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FORMATION AND CONCENTRATION OF URINE

FORMATION OF URINE

Formation of urine is a process important for the whole organism. Not only acid-base balance is modulated by it, but also blood osmolarity, plasma composition and fluid volume, and thus it influences all cells in our body. A healthy adult person produces 1.5-2 liters of urine per day and this process involves three basic mechanisms:

1) Glomerular filtration

2) Tubular reabsorption

3) Tubular secretion

The basic functional unit for the urine formation is called nephron. Very important is the arrangement of nephron: it begins with renal corpuscle (Malpighi) that consists of a glomerulus, which is supplied by afferent glomerular arteriole and drained by efferent glomerular arteriole, and Bowman's capsule (capsula glomeruli, glomerular capsule). Renal tubules have three segments. The proximal tubule, in which we distinguish pars convoluta (initial section) and pars recta, loop of Henle (intermediate tubule), where can be recognized the descending limb and ascending limb (its proximal part is formed by a thick segment of the ascending limb), and distal convoluted tubule (which has conversely first pars recta and then the pars convoluta) that subsequently joins the collecting ducts.

1. Glomerular filtration

The volume of liquid filtered per unit time in all glomeruli can be expressed as the glomerular filtration rate (GFR). Its physiological value is 120 ml/min/1,73m² body surface area, thus 180 l/day. About 99 % of the filtrate gets reabsorbed by the tubular resorption to the extracellular fluid (back into the body), leaving only 1.5-2 l of urine per day. Movement of

the fluid through the filtration membrane is controlled and determined by the ratio of the hydrostatic pressure in the capillaries and oncotic pressure of plasma proteins (less by the hydrostatic pressure of the interstitial fluid and oncotic pressure

2. Tubular reabsorption

As we mentioned above, about 99 % of the filtrate gets reabsorbed by the tubular resorption to the extracellular fluid (back into the body), leaving only 1.5-2 l of urine per day. The main task for renal tubules is therefore an isosmotic tubular reabsorption of primary urine. They absorb water, ions (sodium, chlorides, potassium, calcium, magnesium, bicarbonate or phosphate), urea, glucose and amino acids. All of this is independent on the extracellular fluid volume in the body – we speak about the obligatory resorption. Its primary role is to maintain fluid volume in the body under normal conditions.

Transport can be carried by passive diffusion (in the direction of the concentration or electrical gradient), primary active transport against gradient (needs energy – ATP) or secondary active transport (transport protein uses the concentration gradient created by a primary active transport realized by other transport protein). Substances can be transported by paracellular or transcellular routes. Transport of water is always passive. Na^+/K^+ -ATPase located on the basolateral membrane plays important role in the secondary active transport. It creates a concentration gradient for Na^+ . Transport proteins act as symporters (transport of compound is coupled to the transport of Na^+ in the same direction) or antiporters (transport of compound is coupled to the transport of Na^+ in the opposite direction). To understand the processes in the tubular system, we must imagine tubular epithelial cells, their apical

membrane facing the tubular fluid (primary urine), basolateral membrane, on the other hand, is in contact with the peritubular fluid (here is located the $\text{Na}^+/\text{K}^+-\text{ATPase}$).

3. Tubular secretion

The only difference between secretory and reabsorptive tubular mechanisms lies in the direction of transport; secretory mechanisms involve the addition of substances to the filtrate from the plasma in the peritubular capillaries. The small amount of secretion that does occur, except for the secretion of potassium and uric acid, takes place in the proximal tubule.

Hydrogen ions are also secreted and ammonia is generated, but they are special cases and are discussed below under Regulation of acid-base balance. As in the case of reabsorption, secretion occurs both passively and actively against an electrochemical gradient.

Several drugs are actively secreted, and some of these appear to share a common pathway so that they may compete with each other for a limited amount of energy. This may be turned to therapeutic advantage in the case of penicillin, which is eliminated partly by tubular secretion. The drug probenecid, which can be given simultaneously, competes with penicillin at its secretory site and thus helps to raise the level of penicillin in the blood in the treatment of certain infections. Endogenous (originating within the body) compounds that are secreted also include prostaglandins, bile salts, and hippurate. Uric acid derived from nucleoproteins freely passes the glomerular barrier and is normally largely reabsorbed in the proximal tubule. In some circumstances, however, it is also secreted by other parts of the same convoluted tubule.

The secretion of potassium by the distal tubule is one of the most important events in the kidney as its control is fundamental to the maintenance of overall potassium balance. More than 75 percent of the filtered potassium is reabsorbed in the proximal tubule and in the ascending limb of the loop of Henle, and this percentage remains virtually constant, irrespective of how much is filtered. The amount eliminated in the urine, which is ultimately determined by the dietary intake, is controlled by the distal convoluted tubule. In persons consuming a normal diet, probably about 50 percent of the urinary potassium is secreted into the urine by the distal tubules; this amount can be adjusted according to body need. One of the several factors that influence potassium secretion is a hormone secreted by the cortex of the adrenal gland, aldosterone. In the absence of aldosterone and other mineralocorticoids (adrenocortical steroids affecting electrolyte and fluid balance), potassium secretion is impaired, and potentially dangerous amounts can accumulate in the blood. Excess aldosterone promotes potassium excretion.

Other formation include:

The Filtration Membrane Keeps Blood Cells and Large Proteins in the Bloodstream

Inside the glomerulus, blood pressure pushes fluid from capillaries into the glomerular capsule through a specialized layer of cells. This layer, the filtration membrane, allows water and small solutes to pass but blocks blood cells and large proteins. Those components remain in the bloodstream. The filtrate (the fluid that has passed through the membrane) flows from the glomerular capsule further into the nephron.

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 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.