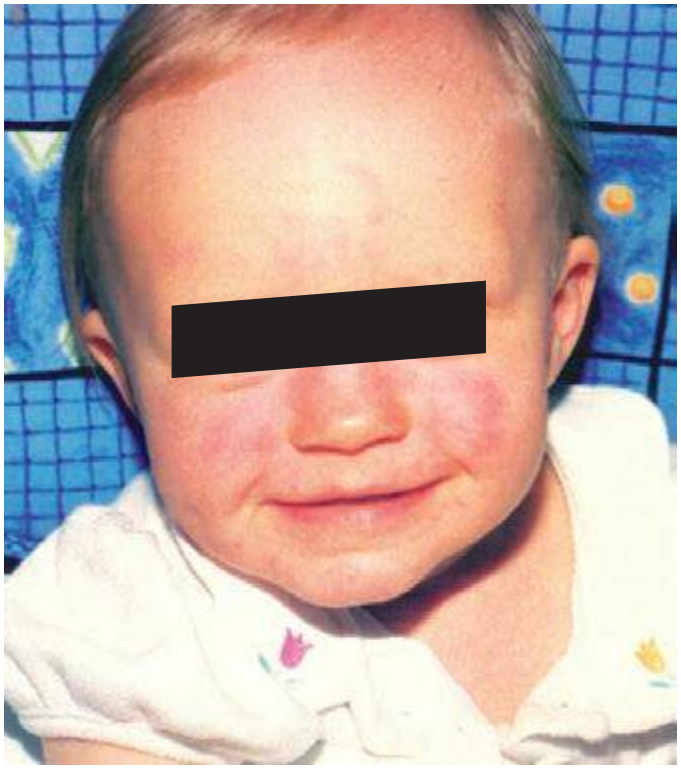

FIGURE 221-2 Young child with erythema infectiosum, or fifth disease, showing typical "slapped-cheek" appearance.

receptor is found in a variety of other cells and tissues, including megakaryocytes, endothelial cells, placenta, myocardium, and liver. Infection of these tissues by B19V may be responsible for some of the more unusual presentations of the infection. Rare individuals who lack P antigen are naturally resistant to B19V infection.

CLINICAL MANIFESTATIONS

Erythema Infectiosum Most B19V infections are asymptomatic or are associated with only a mild nonspecific illness. The main manifestation of symptomatic B19V infection is erythema infectiosum, also known as *fifth disease* or *slapped-cheek disease* **(Fig. 221-2 and Fig. 25e-1*A*)**. Infection begins with a minor febrile prodrome ~7–10 days after exposure, and the classic facial rash develops several days later; after 2–3 days, the erythematous macular rash may spread to the extremities in a lacy reticular pattern. However, its intensity and distribution vary, and B19V-induced rash is difficult to distinguish from other viral exanthems. Adults typically do not exhibit the "slapped-cheek" phenomenon but present with arthralgia, with or without the macular rash.

Polyarthropathy Syndrome Although uncommon among children, arthropathy occurs in ~50% of adults and is more common among women than among men. The distribution of the affected joints is often symmetrical, with arthralgia affecting the small joints of the hands and occasionally the ankles, knees, and wrists. Resolution usually occurs within a few weeks, but recurring symptoms can continue for months. The illness may mimic rheumatoid arthritis, and rheumatoid factor can often be detected in serum. B19V infection may trigger rheumatoid disease in some patients and has been associated with juvenile idiopathic arthritis.

Transient Aplastic Crisis Asymptomatic transient reticulocytopenia occurs in most individuals with B19V infection. However, in patients who depend on continual rapid production of red cells, infection can cause transient aplastic crisis (TAC). Affected individuals include those with hemolytic disorders, hemoglobinopathies, red cell enzymopathies, and autoimmune hemolytic anemias. Patients present with symptoms of severe anemia (sometimes life-threatening) and a low reticulocyte count, and bone marrow examination reveals an absence of erythroid precursors and characteristic giant pronormoblasts. As its name indicates, the illness is transient, and anemia resolves with the cessation of cytopathic infection in the erythroid progenitors.

Pure Red-Cell Aplasia/Chronic Anemia Chronic B19V infection has been reported in a wide range of immunosuppressed patients, including those with congenital immunodeficiency, AIDS **(Chap. 226)**, lymphoproliferative disorders (especially acute lymphocytic leukemia), and transplantation **(Chap. 169)**. Patients have persistent anemia with reticulocytopenia, absent or low levels of B19V IgG, high titers of B19V DNA in serum, and—in many cases—scattered giant pronormoblasts in bone marrow. Rarely, nonerythroid hematologic lineages are also affected. Transient neutropenia, lymphopenia, and thrombocytopenia (including idiopathic thrombocytopenic purpura) have been observed. B19V occasionally causes a hemophagocytic syndrome.

Recent studies in Papua New Guinea and Ghana, where malaria is endemic, suggest that co-infection with *Plasmodium* and B19V plays a major role in the development of severe anemia in young children. Further studies must determine whether B19V infection contributes to severe anemia in other malarial regions.

Hydrops Fetalis B19V infection during pregnancy can lead to hydrops fetalis and/or fetal loss. The risk of transplacental fetal infection is ~30%, and the risk of fetal loss (predominantly early in the second trimester) is ~9%. The risk of congenital infection is <1%. Although B19V does not appear to be teratogenic, anecdotal cases of eye damage and central nervous system (CNS) abnormalities have been reported. Cases of congenital anemia have also been described. B19V probably causes 10–20% of all cases of nonimmune hydrops.

Unusual Manifestations B19V infection may rarely cause hepatitis, vasculitis, myocarditis, glomerulosclerosis, or meningitis. A variety of other cardiac manifestations, CNS diseases, and autoimmune infections have also been reported. However, B19V DNA can be detected by PCR for years in many tissues; this finding is of no known clinical significance, but its interpretation may cause confusion regarding B19V disease association.

DIAGNOSIS

Diagnosis of B19V infection in immunocompetent individuals is generally based on detection of B19V IgM antibodies **(Table 221-1)**. IgM can be detected at the time of rash in erythema infectiosum and

TABLE 221-1 DISEASES ASSOCIATED WITH HUMAN PARVOVIRUS B19 INFECTION AND METHODS OF DIAGNOSIS

Disease	Host(s)	IgM	IgG	PCR	Quantitative PCR
Fifth disease	Healthy children	Positive	Positive	Positive	$>10^4$ IU/mL
Polyarthropathy syndrome	Healthy adults (more often women)	Positive within 3 months of onset	Positive	Positive	$>10^4$ IU/mL
Transient aplastic crisis	Patients with increased erythropoiesis	Negative/positive	Negative/positive	Positive	Often $>10^{12}$ IU/mL, but rapidly decreases
Persistent anemia/pure red-cell aplasia	Immunodeficient or immunocompetent patients	Negative/weakly positive	Negative/weakly positive	Positive	Often $>10^{12}$ IU/mL, but should be $>10^6$ in the absence of treatment
Hydrops fetalis/congenital anemia	Fetus (<20 weeks)	Negative/positive	Positive	Positive amniotic fluid or tissue	n/a

Abbreviations: IU, international units (1 IU equals ~1 genome); n/a, not applicable; PCR, polymerase chain reaction.