Ministry of Public Health of Ukraine
Poltava State Medical University
Department of biological and bioorganic chemistry

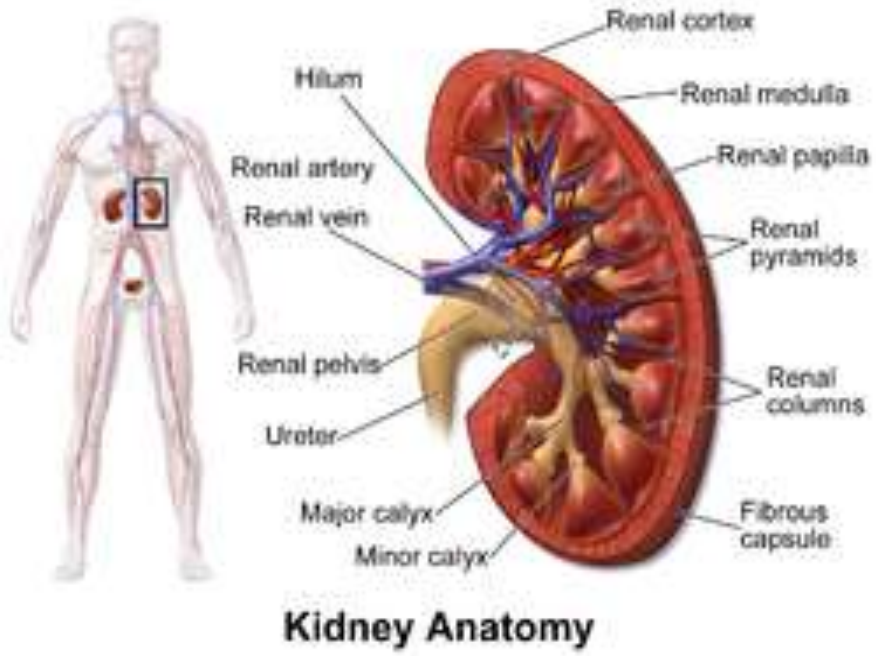
Biochemical functions of the kidney. Biochemistry of urine and urine formation. Patobiochemistry of urine.

Assoc. Prof. Bilets M.V.

Lecture plan

- Biological role of the kidneys.
- Biochemical mechanisms of urine formation in the kidneys.
- Metabolism of the kidneys.
- Chemical composition of urine in norm and pathology.
- Kidneys diseases.

Kidney anatomy



- The kidneys are two reddish-brown bean-shaped organs. They are located on the left and right in the retroperitoneal space, and in adult humans are about 12 centimeters in length. They receive blood from the paired renal arteries; blood exits into the paired renal veins. Each kidney is attached to a ureter, a tube that carries excreted urine to the bladder.

- The nephron is the structural and functional unit of the kidney. Each adult human kidney contains around 1 million nephrons.

https://en.wikipedia.org/wiki/Kidney

Nephron structure

- Each nephron has two major parts:
- **Renal corpuscle (Malpighian body)**
- **Renal tubules**
- **1. Renal corpuscles (Malpighian body)**:

✓ A renal corpuscle consists of a glomerulus surrounded by a glomerular capsule (Bowman's capsule).

✓ The **glomerulus** is a capillary network that arises from an **afferent arteriole** and empties into an **efferent arteriole**. The diameter of the efferent arteriole is smaller than that of the afferent arteriole, which helps maintain a fairly high blood pressure in the glomerulus.

✓ **Bowman's capsule** is double walled cup like structure and it encloses the glomerulus. The wall of glomerulus and the Bowman's capsule consists of a single layer of flattened epithelial cells.

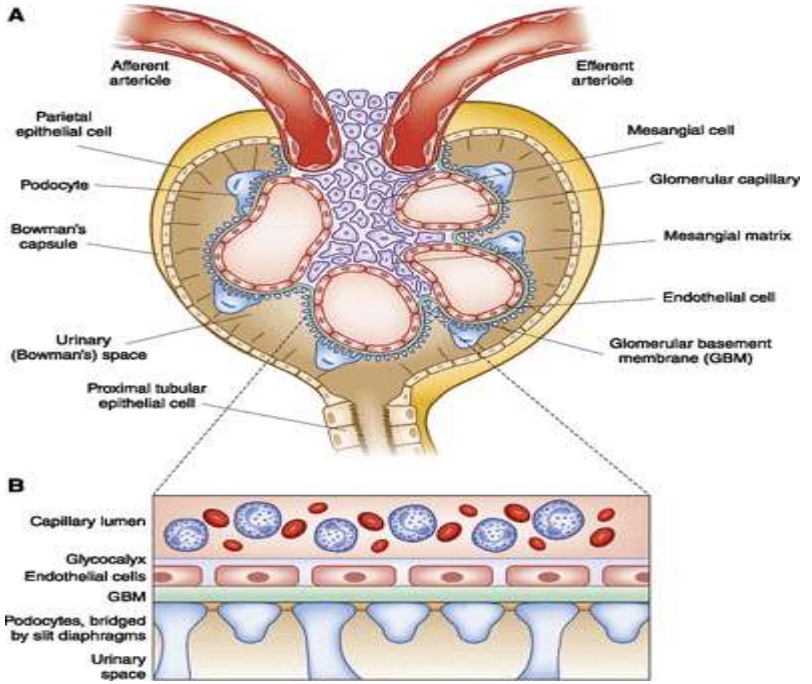
✓ Glomerular capsule consists of **three layers**

1) Outer parietal layer consists of squamous epithelium cells with minute pore of 12nm diameter called **fenestrations**

2) Middle basement membrane which is selectively permiable

3) The inner visceral layer of large nucleated cell called **podocytes**. Podocytes bears finger like projections known as podocels. The areas between the two podocels is filtration slit underlying basement membrane.

- Basic structure of the glomerulus and the glomerular filtration barrier. (A) Each glomerulus is composed of an afferent arteriole, which supplies the glomerular capillaries, and an efferent arteriole, into which they drain. Mesangial cells and mesangial matrix provide structural support for the glomerular capillaries, lined by specialized fenestrated endothelium, and then the glomerular basement membrane. On the urinary side of the glomerular basement membrane are podocytes, with foot processes that wrap around the glomerular capillaries. The urinary space is lined by a cup-like layer of parietal epithelial cells which adhere to the basement membrane of Bowman's capsule. (B) The glomerular filtration barrier is a specialized molecular sieve, with properties that aid filtration of small solutes from the blood to the urine, while limiting the passage of macromolecules such as albumin.



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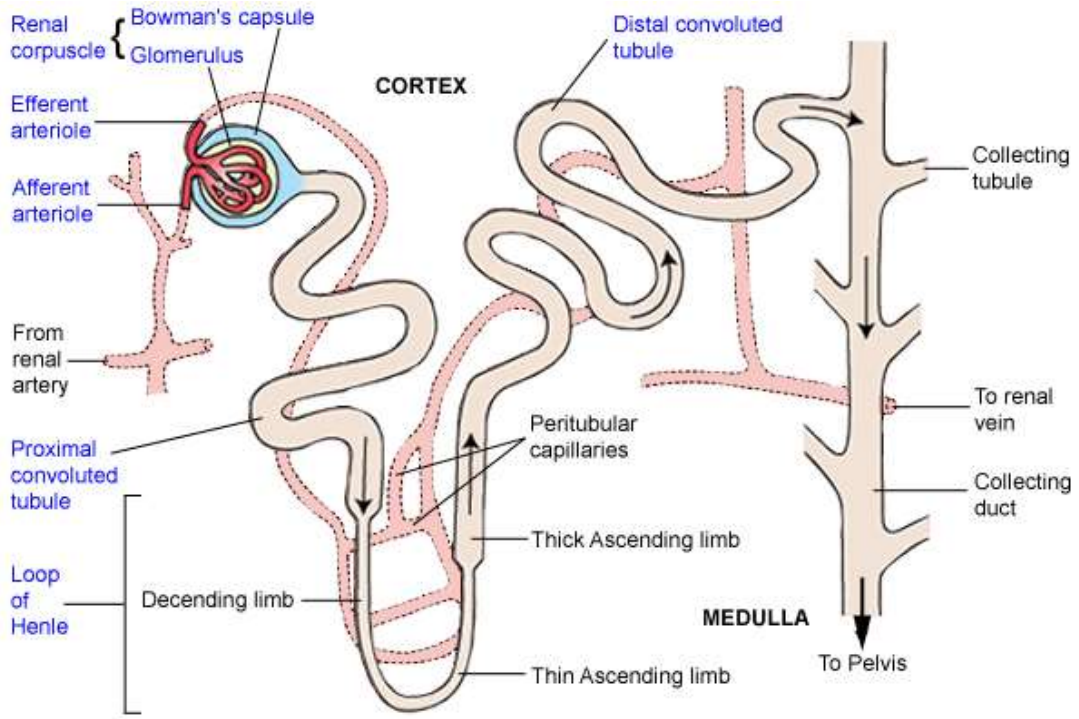
Nephron structure

Types of nephron

✓**Cortical nephron:** 80% of the nephrons are short and located within the cortex.

