



PRIMARY RISK ASSESSMENT

INCREASE IN CONGENITAL PARVOVIRUS B19 INFECTIONS

Date of the signal	Date of the RA	Signal provider	Experts consultation	Method
12/06/2024	20/6/2024	ECDC, University Hospital Leuven	Permanent experts: Caroline Boulouffe (AViQ), Adrae Taame (Vivalis), Anna Schmelz (DGOV), Jorgen Stassijns (Sciensano), Naïma Hammami (Departement Zorg), Bertrand Draguez (RMG)	Meeting 27/06/2024
Date of update	Closing date			
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SIGNAL

Since March 2024, different countries in Europe (Denmark, Netherlands, France,...) are alerting on an increased detection of Parvovirus B19 (B19V). Early March, the Flemish Society of Obstetrics and Gynaecology warned about an epidemic of B19V on their website, and addressed a message to all members asking for increased vigilance in the follow up of pregnant women likely infected with the virus. In June, the University hospital of Leuven alerts on the increase of intrauterine transfusions after infection with B19V. Parvovirus B19 has a cyclic occurrence about 3-4years, but the current incidence seems higher than before.

DESCRIPTION

Event

ECDC published a threat assessment on 5th June 2024 about the increased detection of B19V in different European countries (1).

Parvovirus B19 is a common childhood viral illness, also called fifth disease, "slapped cheek" or erythema infectiosum. After infection (4-14 days of incubation with a viremic peak at +/- day 7 lasting for 1 week) a flu like syndrome appears (fever, malaise, myalgia) (2-4). Several days later a confluent erythema appears on the cheeks, followed by a symmetrical rash predominant on arms, legs, trunk. In adults the rash is often atypical and less pronounced. 20-25% of all infections are asymptomatic (2). Diagnosis is mainly clinical and can be challenging (sometimes difficult to distinguish at the beginning of the disease from for example roseola, measles, rubella,...). Complications include arthritis, arthralgia and transient aplastic crisis.

Serious consequences may occur in pregnant women during the first 20 weeks of pregnancy (anemia, hydrops fetalis, fetal death and miscarriage) and immune compromised patients (4).

Symptoms start appear after the infectious period, so excluding sick children from creches/schools is often not helpful in limiting further spread of virus.

- Currently there is an increase in infections reported from the Sentinel Labs (n=141 till 17/06/2024), possibly reaching full year numbers of the epidemic years 2012 (n=306) and 2017 (n=310) (figure 1). Most reported infections occur in females in age group 5-9y and 30-39y (figure 2).
- A recent article from 3 European fetal reference centers (University hospital Leuven (Belgium), University hospital Leiden (The Netherlands) and 2 university hospitals in Paris (France)) shows a strong increase in the number of intra uterine transfusions performed after B19V infection in 2023 (x3) and till mid 2024 (x5) compared with previous years (figure 3) (5).
- The NRC reports an increased number of performed analyses in 2024 compared to previous years but similar to previous B19V peak year. Although positivity of samples is increasing since 2024 (figure 4, table 1).

Table 1. Number and test specifications performed NRC

PCR confirmation on	2015	2016	2017	2018	2019	2020	2021	2022	2023	2024 (till 13/06)
Serum/blood	14		7	8	9	8	5	14	13	29
Positive PCR on serum/blood	0		0	0	1	0	0	0	2	16
PCR on amniotic fluid	12		32	37	36	25	21	14	17	19
Positive PCR on amniotic fluid	1		0	0	1	0	0	0	0	5
PCR on placenta	1		6	5	3	2	4	2	3	3
Positive PCR on placenta	0		0	0	1	1	0	0	1	2
Number of different Pregnant women	24		38	43	41	29	29	26	31	48

*2016 has a total of 49 test performed and 5 positives.

Type of risk

Unusual but not unexpected

An increase in circulation of Parvovirus B19 is expected as the virus has a tendency to occur in cycles of 3-4 years (typically during spring months) but the increase of number of intra uterine transfusions is much higher than usual (fivefold in 2024). A possible explanation could be the build-up of susceptible people during the COVID-19 pandemic, where circulation of infectious pathogens was reduced.

