

THE HUMAN PARVOVIRUS B19 IN TRANSFUSION MEDICINE

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Introduction

Human parvovirus B19, at 20-25 nm in diameter, is one of the smallest known DNA-containing viruses known to infect man. Antibody to the virus is commonly acquired between the ages five and ten years, and more than 50% of the U.S. population is seropositive by adulthood. Infection has been shown to be transmitted via the respiratory tract. Seroconversion confers lifetime immunity.

Human parvovirus B19 is extraordinarily trophic for human erythroid progenitor cells and replication occurs only in erythroid precursor cells of the bone marrow. The red blood cell P antigen globoside has been shown to act as the viral receptor. This finding explains the tissue distribution of the virus in early erythroid cells, megakaryocytes and endothelial cells in adults and in heart and liver cells of human fetuses.

Clinical Syndromes Caused By The B19

Parvovirus

Active infection by human parvovirus B19 will usually manifest as an asymptomatic seroconversion. There are, however, at least five clinical syndromes associated with B19 infection affecting different high risk groups, with corresponding different pathophysiologies. These five syndromes are:

1) Erythema infectiosum or Fifth's Disease: Acute infection in healthy adults usually results in viremia beginning on the 5th to 6th day of infection, peaking on day 8 to 9. IgM antibodies appear on day 10 to 14 and may stay for several months. IgG antibodies appear in the second week and persist for life. If symptoms occur, these are usually mild itching, headache and malaise accompanied by a low grade fever associated with the viremic phase. There may be a second cluster of symptoms, including arthralgias and evanescent maculopapular rashes over the face ("slapped cheek" appearance in children), trunk and proximal extremities, which occur the second and third week from the start of infection. This second phase of infection is due to B19 virus/anti-IgG complex deposition in joint and skin endothelial cells.

2) Transient Aplastic Crisis (TAC): B19 infection can present with an abrupt onset of severe anemia with absent reticulocytes in patients with underlying hemolytic disorders. This occurs as a single episode in a patient's life, is treated supportively, but may be so severe as to cause death in certain individuals. This syndrome presents with the highest viremia (10¹⁴ genome copies/ml), probably due to the relatively high number of erythrocyte precursors in an already burdened marrow.

3) Hydrops fetalis: There is a low risk of uterine transmission with an even lower probability of disease in fetuses of mothers in their midtrimester of pregnancy when infected with Human parvovirus B19. Diagnosed by fetal ultrasound, this disease is usually cured by intrauterine transfusion.

4) Congenital Infection: Some infected fetuses (three documented cases) are born with B19 DNA in their bone marrows but not in their blood. IVIgG may eliminate detectable DNA in their marrows but low-level, localized infections seem to persist as manifested by these babies' chronic need for blood transfusions.

5) Pure Red Cell Aplasia: Immunosuppressed individuals unable to mount a normal immune response to an acute B19 infection may end up with low antibody levels incapable of neutralizing the B19 infection. Chronic anemia with scattered giant pronormoblasts in the marrow may ensue. IVIgG can be ameliorative or curative in this disease.

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Blood Banking and the B19 Parvovirus

Current blood banking practice does not require routine screening in donated blood. In part, this is because population-based studies have shown a low incidence of DNA-positive donors, ranging from 1/24,000 (.004%) to 6/20,000 (.03%) blood donors. Furthermore, blood products have seldom been reported to transmit human parvovirus B19, and subsequent infection from this method of transmission has not been reliably shown to occur in normal individuals nor in any of the high risk groups mentioned above. Regular recipients of factor concentrates would theoretically be at highest risk of acquiring B19 infection via blood transfusion. This is because factor concentrates are produced by pooling and concentrating the plasma of thousands of donors, then subjecting the pooled plasma to viral inactivating procedures. While lipid-coated viruses (HIV, HBV, etc.) are easily destroyed, the commonly used virucidal treatments have been shown to be ineffective against non-enveloped viruses like human parvovirus B19. There are studies that have shown a higher seroconversion rate in population groups receiving factor concentrates but there is currently no evidence that this particular group of blood product recipients has a higher incidence of B19 infection.

B19 Parvovirus Detection

Detection of human parvovirus B19 DNA is being done by Dr. Jeanne Jordan of the Magee Women's Research Institute using a PCR-based assay. Appropriate sample types include blood, amniotic fluid, bone marrow and tissues. Primers and probes used to amplify the virus are specific for human parvovirus B19. Screening the PCR-amplified samples is accomplished using an enzyme-linked immunoassay detection method. The sensitivity of this assay is approximately 10 virus particles/ml.

Transmission of B19 Parvovirus Infection Via Blood Transfusion

In an effort to find out whether recipients of parvovirus antigen positive (B19 DNA+) blood products are at risk for developing clinically significant parvovirus B19 infection, the Institute for Transfusion Medicine and Dr. Jordan are currently conducting a retrospective study, following the recipients of B19 DNA+ blood for signs and symptoms of any of the clinical syndromes known to

be caused by this virus. A pilot study completed in the spring of 1995 has shown a higher-than-expected incidence of 0.1% B19 DNA positivity among regular community donors. This is three times higher than the highest incidence mentioned in current literature which also used PCR-based technique in their screening procedure.

Twelve of thirteen recipients with satisfactory follow-up have not developed clinical B19 infection, despite nine who were immunosuppressed by hematologic malignancy and/or immunosuppressive drugs. One recipient developed unexplained anemia with very low reticulocyte count four months after receiving his transfusion. He received the red blood cells of a donor who was B19 DNA+ but who had not yet developed B19 specific IgG nor IgM antibodies, theoretically placing this donor at the highest risk of transmitting the disease. This donor also was the only one who reported any symptoms during the viremic phase.

Based on this preliminary data, it appears that human parvovirus B19 is more prevalent than previously thought. Further studies need to be done to better define the risk, if any, of disease transmission via blood transfusion to high risk groups.

For more information about the Human Parvovirus B19, contact Dr. Beatrice Tiangco or [Dr. Joseph Kiss](#) at the Institute for Transfusion Medicine, (412) 209-7326.

Copies of the *Transfusion Medicine Update* can be obtained by contacting [Deborah Small](#) at (412) 209-7320

Prevalence of parvovirus B19 DNA in bone marrow of patients with haematological disorders.

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Patients with haematological disorders (n = 100) were examined for prevalence of parvovirus B19 DNA in the bone marrow and serum, irrespective of B19-related symptoms. B19 DNA was studied using 2 nested PCRs and the serum samples were further analysed with B19-specific IgG, IgM and avidity as well as seroreactivity against linear and conformational epitopes of the B19 VP2 antigen. The latter assays specify whether the IgG antibody response represents acute or past B19 infection. B19 DNA was detected in 4 of the 100 bone marrow samples, whereas all the serum samples were B19 DNA negative. None of the 4 B19 DNA positive patients had symptoms typical of B19 infection and serology showed past infection. Furthermore, 2 were still B19 DNA positive in bone marrow more than 1 y after the first sample indicating virus persistence. The seroprevalence for B19 IgG was 59% and 2 patients were B19 IgM positive. Thus, presence of B19 DNA in bone marrow from patients with haematological disorders is not a general finding in seropositive patients. B19 DNA can persist in bone marrow, but in our material this finding showed no clear correlation with symptomatic B19 infection.
