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Probability of Viremia with HBV, HCV, HIV, and HTLV among Tissue Donors in the United States

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ABSTRACT

BACKGROUND

Tissue-banking organizations in the United States have introduced various review and testing procedures to reduce the risk of the transmission of viral infections from tissue grafts. We estimated the current probability of undetected viremia with hepatitis B virus (HBV), hepatitis C virus (HCV), human immunodeficiency virus (HIV), and human T-lymphotropic virus (HTLV) among tissue donors.

METHODS

Rates of prevalence of hepatitis B surface antigen (HBsAg) and antibodies against HIV (anti-HIV), HCV (anti-HCV), and HTLV (anti-HTLV) were determined among 11,391 donors to five tissue banks in the United States. The data were compared with those of first-time blood donors in order to generate estimated incidence rates among tissue donors. The probability of viremia undetected by screening at the time of tissue donation was estimated on the basis of the incidence estimates and the window periods for these infections.

RESULTS

The prevalence of confirmed positive tests among tissue donors was 0.093 percent for anti-HIV, 0.229 percent for HBsAg, 1.091 percent for anti-HCV, and 0.068 percent for anti-HTLV. The incidence rates were estimated to be 30.118, 18.325, 12.380, and 5.586 per 100,000 person-years, respectively. The estimated probability of viremia at the time of donation was 1 in 55,000, 1 in 34,000, 1 in 42,000, and 1 in 128,000, respectively.

CONCLUSIONS

The prevalence rates of HBV, HCV, HIV, and HTLV infections are lower among tissue donors than in the general population. However, the estimated probability of undetected viremia at the time of tissue donation is higher among tissue donors than among first-time blood donors. The addition of nucleic acid–amplification testing to the screening of tissue donors should reduce the risk of these infections among recipients of donated tissues.

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Hepatitis B virus (HBV), hepatitis C virus (HCV), human immunodeficiency virus (HIV), and human T-lymphotropic virus (HTLV) have all been transmitted by tissue transplantation.[1-3] These viruses have also been transmitted by blood transfusion, almost always as a result of the collection of blood during the so-called viremic window period, before infection can be detected by laboratory testing.[4-7] The probability of collecting blood during this window period has been extensively evaluated.[8-11] However, similar estimates have not been made for tissue donors, even though such estimates would be helpful in evaluating the efficiency of current and future measures designed to ensure the safety of tissue transplantation.

Tissue banks in the United States obtain, process, and distribute a variety of tissues, including heart valves, venous tissue, bone, bone-derived products (such as powders used for dental work), and connective tissue. The vast majority of these tissues come from cadavers, and all are essentially avascular and can be stored for long periods. Although tissue donors may also provide organs for transplantation, the converse is not necessarily true. The infectivity of different tissues varies, in part as a reflection of their anatomical origin and nature, but also as a result of processing after collection. For example, a highly processed bone powder would be much less likely to transmit a viral infection than would a fresh-frozen bone segment. Currently, the measures used to assess tissue donors include a retrospective review of the donor's medical history and testing of cadaveric blood samples for hepatitis B surface antigen (HBsAg) and antibodies against HIV (anti-HIV), HCV (anti-HCV), and HTLV (anti-HTLV).

METHODS

THE STUDY

We estimated the probability of viremia at the time of tissue donation by using the incidence–window-period model developed to estimate the residual risk of viremia among blood donors.[4-6,8] In order to do this, we estimated the incidence rates of HIV, HBV, HCV, and HTLV infection on the basis of measured prevalence rates among tissue donors and available data from other sources. Information on the duration of the window periods of viremia, before seroconversion, for these infections was obtained from the peer-reviewed literature.[8,11]

