Section 1

Anatomy and physiology
Anatomy of the kidney and proximal ureter

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The kidney removes waste via blood filtration followed by tubular reabsorption and secretion. This chapter highlights renal anatomy of the dog and cat, including anatomy of the renal pelvis and proximal ureter.

Gross anatomy

Kidney topography and surface features

The kidneys of the dog and cat are similar in structure and relative size. They are paired, bean-shaped, and located dorsally in the abdominal cavity. Kidneys are retroperitoneal, dorsal to the peritoneal cavity, and covered by parietal peritoneum only. The surface facing laterally is convex; the medial surface is concave, with an indented region called the hilus (hilum) where vessels, nerves, and the ureter enter/exit the kidney. The right kidney is positioned cranial to the left, with its cranial pole situated within a recess of the caudate lobe of the liver.

In the dog, the right kidney is more firmly attached to the dorsal body wall than the left kidney. Thus, the location of the right kidney is more predictable, extending from vertebrae T13 to L2. The left kidney is approximately half a kidney length caudal to the right (Osborne et al. 1972); its looser attachment can result in movement during respiration or body positioning. In the cat, both kidneys are pendulous, moveable, and more caudally located than in the dog. The right kidney is positioned at the level of vertebrae L1 to L4, left kidney at the level of L2 to L3 (Nickel et al. 1973).

The kidney develops embryologically from discrete lobes that fuse for the most part in the dog and cat. The carnivore kidney is classified as unilobar. It is devoid of lobe demarcations externally, presenting a smooth surface encased within a fibrous capsule. Sectioning the kidney reveals an outer layer of dark-colored, highly vascular cortex, surrounding a lighter colored medulla (Figure 1.1).

Renal cortex and medulla

The cut surface of the renal cortex has a relatively rough texture due to collections of capillary tufts (glomeruli) and a labyrinth of tubules (cortical labyrinth). Medullary rays, smooth striations that appear to be radiating out of the medulla toward the periphery of the cortex, are scattered throughout the cortex.

The renal medulla is composed of renal pyramids that fuse to form a central ridge called the renal crest. The pyramids, wedges of medulla separated by interlobar vessels, are apparent in marginal planes of the section. Each pyramid has an apex (papilla) directed toward the renal pelvis. (Renal pyramids are remaining evidence of embryonic lobation.) The medulla contains papillary ducts that open onto the renal crest surface.

Renal pelvis and proximal ureter

Urine collects in the renal pelvis, a dilatation of the proximal end of the ureter. The pelvis is located within the renal sinus, a fat-containing, medial recess situated at the hilus. In the carnivore, the funnel-shaped renal pelvis has irregular margins due to reflection around interlobar vessels. The scalloped outpockets between vessels are referred to as pelvic recesses (Figure 1.1).

The ureter is an extension of the renal pelvis. It runs retroperitoneally along the dorsal wall of the abdominal cavity and through the lateral ligament of the bladder. The pelvis and ureter are lined by transitional epithelium and have smooth muscle walls. Peristaltic contraction waves initiated in the wall of the renal pelvis travel down...
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Figure 1.1 Anatomy of the canine kidney, pelvis, and ureter. (a) The intact kidney appears unilobar and enclosed in a fibrous capsule. Vessels and the ureter connect at the hilus of the kidney. (b) When sliced marginally on a sagittal plane, the cut surface reveals a fibrous capsule, a continuous renal cortex, and a medulla segregated into renal pyramids by interlobar arteries. The papilla of each pyramid is within a recess of the renal pelvis. (c) When sliced transversely, inner and outer zones of medulla can be seen surrounded by cortex. Along the midline, renal pyramids have fused into a renal crest located above the renal pelvis. (d) A mid-sagittal slice of kidney reveals renal crest rather than pyramids. Renal pelvis and fat occupy a space designated renal sinus. (e) External view of an isolated renal pelvis and ureter. (f) Side view of an isolated renal pelvis and ureter. The wall of the renal pelvis is scalloped, divided into pelvic recesses by wall projections around interlobar arteries (modified from Evans, 1993).

