REVIEWS

Review
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Parvovirus B19 infection: characteristics of population immunity in the world

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Abstract
Parvovirus B19 infection (PVI) is one of the relatively new problems in infectology, data on the study of its prevalence in our country began to appear only at the beginning of the twenty-first century. The article presents the results of an analysis of studies from available literature sources highlighting the prevalence of PVI markers at the population level among different social groups of the population at the present stage. The clinical manifestations of PVI are diverse, which requires differential diagnosis, both with exanthemic infectious diseases and with non-infectious pathology. Due to the peculiarity of PVI pathogenesis, it is relevant for various socially significant populations, primarily patients with exanthemic manifestations of various diseases, persons from among blood donors, pregnant women and women planning pregnancy. Furthermore, unlike most countries, our country does not have a system for PVI detecting and reporting in the system of state sanitary and epidemiological supervision, which makes it difficult to conduct research on this topic.

Keywords: *review, parvovirus B19, immunoglobulins G and M, donors, pregnant women, exanthemic infections*

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Обзор
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Парвовирусная B19 инфекция: характеристика популяционного иммунитета в мире

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Аннотация
Парвовирусная B19 инфекция (ПВИ) представляет собой одну из относительно новых проблем в инфектологии, данные по её распространённости в России стали появляться только в начале XXI столетия. В статье приведены результаты анализа исследований из доступных источников литературы, освещаю-

щих распространённость маркеров ПВИ на популяционном уровне среди разных социальных групп населения. Клинические проявления ПВИ разнообразны, что требует дифференциальной диагностики как с экзантемными инфекционными заболеваниями, так и с неинфекционной патологией. В связи с особенностью патогенеза диагностика ПВИ актуальна для разных социально значимых контингентов населения, прежде всего пациентов с экзантемными проявлениями различных заболеваний, лиц из числа доноров крови, беременных женщин и женщин, планирующих беременность. В отличие от большинства стран, в России отсутствует система выявления и учёта ПВИ в системе государственного санитарно-эпидемиологического надзора, что затрудняет проведение исследований на эту тему.

Ключевые слова: *обзор, парвовирус B19, иммуноглобулин G, иммуноглобулин M, доноры, беременные, экзантемные инфекции*

Источник финансирования. Авторы заявляют об отсутствии внешнего финансирования при проведении исследования.

Конфликт интересов. Авторы декларируют отсутствие явных и потенциальных конфликтов интересов, связанных с публикацией настоящей статьи.

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Introduction

Parvovirus (B19) infection (PVI) is an obligate anthroponosis of viral etiology mainly with an aerosol transmission mechanism, as well as transplacental and hemotransfusion routes of transmission, the main clinical symptom of which is infectious erythema, characterized by the appearance of a non-vesicular macula-papular rash, clinically characterized by mild symptoms of general infectious intoxication, arthralgia, joint involvement, inflammatory changes in fetal tissues and the development of aplastic crisis in patients with hemolytic anemia [1-4]. The PVI pathogen is human parvovirus B19 (B19V) (Latin *parvo* — small), which was first discovered by British virologists Y. Cossart et al. in 1974–1975 during laboratory examination of a blood plasma sample from a healthy donor for the presence of HBsAg [5]. The researchers associated the name of the pathogen (B19V) with the well number of the plate containing the serum sample from which it was isolated.

The pathognomonic clinical manifestation of PVI is infectious erythema, described in the XVIII century by the English physician R. Willian long before its etiology was established [6]. However, only in 1899 German physician Sticker singled it out as an independent nosologic form, and in 1905 L. Cheinisse introduced infectious erythema into the classification and defined it as the fifth disease among the 6 classical exanthema [7, 8]. The pathogenic effect of the virus was established only in 1981, when researchers found a correlation between infection of children with squamous cell anemia and the development of aplastic crisis in a number of cases [9]. In 1983, the etiologic role of B19V in the occurrence of infectious erythema was confirmed [10]. In 1984, there were already reports about the development of fetal hydrocele on the background of intrauterine infection with B19V, which ended in premature termination of pregnancy and its death [4, 12]. These scientific facts indicate the expansion of PVI epidemiologic significance and allow us to identify risk groups among people most susceptible to the development of complications of B19V infection. Due to the emergence of specific laboratory diagnostics in modern conditions, the geography of PVI case registration has also expanded. More specifically, it is etiologically confirmed in the territories of South-East Asia, the USA, Europe, and Russia [13]. The epidemic process of PVI is characterized by cyclicity: there are large (10-year) and small (every 3–4 years) cycles.

