https://doi.org/10.17816/PED11381-92

MENINGOCOCCAL INFECTION IN MODERN CONDITIONS: CLINICAL, MICROBIOLOGICAL AND PREVENTIVE ASPECTS

© K.V. Markova [1], N.V. Skripchenko [1, 2], Yu.V. Lobzin [1], V.E. Karev [1], A.A. Vilnits [1, 2], E.Yu. Gorelik [1], E.A. Martens [1], S.V. Sidorenko [1]

[1] North-Pediatric Research and Clinical Center for Infectious Diseases, Saint Petersburg, Russia;
[2] Saint Petersburg State Pediatric Medical University, Saint Petersburg, Russia

For citation: Markova KV, Skripchenko NV, Lobzin YuV, et al. Meningococcal infection in modern conditions: clinical, microbiological and preventive aspects. *Pediatrician (St. Petersburg)*. 2020;11(3):81-92. https://doi.org/10.17816/PED11381-92

Received: 07.04.2020 Revised: 20.05.2020 Accepted: 23.06.2020

The problem of meningococcal infection remains relevant due to the high epidemiological and social significance throughout the world, the unpredictability of the course, a wide range of clinical manifestations (from asymptomatic carriage to extremely severe generalized forms) with a high risk of life-threatening conditions and deaths, and a significant incidence of disability after past illness (loss of limbs, deafness, mental inferiority, and more). The changing serogroup landscape of meningococcal infection with an increase in the incidence of diseases caused by *Neisseria meningitidis* serogroup W, Y and others is noteworthy. The article presents an analytical review of literature and reflects current clinical, epidemiological, diagnostic and preventive trends in the Russian Federation and abroad. The review focuses on the epidemiological features of meningococcal infection, depending on the serogroup affiliation of meningococcus, the variety of clinical manifestations of the generalized form of meningococcal infection, including atypical manifestations, age-related features, depending on the serogroup of the pathogen. New diagnostic approaches and the possibilities of specific prophylaxis are highlighted. Attention is focused on the importance of monitoring the clinical and epidemiological characteristics of meningococcal infection depending on the genetic characteristics of the pathogen, and the need for further in-depth studies of this problem.

Keywords: meningococcal infection; children; diagnosis; prevention.

МЕНИНГОКОККОВАЯ ИНФЕКЦИЯ В СОВРЕМЕННЫХ УСЛОВИЯХ: КЛИНИЧЕСКИЕ, МИКРОБИОЛОГИЧЕСКИЕ И ПРОФИЛАКТИЧЕСКИЕ АСПЕКТЫ

© К.В. Маркова [1], Н.В. Скрипченко [1, 2], Ю.В. Лобзин [1], В.Е. Карев [1], А.А. Вильниц [1, 2], Е.Ю. Горелик [1], Э.А. Мартенс [1], С.В. Сидоренко [1]

[1] Федеральное государственное бюджетное учреждение «Детский научно-клинический центр инфекционных болезней Федерального медико-биологического агентства», Санкт-Петербург;
[2] Федеральное государственное бюджетное образовательное учреждение высшего образования «Санкт-Петербургский государственный педиатрический медицинский университет» Минздрава России, Санкт-Петербург

Для цитирования: Маркова К.В., Скрипченко Н.В., Лобзин Ю.В., и др. Менингококковая инфекция в современных условиях: клинические, микробиологические и профилактические аспекты // Педиатр. – 2020. – Т. 11. – № 3. – С. 81–92. https://doi.org/10.17816/PED11381-92

Поступила: 07.04.2020 Одобрена: 20.05.2020 Принята к печати: 23.06.2020

Проблема менингококковой инфекции сохраняет свою актуальность в связи с высокой эпидемиологической и социальной значимостью во всем мире, непредсказуемостью течения, широким диапазоном клинических проявлений (от бессимптомного носительства до крайне тяжелых генерализованных форм) с высоким риском возникновения жизнеугрожающих состояний и летальных исходов, и значительной частотой инвалидизации после перенесенного заболевания (потеря конечностей, глухота, умственная неполноценность и другое). Обращает на себя внимание меняющийся серогрупповой пейзаж менингококковой инфекции с увеличением случаев заболеваний, вызванных *Neisseria meningitidis* серогруппы W, Y и др. В статье представлен аналитический обзор литературных источников, и отражены современные клинико-эпидемиологические, диагностические и профилак-

тические тенденции в Российской Федерации и за рубежом. В обзоре делается акцент на эпидемиологических особенностях менингококковой инфекции в зависимости от серогрупповой принадлежности менингококка, разнообразии клинических проявлений генерализованной формы менингококковой инфекции, в том числе и атипичных проявлений, возрастных особенностей в зависимости от серогруппы возбудителя. Освещаются новые диагностические подходы, возможности специфической профилактики. Акцентируется внимание на важности мониторинга клинико-эпидемиологических особенностей менингококковой инфекции в зависимости от генетических характеристик возбудителя, и необходимости дальнейшего проведения углубленных исследований данной проблемы.

Ключевые слова: менингококковая инфекция; дети; диагностика; профилактика.

BACKGROUND

Meningococcal infection has not lost its epidemiological and social significance worldwide. It is characterized by a variety of clinical appearances, from asymptomatic carrier state to generalized forms with a high risk of life-threatening conditions and fatal outcomes (8%–15%), reaching 40%–80% at septic shock and a significant frequency (10%–20%) of disability after the disease (deafness, mental disability, loss of limbs, etc.) [8, 9, 11–13].

Twelve serogroups of *Neisseria meningitidis* were identified based on the antigenic properties of the capsule polysaccharide, each of which has different epidemiological features, including prevalence, virulence, immunogenicity, and geographical and temporal distribution. However, six of them can cause the disease of a person (A, B, C, W, Y, and X) [1, 11, 14, 36, 38, 45, 48]. According to R. Tsang et al. [50], these invasive strains belong to several genetic lines known as hypervirulent clones belonging to the following sequence types: ST 32, ST 41/44, ST 11, ST 8, ST 5, and ST 269. According to numerous authors [1, 11, 14, 36, 38, 45, 48, 50], all six serogroups of *N. meningitidis* (A, B, C, W, Y, and X) can cause invasive forms of the disease. This review provides information about current clinical and epidemiological features and diagnostic and preventive aspects of the meningococcal infection.

