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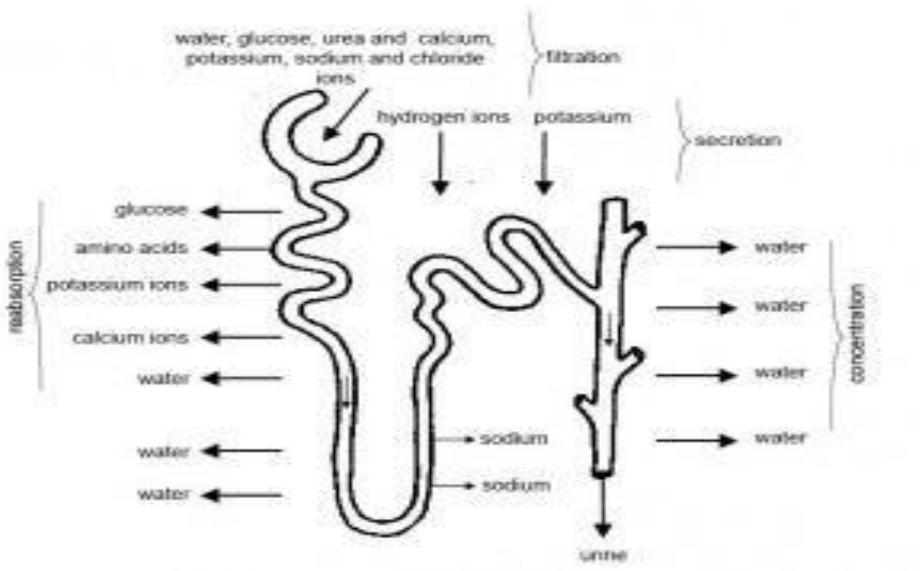
Urine Formation

Each kidney contains over 1 million tiny structures called nephrons. The nephrons are located partly in the cortex and partly inside the renal pyramids, where the nephron tubules make up most of the pyramid mass. Nephrons perform the primary function of the kidneys: regulating the concentration of water and other substances in the body. They filter the blood, reabsorb what the body needs, and excrete the rest as urine.

Waste is excreted from the human body mainly in the form of urine. Our kidneys play a major role in the process of excretion. Constituents of normal human urine include 95 percent water and 5 percent solid wastes. It is produced in the nephron which is the structural and functional unit of the kidney. Urine formation in our body is mainly carried out in three phases namely

1. Glomerular filtration,
2. Reabsorption
3. Secretion.



Mechanism of urine Formation

The mechanism of urine formation involves the following steps:

Glomerular Filtration

Glomerular filtration occurs in the glomerulus where blood is filtered. This process occurs across the three layers- epithelium of Bowman's capsule, endothelium of glomerular blood vessels, and a membrane between these two layers. During filtration, blood enters the afferent arteriole and flows into the glomerulus where filterable blood components, such as water and nitrogenous waste, will move towards the inside of the glomerulus, and nonfilterable components, such as cells and serum albumins, will exit via the efferent arteriole. These filterable components accumulate in the glomerulus to form the glomerular filtrate. Blood is filtered in such a way that all the constituents of the plasma reach the Bowman's capsule, except proteins. Therefore, this process is known as ultrafiltration.

Things that are filtered into the Bowman's capsule from the blood: Water, NaCl, Glucose, H+, Urea/Uric acid.

Things that are not filtered into the Bowman's capsule from the blood: Plasma proteins (too big), Blood cells (too big)**,** Some water, salts, glucose, amino acids.

Normally, about 20% of the total blood pumped by the heart each minute will enter the kidneys to undergo filtration; this is called the filtration fraction. The remaining 80% of the blood flows through the rest of the body to facilitate tissue perfusion and gas exchange.

Reabsorption

Occurs at the proximal convoluted tubule and the Loop of Henle.

