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SPECIAL PAPER

Recommendations of the Polish Paediatric Society, the Polish Society of Vaccinology, and the Polish Society of Family Medicine on meningococcal vaccinations in children and adults in Poland

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ABSTRACT

Invasive meningococcal disease is a dangerous bacterial infection that often leads to death or permanent disability. Immunization is the best strategy to protect individuals against invasive infections caused by Neisseria meningitidis. The effectiveness of vaccines has been demonstrated in many countries where they have been introduced into national vaccination programs.

Meningococcal vaccinations in Poland are recommended in the framework of the National Immunization Program. However, they are not reimbursed, meaning the patient or parent covers vaccination costs. In addition, insufficient public awareness of the disease course and risks associated with meningococcal infection, the need for immunization in the first year of a child's life, the number of doses administered, and the price of the vaccines are barriers to the acceptance and implementation of meningococcal immunization, especially in the youngest children.

Recommendations for physicians implementing meningococcal vaccination in children and adults are the result of the work of an expert group.

KEY WORDS:

meningococcal vaccinations, invasive meningococcal disease, recommendations.

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INTRODUCTION

EPIDEMIOLOGY

Invasive meningococcal disease (IMD) is a relatively rare infectious condition; however, it is always a serious threat to health and life. According to reports by the National Institute of Public Health – National Institute of Hygiene (NIZP-PZH), about 200 annual cases of IMD were reported in Poland before the coronavirus disease 2019 (COVID-19) pandemic [1]. Detailed epidemiological data, including the proportion of individual *Neisseria meningitidis* serogroups, are analysed and published annually by the National Reference Centre for the Diagnosis of Bacterial Infections of the Central Nervous System (KOROUN). Results of KOROUN studies consistently demonstrate that IMD can occur at any age, but the highest incidence is in children under 5 years of age and infants in their first year of life. Among infants, most cases of IMD occur in the latter half of the first year of life, so it is essential to start meningococcal vaccination as early as possible.

According to KOROUN data, serogroup B (MenB) is the most common cause of IMD in the youngest children, accounting for more than 60% of all cases. Serogroups C and W (MenC and MenW, respectively) are responsible for the remaining cases. In 2021, KOROUN confirmed 86 cases of IMD, where MenB was responsible for 58 (67%), MenC for 16 (19%), and MenW for 10 cases (12%). The overall mortality rate was 11.6%, and the mortality rate calculated only for cases with known outcomes was 31.3%. In 2019 (before the COVID-19 pandemic), KOROUN confirmed 167 cases of IMD; MenB accounted for 110 (66%), MenC for 34 (20%), and MenW for 19 cases (11%) [2]. Since 2014, Poland and other European countries have seen a marked increase in the incidence of IMD caused by serogroup W. In children and adolescents, the disease caused by serogroup W may present with non-specific gastrointestinal symptoms, making diagnosis difficult and delaying appropriate treatment [3]. According to data from 2013–2017 published by KOROUN, mortality caused by serogroup W was the highest at 38.5%; the mortality of serogroup B was 13.5%, and serogroup C was 11.2% [4].

DISEASE DIAGNOSIS

Early IMD diagnosis at a family doctor's or paediatrician's office is challenging. The patient may initially present with seemingly harmless upper respiratory tract infection symptoms and fever. However, characteristic IMD symptoms, such as petechiae, do not appear until the advanced stage of the disease and are not present in all patients [5]. Due to the rapid clinical course, the time available for a doctor to recognize the disease and initiate treatment is short. Moreover, doctors working exclusively in primary care do not have the opportunity to gain experience in the recognition, diagnosis, and management of IMD, which may contribute to delayed diagnosis, late referral of patients to hospital resulting in treatment failure, increased risk of complications, and patient death.

PROPHYLAXIS

Vaccines are an effective form of protection against IMD. Table 1 presents the vaccines available in Poland for IMD prophylaxis (MenB, MenACWY, MenC). According to the 2022 national immunization program, meningococcal vaccinations are recommended after 6 or 8 weeks of age, depending on the type of vaccine [6].

