

## Parvovirus

### Introduction

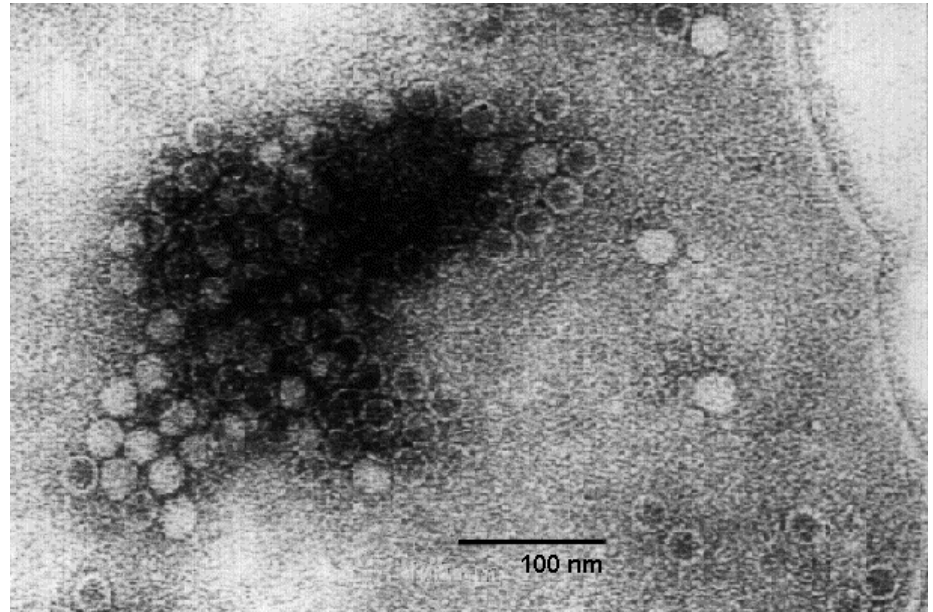
Parvovirus B19, more correctly called Erythrovirus B19 is a common cause of infection in man. It is a member of the Parvoviridae family, a large family of viruses that infect a wide range of animal hosts. B19 is the only member that causes human disease. It was first discovered in 1975, in the blood of a healthy blood donor. B19 was the donation number of the blood unit. A nonspecific result was observed with the Hepatitis B surface Antigen screening test, using counterimmunoelectrophoresis, and on investigation electron microscopy revealed the viral particles.

### The virus

B19 is a small (around 26nm) non-enveloped virus with an icosahedral capsid. The genome is single stranded DNA, 5600 nucleotides in size, and encodes for two capsid proteins (VP1 and VP2), one major non-structural protein (NS1), and several other small peptides. NS1 binds to cellular DNA, is cytotoxic to mammalian cells, and plays a possible role in B19 DNA replication. The capsid is 95% VP2.

The virus has tropism for erythroid tissue (bone marrow), as it requires rapidly dividing cells in the S phase of cell division for replication, and binds to the P antigen of the P blood group system. This antigen is abundant on erythroid cells, endothelial cells, placental cells, and foetal liver and heart cells.

Historically, genetic diversity has been thought to be low -1-2% of genome. But recently new variants have been found with about 10% genetic divergence, dividing B19 into 3 genotypes. Genotype 1 is the most common; the new variants are referred to as genotypes 2 and 3. These new variants are rare, and as yet no data exists on their prevalence in



*A negatively stained preparation of parvovirus as seen by transmission electron microscope. From the Wadsworth Center of the New York State Department of Health.*

New Zealand.

### Clinical Disease

Infection with B19 is common- adult seroprevalence is 50%, reaching 90% in the elderly. Distribution is worldwide.

Transmission is most commonly via respiratory droplets. Mother to foetus and blood transfusion transmission is also possible.

The virus can cause a wide range of disease manifestations. In the immunocompetent host, infection can be asymptomatic, a mild flu like illness, arthropathy, or temporary depression of erythropoiesis. Fifth disease, also known as erythema infectiosum, is the most common manifestation in children and young adults - a typical "slapped cheek" rash on the face is seen.

Arthropathy is more common in adults. In the acute phase of the infection symptoms can mimic rheumatoid arthritis. Symptoms usually resolve after several weeks; however they can occasionally persist for months or even years.

B19 can cause an aplastic crisis in people with underlying haematological disorders. The abrupt onset of severe anaemia is usually self limited but severe complications such as congestive heart failure and bone marrow necrosis can occur.

