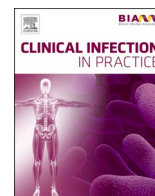




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Practical clinical reviews

The changing face of meningococcal infection

Francesca Knapper

North Bristol NHS Trust, United Kingdom

A B S T R A C T

Meningococcal infection is caused by *Neisseria meningitidis*, a Gram negative diplococci. Invasive meningococcal disease (IMD) is caused by 6 capsular groups. The spectrum of infection is broad, with meningitis and meningococcal sepsis associated with a case fatality of between 4 and 20%. The main burden of disease is felt in the under 1's and this is where vaccination has been focused. Vaccination against MenC begun in 1999, with vaccines against Men ACWY and MenB added to the schedule in 2015. Over the last 10 years rates of IMD in the UK have fallen by over 50%. The impact of COVID-19 on cases has also been felt, with early data suggesting a significant drop in cases during the first wave in 2020. Despite the success of vaccination we need to remain vigilant. Clonal expansion of hypervirulent strains has been seen in epidemics and we have a significant proportion of the population who remain unvaccinated.

In this issue 2 interesting cases of meningococcal sepsis are reported. *Neisseria meningitidis* is a Gram negative diplococci. Twelve capsular groups exist, of which A, B, C, W, X, and Y cause invasive meningococcal disease (IMD). Within these capsular groups are strains defined by multilocus gene typing. In epidemics clonal expansion of hypervirulent strains has been seen (Stephens et al., 2007; Parikh et al., 2020).

Meningococcus is part of normal nasopharyngeal flora. Carriage varies which age but is highest in young adults with up to 24% reported in one study (Christensen et al., 2010). Transmission occurs through aerosol or direct contact with respiratory secretions. Interesting both smoking and passive smoking have been associated with a higher prevalence of IMD. Smokers are more susceptible to carriage but the exact mechanisms behind this are not understood (Murray et al., 2012).

Complex interplay between carriage, acquisition and serotype lead to infection. Meningitis, is the most common presentation, however meningococcal sepsis, pneumonia, pericarditis, arthritis, conjunctivitis, urethritis and pharyngitis can occur (Rosenstein et al., 2001). The presence of the characteristic non blanching purpuric rash is a late sign, but the rapid progression of symptoms can see patients deteriorate over a matter of hours (Thompson et al., 2006). The impact can be devastating with case fatality quoted 4–20% (Wang et al., 2019). In those who survive longterm sequelae can be seen in 10–20%. Hearing loss, amputation and learning difficulties are all complications (Olbrich et al., 2018).

IMD has had the greatest burden of disease in the under 1's, with epidemics seen in older adolescents and young adults. The so called meningitis belt of sub-Saharan Africa historically saw the highest prevalence with epidemics associated with the end of the dry season and seasonal migration for religious festivals (Parikh et al., 2020). Travel

associated infection is seen with pilgrims attending the Hajj and Umrah. Travellers are now required to show a certificate of vaccination against Men ACWY to gain entry to Saudi Arabia (England, 2013; Yezli, 2018)

Since 1999 the UK vaccination schedule has included vaccines against meningococcal infection. Initially a conjugate vaccine against MenC was introduced in 1999. This was replaced with the Men ACWY conjugate vaccine in 2015. The same year a protein based vaccine 4CMenB was included for babies covering MenB (England, 2019). The 4CMenB vaccine covers 4 strains, in the UK it has been reported to be effective against 83% of all MenB cases (Parikh et al., 2016).

At risk groups should also be offered routine vaccination regardless of age. Due to the encapsulated nature of the *Neisseria meningitidis* patients with asplenia, splenic dysfunction or complement disorders are at increased risk of IMD. The drug Eculizumab, which affects the terminal complement pathway is a risk factor for IMD, with vaccination recommended prior to treatment (England, 2013). Clinicians should also note that patients who present with a second episode of IMD should be investigated for underlying complement deficiencies (NICE).

In the UK rates of IMD have steadily fallen with the introduction of vaccination. The first significant decrease was seen in MenC with only 30–40 cases now annually reported (England, 2019).

The emergence and rising incidence of the MenW hypervirulent clonal complex 11 was reported in 2009, with adjustment of the vaccination program accordingly in 2015. This highlighted how epidemics can occur with previously rare serotypes. Interestingly infection with Men W was more often seen in older adults, with European data showing the greatest total number of cases is reported in the >65 age group. It has been reported that this particular MenW can present with more gastro intestinal symptoms than other serotypes and can be associated with a

E-mail address: francesca.knapper@nbt.nhs.uk.

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high mortality (Campbell and Ladhani, 2016; Krone et al., 2019).

MenB is responsible for 80% of cases in the UK currently. UK data from 2019 to 2020 shows that the greatest disease burden is still in the under 1's followed by 1–4 year olds. The trend is generally falling though with only 461 cases reported last year in the UK compared to just over 1000 10 years ago (England, 2019). While case numbers are falling over 50% of IMD is in adults, with the majority of those over 35 unvaccinated and still susceptible. With a general trajectory downward it is important not to miss this infection, particularly in the elderly where the presentation may be less clear.

The impact of social distancing to prevent the spread of COVID-19 has had a significant impact on rates of IMD. Between April and June last year confirmed cases were 76% lower than the same period in 2019 (England, 2019). It remains unclear if data this year will continue to demonstrate this and whether rates rebound with the easing of restrictions.

In conclusion IMD is a serious and important infection. Vaccination has been a huge part of our success in reducing the prevalence in the UK. Despite this we should be vigilant especially inpatients presenting without classic symptoms.

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