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Mini Review Article

Infectious Disease Testing of Blood Donors in the United States: An Educational Review

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Abstract

While the infectious disease risks of blood transfusion are very low and have never been lower, they are not zero. Moreover, this magnitude of safety is an achievement that is often taken for granted, and the process of ensuring the safety of the blood supply is often overlooked or addressed superficially when obtaining consent from patients in advance of transfusion. We review the key aspects of this process in the United States.

Introduction

Transfusion of red blood cells is an acute treatment to increase the blood's oxygen carrying capacity in order to maintain organ and tissue oxygenation. [1] Broadly speaking, indications include symptomatic anemia as well as acute hemorrhage. [1] A common step before transfusion is to obtain informed consent, but the information imparted is sometimes superficial and even outdated or erroneous. [2] Thus, physicians should pursue continuing medical education about the infection risks of transfusion both for the weighing or risks and benefits for their own medical decision making and for educating the patient while obtaining informed consent. One key aspect is the testing of blood donors to minimize infection transmission risk. Our goal is to review the highlights of this process.

Donor Health Questionnaire

The United States relies on nonremunerated volunteer donors for its blood product supply. [3] Prospective blood donors complete an extensive donor health questionnaire (DHQ) prior to donation. [4] Screening questions in the DHQ assess well-being, vaccinations, medical conditions, medications, travel history, and risk behaviors. The DHQ also includes questions that screen for agents that are biologically tested in blood products in the United States such as malaria and prion disease. [5]

Blood products are only collected from volunteer donors determined to be low-risk based on the DHQ. [4] Moreover, the biologic tests have limitations including less than perfect sensitivity including the possibility of a window period infection. [5] Thus, in some ways, the DHQ is the most important screening "test" even though it is not a laboratory test. We hasten to add that one critical limitation of the DHQ is that it relies on

the prospective donor's honesty. [6]

We emphasize that the screening value of the DHQ is critically important and should be included when obtaining consent and making transfusion decisions. However, the details of the DHQ and the donation deferrals for providing certain answers to certain questions are beyond the scope of this article on biological testing. For details, we refer the reader to an excellent recent review. [7]

Overview of Infectious Disease Testing

After donation, a sample of donor blood is tested for immunohematology compatibility as well as infectious disease screening. [8] Infectious disease screening of blood products can be separated into two categories: 1) serological testing to detect antibody and/or antigen levels (performed individually for each donor sample), and 2) nucleic acid testing (NAT) to detect infection-associated DNA or RNA (may be pooled with multiple donor samples to increase cost-effectiveness). [8]

The selection of specific tests for each infectious agent is done based on cost, availability, specificity, and sensitivity. [8] Cost-effective and high-sensitivity tests are preferentially chosen for initial screening followed by highly specific tests for confirmatory testing of initially positive samples. [8] Only non-reactive blood products are released for medical use. [8]

Testing is performed for many, but not all, infectious agents transmissible through blood product transfusion. [5] Decisions on specific agents to test are made based on prevalence in donor populations, transmissibility through transfusion, severity of the disease, and testing availability, quality, and feasibility. [5] The infectious agents tested for in the United States as of October 2021 and their approximate risks are outlined in Table 1. [8] While the risks are not zero, they are very small, and blood products have never been safer. [8]

Bacterial Contamination

Perhaps surprisingly, the highest risk of a transfusion-transmitted infection is from bacterial contamination not viruses or any of the agents in Table 1. If bacterially contaminated blood products are transfused, there is a risk of a septic reaction that can be fatal in vulnerable patients. [5] Platelets are at highest risk because they are required by the FDA to be stored at room temperature. [9] The incidence of bacterial contamination

of platelets is roughly 1 in 2,000 compared to 1 in 30,000 for red blood cells. [10]

