UGS MODULE
PHYSIOLOGY(LECTURE 4)
Renal Concentration and Dilution of Urine

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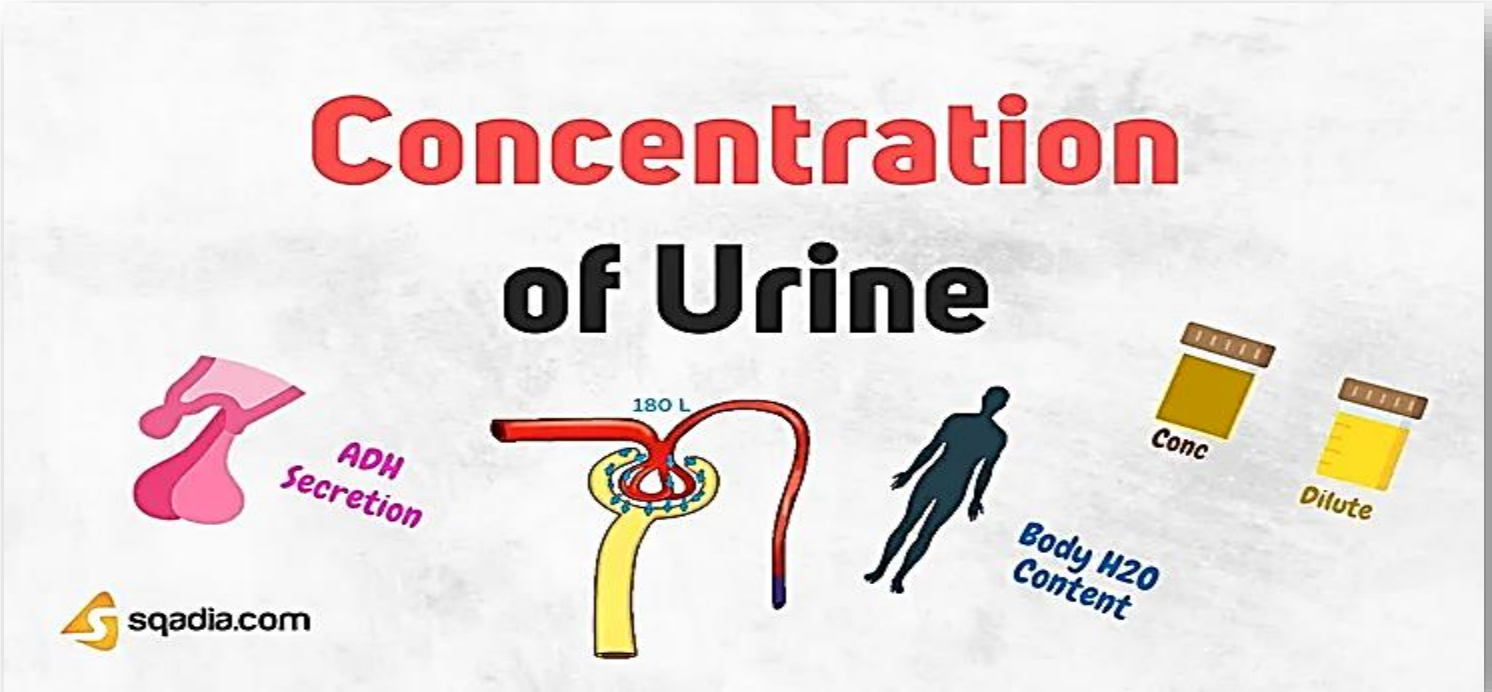


Renal Concentration and Dilution of Urine

- The kidneys can excrete either **concentrated or dilute urine** according to **the water balance of the body**.
- In **dehydration**, water is conserved in the body and **concentrated urine** having **high osmolarity is excreted**.
- While in **hydration**, excess water is eliminated from the body and **dilute urine** having **low osmolarity is excreted**.
- This function is determined by the amount of water reabsorption in renal tubules:

✓ Since water reabsorption is **obligatory in the PCTs (about 65-70 %) and LH (about 15 % in descending limb)**. It is clear that the **final adjustment of the urine volume and osmolarity** depends only on the extent of **facultative water reabsorption in CDs**, which is determined by **2 main factors**:

1) **The ADH blood level:** This hormone renders the CDs highly water permeable and the higher its blood level, the greater the area of CDs that becomes water permeable (and vice versa).
2) **The hyperosmolarity of renal medullary interstitium (MI):** This is developed by the **renal countercurrent multiplier system (LH of juxtamedullary nephrons),** and is the force that causes passive water reabsorption from the MCDs into the renal medulla.

