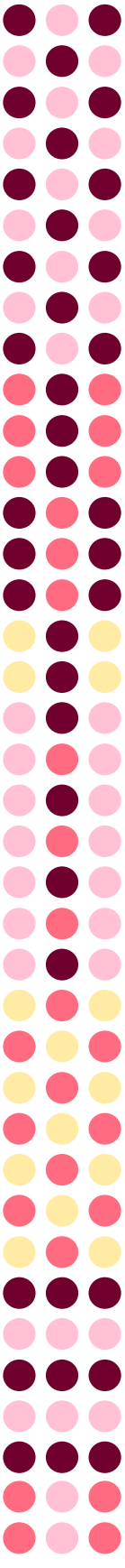
Parvovirus B19: diagnosis, distribution and disease associations

Russcher, A.



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Extreme upsurge of parvovirus B19 resulting in severe fetal morbidity and mortality

Anne Russcher[1†], E.J.T. (Joanne) Verweij[2†], Paul Maurice[3], Jean-Marie Jouannic[3], Alexandra Benachi[4], Alexandre J. Vivanti[4], Roland Devlieger[5]

[†]contributed equally

Affiliations
1. LUCID Medical Microbiology and Infection Control, Leiden University Medical Center, Leiden, Netherlands
2. Division of Fetal Therapy, Department of Obstetrics, Leiden University Medical Center, Leiden, Netherlands
3. Department of Fetal Medicine, Armand-Trousseau Hospital, AP-HP Sorbonne University, Paris, France
4. Department of Obstetrics and Gynecology, Antoine Béclère Hospital, Paris Saclay University, AP-HP, Clamart, France
5. Department of Obstetrics and Gynecology, University Hospitals Leuven, Belgium

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At present, there is an unprecedented upsurge of cases of severe intrauterine infection with parvovirus B19 in northwestern Europe. Parvovirus B19 is well known as the causative agent of erythema infectiosum (also known as fifth disease), a common and usually self-limiting infection in school-aged children. However, when non-immune people acquire the infection during pregnancy, vertical transmission occurs in 33–51% of individuals, and this can lead to severe fetal anaemia and subsequently to life-threatening fetal hydrops [1]. When diagnosed promptly, parvovirus B19 infection in pregnancy can be managed by close monitoring of the fetus using ultrasound to look for signs of fetal anaemia. When anaemia or hydrops occurs, intrauterine transfusion can substantially reduce the risk of fetal death. Therefore, the survival rate after intrauterine transfusion for parvovirus B19 is 67–84% as opposed to 30–50% who do not receive intrauterine transfusion [2]. Intrauterine transfusion for parvovirus B19 requires specific expertise and is mostly performed in national referral centers as these fetuses are deeply anaemic or hydropic and often also suffer from thrombocytopaenia. Timely diagnosis is challenging, as parvovirus B19 infection often is asymptomatic in pregnant people (in 30–50% of cases) or might present as a non-specific febrile illness, which is accompanied by a rash or arthropathy in 30–40% of cases [3].

We report the number of first intrauterine transfusions for fetal anaemia due to proven parvovirus B19 performed in a large part of Northwestern Europe (Leiden, Netherlands; Leuven, Belgium; and Paris, France) since 2010 (figure A). These referral centers for intrauterine transfusion account for at least two thirds of all intrauterine transfusion in these countries, and therefore are a good reflection of intrauterine transfusion activity in this part of Europe. The total number of intrauterine transfusion in the first months of 2024 has already surpassed the annual maximum amount of intrauterine transfusion ever performed in all participating referral centers. Figure B shows the monthly amount of intrauterine transfusion from June 1, 2023 to June 1, 2024. In total, 59 fetuses in this region have been treated with at least one intrauterine transfusion during the current upsurge since Jan 1, 2023, with 44 fetuses receiving intrauterine transfusion since Sept 1, 2023. Of these 59 fetuses, 21 (36%) had adverse outcomes (13 [22%] perinatal death, four [7%] termination of pregnancy due to severe fetal anomalies, and four [7%] ongoing pregnancies with persistent hydrops or severe cerebral anomalies), while the definite outcome is not yet known for 19 pregnancies. Gestational age at first intrauterine transfusion did not differ significantly for the period of Jan 1, 2023, to

June 1, 2024 (mean 21.5 weeks, SD 3.2) compared to Jan 1, 2010, to Dec 31, 2022 (22.4, 2.9; p=0·087). However, gestational age at first intrauterine transfusion was significantly higher in the group with adverse outcomes (22.8, 3.5) compared with the group without adverse outcomes (20.8, 2.8; p=0·010) in the period of Jan 1, 2023, to June 1, 2024.