It should be noted that the taxonomic position of B19V has been revised several times, and the chronology of these changes from 1991 to the present is presented in **Table 1**. B19V was officially classified into the parvovirus family in 1985 [14]. In 2013, it was named Primate *Erythroparvovirus* 1 and assigned to the *Parvoviridae* family, *Parvovirinae* subfamily and *Erythroparvovirus* genus at the congress of virologists in Edinburgh (Scotland). At the 2022 regular convention, its name was not changed [15].

Until 2005, only one species of the *Parvoviridae* family, *Parvovirinae* subfamily, *Erythroparvovirus* genus, *Primate erythroparvovirus 1*, was thought to be pathogenic to humans. However, in 2005 in Sweden, T. Allander described a new respiratory virus from the Parvovirus family, *Bocaparvovirus* genus, called human bocavirus (species HBoV1). It was isolated from infants and children suffering from acute respiratory diseases of the upper and lower respiratory tract by molecular viral screening based on cloning and bioinformatics analysis [16, 17]. This pathogen is the fourth most common virus detected in respiratory samples after adenoviruses, rhinoviruses, and respiratory syncytial

Table 1. The taxonomic position of human B19 parvovirus

Year	Source	Family — subfamily — genus — species
1991	ICTV 5th Report	Parvoviridae — … — Parvovirus — B19 virus
1993	Plenary session vote 10 August 1993 in Glasgow	*Parvoviridae — Parvovirinae — Erythrovirus* — B19 virus
2005	ICTV 8th Report	*Parvoviridae — Parvovirinae — Erythrovirus — Human parvovirus* B19
2013	EC 45, Edinburgh, July 2013; Email ratification 2014	*Parvoviridae — Parvovirinae — Erythroparvovirus — Primate erythroparvovirus 1*
2022	EC 54, July 2022; Email ratification 2023	

virus (it is the cause of acute respiratory viral diseases in children and adolescents in 9–20% of cases) [18–20].

State of the level of population immunity in conditionally healthy individuals

PVI is quite widespread worldwide and causes a wide range of clinical manifestations. A meta-analysis of plasma from 93,636 healthy donor individuals from 17 countries between 1993 and 2019 showed a prevalence of IgG markers at 50.1% (95% CI 43.1–57.1%) and IgM markers at 2.2% (95% CI 1.3–3.7%) [21].

The serologic marker of past infection is the presence of B19V-specific IgG antibodies (previous infection), while IgM antibodies to B19V are the marker of acute PVI infection. There is lifelong immunity after a previous PVI infection. Infection with B19V usually occurs during childhood and adolescence (5–15 years of age). However, adults who are not immune to PVI are also involved in the epidemic process. The prevalence of B19V-specific IgG antibodies in the population depends on age: 2–20% in children under 5 years of age, 15–40% in children aged 5–18 years, and 40–80% in adults [22–24].

However, the seroprevalence of PVI markers differs in different regions of the CIS countries. Thus, when assessing the state of specific immunity in different age groups of the Moscow population in 2015, it was shown that the proportion of seropositive results increased from 25% in children 1–2 years of age to 56.3% in the age group of 30 years and older [22]. At the same time, residents of the Republic of Belarus showed low seroprevalence in pediatric age groups (0–2 years — 8.8%; 3–4 years — 11.8%) and a higher level of seropositive individuals in the age group of 40–44 years (85.4%) [25].

Assessment of the prevalence of population immunity against PVI among conditionally healthy individuals in Russia and abroad (**Table 2**) confirms the ubiquitous nature of the infection. The obtained data testify to active circulation of B19V, rather wide prevalence of PVI (the frequency of occurrence of the PVI marker amounted to 47.4-66.0%) among conditionally healthy individuals. At the same time, the presence of B19V seronegative individuals in all age groups creates conditions for the spread of infection, including in risk groups (blood donors, hematological patients, pregnant women, individuals from organized groups).