✓**Juxtamedulary nephron:** 20% of nephron have long loops of Henle that extend into the medulla.



- **2. Renal tubules:**
- The renal tubule continues from Bowman's capsule and consists of the following parts: **proximal convoluted tubule** (in the renal cortex), **loop of Henle** (in the renal medulla), and **distal convoluted tubule** (in the renal cortex).
  - **1) Proximal convoluted tubules (PCT):** it is proximal part of renal tubules next to Bowman's capsule. It is lined with microvilli. Maximum reabsorption of water, glucose, amino acids and electrolytes takes place here.
  - **2) Loop of Henle:** It is U shaped middle portion of renal tubules. It is composed of ascending and descending loop. Ascending loop is thick walled and impermeable to water while descending loop is thin walled and permeable to water. Counter current mechanism is crucial role of loop of Henle.
  - **3) Distal convoluted tubules (DCT):** It is the distal part of renal tubules that leads to collecting ducts. It is similar in structure and function with PCT.
  - **4) Collecting tubules:** It is not a part of nephron rather it is a part of kidney. The distal convoluted tubules from several nephrons empty into a **collecting tubule**. Several collecting tubules then unite to form a papillary duct that empties urine into **a minor calyx** and then into **major calyx** and finally into **renal pelvis.**

https://www.onlinebiologynotes.com/nephron-structural-anatomy-types/

Functions of the kidneys.

- The main role of the kidneys is maintaining homeostasis. This means they manage fluid levels, electrolyte balance, and other factors that keep the internal environment of the body consistent and comfortable.
- They serve a wide range of functions:
- **Waste excretion**
- The kidneys remove a number of waste products and get rid of them in the urine. For example, kidneys remove urea, uric acid, creatinine, indicant, etc.
- **Reabsorption of nutrients.** They reabsorb other products to help maintain homeostasis. Reabsorbed products include: glucose, amino acids, bicarbonate, sodium, water, phosphate, chloride, sodium, magnesium, and potassium ions
- **Maintaining pH**
- In humans, the acceptable pH level is between 7.36 and 7.44. The kidneys help keep a stable pH within the human body. The kidneys manage the pH through two processes: Reabsorbing and regenerating bicarbonate from urine: Bicarbonate helps neutralize acids. The kidneys can either retain itTrusted Source if the pH is tolerable or release it if acid levels rise. Excreting hydrogen ions and fixed acids: Fixed or nonvolatile acids are any acids that do not occur as a result of carbon dioxide. They result from the incomplete metabolism of carbohydrates, fats, and proteins. They include lactic acid, sulfuric acid, and phosphoric acid.
- **Osmolality regulation**
- Osmolality is a measure of the body's electrolyte-water balance, or the ratio between fluid and minerals in the body. Dehydration is a primary cause of electrolyte imbalance. If osmolality rises in the blood plasma, the hypothalamus in the brain responds by passing a message to the pituitary gland. This, in turn, releases antidiuretic hormone (ADH). In response to ADH, the kidney makes a number of changes, including: increasing urine concentration; increasing water reabsorption; reopening portions of the collecting duct that water cannot normally enter, allowing water back into the body; retaining urea in the medulla of the kidney rather than excreting it, as it draws in water.
- **Endocrine function: Erythropoietin**: This controls erythropoiesis, or the production of red blood cells. The liver also produces erythropoietin, but the kidneys are its main producers in adults. **Renin**: This helps manage the expansion of arteries and the volume of blood plasma, lymph, and interstitial fluid. Lymph is a fluid that contains white blood cells, which support immune activity, and interstitial fluid is the main component of extracellular fluid. **Calcitriol**: This is the hormonally active metabolite of vitamin D. It increases both the amount of calcium that the intestines can absorb and the reabsorption of phosphate in the kidney.

Kidneys metabolism

- The kidneys are an organ with a very good blood supply. They consume 8% of the total oxygen in the blood, although their mass barely reaches 0.8% of the body weight.
- The cortical layer is characterized by an aerobic type of metabolism, the medulla - anaerobic.
- The kidneys have a wide range of enzymes inherent in all actively functioning tissues. At the same time, they differ in their "organ-specific" enzymes, the determination of the content of which in the blood in kidney disease is of diagnostic value. These enzymes primarily include glycine amidotransferase, which transfers the amidine group from arginine to glycine. This reaction is the initial stage in the synthesis of creatine.
- Of the isozyme spectrum, LDH1 and LDH2 are characteristic of the renal cortex, and LDH5 and LDH4 are characteristic of the medulla. In acute renal diseases, an increased activity of aerobic isoenzymes of lactate dehydrogenase (LDH1 and LDH2) and an isoenzyme of alanine aminopeptidase -AAP3 is determined in the blood.
- Along with the liver, the kidneys are an organ capable of gluconeogenesis. This process takes place in the cells of the proximal tubules. The main substrate for gluconeogenesis is glutamine, which simultaneously serves as a buffer to maintain the required pH. Activation of the key enzyme of gluconeogenesis - phosphoenolpyruvate carboxykinase - is caused by the appearance of acidic equivalents in the inflowing blood.
- Consequently, the state of acidosis leads, on the one hand, to stimulation of gluconeogenesis, and on the other, to an increase in the formation of NH3 to neutralize acidic products.

Urine formation

- **Urine:** A liquid excrement consisting of water, salts, and urea, which is made in the kidneys then released through the urethra.
- Urine is formed in three steps: **glomerular filtration, tubular reabsorption and secretion.**
- **Filtration.** During filtration, blood enters the afferent arteriole and flows into the glomerulus where filterable blood components, such as water and nitrogenous waste, will move towards the inside of the glomerulus, and nonfilterable components, such as cells and serum albumins, will exit via the efferent arteriole. These filterable components accumulate in the glomerulus to form the glomerular filtrate.
- Normally, about 20% of the total blood pumped by the heart each minute will enter the kidneys to undergo filtration; this is called the filtration fraction. The remaining 80% of the blood flows through the rest of the body to facilitate tissue perfusion and gas exchange. Reabsorption
- **Reabsorbtion.** The next step is reabsorption, during which molecules and ions will be reabsorbed into the circulatory system. The fluid passes through the components of the nephron (the proximal/distal convoluted tubules, loop of Henle, the collecting duct) as water and ions are removed as the fluid osmolarity (ion concentration) changes. In the collecting duct, secretion will occur before the fluid leaves the ureter in the form of urine.
- **Secretion.** During secretion some substances±such as hydrogen ions, creatinine, and drugs—will be removed from the blood through the peritubular capillary network into the collecting duct. The end product of all these processes is urine, which is essentially a collection of substances that has not been reabsorbed during glomerular filtration or tubular reabsorbtion.

