

FIGURE 1-3

Determinants of the urinary dilution mechanism include 1) delivery of water to the thick ascending limb of the loop of Henle, distal convoluted tubule, and collecting system of the nephron; 2) generation of maximally hypotonic fluid in the diluting segments (*ie*, normal thick ascending limb of the loop of Henle and cortical diluting segment); 3) maintenance of water impermeability of the collecting system as determined by the absence of antidiuretic hormone (ADH) or its action and other antidiuretic substances. GFR—glomerular filtration rate; NaCl—sodium chloride; H₂O—water.

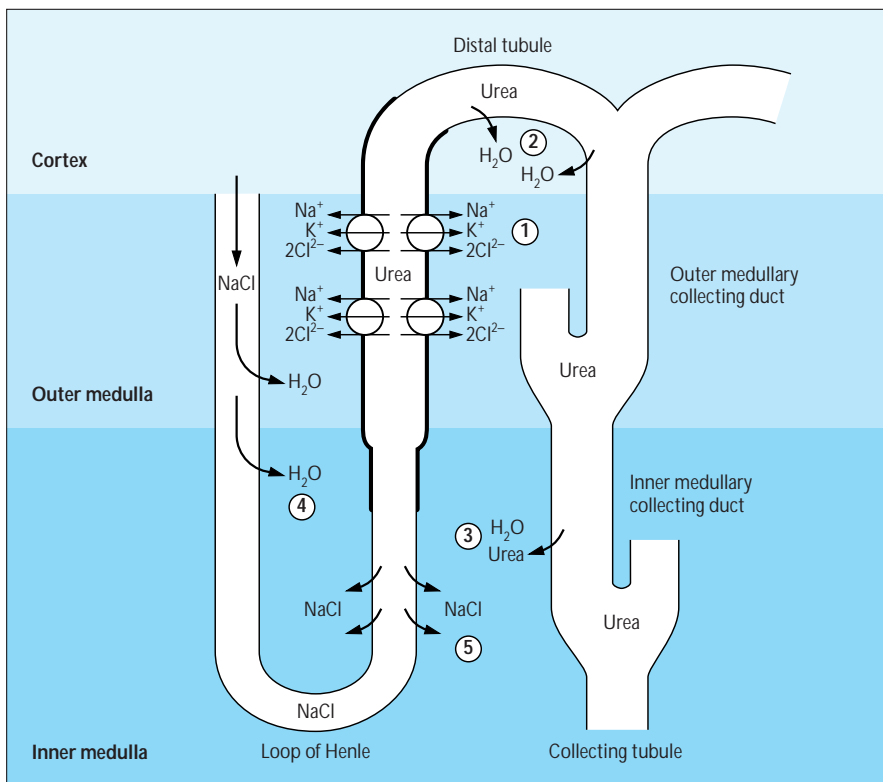


FIGURE 1-4

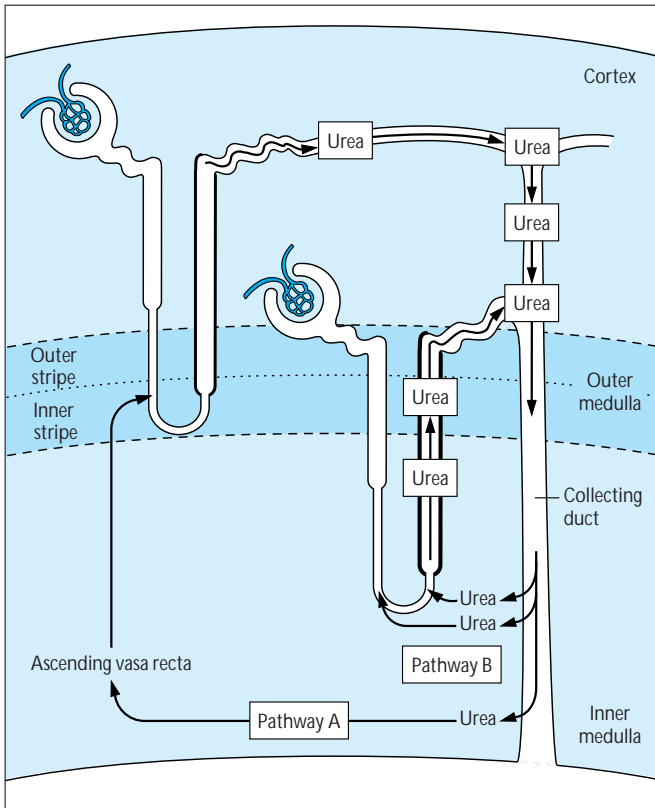
Mechanism of urine concentration: overview of the passive model. Several models of urine concentration have been put forth by investigators. The passive model of urine concentration described by Kokko and Rector [3] is based on permeability characteristics of different parts of the nephron to solute and water and on the fact that the active transport is limited to the thick ascending limb. 1) Through the Na⁺, K⁺, 2 Cl cotransporter, the thick ascending limb actively transports sodium chloride (NaCl), increasing the interstitial tonicity, resulting in tubular fluid dilution with no net movement of water and urea on account of their low permeability. 2) The hypotonic fluid under antidiuretic hormone action undergoes osmotic equilibration with the interstitium in the late distal tubule and cortical and outer medullary collecting duct, resulting in water removal. Urea concentration in the tubular fluid rises on account of low urea permeability. 3) At the inner medullary collecting duct, which is highly permeable to urea and water, especially in response to antidiuretic hormone, the urea enters the interstitium down its concentration gradient, preserving interstitial hypertonicity and generating high urea concentration in the interstitium.

