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CLINICAL PATHOPHYSIOLOGY OF THE RED BLOOD SYSTEM

Tutorial

Vladivostok
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2020

Federal State Budgetary Educational Institution
Pacific State Medical University
Ministry of Public Health of Russia
(FSBEI HE PSMU of Ministry of Public Health of Russia)

CLINICAL PATHOPHYSIOLOGY OF THE RED BLOOD SYSTEM

Tutorial

Рекомендовано Координационным советом по области образования «Здравоохранение и медицинские науки» в качестве учебного пособия для использования в образовательных учреждениях, реализующих основные профессиональные образовательные программы высшего образования уровня специалитета по направлению подготовки 31.05.01 «Лечебное дело»

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2020

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Reviewers:

M.V. Osikov *– Dr. habil. med., professor, head of the Pathological Physiology Department of FSBEI HPE «South Ural State Medical University» of Ministry of Public Health of the Russian Federation*

N.A. Nikolaev *– Professor, Department of Faculty Therapy, Occupational Diseases, Vice-Rector for Medical Activities and Regional Health Care, Federal State Budgetary Educational Institution of Higher Education, Omsk State Medical University, Ministry of Health of the Russian Federation, Doctor of Medical Sciences, Associate Professor*

Authors:

Chagina E.A., Markelova E.V., Malkov V.A., Knish C.V., Shubina A.Yu.

C 60 **Clinical pathophysiology of the red blood system:** tutorial / E.A. Chagina, E.V. Markelova, V.A. Malkov and other authors. – Vladivostok: Medicina DV, – 88 p. Table 7, Figure 40, Bibliography: 15 items.

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The tutorial unravels the concepts: erythron, anemia.

It describes the etiopathogenesis features of the main forms of the red blood system pathology, including in gerontology.

The up-to-date information resources are used as the tutorial basis. In the tutorial, there are case problems and test check tasks.

The tutorial is compiled on “Pathophysiology, clinical pathophysiology” discipline, in accordance with the requirements of the Federal State Educational Standards and is intended for students pursuing specialist’s programs «General Medicine»/

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Table of contents

It describes the etiopathogenesis features of the main forms of the red blood system pathology, including in gerontology.

List of abbreviations

▪ ACTH	– adrenocorticotropic hormone
ATP	– adenosine triphosphoric acid
ATP-ase	– adenosine triphosphatase
ACD	– anemia in chronic diseases
BFU	- burst-forming unit
GM-CSF	– granulocyte-macrophage colony-stimulating factor
DNA	– deoxyribonucleic acid
DPGA	– diphosphoglyceric acid
IDA	– iron deficiency anemia
GT	– gastrointestinal tract
▪ RPI	– reticulocyte production index
CFU	– colony-forming unit
▪ CSF	– colony-stimulating factor
CBV	– circulating blood volume
RNA	– ribonucleic acid
▪ SA	– sideroblastic anemia
▪ MCH (AHGE)	– mean cell haemoglobin
▪ HSC	– hematopoietic stem cell
▪ STH	– somatotropic hormone
▪ TF	– Transforming Factor

- TNFα – tumor necrosis factor
- CDLD – chronic diffuse liver diseases
- CNPD – chronic non-obstructive pulmonary disease
- BCI – blood color index
- EPO – renal erythropoietin
- JGA – juxtaglomerular apparatus
- Fi – Farb index
- GATA-1 – intra-core transcription regulator in erythron
- Hb – hemoglobin
- Ht – hematocrit
- NFE-2 – nuclear factor (derived from erythroids 2), 45 kDa

Introduction

The blood system includes:

- Blood and lymph
- Hemopoietic system
- Organs of blood destruction and immunity
- Blood cells being in connective and epithelial tissues

The red blood system is a functional system supporting the normal life-sustaining activity of the body. It is a complex functional structure combining a set of erythrocytes functioning in the blood-stream, organs of their production and destruction together with a complex of receptors, effectors and regulators providing a normal state and restructuring it in accordance with the changing needs of the body.

This system performs the gaseous exchange function and is able to maintain homeostasis in conditions of multiple factor effect due to effective feedback. In addition to gaseous exchange, erythrocytes perform other functions: participate in water-salt metabolism, in blood buffer systems operation, in adsorption of toxins and protein splitting products, in various enzymatic processes and other processes. The red blood system is a part of the general blood system.

Blood consists of plasma and formed elements – erythrocytes, leucocytes, platelets. In one liter of blood, formed elements, mainly erythrocytes, account for men 4,5-5,7x10^{12}/l (Ht 40,7-50,3%), and for women 3,9-5x10^{12}/l (Ht 36,1-44,3%). The amount of blood in a person is 7-8% of his body weight, so about 5 liters of blood in a person weighing about 70 kg.

