

Committee: Infectious Disease

Title: Improving Investigations of Transfusion Transmitted Infections at State and Local Health Departments

I. Statement of the Problem:

Transfusion transmitted infections (TTIs) have long been recognized as rare but known risks for patients receiving blood products. Reported examples of TTIs include viruses (e.g., HIV, hepatitis viruses, West Nile virus, human herpesvirus 8), bacteria (e.g., skin flora, gram-negative rods, human granulocytic anaplasmosis, ehrlichiosis), parasites, (e.g., babesiosis (*Babesia microti*), Chagas disease (*Trypanosoma cruzi*), malaria (*Plasmodium spp*)), and prions (e.g., variant Creutzfeldt-Jakob disease (vCJD)).^{1, 2,3,4} Although data are limited, it is estimated the incidence of TTIs per unit of blood product released ranges from 1 in 5,000 for bacterial infections (for unscreened platelets) to 1 in 2 million for HIV (for screened donations).⁵

Several measures have been taken to improve blood product safety, including the screening of donors through questionnaire and laboratory testing. While these measures have greatly reduced the incidence of TTIs, particularly for pathogens which are routinely tested in donated blood (e.g. Hepatitis B and C, West Nile virus, HTLV I/II, and HIV 1 and 2); there has been an increase in the number of TTIs due to pathogens such as *Babesia microti* for which screening is typically not done. The risk of TTIs is dynamic, and changes with the emergence of new agents, the changing epidemiology of recognized agents, and the discovery of new data which alters our understanding of transfusion risks.⁶ Pathogens previously not recognized as being transmitted through transfusion that have recently been documented include *Anaplasma phagocytophilum* and newly emerging pathogens such as vCJD.^{7, 8, 9}

Persons receiving blood products are typically more susceptible to infectious diseases compared to the general population.^{10, 11} Because such patients often have co-morbidities, a TTI may not be recognized or readily considered as the source of a patient's fever or illness. Therefore, actions that increase awareness of TTIs and lead to earlier recognition of TTIs can substantially reduce the potential for serious morbidity and mortality.

Epidemiologic and blood product tracing investigations of TTIs are complex, involve multiple agencies and jurisdictions, and require a knowledge of blood collection procedures and transfusion medicine that are not typically found within state and local health departments. Thorough investigations of TTIs can also help prevent additional cases by expediting the identification and removal of additional contaminated blood products collected from the same donor as well as deferring implicated donors from

future donations. Additionally, improved recognition of TTIs should result in more rapid treatment of the recipients of the implicated blood products.

One of the current major concerns in blood safety is the increasing number of TTIs due to *Babesia microti*. The New York City Department of Health and Mental Hygiene identified 11 cases of transfusion transmitted (TT) babesiosis over the course of 18 months.¹² Babesiosis is a regionally occurring disease endemic in the northeastern and upper midwestern states. However, because of the rapid and widespread geographic movement of blood products and the mobility of blood donors, transfusion associated babesiosis may occur in non-endemic areas, posing a diagnostic challenge to clinicians as well as an investigative challenge to local and state health departments. Data suggest that the incidence of tick-transmitted babesiosis is rising, which increases the potential for contamination of the blood supply. This highlights the need to standardize guidance on the epidemiologic investigations of such occurrences and strengthens the argument for creating tool kits for these investigations.

In recognition of the need to better recognize and assess adverse events associated with blood transfusion, including TTIs, the Centers for Disease Control and Prevention (CDC) has developed a hemovigilance module within the National Healthcare Safety Network (NHSN). While few health care facilities are enrolled in the NHSN hemovigilance module at this time (it was only a pilot until February 2010), as enrollment grows, the data collected through this national surveillance system will be used to better estimate the magnitude and trends of adverse events associated with transfusion-related adverse reactions, including TTIs. This may also result in increased recognition of TTIs as healthcare-associated infections (HAIs), further supporting the need to develop resources for state and local health departments, including tool kits.

Similar issues have arisen concerning infections transmitted through organ or tissue transplantation.

II. Statement of the desired action(s) to be taken:

Justification

The purpose of this position statement is to support improved and standardized investigations of TTIs by both public health and the regulatory agencies that have oversight of blood products in the health care community. This would facilitate improved recognition of future cases of TTIs, prevention of additional cases, and rapid initiation of appropriate therapy for patients with TTIs.

Such improvements will require state health departments to develop procedures and expertise in complex TTI investigations and establish contacts with the blood centers and other stakeholders in the blood transfusion community. It is crucial that CDC play a lead role in assisting state HDs in these efforts by developing investigation toolkits for TTIs and by providing enhanced resources to the states in the form of personal consultations.

This position statement is not intended to require that every health department investigate every TTI. Instead, it is to ensure that guidance is available for those investigations which are necessary to perform for public health purposes.

Actions

1. The CDC should develop tool kits containing materials that would facilitate, improve and standardize TTI investigations. These materials would provide guidance on specific TTIs, establish timeframes within which to conduct an investigation to attempt to prevent additional cases, delineate reporting criteria, and incorporate template letters that could be used to notify or make requests for information from physicians, blood banks, blood centers, blood donors and blood product recipients.

Because direct and timely consultation is vital during investigations of TTIs, the CDC should ensure adequate staffing of appropriate subject matter experts to provide real time guidance during such events, particularly for interstate investigations that would benefit from federal coordination.

In addition, the CDC is asked to convene a high level meeting of representatives from the various agencies and organizations which have oversight for, or are involved in the collection, administration or monitoring of blood products. Such agencies include the Food and Drug Administration (FDA), America's Blood Centers®, American Red Cross, AABB® (formerly known as the American Association of Blood Banks), and public health departments. The purpose of this meeting would be to establish formal recognition of joint interests in coordination of TTI investigations and involvement in surveillance (i.e., hemovigilance) efforts.

2. The Food and Drug Administration (FDA) has oversight of blood products and regulates and licenses the centers that collect and distribute blood products to blood banks. As such, the FDA should work with the CDC, the AABB® (formerly known as the American Association of Blood Banks) and blood centers to develop complementary materials for blood centers and blood banks to use when investigating TTIs. Materials should be developed to ensure standardization, completeness and to facilitate collaboration between the blood banks and centers, public health, and healthcare facilities. Such material should be consistent with CDC guidance mentioned above.

III. Public Health Impact:

The major benefits of thorough, standardized investigations of TTIs are to:

1. Prevent future transmission by identifying infectious donors who may pose an ongoing risk of disease transmission;
2. Identify and interdict other components from the implicated donor(s) or unit(s) prior to transfusion;
3. Identify patients who received components from an implicated donation; and
4. Initiate appropriate and timely therapy for infected patients.¹

By providing investigational guidance to public health, the blood industry and health care providers, all stakeholders will be better prepared to recognize and understand the scope

of TTIs, prevent additional cases and fully investigate TTIs due to a previously unrecognized or newly emerging pathogen.

IV. References

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