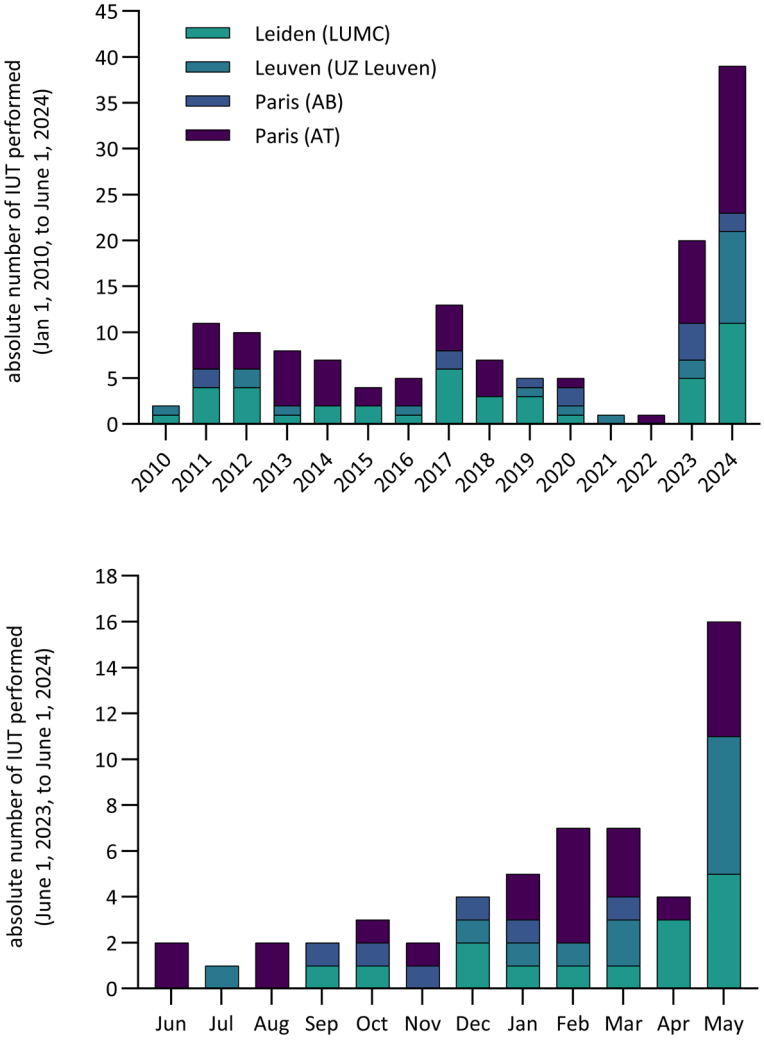

Figure 1: Intrauterine transfusion in Northwestern Europe*. Data are up to June 1, 2024. (A) Annual amount of intrauterine transfusion for parvovirus B19 infection in Leiden, Netherlands; Leuven, Belgium; and Paris, France. The chosen areas represent approximately two-thirds of all intrauterine transfusion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

Recent research [4] shows that the traditional pattern of annual parvovirus B19 epidemics in late spring with superimposed multi-annual epidemics has become disturbed, with local disappearance of multi-annual and annual epidemics since 2014 and the virtual absence of parvovirus B19 infections during and after the COVID-19 pandemic [4]. The resulting increase in susceptible host populations will have led to the large-scale parvovirus B19 epidemic we witness at present, a rebound effect similar to post-pandemic surges of other, also primarily respiratory transmitted, infectious diseases. The proportion of parvovirus B19 fetal cases with adverse outcomes is larger than expected based on existing literature and previous experiences. At present, genotyping of circulating strains does not suggest altered strains with altered virulence [5]. Although gestational age at first intrauterine transfusion did not differ between 2010–22 and the current epidemic in 2023–24, we observed that gestational age at first intrauterine transfusion was significantly higher in the group with adverse outcomes. The considerable proportion of adverse outcomes therefore might be explained by suboptimal awareness for parvovirus B19 infections in general health care or obstetric care, possibly due to its prolonged absence, resulting in late referral and increased risk of adverse outcomes. Considering the ongoing epidemic, we urgently recommend vigilance for parvovirus B19 infections in pregnant people. At present, the threshold of performing a serological test for parvovirus B19 should be low, including (1) pregnant people with febrile illness, exanthema, or painful or swollen joints; (2) pregnant people who have been in contact with an individual with parvovirus B19, and (3) pregnant people with reduced fetal movements or fetal hydrops at routine ultrasound examination. Whether national screening programmes for parvovirus B19 in pregnancy are warranted, particularly in severe epidemic years, is a matter for further study. As pregnant people might present in different stages of parvovirus B19 infection, interpretation of diagnostic tests should be done with care together with a virologist. Early consultation with a fetal medicine specialist is recommended when parvovirus B19 infection in pregnancy is suspected. In the case of a confirmed parvovirus B19 infection, referral to a fetal medicine specialist is indicated for advanced ultrasound examination and frequent follow-up.

We declare no competing interests.

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