

Human Immunodeficiency Virus Variants

Disease Agent:

- Human immunodeficiency virus type-1 (HIV-1), group M, non-B clades
- HIV-1, group O (outlier)
- HIV type-2 (HIV-2)

Disease Agent Characteristics:

- Family: *Retroviridae*; Genus: *Lentivirus*; Species: HIV-1 and HIV-2
- Virion morphology and size: Enveloped, icosahedral nucleocapsid with cone-shaped core structure, spherical to pleomorphic particles, 106-183 nm in diameter (mean: 125 nm)
- Nucleic acid: Linear, positive-sense, single-stranded RNA; ~9.2 kb in length
- Physicochemical properties: Virions are sensitive to treatment with heat, detergents, and formaldehyde

Disease Name:

- Acquired immune deficiency syndrome (AIDS)

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 minimal in the US because of cross-reactivity of screening tests, use of donor questions, and limited geographic distribution of variants.
- Public perception and/or regulatory concern regarding blood safety: Low/Moderate based on transmission of HIV in general, rather than HIV variants
- Public concern regarding disease agent: Low to moderate based on transmission of HIV in general, rather than HIV variants

Background:

- Human lentiviruses consist of two viral species, HIV-1 and HIV-2.
- HIV-1 consists of three identified lineages (groups M, N, and O). Each lineage is made up of numerous subtypes (clades), as well as recombinants of these subtypes.
- HIV-2, some strains of which are indistinguishable from SIVsmm derived from sooty mangabeys, also is made up of several subtypes.
- The initial HIV-1 strain recognized was group M clade B; this subtype is currently the most prevalent

subtype in North America and Europe, whereas clade C is most prevalent worldwide.

- By 2005, over 11 subtypes of HIV-1 group M, as well as 16 common recombinant forms, had been identified (<http://www.hiv.lanl.gov/content/index>).
- In Europe, multiple subtypes and recombinant forms of HIV-1 group M have been detected at high frequency, along with isolated infections with HIV-1 group O and HIV-2 viruses.
- The US remains one of the most genetically homogeneous regions in terms of HIV-1 diversity, with >99% clade B infections (<http://www.hiv.lanl.gov/content/index>). However, an increasing number of HIV-1 subtypes have been detected in US blood donors, and a mix of subtypes could emerge, similar to that seen in Europe.
- Groups N and O HIV-1 have so far been detected primarily in sub-Saharan Africa.

Common Human Exposure Routes:

- Sexual activity (exposure of the oral, rectal, or vaginal mucosa during sex)
- Breast feeding
- Injection-drug use
- Blood transfusions where no HIV screening is carried out or is not capable of detecting N and O variants
- Other parenteral exposures

Likelihood of Secondary Transmission:

- Little data on variants, but, based on M group, secondary transmission could be high

At-Risk Populations:

- Sexually active individuals
- Injection-drug users
- Children born to infected mothers

Vector and Reservoir Involved:

- Infected humans
- Original transmission route of all variants to humans is thought to be from close contact with simian species in Africa.

Blood Phase:

- Acute high-titer plasma viremia followed by chronic intermediate level viremia
- Infected lymphocytes present in blood throughout course of infection

Survival/Persistence in Blood Products:

- Slight reduction in infectivity with storage based on data with HIV-1 clade B

Transmission by Blood Transfusion:

- Well documented for all HIV-1 group M clades and several HIV-2 clades
- Likely occurs with HIV-1 groups N and O and with circulating recombinant strains

Cases/Frequency in Population:

- HIV-1 group M clades present at pandemic level
- HIV-2 and HIV-1 groups N and O present to much lesser extent, primarily in Africa

Incubation Period:

- Seroconversion window period for clade B is ~3 weeks, and the NAT window in minipools is approximately 10 days. Time to acute retroviral syndrome is 21.5 days (range: 5-70 days), whereas time to development of AIDS is in years. Parameters for HIV variants are less well characterized.

Likelihood of Clinical Disease:

- High, although lower for HIV-2 than HIV-1

Primary Disease Symptoms:

- Severe immunodeficiency with opportunistic infections (AIDS)

Severity of Clinical Disease:

- High

Mortality:

- >90% in absence of therapy after prolonged asymptomatic carrier stage

Chronic Carriage:

- Yes

Treatment Available/Efficacious:

- Broad range of highly active anti-retroviral (HAART) drugs has been developed.
- HAART is able to suppress viremia and delay onset of clinical disease in the vast majority of treated individuals infected with all HIV variants, although development of resistance in inadequately treated or nonadherent persons is an increasing concern, as is transmission of drug resistant strains (primary resistance).

Agent-Specific Screening Question(s):

- Current screening questions are based on known HIV exposure risks.
- Questions about travel to or living in Africa and sex partners from Africa are designed to detect exposure to HIV variant strains for which some licensed blood

donor screening assays are less sensitive than for group M strains. However, when a blood donor-screening test with a specific group O claim is used, the Africa travel question is not indicated.

Laboratory Test(s) Available:

- FDA-licensed antibody to HIV-1/HIV-2 serological assays are required, and HIV-1 NAT assays are recommended.
- The combination antibody to HIV-1/HIV-2 serological donor screening assays are sensitive for all group M clades and HIV-2. Performance with variants (N and O) is variable.
- Licensed NAT is highly sensitive for group M clades of HIV-1 but variably sensitive for HIV-1 variants and does not detect HIV-2.

Currently Recommended Donor Deferral Period:

- In the US, FDA-required deferrals vary depending on risk factor (e.g., permanent for any IDU or for a male having sex with another male [MSM] post-1977; 1 year for most other high risk behaviors).
- In the US, indefinite deferral is required for potential exposure in countries where group O is prevalent unless an approved assay sensitive for group O is used.

Impact on Blood Availability:

- Agent-specific screening question(s): There is minimal impact as a result of the Africa deferral question.
- Laboratory test(s) available: Using donor screening assays sensitive for HIV variants has minimal additional impact on donor availability.

Impact on Blood Safety:

- Agent-specific screening question(s): The Africa deferral question has minimal impact given the low prevalence of HIV variants.
- Laboratory test(s) available: Serological blood screening considered effective for all variants, albeit with a prolonged window period for non-B clades and other variants.

Leukoreduction Efficacy:

- Not effective because of plasma viremia

Pathogen Reduction Efficacy for Plasma Derivatives:

- Highly susceptible to inactivation based on data for HIV-1 Group M

Other Prevention Measures:

- Vaccine trials are ongoing

Suggested Reading:

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