Urine Concentrating Mechanisms:
The Countercurrent Multiplier System

Renal Countercurrent Mechanism

Countercurrent system

- It is a system in which the **inflow** of a **current runs parallel, opposite (counter) and close to its outflow** for some distance.
- So, **LH (and vasa recta) acts as countercurrent system**.

Renal countercurrent mechanism:

- It is the **mechanism by which urine is concentrated in the kidney**.
- It **depends on the production and maintenance of a state of hyperosmolarity (hypertonicity) in the renal medullary interstitium (MI)** by the action of the structures that pass in the renal medulla which are:

1. **LH of juxtamedullary nephrons (countercurrent multiplier system)**.
2. **Vasa Recta (countercurrent exchanger system)**.
3. **Medullary collecting ducts (MCDs).**

1. **LH of juxtamedullary nephrons:**

These constitute a **countercurrent multiplier system** that operates **actively** to **construct an osmotic stratification in the renal medulla (i.e. a progressively increasing hyperosmolarity in the renal medulla)**.
So that the osmolarity of the MI gradually increases from **300 mOsm/L in the renal cortex** to **1200-1400 mOsm/L** at the renal papillae.

2. **Vasa Recta (VR):**

These constitute a **countercurrent exchanger system** that operates **passively** to **maintain the hyperosmolarity of the MI**.

3. **Medullary collecting ducts (MCDs).**

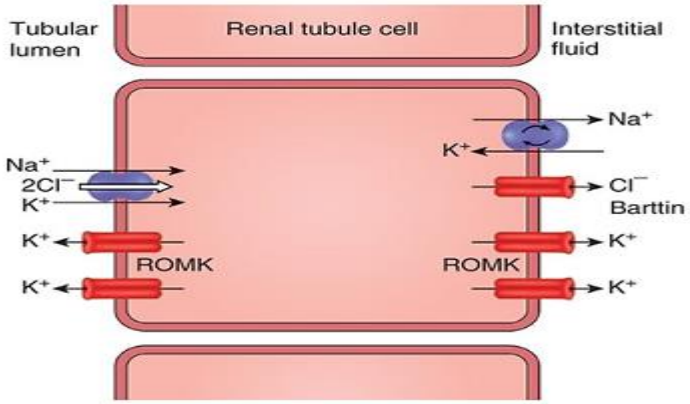
Countercurrent multiplier system

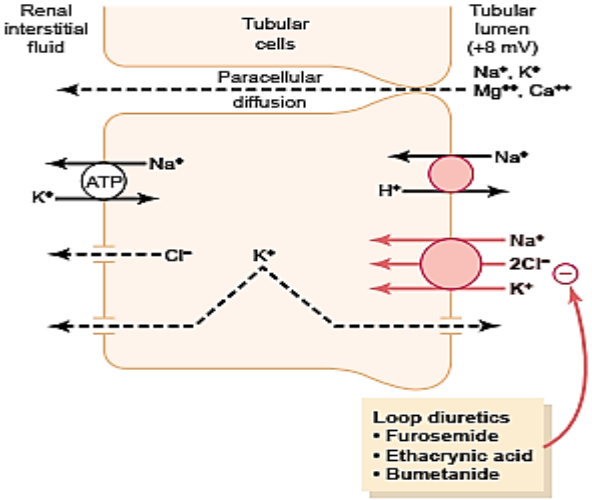
This system consists of **LH of juxtamedullary nephrons** which dip deeply in renal medulla, and is concerned with **production of graded hyperosmolarity in MI** by the following mechanism:

Steps involved in causing hyperosmotic renal medullary interstitium:

Step (1): First assume that the LH is filled with fluid with a concentration of 300mOsm/L, the same as that leaving PCT.

