HUMAN VACCINES & IMMUNOTHERAPEUTICS
2018, VOL. 14, NO. 5, 1203–1215
https://doi.org/10.1080/21645515.2018.1451287

Taylor & Francis
Taylor & Francis Group

COMMENTARY

Vaccination strategies for the prevention of meningococcal disease

Scott Vuocolo[a], Paul Balmer[a], William C. Gruber[b], Kathrin U. Jansen[b], Annaliesa S. Anderson[b], John L. Perez[c], and Laura J. York[a]

[a]Vaccines Medical Development and Scientific/Clinical Affairs, Pfizer Inc, Collegeville, PA, USA; [b]Vaccine Research and Development, Pfizer Inc, Pearl River, NY, USA; [c]Vaccine Research and Development, Pfizer Inc, Collegeville, PA, USA

ABSTRACT

Routine prophylactic vaccination and mass vaccination strategies have been used to control both endemic and epidemic disease caused by *Neisseria meningitidis* globally. This review discusses real-world examples of these vaccination strategies, their implementation, and outcomes of these efforts, with the overall goal of providing insights on how to achieve optimal control of meningococcal disease through vaccination in varied settings. Tailoring immunization programs to fit the needs of the target population has the potential to optimally reduce disease incidence.

ARTICLE HISTORY
Received 17 February 2018
Accepted 8 March 2018

KEYWORDS
Neisseria meningitidis; vaccination strategies; epidemics; epidemiology; prophylaxis

Epidemiology of *Neisseria meningitidis*

Neisseria meningitidis is a major cause of meningitis and septicemia globally.[1] Humans are the only known reservoir for the bacteria, which reside primarily in the nasopharynx.[2] Meningococci are transmitted by droplets from the respiratory tract, and infected individuals can transmit the bacteria up to 24 hours after the initiation of antibiotic treatment.[3] Although colonization occurs in ~10% of adults, rates as high as 42% have been observed among adolescents and young adults due to the social behavior of these populations (ie, kissing, smoking, and alcohol consumption) that predispose them to transmission.[2,4,5] Nasopharyngeal colonization usually does not cause disease; however, for reasons that are not completely understood, the bacteria can penetrate the mucosa, enter the bloodstream, and cause invasive meningococcal disease (IMD).[6]

The incidence of IMD is generally low in industrialized countries (approximately ≤5 cases per 100,000 people), especially since the advent of national meningococcal vaccination programs.[2,7,8] However, a much higher incidence (up to 1000 cases per 100,000 people) has been observed during epidemics, particularly in countries in the African meningitis belt.[9] Overall, the highest incidence of infection occurs in children ≤4 years of age and adolescents and young adults aged 15 to 24 years.[10] IMD typically carries a 10% to 15% mortality rate, even with appropriate antibiotic treatment.[3] Death can occur within 24 to 48 hours after the onset of symptoms, and survivors often have permanent mental and physical impairments.[11]

N meningitidis strains that cause IMD are encapsulated and categorized into 12 serogroups according to the biochemical composition of the capsular polysaccharide.[12] Six serogroups (A, B, C, W, X, and Y) cause the majority of IMD, with serogroup prevalence varying by geographic location.[12] Globally, serogroup A has been responsible for the greatest incidence of IMD and was the causative agent for epidemics in both industrialized and nonindustrialized countries.[13] In the African meningitis belt, serogroup A has been responsible for a constant, low level of endemic disease interspersed with sporadic epidemics. During epidemics, the annual disease incidence can reach 100 cases per 100,000 population.[14] Within smaller communities, IMD can increase by a factor of 10, peaking at 1000 cases per 100,000 population; historically, such epidemics occur almost every year in one of the meningitis belt countries.[14] In 1996, an epidemic of serogroup A in Nigeria resulted in >100,000 infections and >11,000 deaths.[9] Today, IMD due to serogroup A has virtually disappeared from countries within the meningitis belt due to the use of a monovalent meningococcal serogroup A conjugate vaccine licensed in 2014.[15] With the waning of disease caused by serogroup A, epidemics of serogroup X are increasing in many African countries including Niger,[16] Ghana,[17] Kenya,[18] Togo, and Burkina Faso.[19] Serogroup C epidemics are also increasing in the region, as evidenced by the recent increase in IMD due to serogroup C in Niger in 2015 that resulted in 5855 cases and 406 deaths.[20]

Serogroup W has also been implicated in large meningococcal epidemics in Africa.[14] Specifically, during an epidemic in The Gambia in 2012, an incidence rate of 1470 cases of serogroup W per 100,000 population was observed in children <12 months of age.[21] In Australia, the percentage of meningitis cases due to serogroup W increased from 4% to 30% during the 2-year interval between 2013 and 2015.[22] Epidemics of serogroup W have been reported in Mecca among pilgrims attending the annual Hajj[23,24] and in the native countries of pilgrims returning from the Hajj.[25] Among serogroup W isolates, the hypervirulent sequence type 11 (ST11) clone, in particular,

CONTACT Laura J. York Laura.York@Pfizer.com Vaccines Medical Development and Scientific/Clinical Affairs, Pfizer Inc, 500 Arcola Rd, Collegeville, PA 19426 USA.

has been increasing in prevalence since the 2000 Hajj, with disease incidence noted in many regions, including Latin America,[26] Australia,[22] and Canada.[27] The emergence of serogroup W cases in South America, particularly in the southern cone, and in England and Wales[28] was initially thought to be due to the virulent clone disseminating from strains associated with the Hajj.[26] However, genomic analysis later revealed that these strains, although clonal, were genetically different.[29] In the United Kingdom, the number of serogroup W cases began to increase in 2009 and almost doubled from 2013–2014 (95 cases) to 2014–2015 (176 cases).[28] More recently, serogroup W has been responsible for several cases in teenagers that have been characterized by an atypical gastrointestinal presentation that includes nausea, vomiting, and diarrhea.[30] Among 15 cases diagnosed in teenagers aged 15 to 19 years between July 2015 and January 2016, 7 had mainly gastrointestinal symptoms; of these, 5 died within 24 hours of hospitalization.

Serogroup B is an important cause of endemic disease and is responsible for multiple prolonged epidemics in several industrialized countries, including Cuba,[31] Norway,[32] and New Zealand.[33,34] Smaller outbreaks due to a single strain have also been reported in other countries such as France (from 2000–2003)[35,36] and the United States (from 2013–2017), some of which have been associated with colleges and universities.[37,38] In the United States, one lengthy outbreak over 3 academic years occurred at Ohio University beginning in 2008.[39] Recent outbreaks have occurred at Princeton University and the University of California Santa Barbara in 2013, the University of Oregon and Providence College in 2015,[38] Santa Clara University[40] and Rutgers in 2016,[41] and Oregon State University in 2017.[42,43]

Similar to serogroup B, serogroup C has been a major cause of IMD in adolescents and young adults, mostly in industrialized countries.[10,44] In the United Kingdom, disease due to serogroup C declined dramatically after the introduction of a monovalent serogroup C conjugate vaccine into the routine immunization schedule, with a catch-up campaign at the start, in 1999.[45] From 2014 to 2015, only 28 cases of serogroup C disease were identified, which was a substantial decrease from the 848 cases reported from 1999 to 2000.[28] After multiple epidemics of a virulent serogroup C strain in 1990 in Canada, Quebec implemented a mass immunization program using an unconjugated polysaccharide vaccine that resulted in a significant decrease in disease during the following years.[46] However, reemergence of the disease-causing clone in 2001 triggered national recommendations for the inclusion of meningococcal serogroup C conjugate vaccine into the childhood immunization schedule, targeting infants and young adults aged <20 years.[46,47] By 2005, routine vaccination was in place in all provinces in Canada, with the exception of one. Following the initiation of routine vaccination in 2001, IMD due to serogroup C decreased 14% per year over the next 8 years, with reductions in IMD in both vaccinated (78% reduction) and unvaccinated populations (46% reduction).[47]

Serogroup Y was not a global concern before the 1990s; however, an increased incidence of disease was observed during routine active surveillance studies conducted by the Centers for Disease Control and Prevention.[1] From 1992 to 1996, serogroup Y disease began to increase and accounted for approximately 26% of isolates collected in the United States.[1] A steady, although smaller, increase in serogroup Y isolates was observed in Europe from 1995 to 2012.[48,49]

Different vaccination strategies have been used to control disease caused by various *N meningitidis* serogroups in varied settings globally. The following sections will review the vaccines currently available that target these disease-causing serogroups, real-world examples of strategies used to implement these vaccines into diverse populations, the outcomes of these efforts, and pertinent considerations for each approach (Table 1).

Vaccination strategies for meningococcal disease

Vaccination strategies used to manage meningococcal disease vary based on specific conditions within a region or country and the needs of the target population. For instance, routine, age-based prophylactic immunization is often used when typical, or endemic, disease rates prevail in specific age groups. In contrast, mass vaccination is often deployed under epidemic conditions, defined as an increase in cases compared with baseline endemic conditions. Examples of such vaccination strategies are discussed below.

Routine prophylactic immunization in high-risk groups

Meningococcal serogroup C vaccine in infants and adolescents in Europe

From 1994 to 1998, serogroup C accounted for 26% to 34% of cases of confirmed IMD in England and Wales, with the majority of cases occurring in adolescents.[50] From 1998 to 1999, the confirmed number of serogroup C disease cases reached 883 in England,[28] and as a result of escalating disease incidence, 3 novel monovalent protein-conjugate serogroup C vaccines were fast-tracked for approval. The first vaccine approved used a cross-reacting material 197 (CRM_{197}) carrier (Meningitec™, Pfizer Ltd, Kent, UK and Wyeth Pharmaceuticals, Havant, UK)[51]; the other 2 vaccines used either a CRM_{197} (Menjugate®, GlaxoSmithKline Vaccines Srl, Siena, Italy)[52] or a tetanus toxoid carrier (NeisVac-C™, Pfizer Ltd., Kent, UK)[53] (Table 2).