B19V seroprevalence and viral load in blood donors

Viral safety in transfusion of blood and its components is one of the most important problems of transfusiology [31–33]. Modern achievements and scientific discoveries in the field of medicine, development of transplantology, improvement of medical care for the population and increase in invasive interventions — all this has significantly increased the need of therapeutic and preventive medical organizations in blood pro-

Table 2. The frequency of anti-B19V IgG antibodies detection among conditionally healthy of individuals in different countries

Country	Number of persons surveyed	Of these, having IgG-antibodies		Year of publication	Source
		abs.	%		
Russia (St. Peterburg)	317	197	62,1	2020	[24]
Russia	200	123	66,0	2019	[25]
Belarus	942	482	51,2	2014	[23]
Uzbekistan	650	402	61,9	2019	[26]
Tadjikistan	114	54	47,4	2020	[24]
Kazakhstan	480	313	65,2	2020	[24]
Serbia	552	339	59,6	2020	[24]
Guinea	321	173	53,9	2020	[24]
Croatia	1538	986	64,1	2021	[25]

ducts. According to the requirements of domestic regulatory documents, their production is supposed to use raw materials free of viruses or with minimal viral load [34]. Meanwhile, according to domestic and foreign sources, this infection is relevant for such an important contingent of people as blood donors and blood components, since PVI, being a blood borne transmissible agent, is transmitted to recipients — hematological patients and immunocompromised persons [35]. Despite ongoing discussions on the feasibility of donor screening, the European Pharmacopoeia and the US Food and Drug Administration recommend testing donor blood for B19V along with blood borne infections (HIV, hepatitis B, C, D, etc.) [32].

When studying the pathogenesis of PVI, it was found that B19V has tropism to red blood cell precursor cells [36], which often leads to a life-threatening complication, aplastic crisis, in patients with various forms of hemolytic anemia. It has been established that the overwhelming majority of cases of this pathology are caused by B19V [9, 37].

To determine the frequency of occurrence of PVI markers among donors in a number of regions of our country in recent years, screening of varying degrees of scale has been carried out. Thus, during the study of blood serum from 1000 donors in Nizhny Novgorod region, the authors identified 10 (1%) samples that contained B19V DNA with a viral load of 10^3–10^6 copies/mL. IgM was detected in 1 sample. All DNA-positive samples contained IgG antibodies (DNA-negative samples contained IgG antibodies in 29.7%), representing 30.7% of the total number of donors [38].

In a study to determine the occurrence of B19V in donor populations, 510 people (Grozny) and 1011 people (Moscow) were examined [32]. Donors from the Chechen Republic had 7 samples positive for B19V DNA with a viral load of 103 copies/mL or less (1.3%). The second group had 20 (1.9%) positive samples for B19V DNA, of which 8 (0.8%) had a viral load of 104 copies/mL or higher.

A large-scale study of donor plasma used in the industrial production of blood products was conducted in the Kirov region. As a result of the study of several tens of thousands of samples, it was found that 0.003% of donors had a B19V DNA concentration of 106 copies/mL or higher [33], which, can lead to contamination of the entire volume of plasma when pooled.

To evaluate specific humoral immunity, we studied 500 donor plasma samples. It was found that 426 (85.2%) had IgG. Of these samples, PCR detected viral load in 74 (17.4%), and in 12 (2.4%) it exceeded 104 copies/mL.

Thus, even the few studies of donor blood conducted in our country correlate with the data of studies conducted in other countries and show the presence of viral DNA in blood plasma, which indicates the acuteness of the latent epidemic process, and a significant viral load determines the epidemiologic danger of blood products.

A survey of 93,636 blood donors was conducted in 17 countries from 1993 to 2019.According to a random effects model, the pool of B19V DNA prevalence was 0.4% (95% CI 0.3–0.6%; I = 89.7%) [21]. **Table 3** shows the countries with a higher frequency of B19V DNA detection of 104 copies/mL or higher among blood donors.

The prevalence of B19V DNA among blood donors varies from country to country, which can be partly explained by the geographical location of the regions studied, seasonal variations, demographic characteristics, the purpose and sensitivity of the assay used, and the year in which the blood samples were collected (due to the cyclical nature of the epidemic).

Sufficient prevalence of B19V DNA in donor blood samples suggests the need to test donor blood for the amount of DNA of this pathogen in order to improve the epidemiologic safety of blood products and avoid samples with a virus concentration of 104 copies/mL or higher.