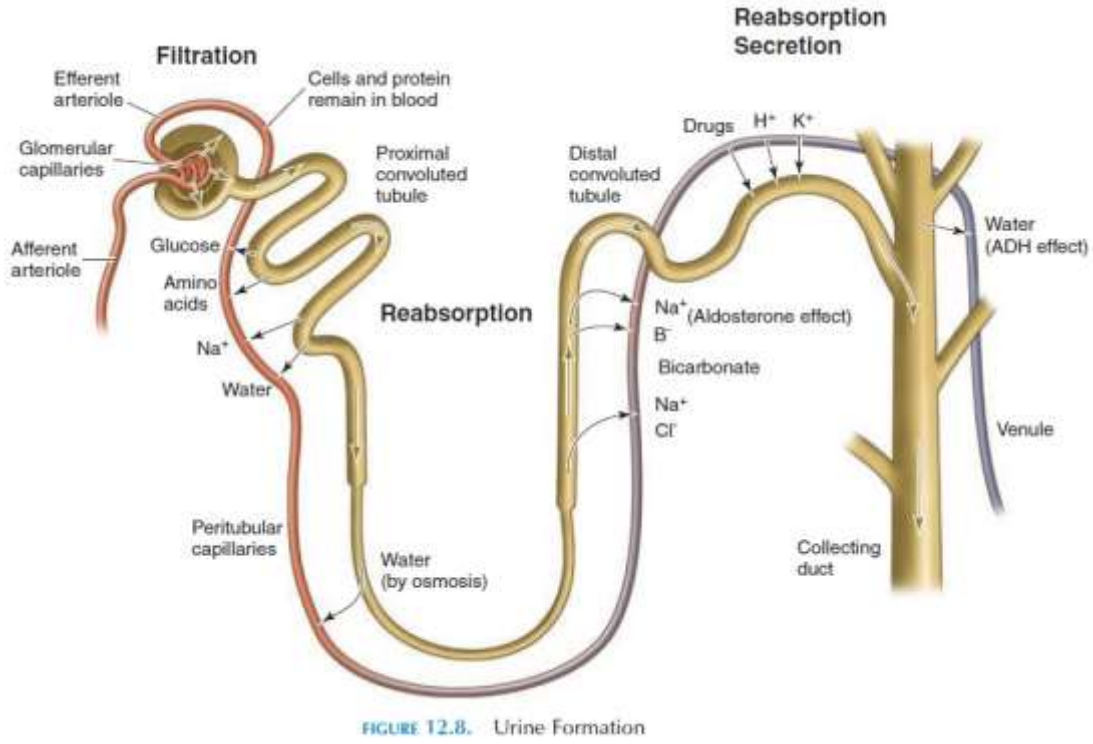


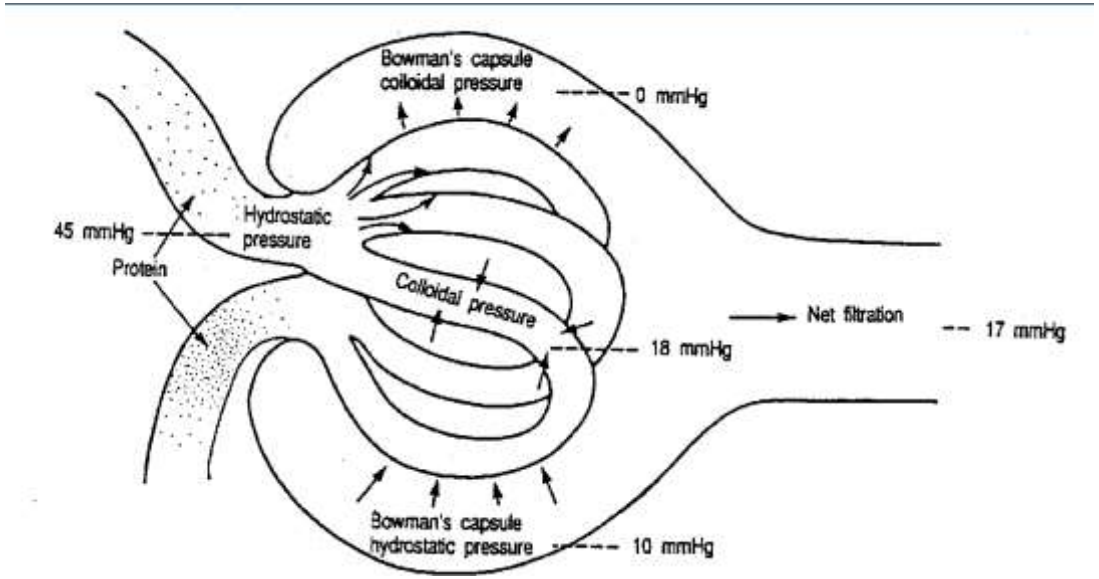
FIGURE 12.8. Urine Formation

https://www.brainkart.com/article/Urine-Formation_21161/

Glomerular filtration

- **Glomerular filtration**
- This takes place through the semipermeable walls of the glomerular capillaries and Bowman's capsule.
- The afferent arterioles supplying blood to glomerular capsule carries useful as well as harmful substances. The useful substances are glucose, aminoacids, vitamins, hormones, electrolytes, ions etc and the harmful substances are metabolic wastes such as urea, uric acids, creatinine, ions, etc.
- The diameter of efferent arterioles is narrower than afferent arterioles. Due to this difference in diameter of arteries, blood leaving the glomerulus creates the pressure known as hydrostatic pressure.
- The **glomerular hydrostatic pressure** forces the blood to leaves the glomerulus resulting in filtration of blood. A capillary hydrostatic pressure of about 7.3 kPa (55 mmHg) builds up in the glomerulus. However this pressure is opposed by the **osmotic pressure** of the blood, provided mainly by plasma proteins, about 4 kPa (30 mmHg), and by **filtrate hydrostatic pressure** of about 2 kPa (15 mmHg in the glomerular capsule.
- The **net filtration pressure** is: 55-(30 +15) = 10mmHg.
- By the net filtration pressure of 10mmHg, blood is filtered in the glomerular capsule.
- Water and other small molecules readily pass through the filtration slits but Blood cells, plasma proteins and other large molecules are too large to filter through and therefore remain in the capillaries.
- The filtrate containing large amount of water, glucose, aminoacids, uric acid, urea, electrolytes etc in the glomerular capsule is known as nephric filtrate of glomerular filtrate.

- The volume of filtrate formed by both kidneys each minute is called the **glomerular filtration rate (GFR).** In a healthy adult the GFR is about 125 mL/min, i.e. 180 litres of filtrate are formed each day by the two kidneys
- As a result of glomerular filtration of blood plasma of the nephron, primary urine is formed. Primary urine is the filtrate of blood plasma. By chemical composition it is similar to blood plasma, only it does not contain proteins.
- Due to the abundant blood supply to the kidneys and the large number of glomerular filtration units (approximately 1 million nephrons per kidney), the body produces about 180 liters of primary urine per day. This corresponds to approximately 120 ml / min. Approximately 99% of primary urine is reabsorbed through the tubular epithelium, so only 1.8–2.0 liters of secondary urine need to be excreted daily.



https://www.semanticscholar.org/paper/Glomerular-filtration%3A-an-overview.-Holechek/ddc843ec192aa3d36ab4720981f3510fe6117c0c/figure/

Control of glomerular filtration

- Three mechanisms control of glomerular filtration (GFR): **renal autoregulation, neural regulation, and hormonal regulation.**
- **Renal autoregulation** The kidneys themselves help maintain a constant renal blood flow and GFR despite normal, everyday changes in blood pressure, like those that occur during exercise. This capability is called renal autoregulation and consists of two mechanisms— the myogenic mechanism and tubuloglomerular feedback.
- **Myogenic autoregulation:** Myogenic constriction of the afferent arteriole occurs due to the ability of the smooth muscle to sense and respond to an increase in arterial pressure. As blood pressure rises, GFR also rises because renal blood flow increases. However, the elevated blood pressure stretches the walls of the afferent arterioles. In response, smooth muscle fibers in the wall of the afferent arteriole contract, which narrows the arteriole's lumen. As a result, renal blood flow decreases, thus reducing GFR to its previous level. Conversely, when arterial blood pressure drops, the smooth muscle cells are stretched less and thus relax. The afferent arterioles dilate, renal blood flow increases, and GFR increases. The myogenic mechanism normalizes renal blood flow and GFR within seconds after a change in blood pressure.

