PARVOVIRUS B19

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What is Parvovirus B19?

Parvovirus B19 is a small, single-stranded DNA virus belonging to the *Erythrovirus* genus of the *Parvoviridae* family that mainly infects human erythroid progenitor cells. It can cause a variety of diseases, dependent on the patient's immunological and haematological status. The virus can be transmitted via the respiratory route, close contact, bone marrow and organ transplantation, vertically from the mother to foetus, and through blood and blood products. Infections occur throughout the year, but outbreaks are more common in late winter, spring and early summer.

Disease manifestations of Parvovirus B19:

- Erythema infectiosum ("slapped cheek" or fifth disease): an innocuous erythematous rash illness usually seen in immunocompetent children. Symptoms begin with a non-specific prodromal illness, with the characteristic "slapped cheek" rash and relative circumoral pallor appearing 2 – 5 days later. This may be followed by a second-stage erythematous rash on the trunk and limbs a few days later. Patients may also complain of pruritis, especially on the soles of the feet.

- Polyarthropathy: an acute polyarthropathy primarily seen during acute infection in adults, especially women. The arthralgia is typically symmetrical, involving the small joints of the hands and feet, and may not always be accompanied by an erythematous rash. Symptoms usually last between one and three weeks, but may persist or recur over several months to years. Both the polyarthropathy and the rash of acute parvovirus B19 infection appear to be immune-complex mediated.

- Transient aplastic crisis: a temporary interruption in red blood cell production seen in patients with high erythroid turnover due to blood loss, haemolysis or other causes. It is characterised by an abruptly worsening anaemia, low reticulocyte count, and the presence of giant pronormoblasts (with the absence of erythroid precursors) in the bone marrow. The severe anaemia may be complicated by congestive cardiac failure, cerebrovascular accidents, and acute splenic sequestration. Red blood cell production resumes with the clearance of infection by neutralising antibodies.

- Pure red cell aplasia: chronic parvovirus B19 infection with persistent anaemia seen in immunocompromised patients, including patients with lymphoproliferative disorders, congenital and acquired immune-deficiencies, and transplant recipients. Persistent infection is established due to a failure to produce neutralising antibodies.

- Hydrops foetalis: intra-uterine infection with parvovirus B19 during the first 20 weeks of pregnancy can lead to non-immune hydrops foetalis and foetal loss. Based on prospective studies, the estimated risk of transplacental transmission amongst women infected during pregnancy is approximately 33%, with a less than 10% risk of foetal loss. Although no evidence of congenital abnormalities could be found in systematic studies, a few case reports have described congenital neurologic and ocular abnormalities, and congenital red cell aplasia.

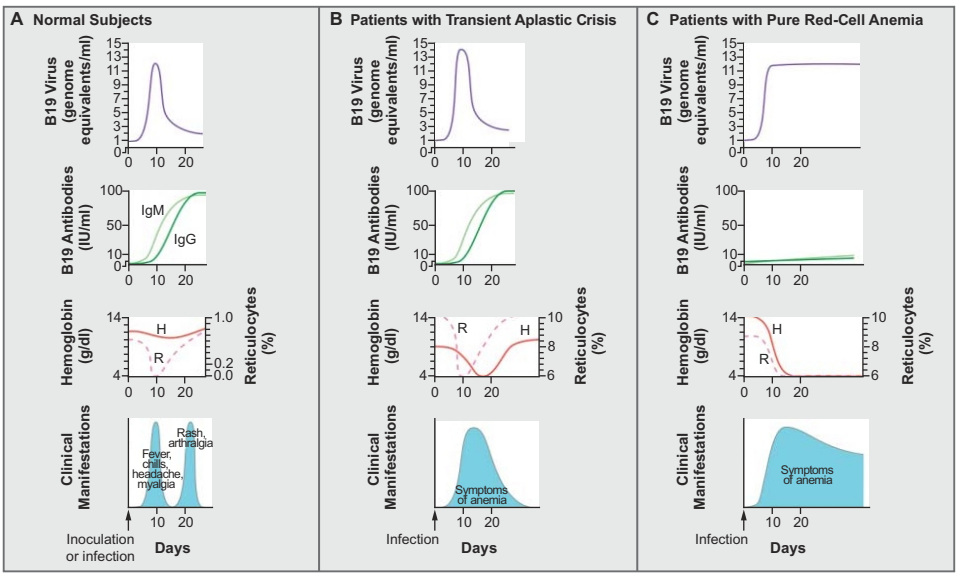

Figure 1: Pathophysiology of parvovirus B19 infection[2]

Panel A – Infection of immunocompetent individuals results in erythema infectiosum or polyarthropathy. The typical rash and joint symptoms correspond to the appearance of specific antiviral antibodies. Reticulocytopaenia occurs during viraemia, but haemoglobin levels do not decline below normal values.
Panel B – Transient aplastic crisis occurs in patients with underlying haemolysis or erythroid stress. Cessation of erythropoeisis causes severe anaemia, because of the higher demand for red cells.
Panel C – Pure red cell aplasia is due to chronic, persistent infection. Anaemia persists because of the failure of the humoral immune response to clear parvovirus B19.

