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Asymptomatic Carriage of *Neisseria meningitidis* in a Randomly Sampled Population

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To estimate the extent of meningococcal carriage in the Norwegian population and to investigate the relationship of several characteristics of the population to the carrier state, 1,500 individuals living in rural and small-town areas near Oslo were selected at random from the Norwegian National Population Registry. These persons were asked to complete a questionnaire and to volunteer for a bacteriological tonsillopharyngeal swab sampling. Sixty-three percent of the selected persons participated in the survey. Ninety-one (9.6%) of the volunteers harbored *Neisseria meningitidis*. The isolates were serogrouped, serotyped, tested for antibiotic resistance, and analyzed by multilocus enzyme electrophoresis. Eight (8.8%) of the 91 isolates represented clones of the two clone complexes that have been responsible for most of the systemic meningococcal disease in Norway in the 1980s. Age between 15 and 24, male sex, and active and passive smoking were found to be independently associated with meningococcal carriage in logistic regression analyses. Working outside the home and having an occupation in transportation or industry also increased the risk for meningococcal carriage in individuals older than 17, when corrections for gender and smoking were made. Assuming that our sample is representative of the Norwegian population, we estimated that about 40,000 individuals in Norway are asymptomatic carriers of isolates with epidemic potential. Thus, carriage eradication among close contacts of persons with systemic disease is unlikely to have a significant impact on the overall epidemiological situation.

The incidence of disease caused by the bacterium *Neisseria meningitidis* reached an epidemic level in the northern part of Norway in 1975 (5). In the following years, the epidemic spread to the whole country, and not until the late 1980s did the incidence of disease start to decrease (14). This epidemic was mainly caused by sulfonamide-resistant, serogroup B organisms belonging to a genetically distinctive group of closely related clones, the ET-5 complex (10).

Although evolution of the disease situation over the last 10 years has been carefully monitored (14), it is not known how and why the pathogenic strains have been spreading in the Norwegian population.

The upper respiratory tract of humans is the only known reservoir of *N. meningitidis*, and most patients with meningococcal disease have not had direct contact with another such patient. Thus, asymptomatic carriers are presumably the major source of transmission of pathogenic strains. The meningococcal carrier state has been shown to be an immunizing event both in children and in adults, leading to the development of bactericidal antibodies (11, 15, 27, 29). While carriage of low-virulence strains may then be beneficial, the transmission of pathogenic strains at the same time represents a risk for the general population. Consequently, it is important to identify the groups of individuals at risk for meningococcal carriage, especially those carrying highly pathogenic strains, to evaluate the feasibility of intervention.

The prevalence of *N. meningitidis* in asymptomatic carriers has been the subject of numerous investigations (see reference 6 for a review). Highly variable carrier rates have been reported (16), with as much as 95% carriage during severe serogroup A epidemics. Even during periods of endemic disease, semisecluded populations, such as military recruits, may present well over 50% carriers (11).

Several characteristics of the populations studied have been related to the frequency of carriage. The carriage rate is low in individuals under 5 years of age (8). It increases throughout childhood and adulthood and then is low again among the elderly (8). Males have more often been reported to be carriers than females (4, 8).

In Belgium, De Wals et al. (13) found that the proportion of carriers among schoolchildren from a densely populated area with residents having a low economic status was three times higher than that among schoolchildren from upper-middle-class families living in a suburban area. The transmission rate is likely to be influenced by the number and quality of social contacts, and reduced social activity has been suggested to explain the decrease in the carriage rate among the elderly (8).

A coincidence between meningococcal carriage and symptoms of upper respiratory tract infections has been demonstrated by Olcén et al. (24) and Young et al. (36), and tonsillectomy has been shown to increase the probability of meningococcal carriage (19). Smoking has also been revealed as an important risk factor for meningococcal carriage (2, 3, 33).

While numerous studies have provided much insight into factors which may be related to carriage rate, they usually have been performed with selected population groups, such as personnel in the armed forces, or in connection with outbreaks, a fact that may not reflect the overall situation in the population. We wanted here to estimate the extent of meningococcal carriage in a randomly sampled population

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and to determine the relative contributions of several characteristics of the individuals to the carrier state. In this report, we present the characteristics of the strains isolated from the carriers, as well as univariate and multivariate analyses of the risk factors associated with the carriage of *N. meningitidis*.

