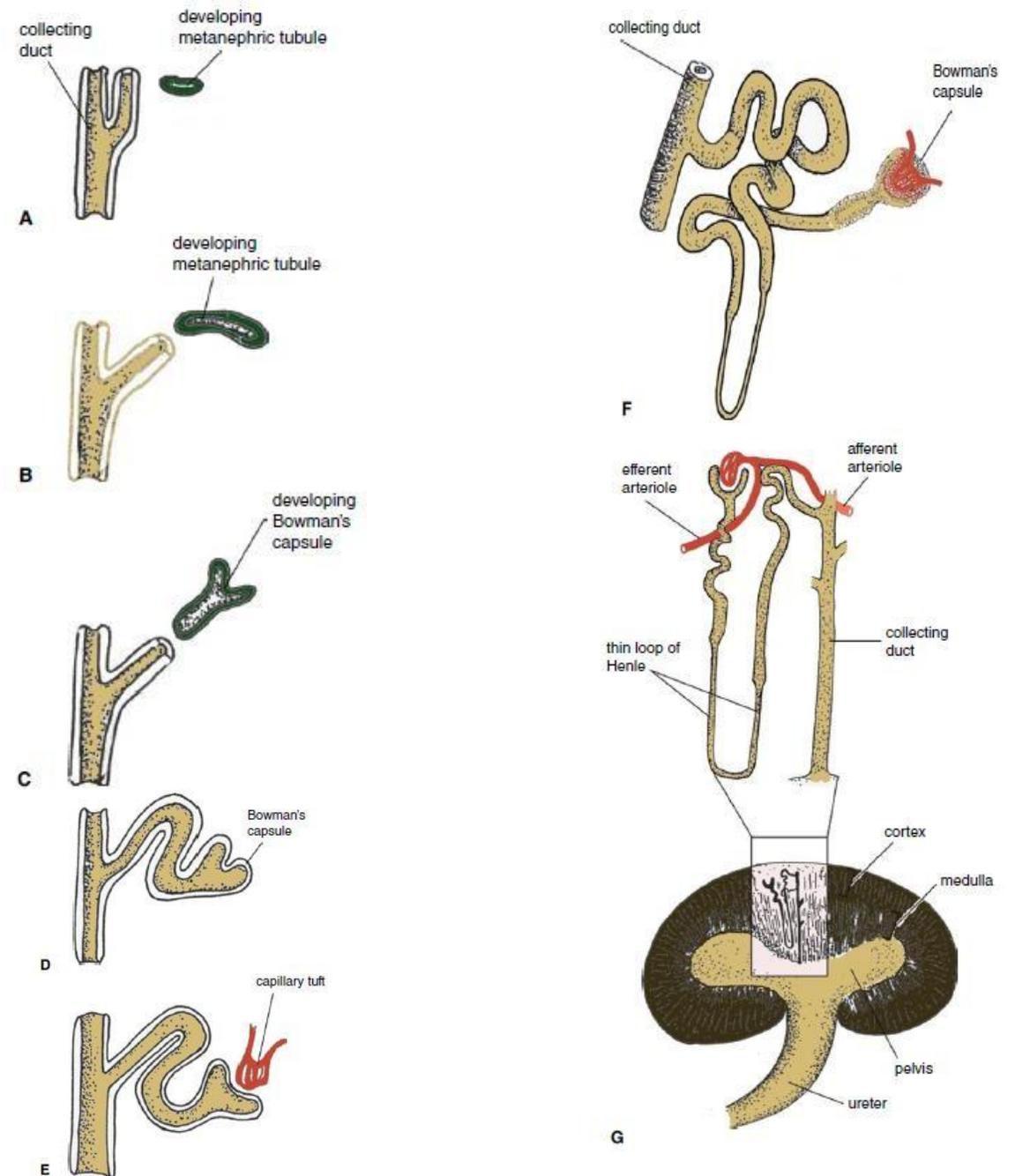


Figure 6. Stages in the formation of a nephron, its relationship to a collecting duct and its final arrangement in the functioning kidney (A to G).

Specification of ureteric buds

- Kidney formation is strongly dependent on a series of reciprocal interactions between the ureteric bud and metanephric mesenchyme. Signals from the metanephric mesenchyme initiate kidney development by inducing the formation of the ureteric bud from the mesonephric duct.
- During early metanephros development, the ureteric buds and the mesenchyme from which the metanephric tissue arises, each promote reciprocal differentiation.

Unilobar kidneys

- In developing kidneys of rodents and rabbits, the renal pelvis gives off a number of branches which project into the metanephric tissue and become the collecting ducts. Under the inductive influence of the collecting ducts, metanephric tissue forms primitive tubules which later become S shaped. One end of each tubule joins to the collecting duct and the other, when invaginated by a glomerulus, becomes the cup-shaped Bowman's capsule. The metanephric tubule continues to elongate, forming a U-shaped bend, the loop of Henle, which extends towards the renal pelvis. The portion of the tubule adjacent to Bowman's capsule becomes coiled and is referred to as the proximal convoluted tubule, while the more distant portion of the tubule, which also coils, is referred to as the distal convoluted tubule. Collectively, the renal corpuscle, the loop of Henle and the proximal and distal convoluted tubules constitute a nephron (Fig 6.).

