Transmission of Parvovirus B19 and Hepatitis E by Plasma Products

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## Disclosures

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<tr>
<th>Conflict</th>
<th>Disclosure - if conflict of interest exists</th>
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<tr>
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<td>Shareholder</td>
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<td>Advisory Committee</td>
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<td>Consultant</td>
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Overview

- Virus epidemiology
- Virus characteristics
- Evidence for transmissibility
- Current prevention strategies
Parvovirus
Epidemiology

- Ubiquitous virus with frequent outbreaks
- Prevalence rises quickly and >90% after age 15 years
- Most often causes a benign illness without sequelae in children
- In adults, can cause acute/chronic arthritis especially in women
- Can cause fetal death in pregnant women
- Case reports of fulminant hepatitis aplastic anemia in some groups
Why are products at risk?

- Large percentage of population exposed
- High levels of viremia in cases
- Evidence for chronic asymptomatic infection in the population
- Non-enveloped, single-strand DNA virus
  - Relatively resistant to viral inactivation methods
- Extremely small size (19-23 nm)
  - Most currently available products are not routinely filtered but, if so, a 35 nm filter most often used
- Available data provides evidence that B19 able to survive current fractionation & inactivation*

B19 Transmission

- B19V transmission reported from red blood cells, platelets, fibrin sealant and IVIG
- A previous study\(^1\) of hemophilia patients found those using plasma-derived products were 7.6 times more likely to have IgG antibodies to B19V
- Manufacturers began voluntary plasma minipool NAT screening in 2000
- FDA study\(^2\) that tested factor products made before and after NAT found that screening had lowered levels of B19V in most products
- No study had evaluated effectiveness of NAT screening in preventing B19V transmission

\(^1\) Soucie JM, et al. Transfusion 2002
Seroprevalence Study

- 1,043 children with bleeding disorders
- Mean age 4.4 years (range 2-7 years)
- 61% white, 12% black, 19% Hispanic
- 65% hemophilia, 31% VWD
- 55% had 1 or more bleeds in last 6 mos
- 33% of patients had never received any blood or blood products and served as controls

Soucie JM, et al. Transfusion 2013
B19V Prevalence by Age and Product Exposure

- **No Product**
- **Recombinant only**
- **Recombinant/Plasma-derived**
- **Plasma-derived only**

95% CI

No Product
### Multivariate Analysis

<table>
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<tr>
<th>Characteristic</th>
<th>OR (95% CI)</th>
<th>p-value</th>
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<tbody>
<tr>
<td>Exposure Group</td>
<td></td>
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<tr>
<td>No factor</td>
<td>reference</td>
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<tr>
<td>Recombinant only</td>
<td>1.1 (0.7 – 1.6)</td>
<td>0.7</td>
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<tr>
<td>Recombinant + Plasma</td>
<td>1.0 (0.6 – 1.8)</td>
<td>0.9</td>
</tr>
<tr>
<td>Plasma-derived only</td>
<td>1.7 (1.2 – 2.4)</td>
<td>0.002</td>
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Adjusted for age, sex, race, treatment type, bleeding frequency, year of test and hemophilia inhibitor status using logistic regression.
Limitations

- Because no data were collected on symptoms, it is not known whether these results represent clinical illness or antibody response to non-infective viral particles.
- Lifetime product exposures were based on clinic records and some patients may have been incorrectly classified – this would have resulted in an underestimate of the product-parvovirus exposure association.
Implications

• This study provides evidence that while the risk of B19V transmission appears to be lower with NAT screening it may not be zero.

• B19V NAT screening cannot be expected to be effective in protecting against transmission of unknown or emerging viruses with similar characteristics.
Hepatitis E
Epidemiology

• Every year world-wide estimated:¹
  • 20 million hepatitis E infections
  • 70,000 hepatitis E-related deaths
  • 3,000 hepatitis E-related stillbirths
• Disease is usually self-limiting but may develop into fulminant hepatitis
• Case fatality rate higher in pregnant women
• Babies at increased risk of prematurity, LBW and perinatal mortality²
• Hepatitis E is found worldwide, but prevalence is highest in East and South Asia

Acute Hepatitis E Among 604 Residents of England and Wales, 2003–2005

Hepatitis E Prevalence in the U.S. by Age and Country of Birth, NHANES 1988-1994

The hepatitis E virus is transmitted primarily by the fecal-oral route, principally by ingestion of contaminated water.

Other transmission routes include:

- Foodborne transmission from ingestion of products derived from infected animals
- Transfusion of infected blood products*
- Vertical transmission from a pregnant woman to her fetus

Are products at risk?

- Present in the population for at least 20 years
- Evidence of transmission by blood
- No screening test available
- Non-enveloped, single-stranded RNA virus
  - Relatively resistant to solvent detergent
- Small size (27-34 nm)
  - Most currently available products are not routinely filtered but, if so, a 35 nm filter most often used
- Similar virus (HAV) was previously found to be transmitted by plasma-derived concentrate*

*Soucie JM, et. al. Transfusion 1998
Time Course

Time course of hepatitis E virus infection

Expert Reviews in Molecular Medicine © 1999 Cambridge University Press
Summary

- CDC has established a surveillance system to monitor the safety of treatment products.
- No hepatitis or HIV infections have been linked to blood products since 1998.
- Blood specimens stored in a serum bank have been used for special studies (porcine parvovirus, West Nile Virus, B19V).
- Maintaining surveillance is important to ensure continued product safety and to detect emerging threats to the blood supply.
Questions?

The findings and conclusions in this report are those of the authors and do not necessarily represent the official position of the Centers for Disease Control and Prevention.