MATERIALS AND METHODS

Ethical issues. Approvals for the study were obtained from the Regional Ethical Committee for Medical Research, the Central Bureau of Statistics, and the Norwegian Data Protection Agency. Written consent was obtained from all the participants or from their legal guardians if they were under the age of 16.

Population sampled. A total of 1,500 individuals living in the municipality of Lørenskog, which includes rural and small-town areas near Oslo, were randomly selected from the Norwegian National Population Registry. These persons were contacted by letter and asked to voluntarily meet at the local health office on weekdays after normal working hours. A questionnaire was enclosed with the information letter. Further general information about the project was made available through the local press and radio.

Collection of throat culture samples. Physicians from the National Institute of Public Health collected the throat samples in a standardized way: under guidance of vision, the tonsillar region on one side, including the crypts and the posterior pharyngeal wall, was scrubbed vigorously with a charcoal-impregnated swab. The samples were placed in modified Stuart's transport medium (30). The physicians recorded the macroscopic appearance of the pharynx and the tonsils for each volunteer. The samples were collected over a 5-week period, in February and March 1991, with the exception of eight samples obtained in a pilot study performed 1.5 weeks earlier. Five hundred persons were called in per week in the first 3 weeks. A second written notice was sent to individuals who had not met after the first letter. Telephone calls were also made to stimulate participation. Twenty-six persons who wanted to participate but were not able to meet at the local health office were sampled at their homes.

Bacterial identification. The throat swabs were plated within 20 h on chocolate agar with colimycin at 7.5 mg/liter, lincomycin at 0.5 mg/liter, amphotericin B at 1.0 mg/liter, and trimethoprim at 5.0 mg/liter. Plates were incubated at 35°C in 10% CO_2 for 2 days, and meningococci were identified by standard methods (28). One colony of *N. meningitidis* from each throat culture was subcultured twice, each time from a new single colony, and preserved at −70°C until further analysis.

Serogrouping and serotyping. Serogroups were determined in an enzyme-linked immunosorbent assay with monoclonal antibodies (MAbs) specific for the A, B, C, W, and Y capsular polysaccharides and by agglutination with commercial polyclonal antisera (Wellcome Reagents Ltd., Beckenham, United Kingdom) for the X and Z serogroups. Serotyping and subtyping were performed with MAbs for serotype antigens 1, 2a, 2b, 2c, 4, 5, 6, 8, 9, 11, 14, 15, 16, and 21 and subtype epitopes P1.1, P1.2, P1.3, P1.4, P1.5, P1.6, P1.7, P1.9, P1.10, P1.12, P1.14, P1.15, and P1.16 by a dot blot method as described by Wedege et al. (35). MAbs were kindly provided by C. E. Frasch, J. T. Poolman, and W. D. Zollinger. The presence of class 1 protein was analyzed by sodium dodecyl sulfate-polyacrylamide gel electrophoresis (SDS-PAGE) (35).

TABLE 1. Proportion of volunteering individuals and participation rate by age and sex in a survey of meningococcal carriage

Age (yr)	No.[a] (%) of:	
	Females	Males
0–4	40/65 (61.5)	36/52 (69.2)
5–9	38/48 (79.2)	37/48 (77.1)
10–14	35/37 (94.6)	31/41 (75.6)
15–19	32/58 (55.2)	36/63 (57.1)
20–24	33/60 (55.0)	19/62 (30.6)
25–29	50/81 (61.7)	40/68 (58.8)
30–34	48/66 (72.7)	36/67 (53.7)
35–39	48/70 (68.6)	37/58 (63.8)
40–44	33/55 (60.0)	31/57 (54.4)
45–49	36/47 (76.6)	40/63 (63.5)
50–54	27/38 (71.0)	21/34 (61.8)
55–59	26/34 (76.5)	12/27 (44.4)
60–64	14/22 (63.6)	19/36 (52.8)
65–69	23/31 (74.2)	17/22 (77.3)
70 or more	25/57 (43.9)	23/33 (69.7)
Total	508/769 (66.1)	435/731 (59.5)

[a] Number of participants/number of selected subjects.

