

Review Article

Parvovirus B19 and Pregnant Women: A Bibliographic Review

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Introduction

Parvovirus B19 (PVB19) is one of the smallest viruses that are known to infect humans [1]. The clinical manifestations of B19V infection vary greatly and depend on age, hematologic and immunologic status. In immunocompetent individuals, the infection can be completely asymptomatic or can cause mild and self-limiting clinical manifestations such as erythema infectiosum or fifth disease during childhood, arthralgias and arthritis in adults, particularly in women [2,3], chronic hemolytic anemia, and fetal death in utero or non-immune hydrops fetalis in pregnant women [4]. Due to the efficient replication of B19V in the erythroid progenitor cells [5].

In temperate climates, the infection may occur throughout the year, Infection is most common in late winter or early spring [6]. During pregnancy, the virus is transmitted through exposure to infected respiratory droplets or blood products and vertically from mother to fetus [7,8]. The vertical transmission of B19 occurs in about one-third of women infected [9]. The proportion of pregnant women susceptible to B19 infection ranges from 34% to 65% in various parts of the world. The incidence of seroconversion during pregnancy is estimated at between 1% and 1, 5% in the endemic period, increasing to 13% in the epidemic period [10]. Non-immune women are most likely to be infected by young children [11].

Parvovirus infection of mothers is diagnosed using serologic or an immune assay enzyme B19 IgM and B19 IgG [12]. Viral DNA can be detected by Polymerase Chain Reaction (PCR) and is considered to be the best indicator of infection in maternal, fetal blood, and amniotic fluid [13].

In these conditions, it seemed necessary to us to study this virus in this article and to answer the various practical questions raised by the occurrence of contagion and/or infection with Parvovirus B19 during pregnancy.

Parvovirus B19: A Few Words of History

Parvovirus B19 particles were first described in 1975 by Cossart, an Australian virologist working in London [1]. While checking normal blood donor's serum in an assay for hepatitis B she noticed an anomalous reaction in position 19 plate B [14]. This

virus was successively called SPLV (Serum Parvovirus like Virus), Aurillac antigen (in France), Nakatani antigen (in Japan), then B19, number of the blood bag where it was isolated for the first time. This explains the name of the virus when there is no parvovirus B1 to B18. The pathogenic role of the virus was first identified in 1981 during erythroblastopenia attacks in patients with sickle cell disease. In 1983, it was recognized as the cause of erythema infectiosum or the 5th pediatric disease [15]. Subsequently, PVB19 infections have been linked to fetoplacental hydrops, Fetal Deaths in Utero (MFIU) secondary to fetal anemia or myocardial involvement [16].

Virology and Pathophysiology of B19V Infection

B19 virus: Virology

Taxonomy: Parvoviruses are common animal and insect pathogens. The Parvoviridae family is divided into two sub-groups: the Parvovirinae infecting vertebrate cells, and the *Densoviridae* infecting invertebrate cells (Table 1) [17]. The Parvovirinae are further subdivided into three groups:

- Genus Parvovirus that replicate autonomously.
- Genus *Dependovirus* that needs helper viruses to replicate.
- Genus *Erythrovirus* that need erythroid cells to replicate.

Parvovirus B19 belongs to the genus *Erythrovirus*.

Morphology: Parvovirus B19 is a small single-stranded DNA virus [18]. Parvovirus B19 is a non-enveloped, 22 to 26 nm icosahedral virus (Figure 1), containing a single strand of DNA of approximately 5,500 nucleotides. As with other parvoviruses, B19 employs overlapping reading frames to encode on-structural proteins and two capsid proteins. The B19 virion is an icosahedron consisting of 60 copies of the capsid proteins.

Most of the capsid consists of VP2, the major structural protein (molecular weight 58 kDa), with 5% or less of the larger VP1 protein, the minor protein (83kDa). Using genetic engineering techniques, the capsid proteins have been expressed in a variety of both mammalian and insect cell lines, where they self-assemble in the absence of DNA and form recombinant empty capsids [19]. VP1 is not required for capsid formation. The limited DNA content and the absence of a lipid envelope makes this virus resistant to heat (56°C for 60 min) and lipid solvents [20].

Genomic structure and organization: As in most animal Parvoviruses, the B19 genome has two large open reading frames, with the single Nonstructural Protein (NS1) encoded by genes on the left side of the genome and the two capsid proteins (VP1 and VP2) by genes on the right side. The non-structural protein, from NS1, sub serves multiple replicative functions and is cytotoxic to host cells [21]. The two structural proteins, Viral Protein1 (VP1) and Viral Protein

