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Review

Meningococcal disease and control in China: Findings and updates from the Global Meningococcal Initiative (GMI)

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ABSTRACT

The Global Meningococcal Initiative (GMI) is a global expert group, including scientists, clinicians and public health officials from a wide range of specialities. The goal of the GMI is to prevent meningococcal disease worldwide through education, research, and co-operation. The Chinese GMI roundtable meeting was held in June 2017. The GMI met with local experts to gain insight into the meningococcal disease burden in China and current prevention and vaccination strategies in place. China experienced five epidemics of serogroup A meningococcal disease (MenA) between 1938 and 1977, with peak incidence of 403/100,000 recorded in 1967. MenA incidence rates have significantly declined following the universal introduction of the MenA polysaccharide vaccine in China in the 1980s. Further, surveillance data indicates changing meningococcal epidemiology in China with the emergence of new clones of serogroup B from serogroup C clonal complex (cc) 4821 due to capsular switching, and the international spread of serogroup W cc11. The importance of carriage and herd protection for controlling meningococcal disease was highlighted with the view to introduce conjugate vaccines and serogroup B vaccines into the national immunization schedule. Improved disease surveillance and standardized laboratory techniques across and within provinces will ensure optimal epidemiological monitoring.

Introduction

Neisseria meningitidis (Nm) is an obligate human pathogen, and is the cause of invasive meningococcal disease (MD).[1] Nm strains can be classified into 12 serogroups (A, B, C, E, H, I, K, L, W, X, Y, Z) based on the immunochemistry of its capsular polysaccharides. Six serogroups (A, B, C, W, X and Y) account for the majority of all cases of MD worldwide.[2,3] The remaining serogroups (E, H, I, J, L and Z) are usually only found in carriage, but can cause invasive disease in immuno-compromised individuals, such as patients with complement deficiencies.[4]

The Global Meningococcal Initiative (GMI) was established in 2009 and is a multidisciplinary group of over 50 scientists and clinicians dedicated to the prevention of MD worldwide through education, research and international co-operation. A number of global and regional GMI meetings have been held since its inception,[5] including this regional meeting in Chengdu, Sichuan province, China in June 2017. Experts were not available to attend the GMI meeting

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from all 34 provinces across China; however, attendees included several representatives from the Chinese Center for Disease Control and Prevention (CDC; Beijing, Shanghai, Guangdong and Liaoning), as well as scientists and clinicians from hospital-based departments relating to infectious disease. Members from Public Health England (United Kingdom [UK]), Institute Pasteur (France) and the World Health Organization also attended to share their experiences and the lessons learned from their vaccination and outbreak programs.

The specific meeting objectives were to: (i) review the global incidence and epidemiology of MD, including China; (ii) provide an update on MD surveillance, prevention and control strategies from both a provincial (Liaoning province and Guangdong province) and national perspective; (iii) discuss the issues faced regarding MD and bacterial meningitis (BM) surveillance, prevention and control strategies with a focus on current barriers to implementation; (iv) highlight the importance of conjugate vaccines and their impact on the prevention of MD; and (v) discuss key learning points from immunization programs used worldwide in outbreak control and preparedness. This paper summarizes the key discussion points and subsequent recommendations from the meeting to help inform global and regional recommendations for MD prevention.

Review of the global incidence and epidemiology of meningococcal disease

The global distribution and incidence of MD varies from 0.11 to 2 cases per 100,000 population in Europe and North America,[6,7] to more than 100 cases per 100,000 population in the “meningitis belt” of sub-Saharan Africa.[8] The incidence of MD in Africa subsequently fell to 0.02 cases per 100,000 between 2011 and 2013 after the introduction of the MenAfriVac® vaccine in 2010.[8] In China, the MD incidence rate is 0.047 cases per 100,000 population based on data from 2006 to 2014 from the National Notifiable Disease Reporting System (NNDRS).[9] However, recent subnational estimates indicate an incidence rate of 1.84 cases per 100,000 population, suggesting that the overall incidence rate for China is underestimated.[10] Historically, China has experienced five epidemics of MD between 1938 and 1977.[10,11] The peak incidence of MD was recorded in 1967 with 403 cases per 100,000 population, >3,040,000 recorded cases and >160,000 deaths with a case fatality rate of approximately 5.5%. Following the universal use of serogroup A MD (MenA) polysaccharide vaccines in China in the 1980s and the introduction of MenA polysaccharide vaccines in to the Expanded Programme for Immunization (EPI) in China in 2008, the reported incidence of MD has steadily declined to <0.52 cases per 100,000 population in 2009[12]; this decline has been particularly evident in the last five years owing to an increasing vaccination coverage rate.