CLINICAL AND EPIDEMIOLOGICAL CHARACTERISTICS OF MENINGOCOCCAL INFECTION

The study of epidemiological and geographical features of the spread of various serogroups of meningococcus is continuing. According to M.V. Abramtseva et al. [1], a serogroup A is characterized by epidemic outbreaks, and serogroups B, C, and Y are characterized by sporadic cases [1]. According to A. Purmohamad [44], in developing countries, including the Western Pacific, Eastern Mediterranean, and African countries, there is an increase in serogroup B; in European and American countries, there is a decrease in serogroup C and even its eradication; there is a tendency to increase serogroup W in some parts of Europe, it is the third most common (after serogroups B and C) [44]. In the Russian Federation, the serogroup characteristics of strains are dominated by *N. meningitidis* serogroups B (27.4%), C (14.1%), and A (10.5%). The number of cases caused by meningococcus serogroup W (8.4%), Y (1.1%), and other serogroups (W/Y, X) continues to increase in 1.7% of cases, but in 36.8% of cases, the serogroup characteristic is not determined[1] [21]. According to A. Purmohamad [44], the prevalence of serogroup B meningococcus in the world reaches 48.5%. According to S. Sridhar, there was also an increase in the frequency of generalized forms of meningococcal infection caused by *N. meningitidis* serogroup B (NmB), despite the constantly changing structure of circulating meningococcal serogroups [46]. However, according to V.N. Racloz [45], M.W. Bijlsma [18], and S. Sridhar [46], it is assumed that the absence of vaccination against meningococcus B in the national calendar of many countries, as well as the use of vaccines that have a protective activity against meningococcus serogroups A, C, W, and Y, may increase the frequency of meningococcus serogroup B. Currently, it is proved that specific vaccination has an effect on the frequency of a spread of various serogroups of meningococci. Thus, according to a number of authors, the use of conjugated serogroup C vaccine resulted in a decrease in the frequency of morbidity caused by a serogroup C [44]. According

[1] About the state of sanitary and epidemiological welfare of the population in the Russian Federation in 2018: State report. Moscow: Federal service for supervision of consumer protection and human welfare. 2019. 254 p.

to R. Tsang [50], the increase in morbidity caused by serogroup W meningococcus is associated with a clonal shift of the strain from ST 22 CC to ST 11 CC. ST 11 CC meningococcus serogroup W clone is a hypervirulent clonal complex and is known in several countries of the world[50].

It should be noted that the gray group view has age-specific features. According to A. Purmohamad [44], meningococci of serogroups C and B have the highest frequency in the age group of 1–4 years and under 1 year, respectively [44]. A serogroup W is most common for middle-aged and older people as reported by R. Tsang [50]. Children of 5 years old are mostly identified with serogroup B strains and those aged 10–24 years with serogroup C strains in the Russian Federation. The proportion of meningococcal serogroup W strains is higher for adolescents and adults than for children of 10 years old[2,3]. It has been reported in the last year that a group C meningococcus causes the disease for men who have sex with men. According to K. Kupferschmidt [35] and J. Lucidarme [36], the first case was discovered in Toronto in 2001, and cases in North America and Europe have also been described. However, the pathogenesis is currently unclear. There are several hypotheses: the first is that men who have sex with men have higher rates of HIV infection than the general population, and this is probably a risk factor. This hypothesis is refused by the fact that many of the men who became ill were HIV negative. In this regard, the second hypothesis is related to the fact that *N. meningitidis* has found a new method of transmission: sometimes the pathogen is detected in the rectum and urethra, and mucosal irritation occurs during oral or anal sex, which can be a risk factor [35, 36]. However, this aspect has not been studied in detail in relation to the reason for the diversity of the gray group view of the age aspect.

[2] About the state of sanitary and epidemiological welfare of the population in the Russian Federation in 2018: State report. Moscow: Federal service for supervision of consumer protection and human welfare. 2019. - 254 p.

[3] Letter of the Federal Service for Surveillance on Consumer Rights Protection and Human Wellbeing dated June 13, 2018 №. 01/7608-2018-32 “About the results of monitoring the incidence of a meningococcal infection and bacterial meningitis in the Russian Federation.”

It is known that meningococcal infection has various clinical forms. *N. meningitidis* is an obligatory human commensal that colonizes the nasopharynx, which is a prerequisite for the transmission and development of a generalized form of a meningococcal infection [39]. Asymptomatic meningococcal carrier state is recognized as an age-dependent phenomenon, the prevalence of which increases in childhood from 4.5% of infants to a peak of 23.7% of 19-year-olds, and then decreases in middle years to 7.8% for 50-year-olds [22, 39]. The capsule is the determining factor of meningococcal virulence, and nonencapsulated meningococci usually do not cause invasive disease [1, 25, 38]. The reasons for determining the absence of a meningococcal capsule are deletion of the gene encoding the capsule and suppression of capsule expression temporarily or permanently by genetic mechanisms [1, 21]. However, the absence of a capsule in meningococcus is because of a change in the phase of genetic capsule synthesis, consisting of five areas: an area A, containing genes necessary for polysaccharide synthesis; an area B, containing genes responsible for lipid modification; an area C, containing *ctr* genes necessary for polysaccharide transport; an area D involved in lipopolysaccharide synthesis; an area E (the function of the *tex* gene homologue present in the area E is currently unknown) [23]. It is important that encapsulated meningococci are genetically diverse because of inter- and intraspecific horizontal genetic exchange.

Absence of areas A and C is the reason for a high proportion (16% ± 4%) of encapsulated meningococci [23]. The loss of the capsule increases the ability of meningococcus to colonize the human nasopharynx and avoid the mechanisms of the human defense system [1, 21, 52]. However, cases of generalized meningococcal infection caused by nonencapsulated meningococci have been described in many studies [26, 30, 51, 52]. The first observation is described by U. Vogel et al. [51] for a 42-year-old immunocompromised adult with severe immunosuppression and a chronic “graft-versus-host” reaction after allogeneic peripheral blood stem cell transplantation. It was known from the medical history of the disease that in January 2001, the patient was diagnosed with an advanced

acute lymphocytic leukemia, and peripheral blood stem cell transplantation from an human leukocyte antigen (HLA)-identical sibling was made (in April 2001) after a myeloablative conditioning regime. The second HLA-identical transplantation of peripheral blood stem cells of a sibling without depletion of T cells was made in February 2003 because of a relapse. The clinical course was complicated by a chronic "graft-versus-host" reaction. The patient was readmitted to the hospital in September 2003 because of chronic progressive diarrhea. Immunosuppression was enhanced. No infectious cause of enteritis could be identified. Clinical signs of sepsis with febrile fever (39°C) and chills were developed during the hospitalization, and there were no pathological elements of the rash. The number of white blood cells was 6.7×10^9/L, the level of C-reactive protein (34.8 mg/L) and interleukin 8 (3279 U/L) were increased. Laboratory tests revealed a nonencapsulated strain of meningococcus. Clinical symptoms of sepsis were disappeared a few h after the start of antibacterial therapy (3 g of piperacillin/combactam iv three times a day) [51].

