Advancing Transfusion and Cellular Therapies Worldwide

Association Bulletin #16-03

Date: February 1, 2016
To: AABB Members
From: Donna M. Regan, MT(ASCP)SBB – President
Miriam A. Markowitz – Chief Executive Officer
Re: Zika, Dengue, and Chikungunya Viruses

Summary
This bulletin was developed by the AABB Transfusion-Transmitted Diseases (TTD) Committee in response to the ongoing outbreaks of Zika virus disease in Mexico, the Caribbean, and Central and South America. It is intended to provide the rationale for blood community action to address the potential threat to blood recipients. The focus of this bulletin is Zika virus, but the measures described should also be effective for chikungunya and dengue viruses. This Association Bulletin supersedes #14-03, which described postdonation information (PDI) and actions for chikungunya and dengue viruses. Included herein are:

- Information about the potential for transfusion-transmitted Zika infection.
- A recommendation to facilitate self-deferral of donors who have traveled to countries that are already experiencing Zika epidemics or those that are likely to experience such epidemics in the near future (see Attachments 1 and 2).
- Educational PDI materials and recommendations for use by blood collection organizations relevant to Zika, dengue, and chikungunya viruses (see Attachments 1 and 2).
- Considerations for the collecting facility in response to PDI reports (see Attachments 1 and 2).

Association Bulletins, which are approved for distribution by the AABB Board of Directors, may include announcements of standards or requirements for accreditation, recommendations on emerging trends or best practices, and/or other pertinent information. This bulletin contains recommendations.

This bulletin applies to AABB members whose collection activities are not in locations currently listed on the Zika-Affected Areas web page maintained by the Centers for Disease Control and Prevention (CDC), http://www.cdc.gov/zika/geo/index.html.

Background
Zika, a flavivirus, is transmitted by *Aedes* mosquitoes, most commonly by *A. aegypti*. This same vector, in addition to *A. albopictus,* transmits dengue (another flavivirus) and chikungunya (an alphavirus).

Zika virus was first described in Africa and spread eastward to cause epidemics in the Pacific starting in 2007 on Yap Island, with subsequent spread in 2013 to French Polynesia and beyond. In 2015, Zika was recognized in Brazil and local (autochthonous) transmission has subsequently been reported in more than 20 countries and territories in the Western Hemisphere including Mexico, the Caribbean, and Central and South America, with its geographic extent increasing rapidly in the region. Travel-associated cases have been reported to CDC for several years, but the only vectorial transmissions in the United States have been in the Commonwealth of Puerto Rico and the US Virgin Islands. Outside of these areas, Samoa and Cape Verde have also reported local transmission and further expansion is to be expected. (Note: malaria is endemic in Cape Verde.)

When symptomatic, Zika infection typically causes a mild dengue-like illness with fever, myalgia, rash, retro-orbital pain, and prostration, that is characteristic of most recognized cases in the current pandemic. Asymptomatic infection occurs in approximately 80% of Zika- (and dengue-) infected individuals. The opposite is true for chikungunya infection where the majority of infected individuals exhibit symptoms, including prolonged arthralgia or joint pain.

- Over 1.7 million chikungunya clinical cases occurred in the Americas, as reported by the Pan-American Health Organization during the 2013-15 outbreak.
- Over 2.3 million dengue clinical cases occurred in the Americas during calendar year 2015.
- To date the exact number of Zika infections is unknown but the number of clinically recognized cases is estimated to exceed hundreds of thousands. Of great concern is the apparent epidemic of microcephaly, a devastating neurodevelopmental abnormality, co-located in space and time with the ongoing Zika epidemic in Brazil There is concern that this may be a consequence of maternal infection and transmission to the developing fetus, an association that is unique for a flavivirus. Zika infection has been confirmed by detection of Zika RNA in the fetus or amniotic fluid in a small number of these cases. CDC has issued a travel advisory recommending that pregnant women avoid travel to areas experiencing a Zika outbreak. In addition, during the French Polynesian outbreak, there was a 20-fold increase in the number of reported Guillain-Barré syndrome cases.