Step (2): There is **a carrier in thick ascending LH (TALH) which actively transported one Na^+, one K^+, and 2 Cl^- (Na^+- K^+ -2Cl^- Transporters) from the tubular lumen into the cells**. Na^+ is actively pumped out by the ATPase in exchange for K^+ .The K^+ diffuses back into the tubular lumen and back into the interstitium via ROMK and other K^+ channels. The Cl^- moves into the interstitium via ClC–Kb channels. **Active transport of these solutes raises the interstitial concentration.**





Step (3): Osmosis of water out of the descending limb of LH raising osmolarity inside it gradually to about 1200 mOsm/L.

Step (4): Additional flow of fluid in LH from PCT, which causes the hyperosmotic fluid previously formed in the descending limb to flow into the ascending limb.

Step (5): Active transport in the ascending limb repeated over and over with the net effect of adding more and more solutes to the medullary interstitium in excess of water.

Countercurrent Multiplier System in the Loop of Henle

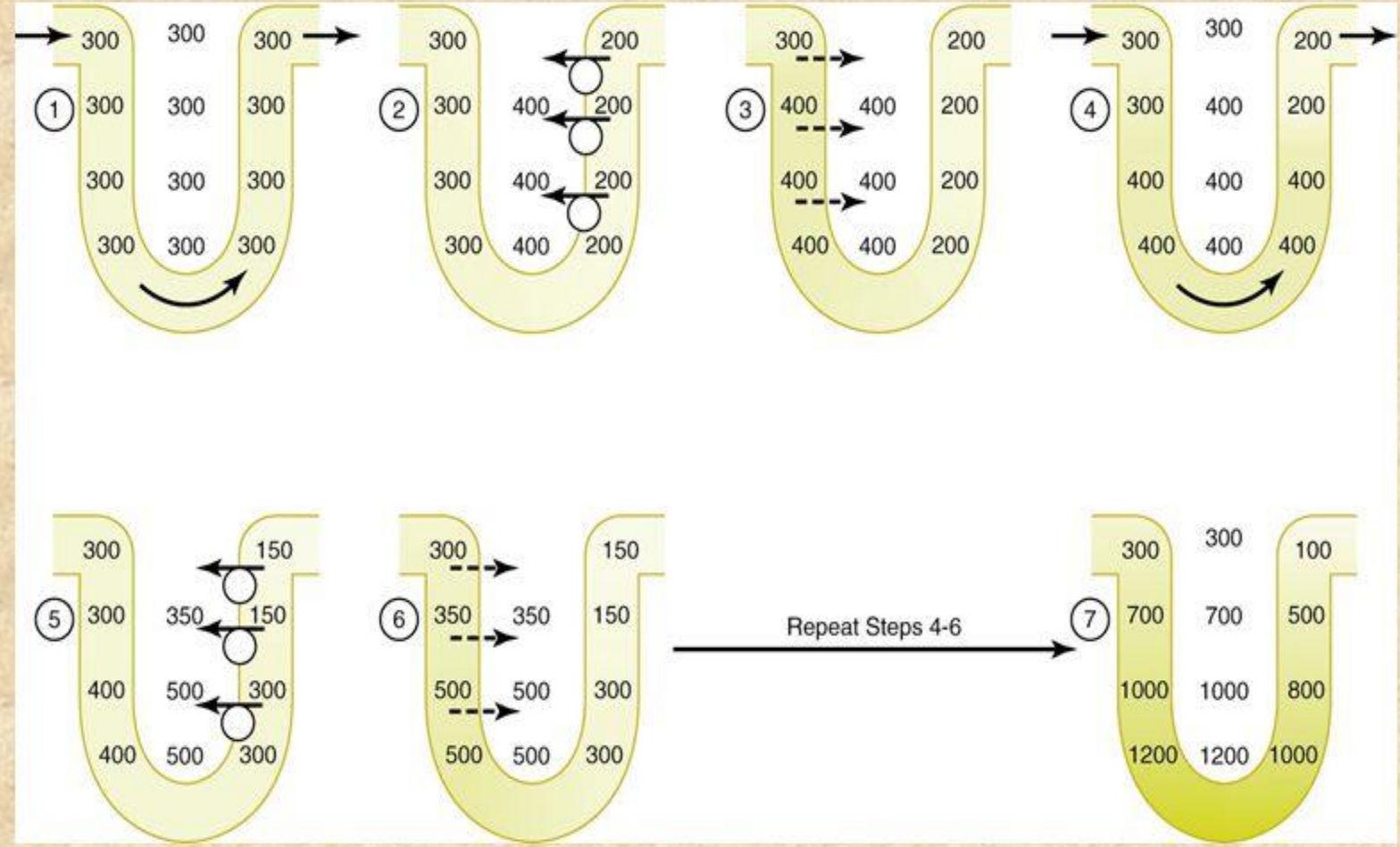


Figure 28-3; Guyton and Hall

The ascending limbs of LH:

Are the segments responsible for creating graded hyperosmolality in MI.

✓ **The distal thick part (TALH):**

- It is **impermeable to water**.
- **Both Na^+ and Cl^-** are **actively transported** from the tubular lumen into the MI. This produces hyperosmolarity in the MI and at the same time, the tubular fluid becomes more **hypotonic (hypoosmotic)** with an osmolality about **100 mOsm/L when delivered to the DCTs**.
- The transport mechanism depends on **a carrier that transports one Na^+, one K^+ & 2 Cl^-** from the tubular lumen into the cells.

✓ **The initial thin part:**

- It is **impermeable to water but highly permeable to Na^+ and Cl^-**.
- **Na^+ and Cl^- diffuse passively (simple diffusion)** down their concentration gradients into MI.

Therefore, the tonicity of tubular fluid progressively decreases as it moves up while hyperosmolarity is developed in MI.