The second case with an unfavorable outcome of the disease for a 13-year-old immunocompetent girl is described by L. M. Hoang et al. [30]. The child was admitted to the hospital at 2 am with a common rash, impaired consciousness, and a slight rigidity of the occipital muscles. Medical history of the patient revealed that at the beginning of the previous day, the girl returned home from school with symptoms of a respiratory infection, back pain, and nausea, and she had fever at night. The epidemiological studies and life history were not burdened, the immune status was normal. Laboratory tests revealed a nonencapsulated strain of meningococcus. Despite ongoing therapy, including antibacterial (ceftriaxone), she was declared dead from a cardiorespiratory insufficiency 5 h after hospitalization. No signs of immunological disease or structural abnormalities were detected on autopsy, and the reticuloendothelial system was fully developed [30]. H. Findlow et al. [26] reported three cases of generalized meningococcal infection caused by nonencapsulated meningococci. Two cases occurred in March and April 2003 with children aged 12 and 13 while the third case had occurred in April 2004 with an 11-year-old girl. Data on vaccination against meningococcal infection for three patients were not provided, but a mass vaccination campaign was conducted in 2002 using a polysaccharide vaccine with a high coverage of the population in this group, so it is likely that patients received the vaccine 1–2 years before the onset of the disease. All three patients had fever, headache, hemorrhagic elements of a rash, and no signs of impaired consciousness. An objective examination revealed the rigidity of the occipital muscles. All the patients lived in different regions without having a contact with each other. All had a diagnostic lumbar puncture: neutrophilic pleocytosis was detected. Patients responded well to treatment with chloramphenicol and were discharged without visible consequences after 1–2 weeks [26]. Another case is described by Z. Xu et al. [52] for an immunocompetent child (a 7-year-old girl) in China. A febrile fever (39°C), vomiting, and rigidity of the occipital muscles attracted attention at admission, but there were no hemorrhagic elements of a rash and loss of consciousness. The epidemiological studies and life history were not burdened, the immune status was normal. The parents refused to perform diagnostic cerebrospinal puncture. A laboratory study revealed a nonencapsulated strain. The girl recovered after an undergoing antibacterial therapy [52].

Consequently, it is considered that the disease caused by an unencapsulated strain is more likely to occur with the most favorable clinical course and a rapid response to antibacterial therapy [51]. It should be noted that the development of a generalized form of meningococcal infection caused by nonencapsulated meningococci is more typical for immunocompromised people [51]. Nevertheless, cases of the disease have been described for people with normal immune status, but the mechanism of development has not been established and requires study [26, 30, 52]. There is an evidence of a variety of clinical appearances of a generalized meningococcal infection: there may be various atypical appearances that differ depending on the serogroup of the pathogen in addition to the classic appearances (meningococcemia, meningitis, and meningoencephalitis),. For example, primary pneumonia is most often associated with serogroup

Y meningococcus [17, 48]. D.S. Stephens [47] states that primary pneumonia caused by serogroup Y is usually found for adults, especially for people over 50 years of age, and is often associated with an unfavorable prognosis for life (mortality reaches 16%). D.S. Stephens in his work indicates that adolescents and young adults with a meningococcal infection caused by serogroups W and C are most likely to develop septic arthritis, usually monoarticular, affecting mainly the knee and hip joints. Arthritic appearances of patients with a meningococcal infection have a diverse pathogenesis [28]. There are three different mechanisms for their development: (1) primary meningococcal arthritis which is an acute form of acute septic arthritis that almost completely affects large joints; (2) arthritis that complicates acute meningococcal disease (secondary septic arthritis); (3) arthritis that is a hypersensitivity reaction (tertiary arthritis). Primary meningococcal ankle arthritis is an infrequent but expected life-threatening orthopedic emergency. If proper treatment is not carried out, the joint may collapse, which will lead to long-term consequences, including disability [28].

Many authors [4, 10, 14, 17, 34, 41] indicate that a meningococcus serogroup W is characterized by a severe course, high mortality (30%–57%), atypical appearances in the form of enteritis, peritonitis, pneumonia, endocarditis, fasciitis, and epiglottis. M. V. Ivanova et al. [4] in their study similarly emphasize the severe and complicated course of a meningococcal infection caused by a serogroup W, only for older children. Other authors [11] draw attention to the subacute onset of the disease: the appearance of scant hemorrhagic rash preferentially localized to the distal extremities on day 4–6. Unusual appearances of a meningococcal disease caused by a serogroup W associated with severe gastrointestinal symptoms, including abdominal pain and diarrhea, followed by the rapid clinical deterioration and death within 24 h after the beginning of the first symptoms were described by J. Bethea [17] and H. Campbell [20]. M. Aung [14] and J. Bethea [17] reported an extremely rare appearance of the meningococcal infection in the form of meningococcal-W-associated myopericarditis. The suspected pathogenesis of myocarditis, is associated either with the early development of pericarditis due to septic bacteremia or with a delay in the immunological response [14, 49]. Interleukin 6 causes significant myocardial depression in vitro [43]. The removal of interleukin 6 from serum samples of patients with meningococcemia eliminates the negative inotropic activity.

However, data concerning the study of clinical features depending on the serogroup of meningococcus of children and adolescents are not numerous. All of the above indicates the feasibility of further studying the features of clinical appearances of diseases caused by meningococci of various serogroups.

DIAGNOSTIC ASPECTS OF A MENINGOCOCCAL INFECTION

The genome of *N. meningitidis* consists of approximately 2.3 million base pairs and contains approximately 2160 genes. Many genes do not have a known function, but there are unique sites specific to the genus, species, or subspecies of the microorganism. According to S. E. Glazkov et al. [3], among a large number of genes important for the life support of a microorganism, there are "household" genes (housekeeping genes). These genes are responsible for intracellular metabolism (i.e., they provide the processes of glycolysis, biosynthesis of amino acids and nucleotides, protein catabolism, and much more). Changes in the structure of housekeeping genes caused by point mutations and recombination processes lead to important changes in small segments of the genome and the appearance of more highly invasive and virulent clonal variants of the pathogen, which may be associated with diagnostic difficulties [3]. An obligatory stage of laboratory diagnostics is a bacteriological study, the purpose of which is to obtain a culture of the pathogen of a meningococcal infection, its identification to the type, determination of the serogroup by detecting a group-specific antigen (capsule polysaccharide), and a sensitivity to bacterial drugs [11, 42]. According to many authors, the advantage of the bacteriological method is its high specificity (there are no cross-false reactions), the ability to determine the sensitivity to antibacterial drugs. However, the main disadvantages of this

