Hypertension and the Kidney

**FIGURE 1-16**

Major transport pathways across proximal tubule cells. At the apical membrane, sodium is transported in conjunction with organic solutes (such as glucose, amino acids, and citrate) and inorganic anions (such as phosphate and sulfate). The major mechanism for sodium entry into the cells is sodium-hydrogen exchange (the isoform NHE3). Chloride transport pathways across the apical membrane may include a coupled sodium chloride entry step or chloride anion exchange that is coupled with sodium-hydrogen exchange.

**FIGURE 1-17**

Sodium transport mechanisms in the thick ascending limb of the loop of Henle. The major sodium chloride reabsorptive mechanism in the thick ascending limb at the apical membrane is the sodium-potassium-chloride cotransporter. This electroneutral transporter is inhibited by furosemide and other loop diuretics and is stimulated by a variety of factors. Potassium is recycled across the apical membrane into the lumen, creating a positive voltage in the lumen. An apical sodium-hydrogen exchanger also exists that may function to reabsorb some sodium bicarbonate. The sodium-potassium ATPase (Na⁺-K⁺ ATPase) at the basolateral membrane again is the driving force. The basolateral chloride channel and possibly other chloride cotransporters are important in mediating chloride efflux across the basolateral membrane. Sodium and chloride are reabsorbed without water in this segment because water is impermeable across the apical membrane of the thick ascending limb. Thus, the tubular fluid osmolality in this nephron segment is hypotonic.
1.11

**FIGURE 1-18**
Mechanisms of sodium chloride reabsorption in the distal tubule. The distal convoluted tubule and subsequent connecting tubule have a variety of sodium transport mechanisms. The distal tubule has predominantly a sodium chloride cotransporter, which is inhibited by thiazide diuretics. In the connecting tubule, sodium channels and a sodium-hydrogen exchange mechanism also are present. Amiloride inhibits sodium channel activity. Again the sodium-potassium ATPase (Na⁺-K⁺ ATPase) on the basolateral membrane provides most of the driving force for sodium reabsorption.

**FIGURE 1-19**
Mechanism of sodium chloride reabsorption in collecting duct cells. Sodium transport in the collecting duct is mainly via amiloride-sensitive sodium channels in the apical membrane. Some evidence for other mechanisms such as an electroneutral sodium-chloride cotransport mechanism and a different sodium channel also has been reported. Again, the basolateral sodium-potassium ATPase (Na⁺-K⁺ ATPase) creates the driving force for overall sodium transport. There are some differences between the cortical collecting duct and the deeper inner medullary collecting duct (IMCD). In the cortical collecting duct, sodium transport occurs in the predominant principal cell type interspersed between acid-base transporting intercalated cells. The principal cell also is an important site of potassium secretion by way of apical potassium channels and water transport via antidiuretic sensitive water channels. Regulation of sodium channels may involve either insertion (from subapical compartments) or activation of preexisting sodium channels.
Neural and sympathetic influences. The neural reflexes serve as the principal mechanisms for the rapid regulation of arterial pressure. The neural reflexes also exert a long-term role by influencing sodium excretion. The pathways and effectors of the arterial baroreflex and atrial pressure-volume reflex are depicted. The arrows indicate increased or decreased activity in response to an acute reduction in arterial pressure which is sensed by the baroreceptors in the aortic arch and carotid sinus.

The insert depicts the relationship between the arterial blood pressure and baroreflex primary afferent firing rate. At the normal level of mean arterial pressure of approximately 100 mm Hg, the sensitivity (∆I/∆P) is set at the maximum level. After chronic resetting of the baroreceptors, the peak sensitivity and threshold of activation are shifted to a higher level of arterial pressure.

The cardiovascular reflexes involve high-pressure arterial receptors in the aortic arch and carotid sinus and low-pressure atrial receptors. In response to decreases in arterial pressure or vascular volume, increased sympathetic stimulation participates in short-term control of arterial pressure. This increased stimulation does so by enhancing cardiac performance and stimulating vascular smooth muscle tone, leading to increased total peripheral resistance and decreased capacitance. The direct effects of the sympathetic nervous system on kidney function lead to decreased sodium excretion caused by decreases in filtered load and increases in tubular reabsorption [26].

The decreases in the glomerular filtration rate (GFR) and filtered sodium load are due to increases in both afferent and efferent arteriolar resistances and to decreases in the filtration coefficient (see Fig. 1-7). Sympathetic activation also enhances proximal sodium reabsorption by stimulating the sodium-hydrogen (Na⁺-H⁺) exchanger mechanism (see Fig. 1-16) and by increasing the net chloride reabsorption by the thick ascending limb of the loop of Henle. The indirect effects include stimulation of renin secretion and angiotensin II formation, which, as discussed next, also stimulates tubular reabsorption. ∆I—change in impulse firing; ∆P—change in pressure; DN—dorsal motor nucleus; NA—nucleus ambiguous; NTS—nucleus tractus solitarii; RBF—renal blood flow; TPR—total peripheral resistance. (Adapted from Vari and Navar [4].)