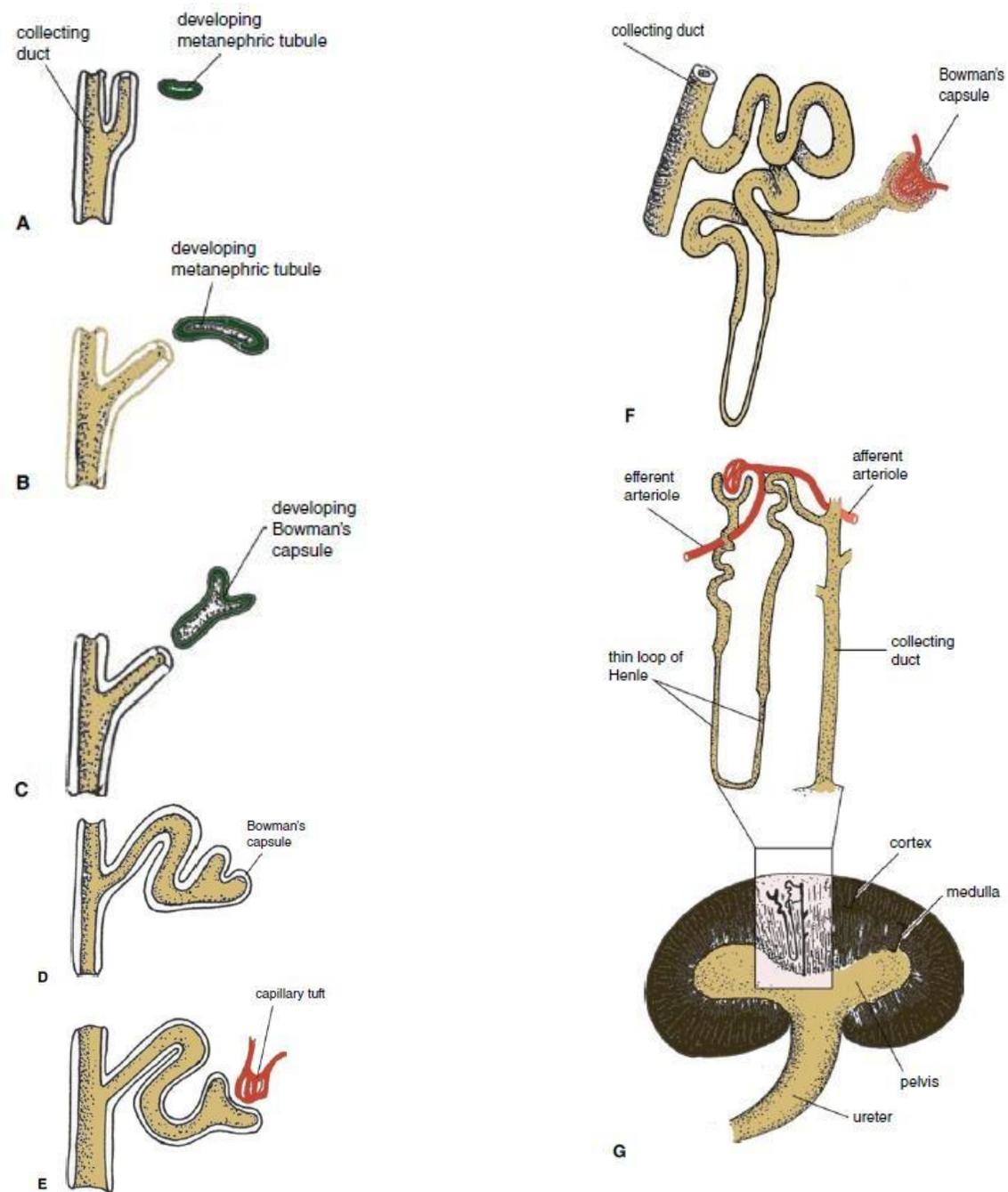


Figure 6. Stages in the formation of a nephron, its relationship to a collecting duct and its final arrangement in the functioning kidney (A to G).

Unilobar kidneys

- With the development of the nephron and collecting duct system, the kidney can be descriptively divided into an outer cortical and inner medullary region. The compact cortex consists mainly of renal corpuscles, along with proximal and distal convoluted tubules, while the medulla consists principally of the loops of Henle and collecting ducts. The conical arrangement of the loops of Henle and collecting ducts is referred to as a medullary pyramid. The base of the pyramid is capped by the cortex, while the apex forms a papilla which projects into the cup-like pelvis. The medullary pyramid, with its associated cortical covering, constitutes a renal lobe composed of subunits referred to as lobules. A renal lobule consists of a collecting duct and the associated nephrons which drain into it. Because the kidneys of rodents and rabbits consist of a single pyramidal structure, they are referred to as unilobar kidneys.

Unilobar kidneys

- Each tubule in the pronephros and mesonephros has its own direct blood supply from the aorta. In contrast, the vascular supply to each nephron in the metanephros derives from a branch of the renal artery. During its differentiation, the position of the metanephros changes from the pelvic region to the lumbar region, where it occupies a position dorsal to the degenerating mesonephros and the developing gonad (Fig 4. and 5.). This change in position may be accounted for in part by migration and also by differential growth of the skeletal and muscular structures in the pelvic and lumbar regions. **With the exception of pigs**, the right kidney in all domestic animals migrates more cranially than the left kidney. In its final position, the right kidney is in direct contact with the caudate lobe of the liver.

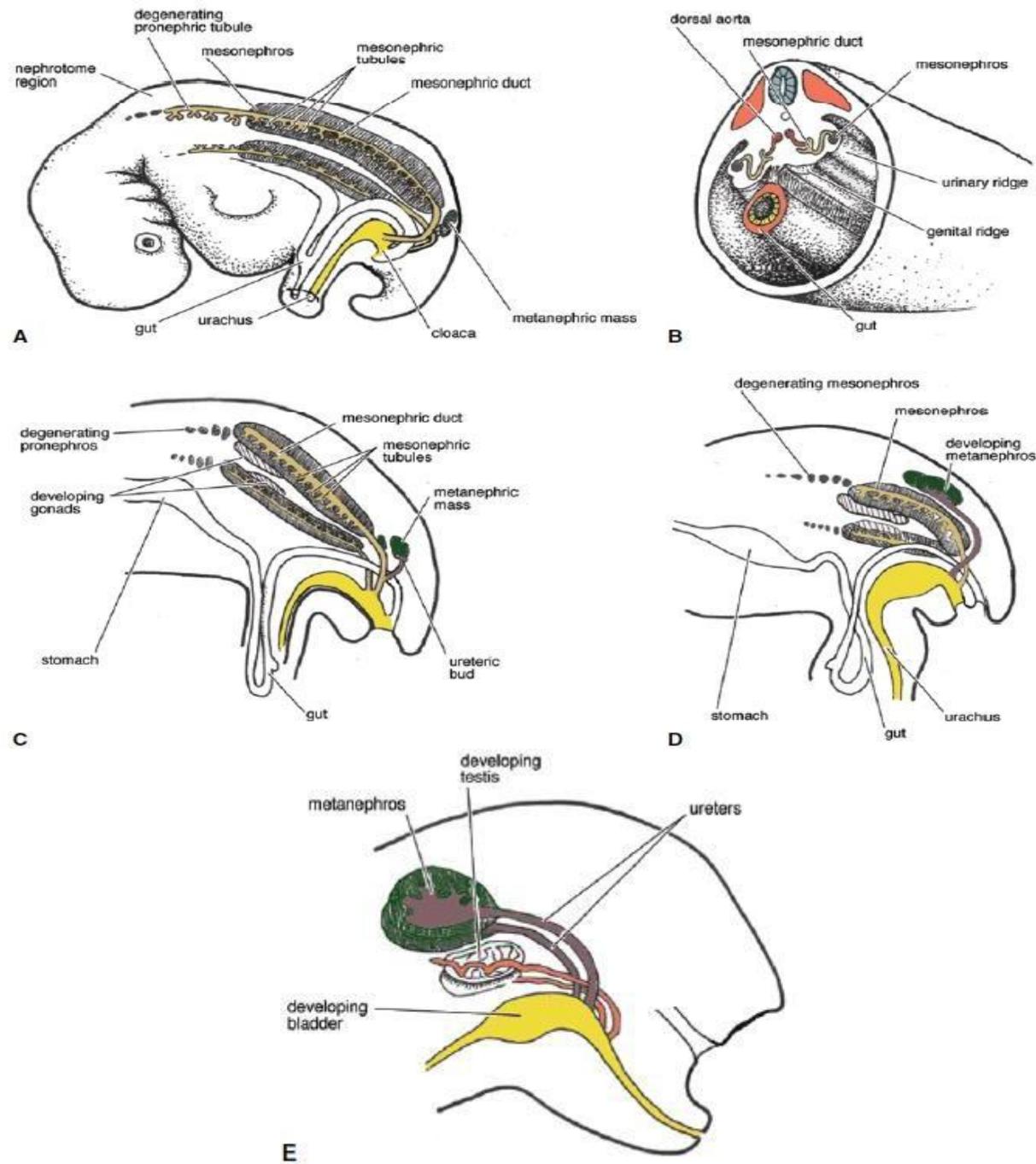


Figure 4. Stages in the formation of the pronephros, mesonephros and metanephros and their relationships to other developing structures (A to E).