The risk posed by Zika virus to the blood supply is unclear, but the potential for transfusion transmission of Zika virus was suggested when 2.8% of blood donors tested positive for Zika RNA during the French Polynesian outbreak. The maximum duration of viremia is unknown but believed to be less than 28 days. Although rigorous proof of transfusion transmission is lacking, there is a credible case undergoing evaluation in Brazil. The high volume of travel between the United States or Canada and Mexico, the Caribbean, or Central or South America will place many US and Canadian travelers at risk for Zika virus infection as this situation evolves. This raises the possibility that, following travel, infected donors who are asymptomatic will present to donor centers and viremic donations will be collected, processed, distributed, and transfused.

In addition, incompletely characterized risks from transfusion persist for chikungunya virus as well as other pathogens causing outbreaks outside of the United States and Canada. Several transfusion-transmission clusters associated with dengue viruses have been documented .

Table 1 provides data from two nationwide surveys (generated by the AABB TTD Committee and administered by America's Blood Centers and the American Red Cross) of more than 50,000 donors in the summer of 2014 (August-September) and winter of 2015 (February), estimating the amount of donor travel to various regions. The results of the survey administered in the winter indicated that 2.25% of otherwise fully qualified donors had travelled in the Western Hemisphere outside of the United States and Canada in the 28 days before their donation.

Table 1. Percent of Presenting, Otherwise Acceptable, Donors Who Would Be Deferred for Travel in Mexico, the Caribbean, or Central or South America

	Travel within 14 Days		Travel within 28 Days	
	Summer Results	Winter Results	Summer Results	Winter Results
Mexico	0.19%	0.40%	0.52%	0.92%
Caribbean	0.16	0.48	0.48	1.18
C. America	0.02	0.13	0.06	0.26
S. America	0.03	0.07	0.07	0.20
Any of above	0.39	0.97	1.17	2.25

Spenser BR, Stramer SL, Dodd RY, et al. Survey to estimate donor loss to 14- or 28-day travel deferral for mitigation of CHIKV, DENV and other acute infections. Presented at AABB Annual Meeting, Anaheim, CA, October 24-27, 2015.

Options to Reduce the Potential Risk of Transfusion Transmission

Use of the current donor history questionnaire will identify and disqualify symptomatic donors. However, there is no regulation, guidance, or standard focused on reducing the risk of Zika, chikungunya, or dengue virus transmission from asymptomatic donors.

Current donor history and deferral criteria for travel to countries and areas where malaria is endemic identify some of the regions affected by Zika virus outbreaks. However, because malaria is not endemic in many of the outbreak sites, the malaria deferrals alone are not sufficient to address this potential risk.

Self-deferral from donation until 28 days after travel to Mexico, the Caribbean, or Central or South America should be an effective measure to reduce the risk posed by Zika virus transfusion transmittion. It is expected to result in the loss of approximately 2.25% of otherwise acceptable donors during the winter months when such travel is more common than in the summer months. It can be implemented more rapidly than a deferral based on the addition of a question to the donor history questionnaire. Thus, at this time, self-deferral is recommended. The attached materials can be used to inform donors of the need to delay donation after such travel.

Some blood collection programs outside the United States (and a limited number of US blood centers) have implemented more extensive temporary donor deferrals, based on use of a question, following travel to any and all countries in the tropics—including those areas in which malaria is not endemic. The use of temporary donor deferrals will help mitigate potential risk from Zika—as well as dengue, chikungunya, and other endemic or emerging acute viral

infections—by preventing donation until resolution of any asymptomatic viremia. As proposed in this Bulletin, the use of donor information sheets to enhance postdonation symptom reporting to blood centers will facilitate quarantine and recall of potentially infectious components from ill donors with exposure in epidemic settings throughout the tropics.

