

Second Edition

Literature Review

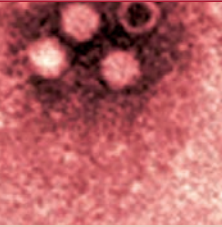
Human Parvovirus B19


Biotrin
www.biotrin.com



Treatment of Parvovirus B19-Associated Polyarteritis Nodosa with Intravenous Immune Globulin.

Viguiet M., Guillemin L., Laroche L. The New England Journal of Medicine
2001;344:19:1481-1482



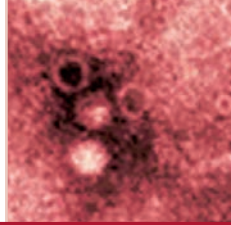
The authors describe a case in which a 33 year old woman identified with Parvovirus B19 associated polyarteritis nodosa was successfully treated with intravenous immune globulin therapy.

The patient presented with symptoms including asthenia (weakness or loss of strength), fever, intense myalgia (pain in muscles) and polyarthritis of the joints of the hands. Parvovirus B19 infection was suspected as her young son had been diagnosed with febrile exanthum three weeks previous.

Serological analysis performed on day 4 of infection was positive for B19 IgM and IgG antibodies. PCR analysis on day 18 revealed the presence of B19 DNA. Skin biopsy and muscle biopsy revealed medium and small vessel vasculitis, respectively. As this data was indicative of B19 associated polyarteritis nodosa* infection, intravenous immune globulin was administered. The patient improved rapidly within one week, and within 1 month she was in remission. IgM antibodies were completely undetectable 1 year after infection, although IgG remained detectable.

Although previous reports describe successful treatments with intravenous (IV) immune globulin, it cannot be ruled out that the recovery of the patient was due to spontaneous regression or a non-specific immunosuppressive effect of immune globulin treatment as recovery did not coincide with disappearance of viremia.

*** *Polyarteritis nodosa is a disease that causes patchy inflammation of the walls of the arteries.***



Diagnosing human Parvovirus B19 infection: Guidelines for test selection.

Jordan J. *Molecular Diagnosis* 2001;6:307-312

Human Parvovirus B19 is the virus responsible for erythema infectiosum or 'fifth disease'. Healthy individuals who become infected with Parvovirus B19 usually develop mild symptoms. However, those most susceptible to B19V are pregnant women and immunosuppressed or immunocompromised individuals such as AIDS and transplant patients.

Once infected, an individual will produce IgM antibodies specific to B19V, 7-10 days after infection. These antibodies usually remain detectable for 2-3 months after infection. Approximately 10-12 days after infection, IgG antibodies specific for B19V are produced. These antibodies remain in the body for years and are thought to confer immunity.

This paper discusses the types of diagnostic tests available to detect B19V and which methods are best for each patient group. During an acute infection B19V DNA is mainly found in blood and reaches levels of 10^{14} particles/ml. The author reports that immunocompetent individuals who have evidence of current or recent infection may lack detectable levels of B19 DNA in their blood when tested by PCR. Evidence to support this came from a study of 40 immunocompetent individuals, who were tested for B19 DNA by PCR. All had shown evidence of seroconversion, B19 IgM and B19 IgG positive. Of these 40, only 45% (18/40) contained B19 DNA using non-nested PCR, whereas the remaining 55% of samples were negative by PCR for B19V DNA. It is suggested that based on this data, PCR should not be used to detect B19V acute infection in immunocompetent persons.

The author suggests that PCR should however be used when detecting Parvovirus B19 within amniotic fluid, umbilical cord blood or fetal tissue. Molecular testing is considered to be a useful diagnostic tool in determining when fetal death is associated with Parvovirus B19 infection, or when trying to diagnose B19V infections in immunosuppressed individuals with low immune response.

It is highlighted that during acute B19V infection, B19V specific antibodies to both the linear and conformational epitopes are produced against the VP1 and VP2 capsids proteins. It is postulated that IgG antibodies to linear epitopes disappear approximately 6 months after infection, thus leaving only antibodies that recognise conformational epitopes.

The author indicates that using E.coli based EIA's can lead to false negative results as they only detect linear antigens. Evidence suggests that Baculovirus systems generate conformational viral antigens and the use of assays based on these antigens results in fewer equivocal, false positive and false negative results. The author also indicated that using a mu capture EIA for detection of Parvovirus B19 IgM antibodies is a more sensitive and specific method than using an indirect assay as high concentrations of IgG antibodies may compete for binding.

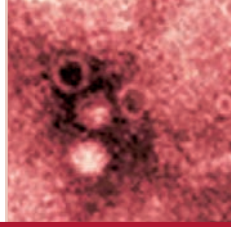
To conclude the author indicates that choosing the correct diagnostic assay to detect Parvovirus B19 infection will depend on the patient being tested. She also emphasises that selecting the correct diagnostic test is of critical importance as inaccurate testing can lead to added expense, misinformation and /or misdiagnosis.

Human Parvovirus B19: Relevance in Internal Medicine

van Elsacker-Niele A.M.W., Kroes A.C.M. The Netherlands Journal of Medicine
1999;54:221-230

Human Parvovirus B19 (B19V) was discovered in 1975 by Cossart *et al.* Members of the Parvovirus family are small, single stranded DNA viruses that lack a viral envelope. Parvovirus B19 has 2 structural proteins (VP1, VP2) and one non-structural protein (NS1). The protein capsid is composed of 4% VP1 and 96% VP2.

It has been postulated that initial viral replication of Parvovirus B19 takes place in the respiratory tract. B19V needs actively dividing cells in order to replicate, hence its target cells are erythroid precursor cells in the bone marrow. B19V enters these cells via the blood group 'P' antigen receptor. The 'P' antigen is found mainly on red blood cell membranes but can also be found on platelets and on tissue from the heart, liver and lungs.