EFFECTIVENESS AND SAFETY OF VACCINES

Countries that have introduced mass meningococcal vaccination have significantly reduced IMD cases. The most comprehensive analysis of the real-world effectiveness of meningococcal vaccines was conducted in the UK. In 1999, the UK introduced mass MenC vaccination in infants with a time-limited catch-up immunization program in children up to the age of 18 years. This led to a rapid and sustained decrease in cases of serogroup C-induced IMD [6]. The MenC/Hib vaccine is administered to children aged 12 months, while MenACWY is administered in the teenage years (9th or 10th year of schooling). In 2015, the UK introduced mass vaccination against MenB in a 2 + 1 schedule (at 8 and 16 days of life and a catch-up dose at 12 months), administered concomitantly with other vaccines recommended in the immunization program (DaTP-Hib-IPV, PCV, RV, and MMR).

ESTIMATED *IN VITRO* VACCINE EFFECTIVENESS IN POLAND

KOROUN conducted *in vitro* studies on MenB isolates using exMATS and gMATS (Meningococcal Antigen Typing System). Studies show that antigens contained in the 4CMenB vaccine are 83.3–86.6%, consistent with those present in MenB isolates from Polish patients. Such a result allows an estimation of the efficacy of the 4CMenB vaccine against *N. meningitidis* serogroup B strains occurring in Poland at the level of at least 83% in addition to 98.5%, 88.6%, and 93.5% against the 3 most common MenB clonal complexes: cc32, cc18, and cc41/44, respectively [7–10]. In addition, tests for MenB-fHbp were conducted using the Meningococcal Antigen Surface Expression (MEASURE) assay to measure the correlation of the expression level of the vaccine antigen (fHbp protein) on the surface of group B meningococci with the bactericidal efficacy of antibodies in human serum determined by serum bactericidal assay (hSBA). The analysis included more than 2150 MenB isolates from

TABLE 1. Meningococcal vaccines available in Poland

Serogroup	Vaccine (Date of latest SmPC/EMA)	Manufacturer	Age restrictions	Number of doses of the complete vaccination schedule depending on the age of the first dose
B	Bexsero (4cMenB) (25.02.2022)	GSK Vaccines	> 8 weeks	Primary vaccinations Infants 2–5 months: 2 or 3 doses Infants > 6 months: 2 doses Booster dose Up to and including 23 months: one dose (time of administration depends on the age of administration of the first dose): for primary vaccination in the first six months of life: 12–15 months of age, with an interval, of not less than 6 months for primary vaccination in the second six months of life: in the second year of life, with an interval, of not less than 2 months for primary vaccination in the second year of life: an interval 12–23 months Booster dose > 2 years of age: should be considered in those at constant risk of exposure to meningococcal disease
			Children, 2–10 years of age inclusive, adolescents (11 years of age and older), and adults up to 50 years of age	Two doses not less than one month apart
	Trumenba (2rLfHbp) (24.05.2022)	Pfizer Manufacturing Belgium N.V.	> 10 years	Primary vaccination: 2 or 3 doses.
A, C, W, Y	MenQUADFI (19.05.2022)	Sanofi Pasteur	> 12 months	One dose
	Menveo (18.01.2022)	GSK Vaccines	> 2 years old	One dose
	Nimenrix (24.05.2022)	Pfizer Manufacturing Belgium N.V.	> 6 weeks	Primary vaccination 2 doses (6 weeks – 6 months) one dose: infants from 6 months, children, adolescents and adults Booster dose In infants from 6 weeks to less than 12 months: one dose at 12 months of age not less than 2 months after the previous dose of vaccine
C	NeisVac-C	Pfizer Manufacturing Belgium N.V.	> 2 months	Primary vaccination 2 doses (2–4 months) one dose: infants after the age of 4 months, older children, adolescents and adults Booster dose In infants younger than 12 months, not less than 6 months after the last vaccination

7 European countries, the USA, and Canada collected between 2000 and 2014. Up to 91% of the analysed isolates were susceptible to vaccine-induced antibodies [11, 12]. MATS, MEASURE, BAST, and gMATS methods allow rapid assessment of hypothetical protein MenB vaccine coverage. When interpreting these results, it should be noted that each method retrospectively assesses theoretical vaccine coverage, which must be confirmed by observations of actual vaccine efficacy [13].

