

Министерство здравоохранения республики Беларусь
Учреждение образования
«Гомельский государственный медицинский университет»

Кафедра патологической физиологии
Обсуждено на заседании кафедры
Протокол №7 от 30.08.2017

МЕТОДИЧЕСКАЯ РАЗРАБОТКА
Для проведения занятия со студентами
3 курса ФПСЗС, обучающихся на английском языке
по патологической физиологии

Тема: Патофизиология системы крови. Изменения общего объема крови. Кровопотеря

Theme: Pathophysiology of blood. Change of total blood volume. Blood loss

Время 3 ак. часа

1.Actuality of the theme. Anemia appear on the base of various diseases, intoxications, bloodloss. Therefore clinicists of various specialities often find them in the practical activity. The quantitative changes erythrocytes and hemoglobin are one of the most important parameters, on the basis of which diagnostics of anemia is carried out. On changes of these parameters also judge about the efficiency of treatment. Using the quantitative characteristics of erythrocytes and hemoglobin, it is possible to define one more clinically important parameter - colour index. Basing on a colour index one can judge about the saturation of erythrocytes by hemoglobin. The value of a colour index (norm, decrease, increase) has diagnostic mean.

Learning goals of the lesson: to know main types of violations of total blood volume, their causes and consequences. To know main type of anemias, their general characteristics.

Educational goals of the lesson: formation of scientific outlook and theoretical basis of future specialists on the basis of fundamental knowledge and the latest achievements of pathological physiology.

Objectives of the lesson:

1. To know main types, causes, and consequences of changes in total blood volume.
2. To know mechanisms of emergency and long-term reactions of compensation for blood loss, principles of therapy for blood loss.
3. To know definition, classifications and general characteristics of anemias.

To repeat the following questions from related disciplines to ensure absolute mastery of the material:

1. Scheme of erythropoiesis (histology, cytology, embryology disciplines).
2. Quantitative parameters of red blood. Methods of determination of erythrocytes count, hemoglobin content (normal physiology discipline).

Control questions of the lesson:

1. Changes in total blood volume: their types, causes and mechanisms of development, importance for the body.
2. Acute blood loss: etiology, pathogenesis, changes in bone marrow and peripheral blood at various times after hemorrhage.
3. Anemia: definition, classifications, general characteristics.
4. Acute and chronic posthemorrhagic anemia: causes, mechanisms of development.
5. Emergency and long-term protective-adaptive reactions of the body with blood loss.
6. Disorders of physiological functions in blood loss and posthemorrhagic conditions, reversible and irreversible changes.
7. Principles of hemorrhage therapy.

Calculation of study time

Total study time 3 ac.hours

№ п/п	Contents	Calculation of study time
1.	Introduction. Motivational characteristic of the theme	3 minutes
2.	Written control of students on the topic of the lesson	15 minutes
3.	Interviews with students about the topic of the lesson	60 minutes
4.	Self-managed student work	15 minutes
5.	Summing up the results of the lesson	5 minutes
6.	Decision of situational tasks	20 minutes
7.	Task for the next lesson	2 minutes




Additional material:

Parameters	SI system	Relative numbers
Hemoglobin:		
<i>female</i>	115,0 – 145,0 g/l	
<i>male</i>	130,0 – 160,0 g/l	
Red blood cells:		
<i>female</i>	$3,7 - 4,7 \cdot 10^{12}/l$	
<i>male</i>	$4,0 - 5,0 \cdot 10^{12}/l$	
Mean corpuscular volume (MCV)	80 – 100 p _h l (10^{-15} l)	
Mean corpuscular hemoglobin (MCH)	$25,4 - 34,6 \times 10^{-15}$ kg/cell	
Mean corpuscular hemoglobin concentration (MCHC)	0,3 – 0,38 kg/ l	
RBC distribution width (RDW) anisocytosis factor	11,5 – 14,5%	
Color index	0,85 – 1,05	
Hematocrit:		
<i>female</i>	0,36 – 0,42	
<i>male</i>	0,40 – 0,48	
Reticulocytes	0,2 – 1,2%	
ESR:		
<i>female</i>	2 – 15 mm/h	
<i>male</i>	1 – 10 mm/h	
Leukocytes:	$4,0 - 9,0 \cdot 10^9/l$	
<i>neutrophils:</i>		
<i>metamyelocytes</i>		0–1%
<i>band</i>	$0,040 - 0,300 \cdot 10^9/l$	1 – 5%
<i>segmented</i>	$2,000 - 5,500 \cdot 10^9/l$	45 – 75%
<i>eosinophils</i>	$0,020 - 0,300 \cdot 10^9/l$	0,5 – 5%
<i>basophils</i>	$0 - 0,0065 \cdot 10^9/l$	0 – 1%
<i>lymphocytes</i>	$1,200 - 3,000 \cdot 10^9/l$	20 – 40%
<i>monocytes</i>	$0,090 - 0,600 \cdot 10^9/l$	2 – 10%
Platelets	$150,0 - 450,0 \cdot 10^9/l$	

