

# THE GLOBAL MENINGOCOCCAL INITIATIVE: MENINGOCOCCAL DISEASE IN ASIA PACIFIC – FINDINGS AND RECOMMENDATIONS FROM THE REGIONAL ROUNDTABLE MEETING, 2014

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## ABSTRACT

**Introduction:** The Global Meningococcal Initiative (GMI) is a global expert group composed of scientists and clinicians with a wide range of specialisations. The initiative seeks to prevent invasive meningococcal disease (MD) globally through education, research and co-operation.

**Aim:** Further understanding of MD and its prevention in Asia Pacific.

**Methods:** A meeting was held in November 2014 where the GMI reviewed global MD data, with a focus on the available data from participating Asia Pacific countries.

**Results:** During this review, many challenges and data gaps were identified in several Asia Pacific countries, and recommendations to address these were formulated. First, MD is under-reported; to improve this, diagnostic techniques and surveillance need to be enhanced in the region, and a standardised case definition is needed. Second, outbreak management guidelines are lacking and should be developed, including a definition of a 'close contact.' Third, reducing meningococcal transmission is expected to enhance control of MD. Research to identify matrices of transmission is a priority. Furthermore, during outbreaks, targeting these group(s) for vaccination is critical for disease control. Finally, increasing awareness of MD among health care providers and health authorities is needed, and advocacy tools should be developed to ensure prevention and management initiatives have the requisite resources.

**Conclusion:** In order to improve the MD situation in Asia Pacific and address the unique outbreak situation (ie, low incidence of MD and outbreaks need to be considered when even a single case is reported), the GMI proposed several activities including the need to strengthen surveillance, improve case reporting, developing guidelines on how to apply different methods of diagnosis, standardising case definitions, developing guidelines for outbreak management and increasing awareness of MD among health professionals.

## INTRODUCTION

- Neisseria meningitidis* remains a leading cause of meningitis and septicaemia globally and is estimated to cause more than 1.2 million cases of invasive meningococcal disease (MD) and 135,000 deaths each year.<sup>1,2</sup>
- MD is associated with substantial morbidity and high fatality rates of 10–20%.<sup>3,4</sup>
- However, in many countries in the Asia Pacific region the true burden of disease is unknown. The reason for this is multifactorial and includes: under-reporting, weak surveillance systems, lack of guidelines and standard case definitions, and lack of awareness and country focus on MD. – Indeed, countries such as Korea and Japan have frequently reported a low incidence of MD, and therefore the disease is not considered a high health care priority.
- In order to better understand MD in Asia Pacific the Global Meningococcal Initiative (GMI) convened its first Asia Pacific regional meeting in Incheon, South Korea on 20–21 November 2014.
- The objectives of this meeting were to:
  - Better understand the epidemiology of MD in Asia over the past decade,
  - Examine the surveillance and prevention strategies in Asia,
  - Discuss key learning points from experience with meningococcal vaccine programmes and how these may be applied elsewhere,
  - Develop recommendations for the control and prevention of MD in Asia, including outbreak preparedness, and
  - Devise means of information dissemination.

## THE GLOBAL MENINGOCOCCAL INITIATIVE

- The GMI, supported by Sanofi Pasteur, is a multidisciplinary group of ~50 scientists and clinicians with diverse expertise from around the world.
- The initiative was formed in 2009 with the goal of preventing MD through education, research, international co-operation and the development of recommendations.
- Given the presence of experts in the field of MD from both the Asia Pacific and elsewhere in the globe, it is hoped that any GMI recommendations will have broad impact and be of medical, scientific and educational value.

## SURVEILLANCE AND EPIDEMIOLOGY OF MD IN ASIA PACIFIC

### INDIA

#### Surveillance

- India does not have a strong surveillance system, which hampers accurate epidemiology and also efforts to control and manage the disease.
  - MD is most certainly under-reported in India:
    - Many patients receive antibiotics from their health care practitioner (HCP) if MD is suspected, and this tends to occur prior to admission to hospital.
    - A single dose of antibiotic can result in a negative culture even if the patient is infected with MD.
    - Another variable that results in under-reporting is that some patients are not seen by HCPs/or at a hospital early in the course of MD, resulting in these patients dying from complications.
  - In addition, within the country, the experts – epidemiologists, microbiologists, clinicians – tend to work apart, only collaborating during outbreaks.
  - Thus data tend to only be available during outbreaks.
- Case definitions are based on the World Health Organization (WHO) guidelines.
- Polymerase chain reaction (PCR) is often only performed by special request or if a study is being undertaken.
- During interepidemic periods, data are collected from the Central Bureau of Health Intelligence (CBHI), Integrated Disease Surveillance Project (IDSP) and individual published reports.
- During outbreak periods, data are obtained from laboratories (eg, the Delhi outbreak), hospitals (eg, Meghalaya) and the community (eg, Tripura).