In 1999, the United Kingdom became the first country to initiate a national immunization campaign focused on serogroup C.[54] This vaccination strategy targeted infants, who received a 3-dose schedule, and children and adolescents 1 to 18 years old, who received a single dose as a catch-up regimen; infants <1 year old and adolescents 15 to 17 years old were vaccinated first in order to target the age groups at highest risk.[45,54] Notably, children and adolescents received the vaccination in a school-based program, leading to vaccine uptake of >85% in these groups.[45]

Monovalent serogroup C conjugate vaccines proved to be immediately effective in controlling disease in the United Kingdom; decreases in IMD incidence were initially observed in vaccinated individuals and later in unvaccinated children and older adults who were not eligible for vaccination, suggesting herd protection.[55] By 2000–2001, 1 year after the vaccination campaign was initiated, 389 cases of invasive meningococcal serogroup C disease were reported, a decrease of 56% compared

Table 1. Meningococcal vaccination programs.

	Vaccination Campaign				Year: Cases[a] (Incidence Rate)[b]	
Serogroup	Location	Year Implemented	Age Group	Vaccine	Prevaccination	Postvaccination
A	Burkina Faso[78,117] (epidemic)	2010	1–29 y	MenAfriVac	2009: 1994	2010: 430 2011: 111 2012: 49 2013: 4
	Chad[89] (epidemic)	2011 (N'Djamena regions)	1–29 y	MenAfriVac	N'Djamena regions 2010: 27	N'Djamena regions 2011: 45 2012: 0 2013: 0
		2012 (Rest of Chad)			Rest of Chad 2010: 28 2011: 110	Rest of Chad 2012: 59 2013: 1
B	United Kingdom[71]	2014	≥2 mo	Bexsero	2012–2013: 595 2013–2014: 424	2014–2015: 418 2015–2016: 444
	Cuba[31] (epidemic)	1989	3.5 mo to <20 y	VA–Mengoc–BC	1984: (14.1) 1985: (13.5) 1986: (11.0) 1987: (8.8) 1988: (8.8)	1989: (6.5) 1990: (4.2) 1991: (2.4) 1992: (1.4) 1993: (0.8) 1994: (0.8)
	Norway[32]	2004		MenBvac	1999–2000: 83 (1.9)	NA
	France[118]	2006	1–19 y	MenBvac	Dieppe region 2003–2006: 28 (8.6) Rest of Seine–Maritime region 2003–2006: 19 (0.5)	Dieppe region 2006–2008:[c] 9 (4.9) 2008–2010: 3 (1.5) Rest of Seine–Maritime region) 2006–2008: 15 (0.7) 2008–2010: 9 (0.4)
	New Zealand[33,34,95]	2004	<20 y	MeNZB	2001: 285 (24.7) 2002: 211 (18.1) 2003: 187 (15.8)	2004: 144 (12.1) 2005: 80 (6.7) 2006: 47 (3.9) 2007: 37 (3.1) 2008: 31 (2.6)
	United States[38,41,111]	2013–2016	10–25 y	Trumenba Bexsero	Colleges/Universities Princeton, 2013: 9 Santa Barbara, 2013: 5 Providence College, 2015: 2 University of Oregon, 2015: 7 Santa Clara, 2016: 3 Rutgers, 2016: 2	
C	Quebec City, Canada[46] (Epidemic)	2001	2 mo to 20 y	Menjugate	2001: 58 (7.84)	2002: 27 (3.63)
	United Kingdom[50] (Epidemic)	1999	2 mo to 17 y	MCCs (Meningitec, Menjugate, NeisVac-C)	1998/1999[d] 537	2000–2001[d]: 103
	Netherlands[60]	2002	14 mo (1-dose series) 1–18 y (catch-up)	MCC	2001: 276	2003: 42
	Spain[119]	2000	2 mo to <6 y	MCCs (Meningitec, Menjugate, NeisVac-C)	1999: 268 (7.04)	2000–2001: 56 (1.46) 2001–2002: 49 (1.26) 2002–2003: 42 (1.08)

(*Continued on next page*)

Table 1. (*Continued*)

	Vaccination Campaign				Year: Cases[a] (Incidence Rate)[b]	
Serogroup	Location	Year Implemented	Age Group	Vaccine	Prevaccination	Postvaccination
ACWY	United States[69]	2005	11–12 y Increased risk: 11–55 y 2–10 y >55 y 11–18 y	MCV4 MCV4 MPSV4 MPSV4	Serogroup C 2004: 27 (0.07) Serogroup Y 2004: 31 (0.08)	Serogroup C 2005: 25 (0.07) 2006: 29 (0.08) Serogroup Y 2005: 39 (0.11) 2006: 42 (0.12)
		2007		MCV4	Serogroup C 2006: 29 (0.08) Serogroup Y 2006: 42 (0.12)	Serogroup C 2007: 36 (0.10) 2008: 38 (0.10) Serogroup Y 2007: 45 (0.12) 2008: 31 (0.08)
		2010	11–12 + 16 y	MCV4	Serogroup C 2009: 28 (0.07) Serogroup Y 2009: 37 (0.10)	Serogroup C 2010: 17 (0.04) 2011: 19 (0.05) Serogroup Y 2010: 27 (0.07) 2011: 27 (0.07)

NA = not available.
[a]Total cases for all age groups.
[b]The campaign was targeted at children <6 years, but in 3 of 19 regions, this age range was extended up to adolescence.
[c]Cases collected during the primary vaccination phase.
[d]Incidence rate is per 100,000

Table 2. Available meningococcal vaccines.

Serogroup	Vaccine Formulation	Vaccine Type	Vaccine Name	Manufacturer
A	MenA-TT	Conjugate	MenAfri Vac[83]	Serum Institute of India
B	MenB-FHbp	Recombinant (FHbp subfamily A and B)	Trumenba[70]	Pfizer
	MenB-4C	Recombinant (FHbp subfamily B, NadA, NHBA, OMV)	Bexsero[72]	GlaxoSmithKline
C	MCC-TT	Conjugate	NeisVac-C[53]	Pfizer
	MCC-TT	Conjugate	Menitorix[120]	GlaxoSmithKline
	MCC-CRM	Conjugate	Menjugate[52]	GlaxoSmithKline
	MCC-CRM	Conjugate	Meningitec[51]	Pfizer
C + Y	Hib-MenCY-TT	Conjugate	MenHibrix[121]	GlaxoSmithKline
ACWY	MenACWY-DT	Conjugate	Menactra[122]	Sanofi Pasteur
	MenACWY-CRM	Conjugate	Menveo[63]	GlaxoSmithKline
	MenACWY-TT	Conjugate	Nimenrix[123]	Pfizer

CRM = cross-reactive material; DT = diphtheria toxoid; FHbp = factor H binding protein; Hib = *Haemophilus influenzae* type B; MCC = meningococcal serogroup C conjugate; NadA = neisserial adhesin A; NHBA = neisserial heparin-binding antigen; OMV = outer membrane vesicles; TT = tetanus toxoid.

with the previous year. By 2014–2015, the total number of cases of serogroup C disease decreased to 28 cases—a reduction of 97% compared with the prevaccination era.[28] Nasopharyngeal carriage rates of serogroup C also declined dramatically in vaccinated individuals (ie, a 66% decrease in vaccinated adolescents).[56] Although monovalent serogroup C conjugate vaccines were effective in reducing disease, the immune response of infants who received the 3-dose schedule waned beginning 1 year after vaccination, whereas protection persisted longer in older children immunized with the catch-up schedule.[45] Thus, a booster dose of monovalent serogroup C vaccine was introduced into the routine immunization schedule at 12 months of age.[57] This program continued to evolve based on the needs of the population, ultimately resulting in the removal of the second dose from the infant schedule and a booster dose in adolescents for those who received the vaccine during infancy.[58]

In addition to the United Kingdom, monovalent serogroup C conjugate vaccines have been used to effectively control endemic meningococcal disease in several European countries as well as Australia and Canada.[59] In the Netherlands in 2002, a single dose of the serogroup C vaccine was introduced as part of routine care in children 14 months old; a 1-dose catch-up campaign included children 1 to 18 years old.[60] Epidemiology, logistics, and economics were driving factors for a 1-dose schedule at 14 months versus a 3-dose schedule in infancy. As a result of this campaign, IMD due to serogroup C in the Netherlands decreased rapidly in all age groups. Although herd protection against serogroup C was evident, vaccinated children and adolescents were afforded the greatest protection.[60] In Spain, where children ≤6 years old were targeted in the initial catch-up campaign, substantial herd protection with monovalent conjugate serogroup C vaccines was not observed. It is likely that the failure to immunize teenagers—the population with the highest carriage rates— contributed to the lack of herd protection.[59]

Quadrivalent serogroup ACWY vaccine in adolescents in the United States

In the United States, the incidence of IMD caused by serogroups ACWY is low in children less than 12 months old compared with global statistics, and as a consequence, routine immunization of young children against these serogroups has not been recommended.[61] The exceptions are infants who are at increased risk of IMD because of immune insufficiencies, those with certain conditions such as functional or anatomic asplenia, or those traveling to endemic areas or exposed to an epidemic.[61] Two quadrivalent vaccines are available in the Unites States; one vaccine includes diphtheria toxin as the carrier protein (MenACWY-D, Menactra®, Sanofi Pasteur, Swiftwater, PA, USA)[62] and the other includes CRM_{197} as the carrier protein (MenACWY-CRM, Menveo®, GlaxoSmithKline Vaccines, Srl, Sovicille, Italy).[63]

