Dinesh kumar
Assistant Professor
Department of Zoology
Multanimal Modi College
Modinagar

MECHANISMS OF URINE CONCENTRATION

RENAL MECHANISMS FOR URINE CONCENTRATION

The ability of the kidney to form urine that is more concentrated than plasma is essential for survival of mammals that live on land, including humans. Water is continuously lost from the body through various routes, including the lungs by evaporation into the expired air, gastrointestinal tract by way of the feces, the skin through perspiration(sweating), and the kidneys through the excretion of urine.

Fluid intake is required to match this loss, but when there is a water deficit in the body, the kidney forms concentrated urine by continuing to excrete solutes while increasing water reabsorption and decreasing the volume of urine formed. The human kidney can produce a maximal urine concentration of 1200 to 1400 mOsm/L, four to five times the osmolarity of plasma.Some desert animals, such as the Australian hopping mouse, can concentrate urine to as high as 10,000 mOsm/L. This allows the mouse to survive in the desert without drinking water; sufficient water can be obtained through the food ingested and water produced in the body by metabolism of the food.

Requirements for Excreting a Concentrated Urine:

The basic requirements for forming a concentrated urine are (1) a high level of ADH, which increases the permeability of the late distal tubules and collecting tubules to water, thereby allowing these tubular segments to reabsorb water, and (2) a high osmolarity (hyperosmolarity) of the renal medullary interstitial fluid, which provides the osmotic gradient necessary for water reabsorption to occur in the presence of high levels of ADH. The renal medullary interstitium surrounding the collecting tubules is normally hyperosmotic, so when ADH levels are high, water moves through the tubular membrane by osmosis into the renal interstitium; from there it is carried away by the vasa recta back into the blood.

Countercurrent Mechanism Produces a Hyperosmotic Renal Medullary Interstitium

The osmolarity of interstitial fluid in almost all parts of the body is about 300 mOsm/L, which is similar to the plasma osmolarity. The osmolarity of the interstitial fluid in the medulla of the kidney is much higher and may increase progressively to about 1200 to 1400 mOsm/L in the pelvic tip of the medulla. This means that the renal medullary interstitium has accumulated solutes in great excess of water. Once the high solute concentration in the medulla is achieved, it is maintained by a balanced inflow and outflow of solutes and water in the medulla.**This maintenance is achieved by vasa recta, which acts as counter- current exchangers**.

The major factors that contribute to the buildup of solute concentration into the renal medulla are as follows:

1. Active transport of sodium ions and co-transport of potassium, chloride, and other ions out of the thick portion of the ascending limb of the loop of Henle into the medullary interstitium
2. Active transport of ions from the collecting tubules into the medullary interstitium
3. Facilitated diffusion of urea from the inner medullary collecting tubules into the medullary interstitium

Steps Involved in Causing Hyperosmotic Renal Medullary Interstitium.

First, assume that the loop of Henle is filled with fluid with a concentration of 300 mOsm/L, the same as that leaving the proximal tubule (Figure 28-4, step 1).

Next, the active ion pump of the thick ascending limb on the loop of Henle reduces the concentration inside the tubule and raises the interstitial concentration; this pump establishes a 200-mOsm/L concentration gradient between the tubular fluid and the interstitial fluid (step 2).

Step 3 is that the tubular fluid in the descending limb of the loop of Henle and the interstitial fluid quickly reach osmotic equilibrium because of osmosis of water out of the descending limb. The interstitial osmolarity is maintained at 400 mOsm/L because of continued transport of ions out of the thick ascending loop of Henle.

Step 4 is additional flow of fluid into the loop of Henle from the proximal tubule, which causes the hyperosmotic fluid previously formed in the descending limb to flow into the ascending limb.
Once this fluid is in the ascending limb, additional ions are pumped into the interstitium, with water remaining in the tubular fluid, until a 200-mOsm/L osmotic gradient is established, with the interstitial fluid osmolarity rising to 500 mOsm/L (step 5).

Then, once again, the fluid in the descending limb reaches equilibrium with the hyperosmotic medullary interstitial fluid (step 6), and as the hyperosmotic tubular fluid from the descending limb of the loop of Henle flows into the ascending limb, stilll more solute is continuously pumped out of the tubules and deposited into the medullary interstitium.

