

## 10 | EPSTEIN-BARR VIRUS

### 10.1 | Agent

- EBV (Human gammaherpesvirus-4, HHV-4)

### 10.2 | 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 kb 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  $-60^{\circ}\text{C}$  or below. Inactivated by heat ( $50\text{--}60^{\circ}\text{C}$  for at least 30 min). EBV survives at room temperature for a few days, 2–3 days at refrigeration temperature, and  $-70^{\circ}\text{C}$  for many years.

### 10.3 | Disease name

- Infectious mononucleosis (heterophile antibody-positive).
  - Heterophile antibodies are antibodies reactive with (usually) equine or bovine RBCs, made in response to EBV infection. The Monospot is a test for heterophile antibodies.
- Burkitt's lymphoma.
- AIDS-related lymphoma.
- Endemic nasopharyngeal carcinoma in wide areas of the developing world including south Asia, the Middle East, North Africa, and the Mediterranean.
- Lymphoproliferative disease including post-transplant lymphoproliferative disease (PTLD).
- Hodgkin's disease.
- Diffuse large B-cell lymphoma.
- Hemophagocytic lymphohistiocytosis.
- Chronic active EBV infection.
- T-cell/NK-cell lymphomas.
- Gastric carcinoma.

### 10.4 | 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

### 10.5 | Background

- Highly endemic and stable in population
- Burkitt's lymphoma (B cell) endemic in central 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.

### 10.6 | Common human exposure routes

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

### 10.7 | Likelihood of secondary transmission

- Moderate

### 10.8 | At-risk populations

- Patients with primary or secondary immunodeficiencies usually associated with impairment of cellular immune response or following bone marrow or solid organ transplantation are at higher risk of developing EBV reactivation (lytic phase) and morbidity.

### 10.9 | Vector and reservoir involved

- Infected humans

### 10.10 | Blood phase

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

### 10.11 | Survival/persistence in blood products

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

### 10.12 | Transmission by blood transfusion

- Suggested, but rare; seroconversion in seronegative recipients has been reported in recipients with DNA detected using molecular methods.
- A prospective, multicenter cohort study among 21 EBV-seronegative pediatric stem cell transplant recipients of EBV-negative grafts identified a single blood donor infected with a strain well matched to the newly infected transplanted patient.

### 10.13 | Cases/frequency in population

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

### 10.14 | Incubation period

- Varies, but for infectious mononucleosis usually 4–7 weeks in adults and 1–2 weeks in children

### 10.15 | Likelihood of clinical disease

- Primary infection is often asymptomatic. Symptomatic infectious mononucleosis is common in adolescents, with 30%–50% of adolescents who seroconvert presenting with symptoms.
- Disease reactivation in immunosuppressed patients is associated with a number of malignancies and hematological diseases.

### 10.16 | Primary disease symptoms (infectious mononucleosis)

- Fever
- Headache
- Pharyngitis

- Lymphadenopathy
- Splenomegaly

### 10.17 | Severity of clinical disease

- In general, infectious mononucleosis is not severe in immunocompetent hosts, although associated splenic rupture can be serious.
- In immunosuppressed patients, disease reactivation can result in life-threatening conditions such as in hemophagocytic lymphohistiocytosis, post-transplant lymphoproliferative disease, nasopharyngeal carcinoma, and other lymphoproliferative disorders.

### 10.18 | Mortality

- Rare, except in immunocompromised patients

### 10.19 | Chronic carriage

- Yes; lifetime latency is typical.

### 10.20 | Treatment available/efficacious

- No drugs are available to treat EBV infection.
- Some antiviral drugs can inhibit viral replication but have no effect on the symptoms of infectious mononucleosis or on the latent phase.
- Specific (not antiviral) therapies are available for EBV-associated malignancies.

### 10.21 | 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.

### 10.22 | Laboratory test(s) available

- No FDA-licensed blood donor screening test exists.
- Serology
  - acute infection established using IgM anti-VCA (viral capsid antigen that peaks at 2–4 weeks after onset),

- rising titers to IgG anti-VCA or anti-EA (early antigen complex consisting of multiple proteins),
- presence of IgG anti-EBNA2 (nuclear antigen that acts as a transcription activator; one of the first viral genes expressed in EBV-infected B cells) in the absence of anti-EBNA1
- heterophile antibodies to sheep and/or horse RBCs.
- NAT in CSF, blood, or lymphoid tissue.

### 10.23 | Currently recommended donor deferral period

- No EBV-specific FDA Guidance or AABB Standard exists.
- Symptomatic individuals with mononucleosis would not be expected to present for donation. Prudent practice would be to defer individuals with infectious mononucleosis at least until signs and symptoms are resolved.

### 10.24 | Impact on blood availability

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

### 10.25 | Impact on blood safety

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

### 10.26 | 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.

### 10.27 | 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.

### 10.28 | Other prevention measures

- Pathogen reduction technology for platelets and plasma (including amotosalen and UV light and riboflavin and UV light) inactivate herpesviruses.

### SUGGESTED READING

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