(Legend continued on next page)

FIGURE 1-4 (continued)

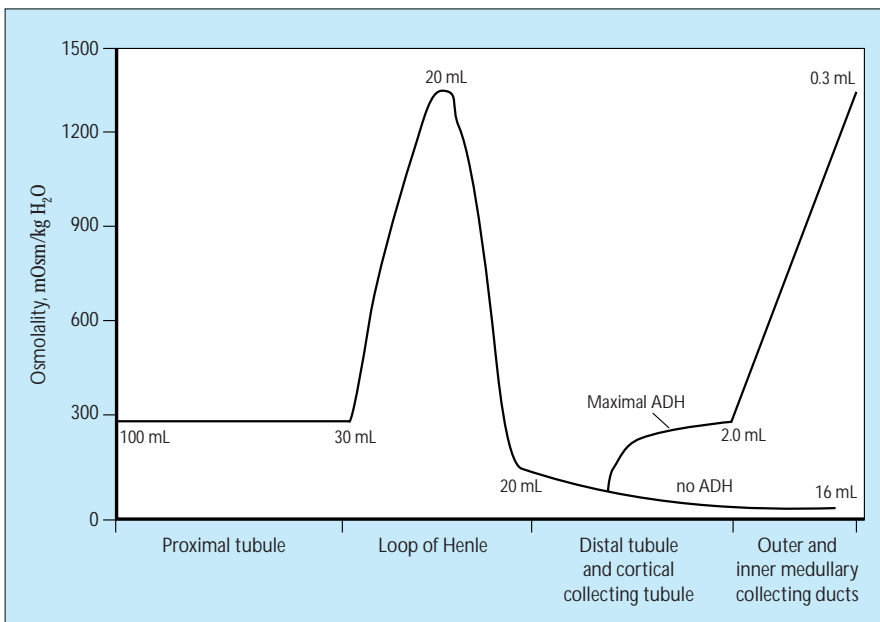
4) The hypertonic interstitium causes abstraction of water from the descending thin limb of loop of Henle, which is relatively impermeable to NaCl and urea, making the tubular fluid hypertonic with high NaCl concentration as it arrives at the bend of the loop of

Henle. 5) In the thin ascending limb of the loop of Henle, NaCl moves passively down its concentration gradient into the interstitium, making tubular fluid less concentrated with little or no movement of water. H_2O —water.

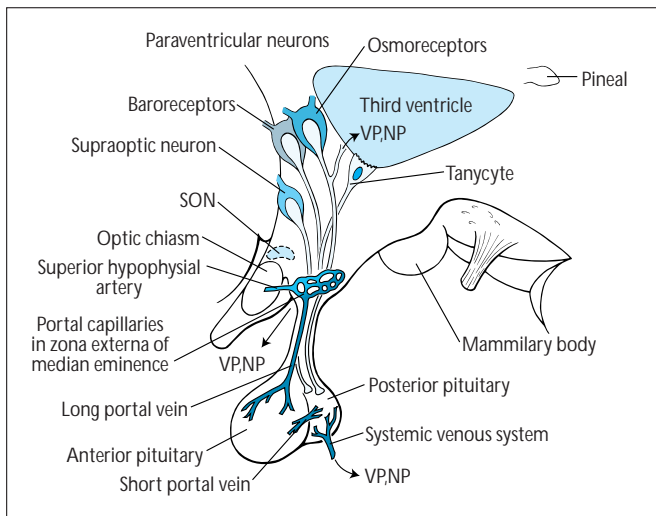
**FIGURE 1-5**

Pathways for urea recycling. Urea plays an important role in the generation of medullary interstitial hypertonicity. A recycling mechanism operates to minimize urea loss. The urea that is reabsorbed into the inner medullary stripe from the terminal inner medullary collecting duct (*step 3* in Fig. 1-4) is carried out of this region by the ascending vasa recta, which deposits urea into the adjacent descending thin limbs of a short loop of Henle, thus recycling the urea to the inner medullary collecting tubule (*pathway A*).