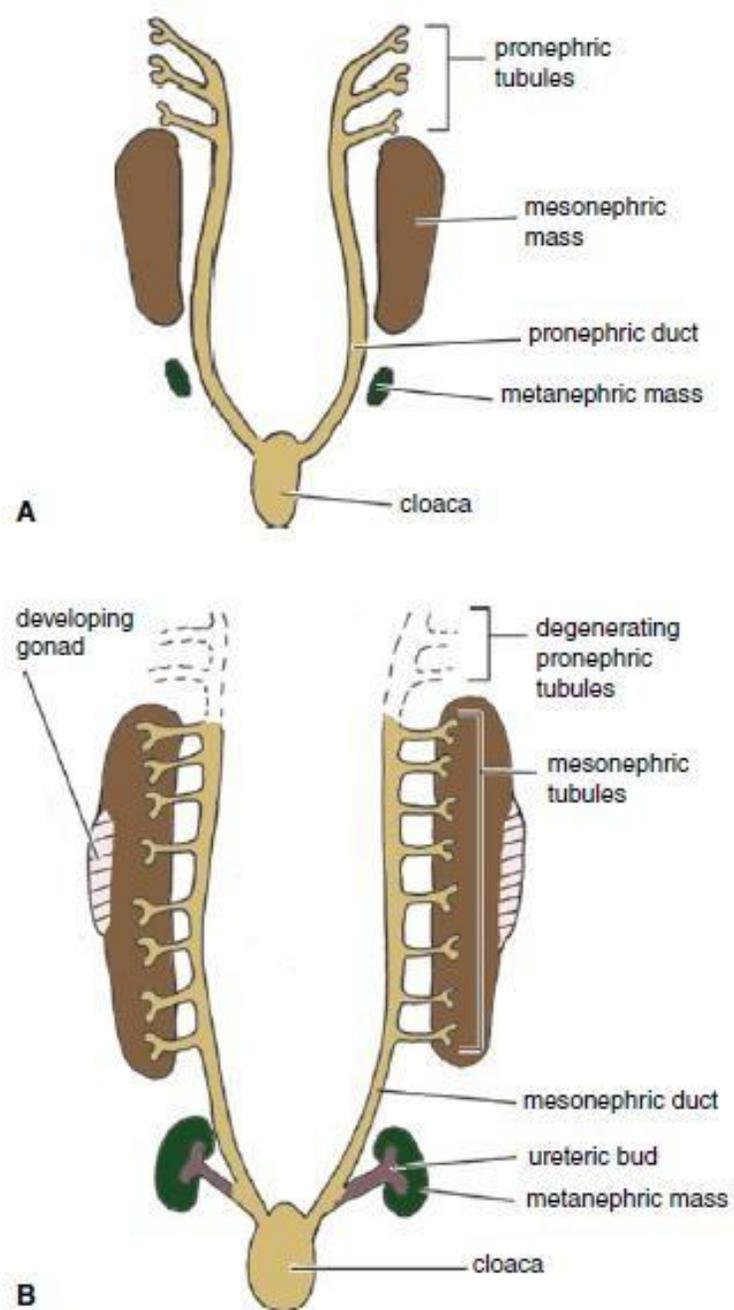
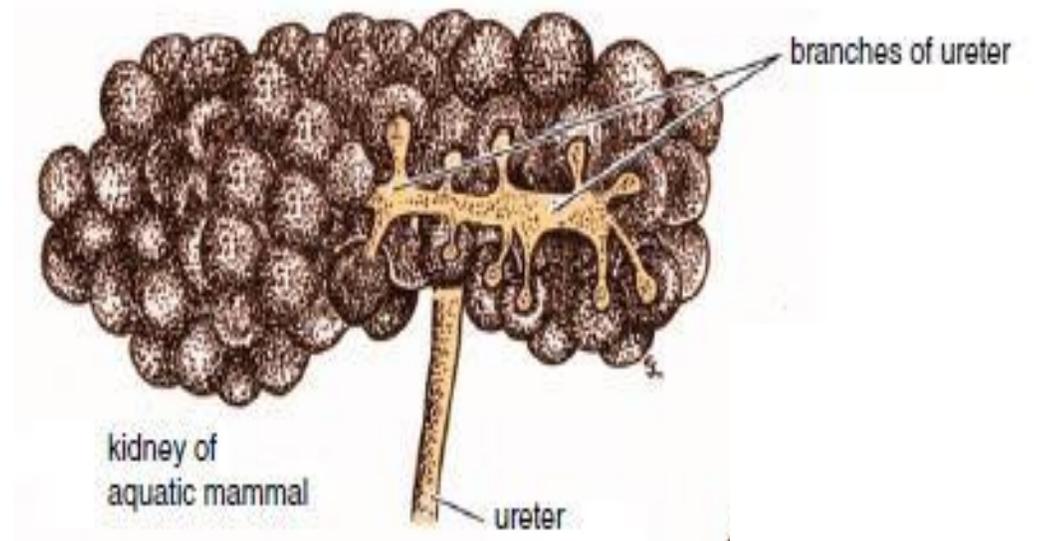


Figure 5. Dorsal views of the developing pronephros, mesonephros and metanephros (A and B).

Multilobar kidneys

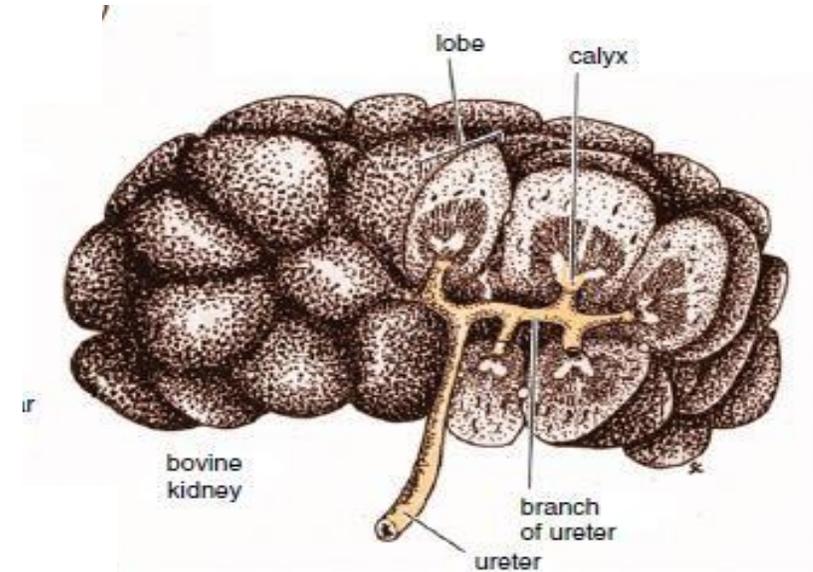
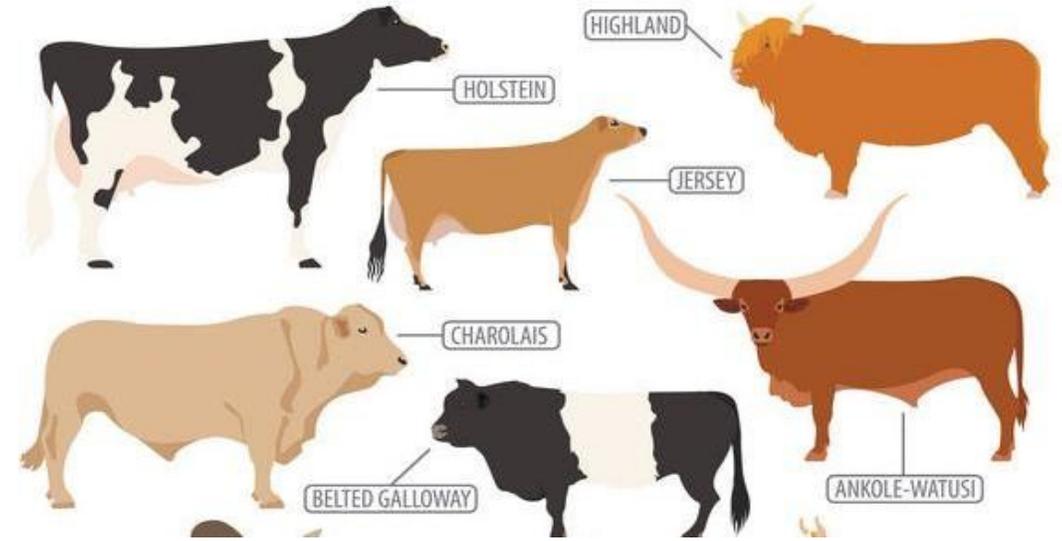
Kidneys of aquatic mammals:

