a glomerulus followed by a tubule. The surrounding capillaries and the interstitial space are also important functional components of the nephron.

Glomerulus

The glomerulus consists of the glomerular vasculature (arterioles and capillaries) supported by the mesangium (mesangial cells and matrix) inside Bowman's capsule (parietal and visceral epithelial cells) (see Fig. 25-1C). The visceral cells of Bowman's capsule are the podocytes, so named because of their numerous "foot processes." The smooth muscle layers of the afferent and efferent arterioles are critical in determining arteriolar tone. The glomerular capillary contacts the mesangium on one side and is separated from the foot processes of the podocyte on the opposite side by the glomerular basement membrane (GBM). The glomerulus filters large volumes of water and solutes while retaining most of the proteins and all of the cells in the blood. The glomerular filtration barrier is composed of the capillary endothelium, the GBM, and the podocyte slit diaphragm.

Lining the inside of the GBM is a single layer of fenestrated endothelial cells. The fenestrations (50 to 100 nm in diameter) provide a barrier to negatively charged large molecules in the blood. The GBM contains laminin, type IV collagen, nidogen, and proteoglycans that restrict movement of large molecules (e.g., albumin) from the capillary into Bowman's space. The GBM contains dense negative charges due to glycoproteins with sialic acid residues that restrict the passage of anionic plasma solutes. It can be the site of deposition of immunocomplexes that cause glomerulonephritis (e.g., membranous glomerulonephritis, lupus nephritis). Autoantibodies to the GBM cause severe inflammation and loss of filtration. The epithelial layer consists of podocytes and the parietal epithelium, which is flat and squamous with very few organelles. At the vascular pole, the parietal epithelium is contiguous with a completely different epithelium—the proximal convoluted tubule.

On the visceral side of Bowman's space are the podocytes, which constitute the outermost layer of the filtration barrier. These cells have a highly interdigitating system of foot processes that rest against the basement membrane. The podocyte cell bodies lie within the extracellular matrix. The spaces between foot processes are filtration slits approximately 40 nm in diameter; they are bridged by slit diaphragms, which are also negatively charged, contributing to the containment of middle-size negatively charged particles in the capillary. In the last decade, there have been momentous advances in identifying the components of the slit diaphragm complex and understanding their functions. A full discussion is not possible here, but major slit diaphragm–associated proteins include nephrin, podocin, neph-1/2/3, FAT-1, R-cadherin, catenin, CD2AP, ZO-1, and α-actinin 4. Mutations of many of these genes cause congenital nephrotic syndrome (see Chapter 28).

Tubules

The parietal epithelium of Bowman's capsule becomes the renal tubule (see Fig. 25-1D) as it leaves the glomerulus. The renal tubule is a prototypical polarized epithelium. Its salient characteristics are summarized in Figure 25-2. A simple cylinder would not suffice in terms of surface area for transport. In the luminal apical membrane, surface amplification is achieved either by protrusions or by a more extensive form of protrusions called the *brush border* in the proximal tubule. Between cells are structures called *tight junctions*. Although they are called tight junctions, some are truly tight (with high resistance to solute and charge movement), whereas others can be quite leaky to solutes. In addition to resistance, these complexes also regulate whether the junction is more permeable to one ion type compared with another (relative and selective permeability). On the other side of the tight junction is the intercellular space, which is contiguous with the interstitial space. The basolateral cell membrane on the interstitial-capillary side amplifies its surface area by infoldings into the cell and interdigitations between two cells.

The movement of a solute can be through a cell (transcellular transport) or around the cell (paracellular transport) (see Fig. 25-2A). Solute transport is an energy-consuming process that requires metabolic fuels. There are many kinds of transport proteins (see Fig. 25-2B). ATPases directly couple hydrolysis of adenosine triphosphate (ATP) to transport. Cotransporters (symporters) move two solutes in the same direction, and countertransporters (antiporters) move two different solutes in opposite directions. Channels function as protein-lined "holes" that allows specific solutes to permeate. Different transporters can also be coupled together to form a new transport system. Finally, there are proteins that protrude outside the cell in the junctional area to provide a conduit for paracellular transport.

Specialized Structures

Interstitium

The space between the tubules and peritubular capillaries constitutes about 5% to 10% of renal volume and harbors interstitial fibroblasts and dendritic cells. In diseases such as interstitial nephritis (see Chapter 29), the interstitium is full of inflammatory cells, which elaborate cytokines and chemokines that profoundly affect filtration and tubular function. The resident fibroblasts are stellate cells with projections that physically contact tubules and capillaries, provide scaffold support, and secrete and maintain matrix. In pathologic conditions, these cells, when stimulated by cytokines, can transform into myofibroblasts and contribute to interstitial fibrosis. Some specialized fibroblasts in the deep cortex are sensors of oxygen and producers of circulating erythropoietin. The dendritic cells are antigen-presenting cells that express major histocompatibility complex (MHC) class II molecules. They are in intimate communication with the renal parenchyma, constantly sampling and responding to the local antigenic environment. Dendritic cells are involved with innate and adaptive immunity and are major players in immunologic homeostasis and diseases of the renal parenchyma.

Juxtaglomerular Apparatus

A unique feature of the nephron is that each thick ascending limb traverses back to and engages in physical contact with its parent glomerulus. The tubular cell at the point of contact is different from the rest of the thick ascending limb and is called the *macula densa*. The tripartite structure comprising the macula densa, the afferent and efferent glomerular arterioles, and the extraglomerular mesangium, a special part of the mesangium that protrudes