method include the duration of obtaining the result, high requirements for taking the material. An early antibiotic therapy (started before the material was collected) makes it difficult to isolate the pathogen, and therefore the proportion of identified cases of the disease decreases [11, 22, 30, 42]. R.E. Nemescu et al. [42] conducted a study to assess the effect of the antibacterial therapy prescribed before the admission to the hospital as per the results of bacteriological research (blood, cerebrospinal fluid, and nasopharyngeal smear) and the reaction of latex agglutination (cerebrospinal fluid). Among 323 cases of generalized meningococcal infection, 80% (257 cases) were meningeal and 20% (66 cases) were meningococcal. From 323 patients with generalized meningococcal infection, 320 samples of cerebrospinal fluid, 248 blood cultures, and 288 nasopharyngeal smears were analyzed. The reaction of a latex agglutination (cerebrospinal fluid) was made in 122 cases. It was found during the course of the study that the implementation of an antibacterial therapy at the prehospital stage contributed to a decrease in the frequency of verification of the etiological diagnosis to 71.9%. The frequency of obtaining a positive result in the bacteriological study of the cerebrospinal fluid decreased from 55.9% to 27.2%, in the reaction of latex agglutination (cerebrospinal fluid) from 84.6% to 58.8%, in the bacteriological study of blood from 14.7% to 3.5%; the use of antibacterial therapy at the prehospital stage had no statistically significant effect in the study of nasopharyngeal smears (18.9% vs. 15%). The percentage of cases where *N. meningitidis* was identified by two methods decreased from 38.5% to 19.2%, and by three methods from 16.9% to 5.6%. In this study, the authors emphasize that the use of an antibacterial therapy at the prehospital stage decreases the frequency of etiological interpretation of the diagnosis [42]. An effective diagnostic method, the result of which does not depend on the use of the antibacterial therapy before the patient's examination, is a molecular genetic study that is aimed at identifying specific fragments of meningococcal DNA in the clinical material [6, 11]. In most studies [2, 5, 17], a number of advantages of this method were found: the maximum diagnostic power because of the possibility of detecting several copies of the bacterial genome in a sample, speed of a research (within a few h), the method is highly sensitive and allows using samples for diagnostics that do not contain live pathogens, but only fragments of their genetic material [19]. G. Maujean et al. [37] described a case where it was necessary to establish an etiological diagnosis postmortem in the decomposed body of a 27-year-old man. The police investigation indicated that the man was seen alive 10 d ago, when he was bothered by a severe headache, vomiting, and fatigue, but he refused to be hospitalized and preferred to stay at home to rest. The main pathoanatomic findings were hemorrhagic elements of a rash on the skin of the trunk, extremities, and on the epicardium. There were no macroscopic or histological signs of meningitis because of postmortem autolysis. The toxicology results were negative. Blood, urine, cerebrospinal fluid, and feces were subjected to bacteriological examination. *Citrobacter freundii* was isolated from blood culture, and the material was sterile during the examination of urine and feces. The study of cerebrospinal fluid revealed presence of bacteria of *Citrobacter koseri* and *Escherichia coli.* However, the presence of these bacteria could not indicate a reliable result given that the body was in the stage of putrefaction. The search was expanded toward *N. meningitidis* taking into account the hemorrhagic elements of the rash. In the study of the cerebrospinal fluid by the polymerase chain reaction was identified in *N. meningitidis* serogroup [37]. This example illustrates the effectiveness of a molecular genetic research.

The main advantage of the bacteriological research method is the determination of a sensitivity to antibacterial drugs. Antimicrobial resistance in N. *meningitidis* strains is reported to be rare [29]. A.E. Deghmane et al. [24] reported a decrease in the sensitivity to third-generation cephalosporins. B.H. Harcourt [29] and S. Bertrand [16] in their study describe meningococci with a reduced penicillin susceptibility. It should be noted that the resistance to antibacterial drugs occurs in individual strains, but in general, resistance to antimicrobial drugs in *N. meningitidis* strains is rare.

The study of epidemiological and geographical features of the pathogen distribution has been

actively expanded in recent years. The study of invasive strains belonging to various genetic lines, known as hypervirulent clones, becomes relevant. The method of multilocus sequence typing is used in order to clarify the clonal complexes among bacterial populations. Individual information about each strain, including ST, is stored in a standardized form in the public PubMLST database. The database should be updated as information accumulates. According to J. Lucidarme [36] and M.A. Korolevoy [5], combining typing results allows monitoring the genetic characteristics of strains isolated by independent researchers, tracking trends in the emergence and circulation of hypervirulent clones, and analyzing evolutionary changes in the population of *N. meningitidis*.

Methods have been introduced to identify bacterial isolates by time-of-flight mass spectrometry with a matrix-activated laser desorption/ionization (MALDI-TOF) in the past years, followed by an automatic identification of isolated cultures of microorganisms based on comparison of the collected initial spectra with a reference spectra of the database. MALDI-TOF has been adopted as a reliable tool for identifying the majority of bacteria cultured in a routine clinical microbiological practice [31]. However, less data are available to identify *Neisseria* using the MALDI-TOF method, the reliability of which is still a matter of a debate. According to M. Kawahara-Matsumizu [32] and F. Morel [40], there may be erroneous definitions of *Neisseria gonorrhoeae* or *N. meningitidis* and other *Neisseria* species [32, 40]. In other words, a comprehensive use of all possible diagnostic methods will allow you to give the correct etiological interpretation of the diagnosis, and provide an opportunity for more complete epidemiological tracking of the prevalence of various pathogen variants in different territories.

Preventive aspects of a meningococcal infection. Vaccination is the most effective way to prevent a meningococcal infection. Vaccines that protect against meningococcus serogroups A, C, W, and Y have been available in the United States for several decades while vaccines designed to protect against meningococcus serogroup B were first licensed in the United States in 2014 [27]. Vaccination against meningococcal infection was included only in the national vaccination calendar for epidemic indications in the Russian Federation[4]. However, attention was drawn to the low awareness of the population about vaccination against a meningococcal infection. N.E. Basta et al. [15] conducted a survey of adolescent parents regarding awareness of a meningococcal infection and the readiness to vaccinate their children. In this survey 1,997,320 people were participated; the survey was held for 12 d. The survey consisted of 27–31 questions regarding demographic indicators, parents' awareness of vaccines against meningococcal infection, and the readiness to vaccinate their child. Participants were provided with educational materials about a meningococcal infection throughout the survey, including general symptoms, severity and risk, data on meningococcal vaccines, and vaccination schedules. Of the 445 parents who answered the questions fully, the average age was 47.6 years, the majority were women (71.7%), and had a bachelor's degree or higher 64.9%. The average age of their children was 16 years. Approximately 89.2% of parents reported that their child had received at least one vaccine previously (against any serogroup of meningococcus at any age); 75.5% of parents were aware of the existence of vaccination against a meningococcal infection, but approximately two-thirds of all respondents did not know about the vaccines MenACWY, Menactra, and Menveo (quadrivalent vaccines against serogroups A, C, W, and Y). Even more people did not hear about the vaccine against meningococcus serogroup B (Becerra, Trumenba). Only 7% of participants knew that vaccines protect against a serogroup B meningococcus. Four out of five parents surveyed reported that they would like their doctor to provide more information about serogroups B, A, C, W, and Y meningococcus vaccines [17]. According to A. Kempe et al. [33], doctors do not have enough knowledge about vaccination against serogroup B meningococcus, and therefore, they often do not discuss about vaccines with their patients.v The situation is even more depressing in our country. According to E. A. Krieger [7], 83.8% of parents

