Epidemiological Report

Carriage Rate and Characteristics of *Neisseria meningitidis* among Dormitory Students

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SUMMARY: In Japan, several meningococcal disease outbreaks have recently been reported among adolescent dormitory residents of schools. However, little is known about meningococcal carriage dynamics in healthy individuals. The purpose of this study was to investigate the carriage rate over time and characteristics of *Neisseria meningitidis* strains among dormitory students. The survey was conducted twice between November 2018 and January 2019 for first- to third-year students ($N = 376$) in a medical school dormitory. The two surveys yielded carriage rates of 0.4% (one positive among 257 students) and 2.1% (two positives among 97 students, including 90 re-participants). No transmission or persistence of a specific strain was observed during the two months. A limited number of students had a history of potential risk behaviors for carriage, such as smoking (3.0% [6/202] aged ≥ 20 years and 5.2% [4/77] aged ≥ 20 years, respectively) and attending parties more than once a week (4.3% [11/257] and 2.1% [2/97], respectively). Two isolates were unencapsulated, consistent with asymptomatic participants.

INTRODUCTION

Meningococcal disease is a life-threatening illness with a rapid onset and progression of symptoms after oral acquisition of *Neisseria meningitidis*. With treatment, the fatality rate is 10–20% (1). Semi-closed populations, such as adolescents in university dormitories, have higher rates of meningococcal carriage and tend to promote outbreaks (2). The USA Centers for Disease Control and Prevention has recommended routine vaccination with a quadrivalent meningococcal conjugate vaccine covering serogroups A, C, W, and Y (MenACWY) since 2005 and has introduced the serogroup B meningococcal vaccine since 2015. This has decreased the disease incidence from 1.20 cases per 100,000 people in 1995 to 0.11 cases per 100,000 people in 2017 (3).

In Japan, the national surveillance data show that the current notification rate for invasive meningococcal

disease is 30 cases per year (approximately 0.03 cases per 100,000 people), reflecting a lower carriage rate than that in the USA and Europe (4–6). However, multiple outbreaks have been reported among dormitory students. These include one at a high school in Miyazaki prefecture with one fatal case (2011), a high school in Mie prefecture (2013), a school in Tokyo (2014), a new recruit at a dormitory in Kagoshima prefecture (2017), and a college in Kanagawa prefecture with one fatal case (2017) (7–11). The meningococcal vaccine (MenACWY) was approved for use in Japan in 2015, but it is not included in routine immunization schedules and is not mandatory prior to school admissions. These outbreaks indicate that Japanese adolescents, especially those living in compact spaces such as dormitories, have a higher risk of contracting the disease. However, little is known about meningococcal carriage dynamics in healthy individuals. The purpose of this study was to investigate the carriage rate and characteristics of meningococcal strains among school students living in dormitories. A study conducting multiple surveys of UK students at 2- to 4-month intervals indicated that MenB acquisition occurred at a rate of 2.8/1,000 person-months, and carriage persisted for months. However, they did not determine whether the isolates were the same or changed over time (12). The study also aimed to observe the acquisition and persistence of specific meningococcal strains over a short time period.

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Table 1. Characteristics of *N. meningitidis* strains obtained in this study

Student	First survey				Second survey			
	Culture	Serogroup	Genotype	<i>ctrA</i>	Culture	Serogroup	Genotype	<i>ctrA</i>
A	+	NT	ST-11026	–				
B	–	–	–	–	+	NT	ST-14239	–
C	–	–	–	–	–	–	–	+

NT, non-typable; ST, sequence type.