The total blood volume taken to calculate body weight (approximately 6-8%), so that an adult male blood volume is approximately 5 liters. In this case 3.5-4 liter normally circulates in bloodstream and heart cavities (the circulating fraction of blood), and 1.5-2 liters deposited in the vessels of the abdominal cavity, lungs, subcutaneous tissue and other tissues (deposited fraction). Forming elements are up 36-48% of total blood volume.

Hematocrit (Ht) – is the ratio of blood cells to plasma volume. Normally equal to 0,41-0,50 for men, women 0,36-0,44).

Table 0. Typical forms of changes in the total volume and / or the ratio of the formed elements and blood plasma

Total blood volume (formed elements/plasma)	Condition of blood volume
	Norm
	Oligocythemic normovolemia
	Polycythemic normovolemia



Normocytic(simple) hypervolemia



Oligocytic hypervolemia



Polycythemic hypervolemia



Normocytic(simple) hypovolemia



Oligocytic hypovolemia



Polycythemic hypovolemia

NORMOVOLEMIA

Normovolemia – is a condition, that characterized by normal total blood volume, combined with a decreased, an increased or a normal Ht. There are oligocytic, polycythemic and normocytic normovolemia. Normocytic normovolemia is normal state of blood.

Oligocytic normovolemia

Oligocytic normovolemia - is a condition with a normal total blood volume with a decreased number of formed elements (mostly red blood cells), accompanied by a fall in hematocrit values below normal (<36%).

The main reasons are:

- massive hemolysis (eg, formation of antierythrocytic Ig; hemolytic action of substances – snake venom, lead compounds, arsenic, phenylhydrazine, etc.);
- prolonged and extreme inhibition of hematopoiesis, mainly of erythropoiesis (eg, aplastic anemia);
- states after blood loss, acute bleeding (in this case, the total blood volume become normal relatively quickly due to transport of fluid from the tissues into the bloodstream, and the number of blood cells is still reduced).

Manifestations:

- anemia (due to the decrease the number of red blood cells) and as a consequence - hemic hypoxia;
- thrombocytopenia (blood loss, or immune reactions autoaggression for platelets);
- reduction of blood coagulability, often combined with a hemorrhagic syndrome;
- leukopenia, which determines the reduction of anticontagious resistance of the organism;
- reduction of blood viscosity. (eg, during hydremic compensate for acute blood loss).

Polycythemic normovolemia

Polycythemic normovolemia -is a condition characterized by normal total blood volume and increasing the number of formed elements, which is accompanied by an increase Ht above normal (>48%).

The main reasons are:

- chronic hypoxia (erythrocytosis is due to the activation of erythropoiesis);
- infusions to patients fractions of blood cells (erythrocytes, leukocytes or platelets);
- erythremia.

Manifestations:

- increase of blood viscosity;
- thrombotic syndrome;
- microcirculation disorders (slowing of blood flow in microvasculature, stasis), which cause reduction of transcapillary exchange in the tissues;
- hypertension (by increasing cardiac output).

HYPERVOLEMIA

Hypervolemia – is a conditions characterized by an increase in total blood volume, and usually changing Ht. There are normocythemic, oligocythemic, polycythemic hypervolemias.

Normocythemic hypervolemia

Normocythemic hypervolemia (simple) – is a condition manifested by an equivalent increase in the amount of formed elements and the liquid part of the CBV. Ht is at the range of normal.