- In aquatic mammals including seals, otters and whales, the terminal end of the ureteric bud gives rise to a number of branches each capped by metanephric tissue forming a kidney lobe, termed a renculus. Each individual lobe is formed in a manner similar to that described for a unilobar kidney. The multilobar kidney in these species resembles a bunch of grapes, with individual lobes draining separately into a branch of the ureter.



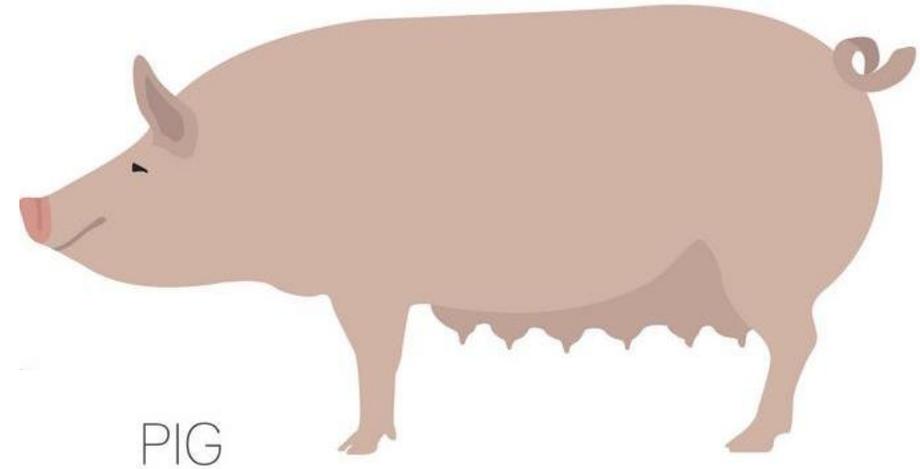
Kidneys of domestic animals:

- In cattle, the ureteric bud, from which the ureter derives, forms two major branches which subdivide into 12 to 25 minor branches. The dilated ends of the minor branches become invaginated forming funnel-shaped calyces. When capped by metanephric tissue, either singly or in pairs, the resulting structure constitutes a kidney lobe. Collecting ducts which radiate from the calyces into the metanephric tissue induce the formation of metanephric tubules. Bovine kidneys and the kidneys of aquatic mammals have some features in common and some distinguishing features. Superficially, kidneys from these species have a multilobar appearance. However, in bovine kidneys, what superficially appear to be individual lobes in some instances arise from fusion of the cortices of adjacent lobes.
- Irrespective of whether or not cortical fusion has occurred, each lobe still retains a distinct pyramidal arrangement. The bovine kidney, therefore, is often referred to as a **multipyramidal kidney**. The fused cortical tissue forms columns which histologically demarcate the boundaries of individual lobes. Unlike the kidneys of other domestic animals, the bovine kidney does not have a pelvis.

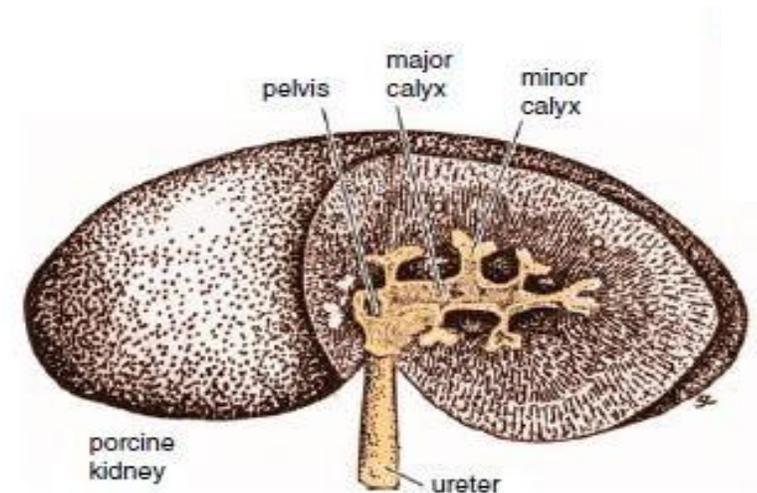


Kidneys of domestic animals:

- The dilated end of the porcine ureteric bud gives rise to the renal pelvis. Two major divisions of the renal pelvis, major calyces, form up to 10 funnel-shaped divisions referred to as minor calyces. When minor calyces are capped by metanephric tissue they constitute the renal lobes.
- Because of fusion of the cortical tissue of adjacent lobes throughout the porcine kidney, its smooth surface imparts the superficial appearance of a unilobar kidney. Despite this superficial appearance, the multilobar structure of the porcine kidney is evident histologically both from its multipyramidal appearance and the separate drainage provided for each lobe by minor calyces.

