Transfusion-Associated Acquired Immunodeficiency Syndrome

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The acquired immunodeficiency syndrome (AIDS) is the most severe manifestation of infection with a newly recognized retrovirus known as HTLV-III/LAV (human T-lymphotropic virus type III/lymphadenopathy-associated virus). Persons with AIDS have a severe disorder of the immune system that renders them susceptible to a number of opportunistic infections and cancers. Over 80% die within 2 years of diagnosis. Thousands of people have developed AIDS. Most are homosexual/bisexual men or intravenous drug users in the United States or highly sexually active heterosexuals in central Africa or Haiti. Many countries, however, are reporting rapid increases in the number of cases. A small proportion of AIDS patients have been infected by contaminated clotting-factor concentrates or by blood transfusions. Although AIDS is a rare complication of blood transfusions, it has evoked more fear of transfusions than other more common infectious agents.

Transfusion-Associated AIDS Cases

As of April 1, 1986, in the United States 2% of the 18,610 patients with acquired immunodeficiency syndrome (AIDS) had a history of no risk for AIDS other than a transfusion of single-donor blood products between 1978 and the onset of symptoms. The 338 patients with possible transfusion-associated AIDS had received their transfusions in 32 different states. Although many had received a large number of units, some had received only 1 unit of blood.

The age of the patients at the time they received their transfusion ranged from 0 (newborn) to 82 years; however, the number of cases among persons who received transfusions when they were infants has been significantly higher than would be expected from the number of units of blood transfused to infants [3]. This suggests that infants may be more susceptible than others to developing AIDS once they are infected with the virus, perhaps because of their immature immune systems.

Transfusion-associated AIDS cases are unique in that we can identify the date on which the person was infected by the virus. For adults, the time between transfusion and the diagnosis of AIDS (incubation period) currently ranges from 4 to 86 months, with a mean of 34 months (Fig. 1). For children, the mean incubation period is shorter (22 months), but the range is similar (4 to 68 months). These figures, however, underestimate the true mean and range of the incubation period since most infected people have only recently become infected, and cases with a very long incubation period have not had a chance to occur; Grouping transfusion-associated AIDS patients by the year in which they received their transfusion demonstrates the effect of this short period of observation and suggests that the mean incubation period may be very long. Furthermore, there is no indication that the incidence of new cases for any of the years of transfusion is beginning to decline. The flat curves suggest a relatively constant risk of disease for a very long time for people with this infection. Mathematical modeling has suggested that the most likely mean incubation period is 5 years [4].

Donor Investigations

The first reported case of transfusion-associated AIDS was an infant who had received a transfusion from a donor who was
healthy at the time of donation, but who developed AIDS 17 months later [5]. A series of 7 complete donor investigations each identified 1 or more donors who were either at risk for AIDS (homosexual/bisexual men or intravenous drug users) or who had an abnormal T-lymphocyte helper-to-suppressor (Th/Ts) ratio [6]. None of these 7 donors had AIDS when they were evaluated. Further donor investigations continued to identify high-risk donors, if all donors were investigated [3]. These donors often had a history of belonging to a group at risk for HTLV-III/LAV infection: 38 were homosexual or bisexual men; 3 were intravenous drug users; 4 had sexual contact with a person at risk for AIDS; and 8 had no risk by history, but had abnormal Th/Ts ratios. All of the donors were apparently healthy when they donated blood and most were still in good health when they were evaluated, up to 6 years after the transfusion: 35 were asymptomatic, 9 had lymphadenopathy, and 9 had AIDS.

Serologic testing of these high-risk donors found that 40 of the 47 tested were seropositive for HTLV-III/LAV [3]. Some of the transfusion-associated AIDS patients had received blood from more than 1 high-risk donor. Therefore, one would not expect all 47 to be seropositive since many homosexual men or intravenous drug users are not infected with the virus; however, if all infected persons do develop antibody, then there should be at least 1 seropositive donor to each case. When each group of high-risk donors to a particular case was considered a donor set, 39 of 40 sets contained at least 1 seropositive donor. The only set with a high-risk donor who was not seropositive was a set that had not been completely investigated, suggesting that the donor who transmitted infection had not been found.

Peripheral blood lymphocytes were collected from these donors up to 5 years after the index donation [3, 7]. Cultures were positive for 23 of 25 seropositive high-risk donors, most of whom were healthy. These donors were essentially all seropositive chronic carriers, most of whom were asymptomatic.

The Mode of Transmission

The specific blood components that can transmit the infection can be determined by identifying the components donated by the high-risk donors. In the 20 cases for which this information is available, 8 persons had donated packed red cells, 7 frozen plasma, 3 whole blood, and 2 platelets [3]. Each of these components appears to be equally capable of transmitting infection. In the few instances in which corecipients of different components from the same infected donor have been studied, all recipients have been infected. Factor VIII and Factor IX concentrates can also transmit infection, but heat treating these products can inactivate the virus [8]. Albumin has not been implicated in the transmission of HTLV-III/LAV and would not be expected to be, since it is routinely heated during preparation. Immunoglobulin preparations have not been implicated in the transmission of infection, and the procedures used to separate them also appear to inactivate the virus [9]. Passive antibody, causing a transient weakly positive HTLV-III antibody test, has been reported after administration of hepatitis B immune globulin [10].

The efficiency of HTLV-III/LAV transmission is relatively low by sexual contact (perhaps 1% per exposure) [11] and extremely low by contaminated needlestick (less than 1% per exposure) [12]; however, transmission via single-donor blood products is apparently very efficient. Studies of recipients of blood from donors who later developed AIDS, or from donors implicated in a case of transfusion-associated AIDS [13] have never identified a recipient who did not acquire infection during a transfusion from an infected donor.