DETERMINATION OF PREVALENCE RATES AMONG TISSUE DONORS

Data on the prevalence of anti-HIV, HBsAg, anti-HCV, and anti-HTLV in tissue donors were obtained from existing databases of the Northwest Tissue Center (for 2001 through 2002), the American Red Cross Tissue Services (for 2000 through 2002), the Musculoskeletal Transplant Foundation (for 2002), the Community Blood Center/Community Tissue Services (for 2001), and LifeNet (for 2002). The data did not include any donor identifiers. During the periods covered, all five centers followed the review and testing standards of the American Association of Tissue Banks.[12] Four of the centers reported confirmed positive results; one reported only the results of the screening tests. For donors at this center, we estimated the rates of confirmed positive results by subtracting the number of false positive results (determined on the basis of specificity analyses of data from the other sites) from the number of reactive screening results. Pooled data were used to determine age- and sex-specific prevalence rates for the markers; prevalence was defined as the number of donors with confirmed positive tests divided by the total number of donors tested.

ESTIMATION OF INCIDENCE RATES AMONG TISSUE DONORS

The incidence rate of new infections among tissue donors was estimated by applying age- and sex-specific incidence rates for first-time blood donors to the tissue-donor population. Prevalence and incidence rates among voluntary donors and donors of directed whole blood were obtained from a research database of blood donors to the American Red Cross Blood Services.[11] Incidence was defined as the number of donors who seroconverted per 100,000 person-years among a group who repeatedly donated blood. Dodd et al.[11] and Janssen et al.[13] reported incidence ratios among first-time donors as compared with those who made repeated donations of 2.42 for HCV infection and 2.43 for HIV infection. No such data were available for HBV and HTLV infections. On the basis of the ratios for HIV and HCV, a ratio of 2.5 was assumed for HBV and HTLV. The ratios were applied to the incidence rates among persons who donate blood repeatedly to estimate incidence rates for first-time blood donations. These incidence rates were adjusted to reflect the difference in prevalence rates between blood and tissue donors by multiplying by the ratios of prevalence rates in the two groups. Prevalence

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and incidence rates for corresponding groups in the general population were also obtained through a search for published epidemiologic data[14-16] and unpublished data from the Centers for Disease Control and Prevention (CDC) (Alter M: personal communication) and were used in a similar manner to derive alternative estimates of incidence rates among tissue donors.

ESTIMATION OF THE PROBABILITY OF VIREMIA

We estimated the risk of infectivity — the probability that any tissue donor was in the viremic window period with an infection that was undetected by means of serologic screening methods at the time of donation — by the method developed by Petersen et al.,[4] Busch et al.,[5] Lackritz et al.,[6] and Schreiber et al.[8] The estimated probability is obtained from the product of the incidence rate and the length of the window period for each infection.

Unless otherwise specified, frequencies were compared with the use of the chi-square test; all reported P values are two-sided. Possible ranges of the estimated risks of infectivity resulting from the collection of tissues during the window periods for these infections were determined by means of Monte Carlo simulation with the use of Crystal Ball software.[17] Basically, possible variations in the prevalence rates among tissue donors and first-time blood donors according to sex and age, incidence rates among those who repeatedly donated blood according to sex and age, overall prevalence and incidence estimates and their assumed sex- and age-based distributions in the general population, incidence ratios for first-time donors as compared with those who repeatedly donated blood, and window periods were incorporated into the incidence- and risk-determination models to derive the 2.5 and 97.5 percentiles of the risk estimates. For prevalence and incidence rates, 95 percent confidence intervals were incorporated into all models except for those for the prevalence of HIV and for the incidence of the three markers in the general population; these models used a 50 percent variation owing to the lack of data on confidence intervals. A variation of 50 percent was also applied to the incidence ratios for HIV, HBV, HCV, and HTLV infections between first-time donors as compared with those who repeatedly donated on the basis of the variations in the incidence rates for HIV[13] and HCV.[11] All the ratios were assumed to follow triangular distributions. The window periods were assumed to follow triangular distributions with different degrees of variation, as reported by Schreiber et al.[8]

