Human Parvovirus B19

Disease Agent:

- Human parvovirus B19 (B19V)

Disease Agent Characteristics:

- Family: *Parvoviridae*; Genus: *Erythrovirus*; Species: human parvovirus B19 (B19V)
- Virion morphology and size: Nonenveloped, icosahedral nucleocapsid symmetry, spherical particles, 23-26 nm in diameter
- Nucleic acid: Linear, negative-sense, single-stranded DNA, ~5.6 kb in length
- Physiochemical properties: Heat resistant (56°C for 60 min), relatively susceptible to inactivation by pasteurization at 60°C for 10 hours and to dry heat in a freeze-dried state (1.5% moisture) at 80°C for 72 hours; stable in lipid solvents; acid stable at pH 3-9; inactivated by other solvents

Disease Name:

- Erythema infectiosum (fifth disease) in children

Priority Level:

- Scientific/Epidemiologic evidence regarding blood safety: Blood components: Very low/Low: In the US there is a higher level of concern for immunocompromised patients, patients with chronic anemia (sickle cell, thalassemia), and bone marrow transplant patients. A Low to Moderate rating is reasonable for pooled plasma and fractionated products based on variable implementation of NAT.
- Public perception and/or regulatory concern regarding blood safety: Very low in the US, with the exception of patients with hemophilia; concern exists for immunocompromised individuals, patients with chronic anemia (sickle cell, thalassemia), and bone marrow transplant patients; Low to Moderate in several European countries with screening programs
- Public concern regarding disease agent: Low

Background:

- Virus discovered in 1974
- Clinical associations discovered in the early 1980s (aplastic anemia, fifth disease, hydrops fetalis)
- Global and endemic infection
- Seasonal, with greater occurrence in late winter and spring
- Periodic focal outbreaks occurring at intervals of several years are typical in temperate climates.

Common Human Exposure Routes:

- Respiratory (droplet infection)
- *In utero* (transplacental) from acutely infected mother

Likelihood of Secondary Transmission:

- High in day-care centers, schools, and household contacts through the respiratory route

At-Risk Populations:

- Children (because of lack of immunity)
- Populations at most risk for serious complications by transfusion route include patients who have shortened RBC survivals, patients who are immunocompromised, and women who are pregnant (because of transmission of infection to the fetus).

Vector Involved:

- None

Blood Phase:

- Virus is tropic for erythroid progenitor cells.
- Extremely high-titer viremia (up to 10^{14} IU/mL) occurs approximately 1 week following infection and persists for approximately 5 days.
- IgM antibody develops 10-14 days postinfection and viremia subsequently declines rapidly, usually disappearing within weeks of IgM development.
- IgM antibody becomes undetectable after several months, but IgG persists long term and is thought to convey immunity to reinfection.
- Infrequently, low-level B19V DNA in association with IgG may persist for months, but transfusion transmission risk has not been established.

Survival/Persistence in Blood Products:

- Survives in blood components and frozen plasma products

Transmission by Blood Transfusion:

- Rarely from blood components (four clinical cases documented in literature); actual frequency of transmission not assessed prospectively.
- Solvent-detergent (SD) treated plasma lots in the US with B19V DNA titers of $>10^7$ IU per mL transmitted to patients and to seronegative volunteers; units with $<10^4$ IU per mL of virus did not transmit.
- Commonly transmitted from Factor VIII and Factor IX concentrates prior to B19V DNA testing
- Very rarely transmitted from intravenous immunoglobulin (IVIG)

Cases/Frequency in Population:

- Half of the population has been infected by late adolescence, with 70-80% infected by adult life.
- Annual incidence in women of childbearing age is 1-1.5% (may be higher in periodic outbreaks).
- Seasonal epidemics generally occur in the late spring.

Incubation Period:

- Approximately 5-6 days to viremia, peaking at days 8-9; slightly longer time interval to disease symptoms

Likelihood of Clinical Disease:

- Most cases asymptomatic
- Erythema infectiosum (fifth disease) in children
- Arthopathy (acute and chronic; more common in adult females)
- Transient aplastic crisis in patients with shortened RBC survival or hemolytic anemias
- Pure RBC aplasia or pancytopenia in immunocompromised patients
- Myocarditis rarely reported
- Hydrops fetalis

Primary Disease Symptoms:

- Acute biphasic illness with fever, chills, headache, and myalgia, followed subsequently by classic fifth disease symptoms associated with the appearance of IgM antibodies (generalized erythematous eruption and joint inflammation) indicative of immune complex formation.

Severity of Clinical Disease:

- Transient aplastic crisis can cause significant morbidity and occasionally be fatal.
- Seronegative pregnant women are at risk for adverse outcomes of pregnancy including giving birth to infants with congenital anemia or for fetal demise due to hydrops fetalis (vertical transmission rate of 33%).

Mortality:

- 5-9% risk of fetal mortality in transplacental infection

Chronic Carriage:

- Chronicity is presumably rare in immunocompetent patients, but virus-specific nucleic acid has been documented to persist in plasma for a year or longer at low concentrations as DNA assays have improved.
- More common in immunocompromised patients who cannot make antibody

Treatment Available/Efficacious:

- Pure RBC aplasia is often effectively treated by IVIG.
- Hydrops fetalis may respond to high dose IVIG.
- Other clinical syndromes are treated with supportive care.

Agent-Specific Screening Question(s):

- No specific question is in use.
- Not indicated because of the rarity of transfusion transmission resulting in clinical disease
- No sensitive or specific question is feasible.

Laboratory Test(s) Available:

- No FDA-licensed blood donor screening test exists.
- NAT is available and can be used in a sensitive or insensitive fashion.
  - Insensitive NAT (detection limit is currently at ~10^5 IU/mL) is used for in-process screening of plasma units intended for fractionation into plasma derivatives.
  - More sensitive testing (detection limit at ~10^3 IU/mL) is used in Germany to make available, upon request, B19V-safe blood components for categories of patients susceptible to severe clinical outcomes of infection.
- B19V antigen tests are available but are not sensitive enough for donor screening.
- IgG and IgM antibody tests are commercially available and licensed in the US for diagnostic testing.
- In the Netherlands, donors with two positive IgG tests at an interval of >6 months are considered B19V-safe, and their components are available for particular categories of susceptible patients upon request.

Currently Recommended Donor Deferral Period:

- No FDA Guidance or AABB Standard exists.
- Prudent practice would be to defer a donor with B19V disease signs and symptoms until they resolve.

Impact on Blood Availability:

- Agent-specific screening question(s): Not applicable
- Laboratory test(s) available: Impact could be relatively high if sensitive NAT were used (donor DNA positivity rates of 0.2%-0.9%) and perhaps higher in communities experiencing epidemics; low if insensitive NAT used (donor DNA positivity rates of 0.03%-0.1%)

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 very low; therefore, benefits of screening may be minimal. However, outcomes could theoretically be severe in particular populations of transfusion recipients (e.g., patients with hemolytic anemias, immunosup-

pressed patients). These recipients might benefit from B19V-safe components.

Leukoreduction Efficacy:

- None, because virus has tropism for RBCs and RBC precursors.

Pathogen Reduction Efficacy for Plasma Derivatives:

- Only partially inactivated by heat and solvent-detergent treatment
- Inactivation appears to be effective if titer of plasma pool is below 10^4-10^5 IU per mL.

Other Prevention Measures:

- None

Suggested Reading:

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