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Rise in carriage of group W meningococci in university students in United Kingdom

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Abstract

MenACWY conjugate vaccination was recently introduced in the UK for adolescents and young adults to reduce disease due to *Neisseria meningitidis* group W (MenW). We conducted a cross-sectional carriage study in first year university students. Despite 71% MenACWY vaccine coverage, carriage of MenW, but not MenY, rose significantly in students.

Neisseria meningitidis causes severe sepsis and meningitis. The main reservoir in most populations is asymptomatic pharyngeal carriage in older adolescents and young adults [*1*]. High carriage rates are particularly evident in semi-closed communities of young adults where individuals live, work and socialize together, including university student populations [*2*]. Meningococcal carriage was previously assessed in university students in the UK in 2009/10 at the University of Nottingham (UoN) when a high prevalence of capsular group Y (MenY) meningococcal carriage was detected [*3*]. This high level of MenY carriage was concomitant with a rise in disease caused by MenY strains in the UK [*4*]. Since 2009, whilst MenY disease has plateaued, capsular group W (MenW) disease has steadily increased [*5*]. This increase is due to the rapid expansion of hyper-virulent strains belonging to the sequence type 11 clonal complex (MenW:ST-11) [*5*]. Based on analysis of whole genome sequence (WGS) data, isolates from the same MenW:ST-11 lineage, termed the 'South American/UK strain' are also endemic in Chile, Brazil and Argentina [*6*], and recently reported in Australia [*7*]. In response, Public Health England (PHE) introduced MenACWY vaccine in the routine adolescent school program for 14-15 year olds and first-year university students [*8*]. A catch-up campaign was used to offer MenACWY vaccine to all 14-18 year olds, with 2015 school leavers (17-18 years of age) being prioritized.

The rationale for targeting the vaccine at older adolescent and young adults stems from: i) carriage studies showing that this demographic represents the principal reservoir of meningococcal carriage and; ii) experience with other polysaccharide conjugate vaccines. Introduction of the MenC monovalent conjugate vaccines previously reduced carriage acquisition of MenC strains in adolescents and young adults [*9*] and there is evidence, albeit limited, to suggest that the quadrivalent vaccine may have a similar effect on carriage of MenCWY strains [*10*, *11*]. Reduced carriage in this population should lead to other age

groups being protected indirectly via herd protection, thus enhancing the public health impact and cost-effectiveness of this targeted vaccination approach.

To assess current trends in meningococcal strain carriage, and to determine the immediate effect of the MenACWY vaccine on carriage of MenW/Y strains, we conducted a cross-sectional study in first-year students at the UoN from registration in September 2015 through to March 2016. MenACWY vaccination coverage in this specific student population increased from 31% (pre-registration) to *ca.* 70% (immediately post-registration) due to a campus-based vaccination campaign targeting 'freshers' [*12*]. We report a significant increase in carriage of MenW strains in first-year university students in the UK.

The Study

The study was approved by the Research Ethics Committee at the UoN and written informed consent was obtained from all participants. Convenience samples of first year students were recruited in September and November 2015 and March 2016. In September students were recruited during registration, while in November and March students were recruited in five dormitories (A-E) with single occupancy rooms. Searches of The UoN Health Service registration database (EMIS Web software; EMIS Health, Leeds, UK) were performed to determine vaccination status in registered first-year students on arrival at the UoN and following the campus-based vaccination campaign. In September, pharyngeal swabs (via mouth) were obtained immediately prior to eligible students receiving MenACWY vaccine. All pharyngeal swabs were immediately inoculated onto GC selective agar (Oxoid, Basingstoke, UK) and incubated at 37°C in air containing 5% CO_2. After 24 and 48 hours, oxidase-positive colonies suggestive of *Neisseria* spp. were selected and identity was confirmed by amplification of the meningococcal gene *crgA* plus *ctrA* and/or *porA* as previously described [*13*]. PCR-based genogrouping was performed as previously described

[*13*, *14*]. The Meningococcal Reference Unit, PHE, Manchester, UK performed serogrouping and serotyping of MenW isolates using dot-blot EIA. Sequence data derived from amplified *porA* and *fHbp* alleles was queried against the PubMLST/Neisseria database (http://pubmlst.org/neisseria). Chi-square tests for significance were performed by using STATCALC (Epi Info version 7.2.0.1; Centers for Disease Control and Prevention, Atlanta, GA, USA).