Renal vessels

In most cases, a single renal artery divides into dorsal and ventral rami before entering the renal hilus (Marques-Sampaio et al. 2007). Further branching gives rise to interlobar arteries that enter kidney parenchyma. Arterial branches are branches of interlobar arteries at the corticomedullary junction. Interlobular arteries (cortical radial arteries) arise from arcuate arteries and run radially through the cortex toward the kidney surface, some extending into the capsule (Nickel et al. 1973). In the cat, additional small branches from renal artery rami travel along the periphery of the kidney to supply the cortical surface and renal capsule (Fuller and Huelke 1973).

Interlobar arteries give off afferent arterioles. Each afferent arteriole gives rise to a ball of capillary loops, called a glomerulus. Glomerular capillaries unite to form an efferent arteriole that feeds a second capillary network surrounding renal tubules. The kidney is unusual in having two capillary beds connected by an arteriole, and thus an arterial portal system. The glomerulus constitutes the first capillary bed.

Efferent arterioles from glomeruli located peripherally in the cortex supply peritubular capillaries around cortical tubules, whereas efferent arterioles from juxtamedullary glomeruli supply peritubular capillaries around medullary tubules (Figure 1.2). In the medulla, the ureter, conveying urine into the bladder. (The distal ureter is discussed in chapters on the lower urinary tract.)

Figure 1.2 From an interlobular artery, blood flows to the glomerulus via an afferent arteriole (a). The glomerulus constitutes the first capillary network within the kidney. Efferent arterioles (e) convey blood to a second capillary bed that supplies the renal tubules, peritubular capillaries (arrows). Efferent arterioles from peripheral glomeruli (upper corpuscle) form a capillary network around cortical tubules; efferent arterioles from juxtamedullary glomeruli (lower corpuscle) form capillary networks around tubules located in the medulla. Medullary vessels (vasa recta) are closely associated with the loop of Henle. Peritubular capillaries drain via venules primarily into the interlobular veins.
the peritubular capillary network forms between descending efferent arterioles and venules that ascend back toward the cortex. These more or less straight vessels and their connections are referred to as vasa recta. They participate in an important countercurrent exchange between vessels and tubules. (Less commonly, peritubular capillaries arise from afferent arterioles or arcuate arterial branches (Christensen 1952; Nickel et al. 1973).)

Kidney veins are generally satellites of arteries. Venules arise from capillary beds surrounding cortical and medullary tubules. Veins travel with arterial branches, emptying into interlobular, arcuate, interlobar, and finally renal veins. A subcapsular venous system drains the renal capsule. In the cat, these veins are located within or immediately under the capsule (capsular veins); in the dog, the veins are deeper within the cortex (stellate veins) (Yadava and Calhoun 1958; Nickel et al. 1973). The cat’s prominent capsular veins continue around the kidney periphery to the hilar region where they drain directly into the renal vein (Fuller and Huelke 1973). In the dog, the stellate veins drain into cortex and eventually into the renal vein (Christensen 1952). (The canine renal vein may also receive a direct contribution from stellate veins near the hilus (Fuller and Huelke 1973).)

Microscopic renal anatomy

Nephron

The nephron (renal corpuscle plus renal tubules) is the functional unit of the kidney. Urine produced within the nephron is further modified as it travels through the collecting duct system. (The term “uriniferous tubule” refers to the nephron plus its associated collecting duct.)

Nephron: renal corpuscle

The renal corpuscle is composed of a spherical complex of capillaries (glomerulus) surrounded by a double-wall capsule (Bowman’s capsule). Arterioles enter/exit the corpuscle at its vascular pole, and ultrafiltrate exits at the opposite end of the corpuscle, the urinary pole.

