REV. HOSP. CLÍN. FAC. MED. S. PAULO 58(4):231-240, 2003

REVIEW

CRITICAL ANALYSIS OF OLD AND NEW VACCINES AGAINST *N. MENINGITIDIS* SEROGROUP C, CONSIDERING THE MENINGOCOCCAL DISEASE EPIDEMIOLOGY IN BRAZIL

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BRICKS LF - Critical analysis of old and new vaccines against *N. meningitidis* serogroup C, considering the meningococcal disease epidemiology in Brazil. **Rev. Hosp. Clín. Fac. Med. S. Paulo 58**(4):231-240, 2003.

Worldwide, the impact of meningococcal disease is substantial, and the potential for the introduction and spread of more virulent strains of *N. meningitidis* or strains with increased resistance to current antibiotics causes concern, making prevention essential.

OBJECTIVES: Review the indications for meningococcal disease vaccines, considering the epidemiological status in Brazil.

METHODS: A critical literature review on this issue using the Medline and Lilacs databases.

RESULTS: In Brazil, MenB and MenC were the most important serogroups identified in the 1990s. Polysaccharide vaccines available against those serogroups can offer only limited protection for infants, the group at highest risk for meningococcal disease. Additionally, polysaccharide vaccines may induce a hypo-responsive state to MenC. New meningococcal C conjugate vaccines could partially solve these problems, but it is unlikely that in the next few years a vaccine against MenB that can promote good protection against multiple strains of MenB responsible for endemic and epidemic diseases will become available.

CONCLUSIONS: In order to make the best decision about recommendations on immunization practices, better quality surveillance data are required. In Brazil, MenC was responsible for about 2,000 cases per year during the last 10 years. New conjugate vaccines against MenC are very effective and immunogenic, and they should be recommended, especially for children less than 5 years old. Polysaccharide vaccines should be indicated only in epidemic situations and for high-risk groups. Until new vaccines against MenC and MenB are available for routine immunization programs, the most important measure for controlling meningococcal disease is early diagnosis of these infections in order to treat patients and to offer chemoprophylaxis to contacts.

DESCRIPTORS: ***Neisseria meningitidis*. Epidemiology. Vaccine. Efficacy. Children.**

Meningococcal diseases (MD) are endemic everywhere in the world, but they have a great potential to cause epidemics. Due to the high mortality rates and serious sequelae when epidemics develop, even a small number of cases cause great concern. Although there are commercially available polysaccharide vaccines to prevent MD caused by the main meningococcus serogroups, such vaccines are unable to produce long-lasting immunity and are poorly effective in preventing MD in infants, the largest group at risk for these infections[1-11].

In February 2002, a new conjugate vaccine against serogroup C meningococcus (MenC) was licensed in Brazil. This vaccine has been included in the vaccination schedule in the United Kingdom since 1999[10,11] . Since this vaccine is little known by pediatricians, we present in this paper a literature review on the association of MenC immunity and prevention of the MD caused by this agent, taking into consideration the epidemiological status in Brazil.

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Received for publication on January 22, 2003.

Immunity against *N. meningitidis*

Newborns acquire IgG class antibodies from their mothers through the placenta; these antibodies are effective against a few meningococcus serogroups. As these antibodies become catabolized, the child becomes susceptible to infections, which occur in general after the third month of life. Non-vaccinated children exhibit a progressive growth of the geometric mean titer (GMT) of antibodies against meningococci in response to the colonization of the airways by different kinds of *Neisseria* (typed or not, including related strains such as *N. lactamica*). A few strains of *E. coli* and other bacteria that normally colonize the intestine have a polysaccharide capsule or other antigens in the capsule wall that are immunologically identical or very similar to the *N. meningitidis* antigens, thus contributing to natural immunization[1,4,7,12,13].