These steps are repeated over and over, with the net effect of adding more and more solute to the medulla in excess of water; with sufficient time, *this process gradually traps solutes in the medulla and multiplies the concentration gradient established by the active pumping of ions out of the thick ascending loop of Henle, eventually raising the interstitial fluid osmolarity to 1200 to 1400 mOsm/L as shown in step 7.*

Thus, the repetitive reabsorption of sodium chloride by the thick ascending loop of Henle and continued inflow of new sodium chloride from the proximal tubule into the loop of Henle is called the countercurrent multiplier. The sodium chloride reabsorbed from the ascending loop of Henle keeps adding to the newly arrived sodium chloride, thus "multiplying" its concentration in the medullary interstitium.

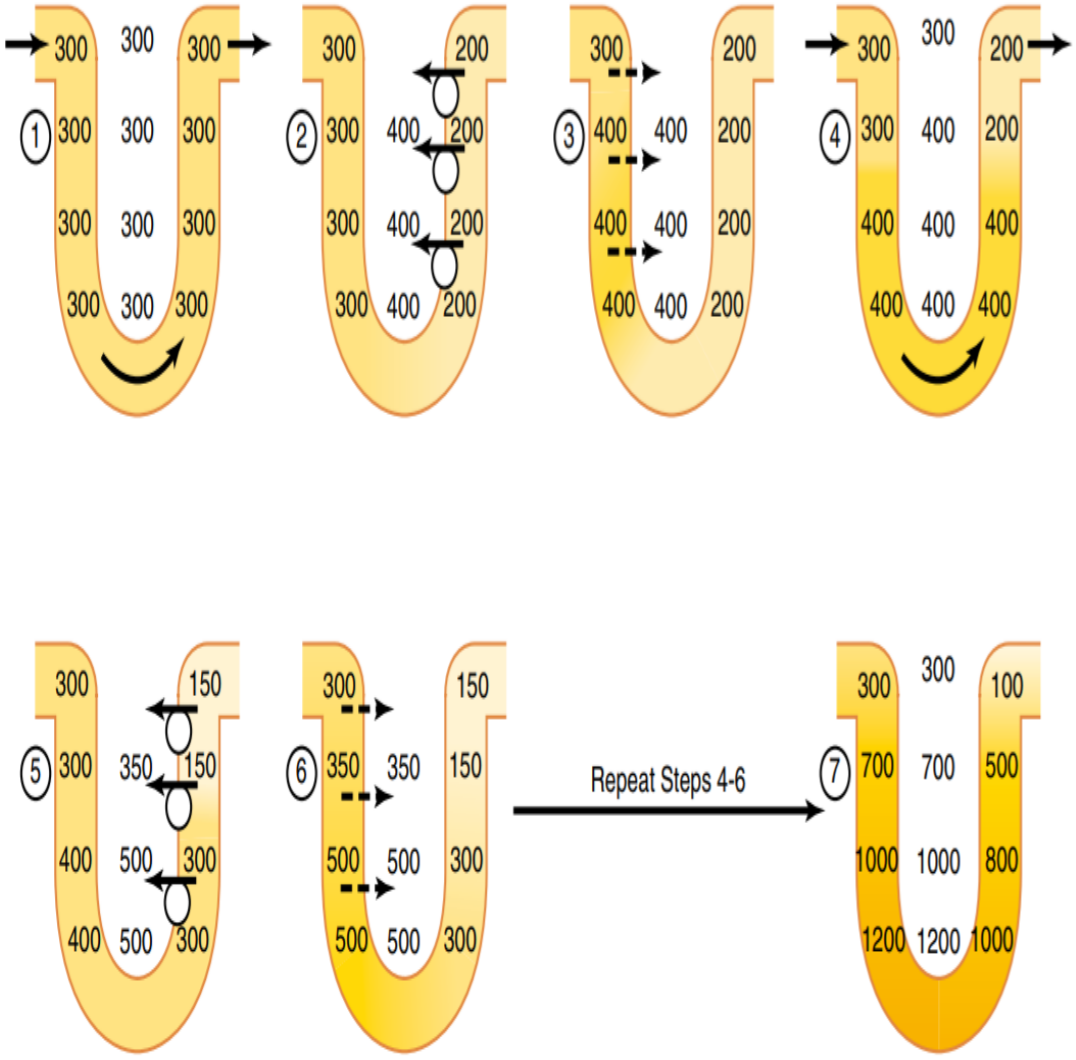

Figure 28-4 Countercurrent multiplier system in the loop of Henle for producing a hyperosmotic renal medulla. (Numerical values are in milliosmoles per liter.)