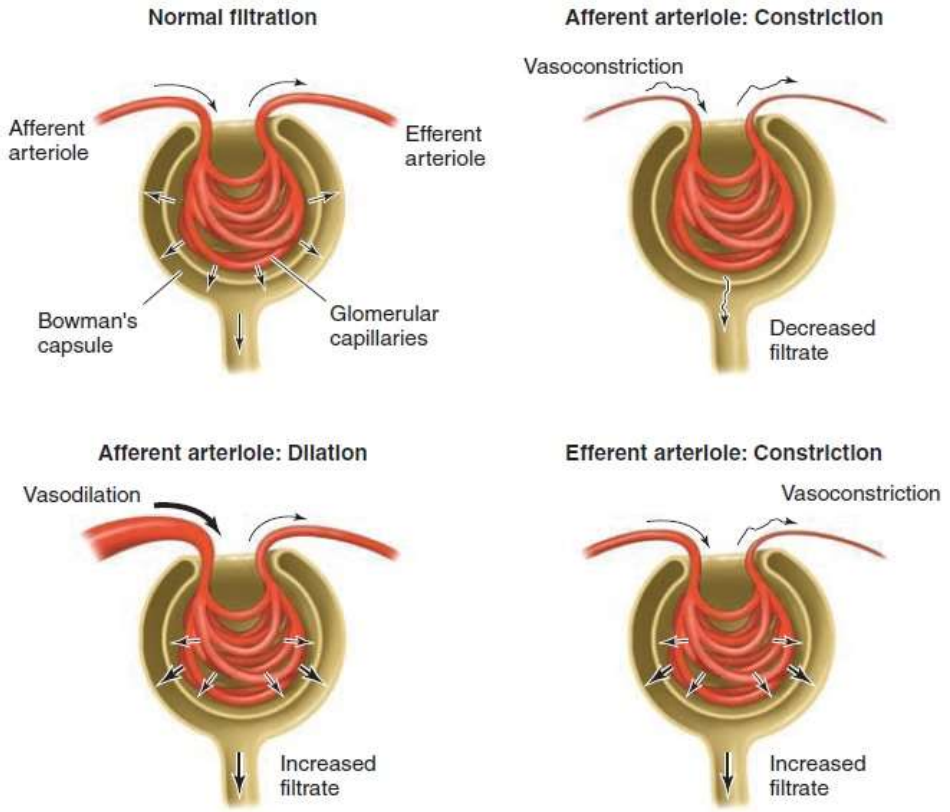


FIGURE 12.9. Control of Glomerular Filtration Rate. Normal Filtration; Afferent Arteriole Constriction; Afferent Arteriole Dilatation; Efferent Arteriole Constriction.

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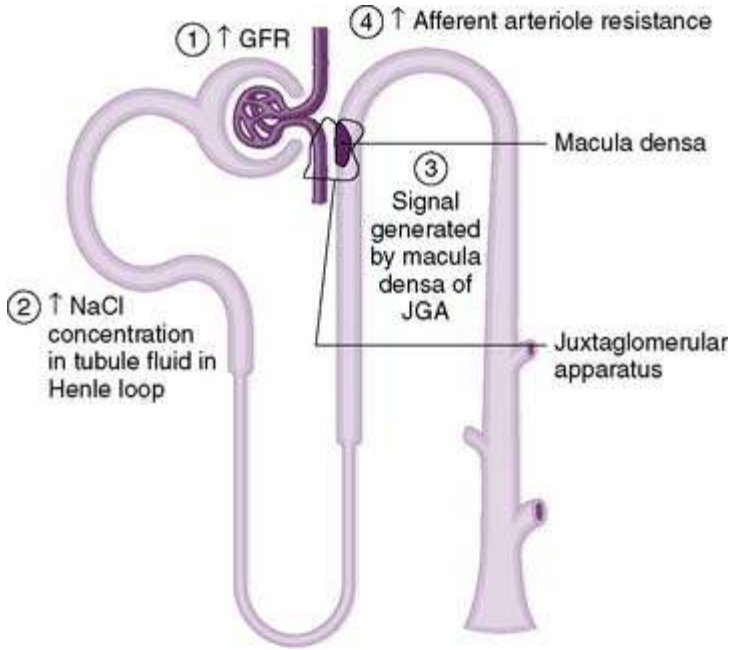
Control of glomerular filtration

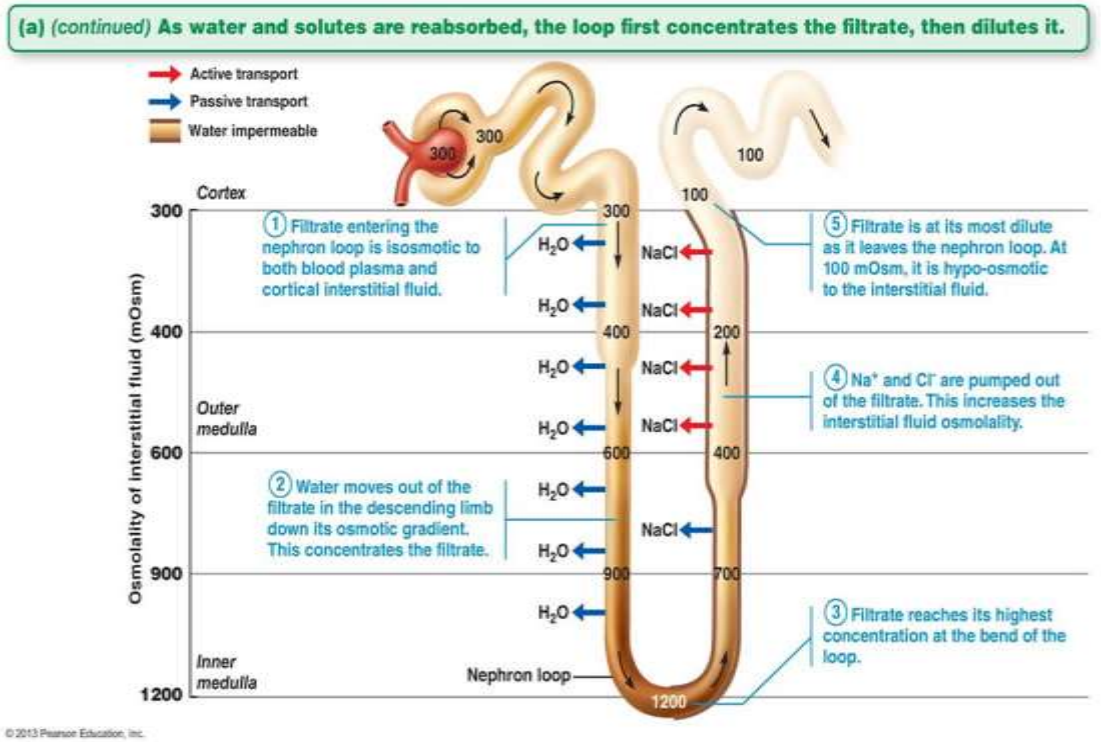
- **Tubuloglomerular feedback:** It is so named because part of the renal tubules—the **macula densa—**provides feedback to the glomerulus. When GFR is above normal due to elevated systemic blood pressure, filtered fluid flows more rapidly along the renal tubules. As a result, the proximal convoluted tubule and loop of Henle have less time to reabsorb Na+ , Cl- , and water. Macula densa cells are thought to detect the increased delivery of Na+ , Cl- , and water and to inhibit release of nitric oxide (NO) from cells in the juxtaglomerular apparatus (JGA). 5 Because NO causes vasodilation, afferent arterioles constrict when the level of NO declines. As a result, less blood flows into the glomerular capillaries, and GFR decreases. When blood pressure falls, causing GFR to be lower than normal, the opposite sequence of events occurs, although to a lesser degree. Tubuloglomerular feedback operates more slowly than the myogenic mechanism.
- **Neural regulation** All the blood vessels of the kidneys, including the afferent and the efferent arterioles, are richly innervated by sympathetic nerve fibres. Activation of renal sympathetic nerves releases norepinephrine. Norepinephrine causes vasoconstriction of afferent arterioles and thus decreases the GFR.
- **Hormonal regulation** Two hormones contribute to regulation of GFR. Angiotensin II reduces GFR; atrial natriuretic peptide (ANP) increases GFR. Angiotensin II is a very potent vasoconstrictor that narrows both afferent and efferent arterioles and reduces renal blood flow, thereby decreasing GFR. Cells in the atria of the heart secrete atrial natriuretic peptide (ANP). Stretching of the atria, as occurs when blood volume increases, stimulates secretion of ANP. By causing relaxation of the glomerular mesangial cells, ANP increases the capillary surface area available for filtration. Glomerular filtration rate rises as the surface area increases.



