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ФІЗІОЛОГІЯ – МЕДИЦИНІ, ФАРМАЦІЇ ТА ПЕДАГОГІЦІ: АКТУАЛЬНІ ПРОБЛЕМИ ТА СУЧАСНІ ДОСЯГНЕННЯ

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However, no relation between rise in the electrolytes excretion and activation of the glomerular filtration is seen since no significant changes in the creatinine excretion index were registered. It is interesting that its concentration in urea also stays almost unchanged as it can be found from the water reabsorption index. Therefore, it can be stated that the rising osmomolarity of urea is caused by changes in the reabsorption values for different ions, not by water reabsorption in the distal kidney tubules. Increased excretion of sodium is primarily caused by its lower reabsorption, and yet retarded transportation in the proximal tubules can also be influential for this process. Thus, sodium excretion and concentration are rising 1.5 times averagely under the 3 % salt load.

Experimental investigations involved various groups of animals at 8:00 and 20:00 and almost no difference in the kidney functional conditions was registered. However, the Na^+ ions concentration has risen by 2.24 times comparing to the control group and this index was a little higher in the 8:00 experiment. This is also proved by lowering of the filtration fraction of Na^+.

The salt load results in increase of concentration and excretion of potassium and sodium, ammonia and titrable acids. Changes in the kidney functionality affect tubular reabsorption and activate secretion while they do not depend on the kidney damage.

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SICKLE CELL DISEASE – UNDERLYING PHYSIOLOGICAL FACTORS FOR PROGNOSIS OF OUTCOME AND DEVELOPMENT OF TREATMENT

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Actuality. Sickle cell disease (SCD) affects millions of people throughout the world and is particularly common among those whose ancestors came from sub-Saharan Africa; Spanish-speaking regions in the Western Hemisphere (South America, the Caribbean, and Central America); Saudi Arabia; India; and Mediterranean countries such as Turkey, Greece, and Italy. Sickle cell disease is the most common inherited blood disorder in the United States, affecting 70,000 to 100,000 Americans. The disease is estimated to occur in 1 in 500 African Americans and 1 in 1,000 to 1,400 Hispanic Americans (L.V. Parice et al., 2016). SCD is characterized by intermittent vaso-occlusive events and chronic hemolytic anemia. Vaso-occlusive complications result in tissue ischemia leading to acute and chronic pain as well as injuring of target organs, including the bones, lungs, liver, kidneys, brain, eyes, and joints. Dactylitis in infants and young children is often the earliest manifestation of sickle cell disease. Recently, it has been revealed that initial and subsequent disorders of CNS are the most permanent injuries in children with SCD. About 50 per cent of children with SCD experience either an overt or silent cerebral infarct; hemorrhagic stroke and aneurysm are more common in adults (M.R. DeBroun, 2016). In children a “splenic sequestration” is indication for splenectomy due to the fact that spleen is particularly subject to infarction; so that the majority of individuals with SCD get asplenic in early childhood, increasing their risk for certain types of bacterial infections (Zora R. Rogers et al., 2011).

The aim of our research was an analysis of physiological factors which influence on the clinical course and prognosis of outcome as well as modern approaches of SCD treatment.

Results and discussion:SCD (or β-thalassemia) is inherent disease which arises from series of mutations in the locus of β-globin at the chromosome 11 that impair the synthesis of β-globin chain. Nowadays, it has been described more than 100 mutations leading to the blockage of different stages of gene expression: transcription, processing of mRNA and translation. Promoter mutations limiting mRNA transcription as well as mutations which impair mRNA splicing usually result in reduce of β-chain synthesis (β+ thalassemia). On the other hand, nonsense-mutations at the encoding zone resulting in the premature finishing of β-globin chain synthesis cause the total absence of the latter (D.J. Weatherhall et al., 2000).

Ordinarily, the Hb molecules exist as single, isolated units in the red cell, whether they have oxygen bound or not; and normal red cells maintain a basic disc shape, whether they are transporting oxygen or not. Sickle Hb (HbS) exists as isolated units in the red cells when they have oxygen bound. When sickle Hb releases oxygen in the peripheral tissues, however, the molecules tend to stick together and form long chains or polymers. These rigid polymers distort the cell and cause it to bend out of shape. While most distorted cells are simply shaped irregularly, a few have a crescent-like appearance under the microscope. When the red cells return to the lungs and pick up oxygen again, the Hb molecules resume their solitary existence (J.A. Detterich, 2016).

Polymerization in the microvasculature may cause vaso-occlusion, leading to painful crisis and end-organ damage, particularly in the kidney, lungs, and bone (S.K. Ballas et al, 2005). Repeated Hb polymerization also damages the red blood cell (RBC) structural integrity by mechanical and oxidative stress, lowering RBC deformability and increasing RBC adhesion properties (F.A. Kuypers, 2014; Diana R. Gutsaeva et al., 2014). Abnormal mechanical properties of RBCs, coupled with increased blood flow as a compensation for decreased oxygen-carrying capacity, affect shear forces on the vascular endothelium (L. Belhassen, 2001). The vascular endothelium is also exposed to chemical stressors from intravascular release of Hb and chronic inflammation (G.J. Kato et al., 2007). Together, mechanical and chemical endothelial stressors are thought

to impair endothelial release of, and response to, nitric oxide, thus impairing vasodilatory reserve (J.A. Detterich, 2016).

