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DEPARTMENT: NURSING

Concentration and formation of urine

URINE CONCENTRATION

When the glomerular filtrate passes through renal tubule, its osmolarity is altered in different segments as described below (Fig. 53.4).

1. BOWMAN CAPSULE

Glomerular filtrate collected at the Bowman capsule is isotonic to plasma. This is because it contains all the substances of plasma except proteins. Osmolarity of the filtrate at Bowman capsule is 300 mOsm/L.

2. PROXIMAL CONVOLUTED TUBULE

When the filtrate flows through proximal convoluted tubule, there is active reabsorption of sodium and chloride followed by obligatory reabsorption of water. So, the osmolarity of fluid remains the same as in the case of Bowman capsule, i.e. 300 mOsm/L. Thus, in proximal convoluted tubules, the fluid is isotonic to plasma.

3. THICK DESCENDING SEGMENT

When the fluid passes from proximal convoluted tubule into the thick descending segment, water is reabsorbed from tubule into outer medullary interstitium by means of osmosis. It is due to the increased osmolarity in the medullary interstitium, i.e. outside the thick descending tubule. The osmolarity of the fluid inside this segment is between 450 and 600 mOsm/L. That means the fluid is slightly hypertonic to plasma.

4. THIN DESCENDING SEGMENT OF HENLE LOOP

As the thin descending segment of Henle loop passes through the inner medullary interstitium (which is increasingly hypertonic) more water is reabsorbed. This segment is highly permeable to water and so the osmolarity of tubular fluid becomes equal to that of the surrounding medullary interstitium. In the short loops of cortical nephrons, the osmolarity of fluid at the hairpin bend of loop becomes 600 mOsm/L. And, in the long loops of juxtamedullary nephrons, at the hairpin bend, the osmolarity is 1,200 mOsm/L. Thus in this segment the fluid is hypertonic to plasma.

5. THIN ASCENDING SEGMENTOF HENLE LOOP

When the thin ascending segment of the loop ascends upwards through the medullary region, osmolarity decreases gradually. Due to concentration gradient, sodium chloride diffuses out of tubular fluid and osmolarity decreases to 400 mOsm/L. The fluid in this segment is slightly hypertonic to plasma.

6. THICK ASCENDING SEGMENT

This segment is impermeable to water. But there is active reabsorption of sodium and chloride from this. Reabsorption of sodium decreases the osmolarity of tubular fluid to a greater extent. The osmolarity is between 150 and 200 mOsm/L. The fluid inside becomes hypotonic to plasma.

7. DISTAL CONVOLUTED TUBULE AND COLLECTING DUCT

In the presence of ADH, distal convoluted tubule and collecting duct become permeable to water resulting in water reabsorption and final concentration of urine. It is found that in the collecting duct, Principal (P) cells are responsible for ADH induced water reabsorption. Reabsorption of large quantity of water increases the osmolarity to 1,200 mOsm/L (Fig. 53.3). The urine becomes hypertonic to plasma.

