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Infection with human T-lymphotropic virus types-1 and -2 (HTLV-1 and -2): Implications for blood transfusion safety

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Abstract

Many countries currently perform antibody screening for HTLV-1 infection in blood donors, and this intervention is likely cost-effective in preventing HTLV-1 related diseases in high prevalence countries. However, a number of high-income countries with low prevalence of HTLV-1 infection also perform universal HTLV-1 screening and debate has arisen regarding the cost-effectiveness of these strategies. Filter-based leukoreduction is likely to substantially reduce HTLV-1 transmission by removing infected lymphocytes, but actual laboratory data on its efficacy is currently lacking. Similarly, cost-effectiveness research on HTLV-1 prevention strategies is limited by poor data on prevalence, transmission efficacy and the cost of treating HTLV1 diseases.

Keywords

HTLV-1; Blood transfusion; Immunoassay; Prevention and control

1. Introduction

Human T lymphotropic virus types-1 and -2 (HTLV-1 and -2) were discovered in the early 1980s and cause chronic infection of humans. Soon after their discovery, it was realized that blood transfusion was associated with high rates of transmission due to the infusion of infected lymphocytes. Transfusion-transmitted HTLV-1 was also associated with the accelerated onset of HTLV associated myelopathy (HAM), a debilitating spinal cord condition and with case reports of adult T-cell leukemia/lymphoma (ATL). Antibody screening for HTLVs was therefore introduced in many countries and remains in place today. In addition to its primary purpose of preventing transfusion transmission, such screening also provides a public health resource in allowing estimation of population prevalence of HTLV infection.

Paradoxically, most countries performing HTLV screening of blood donors have very low prevalence and incidence, while certain countries in Africa with probable high HTLV-1 prevalence in their donors do not currently perform antibody screening due to cost concerns.

Disclosure of interest

The author declares that he has no competing interest.

By analogy to cytomegalovirus, it is likely that filter leukoreduction of blood products reduces the transfusion risk of HTLV, although there are only suggestive data to support this hypothesis and leukoreduction is similarly impractical in many high prevalence countries.

My late colleague Jean Jacques Lefrere was an avid scholar of all threats to transfusion safety. Unbeknownst to me until I researched this article, he had published several articles on HTLV-1 infection, including an early comparison of donor prevalence between endemic Guadeloupe and the non-endemic Paris region and a comprehensive review of HTLV-1 and transfusion safety [1,2]. Our community of scientists will be diminished by the absence of his keen intellect and energy, but we shall also miss him as a faithful and cultivated friend.

2. Early epidemiologic studies of transfusion transmission

Soon after HTLV-1 was discovered and prior to the introduction of HTLV antibody screening, several studies were able to quantify the risk of transfusion-transmitted HTLV-1 infection. In Japan, Okochi et al. were the first to demonstrate transfusion transmission of HTLV-1 [3]. Of the 41 patients who received cellular blood products from HTLV-1 positive donors, 26 (63%) seroconverted to HTLV-1. None of 14 recipients of HTLV-1 positive plasma transfusions seroconverted. Blood products stored less than four days led to seroconversion in 13 of 15 patients while those stored longer did so in 12 of 25 patients ($P = 0.015$). Patients under 30 years of old were more likely to seroconvert than those aged greater than 30. IgG antibodies to HTLV1 were detected from 21 to 47 days after transfusion.

In 1987–1988, Manns et al. performed a similar study in Jamaica with retrospective antibody testing of samples from blood donors and tracing of the recipients [4]. A total of 66 patients had received blood products donated from donors later found to be HTLV-1 infected. Seroconversion occurred in 24 of 54 (44%) recipients of cellular blood products (packed RBC, platelets or whole blood), none of 12 recipients of acellular blood products and 0 of 52 recipients of blood products from HTLV negative blood donors. Significant risk factors for transmission included storage of the blood product for less than one week, male sex and immunosuppression in the transfusion recipient. The median time to HTLV-1 seroconversion in transfusion recipients was 51 days but there was a significant difference between recipients of blood stored for less than one week, almost all of whom seroconverted rapidly and those who received blood stored for more than one week who had seroconversion intervals as long as one year. It should be noted that the tests used at the time of that study were relatively insensitive compared to antibody assays available today, so the contemporary time to seroconversion should be shorter.