Asymptomatic carriers of *N. meningitidis* begin to produce antibodies, on the average, 2 weeks after nasopharyngeal colonization has started. Acquisition of natural immunity against serogroup A meningococcus (MenA) occurs earlier than immunity to other serogroups. In the United States, more than 90% of children aged 18 months have MenA antibodies; the same protection level against MenC is only reached after 6 to 8 years. It is believed that the majority of these antibodies are acquired due to cross-reactivity between *N. meningitidis* antigens and those of enterobacteriae[4,7,12,13]. Tolerance to serogroup B meningococcus (MenB) polysaccharides antigens occurs due to the similarity between MenB capsular antigens and nervous tissue antigens; the majority of the antibacterial antibodies against MenB target sub-capsular antigens[14-16].

Since the 1960's, it has been demonstrated that there is a direct association between the absence of serum antibacterial antibodies and MD susceptibility; however, so far, the titer of antibodies required to protect against the disease is unknown. During epidemics, it has been observed that the majority of children and adults who had antibody titers higher than 2 mg/L (10 times more than those found in patients with agammaglobulinemia) were protected against serogroups A and C infections. There are no studies available on protection titers against serogroups Y and W135[1,3,7,8] .

Complement, especially the C5 and C9 fractions, is also important in protecting against MD, and the spleen plays an essential role in removing incompletely opsonized bacteria from the blood stream. People with complement deficiency or asplenia exhibit a greater risk for MD, and frequently these infections are caused by uncommon serogroups[1,3,5,7,8].

Polysaccharide vaccines against *Neisseria meningitidis*

Currently available polysaccharide vaccines (monovalent A and C, bivalent A/C, and quadrivalent A, C, Y and W135) are safe and effective in reducing the number of cases during epidemics[1-9,17]. However, their immunogenicity is low, especially for younger children[1-9,12-28].

During epidemics, polysaccharide vaccines against MenA and MenC, administered to school age children, adolescents, and adults, demonstrated above 85% efficacy; however, in children under 2, the vaccine against MenC has a low efficiency[1-9,17-28].

In a controlled study performed in Brazil involving 135,000 children aged between 6 and 36 months, Taunay et al.[18] found that the vaccine was effective in only 55% of the individuals between 24 and 36 months of age, and no efficacy was observed in those below 2 years of age, after 17 months of follow-up. Probably, the low efficacy of the vaccine against MenC is due to its reduced capacity to stimulate formation of antibacterial antibodies in children less than 2 years of age[19].

The low immunogenicity of MenA and MenC polysaccharide vaccines in younger children[1-11,20-28] is due to the inability of the polysaccharide antigens to stimulate a T-dependent immunologic response[24-28]. Repeated doses of polysaccharide antigens are not only unable to cause a booster response, but they may actually cause immunologic tolerance[29-33] . Studies conducted with children[29-32] and adults[33] previously vaccinated against MenC who were vaccinated again 1 to 4 years after receiving the first vaccine dose showed low antibacterial antibody titers against MenC (< 1:8), in contrast with those individuals who had never been vaccinated or who had received a new conjugated vaccine against MenC.

It is difficult to assess the clinical importance of these findings. Theoretically, it is possible that individuals who received the MenC polysaccharide vaccine become more prone to developing invasive disease caused by these bacteria due to reduced antibody levels after exposure to MenC[1,29-33] .

Polysaccharide vaccines against MenB have low immunogenicity in humans despite the fact that MenB and MenC polysaccharides are very similar[14-16]. Low immunogenicity of MenB capsule polysaccharides has been one of the main barriers in the development of vaccines against this serogroup of *N. meningitidis*. There are, however, a few indications that antibacterial antibodies against MenB subcapsular antigens may produce some degree of immunity against these bacteria; therefore, the development of new vaccines against MenB is based on these antigens[1,7,15-16].