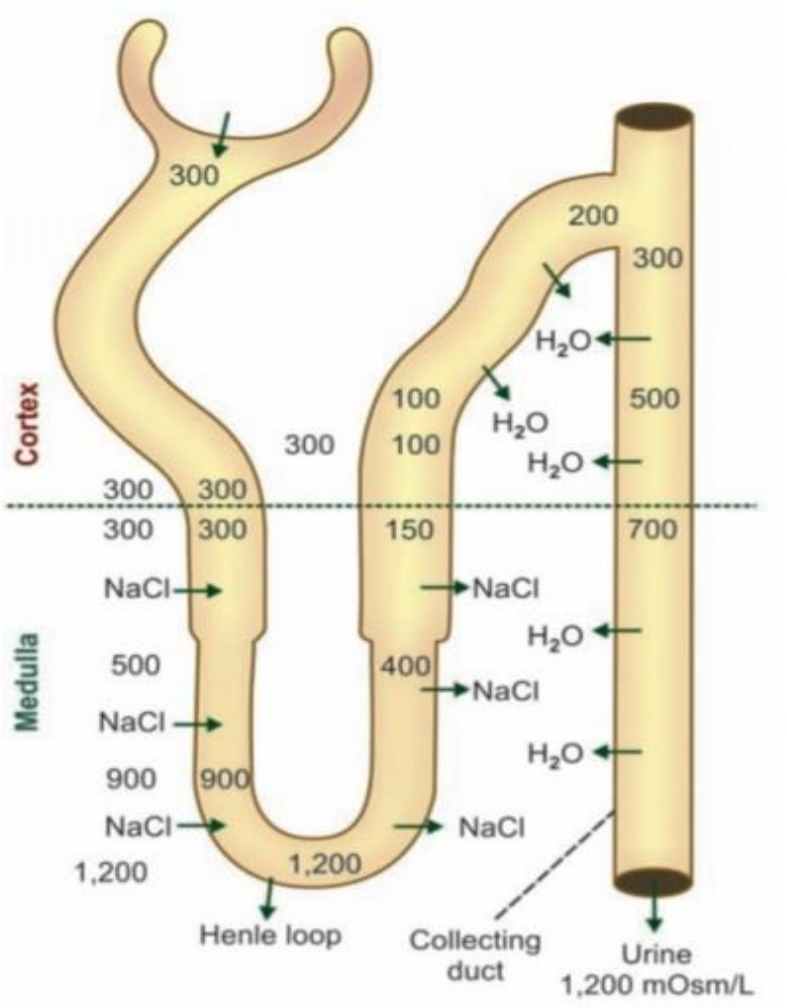


FIGURE 53.3: Role of ADH in the formation of concentrated urine. ADH increases the permeability for water in distal convoluted tubule and collecting duct. Numerical indicate osmolarity (mOsm/L)

