Neisseria meningitidis carriage in Swedish teenagers associated with the serogroup W outbreak at the World Scout Jamboree, Japan 2015

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The aims of the study were to estimate the carrier state of Neisseria meningitidis in Swedish teenagers and its association with an outbreak at the World Scout Jamboree in 2015 as well as to compare sensitivity of throat versus nasopharyngeal swab for optimal detection of carriage. In total, 1,705 samples (cultures n = 32, throat swabs n = 715, nasopharyngeal swabs n = 958) from 1,020 Jamboree participants were collected and sent to the National Reference Laboratory for Neisseria meningitidis for culture and molecular analysis. The overall positivity for N. meningitidis was 8% (83/1,020), whereas 2% (n = 22) belonged to a known sero/genigroup while the majority (n = 61) were non-groupable. Throat sample is clearly the sampling method of choice, in 56 individuals where both throat and nasopharynx samples were taken, N. meningitidis was detected in both throat and nasopharynx in eight individuals, in 46 individuals N. meningitidis was only detected in the throat and in two individuals only in the nasopharynx. Carriage studies are important to provide knowledge of the current epidemiology and association between carrier isolates and disease-causing isolates in a given population. Therefore, planning for a carriage study in Sweden is in progress.

Key words: Neisseria meningitidis; serogroup W; World Scout Jamboree; carriage.

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Neisseria meningitidis (Nm), the causing agent of invasive meningococcal disease (IMD), remains a serious health problem worldwide although the incidence of IMD has decreased in the last decade. This decrease is, at least partly, due to effective polysaccharide–protein conjugate vaccines against serogroups C, Y, W in the Americas and Europe, and the introduction of a serogroup A conjugate vaccine into sub-Saharan Africa (1, 2). Infections due to N. meningitidis can present as a spectrum of clinical illness from mild febrile illness to meningitis and septicemia, but also pneumonia, septic arthritis, pericarditis, conjunctivitis and urethritis (3). Meningococcal disease patterns and incidence can vary dramatically, both geographically and over time in populations, ranging from sporadic cases to local outbreaks or large epidemics. The basis for the dynamic epidemiology of meningococcal disease is still not completely understood; however, it is influenced by differences in serogroups and specific genotypes designated as sequence type (ST) clonal complexes, where serogroup A (ST-5, ST-7), B (ST-41/44, ST-32, ST-18, ST-269, ST-8, ST-35), C (ST-11), Y (ST-23, ST-167), W (ST-11) and X (ST-181) meningococci currently cause almost all invasive disease (4).

Historically, N. meningitidis serogroup W (NmW) was first reported among military recruits in the United States in the late 1960s and its pathogenic potential was recognized by the mid-late 1970s (5, 6). The incidence of NmW has been low and mainly associated with few sporadic cases of IMD worldwide until 2000 when NmW emerged as the cause of a worldwide outbreak being the...
causative agent for the global epidemic that followed and began among Hajj pilgrims in Mecca, Saudi Arabia in 2000. Since then, several NmW epidemics have been described in the African meningitis belt, including a large epidemic in Burkina Faso in 2002 (7, 8) and several outbreaks in South Africa, South America, Europe, the United States and China (9–13).

In Sweden, a striking increase in NmW was seen in 2015, from rarely causing IMD, generally only a few cases per year, range 0–5 since 1990 onwards, to unexpectedly causing more than twice as many cases in 2015 (n = 10). This during a time period when the overall incidence of Nm has been rather stable in Sweden, except for an increase in the total number during 2009–2013, but this increase was mainly due to an increase in NmY disease (14). This increasing trend of NmW seen in the low endemic country Sweden, 2015, has also been observed in several other European countries such as England and Wales, France, Finland and the Netherlands as well as in Australia in the last couple of years and the trend seems to continue at least in Sweden (2016; n = 18) (15–18). The NmW characterized in Sweden 2015 and 2016 was dominated by a single genosubtype, P1.5,2,36-2 corresponding to 80% (8/10) of the cases in 2015 and 94% (17/18) in 2016 (18). This is also the same genosubtype that caused the outbreak associated with the 23rd World Scout Jamboree (15). The 23rd World Scout Jamboree, an international scout camp, organized in Japan, in August 2015 gathered 33 628 participants from 155 countries, including 1 890 Swedish scouts. Directly after their home return, three scouts from Scotland and one relative were diagnosed with IMD. Several suspected cases of IMD were immediately reported in Sweden, but only two additional cases within a week later were verified. No additional cases were reported in Europe or Japan. A prompt massive information campaign was rolled out to alert all participants to be aware of the signs and symptoms of IMD and all Swedish scouts were offered ciprofloxacin as chemoprophylaxis. Throat and/or nasopharyngeal swabs were taken from participants receiving antibiotic prophylaxis to facilitate the decision on the need for further prophylactic treatment to close contacts of returning scouts. Secondly, this was a unique opportunity to estimate the carrier state of meningococci in teenagers in Sweden.

The aims of the present study were to estimate the carrier state of meningococci in Swedish teenagers and its association with the outbreak at the World Scout Jamboree in 2015 and simultaneously compare sensitivity of throat versus nasopharyngeal swab.

MATERIALS & METHODS

All cultures positive for Neisseria and all throat and nasopharyngeal swabs taken in connection with the administration of chemoprophylaxis were sent to the National Reference Laboratory for Neisseria meningitidis at Örebro University Hospital. In total, 1 705 samples (cultures n = 32, throat swabs n = 715, nasopharyngeal swabs n = 958) from 1 020 Jamboree participants were collected.