Finally, in the United States, Donegan et al. studied sera that were banked just prior to the introduction of HIV screening of US donors in 1984–1985 [5]. That repository was tested for HTLV-1 and -2 when commercial HTLV assays became available in the late 1980s and recipients of blood products from the HTLV positives were retrospectively traced in the early 1990s. A total of 26 of 95 (27%) recipients of blood products from HTLV infected donors were themselves found to be HTLV infected by serology and polymerase chain reaction (PCR). Estimated rates of transmission were similar for HTLV-1 (9 of 25 or 36%)

and HTLV-2 (17 of 70 or 24%; $P = 0.30$) infection. However, the duration of refrigerated blood storage played a major role with 74% transmission after 0 to 5 days storage, 44% transmission for 6 to 10 days storage and 0% transmission for 11 to 14 days storage. None of 17 recipients of acellular plasma and cryoprecipitate blood products became infected.

These three studies show rather similar findings, with the exception that the overall transmission rates in the Japanese and Jamaican study were higher than in the USA, probably due to shorter duration of refrigerator storage, the inclusion of a few whole blood units in the Japanese study or differences in the degree of buffy-coat leukoreduction during production of packed red blood cells. Although not a formal retrospective study, a look back study by Kleinman et al. in the same era showed that 16 of 54 (30%) evaluable recipients of blood products from HTLV-1 or HTLV-2 infected donors themselves became infected [6]. In a Canadian lookback study, of 109 HTLV-positive donors, 508 components were transfused, of whom 147 recipients were tested and 18 (12%) were positive [7].

3. Case reports of transfusion-transmitted HTLV-1 infection

Since HTLV infection is often asymptomatic, clinically recognized reports of patients infected via blood transfusion are rare. However, several case reports document the potential for adverse consequences of infection. A French patient who received a heart transplant and required large volumes of transfused red cells, platelets and plasma developed symptoms and signs of HAM within 4 to 5 months and was found to have seroconverted for HTLV-1 in a blood sample drawn at 14 weeks post transfusion [8]. The report also highlights the danger of HTLV infection in patients receiving immunosuppression. Chen et al. in Taiwan reported two cases of HTLV-1 infection and ATL occurring in patients with pre-existing malignancy (Hodgkin’s disease and promyelocytic leukemia) who had received multiple transfusions [9]. The intervals from blood transfusion to ATL diagnosis were six months and 11 years. Although this retrospective report does not definitively implicate the blood transfusions as the source of HTLV-1 infection, it provides suggestive evidence that transfusion-transmitted HTLV-1 carries a risk of ATL. More recently, Hakre et al. report a recent case of transfusion-transmitted HTLV-1 occurring in American soldier in Afghanistan [10]. The US military utilizes “walking blood banks” consisting of fellow soldiers who are called to donate for the wounded colleague. The index patient developed fevers and leukocytosis 1 to 2 years after his initial severe injuries and was found to be HTLV-1 positive; there was no evidence of HAM or ATL by the time of the report. Evaluation of his blood donors found one soldier to be HTLV-1 positive and the proviral DNA sequences of the two viruses were identical.

