Transfusion-Transmitted Diseases Other than AIDS and Hepatitis

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Although the major diseases transmitted by transfusion today are AIDS and hepatitis, many others also are known. These include CMV, syphilis, Chagas disease, babesiosis, parvovirus B19, malaria, Epstein-Barr infection, and many others that have been reported only once or twice. Reducing the risk of transfusion-transmitted diseases is a problem for donor centers where donor screening and laboratory testing for possible carriers is undertaken. Physicians should be aware that the potential for disease transmission is always present when transfusions are administered.

The long-standing concern about transfusion-transmitted hepatitis and the intense and, at times almost hysterical, response to the knowledge that HIV infection also is transfusion-transmitted have overshadowed the fact that still other diseases are spread by blood component transfusion (Table 1) [1]. With some of the diseases all recipients are at risk, and with others only selected groups of recipients are susceptible. Donor selection, pre-donation questioning, and laboratory testing are the measures used to identify potentially infectious donors. The burden of such intervention falls on donor centers and requires relatively little involvement by practicing physicians. Physicians, however, should not be entirely ignorant of donor screening practices, because the family doctor is often called upon to advise donor-patients who have been deferred from donating or in whom some "abnormality" has been found at or after donation.

Of more direct concern to practicing physicians are those cases in which only selected groups of recipients, usually those who are immunosuppressed, are at risk. Here physicians must make judgments about the selection of components that will reduce the risk of disease transmission.

The purpose of this review is to address some transfusion-transmitted diseases. HIV infection and hepatitis, which are discussed elsewhere in this symposium, will not be covered.

CYTOMEGALOVIRUS (CMV)

CMV infections are a well-known complication of transfusion and in some groups of recipients are a major cause of morbidity and mortality. The subject has been well reviewed by Tegtmeier [2] and by Adler [3].

CMV infection, as measured by seroprevalence studies, occurs in from 50 to 100 percent of U.S. adults. Once infected, individuals harbor the viral genome for long periods of time and, even though asymptomatic, are infectious. The presence of

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Abbreviations: CMV: cytomegalovirus STS: serologic test for syphilis

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TABLE 1
Some Infectious Agents That Have Been Transmitted by Blood Component Transfusion

| Viruses                                                                 | Parasites                               |
|------------------------------------------------------------------------|-----------------------------------------|
| Hepatitis A, B, C, delta, and non-A, non-B                              | Plasmodia (malaria)                     |
| HIV-1, HIV-2                                                            | Babesia microti (babesiosis)             |
| HTLV I/II                                                              | Toxoplasma gondii (toxoplasmosis)       |
| Cytomegalovirus                                                        | Trypanosoma cruzi (Chagas disease)      |
| Epstein-Barr virus                                                     | Filaria (filariasis)                     |
| Parvovirus B19                                                         |                                        |
| Spirochetes                                                            |                                        |
| *Treponema pallidum* (syphilis)                                        |                                        |
| *Borrelia burgdorferi* (Lyme disease)*                                  |                                        |
| *Not yet documented*                                                   |                                        |

circulating antibodies indicates a carrier state that is associated with the ability to transmit infection.

Uninfected persons are antibody-negative and are at risk of primary infection by blood component transfusion. Antibody-positive persons are susceptible to reinfection with a different viral strain or to reactivation of the latent virus they harbor. In most cases, CMV infection is clinically unimportant, but in some severely immunosuppressed individuals transfusion-transmitted CMV has life-threatening potential.

Groups said to be at risk of serious consequences from CMV are listed in Table 2. In most medical centers, blood components that contain cellular elements are selected or processed in a way that will reduce or eliminate the risk of CMV transmission before transfusion into them.

The most common way to provide “CMV-negative” components for patients who are at risk is by testing the donor unit for antibodies to CMV and issuing only those components that test negative [4]. Because of the high prevalence of seropositivity in adult populations, this approach has proven difficult for many blood banks. There is a report that donors who have only IgM antibodies are the ones most likely to infect

TABLE 2
Suggested Indications for Use of CMV-Negative Blood Components

1. Newborn infants weighing less than 1,200 grams at birth if the mother is CMV-antibody-negative or if her antibody status is unknown
2. Exchange transfusion in all newborns
3. Intrauterine transfusions
4. Bone marrow transplant recipients
5. Bone marrow transplant candidates who are CMV-antibody-negative or unknown
6. Pregnant women in whom primary infection could pose a risk to the unborn child; does not include women at or near term or women with CMV antibodies
7. Children with documented congenital immune deficiencies
8. Heart, lung, or heart/lung transplant recipients
recipients, but this datum is unconfirmed [5]. Washed or frozen-deglycerolized components seem to be an acceptable alternative, especially for newborns [6]. Recent reports that third-generation leukocyte filters are also effective are promising, especially so because of the ever-increasing demand for “CMV-negative” transfusions [7,8].