The main reasons are:

- a large amount of blood transfusions;
- acute hypoxic state;
- accompanied by ejection the blood from pool;
- heavy physical activity, leading to hypoxia.

Manifestations:

- circulatory disorders due to hyperextension of vessels and heart cavities and microcirculatory disorders.

Oligocythemic hypervolemia

Oligocythemic hypervolemia (hydremia, hemodilution) –is a condition characterized by an increase in total blood volume due to the increase of its liquid part. Ht is lower than normal (<36%).

The main reasons are:

- excessive intake of fluid in pathological thirst (for example, patients with diabetes melitus) and transfusion a large number of plasma substitutes or blood plasma;
- reduction of removing fluid from the body as a result of failure of excretory renal function (eg, renal failure), overproduction of ADH, hyperosmolality of blood plasma.

Manifestations:

- circulatory disorders due to hyperextension of vessels and heart cavities and microcirculatory disorders.

Polycythemic hypervolemia

Polycythemic hypervolemia – is a condition manifested by an increase in total blood volume due to the increase in the number of formed elements. Ht is upper limit of normal (>48%).

The main reasons are:

- erythrocytosis – a group of pathological conditions characterized by an increase in the number of erythrocytes (regardless of the number of white blood cells, platelets);
- polycythemia (polycythemia vera, Vaquez disease) – chronic leukemia with a lesion at the level of progenitor cells myelopoiesis with unlimited proliferation and ability to differentiate mainly in the RBCs as a result is an increased Ht;
- chronic hypoxia of any types (hemic, respiratory, circulatory, tissue, etc.).

Manifestations:

- increased cardiac output (the result of compensatory hyperfunction of the heart due to increased blood volume; however, cardiac output is usually reduced in decompensation heart failure);
- increased blood pressure (due to the increase cardiac output, CBV and the tone of resistive vessels);
- increased blood viscosity;
- increased aggregation and agglutination of blood cells;
- disseminated thrombosis;
- disorders of microcirculation.

HYPOVOLEMIA

Hypovolemia – is a conditions characterized by a decrease in total blood volume and, as a rule, ratio distortion of the formed elements and plasma. There are normocythemic, oligocythemic, polycythemic hypovolemia.

Normocythemmic hypovolemia

Normocythemmic hypovolemia – is a condition manifested by a decrease in total blood volume, while maintaining Ht within normal limits.

The most common reasons:

- acute blood loss;
- shock, vasodilatory collapse.

In this are two cases normocythemmic hypovolemia that caused by deposition of a large blood volume in the venous (capacitance) vessels and intense reduction of CBV.

Manifestations:

Determined by the nature of the reasons that caused it (blood loss, shock, collapse), and the starting compensatory mechanisms to the abatement acute hypoxia.

Oligocythemmic hypovolemia

Oligocythemmic hypovolemia – is a condition characterized by a decrease in total blood volume with a primary decrease in the number of formed elements. Ht is below normal (<36%).

The most common reasons:

- states after acute blood loss;
- erythropenias is a result of massive hemolysis of RBCs (for example, burns a large area of the body, when hemolysis is combined with the plasmorrhagia) and suppression of erythropoiesis (eg, aplastic or aregeneration states).

Manifestations:

- the decline in blood oxygen capacity (as a result erythropenia);
- signs of hypoxia (eg, reducing the oxygen content in blood, acidosis, a decrease of venous blood pO₂, etc.);
- disorders of blood circulation and microcirculation in organs and tissues varying degrees, due to a decrease in CBV.

Polycythemmic hypovolemia

Polycythemmic hypovolemia – is a condition with decreasing total blood, mainly due to a decrease in plasma volume. Ht is above the range of normal (>48%).

The most common reasons:

- states, causing an increased loss of body fluid: repeated vomiting (eg pregnancy or as a result of exogenous intoxication), prolonged diarrhea, polyuria (eg, renal failure), increased and prolonged sweating, and extensive burns of the skin (accompanied plasmorrhagia);
- conditions prevent adequate flow of fluid in the body: the lack of potable water and the impossibility of drinking water (eg due to muscle spasm in tetanus or rabies).