4. Prevalence of infection - HTLV-1

HTLV-1 is widely disseminated and between 5 and 10 million people worldwide are estimated to be infected [11]. Studies of HTLV-1 prevalence among blood donors underestimate prevalence in the general population but are still useful in comparing between nations (Table 1). Endemic clusters of HTLV-1 sero-positivity or infection are present in southern Japan, the islands of the Ryukyu Chain (including Okinawa), and some isolated villages in the north of Japan among aboriginal Ainu populations; rates of infection among persons older than 40 years exceed 15% in these areas. However most seropositive persons

in urban northern Japan are immigrants from areas in the south where infections are endemic [12]. Prevalence among Japanese blood donors has recently been reported to be 0.12% (men) and 0.11% (women) at ages 16 to 19 and 1.29% (men) and 1.66% (women) at ages 60 to 69 [13]. China, Taiwan, Korea, and Vietnam are largely free of infection suggesting that HTLV-1 was not carried by human migrations from these areas to Japan. However, recent investigations have demonstrated pockets of high HTLV-1 prevalence among blood donors in the Chinese cities of Ningde (0.4%) and Putian (0.14%) [14]. Both are in the coastal region of Fujian Province in southeast, leading to speculation about historical contacts with southern Japan as an explanation for their higher HTLV-1 prevalence. High HTLV-1 prevalences (> 15%) in Melanesia and Australian aborigines are attributed to the Melanesian virus type [15].

Another major endemic focus of HTLV-1 infection occurs in the Caribbean, where prevalence in Jamaica, Trinidad and Tobago, Martinique, Barbados, St. Lucia, Haiti, and the Dominican Republic range between 4 and 14% [16,17]. In Jamaica, prevalence varies by geography with the highest rates (10%) observed in the lowland, high-rainfall areas [17]. Seropositivity is found more frequently in persons of lower socioeconomic class and those who lack formal education [16]. Men and women attending clinics for sexually transmitted diseases (STDs) have the highest rate of seropositivity (about 6%) [18]. The rate in blood donors is lower (1 to 5%) [4].

HTLV-1 is also prevalent in South and Central America, including large numbers in Brazil (> 15% in Bahia) and smaller numbers in Colombia, Venezuela, Guyana, Surinam, Panama, and Honduras (5 to 14%). HTLV-1 prevalence among Brazilian donors was 0.14% across three regional blood centers [19]. With the exception of some foci among Native Americans, HTLV-1 is rare in the rest of Central and North America [20].

In the United States, large-scale screening of blood donors has documented a low prevalence of HTLV-1, namely 5.1 per 10^5 first-time donors [21]. In a significant proportion of HTLV-1-positive cases, the donor either has links to an area of endemic infection or has a history of risk-related behaviors, such as injecting drugs [22]. Persons of African ancestry have higher rates of seropositivity [23]. Similarly, migrant populations from Okinawa to Hawaii, from the Caribbean to the United States, and from the Caribbean to the United Kingdom are at increased risk of HTLV seropositivity, as are those who experience exposure through sexual contact or blood transfusion in areas where the virus is endemic [24,25].

In most African countries, HTLV-1 prevalence is poorly understood due to lack of data and high rates of false-positive antibody screening tests, perhaps due to cross-reactivity with malaria antigens [26]. Limited data from the Ivory Coast, Ghana, Nigeria, Zaire, Kenya, and Tanzania suggest prevalence in the range of 5% of the general population [27]. A recent study in South Africa found a prevalence of 0.16% in low-risk black blood donors, suggesting prevalence in the general black population of perhaps 1% [28].

Surveys in the Middle East have not revealed endemic HTLV-1 with the exception of northeastern Iran (Mashhad) and emigrants from that area now residing in Israel and New York [29]. In northeastern Iran, 0.14% of blood donors were found to be seropositive for

HTLV-1 [30]. Surveys in southern India and Indonesia have identified some HTLV-1-positive cases; in the Seychelles in the Indian Ocean, HTLV-1 is highly endemic (> 15%). In most western European countries, HTLV-1 is still uncommon except among immigrants from endemic regions, sex workers and injection drug users may be at increased risk [31]. Among blood donors in Europe, prevalence is generally low, ranging from 0 to 1.7 per 10^5 in Scandinavia and Ireland; 4.5 to 4.8 per 10^5 in France, the Netherlands and UK [32]. Romania was the one exception with prevalence of 53 per 10^5 blood donors.

