

Human T-Lymphotropic Virus Variants

Disease Agent:

- Human T-lymphotropic virus (HTLV) variants (HTLV-III and HTLV-IV)

Disease Agent Characteristics:

- 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

Disease Name:

- No disease associations to date

Priority Level:

- Scientific/Epidemiologic evidence regarding blood safety: Theoretical; 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 US 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

Background:

- The deltaretroviruses HTLV-III and HTLV-IV are HTLV variants, genetically distinct at the nucleic acid level from HTLV-I and II that are screened for in US blood collection facilities.
- These are emergent viruses, mainly in Africa, diverging from other PTLVs that evolved from closely related simian retroviruses.
- It is very probable that additional variants will be found, given current initiatives to screen both non-human primate and human populations for such agents.

Common Human Exposure Routes:

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

Likelihood of Secondary Transmission:

- Whether sexual and/or parenteral transmission will be demonstrated is speculative, but appears likely, based on analogy with HTLV-I and II.

At-Risk Populations:

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

Vector and Reservoir Involved:

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

Blood Phase:

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

Survival/Persistence in Blood Products:

- Not known

Transmission by Blood Transfusion:

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

Cases/Frequency in Population:

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

Incubation Period:

- Not known

Likelihood of Clinical Disease:

- Not known

Primary Disease Symptoms:

- No recognized disease associations to date

Severity of Clinical Disease:

- No recognized disease associations to date

Mortality:

- None recognized to date

Chronic Carriage:

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

Treatment Available/Efficacious:

- Absent disease associations and specific treatment information, extrapolating any data or experience on the efficacy of treatments being studied for HTLV-I and HTLV-II infections is inappropriate.

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.

Laboratory Test(s) Available:

- No FDA-licensed blood donor screening test exists for HTLV variants; however, there is one US-licensed assay available to screen blood donors for HTLV-I and II. 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.
- In general, immunoblot analysis of antibody-reactive individuals from target populations has yielded groups of positives and indeterminates from whom cells have been subjected to NAT using broadly conserved primers. When viral nucleic acid has been amplified, it is analyzed in comparison to known PTLV sequences for phylogenetic characterization. This has allowed identification of HTLV-III and IV in Africa and demonstrated no evidence of variant HTLV infection in US blood donors in one study.
- Reliance on serological cross-reactivity and conservation of nucleic acid sequences across an increasingly diverse group of viruses may not demonstrate the full diversity of this group.

Currently Recommended Donor Deferral Period:

- No FDA Guidance or AABB Standard exists.
- If a donor known to be infected with an HTLV variant presented to donate, a permanent deferral would be prudent.

Impact on Blood Availability:

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

Impact on Blood Safety:

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

Leukoreduction Efficacy:

- Because HTLV-I and HTLV-II are highly WBC associated, it is hypothesized that leukoreduction will reduce the risk of variant transmission by transfusion. Data suggest that effective filtration leukoreduction of RBCs can reduce HTLV-I provirus to below detectable limits, but failures are clearly described.

Pathogen Reduction Efficacy for Plasma Derivatives:

- Frozen plasma and plasma derivatives have not been demonstrated to transmit HTLV-I and II, 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-I and II.

Other Prevention Measures:

- By analogy with HTLV-I and II, 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). *Annals of Internal Medicine* 1993;118:454.
3. Cesaire R, Kerob-Bauchet B, Bourdonne O, Maier H, Amar KO, Halbout P, Dehée A, Désiré N, Dantin F, Béra O, Lézin A. Evaluation of HTLV-I removal by filtration of blood cell components in a routine setting. *Transfusion* 2004;44:42-8.
4. Donegan E, Lee H, Operskalski EA, Shaw GM, Kleinman SH, Busch MP, Stevens CE, Schiff ER, Nowicki MJ, Hollingsworth CG, Mosley JW; Transfusion Safety Study Group. Transfusion transmission of retroviruses: human T-lymphotropic virus types I and II compared with human immunodeficiency virus type 1. *Transfusion* 1994;34:478-83.
5. 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.
6. Lin L, Hanson CV, Alter HJ, Jauvin V, Bernard KA, Murthy KK, Metzel P, Corash L. Inactivation of viruses in platelet concentrates by photochemical treatment with amotosalen and long-wavelength ultraviolet light. *Transfusion* 2005;45:580-90.
7. Pennington J, Taylor GP, Sutherland J, Davis RE, Seghatchian J, Allain JP, Williamson LM. Persistence of HTLV-I in blood components after leukocyte depletion. *Blood* 2002;100:677-81.
8. Wolfe ND, Heneine W, Carr JK, Garcia AD, Shanmugam V, Tamoufe U, Torimiro JN, Prosser AT, LeBreton M, Mpoudi-Ngole E, McCutchan FE, Birx DL, Folks TM, Burke DS, Switzer WM. Emergence of unique primate T-lymphotrophic viruses among central African bushmeat hunters. *Proc Natl Acad Sci USA* 2005;102:7994-9.