EDUCATIONAL COMMENTARY – BLOOD DONOR CENTER: RECENT FDA UPDATES

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Learning Outcomes

On completion of this exercise, the participant should be able to

- understand the purpose of FDA guidance for industry;
- know the latest Zika virus regulations for blood donors;
- know the most up-to-date minimum hemoglobin criteria for donors and the reason for changing them; and
- know the importance of changing the MSM deferral to 1 year.

Introduction

The U.S. Food and Drug Administration (FDA) issues guidances for blood banking establishments to update the industry on current recommended and required practice changes. Within a blood collection facility or blood donor center, this generally involves changes to donor deferral policies. These changes are often the result of new research or the emergence of a new disease. New research and suggested changes are presented in advisory meetings and FDA public workshops where the changes are eventually voted on by the FDA committee members and, if passed, put into effect as recommendations or guidances for the industry to follow. Several important FDA recommendations or guidances have been released in recent years. This commentary will focus on the FDA’s recommendations concerning the Zika virus, minimum hemoglobin criteria for blood donors, and the removal of indefinite deferral for men who have sex with men (MSM) as blood donors.

Zika Virus

The Zika virus is an arbovirus originally isolated from the rhesus monkey in the Zika Forest of Uganda. Zika infection is an exanthematous disease that is primarily transmitted through the bite of an infected *Aedes* species mosquito.\(^1\) The virus is also spread between humans through sexual intercourse and blood transfusions from infected individuals. The virus was first isolated in 1947, and after its discovery was isolated from humans in Africa and Asia. It was not until 2007 that the virus was isolated outside these continents, in Micronesia. It continued to spread globally, to French Polynesia in late 2013, Brazil in 2015, and the continental United States in July 2016.\(^2\) Zika virus became world-known when the World
Health Organization confirmed the link between Zika and the birth defect microcephaly in February 2016, declaring the Zika virus an international public health emergency. In response to the recent Zika outbreak, the FDA has published several industry guidance documents. The initial FDA guidance, published in February 2016, called for the deferral of blood donors based on their symptoms, travel history, and sexual history. Based on their responses to a series of Zika-related questions, potential donors could be deferred for 4 weeks. The most recent guidance, published in August 2016, states that blood products from all donors must be tested using nucleic-acid testing technology or undergo pathogen reduction using an FDA-approved device. There is currently no FDA-approved test for donor testing for the Zika virus. Testing in blood donors was approved using an investigational screening test under an investigational new drug exemption. If a donor tests positive for the Zika virus, the recommended deferral time is 120 days, or until symptoms resolve, whichever is longer. This August 2016 guidance replaces all previous Zika guidances, thus eliminating the need for donor centers to ask donor history questions covering Zika. To implement the change, donor centers were divided into three groups and given one of three implementation deadlines including immediate, 4 weeks, and 12 weeks, depending on Zika risk in the area. By the end of November 2016, all donor centers in the United States will have to meet the testing or pathogen-reduction criteria. The FDA only approves pathogen-reduction technology (PRT) for platelets and plasma. There is no PRT available for red blood cells.

Hemoglobin Requirements

A change to the longstanding minimum hemoglobin requirement for donors was first proposed in the 2007 FDA Proposed Rule. It was not until the November 2011 public workshop, “Hemoglobin Standards and Maintaining Adequate Iron Stores in Blood Donors,” that the decision was finally made through a unanimous vote to change the minimum standards for male hemoglobin levels. Before this change, the minimum hemoglobin requirements for both males and females was 12.5 g/dL. According to the FDA Final Rule published May 22, 2015, the minimum hemoglobin concentration for female donors will remain at 12.5 g/dL, or a hematocrit of 38% or greater, but the minimum hemoglobin concentration for male donors will be increased to 13.0 g/dL, or a hematocrit of 39% or greater. This is the first time since 1958 that the hemoglobin and hematocrit threshold for blood donation has been changed.