5. Prevalence of infection–HTLV-2

HTLV-2 has a more restricted distribution than HTLV-1 and occurs primarily in the Americas and among pygmy tribes in Africa. Amerindians residing in North, Central, and South America show various rates of positivity for HTLV-2 (5 to 30%). Pockets of infection are present among the Seminoles in southern Florida and the Pueblo and Navajo in New Mexico but not among various tribes in Alaska. In Central America, the Guaymi Indians residing in northeastern Panama near the Costa Rican border have high seropositivity rates (> 15%), but this does not hold true for the Guaymi living in southwestern Panama [33]. At some time in the past, HTLV-2 was introduced into injection drug users (IDU) and amplified such that in the United States and southern Europe prevalence ranges from 10 to 15% and higher [34,35]. From IDUs, HTLV-2 has infected members of the general U.S. population via sexual transmission. Nevertheless, HTLV-2 prevalence among U.S. blood donors is much lower at 14.7 per 10^5 first-time donors [21]. The most frequent risk factor for HTLV-2 in seropositive blood donors is previous sexual contact with an IDU [36].

6. HTLV-1 and -2 incidence and residual risk

The blood donation setting is valuable for studies of HTLV-1 and HTLV-2 incidence since a single donor can be tracked prospectively across his or her donations to observe seroconversions. In the United States, several studies have documented HTLV-1/2 incidence ranging from 1–2 per 10^5 person years in the 1990s [37,38] to 0.2 per 10^5 person-years in 2007–2008 (Table 2) [39]. With knowledge of the estimated window period between infection – estimated at 51 days from the transmission studies mentioned above – one may calculate the estimated residual risk of acquiring HTLV-1 from blood transfusions that have been tested. The same studies in the USA estimated residual risk to be 1.59 per 10^6 blood products transfused in the 1990s, falling to 0.29 per 10^6 blood products transfused in 2007–2008. The same reports also included data on hepatitis C virus (HCV) incidence and residual risk. Whereas HCV incidence has been higher than that of HTLV-1, the residual risk of transfusion-transmitted HCV was greatly reduced by the implementation in 1999 of nucleic acid testing (Table 2).

In Canada, there was only one incident case of HTLV infection from 2007–2010 for an estimated incidence of 0.09 per 10^5 and a residual risk of 0.13 per 10^6 [7]. Similarly, incidence has been estimated to be 3.59 per 10^5 in Brazil from 2007–2009 with residual transfusion risk of 5.0 per 10^6 per blood products transfused [19]. In France, incidence among repeat blood donors was 0.4 per 10^5 in France from 2010–2012 and with the residual risk of only 0.05 per 10^6 [40].

7. Current testing and cost effectiveness, by country

Unfortunately, the World Health Organization global database on blood safety does not include HTLV testing as one of its data collected from countries around the world. According to another recent review and supplementary information [41], the following countries test all blood donations for HTLV-1 and -2 antibody: Argentina (endemic regions), Australia, Brazil, Canada, USA, Canada, China (some regions) [14], Colombia, French West Indies, Iran, Israel, Jamaica, Japan, New Zealand, Saudi Arabia, Peru, Sweden, Taiwan, the United Kingdom, Uruguay, the USA and Venezuela (endemic regions). In Europe, HTLV-1/2 antibody testing is currently performed on all blood donations in France, Greece, Ireland, Netherlands, Portugal, Romania, United Kingdom and on first time blood donations in Denmark, Finland, Norway and Sweden [32].