MENB VACCINES

4CMenB

Universal immunization of infants and adolescents with the 4CMenB vaccine is currently being carried out in 9 European countries. The results of vaccination programs in the UK, Italy, Portugal, and South Australia, and on-demand immunization aiming to reduce outbreaks of infection (in Quebec, Canada, and at several universities in the USA), have demonstrated high efficacy of the 4CMenB vaccine in reducing the incidence of MenB IMD among vaccinated persons [14].

The safety assessment performed in the UK 20 months after the 4CMenB vaccine implementation (~1.3 million children had been vaccinated) showed no additional vaccine adverse events (VAEs) compared to events reported during clinical trials. In addition, the overall number of events, based on the MenC vaccine experience, was lower than expected [15].

Furthermore, an observational study in the UK confirmed the safety of using the 4CMenB vaccine in premature infants. In a group of 133 premature infants born before the 35th week of gestation (median age 26.9 weeks of gestation) hospitalized due to causes unrelated to vaccination, the 2 + 1 schedule with co-administration of the vaccine against DTaP-Hib-IPV, PCV, and RV and acetaminophen prophylaxis was used. The control group consisted of premature infants who received only the DTaP-Hib-IPV, PCV, and RV vaccines. The study did not report any differences between children immunized with or without the 4CMenB vaccine regarding the frequency of apnoea, bradycardia, desaturation, or the need for respiratory support. The 4CMenB vaccine can be administered to premature infants with other vaccines and concurrent acetaminophen prophylaxis [16, 17]. After 3 years of universal infant vaccination against MenB, the percentage of children vaccinated with the full 4CMenB schedule in the UK was 88% of the eligible population. No delays in the realization of other immunizations were observed, which indicates the high acceptance level of 4CMenB co-administration with other vaccines by parents and doctors. Vaccines against MenB exhibit only a direct effect by reducing the number of disease cases in the vaccinated group without impacting herd immunity [18].

MENB-FHBP

The safety of the MenB-fHbp vaccine was assessed in 11 clinical trials involving 15,227 subjects aged ≥10 years. The most reported adverse reaction after the first dose of the vaccine was pain at the injection site, reported by 87% of recipients, and muscle pain in 24% of recipients. In addition, Safety was assessed among 1081 students immunized as a part of outbreak control [19–23]. The safety profile was comparable to clinical trials, and all adverse reactions were resolved within 7 days [24].

The post-marketing safety of the MenB-fHbp vaccine was confirmed based on the Vaccine Adverse Event Reporting System (VAERS) database of the US Centers for Disease Control and Prevention (CDC) and the US Food and Drug Administration (FDA). In total, 3,018,899 vaccine doses were administered over 4 years (from 29 October 2014 – 31 December 2018). During that time, 2106 VAEs were reported, 97% by persons aged 10–25 years. The most common events were fever, headache, and local reactions reported by 27% of subjects. Only 2 cases of severe reactions at the injection site were reported, including a case of erysipelas later classified as a VAE. No cases of meningococcal disease were reported [25].

MENACWY VACCINES

In managing health policies aimed at IMD prevention, it is not only the protection that vaccinated individuals receive that is important but also the impact of vaccination in reducing asymptomatic carriage and indirectly reducing disease cases in the unvaccinated population. Teenagers are the leading meningococci carriers in the population [26].

Concurrent with the introduction of infant vaccination against MenB in the UK, widespread vaccination against MenACWY (in response to an increase in infections caused by serogroup W) began among young people aged 13–18 years and those entering higher education. Subsequent analysis of this program showed that the MenACWY vaccine reduced serogroup W infections among vaccinated and unvaccinated individuals. In addition, MenACWY conjugate vaccines reduce carriage and thereby induce herd immunity, while a direct and indirect post-vaccination effect was not observed after vaccination against serogroup B [27, 28].

