Erythrovirus B19 infection

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Abstract

Erythrovirus B19 causes erythema infectiosum or fifth disease, also called slapped cheek syndrome, a common childhood exanthem. Erythema infectiosum is typically an acute, self-limiting, biphasic illness commencing with non-specific flu-like symptoms accompanying viraemia, followed by more specific signs of rash and/or arthropathy coinciding with seroconversion. Most infections are subclinical. Erythrovirus B19 can cause life-threatening illness requiring urgent intervention, depending on age, immune and haematological status. Infection of nucleated red cells causes transient aplastic crisis in patients with haemoglobinopathies, and chronic anaemia in immunocompromised individuals. Up to 50% of women of childbearing age are susceptible, being at risk of fetal loss and hydrops fetalis if infected in the first 20 weeks of pregnancy. Diagnosis depends on the timing and nature of presentation. Aplastic crisis or red cell aplasia presents in the initial viraemic phase, warranting detection by polymerase chain reaction. In patients with rash or arthropathy, specific immunoglobulin M (IgM) and IgG testing is appropriate; IgG testing establishes susceptibility. No antivirals or preventive vaccines are available, but infection control, blood transfusion, intravenous immunoglobulin and reduction of immunosuppression play an important role in management. Infection control is a challenge as index cases are infectious for 10 days before onset of the rash.

Keywords B19v arthropathy; erythema infectiosum; fifth disease; human erythrovirus B19; hydrops fetalis; MRCP; parvovirus B19; pure red cell aplasia; slapped cheek syndrome; transient aplastic crisis

Key points

- Acute erythrovirus B19 infection is a biphasic illness commencing with flu-like symptoms and viraemia, followed by rash and/or arthropathy coinciding with seroconversion
- Patients who are immunocompromised or with haemoglobinopathies present with anaemia in the viraemic phase, requiring DNA detection for diagnosis
- Infection control is challenging as the non-enveloped virus is resistant to degradation in the environment, infections are often subclinical, and patients are infectious for a period of 10 days *before* rash or arthropathy develops
- Contact tracing of pregnant women is important as up to 50% of women of childbearing age are susceptible, and hydrops fetalis can be successfully treated by *in utero* red cell transfusion

The virus and pathogenesis

Human erythrovirus B19 (previously called parvovirus) is a small, non-enveloped, icosahedral, single-stranded DNA virus. It relies on multiplying cells to host viral replication, reflecting the small coding capacity of the 5.6 kbp genome.[1,2]

Humans are the only known host, and productive infection seems to be confined to dividing erythroid progenitor cells. The P antigen, globoside, expressed on mature red blood cells and their precursors, has been identified as the cellular receptor. Individuals who genetically lack P antigen — a rare phenotype observed in the North American Amish population — are innately resistant to erythrovirus B19 infection.[2]

Virus replication in the red cell nucleus results in cell lysis, interrupting red cell production and leading to the reticulocytopenia and fall in haemoglobin that characterize the initial viraemic phase of infection. P antigen is also expressed on the surface of cardiomyocytes, endothelial and placental trophoblast cells. These cell types are not permissive for virus replication, but virus may enter cells and contribute to disease by inducing cellular apoptosis. Putative causal associations with myocarditis, nephritis, hepatitis and encephalitis, sometimes based on DNA detection in tissue, remain as yet unproven.[2]

Epidemiology and transmission

Erythrovirus infection is endemic worldwide, with seasonal outbreaks every few years. Transmission is efficient, with approximately 50% of susceptible household contacts acquiring infection via the respiratory route or contaminated fomites. Most infections are subclinical, and immunity usually persists lifelong.[1] Adult seroprevalence ranges from 40% to 80%. Intrauterine transmission and blood products are also important modes of spread.[1,2]

Clinical syndromes and management

Immunocompetent hosts

Discovered by chance in 1975, parvovirus B19, as it was initially named, was identified as the cause of erythema infectiosum, also known as fifth disease, or 'slapped cheek' syndrome, a common childhood exanthem. Many adults remain susceptible, enabling characterization of the clinical and virological course of experimental infection in volunteers.[3]

Erythema infectiosum is an acute self-limiting biphasic illness. The initial viraemic phase commences 5–10 days after exposure, and lasts around 5 days, with fever, non-specific flu-like