https://basicmedicalkey.com/renal-physiology-2/

Reabsorption

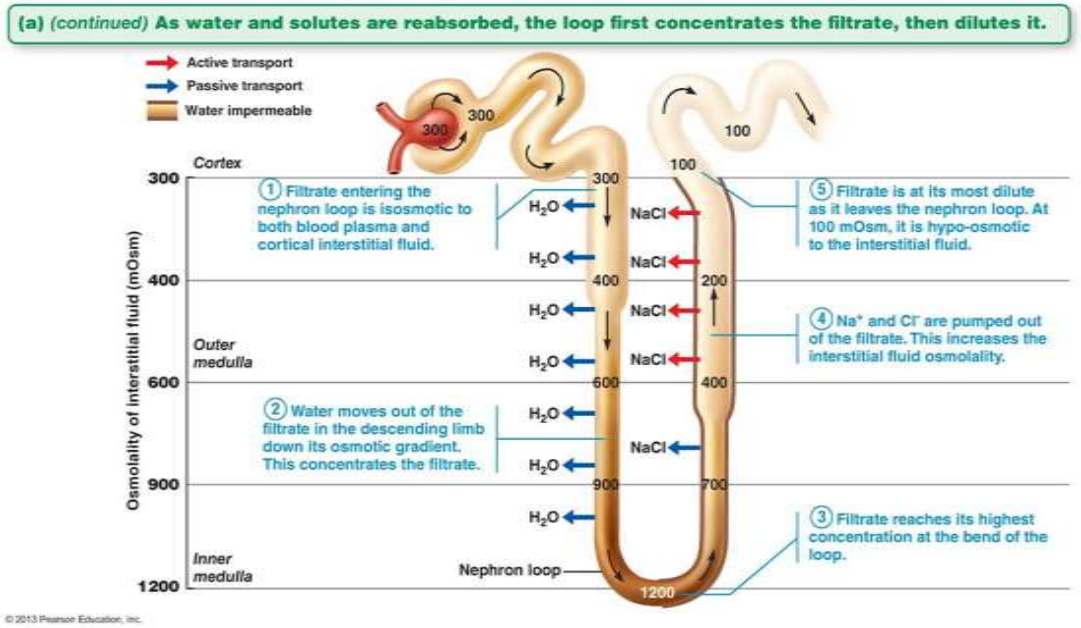
- **Selective reabsorption**
- As the filtrate passes to the renal tubules, useful substances including some water, electrolytes and organic nutrients such as glucose, aminoacids, vitamins hormones etc are selectively reabsorbed from the filtrate back into the blood in the proximal convoluted tubule.
- Reabsorption of some substance is passive, while some substances are actively transported. Major portion of water is reabsorbed by Osmosis.
- Only 60–70% of filtrate reaches the Henle loop. Much of this, especially water, sodium and chloride, is reabsorbed in the loop, so that only 15–20% of the original filtrate reaches the distal convoluted tubule, More electrolytes are reabsorbed here, especially sodium, so the filtrate entering the collecting ducts is actually quite dilute.
- The main function of the collecting ducts is to reabsorb as much water as the body needs.
- Nutrients such as glucose, amino acids, and vitamins are reabsorbed by active transport. Positive charged ions ions are also reabsorbed by active transport while negative charged ions are reabsorbed most often by passive transport. Water is reabsorbed by osmosis, and small proteins are reabsorbed by pinocytosis.



https://www.onlinebiologynotes.com/physiology-urine-formation/

Secretion

- **<u>Tubular secretion</u>**
- Tubular secretion takes place from the blood in the peritubular capillaries to the filtrate in the renal tubules and can ensure that wastes such as creatinine or excess H+ or excess K+ ions are actively secreted into the filtrate to be excreted.
- Excess K+ ion is secreted in the tubules and in exchange Na+ ion is reabsorbed otherwise it causes a clinical condition called Hyperkalemia.
- Tubular secretion of hydrogen ions (H+) is very important in maintaining normal blood pH.
- Substances such as , e.g. drugs including penicillin and aspirin, may not be entirely filtered out of the blood because of the short time it remains in the glomerulus. Such substances are cleared by secretion from the peritubular capillaries into the filtrate within the convoluted tubules.
- The tubular filtrate is finally known as urine. Human urine is usually hypertonic.



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Regulation of body fluids— the process of concentrating and diluting urine

- The primary urine is trasported to the proximal convoluted tubule, where most ions and organic sub-stances are actively or passively reabsorbed. Some reabsorbed solutes include sodium, potassium, calcium, chloride, phosphate, and bicarbonate. Small proteins and peptides are reabsorbed by pinocytosis. A few substances, such as hydrogen ions, urea, ammonia, and creatinine, may be secreted. Water is re-absorbed by osmosis.
- This drastically reduces the volume of the filtrate. As the fluid descends further into the descending limb, more water is reabsorbed and the tubular fluid becomes concentrated. Water and other reabsorbed substances are transported across the lining cells to the surrounding fluid, where they are absorbed into the blood capillaries that surround the tubules.
- The cells in the ascending limb of the loop of Henle are not permeable to water or solutes. The sodium and chloride absorbed here must be actively transported. This process dilutes the tubular fluid (i.e., by removing the solutes alone from the tubular fluid). At the same time, the movement of ions into the interstitial fluid results in concentrating the interstitial fluid surrounding the tubule. As a result, the concentration of interstitial fluid surrounding the loop of Henle progressively increases from the cortex to the deeper parts of the medulla. The volume of water absorbed from the filtrate as it travels through the rest of the renal tubule—distal convoluted tubule and collecting duct—is determined by the ADH level in the blood. ADH increases the permeability of this segment of the tubule. If a person is dehydrated, more ADH is secreted and the permeability of this segment to water increases and more water moves back into the blood. Water absorption is also increased by the action of aldosterone, which in-creases sodium reabsorption from the filtrate, and water moves by osmosis along with the sodium. The fluid from all the nephrons (conveyed by the collect-ing ducts) that finally reaches the pelvis of the kidney is much less in volume, with a high concentration of waste products. Now referred to as urine, from the pelvis, the urine flows into the ureter.
- The permeability properties of the ascending and descending limbs (ascending permeable to water; descending, impermeable), the countercurrent (direction of flow opposite in ascending and descending limbs) flow of fluid in the tubule, the countercurrent flow of blood in the vasa recta, the permeability properties of the collecting duct (permeability to water increased by the presence of ADH), and the active and passive transport of solutes across the tubular cells contribute to the ability of the kidneys to concentrate urine.

