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# Ways to Ensure Safety in the Preparation, Storage and Transfusion of Blood Components in Blood System Diseases

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**Abstract:** This article is devoted to the ways and methods of ensuring safety in the preparation, storage and transfusion of blood components in blood system diseases. The blood transfusion safety system includes work with donors, primary laboratory and virological screening, procurement, storage and clinical use of donor blood components, monitoring of transfusion results and investigation of possible infection cases. A necessary condition for increasing the safety of transfusion is additional testing of donor blood samples for antibodies to the nuclear antigen of the hepatitis B virus, algorithms for checking cases of the initial appearance of infectious symptoms in recipients, and a retrospective review of the event. It describes the detection of signs of viral infections in repeat donors, as well as monitoring the virological status of patients to increase the safety of blood transfusion.

**Keywords:** Blood components, blood system, transfusion, donor, laboratory diagnosis, virus.

## I. INTRODUCTION

Integral parts of the transfusion safety system are administrative measures for the selection of donor personnel, technologies that increase the safety of donor blood during procurement, achievements in laboratory diagnosis of viral infections, as well as reasonable clinical use of components. The main causative agents of infections with parenteral transmission are human immunodeficiency viruses (HIV) types 1 and 2, as well as hepatitis B virus (HBV) and hepatitis C virus (HCV). Almost 40 million people are living with HIV infection, 248 million are living with chronic HBV infection, and 110 million people have antibodies to HCV, of which 80 million have the virus actively replicating. Compared to HIV infection, viral hepatitis B and C are more common infections, 6.7 and 3 times, respectively. HBV and HCV, despite the same target cells and similar clinical manifestations of infections caused by these pathogens, have a number of fundamental differences. This entails differences in the strategy for implementing genetic information and, accordingly, in the pathogenesis of infection both at the level of the affected cell and the entire organism as a whole. Acute hepatitis B is characterized by symptoms of acute liver damage and intoxication, can occur with or without jaundice, and is characterized by a variety of clinical manifestations and disease outcomes. Acute hepatitis C can manifest itself as general malaise, increased fatigue, lack of appetite, and less commonly, nausea, vomiting, jaundice and is accompanied by an increase in the activity of serum aminotransferases [5]. Chronic hepatitis B (CHB), like chronic hepatitis C (CHC), is a long-term inflammatory lesion of the liver that can lead to cirrhosis and primary liver cancer. Clinically, CHB and CHC are manifested by weakness, general malaise, loss of appetite, a feeling of heaviness in the right hypochondrium, enlarged liver, jaundice, increased aminotransferase activity, but in most cases the symptoms of the disease are mild. Of particular interest are latent forms of the disease, as evidenced by the increase in the number of publications on latent HBV and HCV infections in scientific literature databases from 2000 to 2018.

The purpose of this work is to describe a multicomponent system for monitoring the viral safety of transfusions of donor blood components.

## II. LITERATURE REVIEW AND METHODOLOGY

Latent HBV infection was first described in 1978, when a recipient, after a blood transfusion containing antibodies to the HBV core antigen (anti-HBc) in the absence of HBsAg and antibodies to it (anti-HBs), developed acute hepatitis B [6]. In 2008, the European Association for the Study of the Liver introduced the term "latent HBV infection," which meant the presence of HBV DNA in the liver, regardless of its presence in the blood serum, in patients in whom HBsAg is not detected in the blood by available methods [7].

With standard virological screening, the latent form of hepatitis B in a blood donor and its components may not be detected, and blood components collected from such a donor may be transfused to the recipient.

Latent HCV infection was first described in 2004 by Spanish scientist I. Castillo et al. [8], based on a study of 100 patients with liver damage and long-term stable abnormalities in biochemical blood tests. All patients included in the study had a liver biopsy, and in 57% of cases, HCV RNA was detected in the liver tissue using polymerase chain reaction (PCR) with preliminary reverse transcription. The results were confirmed by in situ hybridization: in 48 out of 58 patients, the minus strand of viral RNA was detected in the liver tissue. Since HCV has a positively directed genome, the discovery of the minus strand as a stage in the synthesis of viral genomic RNA confirmed the presence of viral replication. The latent form of HCV infection is determined by the presence of HCV RNA in liver tissue and/or peripheral blood mononuclear cells with multiple negative results of detecting anti-HCV and HCV RNA in peripheral blood and can be asymptomatic.

The range of studies that are included in the standard screening of donor blood is indicated in the regulatory documentation [9] regulating the work of the blood service, and includes the determination of the following viral markers: for HIV this is a combined determination of antibodies and p24/25 antigen, for HBV - the determination of surface antigen (HBsAg), for HCV - determination of total antibodies (anti-HCV). Testing for the presence of viral nucleic acids (HIV RNA, HCV RNA and HBV DNA) is also mandatory. Unlike HIV and HCV, for HBV, when examining donors, antigen and viral nucleic acid are determined, but antibodies are not determined, which are long-term, and in some cases, lifelong evidence of the body's past contact with the virus. Obviously, such a donor examination scheme is incomplete. According to regulatory documentation [9], a history of viral hepatitis is an absolute contraindication to donating blood and its components, regardless of the duration of the disease and the results of treatment. Thus, testing for anamnestic antibodies as an unambiguous fact of previous viral hepatitis B is an obvious need, requiring a revision of the procedure for examining blood donors and its components. The detection of anti-HBs in the blood as the only marker may be the result of specific vaccination against HBV. Antibodies to the HBV e-antigen disappear from the bloodstream over time, so they also cannot serve as an anamnestic marker of past hepatitis B. Thus, of the entire spectrum of antibodies to HBV, the most promising for detecting past HBV are anti-HBc. These antibodies are produced in the body within 2–3 months after the initial infection and are present in the blood for life. According to modern ideas about the pathogenesis of viral hepatitis, after primary infection, elimination of HBV from the body does not occur [10]. The viral genome is stored in hepatocytes most often in the form of a chromatin-stabilized circular covalent closed DNA molecule or in a form integrated into the host genome, which occurs less frequently [10]. The issue of eliminating HCV from the body has not been completely resolved, since there is evidence both for the eradication of the virus after spontaneous recovery and for the persistence of the virus in liver tissue or mononuclear blood cells [11]. Diagnosis of latent forms of HBV and HCV infections is a necessary step for certain treatment programs, including chemotherapy and/or immunosuppressive therapy. With standard laboratory screening, often based only on the diagnosis of HBsAg, less often - HBV DNA, the latent form of HBV in a patient may not be detected. Specific treatment of the underlying disease, including the use of cytostatic drugs, monoclonal antibodies and direct-acting immunosuppressants, can provoke HBV reactivation and the transition of the infection from a latent form to an acutely manifest one, often necessitating interruption of therapy for the underlying disease [12, 13]. Conducting adequate virological screening of a patient is an important aspect of providing high-quality and effective medical care both during the initial visit to the hospital and during treatment.

