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**18/MHS07/006**

**PHARMACOLOGY**

**PHS 212**

**QUESTION**

Explain urine formation and concentration

## **URINE FORMATION**

Urine Formation – by filtering the blood the nephrons perform the following functions

(1) regulate concentration of solutes in blood plasma; this also regulates pH

(2) regulate water concentrations; this helps regulate blood pressure

(3) removes metabolic wastes and excess substances

* Urine Formation:

1. Glomerular Filtration – water and solutes are forced through the capillary walls of the glomerulus into the Bowman’s capsule (glomerular capsule)

* Filtrate – the fluid that is filtered out into bowman’s capsule

Glomerular Filtration Rate is regulated by mechanisms:

1. Autoregulation – the smooth muscle in the afferent arteriole responds to blood pressure changes by constricting and dilating to regulate filtration rate.
2. Sympathetic control – causes afferent arterioles to constrict or dilate when activated by a nerve impulse (fight or flight response to keep blood pressure up)

Renin-angiotensin mechanism – triggered by the juxtaglomerular apparatus; when filtration rate decreases, the enzyme renin is released. Renin converts a plasma protein called angiotensinogen into angiotensin I. Angiotensin I is quickly converted into angiotensin II by another enzyme. Angiotensin II causes 3 changes:

* (1) Constriction of the arterioles – decreases urine formation and water loss
* (2) Stimulates the adrenal cortex to release aldosterone – promotes water reabsorption by causing the absorption of salt
* (3) Stimulates the posterior pituitary to release ADH – antidiuretic hormone – promotes water reabsorption
* (4) Stimulates the thirst and water intake (hypothalamus says we’re thirsty so we get a drink)

Tubular Reabsorption – occurs both passive and actively; glucose, amino acids, and other needed ions (Na, K, Cl, Ca, HCO3) are transported out of the filtrate into the peritubular capillaries (they are reabsorbed back into the blood); about 65% of the filtrate is reabsorbed in the proximal convoluted tubule.

* As these substances are reabsorbed, the blood becomes hypertonic so water easily follows by osmosis
* Reabsorption in the distal convoluted tubule is under hormonal control…aldosterone causes more salt to be absorbed, ADH causes more water to be absorbed

Secretion – waste products such as urea and uric acid, drugs and hydrogen and bicarbonate ions are move out of the peritubular capillaries into the filtrate; this removes unwanted wastes and helps regulate pH

* Urine – filtrate after it has passed through the nephron and undergone filtration, reabsorption, and secretion. The urine passes into the collecting duct, which joins with the minor calyx, major calyx, and eventually the renal pelvis. The renal pelvis joins with the ureter.
* Color – yellow color is due to urochrome – a pigment produced from the breakdown of bile pigments in the intestine
  + Deep yellow to orange – more concentrated, less water
  + Light yellow to clear – less concentrated, more water

**URINE CONCENTRATION**

As already indicated, the [loop of Henle](https://www.britannica.com/science/loop-of-Henle) is critical to the ability of the [kidney](https://www.britannica.com/science/kidney) to concentrate [urine](https://www.britannica.com/science/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](https://www.merriam-webster.com/dictionary/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](https://www.britannica.com/science/vasopressin) (ADH), which is secreted by the hypothalamus and stored in the posterior [pituitary gland](https://www.britannica.com/science/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](https://www.britannica.com/science/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](https://www.britannica.com/science/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](https://www.merriam-webster.com/dictionary/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](https://www.merriam-webster.com/dictionary/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.