Since 2008, some countries in Europe, South America, and Australia have seen a sharp increase in infections caused by MenW, specifically the hypervirulent ST-11 clone. In England, infections caused by this clone in 2008–2009 accounted for only 2% of all cases, increasing to 24% in 2014–2015. Because these infections were associated with high mortality, universal vaccination against MenACWY was introduced among adolescents, replacing the monovalent vaccine against MenC [29]. The most signifi-

cant reduction in the incidence of IMD caused by vaccine serogroups was observed for MenW and MenY in adolescents aged 14–18 years. The actual efficacy of MenACWY vaccines was estimated at 94% (95% CI: 80–90), assuming the residual impact of the previous immunization program with a monovalent MenC vaccine. According to Public Health England, the program's implementation prevented 205–1193 cases of MenW and 60–106 cases of MenY in unvaccinated groups (indirect effect) [30].

In the Netherlands, mass vaccination against MenACWY in response to an increase in MenW-ST-11 infections was conducted in adolescents aged 14–18 years and children aged 14 months using the MenACWY-tetanus toxoid (TT) vaccine (Nimenrix). Since 2020, these vaccinations have entered the routine immunization program. As a result, between 2018 and 2020, a 100% reduction in the incidence of infections caused by serogroups C, W, and Y (95% CI: 14–100) was observed in adolescents aged 14–18 years in addition to an 85% reduction in all other age groups covered by the immunization program (95% CI: 32–97). In addition, a 50% (95% CI: 28–65) decrease in infections caused by serogroups C, W, and Y in age groups not covered by the vaccination program (indirect effect) was observed [31].

In Chile, MenACWY vaccination was initiated in 2012 among children aged 9 months to 4 years due to an increase in infections caused by serogroup W; in 2014, the vaccine was permanently introduced into the immunization program for children aged 12 months [32, 33]. Seven years after the implementation of the immunization program, the incidence of IMD caused by all meningococcal serogroups decreased by 51.3% and by 53% for MenW. The most significant effect was observed in the vaccinated age groups. Among children aged 1–4 years, the incidence of MenW-induced IMD decreased by 92.3%, and mortality was reduced from 23% in 2012 to 0% in 2016. In 2013–2019, the median vaccination coverage was 94%. Due to the lack of vaccination in the adolescent group, no decrease in incidence was observed in the non-vaccinated groups.

EDUCATION

Low awareness of the risks associated with meningococcal infections remains a significant problem in Poland. The importance of education in preventing meningococcal infections was shown by a survey conducted by Kantar Millward Brown in 2017. The survey revealed that 63% of young mothers in Poland knew about the possibility of vaccinating their children against meningococcus, while only 19% of pregnant women would consider immunization during or just after giving birth [34].

CLINICAL PRACTICE

Protecting children against meningococci in the first 6 months of life is crucial. Following the immunization program schedule, infants receive other mandatory vaccinations in the same period. In the first 6 months of life, a child receives 12 intramuscular injections when completing the mandatory immunization program schedule at an outpatient clinic. Therefore, administering the recommended vaccinations, including meningococcal vaccines, often requires scheduling an additional vaccination appointment. Studies indicate that meningococcal immunization should not be deferred except when necessary, because it reduces the number of immunized children [35].

The optimal solution is co-administering meningococcal vaccines with combined polyvalent vaccines (DTPa + IPV + Hib + HBV or DTPa + IPV + Hib), which has been applied in several countries. This allows for the administration of meningococcal vaccines during the same visit, reducing the number of injections and potential errors. Unfortunately, combined vaccines are not reimbursed in Poland, and their purchase by parents often limits their ability to finance additional recommended vaccinations. The situation is further complicated by the fear, both in parents and doctors, of fever occurring after infant meningococcal B vaccination. This is the most common reason for postponing vaccination, despite substantial scientific evidence indicating the benefits of giving the vaccine as early as possible and its high level of safety.

Due to the epidemiology of IMD in Poland, the optimal prophylaxis of meningococcal infection requires use of both the MenB and MenACWY vaccines. However, considering the number of doses administered, completing the full immunization schedule is perceived as expensive, especially when it is initiated in the first 6 months of a child's life. It is then necessary to administer 2 vaccines, 4CMenB and MenACWY, in a 2 + 1 schedule. The cost of meningococcal vaccines, in addition to the low level of awareness of their importance, is often a barrier for parents, including parents of children at increased risk of IMD. These include patients with asplenia, complement deficiency, properdin deficiency, hypogammaglobulinemia, and HIV infection [36, 37]. In these individuals, the likelihood of IMD is 10,000 times higher than in the unaffected population. However, due to the chronic disease and associated costs (both direct and indirect), many such patients have limited access to meningococcal vaccines in practice.

