THE GLOBAL MENINGOCOCCAL INITIATIVE:

A new worldwide expert group to raise awareness and help prevent invasive meningococcal disease

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ABSTRACT

The Global Meningococcal Initiative (GMI) is a new international expert group of scientists and clinicians, chaired by Stanley Plotkin. Collectively, these individuals have expertise in meningococcal clinical practice, epidemiology, immunology, public health, vaccinology, manufacturing, microbiology, and heath economics. The GMI has been formed with the intention to help prevent invasive meningococcal disease worldwide through education, research, and cooperation. Given the geographic variability seen with this disease, the GMI will address these issues at both regional and global levels.

The GMI held their first summit meeting in Barcelona, Spain, on June 18-19, 2010, attended by 23 experts in the field. The scope of the meeting was global, discussing all geographic regions and meningococcal serogroups. Topics of discussion included: worldwide epidemiology, including the African Meningitis Belt, Asia, and the Hajj; introduction of novel vaccines, including MenAfriVac; diagnostic and case confirmation best practice and advice to low-resource regions; variations in regional vaccination strategies across the world. The meeting concluded with discussion on novel prevention strategies, where the importance of serogroup C conjugate vaccine catch-up campaigns in developed countries was highlighted in controlling disease through herd immunity. It became apparent that uncertainty exists concerning the choice between monovalent serogroup and polyvalent serogroup conjugate vaccines, and that data on meningococcal incidence in Asia and other geographic regions are sparse.

INTRODUCTION

- Invasive meningococcal disease (IMD) due to *Neisseria meningitidis*, with meningitis and septicemia being the most common clinical presentations, occurs in 500,000 people and causes 50,000 deaths each year worldwide.[1] There are temporal and geographic variations in IMD incidence, with the majority of disease occurring in the African Meningitis Belt.[2]
- Death can occur in as few as 24 h after symptoms appear.[3] Limb loss, hearing loss, and cognitive deficits may occur in those who survive.[4,5]
- Vaccines are available to serogroups A, C, W-135, and Y; protection against serogroup B has proved more difficult, because of the similarity of serogroup B capsular polysaccharides to human glycoproteins.[6] However, there have been some successes against serogroup B disease, most notably in New Zealand with a vaccine containing outer membrane proteins.

THE GLOBAL MENINGOCOCCAL INITIATIVE

- The newly formed Global Meningococcal Initiative (GMI) was established to help prevent IMD worldwide through education, research, and cooperation. Issues of IMD are to be addressed at both global and regional levels.
- The GMI is an international group of renowned scientists and clinicians whose expertise encompasses meningococcal clinical practice, epidemiology, immunology, public health, vaccinology, manufacturing, microbiology, and heath economics.
- The GMI is supported by an unrestricted grant from sanofi pasteur.

FIRST GMI SUMMIT MEETING

- The First GMI Summit Meeting, held in Barcelona, Spain, on June 18 –19, 2010, comprised 23 experts (**Table 1**).

TABLE 1. Experts Attending the First GMI Summit Meeting

Chairman
Stanley Plotkin, MD, *University of Pennsylvania, Doylestown, PA, USA*

Steering Committee
Carl Frasch, PhD, *Frasch Biologics Consulting, Martinsburg, WV, USA*
Lee Harrison, MD, *University of Pittsburgh, Pittsburgh, PA, USA*
Andrew J. Pollard, FRCPCH, PhD, *University of Oxford, Oxford, UK*
Muhamed-Kheir Taha, MD, PhD, *Institut Pasteur, Paris, France*
Julio Vazquez, PhD, *Institute of Health Carlos III, Madrid, Spain*
Anne von Gottberg, MBBCh, *National Institute for Communicable Diseases, Johannesburg, South Africa*

Summit Members
Richard Adegbola, MSc, PhD, *Bill and Melinda Gates Foundation, Seattle, WA, USA*
Colin Block, MBBCh, PhD, *Hadassah-Hebrew University Medical Centre, Jerusalem, Israel*
Ray Borrow, PhD, *Health Protection Agency, Manchester, UK*
Tom Clark, MD, MPH, *Centers for Disease Control and Prevention, Atlanta, GA, USA*
Benoit Dervaux, PhD, *CRESGE l'Université Catholique de Lille, Lille, France*
Johan Holst, PhD, MSc, *Norwegian Institute of Public Health, Oslo, Norway*
Sheldon Kaplan, MD, *Baylor College of Medicine, Houston, TX, USA*
Marc LaForce, MD, *Meningitis Vaccine Project, Arlington, VA, USA*
Xiaofeng Liang, MD, *National Immunization Program, China CDC, Beijing, China*
Diana Martin, PhD, *Institute of Environmental Science and Research, Poriru, New Zealand*
Stephen Pelton, MD, *Boston University Schools of Medicine and Public Health, Boston, MA, USA*
Marco Safadi, MD, *FCM Da Santa Casa de São Paulo, São Paulo, Brazil*
Samir Saha, PhD, *Institute of Child Health, Dhaka, Bangladesh*
Franklin Sotolongo, MD, *Finlay Institute, Havana, Cuba*
Irina Stanislavovna Koroleva, MD, PhD, *Central Research Institute of Epidemiology, Moscow, Russia*
Annelies Wilder-Smith, MD, PhD, MIH, *National University of Singapore, Singapore*

- Topics considered included current epidemiological and serological trends in IMD in numerous countries throughout the world; current and pending vaccine formulations (polysaccharide, conjugate), valency (monovalent, multivalent), and scheduling; current vaccination strategies; and how to reduce the burden of IMD.