Susceptibility to antibiotics. MICs of sulfadiazine (a sulfonamide) and penicillin G were tested on PDM antibiotic sensitivity medium (AB Biodisk, Solna, Sweden) with horse blood (lysed with saponin for sulfonamide testing). The concentrations of antibiotics ranged from 2 to 400 mg/liter for sulfadiazine and from 0.0125 to 1.6 mg/liter for penicillin G. Isolates were assigned to three categories with regard to their susceptibility to sulfadiazine: susceptible (MIC, 5 mg/liter or lower), intermediate (MIC, 10 to 50 mg/liter), and resistant (MIC, 100 mg/liter or higher).

Electrophoresis of enzymes. Multilocus enzyme electrophoresis was performed as previously described (9). Each isolate was characterized by its combination of alleles at 14 enzyme loci. Distinctive multilocus genotypes were designated electrophoretic types (ETs). Genetic distance between pairs of ETs was expressed as the proportion of enzyme loci at which dissimilar alleles occurred, and clustering was done by the average-linkage method (31). ETs were numbered sequentially according to their genetic relationships as determined by the cluster analysis (dendrogram not shown).

Questionnaire. The participants were asked to list their name, address, age, sex, and marital status. Other questions concerned their current health condition, drugs recently taken, tobacco use, educational level and occupation, either of the subjects themselves or of their parents if they were under the age of 18, type and size of accommodation, type of domestic heating system, and the number of and smoking habits of the household members. The questionnaire was controlled for completeness when sampling took place, and the volunteers were asked to list missing information.

Analysis of data. The questionnaire data were subjected to univariate and multivariate statistical analyses with the statistical package SPSS (Statistical Package for Social Sciences Inc., Chicago, Ill.) and Epi Info (Centers for Disease Control and Prevention, Atlanta, Ga.).

RESULTS

Participation. Of the 1,500 persons randomly selected from the population register, 943 (63%) volunteered for the survey. From the population register, the sex and age

TABLE 2. Characteristics of the 91 isolates of 77 ETs of *N. meningitidis* recovered from carriers

ET	Serogroup[a]	Serotype: subtype[b]	Sulfonamide susceptibility[c]
1	B	15:P1.16	R
2	B	15:P1.2,5	R
3	NG	15:P1.7,16	R
4	B	15:P1.7,16	R
5	NG	15:–	R
6	NG	15:P1.7,16	R
7	B	14:P1.6,9	S
8	B	14:P1.6,12	S
9	B	11:P1.1,7	S
10	X	4:P1.14	S
11	NG	NT:–	I
12	NG	4:–	R
13	B	4:P1.14	S
14	NG	4:P1.14	S
15	NG	4:P1.14	S
16	B	4:P1.14	S
17	NG	4:–	S
18	NG	8:P1.6	S
	B	4:P1.12	S
19	B	NT:–	R
20	B	NT:P1.12	S
21	NG	4:–	R
22	B	NT:P1.15	I
23	B	NT:P1.15	I
24	B	NT:P1.3	R
25	B	NT:–	S
26	NG	4:P1.1,4,14	S
27	B	NT:P1.6	I
28	NG	8:P1.15	S
29	B	14:P1.6,15	R
30	NG	21:P1.1	S
	Z	NT:P1.1	S
31	B	2b:P1.3,6	S
32	B	16:P1.12	I
33	Y	14:P1.6	S
34	NG	14:P1.6	S
35	NG	4:P1.6	S
36	NG	NT:P1.3,6	I
37	W	16:P1.2,5	S
38	NG	14:P1.2,5,6	S (3)
	Y	14:P1.2,5,6	S (3)
39	NG	14:P1.2,5,6	S
40	W	14:P1.6	I
41	Z	4:P1.16	S
42	NG	4:P1.1,7	R
43	B	4:–	S
44	Z	1:P1.15	I
45	NG	4:P1.5	R
46	NG	4:P1.16	S
47	B	8:–	S
	Y	21:P1.1,7	S
48	B	15:P1.2	S
49	NG	8:P1.15	I
50	B	8:P1.15	S
51	B	1:P1.15	I
52	NG	4:P1.16	R
53	NG	4:P1.15	I
54	NG	4:P1.10	I
55	Z	14:P1.1,6,7	S
56	X	4:P1.5	S
57	NG	1:–	I
58	NG	1:P1.2,5	S
59	NG	14:P1.5,6	S
60	C	NT:–	I
61	C	NT:P1.10	S
62	NG	4:P1.5	S
63	NG	16:P1.2,5	S (2)
64	Z	4:P1.16	S
65	NG	NT:P1.1,7	S
66	NG	4:P1.1,7	S
67	NG	4:P1.9	I
68	B	4:–	S
69	B	NT:P1.9	S
70	Z	1:P1.3,6	I
	NG	NT:P1.10	I
	NG	NT:P1.12	I
	NG	NT:P1.14	I (2)
71	NG	16:P1.3,6	S
72	C	2a:P1.2,5	R
	C	2a:–	R
73	NG	4:P1.15	S
74	B	NT:–	I
75	B	11:–	I
76	NG	15:P1.5	S
77	NG	15:P1.6	R