Role of Distal Tubule and Collecting Ducts in Excreting Concentrated Urine

When the tubular fluid leaves the loop of Henle and flows into the distal convoluted tubule in the renal cortex, the fluid is dilute, with an osmolarity of only about 100 mOsm/L (Figure 28-5). The early distal tubule further dilutes the tubular fluid because this segment, like the ascending loop of Henle, actively transports sodium chloride out of the tubule but is relatively impermeable to water.As fluid flows into the cortical collecting tubule, the amount of water reabsorbed is critically dependent on the plasma concentration of ADH. In the absence of ADH, this segment is almost impermeable to water and fails to reabsorb water but continues to reabsorb solutes and further dilutes the urine. When there is a high concentration of ADH, the cortical collecting tubule becomes highly permeable to water, so large amounts of water are now reabsorbed from the tubule into the cortex interstitium.

As the tubular fluid flows along the medullary collecting tubule, there is further water reabsorption from the tubular fluid into the interstitium.The reabsorbed water is quickly carried away by the vasa recta into the venous blood.

When high levels of ADH are present, the collecting tubules become permeable to water, so the fluid at the end of the collecting tubules has essentially the same osmolarity as the interstitial fluid of the renal medulla—about 1200 mOsm/L (see Figure 28-4). Thus, by reabsorbing as much water as possible, the kidneys form highly concentrated urine, excreting normal amounts of solutes in the urine while adding water back to the extracellular fluid and compensating for deficits of body water.