In the United States, adolescents and young adults are at increased risk of IMD compared with the general population.[64,65] To protect against IMD during the peak susceptibility to infection, the Advisory Committee on Immunization Practices (ACIP) has recommended vaccination with a quadrivalent ACWY vaccine for children 11 to 12 years old since 2005.[66] The rationale for vaccination during the preteen years included the decreased frequency of healthcare visits among older children and the supposition that immunity would be durable through adolescence. By 2007, the incidence of IMD caused by serogroups C, W, and Y decreased among those aged 11 to 17 years compared with prevaccination years. This same year, vaccination recommendations were expanded to include adolescents 11 to 18 years of age.[67] With the availability of post-licensure immunogenicity data, the ACIP issued updated recommendations in 2010 to include routine vaccination of adolescents aged 11 or 12 years, with a booster dose at age 16 years, and a 2-dose primary series administered 2 months apart for persons aged 2 through 54 years with certain underlying comorbidities.[68] The goal of this strategy was to strengthen protection during the period of highest risk. Since 2010, IMD caused by serogroups C, W, and Y has steadily decreased among individuals 18 to 22 years of age.[69] Overall, ACWY vaccination in the United States has lead to a decrease in IMD caused by these serogroups; the exception was 2006 when there was a small spike in cases among those 11 to 17 years of age. For example, over a 2-year period from 2013 to 2014, the annual incidence of IMD was 1 case per 100,000 due to these vaccine serogroups among adolescents aged 11 to 17 years and 1 IMD case per 100,000 among adults aged 18 to 22 years compared with 7 IMD cases per 100,000 in each group in 2004, which was before any vaccine recommendations were implemented.[69]

A study that reports the long-term effectiveness of the quadrivalent meningococcal vaccination program in the United States was recently completed by the Centers for Disease Control and Prevention.[70] In adolescents aged ≥11 years who received 1 dose of MenACWY-D, vaccine effectiveness was 69% against serogroups C, W, and Y targeted by the vaccine (there were no cases of serogroup A). For individual serogroups, vaccine effectiveness was 77% and 51% for serogroups C and Y, respectively. Vaccine effectiveness against serogroup W could not be calculated due to the low disease incidence. Vaccine effectiveness against all serogroups was highest in the first year after vaccination (79%), decreasing to 69% and 61% during 1 to <3 and 3 to <8 years after vaccination, respectively. The waning in seroprotection over time supports the strategy of booster dosing in adolescents.

Serogroup B vaccines in the United Kingdom

Although a decrease in overall incidence of IMD was evident in the United Kingdom from 2002–2003 to 2011–2012, 80% of cases during this period were associated with serogroup B.[71] Based on recommendations from the Joint Committee on Vaccination and Immunisation in 2014, the United Kingdom became the first country to include MenB-4C (Bexsero®, 4CMenB; GlaxoSmithKline Vaccines Srl, Sovicille, Italy)[72] in the national childhood immunization schedule (Table 1). MenB-4C is directed against neisserial adhesin A, factor H binding protein (subfamily B), neisserial heparin binding antigen, and outer membrane vesicles containing the porin A (PorA) protein.[72] MenB-4C was offered to infants born on or after July 1, 2015 using a modified 2-, 4-, and 12-month vaccination schedule rather than a 3-dose infant series with booster.[73,74] A catch-up dose was offered to infants born between May 1 and June 30, 2015.[71] Paracetamol use, particularly in those 2 and 4 months of age receiving Bexsero concomitantly with other routine vaccinations, was recommended to offset fever.[75] This vaccination strategy is the first routine and prophylactic use of a meningococcal serogroup B vaccine to protect a target population in the absence of an epidemic. As a follow-up to the routine use of MenB-4C, a national surveillance study was conducted in the United Kingdom that examined vaccine effectiveness in infants for cases diagnosed between September 1, 2015, and June 30, 2016.[76] During the 10-month period, a 50% reduction in MenB incidence was reported among vaccine-eligible infants compared with 4 years before vaccine implementation. This reduction was not dependent on the vaccination status of the infants assessed or strain coverage by the vaccine. Two doses of MenB-4C in infants resulted in an estimated vaccine effectiveness of 82.9% among those <1 year of age.[76]

Mass vaccination and epidemic response

Serogroup A vaccine in the African meningitis belt

The African meningitis belt, which extends from Senegal to Ethiopia, includes more than 350 million people and accounts for the highest meningococcal disease burden worldwide.[11,77] Traditionally, meningitis epidemics in Africa were not managed proactively; vaccination with unconjugated polysaccharide meningococcal vaccines would be initiated when the weekly incidence rate increased above 10 cases per 100,000 population.[78] As a result, vaccination campaigns often began in the late stages of an epidemic or when the epidemic was declining.[78] Although serogroup A polysaccharide vaccines have been shown to be effective in adults and children >2 years old, less than 30% of children aged <1 year develop immunity following vaccination.[79] This overall failure to control disease was likely due to the intrinsic properties of the vaccine, including the relatively short-lived immunity to free polysaccharide antigens, corresponding lack of immunologic memory, and the absence of an effect on carriage.[80]

Development of a monovalent meningococcal A conjugate vaccine was initiated by a partnership between the World Health Organization and the Program for Appropriate Technology in Health (PATH), a nonprofit organization funded by the Bill & Melinda Gates Foundation. The goal of this initiative was to develop an affordable meningococcal group A conjugate vaccine that induced a long-lasting immune response coupled with the potential to reduce carriage and establish herd immunity.[81] The resulting vaccine, called MenAfriVac (PsA-TT, Serum Institute of India, Pune, India) (Table 2), was granted fast-track status by the World Health Organization in June 2010, and the vaccine was prequalified for use in children and adults aged 1 to 29 years.[82,83]

In 2010, MenAfriVac was used prophylactically in Burkina Faso, Mali, and Niger.[78] These countries were chosen for early introduction because of their potential for meningococcal epidemics and the presence of a supportive infrastructure, including surveillance capabilities and support from the Ministries of Health. Mali and Niger chose a regional vaccination campaign in which vaccination of individuals aged 1 to 29 years occurred in 2 phases in 2010 and 2011.[78] Geography factored into the regional vaccination strategy because Mali and Niger both lie only partially within the meningitis belt and have sparsely populated desert regions in the north, where the incidence of disease is low[84]; hence, a regional rather than national campaign was implemented. During the first round of vaccinations in 2010, the 10-day vaccination campaign in Niger and 2-week campaign in Mali resulted in the immunization of 3 million and 4.5 million residents, respectively.[82] In Burkina Faso, which lies completely within the meningitis belt and has one of the highest incidences of IMD in the region,[85] a national immunization campaign was initiated to immunize children and adults 1 to 29 years old over a 10-day period; approximately 11 million residents were vaccinated during this single campaign.[78]

The effects of vaccination in Burkina Faso were evident immediately. By 2012, no cases caused by serogroup A were identified, and IMD caused by serogroup A has not been detected in Burkina Faso, Mali, or Niger through February 2015.[86] Moreover, in a carriage study conducted in Burkina Faso over 4 sampling periods in 2008 and 2009, which was prior to the country-wide mass vaccination that occurred in 2010, the prevalence of serogroup A was 0.39% (80 positive cultures detected in 20,326 samples).[87] In an assessment of carriage conducted 13 months after vaccination, no serogroup A was detected in over 20,000 samples,[88] suggesting that MenAfriVac was effective in reducing carriage and could potentially

eliminate the reservoir of serogroup A in the population. The impact of MenAfriVac was also notable in Chad, another country within the meningitis belt, where the vaccine was introduced in individuals aged 1 to 29 years during a serogroup A epidemic at the end of 2011. The following year, vaccinated regions experienced a 90% decrease in IMD due to serogroup A and a corresponding decrease in carriage.[89] By 2014, >63 million individuals aged 1 to 29 years living within the meningitis belt received 1 dose of MenAfriVac, with more than 217 million doses administered since 2010; due to vaccination efforts, 1146 deaths due to serogroup A were reported in 2014, which is the lowest mortality rate reported since 2004.[11,90] In January 2015, the World Health Organization recommended that MenAfriVac be included in routine infant immunization schedules in sub-Saharan African countries.[83]

Serogroup A disease and MenACWY vaccination during the Hajj

The first epidemic of serogroup A reported internationally after the Hajj occurred in 1987 with 1841 cases confirmed in Saudi Arabia.[91] The majority of cases were concentrated primarily in and around the cities most frequented during the Hajj.[91] Demographically, pilgrims emanated from a multitude of countries. As such, one notable consequence of the epidemic was the far-reaching dissemination of disease that occurred upon the re-entry of the pilgrims to their native countries. A second wave of disease was reported among the contacts of the infected pilgrims.[91]

From 1995 to 1999, the annual incidence rate for meningococcal infections in Saudi Arabia was 0.2/100,000 persons, which equated to a median of 42 cases per year.[24] In 1997, an epidemic of serogroup A disease occurred prior to the Hajj and 72 cases of serogroup A were identified. Three years later, during the 2000 Hajj, a large epidemic of serogroup A and W was identified; 253 cases were confirmed and of these approximately a quarter were due to serogroup A. Beginning in 2001, the government of Saudi Arabia required quadrivalent polysaccharide MenACWY vaccination for all Hajj pilgrims due to the increased prevalence of meningococcal disease.[91,92] No meningococcal epidemic occurred during the 2002 Hajj. From 2002 to 2011, Saudi Arabia documented only 184 cases of meningococcal disease (all serogroups) and of these, only 9% occurred in Hajj pilgrims.[91] Currently, both polysaccharide and quadrivalent vaccines are recommended for use by the Saudi Arabia Ministry of Health, with vaccination required not more than 3 and 5 years, respectively, prior to arrival.[93]