The September sample of 769 first-year students represented 10.9% of the 7,049 first-year students registered in 2015. Carriage rates increased from 14% in late-September 2015 to 39% by mid-November 2015 and 46% in March 2016 (Table 1). The characteristics of enrolled students and behavioral risk factors for carriage were similar at the three time-points. The initial carriage rate of 14% was significantly lower for first-year students in September 2015 than in September 2009 (23.2% [*3*]; $\chi 2 = 34$, 1 df; $p<0.00001$) suggesting a reduction in meningococcal carriage in adolescents in UK, possibly due to an alteration in risk factors for carriage. The MenY carriage rate for incoming students (1.8%) was also lower than that detected in 2009 (2.9% [*3*]; $\chi 2 = 2.0$, 1 df; $p = 0.15$).

In September 2015, carriage of genogroup capsule null locus (cnl), B, Y and W strains was 4.2, 3.3, 1.8 and 0.7%, respectively. Notably, a substantial part of the increase in carriage from September 2015 through March 2016 was the result of a significant increase (0.7 to 8.0%) in carriage of MenW strains (Table 1). No statistically significant change in the carriage of MenY strains was detected (Table 1). Of the 50 students colonized with MenW, 36 (72%) had received MenACWY vaccine either before or during registration, which is consistent with the overall MenACWY coverage in our first-year student cohort. Students colonized with MenW at the latter two sampling points were distributed across all the five dormitories, suggesting widespread dissemination, and 21 (91%) of the MenW carriers in the

last time point (March 2016) had been vaccinated at least 5 months before sampling (Table 2).

Analysis of the genogroup W isolates showed that 47/52 (90%) were serotype 2a (Table 1) and harbored alleles for factor H binding protein (fHbp) peptide 22 and PorA P1.5,2, identical to the corresponding alleles harbored by the MenW:ST-11 clone responsible for the increase in invasive MenW disease in UK [5]. Capsular expression was examined by serogrouping and 32 (62%) of the MenW isolates expressed the W capsular polysaccharide. Of the 21 MenW carriers in March 2016 who had been vaccinated at least 5 months before sampling, 15 (71%) were harboring isolates expressing the W capsule (Table 2).

Conclusions

We detected a rapid rise in carriage of MenW in a university setting. In comparison, carriage of MenC in adolescents and young adults in the UK, including in university students, prior to the introduction of MenC monovalent conjugate vaccines, was rare [*9*]. The rise in MenW carriage is most likely due to acquisition within student dormitories or social spaces on campus, but was unexpected as no such isolates were found in a similar study at the UoN in 2008/09 [*15*], and only a very limited number in a multi-center carriage study involving six UK universities in 2010/11 [*6*, *10*].

The increase in MenW carriage among university students is potentially significant, and merits further monitoring, as it could further contribute to the sustained increase in MenW disease in the UK. Two cases of MenW disease were reported in unvaccinated students in Nottingham during 2015-16. Students attending universities exhibit high mobility and may represent a significant ongoing vehicle for amplification and spread of MenW into communities throughout UK or beyond with important implications for vaccination policy and future research.

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Biographical sketch

Dr. Oldfield is a senior postdoctoral researcher at the School of Life Sciences, University of Nottingham, UK. His research interests include meningococcal carriage dynamics and pathogenesis.

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Table 1. Characteristics of meningococcal carriage in first-year university students, University of Nottingham, UK, 2015–16*