The incidence and prevalence of Nm serogroups continually varies both geographically and temporally.[10,13] Meningococcal epidemiology suggests an increased incidence and prevalence of MD during mass gatherings that involve migration and travel.[14–16] Further, Nm is susceptible to frequent genetic transformations due to natural horizontal DNA exchanges between isolates.[17]

Currently, serogroup B MD (MenB) is the most prevalent globally.[7] Multilocus sequence typing (MLST) of MenB isolates worldwide revealed three major hyperinvasive clonal complexes (ccs) (sequence type [ST]-32, ST-41/44 and ST-269) in Europe and the United States of America (USA).[18] Further, cc ST-11 previously observed among serogroup C MD (MenC) and serogroup W MD (MenW) isolates has since occurred in cases of MenB due to capsular switching.[19,20] MenA is the most common serogroup involved in MD pandemics and is predominantly found in China and Africa.[21] The last major expansion of MenA observed in Africa and China was in the 1980s; however, both nations experienced the same clonal replacement of ST-5 with ST-7 in the 1990s.[21,22] Serogroup X MD (MenX) emerged in Africa in the 1990s, reaching epidemic levels in Niger in 2006.[23] Cases of MenX isolates related to those responsible for meningococcal outbreaks in Niger, Togo and Burkina Faso have recently been recorded in Northern Italy among African and Bangladeshi migrants living in refugee camps.[14] MenW has been known since the 1980s; however, its emergence as an epidemic serogroup was reported in 2000, in Hajj pilgrims returning to France and the UK.[24] Whole genome sequencing (WGS) data suggest a multifocal emergence of MenW isolates worldwide with the identification of two sub-lineages; one in individuals traveling to Mecca and in local South African residents, and the other in South America and the UK.[15] Recently emerging MenC strains in sub-Saharan Africa were different isolates from those previously observed in 1980 and 2012. Following genomic analysis of the new clone of MenC identified in men who have sex with men (MSM), the strain was found to have evolved to acquire the capacity to spread via sexual transmission, as well as by respiratory droplets.[25]

In China, the earliest serogroup A Nm was isolated in the 1950s (Fig. 1) and almost all isolated MenA strains since have been identified as cc1 or cc5. ST-5 and -7 are two major classifications of cc5 MenA, and ST-3 is a major classification of cc1 MenA. ST-5 (cc5 MenA) first emerged in the 1950s, however was gradually replaced by ST-3 (cc1 MenA) in the 1960s. Since 1980, MenA caused by ST-3 has continuously declined, and ST-7 has since been the predominant clone of MenA. In China, the incidence of MenB is increasing. Prior to 2000, invasive cc11, cc32 and cc8 strains were occasionally identified; however, more recently, MenB cc4821 has emerged. From 2003 to 2005, several MD epidemics occurred in the Anhui province, China; the MenC isolates attributed to such outbreaks were identified as the unique cc4821.[26] Genomic analysis

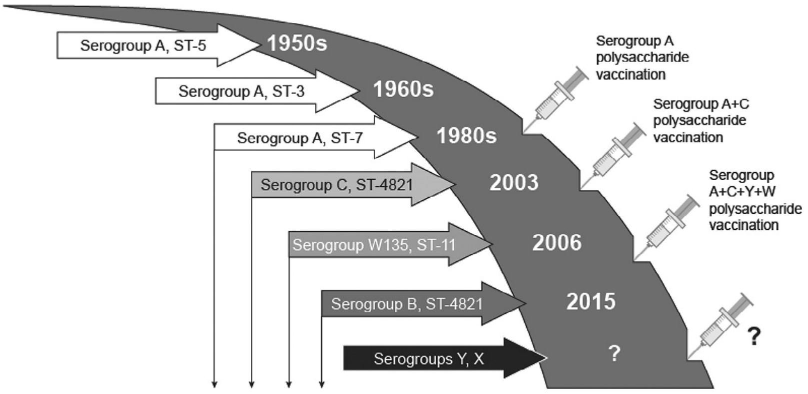

Fig. 1. Molecular epidemiology of *Neisseria meningitidis* in China.