Human T-Cell Lymphotropic Virus Type 1 Exposures Following Blood-borne Virus Incidents in Central Australia, 2002–2012

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We retrospectively audited hospital occupational exposure events over a 10-year period, in a human T-cell lymphotropic virus type 1 (HTLV-1)–endemic area of Central Australia, and report on 53 individuals exposed to HTLV-1 with no transmissions documented (95% confidence interval, 0%–1.5%). This has important implications for the management of exposures including the role of postexposure prophylaxis.

Keywords. HTLV-1; occupational exposure; needlestick.

Human T-cell lymphotropic virus type 1 (HTLV-1) infects 10–20 million people worldwide in a number of distinct geographical regions [1]. Despite being the first recognized human retrovirus, much about its pathogenesis and clinical impact remains unknown. Although there are recognized inflammatory, malignant, and infective sequelae, the majority of infected individuals remain asymptomatic [1].

Similar to human immunodeficiency virus (HIV), HTLV-1 is blood-borne and is capable of transmission via a number of mechanisms including breastfeeding, sexual intercourse, and blood exposure. HTLV-1, however is a cell-associated virus, requiring the transfer of whole cells for infection to occur [1], and is therefore less efficient at transmission than HIV. Prior to routine donor blood screening, HTLV-1–infected blood transfusions were associated with high rates of transmission [1, 2], and higher rates of seropositivity were seen in those with a history of injection drug use [3]. Therefore, it is biologically plausible that HTLV-1 transmission can also occur from occupational needlestick injuries (NSIs). In the setting of contaminated transfusions, seroconversion generally occurs within 3 months and clinical sequelae, especially HTLV-1–associated myelopathy/tropical spastic paraparesis (HAM/TSP), have been described [1, 2].

Central Australia, a geographic region of >1 million km^2, contains a focus of HTLV-1 among Indigenous Australians. True prevalence rates are unknown, but estimates of seropositivity range from 14% of adults in one community [4] to 59.8% in some inpatient groups at Alice Springs Hospital (ASH) [5]. The Northern Territory Department of Health policy for occupational exposures includes testing the source patient for baseline HTLV-1 infection and follow-up serology on the recipient for 6 months to monitor for seroconversion. Postexposure prophylaxis (PEP) with antiretroviral therapy (ART) for substantial exposures is considered on an individual basis—extrapolating from in vitro evidence of anti–HTLV-1 activity and the known benefit of PEP in HIV exposures.

Despite the known risk of transmission via blood, we are aware of only 1 previous report of occupational transmission of infection [6]. Here we describe all occupational exposures to blood from an HTLV-1–seropositive source in the period 1 January 2002 through 30 September 2012 and the resultant rate of viral transmission.

METHODS

We obtained details of occupational exposures from the ASH Infection Control database between 1 January 2002 and 30 September 2012, cross-referencing with Northern Territory Government Pathology Service databases to capture all exposures. For each exposure, the HTLV-1–positive patient was referred to as the "source" and the exposed staff member as the "recipient."

Demographic data including age, sex, and HTLV-1 serological status of the source were recorded along with type of exposure, baseline and follow-up serology of the recipient, and prescription of PEP. Exposures were grouped into 5 risk categories: those involving a hollow-bore needlestick; solid, sharp instrument injuries (eg, scalpel wounds); mucous membrane exposure; bites; and insignificant (included splashes and scratches). Use of PEP with antiretrovirals was recorded.

Two HTLV-1 serological assays were used during the study period: Serodia particle agglutination assay (Tokyo, Japan)

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from 2002 to 2008, and Abbott Architect HTLV-1/2 chemiluminescent enzyme immunoassay (Chicago, Illinois) between 2009 and 2012. Reactive and indeterminate results were sent for confirmation by Western blot analysis at the National Reference Laboratory (Melbourne, Victoria). A positive Western blot requires reactivity to both recombinant envelope proteins (Rgp21 and Rgp46-I) and/or envelope gp46 plus reactivity to at least 3 other viral specific proteins of the gag and pol series.

Confidence intervals (CIs) were calculated using 1-sided 95% confidence intervals. All statistical analysis was performed using Stata software, version 11 (StataCorp). Ethics approval was received from the Central Australian Human Research Ethics Committee.

RESULTS

One hundred and five recipients were identified, 4 having 2 exposures each, resulting in 109 exposure events. One recipient who had 2 exposures was HTLV-1 seropositive and 1 had indeterminate serology at baseline. These recipients were excluded from further analysis, leaving 106 exposures in 103 recipients.

The breakdown of exposure types is shown in Table 1. Fifty-seven exposures (53.8%) involved a hollow-bore NSI, 11 of 106 (10.4%) were with solid, sharp instruments, 24 of 106 (22.6%) involved mucous membrane exposures, and 4 of 106 (3.8%) involved bite injuries. The remaining included splash and scratch exposures [3, 7] with negligible risk of transmission. Use of PEP was documented in 3 (2.8%) NSI incidents—in all cases, lamivudine-zidovudine was prescribed.