There are no licensed blood donor screening tests in the United States to identify Zika, chikungunya, or dengue RNA. Pathogen reduction technologies approved by the Food and Drug Administration have been shown to be effective for reducing arboviral loads and infectivity in platelets (West Nile, dengue and chikungunya viruses) and plasma (West Nile, dengue, chikungunya and Zika viruses).

Information Materials for Donors and Blood Centers

The attached materials were developed by the AABB TTD Committee and are recommended as an addition to donor materials already in use. Collection facilities may elect to use these materials to alert donors to the need for self-deferral after travel to Mexico, the Caribbean, or Central or South America (Attachment 1) and to educate blood donors about the major symptoms consistent with acute tropical infections, including Zika (Attachment 2) in case they experience these symptoms following donation. All tropical areas outside of the United States and Canada are included in the Postdonation Information Sheet because the full extent of the expanding Zika outbreak is unknown. In addition, the blood center information provides considerations for managing donations identified in PDI reports.

Recommendations

At this time, the AABB TTD Committee recommends the following immediate actions:

- Blood collection facilities should implement self-deferral for travel to Mexico, the Caribbean, or Central or South America during the 28 days before donation due to concerns regarding the rapid spread of Zika virus infection. Blood-center-documented donor deferral is not required at this time.
- Donors who do not self-defer are asked to call the blood collection facility if they travelled to Mexico, the Caribbean, Central or South America, or other tropical areas and develop unexplained postdonation illness inclusive of two or more of the listed symptoms—common to Zika, dengue, and chikungunya virus infection—in the 14 days following donation.
    - It is advisable for facilities to recall nontransfused products in the event that an infected donor reports experiencing two or more of these symptoms.
    - If a blood collection facility receives a postdonation report of a confirmed case of Zika, dengue, or chikungunya virus infection, the collection facility should recall any in-date products collected in the 14 days before the onset of symptoms and defer the donor for 28 days following resolution of symptoms.

Suggested Reading

Appassakij H, Promwong C, Rujirojindakul P, et al. The risk of blood transfusion-associated chikungunya fever during the 2009 epidemic in Songkhla Province, Thailand. Transfusion 2014;54:1945-52.

Appassakij H, Khuntikij P, Kemapunamanus M, et al. Viremic profiles in asymptomatic and symptomatic chikungunya fever: A blood transfusion threat? Transfusion 2013;53:2567-74.

Aubry M, Richard V, Green J, et al. Inactivation of Zika virus in plasma with amotosalen and ultraviolet A illumination. Transfusion 2016;56:33-40.

Bogoch II, Brady OJ, Kraemer MUG, et al. Anticipating the international spread of Zika virus from Brazil (letter). Lancet 2016;387:335-6.

Brouard C, Bernillon P, Quatresous I, et al. Estimated risk of chikungunya viremic blood donation during an epidemic on Reunion Island in the Indian Ocean, 2005-2007. Transfusion 2008;48:1333-41.

Centers for Disease Control and Prevention. CDC A-Z Index. [Available at: http://www.cdc.gov/az/a.html (accessed January 27, 2016).] (For full range of CDC publications on chikungunya, dengue and Zika viruses.)

Chiu C, Bres V, Yu G, et al. Genomic assays for identification of chikungunya virus in blood donors, Puerto Rico, 2014. Emerg Infect Dis 2015;21:1409-13.

Duffy MR, Chen T-H, Hancock WT, et al. Zika virus outbreak on Yap Island, Federated States of Micronesia. N Engl J Med 2009;360:2536-43.

Enserink M. An obscure mosquito-borne disease goes global. Science 2015;350:1012-13.

European Centre for Disease Prevention and Control. Rapid risk assessment: Microencephaly in Brazil potentially linked to the Zika virus epidemic—24 November 2015. Stockholm, Sweden: ECDC, 2015.

