The importance of surveillance: Group W meningococcal disease outbreak response and control in England.

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Abstract

Invasive meningococcal disease (IMD) is associated with high morbidity and mortality. Recently, use of the quadrivalent MenACWY conjugate vaccines has extended with the emergence of a hypervirulent MenW:cc11 strain in certain parts of the world, especially South America. In England, MenW:cc11 IMD cases increased rapidly after 2009 and was responsible for 24% of all IMD cases compared to <5% previously, leading to the emergency introduction of a national teenage MenACWY conjugate vaccine programme in August 2015. Unusually, MenW:cc11 cases have been described presenting with severe gastrointestinal symptoms, including abdominal pain and diarrhoea, followed by rapid clinical deterioration and death.

**Commentary**

*Neissseria meningitidis* is a major cause of meningitis and septicaemia, and is notorious for causing large outbreaks and epidemics across the globe. Of the 12 known meningococcal capsular groups, six (A, B, C, W, X and Y) are responsible for nearly all invasive disease.1  The incidence and contribution of different meningococcal capsular groups to the total burden of invasive meningococcal disease (IMD) varies by geography and age, with changes over time due to emerging, re-emerging, evolving and departing strains.

Historically, group W meningococcal (MenW) disease was responsible for less than 5% of all IMD cases in England.2 Since 2009, however, England has been experiencing a year-on-year increase in MenW disease across all regions and age groups, especially older adults and teenagers and, more recently, infants and toddlers.3 In the 2014/15 epidemiological year (July to June), MenW accounted for 24% of all IMD cases in England and this increase was almost entirely due to rapid expansion of one MenW strain belonging to the highly virulent ST-11 clonal complex,4 which is associated with high rates of morbidity and mortality, with a propensity to cause outbreaks and epidemics.5

In the early 2000s, an international Hajj-associated MenW outbreak due to the hypervirulent ST-11 clonal complex was rapidly controlled following mandatory immunisation with the quadrivalent MenACWY vaccine for pilgrims. Since then, however, Increases in endemic MenW:cc11 disease have been observed in sub-Saharan and South Africa, Brazil and several other South American countries, with case fatality rates (CFR) reported to be as high as 25%.6 It is likely that these increases are due to multifocal emergence of different lineages within the hypervirulent ST-11 clonal complexes. Whole genome sequencing of invasive MenW isolates, for example, revealed that the South American strain was distinct from the ‘Hajj outbreak’ strain and from the closely-related South African strain which appeared in 2003.7 The recent UK outbreak strain, too, is now known to be distinct from the Hajj-associated strain and most closely related to the South American strain.5

A report of MenW:cc11 cases in Chile provided useful insight into the clinical characteristics and outcomes in different age groups. 8 In 2012, the 60 group W cases accounted for more than half of all IMD and 25 of the 60 MenW cases (58%) were diagnosed in children (<20 year-olds). Notably, meningococcal disease was only suspected in 2.4% at presentation because most patients did not present with the characteristic features of meningitis (headache, photophobia, neck stiffness) or septicaemia (the typical non-blanching rash). In their cohort, after fever (60% of patients) and cold symptoms (53%), nausea/vomiting (47%) were the major presenting symptoms. The authors also reported a high case fatality rate of 32% (19/60 died), with diarrhoea being the only significant risk factor identified among fatal cases (56% compared to 27% among survivors; p = 0.034). Indeed 8 of the 14 patients with diarrhea (57%) died of their infection.

In England, following reports of teenagers and young adults dying after presenting with vomiting and diarrhoea, we conducted a detailed follow-up of all 15-19 year-olds in England who were diagnosed with group W IMD between July 2015 and January 2016. We found that seven of 15 teenage group W IMD cases presented with an acute (24-48 hour) history of predominantly gastrointestinal symptoms together with or followed by diarrhoea in the 24 hours before attending hospital. 9 In the remaining eight cases, only three had the more characteristic clinical presentations of IMD, two with septicaemia and one with meningitis. None of the 15 MenW cases had been immunised with a MenACWY vaccine. In all, six died (40%), including five who presented with predominantly gastrointestinal symptoms.

MenW and MenY cases in adults have been recognised as having atypical clinical presentations, including pneumonia, septic arthritis and epiglottitis/supraglottitis but these presentations are unusual in children and young adults. Following a large national outbreak of MenC disease in the mid-1990’s, there have been awareness campaigns on the symptoms and signs of IMD in children and young adults. Parents and frontline healthcare professionals alike have been warned to look out for the characteristic symptoms and signs of meningitis and septicaemia. Children, in particular, are known to deteriorate rapidly from development of the first symptoms to death within 24 hours if not diagnosed and treated rapidly.10 Earlier recognition of the signs and symptoms, along with rapid antibiotic treatment and appropriate intensive care support, can lead to improved survival and better long-term outcomes. Unusual clinical presentations, on the other hand, can lead to delays in the recognition of IMD, allowing the disease to progress to shock and multi-organ failure. This appears to be the case with the current hypervirulent MenW:cc11 strain. Delayed diagnosis can also lead to delays in offering chemoprophylaxis to close contacts and in identifying clusters.

