

A SUMMARY OF THE CLINICAL SIGNIFICANCE AND LABORATORY SPECIFICITY OF THE EVALUATION TEST DEFINITIONS

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Currently, the number of laboratory tests by which the various links of blood coagulation are studied exceeds several hundred. However, for the practical physician who is trying to answer questions about the possibility of haemorrhagic complications during surgical interventions, about the cause of bleeding that has already occurred, or about the intensity of intravascular coagulation and the presence of DIC syndrome, as well as about the effectiveness of antithrombotic therapy, the number of laboratory tests is limited to a much smaller number. In this regard, we have subdivided all laboratory tests, with the help of which the state of haemocoagulation is investigated, into several groups depending on the questions posed to the doctor [4,5,6,7,8].

Keywords: *activated partial thromboplastin time, prothrombin time, prothrombin index; clotting factors;*

APTT - activated partial thromboplastin time.

The principle of the APTT method is to determine the clotting time of decalcified plasma after adding a kaolin-kephalin-calcium mixture to it. This mixture activates factors XII, V and VIII of haemocoagulation. Thus, APTT assesses the ability to form fibrin through the sequential interaction of all factors XII, XI, IX, VIII, X, V, II, I. The study is performed using a coagulometer. Manual methods of determination are not standardised and are less accurate. Prolongation of the APTT may occur under the following circumstances:

1. Congenital or acquired defects or deficiencies of factors XII, XI, VIII, VIII, IX, IX, V, X, II, and fibrinogen.;

2. In the presence of antibodies to the listed clotting factors;
3. In Willebrand's disease (severe form);
4. In the presence of inhibitors to phospholipid-dependent reactions, including lupus-type anticoagulants,
5. In the presence of heparin in a blood sample, in overdose of coumarin drugs;
6. In dysfibrinogenemia, or the presence of inhibitors of fibrin polymerization [1,2,3].

APTT is used for screening assessment of the haemocoagulation system, including before surgery, it is mandatory to monitor treatment with unfractionated heparin. The APTT is a baseline study to detect the presence of haemocoagulation inhibitors, including lupus anticoagulant, and to assess the activity of factors VIII, IX, XI and XII. The reagents used must be stable from one sample to another, sensitive to factor deficiencies, reactive to the presence of heparin, and sensitive to the presence of lupus anticoagulant. In addition to universal reagents, reagents can be used that are specially adapted for specific applications, including monitoring treatment with unfractionated heparins and detection of lupus anticoagulants [9,10,11].

Prothrombin time (PT). The prothrombin time measurement is based on the determination of the time of fibrin clot formation in the tested plasma after the addition of thromboplastin-calcium mixture to it. This mixture activates factor VII and ensures the functioning of the external cascade of fibrin formation. As well as the APPT, the study is performed with the help of a coagulometer. Manual methods of determination are not standardised and are less accurate.

Prothrombin time prolongation occurs in:

1. Congenital or acquired deficiency of factors VII, X, V, II and fibrinogen;
2. Vitamin K deficiency;
3. In liver disease;
4. During therapy with indirect anticoagulants;
5. In the presence of inhibitors to the indicated clotting factors and phospholipid-dependent reactions.

The prothrombin test is used to assess the state of the haemocoagulation system, including before surgeries, to assess the state of the liver, to monitor therapy with indirect anticoagulants and to determine the activity of factor VII. The prothrombin time measured in the test can be expressed in seconds or as a percentage of prothrombin according to Quick, which reflects the activity of the entire clotting factor complex involved. The International Normalised Ratio (INR) should be determined to monitor treatment with oral anticoagulants - K antivitamins [9,10].

This requires knowing the International Sensitivity Index (ISI) of the thromboplastin sample with which the test is performed. It is recommended to use thromboplastins with an ISI value of less than 1.5. The presentation of

haemocoagulation results in the form of the patient's prothrombin time compared with its value for normal plasma, or in the form of % prothrombin according to Quick, does not allow standardisation of the study when using different reagents, and thus obtain comparable results in different laboratories [11,12,13,14].

Therefore, these indicators are not recommended for monitoring therapy with oral anticoagulants - antivitamins K. Determination of prothrombin time in capillary blood is possible with the use of combined reagents, which include thromboplastin, fibrinogen and factor V, as well as with the use of special cartridges and portable devices. Calibration of the method for the determination of INR in capillary blood is too labour-intensive for a routine clinical diagnostic laboratory. It is therefore highly desirable that reagents are calibrated by their manufacturer.

