

A Resuscitation Specialist's View of The Problems Arising in The Treatment of Generalized Meningococcal Infection in Children

Ermachenko M.F.^{1,2}, Zemin Yu.A.¹, Ivanov R.A.¹, Sergeeva L.I.¹, Nomokonov V.I.¹, Homeland of Yu.R.^{1,2}, Goruda I.S.^{1,2}, Vanteeva I.A.^{1,2}, Bautina Yu.A.^{1,2}, Sergeeva S.A.^{1,2}, Dengub L.N.¹, Kokorin V.A.^{1,3}, Grafkina Ya.V.⁴, Daro Bratsk*

¹State Budgetary Healthcare Institution "Bratsk Children's City Hospital", Russia, Irkutsk Region.

²Irkutsk State Medical University, Russia, Irkutsk.

³Regional State Budgetary Healthcare Institution "Bratsk District Hospital".

⁴KDRTs "Sanad" LLP, Kazakhstan, Karaganda.

***Corresponding Author:** Daro Bratsk., State Budgetary Healthcare Institution "Bratsk Children's City Hospital", Russia, Irkutsk Region.

Received Date: 20 October, 2025 | **Accepted Date:** 05 November, 2025 | **Published Date:** 10 December, 2025

Citation: Ermachenko M.F., Zemin Yu. A., Ivanov R.A., Sergeeva L.I., Nomokonov V.I., et al, (2025), A Resuscitation Specialist's View of The Problems Arising in The Treatment of Generalized Meningococcal Infection in Children, *Journal of Clinical Surgery and Research*, 6(7); DOI:10.31579/2768-2757/190

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Abstract:

Meningococcal disease is an anthroponotic disease transmitted by meningococcal carriers, patients with meningococcal nasopharyngitis, and generalized forms of the infection. Transmission is via airborne droplets and household contact. The incubation period is 1-7 days. [1]. Meningococcal infection is characterized by a periodicity, with intervals of 10-20 years between peaks, which, according to our observations, has recently become apparent and underscores the relevance of this problem. Children (70-80%) and young adults are predominantly affected.

keywords: meningococcal infection; figures; diagnosis; infectious-toxic

Introduction

Meningococcal infection has a pronounced seasonal nature, is characterized by an acute onset and, despite treatment, often ends fatally due to the development of complications (septic shock, meningococcal meningitis, adrenal damage, cerebral edema) [1, 3, 8, 9, 10, 11]. Most fatalities occur within 1-2 days of illness from fulminant (hypertoxic) meningococemia, and less commonly from the mixed (meningitis and meningococemia) form of infection. In these forms, hemorrhages into the adrenal glands (Waterhouse-Fredericksen syndrome) are most common, leading to the development of refractory septic shock and causing death in almost 100% of victims. [3, 8, 9, 10]. According to the data of the information and analytical review prepared in 2022 by the Russian Reference Center for Monitoring Bacterial Meningitis at the Central Research Institute of Epidemiology of the Federal Service for Surveillance on Consumer Rights Protection and Human Wellbeing, the incidence and mortality from meningococcal infection have a decreasing trend. [17] However, despite the fairly well-studied characteristics of meningococcal infection, its etiology, pathogenesis, and seemingly proven treatment regimens, in 2022 the incidence of GFMI increased by 2 times, amounting to 0.44 per 100 thousand population. In addition, in

2022 the mortality rate from GFMI increased, amounting to 16% (for comparison, in 2020 - 12%). According to the state report of Rospotrebnadzor, in 2024 the incidence rate of generalized forms of meningococcal infection (GFMI) amounted to 0.47 per 100 thousand population [12]. According to some authors, the mortality rate for septic shock developing against the background of meningococcal infection reaches 100%, and a fatal outcome in the overwhelming majority of cases (90.9%) occurs within the first 24 hours of hospitalization [8]. It is characteristic that other authors also cite practically identical figures in their studies [9]. These data confirm the particular severity of the infection and the need for timely, adequate care for patients with meningococcal infection.