[4] Report of the Ministry of health of the RF dated March 21, 2014 No. 125n «About an approval of a national preventive vaccination calendar and a vaccination calendar of epidemic indications (as amended on 24 April 2019)».

vaccinate their children in accordance with the national calendar of preventive vaccinations of the Russian Federation (a survey of 733 parents), only in 5.7% of cases, parents vaccinate their children with additional vaccinations, and vaccination against a meningococcal infection accounts for 2.2% [7]. According to the order of the Ministry of Health of the Russian Federation dated March 21, 2014 No. 125n, "About the approval of the national calendar of preventive vaccinations for epidemic indications (as amended on April 24, 2019)," the vaccination against meningococcal infection is carried out only for people at a risk of infection and meningococcal infection. According to the sanitary rules (SP) 3.1.3542-18, "Prevention of meningococcal infection" dated 20.12.2018, first of all, includes people who have communicated with patients with a generalized form of a meningococcal infection (GFMI), who do not have inflammatory changes in the nasopharynx. In this case, the contact person is given emergency chemoprophylaxis with one of the antibacterial drugs (rifampicin, ciprofloxacin, or ampicillin), taking into account contraindications, and specific prevention is made depending on the serogroup of meningococcus isolated from the cerebrospinal fluid and (or) blood of the patient with GFMI. If it is impossible to determine the serogroup affiliation of meningococcus, emergency immunoprophylaxis with multicomponent vaccines is made. Those who are subject to a military conscription should be vaccinated as planned during the interepidemic period; traveling to areas that are endemic for a meningococcal infection (e.g., tourists, athletes, pilgrims, military personnel, athletes, geologists, and biologists); medical workers of structural divisions that provide specialized medical care in the "infectious diseases" profile, medical workers and laboratory staff working with live meningococcal culture; pupils and staff of institutions of inpatient social services with a day-and-night stay (children's homes, orphanages, and boarding schools); residents of dormitories; taking part in mass international sports and cultural events; children less than 5 years of age inclusive; adolescents aged 13–17 years; persons over 60 years old; persons with primary and secondary immunodeficiency conditions, including those infected with HIV; those who have undergone cochlear implantation; persons with liquorrhea. Insufficient awareness of parents and doctors is a serious obstacle to vaccination, and therefore increases the risk of meningococcal infection, which until now remains an unpredictable disease.

CONCLUSION

Meningococcal infection remains extremely relevant because of the variety of serogroups of meningococci that cause generalized forms of a meningococcal infection, the difference in the nature of the disease course and outcomes, the emergence of new diagnostic approaches, epidemiological and clinical features, and the possibilities of a specific prevention. Continuous monitoring of the clinical and epidemiological characteristics of the pathogen depending on the serogroup of meningococcus, especially in the age aspect, is required in this regard. The need for in-depth research to study the clinical and epidemiological features of the pathogen depending on the genetic characteristics of the strains is worth noting as their understanding could contribute to improving the tactics of a treatment of patients, the possibilities of a specific prevention.

REFERENCES

1. Абрамцева М.В., Тарасов А.П., Немировская Т.И. Менингококковая инфекция. Современные представления о возбудителе, эпидемиологии, патогенезе и диагностике. Сообщение 1 // Биопрепараты. Профилактика, диагностика, лечение. – 2014. – № 3. – С. 4–10. [Abramtseva MV, Tarasov AP, Nemirovskaya TI. Meningococcal infection: Modern insight into epidemiology, pathogenesis, diagnosis and causative agent. *Biopreparaty*. 2014;(3):4-10. (In Russ.)]
2. Глазкова С.Э., Носова Е.С., Бакаева Т.Н., и др. Молекулярно-генетический мониторинг *Neisseria meningitidis* на территории республики Беларусь (2006–2010 гг.) // Здравоохранение (Минск). – 2011. – № 11. – С. 10–14. [Glazkova SE, Nosova ES, Bakayeva TN, et al. Neisseria meningitidis molecular-and-genetic monitoring on territory of the Republic of Belarus (2006–2010). *Zdravookhranenie (Minsk)*. 2011;(11)10-14. (In Russ.)]
3. Глазкова С.Э., Носова Е.С., Титов Л.П. Молекулярно-генетический анализ хаускипинг генов *adk* и *aroE* штаммов *Neisseria meningitidis*, выделенных от больных менингитом // Медицинский журнал. –

2007. – № 4. – С. 47–50. [Glazkova SE, Nosova ES, Titov LP. Molekulyarno-geneticheskiy analiz khauskiping genov *adk* i *aroE* shtammov *Neisseria meningitidis*, vydelennykh ot bol'nykh meningitom *Med Zhurnal*. 2007;(4):47–50. (In Russ.)]

