PARVOVIRUS B19 IN PREGNANCY

By

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ABSTRACT

Parvovirus B19 causes prolonged epidemics of erythema infectiosum. Infection causes clinically significant anemia in individuals with high red cell turnover, including the fetus. Transmission can occur via the respiratory route, hand-to-mouth contact, blood products, and vertically from mother to the fetus. The virus replicates in rapidly proliferating cells, such as erythroblast precursors. In healthy hosts, the virus can cause a range of clinical manifestations, including erythema infectiosum (ie, fifth disease), transient aplastic crisis, chronic red cell aplasia, myocarditis, arthropathy, and nonimmune hydrops fetalis. Approximately 40% women of childbearing age are susceptible, and annual seroconversion rates vary from 1.5% during endemic periods to 10-15% during epidemics. Infection occurs in around 50% of susceptible women exposed at home and 20-30% following occupational exposure (for example, at a primary school). Maternal infection in the first half of pregnancy is associated with a 10% excess fetal loss and hydrops fetalis in 3% of cases (of which up to 60% resolve spontaneously or with appropriate management). No congenital abnormalities or long-term sequelae have been attributed to parvovirus B19 infection. The overall risk of serious adverse outcome of occupational exposure to parvovirus B19 infection during pregnancy is low (excess early fetal loss in 2-6/1,000 pregnancies and fetal death from hydrops in 2-5/10,000 pregnancies). It is not recommended that, susceptible pregnant women be excluded routinely from working with children during epidemics.

Keywords: Erythema Infectiosum, Seroconversion, Childbearing, Epidemics, Occupational Exposure.

INTRODUCTION

Parvovirus B19 (B19V) is the causative agent of the relatively benign childhood disease, erythema infectiosum (fifth disease) (Feldman DM, Timms D, Borgida AF,2010). It is also sometimes referred to as "slapped cheeks disease" because of the telltale red facial rash that children commonly develop when they are infected. Maternal B19V infection can give rise to serious fetal complications during pregnancy (Elsa Giorgio et al., 2010). This inhibits the production of red blood cells. The infection is mainly spread through saliva and nasal secretions. Maternal B19V infection can give rise to serious fetal complications during pregnancy. Up to 50% of women are non-immune and susceptible to B19V infection. Infection may result in anemia, spontaneous abortion and/or hydrops fetalis. Early diagnosis of B19V infection will identify those at risk and may allow for early intervention therapy, thereby improving fetal survival (Lamont RF, Sobel JD, Vaisbuch E, et al., 2011). Parvovirus B-19 is an endemic viral infection that is most frequently seen among preschool and school-age children in the USA. B-19 has historically been referred to as 'slapped cheek' disease or the Fifth disease, because it was the fifth disease that was found to cause rash in children (the first four being measles, scarlet fever, rubella and Duke's disease; exanthem subitum is the sixth). Cossart et al. discovered parvovirus B-19 in 1974. While screening for hepatitis B infection, they obtained false-positive results. When these particles were studied, it was found that, they were in fact a parvovirus. The specification as B-19 arose from the fact that the positive virus was found in the specimen that was on panel B and specimen 19. Soon afterwards, Anderson et al. reported that, parvovirus B-19 was the cause of Fifth disease. Parvovirus B-19 is a linear, nonenveloped, encapsulated, icosahedral, single-stranded DNA virus with a terminal hairpin structure that forms a double-stranded section characteristic of the Parvoviridae family. Parvovirus has been found in individuals of all ages, but the highest incidence of the virus is in patients aged 5 to 15 years.

Objectives

The present study aims to identify the following:

- What is this virus?
- What is the incidence of infection in pregnant women?
- How is it spread?
- When do infections/outbreaks occur?
- What cell types are infected?
- What are the consequences of B19V infection?

Virus

What is it?

- Discovered in 1975 in asymptomatic blood donors (Lamont RF, Sobel JD, Vaisbuch E, et al., 2010).
- Small DNA virus ('parvum' being Latin for small).
- B19V infects only humans.
- Causative agent of erythema infectiosum (fifth disease of childhood) (Health Protection Agency 2012)

Incidence

What is the incidence of infection in pregnant women?

- 1 in 3 chance that a parvovirus will be passed through the placenta to a baby.
- Early fetal loss in 2-6/1,000 pregnancies and fetal death from hydrops in 2-5/10,000 pregnancies (Lamont RF, Sobel JD, Vaisbuch E, et al., 2010).

