PARVOVIRUS B19

(ERYTHEMA INFECTIOSUM, FIFTH DISEASE)
associated

TRANSIENT APLASTIC CRISIS
CHRONIC ANEMIA

CLINICAL MANIFESTATIONS

- Distinctive rash that may be preceded by mild systemic symptoms, including **fever in 15% to 30%** of patients.
- The facial rash can be intensely red with a “**slapped cheek**” appearance thatoften is accompanied by circumoral pallor
- A symmetric, macular, lace-like, and often pruritic rash also occurs on the trunk, moving peripherally to involve the arms, buttocks,and thighs
- The rash can **fluctuate** in intensity and recur with environmental changes,such as **temperature and exposure to sunlight**, for weeks to months
- A brief, mild, nonspecific illness consisting of **fever, malaise, myalgia, and headache** often precedes the characteristic exanthema by **approximately 7 to 10 days**

- **Arthralgia and arthritis** occur in fewer than 10% of infected children but **commonly occur among adults** especially **women**
- **Knees** are involved most commonly in **children**, but a symmetric polyarthropathy of knees, fingers, and other joints is common in adults
- Other manifestations include a mild respiratory tract illness with no rash, a rash atypical for EI that may be rubelliform or petechial, papular purpuric gloves-and-socks syndrome (PPGSS); painful and pruritic papules, petechiae, and purpura of hands and feet, often with fever and an enanthem), polyarthropathy syndrome (arthralgia and arthritis in adults in the absence of other manifestations of EI)
- Human parvovirus B19 infection occurring during pregnancy can cause fetal hydrops,intrauterine growth restriction, isolated pleural and pericardial effusions, and death, but the virus is not a proven cause of congenital anomalies. The risk of fetal death is between 2% and 6% when infection occurs during pregnancy. The greatest risk appears to occur during the first half of pregnancy.

Table 3.45. Clinical Manifestations of Human Parvovirus B19 Infection

Conditions	Usual Hosts
Erythema infectiosum (fifth disease)	Immunocompetent children
Polyarthropathy syndrome	Immunocompetent adults (more common in women)
Chronic anemia/pure red cell aplasia	Immunocompromised hosts
Transient aplastic crisis	People with hemolytic anemia (ie, sickle cell anemia)
Hydrops fetalis/congenital anemia	Fetus (first 20 weeks of pregnancy)
Petechial, papular-purpuric gloves-and-socks syndrome	Immunocompetent adults

- **chronic erythroid hypoplasia with severe anemia** in immunodeficient patients (eg, patients with human immunodeficiency virus [HIV] infection, patients receiving immune suppressive therapy), **and transient aplastic crisis** lasting 7 to 10 days in patients with hemolytic anemias (eg, sickle cell disease and autoimmune hemolytic anemia)
- For children with other conditions associated with low hemoglobin concentrations, including hemorrhage, severe anemia, and thalassemia, parvovirus B19 infection will not result in aplastic crisis but might result in prolongation of recovery from the anemia resulting from these conditions
- Patients with transient aplastic crisis may have a prodromal illness with fever, malaise, and myalgia, **but rash usually is absent**. In addition, human parvovirus B19 infection sometimes has been **associated with decreases in numbers of platelets, lymphocytes, and neutrophils**

ETIOLOGY

- Human parvovirus B19 is a small, nonenveloped, single-stranded DNA virus in the family *Parvoviridae*, genus *Erythrovirus*. Three distinct genotypes of the virus have been described.
- Parvovirus B19 replicates in human erythrocyte precursors, which accounts for some of the clinical manifestations following infection. Human parvovirus B19 associated red blood cell aplasia is related to caspase-mediated apoptosis of erythrocyte precursors.

EPIDEMIOLOGY

- Modes of transmission include **contact with respiratory tract secretions, percutaneous exposure to blood or blood products,and vertical transmission** from mother to fetus.
- Secondary spread among susceptible household members is common, with infection occurring in approximately 50% of susceptible contacts in some studies. The transmission rate in schools is lower, but infection can be an occupational risk for school and child care personnel, with approximately 20% of susceptible contacts becoming infected.
- In young children, antibody seroprevalence generally is 5% to 10%. In most communities, approximately 50% of young adults and often more than 90% of elderly people are seropositive. The annual seroconversion rate in women of childbearing age has been reported to be approximately 1.5%. Timing of the presence of high-titer parvovirus B19 DNA in serum and respiratory tract secretions indicates that people with EI are infectious before rash onset and are unlikely to be infectious after onset of the rash and/or joint symptoms.
- In contrast, **patients with aplastic crises** are contagious from before the onset of symptoms through at least the week after onset.
- Symptoms of the PPGSS can occur in association with viremia and before development of antibody response, and affected patients should be considered infectious.
- The **incubation period** from acquisition of parvovirus B19 to onset of initial symptoms (rash or symptoms of aplastic crisis) is between 4 and 14 days but can be as long as 21 days.