RESULTS

PREVALENCE OF VIRAL INFECTIONS AMONG TISSUE DONORS

Results obtained from 2000 through 2002 from a total of 11,391 tissue donors are shown in Table 1. The data include the numbers of tissue donors with results that were confirmed to be positive and, when necessary, the estimated numbers of confirmed positive results, as explained above. The rate of confirmed positive results (prevalence rate) was 0.093 percent for anti-HIV (95 percent confidence interval, 0.036 to 0.150), 0.229 percent for HBsAg (95 percent confidence interval, 0.139 to 0.319), 1.091 percent for anti-HCV (95 percent confidence interval, 0.896 to 1.286), and 0.068 percent for anti-HTLV (95 percent confidence interval, 0.019 to 0.117). The prevalence rate of anti-HCV was higher among male donors than female donors, whereas the reverse was true for anti-HIV and anti-HTLV.

To check the estimated frequency of confirmed positive results among the unconfirmed reactive results from a single center, we used a recombinant immunoblot assay (RIBA 3.0 SIA test, Chiron) to test 50 serum samples obtained post mortem that were initially reactive for anti-HCV. Thirty-six (72 percent) were positive, seven (14 percent) were indeterminate, and seven (14 percent) were negative. Similarly, we used Western blotting (HIV Western Blot Kit, Cambridge Biotech) to test nine serum samples that were initially reactive for HIV. Seven were negative, and two were indeterminate. Among tissue donors from other tissue centers, 74 percent of samples that were reactive to anti-HCV on initial screening were confirmed to be positive (81 of 110) and 11 percent of samples that were reactive to anti-HIV on initial screening were confirmed to be positive (2 of 19). The differences between these values and values found by evaluation testing were not significant ($\chi^2 = 0.006$, $P = 0.98$ for anti-HCV and $P = 1.00$ for anti-HIV by Fisher's exact test), indicating that the approach used to extrapolate the rates of confirmed positive results was appropriate.

PREVALENCE AND INCIDENCE OF VIRAL INFECTIONS AMONG BLOOD DONORS

Table 2 shows the prevalence rates of confirmed positive results for anti-HIV, HBsAg, anti-HCV, and anti-HTLV among first-time blood donors, strati-

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Table 1. Prevalence of Infectious-Disease Markers among Tissue Donors, According to Age and Sex.*

Marker and Age Group	Male Donors			Female Donors			All Donors		
	No. Tested	Reactive on Screening	Confirmed Positive†	No. Tested	Reactive on Screening	Confirmed Positive†	No. Tested	Reactive on Screening	Confirmed Positive†
		no. (%)			*no. (%)*			*no. (%)*	
Anti-HIV									
<30 yr	1198	3 (0.250)	0.0	543	3 (0.552)	0.5 (0.100)	1,741	6 (0.345)	0.5 (0.031)
30–49 yr	1913	7 (0.366)	3.8 (0.200)	845	3 (0.355)	1.1 (0.134)	2,758	10 (0.363)	5.0 (0.180)
≥50 yr	4742	13 (0.274)	0.0	1669	8 (0.479)	4.6 (0.276)	6,411	21 (0.328)	4.6 (0.072)
Total	7853	23 (0.293)	3.8 (0.049)	3057	14 (0.458)	6.3 (0.206)	10,910	37 (0.339)	10.1 (0.093)
HBsAg									
<30 yr	1195	8 (0.669)	0.7 (0.062)	542	3 (0.554)	1.0 (0.185)	1,737	11 (0.633)	1.7 (0.100)
30–49 yr	1912	17 (0.889)	6.9 (0.362)	845	10 (1.183)	2.4 (0.280)	2,757	27 (0.979)	9.3 (0.337)
≥50 yr	4738	31 (0.654)	11.9 (0.251)	1669	8 (0.479)	2.0 (0.120)	6,407	39 (0.609)	13.9 (0.217)
Total	7845	56 (0.714)	19.6 (0.250)	3056	21 (0.687)	5.4 (0.176)	10,901	77 (0.706)	24.9 (0.229)
Anti-HCV									
<30 yr	1198	6 (0.501)	4.0 (0.334)	543	0	0.0	1,741	6 (0.345)	4.0 (0.230)
30–49 yr	1914	77 (4.023)	63.3 (3.305)	845	12 (1.420)	8.5 (1.007)	2,759	89 (3.226)	71.8 (2.601)
≥50 yr	4745	52 (1.096)	30.7 (0.648)	1670	18 (1.078)	12.6 (0.754)	6,415	70 (1.091)	43.3 (0.675)
Total	7857	135 (1.718)	98.0 (1.247)	3058	30 (0.981)	21.1 (0.690)	10,915	165 (1.512)	119.1 (1.091)
Anti-HTLV									
<30 yr	1197	4 (0.334)	0.0	543	2 (0.368)	0.0	1,740	6 (0.345)	0.0
30–49 yr	1915	11 (0.574)	1.0 (0.052)	845	10 (1.183)	0.9 (0.103)	2,760	21 (0.761)	1.9 (0.068)
≥50 yr	4745	16 (0.337)	0.0	1670	22 (1.317)	5.6 (0.333)	6,415	38 (0.592)	5.6 (0.087)
Total	7857	31 (0.395)	1.0 (0.013)	3058	34 (1.112)	6.4 (0.210)	10,915	65 (0.596)	7.4 (0.068)