Severity of the risk

- **General population: Low**
 - o *B19V illness affects mainly children and is mild, usually in the form of exanthematous disease. Adults may also present rash, transient joint pain/swelling or myalgias.*
- **Non-immune pregnant woman <20weeks gestation: Low to moderate**
 - o *In Belgium 30% of the women of childbearing age are susceptible to parvovirus B19 infection (6). Passage of virus from mother to fetus occurs in 1/3 of cases in a primary infection (33%). The risk of fetal mortality ranges from 5 to 9% (2).*
 - o *Passage varies according to the gestational age at the time of infection: in the first trimester it is high and causes spontaneous abortions in 11 to 15% of cases, in the second trimester the infection results in hydrops fetalis in 4% of children or in death in utero, while fetus in the third trimester usually recover spontaneously(2).*
 - o *Diagnosis can be challenging as Parvovirus B19 infection is often asymptomatic in pregnant women (in 30–50% of cases) or might present as a non-specific febrile illness, which is accompanied by a rash(5).*

	<ul style="list-style-type: none"> - Immune compromised patients and chronic hematological diseases: Moderate <ul style="list-style-type: none"> o <i>Patients in inability to produce neutralizing antibodies with risk for anemia, pancytopenia, graft loss or other complications.</i>
Exposed population	<i>All</i>
Risk of (inter)national dissemination <i>High</i>	<p>The infectious period takes place before symptoms appear. Transmission occurs by respiratory droplets (50% transmission with intra-familial contact), mother to foetus passage or blood transfusion.</p> <p>The ECDC threat assessment indicated current increase in infections in different countries.</p>

PREPAREDNESS & CONTROL MEASURES ALREADY IN PLACE

Preparedness	<p>Given the lack of preventive measures (no vaccine or treatment) and the high proportion of immune women of childbearing age (60%) systematic screening for B19V in all pregnancies is not advised (4,7,8).</p> <p>Antibody determination is indicated if there is a risk: the pregnant woman is in the first 20 weeks of pregnancy, has a child with erythema infectiosum in the family, has an exposure in the professional context, or the pregnant woman herself has symptoms matching B19V infection. This allows to be more mindful of the risk of fetal anemia or hydrops and, if necessary, intervene in a timely manner(9).</p> <p>In Belgium there are 2 surveillance system for Parvovirus B19:</p> <ul style="list-style-type: none"> • Sentinel labs (SL): <ul style="list-style-type: none"> o <i>Providing information on Parvovirus B19 infections in all patients (although most infections are not-lab confirmed, the majority in risk groups)</i> o <i>The network is not stable over time (between 2 and 6 labs/year reporting since 2021) and not geographically representative, but possible to follow up trends.</i> • National Reference lab (ULB) <ul style="list-style-type: none"> o <i>Providing information on performed PCR confirmations of congenital Parvovirus B19 infections (on serum/blood in pregnant woman and babies and PCR in amnion fluid or placenta)</i>
Specific Control Measures	<ul style="list-style-type: none"> • In <u>March and June 2024</u> the Flemish gynecologist association (VVOG) sent out an alert to be vigilant for an increase of Parvovirus infections. A low threshold was recommended for serology testing in case of colds, joint complaints, reduced child movements and fifth disease occurring in the environment of pregnant woman, so that appropriate treatment (intra uterine transfusion) can be done when needed. • In April 2024 this message was repeated in the <u>flash</u> infection diseases by Departement Zorg.

PUBLIC HEALTH IMPACT IN BELGIUM

Low

The threat is only for specific risk groups, such as non-immune pregnant women (with 5-9% risk for foetal death when transmitted).

RECOMMENDATIONS

1. **Surveillance:**

- Optimize surveillance by alerting physicians on the B19V increase and consequently probable increased diagnostic tests analyzed by the NRC.

2. **Control:**

- There is no treatment or vaccine against the infection. Control measures are very limited. It is important to timely diagnose affected women, to carefully follow up further pregnancy (preferably by referral to a fetal medicine specialist) and appropriately treat (by intra uterine transfusion) when needed.