4. Иванова М.В., Скрипченко Н.В., Вильниц А.А., и др. Особенности течения генерализованной менингококковой инфекции, вызванной менингококком серогруппы W135 // Детские инфекции. – 2016. – Т. 15. – № 4. – С. 57–60. [Ivanova MV, Skripchenko NV, Vilnits AA, et al. The Course of Generalized Meningococcal Infection Caused by Meningococcus Serogroup W135. *Detskie infektsii*. 2016;15(4): 57-60. (In Russ.)]
5. Королева М.А. Эпидемиологический мониторинг за гнойными бактериальными менингитами в Российской Федерации: Автореф. дис. … канд. мед. наук. – М., 2014. [Koroleva MA. Epidemiologicheskiy monitoring za gnoynymi bakterial'nymi meningitami v Rossiyskoy Federatsii. Moscow; 2014. (In Russ.)]
6. Костюкова Н.Н., Бехало В.А. Современные менингококковые вакцины: сильные и слабые стороны, ближайшие перспективы // Эпидемиология и вакцинопрофилактика. – 2016. – Т. 15. – № 4. – С. 64–73. [Kostyukova NN, Bekhalo VA. Current Meningococcal Vaccines: Advantages and Disadvantages and New Challenges. *Epidemiol Vakcinoprofil*. 2016;15(4): 64-73. (In Russ.)]
7. Кригер Е.А., Самодова О.В., Рогушина Н.Л., и др. Отношение родителей к вакцинации детей и факторы, связанные с отказом от прививок // Педиатрия. Журнал им. Г.Н. Сперанского. – 2016. – Т. 95. – № 2. – С. 91–95. [Krieger EA, Samorodova OV, Rogushina NL, Borisova TA. Parents' attitudes to vaccination of children and factors of vaccinations refuse. *Pediatriia*. 2016;95(2):91-95. (In Russ.)]
8. Лобзин Ю.В., Скрипченко Н.В., Вильниц А.А., и др. Клинико-эпидемиологические аспекты генерализованной менингококковой инфекции у детей и подростков Санкт-Петербурга // Журнал инфектологии. – 2016. – Т. 8. – № 1. – С. 19–25. [Lobzin YuV, Skripchenko NV, Vilnits AA. Clinical and epidemiological aspectsof generalized meningococcal infectionsin children and adolescents of Saint Petersburg. *Z Infektol*. 2016;8(1):19-25. (In Russ.)]
9. Лобзин Ю.В., Скрипченко Н.В., Середняков К.В., Баиндурашвили А.Г. Опыт применения селективной адсорбции липополисахарида в комплексной терапии менингококкового сепсиса у детей (клинические наблюдения) // Медицина: целевые проекты. – 2015. – № 22. – С. 56–59. [Lobzin YuV, Skripchenko NV, Serednyakov KV, Baindurashvili AG. Opyt primeneniya selektivnoy adsorbtsii lipopolisakharida v kompleksnoy terapii meningokokkovogo sepsisa u detey (klinicheskie nablyudeniya). *Meditsina: tselevye proekty*. 2015;(22):56-59. (In Russ.)]
10. Нагибина М.В., Венгеров Ю.Я., Матосова С.В., и др. Генерализованная форма менингококковой инфекции, вызванная *N. meningitidis* серогруппы W, на территории г. Москвы в 2011–2016 гг. // Инфекционные болезни: новости, мнения, обучение. – 2018. – Т. 7. – № 1. – С. 100–105. [Nagibina MV, Vengerov YuYa, Matosova SV, et al. Generalized meningococcal disease caused by *N. meningitidis* serogroup W in Moscow in the years 2011–2016. *Infektsionnye bolezni: novosti, mneniya, obuchenie*. 2018;7(1):100-105. (In Russ.)]
11. Скрипченко Н.В., Вильниц А.А. Менингококковая инфекция у детей: руководство для врачей. – СПб.: Тактик-Студио, 2015. – 840 с. [Skripchenko NV, Vil'nits AA. Meningokokkovaya infektsiya u detey: rukovodstvo dlya vrachey. Saint Petersburg: Taktik-Studio; 2015. 840 p. (In Russ.)]
12. Фельдблюм И.В., Новгородова С.Д., Гореликова Е.В. Эпидемиология и новые возможности специфической профилактики менингококковой инфекции в условиях реального времени // Поликлиника. – 2018. – № 2. – С. 24–27. [Feldblyum IV, Novgorodova SD, Gorelikova EV. Epidemiology and new opportunities for real-time specific prevention of meningococcal infection. *Poliklinika*. 2018;(2):24-27. (In Russ.)]
13. Ali A, Jafri RZ, Messonnier N, et al. Global practices of meningococcal vaccine use and impact on invasive disease. *Pathog Glob Health*. 2014;108(1):11-20. https://doi.org/10.1179/2047773214Y.0000000126.
14. Aung M, Raith E, Williams E, Burrell AJ. Severe meningococcal serogroup W sepsis presenting as myocarditis: A case report and review of literature. *J Intensive Care Soc*. 2019;20(2):182-186. https://doi.org/10.1177/1751143718794127.
15. Basta NE, Becker AB, Li Q, Nederhoff D. Parental awareness of Meningococcal B vaccines and willingness to vaccinate their teens. *Vaccine*. 2019;37(4):670-676. https://doi.org/10.1016/j.vaccine.2018.11.078.
16. Bertrand S, Carion F, Wintjens R, et al. Evolutionary changes in antimicrobial resistance of invasive Neisseria meningitidis isolates in Belgium from 2000 to 2010: increasing prevalence of penicillin nonsusceptibility. *Antimicrob Agents Chemother*. 2012;56(5): 2268-2272. https://doi.org/10.1128/AAC.06310-11.
17. Bethea J, Makki S, Gray S, et al. Clinical characteristics and public health management of invasive meningococcal group W disease in the East Midlands region of England, United Kingdom, 2011 to 2013. *Euro Surveill*. 2016;21(24). https://doi.org/10.2807/1560-7917.ES.2016.21.24.30259.
18. Bijlsma MW, Bekker V, Brouwer MC, et al. Epidemiology of invasive meningococcal disease in the Netherlands, 1960–2012: an analysis of national surveillance data.