In the **proximal convoluted tubule*:***

- Selective reabsorption: Nephron actively transports glucose, amino acids, and Na+ ions back into the blood (useful molecules – takes ATP).
- Negative ions (i.e. Cl-) follow the positive ion (Na+) **passively**

More ions/molecules moving back into the blood **concentrates** the blood making an **osmotic gradient** (Difference in concentration between two solutions)

- This causes water to reenter the blood vis **osmosis**.
- This causes the **filtrate** to become concentrated as it moves through the **proximal convoluted tubule.**

In the Loop of Henle:

- In the descending loop: not permeable to ions, permeable to water.
- Water leaves nephron, urine becomes more concentrated.
- In the ascending loop: permeable to ions, not permeable to water.
- Na+ leaves the nephron, fluid around **descending loop** becomes concentrated
- This allows for **more water reabsorption** (back into the blood) anytime the nephron passes back into that region (even the collecting duct!)

Secretion

During secretion some substances such as hydrogen ions, creatinine, and drugs—will be removed from the blood through the peritubular capillary network into the collecting duct. The end product of all these processes is urine, which is essentially a collection of substances that has not been reabsorbed during glomerular filtration or tubular reabsorption.

Urine is mainly composed of water that has not been reabsorbed, which is the way in which the body lowers blood volume, by increasing the amount of water that becomes urine instead of becoming reabsorbed. The other main component of urine is urea, a highly soluble molecule composed of ammonia and carbon dioxide, and provides a way for nitrogen (found in ammonia) to be removed from the body. Urine also contains many salts and other waste components. Red blood cells and sugar are not normally found in urine but may indicate glomerulus injury and diabetes mellitus respectively.