One evidence-based recommendation for change in minimum hemoglobin levels was presented as a result of 2008 research by Barbara Bryant, who conducted a study comparing finger-stick hemoglobin levels with iron status of both male and female donors. The study found that 10% of women with a hemoglobin level of less than 12.5 g/dL were iron deficient, while 46% of men were iron deficient at a hemoglobin level of 12.5 g/dL. Although men have greater iron stores, at about 1 gram, compared to women, who have about 350 mg, once a man’s hemoglobin concentration reaches the previous blood donation cutoff of 12.5 g/dL they are almost five times more likely to be iron deficient than a woman with...
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the same iron concentration.\textsuperscript{7} It is this finding that led to the recommendation to raise the male minimum hemoglobin to 13 g/dL.

Human Immunodeficiency Virus and MSM

In December 2015, the FDA published a revised recommendation for reducing the risk of human immunodeficiency virus transmission (HIV) through blood and blood products. The FDA recommended that blood collection facilities change the donor deferral time for men who have sex with men from indefinitely to 12 months since the last sexual contact with another man.\textsuperscript{8} This decision takes into account many years of research as well as the vast improvements in technology used to detect HIV. AIDS was first recognized in the early 1980s and the first blood-donor deferral policy was enacted in 1983. The initial policy was based on an early understanding of risk factors for contracting AIDS and was composed only of a questionnaire to defer donors who fell into the at-risk category. It was not until 2 years later that the first screening tests for HIV were approved. Until the 2015 FDA guidance, the indefinite deferral for MSM remained in place.

The FDA reviewed a variety of quantitative and qualitative studies when determining if changing the MSM deferral length would improve the safety of the blood supply. The current risk for acquiring an HIV infection from a blood transfusion is 1 in 1.47 million transfusions.\textsuperscript{9} Even with such a minimal risk, the current research shows that there is still room for improvement. One of the considerations for the change was an operational assessment of quarantine-release errors. If the deferral period is changed to allow potentially HIV-positive individuals to donate blood, it is essential that there be strict rules and policies in place that prevent donated blood from being released from quarantine before infectious disease testing is completed. On review of the FDA-reported errors, it was found that quarantine-release errors that led to a patient acquiring HIV are extremely rare due to advances in computerized inventory management.\textsuperscript{10} The development of nucleotide amplification test technology has significantly lowered the number of false-negative results by narrowing the window period of detectability. The current window period, the time between infection and detectability, is approximately 9 days. The likelihood that an individual would donate blood during this 9-day period is low, and some have even suggested that this negates the need for a deferral period.\textsuperscript{8} However, the current rate of new HIV infections in the United States is 50,000 a year, so research suggests that completely eliminating the deferral time could increase the blood transfusion–acquired HIV infections four-fold.\textsuperscript{8}

Another important concern is donor honesty when filling out a donor history questionnaire. A study review found that many MSM find the indefinite deferral policy to be inappropriate and discriminatory, so they donate despite the rules telling them they cannot.\textsuperscript{11} This practice places the blood supply at risk because of the tendency to lie before donating blood. The same group of individuals who participated in the study also said that they would be more understanding and less likely to lie if the deferral time was reduced to one year. The most convincing evidence that changing the MSM deferral length to one year
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would increase the safety of the blood supply comes from a study in countries that have changed their deferral period. These countries include Argentina, Australia, Brazil, Hungary, Japan, Sweden, and the United Kingdom. Australia has seen a drastic increase in compliance since institution of the one-year deferral period for MSM, with a compliance rate for deferrals at more than 99.7%.12 The current literature review and data analysis has led to the change in MSM deferral length from indefinitely to one year from the last MSM sexual contact.

Summary

FDA regulations and recommendations with regard to the blood supply are in place to maintain the safest blood supply possible and maintain the safety of blood donors. The regulations are constantly reviewed and updated as new research becomes available. At the time this commentary is published, the three most recent FDA industry guidance documents should all be in effect at blood establishments around the country.

References


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