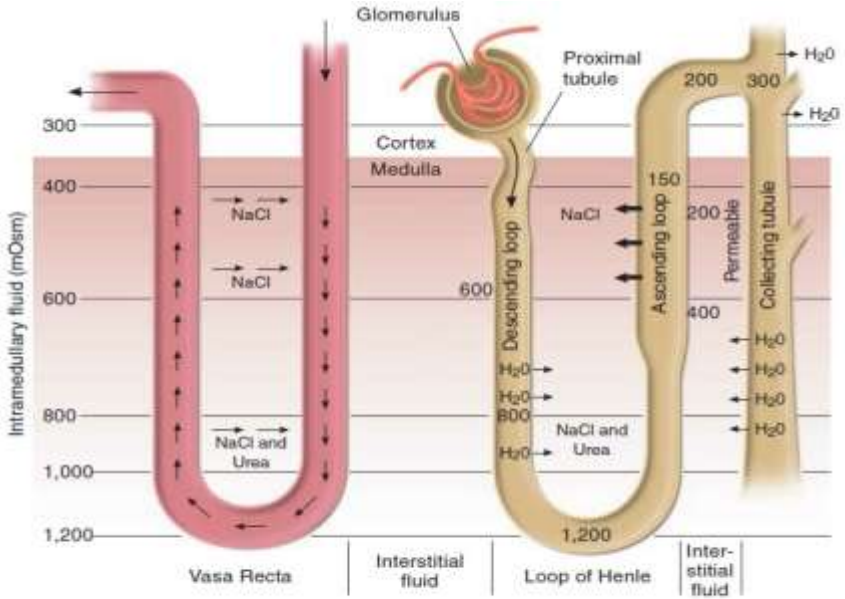

FIGURE 12.10. Countercurrent Mechanisms for Concentrating Urine. Antidiuretic hormone (ADH) alters the permeability of the collecting duct to water. When ADH level is increased, more concentrated urine is formed.

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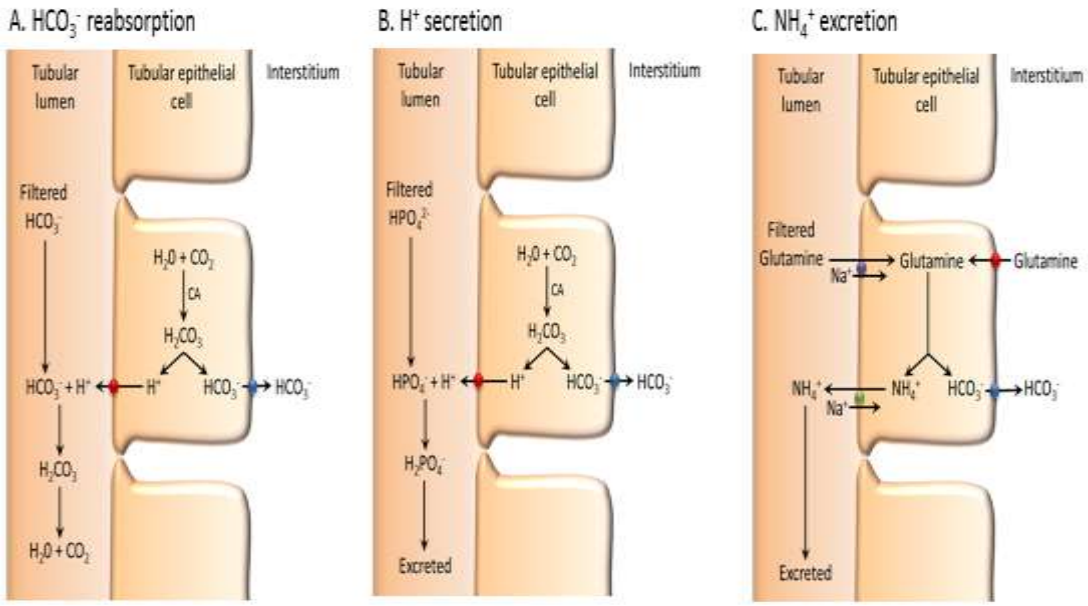
Regulation of Ph

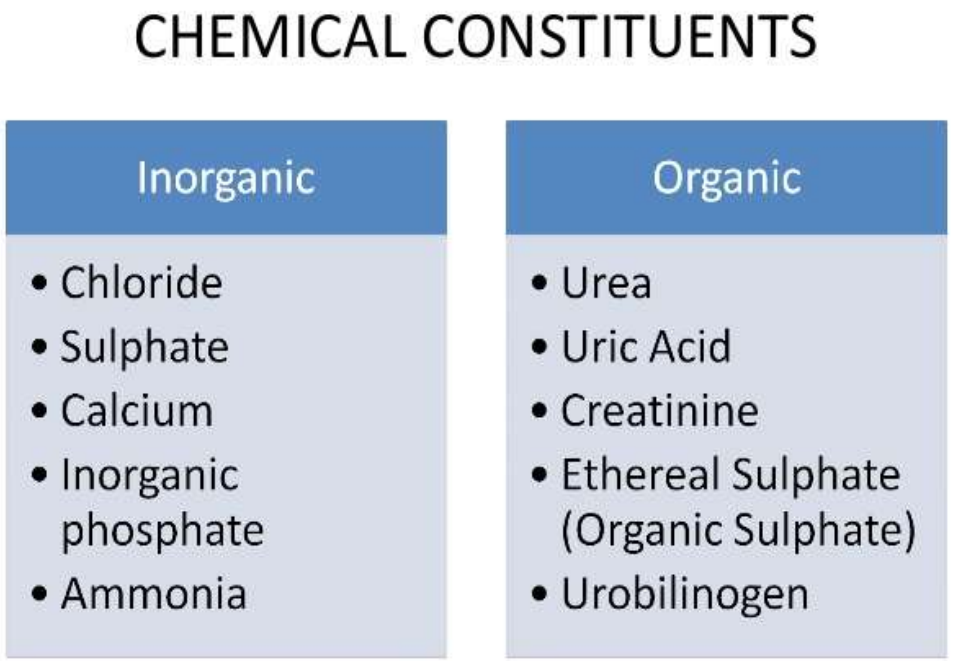
- The kidney is important in acid-base balance. It can regulate the body pH by conserving or eliminating the bases (e.g., bicarbonate) or acids (e.g., hydrogen ions). The kidney has the capacity to secrete hydro-gen ions into the tubular fluid. Large quantities of hy- drogen ions can be eliminated because of the presence of buffers in the urine that combine with the hydrogen ions.
- The three major urinary buffers are bicarbonate (HCO3-), phosphate (HPO4—) and ammonia (NH3). Bi-carbonate present in the filtrate combines with hydrogen ions to form carbonic acid (a weak acid). This acid dissociates into water and carbon dioxide. The carbon dioxide diffuses into the cells and is used to form more bicarbonate ions.
- H+HCO3-⟶ H2CO3⟶ H2O+CO2
- Similarly, filtered phosphate combines with the secreted hydrogen ions and is excreted. The tubular cells manufacture ammonia from the amino acid glu-tamine. The ammonia combines with hydrogen ions and is also excreted.
- When the blood pH is alkaline, fewer hydrogen ions are secreted and more bases excreted.



http://www.nataliescasebook.com/tag/renal-acid-base-regulation

The composition of urine

- ***Volume of urine*** - 1500–2000 mL/24 hour
- Physical characteristics that can be applied to urine include color, turbidity (transparency), smell (odor), pH (acidity – alkalinity) and density. Many of these characteristics are notable and identifiable by by vision alone, but some require laboratory testing.
- ***Color.*** Typically yellow-amber, but varies according to recent diet and the concentration of the urine. Drinking more water generally tends to reduce the concentration of urine, and therefore causes it to have a lighter color. Dark urine may indicate dehydration. Red urine indicates red blood cells within the urine, a sign of kidney damage and disease.
- ***Smell.*** The smell of urine may provide health information. For example, urine of diabetics may have a sweet or fruity odor due to the presence of ketones (organic molecules of a particular structure) or glucose. Generally fresh urine has a mild smell but aged urine has a stronger odor similar to that of ammonia.
- The ***pH*** of normal urine is generally in the range 4.6 – 8, with a typical average being around 6.0. Much of the variation occurs due to diet. For example, high protein diets result in more acidic urine, but vegetarian diets generally result in more alkaline urine (both within the typical range of 4.6 – 8).
- ***Density.*** Density is also known as ***"specific gravity".*** This is the ratio of the weight of a volume of a substance compared with the weight of the same volume of distilled water. The density of normal urine ranges from 0.001 to 0.035.
- ***Turbidity.*** The turbidity of the urine sample is gauged subjectively and reported as clear, slightly cloudy, cloudy, opaque or flocculent. Normally, fresh urine is either clear or very slightly cloudy. Excess turbidity results from the presence of suspended particles in the urine, the cause of which can usually be determined by the results of the microscopic urine sediment examination. Common causes of abnormal turbidity include: increased cells, urinary tract infections or obstructions.



https://www.slideshare.net/janicedesa/normal-constituents-of-urine

- **Polyuria** is excessive or an abnormally large production or passage of urine (greater than 2.5 L or 3 Lover 24 hours in adults). Increased production and passage of urine may also be termed diuresis. Polyuria often appears in conjunction with polydipsia (increased thirst), though it is possible to have one without the other, and the latter may be a cause or an effect. Polyuria is usually viewed as a symptom or sign of another disorder (not a disease by itself).
- The most common cause of polyuria in both adults and children is uncontrolled diabetes mellitus. In the absence of diabetes mellitus, the most common causes are decreased secretion of aldosterone due to adrenal cortical tumor, primary polydipsia (excessive fluid drinking), central diabetes insipidus and nephrogenic diabetes insipidus.Polyuria may also be due to various chemical substances, such as diuretics, caffeine, and ethanol. It may also occur after supraventricular tachycardias, during an onset of atrial fibrillation, childbirth, and the removal of an obstruction within the urinary tract.