Mass vaccination in epidemics

Outer membrane vesicle vaccines

In regions around the globe, epidemics caused by meningococcal serogroup B are continually emerging; epidemics occurring in Cuba,[31] Norway,[32] and New Zealand[94] were noted for their longevity and number of confirmed cases. In each of these countries, an outer membrane vesicle (OMV) vaccine specifically targeted to the epidemic strain was developed in response to the epidemic. The immune response induced by these vaccines is highly specific for the immunizing strain, which is likely due to the specificity of the PorA response; as a result, the coverage afforded by OMV vaccines is limited to the epidemic strain.[95]

In Cuba, the introduction of an OMV vaccine (VA-Mengoc-BC, Finlay Instituto, Havana, Cuba) in 1988 led to a substantial decline in IMD among vaccinated and unvaccinated individuals.[31] In Norway, another OMV vaccine (MenBvac, Norwegian Institute of Public Health, Oslo, Norway) was developed in response to a 16-year epidemic that began in 1975[32,96]; this same OMV vaccine was subsequently used to address an epidemic in France that was caused by a similar strain.[36] In New Zealand, an epidemic in the early 1990s led to the development of an OMV vaccine to target the disease-causing strain.[95] Details of this epidemic and vaccine are discussed below.

A prolonged epidemic of meningococcal B disease occurred in New Zealand starting in 1991, with the majority of cases caused by a single epidemic strain.[33,34] At the peak of the epidemic in 2001, the annual IMD incidence was 17.4 cases per 100,000 population.[97] The epidemic affected younger populations, with individuals <20 years old accounting for approximately 80% of all cases; among these, half were <5 years old.[98] In response, a strain-specific OMV vaccine directed against the serogroup B epidemic strain (MeNZB™, Chiron/NZ Ministry of Health, Wellington, New Zealand) was developed through the cooperation of government, academic, and pharmaceutical partners.[95] MeNZB was included in the national immunization program in New Zealand from 2004 to 2006. Vaccination was subsidized by the government and therefore offered free of charge to children and young adults <20 years old; infants and preschool children continued to be vaccinated until 2008; the last phase of the program, after which MeNZB was no longer available in New Zealand, was completed in 2011 and was limited to those with a high risk of disease.[99] MeNZB was administered in a 3-dose schedule to children and young adults, with a booster dose added in 2006 for children who received their first dose before 6 months of age.[100-104] In total, more than 1 million people in New Zealand were immunized during the vaccination campaign.[99] By 2004, when the MeNZB vaccination campaign was initiated, the epidemic in New Zealand had begun to wane. Despite this, a prospective efficacy trial demonstrated that MeNZB significantly decreased the risk of infection by 4-fold in vaccinated individuals and had an effectiveness of 73%.[104] By 2009, the incidence rate for IMD declined to 3.3 per 100,000 population compared with 17.4 per 100,000 population at the peak of the epidemic. By 2014, IMD due to serogroup B had an incidence rate of 1.0 case per 100,000 population,[8] resulting in the lowest rate of disease in those ≥5 years old since 1997.[8]

Recombinant meningococcal serogroup B vaccines in the United States

Although OMV vaccines have been effective in controlling epidemics dominated by a single disease-causing clone in several countries, including Cuba,[31] Norway,[32] France,[36] and New Zealand,[33,34] these vaccines have not been effective for the prevention of endemic disease caused by diverse serogroup B strains.

In 2013 when 2 serogroup B outbreaks occurred on college campuses in the United States (ie, Princeton University and University of California Santa Barbara), there were no licensed MenB vaccines available.[37] In response to this acute unmet medical need, the US Food and Drug Administration granted breakthrough therapy designation to 2 MenB vaccines, MenB-FHbp (Trumenba®, Bivalent rLP2086; Pfizer Inc, Collegeville, PA) and MenB-4C, which were subsequently licensed in 2014 and 2015, respectively, for the prevention of invasive serogroup B disease in individuals aged 10 to 25 years.[70,72] MenB-4C had previously received approval in Europe for individuals ≥2 months old.[105] The different vaccination campaigns implemented using these licensed serogroup B vaccines in response to recent college outbreaks in the United States are discussed below.

Beginning in 2013, 9 cases of serogroup B have been associated with Princeton University (Princeton, NJ, USA), the ninth case occurring in a Drexel student after contact with Princeton students who traveled to Drexel for a social event.[106] Also in 2013, 5 cases were identified at the University of California, Santa Barbara (UCSB; Santa Barbara, CA, USA).[38] In response to these outbreaks, mass vaccination strategies were implemented with MenB-4C, which was not licensed in the United States at the time, administered in a 2-dose series at least 1 month apart for approximately 7500 and 20,000 undergraduates, faculty, and staff at Princeton and UCSB, respectively.[38] With the exception of the Drexel University student,[106] additional cases have not been associated with the Princeton University or UCSB outbreaks after the initiation of the vaccination campaign.[107] In response to the Drexel University case which occurred after the vaccination clinics, Princeton University decided to offer the vaccine to all incoming freshmen.[106]

In 2015, additional serogroup B outbreaks occurred at Providence College (Providence, RI, USA)[108] and the University of Oregon (Eugene, OR, USA).[109] Providence College identified 2 cases of serogroup B disease, resulting in an attack rate of 44 cases per 100,000 students, which is approximately 500-fold higher than the national incidence of 0.15 cases per 100,000 among persons aged 17 to 22 years in the United States.[108] At the University of Oregon, 6 students and 1 parent were diagnosed with IMD, resulting in 1 fatality. The vaccination campaign at Providence College used MenB-FHbp exclusively[108]; the University of Oregon vaccinated primarily with MenB-FHbp, with MenB-4C available at off-campus pharmacies.[38] Although MenB-FHbp was used in both outbreaks, there were a number of notable strategic differences.

Providence College provided vaccine to all eligible students and staff <25 years of age using an opt-out strategy, whereby any individual declining vaccination was required to complete an opt-out form.[108] The first vaccination clinic at Providence College occurred 6 days after 2 cases were confirmed to be due to serogroup B infections; a make-up day was scheduled 3 days later. The second and third doses were administered approximately 2 and 7 months after the first dose, with a single make-up day scheduled within 3 days of each dose. Vaccine uptake among eligible students ranged from 94% for dose 1 to 77% for dose 3.[110] No additional serogroup B cases have been reported as of November 2016. A baseline carriage study at Providence College indicated that of the 25% of students who were carriers of *N meningitidis*, 4% were positive for serogroup B; however, no carriers were positive for the outbreak strain at baseline, making it difficult to assess vaccine effectiveness against carriage.[108]

In contrast, the University of Oregon provided vaccine for all eligible students using an opt-in strategy.[38] Students were required to provide their university identification card, medical insurance, and pharmacy card to receive the vaccine; uninsured students were provided with assistance in obtaining the vaccine. The first vaccination clinic was conducted approximately 45 days after the first case of serogroup B disease was identified and occurred over 4 consecutive days. A second clinic was conducted 2 months later and occurred over 2 days. No make-up vaccinations occurred outside of these periods. Among those eligible for vaccination, vaccine uptake was 46% for dose 1 and 29% for dose 2.[38] After the vaccination campaign, 3 cases of serogroup B disease were reported. Two cases occurred after the first vaccination clinic. A third case occurred after the second vaccination clinic in a father who had visited the campus.

In 2016, 3 serogroup B cases were reported at Santa Clara University (Santa Clara, CA, USA).[111] The university responded by organizing two 3-day vaccination clinics in which MenB-4C was administered to eligible students. In response to 2 serogroup B cases reported at Rutgers University (New Brunswick, NJ, USA), MenB-FHbp was offered to eligible students and faculty.[41] All undergraduate students were required to submit a vaccination verification form or complete a declination form, confirming that the risks of meningococcal disease were understood. Studies are currently underway to examine any reduction in serogroup B carriage following these college-based vaccination campaigns.

At another university in Oregon, Oregon State University, 6 cases of MenB were reported in late 2016 to 2017,[42,112] which prompted the University to require that all students aged ≤25 years be vaccinated against MenB; both MenB-FHbp and 4C-MenB were available to students at the student health center.[42,43] The University had previously required vaccination for incoming students but amended the policy to include all students that were within the age requirement and issued a deadline for vaccination of February 15, 2018.[42,43]

In 2014, a serogroup B vaccination campaign targeting individuals 2 months to 20 years was implemented in the Saguenay-Lac-Saint-Jean region of Quebec.[113] This area had experienced a hyperendemic rate of serogroup B disease with an annual incidence rate >10/100,000 from 2006 to 2013 compared with rates of 0.33/100,000 in Canada and 0.76/100,000 in Quebec.[113] The highest incidence was reported in infants, followed by adolescents. In response, a vaccination campaign targeting approximately 60,000 individuals aged 2 months to 20 years, was implemented. Those aged 2 to 5 months received 4 doses, 6 to 11 months received 3 doses, and ≥1 years received 2 doses. In the course of the vaccination campaign, approximately 45,000 individuals received at least 2 doses of MenB-4C. As a result of the vaccination efforts, serogroup B disease across

the region decreased dramatically and no cases have been reported in vaccinated individuals through January 2016; two cases have been reported among those who were not vaccinated.[114]

Conclusion

Neisseria meningitidis infection causes serious disease worldwide. The introduction of vaccines targeting disease-causing serogroups, such as vaccination against serogroup C in the United Kingdom and serogroup A in Africa, has led to dramatic decreases in IMD incidence.[55,86]

Ongoing meningococcal vaccination campaigns should focus on implementing strategies that maximize the potential for disease prevention, which includes identifying groups most likely to carry and potentially be responsible for transmission across the population. Meningococcal conjugate vaccines clearly demonstrate a reduction in carriage, suggesting these vaccines have the ability to provide both direct protection to vaccinated individuals and herd protection to their close contacts by preventing transmission.[115] Routine prophylactic vaccination strategies targeting those at greatest risk aim to reduce IMD burden and prevent epidemic disease. The impact of recent infant and adolescent serogroup vaccination strategies should be revealed by ongoing surveillance in the coming years.