Approximately 80% of bacterial contamination of blood products occurs from the skin of donors. [11] The most common organisms implicated in septic reactions due to bacterial contamination of platelets are coagulase-negative Staphylococci such as Staphylococcus epidermidis. [11] The most common organism implicated in septic reactions due to bacterial contamination of red blood cells is Yersinia enterocolitica. [11]

Blood banks and blood donor centers are required to implement strategies to prevent and detect bacteria. Numerous strategies are used to decrease the risk of bacterial transmission at different stages. The DHQ is used to exclude prospective donors presenting on the day of donation with fever or symptomatic infections. [11] Skin sites, the most common source of bacterial contamination, are decontaminated prior to phlebotomy using iodine or chlorhexidine. [11]

In addition, the initial volume of blood collection (approximately 50 mL) has the highest risk of skin contamination and is diverted away into a diversion pouch instead of going into the product to be used for transfusion. [11] Donors are also instructed to inform the donor center if they feel unwell in the days following donation in case they could have had sub-clinical bacteremia at the time of donation. In such cases, the medical director of the donor center can decide to have the donated product(s) discarded.

Infectious agent	***Mechanism of testing***	***Estimated Risk of Transfusion Transmission***
Human immunodeficiency virus 1	Antibody serology and NAT	1:2,000,000
Human immunodeficiency virus 2	Antibody serology	
Hepatitis C virus	Antibody serology and NAT	1:2,000,000
Human T-lymphotropic virus 1/2	Antibody serology	1:3,000,000
Hepatitis B core antigen	Antibody serology	1:1,700,000
Hepatitis B surface antigen	Antigen serology	
Hepatitis B virus	NAT	
West Nile virus	NAT	Rare with testing, 1 case per year
Zika virus (discontinued 5/2021)	NAT	No cases reported in the United States
Babesia (in endemic states)	NAT	1:20,000 (endemic) to 1:1,000,000 (national)
Trypanosoma cruzi (performed on initial donation)	Antibody serology	No cases reported since routine testing
Treponema pallidum	Antibody serology	Last reported case in 1966

Table 1: FDA-required tests for blood donors in the United States and risks of transmission.

Pathogen Inactivation

Finally, another recent advancement is pathogen inactivation. The method called photoactivation involves the adding of a photosensitizer such as a psoralen followed by treating the unit with ultraviolet A light. [5] The bacterial load can be decreased in platelet products by using pathogen inactivation treatments. [11] Alternatively, the method of adding a solvent/detergent effectively inactivates enveloped viruses. [5] In sum, these and other pathogen inactivation methods decrease bacterial contamination of platelets, inactivate parasites and viruses, and decrease risks associated with emerging pathogens and unknown pathogens. [5]

Teaching Points

- Blood transfusion confers a risk of infection transmission. Numerous strategies have been employed to decrease these risks while maintaining the blood supply.
- Even though it is not a biologic test, the pre-donation donor health questionnaire (DHQ) is a vital screening tool for prospective blood donors.
- Negative results from tests for infectious agents in donated blood are required to release blood products for allogeneic use in standard medical practice.
- Tests are required in the United State for HBV, HCV, HIV, HTLV, T pallidum, WNV, Babesia (endemic states), and T cruzi (first donation).
- The risks of HBV, HCV, HIV, and HTLV are roughly one in 1-3 million each.
- The risk of Babesia is higher than this range in certain endemic states.
- The risks of T pallidum, T cruzi, and WNV are lower.
- The highest risk of transfusion-transmitted infection is bacterial contamination.
- Platelet products are required by the FDA to be stored at room temperature and have a higher rate of bacterial contamination than red blood cells.
- The most common organisms implicated in septic reactions from platelets are coagulase-negative Staphylococci such as Staphylococcus epidermidis.
- The most common organism implicated in septic reactions from red blood cells is Yersinia

enterocolitica.

- The risk of bacterial contamination can be decreased by the DHQ, skin decontamination, diversion pouches, screening for bacteria, pathogen inactivation, and post-donation notifications of changes to the donor's health.

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