[a] NG, nonserogroupable.
[b] NT, nonserotypeable; –, nonsubtypeable.
[c] S, susceptible; I, intermediate; R, resistant. The numbers of isolates, if greater than one, with the same characteristics are indicated in parentheses.

distributions for the 1,500 individuals were obtained, and these were compared with the age and sex distributions for the survey participants (Table 1). Overall, the participation was higher among females (66.1%) than among males (59.5%). The highest rate of participation occurred among 5- to 14-year-old persons, with over 80% for both sexes combined. The lowest rate (30.6%) was among 20- to 24-year-old males, with the exception of age groups over 80. The youngest participant was 2.5 months old, and the oldest one was 94 years old.

Fifty-six of the nonvolunteers or their family members called and gave the following reasons for not participating in the study: moving (43%), illness (27%), death (5%), military service (4%), and imprisonment (2%). The remaining 20% just did not want to participate.

Overall carriage rate. *N. meningitidis* was identified in 91 samples, for an overall carriage rate of 9.6%. None of the samples harbored *N. gonorrhoeae* or *N. polysaccharea*. *N. lactamica* was definitively identified in 29 samples and was suspected in another 34 samples, but the strains were not kept for complete identification. Nineteen of the 29 *N. lactamina* strains were from children between 0 and 8 years old.

Strain characteristics. The *N. meningitidis* isolates are listed in Table 2 according to the genetic relationships of their ETs. Full ET data are available upon request from D.A.C. Serogroup, serotype, and sulfonamide susceptibility are given for each isolate. All isolates were susceptible to penicillin G (MIC of 0.05 mg/liter or lower).

Six serogroups were represented, B (28 isolates), C (4 isolates), W (2 isolates), X (2 isolates), Y (5 isolates), and Z (6 isolates). Nearly 50% of the isolates were nonserogroupable. Ten serotypes were represented among the 91 isolates, with the dominant ones being serotype 4 (28.6%) and serotype 14 (16.5%). Other serotypes were represented by less than 10% of the isolates, and 19 (20.9%) isolates were nonserotypeable. Individual isolates reacted with up to three subtype MAbs, one of which was P1.6. Twenty-one subtype

