

Epstein–Barr Virus

Agent:

- EBV (HHV-4)

Disease Agent Characteristics:

- Family: *Herpesviridae*; Subfamily: *Gammaherpesvirinae* (EBV); Genus: *Lymphocryptovirus* (EBV)
- Virion morphology and size: Enveloped, icosahedral nucleocapsid symmetry, spherical to pleomorphic particle, 120-220 nm in diameter. Between the capsid and the envelope is an amorphous layer of proteins termed the tegument.
- Nucleic acid: Linear, double-stranded DNA about 184 kbp in length
- Physicochemical properties: Nonionic detergents solubilize the envelope; virus inactivated by standard disinfectants, UV light, and gamma-irradiation; infectivity sensitive to acid pH and high temperatures; virus stable at low temperatures, especially at -60°C or below. Inactivated by heat ($50-60^{\circ}\text{C}$ for at least 30 min). EBV survives at room temperature for a few days, 2-3 days at refrigeration temperature, and -70°C for many years.

Disease Name:

- (Heterophile-positive) infectious mononucleosis
- Burkitt's lymphoma
- AIDS-related lymphoma
- Posttransplant lymphoproliferative disease (PTLD)
- Nasopharyngeal carcinoma

Priority Level:

- Scientific/Epidemiologic evidence regarding blood safety: Very low
- Public perception and/or regulatory concern regarding blood safety: Absent
- Public concern regarding disease agent: Absent

Background:

- Endemic and stable in population
- Burkitt's lymphoma (B cell) endemic in central part of Africa and New Guinea, with an annual incidence of 6-7 cases per 100,000 with peak incidence at 6-7 years of age
- Nasopharyngeal carcinoma incidence rates are less than 1 per 100,000 except in southern China where an annual incidence of more than 21 per 100,000 is reported.
- More serious disorders are confined largely to the immunocompromised and are rare.

Common Human Exposure Routes:

- Exposure to infected secretions (e.g., saliva, semen, breast milk) via respiratory tract and mucous membranes; parenteral exposure (transfusion) rare

Likelihood of secondary transmission:

- Moderate

At-Risk Populations:

- Typically greater risk of disease in immunocompromised hosts or following bone marrow or solid organ transplantation

Vector and Reservoir Involved:

- Infected humans

Blood Phase:

- EBV persists life-long in B-lymphocytes as latent virus that can be reactivated.

Survival/Persistence in Blood Products:

- EBV genomes are detectable in viable B-cells for duration of RBC storage.

Transmission by Blood Transfusion:

- Documented through seroconversion in seronegative recipients and in case reports using molecular methods.

Cases/Frequency in Population:

- Up to 95% of the population is infected by 40 years of age.

Incubation Period:

- Varies, but usually 4-7 weeks in adults and 1-2 weeks in children

Likelihood of Clinical Disease:

- Symptomatic infectious mononucleosis is relatively common in a seronegative individual especially during adolescence or young adulthood following exchange of saliva.
- Other manifestations of EBV are rare in the US.

Primary Disease Symptoms:

- Fever
- Headache
- Pharyngitis
- Lymphadenopathy

Severity of Clinical Disease:

- In general, infectious mononucleosis is not severe in immunocompetent hosts; however, posttransplant

lymphoproliferative disease and nasopharyngeal carcinoma are life threatening.

Mortality:

- Rare, except in immunocompromised patients

Chronic carriage:

- Yes; lifetime latency is typical.

Treatment Available/Efficacious:

- No drugs are available to treat EBV infection, and thus therapy is largely supportive. Specific (not antiviral) therapies are available for EBV-associated malignancies.

Agent-Specific Screening Question(s):

- No specific question is in use.
- Not indicated because the primary infection is usually asymptomatic and because up to 95% of donors are seropositive.
- No sensitive or specific question is feasible because the virus is ubiquitous.

Laboratory Test(s) Available:

- No FDA-licensed blood donor screening test exists.
- Serology (acute infection established using IgM anti-VCA, rising titers to IgG anti-VCA or anti-EA, presence of IgG anti-EBNA2 in the absence of anti-EBNA1; heterophile antibodies to sheep and/or horse RBCs); NAT for EBV in CSF, blood, or lymphoid tissue can detect virus

Currently Recommended Donor Deferral Period:

- No FDA Guidance or AABB Standard exists.
- Prudent practice would be to defer donor with infectious mononucleosis at least until signs and symptoms are resolved. It should be noted that US regulatory agencies require that any donor with viral hepatitis after the age of 11, including that associated with infectious mononucleosis, be indefinitely deferred.

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 EBV is typically present within circulating B-lymphocytes, leukoreduction should be effective. This has only been demonstrated in vitro with a 4 log reduction in viral genomes to undetectability in leukoreduced RBCs.

Pathogen Reduction Efficacy for Plasma Derivatives:

- EBV is primarily B cell-associated, and plasma viremia is rare.
- Multiple pathogen reduction steps used in the fractionation process have been shown to be robust in the removal of enveloped viruses

Other Prevention Measures:

- None

Suggested Reading:

1. Alifieri C, Tanner J, Carpenter L, Perpète C, Savoie A, Paradis K, Delage G, Joncas J. Epstein-Barr virus transmission from a blood donor to an organ transplant recipient with recovery of the same virus strain from the recipient's blood and oropharynx. *Blood* 1996;87:812-7.
2. Griffin BE, Xue SA. Epstein-Barr virus infections and their association with human malignancies: some key questions. *Ann Med* 1998;30:249-59.
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4. Qu L, Triulzi DJ, Rowe DT, Donnenberg AD. Stability of lymphocytes and Epstein-Barr virus during red blood cell storage. *Vox Sang* 2007;92:1-5.
5. Rickinson AB, Kieff E. Epstein-Barr virus. In: Knipe DM, Howley PM, editors. *Fields virology*, 5th ed. Philadelphia: Lippincott Williams & Wilkins; 2007. p. 2655-700.
6. Sokal EM, Antunes H, Beguin C, Bodeus M, Wallemacq P, de Ville de Goyet J, Reding R, Janssen M, Buts JP, Otte JB. Early signs and risk factors for the increased incidence of Epstein-Barr virus-related posttransplant lymphoproliferative diseases in pediatric liver transplant recipients treated with tacrolimus. *Transplantation* 1997;64:1438-42.
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