VIROLOGY - CHAPTER TWENTY SIX

PARVOVIRUSES AND FIFTH DISEASE

Dr. Margaret Hunt
Professor Emerita
University of South Carolina School of Medicine

Dr Richard Hunt
Professor
University of South Carolina School of Medicine

Figure 1A. This electron micrograph depicts a number of parvovirus H-1 virions of the Parvoviridae family of DNA viruses. The Parvoviridae family of viruses also contains the Parvovirus B19 virion, which is responsible for causing erythema infectiosum, or *"Fifth Disease"*. CDC

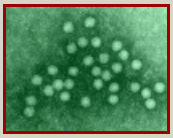

Figure 1B Parvoviruses are the smallest known DNA-containing viruses. The capsids have icosahedral symmetry, and are approximately 25nm in diameter. © Dr Linda Stannard, University of Cape Town, South Africa. Used with permission

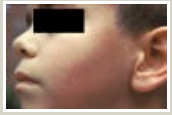

Figure 2. The left side of this boy's face displays signs of erythema infectiosum, or Fifth disease. CDC

Figure 3. The hands of an elementary school youngster showing symptoms of erythema infectiosum, or Fifth disease. CDC

Fifth disease is one of the common childhood rashes and is caused by human parvovirus B-19 (figure 1). It is also called *erythrema infectiosum* or slapped face disease because of the rash on the cheeks. It is called fifth disease because it was the fifth of a series of rashes, ordered in the sequence that they were reported, that all look very similar. The others are measles (Rubeola), scarlet fever (Scarlatina), German measles (3-day measles, rubella) and Dukes' disease. About half of the US population has been infected by parvovirus B-19 and infection results in life-long immunity.

Is there a sixth disease?	What is Duke's disease?

Fifth disease is common in children, is usually mild and quickly resolves without intervention. It does not require treatment but it can cause serious problems in some members of the population. A child with fifth disease shows symptoms from a few days to as long as two weeks after infection but usually they resolve after about a week. The rash can look like the redness of a slapped face (figure 2), intensely red on the cheeks with a pale ring around the mouth (circumoral pallor). It may extend to the rest of the body as a lacy rash (figure 3). Sometimes there is itching. Before the manifestation of the rash, the child may have cold-like symptoms and perhaps a low fever. Most people are infected early in life and become immune but adults can be infected. As with children, adults sometimes manifest no symptoms but they can also get the typical rash. This can be accompanied by swelling of the joints on both sides of the body which usually subsides in a few weeks, though the swelling can persist for longer.

The disease can be spread from person to person before the rash appears. Since the patient often has cold-like symptoms before the onset of rash and the virus is found in respiratory tract secretions, spread is likely to result from aerosols (sneezing) or other contact (via the hands etc) with the secretions. By the time of the rash, the viremia has subsided and the patient is no longer infectious. This is in contrast with other similar diseases in which the patient with the rash is contagious. (e.g measles). Usually, about half of the family contacts of an infected person contracts the disease.

IMMUNE RESPONSE

Two weeks after infection about 90% of patients show IgM antibodies. The level peaks peaks after about a month and may persist for several more months. IgG appears after about three to four weeks and persists indefinitely leading to lifelong immunity.

Table 1
PARVOVIRUS B-19 SEROLOGY

Serology	Interpretation
IgG-	No past infection Patients susceptible to

IgM-	infection
IgG+ IgM-	There has been a past infection Patient probably immune
IgG + or - IgM equivocal	Current or recent infection Patient should be retested in a few weeks
IgG+ IgM+	Ongoing or recent infection Fetus may be at risk if patient pregnant
IgG- (or equivocal) IgM+	Current infection Patient should be retested in a few weeks

Adapted from Biotrin International, Dublin Ireland

DIAGNOSIS

Diagnosis is from the rash but there is also a serology test. The presence of anti-viral IgM indicates a recent infection.

ANEMIA

In patients with chronic anemia, such as in sickle cell anemia in which there are short-lived erythrocytes, a fifth disease infection can be very serious as a temporary aplastic crisis may result. This is because the virus replicates in red blood cell precursors and temporarily interferes with red blood cell production. These patients do not usually have the characteristic rash and in fact may show pallor and malaise. As the infection resolves so do the symptoms.

Other people who may need medical attention as a result of parvovirus B-19 infection are those with compromised immune systems (organ transplant patients, patients with leukemia, other forms of cancer or an HIV infection).

INFECTION DURING PREGNANCY

Usually, the virus has no effect on pregnant women or their fetus, even if the mother is not one of the 50% of the population with life-long immunity as a result of a prior infection. In about a third of maternal infections the virus crosses the placenta; however, in about 5% of maternal infections that occur in the first half of the pregnancy, the mother may develop a serious anemia that may result in miscarriage.

In the fetus, the virus replicates in erythroid cells causing fetal anemia and non-immune hydrops fetalis (NIHF) in about three quarters of cases and idiopathic NIHF in the remainder. Hydrops usually occurs about 4 weeks after maternal infection.

TREATMENT

There is no vaccine and no treatment for fifth disease although the fever symptoms can be addressed. In adults, aspirin may help with the joint pain. In cases of severe anemia, hospitalization and blood transfusion may be necessary. If there is a compromised immune system, passive immune globulin may be required. In fetal anemia, intrauterine blood transfusion may be necessary.

PARVOVIRUSES

Parvoviruses are small (30nm - *parvum* = small), naked icosahedral DNA viruses with a single DNA strand of about 5kB. The packaged DNA may be either sense (same as the mRNA) or anti-sense. The two forms are packaged in about equal proportions. Replication of the virus requires that the host cell be undergoing DNA replication (that is, in S phase) yet unlike many other viruses, they cannot initiate cell DNA synthesis. This means that parvoviruses are restricted to the dividing cells of the body such as the erythropoietic and immune systems.

After infection the single strand DNA enters the nucleus where host cell repair enzymes

convert it to double stranded DNA. There are three promoters from which host cell RNA polymerase makes three transcripts that have different 5' ends but the same 3' end. There is also RNA splicing so that several proteins of related sequence result. The virus makes a replication enzyme but this is not a polymerase. It cleaves the DNA closed circle to make the single strand genomic DNA.

The human parvovirus B19 is different from the parvoviruses which cause problems in cats and dogs. Humans appear to be the only natural host for human parvoviruses. In dogs, a parvovirus can cause severe disease. Feline panleukopenia in cats is caused by a parvovirus and can cause mortality as a result of immune system destruction.

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