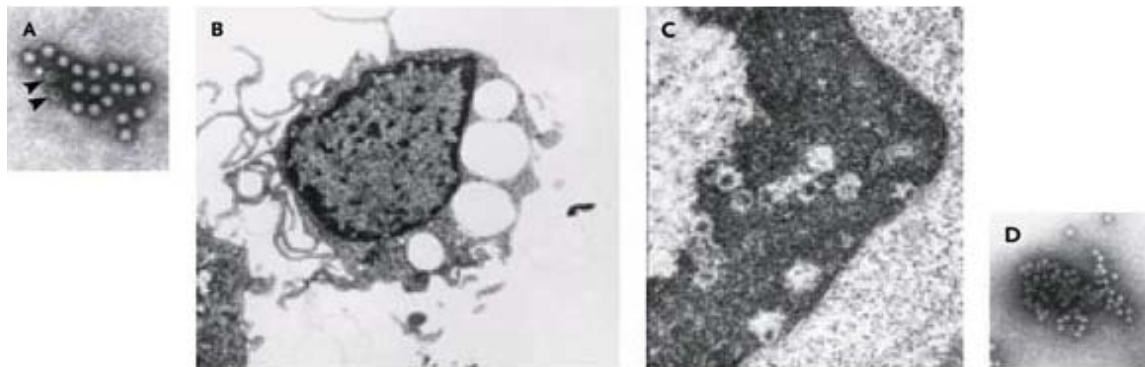


Figure 1: Transmission Electron Micrographs Showing Native Parvovirus B19 in Serum and Cells and Recombinant Capsid [14]. Panel A shows symmetric, icosahedral particles, about 25 nm in diameter, and empty capsids (arrowheads) in serum from an infected. Panel B shows human erythroid progenitor cells infected in vitro with the virus; vacuoles and cytoplasmic pseudopods are present (x10,000). In Panel C which shows part of Panel B at higher magnification, margined chromatin contains assembled capsids (x100,000). Panel D shows empty recombinant parvovirus capsids produced in a baculovirus system (x154,000).

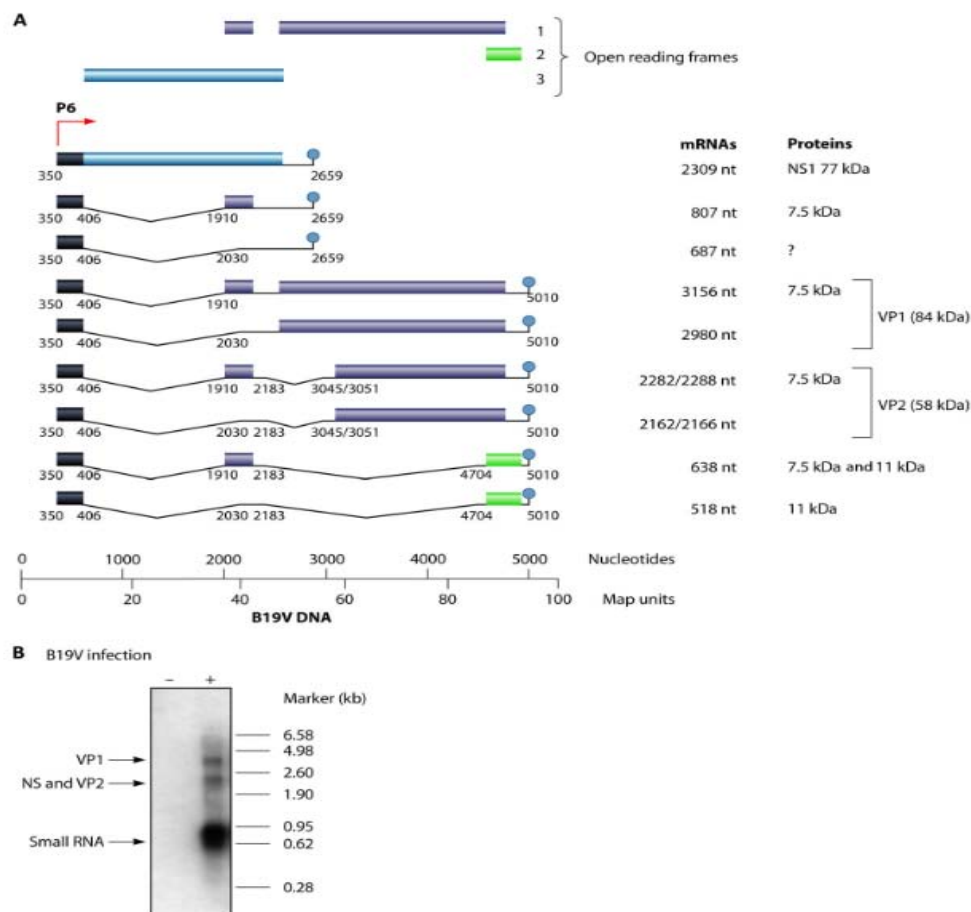


Figure 2: Schematic Representation of B19V Genome Organization and Functional Mapping [22-24]. (A) Transcription map of B19V genes. The 9 main transcripts are represented. (B) Expression of viral mRNAs in primary erythroid cells. The viral mRNAs were detected by Northern blotting, using a radiolabeled probe in non-infected and infected primary erythroid cells as described previously.

2 (VP2), arise from alternative splicing so that VP1 is the same as VP2 except for an additional 226 amino acids at its amino-terminal (Figure 2) [22-24].

NS1 is a 671 amino acid long protein that has an MW of ~75 kDa.

