Retesting of bone donors 2 months after donation guarantees sufficient safety of bone allografts

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Both allogeneic bone grafting and blood transfusion may transmit infections from the donor to the recipient. The most effective means to reduce the risk of infection is careful donor selection and screening of donors for markers of infection. The risk of blood transfusion-transmitted HIV infection in Finland, calculated with the incidence/window period model, is approximately 1:3,300,000. The calculated risk for hepatitis B (HBV) and C (HCV) is 1:217,000 and 1:147,000 donations, respectively. In bone banking we can further reduce the risks by retesting the living donors. Retesting 2 months after donation seems to be sufficient, at least in countries with a low incidence of transplantation-transmitted infections.

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Femoral head allografts harvested in primary hip arthroplasties can transmit HIV, hepatitis B (HBV) and hepatitis C (HCV) (Patijn et al. 1993, Tomford 1995). A case of HTLV transmission by bone allografting has recently been described (Sanzén and Carlsson 1997). According to the Common Standards for Musculoskeletal Tissue Banking (EATB and EAMST 1997), antibodies to HIV 1 and 2 and to HCV should be retested 6 months following bone donation, but this is difficult to arrange (Norman-Taylor et al. 1997). Retesting may be replaced by performing a p24 antigen or PCR test for HIV and a PCR test for HCV (EATB and EAMST 1997). However, clinical studies have shown that the p24 antigen test for HIV does not increase the sensitivity greatly, compared to an antibody to find the infection in blood donors (Alter et al. 1990, Busch et al. 1990). Direct virus detection assays are more expensive and there is still a "window" period of approximately 2 weeks (Busch et al. 1995). Viral inactivation with heat and gamma-irradiation has been used to make retesting unnecessary (Strong et al. 1991), but these methods are also expensive and they destroy the structure and osteoinductive capacity of the bone, without giving any guarantee against viral sterility (Munting et al. 1988, Strong et al. 1991, Tomford 1995).

In countries with a low prevalence of transfusion-transmitted diseases, as in Scandinavia (Lindholm 1994, Kantanen et al. 1996), the long retesting time might be shortened to 2 months. Risks of infections from bone grafting can be compared to those of allogeneic blood transfusion; both are directly related to the risk of viral transmission via blood (Tomford 1995). The annual number of blood donors is high and the incidence of infectious diseases can be estimated on the basis of seroconversions among repeat blood donors (Schreiber et al. 1996). We compared the risk of viral infections in the window period among Finnish blood donors to that of donors at Tampere University Hospital Bone Bank.

Material and methods

The Finnish Red Cross Blood Transfusion Service collects some 360,000 units of blood from 210,000 blood donors annually. About 450,000 units of red cells, platelets and fresh frozen plasma are annually distributed to hospitals. Finnish hospitals collect roughly 1,500 femoral heads for allografting annually. Of these, approximately 200 are collected by the Tampere University Hospital Bone Bank. After selection, the donors are tested according to the international donor screening criteria for HIV antibodies, HCV antibodies, hepatitis B surface antigen (HBsAg), HBV core protein antibodies (anti-HBc), alanine aminotransferase and syphilis (EATB and EAMST 1997). Blood donors in Finland are also tested for HTLV-I and -II. At the Tampere University Hospital Blood Bank, living bone donors are retested for HIV, HBV and HCV 2 months after donation at their follow-up visit.

The risk of a blood donation during the window period of an infection in Finland has been calculated ac-

Table 1. Estimated residual risk of an infection after a blood donation in Finland. The figures are based on data from repeat blood donors from 1993 to 1996

Virus	Incidence per 100,000 donors	Length of window period	Estimated residual risk per million donations (95% CI)
HIV	0.50	22 days [a] (6–38)	0.30 (0.02–0.91)
HBV	2.99	56 days [b] (24–128)	6.80 (2.85–12.35)
HCV	3.76	66 days [b] (38–94)	4.59 (1.36–13.70)