		Genogroup											
		Capsule null locus		**Non-groupable**[a]		**B**		**Y**		**W**[b]		**Non-BYW**	
Time point	Carriage rate	No. of isolates (% carried strains)	% of all participants (95% CI)	No. of isolates (% carried strains)	% of all participants (95% CI)	No. of isolates (% carried strains)	% of all participants (95% CI)	No. of isolates (% carried strains)	% of all participants (95% CI)	No. of isolates (% carried strains)	% of all participants (95% CI)	No. of isolates (% carried strains)	% of all participants (95% CI)
SEP	110/769 (14%)	32 (29.1)	4.2 (2.8-5.6)	9 (8.2)	1.2 (0.4-1.9)	25 (22.7)	3.3 (2.0-4.5)	14 (12.7)	1.8 (0.88-2.8)	5 (4.5)[c]	0.7 (0.1-1.2)	25 (22.7)	3.3 (2.0-4.5)
NOV	136/353 (39%)	32 (23.5)	9.1# (6.1-12.1)	9 (6.6)	2.5 (0.9-4.2)	30 (22.1)	8.5# (5.6-11.4)	8 (5.9)	2.3 (0.7-3.8)	24 (17.6)[d]	6.8# (4.2-9.4)	33 (24.3)	9.3# (6.3-12.4)
MAR	133/288 (46%)	46 (34.6)	16.0# (11.7-20.2)	5 (3.8)	1.7 (0.2-3.2)	17 (12.8)	5.9 (3.2-8.6)	11 (8.3)	3.8 (1.6-6.0)	23 (17.3)[e]	8.0# (4.9-11.1)	31 (23.3)	10.8# (7.2-14.3)

*CI = confidence interval

[a] Isolates lacking *ctrA*

[b] Overall, of the 52 genogroup W isolates, 47 (90%) were serotype 2a and 32 (62%) expressed serogroup W capsule

[c] Of the W:2a isolates, 2/4 (50%) expressed serogroup W capsule

[d] Of the W:2a isolates, 12/23 (52%) expressed serogroup W capsule

[e] Of the W:2a isolates, 15/20 (75%) expressed serogroup W capsule

Significant difference compared to genogroup-specific carriage rate in September ($p<0.001$)

Table 2. MenW carriers in each of five dormitories and their respective MenACWY vaccination status

Time point[a]	MenACWY vaccination status[b]	Dormitory											
		A		B		C		D		E		**Total**	
		No. (%) of MenW carriers	No. (%) of individuals sampled	No. (%) of MenW carriers	No. (%) of individuals sampled	No. (%) of MenW carriers	No. (%) of individuals sampled	No. (%) of MenW carriers	No. (%) of individuals sampled	No. (%) of MenW carriers	No. (%) of individuals sampled	**No. (%) of MenW carriers**	**No. (%) of individuals sampled**
NOV	Vaccinated	3 (50)	45 (69)	4 (80)	50 (78)	2 (50)	52 (68)	3 (75)	43 (57)	4 (80)	67 (93)	**16 (67)[c]**	**257 (73)**
	Non-vaccinated	3 (50)	18 (28)	1 (20)	12 (19)	2 (50)	24 (31)	1 (25)	31 (41)	1 (20)	5 (7)	**8 (33)[d]**	**90 (25)**
	Un-assigned[e]	0	2 (3)	0	2 (3)	0	1 (1)	0	1 (1)	0	0	**0**	**6 (2)**
	Total	6 (100)	65 (100)	5 (100)	64 (100)	4 (100)	77 (100)	4 (100)	75 (100)	5 (100)	72 (100)	**24 (100)**	**353 (100)**
MAR	Vaccinated	9 (100)	50 (79)	3 (75)	43 (65)	4 (80)	57 (77)	3 (100)	24 (65)	2 (100)	39 (81)	**21 (91)[f]**	**213 (74)**
	Non-vaccinated	0	13 (21)	1 (25)	23 (35)	1 (20)	17 (23)	0	13 (35)	0	9 (19)	**2 (9)[g]**	**75 (26)**
	Total	9 (100)	63 (100)	4 (100)	66 (100)	5 (100)	74 (100)	3 (100)	37 (100)	2 (100)	48 (100)	**23 (100)**	**288 (100)**

[a] Students at the September 2015 time-point were recruited during registration and are not shown. Of these, 76/769 (10%) were not living in dormitories. The carriage rate for this specific group (9.2% [95% CI = 2.7%-15.7%]) was lower compared to those students living in dormitories (14.9% [95% CI = 12.2%-17.5%]), but the difference was not statistically significant ($p>0.05$)

[b] Students received MenACWY vaccine prior to or during registration (September 2015)

[c] Of these, 8/16 (50%) expressed serogroup W capsular polysaccharide

[d] Of these, 5/8 (63%) expressed serogroup W capsular polysaccharide

[e] Vaccination history unavailable

[f] Of these, 15/21 (71%) expressed serogroup W capsular polysaccharide

[g] Of these, 1/2 (50%) expressed serogroup W capsular polysaccharide