NS1 contains two nuclear localization signals. NS1 contains a DNA binding and endonuclease domain at the N-terminus

In short, NS1 is a multifunctional protein and plays various roles during B19V infection [25]. VP2 is the predominant protein,

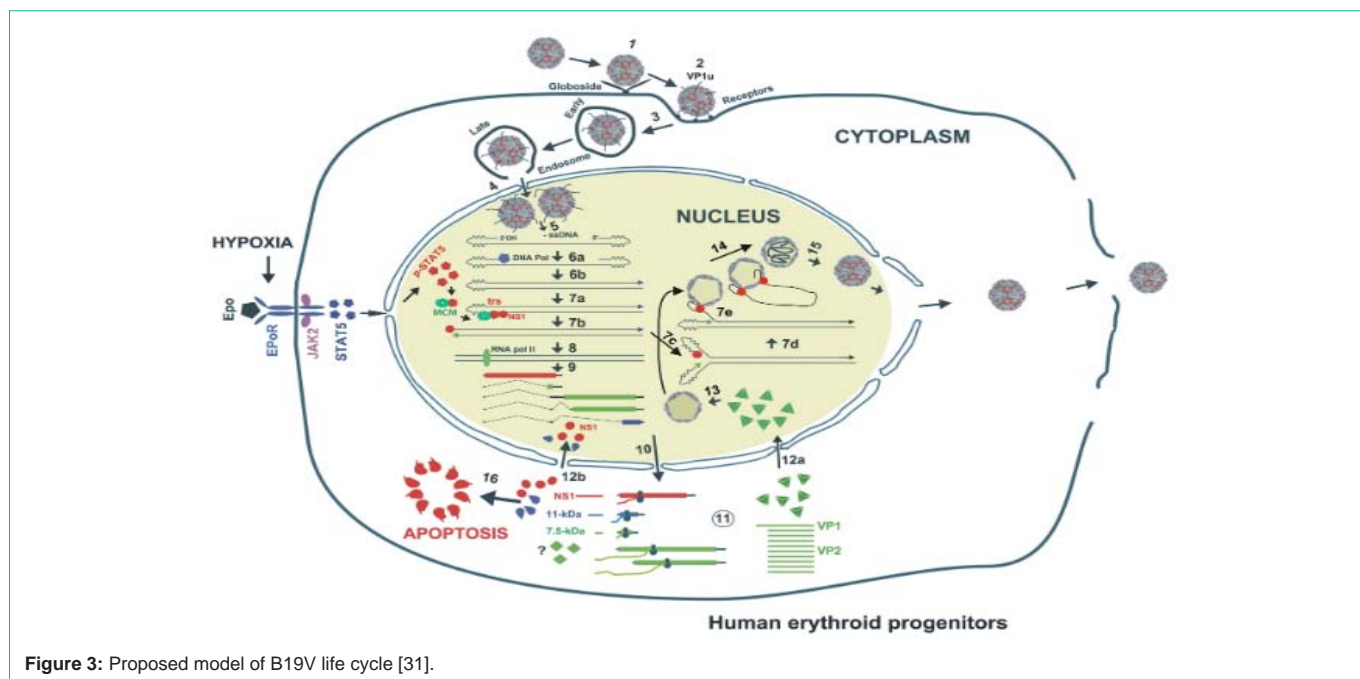


Figure 3: Proposed model of B19V life cycle [31].