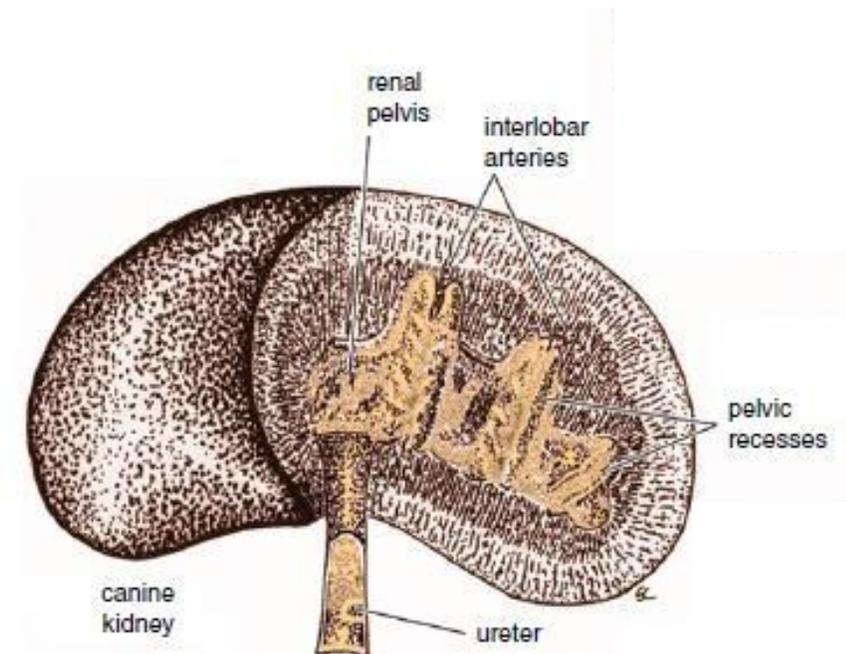


PIG



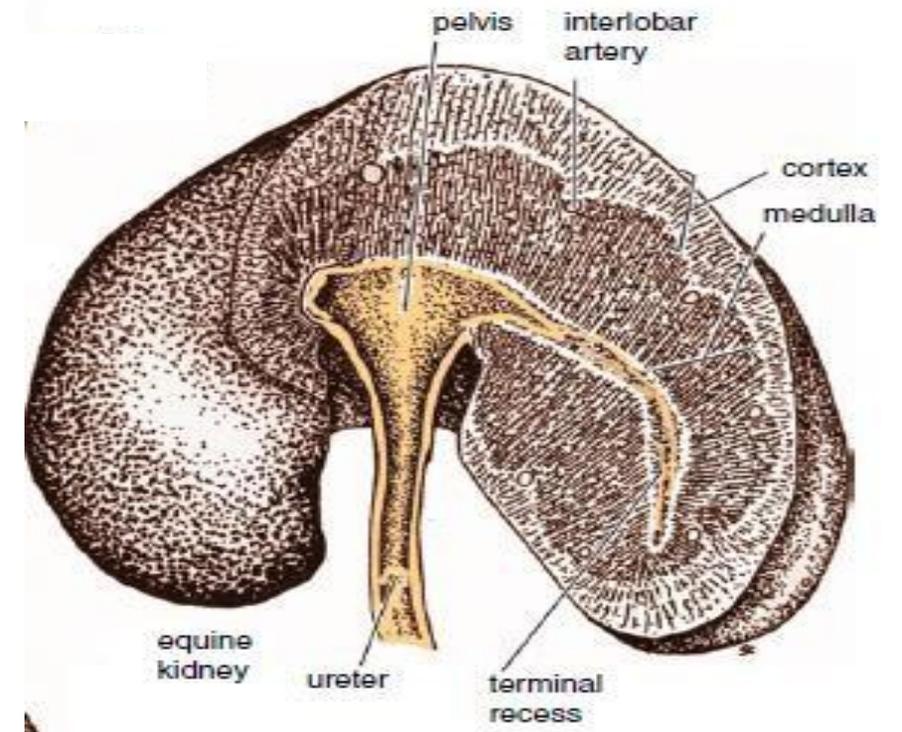
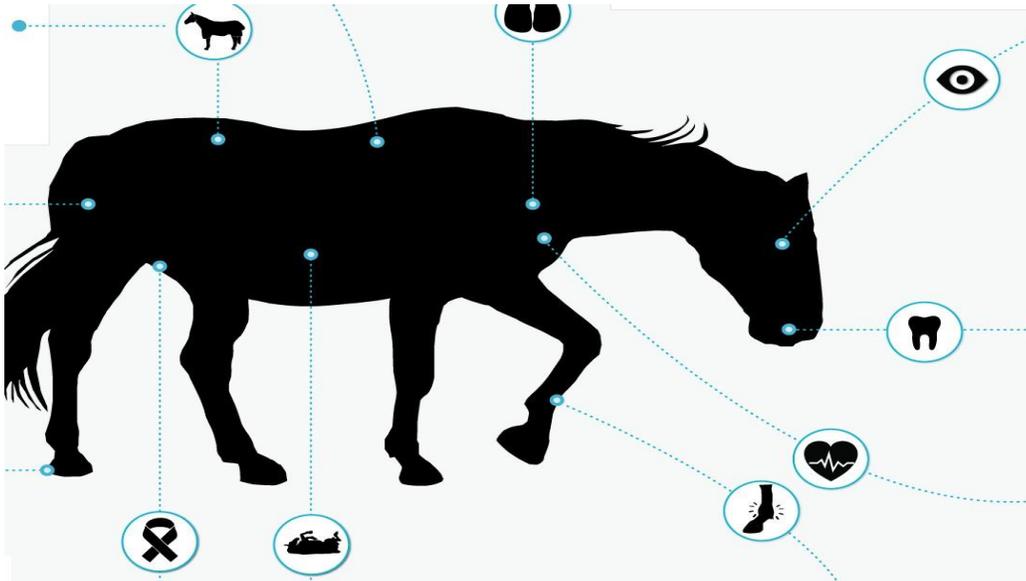
Kidneys of domestic animals:

- In domestic carnivores, complete fusion of the cortical areas of adjacent lobes imparts the superficial appearance of a unilobar kidney. Fusion of the apices of medullary pyramids leads to the formation of a ridge-like common papilla, the renal crest, a prominent feature of canine kidneys. This fusion of the pyramidal apices conveys the impression that kidneys of carnivores are unilobar. However, the multilobar structure of kidneys of carnivores is confirmed by the presence of cortical columns and the position of the interlobar arteries which delineate individual lobes. A feature of the kidneys of domestic carnivores is the presence of deep out-pouchings of the lateral walls of the renal pelvis, referred to as lateral recesses.
- **The kidneys of sheep and goats develop in a manner comparable to those of domestic carnivores with many similar morphological features.**



Kidneys of domestic animals:

- Equine kidneys, which consist of 40 to 60 lobes and develop in a manner similar to those of domestic carnivores, have a smooth cortical surface with a common draining area, the renal crest. Extensions of the poles of the renal pelvis form two structures, termed the terminal recesses, into which some collecting ducts drain.



Bladder

- During development of the hindgut, the urorectal septum divides the cloaca into the rectum dorsally and the primitive urogenital sinus ventrally. At the point of entry of the mesonephric duct, the primitive urogenital sinus divides into the cranial vesico-urethral canal, the primordium of the bladder, and a caudal urogenital sinus proper (Fig 8.).
- In the male embryo, the caudal urogenital sinus gives rise to the penile urethra, and in the female embryo to the urethra and vestibule. As the terminal portions of the mesonephric and ureteric ducts are gradually incorporated into the wall of the developing bladder, each duct system develops its own separate opening into the bladder primordium. Subsequently, in the male embryo, the mesonephric ducts converge before entering the prostatic urethra. The ureters undergo a cranial displacement relative to the mesonephric ducts (Fig 8.), so that each ureter enters the bladder on its dorsal surface, cranial to the neck of the bladder.