Renal corpuscles are typically scattered throughout the cortex, although there is a small region immediately below the capsule where they are absent in the canine (Sherwood et al. 1969; Bulger et al. 1979). The number of corpuscles per kidney varies with species: 400,000–600,000 in the dog (Horster et al. 1971; Finco and Duncan 1972; Eisenbrandt and Phemister 1979) and approximately 200,000 in the cat (Kunkel 1930).

The glomerulus is formed by an afferent arteriole that gives rise to a ball of capillary loops, which then coalesce, into an efferent arteriole. The diameter of the afferent arteriole is usually larger than that of the efferent. Arteriolar size is autoregulated to maintain a consistent glomerular filtration rate over a wide range of systemic arterial pressures. Intraglomerular mesangial cells and matrix occupy the spaces between capillary loops within the glomerulus (see below).

The blind-ended beginning of the renal tubule, called Bowman’s capsule, surrounds the glomerulus. The capsule is cup-shaped, with inner and outer layers separated by a cavity, the urinary space. The outer layer of the capsule, called the parietal layer, is continuous with the epithelial cells of the proximal tubule at the urinary pole of the renal corpuscle. The inner layer of the cup, called the visceral layer, is composed of specialized cells called podocytes.

Podocytes have elaborate primary and secondary processes (foot processes) that interdigitate with processes of neighboring podocytes. Podocytes cover glomerular endothelial cells and intraglomerular mesangial cells. An intervening glomerular basement membrane (GBM) separates podocytes from endothelial cells and intraglomerular mesangial cells. The GBM is formed by fusion of podocyte and endothelial cell basal laminae (Figure 1.3a) (Abrahamson 1987).

Mesangial cells are found among glomerular capillaries (intraglomerular) and also outside the glomerulus near its vascular pole (extraglomerular). The latter are associated with the juxtaglomerular apparatus (described below). Mesangial cells function to maintain a “clean” GBM for blood filtration, by extending cytoplasmic processes between the GBM and endothelial cells for phagocytosis of debris. Additionally, mesangial cells secrete...
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A variety of biologically active molecules and proliferate in response to glomerular injury. The mesangium (mesangial cells and associated matrix) provides physical support for the glomerulus (Sakai and Kriz 1987). Glomerular endothelial cells and mesangium together are surrounded by the GBM.

Renal “filter”

Urine formation begins as an ultrafiltrate within the urinary space of the renal corpuscle. The three major components of the renal “filter” are as follows (Figure 1.3b):

1. Endothelial cells of the glomerulus
2. GBM
3. Podocytes of the visceral layer of Bowman’s capsule

Endothelial cells possess large fenestrations (pores); however, negatively charged material occupies much of this space. This represents the first barrier to filtration (Rostgaard and Qvortrup 2002). The GBM is thought to be the main filtration barrier to cells and large molecules. The GBM is also negatively charged. Podocyte foot processes form a discontinuous covering on the urinary space side of the GBM. Spaces between apposing foot processes are referred to as filtration slits.

Filtration of smaller molecules is blocked by the presence of a thin negatively charged membrane within the filtration slits (slit diaphragm) (Rodewald and Karnovsky 1974).

Taken together, passage through the renal “filter” is dependent on molecular size and charge. Blood cells and most proteins are too large to pass through endothelial fenestrations, and negatively charged macromolecules are repelled by negatively charged components of the “filter.”

Nephron: tubular components

In addition to the renal corpuscle, the nephron has the following renal tubules: proximal convoluted tubule, loop of Henle, and distal convoluted tubule (Figure 1.4).

Proximal convoluted tubule

Ultrafiltrate within the urinary space travels first into the proximal convoluted tubule (PCT). This highly coiled tubule is the major tubule type of the cortical labyrinth. PCT cells feature apical intercellular tight junctions that limit intercellular (paracellular) movement of molecules from the lumen to the intercellular compartment. The PCT contains the only renal tubular epithelial cells with intercellular gap junctions (evidence of intercellular communication). The following cellular features exhibited by simple cuboidal epithelium of the PCT may be present to varying degrees on other renal tubular epithelial cells:

- **Microvilli (brush border):** An apical membrane modification that provides increased surface area for absorption, modification, and intracellular transport of luminal material.
- **Basolateral intercellular interdigitations:** They are extensive and serve to increase available cell membrane for transcellular transport of materials.
- **Mitochondria:** They provide energy for the extensive reabsorption that occurs within the tubule. Vertically oriented mitochondria are closely associated with...
infoldings of the basolateral cell membrane, producing a striated appearance. This close association provides energy for intramembranous transport pumps.