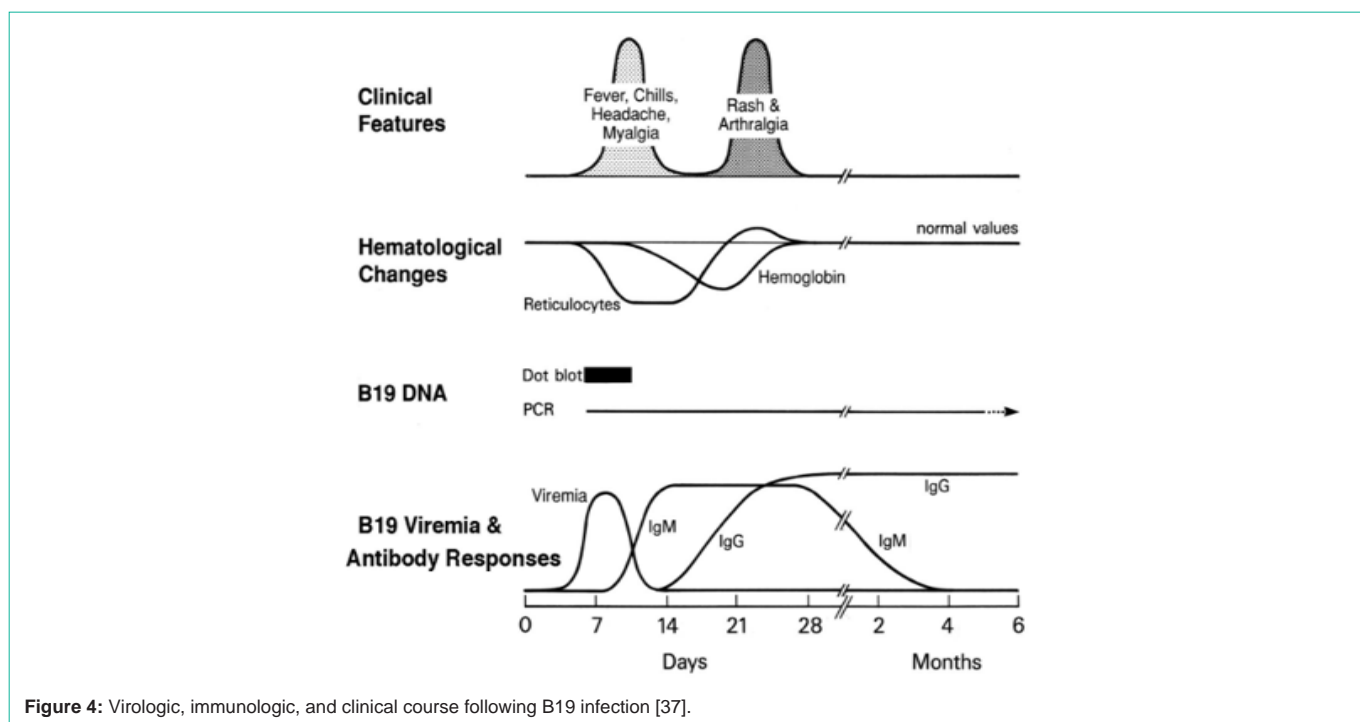


Figure 4: Virologic, immunologic, and clinical course following B19 infection [37].

comprising 95% of the virus capsid. VP1 is the same as VP2 except for an additional 226 amino acids at its amino-terminal [26]. VP1 makes up only 5% of the capsid, has its unique region external to the viral capsid itself, and is thought to be the main target of neutralizing antibodies. Sequence analysis reveals that NS1 is highly conserved, while VP1 and VP2 show greater variation [27]. Despite variations in VP1 and VP2, the antigens are commonly and successfully used in serologic tests.

B19V as a species is subdivided into three genotypes, the

prototype genotype 1, and two variant genotypes 2 and 3. At the nucleotide level, the diversity between genotype clusters is about 10%, while the diversity within each genotype cluster is normally lower than 2% for genotype 1 and in the range 3-10% for genotypes 2 and 3 [28]. All genotypes co-circulate, but with different frequencies and geographical distributions [29].

Pathogenesis and Infection

Viral life cycle

The only known natural host cell of parvovirus B19 is the human

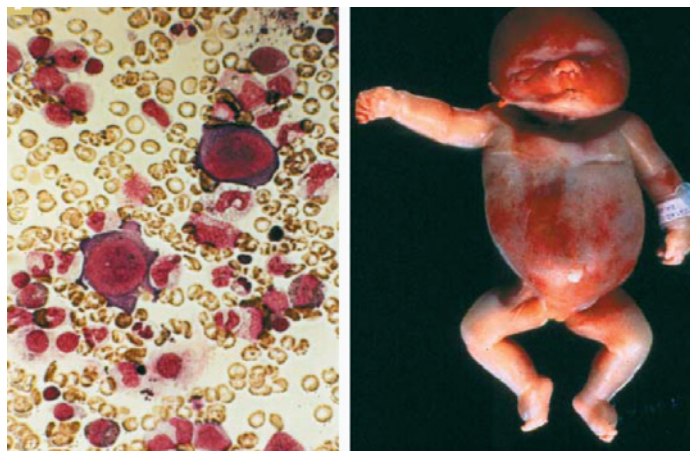


Figure 5: B19-associated hydrops fetalis [55]. Panel A shows a bone marrow aspirate with no mature erythroid precursors and with characteristic giant pronormoblasts. In Panel B, hydrops fetalis is evident in an infant who was infected in utero in midtrimester.

Table 1: Excerpt of the current classification of the subfamily Parvoviridae, including proposed members of the genus Erythrovirus placed tentatively [17].

Genus	Virus	Natural hosts(s)	Clinical spectrum
Parvovirus	<i>Aleutian mink disease virus</i>	Mink, ferret, skunk,raccoon	Immune complex disease and fetal death
	<i>Canine parvovirus</i>	Dog	Enteritis, myocarditis
	<i>Mice minute virus</i>	Mouse, rat	No known disease
	<i>Porcine parvovirus</i>	Pig	Abortion, fetal death
Dependovirus	<i>Adeno-associated virus 1 to 6</i>	Human	No known disease
	<i>Avian adeno-associated virus</i>	Birds	No known disease
	<i>Canine adeno-associated virus</i>	Dog	No known disease
	<i>Bovine adeno-associated virus</i>	Cow	No known disease
Erythrovirus	<i>Parvovirus B19</i>	Human	Erythema infectiosum, aplastic crisis, arthritis, hydrops fetalis, etc.
	<i>Parvovirus V9^a</i>	Human	Aplastic crisis?
	<i>Chipmunk parvovirus^a</i>	Chipmunk	No known disease
	<i>Simian Parvovirus^a</i>	Cynomolgus monkeys	Anemia
	<i>Pig-tailed macaque Parvovirus^a</i>	Pig-tailed macaques	Anemia and immunosuppression
	<i>Rhesus Parvovirus^a</i>	Rhesus monkeys	Anemia

^aProposed member of genus.

erythroid progenitor. Like other non-enveloped DNA viruses the Parvovirus B19 life cycle includes the following stages: binding to host cell receptor, internalization, translocation of the genome to the host nucleus, DNA replication, RNA transcription, assembly of capsid, packing the genome, and cell lines is with release of the mature virion [3] (Figure 3). The P antigen on the red blood cell is a cellular receptor of the Parvovirus B19. However, all P antigen expressing cells are not permissive to B19V. Various other co-receptors like integrin α 5 β 1, and antibody-mediated B19V entry routes are presumed to be involved in B19V entry [30].