Purpose of the study

To analyze the causes of fatal outcomes of generalized forms of meningococcal infection using the example of the intensive care unit of the Bratsk Children's City Hospital for the period from 1988 to 2024.

Material and methods

During the analyzed period (1988-2024), 119 children with the diagnosis of generalized meningococcal infection, meningococemia and/or meningococcal meningitis, and/or mixed form, including 10 with a fulminant form, were treated in the intensive care unit of the Bratsk Children's City Hospital. The years (2009, 2011, 2014, 2019) when patients with meningococcal infection were not admitted to the intensive

care unit are noted. The average age of patients was 1.4 years (min - 4 months, max - 11 years). Boys - 54.6% (65 patients), girls - 45.4% (54 patients). The average bed-day in the intensive care unit was 4 days (min - 1 bed-day, max - 14 bed-days). The mortality rate in this group of patients was 12.6% (15 patients), which is comparable with data from the Federal Budgetary Institution of Health "Center for Hygiene Education of the Population" of Rospotrebnadzor [16].

Cause of death:	Period 1988 – 2024
Lightning form, ITSH (III – IV century)	10
Late hospitalization	2
Severe concomitant pathology	1
Incorrect tactics at the pre-hospital stage	1
Incorrect hospital tactics	1
Total:	15

Table 1: The main causes of deaths are reflected in Table No. 1

Results and discussion:

Our data show that the most common cause of death is the rapid progression of meningococcal infection (in 10 of 15 cases), with the development of refractory septic shock, with or without Waterhouse-Friderichsen syndrome (adrenal hemorrhage). In these cases, even appropriate prehospital and in-hospital management failed to produce the desired results. Late hospitalization resulted in underestimation of the child's condition during the pre-hospital phase. Symptoms such as high fever, nonspecific signs of intoxication (lethargy, weakness, headache, loss of appetite) in the absence of characteristic skin rashes, meningeal symptoms, and vomiting are sometimes misinterpreted as signs of acute respiratory viral infection. In these cases, appropriate treatment is prescribed with a recommendation for a follow-up examination by a local physician the following day. This lost time resulted in two fatal outcomes; in both cases, the children were hospitalized only after a second call to the ambulance. In one case, the cause of death was the administration of penicillin during the prehospital phase. The diagnosis of meningococcal infection was correct, but the administration of a bactericidal antibiotic without considering the risk of endotoxemia led to the development of refractory septic shock. The cause of death, related to improper hospital management, was the early discontinuation of chloramphenicol and the switch to penicillin. The patient's general condition 36 hours after treatment was mistakenly assessed as severe with improvements (decreased temperature, no new rash, adequate diuresis, and relatively stable hemodynamics despite the use of cardiotonic agents). The administration of penicillin led to a deterioration in the patient's condition, a return of shock symptoms, and ultimately, death. Taking into account the analyzed period, we compared modern approaches to the treatment of meningococcal infection and treatment regimens used in our department in earlier years. Before the introduction of Clinical Guidelines (CG) for the treatment of meningococcal infection in children, in our practice we used the methodological recommendations of the Ministry of Health of the RSFSR of the Leningrad Research Institute of Children's Infections dated January 16, 1985, "Meningococcal Infection in Children (Clinical Features, Diagnosis, Treatment)", which included the administration of massive doses of glucocorticosteroids, the administration of antibiotics, infusion therapy, antithrombotic therapy, as well as a detailed symptomatic treatment. From the perspective of a resuscitation specialist or intensive care physician, these guidelines placed somewhat more