Blood subtly reflects the effect of various exogenous and endogenous factors on the body. Thus, with anemia, in most cases, the amount of erythrocytes in the blood decreases (Ht is below normal), but the circulating blood volume (CBV) remains normal due to plasma. In this case, due to the hemoglobin deficiency, the oxygen capacity of the blood decreases and hemic hypoxia develops.

With an increase in the number of erythrocytes in the blood against the normal CBV background, excluding some pathology forms, one may talk of compensatory erythrocytosis caused by hypoxia of various genesis, neutralized by increasing in the oxygen capacity of the blood. A significant increase of Ht may indicate an increase in blood viscosity and microcirculation processes disruption.

The blood system diseases by its prevalence, severity and possible consequences pose a serious problem for modern medicine. At the same time, the progress in studying the genesis of the blood system pathology dictates the urgent need to generalize and systematize constantly accumulating material.

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Chapter I

1. The concept of erythron

The term "erythron" was introduced by English therapists Castle and Minot in 1953, they defined it as the entire mass of erythroid cells of the body, inclusive nuclear bone marrow forms, reticulocytes, and mature erythrocytes. As defined by modern functional hematology, erythron combines a totality of erythrocytes functioning in the vascular bed, organs of their production and breakdown with a complex of receptors and effectors that ensure the system constancy and its variation according to the body needs under the specific conditions, as well as the erythrokinetics processes and quantitative characteristics (erythron volume).

It was stated that erythrocytes in the norm do not represent a homogeneous mass of cells detected by a smear or a native erythrocytes preparation microscopy, but form a system in which cells of different age, morphology and functional state are consistently combined. Qualitative differences between individual erythrocytes are found, for example, when determining their resistance to hemolytics of different nature by the dispersion analysis method, etc.

An important characteristic of the blood system physiology and pathology is the quantitative and qualitative composition of the erythrocyte population, one of the most important parts of erythron.

The red blood system is one of the examples of balanced biological systems. In case of the dynamic equilibrium impairment, not only quantitative indicators but also qualitative ones vary – changes occur in the distribution of the cells by diameters, physicochemical properties, biochemical composition. Therefore, the qualitative composition of the erythrocytes population in the vascular bed is an adjustable sign of erythron.

The fundamental difference between erythron and other tissues of the body is that the destruction of erythrocytes is carried out mainly by macrophages due to a process called erythrophagocytosis (Figure 1). The

resulting products of destruction and, primarily, iron, are used to build new cells. Thus, erythron is a partially closed-loop system in which, under normal conditions, the number of erythrocytes destroyed corresponds to the number of newly formed erythrocytes.

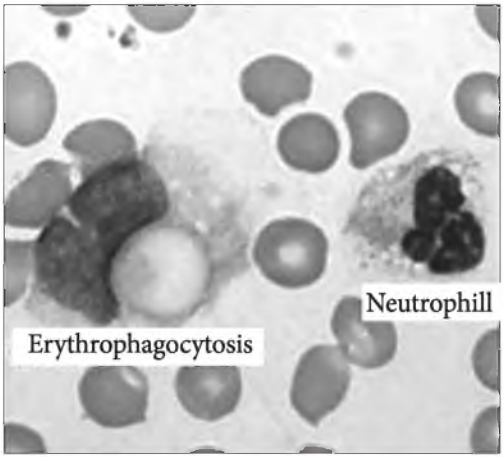

Figure 1. Macrophage with phagocytosed erythrocyte (H.B. Kolesnik, 2010).

Erythrocytes live from 60 to 120 days in the blood flow. The blood cell survival in men is 10-20 days longer than in women.

When the erythrocyte aging, its membrane properties change, and the cationic exchange with plasma is also significantly disrupted. In old erythrocytes, there is a "malfunction" of the antioxidant enzyme system, which is represented by super-oxides mutase, glutathione peroxidase, and catalase, which leads to the strengthening of peroxide oxidation of lipids and acid radicals accumulation. At the same time, the membrane loses sialic acid, which reduces the negative charge of the erythrocyte. Finally, the antigenic composition of the membrane changes at the erythrocyte aging, as antigenic determinants are unmasked, capable to form complexes with immunoglobulins, so those old erythrocytes are recognized by the immune system cells as non-self ones. All these processes lead to the erythrocyte destruction in prospect. Up to 20% of erythrocytes are destroyed as a result of intravascular hemolysis (Fig. 2). At the same time, hemoglobin enters the plasma directly and is bound by a special plasma protein related to $\alpha_2$globulins – haptoglobin. Very soon about half of the generated haptoglobin-hemoglobin complexes leave the plasma and are absorbed by