Manifestations:

- organs and tissues microcirculation disorders due to hypovolemia, and polycythemia;
- increase blood viscosity, aggregation of blood cells in microcirculation vessels of organs and tissues and disseminated microthrombosis;
- the signs of main pathologies causing polycythemmic hypovolemia (eg, shock, diabetes insipidus, renal failure, burn patients, etc.).

BLOOD LOSS

Blood loss – is a pathological condition as a result of hemorrhage that lead to disturbances of vital activity of the organism in a various degree.

Etiological factors of blood loss:

1. violation of the blood vessels integrity (injury, damage by pathological processes);
2. increased permeability of the vascular wall;
3. decrease of blood clotting (haemorrhagic syndrome).

Pathogenesis of bleeding has three stages:

1. initial
2. compensatory
3. terminal

1. **Initial stage.** Decreased CBV (hypovolemia), decreased cardiac output and blood pressure develop circulatory hypoxia.

2. **Compensatory.** Distinguish the following phases of compensatory reactions:

- 1) ***Vascular reflex phase*** lasts 8-12 hours from the start of hemorrhage. It is characterized by spasm of peripheral vessels due to release of adrenal catecholamines, which results leads to reduce the volume of bloodstream ("centralization" of blood circulation) and helps maintain blood flow to vital organs (brain and heart). At the same time there is activation of the renin-angiotensin-aldosterone system that leads to activation the processes of sodium and water reabsorption in the proximal tubules of the kidneys, accompanied by a decrease in diuresis and water retention in the body. During this period, the loss of blood plasma and blood cells and as a result equivalent compensatory out of blood from pool, as a result the hematocrit about norm ("hidden" anemia). Early signs of acute blood loss are leukopenia (in some cases, may be leukocytosis) and thrombocytopenia.
- 2) ***Hydremic phase*** (in 1-2 days after blood loss). On this stage there is restoration of plasma volume. Mobilize tissue fluids in to blood stream. "Dilution" of blood is accompanied by a progressive decrease in the number of RBCs and hemoglobin in a unit volume of blood. The anemia has normochromic, normocytic character.
- 3) ***Phase of bone marrow*** (develop into 4-5th day after the hemorrhage). Juxtaglomerular apparatus of kidneys is response to hypoxia by overproduction of erythropoietin, which stimulates activity of unipotent progenitor cells of erythropoiesis - CFU-E. In case of sufficient regenerative capacity of bone marrow there is increase of young forms of red blood cells (reticulocytes) in the blood (after 4-5 days). It is accompanied by changes in the size of red blood cells (macrocytosis) and cell shape (poikilocytosis). In the blood can appear RBCs with basophilic granules, sometimes single normoblasts, develops a mild leukocytosis (up to $12 \times 10^9/l$) with a left shift to metamyelocytes (rarely up to myelocytes) and increase in platelet counts (up to $500 \times 10^9/l$ or more).

Protein compensation is realized by activation proteosynthesis in the liver, start from few hours after the bleeding, can be founded 1,5-3 weeks.

3. **Terminal stage** may occur in acute massive blood loss exceeding 50% of CBV, absence of adequate treatment, insufficiency of adaptation (due to severe diseases, effect of unfavorable exogenous and endogenous factors).

In the case of acute blood loss (more than 15% of CBV) significantly reduced venous return to the right heart, which leads to a decrease in cardiac output, a progressive drop in blood pressure and slowing down blood flow. In response to a decrease in central hemodynamics occurs systemic vasoconstriction, release deposited blood, and develops tachycardia and other compensatory mechanisms of hypovolemia. It allows maintaining blood pressure in the subcritical level (90-85/45-40 mm Hg) until a certain time (until blood loss does not exceed 40-45% of CBV). Continuing bleeding leads to the depletion of the body's adaptive systems (involved in the fight against hypovolemia), thus developed hemorrhagic shock. In this case the protective reflexes of macrocirculatory system are already insufficient to ensure adequate cardiac output, resulting in systolic blood pressure falls rapidly to critical numbers (50-40 mm Hg). Ultimately disturbed blood flow to organs and body systems, develops oxygen starvation, and death due to respiratory paralysis and cardiac arrest.