There has been relatively little work on the cost-effectiveness of HTLV screening. Couroce et al. estimated a cost of € 475,000–950,000 per infection prevented for testing of all blood donations, as contrasted to € 140,000–280,000 per infection prevented (but also allowing one case of HTLV-1 transmission) using a strategy of testing only first-time blood donors [42]. Stigum et al. recognized the dependence of cost-effectiveness on the underlying HTLV-1 prevalence in the blood donor population [43]. At a prevalence of 1 per 10^5, cost was $ 9.2 million per life saved or $ 420,000 per quality adjusted life year. At a prevalence of 1 per 10^4, cost was $ 0.9 million per life saved and $ 41,000 per QALY. Seed et al. noted a residual risk for HTLV-1 in Australia at well less than one per million included that cost-effectiveness would be difficult to estimate at such a low risk [44].

8. Gaps in knowledge and controversies

At present, the main gaps in knowledge regarding transfusion-transmitted HTLV-1 can be ascribed to inadequate prevalence data in some regions of Africa and Asia, uncertainty regarding the effectiveness of leukoreduction, and the cost effectiveness of less-than-universal antibody screening. Cassar and Gessain made a comprehensive survey of HTLV-1 prevalence across the globe but noted that their global estimate of 5 million to 10 million cases was substantially limited by inadequate data on HTLV-1 prevalence, particularly in the very populous countries of India and China [11]. Similarly, data from likely high prevalence regions in Africa are spotty and would benefit from a systematic survey among blood donors.

In general, it is reasonable to think that leukoreduction substantially reduce the risk of HTLV-1 transmission since the provirus is integrated in CD4+ lymphocytes and there is little cell-free virus. Laperche et al. suggest a tenfold reduction in transmission risk associated with leukodepletion although they recognized that this estimate is uncertain [40]. Hewitt et al. performed a look-back study of blood transfusions in the United Kingdom and found that only 1 of 96 filter-leukoreduced or buffy coat reduced blood products transmitted HTLV-1 as compared to 5 of 17 blood products that were not leukoreduced [45]. Buffy coat reduced blood products made up the minority of the former group and so that method should not be equated with filter-leukoreduction. Finally, Sobata et al. performed quantitative PCR on 300 blood donations from HTLV-1 positive donors in the Tokyo region [46]. By analyzing the

distribution of proviral loads and assuming that 80% of fresh cellular products from seropositive donors transmitted infection, they set a transmission cutoff at a proviral load of 0.9 per 10^4 cells or 9×10^4 HTLV-1 positive leukocytes in a typical cellular blood product. Since leukoreduction must achieve a standard of less than 1 to 5×10^6 leukocytes per RBC or platelet unit it would seem that leukoreduced blood products, although safer, still carry a theoretical risk of HTLV-1 transmission from donors with high proviral load.

Although there is some literature on the cost-effectiveness of HTLV screening, additional work is needed to evaluate alternative strategies, particularly HTLV-1 antibody screening of first time donors only and the effectiveness of leukoreduction. Data on the clinical outcomes of HTLV-1 infection and on the survival of blood transfusion recipients is available but needs to be assembled in a critical fashion. Less data are available on the cost of treating HTLV-1 diseases including ATL and HTLV-1 associated myelopathy. A couple of Scandinavian countries have already made the decision to scale back testing to first time donors only and there is currently debate in mainland France on the cost-effectiveness of continuing HTLV-1 antibody screening.

9. Conclusions and future directions

In conclusion, there is currently a mismatch of prevention strategies for transfusion transmission of HTLV-1 across the world, with high-income countries performing expensive testing in very low prevalence and incidence settings. In contrast, many low and middle-income countries with much higher endemicity of HTLV-1 are currently performing no or ineffective HTLV-1 screening. A shift in global priorities and resources would seem to be in order, with the potential adoption of less costly screening strategies in low prevalence countries and institution of at least antibody screening in high prevalence countries that currently perform no testing. An additional benefit of broader introduction of HTLV screening of blood donors would be the generation of prevalence data that can be compared across countries. Better information on HTLV-1 prevalence is needed from India, China and many countries in sub-Saharan Africa in order to gauge the necessity for better prevention measures for HTLV-1 transfusion transmission. Finally, research on the efficacy of filter leukoreduction and pathogen inactivation technologies is needed to guide policies in countries that could afford these approaches instead of antibody screening.