Pathogenesis and Immune Response

After primary infection, mild symptoms of fever and general illness usually start after 6-10 days when viremia is highest. These symptoms will recede within a week [32,33]. During the second week after infection, the viremia titer decreases, and IgM antibodies are detected. In the third week, the well-known slapped cheeks and rash and the possible arthralgia occur, which coincides with an IgG

antibody response [34]. These IgG antibodies can persist for years, while the IgM antibodies disappear after 6-10 weeks (Figure 4).

Recovery involves production of IgM antibody 10 to 12 days post infection, coinciding with a peak in virus level. IgM usually persists in serum samples for approximately 3 months but may be found for several months [35]. IgG antibody is detectable in volunteers about 2 weeks after inoculation and presumably persists for life and protects against secondary infections. IgA may also be detected and probably plays a role in protection against infection by the natural nasopharyngeal route [36].

Parvovirus B19 and Autoimmunity

Apart from Rheumatoid Arthritis (RA), B19 infection has been associated with the onset of numerous autoimmune disorders including Systemic Lupus Erythematosus (SLE) [38], other connective tissue diseases, and systemic vasculitides. Although a few cases of erosive RA and SLE have been associated with B19 infection, the

Table 2: General characteristics of studies reporting on outcome of fetuses with parvovirus B19 (PB19) infection included in systematic review.

Authors (years)	Period of study	Country	Number of serum samples tested	Clinical Symptoms	Fetal Effects
[56]	1999-2004	Sendai, Japan	478 ↓ 100 pregnant women had been exposed to B19 (21%) 49 51 ↓ ↓ Symptomatic Asymptomatic	Facial Rash (51%) (25/49) Most common Infection ↓ Children living at home	Hydrops fetalis et fetal death 7% (7/100) >20 weeks
[57]	2005-2010	Bologna, Italy	72 ↓ 68 pregnant women had been exposed to B19 (94.1%) 29 39 ↓ ↓ Symptomatic Asymptomatic	Rash, fever and polyarthralgia (79.3%) 23/29	-10,2% fetal deaths -11,9 % Hydrops fetalis
[58]	2004	Stuttgart, Germany	1018	-	- 6.3% fetal deaths (64/1018) -3.9 % Hydrops fetalis (40/1018)
[59]	1985-1988 and 1992-1995	London	420 pregnant women with B19 infection	-	Fetal loss averaged 9%
[60]	2010	Germany	236 pregnant women with B19 infection	-	-18.8% fetal loss(8/236) - 23.6 % Hydrops fetalis (10/236)
[61]	2014	Paris, France	-	-	20 cases of congenital parvovirus B19 Infection (1/20 (neonatal death))

virus is probably an extremely rare cause of these diseases. Systemic vasculitides including, for example, Henoch-Schönlein purpura, periarteritis nodosa, and giant cell arteritis can occur after acute B19 infection [39]. The role of B19 in these disorders is not clear and in some cases, the infection may be a pure coincidence and in other cases, it can be a triggering or even a rare aetiological factor [40].

Parvovirus B19 Infection in Pregnancy

Acute parvovirus B19 infection is a risk for pregnant women. Since B19 infection occurs mainly during childhood, children represent a main source for virus transmission.

Human parvovirus B19 infection is widespread. Approximately 30-50% of pregnant women are nonimmune, and vertical transmission is common following maternal infection in pregnancy. The magnitude of B19 has been studied in many developed countries [41] whereby the prevalence of specific B19 antibodies among pregnant women has been found to range from 1 to 5% with a transmission rate to the fetus of about 17-33% [42].

Approximately 50% to 75% of women of reproductive age have developed immunity to parvovirus B19 [43,44]. Without known exposure, about 1% to 3% of susceptible pregnant women will develop serologic evidence of infection in pregnancy [45]. Rising to over 10% in epidemic periods [46]. Where there is extensive opportunity for exposure to parvovirus B19, such as in a daycare center or school, it is estimated that 20% to 30% of susceptible women will develop an infection, while 50% of susceptible women exposed through household contacts will become infected [47]. The risk of infection in pregnant women with one child is (are) 3 times more than nulliparous women, but this risk for women with three or more children is (are) 7,5 times more. The other risk factors are working in the school, care centers, and other full stress jobs [48,49].

Fetal Effects of Parvovirus B19 Infection

Primary PVB19 infection during pregnancy is potentially fatal to the fetus. Transplacental passage would occur at the time of the maximum peak of viremia following maternal contamination

approximately one week. It is made possible by the expression of the P antigen on the surface of placental cells. The actual incidence of a fatal outcome for the fetus after parvovirus B19 infection remains difficult to establish. Vertical transmission of B19 has been shown to occur throughout pregnancy from 7-8 weeks of amenorrhea [50].

