Herpes Viruses (Other Than CMV, EBV, and HHV-8)

Disease Agent:

- Herpes simplex viruses 1 and 2 (HSV-1,2)
- Varicella-zoster virus (VZV)
- Human herpesviruses-6,7 (HHV-6,7)

Disease Agent Characteristics:

- Family: *Herpesviridae*; Subfamilies: *Alphaherpesvirinae* (HSV-1,2; VZV), *betaherpesvirinae* (HHV-6,7); Genus: *Simplexvirus* (HSV-1,2); *Varicellovirus* (VZV); *Roseolovirus* (HHV-6,7)
- Virion morphology and size: Enveloped; icosadeltahedral nucleocapsid symmetry, spherical to pleomorphic particles, 160-200 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 125-170 kbp in length
- Physicochemical properties: Nonionic detergents solubilize the envelope; virus stable when frozen, especially at –80°C or below; virus inactivated by UV light, gamma-irradiation, standard disinfectants, and heating. Herpes viruses do not, in general, survive for long periods outside the host.
- *Herpesviridae* cause primary infection followed by lifelong latency with the opportunity for reactivation of productive infection.
  - HSV-1,2 and varicella are latent in nerve cells.
  - HHV-6,7 are latent in lymphocytes.

Disease Name:

- Multiple, including oropharyngeal and genital herpes (HSV-1,2); varicella (chickenpox), herpes zoster, or shingles (VZV); and exanthem subitum or roseola infantum (HHV-6,7)

Priority Level

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

Background:

- Primary infections are followed by lifelong latency of this family of viruses, which raises the issue of reactivation syndromes in both healthy and immunocompromised hosts.
- Rates of infection are stable in US population, except for a marked decrease in the incidence of primary VZV infection with introduction of universal immunization.

Common Human Exposure Routes:

- Contact with infected human secretions (saliva, semen) most common; aerosols also possible

Likelihood of Secondary Transmission:

- Moderate

At-Risk Populations:

- All populations at risk for infection for most of these agents
- Typically greater risk of disease in immunocompromised hosts or following bone marrow or solid organ transplantation

Vector and Reservoir Involved:

- Infected humans

Blood Phase:

- HSV and VZV viremia in symptomatic neonates, and immuncompromised hosts is well described.
- Viremia in immunocompetent hosts occurs with both primary and recurrent HSV and VZV infection, but for short intervals and at relatively low levels
- HHV-6,7 circulates as latent virus in lymphocytes over the long-term (lifelong) and can reactivate later in life and in association with immunosuppression.

Survival/Persistence in Blood Products:

- Unknown

Transmission by Blood Transfusion:

- While the lymphocyte association of HHV-6,7 suggests the possibility of transfusion transmission, well-documented case reports or series are not available.
- Case reports of HHV-6 transmission by peripheral blood stem cells have used molecular methods to detect integrated donor HHV-6 DNA in the chromosomes of engrafted donor cells. This appears to be transmission of latent infection rather than of active infection. Furthermore, transplant recipients may reactivate preexisting HHV-6 infection, thereby confounding the evaluation of potential transfusion transmission.
- Although viremia occurs during both primary and reactivation infections with HSV and VZV, transmission by blood has never been reported for HSV-1, HSV-2, and VZV.

Cases/Frequency in Population:

- HSV: 50-80% adults seropositive
- VZV: Up to 95% seropositive
- HHV-6: >90% seropositive
- HHV-7: 70-90% seropositive

Incubation Period:

- HSV-1,2: 2-12 days
- VZV: 10-21 days
- HHV-6,7: 5-15 days

Likelihood of Clinical Disease:

- HSV: Mucocutaneous disease (orolabial and genital herpes) common. Severe disease is rare in immunocompetent hosts, but, if it occurs, it can be deadly (e.g., severe encephalitis).
- VZV: Varicella (chickenpox) was previously very common (about 4 million cases/year in the US before recommendations for universal vaccination), but rates have fallen 75-85% and continue to decline; herpes zoster due to reactivation of latent virus continues to increase after age 60 years with lifetime risk ~50% among persons who survive to 85 years (1.7 cases/1000 population in the US)
- HHV-6,7: High in children; prevalent in febrile children if sought

Primary Disease Symptoms:

- HSV-1 and -2
  - Gingivostomatitis and orolabial ulcers (cold sores) primarily from HSV-1
  - Genital herpes primarily with HSV-2
  - Aseptic meningitis (sometimes recurrent)
  - Encephalitis and disseminated infections seen in neonates and immunocompromised hosts
- VZV
  - Disseminated rash (chickenpox or varicella) and dermatomal rash (zoster)
  - Widespread visceral dissemination in immunocompromised hosts
- HHV-6,7
  - Exanthem subitum (or roseola infantum) is a very common self-limited, benign childhood rash. Nonspecific febrile illness is also frequently observed.
  - Reactivation of latent HHV-6,7 in immuncompromised hosts can result in disseminated infection of multiple organs and is assocatiated with poor clinical outcomes, especially in recipients of hematopoetic transplantation.

Severity of Clinical Disease:

- Primary infections in well hosts are generally self-limited with full recovery. Reactivation of latent infections with HSV-1 and 2 causes self-limited illness. Reactivation of VZV as shingles generally heals with few sequelae but can cause relatively severe disability because of postherpetic neuralgia. HHV-6,7 infections in children are usually benign. Reactivation of any of these viruses in the immune compromised host can cause severe disease.

Mortality:

- Rare, except in immunocompromised patients

Chronic Carriage:

- Yes; lifetime latency is typical.

Treatment Available/Efficacious:

- There are a variety of nucleoside analog drugs used to treat herpes virus infections, including acycloguanosine (acyclovir), famciclovir, valacyclovir, ganciclovir and valgancylovir, cidofovir, and foscarnet. All of these drugs suffer from the selection of resistant herpes mutants. As with HSV, acyclovir (or other nucleoside analogs) can be useful, particularly in preventing VZV disease, and varicella immunoglobulin also can be used. Unlike herpes simplex virus and VZV, there are no drugs proven effective for HHV-6 or 7, although there is uncontrolled evidence suggesting that several of the above drugs have promise for HHV-6 infections.

Agent-Specific Screening Question(s):

- No specific question is in use.
- Not indicated because transfusion transmission has not been definitively demonstrated
- No sensitive or specific question is feasible. Most infections are aquired during childhood, and the prevelance of latent infections is so high as to make questions impractical.

Laboratory Test(s) Available:

- No FDA-licensed blood donor screening test exists.
- Serology, NAT, and cultivation of viruses

Currently Recommended Donor Deferral Period:

- No FDA Guidance or AABB Standard exists.
- Persons with symptomatic primary genital or orolabial HSV may not feel well on the day of donation and would often be deferred.
- Deferral practices for recurrent HSV infection, if reported by the donor, vary by collection facility.
- Prudent practice would be to defer prospective donors with primary (chickenpox) or recurrent (shingles/zoster) varicella until signs and symptoms are gone.

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:

- Viruses that have a blood phase (HHV-6,7) are typically present within WBCs; therefore, leukoreduction is likely to be effective by analogy to human cytomegalovirus. However, cell-free virus also has been detected in cases of primary infection in children.

Pathogen Reduction Efficacy for Plasma Derivatives:

- These viruses are primarily WBC associated, but plasma viremia may be present. Because these viruses are lipid enveloped and relatively labile, any free virus in plasma should be sensitive to the many measures used in the fractionation process.

Other Prevention Measures:

- None

Suggested Reading:

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