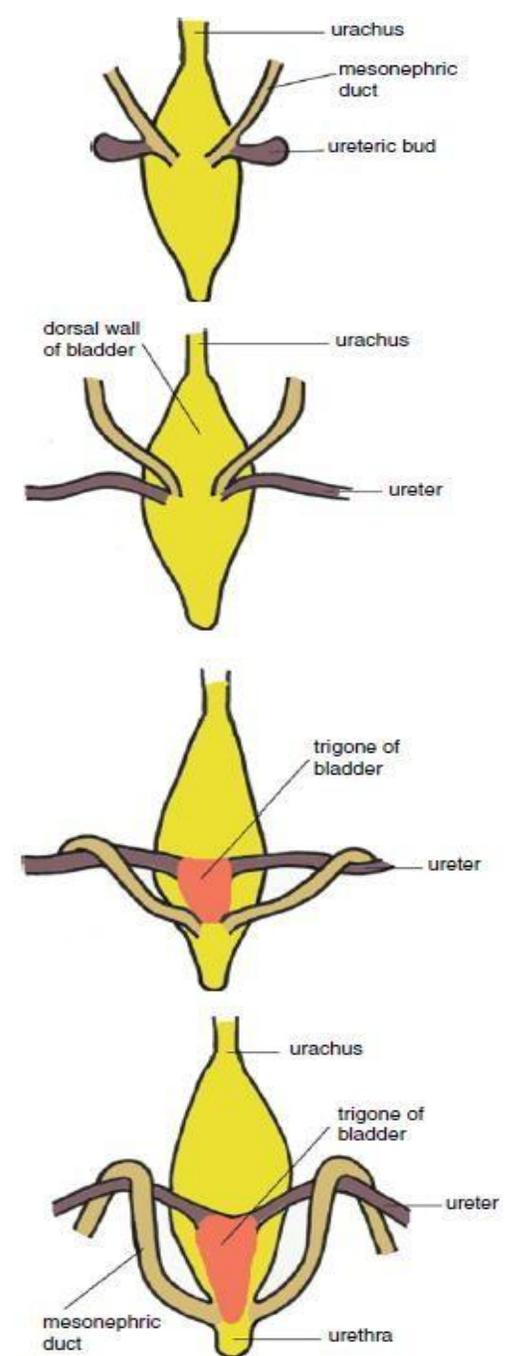


Figure 8. Sequential stages in the development of the bladder, ureters and associated structures.

Bladder

- As the mesonephric ducts and ureters are of mesodermal origin, a triangular area of the dorsal wall of the bladder, the trigone, is lined by epithelium of mesodermal origin, while the epithelial lining of the remainder of the bladder is derived from endoderm.
- Non-epithelial components of the bladder develop from splanchnic mesoderm. The embryological origins of the cells, tissues and structures of the urinary system are shown in Figure 9.

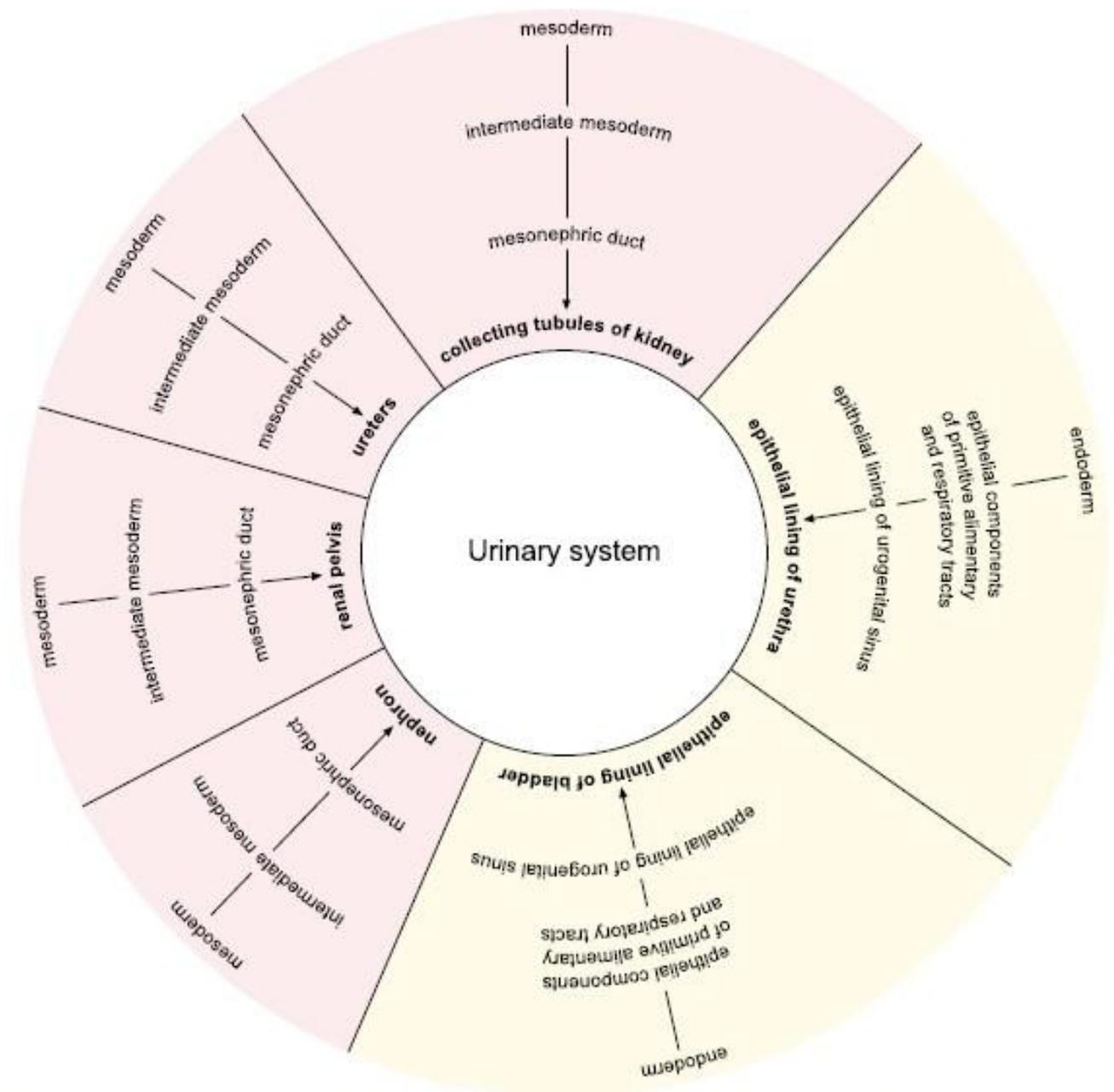


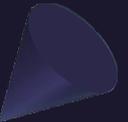
Figure 9. Derivatives of germ layers from which cells, tissues, structures and organs of the urinary system are formed. Structures in bold print are arranged alphabetically (based on Figure 9.3).

Summary

- Intermediate mesoderm gives rise to nephrons, the functional units of the kidney. Three sequential urinary systems develop, pronephros, mesonephros and metanephros. The pronephros and duct, before regressing, induce formation of the mesonephros.
- The metanephros replaces the mesonephros as the definitive kidney in reptiles, avian species and mammals.
- The ureteric bud, which originates from the mesonephric duct, grows into the metanephric mesenchyme, inducing nephron formation.
- Apart from the mesodermal trigone, the bladder develops from the cranial portion of the urogenital sinus and its epithelial lining is derived from endoderm.