Emerging Infectious Diseases Working Group. Chikungunya virus. Bethesda, MD: AABB, 2014. [Available at http://www.aabb.org/tm/eid/Documents/chikungunya-virus.pdf (accessed January 27, 2016).]

Emerging Infectious Diseases Working Group. Dengue Viruses (with comments on Zika virus, another mosquito-borne flavivirus). Bethesda, MD: AABB, 2014. [Available at: http://www.aabb.org/tm/eid/Documents/dengue-viruses.pdf (accessed January 27, 2016).]

Fauci AS, Morens DM. Zika virus in the Americas—Yet another arbovirus threat. N Engl J Med 2016 (in press). [Available at http://jama.jamanetwork.com/article.aspx?articleid=2485361 (accessed January 28, 2016).]

Gourinat A-C, O'Connor O, Calvez E, et al. Detection of Zika virus in urine. Emerg Infect Dis 2015;21:84-6.

Hennessey M, Fischer M, Staples JE. Zika virus spreads to new areas—Region of the Americas, May 2015-January 2016. MMWR Morb Mortal Wkly Rep 2016;65(3):1-4.

Herriman R. Transfusion-associated Zika virus reported in Brazil. Outbreak News Today, December 18, 2015. [Available at: http://www.outbreaknewstoday.com/transfusion-associated-zika-virus-reported-in-Brazil-76935/ (accessed January 27, 2016).]

Liumbruno MG, Calteri D, Petropulacos K, et al. The chikungunya epidemic in Italy and its repercussion on the blood system. Blood Transfusion 2008;6:199-210.

Matos D, Tomashek K, Perez-Padilla J, et al. Probable and possible transfusion-transmitted dengue associated with NS1 antigen–negative but RNA confirmed-positive red blood cells. [Available at: http://onlinelibrary.wiley.com/doi/10.1111/trf.13288/full (accessed January 27, 2016).]

Musso D, Nhan T, Robin E, et al. Potential for Zika virus transmission through blood transfusion demonstrated during an outbreak in French Polynesia, November 2013 to February 2014. Euro Surveill 2014;19(14):pii=20761.

Pan American Health Organization. Chikungunya: PAHO/WHO Data, Maps and Statistics [Available at: http://www.paho.org/hq/index.php?option=com_topics&view=article&id=343&Itemid=40931&lang=en (accessed January 27, 2016).]

Pan American Health Organization. Dengue: PAHO/WHO Data, Maps and Statistics. [Available at: http://www.paho.org/hq/index.php?option=com_topics&view=rdmore&cid=6290&Itemid=40734&lang=en (accessed January 27, 2016).]

Pan American Health Organization. Zika: PAHO/WHO Data, Maps and Statistics. [Available at: http://www.paho.org/hq/index.php?option=com_topics&view=article&id=427&Itemid=41484 (accessed January 27, 2016).]

Sabino E, Loureiro P, Lopes M, et al. Transfusion-transmission of dengue virus and associated clinical symptomatology during the 2012 epidemic in Brazil. [Available at: https://jid.oxfordjournals.org/content/early/2015/07/09/infdis.jiv326.full (accessed January 28, 2016).]

Schuler-Faccini L, Ribeiro EM, Feitosa IML, et al. Possible association between Zika virus infection and microencephaly—Brazil, 2015. MMWR Morb Mortal Wkly Rep 2016;65(3):1-4.

Spencer B, Stramer S, Dodd R, et al. Survey to estimate donor loss to 14- or 28-day travel deferral for mitigation of CHIKV, DENV and other acute infections. (abstract) Transfusion 2015;55:3A.

WHO reaction to Zika virus – Americas, Asia (web posting). Brookline, MA: International Society for Infectious Diseases, 2016. [Available at: http://www.proMEDmail.org (accessed January 29, 2016).]

Attachment 1

What is the purpose of the Donor Self-Deferral Information Sheet to Reduce the Risk of Transfusion-Transmitted Zika?