Lancet Infect Dis. 2014;14(9):805-812. https://doi.org/10.1016/s1473-3099(14)70806-0.
19. Braunova A, Krbkova L, Rainetova P, et al. Clinical and laboratory characteristics of enteroviral meningitis in children, including qRT-PCR and sequencing analysis. *Biomed Pap Med Fac Univ Palacky Olomouc Czech Repub*. 2019;163(4):355-361. https://doi.org/10.5507/bp.2018.082.
20. Campbell H, Ladhani S. The importance of surveillance: Group W meningococcal disease outbreak response and control in England. *Int Health*. 2016;8(6):369-371. https://doi.org/10.1093/inthealth/ihw037.
21. Caugant DA, Tzanakaki G, Kriz P. Lessons from meningococcal carriage studies. *FEMS Microbiol Rev*. 2007;31(1):52-63. https://doi.org/10.1111/j.1574-6976.2006.00052.x.
22. Christensen H, May M, Bowen L, et al. Meningococcal carriage by age: a systematic review and meta-analysis. *Lancet Infect Dis*. 2010;10(12):853-861. https://doi.org/10.1016/s1473-3099(10)70251-6.
23. Claus H, Maiden MCJ, Maag R, et al. Many carried meningococci lack the genes required for capsule synthesis and transport. *Microbiology*. 2002;148(Pt 6):1813-1819. https://doi.org/10.1099/00221287-148-6-1813.
24. Deghmane AE, Hong E, Taha MK. Emergence of meningococci with reduced susceptibility to third-generation cephalosporins. *J Antimicrob Chemother*. 2017;72(1):95-98. https://doi.org/10.1093/jac/dkw400.
25. Feavers IM, Maiden MCJ. Recent Progress in the Prevention of Serogroup B Meningococcal Disease. *Clin Vaccine Immunol*. 2017;24(5). https://doi.org/10.1128/CVI.00566-16.
26. Findlow H, Vogel U, Mueller JE, et al. Three cases of invasive meningococcal disease caused by a capsule null locus strain circulating among healthy carriers in Burkina Faso. *J Infect Dis*. 2007;195(7):1071-1077. https://doi.org/10.1086/512084.
27. Folaranmi T, Rubin L, Martin SW, et al. Centers for Disease Control (CDC). Use of Serogroup B Meningococcal Vaccines in Persons Aged ≥10 Years at Increased Risk for Serogroup B Meningococcal Disease: Recommendations of the Advisory Committee on Immunization Practices, 2015. *MMWR Morb Mortal Wkly Rep*. 2015;64(22):608-612.
28. Gómez BO, Feito CR, Vázquez DG, et al. Primary Meningococcal Septic Arthritis Case Report and Literature Review of an Unusual Manifestation of Meningococcal Disease. *Bull Hosp Jt Dis (2013)*. 2019;77(2):140-145.
29. Harcourt BH, Anderson RD, Wu HM, et al. Population-Based Surveillance of Neisseria meningitidis Antimicrobial Resistance in the United States. *Open Forum Infect Dis*. 2015;2(3):ofv117. https://doi.org/10.1093/ofid/ofv117.
30. Hoang LM, Thomas E, Tyler S, et al. Rapid and fatal meningococcal disease due to a strain of Neisseria meningitidis containing the capsule null locus. *Clin Infect Dis*. 2005;40(5):e38-42. https://doi.org/10.1086/427875.
31. Hong E, Bakhalek Y, Taha MK. Identification of Neisseria meningitidis by MALDI-TOF MS may not be reliable. *Clin Microbiol Infect*. 2019;25(6):717-722. https://doi.org/10.1016/j.cmi.2018.09.015.
32. Kawahara-Matsumizu M, Yamagishi Y, Mikamo H. Misidentification of Neisseria cinerea as Neisseria meningitidis by Matrix-Assisted Laser Desorption/Ionization Time of Flight Mass Spectrometry (MALDI-TOF MS). *Jpn J Infect Dis*. 2018;71(1):85-87. https://doi.org/10.7883/yoken.JJID.2017.183.
33. Kempe A, Allison MA, MacNeil JR, et al. Adoption of Serogroup B Meningococcal Vaccine Recommendations. *Pediatrics*. 2018;142(3). https://doi.org/10.1542/peds.2018-0344.
34. Knol M, Ruijs WLM, Melker HE, et al. Sudden increase of invasive meningococcal disease serogroup W in 2015 and 2016. *Infectieziekten Bulletin*. 2017;28(1):23-28.
35. Kupferschmidt K. Infectious diseases. Bacterial meningitis finds new niche in gay communities. *Science*. 2013;341(6144):328. https://doi.org/10.1126/science.341.6144.328.
36. Lucidarme J, Hill DM, Bratcher HB, et al. Genomic resolution of an aggressive, widespread, diverse and expanding meningococcal serogroup B, C and W lineage. *J Infect*. 2015;71(5):544-552. https://doi.org/10.1016/j.jinf.2015.07.007.
37. Maujean G, Guinet T, Fanton L, Malicier D. The interest of postmortem bacteriology in putrefied bodies. *J Forensic Sci*. 2013;58(4):1069-1070. https://doi.org/10.1111/1556-4029.12155.
38. McNamara LA, Potts CC, Blain A, et al. Invasive Meningococcal Disease due to Nongroupable Neisseria meningitidis-Active Bacterial Core Surveillance Sites, 2011-2016. *Open Forum Infect Dis*. 2019;6(5):ofz190. https://doi.org/10.1093/ofid/ofz190.
39. Miglietta A, Innocenti F, Pezzotti P, et al. Carriage rates and risk factors during an outbreak of invasive meningococcal disease due to *Neisseria meningitidis* serogroup C ST-11 (cc11) in Tuscany, Italy: a cross-sectional study. *BMC Infect Dis*. 2019;19(1):29. https://doi.org/10.1186/s12879-018-3598-3.
40. Morel F, Jacquier H, Desroches M, et al. Use of Andromas and Bruker MALDI-TOF MS in the identification of *Neisseria*. *Eur J Clin Microbiol Infect Dis*. 2018;37(12):2273-2277. https://doi.org/10.1007/s10096-018-3368-6.
41. Mustapha MM, Marsh JW, Harrison LH. Global epidemiology of capsular group W meningococcal disease (1970–2015): Multifocal emergence and persistence of hypervirulent sequence type (ST)-11 clonal com-

plex. *Vaccine*. 2016;34(13):1515-1523. https://doi.org/10.1016/j.vaccine.2016.02.014.
42. Nemescu RE, Iancu LS, Dorneanu OS, et al. Influence of antibiotic therapy prior to admission on the efficacy of classical methods for the diagnosis of meningococcal disease. *Rev Med Chir Soc Med Nat Iasi*. 2014;118(2):497-502.
43. Pathan N, Hemingway CA, Alizadeh AA, et al. Role of interleukin 6 in myocardial dysfunction of meningococcal septic shock. *Lancet*. 2004;363(9404):203-209. https://doi.org/10.1016/s0140-6736(03)15326-3.
44. Purmohamad A, Abasi E, Azimi T, et al. Global estimate of *Neisseria meningitidis* serogroups proportion in invasive meningococcal disease: A systematic review and meta-analysis. *Microb Pathog*. 2019;134:103571. https://doi.org/10.1016/j.micpath.2019.103571.
45. Racloz VN, Luiz SJ. The elusive meningococcal meningitis serogroup: a systematic review of serogroup B epidemiology. *BMC Infect Dis*. 2010;10:175. https://doi.org/10.1186/1471-2334-10-175.
46. Sridhar S, Greenwood B, Head C, et al. Global incidence of serogroup B invasive meningococcal disease: a systematic review. *Lancet Infect Dis*. 2015;15(11):1334-1346. https://doi.org/10.1016/s1473-3099(15)00217-0.
47. Stephens DS, Apicella MA. *Neisseria meningitidis*. In: Mandell, Douglas, and Bennett's principles and practice of infectious diseases. Ed. by J.E. Bennett, R. Dolin, M.J. Blaser. Philadelphia: Elsevier Saunders; 2015. p. 2425-2445.
48. Stephens DS. Biology and pathogenesis of the evolutionarily successful, obligate human bacterium Neisseria meningitidis. *Vaccine*. 2009;27: B71-B77. https://doi.org/10.1016/j.vaccine.2009.04.070.
49. Taldir G, Parize P, Arvis P, Faisy C. Acute right-sided heart failure caused by *Neisseria meningitidis*. *J Clin Microbiol*. 2013;51(1):363-365. https://doi.org/10.1128/JCM.02264-12.
50. Tsang R, Hoang L, Tyrrell GJ, et al. Increase in *Neisseria meningitidis* serogroup W invasive disease in Canada: 2009-2016. *Can Commun Dis Rep*. 2017;43(7-8):144-149.
51. Vogel U, Claus H, von Muller L, et al. Bacteremia in an immunocompromised patient caused by a commensal *Neisseria meningitidis* strain harboring the capsule null locus (cnl). *J Clin Microbiol*. 2004;42(7):2898-2901. https://doi.org/10.1128/JCM.42.7.2898-2901.2004.
52. Xu Z, Zhu B, Xu L, et al. First case of *Neisseria meningitidis* capsule null locus infection in China. *Infect Dis (Lond)*. 2015;47(8):591-592. https://doi.org/10.3109/00365548.2015.1010228.

