RENAL PHYSIOLOGY (PART 4)

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Lec. 4

DILUTED AND CONCENTRATED URINE

❖ **The basic requirements for forming a concentrated urine are:-**

(1) a high level of ADH, which increases the permeability of the distal tubules and collecting ducts to water, thereby allowing these tubular segments to avidly reabsorb water, and

(2) a high osmolarity 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 ducts 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.
- Thus, the urine-concentrating ability **is limited** by the level of ADH and by the degree of hyperosmolarity of the renal medulla.

What is the process by which renal medullary interstitial fluid becomes hyperosmotic?

- This process involves the operation of the **countercurrent multiplier** mechanism
- The countercurrent multiplier mechanism depends on the special *anatomical arrangement of the loops of Henle* and *the vasa recta*, (the specialized peritubular capillaries of the renal medulla.)
- Urea recirculating.

The major factors that contribute to the buildup of solute concentration into the renal medulla

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 ducts** into the medullary interstitium

3. Facilitated diffusion of **urea** from the **inner medullary collecting ducts** into the medullary interstitium

4. Diffusion of only small amounts of water from the **medullary tubules** into the medullary interstitium— far less than the reabsorption of solutes into the medullary interstitium

SPECIAL CHARACTERISTICS OF THE LOOP OF HENLE THAT CAUSE SOLUTES TO BE TRAPPED IN THE RENAL MEDULLA

- A major reason for the high medullary osmolarity is active transport of sodium and co-transport of potassium, chloride, and **other ions from the thick ascending loop of Henle** into **the interstitium**.
- Because the **thick ascending limb** is **virtually impermeable to water**, *the solutes pumped out are not followed by osmotic flow of water into the interstitium.*
- Thus, the active transport of sodium and other ions out of the thick ascending loop adds solutes in excess of water to the renal medullary interstitium.

- There is some **passive reabsorption** of sodium chloride from the thin ascending limb of Henle's loop, which is also impermeable to water, adding further to the high solute concentration of the renal medullary interstitium.
- The **descending limb of Henle's loop**, in contrast to the ascending limb, is very permeable to water, *and the tubular fluid osmolarity quickly becomes equal to the renal medullary osmolarity*
- Therefore, water diffuses out of the descending limb of Henle's loop into the interstitium and the tubular fluid osmolarity gradually rises as it flows toward the tip of the loop of Henle.

Table 29-1 Summary of Tubule Characteristics—Urine Concentration

		Permeability		
	Active NaCl Transport	**H_2O**	**NaCl**	**Urea**
Proximal tubule	++	++	+	+
Thin descending limb	0	++	+	+
Thin ascending limb	0	0	+	+
Thick ascending limb	++	0	0	0
Distal tubule	+	+ADH	0	0
Cortical collecting tubule	+	+ADH	0	0
Inner medullary collecting duct	+	+ADH	0	+ADH

ADH, antidiuretic hormone; NaCl, sodium chloride; 0, minimal level of active transport or permeability; +, moderate level of active transport or permeability; ++, high level of active transport or permeability; +ADH, permeability to water or urea is increased by ADH.

Steps Involved in Causing Hyperosmotic Renal Medullary Interstitium

- **how the renal medulla becomes hyperosmotic?**
- 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.
- 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 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 200mOsm/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, still 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 6

- *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.

