

The perception of *extracellular blood volume* is determined, in part, by the integration of arterial tone, cardiac stroke volume, heart rate, and the water and solute content of extracellular fluid. Na^+ and accompanying anions are the most abundant extracellular effective osmoles and together support a blood volume around which pressure is generated. Under normal conditions, this volume is regulated by sodium balance (Fig. 309-4B), and the balance between daily Na^+ intake and excretion is under the influence of *baroreceptors* in regional blood vessels and vascular hormone sensors modulated by atrial natriuretic peptides, the renin-angiotensin-aldosterone system, Ca^{2+} signaling, adenosine, vasopressin, and the neural adrenergic axis. If Na^+ intake exceeds Na^+ excretion (positive Na^+ balance), then a rising blood volume will trigger a proportional increase in urinary Na^+ excretion. Conversely, when Na^+ intake is less than urinary excretion (negative Na^+ balance), blood volume will fall and trigger enhanced renal Na^+ reabsorption, leading to decreased urinary Na^+ excretion.

The renin-angiotensin-aldosterone system is the best-understood hormonal system modulating renal Na^+ excretion. Renin is synthesized and secreted by granular cells in the wall of the afferent arteriole. Its secretion is controlled by several factors, including β_1 -adrenergic stimulation to the afferent arteriole, input from the macula densa, and prostaglandins. Renin and ACE activity eventually produce angiotensin II that directly and indirectly promotes renal Na^+ and water reabsorption. Stimulation of proximal tubular Na^+/H^+ exchange by angiotensin II directly increases Na^+ reabsorption. Angiotensin II also promotes Na^+ reabsorption along the collecting duct by stimulating aldosterone secretion by the adrenal cortex. Constriction of the efferent glomerular arteriole by angiotensin II indirectly boosts the filtration fraction and raises peritubular capillary oncotic pressure to promote tubular Na^+ reabsorption. Finally, angiotensin II inhibits renin secretion through a negative feedback loop. Alternative metabolism of angiotensin by ACE2 generates the vasodilatory peptide angiotensin 1-7 that acts through Mas receptors