Infectious Disease Testing for Blood Transfusions

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To address questions relative to the safety of the blood supply, the National Heart, Lung and Blood Institute, together with the Office of Medical Applications of Research of the National Institutes of Health (NIH), convened a Consensus Development Conference on Infectious Disease Testing for Blood Transfusions. The conference, held early in 1995, was cosponsored by the Transfusion Medicine Branch of the NIH Clinical Center and the National Institute of Allergy and Infectious Diseases. The panel’s findings are summarized below.

The United States has had an organized blood collection system for more than 50 years. During this time, various blood tests have been mandated, recommended by regulatory authorities, or adopted voluntarily to make blood transfusions as safe as possible. In the last 10 years alone, blood collection agencies have implemented five new tests for donated blood.

The continuing contribution that some of these tests make to transfusion safety has been uncertain. This is particularly true of the hepatitis B core antibody (anti-HBc) test, the serum alanine aminotransferase (ALT) test, and the serological test for syphilis (STS). It has been many years since any transmission of syphilis by blood transfusion has occurred. In addition, now that a more specific assay for hepatitis C virus (HCV) is available, the continuing need for the nonspecific tests for post-transfusion non-A, non-B (PT-NANB) hepatitis, with their low positive predictive values and frequent false positives, should be reconsidered. False positive values not only contribute to unnecessary deferral of donors and attendant loss of useful blood but also result in emotional, psychological, and financial costs to the donor.

To maintain the safety of blood transfusions, it is also important to establish mechanisms to cope with the entry into the community of new infectious diseases that may be blood-borne and, therefore, a hazard of transfusion. Chagas disease is one example.

Background for the Role of ALT and Anti-HBc Testing

The ALT and anti-HBc tests were introduced in 1986-1987 to identify donors at risk of transmitting PT-NANB hepatitis. Several years later, HCV was identified, a test for antibodies to HCV was developed, and HCV was shown to be responsible for at least 90% of the cases of PT-NANB hepatitis. The more sensitive second-generation test for anti-HCV, combined with improved donor selection, has effectively eliminated 85% to 90% of post-transfusion hepatitis due to HCV, and a newer test will likely further improve this level of protection.

The ALT Test

The ALT test might still be useful in reducing the risk of post-transfusion HCV, and non-A, non-B, non-C agents. However, this utility must be weighed against the costs and unnecessary donor deferrals it produces.

Setting criteria for discarding units of donated blood because of ALT elevations has been difficult. Modest elevations are common in apparently healthy blood donors. They may reflect factors not related to transfusion-transmitted diseases. Furthermore, values of ALT in normal males are higher than those in normal females so that a single cutoff value for ALT results in deferral of a higher proportion of men than women. Finally, different methods are available to measure ALT, and the interpretation of the test is affected by the assay and laboratory used.

Prior to the introduction of anti-HCV testing, surrogate markers, including ALT, may have contributed to a reduction in the overall post-transfusion hepatitis rate by 30% to 40%. However, data show that added to anti-HCV testing, retention of the ALT test provides little or no additional value. Furthermore, there are no data to indicate that ALT screening is useful in detecting HCV infection in the “window period” prior to anti-HCV seroconversion or in detecting post-transfusion hepatitis not identified by the anti-HCV test.

Although the direct cost of the test is low, the indirect costs are high: the loss of approximately 200,000 usable units of blood and the temporary or permanent deferral of about 150,000 donors annually; the cost to the health care system of evaluating donors with elevated ALT; and the
unwarranted anxiety and stress and risk of insurance denial for healthy deferred donors. The panel, therefore, recommends that ALT testing of volunteer blood donors be discontinued. Persons previously deferred for only an isolated elevation in ALT may now be re-evaluated for donor eligibility.

**The Anti-HBc Test**

Although there is no reason to retain the anti-HBc test to prevent post-transfusion HCV, it is recommended that use of the test be continued. Anti-HBc testing is likely to help reduce the risk of hepatitis B virus (HBV) transmission. Also, because of the overlapping epidemiology of HBV and HIV, anti-HBc testing serves as a surrogate marker for HIV, primarily for recently infected donors who are in the window period of HIV infection prior to the detectability of HIV antibodies. Nonetheless, the present anti-HBc test produces many false positive results. Its positive predictive value for past or present infection with the hepatitis B virus must be improved.

**The Syphilis Test**

Because the contribution of the serologic test for syphilis in preventing transfusion-transmitted syphilis is not understood, the panel concludes that use of this test should continue. Syphilis is one of the oldest recognized infectious risks of blood transfusion, and serologic tests for syphilis have been routinely carried out for more than 50 years. In recent years, transfusion-transmitted syphilis has become exceptionally rare. Such factors as improved donor selection processes, the uniform application of testing to all donors, and the use of refrigerated blood for transfusion may possibly contribute to the absence of reported cases, but few data specifically address these issues. In addition, it is not certain that current surveillance would detect a rare case of transfusion-transmitted syphilis. Antibiotics received by many hospitalized, transfused patients may partially treat transfusion-transmitted syphilis, obscuring the diagnosis but not necessarily preventing long-term complications of the infection. Current blood storage conditions may not provide an adequate margin of safety against transfusion-transmitted syphilis if donor screening were eliminated. Although *Treponema pallidum*, the organism responsible for syphilis, may lose its viability after several days of refrigerated storage, a few organisms may survive up to 96 hours under such storage conditions, and some units of blood are refrigerated for shorter periods prior to transfusion. In addition, platelet concentrates are stored at room temperature. More information is needed to better assess this issue. The data also do not support the rationale that the serological test for syphilis has value as a surrogate marker for other transfusion-transmitted diseases, especially HIV.

**Management of Potential Threats to Transfusion Safety**

Public health surveillance and collaboration between public health and medical specialists are critical in responding to emerging infectious disease threats to the blood supply. An organized multidisciplinary approach to these threats must be formulated. In particular, the blood transfusion community should arrange for periodic communication with the Centers for Disease Control and Prevention to proactively review emerging infectious disease threats to the United States. In assessing a potential threat to transfusion safety, numerous issues need to be addressed, including its potential transmissibility through blood products; the length of the asymptomatic but infectious period; its severity, incidence, and prevalence in the donor population; and its potential for secondary spread. Once a potential threat to transfusion safety has been identified, the appropriate responses will balance the magnitude of the problem against the need to maintain an adequate blood supply and the availability of procedures to remove the threat from the donor pool. Intervention strategies may include redesigning donor recruitment and selection practices; implementing reliable assays or, in their absence, instituting surrogate testing; and evaluating outcomes to demonstrate that the interventions favorably influence component safety. Implementation of a response will also require training personnel, obtaining new equipment and supplies, preparing procedures and policies, and supervising blood banks closely to ensure that the changes entailed do not produce errors.

**Future Research**

More research is needed on a wide range of issues, including better understanding of viral and bacterial agents that threaten the blood supply; improved tests for infectious agents and methods for eliminating or inactivating them in blood components; implications of transfusion-transmitted diseases in neonates; improved understanding of donor motivation and impact of deferral; and development of artificial blood components.