Conjugated vaccines against MenA and MenC

After the conjugated vaccines were

developed and had proven to be highly effective against *Haemophilus influenzae* type b (Hib) in infants, there have been many attempts to develop new vaccines against *N. meningitidis* by conjugating the bacteria capsule polysaccharides with the same carrier proteins used in the development of conjugated vaccines against Hib. Although MenA, MenC, MenY, and MenW-135 polysaccharides have been conjugated with different kinds of proteins, published data on safety and immunogenicity of these vaccines in humans only deal with MenA ad MenC[31-41] .

A number of studies have already demonstrated that the new conjugated vaccines against MenA and MenC are highly immunogenic in children, adolescents, and adults[9,29-40]. Twumasi et al.[34] assessed the immunologic response in 304 children (aged between 8 and 10 weeks) after 3 doses of a conjugated vaccine A/C, compared with the polysaccharide vaccine. The conjugated vaccine was found to be as safe as the polysaccharide vaccine. Moreover, antibody titers after 2 doses of the conjugated vaccine were higher than those obtained after the use of the polysaccharide vaccine. In children over 6 months of age, a conjugated vaccine dose induced higher antibody titers against MenC than 2 doses of the same vaccine administered at 2 and 6 months.

Similar results have been observed by different investigators in studies performed in the United States[36], United Kingdom[9,35,39,41], and Africa[29,31,34]. In all these studies, MenC bactericidal antibody production after administration of conjugated vaccines was much higher than that obtained after the use of the polysaccharide vaccine. One month after the meningococcal conjugated vaccination, 91% to 100% of children had serum bactericidal antibody (SBA) ≥ 8, and 89% to 100% had a ≥ 4-fold increase. Serum bactericidal geometric mean titers (GMTs) of anti-MenC antibodies increased more than 50 times after administration of 3 different meningococcal C conjugated vaccines. By 6 months, GMTs decreased, but IgG antibody avidity increased. After a polysaccharide vaccine booster, there is a further increase in avidity and higher GMT, suggesting that conjugated vaccines can induce immunologic memory[1,42].

Conjugated MenC vaccines contain no live component and cannot give anyone meningitis or septicemia. The main adverse events include local transient reactions that normally resolve within 1 or 2 days. Less than 5% of vaccinated infants and toddlers develop local erythema or swelling ≥ 3 cm within 7 days at the meningococcal conjugated vaccine injection site, and 2% have low fever. Children above 5 years and adolescents presented the highest rate of local reactions that include redness and/or edema (25%) and pain in the injection site (1%), and the same rate of increased temperature. All such reactions remitted within 1 or 2 days and were not significantly higher than those observed after administration of vaccines against hepatitis B, Hib, and inactivated poliovirus vaccine[1,31-42].

Presentations and dosage administration – Three MenC conjugated vaccines licensed in Europe and 2 in Brazil are currently commercially available. Two of the 3 meningococcal conjugated vaccines contain short-chain oligosaccharides (10 µg) derived from serogroup C capsular polysaccharide (O-acetylated), coupled to CRM_{197}, a nontoxic mutant of diphtheria toxin (Chiron Vaccines and Wyeth Lederle Vaccines and Pediatrics). The third contains serogroup C polysaccharide (10 µg of O-acetylated), conjugated to tetanus toxoid (MCC-TT; North American Vaccine – NAVA)[42].

The United Kingdom was the first country to license and recommend routine immunization with MenC conjugated vaccines in 1999. Single dose vaccine is recommended for children older than 1 year; when the immunization program is initiated in children aged 5 to 12 months, 2 doses were recommended, and between 2 and 5 months, 3 doses, with a 1-month interval (Table 1)[10,11,42] .

Table 1 - Immunization schedule for conjugated vaccines against *N. meningitidis* C used in the United Kingdom.

Age group	Conjugated vaccine	Comments
< 5 months	3 doses, with a minimum 4 week interval	In the United Kingdom, conjugated vaccines are recommended for 2-, 3-, and 4-month-old children together with the vaccines DPT-Hib and poliovirus oral vaccine.
5 to 12 months	2 doses, with one month interval	
Children over 1 year, adolescents and adults *	1 dose only	

*After the age of 2, immunocompromised individuals should receive a quadrivalent polysaccharide vaccine dose.

