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Meningococcal carriage in adolescents in the United Kingdom to inform timing of an adolescent vaccination strategy

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Summary *Objectives:* Recent development of serogroup B meningococcal (MenB) vaccines highlights the importance of pharyngeal carriage data, particularly in adolescents and young adults, to inform implementation strategies. We describe current UK carriage prevalence in this high risk population and compare methods of carriage detection.
Methods: In this multisite study, pharyngeal swabs were collected on 3–4 occasions over 6–12 months, from 1040 school and university students, aged 10–25 years. Meningococcal carriage was detected by standard culture combined with seroagglutination or PCR of cultured isolates, or by direct PCR from swab. The factor H binding protein (fHBP) variants present in meningococcal isolates were determined.
Results: Meningococcal serogroups B and Y were most common, with carriage up to 6.5% and 5.5% respectively, increasing throughout adolescence. Identification by seroagglutination was often unreliable, and the sensitivity of direct PCR detection was 66% compared to culture combined with PCR. Of MenB isolates, 89.1% had subfamily A variants of fHBP. The acquisition rate of MenB carriage was estimated at 2.8 per 1000 person-months.
Conclusions: If vaccination is to precede the adolescent rise in MenB carriage, these data suggest it should take place in early adolescence. Studies assessing vaccine impact should use molecular methods to detect carriage.

Introduction

Neisseria meningitidis remains a leading cause of meningitis and septicaemia globally. There are 700–1200 cases of invasive disease annually in the UK with a case fatality rate of 5–15%.[1,2] Invasive disease is almost exclusively due to 6 capsular serogroups (A, B, C, W, X or Y) and effective capsule-based glycoconjugate vaccines are currently available for the prevention of A, C, W and Y infection.[3] Serogroup B meningococcus (MenB) now accounts for 80–90% of invasive disease in the UK,[2,4] 65% across Europe,[5] and 30% in North America.[6] The MenB capsule has a structure identical to human polysialic acid and is therefore poorly immunogenic, which has historically hampered vaccine development. Recently, a MenB vaccine based on four subcapsular antigens (4CMenB, 'Bexsero', Novartis, Italy) has been licensed in Europe while a vaccine composed of two lipidated factor H binding proteins (bivalent rLP2086, 'Trumenba', Pfizer, USA) has been licensed in the USA.

The human pharynx is the only effective reservoir for *N. meningitidis*, where it is carried as a commensal. Carriage prevalence is age-related with carriage rates of up to 20–50% being reported in late adolescence.[7] Carriage is also associated with social risk factors, including visiting night clubs, kissing, smoking, and living in closed communities such as military or university residences.[8–10] The relationship between carriage and disease is complex. Most disease is caused by a limited number of 'hyperinvasive' strains, although these are commonly carried harmlessly, and pharyngeal isolates are often non-pathogenic strains.[11] Nonetheless, carriage data remain invaluable for predicting disease epidemiology, and a vaccine which reduces carriage of invasive strains is likely to confer a herd immunity effect, as has been seen with meningococcal serogroup C (MenC) conjugate vaccines.[12]

The aim of this study was to address the relative paucity of recent information about carriage in UK adolescents, by sequentially collecting posterior pharyngeal swabs from students at secondary school (typically attended from 11 to 18 years of age in the UK) and first year of university. As both MenB vaccines include a recombinant factor H binding protein (fHBP) component - a meningococcal virulence factor which aids evasion of innate immunity - the study characterised the fHBP variant type of all meningococci isolated to add to epidemiological data on current strains circulating in the UK. In considering the likely need to assess the impact of vaccination on carriage in future studies, the study also explored laboratory methodologies for detecting carriage.

Methods

Study design and population

A longitudinal epidemiological study was performed to collect pharyngeal swabs from secondary school and first year university students, aged 10–25 years, during a 6–12 month period. Participants were enrolled and first swabbed between March–May 2011, across 13 secondary schools and 5 universities from 4 recruiting sites in the UK (Oxford, London, Bristol and Southampton). The study was approved by National Research Ethics Service Committee South Central (Oxford B: 10/H0605/80). Written informed consent was obtained from participants over the age of 18 and from their parent(s) or legal guardian (s) (with the child's assent) below this age. Approximately equal numbers were to be recruited in each of 5 age cohorts: 10–12, 13–14, 15–16, 17–18 and 19–25 years old.

The second study visit occurred two months after enrolment (during May–July 2011), at which time any additional participants required were enrolled to fulfil the target sample size. The third visit of the main study period occurred 6 months after initial enrolment period (September–October 2011). Students who were in their penultimate school year at enrolment (year 12), were invited for an additional visit 12 months after enrolment (February–March