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A Modern View Of Hemostasis Pathology In The Aspect Of Medical Biology

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Abstract: In our work, we analyzed the problems of hemostasis disorders based on literature analysis.

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Introduction: The hemostasis system is an evolutionarily developed, multi-component protective device of the body. It ensures the processes of formation of a fibrin clot and maintaining blood in a liquid state.

Physiological clot formation and lysis is a series of well-regulated and balanced interactions between plasma factors, enzyme cofactors, their regulators, and various blood cells, as well as the vascular endothelium.

The main mechanism of activation of hemostasis components is limited proteolysis, in which an active enzyme is formed from an inactive precursor, catalyzing the process of blood clotting or lysis of the fibrin clot.

When compensatory-adaptive hemocoagulation mechanisms fail, the process of blood microcoagulation is triggered, which accompanies many pathological conditions, in particular, thermal burns.

Disorders of the hemostasis system occur as disseminated intravascular coagulation (DIC syndrome), the development of which leads to progression, a sharp aggravation, and often an unfavorable outcome of the pathological process.

DIC syndrome is always secondary to a general disturbance of homeostasis. It is characterized by excessive activation of the hemostasis system, leading to excessive thrombin generation (thrombinemia), accelerated intravascular fibrin synthesis with subsequent blockade of microcirculation in target organs. (lungs, kidneys, liver, gastrointestinal tract, brain). In this case, hypoxia, acidosis, and intoxication with various metabolites of protein, lipid, and carbohydrate metabolism develop in the body. DIC syndrome is accompanied by a decrease in anticoagulant potential, depression of fibrinolysis, which leads to the accumulation of fibrin microclots in the bloodstream and the development of multiple organ failure.

The study of DIC syndrome under the influence of a thermal agent on the body began in the 1960-1980s. The data obtained allowed researchers to conclude that DIC syndrome in severe burns is related to disorders in the lungs, kidneys, gastrointestinal tract, etc.).

However, the main methods for studying the hemostasis system in those years were such as determining blood clotting according to Lee and White, prothrombin time, thrombin time, plasma recalcification time, fibrinogen content, and total fibrinolytic activity.

The earliest possible diagnosis of DIC syndrome is a critical task, the successful solution of which is the key to a favorable outcome of the pathological process. Rapid correction of hemostasis normalizes blood supply in parenchymatous organs, restores their function and biosynthesis of biologically active compounds that regulate the coagulation and anticoagulation systems.

Changes in hemostasis system parameters can precede the clinical picture of DIC syndrome by 1-1.5 days, which allows it to be diagnosed at an early preclinical stage. Laboratory tests, on the basis of which the diagnosis of DIC syndrome is made, must meet the

following criteria: informativeness, efficiency and accessibility for clinical practice, as well as the comparative simplicity of the method.

To date, the following tests meet these requirements. 1/. Study of the activity of antithrombin III - the main biological regulator of the hemostasis system, one of the most powerful natural blood anticoagulants, the main physiological inhibitor of thrombin.

Its level in the bloodstream determines the direction of the pathological process in extreme conditions. Determination of AT III activity is a key test for diagnosis and monitoring of therapy of patients with DIC syndrome. 2/. Analysis of the activity of HPA-dependent fibrinolysis. The most "vulnerable" already at the early stages of the formation of DIC syndrome. 3/. Counting the number of platelets, the degree of reduction of which reflects the severity of disseminated intravascular coagulation. 4/. Determination of the content of soluble fibrin-monomer complexes - a marker of activation of intravascular blood coagulation, allowing quantitative determination of the level of thrombinemia. 5/. Identification of fragmented erythrocytes, which contribute to the activation of the coagulation system and are of great importance for the diagnosis of DIC syndrome.

However, in the literature we studied, we did not find any works devoted to a systematic and in-depth study of the dynamics of the indicators of the coagulation and anticoagulation systems of the blood during thermal exposure to the body during shock and acute toxemia using modern research methods.

A comparative analysis of the diagnostic value of each laboratory test for characterizing various links of the hemostasis system has not been conducted. A set of effective laboratory studies sufficient for establishing a diagnosis of DIC syndrome based on the results of blood sample analysis has not been identified.

At present, there are no algorithms for comprehensive diagnostics and assessment of the state of various links in the hemocoagulation system, endogenous anticoagulants and fibrinolysis based on laboratory analysis of blood samples.

Further analysis of the literature showed that the task of the hemostasis system in humans is to prevent blood loss when the integrity of the circulatory system is compromised. The plasma coagulation link is one of the important components of this system, the task of which is to form a gel at the site of damage to prevent fluid leakage.

More than 30 proteins are involved in blood plasma coagulation, interacting with each other to form a huge network of biochemical reactions.

Such a complex system requires appropriate regulation. This leads to the fact that even small disturbances in the delicate balance of pro- and anticoagulant reactions can lead to serious consequences for the body: thrombosis and bleeding.

Hemophilia - the disease of "royalty" - is an old but still relevant disease.

It is noted in the literature that hemophilia is one of the diseases known since ancient times. The first known descriptions of symptoms similar to the manifestations of hemophilia were made in Hebrew in the 2nd century BC.

The authors of literary sources noted the fact that the biblical sages, thanks to the tradition of meticulously tracking genealogies, penetrated into the essence of hemophilia more deeply than doctors and biologists of the early 20th century. Thus, hemophilia as a hereditary disease was described in the Talmud in the 5th century CE, where a description of cases of death of boys from ritual circumcision is given.