Frequency of detection of PVI markers in pregnant women and its impact on the fetus

Another socially significant group that is subject to epidemiologic monitoring for PVI are pregnant women or those who are planning pregnancy. This is due to the increased risk of endogenous fetal damage and subsequent adverse events that may occur during pregnancy against the background of intrauterine infection with this pathogen. Workers of kindergartens and schools are most often exposed to infection. Kindergarten teachers have a 3-fold higher risk of developing acute PVI compared to other pregnant women, and school teachers have a 1.6-fold higher risk [44]. When a pregnant woman is infected with PVI, the risk of transmitting the virus to the fetus averages 17–33% [11, 45]. At the same time, the risk of transplacental infection of the fetus is 35–51% of cases [43, 46], the frequency of unfavorable pregnancy outcomes is 20–30%, and fetal death is 10–15% [47]; therefore, PVI is considered as a component of the TORCH complex [48]. According to WHO experts, the risk of fetal death when a woman is infected with B19V in the first 12 weeks of pregnancy, at 13-20 weeks and after 20 weeks is 19, 15 and 6%, respectively [49]. It should be noted that PVI is rarely recognized during pregnancy, as in most cases it is asymptomatic or occurs as a respiratory infection.

The mechanism of the pathogen's negative effect is related to the tissue tropism of the virus, which is capable of affecting placental cells, since the P-antigen (globoside), which is the main receptor for B19V, is located on the surfaces of trophoblast and chorionic villus cells [11]. Furthermore, specific inflammatory changes can lead to placental dysfunction and unfavorable pregnancy outcome even in the absence of fetal infection.

Table 3. The frequency of B19V DNA detection in blood donors in different countries

Country	Number of donors surveyed	Of these having DNA B19V 10^4 copies/ml and above		Year of publication	Source
		abs.	%		
Great Britain	1000	9	0,9	2004	[34]
Ghana	1000	13	1,3	2004	[34]
South Africa	360	2	0,6	2004	[34]
USA	5020	44	0,9	2007	[35]
China	3957	23	0,6	2011	[36]
Russia	1521	27	1,9	2012	[29]
Russia	500	12	2,4	2019	[29]
Iran	500	6	1,2	2018	[37]
Brazil	480	9	1,9	2019	[38]

In this case, the cause of intrauterine fetal death is placental insufficiency [50]. Against the background of erythropoiesis suppression, anemia is observed in the fetus and aplastic crisis may occur with subsequent hypoxia causing dysfunction of its various organs [51]. When viral myocarditis develops, cardiac rhythm disturbances occur, which may lead to fetal cardiac arrest and death [52]. The main clinical manifestation of congenital PVI is thought to be nonimmune fetal hydrocele, which develops in 80% of cases in the second trimester of pregnancy [53, 54]. Congenital PVI may also manifest with hepatosplenomegaly, sickle cell anemia, developmental delay and other pathological conditions [50].

Given the negative impact of B19V on the fetus, the screening of pregnant women in the I and II trimesters of pregnancy for markers of specific humoral immunity in is reasonable. In a number of foreign countries, this infection is referred to infections of the TORCH group, and therefore women planning pregnancy and pregnant women are examined for PVI. In our country, publications on this topic are rare and contradictory. To determine the risk of possible infection of women during pregnancy, the presence of markers of specific antiviral immunity, indicating acute (IgM antibodies) and past (IgG antibodies) PVI, is determined in blood plasma samples. The results of serologic examination of women and prediction of possible fetal complications are shown in **Table 4**.

Screening and monitoring of the serologic status of pregnant women can determine the course of action, the need for additional testing and preventive measures.

The prevalence of PVI markers among pregnant women in different regions of the world varies widely, which can be partly explained by the geographical location of the regions, natural factors, demographic characteristics and national traditions, the sensitivity of the assay used, and different manifestations of the cyclical nature of the epidemic process.

Determination of the prevalence of markers of specific antiviral immunity in the group of pregnant women in different countries shows that up to half of pregnant women (25–46%) are at risk of infection and transplacental transmission of this disease to the fetus (**Table 5**). The active spread of PVI among women of childbearing age indicates the risk of infection of women during pregnancy with the possibility of unfavorable outcomes and can lead to various complications, especially in the first trimester of pregnancy.