**Loop of Henle**

The loop of Henle is a straight tubular loop that initially descends from cortex into the medulla and then ascends back to the cortex. It is composed of a thick descending limb, thin limbs of the loop, and a thick ascending limb:

- The thick descending limb of Henle’s loop is often described with proximal tubules and referred to as the proximal straight tubule. This segment is lined by simple cuboidal epithelium. It has less extensive cellular modifications than the PCT (shorter microvilli, fewer cellular interdigitations, and smaller mitochondria).

- The descending and ascending thin limb of Henle’s loop begins with an abrupt change to simple squamous epithelium. This thin segment descends into the medulla and then abruptly turns to ascend toward the cortex. Ultrastructural characterization of this epithelium reveals a heterogeneous cellular population that varies with species, length of loop, and specific region. Microvilli and lateral interdigitations are underdeveloped or absent, and organelles are sparse in most thin limb regions. The thin limbs of Henle’s loop in combination with its surrounding vascular network (vasa recta) play an important role in concentrating urine and maintaining a medulla high in solute concentration.

- The thick ascending limb (TAL) of Henle’s loop is the last segment of the loop of Henle. Its simple cuboidal epithelium is similar to the PCT but with less developed microvilli. The TAL ascends into the cortex to the vicinity of the vascular pole of its glomerulus of origin. TAL epithelial cells in the vicinity of the afferent arteriole will become a specialized group of cells called the macula densa, a component of the juxtaglomerular apparatus (described below).

Ultrafiltrate within Henle’s loop travels next into the distal convoluted tubule (DCT). This tubule is shorter in length and has less developed microvilli than the PCT. Similar to PCT cells, there are many basolateral interdigitations; differing from the PCT, DCT has an even higher concentration of mitochondria.

**Connecting tubule**

The connecting tubule (CNT) runs from the DCT to a cortically located collecting duct within a medullary ray. The classification of this tubule as part of the nephron (i.e., derived from the nephrogenic ridge) or as part of the collecting duct (i.e., ureteric bud derivation) is open to debate. Interestingly, it has been shown in a variety of mammalian species (rats, rabbits, and humans) that CNTs pass in close proximity to the afferent arteriole, feeding the glomerulus of origin (Barajas et al. 1986; Vio et al. 1988; Dorup et al. 1992). There is evidence of paracrine signaling occurring between CNTs and afferent arterioles, a feedback arrangement. The epithelium of the CNT is simple cuboidal with less mitochondria and less intercellular interdigitations than PCT epithelium.

**Collecting duct system**

Nephrons (including CNTs) drain into a collecting duct system. Several nephrons join the same collecting duct and several collecting ducts unite to form a papillary duct. The renal medulla contains collecting ducts, papillary ducts, and the loops of Henle. Papillary ducts open onto the renal crest surface. There is a progressive change from cuboidal to columnar epithelium along the collecting duct system.

Collecting ducts have two cell types: principal and intercalated cells. The principal cells (collecting duct cells, light cells) are cuboidal, with short microvilli. These cells have distinct lateral borders that are noninterdigitating. Additionally, the cell base is filled with infoldings that displace organelles and create a visibly lighter zone. The darker appearing intercalated cells (dark cells) are most frequently found in collecting ducts, although low numbers can occur in the DCT and CNT. Several subtypes of intercalated cells exist with differing roles in acid or bicarbonate secretion. The intercalated cell has many mitochondrial, but basal infoldings are absent.