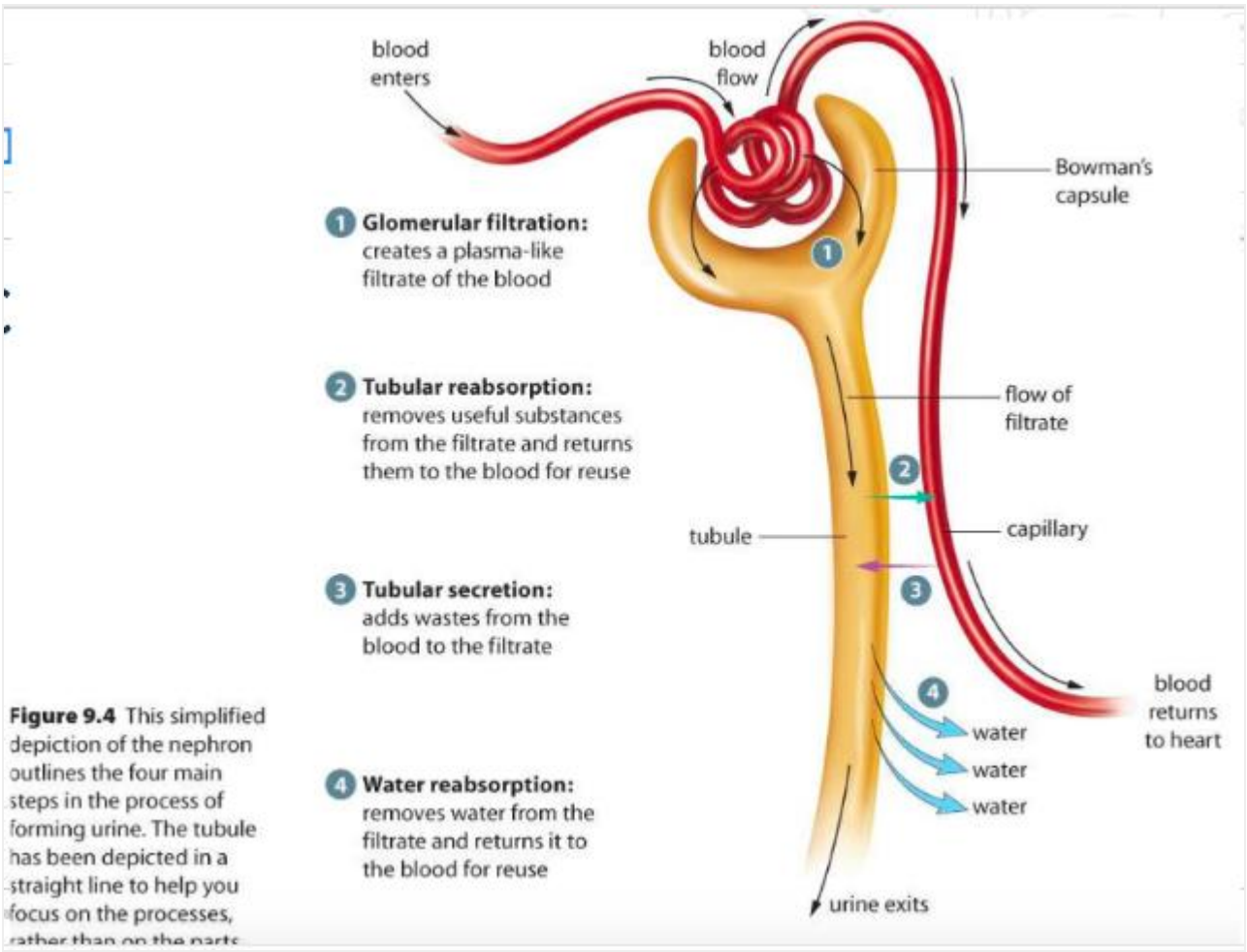
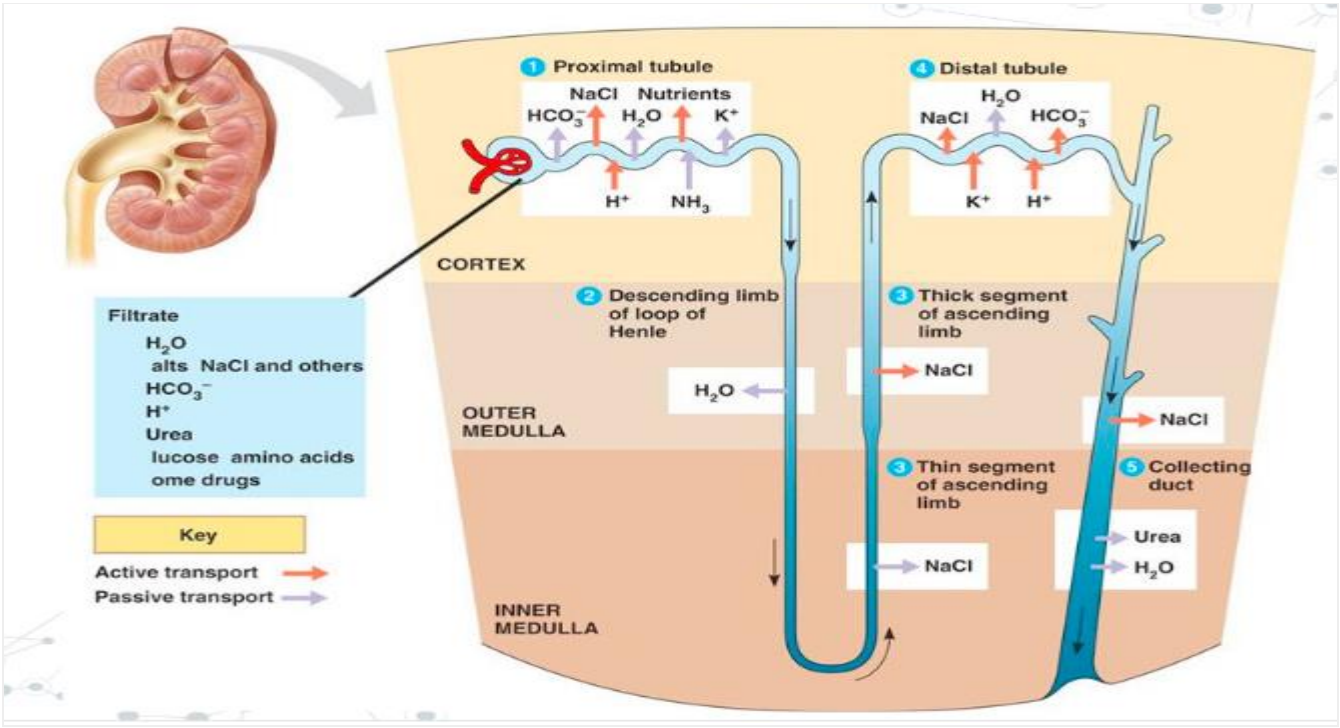