In Brazil, the first conjugated MenC vaccine was licensed in February 2002 (Meningitec, Wyeth Laboratories). The serogroup C polysaccharide conjugated to tetanus toxoid (NeisVac-C, Baxter) was also licensed in 2002. The manufacturer's recommendations should be followed with regard to the number of doses and administration intervals.

Efficacy of conjugated vaccines in the United Kingdom (UK) – Conjugated MenC vaccines have had a high efficacy against MD[41,42]. From November 1999 until November 2000, about 14 million people younger than 18 years had been immunized with conjugated MenC vaccines in the UK. Age-specific vaccine efficacy had been estimated to be 88% in children aged 12 to 30 months and 96% in adolescents aged 15 to17 years. Additionally, conjugated MenC vaccines reduced carriage of serogroup C meningococci in 15 to 17 year-old school students in the UK by 66% and produced no significant changes in carriage of meningococci expressing other disease-associated serogroups[42]. These vaccines were highly immunogenic and induced immunologic memory after a single dose in UK toddlers. There was no serious adverse event associated with their use in children and adolescents[41-43].

Comments on the use of conjugated MenC vaccines, considering the epidemiology of MD in Brazil.

In Brazil, local meningococcal meningitis outbreaks caused by serogroups B and C have occurred since the 1980s.[44-46] The Health Ministry and the State of São Paulo Health Secretary data indicate that in this country prevalence and mortality rates of MD are extremely high, especially in children younger than 5 years (Tables 2 and 3)[45,46]. Although serogroup B is the most prevalent in children with MD, a progressive increase in the number of serogroup C cases has been recorded. While in the 1980s, over 80% of meningitis cases due to *N. meningitidis* were ascribed to MenB, in the 1990s, this rate came down to 50% to 60%, while MenC reached a 40% to 50% level (Table 4)[1,45,46].

In different countries, there has been an increase not only in the incidence rate of MD caused by MenC, but also an increase in the mortality

Table 2 - Meningococcal disease in Brazil. Distribution of confirmed cases, prevalence coefficient, mortality numbers, and rates, in the year 2000.

Age group (years)	Cases (number)	Coefficients /100,000	Deaths (number)	Mortality rate (%)
< 1	817	24.5	197	24
1 – 4	1,379	10.3	273	20
5 – 9	825	4.7	120	15
10-14	497	2.7	67	13
15-19	305	1.7	36	12
20 – 29	311	1.1	60	19
30 – 39	193	0.8	44	23
40 –49	121	0.7	23	19
50 – 59	83	0.7	22	27
60 – 69	30	0.4	8	27
70 –79	21	0.5	11	52
> 80	1	0.07	0	0
Total	4,583	6.1	862	22

Source: Health Ministry, "Fundação Nacional de Saúde" (unpublished and not final data, March 2002).

Table 3 - Number of cases, mortality numbers, and rate of Meningococcal diseases according to age group. State of São Paulo, year 2000.

Age group (years)	Cases (number)	Deaths (number)	Mortality rate (%)
< 1	343	76	22
1 – 4	592	118	20
5 – 9	263	34	13
10-14	105	16	15
15-19	88	9	10
20 – 39	166	32	19
³ 40	86	21	24
Total	1,643	306	19

Source: São Paulo, "Centro de Vigilância Epidemiológica"[46].

Table 4 - Meningococcal disease cases rate, by serogroup. State of São Paulo, 1982 - 2001.