The descending limbs of LH:

- Receive **isotonic (iso-osmotic) fluid** from the **PCTs**.
- Their walls are:
- **Highly permeable to water.**
- **Impermeable to reabsorption of solutes (namely Na^+ and Cl^-).**
- Accordingly water passively diffuses outward down an osmotic gradient into the MI (which is hypertonic by the countercurrent multiplier effect of the ascending limb).
- As a result, the **tubular fluid becomes hypertonic, and its hypertonicity increases gradually as it flows downwards reaching 1200 (up to 1400) mOsm/L at the tips of the renal pyramids.**
- The **reabsorbed water in the LH is about 15% of the filtered water in the glomeruli, and it is also an obligatory reabsorption as that occurring in the PCTs.**

Causes of renal MI hyperosmolality:

1. **The thick ascending limb of LH (TALH):**
   - **Impermeable to water.**
   - **Active reabsorption of Na^+, K^+, and Cl^- (by common carrier protein that transports one Na^+, one K^+ & 2 Cl^-) with passive reabsorption of +ve ions**.
   - There is a backleak of K^+ out of the cells into the lumen, creating a lumen-positive trans-epithelial potential difference (compared with interstitial fluid). This allows paracellular movement of cations (Ca^{2+}, Mg^{2+}, Na^+, K^+) out of the tubular lumen.

2. The medullary collecting duct (MCD):

ADH increases permeability to water → water reabsorption **(facultative water reabsorption)**→↑ concentration of **urea** in the tubular fluid→ diffuses to medullary interstitium **(urea recycling)**.

3. Transport of additional Na^+ and Cl^- into the medullary interstitium from the **thin ascending limb of the LH.**

Countercurrent exchanger system of the vasa recta

Without a special medullary vascular system, the flow of blood in the medulla will wash out excess solutes and prevent the previous mechanisms from increase the osmolarity of the medullary interstitium.