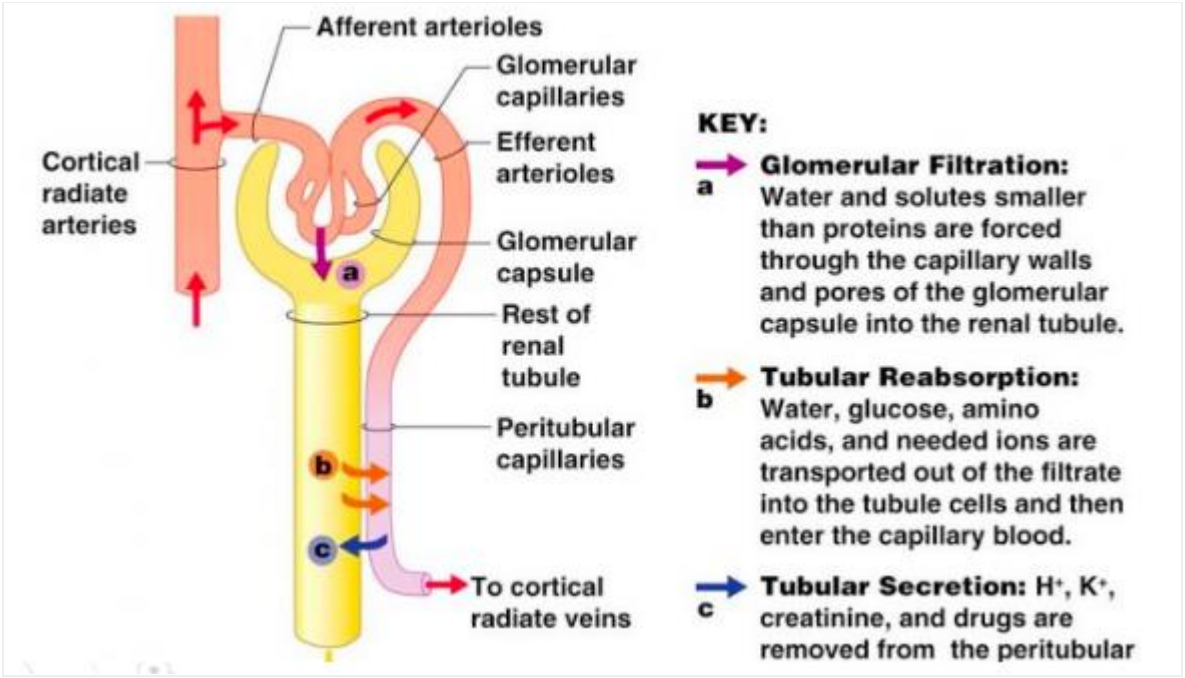
Figure 9.4 This simplified depiction of the nephron outlines the four main steps in the process of forming urine. The tubule has been depicted in a straight line to help you focus on the processes, rather than on the parts

Simplified nephron/capillary interaction

There is a countercurrent exchange occurring between the nephron and the peritubular capillary network. This allows for osmotic gradients to be maintained throughout the formation process and more efficient