In order to prevent acute fetal PVI, the monitoring of the pregnant woman depends on the gestational age at which the infection occurred. In the first trimester, ultrasound (collar space screening, Doppler venous hemodynamics) is used to detect anemia. At up to 20 weeks of gestation, fetal screening should be started no later than 4 weeks after maternal illness or seroconversion. If the ultrasound shows fetal hydrocele, the woman should be warned of the possible consequences

Table 4. Results of serological examination of women and prediction of possible fetal complications

Result	Interpretation of the obtained data
IgG+, IgM–	A past infection (there is no risk to the fetus)
IgG+, IgM+	Infection during the last 7–120 days (possible risk to the fetus)
IgG–, IgM+	Acute infection (maximum risk to the fetus)
IgG–, IgM–	The mother does not have a specific immunity — there is a risk of infection. There are no signs of acute infection. If the woman contacted with infected patient, then it is necessary to repeat the serological examination after three weeks. In this case, the appearance of IgM antibodies indicates an acute infection

Table 5. IgG seroprevalence in pregnant women in different countries

Country	The number of women surveyed	Of them having IgG antibodies, %	Year of publication	Source
Tunisia	404	76,2	2011	[50]
Finland	558	58,6	2005	[51]
Jordan	439	51,3	2006	[52]
Netherlands	2567	70	2005	[53]
Italy	1893	69,5	2022	[54]
Russia	233	56,2	2019	[55]
Iran	1954	54	2016	[56]
Kuwait	1047	53,3	1999	[57]

of the disease. If no fetal abnormalities are detected, ultrasound examinations are continued at 1–2 week intervals. In the high-risk group, weekly Doppler examination of the middle cerebral artery, peak systolic blood flow velocity and venous duct blood flow is recommended [11].

It should be emphasized that due to the lack of available means of specific prophylaxis, the main attention should be focused on measures aimed at identifying non-immune pregnant women, preventing their infection and careful clinical and serological monitoring during pregnancy. All of this points to the necessity of introducing mandatory screening of pregnant women for the presence of PVI markers.

Frequency of detection of PVI markers in patients with exanthemic manifestations of the infectious process

Since 2002, a strategic plan for the elimination of endemic measles and rubella infection and prevention of congenital rubella infection has been implemented in Russia in accordance with the recommendations of the WHO Regional Office for Europe. The success achieved in reducing the incidence of these infections has led to greater attention being paid to other diseases with exanthemic manifestations of the infectious process. The onset of exanthema usually occurs early in the disease and is the leading clinical symptom for differential diagnosis. One of these most common infections includes PVI. The main form of the disease is infectious erythema (fifth disease), which is registered in the International Classification of Diseases (ICD-10) under the code B08.3 [62].

Since the discovery of the virus, a large number of scientific studies have been conducted abroad to investigate the epidemiology, diagnosis, and clinical manifestations of PVI. In our country, studies have been conducted only since the beginning of the current century, and their number is clearly insufficient to determine the prevalence of PVI markers, especially in socially important groups.

However, some data on the prevalence of PVI among examined persons with exanthemic manifestations of the infectious process in some regions of our country and other countries have been obtained from available sources (**Table 6**).

The largest number of examined patients was in the Republic of Belarus, where the highest proportion

Table 6. The frequency of detection of anti-B19V IgM antibodies in patients with exanthemic manifestations of the infectious process

Country	The number of examined persons with exanthema	Of those with anti-B19V IgM antibodies, %	Year of publication	Source
Russia, Southern Federal District	184	8,2	2008	[58]
Russia, Northwestern Federal District	465	20,4	2012	[59]
Russia, Northwestern Federal District	336	14,9	2015	[59]
Belarus	4919	27,8	2021	[60, 61]
Argentina	141	14,9	2012	[62]
Russia	69	20,1	2019	[55]
Italy	390	5,1	2015	[63]
Iran	583	19,2	2016	[64]
Cuba	298	10,7	2019	[65]
Bulgaria	1266	22	2016	[66]

of acute PVI among all acute exanthemic diseases was detected. If we consider the age structure, it is dominated by children. IgM antibodies to B19V was detected in the age groups 4–6 years (22,5%) and 7–10 years (22,6%), which indicates that the main form of PVI disease in childhood is infectious erythema, and the least amount of acute PVI marker was determined in older age groups — 40–49 years (3,05%) and 50–64 years (1,6%).

