Human Herpesvirus-8

Disease Agent:

- Human herpesvirus 8 (HHV-8)

Disease Agent Characteristics:

- Family: *Herpesviridae*; Subfamily: *Gammaherpesvirinae*; Genus: *Rhadinovirus*
- Virion morphology and size: Enveloped, icosadeltahedral nucleocapsid symmetry, spherical to pleomorphic virions, 120-200 nm in diameter
- Nucleic acid: Circular in latent phase and linear in lytic phase, double-stranded DNA genome, ~170-210 kb in length
- Physicochemical properties: Fragile particle that is sensitive to brief treatments with organic solvents, degradation by detergents, proteases, heating to 60°C, prolonged storage at temperatures of –10°C or above, and extremes of pH (<6.2 or >7.8).

Disease Name:

- Kaposi's sarcoma (KS)
- Primary effusion lymphoma (PEL)
- Multicentric Castleman's disease (MCD)

Priority Level:

- Scientific/Epidemiologic evidence regarding blood safety: Very low; no disease has been documented although transfusion transmission occurs in the absence of leukoreduction.
- Public perception and/or regulatory concern regarding blood safety: Low
- Public concern regarding disease agent: Very low

Background:

- Discovered in 1994 in patients with Kaposi's sarcoma
- In retrospect, HHV-8 is an ancient human infection having entered human populations thousands of years ago.
- Rates of clinical disease caused by HHV-8 increased during the HIV epidemic.

Common Human Exposure Routes:

- Horizontal (occurring in children in endemic areas, such as Africa). Exact mechanism is unknown, but postulated transmission route is from saliva because of replication of virus in oropharynx.
- Sexual transmission in males who have sex with males (MSM): postulated route is from saliva via the oral–genital or oral–oral route.
- Heterosexual transmission is not considered to be an important route of spread in recent population-based serological studies in the US.
- Injection-drug use suspected, based on epidemiologic studies
- Transplantation of organs from infected donors

Likelihood of Secondary Transmission:

- Person-to-person transmission (probably in saliva) is the major route of transmission in endemic populations.

At-Risk Populations:

- Pediatric populations in Africa
- MSM
- Transplant recipients (most frequently because of reactivation in patients who were seropositive prior to transplant)

Vector and Reservoir Involved:

- Human reservoir

Blood Phase

- HHV-8 may be found in peripheral blood mononuclear cells (PBMCs) from 35 to 75% of patients with KS and less frequently in asymptomatic populations.
- The virus is highly cell associated and has not been readily identified as free virus in plasma except in immunosuppressed HIV-infected patients.

Survival/Persistence in Blood Products:

- Survival of the virus in blood products has not been formally assessed.
- Among African children who received transfusion, transfusion transmission was significantly associated with use of blood ≤4 days old compared with older units.

Transmission by Blood Transfusion:

- A study of transfusion recipients in Uganda provides strong evidence of transfusion transmission by relatively fresh (≤4 days old) nonleukoreduced whole blood from seropositive donors compared with that from seronegative donors.
- Other studies in highly endemic populations of African children strongly suggest transfusion-transmission with nonleukoreduced products.
- Two postsurgical seroconversions in cardiac surgery patients receiving nonleukoreduced components have been described in the US; transfusion-transmission was suspected but not proven.
- Two previous small studies in the US and Jamaica showed lack of transmission in 32 recipients receiving components from HHV-8 seropositive units.
- Evaluation of linked donor-recipient blood samples from the US TTVS study during the 1970s showed no difference in seroconversion rates between

transfused patients and untransfused surgical control patients.

Cases/Frequency in Population:

- In endemic areas, seropositivity rates begin increasing at age 2 and rise until puberty.
- The seroprevalence in US general population has not been precisely determined due largely to uncertain performance characteristics of available antibody assays. The most comprehensive population-based study (the Third National Health and Nutrition Examination Survey 1988-1994 cohort) estimated that seroprevalence ranged from 1.5 to 7.4% depending on the antigen used in the assay and the assay cut-off value. When stringent (i.e., conservative) cutoffs were used, seroprevalence was similar in men and women and was higher in groups whose demographic profiles were suggestive of poorer socioeconomic conditions.
- Antibody prevalences of 10-25% in MSM without HIV and 30-60% in MSM with HIV are reported, but comparison of studies is confounded by differences in assays.
- Seroprevalence in US blood donors also varies depending upon antibody assay characteristics. The most comprehensive study reported rates of 3-3.5% in blood donors, based on concordance of at least two antibody assays.
- Infection and disease are rare among children in the US and Europe; in contrast, seroprevalence rates are above 50% in many African populations.

Incubation Period:

- Unknown

Likelihood of Clinical Disease:

- Most infections, in otherwise healthy hosts, are asymptomatic.
- Rare primary infection manifesting as febrile syndrome in immunocompetent patients
- Disease is uncommon except in the setting of HIV infection or immunosuppression (as in transplant recipients) and occurs years after infection.
- HHV-8 identified as causative agent of all four forms of KS: HIV-related, classical (old men in the Mediterranean), endemic (Africa), and iatrogenic (post-transplant); PEL in HIV positive men, and MCD (a lymphoproliferative disorder of B cells)

Primary Disease Symptoms:

- Usually none, but rarely an acute viral syndrome can be seen

Severity of Clinical Disease:

- KS, PEL, and MCD are all severe.

Mortality:

- High in PEL and MCD
- KS in AIDS patients will respond both to highly active antiretroviral therapy and specific treatment for the tumor(s).

Chronic Carriage:

- Chronic (latent) infection is characteristic, but viremia is rarely detectable by NAT in healthy individuals, including blood donors.

Treatment Available/Efficacious:

- No direct treatment of HHV-8 infection is available, but treatment of the underlying immunosuppression in patients with HIV-related KS (using antiretrovirals) or posttransplant KS (by stopping immunosuppressive drugs) may lead to KS regression.
- A variety of chemotherapy regimens and radiation are used for local control and palliation of advanced KS.

Agent-Specific Screening Question(s):

- There is no question specific for HHV-8 risk.
- The current question on MSM activity since 1977 identifies a subpopulation with higher rates of infection than the general population.
- The current question on history of injection-drug use also may identify a subpopulation with a higher risk of infection.

Laboratory Test(s) Available:

- No FDA-licensed blood donor screening test exists.
- Multiple research EIA and IFA antibody assays to multiple antigens have been developed. There is poor agreement among antibody assays and between laboratories when serology has been applied in low-risk blood donor populations.
- PCR tests applied to PBMC or to serum/plasma exist in research settings. However, most antibody-positive blood donors are negative for HHV-8 DNA in PBMC.

Currently Recommended Donor Deferral Period:

- No FDA Guidance or AABB Standard exists.

Impact on Blood Availability:

- Agent-specific screening question(s): Not applicable
- Laboratory test(s) available: Antibody testing would defer from 0.5 to >7% of current donors based on studies of a variety of serological assays.

Impact on Blood Safety:

- Agent-specific screening question(s): Not applicable
- Laboratory test(s) available: Uncertain as clinically significant HHV-8 disease arising from transfusion has not been documented.

Leukoreduction Efficacy:

- HHV-8 is highly cell-associated in PBMC, and leukoreduction would be expected to be effective (as is the case with cytomegalovirus); however, specific studies of HHV-8 and leukoreduction on efficacy have not yet been reported.

Pathogen Reduction Efficacy for Plasma Derivatives:

- No specific data are available for this virus, but fractionation and inactivation techniques in use for plasma derivatives should be robust.

Other Prevention Measures:

- None

Suggested Reading:

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