Infection during pregnancy has a 24-33% chance of mother to foetus transmission, with the highest risk in the second trimester. Spontaneous abortion can occur, or the foetus can develop hydrops fetalis, in which fetal anaemia leads to heart failure and oedema. In surviving babies there are usually no other congenital deformities, but they can be born with chronic anaemia.

### Laboratory Diagnosis

Infection can be diagnosed by serology and / or by PCR, both of which are available at Canterbury Health Laboratories (CH Labs). Serology is recommended in immunocompetent individuals, including pregnant women, patients with erythema infectiosum or transient aplastic crisis.

# Parvovirus

Clinical Presentation	Specimen(s) of choice	Primary test of choice	Additional Tests
Immune status	Serum	Parvovirus IgG	
Infection during pregnancy 1 <sup>st</sup> trimester	Serum	Parvovirus IgM	Parvovirus IgG Parvovirus IgG avidity
Infection during pregnancy 2 <sup>nd</sup> and 3 <sup>rd</sup> trimester (mother)	Serum	Parvovirus IgM(serum)	DNA by PCR
Infection during pregnancy 2 <sup>nd</sup> and 3 <sup>rd</sup> trimester (foetus)	Amniotic fluid Foetal tissue (heart, lung, liver, placenta)	DNA by PCR	
Polyarthropathy	Serum	Parvovirus IgM	Parvovirus IgG
Erythema infectiosum	Serum	Parvovirus IgM	Parvovirus IgG
Aplastic crisis	Serum	DNA by PCR	Parvovirus IgM Parvovirus IgG
Infection in the immunocompromised	Serum Bone marrow cells	DNA by PCR	

PCR was used at CH Labs. This nested (two step) PCR was very long and it was often difficult to obtain a result on the same day the sample was received. Conventional PCR gives only an end point positive or negative result.

We have now developed a real-time PCR using the Roche Lightcycler. The new PCR targets a conserved sequence of the NS1 protein. Real time PCR is much faster and less labour intensive than conventional PCR. The results are easier to interpret and troubleshoot, as the PCR reaction is monitored cycle by cycle.

This new test performs as well as the old method, with the same sensitivity, and offers significant improvements both to our lab workflow and result turn around times.

## References

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- Baylis S et al. Evaluation of different assays for the detection of Parvovirus B19 DNA in human plasma. Journal of Virological Methods 121 (2004) 7-16
- Specter et al. Clinical Virology Manual, 3<sup>rd</sup>

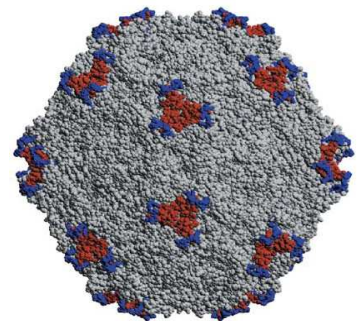
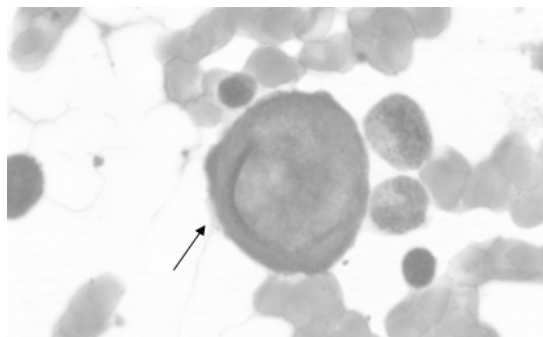
However antibodies are not detectable in some immunocompromised patients with chronic and persistent infection. During aplastic crisis IgM antibodies may not be present until some days after crisis onset. In these situations, and for the prenatal diagnosis of non-immune fetal hydrops, PCR testing is helpful.

B19 can be detected by PCR in serum, urine, CSF, pleural fluid, respiratory secretions, peripheral mononuclear cells, bone marrow, tissue, synovial fluid, joint aspirates and amniotic fluid.

Parvovirus is very difficult to grow in cell culture, and this technique is not used routinely for diagnostic testing.

## New Real Time PCR at CH Labs

Until recently a conventional gel based



*Bone marrow showing giant erythroblast, The cytopathic effect of B19 parvovirus infection of the erythroid progenitor cell and erythroid hypoplasia:Leishman stained*