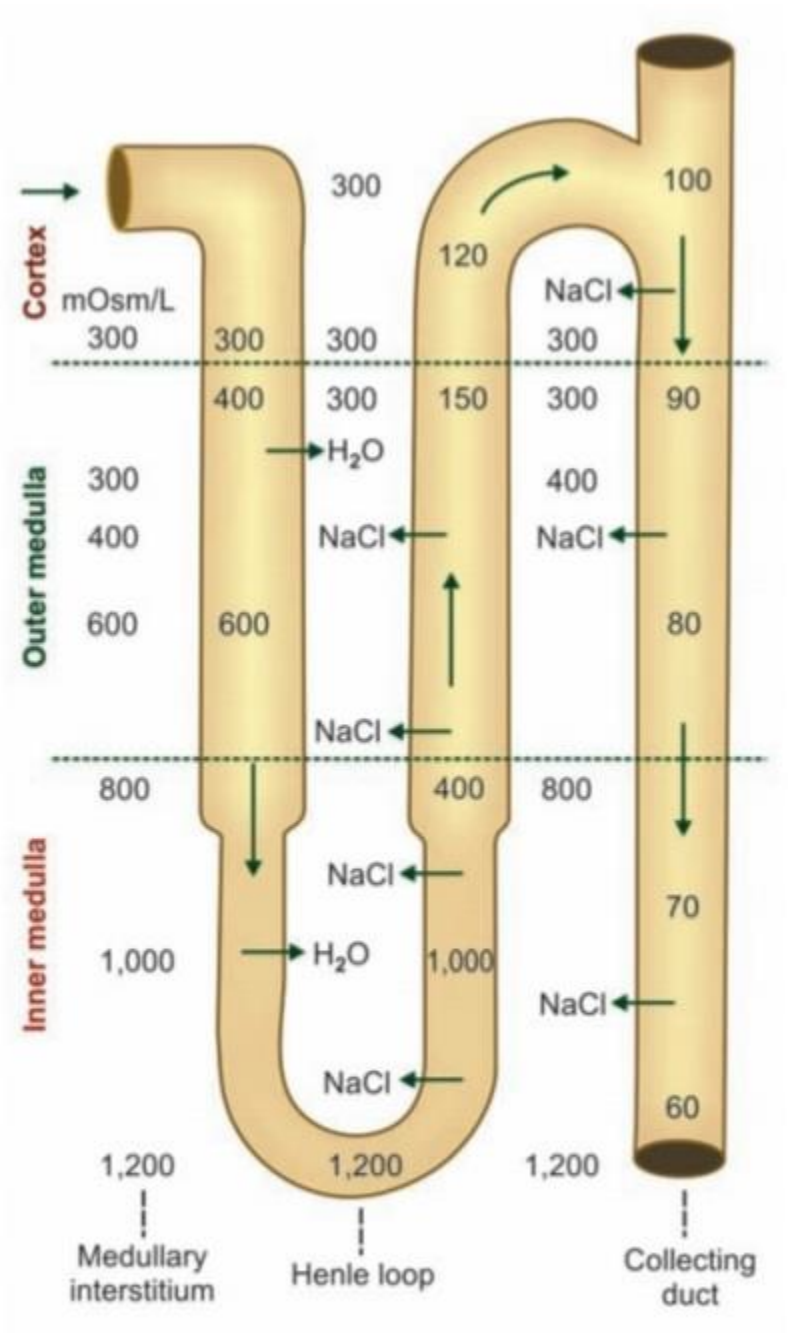


FIGURE 53.4: Mechanism for the formation of dilute urine. Numerical indicate osmolarity (mOsm/L)

URINE FORMATION

The kidney's ability to perform many of its functions depends on the three fundamental functions of *filtration*, *reabsorption*, and *secretion*, whose sum is called renal clearance or renal excretion. That is:

Urinary excretion rate = Filtration rate – Reabsorption rate + Secretion rate

Although the strictest sense of the word *excretion* with respect to the urinary system is urination itself, renal clearance is also conventionally called excretion (for example, in the set term *fractional excretion of sodium*).

Filtration

The blood is filtered by nephrons, the functional units of the kidney. Each nephron begins in a renal corpuscle, which is composed of a glomerulus enclosed in a Bowman's capsule. Cells, proteins, and other large molecules are filtered out of the glomerulus by a process of ultrafiltration, leaving an ultra filtrate that resembles plasma (except that the ultra filtrate has negligible plasma proteins) to enter Bowman's space. Filtration is driven by Starling forces.

The ultra filtrate is passed through, in turn, the proximal convoluted tubule, the loop of Henle, the distal convoluted tubule, and a series of collecting ducts to form urine.

In renal physiology, **ultrafiltration** occurs at the barrier between the blood and the filtrate in the glomerular capsule (Bowman's capsule) in the kidneys. As in nonbiological examples of ultrafiltration, pressure (in this case blood pressure) and concentration gradients lead to a separation through a semipermeable membrane (provided by the podocytes). The Bowman's capsule contains a dense capillary network called the glomerulus. Blood flows into these capillaries through the afferent arterioles and leaves through the efferent arterioles.

The high hydrostatic pressure forces small molecules in the tubular fluid such as water, glucose, amino acids, sodium chloride and urea through the filter, from the blood in the glomerular capsule across the basement membrane of the Bowman's capsule and into the renal tubules. This process is called ultrafiltration; the resulting fluid, virtually free of large proteins and blood cells, is referred to as glomerular filtrate, or ultra filtrate. Further modification of ultra filtrate, by reabsorption and secretion, transforms it into urine.

Glomerular pressure is about 75 millimetres of mercury (10 kPa). It is opposed by osmotic pressure (30 mmHg, 4.0 kPa) and hydrostatic pressure (20 mmHg, 2.7 kPa) of solutes present in capsular space. This difference in pressure is called effective pressure (25 mmHg, 3.3 kPa).

In haemodialysis centres, ultrafiltration takes place in a hemofilter on the haemodialysis machines, when the blood pressure is greater than the dializate pressure (difference = transmembrane pressure (TMP)). This removes fluid from the blood while keeping its blood cells intact.

Reabsorption

Tubular reabsorption is the process by which solutes and water are removed from the tubular fluid and transported into the blood. It is called *reabsorption* (and not *absorption*) both because these substances have already been absorbed once (particularly in the intestines) and because the body is reclaiming them from a post glomerular fluid stream that is well on its way to becoming urine (that is, they will soon be lost to the urine unless they are reclaimed).

Reabsorption is a two-step process beginning with the active or passive extraction of substances from the tubule fluid into the renal interstitium (the connective tissue that surrounds the nephrons), and then the transport of these substances from the interstitium into the bloodstream. These transport processes are driven by Starling forces, diffusion, and active transport.