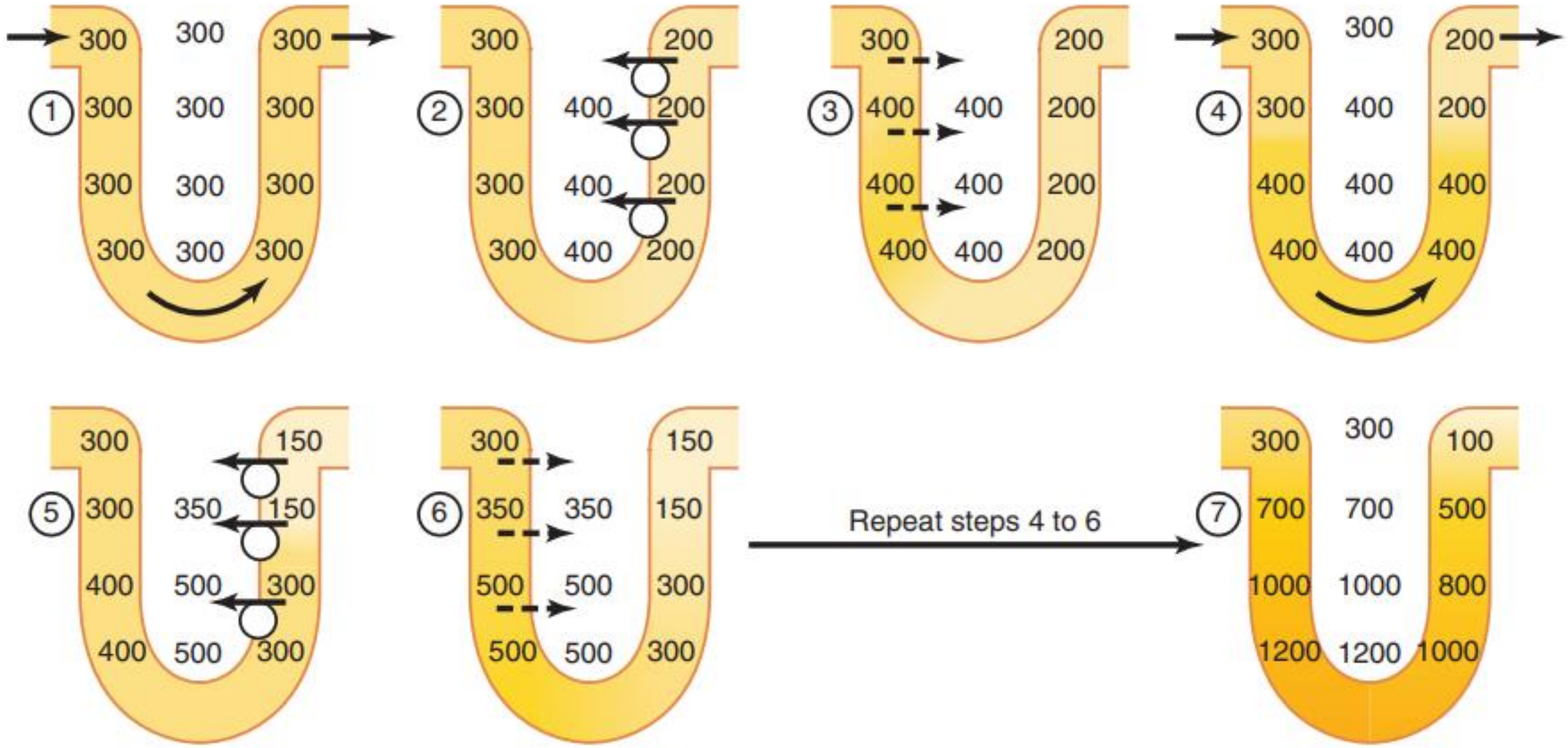


Figure 29-4. Countercurrent multiplier system in the loop of Henle for producing a hyperosmotic renal medulla. (Numerical values are in milliosmoles per liter.)

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.**
- 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, where it is swept away by the rapidly flowing peritubular capillaries

- The fact that these large amounts of water are reabsorbed into the cortex, rather than into the renal medulla, *helps to preserve the high medullary interstitial fluid osmolarity.*

UREA CONTRIBUTES TO HYPEROSMOTIC RENAL MEDULLARY INTERSTITIUM AND FORMATION OF CONCENTRATED URINE

- 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 a water deficit and blood concentration of ADH is high,
- large amounts of **urea are passively reabsorbed** from the inner medullary collecting ducts into the interstitium.