- **Oliguria** or hypouresis is the low output of urine specifically more than 80 ml/day but less than 100ml/day. The decreased output of urine may be a sign of dehydration, kidney failure, hypovolemic shock, hyperosmolar hyperglycemic nonketotic syndrome (HHNS), multiple organ dysfunction syndrome, urinary obstruction/urinary retention, diabetic ketoacidosis (DKA), preeclampsia, and urinary tract infections, among other conditions.
- The decreased output of urine may be a sign of dehydration, kidney failure, hypovolemic shock, hyperosmolar hyperglycemic nonketotic syndrome (HHNS), multiple organ dysfunction syndrome, urinary obstruction/urinary retention, diabetic ketoacidosis (DKA), preeclampsia, and urinary tract infections, among other conditions.
- Beyond oliguria is anuria, which represents an absence of urine, clinically classified as below 80 or 100 ml/day, which represents an absence of urine, clinically classified as below 80 or 100 ml/day.
- Anuria is often caused by failure in the function of kidneys. It may also occur because of some severe obstruction like kidney stones or tumours. It may occur with end stage kidney disease.

- Depending on the mechanism of entry of various substances into the urine, they are divided into several groups:

✓ 1) substances that enter the urine as a result of filtration in the glomeruli of the renal corpuscles (creatinine, urea, inulin);

✓ 2) substances, the concentration of which in urine is determined by the ratio processes of secretion and reabsorption in the renal tubules (electrolytes);

✓ 3) substances excreted in the proximal nephron (organic acids, bases)

✓ 4) substances that are practically absent in blood plasma and entering the urine from the cells of the renal tubules ammonia, some enzymes)

✓ 5) substances that are normally almost completely reabsorbed from ultrafiltrate in the proximal nephron (sugars, amino acids).

- Substances of **1-4 groups** are called **nonthreshold**, because their presence in urine is not related to blood concentration. **Group 5** substances are **threshold**, since with intact kidneys, they appear in the urine, when their concentration in the blood exceeds a certain value (threshold).
- The appearance of threshold substances in the urine can also be against the background of their normal content in the blood in violation of the reabsorption mechanism.
- In the clinical diagnosis of kidney disease is important assigned to laboratory analysis of urine and identification of biochemical changes in blood.
- In urine with kidney disease with impaired filtration, it is noted appearance of:

✓ protein (proteinuria);

✓ erythrocytes (hematuria);

✓ hemoglobin (hemoglobinuria);

✓ leukocytes (leukocyturia);

✓ bacteria (bacteriuria).

Pathological components of urine

- **Pathological components** of urine are substances that are not found in normal urine in analytically determined quantities. These are primarily proteins, glucose, acetone (ketone) bodies, bile and blood pigments.
- ***Protein.*** Normal human urine contains a minimal amount of protein, the presence of which cannot be proved by ordinary qualitative tests for the presence of protein. With a number of diseases, especially with kidney disease, the protein content in the urine can increase dramatically (proteinuria). The source of urine protein is serum proteins, as well as, to some extent, proteins of the kidney tissue. Proteinurias are divided into two large groups: ***renal and extrarenal.*** In renal proteinuria, proteins (mainly blood plasma proteins) enter the urine due to organic damage to the nephron, an increase in the pore size of the renal filter, and as a result of a slowdown in blood flow in the glomeruli. Extrarenal proteinuria is caused by damage to the urinary tract or prostate gland.
- ***Blood.*** In urine, blood can be found either in the form of red blood cells (hematuria) or as dissolved blood pigment (hemoglobinuria). Hematuria are renal and extrarenal. Renal hematuria is the main symptom of acute nephritis. Extrarenal hematuria in inflammatory processes or trauma of the urinary tract. Hemoglobinuria is usually associated with hemolysis and hemoglobinuria.
- ***Glucose.*** Normal human urine contains minimal amounts of glucose that are not detectable by conventional quality samples. In pathological conditions, the content of glucose in the urine increases (glucosuria). For example, in diabetes mellitus, the amount of glucose excreted in the urine can reach several tens of grams per day. Normally, glucose is completely reabsorbed in the proximal tubules. When the renal threshold (8.8-9.9 mmol / L) is exceeded, it begins to be excreted in the urine.
- ***Ketone (acetone) bodies.*** In normal urine, these compounds are found only in trace amounts (no more than 0.01 g per day). They are not detectable by conventional quality tests. When large amounts of ketone bodies are released, the qualitative tests become positive. This phenomenon is pathological and is called ketonuria. For example, with diabetes mellitus, up to 150 g of ketone bodies can be released daily. Ketone bodies are excreted in the urine not only in diabetes mellitus, but also during fasting, excluding carbohydrates from food. Ketonuria is observed in diseases associated with increased consumption of carbohydrates: for example, with thyrotoxicosis, hemorrhages in the subarachnoid spaces, craniocerebral trauma. In early childhood (prolonged diseases of the digestive tract (dysentery, toxicosis) can cause ketonemia and ketonuria as a result of hunger and exhaustion. Ketonuria is often observed in infectious diseases: scarlet fever, flu, tuberculosis, meningitis.

Pathological components of urine

- ***Bilirubin.*** Normal urine contains a minimal amount of bilirubin that cannot be detected by conventional quality tests. An increased release of bilirubin, in which routine quality tests for bilirubin in the urine are positive, is called bilirubinuria. It occurs with blockage of the bile duct and liver parenchyma disease. The release of bilirubin into the urine is especially pronounced in obstructive jaundice. With stagnation of bile, the bile-filled tubules are injured and pass bilirubin into the blood capillaries. If the liver parenchyma is affected, bilirubin enters the bloodstream through the destroyed liver cells. Bilirubinuria is manifested when the level of direct bilirubin in the blood is above 3.4 μmol / L. Indirect bilirubin cannot pass through the kidney filter. This becomes possible with significant kidney damage.
- ***Urobilin.*** In urine, urobilin, or rather stercobilin, is always present in small quantities. Its concentration increases sharply with hemolytic and hepatic jaundice. This is due to the loss of the liver's ability to retain and destroy the mesobilinogen (urobilinogen) absorbed from the intestine. On the contrary, the absence of urobilinogen in the urine in the presence of bile pigments (bilirubin) indicates the cessation of the flow of bile into the intestine due to blockage of the bile duct.
- ***Porphyrins.*** Normally, urine contains only very small amounts of type I porphyrins (up to 300 μg per day). However, the release of porphyrins can sharply increase (10-12 times) in liver disease and pernicious anemia. In congenital porphyria, there is an overproduction of type I porphyrins (uroporphyrin I and coproporphyrin I). In these cases, up to 10 mg of a mixture of these porphyrins is found in the daily amount of urine. In acute porphyria, urinary excretion of increased amounts of uroporphyrin III, coproporphyrin III, and porphobilinogen is noted.