Five-year view

Vaccination strategies against IMD include mass vaccination, routine vaccination, and a combination of the two approaches. Important considerations in determining the strategy to be used include understanding the disease epidemiology by age and serogroup and the vaccines available.

Currently, IMD is historically low in many regions of the world, with vaccination campaigns such as those in the African meningitis belt, Europe, and Canada successfully reducing IMD incidence by targeting relevant disease-causing serogroup (s) in at-risk populations.[46,116] As IMD incidence is unpredictable, vaccination strategies will need to be updated to combat ongoing changes in meningococcal epidemiology and disease. A proactive strategy, which has been successful for vaccinating large numbers of students on University campuses in the United States,[38] highlights the success that can be achieved through preemptive immunization. The United Kingdom also was responsive to changing needs and incorporated serogroup C booster dosing into the routine infant immunization program upon the realization that catch up vaccination schedules in older children afforded longer protection. The availability of licensed vaccines for the 5 serogroups responsible for the majority of IMD, coupled with the correct implementation and programmatic strategy, should aim to reduce the incidence and reservoirs of IMD through optimizing worldwide vaccination.

Over the next 5 years, more information on the potential effectiveness of recently licensed serogroup B vaccines will become available. The breadth of coverage that these vaccines will provide against disease in terms of clonal complexes and relevant protein antigens expressed by genetically-diverse strains will be determined. These data will potentially support more widespread use of serogroup B vaccines to control endemic disease and inform on the ability of these vaccines to interrupt transmission if vaccination programs are implemented in adolescents and young adults. Development of a serogroup ABCWY pentavalent vaccine over the next 5 to 10 years will potentially simplify vaccination schedules and ensure more comprehensive coverage against the serogroups responsible for the majority of disease. Vaccination strategies should also aim to reduce carriage and bacterial reservoirs, which should result in a reduction in disease transmission.

Disclosure of potential conflicts of interest

All authors are employees of Pfizer Inc and may hold stock and/or stock options.

Acknowledgments

All authors have contributed to the development of this manuscript. The authors would like to thank Cynthia Burman, PharmD, Pfizer Inc, for critical review of the manuscript. Editorial assistance and medical writing were provided by Susan E. DeRocco, PhD, of Complete Healthcare Communications, LLC, a CHC Group company, and was funded by Pfizer Inc.

Funding

This manuscript was funded by Pfizer Inc.

References

1. Rosenstein NE, Perkins BA, Stephens DS, Lefkowitz L, Cartter ML, Danila R, Cieslak P, Shutt KA, Popovic T, Schuchat A, et al. The changing epidemiology of meningococcal disease in the United States, 1992–1996. J Infect Dis. 1999;180(6):1894–901. doi:10.1086/315158. PMID:10558946.
2. Centers for Disease Control and Prevention. Meningococcal disease. [accessed 2017 October 2] http://www.cdc.gov/vaccines/pubs/pinkbook/downloads/mening.pdf.
3. Kimberlin DW, Brady MT, Jackson MA, Long SS, (Eds.). Red Book 2015. 30th ed. Elk Grove Village, IL: American Academy of Pediatrics; 2015. p. 152.
4. Christensen H, May M, Bowen L, Hickman M, Trotter CL. Meningococcal carriage by age: a systematic review and meta–analysis. Lancet Infect Dis. 2010;10(12):853–61 doi:10.1016/S1473-3099(10)70251-6. PMID:21075057.
5. Caugant DA, Hoiby EA, Magnus P, Scheel O, Hoel T, Bjune G, Wedege E, Eng J, Froholm LO. Asymptomatic carriage of Neisseria meningitidis in a randomly sampled population. J Clin Microbiol. 1994;32(2):323–30. PMID:8150942.
6. Carbonnelle E, Hill DJ, Morand P, Griffiths NJ, Bourdoulous S, Murillo I, Nassif X, Virji M. Meningococcal interactions with the host. Vaccine. 2009;27(suppl 2):B78–89. doi:10.1016/j.vaccine.2009.04.069. PMID:19481311.
7. Trotter CL, Ramsay ME. Vaccination against meningococcal disease in Europe: review and recommendations for the use of conjugate vaccines. FEMS Microbiol Rev. 2007;31(1):101–7. doi:10.1111/j.1574-6976.2006.00053.x. PMID:17168998.
8. Environmental Health Indicators New Zealand. Notifications of meningococcal disease. [accessed 2017 October 2] http://www.ehinz.ac.nz/assets/Factsheets/Released-2015/EHI72-NotificationsOfMeningococcalDiseaseInNZ1997-2014-released201508.pdf.
9. Mohammed I, Nasidi A, Alkali AS, Garbati MA, Ajayi-Obe EK, Audu KA, Usman A, Abdullahi S. A severe epidemic of meningococcal meningitis in Nigeria, 1996. Trans R Soc Trop Med Hyg. 2000;94(3):265–70. doi:10.1016/S0035-9203(00)90316-X. PMID:10974995.