Fortunately, the medullary blood flow has 2 characteristics:

1. It is **very sluggish representing 1-2% of the total RBF**. So, removal of solutes is minimized.
2. **The vasa recta function as a countercurrent exchanger** that **prevents wash out of solutes from the medulla. HOW?**

- Fluid flows through along U tubule, with its arms lying very close to each other so that fluid and solutes can exchange readily between the 2 arms (countercurrent exchanger).

- Thus, **as the blood flows down the descending limb, NaCl and urea diffuse into the blood from the highly concentrated interstitium while water diffuses outward into the interstitium**. Both effects cause the **blood osmotic concentration to raise progressively higher to a maximum of 1200 mOsm/L** at **the tips of vasa recta**.

- As the **blood flows back up the ascending limb, all the NaCl and urea diffuses back out the blood into the interstitium while water diffuses back into blood.**
- Therefore, **by the time the blood leaves the medulla with osmolarity slightly greater than that of the blood that had initially enter the vasa recta**. As a result, **blood flowing through the vasa recta carries only minute amounts of medullary interstitial solutes away from the medulla**.

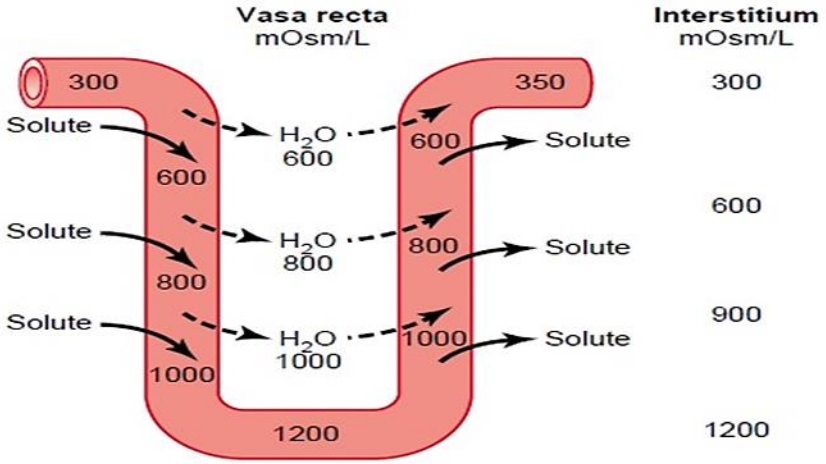


Figure 28–6

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.)

- In this way, **solutes are trapped in the MI while excess water is removed from it**, and both effects help **maintenance of MI hyperosmolarity**.
- **The excess water comes from 2 sources:**
  - **Water that diffuses from the descending limbs of both VR and LH.**
  - **Water that is reabsorbed from the MCDs.**
- **The countercurrent exchanger function of VR is helped by:**
- **They are highly permeable to both solutes and water.**
- **Blood flow is sluggish and small (about 2% of total RBF).**
- **Thus, the main function of VR is to maintain the renal MI hyperosmolarity**.

Urea Recycling

Urea reabsorption from the medullary collecting ducts and urea diffusion from the medullary interstitium into the thin limb of loop of Henle).