Only 53 of 106 (50%) of recipients had follow-up serology. Of these, there were no documented seroconversions, with an estimated risk of transmission of 0% (1-sided 95% CI, 0%–1.5%). Of the highest risk exposure category (hollow-bore NSIs), 27 of 57 (47.4%) had follow-up serology with no transmission (0%; 95% CI, 0%–2.9%). Of those followed up, 49 (92.4%) had at least 1 follow-up serology test at >60 days postexposure and 41 (77.4%) at >90 days postexposure.

DISCUSSION

HTLV-1 is a cell-associated retrovirus transmissible via a number of mechanisms similar to HIV. Evidence of transmission from blood transfusions [1, 2] and injection drug use [3] suggests that there is potential risk of transmission from occupational blood exposures. However, the sole published case report of occupationally acquired infection is of a midwife working in West Africa who had been exposed to infected blood while assisting in childbirth [6].

Despite the seemingly low risk of transmission, the potential consequences are substantial. The sole report of occupationally acquired infection was likely only detected as the patient suffered from HAM/TSP [6]; evidence from transfusion cohorts suggests this is a significant risk, perhaps even within a few years of infection [2]. Much less commonly, HTLV-1–associated uveitis has been seen [7]. Infective sequelae (eg, strongyloidiasis and bronchiectasis) have not been described and are perhaps much harder to quantify. The most dire HTLV-1–associated condition, adult T-cell leukemia/lymphoma (ATLL), is unlikely to be seen given its long latency period and association with transmission from breastfeeding [1].

Little is known about the role of ART. HTLV-1 has many enzymes functionally similar to those in HIV, and a number of antiretrovirals have some in vitro activity against HTLV-1, including the nucleoside/nucleotide reverse transcriptase inhibitors and raltegravir, an integrase inhibitor [8, 9]. In general, the results of ART in HTLV-1 have been disappointing—both on proviral load and clinical course—with the exception of zidovudine in the treatment of ATLL. The ineffectiveness of ART is possibly explained by the differing mechanisms of HTLV-1 infection compared with HIV. In established disease, cellular mitosis is the predominant determinant of proviral load, a setting where ART probably has little to offer. However, in early infection, the cell-associated HTLV-1 is transmitted largely by cell-to-cell synapses where, theoretically, ART may be of some benefit [9]. Regardless, the role of PEP in HTLV-1 infection is

Table 1. Occupational Exposure Injuries and Follow-up

Type of Exposure	Total No. of Exposures	No. of Exposures With Follow-up Serology	Transmission Rate[a], % (1-Sided 95% CI)	Duration of Follow-up, d, Median (Range)
Hollow-bore needlestick	57	27	0 (0–2.9)	116 (42–1894)
Solid sharp	11	5	0 (0–14.8)	124 (103–681)
Mucous Membrane	24	14	0 (0–5.5)	97 (57–1325)
Bite wound	4	3	0 (0–23.4)	117 (84–470)
Other[b]	10	4	0 (0–18.1)	142 (26–185)
All	106	53	0 (0–1.5)	117 (26–1894)

Abbreviation: CI, confidence interval.

[a] Of those with follow-up serology performed.

[b] "Other" injury included splash and scratch injuries.

based on little clinical evidence and is only considered in high-risk exposures, after suitable counseling, explaining the low rates of PEP prescribed in our study.

Our study has some limitations. First, HTLV-1 transmission is dependent on proviral load in the source [10], which could not be quantified in our study as this was not routinely available during the period under study. A large proportion of HTLV-1 carriers have a negligible proviral load even in the absence of specific therapy [11]; therefore, many of the exposures in our study likely carried a negligible risk of transmission regardless of the volume of blood or mechanism involved. Recently, proviral load testing has become available, which may allow a better quantification of risk in the future. Furthermore, the true seroconversion time following HTLV-1 exposure is unclear, but extrapolating from transfusion-associated infections probably lies between 2 and 3 months [1]. Given that the median follow-up in our study was 117 days, it is unlikely seroconversion was missed in those who did complete follow-up.

Our low follow-up rate (50%) is perhaps attributable to the high staff turnover at ASH. A large number of recipients had finished their contract by the time follow-up serology was required. Regardless, our study allows for some quantification of the risk of transmission, in the order of 1% at the very most and much less than the high rates reported with blood transfusion. If the risk is of a similar degree to that of HIV—an estimated 0.3% transmission risk with an NSI and only 0.09% with a mucous membrane exposure [12]—then our study was underpowered and would have required approximately 350 exposures to demonstrate 1 infection in the setting of an NSI. Although it may be underpowered, our study is the only published case series on follow-up of occupational exposures to HTLV-1, and although it failed to demonstrate viral transmission, it certainly aids in the quantification of risk.

In conclusion, in the only published case series of occupational exposure to HTLV-1 infection published to date, we found no evidence of seroconversion in 53 exposed healthcare workers with follow-up serology, despite only 3 having received PEP. This has important implications for the future management of such exposures. We suggest that reassurance and follow-up without PEP is reasonable for all but massive exposures, where PEP with ART may be considered. Our finding should be confirmed in further research, including proviral load measurement and a much larger number of exposures.

Note

Potential conflicts of interest. J. D. has received research funding from Gilead, and reimbursement for travel and accommodation expenses to attend educational meetings on viral hepatitis. All other authors report no potential conflicts.

All authors have submitted the ICMJE Form of Disclosure of Potential Conflicts of Interest. Conflicts that the editors consider relevant to the content of the manuscript have been disclosed.

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