Summary of urine formation



Another summary of urine formation

The Concentration of Urine

As already indicated, the loop of Henle is critical to the ability of the kidney to concentrate urine. The high concentration of salt in the medullary fluid is believed to be achieved in the loop by a process known as countercurrent exchange multiplication. The principle of this process is analogous to the physical principle applied in the conduction of hot exhaust gases past cold incoming gas so as to warm it and conserve heat. That exchange is a passive one, but in the kidney the countercurrent multiplier system uses energy to "pump" sodium and chloride out of the ascending limb of the loop into the medullary fluid. From there it enters (by diffusion) the filtrate (isotonic with plasma) that is entering the descending limb from the proximal tubule, thus raising its concentration a little above that of plasma. As this luminal fluid in turn reaches the ascending limb, and subsequently the distal tubule, it in turn provides more sodium to be pumped out into the surrounding fluid or blood, if necessary, and transported (by diffusion) back into the descending limb; this concentrating process continues until the osmotic pressure of the fluid is sufficient to balance the resorptive power of the collecting ducts in the medulla, through which all of the final urine must pass. This resorptive capacity in the ducts is regulated by antidiuretic hormone(ADH), which is secreted by the hypothalamus and stored in the posterior pituitary gland at the base of the brain. In the presence of ADH, the medullary collecting ducts become freely permeable to solute and water. As a consequence, the fluid entering the ducts (en route to the renal pelvis and subsequent elimination) acquires the concentration of the interstitial fluid of the medulla; i.e., the urine becomes concentrated. On the other hand, in the absence of ADH, the collecting ducts are impermeable to solute and water, and, thus, the fluid in the lumen, from which some solute has been removed, remains less concentrated than plasma; i.e., the urine is dilute.

The secretion of ADH by the hypothalamus and its release from the posterior pituitary is part of a feedback mechanism responsive to the tonicity of plasma. This interrelation between plasma osmotic pressure and ADH output is mediated by specific and sensitive receptors at the base of the brain. These receptors are particularly sensitive to sodium and chloride ions. At normal blood tonicity there is a steady receptor discharge and a steady secretion of ADH. If the plasma becomes hypertonic (i.e., has a greater osmotic pressure than normal), either from the ingestion of crystalloids such as common salt, or from shortage of water, receptor discharge increases, triggering increased ADH output, and more water leaves the collecting ducts to be absorbed into the blood. If the osmotic pressure of plasma becomes low, the reverse is the case. Thus water ingestion dilutes body fluids and reduces or stops ADH secretion; the urine becomes hypotonic, and the extra water is

excreted in the urine.

The situation is complex because there are also receptors sensitive to changes in blood volume that reflexively inhibit ADH output if there is any tendency to excessive blood volume. Exercise increases ADH output and reduces urinary flow. The same result may follow emotional disturbance, fainting, pain, and injury, or the use of certain drugs such as morphine or nicotine. Diuresis is an increased flow of urine produced as the result of increased fluid intake, absence of hormonal activity, or the taking of certain drugs that reduce sodium and water reabsorption from the tubules. If ADH secretion is inhibited by the drinking of excess water, or by disease or the presence of a tumour affecting the base of the brain, water diuresis results; and the rate of urine formation will approach the rate of 16 millilitres per minute filtered at the glomeruli. In certain disorders of the pituitary in which ADH secretion is diminished or absent—e.g., diabetes insipidus—there may be a fixed and irreversible output of a large quantity of dilute urine.

Regulation of Urine Concentration

The nephron loop of juxtamedullary nephrons is the apparatus that allows the nephron to concentrate urine. The loop is a countercurrent multiplier system in which fluids move in opposite directions through side-by-side, semi-permeable tubes. Substances are transported horizontally, by passive or active mechanisms, from one tube to the other. The movement of the transported substances up and down the tubes results in a higher concentration of substances at the bottom of the tubes than at the top of the tubes.

The descending limb of the nephron loop is permeable to H_2O, so H_2O diffuses out into the surrounding fluids. Because the loop is impermeable to Na^+ and Cl^- and because these ions are not pumped out by active transport, Na^+ and Cl^- remain inside the loop. As the fluid continues to travel down the descending limb of the loop, it becomes more and more concentrated, as water continues to diffuse out. Maximum concentration occurs at the bottom of the loop.