EPIDEMIOLOGY AND SEROLOGY OF IMD

- In most countries, the greatest burden of disease is found in infants <1 year of age. Even among developed nations, incidence rates are high. For example, in Canada, the incidence rate is 7.8 cases per 100,000 infants <1 year of age.
- In many Western countries, such as the United States, Canada, and the United Kingdom, a second peak in disease burden is observed among adolescents. However, this is not universal. For example, there is no adolescent peak in Brazil and some other countries in Latin America, or in the African Meningitis Belt.
- In some countries, a third peak is also observed in the elderly.[7]

SURVEILLIANCE

- IMD surveillance is highly variable and data on incidence and the serogroups to which IMD is attributable are often incomplete (**Table 2**).
- To capture the true burden of IMD, accurate surveillance systems are needed, which requires uniformly and consistently applied case definitions. Diagnoses based solely on clinical examination are not reliable because the clinical symptoms of IMD are not unique or always obvious.
- Definitive diagnosis requires laboratory assessment, ideally the detection of *N meningitidis* from otherwise sterile body sites. Bacterial culture is the gold standard but may lead to underreporting due to low sensitivity and, in some countries, common antibiotic use prior to sample acquisition. Polymerase chain reaction (PCR) is an important adjunct to bacterial culture; it is the most sensitive technique now available and where resources are available should be added to cultures for diagnostic purposes.
- Other techniques, such as commercial biochemical test strips and latex agglutination kits, are also available in some countries but have limited sensitivity.
- Partnerships between resource-rich and resource-poor regions of the world may help to overcome the paucity of surveillance data in regions of the world thought to underreport IMD.

TABLE 2. Incidences and Predominant Serogroups

Geographic region	Incidence	Predominant serogroup (s)
Africa		
African Meningitis Belt	Very high incidence (up to 1000 per 100,000); Highest in age group 0–19 year olds	A + others
South Africa	Incidence 3.7 per 100 000 population in 2005; Highest rates in children <1 year old; increases in winter and spring	W-135
Asia		
Bangladesh	46% of all cases in 0–2 year olds, 50% of whom are 0–6 months of age	A (80%)
China	9.2–14.2 per 100,000 (most cases in winter); mainly in <1 year olds	C (38%), A (36%)
Saudi Arabia (Hajj pilgrims)	1 in 70 of these develop IMD on return from Hajj	Last large W-135 epidemic in 2001
Europe/North America		
Western Europe	Peaks in infants (<1 year) Second peak in adolescents Third peak in elderly (≥65 years)	B
Russia	1.3 cases per 100,000 individuals, mainly in infants	A, C B common in east
North America	0.4 cases per 100,000	Y, C, B
Pacific region		
Australia	Occasional endemic cases	B or C
New Zealand	Serogroup B epidemic countered by MenNZB vaccine. 40 cases in 2009, 3.3% attributed to serogroup B strain	C (previously B)
South America		
Brazil	Highest incidence in South America	B (37%), C (51%)
Argentina, Chile, Uruguay, Paraguay	Limited data	B, W-135 increasing in Argentina
Columbia	Limited data	B and Y in the same proportion

VACCINES

- Several commercial vaccines against meningococcal disease are licensed in various countries, including monovalent (Group A and C), bivalent (A/C) and quadrivalent (A/C/W-135/Y) polysaccharide vaccines; as well as monovalent and quadrivalent protein conjugated polysaccharide vaccines of analogous composition.
- The efficacy against Groups A and C has been demonstrated in clinical trials, whereas other valences have been licensed on the basis of induction of bactericidal antibodies, which is a correlate of protection.
- The use of these vaccines depends on epidemiological factors such as the incidence and peak age of disease, and also taking into account the ability of conjugate vaccines to induce antibodies in infants.
- Conjugate vaccines also have the advantage of not inducing hyporesponsiveness to booster vaccination.

STRENGTHS AND WEAKNESSES OF CURRENT VACCINATION STRATEGIES

- Current IMD vaccination programs in various countries are summarized in **Table 3**.