Developmental Anomalies of Urinary System



1. Renal agenesis

- Unilateral or bilateral renal agenesis is associated with developmental failure of one or both ureteric buds. As a consequence of this failure, induction of the metanephric mass, which is required for the formation of renal tubules, does not occur. Survival is not threatened by unilateral renal agenesis, whereas bilateral renal agenesis is incompatible with life.

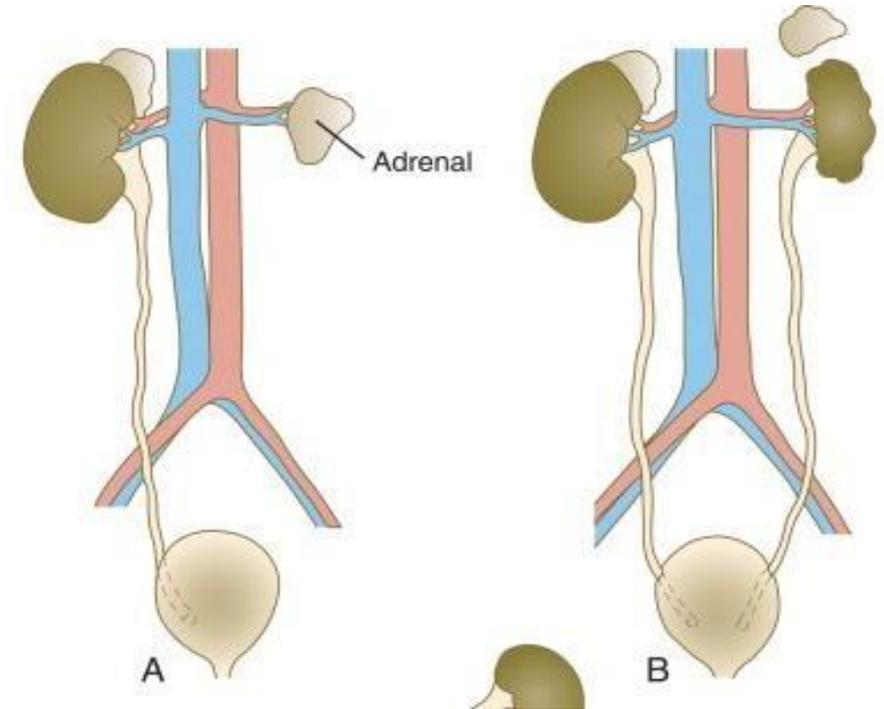
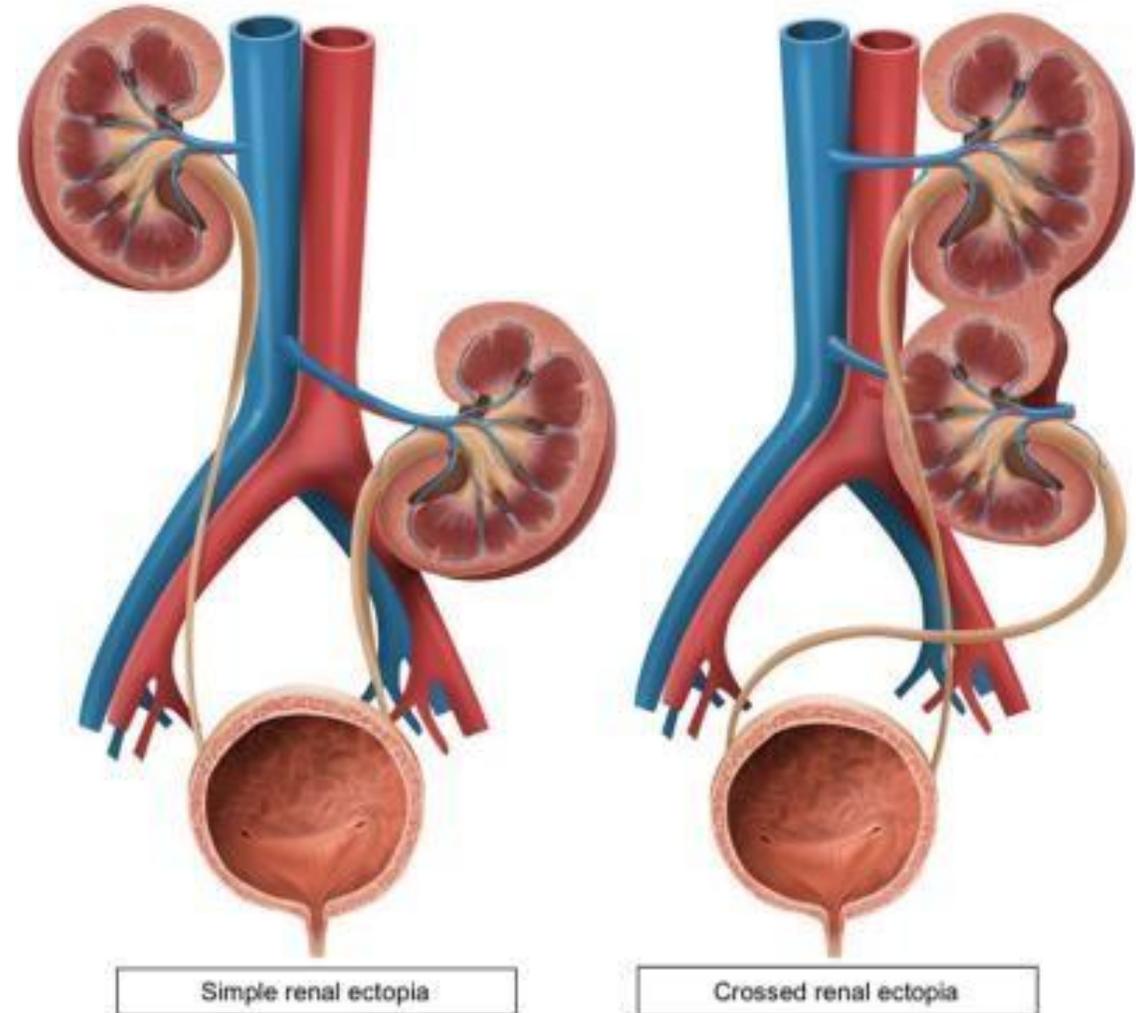


Figure 10. Common renal anomalies. (a) Unilateral renal agenesis. The ureter is also missing. (b) Unilateral renal hypoplasia