❖ **The mechanism for reabsorption of urea into the renal medulla is as follows:**

- As **water** flows up the ascending loop of Henle and into the distal and cortical collecting tubules, **little urea** is reabsorbed because these segments are **impermeable to urea**

- In the presence of **high** concentrations of **ADH**, water is reabsorbed rapidly from the cortical collecting tubule and the urea concentration increases rapidly **because** urea is not very permeant in this part of the tubule.
- As the tubular fluid flows into the inner medullary collecting ducts, still more water reabsorption takes place, causing an even higher concentration of urea in the fluid
- This high concentration of urea in the tubular fluid of the **inner medullary collecting duct** causes urea to diffuse out of the tubule into the renal interstitial fluid.

- This diffusion is greatly facilitated by specific urea transporters, UT-A1 and UT-A3. These urea transporters are activated by ADH, increasing transport of urea out of the inner medullary collecting duct even more when ADH levels are elevated.
- The simultaneous movement of water and urea out of the inner medullary collecting ducts maintains a high concentration of urea in the tubular fluid and, even though urea is being reabsorbed.

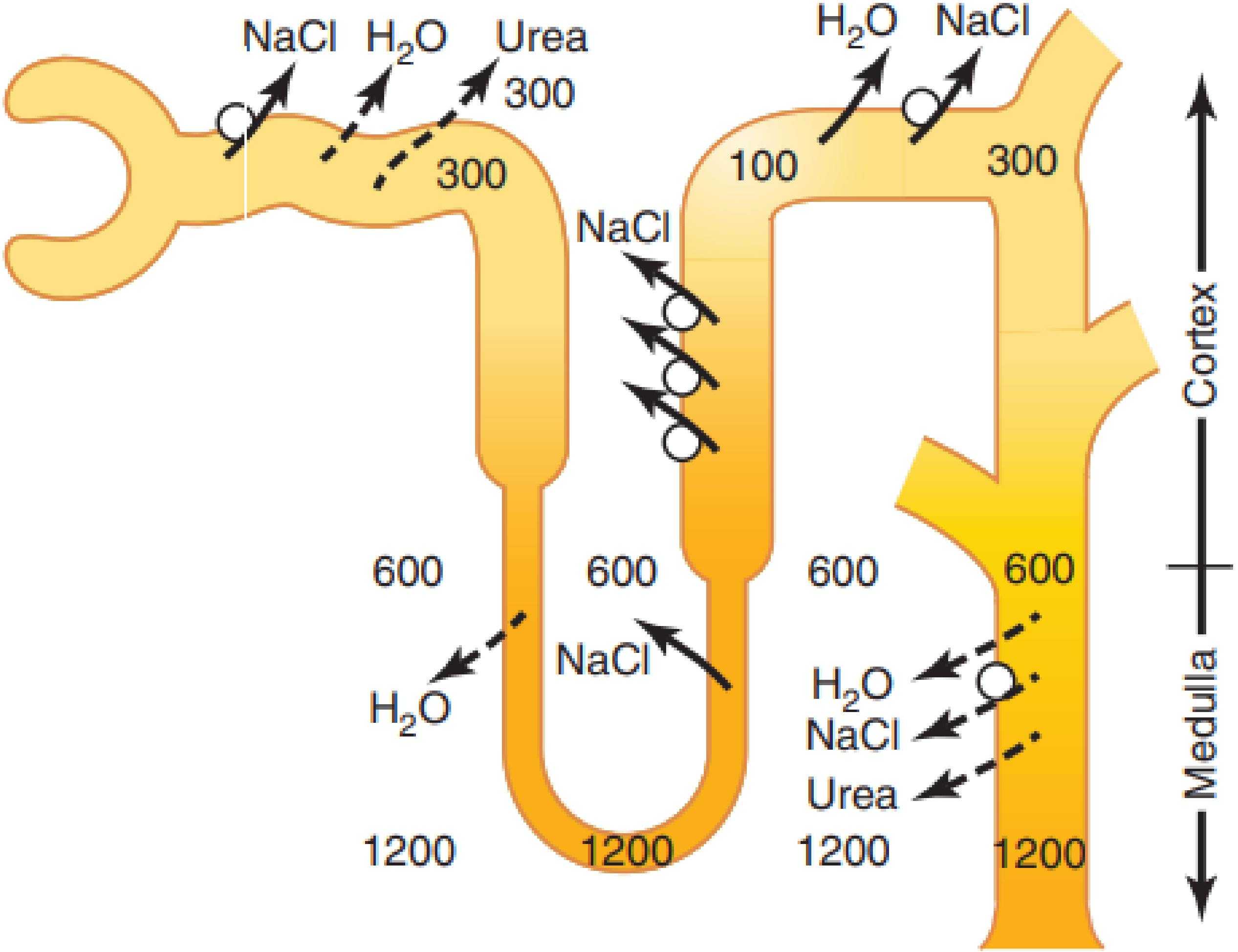


Figure 29-5. Formation of a concentrated urine when antidiuretic hormone (ADH) levels are high. Note that the fluid leaving the loop of Henle is dilute but becomes concentrated as water is absorbed from the distal tubules and collecting tubules. With high ADH levels, the osmolarity of the urine is about 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.)

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

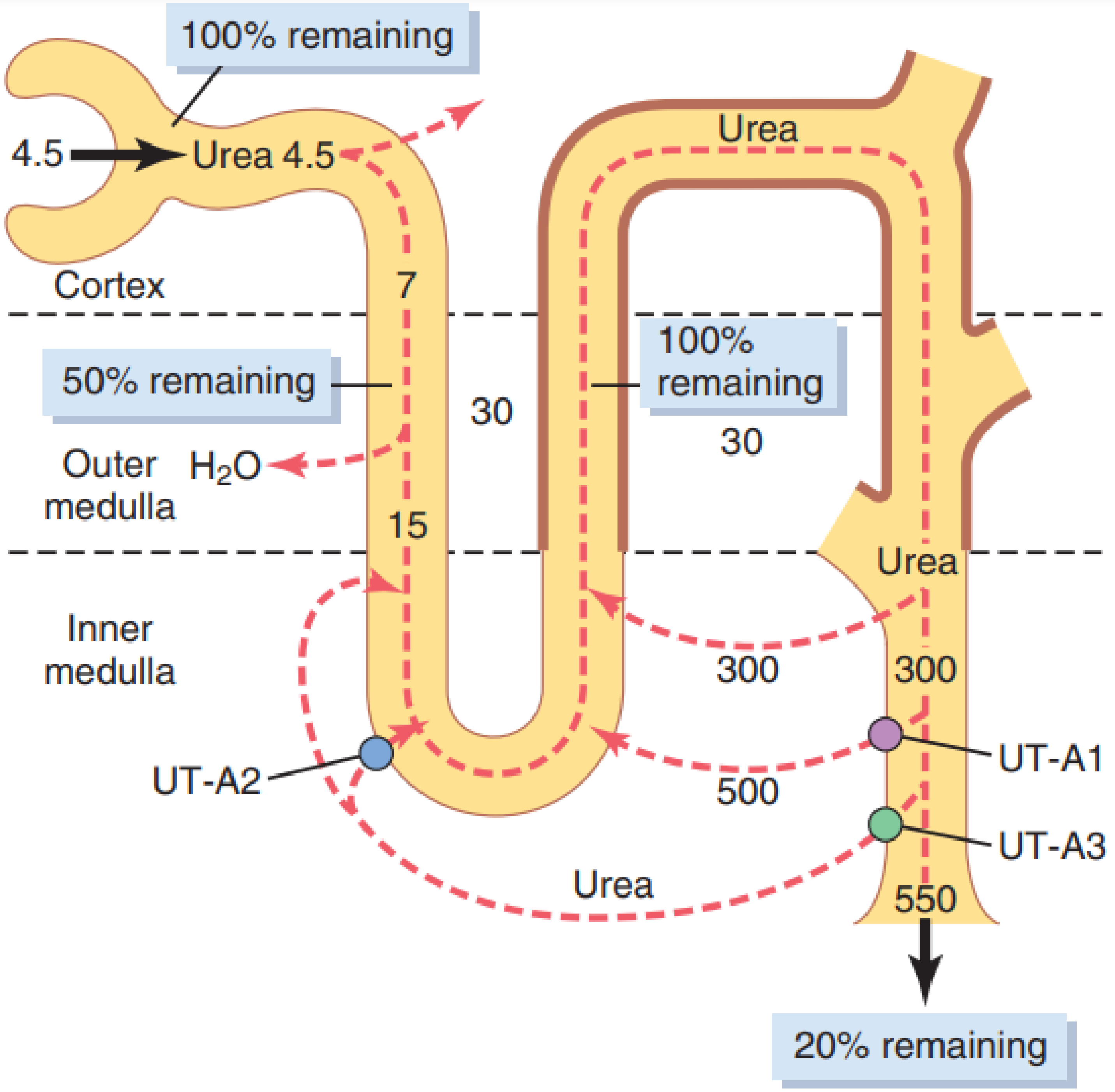
- A healthy person usually excretes about 20 to 50 percent of the filtered load of urea.
- In general, the rate of urea excretion is determined mainly by
- (1) the concentration of urea in the plasma,
- (2) the glomerular filtration rate (GFR), and
- (3) renal tubular urea reabsorption.
- In the proximal tubule, 40 to 50 percent of the filtered urea is reabsorbed, but even so, the tubular fluid urea concentration increases because urea is not nearly as permeant as water.

