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PHARMACOLOGY

PHS 212

ASSIGNMENT: Explain urine formation and concentration

ANSWER :

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:

* Glomerular filtration
* Tubular reabsorption
* Tubular secretion

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

The volume of filtrate formed by both kidneys per minute is termed the glomerular filtration rate (GFR). The heart pumps about 5 L blood per min under resting conditions. Approximately 20 percent or one liter enters the kidneys to be filtered. On average, this liter results in the production of about 125 mL/min filtrate produced in men (range of 90 to 140 mL/min) and 105 mL/min filtrate produced in women (range of 80 to 125 mL/min). This amount equates to a volume of about 180 L/day in men and 150 L/day in women. Ninety-nine percent of this filtrate is returned to the circulation by reabsorption so that only about 1–2 liters of urine are produced per day.

GFR is influenced by the hydrostatic pressure and colloid osmotic pressure on either side of the capillary membrane of the glomerulus. Recall that filtration occurs as pressure forces fluid and solutes through a semipermeable barrier with the solute movement constrained by particle size. Hydrostatic pressure is the pressure produced by a fluid against a surface. If you have a fluid on both sides of a barrier, both fluids exert a pressure in opposing directions. Net fluid movement will be in the direction of the lower pressure. Osmosis is the movement of solvent (water) across a membrane that is impermeable to a solute in the solution. This creates a pressure, osmotic pressure, which will exist until the solute concentration is the same on both sides of a semipermeable membrane. As long as the concentration differs, water will move. Glomerular filtration occurs when glomerular hydrostatic pressure exceeds the luminal hydrostatic pressure of Bowman’s capsule. There is also an opposing force, the osmotic pressure, which is typically higher in the glomerular capillary.

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

Glomerular Filtration Rate is regulated by mechanisms:

* Autoregulation – the smooth muscle in the afferent arteriole responds to blood pressure changes by constricting and dilating to regulate filtration rate.
* 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:

* Constriction of the arterioles – decreases urine formation and water loss
* Stimulates the adrenal cortex to release aldosterone – promotes water reabsorption by causing the absorption of salt
* Stimulates the posterior pituitary to release ADH – antidiuretic hormone – promotes water reabsorption
* 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

Tubular secretion

Tubular secretion is the transfer of materials from peritubular capillaries to the renal tubular lumen; it is the opposite process of reabsorption. This secretion is caused mainly by active transport and passive diffusion.Usually only a few substances are secreted, and are typically waste products. Urine is the substance leftover in the collecting duct following reabsorption and secretion.

The mechanisms by which secretion occurs are similar to those of reabsorption, however these processes occur in the opposite direction.

* Passive diffusion—the movement of molecules from the peritubular capillaries to the intersitial fluid within the nephron.
* Active transport—the movement of molecules via ATPase pumps that transport the substance through the renal epithelial cell into the lumen of the nephron.

Renal secretion is different from reabsorption because it deals with filtering and cleaning substances from the blood, rather than retaining them. The substances that are secreted into the tubular fluid for removal from the body include:

* Potassium ions (K+)
* Hydrogen ions (H+)
* Ammonium ions (NH4+)
* Creatinine
* Urea
* Some hormones
* Some drugs (e.g., penicillin)

Urine concentration

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.