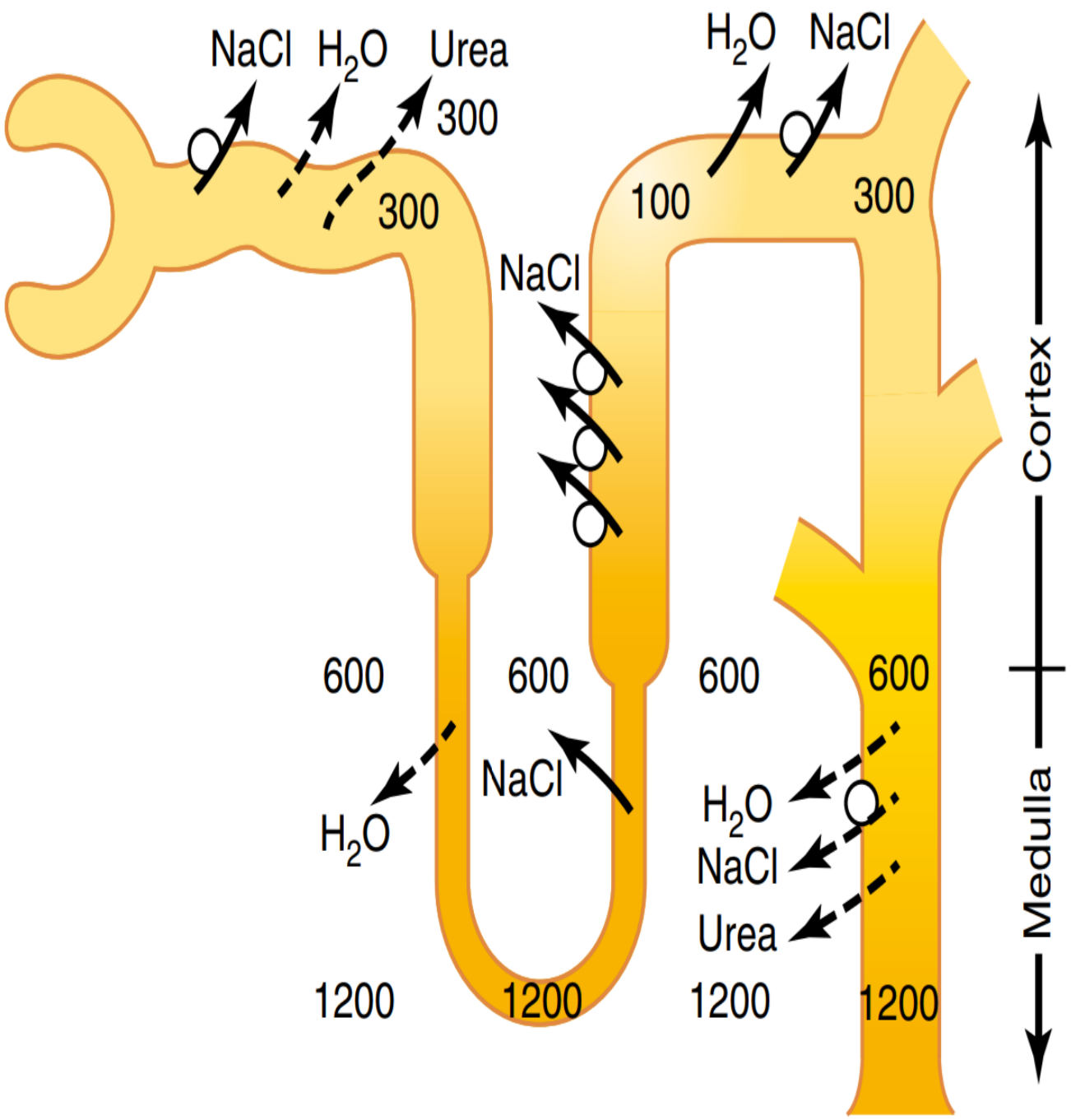

Figure 28-5 Formation of a concentrated urine when antidiuretic hormone (ADH) levels are high. Note that the fluid leaving the loop of Henle is dilute but becomes concentrated as water is absorbed from the distal tubules and collecting tubules. With high ADH levels, the osmolarity of the urine is about the same as the osmolarity of the renal medullary interstitial fluid in the papilla, which is about 1200 mOsm/L. (Numerical values are in milliosmoles per liter.)

Urea Contributes to Hyperosmotic Renal Medullary Interstitium and Formation of Concentrated Urine

Thus far, we have considered only the contribution of sodium chloride to the hyperosmotic renal medullary interstitium. However, urea contributes about 40 to 50 percent of the osmolarity (500 to 600 mOsm/L) of the renal medullary interstitium when the kidney is forming a maximally concentrated urine. Unlike sodium chloride, urea is passively reabsorbed from the tubule. When there is water deficit and blood concentration of ADH is high, large amounts of urea are passively reabsorbed from the inner medullary collecting tubules into the interstitium.

Recirculation of Urea from Collecting Duct to Loop of Henle Contributes to Hyperosmotic Renal Medulla.

In the proximal tubule, 40 to 50 percent of the filtered urea is reabsorbed, but even so, the tubular fluid urea concentration increases. The concentration of urea continues to rise as the tubular fluid flows into the thin segments of the loop of Henle, partly because of water reabsorption out of the descending loop of Henle but also because of some secretion of urea into the thin loop of Henle from the medullary interstitium (Figure 28-6).A moderate share of the urea that moves into the medullary interstitium eventually diffuses into the thin loop of Henle and then passes upward through the ascending loop of Henle, the distal tubule, the cortical collecting tubule, and back down into the medullary collecting tubule again. In this way, urea can recirculate through these terminal parts of the tubular system several times before it is excreted. Each time around the circuit contributes to a higher concentration of urea.This urea recirculation provides an additional mechanism for forming a hyperosmotic renal medulla.