Tubular organization gives rise to regions within the renal medulla (see Figure 1.4):

- Distinct inner and outer zones of the medulla are due to a difference in renal tubular segments.

- The inner zone of the medulla contains only thin limbs of Henle’s loop, collecting ducts, vasa recta, and a relatively large component of interstitium. (Collecting ducts originate in a medullary ray of the cortex.)

- The outer zone of the medulla is where the thick limbs of the loop of Henle are located. It is subdivided generally into an inner stripe and an outer stripe (except in the dog). The junction of the inner and outer stripes correlates with the transition from thick tubules to thin segments of the descending limb of Henle’s loop. In the cat and most species, this transition occurs within the outer zone. In the dog, this transition occurs at or near the corticomedullary junction, and therefore the outer stripe is absent (Bulger et al. 1979).

- The cat and dog normally have long loops of Henle. Even peripherally located corpuscles have loops of
Henle that extend all the way to the inner zone of the medulla (Beeuwkes and Bonventre 1975; Bulger et al. 1979). (In most mammals, the length of Henle's loop is variable and related to the position of its associated corpuscle within the cortex. Peripherally located corpuscles have shorter loops of Henle, only reaching the outer medulla, and juxtamedullary corpuscles have long loops of Henle, extending deep into the medulla (Schmidt-Nielsen and O’Dell 1961).)

**Juxtaglomerular apparatus**

The juxtaglomerular apparatus (JGA) is an anatomically distinct region at the vascular pole of the glomerulus. The JGA has three components: juxtaglomerular cells, macula densa cells, and extraglomerular mesangial cells (Figure 1.5).

Juxtaglomerular cells are modified smooth muscle cells in the walls of afferent and rarely efferent arterioles. The cells contain renin granules and may be referred to as granular cells. The release of renin in response to signals from the macula densa cells generates a cascade of reactions leading to increased systemic blood pressure, thus increasing glomerular perfusion pressure.

The macula densa is a specialization of epithelial cells in the TAL of Henle’s loop near the afferent and efferent arterioles. The cells are tall columnar versus the adjacent cuboidal epithelium. Cells of the macula densa detect changes in luminal sodium chloride concentration. In response, they generate paracrine signals that result in changes in arteriolar resistance and renin release by juxtaglomerular cells.

Extraglomerular mesangial cells are interposed between the two arterioles and macula densa cells. The cells are continuous with intraglomerular mesangial cells. A key feature of extraglomerular cells is the gap junctions they form with neighboring cells including juxtaglomerular cells, normal smooth muscle cells, and other mesangial cells (but not with macula densa cells). Although their entire role is unclear, the cells are thought to take part in coordinating JGA activities through gap junction communication. Also, because of their observed cytoskeletal “bridging” within the juxtaglomerular region, they are thought to help structurally reinforce this region.

**Renal interstitium, lymphatics, and nerves**

The interstitium—a composite of fibers, matrix, and cells—provides structural support for the kidney. The major cell type is the fibroblast, functioning to produce stroma and maintain structural connections to other cells, nerves, and epithelial basement membranes (Kaisling et al. 1996). Dendritic cells are also present, playing a role in immune regulation within the kidney (Dong et al. 2005). Macrophages and rarely lymphocytes may be present under normal conditions (Kaisling et al. 1996).

Lymphatic vessels are located within the renal cortex in association with vessels, encircling corpuscles and tubules and penetrating the renal capsule. The renal medulla lacks lymph vessels (Albertine and O’Morchoe 1980; Eliska 1984). Connective tissue sheaths surrounding vessels and tubules may serve as an avenue for lymph to move out of the medulla.

Sympathetic nerves typically travel along periarterial connective tissue sheaths (Barajas 1978) and innervate vascular smooth muscle (Fourman 1970). Tubules in close proximity to the arteries may be under a direct neuronal influence (Barajas 1978). Efferent innervation is still not completely understood and even less is known about the afferent innervation of the kidney.
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References