Year	Serogroup B	Serogroup C
1982	70.1	4.6
1983	77.3	5.9
1984	86.1	3.4
1985	83.1	6.1
1986	63.6	11.0
1987	75.2	10.9
1988	78.5	8.6
1989	76.6	16.6
1990	62.3	33.7
1991	45.8	50.0
1992	57.3	39.5
1993	58.1	39.5
1994	59.7	36.8
1995	57.0	41.8
1996	61.0	36.7
1997	61.2	33.3
1998	62.1	34.4
1999	65.6	30.8
2000	59.9	35.9
2001	56.5	38.4

Source: São Paulo, "Centro de Vigilância Epidemiológica", "Serviço de Vigilância Epidemiológica" (up to 1997) and "Sistema de Informação de Agravos de Notificação" (1998 to 2001)/"Divisão de Doenças de Transmissão Respiratórias)"/"Centro de Vigilância Epidemiológica". Data collected up to 01/31/2002[46].

rate associated with this serogroup[4,6-9-11]. This problem has been attributed to the emergence and spread of highly aggressive MenC strains belonging to the ET-37 complex[1,47-49]. Unfortunately, in Brazil, the etiological agent is identified in less than 50% of the cases and serogrouping is performed in approximately one-third of the cases[1,45,46].

Since it is not always possible to isolate the bacterial meningitis agents, and very often, the isolates are not typed, the prevalence of MD is underestimated. Even so, during the last 10 years, the number of MD cases has been extremely high. In the 1990's, an average of 5,680 MD cases and 1,085 deaths (19%) have been reported each year. Distribution of the number of MD cases and deaths, and mortality rate due to MD in Brazil in 2000, separated by age-groups, is reported in table 2[1]. Almost half the cases and deaths (45%) occurred in children under 5 years[45]. In the state of São Paulo, the incidence rate of MD in children under 1 year ranged between 40 and 69 per 100,000, and in the age group of 1 to 4 years, between 15 and 30 per 100,000, a definitely higher number than in other age groups[44]. In children under 1 year and in the cases of septicemia, mortality rates due to MD are also very high when compared to the rest of the population, reaching 28% and 40%, respectively[1,44-46].

Assuming that MenC is responsible for at least 40% of all MD cases and deaths in Brazil, the annual number of cases and incidence of death ascribed to that agent is extremely high (over 2,200 cases and 400 deaths each year). Considering the epidemiological hazard caused by the MenC disease, as well as the safety and efficacy of the conjugated vaccine, there is no doubt that this new vaccine should contribute significantly to the reduction of morbidity and mortality caused by MD in this country[1]. It should be pointed out that conjugate vaccines against MenC do not offer protection against MenB; therefore, these vaccines will not confer full protection against MD.

The licensed vaccine has a high cost (approximately R $140.00), which should hinder its use in public health. Additionally, the vaccine is recommended as a 3-dose schedule, intramuscular, for infants. Many parents and doctors may feel reluctant to administer more injections to such very young persons.[1]

Lastly, there are some issues associated with the duration of immunity provided by the vaccine and also with the impact of immunization in the community. Since this is a new product, the duration of the protection provided by conjugated vaccines is unknown[10,11]. All studies conducted so far have shown that the conjugated vaccines against MenC should provide long-term immunity, just like the Hib vaccines[29-43]. However, it is only through the follow-up of vaccinated populations that a definitive answer may be provided in this case[1,10,11,39-43].

A few studies have demonstrated that the new conjugated MenC vaccines are capable of eliminating the carrier condition similar to what occurred with vaccination against Hib[8,9,42,50-52]. With the reduction of both oropharyngeal colonization and the number of MenC carriers, it is quite likely that conjugated vaccines will significantly contribute to herd immunity[42,49-52]; however, there are some indications that different *N. meningitidis* strains may, through a gene exchange that controls production of the polysaccharide capsule, switch their serogroup. The switch of serogroup C to B and of B to C has already been confirmed both in vitro and in vivo[4,54,55]. The United Kingdom's Epidemiologic Surveillance Service has not observed this kind of problem so far. However, it is still unknown whether massive use of these vaccines in a set population may cause a selective pressure for such genetic switches. Strict epidemiologic surveillance should be maintained in order to secure early identification of this phenomenon[1,39-43,49].