To assess the frequency of IgM antibodies to B19V in the Northwestern Federal District before and after the adoption of restrictive measures due to the COVID-19 pandemic, the St. Petersburg Regional Center for Measles and Rubella Surveillance examined blood sera from its collection. IgM antibodies to B19V (a laboratory marker of acute PVI) were tested in 1695 samples from 11 territories of the district.

PVI was laboratory confirmed in 198 (11.7%) samples. For comparison: in 2012, the proportion of positive samples out of the number of samples tested was 20.4%, and in 2015, 14.9% (Table 6). On the territory of Russia, restrictive measures in connection with COVID-19 were introduced from 30.03.2020. In 2020, the proportion of positive samples with confirmed PVI was 8.9%; in 2021, it was 10.2%. In 2022, the social restrictions were completely removed. When serum samples from patients with fever and rash were examined, IgM antibodies to B19V were detected in 14.8% of cases. These studies show that the restrictive measures introduced in connection with the COVID-19 pandemic played a role, especially in reducing the incidence of acute PVI, as well as other infections with aerosol transmission.

In conducting our own studies of patients with exanthemic manifestations of various diseases, 69 patients admitted to an infectious disease hospital in St. Petersburg were examined. The distribution of samples with detected IgM antibodies to B19V in the serum of patients with various exanthemic diseases is presented in **Table 7.**

According to the results of the study, it should be noted that in none of the cases were patients diagnosed with PVI. Thus, the problem of early diagnosis of PVI in patients admitted to an infectious disease hospital with exanthema syndrome is caused by objective difficulties associated with the diversity of manifestations in the clinical picture. In addition, insufficient knowledge of physicians of the main clinical syndromes characteristic of PVI, in the form of a relatively small proportion of this infection among other infectious diseases, plays an important role.

Conclusion

The results of the literature review showed the presence of latent PVI epidemic process among different social groups in the population of many countries. The results suggest that in order to prevent blood borne infection with B19V, it is important to include B19V DNA testing and quantitation in the list of mandatory testing of donor blood in order to improve the epidemiologic safety of blood products and to reject samples with a virus concentration of 104 or more copies/mL.

Table 7. The proportion of laboratory-confirmed B19 PVI in different preliminary diagnoses

Preliminary clinical diagnosis	The number of serums, abs.	The number of anti-B19V IgM positive samples, abs.	The proportion of laboratory-confirmed PVI, %
I class			
Exanthema of unclear etiology	32	7	21.9
Infectious mononucleosis	6	2	33,3
HIV infection	1	0	0
Herpesvirus infection	1	1	100
Thrombocytopenia	2	0	0
Toxicoderma	4	0	0
Fever of unknown origin	2	0	0
Pseudotuberculosis	1	0	0
Total	49	10	20,4
X class			
Acute respiratory viral infections of the upper respiratory tract	14	1	7,1
Tonsillitis	2	1	50,0
Bronchitis	2	1	50,
Pneumonia	2	1	50,0
Total	20	4	20,0
In total	69	14	20,3

B19V poses a potential risk to pregnant women. The risk of infection of pregnant women, the possibility of transplacental transmission with the possibility of severe congenital disease is quite high. In our country there are no accurate data on the frequency of PVI among women of childbearing age, the frequency of congenital infection. Therefore, all pregnant women and women planning pregnancy should be screened for PVI markers regardless of age and number of pregnancies. Immunologic screening of pregnant women at risk will not only allow timely detection of PVI, but will also help to reduce the development of pregnancy pathology and fetal deaths. The acute form of PVI is common among infectious diseases with exanthemic manifestations and in respiratory diseases with atypical course. However, the final diagnosis of PVI can be made only on the basis of the results of laboratory tests. In this regard, patients with exanthema need to conduct laboratory tests to detect specific IgM-antibodies not only to measles and rubella viruses, but also to B19V for the differential diagnosis of exanthemic diseases.

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Участие авторов. *Никишов О.Н., Кузин А.А., Лаврентьева И.Н., Антипова А.Ю.* — сбор и обработка материала, статистическая обработка, написание текста, концепция и дизайн исследования; *Никишов С.Н.* — концепция и дизайн исследования, редактирование. Все авторы подтверждают соответствие своего авторства критериям ICMJE, внесли существенный вклад в проведение поисково-аналитической работы и подготовку статьи, прочли и одобрили финальную версию до публикации.

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