* Anti-HIV denotes antibody to human immunodeficiency virus, HBsAg hepatitis B surface antigen, anti-HCV antibody to hepatitis C virus, and anti-HTLV antibody to human T-lymphotropic virus.
† Fractional values are presented as a result of the estimation of the numbers of true positive results for one tissue bank.

fied according to sex and age. Incidence rates of new infections were obtained for those who repeatedly donated blood in the period from 2000 through 2001, according to sex and age group, as previously published.[11] For HBsAg, the incidence was adjusted as described by Schreiber et al.[8] and Korelitz et al.[18] This adjustment involves multiplying the incidence rate by a correction factor (2.38) to compensate for the transient expression of HBsAg in acute infections.

PREVALENCE AND INCIDENCE OF VIRAL INFECTIONS IN THE GENERAL POPULATION

According to U.S. data from the CDC[16] (and from the AIDS [Acquired Immunodeficiency Syndrome] Public Information Data Set at www.cdc.gov/hiv/software/apids.htm), the current prevalence of HIV infection (excluding AIDS) is approximately 0.20 percent. The incidence of HIV infection is estimated to be 40,000 cases per year, with approximately 70 percent of cases in males and 30 percent in females; the age distribution of incident HIV infections is not available. The age distribution of patients with AIDS — 18.30 percent of whom are less than 30 years of age, 70.85 percent 30 to 49 years of age, and 10.85 percent 50 years of age or older — was assumed for HIV infections.

For viral hepatitis, the CDC estimates that 78,000 HBV infections and 25,000 HCV infections occurred in 2001 (from the Division of Viral Hepatitis, at www.cdc.gov). The age distribution of incident HBV infections for 2000 — 37.09 percent younger than 30 years of age, 46.80 percent 30 to 49 years of age, and 16.11 percent 50 years of age or older —

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Table 2. Prevalence of Infectious-Disease Markers among First-Time Donors of Whole Blood in 2001, According to Age and Sex.*