A detailed description of hemophilia was made by John Conrad Otto, a researcher from Philadelphia. In 1803, he published his scientific work on the topic of excessive bleeding. While studying the genealogy of one of the families in detail, Otto concluded that there is a hereditary tendency to excessive bleeding in boys.

Later, the famous scientist Johann Lukas Schonlein called this disease "hemorrhage", which in Latin means "tendency to bleed". It is assumed that the students who listened to Schonlein's lectures "christened" the disease with a more euphonious, but meaningless name "hemophilia".

However, it is still generally accepted that the term "hemophilia" was proposed in 1828 by F. Hopff. As an independent disease, hemophilia was described only in 1874 by V. Fordyce. In Russia, a detailed description of this disease belongs to the privat-docent of Moscow University A.P. Poletaev, who in 1913 in the book "Hemorrhagic diseases" described the features of its inheritance and clinical symptoms. A steady increase in the number of patients with hemophilia is noted, which is associated with progress in treatment, patients reaching reproductive age, as well as an increase in the frequency of spontaneous mutations, leading to an increase in the number of patients and carriers of hemophilia.

It is currently known that the genes of hemophilia A and B are localized in the sex X chromosome.

Statistical data have shown that the frequency of hemophilia A in the population is 1 in 10,000, and hemophilia B - 1 in 60,000 births. It is important to note that all other hemorrhagic diathesis are much less

common - 1:500,000.

Hemophilia is a hereditary disease that manifests itself as a deficiency of blood clotting factors VIII (hemophilia type A) or IX (hemophilia type B). This trait is inherited along the X chromosome. Women are carriers of the pathological gene, while it is mainly men who suffer from the disease.

In a woman with hemophilia, both her parents have the abnormal gene in their X chromosome. In a sick man, all sons will be healthy, and all daughters will be carriers. A carrier woman and a healthy father have a 50% chance of having both an affected son and a carrier daughter.

Experts have noted that hemophilia is caused not only by inherited genetic abnormalities, but also by spontaneous mutations. If the disease appears in a family with no history of hemophilia, this variant is called sporadic. The frequency of occurrence of sporadic "new" cases of hemophilia can reach 1/3 of all cases of the disease.

The gene responsible for hemophilia A or B is located on the X chromosome. Hemophilia A is caused by a deficiency or molecular abnormality of the procoagulant portion of factor VIII (antihemophilic globulin) with a recessive, X-linked inheritance pattern.

Hemophilia B is a hereditary coagulopathy caused by a deficiency in factor IX activity (the plasma component of thromboplastin). Like hemophilia A, it is transmitted in an X-linked recessive manner.

To date, the genes controlling the synthesis of factors VIII or IX and responsible for the development of hemophilia have been mapped. It has been established that the gene encoding the synthesis of factor VIII is located on the long arm of the X chromosome in the Xq 28 locus and consists of 26 exons and 25 introns (the mature protein contains 2332 amino acids), and the factor IX gene is located in the Xq 27 locus of the long arm of the X chromosome and consists of 8 exons and 7 introns.

The factor VIII gene is large in size and contains about 186 thousand base pairs of DNA. Defects of this gene can be of different nature: duplications, deletions, frame shifts, inclusions of new bases. In more than half of the cases, nucleotide sequence inversion occurs. The factor IX gene has a size of about 34 thousand base pairs. The incidence of hemophilia type B is 3-5 times lower than type A.

Hemophilia type C, associated with a deficiency of factor XI (PTA factor) of blood coagulation, is also distinguished. It has an autosomal nature of inheritance and is manifested by a mild or moderate tendency to bleeding, but is often asymptomatic.

Hemophilia A is often called the "royal" (less often - "crowned") disease. This is due to the fact that the most famous carrier of hemophilia in history was Queen Victoria. It is assumed that a de novo mutation occurred in her genotype, since hemophiliacs were not registered in the families of her parents. Queen Victoria passed on the mutated gene to her son Leopold (Duke of Albany) and some of her daughters.

This led to the spread of haemophilia in the royal families of Europe, including the royal families of Spain, Germany and Russia. The Queen's grandsons and great-grandsons, born to daughters or granddaughters, suffered from haemophilia, including the Russian Tsarevich Alexei, son of the Russian Emperor Nicholas II.

Hemophilia B as a separate disease was identified only in 1952. This form is often called "Christmas disease" after the name of the first sick boy, in whom its presence was confirmed during examination. There are two types of hemostasis - vascular-platelet (primary) and coagulation. The enzymatic cascade of coagulation hemostasis has internal (contact) and external activation pathways.

Both pathways are closed by the formation of the prothrombinase complex, consisting of factors X (Stewart-Prower) and V (proaccelerin), calcium ions and phospholipid matrices. The external pathway is initiated by tissue thromboplastin (factor II) entering the blood. In laboratory diagnostics, this pathway is assessed using the prothrombin (thromboplastin) test.

Other hemostasis tests that should be performed in individuals suspected of having hemophilia and related disorders include prothrombin time (PT), activated partial thromboplastin time (APTT), bleeding time, and platelet count.

In hemophilia, only APTT will be elevated. It should be remembered that, especially in mild cases of the disease, all laboratory parameters may be normal. This is primarily characteristic of stressful situations (operations, injuries), since back in 1772 it was noted that blood taken after stress clots faster.

Thus, summing up the literature review, it can be said that the above methods allow only a rough identification of gross violations in the blood coagulation system. They do not provide an opportunity to assess the level of thrombinemia, the content of components of the fibrinolytic system, the activity of individual physiological anticoagulants, changes in which underlie microthrombosis.

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