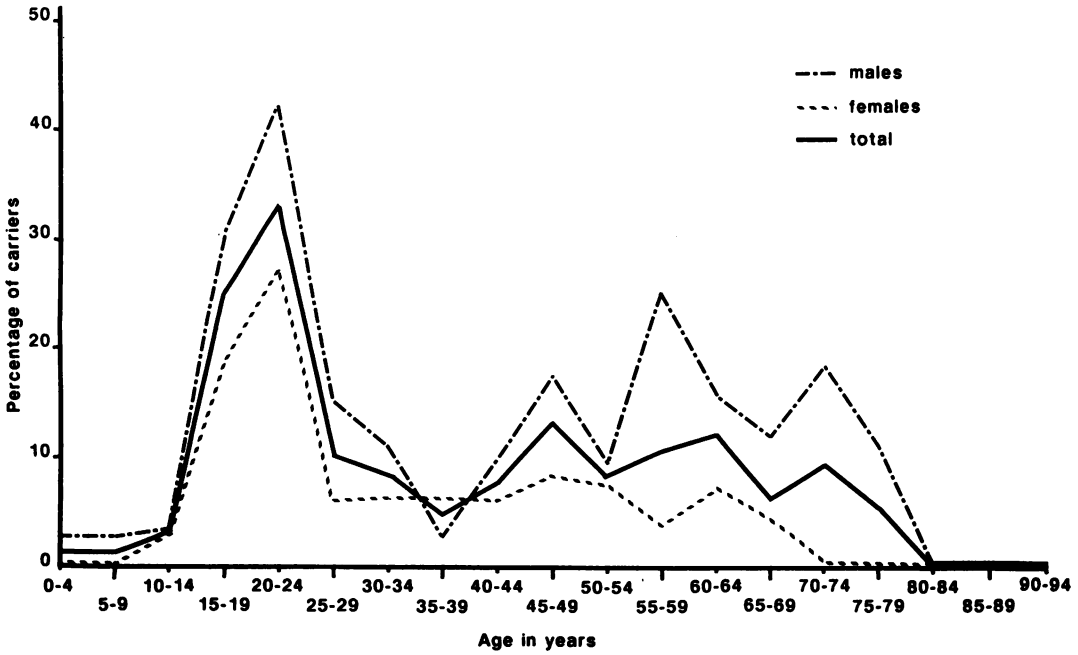

FIG. 1. Percentages of carriers of *N. meningitidis* according to age among males, females, and all participants in a random sample of the Norwegian population.

combinations were distinguished, but none of them represented 10% of the isolates. Fifteen isolates did not react with any of the subtype MAbs, and 5 of these did not reveal a class 1 protein in SDS-PAGE (data not shown).

On the basis of allelic variations at 14 enzyme loci, 77 ETs were identified among the 91 isolates, and only 7 ETs were represented by multiple isolates. The most frequently identified ET, ET-38, included 6 isolates, which were all 14: P1.2,5,6.

Six isolates belonged to the ET-5 complex, which has been responsible in large part for the Norwegian epidemic since the mid-1970s (here represented by ET-1 through ET-6). Only one of these six isolates was ET-5 itself. This isolate, however, did not react with any of the subtype MAbs. Two isolates belonged to the ET-37 complex (designated ET-72 in Table 2), the second dominant clone complex causing disease in Norway since the mid-1980s. Carriers of these potentially virulent strains were again contacted, and they and their family members who were also found to be meningococcal carriers of the same isolates were offered treatment with antibiotics (rifampin or ciprofloxacin) to eliminate the bacteria and avoid transmission to nonprotected individuals.

Carriage detection according to physician. Altogether, six physicians took the throat samples, with from 23 to 424 recorded samples per physician. Carriage detected by each physician varied from 6.2 to 14.0%, but the overall differences were not statistically significant ($\chi^2 = 5.7$; $P = 0.336$).

Carriage in relation to age and sex. The percentages of carriers among males, females, and the whole population sampled according to age groups are shown in Fig. 1 and summarized in Table 3. In all age classes but one (persons 35 to 39 years old), the carriage rate proved higher in males than in females. Overall, the male/female ratio was 1.87 ($\chi^2 = 9.6$; $P = 0.002$). Among the 217 children below age 15, only 4 (1.8%) carriers were identified (Table 3). After the age of 15, the carriage rate increased sharply, reaching 32.7% in persons 20 to 24 years old, both sexes combined, and 42.1% in males. After the age of 25, the carriage rate decreased rapidly in both sexes but remained at about 10%. The oldest carrier was a 77-year-old man.

Carriage in relation to health conditions. The relationship between carriage and appearance of the pharynx noted by the physicians who took the samples, as well as the parameters of health from the questionnaire, is given in Table 4. The presence or absence of the tonsils and redness of the pharynx were not associated with carriage, but exudate over the tonsillar surface was more often noted among carriers

TABLE 3. Meningococcal carriage rate by age and sex

Age (yr)	Females			Males		
	No.[a] (%)	OR (95% confidence interval)	*P*	No.[a] (%)	OR (95% confidence interval)	*P*
0–14	1/113 (0.9)	1.00		3/104 (2.9)	1.00	
15–24	15/65 (23.0)	33.60 (4.45–700.51)	<0.001	19/55 (34.5)	17.77 (4.58–80.64)	<0.001
>24	19/330 (5.8)	6.84 (0.95–138.80)	0.031	34/276 (12.3)	4.73 (1.35–19.78)	0.006
Total	35/508 (6.9)			56/435 (12.9)		

[a] Number of carriers/total number of participants.