Marker and Age Group	Male Donors		Female Donors		All Donors	
	No. Tested	Confirmed Positive	No. Tested	Confirmed Positive	No. Tested	Confirmed Positive
		no. (%)		*no. (%)*		*no. (%)*
Anti-HIV						
17–29 yr	387,087	48 (0.012)	411,668	14 (0.003)	798,755	62 (0.008)
30–49 yr	279,487	63 (0.023)	312,883	26 (0.008)	592,370	89 (0.015)
≥50 yr	117,908	6 (0.005)	122,924	5 (0.004)	240,832	11 (0.005)
Total	784,482	117 (0.015)	847,475	45 (0.005)	1,631,957	162 (0.010)
HBsAg						
17–29 yr	387,405	366 (0.094)	412,160	177 (0.043)	799,565	543 (0.068)
30–49 yr	279,655	385 (0.138)	313,148	154 (0.049)	592,803	539 (0.091)
≥50 yr	117,977	101 (0.086)	122,985	69 (0.056)	240,962	170 (0.071)
Total	785,037	852 (0.109)	848,293	400 (0.047)	1,633,330	1252 (0.077)
Anti-HCV						
17–29 yr	387,184	261 (0.067)	411,891	200 (0.049)	799,075	461 (0.058)
30–49 yr	279,353	2201 (0.788)	312,825	1445 (0.462)	592,178	3646 (0.616)
≥50 yr	117,843	521 (0.442)	122,862	340 (0.277)	240,705	861 (0.358)
Total	784,380	2983 (0.380)	847,578	1985 (0.234)	1,631,958	4968 (0.304)
Anti-HTLV						
17–29 yr	386,724	10 (0.003)	411,637	9 (0.002)	798,361	19 (0.002)
30–49 yr	279,173	24 (0.009)	312,656	67 (0.021)	591,829	91 (0.015)
≥50 yr	117,754	15 (0.013)	122,801	35 (0.029)	240,555	50 (0.021)
Total	783,651	49 (0.006)	847,094	111 (0.013)	1,630,745	160 (0.010)

* Both volunteer donors and directed donors are included in this analysis.

was assumed for cases of HBV. The age distribution for incident HCV infections for 2001 was 29 percent younger than 30 years of age, 64 percent 30 to 49 years of age, and 7 percent 50 years of age or older, and the male:female ratio was 1.7:1 (Alter M: personal communication).

No current prevalence data are available for HBV or HCV. On the basis of testing of serum samples from persons who participated in the Third National Health and Nutrition Examination Survey from 1988 through 1994, McQuillan et al.[15] reported a prevalence rate of HBsAg of 0.42 percent, and Alter et al.[14] reported a prevalence of anti-HCV of 1.8 percent. Furthermore, the study by McQuillan et al.[15] showed a male:female ratio of 1.4:1 with respect to the prevalence of total HBV infections. These data are assumed to represent the current status and were used in this assessment. No data are available on HTLV infection in the general population.

ESTIMATED INCIDENCE RATES AMONG TISSUE DONORS

By extrapolating from the rates among first-time blood donors, we estimated that the incidence rates among tissue donors were 30.118 per 100,000 person-years for HIV, 18.325 per 100,000 person-years for HBsAg, 12.380 per 100,000 person-years for HCV, and 5.586 per 100,000 person-years for HTLV (Table 3). The prevalence ratios for tissue donors relative to those in the general population were 0.46 for HIV, 0.54 for HBsAg, and 0.61 for HCV; the corresponding estimated incidence rates per 100,000 person-years for tissue donors were 7.099, 15.100, and 4.910, respectively (Table 4). The estimates derived from the blood-donor approach were higher than those derived from the general-population approach. Prevalence and incidence data from blood donors are less likely to be underestimates, owing to the systematic testing of each donation.

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Table 3. Estimated Incidence of HIV, HBsAg, HCV, and HTLV among Tissue Donors.