TABLE 3. Current IMD Vaccination Programs

Country	Vaccine	Vaccination schedule
Argentina	MenAC MenC conjugate MenB	Outbreak management
Australia	MenC conjugate	12 months of age
Brazil	MenAC MenC conjugate	≥2 years of age 3, 5, and 12 months of age
Canada	MenC conjugate vaccine MenACYW-135 conjugate	2, 4, and 12 months of age Adolescent booster in some provinces
	Both formulations used for adolescent booster	2–55 years of age, if high risk
China	MenA MenAC	2 doses between 6–18 months of age 3 and 6 years of age
Cuba	MenBC	3 and 5 months of age
France	MenC conjugate	1 dose after 12 months of age
Greece	MenC conjugate	2, 4, and 15–18 months of age groups
Italy	MenC conjugate	2 months–2 years of age
Japan	No routine IMD vaccination strategy	
Mexico	No routine IMD vaccination strategy	
New Zealand	MenNZB	Routine vaccination stopped; still available for high-risk groups
Paraguay	MenAC	Only high-risk or special-needs groups
Russia	MenAC	Contacts with the infected
Saudi Arabia	Quadrivalent meningococcal	All health care workers and internal Hajj pilgrims, residents in Hajj region aged 2–55 years
South Africa	Quadrivalent polysaccharide only	Only high-risk groups and potentially for outbreak management
Spain	MenC conjugate	2, 6, and 15–18 months of age
UK	MenC conjugate (combined with Hib at 12 months of age)	3, 4, and 12 months of age
USA	MenACYW-135 conjugate	11–18 years of age (2–10, 19–55 years if high risk; 13–18 years for catch-up)

Europe

- Vaccination of infants against serogroup C with MenC is common in EU countries, but protective bactericidal antibodies decline over time, which is likely to result in reduced clinical protection. Previous catch-up campaigns targeted adolescents. Adolescents are not currently given a booster dose, but several countries are considering introducing one to sustain immunity.
- Exclusive use of MenC vaccine in Europe is currently warranted by the low incidence of IMD due to serogroups A, Y, and W-135. Licensed conjugate (and polysaccharide) vaccines against A, W-135, and Y serogroups are available. Routine vaccination against these serotypes in Europe is currently not cost effective, as the serogroups are rare. This may change if increases in serogroup A, Y, or W-135 were to occur.

New Zealand

- Introduction of the Meningococcal B Immunization Program, using the MenNZB vaccine, resulted in the control of the New Zealand's epidemic due to *N. meningitidis* that was dominated by the strain B:4:P1.7b,4 with a 3.7-fold reduced risk of serogroup B-specific IMD. Disease resurgence is a matter of concern because the program has now ended.

North America

- In the United States, because of the circulation of serogroups C and Y, routine immunization is carried out at 11–12 years (with routine catch-up to 18 years) using the conjugate quadrivalent (A,C,Y, W-135) formulation.
- In Canada most disease is serogroup C. Children are routinely vaccinated with MenC vaccine (similar to Europe), and sometimes quadrivalent (A,C,Y,W-135) vaccine. Adolescent booster using both conjugate formulations has been introduced in some provinces. Vaccines are also available for those considered at high risk.

South America

- Brazil is the only country with a routine vaccination program in infants and a comprehensive surveillance system, but it lacks a catch-up component. The country has the highest documented levels of IMD in South America.
- In other countries, the overall burden of IMD was thought to be low, but accurate surveillance data are lacking. Hence, large-scale vaccination programs are currently not thought to be cost effective by regional governments. More accurate surveillance is required to determine the true prevalence.

African Meningitis Belt

- The introduction of the conjugate vaccine against group A (MenAfriVac) is anticipated to have a large positive impact on morbidity and mortality of IMD in this region, where 90% of the IMD is attributable to this serogroup. MenAfriVac will first be introduced to Mali, Niger, and Burkina Faso during 2010–2011, starting in September 2010.

Asia

- Discussions among the GMI showed that epidemiological data from many regions of Asia are sparse. Serogroup A is responsible for most reported disease in the region, apart from China and Russia where serogroups A and C are equally prevalent. Serogroup B is also common in some parts of eastern Russia.

PROPOSED RECOMMENDATIONS FOR THE PREVENTION OF IMD

- Conjugate vaccines should replace polysaccharide vaccines particularly in children, where cost, availability, and licensing allow, because of immunologic advantages of conjugate vaccines; polysaccharide vaccines are still recommended where conjugate vaccines are not available.
- Measures should be taken to avoid repeated dosing with polysaccharide vaccines to prevent hyporesponsiveness.
- Global surveillance for IMD should be strengthened to determine the true burden of IMD worldwide.
- Ideally, given its morbidity and mortality risk, all high-risk individuals should consider being vaccinated.
- Vaccination against IMD should be recommended to travellers who will visit high-risk areas. An example of this is vaccination of Islamic pilgrims to the Hajj, where vaccination with a quadrivalent vaccine is mandatory.
- Given the complexity of IMD epidemiology and geographic variations, vaccination strategies should be tailor-made to regions and countries. Future meetings of the GMI aim to develop recommendations specific for each region of the world.

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