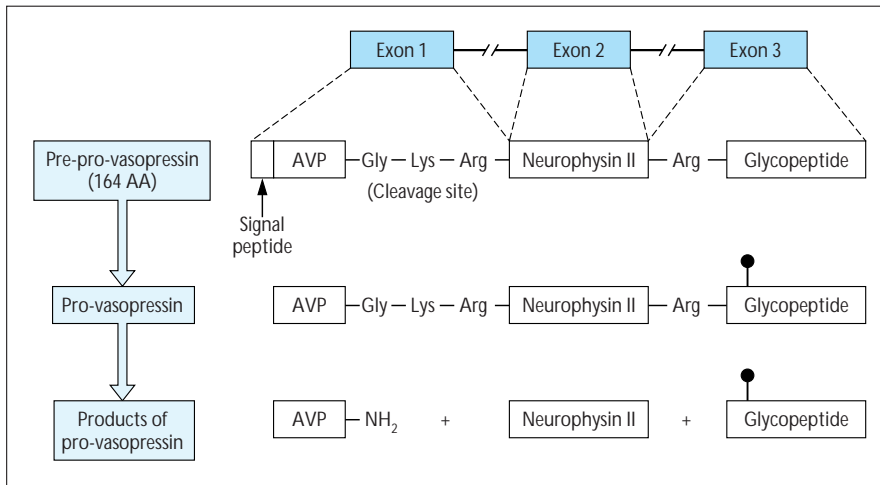
Some of the urea enters the descending limb of the loop of Henle and the thin ascending limb of the loop of Henle. It is then carried through to the thick ascending limb of the loop of Henle, the distal collecting tubule, and the collecting duct, before it reaches the inner medullary collecting duct (*pathway B*). This process is facilitated by the close anatomic relationship that the hairpin loop of Henle and the vasa recta share [4].

**FIGURE 1-6**

Changes in the volume and osmolality of tubular fluid along the nephron in diuresis and antidiuresis. The osmolality of the tubular fluid undergoes several changes as it passes through different segments of the tubules. Tubular fluid undergoes marked reduction in its volume in the proximal tubule; however, this occurs iso-osmotically with the glomerular filtrate. In the loop of Henle, because of the aforementioned countercurrent mechanism, the osmolality of the tubular fluid rises sharply but falls again to as low as 100 mOsm/kg as it reaches the thick ascending limb and the distal convoluted tubule. Thereafter, in the late distal tubule and the collecting duct, the osmolality depends on the presence or absence of antidiuretic hormone (ADH). In the absence of ADH, very little water is reabsorbed and dilute urine results. On the other hand, in the presence of ADH, the collecting duct, and in some species, the distal convoluted tubule, become highly permeable to water, causing reabsorption of water into the interstitium, resulting in concentrated urine [5].

**FIGURE 1-7**

Pathways of antidiuretic hormone release. Antidiuretic hormone is responsible for augmenting the water permeability of the cortical and medullary collecting tubules, thus promoting water reabsorption via osmotic equilibration with the isotonic and hypertonic interstitium, respectively. The hormone is formed in the supraoptic and paraventricular nuclei, under the stimulus of osmoreceptors and baroreceptors (see Fig. 1-11), transported along their axons and secreted at three sites: the posterior pituitary gland, the portal capillaries of the median eminence, and the cerebrospinal fluid of the third ventricle. It is from the posterior pituitary that the antidiuretic hormone is released into the systemic circulation [6]. SON—supraoptic nucleus; VP—vasopressin; NP—neurophysin.

**FIGURE 1-8**

Structure of the human arginine vasopressin (AVP/antidiuretic hormone) gene and the prohormone. Antidiuretic hormone (ADH) is a cyclic hexapeptide (mol. wt. 1099) with a tail of three amino acids. The biologically inactive macromolecule, pre-pro-vasopressin is cleaved into the smaller, biologically active protein. The protein of vasopressin is translated through a series of signal transduction pathways and intracellular cleaving. Vasopressin, along with its binding protein, neurophysin II, and the glycopeptide, are secreted in the form of neurosecretory granules down the axons and stored in nerve terminals of the posterior lobe of the pituitary [7]. ADH has a short half-life of about 15 to 20 minutes and is rapidly metabolized in the liver and kidneys. Gly—glycine; Lys—lysine; Arg—arginine.