10. Dwilow R, Fanella S. Invasive meningococcal disease in the 21st century-an update for the clinician. Curr Neurol Neurosci Rep. 2015;15 (3):2. doi:10.1007/s11910-015-0524-6. PMID:25637287.
11. World Health Organization. Meningococcal Meningitis Fact Sheet No 141. [accessed 2017 October 16] http://www.who.int/mediacentre/factsheets/fs141/en/#.
12. Harrison OB, Claus H, Jiang Y, Bennett JS, Bratcher HB, Jolley KA, Corton C, Care R, Poolman JT, Zollinger WD, et al. Description and nomenclature of *Neisseria meningitidis* capsule locus. Emerg Infect Dis. 2013;19(4):566–73 doi:10.3201/eid1904.111799. PMID:23628376.
13. Stephens DS, Greenwood B, Brandtzaeg P. Epidemic meningitis, meningococcaemia, and *Neisseria meningitidis*. Lancet. 2007;369(9580):2196–210 doi:10.1016/S0140-6736(07)61016-2. PMID:17604802.
14. Mueller JE, Gessner BD. A hypothetical explanatory model for meningococcal meningitis in the African meningitis belt. Int J Infect Dis. 2010;14(7):e553–559. doi:10.1016/j.ijid.2009.08.013. PMID:20018546.
15. World Health Organization. Reducing mortality from emerging diseases. Wkly Epidemiol Rec. 2015;90:121–3. PMID:25816447.
16. Boisier P, Nicolas P, Djibo S, Taha MK, Jeanne I, Mainassara HB, Tenebray B, Kairo KK, Giorgini D, Chanteau S. Meningococcal meningitis: unprecedented incidence of serogroup X-related cases in 2006 in Niger. Clin Infect Dis. 2007;44(5):657–63 doi:10.1086/511646. PMID:17278055.
17. Gagneux SP, Hodgson A, Smith TA, Wirth T, Ehrhard I, Morelli G, Genton B, Binka FN, Achtman M, Pluschke G. Prospective study of a serogroup X Neisseria meningitidis outbreak in northern Ghana. J Infect Dis. 2002;185(5):618–26. doi:10.1086/339010. PMID:11865418.
18. Materu S, Cox HS, Isaakidis P, Baruani B, Ogaro T, Caugant DA. Serogroup X in meningococcal disease, Western Kenya. Emerg Infect Dis. 2007;13(6):944–5. doi:10.3201/eid1306.070042. PMID:17582900.
19. Delrieu I, Yaro S, Tamekloe TA, Njanpop-Lafourcade BM, Tall H, Jaillard P, Ouedraogo MS, Badziklou K, Sanou O, Drabo A, et al. Emergence of epidemic Neisseria meningitidis serogroup X meningitis in Togo and Burkina Faso. PLoS ONE. 2011;6(5):e19513. doi:10.1371/journal.pone.0019513. PMID:21625480.
20. World Health Organization.Rapidly growing outbreak of meningococcal disease in Niger. 2015. [accessed 2018 March 20] http://www.who.int/mediacentre/news/situation-assessments/meningitis-niger/en/.
21. Hossain MJ, Roca A, Mackenzie GA, Jasseh M, Hossain MI, Muhammad S, Ahmed M, Chidiebere OD, Malick N, Bilquees SM, et al. Serogroup W135 meningococcal disease, The Gambia, 2012. Emerg Infect Dis. 2013;19(9):1507–10. doi:10.3201/eid1909.130077. PMID:23965435.
22. Carville KS, Stevens K, Sohail A, Franklin LJ, Bond KA, Brahmi A, Romanes F, Ong KS. Increase in meningococcal serogroup W disease, Victoria, Australia, 2013–2015. Emerg Infect Dis. 2016;22 (10):1785–7 doi:10.3201/eid2210.151935. PMID:27648521.
23. Yousuf M, Nadeem A. Fatal meningococcaemia due to group W135 amongst Haj pilgrims: implications for future vaccination policy. Ann Trop Med Parasitol. 1995;89(3):321–2 doi:10.1080/00034983.1995.11812960. PMID:7668926.
24. Lingappa JR, Al-Rabeah AM, Hajjeh R, Mustafa T, Fatani A, Al-Bassam T, Badukhan A, Turkistani A, Makki S, Al-Hamdan N, et al. Serogroup W-135 meningococcal disease during the Hajj, 2000. Emerg Infect Dis. 2003;9(6):665–71. doi:10.3201/eid0906.020565. PMID:12781005.
25. Aguilera JF, Perrocheau A, Meffre C, Hahne S, W135 working group outbreak of serogroup W135 meningococcal disease after the hajj pilgrimage, Europe, 2000. Emerg Infect Dis. 2002;8(8):761–7. doi:10.3201/eid0808.010422.
26. Abad R, Lopez EL, Debbag R, Vazquez JA. Serogroup W meningococcal disease: global spread and current affect on the Southern Cone in Latin America. Epidemiol Infect. 2014;142(12):2461–70 doi:10.1017/S0950268814001149. PMID:24831052.
27. Tsang RSW, Deeks SL, Wong K, Marchand-Austin A, Jamieson FB. Invasive serogroup W Neisseria meningitidis (MenW) in Ontario, Canada shows potential clonal replacement during the period January 1, 2009 to June 30, 2016. [accessed 2017 March 27] http://www.phac-aspc.gc.ca/publicat/ccdr-rmtc/16vol42/dr-rm42-12/ar-06-eng.php.
28. Public Health England. Meningococcal disease: laboratory confirmed cases in England and Wales; invasive meningococcal C infections by epidemiological year and age group, England. (1998 and 1999 to 2014 and 2015). [accessed 2017 November 2] https://www.gov.uk/government/publications/meningococcal-disease-laboratory-confirmed-cases-in-england-and-wales.
29. Lucidarme J, Hill DM, Bratcher HB, Gray SJ, du Plessis M, Tsang RS, Vazquez JA, Taha MK, Ceyhan M, Efron AM, et al. Genomic resolution of an aggressive, widespread, diverse and expanding meningococcal serogroup B, C and W lineage. J Infect. 2015;71(5):544–52 doi:10.1016/j.jinf.2015.07.007. PMID:26226598.
30. Campbell H, Parikh SR, Borrow R, Kaczmarski E, Ramsay ME, Ladhani SN. Presentation with gastrointestinal symptoms and high case fatality associated with group W meningococcal disease (MenW) in teenagers, England, July 2015 to January 2016. Euro Surveill. 2016;21 (12) doi:10.2807/1560-7917.ES.2016.21.12.30175. PMID: 27035055.
31. Rodriguez AP, Dickinson F, Baly A, Martinez R. The epidemiological impact of antimeningococcal B vaccination in Cuba. Mem Inst Oswaldo Cruz. 1999;94(4):433–40 doi:10.1590/S0074-02761999000400002. PMID:10445998.
32. Fredriksen JH, Rosenqvist E, Wedege E, Bryn K, Bjune G, Froholm LO, Lindbak AK, Mogster B, Namork E, Rye U, et al. Production, characterization and control of MenB-vaccine "Folkehelsa": an outer membrane vesicle vaccine against group B meningococcal disease. NIPH Ann. 1991;14(2):67–79; discussion 79–80. PMID:1812438.
33. Martin DR, Walker SJ, Baker MG, Lennon DR. New Zealand epidemic of meningococcal disease identified by a strain with phenotype B:4:P1.4. J Infect Dis. 1998;177(2):497–500. doi:10.1086/517385. PMID:9466547.
34. Dyet KH, Martin DR. Clonal analysis of the serogroup B meningococci causing New Zealand's epidemic. Epidemiol Infect. 2006;134 (2):377–83. doi:10.1017/S0950268805004954. PMID:16490143.
35. Grodet C, Dequin PF, Watt S, Lanotte P, de Gialluly C, Taha MK, Alonso JM, Quentin R, Goudeau A, Mereghetti L. Outbreak in france of neisseria meningitidis B:15:P1.12 belonging to sequence type 1403. Clin Microbiol Infect. 2004;10(9):845–8. doi:10.1111/j.1469-0691.2004.00935.x. PMID:15355418.
36. Caron F, du Chatelet IP, Leroy JP, Ruckly C, Blanchard M, Bohic N, Massy N, Morer I, Floret D, Delbos V, et al. From tailor-made to ready-to-wear meningococcal B vaccines: longitudinal study of a clonal meningococcal B outbreak. Lancet Infect Dis. 2011;11(6):455–63 doi:10.1016/S1473-3099(11)70027-5. PMID:21489881.
37. Folaranmi T, Rubin L, Martin SW, Patel M, MacNeil JR. 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):608–12. PMID:26068564.
38. Atkinson B, Gandhi A, Balmer P. History of meningococcal outbreaks in the United States: implications for vaccination and disease prevention. Pharmacotherapy. 2016;36(8):880–92. doi:10.1002/phar.1790. PMID:27332671.
39. Mandal S, Wu HM, MacNeil JR, Machesky K, Garcia J, Plikaytis BD, Quinn K, King L, Schmink SE, Wang X, et al. Prolonged university outbreak of meningococcal disease associated with a serogroup B strain rarely seen in the United States. Clin Infect Dis. 2013;57 (3):344–8. doi:10.1093/cid/cit243. PMID:23595832.
40. Biswas HH, Han GS, Wendorf K, Winter K, Zipprich J, Perti T, Martinez L, Arellano A, Kyle JL, Zhang P, et al. Notes from the field: outbreak of serogroup B meningococcal disease at a University – California, 2016. MMWR Morb Mortal Wkly Rep. 2016;65(20):520–1 doi:10.15585/mmwr.mm6520a3. PMID:27227576.
41. Rutgers Student Health. Rutgers recommends meningitis B vaccine. [accessed 2016 August 31] http://health.rutgers.edu/meningitis/.