A relevant property of B19V is its ability to cross the placental barrier and infect the fetus [51]. When in the fetal circulation, the virus can infect erythroid progenitor cells, in liver and/or bone marrow depending on the gestational age, and can be detected in erythroid cells circulating in the vessels of several tissues, in endothelial placental cells as well as in the amniotic fluid.

Parvovirus B19 infection during pregnancy can cause severe anemia, Nonimmune Hydrops Fetalis (NIHF), miscarriage, or even fetal death in utero [52] (Figure 5 and Table 2). Intrauterine growth retardation, myocarditis, pleural effusion, pericardial effusion, pericardial effusion and brain involvement of the fetus may occur following infection with the virus. Although, Parvovirus B19 is not related to congenital malformations [53].

The vertical transmission of B19V occurs in about one third of women infected during pregnancy. Consequently, in the first trimester, the risk of fetal loss is 5-10%, while in the second trimester is about 11-12, 5%. It is considered that up to 20% nonimmune hydrops fetalis may be caused by B19V [54].

Epidemiological Studies

Infection with B19 is very common and cases of infection have been reported all over the world in all seasons. Parvovirus B19 is active worldwide with neither ethnical nor geographical boundaries, albeit with some regional differences [18].

Generally, seropositivity is lowest among young children, rises to around 50% at puberty [41]. And in-creases further at lower rates throughout adulthood. Seropositivity is correlated with age, a history of transfusion, and urban residency.

Worldwide, the prevalence of PVB19 in pregnant women is variable, generally between 60% and 80%, with lower prevalence in

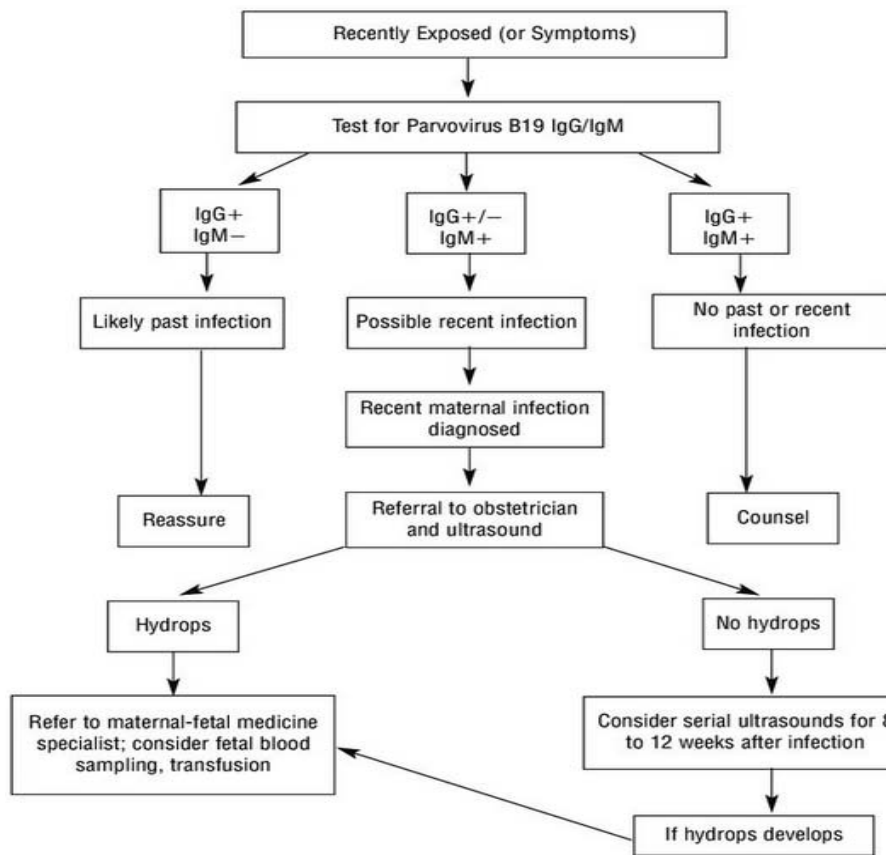


Figure 6: Management of a pregnant woman exposed to parvovirus B19 infection [92].

Asian regions [62].

Data on the seroprevalence of women susceptible to B19 infection in early pregnancy report a value of 26% to 43.5% in European countries and Japan [43,49,63].

In developing countries, the percentages are very similar, although the incidence and extent of infection have been studied in smaller population samples (Table 3).

Up to 2374 B19 infections occur annually in Japan among pregnant women. The risk of fetal death after infection is 9% during the first 20 weeks of pregnancy and up to 107 fetal deaths per year. Similarly, 2.9% risk of fetal hydrops between 9-20 weeks of pregnancy or 21 cases are estimated each year [63].