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Table 1

HTLV-1 and -2 seroprevalence among blood donors in various countries.

Region	Country	N Pos/N tested	Prevalence	Reference
Americas	*Argentina*	129/14,228	0.9%	Biglione M, J AIDS 1999
	Brazil	327/281,760	0.12%	Carneiro-Proietti AB, AIDS Res Human Retrov 2012 (adjusted for HTLV-1 vs. HTLV-2)
	Canada		8.1×10^{-5}	O'Brien S, Transfusion Med 2013 (adjusted for HTLV-1 vs. HTLV-2)
	Chile	37/3,437	1.1%	Cartier L, Truth and Questions 1996 Vasquez P, Blood 1991
	Cuba	0/1600	–	Hernandez Ramirez P, Vox Sang 1991
	Dominican Republic	23/1955	1.2%	Koenig R, AIDS Res Hum Retrov 1992
	Guadeloupe	272/97,150	0.3%	Rouet F, Transfusion 1999 and Rouet F, J Clin Microbiol 2001
	Guyana	13/1035	1.3%	Pouliquen JF, J Clin Microbiol 2004
	Jamaica	376/15,022	2.5%	Brady-West, West Indian Med J 2000
	Nicaragua	1/410	0.2%	Qiu X, J Med Virol 2008
	Surinam	3/77	–	Alberga H, Ned Tijdschr Geneeskd 1996
	Trinidad & Tobago	16/1089	1.5%	Daisley H, Trop Med Parasitol 1991
	United States	104/2,047,740	5.1×10^{-5}	Chang YB, J Infect Dis 2014
	Uruguay	2/266	0.8%	Muchnik G, JAIDS 1992
	Venezuela	23/23,413	0.1%	Leon G, Rev Panam Salud Publica 2003
Europe	Denmark	1/119,973	0.8 per 10^{-5}	Laperche S, Vox Sang 2009; Dickmeiss E Ugeskr Laeger 2001; Christiansen PB, Vox Sang 1995
	Finland	0/52,124	–	Laperche S, Vox Sang 2009
	France	54/1,115,030	4.8×10^{-5}	Laperche S, Vox Sang 2009
	Germany	0/100,852	–	Nubling M, Vox Sang 2001
	Greece	29/1,524,568	1.9×10^{-5}	Laperche S, Vox Sang 2009
	Ireland	0/55,524	0	Laperche S, Vox Sang 2009
	The Netherlands	5/110,307	4.5×10^{-5}	Laperche S, Vox Sang 2009
	Norway	0/41,421	–	Laperche S, Vox Sang 2009
	Romania	115/215,732	53.3×10^{-5}	Laperche S, Vox Sang 2009
	Sweden	2/117,383	1.7×10^{-5}	Laperche S, Vox Sang 2009
	Switzerland	1/1,266,466	0.08×10^{-5}	Boni J, J Med Virol 2004
	United Kingdom	40/850,801	4.7×10^{-5}	Laperche S, Vox Sang 2009
Africa	*Guinea*	22/1785	1.2%	Gessain A, JAIDS 1993
	La Reunion	2/114,187	1.8×10^{-5}	Aubry P, Bull Soc Patho Exot 2013
	Malawi	4/159	2.5%	Candotti D, J Med Virol 2001
	Mali	11/799	1.4%	Diarra AB, Transfus Clin Biol 2014
	Mozambique	18/1989	0.9%	Vicente AC, PLOS Neglect Trop Dis 2011
	Niger	3/600	0.5%	Develoux M, Med Trop 1996
	Nigeria	15/736	2.0%	Olaleye DO, Int J Epidemiol 1995
	Senegal	8/4900	0.2%	Diop S, J Clin Microbiol 2006
	Tunisia	0/500	–	Mojaat N, JAIDS 1999

