ESAN FAITH

18/MHS07/017

PHARMACOLOGY

PHS 212

WRITE ON THE FORMATION AND CONCENTRATION OF URINE

**Formation of urine**

There are two kidneys which are bean-shaped and are approximately 10cm long, 5.5cm wide and 3cm thick. Each kidney weighs about 150g and has a marked indentation medially - the hilus - where the renal artery and renal nerves enter and the renal vein and ureter leave. Between them, the kidneys make approximately 30ml or more of urine every hour.

Approximately 25 per cent of the cardiac output goes to the kidneys where organic waste products are removed in the million or so nephrons in each kidney. Normal urine production, therefore, depends on normal blood flow to the kidneys. The nephron is the functional unit of the kidney. Nephrons permit the passage of some substances out of the body but restrict the passage of others, for example, blood cells and large proteins.

Urine formation begins as a process of ultrafiltration of a large volume of blood plasma from the glomerular capillaries into the [capsular](https://www.britannica.com/science/capsular-urine) space, [colloids](https://www.britannica.com/science/colloid) such as proteins being held back while [crystalloids](https://www.britannica.com/science/crystalloid) (substances in true solution) pass through. In humans, the average capillary diameter is 5 to 10 micrometres (a micrometre is 0.001 millimetre). The wall of each loop of capillaries has three layers. The inner layer consists of flat nucleated endothelial cells arranged to form numerous pores, or fenestrae, 50–100 nanometres in diameter (a nanometre is 0.000001 millimetre), which allow the blood to make direct contact with the second layer, a [basement membrane](https://www.britannica.com/science/basement-membrane). The basement membrane of the capillaries, similar to that which occurs in the lining of many other structures and organs, is a continuous layer of hydrated collagen and glycopeptides. Although once thought to be [homogeneous](https://www.merriam-webster.com/dictionary/homogeneous), it appears to consist of three layers that differ in the content of polyanionic glycopeptides. The membrane is negatively charged (anionic), owing to its relatively high content of sialic and aspartic acids. Also present are glycosaminoglycans, such as heparin sulfate. The third, external layer consists of large epithelial cells called podocytes. These cells make contact with the outer surface of the basement membrane by slender cytoplasmic extensions called pedicels (foot processes). These processes are slightly expanded at their point of contact with the basement membrane and are separated from each other by slitlike spaces about 20 to 30 nanometres across. A fine membrane (slit diaphragm) closes the slitlike spaces near the basement membrane.

**THE CONCENTRATION OF 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.