3. **Communication:**

- Alert gynecologists and midwives on the current increased circulation of Parvovirus B19 and remind them on the possible impact on early pregnancies. Encourage them to timely diagnose (sometimes no specific symptoms) and carefully follow up further pregnancy (preferably referral to a fetal medicine specialist) to be able to treat appropriately when needed.
- Raise awareness in GPs and pediatricians on the current increase of B19V infections and the possible challenging diagnosis. Stimulate to explain possible impact to certain risk groups and educate (disease symptoms, hygienic measures and appropriate health-seeking behavior).
- In case of an outbreak in a nursery/crèche/school, inform occupational physician to evaluate if possible actions for pregnant employees should be done.

ACTIONS

1. Sciensano drafts a message to gynecologists and midwives for distribution by the Vlaamse Vereniging voor Obstetrie en Gynaecologie (VVOG), the Collège Royal des Gynécologues Obstétriciens de Langue française de Belgique (crGOLFb) and to midwives by Belgian Midwives Association.
2. Sciensano drafts message to GPs and pediatricians for distribution by the Société Scientifique de Médecine Générale (SSMG), the Collège de Médecine Générale (CMG), Domus Medica, Belgische vereniging Kinderartsen-Société Belge de Pédiatres (BVK-SBP), the Belgian Academy of Paediatrics (BAoP) and ONE.

FIGURES & TABLES

Figure 1. Number of reported B19V cases by the Sentinel laboratories

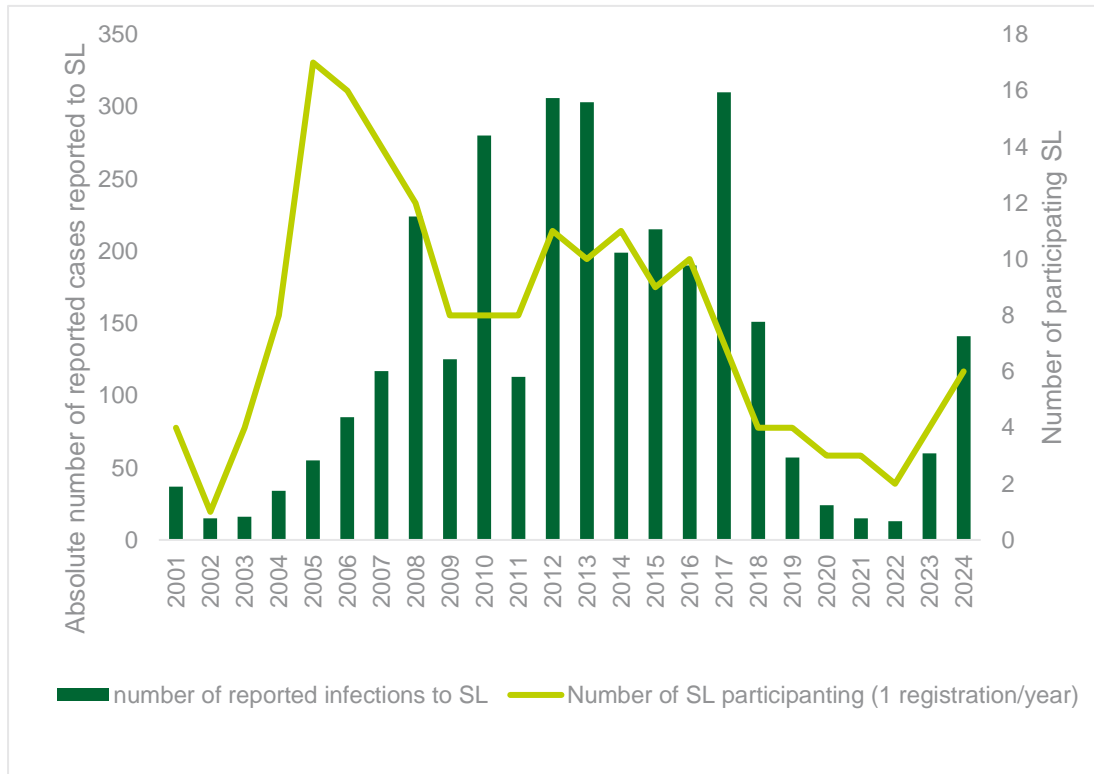


Figure 2. Number of reported B19V cases by the Sentinel laboratories by agegroup and gender

