



***Neisseria meningitidis* user information**

Neisseria species are Gram negative cocci, 0.6 - 1.0 μM in diameter, occurring singly but more often in pairs with adjacent sides flattened; they are non-motile due to a lack of flagella and are oxidase and catalase positive (except *Neisseria elongata*).

N. meningitidis, often referred to as meningococcus, is a species which can only be found in humans, mostly in the normal nasopharyngeal flora as asymptomatic carriage in ~5-11% of adults, increasing in prevalence throughout childhood and peaking at 25% in 18-20 year olds. Carriage episodes may last for many months and most will be with strains that are non-capsulated and thus mainly non-pathogenic. However, when a pathogenic encapsulated strain is present there is the potential for very severe and invasive disease with a high mortality (~5% in the UK) and morbidity. The disease causes irreversible injuries such as loss of limb, brain damage, and visual impairment in some cases. Although ~97% of cases are sporadic, this organism has the potential to form epidemics via transmission through respiratory droplets. It is not fully understood why disease develops in some individuals but not in others. Age, season, smoking, preceding influenza A infection and living in 'closed' or 'semi-closed' communities, such as university halls of residence or military barracks have all been identified as risk factors.

Meningococcal disease is most commonly diagnosed in infants, adolescents and young adults. There are twelve serogroups of *N. meningitidis* which have been identified, six of which (A, B, C, W, X and Y) can cause epidemics, though virulence and geographical distribution differ between the serotypes. The potential for rapid spread of infection and the severity of the illness means that efficient diagnosis and immediate antibiotic treatment is crucial.

Meningococcal infection most commonly presents as either meningitis, septicemia, or a combination of both. Less commonly, individuals may present with pneumonia, myocarditis, endocarditis, pericarditis, arthritis, conjunctivitis, urethritis, pharyngitis and cervicitis (Rosenstein et al., 2001). The incubation period is from two to seven days and the onset of disease varies from fulminant with acute and overwhelming features, to insidious with mild prodromal symptoms. Early symptoms and signs are usually malaise, pyrexia and vomiting. Headache, neck stiffness, photophobia, drowsiness or confusion and joint pains may variably occur. In meningococcal septicemia, a rash may develop, along with signs of advancing shock and isolated limb and/or joint pain. The rash may be non-specific early on but as the disease progresses the rash may become petechial or purpuric and may not blanch. This can readily be confirmed by gentle pressure with a glass (the 'glass test') when the rash can be seen to persist.

Vaccination against meningococcal disease in the UK as of 2016 is as follows; one dose of 4CMenB vaccine (for serogroup B) at two and four months; one dose Hib/Menc (Serogroup C) and one dose of 4CMenB (serogroup B) at one year (and an associated booster vaccine); and one dose of

MenACWY (covering serogroups A, C, W and Y) at 14 years (also has an associated booster) (Green book – Chapter 22, page 6, table 2).

MenB IMD cases fell between 2001 to 2002 and 2013 to 2014, likely because of secular trends. MenB accounted for nearly 90% of cases during 2006 to 2011, with an overall incidence of nearly 2 per 100,000. The implementation of 4CMenB (Bexsero®) into the national infant immunisation programme since September 2015 resulted in a large and significant reduction in MenB IMD cases in vaccinated children. MenB invasive cases have predominated with the early re-emergence of disease since restrictions to control the COVID-19 pandemic were withdrawn in July 2021. Following the easing of restrictions after July 2021, there was a notable increase in serogroup B cases, with numbers in adolescents and young adults comparable to those observed pre-pandemic. Invasive meningococcal disease (IMD) cases in other age groups and from other serogroups remained very low throughout 2021 to 2022. MenB cases began to increase in all age groups in 2022 to 2023 whereas non-MenB disease has remained very low.

The MenC conjugate vaccine was implemented into the UK national immunisation programme in 1999 and was highly effective in preventing MenC invasive disease across all age groups through direct and indirect (herd) protection. MenC is currently well-controlled, with only 30 to 40 cases annually prior to the pandemic. Current cases are mainly diagnosed in adults born outside the UK who were unvaccinated against MenC disease and small numbers of cases arising in previously-vaccinated children.

MenW cases increased with the emergence and rapid expansion of a hyperinvasive strain belonging to the ST-11 complex in 2010 and is now controlled following implementation of an emergency MenACWY immunisation programme for teenagers in August 2015. MenACWY vaccination is now routinely offered at 13 to 14 years as mentioned above, and MenW invasive disease cases are currently very low across all age groups.

MenY disease remains uncommon in the UK and predominantly affects older adults and those with underlying health conditions. MenY invasive disease cases declined further across all age groups following implementation of an emergency MenACWY immunisation programme for teenagers in August 2015 and remain low with the routine teenage MenACWY vaccination, although a small number of invasive cases has arisen from individuals with Serogroup Y (ST1466) organisms infecting the urogenital or anorectal areas.

Other meningococcal groups rarely cause invasive disease in the UK, with most cases occurring in those with underlying health conditions. In other parts of the world different serogroups may predominate. Large epidemics of both capsular group A and W meningococcal infection have occurred in association with Hajj pilgrimages, and proof of vaccination against A, C, W and Y capsular groups is now a visa entry requirement for pilgrims and seasonal workers travelling to the Kingdom of Saudi Arabia. Epidemics arise unpredictably throughout sub-Saharan Africa with MenA previously predominating before the successful introduction of MenA conjugate vaccine. Subsequent outbreaks have been due to serogroups C, W and X.

Diagnosis of invasive disease is traditionally through detection of *N. meningitidis* using Gram staining and culture of CSF and/or blood, joint fluid and pleural fluid. However, these methods are limited as they may not be sensitive enough to detect cases where the organisms are in low numbers within the specimens collected, or the patient may have had prior antibiotic therapy, and these methods may take up to 72 hours before a result is available. NAAT testing provides a rapid, sensitive and definite method for identifying *N. meningitidis* in invasive specimens from patients suspected of

meningococcal infection. Importantly, meningococcal DNA can be found in the CSF up to 96 hours after commencing antibiotics.

Clients may also choose to send a throat swab for screening; use of intravenous antibiotics in the community prior to hospital admission may decrease the yield of *N. meningitidis* from blood and CSF samples, however nasopharyngeal swabs are less affected by prior antibiotic therapy and have been shown to yield *N. meningitidis* in 40-50% of clinical cases.

Micropathology Ltd employs a probe-based real-time PCR assay for the amplification and qualitative detection of *Neisseria meningitidis*. Following the detection of *N. meningitidis* in a specimen, Micropathology Ltd offers typing assays for the identification of serogroups A, B, C, W and Y. UKAS accredited specimen types for this assay include CSF, EDTA whole blood, nasopharyngeal swabs and joint fluid. However, UKAS accredited sample types for *N. meningitidis* typing is any sample that tests positive for *N. meningitidis*. Other samples may be tested and reported alongside an appropriate caveat stating that the sample provided is not accredited or validated for this assay. The turnaround time for specimen that request *N. meningitidis* testing is 'same day', while typing for serogroup B may require up to four days and for serogroups A/C/W/Y may require up to seven days (please see our laboratory user handbook):

https://www.micropathology.com/PDF%20Documents/Laboratory_User_Handbook.pdf

Where there is a delay, we are usually confirming a result and addressing clinical data given with the specimen.

References

Rosenstein NE, Perkins BA, Stephens DS et al. (2001) Meningococcal disease. N Engl J Med 344(18): 1378-88.

Department of Health (2022) Meningococcal (Green Book- Chapter 22). London: Department of Health- Sept 2016 (chapter last updated in 2022, table last updated in 2016)

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