RECOMMENDATIONS

1. VACCINATIONS IN CHILDREN WITHIN THE FIRST 6 MONTHS OF LIFE

Infants in the first year of life, including those born prematurely, are at highest risk of developing IMD. Among the aetiological agents of IMD in this age group, we observe the predominance of serogroup B cases, with

TABLE 2. Different vaccination schedules for children aged 0–6 months old with the use of highly combined vaccines

Scheme 1		Scheme 2 (#)	
Age	**Vaccines**	**Age**	**Vaccines**
6 weeks	5 in1/6 in1 + PCV 10/13 + RV **MenACWY (1)**	6 weeks	5 in1/6 in1 + PCV 10/13 + RV
		8 weeks	**MenB (1)** + **MenACWY (1)** + prophylactic acetaminophen
10 weeks	RV **MenB (1)** + prophylactic acetaminophen	10 weeks	RV
14 weeks	5 in1/6 in1 + PCV 10/13 (+ RV*) **MenACWY (2)**	14 weeks	5 in 1/6 in 1 + PCV 10/13 (+ RV*)
		16 weeks	**MenB (2)** + **MenACWY (2)** + prophylactic acetaminophen
18 weeks	**MenB (2)** + prophylactic acetaminophen		
22 weeks	5 in 1/6 in 1	22 weeks	5 in1/6 in1
13 months	5 in 1/6 in 1 + PCV 10/13 + **MenACWY (3)**	13 months	**MenACWY (3)** + **MenB (3)** + prophylactic acetaminophen
14 months	MMR + Varicella **MenB (3)** + prophylactic acetaminophen	14 months	5 in 1/6 in 1 + PCV 10/13 MMR + Varicella

MenB – 4CMenB, recombinant meningococcal B protein vaccine, MenACWY – meningococcal A, C, W, Y conjugate vaccine, MMR – vaccine against measles, mumps, and rubella, PCV – pneumococcal vaccine, RV – vaccine against rotavirus, RV – the last dose of 3-dose rotavirus vaccine*
 # – schedule two can be administered with DTPw (whole-cell pertussis vaccine)
5 in 1 – combined vaccine against diphtheria, tetanus, pertussis, polio, and H. influenzae type b with an acellular pertussis component
6 in 1 – combined vaccine against diphtheria, tetanus, pertussis, polio, hepatitis B, and H. influenzae type b with an acellular pertussis component

a high proportion of serogroup C and an increasing proportion of cases caused by serogroup W. For this reason, **meningococcal vaccination should be started as early as possible, preferably in the first 6 months of life**. To ensure optimal protection against the most common serogroups of *N. meningitidis*, we recommend using both **MenB and MenACWY vaccines** in infants, including those born prematurely. If it is not possible to give both products (e.g. due to the cost of the vaccines), we recommend starting with vaccination against MenB and giving a vaccine against MenACWY as soon as possible, because both are required for complete IMD prophylaxis. Parents of all infants, especially those born prematurely, should be offered combined vaccines with an acellular pertussis component (6-in-1 – DTPa + Hib + IPV + Hepatitis or 5-in-1 – DTPa + Hib + IPV) in addition to meningococcal vaccines, which facilitates timely completion of vaccination with significantly fewer injections. MenB and MenACWY vaccines can be administered simultaneously during a single visit at separate injection sites. Previous studies have confirmed the efficacy and safety of the co-administration of the MenB vaccine [38–41].

Two schedules are available for infants starting the 4CMenB (Bexsero) vaccination in the first 6 months of life: 2 + 1 and 3 + 1. Due to the similar immunogenicity and efficacy of both immunization schedules, we recommend using the 2 + 1 schedule, which can be completed only when the interval between the first and second dose of the 4CMenB vaccine is not less than 2 months. The 3 + 1 schedule is used when the second dose is given earlier (not less than one month) and in children at risk (e.g. congenital asplenia). In all cases, the full 2- or 3-dose 4CMenB primary vaccination schedule should be completed by administering a booster dose in the second year of life, with an interval of at least 6 months between the primary vaccination cycle and the booster dose [17].