Recommendations for MD prevention

It is estimated that in Brazil, MenC is responsible for about 2,000 cases of MD every year. Due to the high prevalence and mortality rates of MD, we consider that the conjugated MenC vaccine should be primarily prescribed for children under 5 years, who constitute the largest risk group. The vaccine, because of its enhanced immunogenicity, should also be offered to other risk groups, such as

immunocompromised patients (children, adolescents, and adults with complement deficiency, HIV infection, functional and anatomical asplenia, or undergoing bone marrow transplantation). MD risk groups should receive the quadrivalent vaccine in order to broaden the protection spectrum against serogroups A, Y, and W-135, which are not included in the conjugated vaccine against MenC. Polysaccharide vaccines should only be indicated in the case of epidemics, due to their low efficacy and lack of induction of immunologic memory.

It should be emphasized that conjugated MenC vaccines provide specific serogroup protection; therefore, they will not protect against the serogroups that are not included in the vaccine. If MD is suspected in the absence of prior vaccinations, blood and liquor culture should be performed, and treatment should be initiated as soon as possible. Individuals with intimate contacts with MD victims should receive chemoprophylaxis, when so indicated, because vaccines will only give protection after at least 2 weeks, and the majority of secondary cases occur during the first 2 weeks after contact[20].

It is essential to improve epidemiologic surveillance and to establish laboratories capable of promptly identifying the primary MD pathogens with serogrouping and identification of serogroups, subtypes, and immune types responsible for the epidemics. Unfortunately, in Brazil, many of the MD diagnostics are still based on clinical and laboratory data without isolation of *N. meningitidis* in culture, and even when the type of bacteria is identified, the serogroup is not identified in most cases.

Regarding the possibility of vaccination against MenB, one of the most common MD pathogens in Brazil, the problem is even more serious, because of the need to identify not only the serogroup, but also the serotypes, subtypes, and immune types of that pathogen. Although, since the 1980's, the strain ET-5 has been the most prevalent cause of epidemics, there is large variability among the strains that have been identified in different countries and at different times[1,4,7-9,52,53]. Currently, at least 14 serotypes, 12 subtypes, and 12 immunotypes of MenB are known. In addition, a large portion of the invasive disease strains is still not typed. Consequently, the indications for vaccination against this pathogen remain questionable, especially when the serotype causing the MD is unknown and the 2-dose regimen is used to immunize children under 4 years[1,16].

The finding that class-1 OMP proteins play an essential role in the induction of bactericidal antibodies has stimulated research in the field of polyvalent vaccines, in an attempt to provide protection against several subtypes of MenB. Although it has been evident that hexavalent vaccines may induce response to more than one OMP-1 type[57], such vaccines need improvement to offer a broader clinical protection spectrum against the dreaded MD[1-9,48].

By the end of 2000, the genetic sequencing of *N. meningitidis* was completed[58,59], and it is expected that in a few years vaccines with a broader protection spectrum against several strains of this bacteria will become available. In the meantime, it is fundamental that the population and doctors watch for the primary signs and symptoms of the disease to allow a prompt diagnosis and adequate treatment as well as chemoprophylaxis for the contacts.

It is estimated that the incidence of sporadic cases of MD in household contacts is 4 cases per 1,000 people exposed, that is, 500 to 800 times higher than that reported in the population as a whole. The majority of secondary cases occur in the first days after development of the index case; it is thus recommended that prophylaxis be administered early to the following groups, and if possible, within 24 hours after confirmation of the index case[1-3]:

1) household contacts;
2) day care units contacts;
3) people exposed to oral secretions of infected individuals (kissing, mouth-to-mouth breathing, endotracheal intubation).