MATERIALS AND METHODS

This cross-sectional study surveyed meningococcal carriage rates and evaluated the associated risk factors in a population of first- to third-year students ($N = 376$) in a medical school dormitory. The survey was conducted twice, first in November 2018 and again in January 2019. Students participated in one or both surveys. To determine the status of live bacteria, pharyngeal swabs were collected on-site and cultured at BML, Inc., Tokyo, Japan. Briefly, samples were cultured on modified Thayer-Martin medium and chocolate agar medium at 5% CO₂ at 35°C for 18–24 h. After culturing, suspected colonies were identified using the oxidase test, Gram staining, and mass spectrometry, VITEK-MS (WAKENYAKU, Co., LTD., Kyoto, Japan). Isolates were then sent to the National Institute of Infectious Diseases to determine serogroup and sequence type (ST) following multilocus sequence typing (13). To detect encapsulated meningococci with high sensitivity, the capsular *ctrA* gene was tested using loop-mediated isothermal amplification (LAMP) at the National Defense Medical College Research Institute (14). To maintain testing accuracy over time, the number of investigators who performed swabbing was limited. The acquisition rate was calculated as the number of new meningococcal carriages occurring during the study period divided by the total person-time of all initially negative subjects (12). Any acquisition was assumed to have occurred halfway between assessments. Self-administered questionnaires were used to investigate demographics and behaviors during the previous month (e.g., smoking, participation in parties, and food sharing). The study was approved by the Ethics Committee of the National Defense Medical College (No. 2995) and Ethics Committee of Jichi Medical University (No. 18-0045). Written informed consent was obtained from all participants.

RESULTS

The survey was conducted twice. During the first survey in November 2018, 257 (68%) of the 376 healthy students participated in the study. One student (student A) tested positive on culture (Table 1). Two months later, a second survey was conducted with 97 students (26%). Ninety participants were also participants in the first survey. One student (student B) tested positive on culture but was negative for the *ctrA* gene on LAMP. Another student (student C) tested negative on culture but was positive on LAMP. Student A was not included in the second survey. Students B and C tested negative on culture and LAMP in the first

survey. These results yielded carriage rates of 0.4% (1/257) and 2.1% (2/97), respectively. The two isolates from students A and B were unencapsulated strains that had different ST, while the isolate from student C was believed to be encapsulated (Table 1). The 90 students who participated in both surveys were all negative in the first survey, and two (students B and C) were positive in the second survey. This yielded an estimated acquisition rate of 10.8/1,000 person-months.

Three students with positive cultures attended parties. They shared food and drink and were involved in kissing and club activities during the previous month. These behaviors are possible routes of meningococcal carriage. However, these rates were not higher than those who tested negative for *N. meningitidis* (Table 2). Students A, B, and C did not receive recent antibiotic treatment. Among the students who tested negative for *N. meningitidis*, 11 in the first survey and three in the second survey were administered antibiotics. Nine and 16 students had received meningococcal vaccination prior to the first and second surveys, respectively; all were negative for *N. meningitidis*.

DISCUSSION

In the USA and European countries, the association between social behaviors and meningococcal carriage has been studied. Among the university student population in the USA, the carriage rate was approximately 15%. Carriage was associated with attending bars/parties more than once a week (78.6% of carriers vs. 50.8% of non-carriers) and tobacco/marijuana use in the previous month (50.4% of carriers vs. 26.2% of non-carriers) (15). Attending pubs/clubs and cigarette smoking were independently and strongly associated with an increased risk of meningococcal carriage in a young British population (76.9% of carriers vs. 59.1% of non-carriers) (16). In contrast, low carriage rates among dormitory students were observed in the current study (0.4% and 2.1%). The proportion of smokers (3.0% [6/202] aged ≥ 20 years in the first survey; 5.2% [4/77] aged ≥ 20 years in the second survey) was lower than the proportion of ever-smokers among university students in a previous study (18.3%) (17). This may be because the population in the current study was comprised of medical students. The low proportion of students who attended parties more than once a week (4.3% [11/257]; 2.1% [2/97]) in the previous month may also have contributed to the low carriage rate among students. The lower carriage rate in the Japanese population (0.4–0.84%) than that in Western countries (4,5) indicates a smaller chance of introducing *N. meningitidis* into dormitories. Additionally, the students