Region	Country	N Pos/N tested	Prevalence	Reference
Middle East	Saudi Arabia	5/181,704	2.8×10^{-5}	Kawashsti M, Egypt Immunol 2005; Balkhy ZA, Milit Med 2004; Ul-Hassan Z, Saudi Med J 2004; El-Hazmi MM, Saudi Med J 2004; Arif M, Ann Trop Med Parasitol 1998; Bernvil SS, Transfus Sci 1997
	Oman	0/1586	–	Know-Macaulay H, Scan J Infect Dis 1997
	Kuwait	1/10,819	9.2×10^{-5}	Al-Mufti S, JAIDS 1997
	Iran	208/28,928	0.7%	Abbaszadegan MR, J Clin Microbiol 2003
	Iraq	7/68,857	10.2×10^{-5}	Stienlauf S, Emerg Infect Dis 2009
	Israel	3/294,342	1.0×10^{-5}	Stienlauf S, Emerg Infect Dis 2009
	Lebanon	2/4429	4.5×10^{-4}	Tamim H, Am J Infect Control 2004; Naman R, J Infect 2002
	Turkey	4/35,054	11.4×10^{-5}	Sertoz R, Mikrobiyol Bul 2010; Stienlauf S, Emerg Infect Dis 2009
Asia	*India*	14/10,000	0.1%	Kumar H, Indian J Pathol Microbiol 2006
	Indonesia	0/79	–	Tanggo Y, Intervirology 2000
	Japan	3787/1,196,321	0.3%	Satake M, J Med Virol 2012
	Korea, South	1/15,173	6.6×10^{-5}	Kwon SY, J Med Virol 2008
	Nepal	0/413	–	Nakashima K, J Trop Med Hyg 1995
	Russia	7/111,109	6.3×10^{-5}	Stienlauf S, Emerg Infect Dis 2009
	Taiwan	1793/2,578,238	6.9×10^{-4}	Lu SC, Int J Hematol 2003
	Turkmenistan	3/1510	0.2%	Senyuta N, Int J Cancer 1998
Oceania	Australia	16/4,571,448	0.3×10^{-5}	Seed CR, Int Med J 2005; Whyte GS, Med J Australia 1997
	French Polynesia	1/395	0.3%	Chungue E, Eur J Epidemiol 1993
	Hawaii (USA)	N/A	0.2%–0.8%	Dixon PS, West J Med 1990
	New Zealand	0/111	–	Reddy D, J Med Virol 1987
	Samoa	0/50	–	Reddy D, J Med Virol 1987

Where more than one reference is given, similar data from the two studies were combined. Grey shading indicates countries with higher prevalence. Adapted from European Centre for Disease Prevention and Control. In italics: geographical distribution of areas with a high prevalence of HTLV-1 infection. Stockholm: ECDC; 2015.

Table 2

Incidence and estimated residual risk of (a) HTLV-1/2 and (b) hepatitis C virus (HCV) transmission in US blood donors.

Year	Incidence per 10^5 person-years	Residual risk per 10^6 transfused blood units	Reference
HTLV-1 and -2			
1991–1993	1.12	1.59	Schreiber, NEJM 1996
1991–1996	1.59	–	Glynn, JAMA 2000
1998–2001	0.66	0.92	Dodd, Transfusion 2002
2007–2008	0.21	0.29	Zou, Trans Med Rev 2012
HCV			
1991–1993	4.32	9.70	Schreiber, NEJM 1996
1991–1996	3.25	–	Glynn, JAMA 2000
1998–2001	2.09	3.63/0.52[a]	Dodd, Transfusion 2002
2007–2008	2.98	0.60[a]	Zou, Trans Med Rev 2012

[a]With nucleic acid testing (NAT).