Indirect reabsorption

In some cases, reabsorption is indirect. For example, bicarbonate (HCO_3^-) does not have a transporter, so its reabsorption involves a series of reactions in the tubule lumen and tubular epithelium. It begins with the active secretion of a hydrogen ion (H^+) into the tubule fluid via a Na/H exchanger:

- In the lumen
  - The H^+ combines with HCO_3^- to form carbonic acid (H_2CO_3)
  - Luminal carbonic anhydrase enzymatically converts H_2CO_3 into H_2O and CO_2

- CO_2 freely diffuses into the cell

- In the epithelial cell
  - Cytoplasmic carbonic anhydrase converts the CO_2 and H_2O (which is abundant in the cell) into H_2CO_3
  - H_2CO_3 readily dissociates into H^+ and HCO_3^-
  - HCO_3^- is facilitated out of the cell's bilateral membrane

Influence of hormones

Some key regulatory hormones for reabsorption include:

- aldosterone, which stimulates active sodium reabsorption (and water as a result)
- antidiuretic hormone, which stimulates passive water reabsorption

Both hormones exert their effects principally on the collecting ducts.

Tubular secretion

This occurs simultaneously during reabsorption of filtrate. Substances, generally produced by body or the by-products of cell metabolism that can become toxic in high concentration, and some drugs (if taken). These all are secreted into the lumen of renal tubule. Tubular secretion can be either active or passive or co-transport. Substances mainly secreted into renal tubule are; H+, K+, NH3, urea, creatinine, histamine and drugs like penicillin. Tubular secretion occurs at Proximal Convoluted Tubule (PCT) and Distal Convoluted Tubule (DCT); for example, at proximal convoluted tubule, potassium is secreted by means of sodium-potassium pump, hydrogen ion is secreted by means of active transport and co-transport, i.e. antiporter, and ammonia diffuses into renal tubule