emphasis on preventing severe complications of meningococcal infection than current clinical guidelines. For example, if a patient presented with symptoms of septic (infectious-toxic) shock, the initial therapy recommended was the administration of bacteriostatic chloramphenicol (IV) at a dose of 80-100 mg/kg/day, either intramuscularly or intravenously, with a 6-hour interval for 24-48 hours. These recommendations were justified by the significant risk of worsening the condition and causing death due to possible endotoxemia associated with the use of bactericidal antibiotics (penicillin) before the patient recovered from shock. As resuscitation specialists, we believe this approach to treatment is pathogenetically justified, and the cases and causes of death we cited, in our opinion, support this view. Unfortunately, intensive care physicians are well aware of the complexity of treating septic shock, the mortality rate of which remains very high today [15]. Treating septic shock, even in a hospital setting, is a challenging task in all countries [1, 2, 3, 4, 5, 6, 7, 10, 11]. In our opinion, the development of septic shock at the prehospital stage significantly increases the risk of an unfavorable outcome. In this regard, we believe it is very important and appropriate to use current recommendations to administer antibacterial drugs only when rapid (up to 90 minutes) hospitalization is impossible, at least in some patients (suspected meningitis, absence of hemorrhagic rash). However, parenteral use of chloramphenicol is currently extremely limited due to its toxicity and the potential for severe adverse reactions, as reflected in current guidelines for meningococcal infection. Indeed, data from various studies necessitate a serious reconsideration of previously existing approaches to antibacterial therapy. The incidence of irreversible aplastic anemia following oral or intravenous chloramphenicol use is known to vary widely among different investigators and is estimated to range from 1:6,000 to 1:45,000 cases of use [13]. According to the Scottish Antimicrobial Prescribing Group, the incidence of aplastic anemia in patients taking chloramphenicol is estimated to be 1 in 24,000–40,000 patients and is often dose-independent. Only 22% of cases of aplastic anemia developed during or shortly after treatment. In other cases, this severe complication arose weeks and even months after the treatment [14]. Currently, according to the State Register of Medicines, there is no approved parenteral form of chloramphenicol in the Russian Federation. We can note that, fortunately, over the years of parenteral use of chloramphenicol, we have never observed any such adverse reactions. At the same time, in our neighboring Republic of Kazakhstan, intravenous chloramphenicol is approved for use and is included in clinical guidelines

for the treatment of meningococcal infection [16]. In our opinion, the previously accepted prescription of antithrombotic therapy deserves special attention. Current guidelines note the potential for serious complications of meningococcal infection, such as deep necrosis and mummification of the distal extremities. Surgical treatment is recommended, with no options for preventing these complications. This problem remains relevant today, as evidenced by the following example from the UK: A 3-year-old girl was called to see a doctor because of fever, drowsiness, and a rash. The doctor suspected meningococcal infection and administered an intramuscular injection of penicillin. Her condition worsened, with altered consciousness, shock, and widespread purpura. The child was urgently hospitalized in the intensive care unit, where microscopy of the skin area affected by the purpura revealed meningococci. Multiple organ failure required inotropic support and mechanical ventilation. Three fingers of her left hand were amputated due to necrosis. Five days later, the child's condition improved, and she was transferred from the intensive care unit. [2] Similar complications have been described elsewhere [6]. Antithrombotic therapy was not used in this case. During the specified observation period, we managed to avoid such complications in our practice. We believe this was facilitated by the use of heparin at a dose of 150-300 U/kg/day intravenously, depending on the patient's age and weight, as well as clinical and laboratory data. In our opinion, the use of heparin in the treatment of generalized forms of meningococcal infection, in the setting of DIC syndrome, is pathogenetically justified, of course, taking into account the clinical situation and known contraindications.

Conclusions

1. Emergency medical personnel and local physicians should be alert for meningococcal infection when examining a child with severe symptoms of intoxication. If meningococcal infection is suspected, the child should be urgently hospitalized for diagnosis and treatment.
2. The administration of bactericidal drugs at the pre-hospital stage carries a serious risk of developing endotoxemia with subsequent development of severe hemodynamic disorders, which requires careful consideration of all risk factors before starting antibacterial therapy.
3. The use of heparin or (if possible) low molecular weight heparins helps to avoid serious complications such as tissue necrosis with subsequent amputation of parts of the limbs, as well as delayed impairment of renal and myocardial function.

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