

Human Parvovirus PARV4

Disease Agent:

- Human parvovirus 4 (PARV4)

Disease Agent Characteristics:

- Family: *Parvoviridae*; Genus: *Parvovirus* (proposed); Species: human parvovirus 4
- Virion morphology and size: Nonenveloped, icosahedral nucleocapsid symmetry, spherical particles, 20-25 nm in diameter
- Nucleic acid: Linear, negative and positive single-stranded DNA, ~5.3 kb in length. The genome comprises two main open reading frames, but unlike B19V, the two ORFs do not overlap.
- Physicochemical properties: Not described in the literature but it is expected that due to similarity to B19V and other parvoviruses it might have similar properties. Thus, it should be resistant to wet or dry heat during the manufacturing of clotting factors from plasma pools and to solvent/detergent treatment. It is presumably inactivated by formalin, β -propiolactone and gamma irradiation.

Disease Name:

- Disease association unknown.
- Reports of PARV4 detection in CSF of two patients with encephalitis of unknown etiology, and in cases of fetal hydrops.
- Possible association with rashes and exacerbation of hepatitis in hemophiliacs, but causation is disputable.

Priority Level:

- Scientific/Epidemiologic evidence regarding blood safety: Theoretical for blood components; disease associations and transfusion transmission have not been proven, but if so, immunocompromised patients expected to be at greatest risk.
- Public perception and/or regulatory concern regarding blood safety: Very low in the US; concern exists about the possible pathogenicity of PARV4 in manufactured plasma pool derivatives
- Public concern regarding disease agent: Absent

Background:

- Virus discovered in 2005 from an injection drug user with general symptoms of primary viremia. Found in individuals with a history of IDU or HIV or HCV infection. Antibodies found in high concentrations in high-risk groups and persons with hemophilia. Occurs mainly in lymphoid tissues, bone marrow and blood of IDUs.
 - 3 genotypes:
 - Genotype 1 most prevalent; DNA detected in plasma pools world-wide ranging from 4-5% in

currently manufactured plasma pools in Europe to 26% in China. Prevalent in younger European and US populations

- Genotype 2 was first identified in plasma pools.
- Genotype 3 is restricted to healthy individuals in sub-Saharan Africa. It is found in children suggesting a different route of transmission such as respiratory or fecal-oral routes or even through unrecognized blood contact.
- Global and endemic infection strongly associated with HIV and HCV in developed countries
- Blood component transmission suspected but not proven
- High seroreactivity in injection drug user populations in developed countries indicate likely source of transmission. May be associated with unsafe needle injections
- Other newly described human parvoviruses include the bocaviruses (HBoV) 1-4. They are closely related to bovine and canine parvoviruses. HBoV genotypes have been found worldwide, indicating their global circulation. HBoV DNA was detected by quantitative, real-time PCR in 5.5% of serum samples obtained from healthy blood donors in Italy.
 - HBoV1 was originally identified from nasopharyngeal aspirates of children with respiratory tract infections; DNA and antibody have been detected in association with acute respiratory illness. DNA also found in serum, feces, urine, saliva and CSF of children in Spain. Seroprevalence among adults exceeds 90%; DNA reported in 4%-32% of tonsils and adenoids of young children (versus none for HBoV2-4 or PARV4 DNA). The presence of mRNA as an indication of DNA replication has been demonstrated in the nasopharynx.
 - HBoV 2-4 have been detected in stool samples from young children with acute gastroenteritis (nausea and watery, bloody diarrhea).

Common Human Exposure Routes:

- Injection drug use
- Possibly *in utero* (transplacental) as reflected by detection in cases of fetal hydrops
- Other routes possible for PARV4 genotype 3 in sub-Saharan Africa

Likelihood of Secondary Transmission:

- Likely, as virus appears to be readily transmissible within the drug user population in developed countries and in general population in African countries

At-Risk Populations:

- Possibly immunocompromised plasma product recipients
- Possibly pregnant women

Vector and Reservoir Involved:

- Unknown

Blood Phase:

- Cellular tropism unknown. Viral DNA found in plasma, bone marrow, lymphoid tissue, liver and other organs and tissues.
- High-titer viremia during primary infection (up to 10¹⁰ DNA copies/mL), but usually <10⁵ DNA copies/mL especially in pre-school children
- Reported detection of low-level DNA concentrations in plasma of approximately 2% of 200 US blood donors from Los Angeles; this may reflect low-level chronic viremia or nucleic acid circulating in the blood similar to B19V. The extent of cross-neutralization by seroreactive plasma in plasma pools, as is assumed for B19V, is unknown.

Survival/Persistence in Blood Products:

- PARV4 DNA detected in blood components, in source and frozen plasma, and in virally inactivated clotting factors

Transmission by Blood Transfusion:

- Transmission from blood components has not been formally assessed
- Transmission from plasma products strongly suspected from studies of seroconversion in hemophiliacs
- Solvent-detergent and heat-treated plasma lots can be infectious.

Cases/Frequency in Population:

- PARV4 DNA detected in approximately 2% of 200 blood donors from Los Angeles, CA
- Seroprevalence in injection drug use populations is approximately 6%.

Incubation Period:

- Unknown

Likelihood of Clinical Disease:

- No confirmed disease associations; most infections asymptomatic
- PARV4 in CSF and plasma of two encephalitis patients in India
- PARV4 DNA detected in three cases of fetal hydrops
- PARV4 seroconversion observed among patients with hemophilia, concurrent with rash and unexplained hepatitis

Primary Disease Symptoms:

- Association with disease is unclear.

Severity of Clinical Disease:

- Association with disease is unclear.

Mortality:

- Unknown

Chronic Carriage:

- Viral particles detected in multiple tissues and possibly sequestered there for life as is the case for B19V. The high

rate of detection (2% in healthy blood donors) may be explained by low-level viremia or nucleic acid circulating in the blood over extended periods, as has been reported for B19V.

Treatment Available/Efficacious:

- None reported

Agent-Specific Screening Question(s):

- No specific question is in use.
- Not indicated because of the absence of confirmed transfusion transmission and associated clinical disease
- No sensitive or specific question is feasible.

Laboratory Test(s) Available:

- No FDA-licensed blood donor screening or diagnostic test exists.
- Nested PCR and real-time PCR assays have been used.
- IgG and IgM antibody tests have been developed by academic laboratories using virus-like particles for antibody capture.

Currently Recommended Donor Deferral Period:

- No FDA Guidance or AABB Standard exists.

Impact on Blood Availability:

- If low-level NAT-positive donors are excluded, the results of one reported study indicate that approximately 2% of donors in the US would be deferred from donation.

Impact on Blood Safety:

- Agent-specific screening question(s): Not applicable
- Laboratory test(s) available: NAT screening could decrease transmission rate by removal of viremic units. Extent of clinical disease because of transfusion transmission is unknown but thought to be low; therefore, benefits of screening may be small. However, outcomes could theoretically be severe in particular populations of transfusion recipients such as immunosuppressed patients. It has been speculated that these recipients might benefit from PARV4-safe components.

Leukoreduction Efficacy:

- Unknown but highly unlikely

Pathogen Reduction Efficacy for Plasma Derivatives:

- PARV4 is not totally inactivated by heat and solvent-detergent treatment.

Other Prevention Measures:

- None

Suggested Reading:

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