

concentration  $<20$  mM, in the absence of a cause of hypervolemic hyponatremia, predicts a rapid increase in plasma  $\text{Na}^+$  concentration in response to intravenous normal saline; saline therapy thus induces a water diuresis in this setting, as circulating AVP levels plummet.

The *renal* causes of hypovolemic hyponatremia share an inappropriate loss of  $\text{Na}^+\text{-Cl}^-$  in the urine, leading to volume depletion and an increase in circulating AVP; urine  $\text{Na}^+$  concentration is typically  $>20$  mM (Fig. 53-5). A deficiency in circulating aldosterone and/or its renal effects can lead to hyponatremia in primary adrenal insufficiency and other causes of hypoaldosteronism; hyperkalemia and hyponatremia in a hypotensive and/or hypovolemic patient with high urine  $\text{Na}^+$  concentration (much greater than 20 mM) should strongly suggest this diagnosis. Salt-losing nephropathies may lead to hyponatremia when sodium intake is reduced, due to impaired renal tubular function; typical causes include reflux nephropathy, interstitial nephropathies, postobstructive uropathy, medullary cystic disease, and the recovery phase of acute tubular necrosis. Thiazide diuretics cause hyponatremia via a number of mechanisms, including polydipsia and diuretic-induced volume depletion. Notably, thiazides do not inhibit the renal concentrating mechanism, such that circulating AVP retains a full effect on renal water retention. In contrast, loop diuretics, which are less frequently associated with hyponatremia, inhibit  $\text{Na}^+\text{-Cl}^-$  and  $\text{K}^+$  absorption by the TALH, blunting the countercurrent mechanism and reducing the ability to concentrate the urine. Increased excretion of an osmotically active nonreabsorbable or poorly reabsorbable solute can also lead to volume depletion and hyponatremia; important causes include glycosuria, ketonuria (e.g., in starvation or in diabetic or alcoholic ketoacidosis), and bicarbonaturia (e.g., in renal tubular acidosis or metabolic alkalosis, where the associated bicarbonaturia leads to loss of  $\text{Na}^+$ ).

Finally, the syndrome of “cerebral salt wasting” is a rare cause of hypovolemic hyponatremia, encompassing hyponatremia with clinical hypovolemia and inappropriate natriuresis in association with