Although the level of risk for transfusion-transmitted Zika virus infection is not understood, the following are notable considerations:

- There are severe consequences of Zika virus infection for fetuses.
- Zika RNA has been detected in otherwise qualified donors.
- A probable case of transfusion transmission of Zika virus has been reported in Brazil.
- There is a risk that an infectious unit could be transfused to a woman during a recognized or unrecognized pregnancy, to a fetus via intrauterine transfusion, or to recipients otherwise susceptible to severe morbidity.
- Zika virus has spread rapidly in the Western Hemisphere outside the United States and Canada.

Therefore, it is a prudent precaution to ask donors who have travelled to countries in the Western Hemisphere with, or at risk for, Zika epidemics (Mexico, the Caribbean, and Central and South America) to refrain from donating blood until they have been back in the United States or Canada for 28 days after leaving such areas. AABB recommends providing this information to donors when they present to donate and before completion of the donor history. At this time, there is no recommendation for the formal addition of a question to the donor history questionnaire.

Donor Self-Deferral Information Sheet to Reduce the Risk of Transfusion-Transmitted Zika

Thank you for coming in to donate today: If you have travelled to Mexico, the Caribbean, and or Central or South America in the last 28 days, we are asking you not to donate today, but to return for your donation more than 28 days after your return to the United States. We are doing this for the following reasons:

- Zika virus infection is spreading rapidly in the Western Hemisphere, outside the United States and Canada.
- Zika virus infection is mild in most people, but there is concern that Zika is causing serious brain injury to infants whose mothers have been infected during pregnancy and an increase in cases of Guillain-Barré syndrome, a temporary but serious disorder causing paralysis.
- Zika virus can be present in the blood of an infected person who has no symptoms of illness.
- There is concern that Zika virus can be transmitted by blood.

For further information speak with staff in the donor room or call xxx-xxx-xxxx.

Attachment 2

What is the purpose of the Postdonation Information Sheet?

The Postdonation Information Sheet was developed in light of current Zika, dengue and chikungunya virus outbreaks worldwide and the possibility that donors who travel to those areas may become infected. The Information Sheet is designed to inform any donor who has travelled to Mexico, the Caribbean, Central or South America or other tropical areas in the last 28 days and who develops signs and symptoms consistent with these acute viral infections within 14 days of donation.

Directions are provided for the donor to call the blood center if the designated signs or symptoms of infection develop after donation. If your organization chooses to use the Postdonation Information Sheet, it should be provided to the donor with your standard postdonation information materials.

If a donor reports two or more of the listed symptoms after such travel in the specified period, it is advisable to recall nontransfused products. There is no recommendation to defer the donor since donors must be well and healthy when they return to donate

In addition, if a donor reports a confirmed case of Zika, dengue, or chikungunya virus infection, all in-date products collected in the 14 days before the onset of symptoms should be quarantined and recalled, and the donor deferred for at least 28 days following resolution of symptoms.

Postdonation Information Sheet

Thank you for your donation today. Travel to the tropics puts you at risk of getting infections not found in the United States and Canada. Of most concern at this time are tropical diseases caused by Zika, dengue, and chikungunya viruses, which are transmitted to humans by infected mosquitoes.

You were asked not to give blood if you traveled in the last 28 days to Mexico, the Caribbean, or Central or South America. You may have donated anyway. You might have been infected during your travel, but remained well. If you have traveled anywhere in Mexico, Central or South America, the Caribbean, or elsewhere in the tropics (for example, in the islands of the South Pacific) in the last 28 days before you donated today and then you develop two or more of the symptoms listed below any time within the next 14 days, PLEASE notify us as soon as possible at (XXX) XXX-XXXX.

- Fever ≥100 F
- Muscle and/or joint aches or weakness
- Headache
- Eye pain including conjunctivitis (pink eye)
- A rash

By notifying us, you may prevent the blood that you donated today from being used and potentially infecting a patient receiving a transfusion.