42. Oregon State University Student Health Services. Meningococcal Disease. [accessed 2018 February 12] http://studenthealth.oregonstate.edu/meningococcal-disease.
43. OSU hit with 6th case of meningococcal disease; all students under 26 will need a vaccination. [accessed 2018 February 12] http://www.oregonlive.com/health/index.ssf/2017/12/osu_hit_with_6th_case_of_menin.html.
44. Harrison LH. Epidemiological profile of meningococcal disease in the United States. Clin Infect Dis. 2010;50(suppl 2):S37–44 doi:10.1086/648963. PMID:20144015.
45. Trotter CL, Andrews NJ, Kaczmarski EB, Miller E, Ramsay ME. Effectiveness of meningococcal serogroup C conjugate vaccine 4 years after introduction. Lancet. 2004;364(9431):365–7. doi:10.1016/S0140-6736(04)16725-1. PMID:15276396.
46. De Wals P, Deceuninck G, Boulianne N, De Serres G. Effectiveness of a mass immunization campaign using serogroup C meningococcal conjugate vaccine. JAMA. 2004;292(20):2491–4. doi:10.1001/jama.292.20.2491. PMID:15562128.
47. Sadarangani M, Scheifele DW, Halperin SA, Vaudry W, Le Saux N, Tsang R, Bettinger JA. Investigators of the canadian immunization monitoring program , ACTive. The impact of the meningococcal serogroup c conjugate vaccine in canada between 2002 and 2012. Clin Infect Dis. 2014;59(9):1208–15 doi:10.1093/cid/ciu597. PMID:25069868.
48. Ladhani SN, Lucidarme J, Newbold LS, Gray SJ, Carr AD, Findlow J, Ramsay ME, Kaczmarski EB, Borrow R. Invasive meningococcal capsular group Y disease, England and Wales, 2007–2009. Emerg Infect Dis. 2012;18(1):63–70. doi:10.3201/eid1801.110901. PMID:22261040.
49. Toros B, Hedberg ST, Unemo M, Jacobsson S, Hill DM, Olcen P, Fredlund H, Bratcher HB, Jolley KA, Maiden MC, et al. Genome-based characterization of emergent invasive Neisseria meningitidis serogroup Y isolates in Sweden from 1995 to 2012. J Clin Microbiol. 2015;53(7):2154–62. doi:10.1128/JCM.03524-14. PMID:25926489.
50. Miller E, Salisbury D, Ramsay M. Planning, registration, and implementation of an immunisation campaign against meningococcal serogroup C disease in the UK: a success story. Vaccine. 2001;20(suppl 1):S58–67. doi:10.1016/S0264-410X(01)00299-7. PMID:11587814.
51. Meningtec® (Meningococcal serogroup C oligosaccharide conjugate vaccine). Package Leaflet: Information for the User, Pfizer Ltd, Kent, UK, 2011.
52. Menjugate® (Meningococcal Group C–CRM197 Conjugate Vaccine). Product Monograph, GlaxoSmithKline Inc, Ontario, Canada, 2015.
53. NeisVac-C® (Meningococcal group C polysaccharide conjugate vaccine adsorbed). Product Monograph, Pfizer Ltd, Kent, UK, 2016.
54. Handysides S. Vaccination programme for group C meningococcal infection is launched in the United Kingdom. Eurosurveillance. 1999;3(30):1365.
55. Ramsay ME, Andrews NJ, Trotter CL, Kaczmarski EB, Miller E. Herd immunity from meningococcal serogroup C conjugate vaccination in England: database analysis. BMJ. 2003;326(7385):365–6. doi:10.1136/bmj.326.7385.365. PMID:12586669.
56. Maiden MC, Stuart JM. U. K. Meningococcal Carriage Group. Carriage of serogroup C meningococci 1 year after meningococcal C conjugate polysaccharide vaccination. Lancet. 2002;359(9320):1829–31. doi:10.1016/S0140-6736(02)08679-8. PMID:12044380.
57. Health England. Meningococcal: the Green Book, Chapter 22. [accessed 2016 August 25] https://www.gov.uk/government/publications/meningococcal-the-green-book-chapter-22.
58. Public Health England. Changes to the meningococcal C conjugate (MenC) vaccine schedule 2013–2015. [accessed 2017 March 27] https://www.gov.uk/government/uploads/system/uploads/attachment_data/file/336171/MenC_information_for_healthcare_professionals_V7_.pdf.
59. Trotter CL, Maiden MC. Meningococcal vaccines and herd immunity: lessons learned from serogroup C conjugate vaccination programs. Expert Rev Vaccines. 2009;8(7):851–61. doi:10.1586/erv.09.48. PMID:19538112.
60. de Greeff SC, de Melker HE, Spanjaard L, Schouls LM, van Derende A. Protection from routine vaccination at the age of 14 months with meningococcal serogroup C conjugate vaccine in the Netherlands. Pediatr Infect Dis J. 2006;25(1):79–80. doi:10.1097/01.inf.0000195594.41449.c6. PMID:16395110.
61. MacNeil JR, Rubin L, McNamara L, Briere EC, Clark TA, Cohn AC, Meningitis, Vaccine Preventable Diseases Branch DoBDNCfI, Respiratory Diseases CDC. Use of MenACWY-CRM vaccine in children aged 2 through 23 months at increased risk for meningococcal disease: recommendations of the Advisory Committee on Immunization Practices, 2013. MMWR Morb Mortal Wkly Rep. 2014;63(24):527–530. PMID:24941332.
62. Menactra (meningococcal [groups A, C, Y and W-135] polysaccharide diphtheria toxoid conjugate vaccine). Full Prescribing Information, Sanofi Pasteur, Swiftwater, PA. 2016.
63. Menveo® (Summary of Product Characteristics, meningococcal [groups A, C, Y and W-135] oligosaccharide diphtheria CRM197 conjugate vaccine). summary of product characteristics. Via Fiorentia, Italy: GSK Vaccines, Srl. 2017.
64. MacNeil JR, Rubin L, Folaranmi T, Ortega-Sanchez IR, Patel M, Martin SW. Use of serogroup b meningococcal vaccines in adolescents and young adults: recommendations of the Advisory Committee on Immunization Practices, 2015. MMWR Morb Mortal Wkly Rep. 2015;64(41):1171–6 doi:10.15585/mmwr.mm6441a3. PMID:26492381.
65. Cohn AC, MacNeil JR, Clark TA, Ortega-Sanchez IR, Briere EZ, Meissner HC, Baker CJ, Messonnier NE. Centers for Disease Control and Prevention. Prevention and control of meningococcal disease: recommendations of the Advisory Committee on Immunization Practices (ACIP). MMWR Recomm Rep. 2013;62(RR-2):1–28 PMID:23515099
66. Bilukha OO, Rosenstein N. National Center for Infectious Diseases, Centers for Disease Control and Prevention. Prevention and control of meningococcal disease. Recommendations of the Advisory Committee on Immunization Practices (ACIP). MMWR Recomm Rep. 2005;54(RR-7):1–21.
67. Centers for Disease Control and Prevention. Revised recommendations of the Advisory Committee on Immunization Practices to vaccinate all persons aged 11–18 years with meningococcal conjugate vaccine. MMWR Morb Mortal Wkly Rep. 2007;56(31):794–5. PMID:17694617.
68. Centers for Disease Control and Prevention. Updated recommendations for use of meningococcal conjugate vaccines — Advisory Committee on Immunization Practices (ACIP), 2010. MMWR Morb Mortal Wkly Rep. 2011;60(3):72–76. PMID:21270745.
69. Centers for Disease Control and Prevention. Active Bacterial Core Surveillance (ABCs) Surveillance Reports. [accessed 2017 November 29] http://www.cdc.gov/abcs/reports-findings/surv-reports.html.
70. Cohn AC, MacNeil JR, Harrison LH, Lynfield R, Reingold A, Schaffner W, Zell ER, Plikaytis B, Wang X, Messonnier NE, et al. Effectiveness and duration of protection of one dose of a meningococcal conjugate vaccine. Pediatrics. 2017;139(2) doi:10.1542/peds.2016-2193. PMID:28100689.
71. Joint Committee on Vaccination and Immunisation. JCVI position statement on use of Bexsero® meningococcal B vaccine in the UK. March 2014. [accessed 2017 October 2] https://www.gov.uk/government/uploads/system/uploads/attachment_data/file/294245/JCVI_Statement_on_MenB.pdf.
72. Bexsero (meningococcal group B vaccine). Full Prescribing Information, Novartis, Cambridge, MA: 2016.
73. Bexsero® (meningococcal group B vaccine). Summary of Product Characteristics. GlaxoSmithKline Research Triangle Park, NC. 2017.
74. Public Health England. Immunisation against meningococcal B disease for infants aged from two months. [accessed 2018 February 12] https://www.gov.uk/government/uploads/system/uploads/attachment_data/file/501588/PHE_MenB_informationforhealthprofessionals_FINAL_18022016.pdf.