Creatinine clearance

- Hemorenal tests are based on content comparison certain substances in the blood and urine.
- These tests can be used to assess the ability of the kidneys to remove from organism this or that compound. From the word "clear" - to clean, these tests often called clearance.
- It is known that creatinine is filtered by the kidneys and is not exposed to reabsorption, hence creatinine clearance – characterizes glomerular filtration and corresponds to the amount of secreted primary urine.

Creatinine clearance (CrCl) is the volume of blood plasma cleared of creatinine per unit time. It is a rapid and cost-effective method for the measurement of renal function. Creatinine clearance is a good estimation of the glomerular filtration rate because in the process of urine formation, reatinine is filtered, but almost not reabsorbed. This makes it possible to assess precisely the filtration capacity of the kidneys.

Normal creatinine clearance –
80-120 ml/min.

Renal failure. Acute renal failure

- **There are 2 types of renal failure:**
- 1**.** ***Functional renal failure (transient)*** - transient state impairment of renal function, which can develop with acute flowing nephritis with pronounced hypertensive syndrome or occurs immediately after the birth of the child due to the shutdown of the placenta as organ of excretion of metabolic products.
- 2. Organic renal failure- divided into **acute renal failure and chronic renal failure**, based on there are pronounced changes in the structures of the renal tissue and are manifested severe changes in homeostasis.
- **Acute renal failure (ARF)** is a nonspecific a syndrome that develops as a result of acute transient or irreversible loss of homeostatic functions of the kidneys due to hypoxia renal tissue with subsequent predominant damage tubules and swelling of the insterstitial tissue.
- The main syndromes of acute renal failure are increasing azotemia, electrolyte imbalance, decompensated metabolic acidosis and impaired kidney ability to excrete water.
- The main clinical signs in acute renal failure are oliguria (daily diuresis less than ¼ - ⅓ volume, in children - less than 300 ml / m2) and azotemia (urea exceeds 16.65 mmol / l).
- The following stages of acute renal failure are distinguished:
- ***Stage 1*** - initial or shock, proceeds from one to three days. The main clinical signs are pronounced edematous syndrome, hypertension. In laboratory diagnostics, oliguria is isolated, hyperkalemia, increasing azotemia, rapid decrease relative density of urine, hypernatremia, which changes to hyponatremia.
- ***Stage 2*** - oligoanuric. Clinical features: decrease diuresis less than 30%, increasing intoxication, dyspeptic, edematous, neurological syndromes, metabolic acidosis, water-electrolyte imbalance. Laboratory diagnostics: in general urine analysis, the relative density continues to fall, increased proteinuria, hematuria, leukocyturia. In the blood is growing azotemia, anemia, hypoproteinemia, hyponatremia, hyperkalemia, changes occur in the water-electrolyte balance of magnesium and phosphorus increase, and calcium and chlorides decrease.
- ***Stage 3*** - restoration of diuresis. Laboratory diagnostics: oliguria is replaced by polyuria, hypo- and isostenuria are expressed. Gradually the function of urine concentration is restored, water-electrolyte violations disappear.
- ***Stage 4*** - recovery. At this stage there is restoration of kidney function.

Chronic renal failure

- **Chronic renal failure (CRF)** is irreversible impairment of homeostatic renal function associated with severe progressive kidney isease that occurs in his the final stage.
- The term "uremia" is identified with end-stage chronic renal failure.
- Each stage corresponds to certain disorders of the excretory functions - creatininemia, magnesium, calcium, and endocrine functions – hemoglobinemia.
- The leading syndromes of chronic renal failure are azotemia, anemia, hypertension, disturbance of CBS and water-electrolyte balance, the nature and severity of these syndromes mainly correlate with a degree of chronic renal failure. And also such syndromes as: osteodystrophy, disorders of hemostasis and impaired immunity.

Glomerulonephritis

- ***Glomerulonephritis*** is a bilateral diffuse immunological-inflammatory kidney disease with a predominant lesion vessels of the glomeruli - proceeds in the form of an acute or chronic process with repeated exacerbations and remissions.
- The following variants of glomerulonephritis are distinguished:

✓ 1) nephritic - manifested by hematuria, proteinuria, hypertension, oliguria, cylinduria, leukocyturia, hypovolemia, hypocomplementemia, encephalopathy;

✓ 2) nephrotic - high proteinuria, edema, hypoproteinemia, possibly arterial hypertension, erythrocyturia, azotemia;

✓ 3) mixed - severe nephrotic syndrome, significant hematuria, hypertension;

✓ 4) hematuric - hematuria predominates in the urinary syndrome;

✓ 5) isolated urinary syndrome, manifested extrarenal symptoms that are mild.

- In the general analysis of urine, it is noted proteinuria up to 3 g/l, massive proteinuria may last no more 1-3 weeks, moderate persists up to several months. Proteinuria can be selective with the release of albumin or non-selective when other serum proteins are also found in urine. Microhematuria - persistent symptom, lasts longer than proteinuria. Macrohematuria occurs in 12-18% of cases, urine can be red or brown due to the transition of heme to hematin during an acidic reaction of urine.
- In the blood - the concentration of serum protein may be slightly reduced due to hypervolemia. Dysproteinemia with a decrease inalbumin / globulin ratios due to α2- and γ-globulins. Compensated metabolic acidosis. Hyperkalemia is observed only with a severe course of the disease. Sodium and urinary acid is increased. Malignant glomerulonephritis is characterized by also hypoproteinemia and hypercholesterolemia, early development of renalfailure.
- Chronic glomerulonephritis is biochemically manifested hypoproteinemia, hypercholesterolemia, signs of chronic renal failure.

Pyelonephritis

- Pyelonephritis is a nonspecific inflammatory process with predominant lesion of the interstitial tissue of the kidney of its calyceral system.
- Laboratory diagnostics. In the general analysis of urine, there is leukocyturia, pyuria (pus in the urine), bacteriuria, leukocyte casts, destruction of the renal papillae is accompanied by hematuria.
- In the blood - dysproteinuria with a decrease in albumin-globulin coefficient and hypergammaglobulinemia, increased C-reactive squirrel. Bilateral kidney damage leads to renal failure with azotemia, acidosis.

Kidney stone disease

- Kidney stone disease (nephrolithiasis) – chronic a disease characterized by a violation of metabolic processes in the body and local changes in the kidneys with the formation in the parenchyma, calyxes and pelvis stones formed from mineral and organic components of urine.
- Laboratory diagnostics. In the general analysis of urine micro- and gross hematuria, often after exercise. Oxalaturia or hyperuricemia (uric acid salts - urates), bacteriuria.
- In a biochemical blood test - a violation of purine or phosphate-calcium metabolism (hypercalcemia and hypophosphatemia).

Types of Kidney Stones

- **Calcium oxalate stones** ***(calcium oxolate mono-, di- and trihydrates)*** – the most common type. This occurs when the urine contains low levels of citrate and high levels of calcium and either oxalate or uric acid. Calcium oxalate stones are linked with foods high in oxalate. These include beets, black tea, chocolate, nuts, potatoes, and spinach.
- **Calcium phosphate stones** ***(apatite, brushite, octacalcium phosphate)*****–** by abnormalities in the way the urinary system functions.
- **Struvite stones** ***(tripel phosphate, newberite, amorphous phosphate, vitlockite)*** – are more common in women, it forms as a result of certain types of urinary tract infections. These stones tend to grow quickly and become large, sometimes occupying the entire kidney. If left untreated, they can cause frequent and sometimes severe urinary tract infections and loss of kidney function.
- **Uric acid stones** ***(uric acid and its salts (anhydrous uric acid, uric acid dihydrate, ammonium urate, sodium monourate)*** – are more common in men; they tend to occur in people who don't drink enough water or have a diet high in animal protein. They are also more likely to occur in people who have gout, a family history of this type of kidney stone, or in those who've had chemotherapy.
- **Cystine stones** – are caused by a hereditary genetic disorder called cystinuria that can lead to excessive amounts of the amino acid cystine collecting in the urine. This can result in the formation of stones in the kidneys, bladder, and ureters, which transport urine from the kidneys to the bladder.

https://amazedbytruth.com/kidney-stones/

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