DIAGNOSTIC TESTS

- Parvovirus B19 **cannot be propagated in standard cell culture**. In the immunocompetent host, detection of serum parvovirus B19-specific **immunoglobulin (Ig) M antibodies is the preferred diagnostic test for parvovirus B19-associated rash illness**.
- **A positive IgM test result indicates that infection probably occurred within the previous 2 to 3 months**. On the basis of immunoassay results, IgM antibodies may be detected in 90% or more of patients at the time of the EI rash and by the third day of illness in **patients with transient aplastic crisis**.
- **Serum IgG antibodies appear by approximately day2 of EI and persist for life**; therefore, presence of parvovirus B19 IgG is not necessarily indicative of acute infection
- However, their sensitivity and specificity may vary, particularly for IgM. **The optimal method for detecting transient aplastic crisis or chronic infection** in the immunocompromised patient is demonstration of high titer of viral DNA by polymerase chain reaction (PCR) assays. Because parvovirus B19 DNA can be detected at low levels by PCR assay in serum for months and even years after the acute viremic phase, detection does not necessarily indicate acute infection. Low levels of parvovirus B19 DNA also can be detected by PCR in tissues (skin, heart, liver, bone marrow), independent of active disease.

TREATMENT

- For most patients, **only supportive care is indicated**. **Patients with aplastic crisis** may require transfusion. For treatment of chronic infection in **immunodeficient patients**, Immune Globulin Intravenous (IGIV) therapy often is effective and should be considered.
- Some cases of parvovirus B19 infection concurrent with **hydrops fetalis** have been treated successfully with intrauterine blood transfusions of the fetus.

- **ISOLATION OF THE HOSPITALIZED PATIENT:**
- In addition to **standard precautions**, **droplet precautions** are recommended for hospitalized children with aplastic crises, children with PPGSS, or immunosuppressed patients with chronic infection and anemia for the duration of hospitalization.
- For patients with **transient aplastic or erythrocyte crisis**, these precautions should be maintained for 7 days or until the reticulocyte count has recovered from suppression to at least 2%.
- Neonates who had **hydrops** attributable to parvovirus B19 in **utero** do not require isolation if the hydrops is resolved at the time of birth.
  Pregnant health care workers should be informed of the potential risks to their fetus from human parvovirus B19 infections and about preventive measures that may decrease these risks (eg, attention to strict infection control procedures and not caring for immunocompromised patients with chronic parvovirus B19 infection or patients with parvovirus
  B19-associated aplastic crises, because patients in both groups are likely to be contagious).

CONTROL MEASURES:

- Women who are exposed to children at home or at work (eg, teachers or child care providers) are at increased risk of infection with parvovirus B19. However, because school or child care center outbreaks often indicate wider spread in the community, including inapparent infection, women are at some degree of risk of exposure from other sources at home or in the community. In view of the high prevalence of parvovirus B19 infection, the low incidence of adverse effects on the fetus, and the fact that avoidance of child care or classroom teaching can decrease but not eliminate the risk of exposure,
routine exclusion of pregnant women from the workplace where EI is occurring is not recommended. Women of childbearing age who are concerned can undergo serologic testing for IgG antibody to parvovirus B19 to determine their susceptibility to infection.
• Pregnant women who discover that they have been in contact with children who were in the incubation period of EI or with children who were in aplastic crisis should have the relatively low potential risk of infection explained to them. The American College of Obstetrics and Gynecology recommends that **pregnant women exposed to parvovirus B19 should have serologic testing performed to determine susceptibility and possible evidence of acute parvovirus B19 infection. Pregnant women with evidence of acute parvovirus B19 infection should be monitored closely** (eg, serial ultrasonographic examinations) by their obstetric provider. In pregnant women with suspected or proven intrauterine parvovirus B19 infection, amniotic fluid and fetal tissues should be considered infectious and contact precautions should be used in addition to standard precautions if exposure is likely.

- Children with EI may attend child care or school, because they no longer are contagious once the rash appears.
  • Transmission of parvovirus B19 is likely to be decreased through use of routine infectioncontrol practices, including hand hygiene and proper disposal of used facial tissues.
  • In July 2009, the US Food and Drug Administration issued a guidance for nucleic acid amplification testing to reduce the possible risk of parvovirus B19 transmission by plasma-derived products
- The goal was to identify and prevent the use of plasma-derived products containing high levels of virus. Human parvovirus B19 viral loads in manufacturing pools should not exceed 104 IU/mL.