Culture

The bacteria were cultured on chocolate agar at 36 °C in 5% CO₂ overnight. Species identity was determined by MALDI TOF MS (Burker Daltonics, Bremen, Germany), according to manufacturer’s instructions, in addition with sugar utilization test. All N. meningitidis were serogrouped by agglutination using Difco™ Neisseria Meningitidis Antisera (BD, New Jersey, USA) according to manufacturer’s instructions and finally preserved and stored at -70 °C.

Molecular analysis

DNA from the throat and nasopharynx swabs were automatically extracted using the Diasorin Bullet robot (Diasorin, Saluggia, Italy) with the BUGS'n BEADS™ kit (Diasorin), according to the manufacturer’s instructions. Identification and genogrouping of N. meningitidis was conducted by real-time PCR as previously described (19).

RESULTS

Sampling was conducted in 54% (1 020/1 890) of the Swedish participants of the 23rd World Scout Jamboree, with a mean and modal age of 19 and 15 years, respectively. The overall positivity for N. meningitidis in this group was 8% (83/1 020) and 2% (n = 22) belonged to a known sero/genogroup, whereas the majority (n = 61) were non-groupable (Table 1). NmW dominated among the 22 groupable Nm-positive samples (n = 11) followed by NmY (n = 4), NmB (n = 4) and NmC (n = 3).

To assess the sensitivity of throat versus nasopharyngeal swab for optimal sampling for N. meningitidis, 112 samples from 56 individuals, from which both throat and nasopharyngeal swabs were available, were compared. In eight individuals, N. meningitidis was detected in both throat and nasopharynx, in 46 individuals N. meningitidis was only detected in the throat and in two individuals only in the nasopharynx. The sensitivity of PCR was about 12-fold as high as culture for the throat swabs, 49 samples were only PCR positive compared to four samples that were only culture positive (Fig. 1).
DISCUSSION

This is a first estimation of carriage of meningococci in Swedish teenagers. Our results showed an 8% (83/1,020) carriage rate among the teens who participated at the World Scout Jamboree in 2015. These numbers correspond quite well with the overall estimation of carriage in a population, which in most publications usually is around 10% (20, 21). However, no carriage studies regarding \textit{N. meningitidis} have been conducted in Sweden so far; consequently, we cannot compare the results from this study to other age groups or other countries. It might not even be possible to extrapolate the number from the present study to obtain a view of the carriage rate of \textit{N. meningitidis} in teenagers in Sweden. The reasons for this are the limited number of samples and that the samples collected are all from individuals who during a short period of time lived close together during the World Scout Jamboree in 2015, factors known to the increase the spread and colonization of \textit{N. meningitidis}.

Of the groupable \textit{N. meningitidis} (22/83, in total 2%), half (n = 11) belonged to NmW. It is a well-known fact that \textit{N. meningitidis} and NmW previously have been responsible for outbreak situations at large mass gathering such as Hajj and Umrah and knowing that the carriage rates of \textit{N. meningitidis} peaks in teens, the outbreak at the World Scout Jamboree in 2015 could have got much larger proportions. A reason that only participants from Scotland and Sweden got affected might reflect the on-going increase in NmW in both countries together with different vaccine recommendations in different countries before travelling to the Jamboree. In a previous study, we confirmed by whole-genome sequencing that the Jamboree-associated cases constituted a genuine outbreak and that this was due to a novel and rapidly expanding strain descended from the strain that has recently expanded in South America and the United Kingdom (15). In our further investigation by Eriksson et al., where all NmW associated with IMD in Sweden from 1995 to June 2017 were whole-genome sequenced, it was shown that the Jamboree-associated isolates clustered together and no subsequent spread was identified in Sweden by this specific strain after the return to Sweden. The overall increase in NmW in association with IMD in Sweden seen in the last couple of years is instead caused by a related subcluster of the cc11 South American/UK strain referred to as the novel 2013 UK strain because of its emergence in the UK in 2013 (15, 18).

The results also showed that there were relatively large differences in the proportion of meningococci being non-groupable between culture-positive (12/31) and PCR-positive (53/66) individuals, and the absolute number of groupable \textit{N. meningitidis} were
less among PCR-positive subjects (14 vs 19). Grouping of carriage isolates is challenging whether using phenotypic or genotypic approaches. High percentages of isolates recovered from healthy carrier’s displays low level or complete absences of expression of the genes required for capsule production during carriage, this due to phase variation, deletions or insertion of genetic mobile elements or a complete absence of the capsule genes (22–24).

Regarding the sampling methods throat sampling is clearly the sampling method of choice, which is consistent with previous studies (25–27). In addition, sensitivity can be improved by using PCR, which is more sensitive than culture for identification of asymptomatic carriers (28, 29). In a recent publication by Manigart et al. (30), they introduced an improved method for molecular detection of meningococcal carriage, in which they ran PCR after a pre-incubation in Todd Hewitt broth overnight, which enhanced the detection of meningococcal carriage in children >2-fold compared to conventional culture (13.2% vs 5.7%; p < 0.0001).

To conclude, performance of carriage studies is important to provide knowledge of the current epidemiology and association between carrier isolates and disease-causing isolates in the population and the dynamic dissemination between different countries. Planning for a carriage study is in progress in Sweden. Such a study has previously not been performed.

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