Although the change to hemoglobin (Hb) is usually simple and uniform (a single amino acid substitution Glu vs Val in the β-globin chain), SCD is characterized by broad differences in clinical manifestation. Phenotype variation in SCA is thought to arise from both environmental and genetic factors (eg, β-gene cluster haplotype, degree of fetal hemoglobin (HbF) expression, or effects of other epistatic genes). The environmental factor that the most clearly influences SCD phenotype is hypoxia, which drives sickle Hb (HbS) polymerization and the resulting well-characterized alterations in RBC physiology and the microcirculation. Moreover, nonpolymerized, solution-phase HbS may promote oxidative stress, even in RBCs under normal physiologic O_2 gradients (Stephan C. Rogers, 2016).

The broad investigations have confirmed the limited abilities of patients with SCD for adaptation to different physiological factors. Thus, exercise and physical activity are known to induce marked metabolic changes, including lactic acidosis, tissue hypoxia and dehydration, all of which predispose towards HbS polymerization and vaso-occlusion. Studies suggest that even moderate exercise can induce significant hypoxia in children with SCD, impaired heart rate recovery, abnormal increases in pulmonary artery pressureand increased oxidative stress.Several studies have reported episodes of sudden death after intense exercise in people with sickle cell trait. Causes of death include rhabdomyolysis, exertional heat stroke and sudden cardiac arrhythmias (Robert I. Liem et al., 2017; Luca D. Carbonare et al., 2015). Nevertheless, the potential adverse effects of exercise have to be balanced against the probable cardiovascular and social benefits, and in general individuals with SCD should be encouraged to participate in exercises and sporting activities (Natalie A. Bello et al., 2017).

Risk factors for individuals with SCD also include dehydration, fluctuations of ambient temperatures and being at high altitudes. In case of dehydration, cells with a markedly increased HbS concentration are a prominent feature of sickle cell disease, as a consequence of the loss of K^+, Cl^- and water from the erythrocyte. The extreme dependence of polymerization kinetics on HbS concentration means that these dehydrated erythrocytes rapidly sickle when deoxygenated. Blockade of K^+ loss from the erythrocyte should, therefore, prevent the increase in HbS concentration and reduce erythrocyte sickling. Detailed knowledge of the mechanisms leading to cell dehydration makes this a viable therapeutic option. Two ion transport pathways, the K^+-Cl^- contraport and the Ca^{2+}-activated K^+ channel play prominent roles in the dehydration of sickle erythrocytes (Fiona C. Brown, 2015).

Extremes of both hot and cold weather have been found to precipitate acute complications. Many patients with SCD report that exposure to cold results in acute pain, usually starting within a few hours. On cold exposure, peripheral vasoconstriction occurs and the velocity of blood flowing through the vasculature of these areas is reduced. This results in greater deoxygenation of blood in the peripheries, and red cells spending a longer period of time in the deoxygenated part of the circulation. HbS polymerization therefore occurs more readily, and more rigid, sickle red cells are produced which subsequently cause vaso-occlusion, presumably in tissues near to the areas exposed to cold. Countering this adverse effect of cold exposure is the fact that the rate of HbS polymerization decreases at lower temperatures; at 20–30°C, a 1°C increase in temperature halves the delay time before hemoglobin gelation starts to occur (S.H. Embury, 2000).

The harmful effects of high altitude in SCD for many years, principally was due to potential problems associated with low oxygen partial pressures in high altitude. The most frequently reported complication at altitude of aircraft above 2000 m is acute splenic infarction in people with SCD (D.J. Weatherhall, 1994). Nowadays, the preflight transfusions or oxygen supplementation are only recommended if a patient has preexisting complications, such as lung or cerebrovascular disease.

A link between cigarette smoking and "acute chest syndrome" in sickle cell anemia is suggested. Acute chest syndrome in the patient with sickle cell anemia is characterized by fever, leukocytosis, cough, chest pain, and pulmonary infiltrates in the chest radiograph. Although the exact mechanism of the relationship between smoking and the development of acute chest syndrome remains speculative, cigarette smoking joins infection, hypoxia, acidosis, infarction, dehydration, and analgesics as a causative factor in adolescent and adult patients with SCD. Behavioral modification of the smoking habit in patients with sickle cell anemia may decrease the frequency of acute chest syndrome and sequelae of sickle cell lung disease (R.C. Young, 1992).