Bleeding time. The bleeding time should be determined according to the method proposed by Duke. This involves puncturing the skin at the earlobe, as this is where the skin thickness is the same in the vast majority of cases. Exceptions are those who have had earlobe scarring due to suppuration following earring hole procedures. A stopwatch is started at the same time as the skin puncture and a drop of blood is removed with filter paper as soon as it appears. As soon as a drop of blood does not appear, the stopwatch is switched off and the duration of bleeding is recorded. The Ivy method is more standardised and is widely used abroad. It consists of applying a scratch to the front surface of the forearm. The rest of the procedure is the same. Prolongation of bleeding time indicates a defect in the platelet link of haemocoagulation. This may be as a result of a decrease in the number of platelets or a defect in their qualitative characteristics - the ability to adhere, aggregate, release reaction or retraction of the blood clot. With prolongation of bleeding time, it is necessary to determine the number of platelets in the blood. In the absence of thrombocytopenia, it is necessary to establish thrombocytopathy and make special studies of the functional activity of platelets [14,15,16].

Fibrinogen determination. To determine fibrinogen in clinical practice, several methods are used: weight «dry-air» method (modified by R.A. Rutberg), turbidimetric method, kinetic method using reptilase, or immunological methods. The weight method as modified by R.A. Rutberg does not meet modern requirements and should not be used. The most common is the method of fibrinogen determination according to Clauss. The essence of the method is the interaction of fibrinogen of diluted plasma of the subject with thrombin added in increased concentration (to exclude the effect of antithrombins). Under these conditions, the reaction time of clot formation depends only on the amount of fibrinogen. It is not possible to determine fibrinogen according to Clauss with manual methods (without the use of a coagulometer).

Thrombin time. This test reflects the interaction of thrombin with fibrinogen, the final step in blood clotting. When thrombin is added to the test plasma, the time from

the addition of the reagent to the formation of a clot is measured. Prolongation of thrombin time may result from a decrease in the amount of fibrinogen in the plasma, disruption of the fibrinogen structure (dysfibrinogenemia), the presence in the plasma of heparin or heparin-like substances, direct thrombin inhibitors (hirulog and other hirudin preparations), as well as in the presence in the plasma of other thrombin inhibitors, including fibrin or fibrinogen degradation products.

Barium plasma test. In clinical practice, it is very important to quickly differentiate haemophilia A (factor VIII deficiency) from haemophilia B (factor IX deficiency). In general, the activity of the respective factors is tested using standardised factor-deficient plasmas (deficiency plasmas). In the absence of deficient plasmas, the barium plasma test may be used. The principle of the method is that when barium sulphate is added to the plasma, proteins of the prothrombin complex, which include factors II, VII, IX and X, are adsorbed on it, while other haemocoagulation factors remain quantitatively unchanged in the «barium» plasma. Therefore, the addition of barium plasma to the plasma of a patient with haemophilia A, i.e. with a deficiency or defect of factor VIII, should lead to normalisation of the prolonged APTT time, whereas in the presence of haemophilia B, or defect of factor IX, normalisation of APTT does not occur [17].

Determination of blood fibrinolytic activity. There are several methods for assessing blood fibrinolytic activity. Unfortunately, the accuracy of these methods is achieved by increasing the complexity of their execution. The most popular remains the method of determining the time of euglobulin clot lysis. At the same time, the invention of methods using chromogenic substrates has allowed the wider use of such additional methods as the assessment of plasminogen activator inhibitor and tissue plasminogen activator levels. The value of plasminogen determination is limited to the conclusions about its consumption by the organism to dissolve excessive amounts of fibrin in the vascular bed. From a practical point of view, the activity of blood fibrinolysis can also be judged by the level of D-dimer. Prolongation of the bleeding time with normal values of ACTH and prothrombin time allows to suspect disorders of the platelet link of haemostasis, which may be due to a decrease in the number of platelets in the circulating blood or platelet dysfunction. After establishing prolongation of the bleeding time, which should be determined by puncturing the lobes of both ears, the first step is to count the number of platelets.

Thus, in the absence of thrombocytopenia but prolonged bleeding time, thrombocytopathy, i.e. impaired blood platelet function, should be suspected. In this case, it is necessary to determine which specific platelet function is impaired [18,19].

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