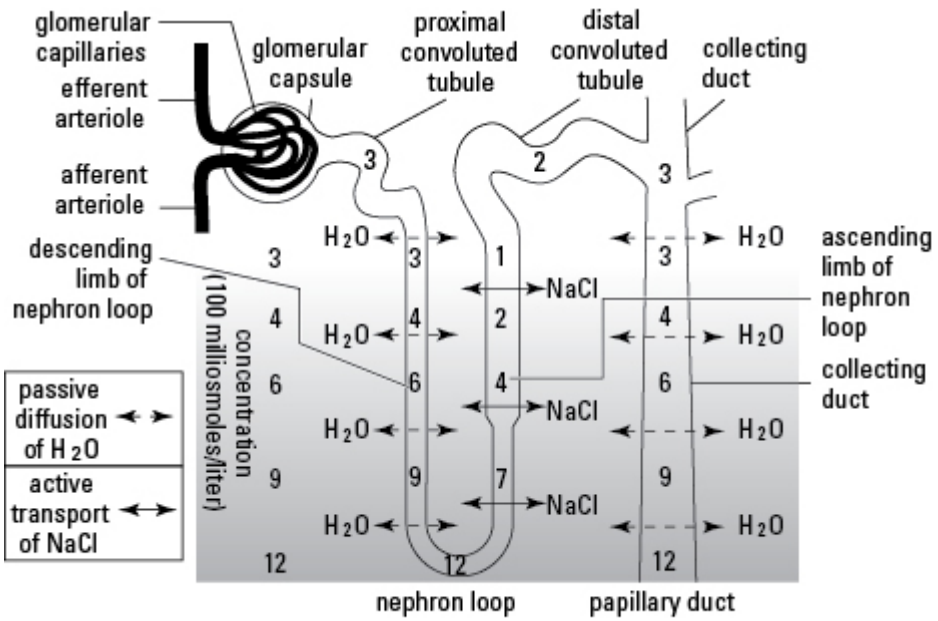
The ascending limb of the nephron loop is impermeable to water, but Na^+ and Cl^- are pumped out into the surrounding fluids by active transport. As fluid travels up the ascending limb, it becomes less and less concentrated because Na^+ and Cl^- are pumped out. At the top of the ascending limb, the fluid is only slightly less concentrated than at the top of the descending limb. In other words, there is little

change in the concentration of the fluid in the tubule as a result of traversing the nephron loop. In the fluid surrounding the nephron loop, however, a gradient of salt (Na^+, Cl^-) is established, increasing in concentration from the top to the bottom of the loop. Fluid at the top of the collecting duct has a concentration of salts about equal to that at the beginning of the nephron loop (some water is reabsorbed in the DCT). As the fluid descends the collecting duct, the fluid is exposed to the surrounding salt gradient established by the nephron loop. Without ADH, the collecting duct is impermeable to H_2O. Two outcomes are possible:

- If water conservation is necessary, ADH stimulates the opening of water channels in the collecting duct, allowing H_2O to diffuse out of the duct and into the surrounding fluids. The result is concentrated urine (refer to Figure 1).
- If water conservation is not necessary, ADH is not secreted and the duct remains impermeable to H_2O. The result is dilute urine.

The vasa recta delivers O_2 and nutrients to cells of the nephron loop. The vasa recta, like other capillaries, is permeable to both H_2O and salts and could disrupt the salt gradient established by the nephron loop. To avoid this, the vasa recta acts as a countercurrent multiplier system as well. As the vasa recta descends into the renal medulla, water diffuses out into the surrounding fluids, and salts diffuse in. When the vasa recta ascends, the reverse occurs. As a result, the concentration of salts in the vasa recta is always about the same as that in the surrounding fluids, and the salt gradient established by the nephron loop remains in place.

Figure 1. The loop is a countercurrent multiplier system in which fluids move in opposite directions through side-by-side, semi-permeable tubes. This process regulates the concentration of urine.



Regulation of Urine Concentration