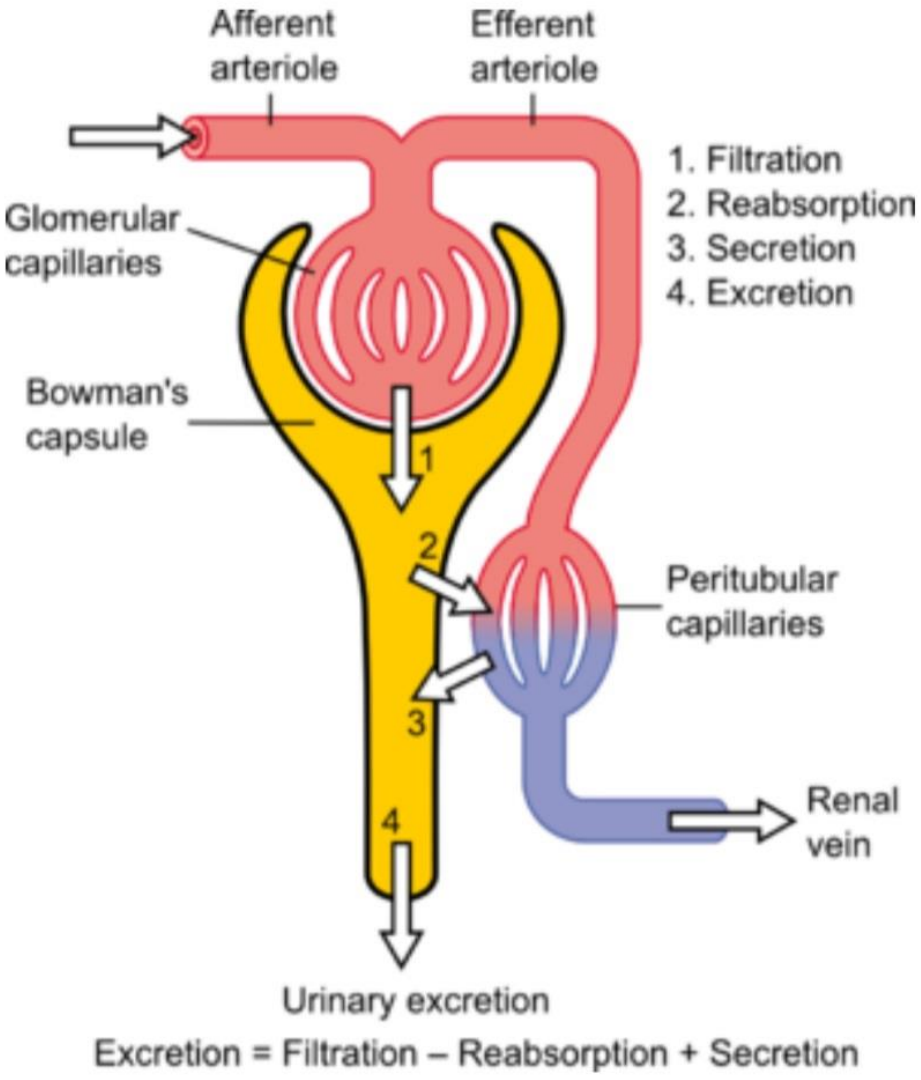
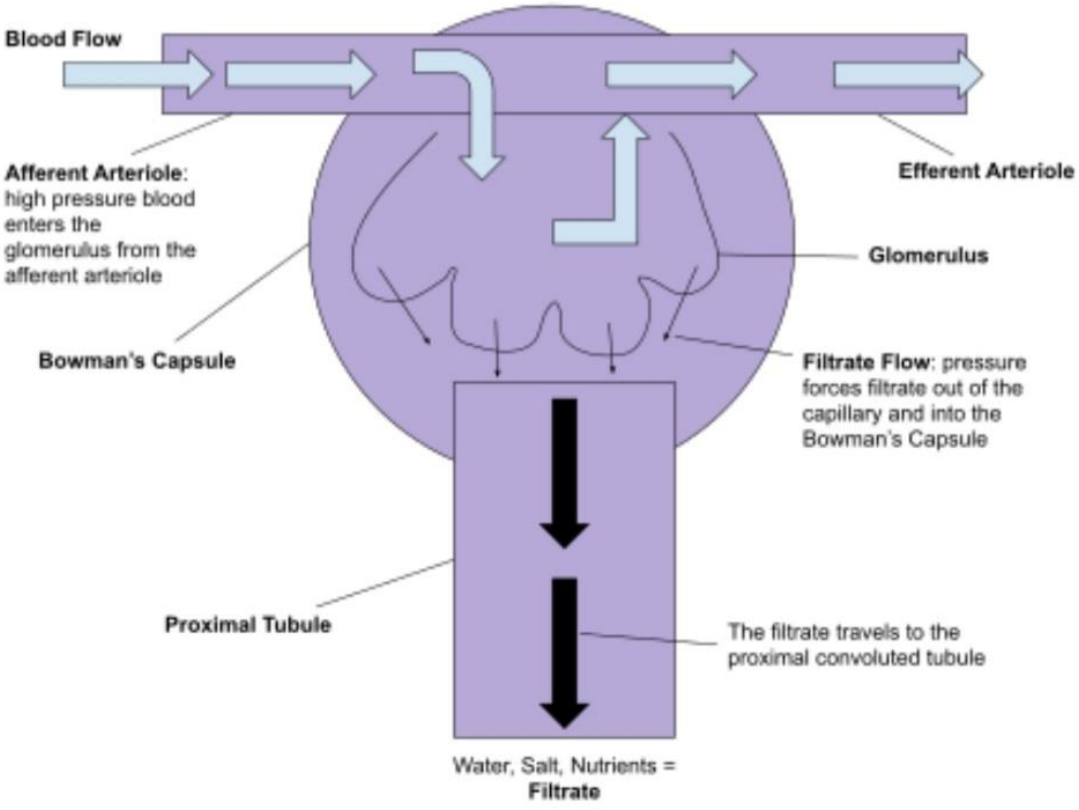


Diagram showing the basic physiologic mechanisms of the kidney


Blood Flow
Afferent Arteriole: high pressure blood enters the glomerulus from the afferent arteriole
Efferent Arteriole
Glomerulus
Bowman's Capsule
Filtrate Flow: pressure forces filtrate out of the capillary and into the Bowman's Capsule
Proximal Tubule
The filtrate travels to the proximal convoluted tubule
Water, Salt, Nutrients = Filtrate