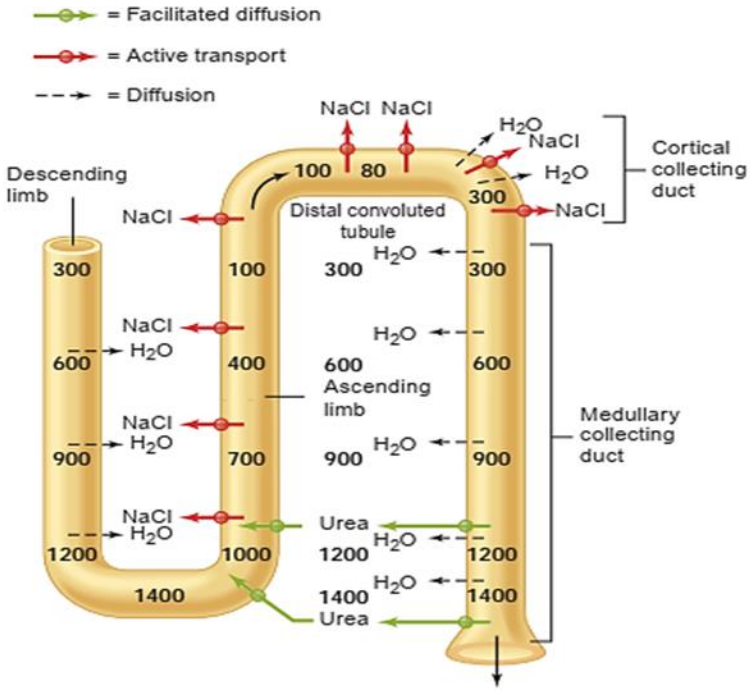


Figure 14.18 AP|R Simplified depiction of the generation of an interstitial fluid osmolarity gradient by the renal countercurrent multiplier system and its role in the formation of hyperosmotic urine in the presence of vasopressin. Notice that the hyperosmotic medulla depends on NaCl reabsorption and urea trapping (described in Figure 14.20).

Role of ADH in the Mechanism of Urine Concentration and Dilution

- ✓ Either **a small increase in plasma osmolarity (~1%) or a significant decrease (a greater than 10% loss) in plasma volume** (from, for example, hemorrhage or severe dehydration) will elicit release of antidiuretic hormone (ADH) from the posterior pituitary gland.
- ✓ **ADH binds to V2 receptors on principal cells of the renal collecting ducts.**
- ✓ The ADH increases apical water channels, or **aquaporins** (in the principal cells, **AQP-2)**, In the presence of high concentrations of ADH, water reabsorption occurs from the **cortical collecting duct (about 10 %)** until the fluid in this segment becomes iso-osmotic to the interstitial fluid and peritubular plasma of the cortex—that is, until it is once again at 300 mOsm/L.
- ✓ The iso-osmotic tubular fluid then enters and flows through the medullary collecting ducts.
- ✓ In the presence of **high plasma concentrations of ADH**, **(about 4.7 %)** of water diffuses out of the medullary collecting ducts into the medullary interstitial fluid as a result of the high osmolarity that the loop countercurrent multiplier system and urea trapping establish there. Thus, leading to a **total water reabsorption of about 99.7% and a urine volume about 0.5 liter (obligatory urine volume) daily with an osmolarity of about 1400 mOsm/L (hypertonic urine)**.

- ✓ By this means, the **final urine is hyperosmotic**. By retaining as much water as possible, the kidneys minimize the rate at which dehydration occurs during water deprivation.
- ✓ **At the normal rate of ADH secretion, about 10 % of water is reabsorbed in the CCD and 4.2 % is reabsorbed in the MCDs, leading to a total water reabsorption of about 99.2% and a urine volume about 1.5 liters daily with an osmolarity about 400 mOsm/L.**