- 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
- The passive secretion of urea into the thin loops of Henle is facilitated by the **urea transporter UT-A2**.

- The thick limb of the loop of Henle, the distal tubule, and the cortical collecting tubule are all relatively impermeable to urea, and very little urea reabsorption occurs in these tubular segments.
- When the kidney is forming concentrated urine and high levels of ADH are present, reabsorption of water from the distal tubule and cortical collecting tubule further raises the tubular fluid concentration of urea.
- As this urea flows into the inner medullary collecting duct, the high tubular fluid concentration of urea and the urea transporters UT-A1 and UT-A3 cause urea to diffuse into the medullary interstitium.

- A moderate share of the urea that moves into the medullary interstitium eventually **diffuses into** the thin loop of Henle and *<u>then passes upward through the ascending loop of Henle</u>*, the distal tubule, the cortical collecting tubule, and back down into the medullary collecting duct again.
- In this way, urea can recirculate through these terminal parts of the tubular system several times before it is excreted.

- This urea recirculation provides an additional mechanism for forming a **hyperosmotic renal medulla**. Because urea is one of the most abundant waste products that must be excreted by the kidneys, this mechanism for concentrating urea before it is excreted is essential to the economy of the body fluid when water is in short supply.


100% remaining
4.5
Urea 4.5
Cortex
7
50% remaining
30
Outer medulla
H_2O
15
Inner medulla
UT-A2
Urea
100% remaining
30
300
500
Urea
Urea
300
UT-A1
UT-A3
550
20% remaining

COUNTERCURRENT EXCHANGE IN THE VASA RECTA PRESERVES HYPEROSMOLARITY OF THE RENAL MEDULLA

- Blood flow must be provided to the renal medulla to supply the metabolic needs of the cells in this part of the kidney.
- Without a special medullary blood flow system, the solutes pumped into the renal medulla by the countercurrent multiplier system would be rapidly dissipated.
- Two special features of the renal medullary blood flow contribute to the preservation of the high solute concentrations:
- 1. The medullary blood flow is low
- 2. The vasa recta serve as countercurrent exchangers, minimizing washout of solutes from the medullary interstitium.

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