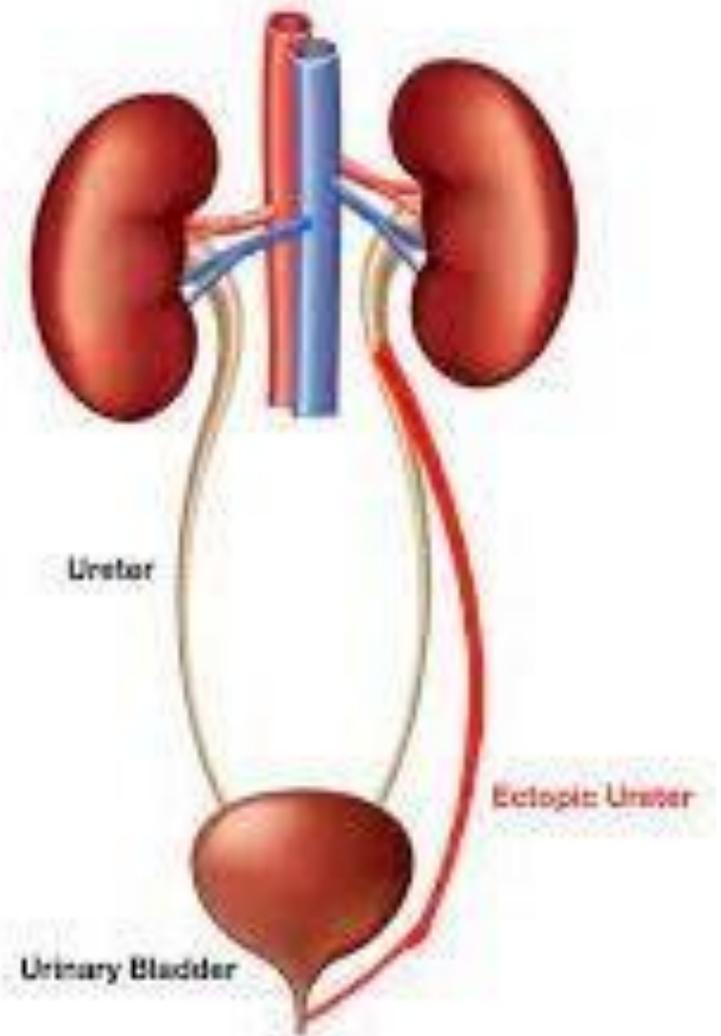
2. Ectopic kidney

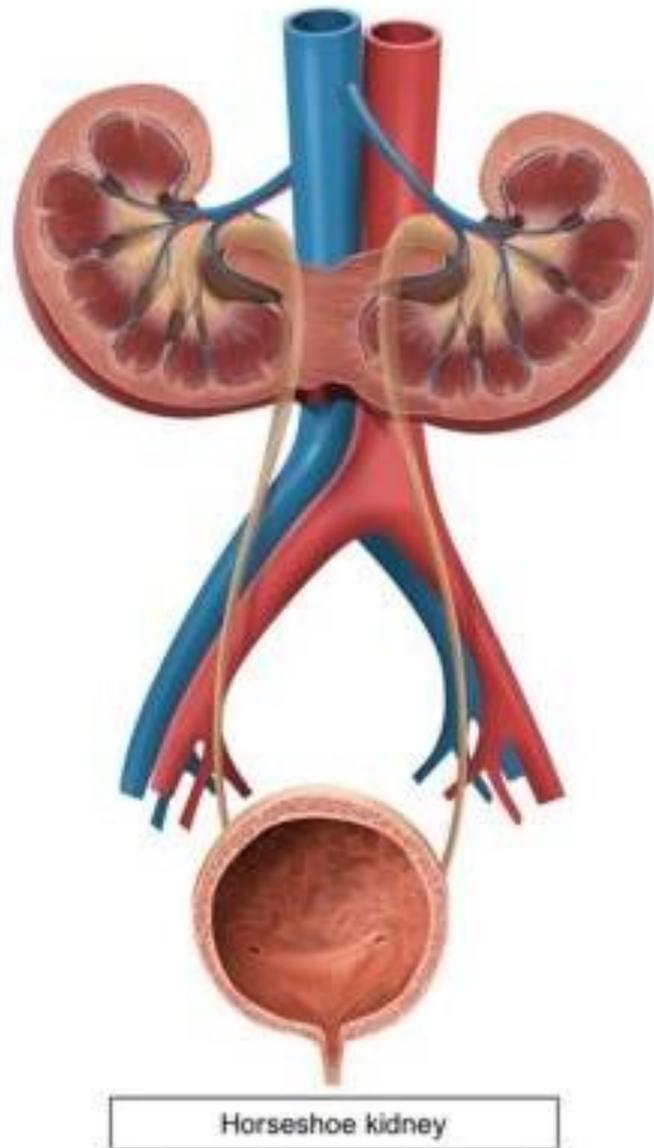
- When the metanephros gives rise to a kidney which remains in the sacral region, such a kidney is referred to as an ectopic or pelvic kidney. The frequency of this condition which may be unilateral or bilateral, is approximately 1 in 400, with a higher incidence in male than in female newborns.



3. Ectopic ureter

- If the process of ureteric bud differentiation is disrupted, the ureter may retain an attachment to the urethra, thus forming an ectopic ureter. This condition results in urinary incontinence as the ureter bypasses the bladder, resulting in a lack of voluntary control of urination. Ectopic ureters are diagnosed more commonly in female animals than in male animals and are generally seen in pups. The breeds most commonly affected are Golden Retrievers, Labrador Retrievers, and Siberian Huskies.





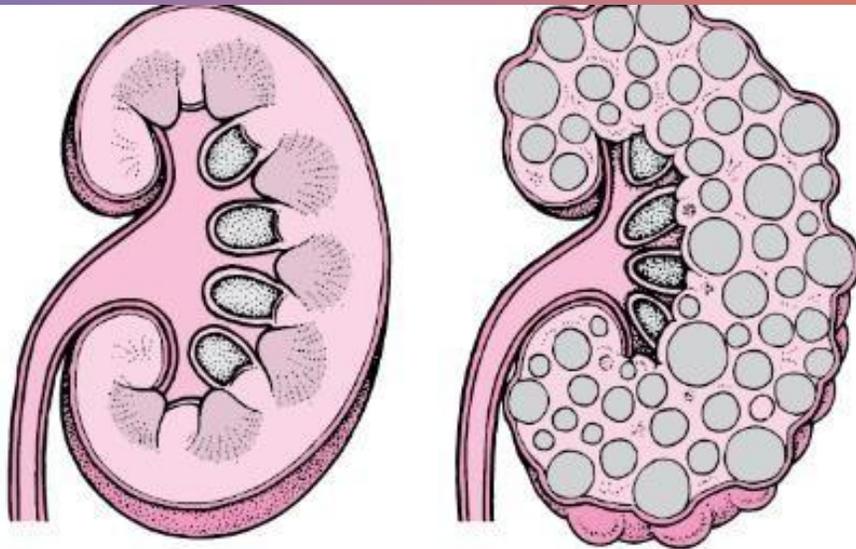
4. Horseshoe kidney

- The term ‘horseshoe kidney’ is used to describe an abnormal renal structure, formed by the fusion of the caudal poles of bilateral pelvic kidneys, because of its shape. This anomaly has been reported in humans and in domestic animals.



5. Congenital cystic kidney

- An anomaly which may result either from the failure of developing nephrons to join with their collecting ducts or from the formation of cysts in rudimentary nephrons is referred to as a congenital cystic kidney.
- Cyst formation arises from the accumulation of urine within nephrons which fail to connect to their collecting duct system. An inherited disease in Persian cats, referred to as feline polycystic kidney disease, which has an autosomal dominant pattern of inheritance, is reported to occur at high frequency in the Persian cat population worldwide.



Normal Kidney

Polycystic Kidney

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Thank you for your attention