◆ Information about the authors

Ksenija V. Markova — Postgraduate Student, Department of Neuroinfections and Organic Pathology of the Nervous System. Federal State Financed Institution Pediatric Research and Clinical Center for Infectious Diseases under the Federal Medical Biological Agency, Saint Petersburg, Russia. E-mail: ksenija-sidorova@mail.ru.

Natalia V. Skripchenko — MD, PhD, Dr Med Sci, Honored Scientist of the Russian Federation, Professor, Deputy Director for Research, Federal State Financed Institution Pediatric Research and Clinical Center for Infectious Diseases, Saint Petersburg, Russia; Head of the Department of Infectious Diseases, Saint Petersburg State Pediatric Medical University, Saint Petersburg, Russia. E-mail: snv@niidi.ru.

Yuriy V. Lobzin — MD, PhD, Dr Med Sci, acad. Russian Academy of Sciences. Federal State Financed Institution Pediatric Research and Clinical Center for Infectious Diseases under the Federal Medical Biological Agency, Saint Petersburg, Russia. E-mail: niidi@niidi.ru.

Vadim E. Karev — MD, PhD, Dr Med Sci, Head of the Department of Tissue and Pathomorphological Methods. Federal State Financed Institution Pediatric Research and Clinical Center for Infectious Diseases under the Federal Medical Biological Agency, Saint Petersburg, Russia. E-mail: vadimkarev@yandex.ru.

◆ Информация об авторах

Ксения Витальевна Маркова — аспирант, отдел нейроинфекций и органической патологии нервной системы. ФГБУ «Детский научно-клинический центр инфекционных болезней Федерального медико-биологического агентства», Санкт-Петербург. E-mail: ksenija-sidorova@mail.ru.

Наталья Викторовна Скрипченко — д-р мед. наук, Заслуженный деятель науки Российской Федерации, профессор, заместитель директора по научной работе, ФГБУ «Детский научно-клинический центр инфекционных болезней Федерального медико-биологического агентства», Санкт-Петербург; заведующая кафедрой инфекционных болезней ФП и ДП, ФГБОУ ВО «Санкт-Петербургский государственный педиатрический медицинский университет» Минздрава России, Санкт-Петербург. E-mail: snv@niidi.ru.

Юрий Владимирович Лобзин — академик РАН, заслуженный деятель науки РФ, д-р. мед. наук, профессор, директор. ФГБУ «Детский научно-клинический центр инфекционных болезней Федерального медико-биологического агентства», Санкт-Петербург. E-mail: niidi@niidi.ru.

Вадим Евгеньевич Карев — д-р. мед. наук, руководитель отдела тканевых и патоморфологических методов исследования. ФГБУ «Детский научно-клинический центр инфекционных болезней Федерального медико-биологического агентства», Санкт-Петербург. E-mail: vadimkarev@yandex.ru.

◆ Information about the authors

Alla A. Vilnits — MD, Ph.D., Art. Scientific Member of the Department of Neuroinfections and Organic Pathology of the Nervous System, Federal State Financed Institution Pediatric Research and Clinical Center for Infectious Diseases, Saint Petersburg, Russia; Associate Professor of the Department of Infectious Diseases, Saint Petersburg State Pediatric Medical University, Saint Petersburg, Russia. E-mail: vilnitz@mail.ru.

Eugeniy Yu. Gorelik — MD, Ph.D, Acting Head of the Department of Neuroinfections and Organic Pathology of the Nervous System. Federal State Financed Institution Pediatric Research and Clinical Center for Infectious Diseases under the Federal Medical Biological Agency, Saint Petersburg, Russia. E-mail: e.gorelik@mail.ru.

Elvira A. Martens — Head of the Laboratory of Medical Microbiology. Federal State Financed Institution Pediatric Research and Clinical Center for Infectious Diseases under the Federal Medical Biological Agency, Saint Petersburg, Russia. E-mail: eamartens@yandex.ru.

Sergey V. Sidorenko — Head of the Department of Molecular Microbiology and Epidemiology. Federal State Financed Institution Pediatric Research and Clinical Center for Infectious Diseases under the Federal Medical Biological Agency, Saint Petersburg, Russia. E-mail: e-mail:sidorserg@gmail.com.

◆ Информация об авторах

Алла Ароновна Вильниц — канд. мед. наук, ст. научн. сотрудник отдела нейроинфекций и органической патологии нервной системы, ФГБУ «Детский научно-клинический центр инфекционных болезней Федерального медико-биологического агентства», Санкт-Петербург; доцент кафедры инфекционных болезней ФП и ДП, ФГБОУ ВО «Санкт-Петербургский государственный педиатрический медицинский университет» Минздрава России, Санкт-Петербург. E-mail: vilnitz@mail.ru.

Евгений Юрьевич Горелик — канд. мед. наук, исполняющий обязанности руководителя отдела нейроинфекций и органической патологии нервной системы. ФГБУ «Детский научно-клинический центр инфекционных болезней Федерального медико-биологического агентства», Санкт-Петербург. E-mail: e.gorelik@mail.ru.

Эльвира Акрамовна Мартенс — заведующая лабораторией медицинской микробиологии. ФГБУ «Детский научно-клинический центр инфекционных болезней Федерального медико-биологического агентства», Санкт-Петербург. E-mail: eamartens@yandex.ru.

Сергей Владимирович Сидоренко — руководитель отдела молекулярной микробиологии и эпидемиологии. ФГБУ «Детский научно-клинический центр инфекционных болезней Федерального медико-биологического агентства», Санкт-Петербург. E-mail: e-mail:sidorserg@gmail.com.