**SYPHILIS**

Transfusion-transmitted syphilis is almost non-existent today, despite the increase in reported primary and secondary syphilis. All donations are tested, using a serologic test for syphilis (STS), hence only those very few donors who are STS-negative but spirochetic pose any risk. In addition, the spirochete does not survive well at 4°C, the temperature at which red blood cell components are stored. For this reason, only red cell components stored for less than four days or platelets, which are stored at 22°C, can transmit the disease. Occasional cases of transmission from platelets donated by such individuals have been reported [9].

**MALARIA**

Although no cases of transfusion-related malaria have been reported to the Centers for Disease Control for the most recent two years, the risk of transmission remains. Worldwide travel and recent immigration patterns from endemic areas make it almost certain that cases will continue to occur. Because transfusion-transmitted malaria is so infrequent, the correct diagnosis is often delayed. This fact is unfortunate because early treatment is effective, and delay can be fatal. Serologic testing can detect some carriers but is not indicated for donor screening. Current regulations do not allow individuals to donate for three years after they have had malaria, have taken malarial prophylaxis, or have visited in or immigrated from endemic areas. This screening approach is generally effective, as evidenced by the very low incidence of cases.

**CHAGAS DISEASE**

Chagas disease is widespread and well-known in the Western hemisphere, especially in South America, Central America, and Mexico. Perhaps as many as 10–15 million persons are infected, many of whom are essentially asymptomatic. Acute infection can be fatal, but this result is unusual. More often a chronic carrier state follows infection. At times it is symptomatic with cardiac and visceral involvement; more often, no significant symptoms are noted, but patients become carriers and are infectious.

Transfusion-transmitted Chagas disease has been reported twice in North America [10,11]. In each case the suspected carrier had emigrated from South or Central America. Thus, the increasing number of individuals from endemic areas who now live in the U.S. represents a new problem for blood-collecting agencies. There is no good test for donor screening. Current tests have a false-positive rate of 1–3 percent. Adding such a test to the donor-processing routine will be difficult, because so many donors who are not infected will have to be notified about the positive finding and placed on lists of deferred donors. In a like manner, to select Hispanics for testing or to defer them without testing would be socially unacceptable. The Public Health Service is addressing this problem, but no easy solution seems forthcoming. One author has called for an interim policy of not accepting blood from selected donors who have resided in endemic regions [12].
BABESIOSIS

Babesiosis has been transmitted by transfusion throughout the world [13,14]. Splenectomized recipients seem to be at increased risk [15], and at least one fatal case is reported [16]. There is a reservoir of infected individuals, at first thought to be localized to eastern Long Island and adjacent Connecticut, but now reported in other areas. One study of antibody prevalence in the Cape Cod-Boston, Massachusetts, area found positive results in 3.3–4.9 percent of donors tested [17]. It is not known how many, if any, of these antibody-positive persons are infectious. There is no consensus about what, if anything, should be done to limit the spread of transfusion-transmitted babesiosis. Neither additional questioning about tick bites nor geographic restrictions on summer bloodmobiles seem indicated. Serological testing and/or examination of blood films from all donors is not practical. No reasonable solution to the problem is obvious; the fact that it is, at present, a minor problem, suggests that no action will be forthcoming.

PARVOVIRUS B19 INFECTIONS

Parvovirus B19 has been identified as the etiologic agent of erythema infectiosum (fifth disease) in children and as a major cause of the transient aplastic crises seen in patients with hemolytic anemias. It has also been reported to cause severe chronic anemia, particularly in immunodeficient patients.

Parvovirus B19 seroconversion and infection have been reported after transfusion of factor VII concentrates [18]. So far, the number of reports is small, but the potential for increased interest and awareness is present, especially since a test for antibodies to parvovirus B19 is becoming more readily available. It may be that in the near future it will be considered appropriate to use parvovirus B19-negative components for selected patients, in a manner similar to current practice with CMV.

LYME DISEASE

The association of the spirochete Borrelia burgdorferi with Lyme disease has prompted an interest in whether infected individuals who donate blood could transmit the infection to their recipients [19]. There are no reported cases to date, but the setting for such transmission seems so likely that it should be only a matter of time until the first case of transfusion-transmitted Lyme disease is reported. The infection is common, especially during the summer months and especially in the upper northeastern region of the country. There is a period of spirochetemia during which patients may be essentially asymptomatic and therefore eligible to donate blood. The organism survives in blood products under the storage conditions generally used, although these experiments were done using relatively large innocula of Borrelia [20]. It only remains for some astute clinician to suspect Lyme disease and collect the appropriate blood samples before it is added to the ever-growing list of transfusion-transmitted diseases.

The American Association of Blood Banks, in response to the public's interest in this problem, has issued a statement suggesting that: (1) donor testing is not appropriate, even in endemic areas; (2) additional questions at the time of blood donation are not necessary; and (3) neither a tick bite nor a history of Lyme disease with recovery are cause for donor deferral.

While many other diseases have been transmitted by transfusion, in each case the number is small and none are a major problem. Transfusion is safer today than it has
ever been. It will be safer tomorrow than it is today, but it will never be absolutely safe. The only transfusion that cannot possibly transmit disease is the one not given.

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