[a] Schreiber et al. 1996
[b] Couroucé and Pillonel 1996

cording to Schreiber and coworkers (1996) using the incidence rates of seroconversions among donors who have donated blood more than once (Table 1). To estimate the risks of infection from allogeneic bone grafting blood and bone donor populations were assumed to be identical for acquiring virus infections. To estimate the value of retesting, 2 months after donation, the reported infectious window periods were utilized (Schreiber et al. 1996). The "window period" runs from when blood is capable of transmitting an infection until a detectable laboratory marker of the infection appears. Third-generation HIV antibody tests have been reported to detect 95–97% of the recent infections in 3 months (Canadian Medical Association 1995). The sensitivity in 2 months is about 85–90%. HIV RNA PCR tests reduce the length of the window period by 50%, compared to the HIV antibody test (Busch et al. 1995). The window periods of HBV and HCV infections are longer and, after transmission of infection, only about 50% of the patients have seroconverted at 2 months (Schreiber et al. 1996, Couroucé and Pillonel 1996). A slightly higher percentage of HTLV-I and -II infections could be obtained by testing the patients 2 months after transmission (Couroucé and Pillonel 1996, Schreiber et al. 1996).

Results

The incidence of HIV among Finnish blood donors is 1:200,000. Since 1986, not a single case of HIV infection due to blood transfusion is known to have occurred in Finland. The calculated residual risk of developing an infection after a blood donation in Finland is 1:3,300,000. There has never been an HIV-positive bone donor in Tampere Bone Bank or in other bone banks in Finland. Assuming that blood and bone donor populations in Finland are similar regarding the epidemiology of infectious diseases and that bone donors are not retested, it can be estimated that there will occur 1 HIV infection among allograft bone recipients in 2000 years. Retesting after 2 months will further reduce the figure to 1/7.

The incidence of HBV and HCV infections among Finnish blood donors is 1:34,000 and 1:27,000, respectively. The estimated risks of HBV and HCV transmission by blood transfusion are 1:218,000 and 1:147,000, respectively. In Tampere Bone Bank, 2.5% of the donors have been discarded because of positive hepatitis serology, including every donor with increased alanine aminotransferase activity or a medical history of HBV or HCV infection, even though the person has recovered from infection. During the last year, 2 donors were found to be HBV antibody positive. Both were no longer infectious, but despite this, the tissues were rejected. 1 donor had HCV antibodies and in 1 case an HCV infection was suspected. In 1 case, increased alanine aminotransferase activity was the reason for rejection. According to the estimated risk figures of HBV and HCV infections in Finnish blood donors, 1 HBV and 1 HCV infection will occur in bone allograft recipients in 100 years, if the donors have not been retested. With retesting, the same figure would be 1 infection in 200 years.

Since 1995, blood donors in Finland have been tested for antibodies to HTLV-I and -II viruses. The seroprevalence of HTLV in Finnish blood donors has been approximately 1:80,000. No seroconversions have been encountered and therefore the residual risk of a blood donation in the window period cannot be calculated. Finnish bone banks have not tested donors for HTLV-I and -II. It can be estimated that, even without testing bone allograft donors in Finland, there will be only 1 HTLV transmission in 50 years. Freezing of the bone allograft will further reduce the infectivity by HTLV, since frozen blood products have not been reported to transmit HTLV (Donegan et al. 1994).

Discussion

Most bone banks have to rely on donor retesting, because adequate sterilization methods are not clinically available. Therefore, surgeons and bone bank person-

Table 2. Estimated residual risk of HIV and hepatitis C (HCV) using the antibody or PCR test at donation or additional antibody retesting 2 months after donation in Finland and the United States (calculated per million donations)

	Finland	United States	Reduction [a]
HIV antibody test	0.30	2.03 [b]	–
HIV PCR test	0.15	1.02 [c]	50%
HIV antibody retesting	0.05	0.30	85%
HCV antibody test	4.59	9.70 [b]	–
HCV PCR test	1.38	2.91 [b]	70%
HCV antibody retesting	2.30	4.85	50%

[a] compared with antibody test performed only at donation
[b] Schreiber et al. 1996
[c] Busch et al. 1995

nel dealing with bone allografts should be aware of the risks of transfusion-transmitted diseases in the population and the limits of the screening tests used.