How is it Spread?

- Transmission is greatest during viremia and before the symptoms arises.
- The virus is spread via aerosol droplets through the respiratory route (Cossart et al.).
- Transmitted by hand-to-mouth contact, blood or blood products and nosocomial infection.
- Can be spread transplacentally to the fetus during active maternal infection (33% transmission rate across the placenta).
- During outbreaks, infection rates of 25 and 50% have been noted in the school and home, respectively, (Stelma FF, Smismans A, Goossens VJ, et al., 2008).

When do infections/outbreaks occur?

- Parvovirus B19 infection can occur at any time.
- The majority of the outbreaks tend to be in the winter and spring time (De Jong EP, Walther FJ, Kroes AC, et al, 2011).

What cell types are infected?

- Preferentially infects and replicates in erythroid cells.
- Following B19V infection, erythrocytes will lyse arresting erythropoiesis.
- Lymphocyte, granulocyte and platelet counts may also fall during infection.
- The B19V incubation period is usually 4-14 days, (Tolfvenstam T, Broliden K, 2011).

Clinical Manifestation

What are the consequences of B19V infection

- Most pregnant women are asymptomatic
- Some may experience exanthem and arthralgia. (Feldman DM, Timms D, Borgida AF, 2010).

Fetal Anemia

- B19V preferentially infects and replicates in the erythroid cells
- Active B19V infection causes fetal anemia.
- Anemia is an underlying factor in the development of hydrops, ascites and can lead to fetal loss.

Non-immune Hydrops Fetalis (NIHF)

- B19V infection induces severe anemia, which leads to NIHF.
- The most common form of hydrops is NIHF (~75% of cases).
- 10-20% of cases of idiopathic NIHF are B19V-associated.
- Hydrops usually occur 2-4 weeks after maternal B19V infection.
- On average, there is a 10% risk of hydrops following B19V infection (Lamont RF, Sobel JD, Vaisbuch E, et al).

Fetal Loss

- Up to 10% of B19V infections during pregnancy are associated with fetal loss 11.
- The majority of fetal losses due to B19V infection occur in the 2nd trimester.

- Fetal deaths usually occur at 4-6 weeks of post infection, but have been reported up to 12 weeks after symptomatic infection. The reason is uncertain, but may be related to multisystem organ damage (Ergaz Z, Ornoy A, 2006).

Congenital Anomalies

- Central nervous system
- Craniofacial, and
- Eye anomalies (de Haan TR, de Jong EP, Oepkes D, Vandenbussche FP, Kroes AC, and Walther FJ, 2008).

Diagnosis

What is the Immune Response to the following B19V infection?

General Principles:

- All pregnant women who have a non-vesicular rash, or contact with someone suffering from a non-vesicular rash, should be investigated for parvovirus and rubella infection - irrespective of past history, previous serology or gestation. (Crane J, 2002).
- Contact is defined as being in the same room for >15 minutes or face-to-face contact; however, for parvovirus, this is probably over-cautious, the main risk of infection being from household contacts or prolonged occupational contact (Roberts AB, Mitchell JM, Lake Y, Pattison NS, 2001).
- The IgM result confirms or excludes infection in the 4 weeks prior to the sample. This also means that, parvovirus infection cannot be excluded if investigation starts >4 weeks after onset of the rash (Mari G, 2000)

When/what to Test

- Test for parvovirus B19 (and rubella) IgM and IgG as soon as possible after contact with, or symptoms of, a rash illness. Include details of dates of illness/contact, details of rash, gestation, etc. (GL Gilbert, 2000).
- Positive IgG with negative IgM will confirm immunity and the patient can be reassured.
- If IgM is detected, but IgG is not detected, a further sample should be taken immediately. If the repeat sample is positive for IgM further testing, confirmation by alternative assay is required - eg, detection of high titre B19.
- Virus DNA or IgG seroconversion using an antenatal booking blood (discussed with a microbiologist).
- If neither IgG nor IgM is detected, a further sample should be tested one month later (Johnson DR, Fisher RA, Helwick JJ, Murray DL, Patterson MJ, Downes FP, 1994).
- If both are negative, the woman can be reassured that, she has no evidence of parvovirus infection, but is susceptible (Elsa Giorgio et al. 2010).
- IgM antibodies are present in 90% of the patients, approximately 2 weeks after the infection.
- IgM levels can peak around 30 days postinfection and may last up to 4 months (Roberts AB, Mitchell JM, Lake Y, Pattison NS. 2001)
- IgG antibodies start to appear after 3-4 weeks and most probably persist for life (Johnson DR, Fisher RA, Helwick JJ, Murray DL, Patterson MJ, Downes FP, 1994) (Table 1).