### III. MULTICOMPONENT SYSTEM FOR MONITORING VIRAL SAFETY OF TRANSFUSIONS

The development of a system for improving the safety of transfusions of donor blood components is complex and involves various stages, from working with donors before the procurement of components and ending with the investigation of cases of possible transfusion transmission of infection. Describing all the stages at which measures and system solutions can be taken to improve safety, we can conditionally identify six main ones presented.

### IV. DISCUSSION AND RESULTS

- 1) Working with donor personnel to improve the infectious safety of transfusions of donor blood components. Administrative measures to select donors from individuals at low risk of infection are an effective method that increases the safety of transfusions even before laboratory tests. Such measures include: attracting gratuitous donors, developing a policy to create comfortable conditions at all stages of donation (reducing queues, the presence of wireless networks in waiting areas, informing after donation via SMS and/or e-mail that there are no deviations in the results of laboratory tests and the fact clinical use of prepared components, which also additionally guides donors to a repeat visit). All of these measures create an environment for the formation of a target group of repeat donors, the procurement of components from which is preferable.



- 2) Primary clinical and laboratory blood testing as part of a system for improving transfusion safety. A primary clinical and laboratory study is carried out before donating blood and its components, and its results make it possible to prevent donors with abnormalities in any peripheral blood parameters from donating. These deviations are a temporary contraindication to donation, with the exception of a repeated increase in serum alanine aminotransferase (ALT) activity by 2 or more times. In addition to routine tests, additional laboratory tests may also be important. Deviations in the leukocyte formula may indicate the onset of an infectious disease caused by a pathogen with parenteral transmission. Below is a description of an observation that illustrates this assumption.
- 3) Increasing the infectious safety of donor blood components at the stage of virological screening. One of the most objective methods of ensuring the safety of transfusions is virological screening of donor blood samples. As stated earlier, for HBV, no antibodies are detected in donors during decretal testing. To eliminate this discrepancy, the Federal State Budgetary Institution “National Medical Research Center of Hematology” of the Ministry of Health of Uzbekistan “The procedure for examining donor blood and rejecting components based on the results of laboratory testing for infectious markers” was developed and introduced into practice in 2014, which includes screening of donor blood for anti-HBc at each donation and exclusion from donation based on the detection of this marker. The introduction of this protocol made it possible to exclude the transmission of HBV to patients with secondary immunodeficiency, despite the high transfusion load [14]. From March 2014 to January 2019 at the Federal State Budgetary Institution
- 4) “National Medical Research Center of Hematology” Ministry of Health was highly Completed 54,007 transfusions to 3,526 patients: 4,609 plasma transfusions, 20,785 - erythrocyte suspension, 27,257 - platelet concentrate and 1,356 - cryoprecipitate. To assess the frequency of detection of infection markers within the framework of the current protocol, 26,113 donations were analyzed: 8,134 (31.1%) from primary and 17,979 (68.9%) from repeat donors, respectively. In 6 blood samples from repeat donors, previously examined for anti-HBc, the appearance of this marker was recorded. Moreover, in 3 cases this was the only marker of HBV. Other markers of HBV, including viral DNA, were also detected in 2 samples, and markers of HIV infection were also detected in 1 sample. The simultaneous detection of anti-HBc and other markers of infection in some donors indicates the possible role of this marker in increasing the sensitivity of the entire set of tests for possible infection of blood components. The simultaneous detection of several markers of infections is reliable evidence of the risk behavior of the donor in general. Analysis of risk indicators for coinfection or superinfection showed that a positive anti-HBc test increases the likelihood of detecting other markers by 3–100 times.

## V. CONCLUSION

Thus, the possibility of transmitting infections through donated blood and its components remains, since there is no way to guarantee complete eradication of infectious agents. At the same time, there is a set of measures to improve the viral safety of transfusions. Activities carried out at different stages differ significantly both in nature and in resource and labor costs. However, all existing measures are not mutually exclusive, but complementary, creating a general system for increasing the viral safety of transfusions of blood and its components. The introduction of new diagnostic markers, in particular anti-HBc, helps to identify latently infected individuals among donors of blood and its components, which reduces the risk of transfusion transmission of infections, including recipients of multiple transfusions who are in a state of immunodeficiency. An indispensable condition for effective monitoring of transfusion safety is the full identification of primary infected individuals among recipients of blood components and the implementation of a set of measures to investigate the possible causes of the infection.

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