Laboratory testing:

Serology

- IgM antibodies usually appear 3 – 4 days after the onset of symptoms and persist for 2 – 3 months after acute infection. Occasionally IgM antibodies may not appear until 7 – 10 days after the onset of symptoms in patients with erythema infectiosum or transient aplastic crisis. A second sample, taken approximately 14 days after the onset of symptoms, is indicated in these cases.
- IgG antibodies are detectable by approximately the 7th day of illness and persist lifelong.
- Serology is unhelpful for the diagnosis of chronic parvovirus B19 infection and pure red cell aplasia as immunocompromised patients typically fail to mount an adequate immune response and antibodies may only be detectable at low levels or not at all.
- Pregnant women are frequently asymptomatic during acute infection with parvovirus B19. By the time foetal symptoms are evident, 2 – 12 weeks after maternal infection, the mother may already have high titres of IgG and no detectable IgM. Less than one third of foetal blood samples, taken whilst foetal symptoms are present, have detectable levels of IgM or IgG.

PCR

- Parvovirus B19 viraemia usually lasts only 2 – 4 days in the immunocompetent individual. However, even in immunocompetent people, low levels of parvovirus B19 DNA may be detectable in serum for more than 4 months after acute infection, and for years in bone marrow, synovium, heart, and other tissues. Thus the detection of DNA in tissues does not necessarily prove that disease is due to parvovirus B19 infection.
- Parvovirus B19 DNA detection by PCR is unhelpful for confirming the diagnosis when a patient presents with symptoms of erythema infectiosum or polyarthropathy as these are due to immune-complex formation, with resultant low level or absent parvovirus B19 viraemia.
- In contrast, patients with transient aplastic crisis and pure red cell aplasia are usually viraemic at the time of presentation, and parvovirus B19 DNA can readily be detected in the patient's blood.
- The detection of low levels of parvovirus B19 DNA in maternal blood may not be related to recent infection due to the reason stated above. To confirm intra-uterine infection, parvovirus B19 DNA may be detected by PCR in foetal blood or amniotic fluid.

Treatment:

In the vast majority of patients, infection with parvovirus B19 is benign, self-limiting and results in lifelong immunity. Treatment consists mainly of symptomatic relief, e.g. non-steroidal anti-inflammatory drugs for the arthralgia. Frequent hand washing is recommended to help reduce the spread of parvovirus B19.

Specific treatment may be necessary in patients presenting with transient aplastic crisis or pure red cell aplasia. Patients with transient aplastic crisis commonly respond well to blood transfusion and supportive care alone. Immunosuppressed patients with documented, chronic parvovirus B19 infection may require a temporary interruption in their immunosuppression, to allow their own immune system to mount a response and clear the infection. The administration of immunoglobulins may be needed in cases where the interruption of immunosuppression is ineffectual or impractical. An intravenous pooled immunoglobulin (IVIG) regimen of 400 mg/kg body weight for 5 – 10 days has proven to be effective in resolving the anaemia and reducing the parvovirus B19 viraemia level within one to two weeks of treatment.

Intra-uterine blood transfusions have been shown to reduce the mortality rate of hydrops foetalis due to parvovirus B19 infection during pregnancy from approximately 50% to 18%. However, intra-uterine blood transfusions are not without risk, and hydrops foetalis due to parvovirus B19 has been known to resolve spontaneously without any residual sequelae seen at birth.

Prevention:

The only measures currently available to prevent parvovirus B19 infection are those designed to interrupt virus transmission, e.g. frequent hand washing. There is no need to isolate patients presenting with erythema infectiosum, as the viraemia occurs before the symptoms. However, patients with transient aplastic crisis and pure red cell aplasia are both viraemic and infectious at presentation, and should thus be separated from high risk contacts. The US CDC recommends droplet precautions for 7 days for patients with transient aplastic crisis, and patients with pure red cell aplasia should be isolated for the duration of their hospitalisation.

Summary:

DISEASE	PATIENT POPULATION	ACUTE OR CHRONIC	DIAGNOSIS
Erythema infectiosum	Immunocompetent children	Acute	Serology
Polyarthropathy	Immunocompetent adults	Acute or chronic	Serology
Transient aplastic crisis	Patients with increased erythropoesis	Acute	PCR
Pure red cell aplasia	Immunocompromised patients	Chronic	PCR
Congenital infection	Foetus	Acute or chronic	Serology and PCR

References:

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