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MATRIC NO; 18/MHS02/174

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:

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:

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:

- (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

Glomerular Filtration Rate (GFR)

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.

Table 2. Calculating Urine Formation per Day

Flow per minute (mL) Calculation

Renal blood flow 1050 Cardiac output is about 5000 mL/minute, of which 21 percent flows through the kidney.

$$5000 * 0.21 = 1050 \text{ mL blood/min}$$

Renal plasma flow 578 Renal plasma flow equals the blood flow per minute times the hematocrit. If a person has a hematocrit of 45, then the renal plasma flow is 55 percent.

$$1050 * 0.55 = 578 \text{ mL plasma/min}$$

Glomerular filtration rate 110 The GFR is the amount of plasma entering Bowman's capsule per minute. It is the renal plasma flow times the fraction that enters the renal capsule (19 percent).

$$578 * 0.19 = 110 \text{ mL filtrate/min}$$

Urine 1296 ml/day The filtrate not recovered by the kidney is the urine that will be eliminated. It is the GFR times the fraction of the filtrate that is not reabsorbed (0.8 percent).

$$110 \times .08 = 0.9 \text{ mL urine /min}$$

Multiply urine/min times 60 minutes times 24 hours to get daily urine production.

$$0.9 \times 60 \times 24 = 1296 \text{ mL/day urine}$$

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. Net Filtration Pressure (NFP)

NFP determines filtration rates through the kidney. It is determined as follows:

$$\text{NFP} = \text{Glomerular blood hydrostatic pressure (GBHP)} - [\text{capsular hydrostatic pressure (CHP)} + \text{blood colloid osmotic pressure (BCOP)}] = 10 \text{ mm Hg}$$

That is:

$$\text{NFP} = \text{GBHP} - [\text{CHP} + \text{BCOP}] = 10 \text{ mm Hg}$$

Or:

$$\text{NFP} = 55 - [15 + 30] = 10 \text{ mm Hg}$$

As you can see, there is a low net pressure across the filtration membrane. Intuitively, you should realize that minor changes in osmolarity of the blood or changes in capillary blood pressure result in major changes in the amount of filtrate formed at any given point in time. The kidney is able to cope with a wide range of blood pressures. In large part, this is due to the autoregulatory nature of smooth muscle. When you stretch it, it contracts. Thus, when blood pressure goes up, smooth muscle in the afferent capillaries contracts to limit any increase in blood flow and filtration rate. When blood pressure drops, the same capillaries relax to maintain blood flow and filtration rate. The net result is a relatively steady flow of blood into the glomerulus and a relatively steady filtration rate in spite of significant systemic blood pressure changes. Mean arterial blood pressure is calculated by adding $1/3$ of the difference between the systolic and diastolic pressures to the diastolic pressure. Therefore, if the blood pressure is 110/80, the difference between systolic and diastolic pressure is 30. One third of this is 10, and when you add this to the diastolic pressure of 80, you arrive at a calculated mean arterial pressure of 90 mm Hg. Therefore, if you use mean arterial pressure for the GBHP in the formula for calculating NFP, you can determine that as long as mean arterial pressure is above approximately 60 mm Hg, the pressure will be adequate to maintain glomerular filtration. Blood pressures below this level will impair renal function and cause systemic disorders that are severe enough to threaten survival. This condition is called shock.

Determination of the GFR is one of the tools used to assess the kidney's excretory function. This is more than just an academic exercise. Since many drugs are excreted in the urine, a decline in renal function can lead to toxic accumulations. Additionally, administration of appropriate drug dosages for those drugs primarily excreted by the kidney requires an accurate assessment of GFR. GFR can be estimated closely by intravenous administration of inulin. Inulin is a plant polysaccharide that is neither reabsorbed nor secreted by the kidney. Its appearance in the urine is directly proportional to the rate at which it is filtered by the renal corpuscle. However, since measuring inulin clearance is cumbersome in the clinical setting, most often, the GFR is estimated by measuring naturally occurring creatinine, a protein-derived molecule produced by muscle metabolism that is not reabsorbed and only slightly secreted by the nephron.

The concentration of urine

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.

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.