Earlier risk analyses have been based on seroprevalence studies (Buck et al. 1989). However, the actual risk of transmission of an infection can be calculated only if the incidence of new infections and the length of the window periods are known. HIV, HBV and HCV tests have been developed during the last few years and, consequently, the sensitivity of the tests has increased. Third-generation anti-HIV tests used at present have a median window period of only 22 days, compared to 45–60 days achieved by old viral lysate-based first-generation anti-HIV assays (Horsburgh et al. 1989, Busch et al. 1995). According to Tomford, the p24 antigen test does not seem to improve the safety vis à vis HIV, compared to the present third-generation antibody test (Tomford 1995). HIV RNA PCR tests reduce the window period by 50%, equalling 11 days, but raise the costs and do not improve the safety as compared to retesting (Busch et al. 1995).

Schreiber and coworkers (1996) have published estimates on blood donors with infections in the United States, based on the incidence/window period model. We have used the same model to estimate the risks in the Finnish blood donor population (Table 1). The estimated risk for HIV in Finland is 1/7 and for hepatitis 1/2 of that in the United States. The assumption that blood and bone donor populations are identical was essential for estimating risks among the few bone and soft tissue donors. Although there are reports of a higher prevalence of hepatitis among cadaver bone donors compared to blood donors, the incidence of new infections, at least among living bone donors, is lower (Lefrère et al. 1997). Living bone donors represent an older age-group with less risk behavior who therefore run a lower risk of residual HIV or hepatitis infection (Tomford 1995).

Using the estimated data for the United States and Finland, one can compare these two populations (Table 2). Retesting for HIV 2 months after donation seems to be sufficient in both countries. In the United States, where approximately 200,000 bone and soft tissue transplantations are performed annually (Buck et al. 1989, Strong et al. 1991), retesting would reduce the estimated transmission of HIV infection to 1 in 15 years. In the Finnish donor population, the same estimated risk level is reached without retesting. With retesting, the estimated risk is 1 infection in more than 10,000 years. Retesting of bone donors for HBV and HCV infections after 2 months is more problematic, because of their long window periods (Table 1). That is why, the HCV PCR test is better than retesting. However, the same risk level reached with the PCR test in the United States is reached by retesting in Finland. Hepatitis is a less serious disease than HIV and, therefore, the HCV antibody test seems to be sufficient, at least in Scandinavian countries with their lower incidence of hepatitis C infection (Pereira et al. 1993, Lindholm 1994).

In Finland, bone donors have not been tested for HTLV infections. One of the reasons for this has been the low seroprevalence rate of HTLV in Finnish blood donors (1:80,000). Reports from endemic areas show that only 2–4 % of the seropositive persons develop symptoms and the incubation period of the disease is at least some decades (Manns et al. 1992, Pillonel et al. 1996, Rabkin et al. 1996). It has also been shown that the risk of HTLV transmission by blood products appears to diminish with longer duration of storage. According to Donegan et al. (1994), blood products more than 10 days old were not found to transmit HTLV infections. Surprisingly, a probable transmission of HTLV by allograft bone has recently been reported (Sanzén and Carlsson 1997).

It is important that medical staff of the bone bank carefully interview potential bone donors. The donors should complete and sign a structured questionnaire concerning their risk behavior for transplantation-transmitted diseases. After this, the physician-in-charge should decide if the donation is justified and start the serological screening. Retesting of donors during their follow-up visit to the hospital 2 months after donation is advisable, to further increase the safety of bone allografts. Retesting also confirms the negative test results obtained at donation. Despite thorough donor selection and repeated screening tests, viruses may be transmitted by bone allografts, because of the infectious window period.

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