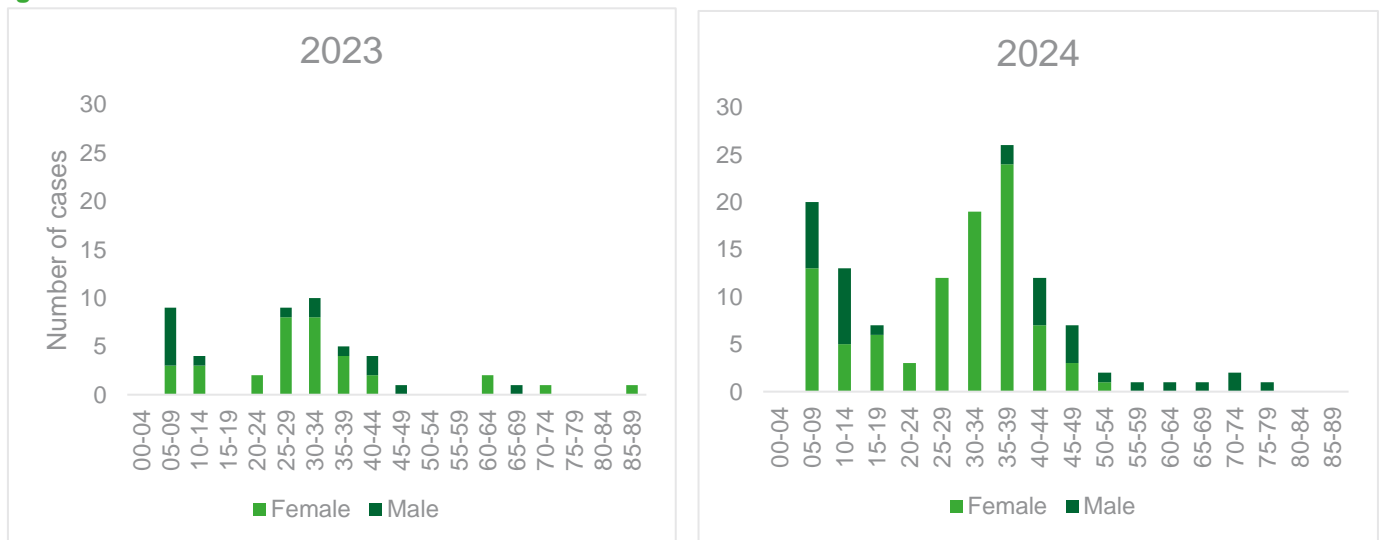


Figure 3. Intrauterine transfusions after B19V infection in Northwestern Europe (5)