#### Epidemiology

- Most reported cases thus far are due to serogroup A, with rare reports of isolation of serogroup B and C.
- The majority of cases occur in late winter and early spring.
- Outbreaks more frequently observed post 2005.

### JAPAN

#### Surveillance

- Japan's surveillance system is named The National Epidemiological Surveillance on Infectious Disease (NESID).
  - Since 1999, detection/isolation of meningococci from meningitis patients: all cases are reported from hospital.
  - From April 2013, meningococcal bacteremia without focus has been added to notifiable disease as an invasive MD (IMD), in addition to meningococcal meningitis.
- Detection of MD is reliant on clinicians' ability to suspect meningococci.
  - All hospitals have laboratories where they perform culture and PCR.
  - Following confirmation, the disease is reported to the local health department, which also undertakes a PCR. For more detailed testing the sample is sent to NESID.
- Generally accepted that sample collection needs improvement.

#### Epidemiology

- Japan is unique in that it has a low incidence of MD (Figure 1).
- From 1999 to 2013 the rate of MD was highest in adolescents and males (59%).
- Since 2013 the incidence of cases in males increased to 69% and the age cohort affected shifted (Table 1; Figure 1).
- The major serogroup isolated is Y (Table 1).

### KOREA

#### Surveillance

- In Korea the Division of Tuberculosis and Bacterial Respiratory Infectious Diseases, Korea Centers for Disease Control and Prevention (KCDC) works as a central laboratory.
- There is a passive surveillance system in place, but reporting varies across medical facilities.
- Reporting of meningococcal meningitis cases is mandatory.
- There are 3 sources of surveillance data:
  - KCDC,
  - Health Insurance Review and Assessment Service (HIRA), mandatory governmental health insurance,
  - Individual report papers.
- Data reported by sources vary widely (Figure 2).
- In addition, the diagnostic criteria do not reflect the pathogen-specific diagnosis (ie, reliant on culture).
- Many patients receive antibiotics from HCPs, which may impact on the results of the culture.

#### Epidemiology

- Few reliable epidemiology data are available in Korea.
- Impacted age cohorts vary across the 3 reporting systems in Korea, as do the incidence rates (Table 1).

FIGURE 1. Age and Gender Distribution of MD Cases, Japan, April 2013–Aug 2014

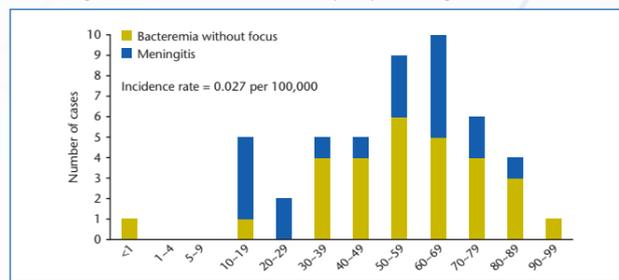
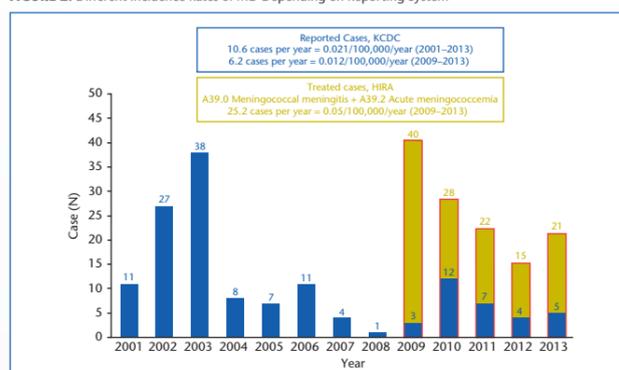