Carriage Rate among Dormitory Students

Table 2. Student demographics and behaviors

		First survey (N = 257)						Second survey (N = 97)					
Demographics		Total	%	Nm+	%	Nm–	%	Total	%	Nm+	%	Nm–	%
Sex	Male	160	62.3	1	100.0	159	62.1	63	64.9	1	50.0	62	65.3
Age (yr)	Median	20	–	22	–	20	–	21	–	20.5	–	21	–
	IQR	19–21				19–21		20–22				20–22	
Nm vaccinated	no	217	84.4	0	0.0	217	84.8	66	68.0	1	50.0	65	68.4
Behaviors during the past month		Total	%	Nm+	%	Nm–	%	Total	%	Nm+	%	Nm–	%
Smoking	yes	6	3.0	0	0.0	6	3.0	4	5.2	0	0.0	4	5.3
Participating in parties	≥1 / wk	11	4.3	0	0.0	11	4.3	2	2.1	0	0.0	2	2.1
	≥1 / mo	145	56.4	0	0.0	145	56.6	53	54.6	2	100.0	51	53.7
	no	100	38.9	1	100.0	99	38.7	42	43.3	0	0.0	42	44.2
	unknown	1	0.4	0	0.0	1	0.4	0	0.0	0	0.0	0	0.0
Kissing	yes	103	40.1	0	0.0	103	40.2	34	35.1	2	100.0	32	33.7
Sharing food and drinks	yes	212	82.5	1	100.0	211	82.4	61	62.9	2	100.0	59	62.1
Upper respiratory tract infection	yes	94	36.6	1	100.0	93	36.3	24	24.7	0	0.0	24	25.3
Antibiotics	no	233	90.7	1	100.0	232	90.6	91	93.8	2	100.0	89	93.7

Nm, *Neisseria meningitidis*; IQR, interquartile range.

in the current study were all living independently in private bedrooms. Since this setup enables a lower frequency of personal contact than shared rooms, the rate of bacterial transmission may have been reduced (9).

The rates of students who had a history of meningococcal vaccination were 3.5% and 16.5% in the first and second surveys, respectively. The vaccine is currently not included in the routine immunization schedule in Japan and is optional, mainly for those traveling to endemic countries. Given the limited use of the vaccine, these rates seem relatively high, but they are still too low to provide herd protection against meningococcal carriage (18).

There was a discrepancy between the culture and LAMP results for student C, who had no history of antibiotic drug administration. The same researcher obtained pharyngeal swabs from the same student, and the culture samples were maintained at room temperature. After obtaining the swab from student C, the number of live bacteria may have decreased below the detection limit of the culture method; however, the *ctrA* gene was still stable and detectable on LAMP. The isolates from students A and B were encapsulated, which was consistent with the absence of *ctrA* on LAMP.

Periodic follow-up of this population could provide information regarding meningococcal acquisition from outside the school, persistence in individuals, and transmission among the population. The isolates from students B and C could not be discriminated but might be different strains given the presence of the *ctrA* gene in the isolate from student C. Students A, B, and C presumably acquired *N. meningitidis* strains from

different routes at different time periods. In particular, students B and C possibly acquired the strain during the period between the two surveys. We estimated an acquisition rate of 10.8/1,000 person-months among students who participated in both surveys. This seems higher than the 2.8/1,000 person-months in adolescents (aged 10–25 years) in the UK (12). This might be partly because our subjects were in a high-risk age group. However, correct interpretation of this acquisition rate is difficult as the number of subjects in our study was small. Unfortunately, since student A was not tested in the second survey, the persistence period was unknown.

ST-11026 and ST-14239 isolates have been reported only in Japan in the PubMLST database. ST-11026 has been a major isolate among recent unencapsulated meningococci identified in Japan (Takahashi H, unpublished data). Most unencapsulated *N. meningitidis* strains were from healthy individuals, but some were obtained from the blood and spinal fluid. The trends in the number of patients/carriers and geographical distribution of these strains should be further investigated.

A major limitation of this study is that the results may not reflect the entire target population because the participation rates were low. The behavioral factors tested in the questionnaire were not identified as risks for meningococcal carriage because the number of positive samples was too small.

In summary, an encapsulated strain and two unencapsulated strains were isolated from healthy individuals. Little is known about the effects of unencapsulated meningococci on individuals and populations (19). Further studies targeting high-risk

populations using the LAMP test, culture, and other identification methods are needed to address questions regarding carriage dynamics and the prerequisites for a meningococcal outbreak.

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Conflict of interest None to declare.

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