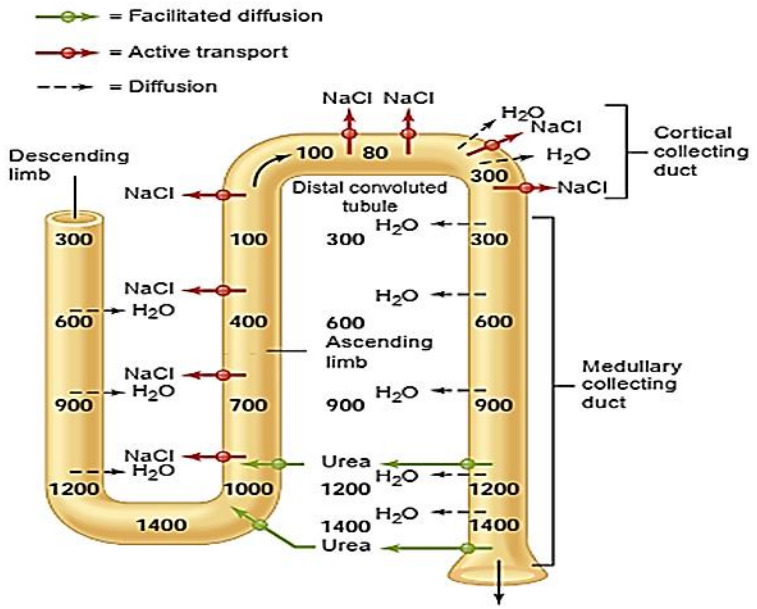
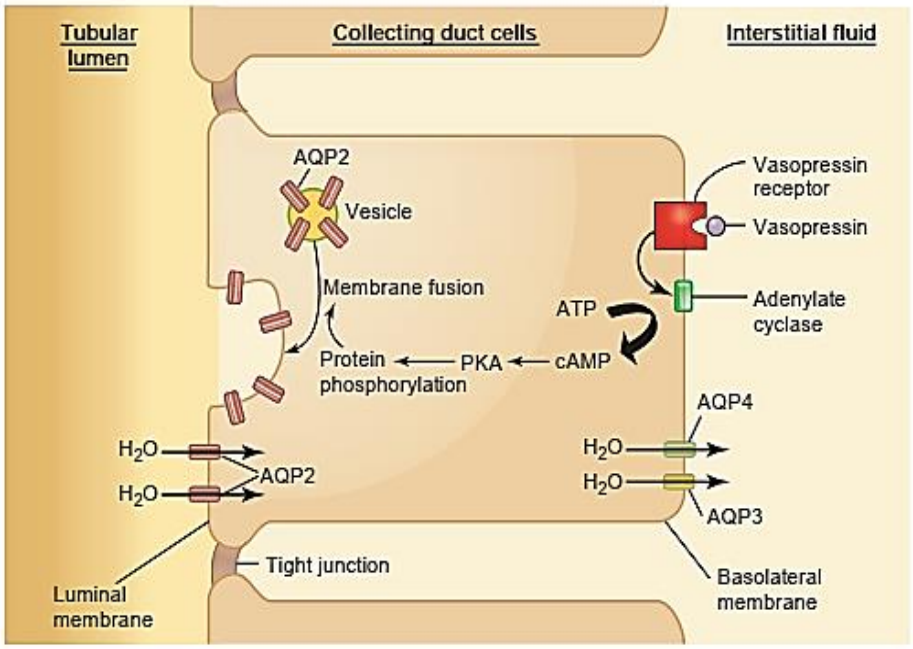


Figure 14.18 AP|R Simplified depiction of the generation of an interstitial fluid osmolarity gradient by the renal countercurrent multiplier system and its role in the formation of hyperosmotic urine in the presence of vasopressin. Notice that the hyperosmotic medulla depends on NaCl reabsorption and urea trapping (described in Figure 14.20).



- ✓ In contrast, **when plasma ADH concentration is low, both the cortical and medullary collecting ducts are relatively impermeable to water.**
- ✓ This occurs in cases of **hydration and after drinking large amounts of water.**
- ✓ It is produced secondary to **decreased secretion of ADH (as a result of both hypervolemia and blood hypotonicity)**.
- ✓ As a result, a **large volume of hypo-osmotic (dilute) urine is excreted, thereby eliminating an excess of water in the body**. When the excess fluid is excreted, the plasma osmolarity will increase.
- ✓ **In severe cases of diabetes insipidus**, almost the whole length of the CDs become water-impermeable, thus water reabsorption is markedly decreased. In addition, there is continuous Na^+ reabsorption, so the osmolarity of the tubular fluid in the CCDs decreases to about 90 mOsm/L and is further decreased in the MCDs, leading to excretion of a **large volume of dilute (hypo-osmotic) urine** with an osmolality less than 80 mOsm/L (about 50 mOsm/L).

- ✓ In cases of **complete absence of ADH, the urine osmolarity becomes about 30 mOsm/L, and its volume about 23.3 liters/day**.

