

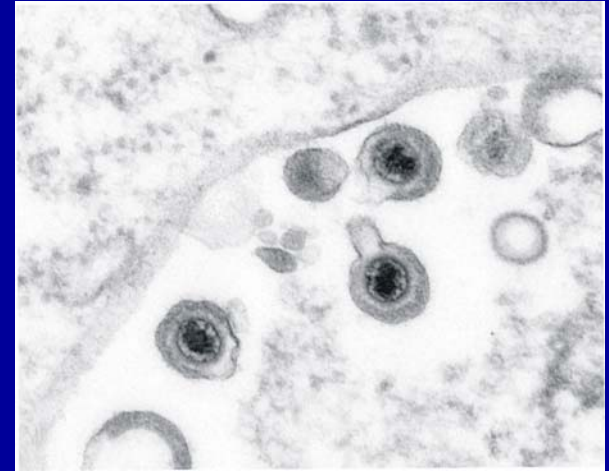
Human Herpesvirus 8 (HHV-8) and Blood Safety: Case Example of Unresolved Scientific Evidence

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Human Herpesvirus 8 (HHV-8)



- **Discovered in 1994**
- **Enveloped DNA virus**
- **Closely related to Epstein-Barr virus**
- **Establishes latency and persists in the host**
- **Primarily cell-associated**
- **Seropositivity (presence of antibody) often does not imply presence of virus in the blood**
- **Variety of serologic assays, variety of estimates of seroprevalence in blood donors**
- **No FDA-approved serologic assay**

Diseases Caused by HHV-8

- **Kaposi's sarcoma (KS)**
- **Other diseases**
 - **Primary effusion lymphomas (PEL)**
 - **Multicentric Castleman's disease**
- **Estimated Annual Risk of Developing KS**
 - **1 in 1,000,000 in healthy persons**
 - **1 in 80 in organ transplant recipients**
 - **1 in 50 in persons with HIV**
 - **1 in 20 in persons seropositive for both HIV and HHV-8**

Evidence that HHV-8 May Pose a Risk to the Blood Supply

- **Infectious human herpesvirus 8 found repeatedly in a healthy North American blood donor.**
- **HHV-8 associated with:**
 - **having ever injected drugs**
 - **increasing frequency of injection drug use**
 - **cumulative years of injection drug use**
 - **hepatitis C virus (HCV) infection**

HHV-8 Seroprevalence in Blood Donors

Lab	Seropositive KS controls (%) (n=40)	Seropositive REDS donors (%) (n=1000)
D	40 (100)	5 (0.5)
B	39 (100)*	17 (1.7)
A	40 (100)	24 (2.4)
C	40 (100)	27 (2.7)
F	40 (100)	37 (3.7)
E	40 (100)	51 (5.1)

* Tested only 39 of 40 controls.

- **Best estimate of seroprevalence: 3.5%**
- **0/138 had HHV-8 DNA in PBMC, including 55 who tested seropositive in ≥ 1 laboratory.**

Studies of Transfusion Transmission of HHV-8—Literature Highlights

- **No HHV-8 seroconversion in**
 - 14 recipients of blood from HIV/HHV-8 seropositive US donors.
 - 18 recipients of blood from HHV-8 seropositive donors in Jamaica.
- **In Uganda, HHV-8 seropositivity in children correlated with the number of blood transfusions they received.**

Studies of Transfusion Transmission of HHV-8—CDC Studies

- **Uganda transfusion study (unpublished)**
 - 1800 donors and 1800 recipients
 - Mean units transfused: 1.5
 - Primarily whole blood or packed cells
 - Those receiving HHV-8 seropositive blood were approximately twice as likely to seroconvert (3% vs. 1.5%)
- **FACTS HHV-8 study (in press)**
 - Specimens from pre- and post-transfusion cardiac surgery patients in the US, 1986-1989
 - 2/284 (0.7%) of HHV-8 seronegative patients seroconverted
 - 0.082% transfusion risk per transfused component

Discussion of FACTS HHV-8 Study

- **We cannot definitively say whether infection was transfusion-acquired, but...**
 - No seroconverters in the non-transfused group.
 - Community-acquired infection unlikely at that age.
 - Both seroconverters received many transfused units.
- **0.082% per transfused unit probably an upper bound on current transmission rates in the US.**
 - More stringent donor requirements since 1988
 - Laboratory testing now done for more agents which share risk factors with HHV-8
 - Leukoreduction eliminates most white blood cells, the presumed reservoir for HHV-8 in blood.

Technical Challenges of HHV-8 Serologic Assay Development

- HHV-8 serologic assays are useful for epidemiologic studies.**
- Diagnosis of individuals is more difficult.**
- True seroprevalence in blood donors is low (~3.5%), so seroassays must be highly specific to avoid false positives.**
- Among truly infected individuals at low risk for KS, weak seroreactivity is the rule, so seroassays must also be highly sensitive.**

General Requirements for Resolving Scientific Evidence

- Continuing collaborative, multi-agency efforts
- Determining that HHV-8 and blood safety is a priority

Specific Steps to Take

- **Determine the precise risk of HHV-8 transmission via transfusion.**
 - **Linked donor-recipient repository from 1970s (TTVS)**
 - **Current linked donor-recipient repositories (e.g. RADAR)**
- **Study effect of leukoreduction on HHV-8 viral load**
- **Estimate burden of disease associated with transfusion-acquired HHV-8 infection.**
- **Should donor screening be indicated, assays must be developed to have these characteristics:**
 - **High sensitivity**
 - **High specificity**
 - **High-throughput capability**