Acute Hemorrhage

Acute hemorrhage occurs after injury of a large vessel. In this case cellular elements and liquid part of the blood are lost proportionally (simple hypovolemia).

Acute loss of the blood up to 10% of the blood volume and slow loss of even greater amounts may have no significant manifestations. Sudden loss of 25-40% and more of the blood is dangerous for life. Loss of 60% of blood is lethal.

A state of hemostasis system plays an important role; thus, in its disorder, a damage of even not so large vessel may lead to acute blood loss.

In clinical manifestations following changes play the critical role:

- acute disorder of the systemic blood circulation;
- critical decrease in arterial blood pressure;

- decrease in heart filling and systolic heart volume, coronary insufficiency (decrease of coronary blood supply);
- development of acute hypoxia of circulatory type;
- acute kidney insufficiency;
- acute posthemorrhagic anemia;
- hemorrhagic shock may occur if a compensation fails and is characterized by extreme disorder of all vital functions, loss of consciousness and death if not treated.

Chronic Hemorrhage

Causes of a chronic hemorrhage, as a rule, are of endogenous origin. They are bleeding from stomach or intestine ulcer, cancer of stomach or intestine, bronchial hemorrhage with pulmonary tuberculosis, massive menses in women, uterine hemorrhages. Chronic blood loss is accompanied by the development of the deficit of iron. In gastrointestinal bleeding the RBCs is rapidly digested and the iron may be reutilized. Important pathogenic component in the development of clinical disorders in the chronic hemorrhage appears anemia and hemic type of hypoxia.

In pathophysiological and clinical manifestations dominate following signs:

- insufficiency of tissue respiration due to the development of hemic and tissue hypoxia;
- disorder of tissue metabolism;
- acid-base disbalance (non-respiratory acidosis);
- iron-deficiency anemia
- disorder of the bone marrow due to its chronic suffering from hypoxia;
- development of chronic posthemorrhagic anemia.

ANEMIA

Anemia – clinical –hematological syndrome characterized by deficiency of hemoglobin or/ and erythrocytes content in units of blood.

Table 1 Classification of anemia

According to cause:	primary secondary
According to the rate of development:	acute chronic
According to mechanism:	post-hemorrhagic hemolytic dyserythropoietic
According to hemopoietic type:	erythroblastic megaloblastic
According to regenerative ability of bone marrow:	regenerative >1.5% of reticulocytes hyperregenerative >15% of reticulocytes hyporegenerative 0,2-1% of reticulocytes aregenerative (aplastic) < 0,2% of reticulocytes
According to color index:	Normochromic: CI=0,8–1,05; MCH 25,4-34,6 pg Hyperchromic: CI > 1,05; MCH >34,6pg hypochromic: CI <0,8; MCH <25,4pg
According to Er size:	normocytic — 7,2–8,3 mcm (MCV=80-100fl) microcytic — < 7,2 mcm (MCV<80fl) macrocytic — > 8,3–12 mcm (MCV>100fl) megalocytic — 12–15 mcm (MCV=110-120fl)
According to severity:	mild — Hb 110-90 g/l; Er >3,0·10 ¹² /l medium — Hb – 90–70g/l; Er – 3,0 – 2,0·10 ¹² /l severe – Hb <70g/l; Er< 2,0·10 ¹² /l

Questions for self-control of knowledge:

1. Describe standard forms of changes in the total blood volume.

2. What is the etiology oligocythemic and polycythemic hypovolemia?
3. What is the etiology oligocythemic and polycythemic hypervolemia?
4. Tell about the general mechanisms of compensatory-adaptive mechanisms for blood loss.
5. What is the mechanism of immediate protective-adaptive reactions formation of the organism in blood loss?
6. What is the mechanism of long-term protective-adaptive reactions formation of the organism in blood loss?
7. Define the concept of anemia, what are the principles of classification?
8. What are the main iron reserves in the body?
9. List the laboratory parameters that characterize the state of red blood cells in acute blood loss?
10. List the laboratory parameters that characterize the state of red blood cells in chronic blood loss?

Tasks for self-managed student work:

1. Methods of diagnosis of acute blood loss. Principles of prevention and therapy.
2. Mechanisms of blood loss compensation

Literature

Basis literature:

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