75. National Health Service. Using paracetamol to prevent and treat fever after MenB vaccination. [accessed January 4 2018] https://www.gov.uk/government/uploads/system/uploads/attachment_data/file/483408/9413-paracetamol-menB-2page-A4-08-web.pdf.
76. Parikh SR, Andrews NJ, Beebeejaun K, Campbell H, Ribeiro S, Ward C, White JM, Borrow R, Ramsay ME, Ladhani SN. Effectiveness and impact of a reduced infant schedule of 4CMenB vaccine against group B meningococcal disease in England: a national observational cohort study. Lancet. 2016;388(10061):2775–82. doi:10.1016/S0140-6736(16)31921-3. PMID:28100432.
77. Frasch CE, Preziosi MP, LaForce FM. Development of a group A meningococcal conjugate vaccine, MenAfriVac(TM). Hum Vaccin Immunother. 2012;8(6):715–24 doi:10.4161/hv.19619. PMID:22495119.
78. Djingarey MH, Barry R, Bonkoungou M, Tiendrebeogo S, Sebgo R, Kandolo D, Lingani C, Preziosi MP, Zuber PL, Perea W, et al. Effectively introducing a new meningococcal A conjugate vaccine in Africa: the Burkina Faso experience. Vaccine. 2012;30(suppl 2):B40–45. doi:10.1016/j.vaccine.2011.12.073. PMID:22607898.
79. Al-Mazrou Y, Khalil M, Borrow R, Balmer P, Bramwell J, Lal G, Andrews N, Al-Jeffri M. Serologic responses to ACYW135 polysaccharide meningococcal vaccine in Saudi children under 5 years of age. Infect Immun. 2005;73(5):2932–9. doi:10.1128/IAI.73.5.2932-2939.2005. PMID:15845499.
80. Girard MP, Preziosi MP, Aguado MT, Kieny MP. A review of vaccine research and development: meningococcal disease. Vaccine. 2006;24(22):4692–700 doi:10.1016/j.vaccine.2006.03.034. PMID:16621189.
81. Jodar L, LaForce FM, Ceccarini C, Aguado T, Granoff DM. Meningococcal conjugate vaccine for Africa: a model for development of new vaccines for the poorest countries. Lancet. 2003;361(9372):1902–4. doi:10.1016/S0140-6736(03)13494-0. PMID:12788589.
82. LaForce FM, Okwo-Bele J-M. Eliminating epidemic group A meningococcal meningitis in Africa through a new vaccine. Health Aff (Millwood). 2011;30(7):1049–57. doi:10.1377/hlthaff.2011.0328. PMID:21653956.
83. World Health Organization. Meningococcal A conjugate vaccine: updated guidance, February 2015. Wkly Epidemiol Rec. 2015;90 (8):57–68. PMID:25702330.
84. Novak RT, Kambou JL, Diomande FV, Tarbangdo TF, Ouedraogo-Traore R, Sangare L, Lingani C, Martin SW, Hatcher C, Mayer LW, et al. Serogroup A meningococcal conjugate vaccination in Burkina Faso: analysis of national surveillance data. Lancet Infect Dis. 2012;12(10):757–64 doi:10.1016/S1473-3099(12)70168-8. PMID:22818241.
85. Centers for Disease Control and Prevention. Evaluation of meningitis surveillance before introduction of serogroup a meningococcal conjugate vaccine – Burkina Faso and Mali. MMWR Morb Mortal Wkly Rep. 2012;61(50):1025–8. PMID:23254257.
86. World Health Organization. Meningitis weekly bulletin, inter country support team – West Africa. [accessed 2016 August 31] http://www.meningvax.org/epidemic-updates.php.
87. Kristiansen PA, Diomande F, Wei SC, Ouedraogo R, Sangare L, Sanou I, Kandolo D, Kabore P, Clark TA, Ouedraogo AS, et al. Baseline meningococcal carriage in Burkina Faso before the introduction of a meningococcal serogroup A conjugate vaccine. Clin Vaccine Immunol. 2011;18(3):435–43. doi:10.1128/CVI.00479-10. PMID:21228139.
88. Kristiansen PA, Diomande F, Ba AK, Sanou I, Ouedraogo AS, Ouedraogo R, Sangare L, Kandolo D, Ake F, Saga IM, et al. Impact of the serogroup A meningococcal conjugate vaccine, MenAfriVac, on carriage and herd immunity. Clin Infect Dis. 2013;56(3):354–63 doi:10.1093/cid/cis892. PMID:23087396.
89. Gamougam K, Daugla DM, Toralta J, Ngadoua C, Fermon F, Page AL, Djingarey MH, Caugant DA, Manigart O, Trotter CL, et al. Continuing effectiveness of serogroup A meningococcal conjugate vaccine, Chad, 2013. Emerg Infect Dis. 2015;21(1):115–8 doi:10.3201/eid2101.140256. PMID:25536336.
90. Meningitis Vaccine Project. MVP News Digest, Q4 2014. [accessed 2017 March 27] http://www.meningvax.org/files/MVP_newsdigest_2014_Q4_42_EN.pdf.
91. Yezli S, Wilder-Smith A, Bin Saeed AA. Carriage of *Neisseria meningitidis* in the Hajj and Umrah mass gatherings. Int J Infect Dis. 2016; [Accepted for publication].
92. Centers for Disease Control and Prevention. 2016. Yellow Book Travelers' Health. 2016;Chapter 4 Select Destinations
93. Saudi Arabia Ministry of Health. Meningococcal Meningitis. [accessed 2018 February 12] https://www.moh.gov.sa/en/Hajj/HealthGuidelines/HealthGuidelinesDuringHajj/Pages/MeningococcalMeningitis.aspx.
94. Baker MG, Martin DR, Kieft CE, Lennon D. A 10-year serogroup B meningococcal disease epidemic in New Zealand: descriptive epidemiology, 1991–2000. J Paediatr Child Health. 2001;37(5):S13–19. doi:10.1046/j.1440-1754.2001.00722.x. PMID:11885731.
95. Holst J, Oster P, Arnold R, Tatley MV, Naess LM, Aaberge IS, Galloway Y, McNicholas A, O'Hallahan J, Rosenqvist E, et al. Vaccines against meningococcal serogroup B disease containing outer membrane vesicles (OMV): lessons from past programs and implications for the future. Hum Vaccin Immunother. 2013;9(6):1241–53 doi:10.4161/hv.24129. PMID:23857274.
96. World Health Organization. Control of epidemic meningococcal disease. WHO practical guidelines. 2nd edition. [accessed 2017 November 2] http://www.who.int/csr/resources/publications/meningitis/whoemcbac983.pdf.
97. Dyet K, Devoy A, McDowell R, Martin D. New Zealand's epidemic of meningococcal disease described using molecular analysis: implications for vaccine delivery. Vaccine. 2005;23(17-18):2228–30. doi:10.1016/j.vaccine.2005.01.050. PMID:15755601.
98. Lennon D, Jackson C, Wong S, Horsfall M, Stewart J, Reid S. Fast tracking the vaccine licensure process to control an epidemic of serogroup B meningococcal disease in New Zealand. Clin Infect Dis. 2009;49(4):597–605 doi:10.1086/603552. PMID:19622040.
99. New Zealand Ministry of Health. Meningococcal B immunisation programme and MeNZB^{TM} vaccine. [accessed 2017 March 27] http://www.health.govt.nz/our-work/preventative-health-wellness/immunisation/immunisation-programme-decisions/meningococcal-b-immunisation-programme-and-menzbtm-vaccine.
100. Feiring B, Fuglesang JB, Oster P, Naess LM, Helland OS, Tilman S, Rosenqvist E, Bergsaker MA, Nokleby H, Aaberge IS. Persisting immune responses indicating long-term protection after booster dose with meningococcal group B outer membrane vesicle vaccine. Clin Vaccine Immunol. 2006;13(7):790–6 doi:10.1128/CVI.00047-06. PMID:16829617.
101. Holst J, Feiring B, Fuglesang JE, Hoiby EA, Nokleby H, Aaberge IS, Rosenqvist E. Serum bactericidal activity correlates with the vaccine efficacy of outer membrane vesicle vaccines against *Neisseria meningitidis* serogroup B disease. Vaccine. 2003;21(7-8):734–7. doi:10.1016/S0264-410X(02)00591-1. PMID:12531351.
102. Oster P, O'Hallahan J, Aaberge I, Tilman S, Ypma E, Martin D. Immunogenicity and safety of a strain-specific MenB OMV vaccine delivered to under 5-year olds in New Zealand. Vaccine. 2007;25(16):3075–9 doi:10.1016/j.vaccine.2007.01.023. PMID:17289223.
103. Wong SH, Lennon DR, Jackson CM, Stewart JM, Reid S, Ypma E, O'Hallahan JM, Oster P, Mulholland K, Martin DR. Immunogenicity and tolerability in infants of a New Zealand epidemic strain meningococcal B outer membrane vesicle vaccine. Pediatr Infect Dis J. 2009;28(5):385–90 doi:10.1097/INF.0b013e318195205e. PMID:19384263.
104. Kelly C, Arnold R, Galloway Y, O'Hallahan J. A prospective study of the effectiveness of the New Zealand meningococcal B vaccine. Am J Epidemiol. 2007;166(7):817–23 doi:10.1093/aje/kwm147. PMID:17615088.
105. European Medicines Agency. Bexsero EPAR summary for the public. [accessed 2017 March 27] http://www.ema.europa.eu/docs/en_GB/document_library/EPAR_-_Summary_for_the_public/human/002333/WC500137857.pdf.

106. National Foundation for Infectious Diseases. Addressing the challenges of serogroup B meningococcal disease outbreaks on campuses: A report by the National Foundation for Infectious Diseases. [accessed 2018 February 12] http://www.nfid.org/meningococcal-b.
107. National Meningitis Association. Serogrlloup B meningococcal disease outbreaks on U.S. college campuses. [accessed 2018 February 12] http://www.nmaus.org/disease-prevention-information/serogroup-b-meningococcal-disease/outbreaks/.
108. Soeters HM, McNamara LA, Whaley M, Wang X, Alexander-Scott N, Kanadanian KV, Kelleher CM, MacNeil J, Martin SW, Raines N, et al. Serogroup B meningococcal disease outbreak and carriage evaluation at a college – Rhode Island, 2015. MMWR Morb Mortal Wkly Rep. 2015;64(22):606–7. PMID:26068563.
109. University of Oregon. Meningococcemia diagnosed in another UO student; vaccination efforts continue. [accessed 2018 February 12] http://around.uoregon.edu/content/meningococcemia-diagnosed-another-uo-student-vaccination-efforts-continue.
110. Soeters H, McNamara L, Whaley M, Wang X, Alexander-Scott N, Goodwin K, Kanadanian K, Kelleher C, MacNeil J, Martin S, et al. Meningococcal carriage evaluation in response to a serogroup B meningococcal disease outbreak and mass vaccination campaign at a college-Rhode Island. Paper presented at: IDWeek (abstract number 1872). 2015 October 7–11; San Diego, CA.
111. Santa Clara County Public Health. Meningococcal Meningitis. [accessed 2016 August 31] https://www.sccgov.org/sites/sccphd/en-us/Residents/DiseaseInformation/meningitis/Pages/meningitis.aspx.
112. The Associated Press. Second Oregon State student sick with meningoccocal disease. [accessed 2018 February 13] http://www.oregonlive.com/education/index.ssf/2016/11/second_oregon_state_student_si.html.
113. de Serres G. Results of a mass immunization campaign with 4CmenB vaccine in the Saguenay-Lac-Saint-Jean region. Paper invited to be presented at: Meeting of the Advisory Committee on Immunization Practices (ACIP). 2016 February 24; Atlanta, GA, USA Requests for slide presentation files at acip@cdc.gov.
114. Banzhoff A. Multicomponent meningococcal B vaccination (4CMenB) of adolescents and college students in the United States. Ther Adv Vaccines. 2017;5(1):3–14. doi:10.1177/2051013616681365. PMID:28344804.
115. Read RC, Baxter D, Chadwick DR, Faust SN, Finn A, Gordon SB, Heath PT, Lewis DJ, Pollard AJ, Turner DP, et al. Effect of a quadrivalent meningococcal ACWY glycoconjugate or a serogroup B meningococcal vaccine on meningococcal carriage: an observer-blind, phase 3 randomised clinical trial. Lancet. 2014;384(9960):2123–31. doi:10.1016/S0140-6736(14)60842-4. PMID:25145775.
116. Maiden MC, Frosch M. Can we, should we, eradicate the meningococcus? Vaccine. 2012;30(suppl 2):B52–56. doi:10.1016/j.vaccine.2011.12.068. PMID:22607899.
117. Lingani C, Bergeron-Caron C, Stuart JM, Fernandez K, Djingarey MH, Ronveaux O, Schnitzler JC, Perea WA. Meningococcal meningitis surveillance in the African meningitis belt, 2004–2013. Clin Infect Dis. 2015;61(Suppl 5):S410–415. doi:10.1093/cid/civ597. PMID:26553668.
118. Noah N, Henderson B. Surveillance of bacterial meningitis in europe 1999/2000. 2002. [accessed 2018 March 20] http://ecdc.europa.eu/en/publications/Publications/0202_SUR_Surveillance_of_Bacterial_Meningitis.pdf
119. Larrauri A, Cano R, Garcia M, Mateo S. Impact and effectiveness of meningococcal C conjugate vaccine following its introduction in Spain. Vaccine. 2005;23(32):4097–100. doi:10.1016/j.vaccine.2005.03.045. PMID:15908059.
120. Menitorix (Meningococcal polysaccharide conjugate vaccine (Hib-MenC)). Full Prescribing Information, GlaxoSmithKline, Victoria, Australia, 2016.
121. MENHIBRIX (Meningococcal Groups C and Y and Haemophilus b Tetanus Toxoid Conjugate Vaccine). Full Prescribing Information, GlaxoSmithKline, Rixensart, Belgium, 2013.
122. Menactra® (MCV4). Full Prescribing Information. Sanofi Pasteur, 2011.
123. Nimenrix®, Product Monograph. (Meningococcal polysaccharide groups A, C, W-135 and Y conjugate vaccine). Full Prescribing Information, Pfizer Canada Inc, Kirkland, QC, Canada, 2016.