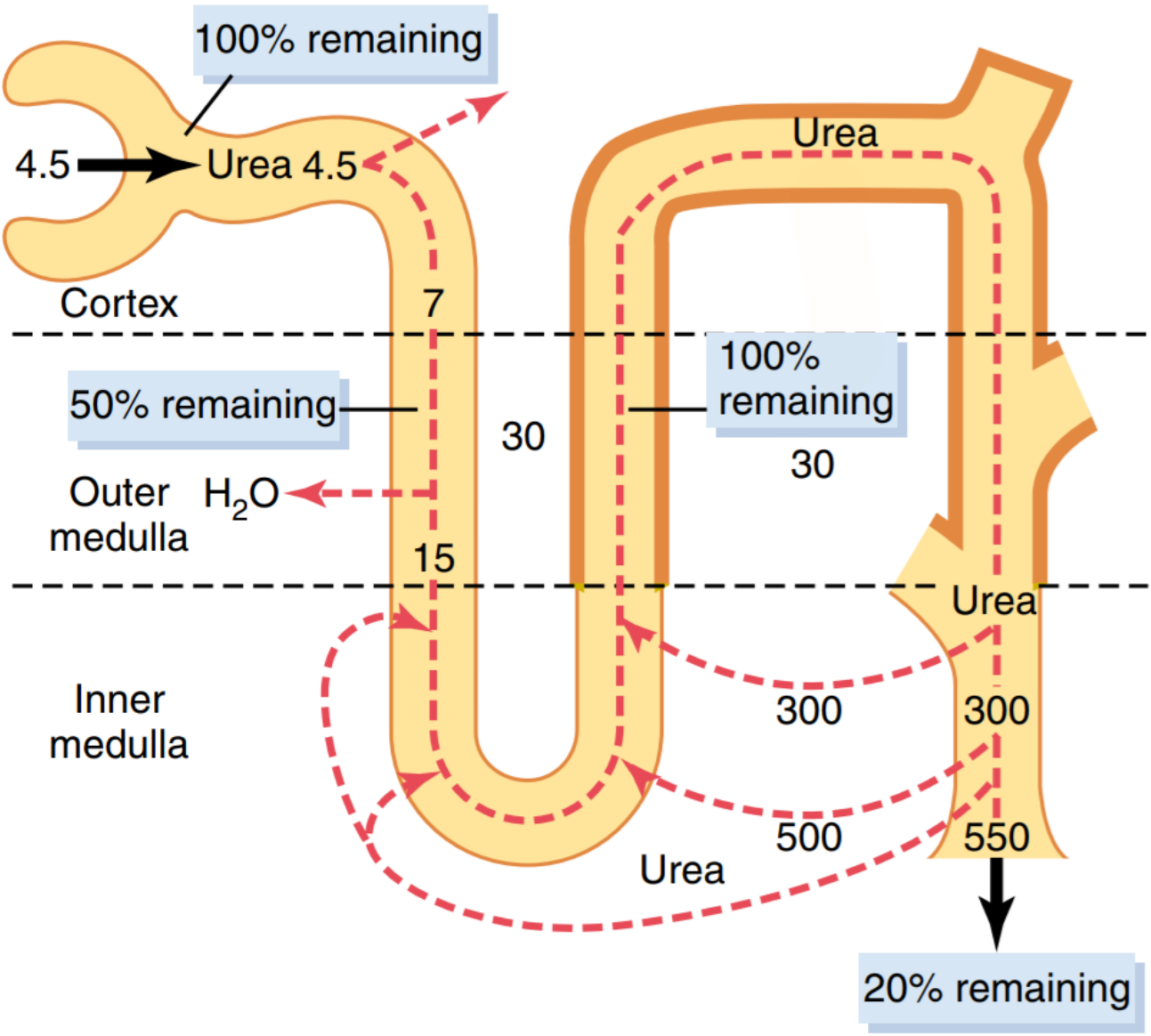

Figure 28-6 Recirculation of urea absorbed from the medullary collecting duct into the interstitial fluid. This urea diffuses into the thin loop of Henle and then passes through the distal tubules, and it finally passes back into the collecting duct. The recirculation of urea helps to trap urea in the renal medulla and contributes to the hyperosmolarity of the renal medulla. The *heavy tan lines*, from the thick ascending loop of Henle to the medullary collecting ducts, indicate that these segments are not very permeable to urea. (Numerical values are in milliosmoles per liter of urea during antidiuresis, when large amounts of antidiuretic hormone are present. Percentages of the filtered load of urea that remain in the tubules are indicated in the blue boxes.)

Countercurrent Exchange in the Vasa Recta Preserves Hyperosmolarity of the Renal Medulla

There are two special features of the renal medullary blood flow that contribute to the preservation of the high solute concentrations:

1. The medullary blood flow is low. This sluggish blood flow helps to minimize solute loss from the medullary interstitium.
2. The vasa recta serve as countercurrent exchangers, minimizing washout of solutes from the medullary interstitium.

The countercurrent exchange mechanism operates as follows (Figure 28-7): Blood enters and leaves the medulla by way of the vasa recta. The vasa recta are highly permeable to solutes in the blood. As blood descends into the medulla toward the papillae, it becomes progressively more concentrated, partly by solute entry from the interstitium and partly by loss of water into the interstitium. By the time the blood reaches the tips of the vasa recta, it has a concentration of about 1200 mOsm/L, the same as that of the medullary interstitium. As blood ascends back toward the cortex, it becomes progressively less concentrated as solutes diffuse back out into the medullary interstitium and as water moves into the vasa recta.

