

COLLECTING DUCT

The collecting duct modulates the final composition of urine. The two major divisions, the cortical collecting duct and inner medullary collecting duct, contribute to reabsorbing ~4–5% of filtered Na^+ and are important for hormonal regulation of salt and water balance. Cells in both segments of the collecting duct express vasopressin-regulated water channels (aquaporin-2 on the apical membrane, aquaporin-3 and -4 on the basolateral membrane). The antidiuretic hormone vasopressin binds to the V2 receptor on the basolateral membrane and triggers an intracellular signaling cascade through G protein-mediated activation of adenylyl cyclase, which raises intracellular levels of cyclic AMP. This signaling cascade stimulates the insertion of water channels into the apical membrane of collecting duct cells to promote water permeability, water reabsorption, and production of concentrated urine. In the absence of vasopressin, collecting duct cells are water impermeable, and urine remains dilute.

The cortical collecting duct contains *high-resistance epithelia* with two cell types. Principal cells are the main water-reabsorbing, Na^+ -reabsorbing, and K^+ -secreting cells, and the site of action of aldosterone, K^+ -sparing diuretics, and mineralocorticoid receptor antagonists such as spironolactone and eplerenone. The other cells are type A and B intercalated cells. Type A intercalated cells mediate acid secretion and bicarbonate reabsorption also under the influence of aldosterone. Type B intercalated cells mediate bicarbonate secretion and acid reabsorption.

Virtually all transport is mediated through the cellular pathway for both principal cells and intercalated cells. In principal cells, passive apical Na^+ entry occurs through an amiloride-sensitive, epithelial Na^+ channel (ENaC) with basolateral exit mediated by the Na^+/K^+ -ATPase (**Fig. 309-3E**). This Na^+ reabsorptive process is tightly regulated by aldosterone and is physiologically activated by a variety of proteolytic enzymes that cleave extracellular domains of ENaC; plasmin in the tubular fluid of nephrotic patients, for example, activates ENaC, leading to sodium retention. Aldosterone enters the cell across the basolateral membrane, binds to a cytoplasmic