Laboratory Testing Options, Applications and Interpretation

Two circumstances lead to the diagnosis of parvovirus B19 infection in pregnant women: the occurrence of maternal clinical signs, mainly rash and arthritic manifestations, and the incidental finding of a fetoplacental hydrops [63]. The search for parvovirus B19 in the laboratory is based on a multiparametric approach, combining the immunological search for specific antibodies and the molecular detection of viral DNA [78].

Cell culture

The detection of viral particles in serum or bone marrow is not

commonly used. In fact, PVB19 culture is only obtained by inoculating samples with fresh human marrow cells from a healthy donor. It is a cumbersome and expensive technique reserved for research [3].

Serology

A variety of methods can be used to detect parvovirus B19 antibodies (Table 4), and an international standard for B19 IgG assays has been developed and tested in collaborative studies [79,80]. Numerous diagnostic kits are available, most of which are based on enzyme immunoassay, immunofluorescence, or immunoblot techniques.

In general, IgM to B19 appears 7 to 10 days after infection, is followed with in a few days by IgG, and remains positive for 2 to 4 months. In contrast, immunocompromised hosts may not develop antibodies, or IgM can develop but remain positive for months or years as an indicator of persistent infection, without development of IgG. A positive IgM test will indicate primary infection. If IgM and IgG negative, the patient is at risk of primary infection and further tests are required if there is a strong clinical suspicion [81].

When only IgG is positive, the doubt may persist if the antibody test was performed at a distance from the clinical point of call or the contact person: if the levels are low and stable, it is certainly an old infection; if the levels are high or have ascending kinetics, it may be a re-infection or a primary infection with IgM that has already disappeared from the serum [82].

Table 3: Prevalence of Parvovirus B19 infection among normal and at risk pregnant women.

Reference number	Year	Country	Total number of serum samples tested	Number of serum samples infected by B19	Percentage B19 positive
[64]	2016	Ardabil, Iran	350	242	69.10%
[65]	2014	Azerbaijan, Iran	86	65	75.60%
[66]	2014-2015	Mwanza, Tanzania	258	142	55%
[67]	2013	Ogbomoso, Nigeria	231	55	24%
[68]	2012	Sudan	147	73	49.70%
[69]	2011	Tunisie	404	307	76.20%
[70]	2007	Cordoba, Spain	42	27.7	66%
[71]	2007-2008	Tripoly, Libya	150	100	66%
[72]	2007-2008	Bialystok, Poland	55	24	43%
[73]	2008-2009	Khartoum state, Sudan	500	287	57.40%
[74]	2003-2010	Milan, Italy	37	29	78.30%
[75]	1999	Kuwait	1047	560	53.30%
[56]	1999-2004	Sendai, Japan	478	100	21%
[76]	1999-2008	Oslo, Norway	1349	832	61.70%
[77]	1998-2000	Nijmegen, The Netherlands	2567	1788	70%

Table 4: Parvovirus B19 Serologic assays [80].

Manufacture	Method ^a	Antigen and Source	FDA approved
Botrin International (Dublin Ireland)	Indirect IgG EIA and class-capture IgM EIA	Baculovirus-expressed VP2 ^a	Yes
Diasorin (Saluggia, Italy)	Indirect IgG EIA and class-capture IgM CLIA-Liaison platform	Baculovirus-expressed VP2 ^a	No
Denka Seiken (Tokyo, Japan)	Indirect IgG and IgM EIA	Baculovirus-expressed VP2 ^a and VP2	No
Medac Diagnostika (Wedel, Germany)	Indirect IgG EIA and class-capture IgM EIA	Baculovirus-expressed VP2 ^a and VP2	No
Euroimmun(LÜbeck, Germany)	Indirect IgG EIA and class-capture IgM EIA	yeast-expressed VP2	No
IBL(Hamburg, Germany)	Indirect IgG and IgM EIA	<i>E.coli</i> -expressed VP1	No
Focus Parvovirus Dxselect (Cyprus, CA)	Indirect IgG and IgM EIA	Recombinant VP1	No
Mikrogen (Martinsried, Germany)	Indirect IgG and IgM and Strip immunoassay	<i>E.coli</i> -expressed VP1 baculovirus-expressed VP2	No
Botrin International (Dublin Ireland)	Indirect IgG and IgM immunofluorescence (IFA) ^b	Baculovirus-expressed VP1	No

^aVP2 comprises >95% of capsid antigen and appears to be conserved among genotypes.

^bPretreatment with adsorbent reagent is needed to prevent interference from rheumatoid factors.

^cEIA: Enzyme Immunoassay; CLIA: Chemiluminescence Immunoassay.

Viral DNA detection (PCR)

PCR techniques to quantify viral DNA are commonly used. The most widely used technique is real-time PCR, which gives very rapid results with very high sensitivity [3].

The search for DNA in maternal blood can sometimes help in diagnosis because PCR is positive in the first month following primary infection; DNA then decreases progressively. This PCR can also be performed on abortion products or fetal tissue taken during an autopsy. A preliminary study has shown that amniotic fluid samples are much richer in virus than maternal blood collected at the same time [83]. In the case of low IgM and viral DNA levels with a strong suspicion of contagion, it is possible to test for antibodies to VP2 and VP1, thus allowing a very early diagnosis of seroconversion and thus the implementation of fetal surveillance [84].