TABLE 1. Epidemiology of MD in the Asia Pacific Region

	India	Japan	Korea	The Philippines
Quality of data.	Mostly only available during outbreaks.	Detection of MD is reliant on clinicians' ability to suspect meningococci. Surveillance system in place and laboratory resources good.	Little reliable epidemiological data.	Only the septicaemic form, meningococemia, is reported.
Data source.	Recently there were 3 major outbreaks in India (Delhi/NCR [2005], Meghalaya [2008–09] and Tripura [2009]).	NESID.	KCDC, HIRA and individual published reports.	PIDSR.
Incidence.	Not reliably known.	0.027/100,000 during 2013–2014.	0.012–0.05/100,000/year in general population (by KCDC or HIRA data) 6.8/100,000/year in children (aged <5 years) (in a CSF PCR study).	0.02–0.1/100,000/year.
Age groups affected.	An increase in the proportion of cases in young adults has recently been reported.	Since 2013 MD has become more prevalent in individuals aged 50 years and older.	Vary across the 3 reporting systems.	The number of cases was greatest in infants and young children (case fatality high; females more than males).
Predominant serogroups.	Serogroup A with rare reports of B and C.	Serogroup Y, followed by C and B (but these data are based on only 48 cases).	No predominant serogroups at this time.	Serogroup A, although B has been documented.
Case definition.	<b>Suspect:</b> sudden onset of fever >38.5°C rectal or 38.0°C axillary with stiff neck (in patients <1 year of age, bulging fontanel). <b>Probable:</b> suspect case as defined above, with Gram stain showing diplococci or ongoing epidemic or purpurial rash. <b>Confirmed:</b> suspect or probable case as above, with either positive cerebrospinal fluid (CSF)/blood culture or positive CSF antigen detection for meningococcus or positive PCR test.	Meningococcal disease with either culture or PCR positive cases are confirmed cases and need to be reported within 7 days after the diagnosis.	Differ depending on location and situation, ie, outbreak definition different from non-outbreak situations.	<b>Suspect:</b> Acute fever with haemorrhagic rash and/or meningial signs. <b>Probable:</b> A suspect case with turbid CSF OR gram negative diplococci from CSF, blood or skin OR close contact with a confirmed case during the previous 10 days. <b>Confirmed:</b> A suspect case with <i>Neisseria meningitidis</i> isolated from a sterile site (CSF, blood, skin) OR presence of <i>N. meningitidis</i> DNA from a sterile site (CSF, blood, skin).

CSF, cerebrospinal fluid; HIRA, Health Insurance Review and Assessment Service; KCDC, Korea Centers for Disease Control and Prevention; MD, meningococcal disease; NESID, the National Epidemiological Surveillance on Infectious Disease; PCR, polymerase chain reaction; PIDSR, the Philippine Integrated Disease Surveillance and Response.

FIGURE 2. Different Incidence Rates of MD Depending on Reporting System<sup>5,6</sup>



HIRA, Health Insurance Review and Assessment Service; KCDC, Korea Centers for Disease Control and Prevention; MD, meningococcal disease.

## THE PHILIPPINES

### Surveillance

- In 2005, the PIDSR was created in response to the International Health Regulations of the WHO.
- Only the septicaemic form, meningococemia, is reported; thus, the surveillance data are skewed and reflect a high case fatality.
- Surveillance for bacterial meningitis has been adopted by the National Epidemiology Center (NEC) as a surrogate for Invasive Bacterial-Vaccine Preventable Disease (IB-VPD) Surveillance.
- Surveillance for MD is based on clinical case definitions, which can be used in all types of health care settings.
- For confirmation of MD, PCR is mostly used in the central laboratory, but PCR is also available in local hospitals.

### Epidemiology

- According to data reported to PIDSR from 2008 through 2013, the number of meningococemia cases increased from 73 cases in 2008 to 182 in 2013.
  - An average of 100 cases are reported every year, without seasonal variation (Table 1).
  - Those most affected are shown in Table 1 and Figure 3.
  - Table 1 also highlights the predominant serogroups.

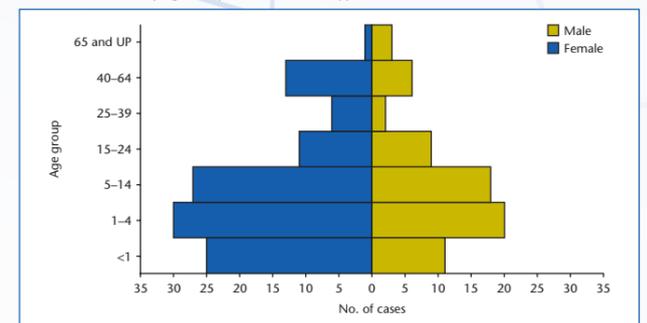
## PREVENTION AND OUTBREAK RESPONSE IN ASIA PACIFIC

### INDIA

#### Prevention

- During interepidemic periods:
  - Immunoprophylaxis: high-risk population (eg, health care workers).
  - Chemoprophylaxis: close contacts.
- During epidemic situations:
  - Social distancing: closure of schools/colleges/cinema halls, etc.
  - Immunoprophylaxis: high-risk population (eg, health care workers).
  - Chemoprophylaxis: close contacts.