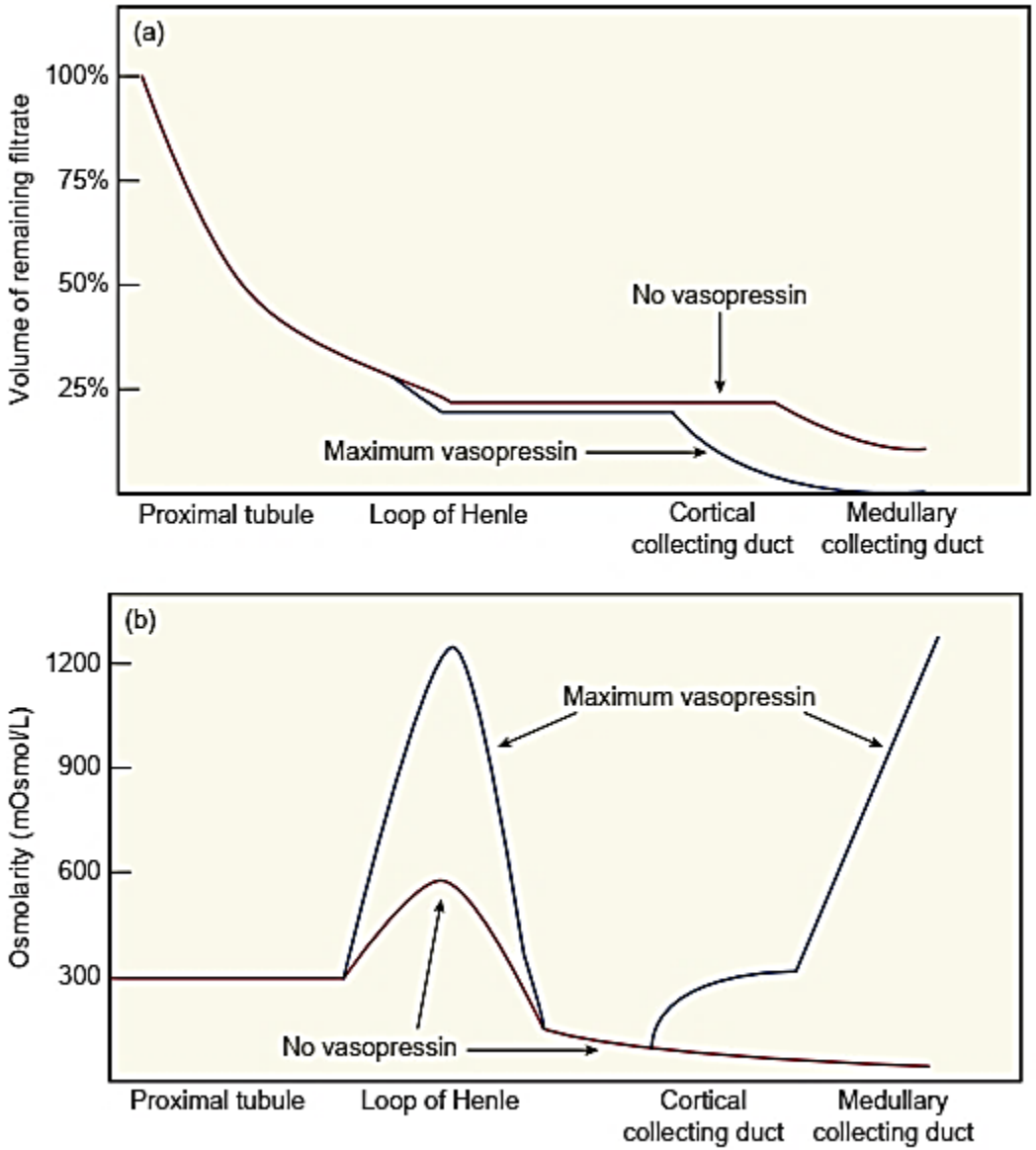


Figure 14.21 The effect of no vasopressin and maximum vasopressin concentration in the blood on (a) the volume remaining in the filtrate in the nephron as well as (b) the osmolarity of the tubular fluid along the length of the nephron.

Thank You