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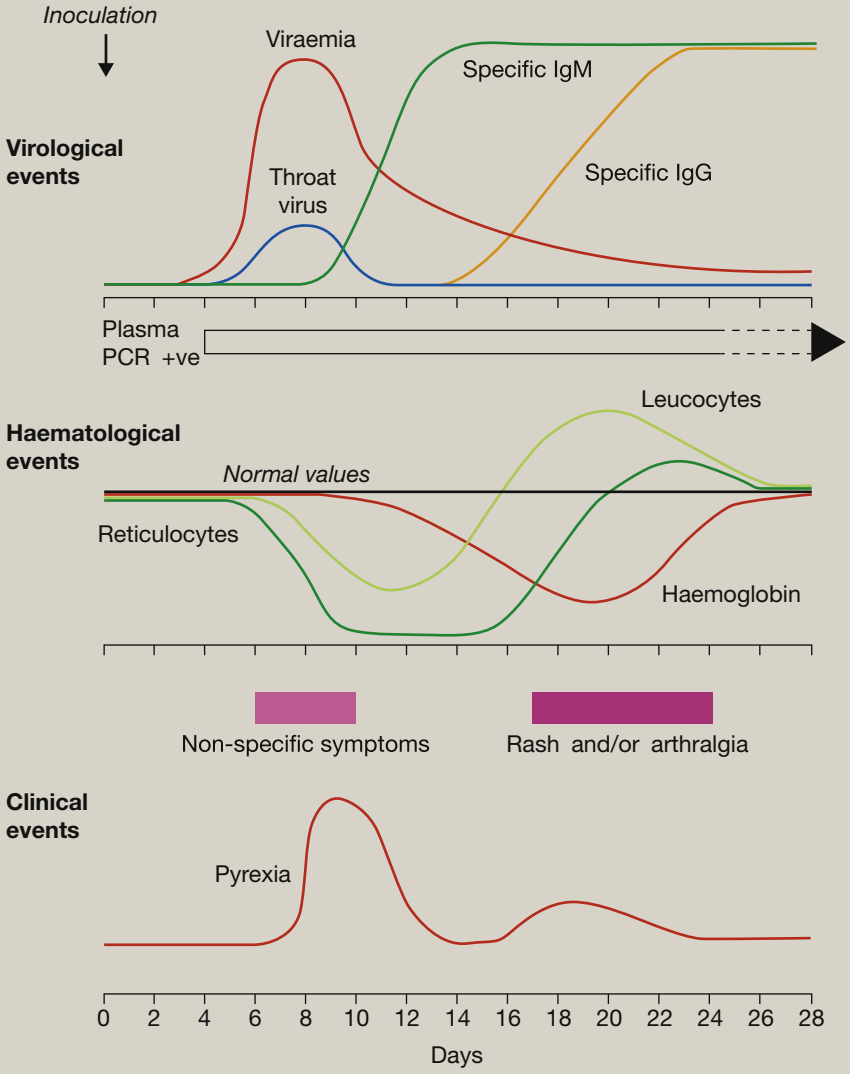
symptoms and spread to susceptible contacts (Figure 1). Virus invades and destroys erythrocyte progenitor cells, causing a significant drop in the reticulocyte count and haematocrit. Red cell production recovers within 14 days. As the half-life of red cells is 120 days, infection does not usually cause recognizable anaemia.[1–3]

The onset of the second phase, characterized by rash and arthropathy, coincides with the appearance of erythrovirus B19 specific antibodies and immune complex formation. Individuals are no longer infectious. The erythematous maculopapular rash also heralds the end of the 13–18-day incubation period, the interval between exposure and onset of the rash (Figure 1).

'Slapped cheek' describes the classic malar rash and associated circumoral pallor seen in children. The rubella-like rash on the trunk and limbs can be subtle and reticular (like lace), and is often evanescent, recurring in response to sunlight, heat, emotion or exercise, after apparent resolution (Figure 2).[1,2]

Symmetrical hand, wrist and knee joint arthritis, or arthralgia, occurs more often in adults, especially women, as with rubella (Figure 2). There is no joint destruction, but similarity to rheumatoid arthritis often generates rheumatology referrals. Joint pain usually resolves within a few weeks, but persistent arthropathy sometimes develops. Management is symptomatic.[1–3]

Acute parvovirus infection, a biphasic illness in the normal host: evolution of clinical features and haematological indices, detection of viraemia and serological responses



Source: Adapted from Heegaard ED, Brown KE. Human Parvovirus B19. *Clin Microbiol Rev* 2002; 15(3): 485–505.

Figure 1

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