IMD presentation with primarily gastrointestinal symptoms has been described rarely prior to the emergence of the current W:cc11 strain and it is not yet clear whether these severe symptoms are a characteristic of the capsular group, this hypervirulent strain, the age of the cases (adolescents) or a combination of these. It is important that clinicians are aware that severe gastrointestinal symptoms, including nausea, vomiting, abdominal pain and diarrhoea may be due to IMD. We were unable to identify any specific clinical feature that might help distinguish IMD from the more common, self-limiting causes of vomiting and diarrhoea, apart from the observation that they deteriorated rapidly over a period of hours and most fatal cases died within 24 hours of the first symptoms.

In Chile, in response to the increase in group W IMD cases and the high CFR, conjugate MenACWY vaccination was offered to children aged 9 months to 5 years from October 2012. 6,11 This successfully protected children in the vaccine-eligible age-groups but did not have a broader population impact, with ongoing increases continuing in older children and adults. Teenagers and young adults are the main carriers and transmitters of meningococci12, and, although IMD cases are lower in this age group compared to infants and young children, vaccinating the age group with the highest carriage rates using a vaccine that is known to prevent carriage acquisition, has the potential to provide indirect (herd) protection across the population over time.

Following the continued increase of MenW disease in England, the national advisory group of experts, the Joint Committee on Vaccination and Immunisation, recommended conjugate MenACWY immunisation for all 13-18 year olds and new university entrants up to 25 years as an emergency, national outbreak control measure over a two year period (August 2015 to mid-2017).3 The MenACWY conjugate vaccine has, therefore, replaced the MenC conjugate vaccine in the routine adolescent (aged 13-14 years) and the new university entrants’ programmes. It is hoped that this programme will provide both direct protection to vaccinated teenagers and herd protection to the wider population by preventing carriage acquisition in teenagers and young adults.

Other countries in Europe and elsewhere are now witnessing an increase in MenW disease, including local, national and international outbreaks due to the hypervirulent MenW:cc11 strain.5,13 In England, it is hoped that the rapid implementation of a national outbreak control MenACWY vaccination programme will curb the ongoing rise in MenW cases and control the disease across all age groups in the coming years; teenagers may already be directly benefitting from the programme (PHE unpublished data). Good quality enhanced surveillance has been key in generating data that have furthered our understanding of IMD and the vaccines designed to protect against this devastating infection. In England, Public Health England (PHE) has been conducting enhanced national surveillance of IMD for the past two decades, alongside a national reference unit (the PHE Meningococcal Reference Unit, MRU) for confirmation, grouping, molecular and, since 2010, genomic characterisation of invasive meningococcal isolates across the country. The MRU also provides a free national service for PCR-testing of clinical samples from patients with suspected IMD. More than 20,000 clinical samples are tested annually across all age groups, with a positivity rate of nearly 7%.14 This high referral for testing ensures high case ascertainment 15 and, by combining laboratory data with clinical follow-up of confirmed IMD cases using standardised questionnaires for clinicians, provides a detailed – and near-realtime – insight into changing epidemiology of IMD across the country. It is because of the enhanced surveillance, knowledge gained from past meningococcal immunisation programmes and experiences in other countries that a national outbreak control programme from MenW was installed so rapidly after only 176 cases were diagnosed across a population of 50 million in the 2015/16 epidemiological year.

The UK was the first country to include MenC conjugate vaccine in its national schedule in 1999 following accelerated vaccine development and licensure based on serological markers of protection.16 Greater understanding of the mechanisms behind the marked and continuing impact on MenC disease control generated by national surveillance and, in particular, the importance of the impact of vaccination on carriage, has helped inform the successful rollout of the MenA vaccination programme across sub-Saharan Africa and the current adolescent MenACWY vaccination programme in the UK. Enhanced surveillance strategies following the recent introduction of the infant MenB vaccine in the UK immunisation programmes will similarly be fundamental in establishing the safety, impact and effectiveness of this vaccine and in better informing MenACWY vaccine use in adolescents.17

Authors’ contributions

HC and SL conceived the commentary and drafted the manuscript. Both authors read and approved the final manuscript.

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