Infants starting **MenACWY** (Nimenrix) vaccination in the first 6 months of life receive 2 doses of the vaccine at a 2-month interval. The booster dose should be administered at the age of 12 months, at least 2 months after the previous dose of the vaccine. The Nimenrix vaccine can be administered simultaneously with a combined vaccine containing an acellular pertussis component and a 10-valent pneumococcal conjugate vaccine. In children above one year of age, the Nimenrix vaccine can be administered at the same time as vaccines against viral hepatitis A (HAV) and B (HBV), measles-mumps-rubella (MMR), measles-mumps-rubella-varicella (MMRV), 13-valent pneumococcal conjugate vaccine, or seasonal flu vaccine without adjuvants.

An increase in TT antibodies has been observed after Nimenrix vaccine administration; therefore, whenever possible, Nimenrix and TT-containing vaccines (e.g. DTaP-HBV-IPV/Hib vaccine) should be given at the same time, or the Nimenrix vaccine should be given at least one month before the TT-containing vaccine [31].

Table 2 presents the meningococcal vaccination schedules.

2. VACCINATIONS IN CHILDREN AFTER THE FIRST 6 MONTHS OF LIFE

If meningococcal vaccination has not been initiated in the first 6 months of a child's life, we recommend completing it as soon as possible. Children under 5 years of age still have a much higher risk of developing IMD than

TABLE 3. Recommended meningococcal vaccination schedules in children over 6 months of age

Scheme for children aged 6–12 months		
Primary vaccination	The first visit	MenACWY + MenB
	The second visit: no less than after 2 months	MenB
Booster vaccination	The third visit in the 2nd year of life	MenACWY+ MenB
Scheme for children aged 12–23 months		
Primary vaccination	The first visit	MenB + MenACWY
	The second visit: not less than after 2 months	MenB
Booster vaccination	The third visit in 3rd–4th year of life One dose with an interval of 12–23 months between the primary vaccination and the booster dose.	MenB
Scheme for children aged > 2 years, adolescents, and adults		
Vaccination	The first visit	MenB + MenACWY
Vaccination	The second visit – not less than after one month	MenB

MenB – 4cMenB, recombinant protein vaccine against meningococcus B, MenACWY – meningococcal A, C, W, Y conjugate vaccine

the general population, although their risk is lower than that of infants. Furthermore, the type and frequency of social interactions (e.g. nursery, kindergarten, older siblings) and meningococcal carriage rates increase with age. Therefore, for children previously unvaccinated against meningococci, we recommend that every vaccination and routine health check visit be used as an opportunity to administer MenB and MenACWY vaccines. Both vaccines can be given simultaneously and with other vaccines [17, 31]. It is important to remember that, in the second year of life, the Nimenrix vaccine should be given simultaneously with a TT-containing vaccine or one month before the TT-containing vaccine (no data are available for persons above 2 years of age) [31].

Table 3 shows the recommended vaccination schedules against MenB and MenACWY after the first 6 months of life.

3. VACCINATIONS OF ADOLESCENTS AND YOUNG ADULTS

Immunization of adolescents is essential, mainly because of the importance of this age group in *N. meningitidis* transmission. Meningococcal carriage is found in 25% of people in this age group, and studies have shown that the effectiveness of mass vaccination against MenACWY can be measured by a decrease in the carriage [26, 28]. Therefore, we recommend vaccinating all adolescents against MenACWY to protect them individually, to improve the epidemiological situation, and to increase the level of protection in the general population. Vaccination against MenB acts as effective individual prophylaxis because there is no evidence that it leads to a decrease in carriage [27, 42]. In addition, we recommend meningococcal vaccination for adolescents starting university, planning to live in boarding schools or dormitories, and those traveling abroad due to close contact with large groups of people, which increases the risk of *N. meningitidis* infection. Routine health check visits at 10, 14, and 19 years of age provide good opportunities for meningococcal vaccination.