Viral replication in these cells causes a cessation of erythropoiesis. The virus is neutralised by the production of IgM antibodies and life long immunity is conferred by the production of IgG antibodies.

Parvovirus B19 has been identified as the causative agent of erythema infectiosum or 'fifth disease'. The characteristic feature of this illness is erythema of the face, and a maculopapular rash of the trunk and limbs. The onset of the rash has been shown to coincide with the production of neutralising antibodies.

Parvovirus B19 has been implicated in a number of other clinical symptoms including aplastic crisis in individuals with chronic haemolytic anaemia. Aplastic crisis is caused by the rapid decrease in erythrocytes numbers due to viral replication. In an immunocompetent host this has little effect but in those patients with a high erythrocyte turnover the condition can be life threatening.

Parvovirus B19 has also been associated with acute forms of arthritis. Approximately 5% of children with Parvovirus B19 infection suffer joint pain. Girls are more severely affected than boys, and in infected adults more women suffer arthritic symptoms than men.

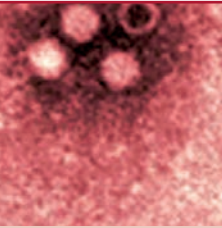
Parvovirus B19 in pregnancy can lead to hydrops fetalis and intrauterine fetal death. Research indicates that there is approximately a 33% transmission rate of the virus from mother to fetus and about 9% of maternal Parvovirus cases result in fetal death. B19V accounts for 10% of all cases of non-immune hydrops fetalis increasing to 36% during epidemic periods. Approximately, 53% of maternal Parvovirus infections are asymptomatic and fetal distress may go unnoticed in the first 18 weeks of pregnancy.

Diagnosis of the infection is often difficult. Fetal death may occur up to 11 weeks after confirmed maternal infection and IgM antibodies may have dropped to undetectable levels by this time

Detection and control of B19V is complicated by the fact that most symptoms of the virus occur after the viraemic (and infectious) period has passed. In routine practice detection of specific IgM and IgG antibody is used. Tests based on Baculovirus capsid antigen are generally considered the best. Patients who develop aplastic crisis as a result of chronic Parvovirus B19 infection may be treated with immunoglobulin preparations.

Parvovirus B19 Infection in Humans.

Modrow S., Gigler A., Hemaue A. Biomedical Progress 1997;10:45-50



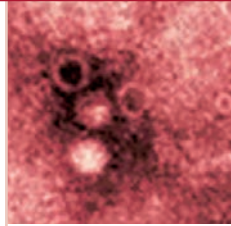
Parvovirus B19 is a member of the erythrovirus genus which is part of the Parvoviridae family. It has been reported that Parvovirus B19 has a small icosahedral capsid, surrounded by a lipid bilayer. The capsid is composed of two structural proteins, VP1 and VP2. VP2 is the major capsid protein (95%) whereas the minor capsid protein is VP1 (5%). In addition to these two structural proteins Parvovirus B19 is thought to have a non structural protein (NS1).

Evidence suggests that Parvovirus B19 is tropic for erythroid progenitor cells in bone marrow and for pronormoblasts of fetal liver. The virus uses the blood group 'P' antigen as its receptor. Seroprevalence rates of 70% have been reported for Parvovirus B19. By the age of 15 approximately 50% of children appear to have been infected. During the early stages of the virus the level of viremic particles in the blood can reach between 10^{12} or 10^{13} particles per ml. The most common route of transmission for B19V is the respiratory system, however it is also known to be transmitted by blood. As B19V lacks a lipid envelope it is very stable and cannot be destroyed by dry heat treatment or solvent detergents.

Parvovirus B19 infection is characterised by a rash and is referred to as 'slapped cheek syndrome' or 'fifth disease'. In general infection with B19V is mild. However in pregnant women or those who are immunocompromised symptoms can be very severe. Parvovirus B19's tropism for erythroid progenitor cells means that individuals with haemolytic disorders such as sickle cell anaemia may be subject to transient aplastic crises (TAC) which can result in life threatening anaemias. B19V infection in the second and third trimester of pregnancy can cause hydrops fetalis which can lead to miscarriage. Reports suggest that there is approximately a 33% transmission rate from mother to fetus and the virus is believed to be passed through the placenta from mother to child.

The most common methods used to detect B19V infection are ELISAs, Western Blots and PCR. These assays contain B19V antigen which is used to detect the presence of Parvovirus B19 IgG and IgM antibodies in serum. Using VP2 antigens is of particular interest for IgM capture assays. IgM is considered to be the first serological marker for B19V infection. IgM antibodies can be detected 6 to 10 days after virus production. IgG antibodies are produced approximately 12 days after infection and persist for life. The presence of IgG antibodies specific for B19V is indicative of past infection. In chronic forms of infection the pattern of antibody production appear to differ and reports suggest that IgG specific for NS1 has been detected in patients with chronic arthritis.

To conclude the authors discuss current treatments available for B19V infection. Treatment of B19V in healthy individuals is considered unnecessary. They do however recommend that patients suffering from TAC as a result of B19V infection should be given blood transfusions and those who suffer from persistent B19V infection may be treated with intravenous immunoglobulin.



Parvovirus B19 Product Range

Product Description

Catalogue Number

Parvovirus IgG & IgM IFA
6 x 10 well slide

V119IF

Parvovirus IgG EIA
96 well EIA

V519IG

Parvovirus IgM EIA
96 well EIA

V619IM

Parvovirus IgG EIA (FDA approved)
96 well EIA

V519IGUS

Parvovirus IgM EIA (FDA approved)
96 well EIA

V619IMUS



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