19 | HUMAN IMMUNODEFICIENCY VIRUS VARIANTS

19.1 | Disease agent

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

19.2 | 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: Two copies of linear, positive-sense, single-stranded RNA; ~9.2 kb in length.
- Physicochemical properties: Virions are sensitive to treatment with heat, detergents, and formaldehyde.

19.3 | Disease name

- Acquired immune deficiency syndrome (AIDS)

19.4 | Priority level

- Scientific/Epidemiologic evidence regarding blood safety: Moderate; although the most common groups and clades are transfusion-transmitted, transfusion transmission of some variants has not been documented. Assuming variants are transmissible, the risk would be minimal in the United States because of cross-reactivity of screening tests, use of donor questions, and their limited geographic distribution.
- Public perception and/or regulatory concern regarding blood safety: Moderate based on transmission of HIV in general, rather than HIV variants.
- Public concern regarding disease agent: Moderate based on transmission of HIV in general, rather than HIV variants.

19.5 | 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 simian immunodeficiency virus (SIVsmm) derived from sooty mangabey monkeys, also is made up of several groups.
- The initial HIV-1 strain recognized was group M clade B; this subtype remains the most prevalent subtype in North America, South America, and Europe, whereas clade C is most prevalent in Africa and most of Asia.
- By 2021, over 11 subtypes of HIV-1 group M, as well as many circulating recombinant forms (CRF), have been identified (http://www.hiv.lanl.gov/content/index). One HIV-2 CRF had also been identified.
- 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.
- 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).
- Identified variants remain a tiny proportion of HIV infections in blood donors in the United States, accounting for <1% of sequenced isolates from donor specimens. Groups N and O HIV-1 have so far been detected primarily in sub-Saharan Africa.

19.6 | Common human exposure routes

- Sexual activity (unprotected mucosal exposure)
- Injection-drug use
- Blood transfusions where no HIV screening is done or assays not capable of detecting N and O variants
- Other parenteral exposures

19.7 | Likelihood of secondary transmission

- Few data on variants exist, but based on M group, secondary transmission including transfusion transmission could be high.

19.8 | At-risk populations

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

19.9 | 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.

19.10 | Blood phase

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

19.11 | Survival/persistence in blood products

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

19.12 | Transmission by blood transfusion

- Well documented for all HIV-1 group M clades and HIV-2 groups A and B
- Likely occurs with HIV-1 groups N and O and with CRFs

19.13 | 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

19.14 | Incubation period

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

19.15 | Likelihood of clinical disease

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

19.16 | Primary disease symptoms

- Severe immunodeficiency with opportunistic infections (AIDS)

19.17 | Severity of clinical disease

- High

19.18 | Mortality

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

19.19 | Chronic carriage

- Yes

19.20 | Treatment available/efficacious

- A broad range of anti-retroviral therapy (ART) drugs have been developed.
- Combination ART 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 a concern, as is transmission of drug resistant strains (primary resistance).

19.21 | Agent-specific screening question(s)

- Variant-specific questions are not used. HIV exposure questions are thought to adequately cover variants.
- Current screening questions are based on previous HIV diagnosis, on known HIV exposure risks, and use of ART to treat or prevent HIV infection.

- Questions about risk behaviors focus on the last 3 months and include sexual, parenteral, and body fluid exposures.
- The FDA published guidance in May 2023 to update donor criteria in the United States to emphasize behaviors rather than gender or sexual preferences.

19.22 | Laboratory test(s) available

- Currently required FDA-licensed HIV-1/HIV-2 donor screening assays (antibody and NAT) used in the United States are sensitive for all group M clades, group O and HIV-2. Performance with other variants (e.g., N) may be variable.

19.23 | Currently recommended donor deferral period

- In the United States, updated FDA-required deferrals were adopted in April 2020, updated in May 2023, and are mostly 3-month deferrals (e.g., IDU, other sexual exposures exchanging money or drugs for sex, needlestick or body fluid exposure, among others).
  - In May 2023, the FDA released final guidance to update donor criteria in the United States to emphasize behaviors rather than gender or sexual preferences. No deferral is required for those with a single sexual partner in the past 3 months; 3-month deferrals are in place for those with a new sexual partner or multiple partners and have participated in anal sex in the last 3 months.
  - A 3-month or 2-year deferral is in place for those taking pre-exposure prophylaxis (PrEP) to prevent an HIV infection, either oral or injectable, respectively.
- Receipt of treatment for HIV infection remains a permanent deferral.

19.24 | Impact on blood availability

- Agent-specific screening question(s): There is minimal impact related to HIV variants.
- Laboratory test(s) available: Using donor screening assays sensitive for HIV variants has minimal additional impact on donor availability.

19.25 | Impact on blood safety

- Minimal due to rarity of variants in donors

19.26 | Laboratory test(s) available

- Serology and NAT are effective for all variants, albeit with a presumed prolonged window period for non-B clades and other variants.

19.27 | Leukoreduction efficacy

- Not effective because of plasma viremia

19.28 | Pathogen reduction efficacy for plasma derivatives

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

19.29 | Other prevention measures

- Vaccine trials have been ongoing for decades; however, no vaccine has been effective, thus prevention is strictly based on behavioral strategies and antiretrovirals used for pre- and post-exposure prophylaxis.

SUGGESTED READING

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