4. VACCINATION OF PATIENTS AT RISK

Patients with functional or anatomical asplenia, complement deficiency, hypogammaglobulinemia following haematopoietic stem-cell transplantation, infection with HIV, and patients taking eculizumab or ravulizumab are at significantly increased risk of developing IMD [36, 37]. In addition, laboratory workers who are in contact with biological material containing *N. meningitidis* bacteria are at risk of developing IMD. Therefore, we recommend vaccination against MenB and MenACWY in these high-risk groups. Clinical studies involving subjects aged 2–17 years with complement deficiency, asplenia, or spleen dysfunction reported that the schedule comprising 2 doses of the 4CMenB vaccine administered at a 2-month interval produced high immunogenicity [17, 43]. Adolescents and adults living in highly populated areas or traveling to endemic areas also represent a group at increased risk of developing IMD. Table 4 presents the patients at risk of developing IMD.

Booster doses for patients at risk

The need for and timing of a booster dose of the 4CMenB vaccine in at-risk individuals has not been established; therefore, administering booster doses of the conjugated MenACWY vaccine to persons at risk is not currently recommended. However, one dose of the MenACWY conjugate vaccine and 2 doses of the 4CMenB vaccine given 8 weeks apart is recommended for unvaccinated children aged 2–10 years. Regardless of previous vaccination, it is recommended that children aged 10 years or older receive one dose of MenACWY and MenB vaccine and one additional dose of MenB vaccine administered after 4 weeks [44].

TABLE 4. Recommended meningococcal vaccination for high-risk groups (children, adolescents, and adults)

High risk group	Recommended vaccinations
Anatomical or functional asplenia	MenB + MenACWY
Disorders of complement	MenB + MenACWY
Infected with human immunodeficiency virus	MenB + MenACWY
Patients after (bone marrow) hematopoietic stem cell transplantation	MenB + MenACWY
Patients taking eculizumab or ravulizumab	MenB + MenACWY
Microbiology laboratory workers at risk of meningococcal infection	MenB + MenACWY
Travelers to endemic areas	MenB + MenACWY
People living in crowded conditions	MenB + MenACWY

MenB – 4cMenB, recombinant protein vaccine against meningococcus B, MenACWY – meningococcal A, C, W, Y conjugate vaccine

Patients undergoing treatment affecting their immune system (radiotherapy, corticosteroid treatment, chemotherapy) may not obtain optimal benefits from vaccination with the MenB-fHbp vaccine (Trumenba). According to the registered administration schedule, the Trumenba vaccine in the primary vaccination cycle is administered in a 2-dose (given at 6-month intervals) or 3-dose (2 doses given at least one month apart, and a third dose given at least 4 months after the second dose) schedule. Administering a booster dose after each dosing regimen should be considered in people at continuous risk of developing IMD [12].

Regarding MenB vaccines, the recommendations for Bexsero and Trumenba are different; these vaccines should not be given interchangeably.

POST-VACCINATION FEVER PROPHYLAXIS

We recommend that parents of vaccinated children be informed that fever is a natural symptom that can occur after any immunization. It is caused by the activation of the immune system, which reacts to vaccine antigens, and the absence of a fever does not mean that the vaccine will be less effective. When the MenB vaccine is given to children under 6 months of age, fever (> 38.0°C) is more frequent than with other vaccines and more frequent in children in case of co-administration with other vaccines [45, 46]. Therefore, we recommend prophylactic administration of acetaminophen to every infant vaccinated against MenB in the first 6 months of life, regardless of whether the vaccine is given alone or concomitantly with other vaccines (Table 5 presents the acetaminophen dosing schedule). Acetaminophen reduces the incidence and severity of fever without affecting the immunogenicity of the 4CMenB vaccine or other concomitantly administered vaccines. It should be emphasized that only acetaminophen (in such an indication) has been assessed in clinical studies [46]; however, if a fever occurs despite the antipyretic prophylaxis, both acetaminophen and ibuprofen can be used to reduce the fever.