The most usual therapy, which patients with SCD receive, is hemotransfusion for maintenance of Hb level at 90–100 g/L that is critical for normal growth and development of children as well as prophylactic of skeleton deformations. Supporting therapy includes binding and elimination of the excess of iron which results from chronic hemolysis. Progressing of tolerance for hemotransfusions is the indication for splenectomy. Modern therapeutic approaches target the “root cause” of SCD (ie, by replacement of the abnormal hemoglobin), as do stem cell transplantation and gene therapy, or one or more of the many damaging and interwoven pathways responsible for the disease’s cardinal manifestations – episodic severely painful vaso-occlusive episodes, hemolytic anemia, and progressive multiorgan damage (Marilyn J. Telen, 2016). One of the most promising approaches is regulation of fetal hemoglobin (HbF) transcription in adults (I. Akinsheye et al., 2011). It is reported that HbF is the most powerful modulator of the clinical and hematologic features of sickle cell anemia. To protect against various complications of disease, different concentrations of HbF were postulated to be required, although any increment in HbF had a beneficial effect on mortality (O.S. Platt et al.,

1994). Higher HbF levels were associated with a reduced rate of acute painful episodes, fewer leg ulcers, less osteonecrosis, less frequent acute chest syndromes, and reduced disease severity. However, HbF level had a weak or no clear association with priapism, urine albumin excretion, stroke and silent cerebral infarction, systemic blood pressure, and perhaps sickle vasculopathy as estimated by tricuspid regurgitant velocity (M.N. Steinberg et al., 2009). Studies suggest that deoxyHb polymerization is prevented at physiologic venous and capillary O_2 saturations of 40 % to 70 % when HbF/F-cell is 9 to 12 pg. HbS polymer is not present in the erythrocytes of HbS-HPFH, either experimentally or after calculating the HbS polymer fraction at 70% O_2 saturation. HbS polymer is present at 70 % O_2 saturation in sickle cell anemia, and the polymer fraction rises steeply as O_2 saturation falls (M.H. Steinberg et al., 2014).

Conclusions

1. Analysis of reported figures has indicated that patients with SCD have limited abilities for adaptation to different physiological factors.
2. Such physiological factors as physical exercises, hypoxia, dehydration, extreme temperatures and high altitudes have a substantial effect on the clinical course of SCD. These factors are beneficial for polymerization of HbS resulting in progression of sickle RBCs hemolysis, increase of hypoxia severity and oxidative stress that significantly impact disease prognosis and outcome. When these factors are brought under control it will ultimately augment measures aimed at managing the clinical disorders of sickle cell disease.
3. Modern therapeutic approaches focus on stem cell transplantation and gene therapy. HbF reduces polymerization of HbS and protects against various complications of SCD, so that expression of its genes in SCD patients is, perhaps, one of the most promising methods of therapy.

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THE DIRECTIONS OF STUDENT'S HEALTH IN TERMS OF TRAINING LOAD EFFECTS ON THE BODY

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Topicality. The life of a person depends on the state of health of the body and the extent of using its psycho-physiological potential. All aspects of human life in a wide range of social life, industrial-labor, socio-economic, family-household, spiritual, health, and educational – are ultimately determined by the level of health. Health affects the quality of the labor resources, on the productivity of social labor, and thereby the dynamics of economic development of society.

Aim. The level of health and physical development – one of the most important conditions for quality of the workforce. Depending on their indicators: estimating the possibility of human participation in certain areas of labor activity. Therefore, already at the stage of choosing a specialty and type of professional training occurs objectively posed and solved the problem of psycho-physiological personality matching specific types of professional activity.

Results. The state of health is reflected in all spheres of people's lives. Completeness and intensity of the various life manifestations of a person directly depends on the level of health, its "qualitative" characteristics, which largely determine the image and style of life of a person: the level of social, economic and labor activity, the degree of migration mobility of people, familiarizing them with modern cultural achievements, science, art, technics and technology, the nature and ways of leisure and recreation. At the same time, there is an inverse relationship: the style of a person's life, the degree and nature of his activity in everyday life, especially in working life, largely determine the state of his health. Such interdependence offers great opportunities for prevention and promotion of health.

The most widely used now was the functional methods to the study of human health. Its peculiarity lies in the individual's ability to exercise its inherent biological and social functions, in particular, to carry out socially useful labor, productive activity. Their loss is the most common and the most important for a person, family, community, social consequence of human diseases.

The need for health is universal, it is inherent in individuals as well as in society as a whole. Attention to one's own health, the ability to provide individual prevention of its disorders, conscious orientation to the health of various forms of life activity are all indicators of a person's general culture. In recent years, attention has been paid to the healthy lifestyle of students, which is associated with the concern of the public about the health of specialists graduated from higher education, the increase in morbidity in the process of professional training, and subsequent decline in efficiency.

Study of value orientations of students on healthy lifestyle allows you to select among these four groups of probation. The first group includes the absolute, universal values; the students received an assessment of great importance (from 69 % to 93 %). These include: a successful family life, courage and honesty, health, the full development of personality, intellectual abilities, will power and concentration, communication skills, possess the beauty and expressiveness of movements. The second group of "pre-emptive