FIGURE 3. MD Cases by Age Group and Sex in the Philippines, 2013 (N=182)



## Outbreak response

- Outbreaks have been more frequently reported from 2005 onwards.
- Of note, for the first time, there were 2 major outbreaks in the northeast region of the country (Meghalaya 2008–2009 and Tripura 2009).
  - Experts report never detecting outbreaks in this region before.
  - This affected treatment, as patients were initially treated incorrectly as clinicians did not suspect MD.
- Also of note, during recent outbreaks a shift in the affected age group was observed, ie, for the first time there was an increase in the proportion of cases in young adults.
- The decision to undertake mass vaccination following an outbreak is based upon the attack rate within an area.

## JAPAN

### Prevention

- Immunisation is not obligatory but individuals should be vaccinated upon individual request based on the national recommendations.
- MCV4 available in 2015.
  - It will be a voluntary vaccine, available only in the private market (ie, those who wish to be vaccinated will have to purchase the vaccine themselves).
- Although serogroup B has been detected recently, it is unclear when the vaccine against MD strain B will be licensed in Japan.

## Outbreak response

- The only outbreak in Japan (high school dormitory) was caused by serogroup B (May 2011).
- Because of the few cases of MD in Japan, the advice was not to follow WHO/CDC guidelines for outbreaks.

## KOREA

### Prevention

- There are few cases and secondary cases are rare except in the military but close contacts always receive prophylaxis.
- The emphasis in Korea is on attempting to determine who is at risk.

## Outbreak response

- There are no guidelines for the management of MD outbreaks in Korea.
- In 2011, there was an outbreak of IMD in the Korean Army.
- The country has a good emergency outbreak system and general outbreak guidelines are in place.
- There is a risk of outbreaks in Korea due to a lack of herd protection.

## THE PHILIPPINES

### Prevention

- Meningococcal vaccines are not part of the Philippine Expanded Programme on Immunization, but available data support their use in certain conditions or selected populations.
- Two meningococcal vaccines are available, the tetravalent meningococcal (ACYW-135) conjugate vaccine (MCV4) and the tetravalent meningococcal polysaccharide vaccine (MPSV4) but the conjugate is preferred.

## Outbreak response

- During the 2005 outbreak, two vaccines were used, the bivalent polysaccharide A and C vaccine and the tetravalent polysaccharide vaccine; the former was used extensively.
- The target groups for mass vaccination were children aged 2–5 years and those >50 years of age.

## RECOMMENDATIONS

Based on the findings from the meeting a number of key recommendations, specific for the Asia Pacific region were determined (Table 2)

TABLE 2. GMI Recommendations

In many countries in the Asia Pacific region, surveillance systems need to be strengthened, especially in countries where there have been several recent outbreaks.
It is generally accepted that the incidence rates in the Asia Pacific region are unlikely to reflect the true burden of disease, and the reason for this is multifactorial.
It was felt that the GMI should write guidelines on how to apply different methods of diagnosis in different settings (based on resources available).
In addition, a standardised case definition is needed in the region.
Outbreak management guidelines are lacking in the region and should be developed.
Increasing awareness of MD among health care providers and health authorities should be a goal of the GMI. This will assist in directing resources that GMI members feel are already available in their respective countries, to be directed toward MD as needed.
Determining those cohorts who carry meningococci is crucial for controlling transmission of MD and ensuring herd protection.
It was noted that the GMI members could reach out to funding bodies/apply for grants for training courses on areas of importance, e.g., PCR training.

## CONCLUSIONS

- The true burden of MD disease is unknown in the Asia Pacific region for a number of reasons (including under-reporting, weak surveillance systems, lack of guidelines and standard case definitions, and lack of awareness and focus on MD).
  - Indeed, in Korea, data discrepancies between the different surveillance systems employed emphasise this point, and also suggest potential under-reporting of MD in the country by some systems.
- In some countries in the region, MD has recently become a major public health issue (in particular due to more frequent outbreaks).
- To improve the MD situation in Asia Pacific and address the unique outbreak situation (ie, low incidence of MD and outbreaks of only a single case) the GMI developed the recommendations described herein and emphasised that there is a need to:
  - Strengthen surveillance throughout the region,
  - Improve case reporting,
  - Develop guidelines on how to apply different methods of diagnosis,
  - Standardise case definitions,
  - Develop guidelines for outbreak management,
  - Increase awareness of MD among health professionals, the public and policy makers.

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