Chemoprophylaxis may be performed with rifampicin, ciprofloxacin, or ceftriaxone and is 90% to 95% effective in reducing the *N. meningitidis* carrier status. It is recommended up to 14 days after exposure; after this period, it is likely that this procedure will bring little or no benefit to the contacts. Throat and nasopharyngeal cultures are of no value for deciding who should receive chemoprophylaxis because of the asymptomatic colonization of the respiratory tract[3,4].

Current indications for polysaccharide vaccines:

1. **Epidemics:** according to the experience acquired in control of meningococcal C epidemics, an epidemic is defined as the occurrence of 3 or more cases (confirmed or probable) of meningitis caused by this pathogen in a period shorter than 3 months or an incidence rate of at least 10 in 100,000 inhabitants. This rate is calculated based on the whole population data and not on specific age groups. These parameters also apply to other meningococcal groups (A, Y, and W135);
2. **High-risk groups for meningococcal infections:** individuals with anatomic or functional asplenia deficiency of the terminal section of complement, as well as individuals working in laboratories and who have a greater possibility of exposure to these bacteria;

3. **Military:** the high incidence of MD in non-vaccinated recruits and the excellent efficacy of MenA and MenC vaccines warrant indication for this group;
4. **Individuals traveling to hyperendemic disease areas or where the disease occurs as epidemics:** especially those traveling, during the dry season (December to June) to Africa's sub-Sahara, where the disease is prevalent.

At-risk children, especially if vaccinated before they are 4 years, should be vaccinated again after 2 to 3 years; although there are no studies on the need to revaccinate individuals over 4 years; if they remain as high-risk individuals, revaccination may be considered 3 to 5 years after the initial dose[1-3].

RESUMO

BRICKS LF - Análise crítica das antigas e novas vacinas contra a *N. meningitidis* do sorogrupo C, considerando a epidemiologia da doença meningocócica no Brasil. **Rev. Hosp. Clín. Fac. Med. S. Paulo 58** (4):231-240, 2003.

Em todo o mundo, o impacto das doenças meningocócicas é enorme e o potencial para a introdução e disseminação de cepas da *N. meningitidis* mais virulentas ou com aumento da resistência aos antibióticos atualmente utilizados causa grande preocupação, tornando a prevenção essencial.

OBJETIVO: Rever as indicações das vacinas para doenças meningocócicas, considerando a situação epidemiológica do Brasil.

MÉTODOS: Revisão crítica sobre o tema, usando as bases de dados Medline e Lilacs.

RESULTADOS: Os sorogrupos B e C foram os mais prevalentes no Brasil, na década de 90. As vacinas polissacarídicas disponíveis contra esses sorogrupos oferecem proteção limitada aos lactentes e podem induzir tolerância ao MenC. As novas vacinas

conjugadas contra o MenC podem solucionar parcialmente esse problema, mas é improvável que, em curto prazo, sejam licenciadas novas vacinas contra o MenB.

CONCLUSÕES: Para tomar as melhores decisões sobre as recomendações em práticas de imunização, é necessário que se disponha de dados precisos da vigilância epidemiológica, com identificação dos sorogrupos mais prevalentes em cada faixa etária. Estima-se que, no Brasil, o MenC seja responsável por 2.000 casos de doenças meningocócicas , a cada ano. As novas vacinas conjugadas contra o MenC são seguras, efetivas e imunogênicas, devendo ser recomendadas, particularmente, para crianças menores de 5 anos. As vacinas polissacarídicas devem ser recomendadas apenas para os grupos de alto risco ou em situações epidêmicas. Enquanto novas vacinas contra o MenC e MenB não forem incorporadas ao calendário de vacinação de rotina, as mais efetivas medidas para controlar as doenças meningocócicas são o diagnóstico e tratamento precoces e a quimioprofilaxia para contactantes.

DESCRITORES: ***N. meningitidis*. Epidemiologia. Vacina. Eficácia. Crianças.**

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