NAME: BASORUN MORENIKE ABIBAT

MATRIC NUMBER: 18/MHSO7/010

DEPARTMENT: PHARMACOLOGY

COURSE CODE: PHS 212

**The Process of Urine Formation**

Urine formation is a very sophisticated process that takes place in the kidneys. This important process provides a mechanism for the body to get rid of metabolic wastes and toxins, which can be deadly if allowed to accumulate in the body. Basically, the process of urine formation takes place in three (3) stages, as blood plasma flows through the nephrons. (Nephrons are microscopic tube-like structures in the kidneys that filter the blood and cause wastes to be removed.  They are the most basic structures of the kidney's anatomy.  Each kidney contains over one million nephrons.) As the blood plasma flows through the nephrons, its composition changes.  Fluids comprising excess water, salt and metabolic waste products are extracted from the blood as it enters the Bowman's capsule in the nephrons. This fluid in the in the Bowman's capsule is called glomerular filtrate.  It is similar to blood plasma except that it has almost no protein. Blood plasma is a clear fluid that surrounds blood cells. As the fluid moves through the renal tubule it is called tubular fluid.  It is different form glomerular filtrate because of substances which are removed and added by the tubule cells. Finally, when the fluid moves into the collecting tubule it is called urine.

The three (3) distinct stages of urine formation are referred to as:

1. Glomerular filtration,

2. Tubular reabsorption and secretion, and

3. Water conservation.

Stage 1 of Urine Formation**: GLOMERULAR FILTRATION**

Glomerular filtration is a process in which water and some other substances in the blood plasma pass from the capillaries of the glomerulus into the Bowman's capsule. Very small molecules can pass through the filtration membrane into the Bowman's capsule. This includes water, electrolytes, glucose, fatty acids, amino acids, nitrogenous wastes, and vitamins. These substances have about the same concentration in the glomerular filtrate (fluid in the in the Bowman's capsule) as in the blood plasma. Some substances are retained in the bloodstream because they are bound to plasma proteins that cannot get through the membrane. For example, most calcium, iron, and thyroid hormone in the blood are bound to plasma proteins that retard their filtration by the kidneys. The small fractions that are not bound to plasma protein, however, passes freely through the filtration membrane and appears in the urine. Kidney infection and trauma can damage the filtration membrane (located in the Bowman's capsule). This allows albumin (a protein) or blood cells to filter through. Kidney disease can sometimes be detected by the presence of protein (especially albumin) or blood in the urine. The medical terms for the presence of protein and blood in the urine are proteinuria (albuminuria) and hematuria, respectively. Glomerular filtration must be precisely controlled. If it is too high, fluid flows through the renal tubules too rapidly for them to reabsorb the required amount of water and solutes. If it is too low, fluid flows too slowly through the tubules and wastes that should be eliminated are reabsorbed into the bloodstream. Renal auto-regulation is the ability of the nephrons to adjust their own blood flow. It allows them to maintain a relatively stable glomerular filtration rate in spite of changes in arterial blood pressure.

Stage 2: **TUBULAR REABSORPTION AND SECRETION**

The second stage of urine formation is tubular reabsorption and secretion. This involves removal and addition of chemicals, after glomerular filtrate leaves the Bowman's capsule and enters the renal tubule. The Renal tubule is very long, which increases its absorptive surface area. It reabsorbs about 65% of the glomerular filtrate, while it removes some substances from the blood. Tubular reabsorption is the process of reclaiming water and other substances from the tubular fluid (glomerular filtrate which passes from the Bowman's capsule to the renal tubule) and returning them to the blood. Sodium reabsorption is the key to everything else. It creates the environment for water and other substances to be reabsorbed. Glucose is transported along with sodium irons by carriers called sodium-glucose transport proteins. Normally all glucose in the tubular fluid is reabsorbed and there is none in the urine. Water reabsorption is a significant function of the kidney. The amount of water reabsorption is continually regulated by hormones according to the body's state of hydration. The more hydrated the body, the less water is reabsorbed, and vice versa. Nitrogenous wastes such as urea diffuses through the renal tubule with water. The kidneys remove about 50% of the urea in the blood thus keeping its concentration down to a safe level, but not completely clearing the blood of it. Almost all uric acid is first reabsorbed by the renal tubule but later parts of the nephron secretes it back into the tubular fluid. Creatinine is not reabsorbed at all. It is too large to diffuse through water channels in the plasma membrane, and there are no transport proteins for it. All creatinine filtered by the glomerulus is, therefore, excreted in the urine. After water and other substances leave the surface of the renal tubule, they are reabsorbed by the capillaries, into the bloodstream. Tubular secretion is the process in which renal tubule extracts chemicals from the capillary's blood and secretes them into the tubular fluid. This process serves two main purposes: Waste removal. Urea, uric acid, bile acids, ammonia, and creatinine are secreted into the renal tubule. Tubular secretion clears the blood of pollutants and drugs as well. One reason why so many drugs (prescription drugs) must be taken three to four times per day is to maintain the therapeutically effective drug concentration in the blood, to compensate for the rate of clearance, through tubular secretion. Maintaining the acid-base balance. Tubular secretion of hydrogen and bicarbonate irons serves to regulate the pH of the body's fluids.

Stage 3: **WATER CONSERVATION**

The third and final stage of urine formation is water conservation. The kidneys are not only responsible for eliminating metabolic wastes from the body but they also prevent excessive water loss, in doing so. This is very important in maintaining the body's fluid balance. Urine is made up mostly of water. It plays a significant role in the entire process of waste elimination. If, however, too much water is removed from the body, it results in dehydration, which could lead to other serious medical conditions. When tubular fluid leaves the renal tubule, it goes to the collecting tubule (or collecting duct). At this stage the tubular fluid becomes urine. The renal tubule of several nephrons drains into the collecting tubule. This results in a significant amount of water being drained into the collecting tubule. If all this water was eliminated, it would amount to about 36 liters of urine per day. One can only imagine the devastating effects this would have on the body as this far exceeds the average volume of urine excreted by an adult, of 1 to 2 liters per day. The collecting tubule receives tubular fluid from numerous nephrons. As it moves along the collecting tubule it become more and more concentrated. This causes water to be reabsorbed into the bloodstream, by the process of osmosis. The relative concentration of the urine depends on the body's state of hydration. For example, if you drink a large volume of water, you will produce a large volume of urine which is less concentrated. On the other hand, if you are dehydrated, your urine is much more concentrated and the volume is much lower. The collecting duct can adjust water reabsorption, depending on the body's need for water conservation or removal.

**The concentration of urine**

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 counter current 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 counter current 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.