20 | HUMAN T-LYMPHOTROPIC VIRUS VARIANTS

This fact sheet is archived and will not be further updated without further evidence that the pathogen(s) pose a threat in the context of transfusion medicine.

20.1 | Disease agent

- Human T-lymphotropic virus (HTLV) variants (HTLV-3 and HTLV-4)

20.2 | Disease agent characteristics

- HTLV-1, HTLV-2, HTLV-3, and HTLV-4 belong to the primate T-lymphotropic viruses group (PTLV).
- HTLV-3 and HTLV-4 are divergent from HTLV-1 and HTLV-2.
- Family: *Retroviridae*; Genus: *Deltaretrovirus*.
- Virion morphology and size: Enveloped, icosahedral nucleocapsid symmetry, spherical particles, 150–200 nm in diameter.
- Nucleic acid: Linear, positive-sense single-stranded RNA; HTLV-I has a genome of 8.5 kb in length whereas other primate T-lymphotropic retroviruses (PTLVs) range from 8.5 to 9.0 kb in length.
- Physicochemical properties: Sensitive to treatment with heat, detergents, and formaldehyde.

20.3 | Disease name

- No disease associations to date

20.4 | Priority level

- Scientific/Epidemiologic evidence regarding blood safety: Low; although the wild-type agents are transfusion transmitted, transfusion transmission of the variants has not been documented. If variants are transmissible, the risk would be very low in the United States because of cross-reactivity of screening tests, use of donor questions, and limited global distribution of variants.
- Public perception and/or regulatory concern regarding blood safety: Absent
- Public concern regarding disease agent: Absent

20.5 | Background

- The deltaretroviruses HTLV-3 and HTLV-4 are variants, genetically distinct at the nucleic acid level from HTLV-1 and 2 that are screened for in US blood collection facilities.
- These are emergent viruses, mainly in Central Africa (Cameroon and South Cameroon), diverging from other PTLVs that evolved from closely related simian retroviruses.
- It is likely that additional variants will be found if research initiatives screen both non-human primate and human populations for such agents.
- To date a small number of human HTLV-3 and 4 infections have been reported, but no disease associations are established.

20.6 | Common human exposure routes

- Data on exposure routes to date are mostly confined to screening studies in populations that reside in Central Africa, and these have generally been selected for those with extensive contact with nonhuman primates (hunting, butchering, and pet keeping).

20.7 | Likelihood of secondary transmission

- Whether sexual and/or parenteral transmission occurs is speculative.

20.8 | At-risk populations

- Current data are limited to populations residing in Central Africa who have extensive contact with nonhuman primates (e.g., hunting, butchering, and pet keeping).

20.9 | Vector and reservoir involved

- Not known to be vector transmitted; reservoir is nonhuman primates.

20.10 | Blood phase

- Longitudinal studies are not available, but, if the analogies to HTLV-1 and 2 are correct, these will be chronic, lifelong infections.

20.11 | Survival/persistence in blood products

- Not known

20.12 | Transmission by blood transfusion

- Although wild-type HTLV is transfusion-transmitted via cellular blood components, transmission of the variants has not been documented, but likely.

20.13 | Cases/frequency in population

- These viruses exist at the case report level in humans in Central Africa.

20.14 | Incubation period

- Not known

20.15 | Likelihood of clinical disease

- Not known

20.16 | Primary disease symptoms

- No recognized disease associations to date

20.17 | Severity of clinical disease

- No recognized disease associations to date

20.18 | Mortality

- None recognized to date

20.19 | Chronic carriage

- Unknown, but reasonable to assume that long-term carriage will be demonstrated

20.20 | Treatment available/efficacious

- There are no data and there are no effective antiviral treatments for HTLV-1 or 2 infections.

20.21 | Agent-specific screening question(s)

- No specific question is in use.
- Not indicated because of the rarity of human infection and transfusion transmission and disease association have not been demonstrated.
- No sensitive or specific question is feasible.