Interpretation

Management

How can effective patient management be achieved?

- Through screening and assessing a pregnant women.
- By treatment of the women infected with B19V.
- Through education of pregnant women about B19V, (Health Protection Agency, 2011).

Screening

Before or During Pregnancy

- Appropriate patient management is dependent on accurate B19V diagnosis (NICE CKS, 2010).
- Screening patients for B19V antibody status will determine the need for further follow-up.
- An IgG-positive, IgM-negative patient should be reassured that, B19V infection is not a cause for concern during their pregnancy (Divakaran TG, Waugh J, Clark TJ, Khan KS, Whittle MJ, Kilby MD, 2001).

Result	Indication	Action
IgG+, IgM	Past Infection (immune)	Reassure Patient
IgG-, IgM-	- No Past Infection (non-immune)	Repeat Testing
IgG+, IgM+	Recent Infection	Fetal Evaluation
IgG-, IgM+	Recent Infection	Fetal Evaluation

Table 1. A Proposed Algorithm of Care for B19V Antibody

Treatment for B19V Infection During Pregnancy

- For moderate to severe hydrops, fetal blood sampling may be appropriate (Rodis JF, Hovick TJ, Jr, Quinn DL, Rosengren SS, Tattersall P, 1988).
- If the reticulocyte count is high, marrow aplasia is already in the resolution stage and hydrops should resolve without therapy.
- If hydrops develop, an intrauterine blood transfusion via cordocentesis should be considered (Morita E, Nakashima A, Asao H, Sato H, Sugamura K, 2003).
- The severely anemic fetus with a low reticulocyte count may benefit from immediate transfusion.
- High-titre intravenous immunoglobulin has been reported to be an effective therapy.
- Ultra-sound exams should be performed every 1-2 weeks for up to 6-8 weeks (De Haan TR, de Jong EP, Oepkes D, Vandenbussche FP, Kroes AC, Walther FJ, 2008).

Education

- It will allow them to avoid situations that involve possible risk of exposure. (Health Protection Agency, 2011).
- Patient monitoring of fetal movement would also serve as an important aid to fetal surveillance in women beyond gestation week 28. (Divakaran TG, Waugh J, Clark TJ, Khan KS, Whittle MJ, Kilby MD, 2001)

Discussion

The main aim is appropriate monitoring of pregnant woman with parvovirus infection.

At present, there is no role for a routine antenatal screening programme for human parvovirus B19 and infection in pregnancy is not an indication for therapeutic termination. Women, particularly those working in close contact with young children, should be given information about human parvovirus B19 infection during pregnancy. This information should not be given only in antenatal clinics, but also in preconception and family planning clinics. Human parvovirus B19 is an important cause of nonimmune hydrops. A significant proportion of these fetuses might recover spontaneously. However, there are no clinical or ultrasonographic criteria to predict this. Therefore, it is prudent to refer pregnancies complicated by nonininiune hydrops to fetal medicine centres with facilities for intrauterine transfusion.

Recommendations

- Pregnant women exposed to, or who develop symptoms of, parvovirus B19 infection should be assessed to determine whether they are susceptible to infection (non-immune) or have a current infection by determining their parvovirus B19 G and immunoglobulinM status.
- If parvovirus B19 IgG is present and IgM is negative, the woman is immune and can be reassured that, she will not develop infection and that the virus will not adversely affect her pregnancy.
- If a recent parvovirus B19 infection has been diagnosed in the woman, then referral to an obstetrician or a maternal-fetal medicine specialist should be considered.

Conclusion

Most women with B19 infection in pregnancy had a satisfactory outcome, but there is nevertheless a substantial risk of fetal loss and non immune hydrops in the second trimester. An early diagnosis of the fetal anemia due to parvovirus infection is possible. If a maternal infection is suspected, the woman should be referred to a tertiary center for fetal maternal medicine.