PCR also appears to be of particular interest for the analysis of MFIU in the first and third trimesters of unknown etiology [85,86].

Anatomopathological analysis

This analysis allows the detection of intranuclear viral inclusions and margined chromatin, particularly in erythroid progenitors (lungs, liver, thymus, kidneys, etc.). PVB19 is suspected to cause malformations in the fetus, but very few cases are reported and they only concern spontaneous abortions. Ocular anomalies, myocardial necrosis, and intestinal vascular accidents have been described [88].

Ultrasound examination of the fetus

Ultrasound monitoring, by evaluating the degree of hydrops and performing Doppler analysis of the systolic peak of the middle cerebral artery, will allow the severity of fetoplacental hydrops to be assessed. It will make it possible to distinguish between two types of anasarca: early anasarca and pericardial anasarca [89].

Antenatal biological diagnosis

Prenatal diagnosis of fetal B19 infection is made by testing for the virus or viral genome in amniotic fluid (PCR) or fetal blood.

Table 5: Diagnostic techniques and samples used for diagnosing congenital parvovirus B19 infections [87].

Sample	Technique
Maternal serum	IgG/IgM, ELISA, Western blot, immunofluorescence
Maternal serum	<i>In situ</i> hybridization
Maternal serum	AFP (elevated prior to detection of hydrops)
Maternal serum	AFP (elevated)
Maternal serum	PCR
Maternal serum	IgG antibodies against viral non-structural protein NSI
Amniotic fluid	PCR
Amniotic fluid	PCR, Southern blot, chemiluminescence
Amniotic fluid	Enzymatic amplification of parvovirus B19 (segment)
Fetal blood	PCR, dot-blot hybridization, <i>in situ</i> hybridization
Fetal blood	Enzymatic amplification of parvovirus B19 (segment)
Fetal serum	PCR
Fetal heart tissue	Microscopy: VP1 and VP2 viral particles
Fetal tissue	Microscopy: histology was found to be as sensitive as PCR

Ig: Immunoglobulin; ELISA: Enzyme-Linked Immunosorbent Assay; AFP: Alpha-Fetoprotein; PCR: Polymerase Chain Reaction (DNA test).

B19 infection during pregnancy can affect the fetus and result in hydrops or fetal death. Anasarca is the predominant ultrasound feature in fetuses with parvovirus B19 infection. Obtaining a diagnosis of maternal infection will allow fetal evaluation and treatment by intrauterine blood transfusion. Unfortunately, mothers are often unaware that they have an infection until fetal symptoms are noted. Confirmation of PVB infection requires laboratory analysis, which is complicated by the nature of the viral infection and the immune response [90].

Management of Infection to B19

After contact, surveillance at any term is maintained for 12 weeks because there is considered to be a 10% risk of complications before 28SA that drops to less than 1% but still exists after 28SA. A latency of 6 weeks on average between maternal infection and the appearance of fetoplacental anasarca is also noted in the literature [91]. In case of contagion, maternal serology should be checked to determine the initial status and recheck 2 to 3 weeks later (Figure 6).

Prognosis, Prevention and Therapeutic Approaches

Prognosis

Several studies have shown that the short- and long-term prognosis of children born alive to mothers infected with PVB19 is excellent, with 98% of children surviving without sequelae, even if the mother is infected, in only 17 to 33% of cases [59,93].

The prognosis is clouded by spontaneous abortions and hydrops. The prognosis is clouded by spontaneous abortion and anasarca. Indeed, the prognosis of fetuses in anasarca having been transfused in utero is considered favorable in the light of several studies [94,95].

Prevention

Mothers of young children, as well as women working in schools and daycare centers, are most at risk of exposure to B19 infection.

Excluding infected people from the workplace, daycare or school is not likely to prevent the spread because infected people are contagious before symptoms appear [58].

To reduce the risk of infection, pregnant women should:

- Wash their hands thoroughly after touching tissues used by infected children and dispose of tissues immediately.

- Avoid sharing glasses or utensils with anyone who has or has been exposed to the disease.

No systematic prevention or screening methods are effective.

Therapeutic approaches

There is no specific antiviral treatment for PVB19. The primary infection of the immunocompetent subject generally does not require any specific treatment. In patients with chronic hemolysis, transfusion of packed blood cells and injection of polyvalent immunoglobulins may be warranted.

Intrauterine blood transfusion has been proposed as a treatment for the fetus with severe B19-induced anemia and hydrops. However, the natural history of infection in the untreated fetus is not known, and the benefit of intrauterine blood transfusion is as yet unproven. Several investigators have reported spontaneous resolution of nonimmune hydrops. A survey of perinatal obstetricians in the United States and Canada reported that 34% of the cases of nonimmune hydrops resulting from parvovirus infection resolved spontaneously, the majority within 8 weeks [96]. In the absence of such treatment, fetal death occurs in 90% of cases [97].

B19 vaccine

As far as is currently known, no vaccine is currently available. A Phase I study working on a recombinant vaccine comprising the capsid proteins VP1 and VP2 seems to confirm the good immunogenicity of these proteins inducing the production of a high level of antibodies persisting at least one year [98].

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