Marker and Age Group	Male Donors					Female Donors					All Tissue Donors		
	Total No.	Prevalence Ratio (Tissue: 1st-Time Blood Donors)	Incidence Rate in 1st-Time Blood Donors	Estimated Incidence Rate in Tissue Donors	No. of Cases Expected among Tissue Donors	Total No.	Prevalence Ratio (Tissue: 1st-Time Blood Donors)	Incidence Rate in 1st-Time Blood Donors	Estimated Incidence Rate in Tissue Donors	No. of Cases Expected among Tissue Donors	Total No.	Estimated Incidence Rate	Estimated No. of Cases Expected
			no./100,000 person-yr					*no./100,000 person-yr*				*no./100,000 person-yr*	
Anti-HIV													
<30 yr	1198		12.836	42.012	0.5	543		4.100	158.823	0.9	1,741	78.444	1.4
30–49 yr	1913		5.066	16.581	0.3	845		0.876	33.921	0.3	2,758	21.894	0.6
≥50 yr	4742		1.268	4.150	0.2	1669		1.731	67.076	1.1	6,411	20.532	1.3
Total	7853	3.27	5.547	18.154	1.4	3057	38.74	1.969	76.278	2.3	10,910	30.118	3.3
HBsAg													
<30 yr	1195		14.967	34.416	0.4	542		7.529	28.047	0.2	1,737	32.428	0.6
30–49 yr	1912		9.140	21.017	0.4	845		2.144	7.987	0.1	2,757	17.024	0.5
≥50 yr	4738		7.244	16.658	0.8	1669		2.826	10.529	0.2	6,407	15.061	1.0
Total	7845	2.30	9.791	22.514	1.8	3056	3.73	3.788	14.112	0.4	10,901	18.325	2.0
Anti-HCV													
<30 yr	1198		7.305	23.955	0.3	543		6.124	18.044	0.1	1,741	22.111	0.4
30–49 yr	1914		4.780	15.674	0.3	845		4.941	14.559	0.1	2,759	15.332	0.4
≥50 yr	4745		2.946	9.662	0.5	1670		1.724	5.080	0.1	6,415	8.469	0.5
Total	7857	3.28	4.753	15.587	1.2	3058	2.95	4.482	13.206	0.4	10,915	12.380	1.4
Anti-HTLV													
<30 yr	1197		0.000	0.000	0.0	543		1.054	16.913	0.1	1,740	5.278	0.1
30–49 yr	1915		0.000	0.000	0.0	845		0.300	4.816	0.0	2,760	1.475	0.0
≥50 yr	4745		0.000	0.000	0.0	1670		1.781	28.571	0.5	6,415	7.438	0.5
Total	7857	2.04	0.000	0.000	0.0	3058	16.04	0.868	13.925	0.4	10,915	5.586	0.6

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Table 4. Estimated Probability of Viremia Undetected by Testing Methods at the Time of Tissue Donation, According to the Blood-Donor Approach and the General-Population Approach.*

Agent	Window Period†	Estimated Incidence		Estimated Probability		Nucleic Acid–Amplification Testing	
		Blood-Donor Approach	General-Population Approach	Blood-Donor Approach	General-Population Approach	Window Period‡	Projected Probability§
	days	*no./100,000 person-yr*		*no./100,000 tissue donors (95% CI)*		*days*	*no./100,000 tissue donors*
HIV antibody	22	30.118	7.099	1.815 (0.577–4.451)	0.428	7	0.578
HBsAg	59	18.325	15.100	2.962 (1.466–5.254)	2.441	20	1.004
HCV antibody	70	12.380	4.910	2.374 (1.367–6.002)	0.942	7	0.237
HTLV antibody	51	5.586	—	0.780 (0.344–2.432)	—	—	—

* The blood-donor and general-population approaches are explained in the Methods section. No data on HTLV were available for use with the general-population approach. CI denotes confidence interval.
† Data on the window periods are from Dodd et al.[11]
‡ Data on the window periods are from Jackson et al.[19]
§ Values are the projected probability of collecting tissues from donors during the viremic window period for HIV, HCV, and HBV infections after the implementation of nucleic acid–amplification testing of individual specimens.