References

[1]. Feldman DM, Timms D, Borgida AF, (2010). "Toxoplasmosis, parvovirus, and cytomegalovirus in pregnancy". *Clin Lab Med*. Vol.30, No.3, pp.709-20.

[2]. Elsa Giorgio et al. (2010). "Parvovirus B19 During Pregnancy: a review". *J Prenat Med*, Vol.4, No.4, pp.63-66.

[3]. Cossart YE, Field AM, Cant B, et al. (1975). "Parvovirus-like particles in human sera". *Lancet*, Vol.1, pp.72-3.

[4]. Anderson MJ, Jones SE, Fisher-Jock SP, et al. (1983). "Human parvovirus, the cause of erythema infectiosum (Fifth disease)?". *Lancet*, Vol.1, pp.1378.

[5]. Lamont RF, Sobel JD, Vaisbuch E, et al., (2010). "Parvovirus B19 infection in human pregnancy". *BJOG*. Vol.118, No.2, pp.175-86.

[6]. Health Protection Agency, (2012). "Increased parvovirus B19 activity in England and Wales". *Health Protection Report*, Vol.6, No.24.

[7]. Stelma FF, Smismans A, Goossens VJ, et al., (2008). "Occupational risk of human Cytomegalo virus and Parvovirus B19 infection in a female day care personnel in the Netherlands; a study based on seroprevalence". *Eur J Clin Microbiol Infect Dis*, Vol.28, No.4, pp.393-7.

[8]. De Jong EP, Walther FJ, Kroes AC, et al., (2011). "Parvovirus B19 infection in pregnancy: new insights and management". *Prenat Diagn*. Vol.31, No.5, pp.419-25. doi: 10.1002/pd.2714. Epub 2011 Feb 24.

[9]. Tolfvenstam T, and Broliden K. (2009). "Parvovirus B19 infection". *Semin Fetal Neonatal Med*, Vol.14, No.4, pp.218-21.

[10]. Ergaz Z, and Ornoy A. (2006). "Parvovirus B19 in pregnancy". *Reprod Toxicol*, Vol.21, No.4, pp.421–35.

[11]. De Haan TR, de Jong EP, Oepkes D, Vandenbussche FP, Kroes AC, and Walther FJ. (2008). "Infection with human parvovirus B19 (fifth disease') during pregnancy: potential life-threatening implications for the foetus". *Ned Tijdschr Geneeskd*. Vol.152, No.21, pp.1185-90.

[12]. Crane J. (2002). "Parvovirus B19 infection in pregnancy". *J Obstet Gynaecol Can*. Vol.24, No.9, pp.727-743.

[13]. Roberts AB, Mitchell JM, Lake Y, Pattison NS. (2001). "Ultrasonographic surveillance in red blood cell alloimmunization". *Am J Obstet Gynecol*, Vol.184, pp.1251-5. [PubMed]

[14]. Mari G. (2001). "Non invasive diagnosis by Doppler ultrasonography of fetal anemia due to maternal red-cell alloimmunization". *N Engl J Med*. Vol.342, pp.9-14.

[15]. GL Gilbert, (2000). Parvovirus B19 infection and its significance in pregnancy, in Communicable Diseases Intelligence.

[16]. Johnson DR, Fisher RA, Helwick JJ, Murray DL, Patterson MJ, Downes FP. (1994). "Screening maternal serum alpha-fetoprotein levels and human parvovirus antibodies". *Prenat Diag*. Vol.14, pp.455-8.

[17]. Health Protection Agency (2011). *Guidance on Viral Rash in Pregnancy*.

[18]. Parvovirus B19 infection, (2010). *NICE CKS*.

[19]. Divakaran TG, Waugh J, Clark TJ, Khan KS, Whittle MJ, and Kilby MD. (2001). "Non invasive techniques to detect fetal anemia due to red blood cell alloimmunization: a systematic review". *Obstet Gynecol*, Vol.98, pp.509-17.

[20]. Rodis JF, Hovick TJ, Jr, Quinn DL, Rosengren SS, and Tattersall P. (1988). "Human parvovirus infection in pregnancy". *Obstet Gynecol*, Vol.72, pp.733-8.

[21]. Morita E, Nakashima A, Asao H, Sato H, and Sugamura K. (2003). "Human parvovirus B19 non structural protein (NS1) induces cell cycle arrest at G(1) phase". *J Virol,* Vol.77, No.5, pp.2915-21.

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