The maintenance of the tonicity of body fluids within a very narrow physiologic range is made possible by homeostatic mechanisms that control the intake and excretion of water. Critical to this process are the osmoreceptors in the hypothalamus that control the secretion of antidiuretic hormone (ADH) in response to changes in tonicity. In turn, ADH governs the excretion of water by its end-organ effect on the various segments of the renal collecting system. The unique anatomic and physiologic arrangement of the nephrons brings about either urinary concentration or dilution, depending on prevailing physiologic needs. In the first section of this chapter, the physiology of urine formation and water balance is described.

The kidney plays a pivotal role in the maintenance of normal water homeostasis, as it conserves water in states of water deprivation, and excretes water in states of water excess. When water homeostasis is deranged, alterations in serum sodium ensue. Disorders of urine dilution cause hyponatremia. The pathogenesis, causes, and management strategies are described in the second part of this chapter.

When any of the components of the urinary concentration mechanism is disrupted, hypernatremia may ensue, which is universally characterized by a hyperosmolar state. In the third section of this chapter, the pathogenesis, causes, and clinical settings for hypernatremia and management strategies are described.
1.2 Disorders of Water, Electrolytes, and Acid-Base

Physiology of the Renal Diluting and Concentrating Mechanisms

Principles of normal water balance. In most steady-state situations, human water intake matches water losses through all sources. Water intake is determined by thirst (see Fig. 1-12) and by cultural and social behaviors. Water intake is finely balanced by the need to maintain physiologic serum osmolality between 285 to 290 mOsm/kg. Both water that is drunk and that is generated through metabolism are distributed in the extracellular and intracellular compartments that are in constant equilibrium. Total body water equals approximately 60% of total body weight in young men, about 50% in young women, and less in older persons. Infants’ total body water is between 65% and 75%. In a 70-kg man, in temperate conditions, total body water equals 42 L, 65% of which (22 L) is in the intracellular compartment and 35% (19 L) in the extracellular compartment.

Assuming normal glomerular filtration rate to be about 125 mL/min, the total volume of blood filtered by the kidney is about 180 L/24 hr. Only about 1 to 1.5 L is excreted as urine, however, on account of the complex interplay of the urine concentrating and diluting mechanism and the effect of antidiuretic hormone to different segments of the nephron, as depicted in the following figures.
Diseases of Water Metabolism

FIGURE 1-2
Determinants of the renal concentrating mechanism. Human kidneys have two populations of nephrons, superficial and juxtamedullary. This anatomic arrangement has important bearing on the formation of urine by the countercurrent mechanism. The unique anatomy of the nephron [1] lays the groundwork for a complex yet logical physiologic arrangement that facilitates the urine concentration and dilution mechanism, leading to the formation of either concentrated or dilute urine, as appropriate to the person's needs and dictated by the plasma osmolality. After two thirds of the filtered load (180 L/d) is isotonicly reabsorbed in the proximal convoluted tubule, water is handled by three interrelated processes: 1) the delivery of fluid to the diluting segments; 2) the separation of solute and water (H₂O) in the diluting segment; and 3) variable reabsorption of water in the collecting duct. These processes participate in the renal concentrating mechanism [2].

1. Delivery of sodium chloride (NaCl) to the diluting segments of the nephron (thick ascending limb of the loop of Henle and the distal convoluted tubule) is determined by glomerular filtration rate (GFR) and proximal tubule function.
2. Generation of medullary interstitial hypertonicity, is determined by normal functioning of the thick ascending limb of the loop of Henle, urea delivery from the medullary collecting duct, and medullary blood flow.
3. Collecting duct permeability is determined by the presence of antidiuretic hormone (ADH) and normal anatomy of the collecting system, leading to the formation of a concentrated urine.