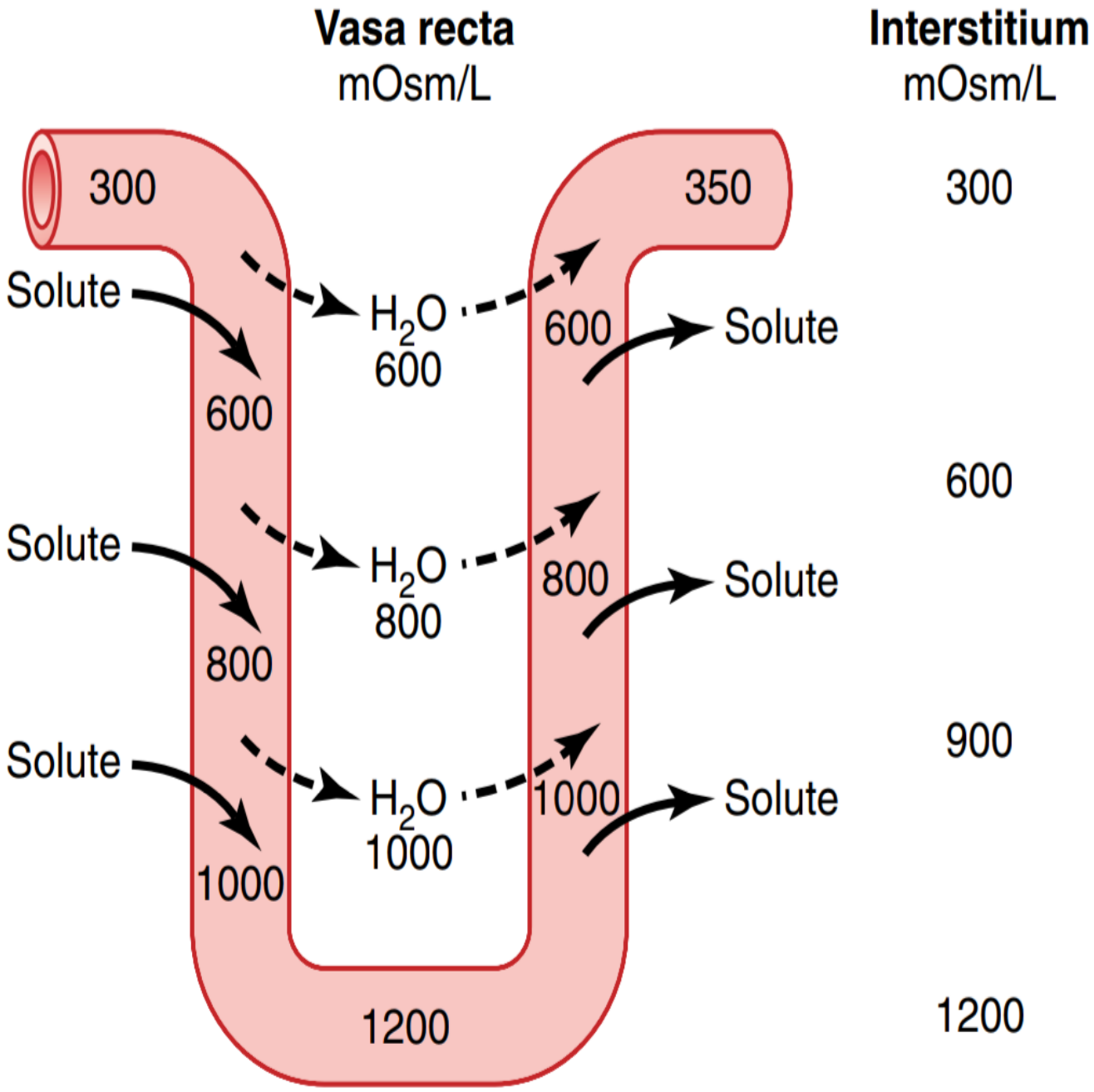

Figure 28-7 Countercurrent exchange in the vasa recta. Plasma flowing down the descending limb of the vasa recta becomes more hyperosmotic because of diffusion of water out of the blood and diffusion of solutes from the renal interstitial fluid into the blood. In the ascending limb of the vasa recta, solutes diffuse back into the interstitial fluid and water diffuses back into the vasa recta. Large amounts of solutes would be lost from the renal medulla without the U shape of the vasa recta capillaries. (Numerical values are in milliosmoles per liter.)

Although there are large amounts of fluid and solute exchange across the vasa recta, there is little net dilution of the concentration of the interstitial fluid at each level of the renal medulla because of the U shape of the vasa recta capillaries, which act as countercurrent exchangers. Thus, the vasa recta do not create the medullary hyperosmolarity, but they do prevent it from being dissipated.

REFERENCE:-

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