20.22 | Laboratory test(s) available

- No FDA-licensed blood donor screening test exists for HTLV variants; however, there are US-licensed assays required for screening all donors and donations for HTLV-1 and 2.
  - One-time donor screening has been implemented in some EU countries and proposed in US, based on the low prevalence and incidence of HTLV-1 and 2 infections among donors and the widespread use of leukoreduction.
- HTLV antibody assays have been used to screen target populations for HTLV variants, both in Africa and among US blood donors, relying on serological cross-reactivity.
- When viral nucleic acid was amplified from seroindeterminate blood donor samples and analyzed in comparison to known PTLV sequences for phylogenetic characterization, HTLV-3 and 4 were identified. However, these variants have never been identified in US blood donors.
- Reliance on serological cross-reactivity and the highly conserved nucleic acids of these agents may not demonstrate the full diversity of this group.

20.23 | Currently recommended donor deferral period

- No FDA Guidance or AABB Standard exists.
- HTLV-infected donors should be permanently deferred.

20.24 | Impact on blood availability

- Agent-specific screening question(s): Not applicable
- Laboratory test(s) available: Not applicable

20.25 | Impact on blood safety

- Agent-specific screening question(s): Not applicable
- Laboratory test(s) available: Not applicable

20.26 | Leukoreduction efficacy

- Because HTLV-1 and HTLV-2 are highly WBC associated, leukoreduction will reduce the risk of variant transmission by transfusion. Data suggest that effective leukoreduction reduce HTLV-1 provirus to below detectable limits.

20.27 | Pathogen reduction efficacy for plasma derivatives

- Frozen plasma and plasma derivatives have not been demonstrated to transmit HTLV-1 and 2, presumably related to their WBC association and the effect of freezing and fractionation on virus.
- Probably highly susceptible to inactivation by many methods currently used in fractionation based on data for HTLV-1 and 2.

20.28 | Other prevention measures

- By analogy with HTLV-1 and 2, consider advising infected mothers to avoid breast-feeding their infants.

SUGGESTED READING

1. Busch MP, Switzer WM, Murphy EL, Thomson R, Heneine W, for the Retrovirus Epidemiology Donor Study. Absence of evidence of infection with divergent primate T-lymphotropic viruses in United States blood donors who have seroindeterminate HTLV test results. Transfusion. 2000;40:443–9.
2. Centers for Disease control and Prevention and the US Public Health Service working group. Guidelines for counseling persons infected with Human T-Lymphotropic type I (HTLV-I) and type II (HTLV-II). Ann Intern Med. 1993;118:454.
3. Cesaire R, Kerob-Bauchet B, Bourdonne O, Maier H, Amar KO, Halbout P, et al. Evaluation of HTLV-I removal by filtration of blood cell components in a routine setting. Transfusion. 2004;44:42–8.
4. Crowder LA, Haynes JM, Notari EP, Dodd RY, Stramer SL. Low risk of human T-lymphotropic virus infection in U.S. blood donors; Is it time to consider a one-time selective testing approach? Transfusion. 2023;63(4):764–73.
5. Donegan E, Lee H, Operskalski EA, Shaw GM, Klein- man SH, Busch MP, et al. Transfusion transmission of retroviruses: human T-lymphotropic virus types I and II compared with human immunodeficiency virus type 1. Transfusion. 1994;34:478–83.
6. Jauvin V, Alfonso RD, Guillemain B, Dupuis K, Fleury HJ. In vitro photochemical inactivation of cell-associated human T-cell leukemia virus type I and II in human platelet concentrates and plasma by use of amotosalen. Transfusion. 2005;45:1151–9.
7. Lin L, Hanson CV, Alter HJ, Jauvin V, Bernard KA, Murthy KK, et al. Inactivation of viruses in platelet concentrates by photochemical treatment with amotosalen and long-wavelength ultraviolet light. Transfusion. 2005;45:580–90.
8. Pennington J, Taylor GP, Sutherland J, Davis RE, Seghatchian J, Allain JP, et al. Persistence of HTLV-I in blood components after leukocyte depletion. Blood. 2002;100:677–81.
9. Mahieux R. Antoine Gessain HTLV-3/STLV-3 and HTLV-4 viruses: discovery, epidemiology, serology and molecular aspects. Viruses. 2011;3(7):1074–90. https://www.ncbi.nlm.nih.gov/pmc/articles/PMC3185789/
10. Wolfe ND, Heneine W, Carr JK, Garcia AD, Shan- mugam V, Tamoufe U, et al. Emergence of unique primate T-lymphotrophic viruses among central African bushmeat hunters. Proc Natl Acad Sci USA. 2005;102:7994–9.