TABLE 5. Prophylactic dosage of oral acetaminophen (120 mg/5 ml) after MenB vaccination in children aged 0–6 months

Dose 1	2.5 ml (60 mg) 30 min. before or simultaneously with vaccination
Dose 2	2.5 ml (60 mg) 4–6 hours after the first dose
Dose 3	2.5 ml (60 mg) 4–6 hours after the second dose

VACCINATION FINANCING

A significant increase in the proportion of children and adolescents vaccinated against meningococci seems impossible without introducing at least partial reimbursement of meningococcal vaccines and 5-in-1 or 6-in-1 combined vaccines. Introducing free or subsidized combined vaccines will increase the accessibility to meningococcal vaccination, which will translate into a reduction in IMD incidence and a subsequent reduction in treatment costs and the number of complications and late sequelae, which also include an increased risk of premature death and a reduction in life expectancy by up to 16 years [47, 48].

We believe that free meningococcal vaccination should be introduced for patients at risk. This small group is at an exceptionally high risk of developing IMD. We believe that partial or full reimbursement of MenB and MenACWY vaccines should be considered for all infants. Full reimbursement can be considered for children starting vaccination in the first 2 years of life when the benefits are the greatest. Similar measures, among others, are in place in the Czech Republic. Infant vaccination against MenB provides individual protection for this group of children who are especially vulnerable to IMD. Immunization of adolescents against MenACWY will significantly reduce meningococcal transmission in the community [49]. Therefore, we recommend reimbursement of adolescent vaccination against MenACWY because this will reduce the carriage and incidence of the disease in other age groups. These measures allow both direct and indirect effects of meningococcal vaccinations [50, 51]. Another crucial issue is the reimbursement of meningococcal vaccines for all children living in orphanages and other educational care facilities, who are especially vulnerable to infection.

EDUCATIONAL ACTIVITIES

The knowledge of the risk of IMD and the potential for its prevention by vaccination in Poland remains very low [34]. Therefore, in addition to personalized actions proactively recommending vaccination during routine medical appointments, it is also necessary to carry out and regularly repeat a nationwide education campaign to improve public awareness of the risks associated with *N. meningitidis* infection and the possibility of its prevention through vaccination. Care should be taken to ensure that future versions of the education campaign always include up-to-date information on the epidemiology of IMD, the course of the disease (including the atypical course as currently described for MenW infection), possible complications, long-term sequelae, and the availability, safety, and efficacy of vaccination. Planned educational programs produce better results than *ad hoc* actions. Promotional activities targeting adolescents and students may also be beneficial [52]. In this age group, the immunization program schedule includes few mandatory vaccinations, and the fear of vaccination among adolescents is low. In this case, meningococcal vaccination can be combined with vaccination against HPV or tetanus, diphtheria, and pertussis. We believe that the annual influenza vaccination and COVID-19 vaccination campaigns represent opportunities to carry out meningococcal vaccination.

Attention should be paid to the role of midwives who care for women during pregnancy and after childbirth, because they can significantly influence the mother's decisions regarding immunization in the first months of a child's life. In addition, the whole family should be involved in vaccination education because a meningococcal disease can occur at any age.

RECOMMENDATIONS – SUMMARY

1. Initiation of meningococcal vaccination in the first 6 months of life with MenACWY and MenB vaccines (after 6 or 8 weeks of age, respectively).
2. Simultaneous administration of the MenB and MenACWY vaccines during one visit (after 8 weeks of age).
3. MenB vaccination in children within the first 6 months of life following a:
   a. 2 + 1 schedule,
   b. 3 + 1 schedule in infants belonging to groups at increased risk of IMD.
4. MenACWY and MenB vaccination in adolescents and young adults, especially adolescents entering university, planning to live in boarding schools or dormitories, or traveling abroad.
5. Vaccination of patients belonging to groups at increased risk of IMD with simultaneous administration of MenACWY and MenB vaccines.
6. Use of booster doses of MenACWY and MenB vaccines in patients at highest risk of developing IMD (over 10 years of age).
7. Prophylactic administration of acetaminophen to every infant vaccinated against MenB in the first 6 months of life, especially if other vaccines are administered during the same visit.
8. Use of vaccination and routine health check visits to actively promote meningococcal immunization.
9. Introduction of free vaccinations for patients in IMD risk groups.
10. Take urgent action to enable reimbursement of meningococcal vaccines in the general population.

DISCLOSURE

The authors declare no conflict of interest.

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