ESTIMATED RISK OF INFECTIVITY AMONG TISSUE DONORS

Table 4 shows the estimated probability of viremia at the time of tissue donation that was undetected on screening with the use of current serologic methods, as well as the projected effect of nucleic acid–amplification testing of individual samples on the window periods of infection and the projected probabilities. The estimates of incidence rates that were derived from the blood-donor approach were used for the projection.

DISCUSSION

Our prevalence results were based on data from five tissue banks across the United States. A survey of tissue banks accredited by the American Association of Tissue Banks, conducted in June 2000 for calendar year 1999, showed rates of reactivity on screening of 0.35 percent for HIV (66 of 19,091 donations), 0.94 percent for HBsAg (179 of 19,090 donations), 1.49 percent for HCV (285 of 19,130 donations), and 0.53 percent for HTLV (101 of 19,072 donations).[20] Our results — 0.34 percent, 0.71 percent, 1.51 percent, and 0.60 percent, respectively — are close to those of the survey. Such consistency suggests that our data are representative of the tissue-donor population in the United States.

The measured prevalence rates among tissue donors fall between those found among first-time blood donors and those attributed to the general population. This is not surprising, since tissue donors, although more representative of the general population than are blood donors, are carefully selected on the basis of medical history, physical examination, and interviews with the next of kin. Such a process, however, is not as effective as the face-to-face interview that is conducted with blood donors.[21]

By imputing rates from first-time blood donors and, separately, from the general population, we used an indirect approach to assign incidence rates to tissue-donor populations. For our primary estimates, we adjusted these rates to reflect the different prevalence rates among the tissue donors and the populations used for comparison. We used the resulting incidence rates with estimated window periods to estimate the probability of viremia at the time of tissue donation that would have gone undetected on screening with the use of current serologic tests.

Our data are based on information from 11,391 tissue donors. Donations from approximately 20,000 tissue donors are processed annually in the United States, generating roughly 1 million separate products. According to our estimates, the probability that a donor is viremic at the time of donation is 1 in 55,000 in the case of HIV infection, 1 in 34,000 in the case of HBV infection, 1 in 42,000 in the case of HCV infection, and 1 in 128,000 in the case of HTLV infection. We suggest that the respective upper bounds of these figures would be 1 in 22,000,

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1 in 19,000, 1 in 17,000, and 1 in 41,000; in other words, 1 or fewer donors would be viremic per year. These figures clearly indicate that the risk of infectivity is low, and in fact, most transplanted products are treated to reduce or eliminate the risk of infectivity. However, since tissues from a single donor may be used in an average of 50 patients, a single donor has the potential to infect an unknown, although probably small, number of recipients.[2]

The implementation of nucleic acid–amplification testing of "minipools" (pools of 16 to 24 blood donations) has markedly reduced the residual risk of viremia and transfusion-transmitted infection; the reduction in risk is directly proportional to the decrease in the length of the window period achieved by the use of this approach, by 5 days for HIV and by 60 days for HCV.[11,22] Studies have shown that nucleic acid–amplification testing of individual donations would reduce the window period to 7 days for HIV and HCV and to 20 days for HBV.[19,23] If individual testing were to be used for tissue donors, the probability of donor viremia would be reduced to 1 in 173,000 for HIV, 1 in 421,000 for HCV, and 1 in 100,000 for HBV. Assuming that it would cost approximately $150 ($50 per virus on the basis of current charges) to test each donor for the three viruses, the overall cost of eliminating one potentially infectious donor would be $4.0 million in the case of HIV infection, $2.3 million in the case of HCV infection, and $2.6 million in the case of HBV infection. Presumably, that cost would be spread over 1 million or more tissue products each year. Currently, efforts are under way to implement nucleic acid–amplification testing of cadaveric samples.

Overall, we believe that current measures used to evaluate tissue donors are effective and that the probability of collecting products from a viremic donor is low, but not negligible. On the basis of the model used for donated blood, this probability could be further reduced by the addition of nucleic acid–amplification testing at an approximate cost of less than $5 per product.

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APPENDIX

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