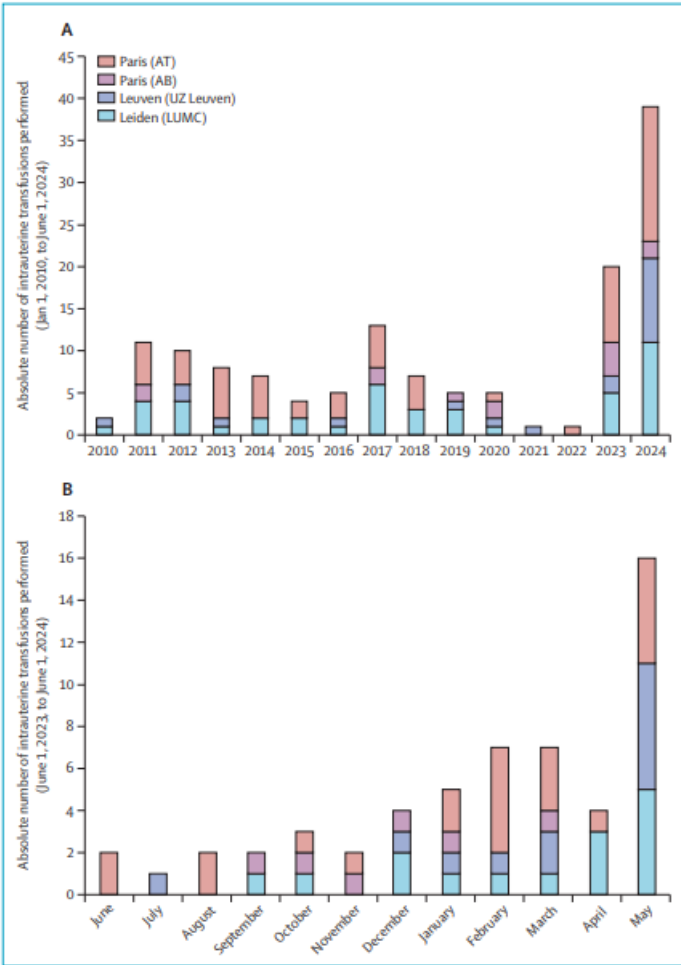
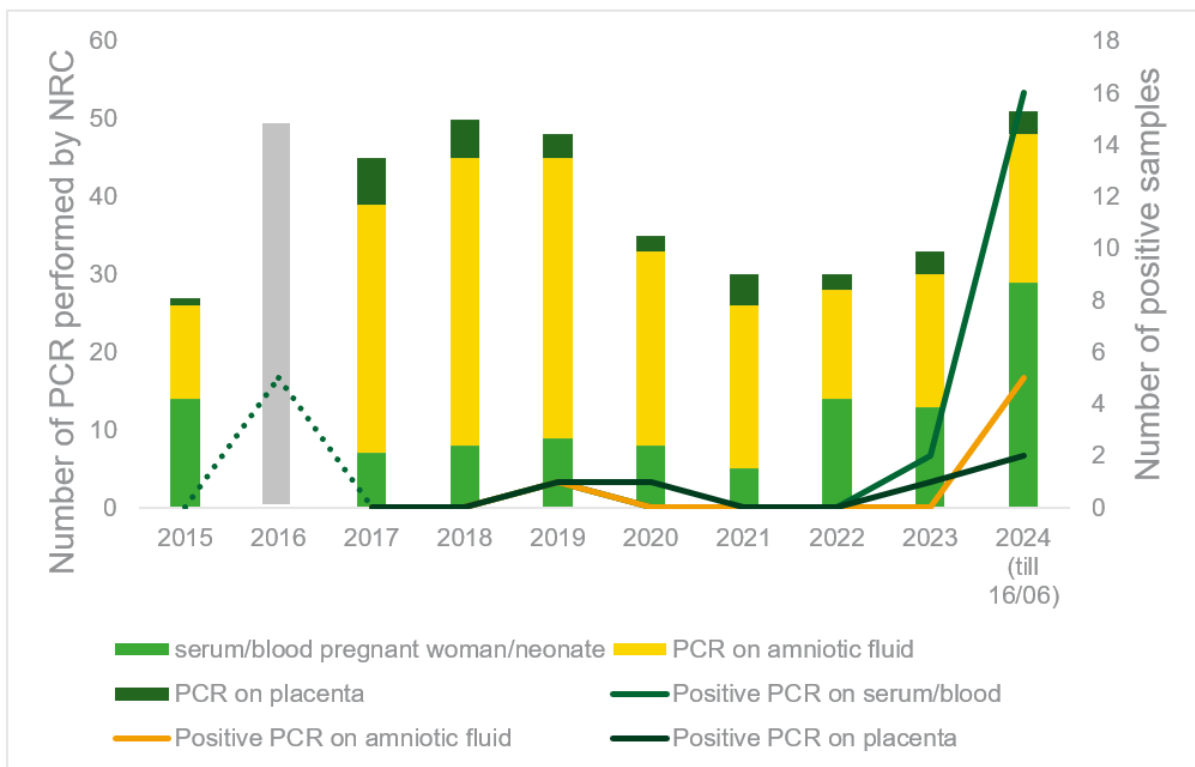


Figure: Intrauterine transfusion in Northwestern Europe
 Data are up to June 1, 2024. (A) Annual amount of intrauterine transfusion for parvovirus B19 infection in Leiden, Netherlands; Leuven, Belgium; and Paris, France. The chosen areas represent approximately two-thirds of all intrauterine transfusion activity combined in these countries. (B) Monthly amount of intrauterine transfusion from May 1, 2023, to June 1, 2024. AT=Armand-Trousseau hospital. AB=Antoine-Bécère hospital. LUMC=Leiden University Medical Center. UZ Leuven=University Hospitals Leuven.

Figure 4. Test type and positivity of B19V samples analyzed by the NRC



*Test type not specified in 2016

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