TABLE 4. Meningococcal carriage rate in relation to health conditions

Factor	No.[a] (%)	OR (95% confidence interval)	P
Presence of pharyngeal exudate			
No	84/917 (9.2)	1.00	
Yes	5/17 (29.4)	4.13 (1.24–13.03)	0.005
Pharyngeal inflammation			
No	78/822 (9.5)	1.00	
Yes	11/104 (10.6)	1.13 (0.55–2.28)	0.723
Tonsils			
Present	69/751 (9.2)	1.00	
Small or absent	19/175 (10.9)	1.20 (0.68–2.12)	0.498
Influenza-like illness in the month before sampling			
No	47/460 (10.2)	1.00	
Yes	44/479 (9.2)	0.89 (0.56–1.40)	0.593
Other disease			
No	83/799 (10.4)	1.00	
Yes	6/124 (4.8)	0.44 (0.17–1.07)	0.051
Recent use of antibiotics			
No	86/829 (10.4)	1.00	
Yes	4/108 (3.7)	0.33 (0.10–0.97)	0.027
Use of other drugs			
No	75/765 (9.8)	1.00	
Yes	15/169 (8.9)	0.90 (0.48–1.65)	0.711
Use of a dietary iron supplement			
No	81/817 (9.9)	1.00	
Yes	10/115 (8.7)	0.87 (0.41–1.79)	0.680

[a] Number of carriers/total number of participants.

TABLE 5. Meningococcal carriage rate in relation to marital status, education, and occupation for individuals over 17 years old

Factor	No.[a] (%)	OR (95% confidence interval)	P
Marital status			
Single	23/101 (22.8)	1.00	
Married	45/505 (9.7)	0.33 (0.18–0.60)	<0.001
Widowed, divorced, or separated	9/77 (11.7)	0.58 (0.23–1.42)	0.196
Basic education (yr)			
7	17/157 (10.8)	1.00	
9	35/237 (14.8)	1.43 (0.74–2.77)	0.258
12	28/280 (10.0)	0.92 (0.46–1.82)	0.785
Further education			
None	22/130 (16.9)	1.00	
University	10/141 (7.1)	0.37 (0.16–0.87)	0.012
Other	47/388 (12.1)	0.68 (0.38–1.22)	0.162
Working status			
At home	13/174 (7.5)	1.00	
Student	13/52 (25.0)	4.13 (1.64–10.41)	<0.001
Outside the home	56/465 (12.0)	1.70 (0.87–3.35)	0.097
Profession			
Transportation or industry	26/115 (22.6)	3.10 (1.71–5.62)	<0.001
Other	35/407 (8.6)	1.00	

[a] Number of carriers/total number of participants.

than among noncarriers (crude odds ratio [OR] = 4.13; P = 0.005). A combination of these clinical signs did not show a significant association with carriage.

About half of the participants had suffered symptoms of throat infection or influenza-like illness in the month before the sample was taken, but no association with meningococcal carriage was revealed (Table 4). The carriage rate, however, was lower in individuals reporting disease other than throat infection than among healthy ones (P = 0.051). Antibiotics had been used in the last 3 months before the sample was taken by a larger proportion of noncarriers than carriers (P = 0.027). Of the only four carriers who claimed to have taken antibiotics, two did not remember what type of drug was prescribed and two were treated with low-dose tetracycline.

No significant relationship between carriage and the use of drugs other than antibiotics or a dietary iron supplement was detected.

Carriage in relation to marital status, education, and occupation. Analyses of marital status and working status were performed for individuals older than 17 years (Table 5). The carriage rate was higher among single and widowed, divorced, or separated individuals and lower among those working at home. Among individuals working outside the home, the sex ratio (2.34; χ^2 = 10.26; P = 0.001) was more pronounced among carriers than in the whole population. We found significant differences in the proportion of carriers according to profession, with a carriage rate of 22.6% in individuals working in transportation or industry (OR = 3.10; $P < 0.001$). The carriage rate was not related to the level of basic education (Table 5), but it was lower among persons with university-level education. It was also lower among individuals below 18 years of age whose parents had completed junior high school (P = 0.018) than among the others (data not shown).

Carriage in relation to living conditions. None of the parameters analyzed showed an overall significant association with meningococcal carriage, but individuals living in a relatively old house were more likely to be carriers than individuals living in a house that was less than 10 years old (Table 6).

Carriage in relation to smoking. There were nearly three times as many carriers among smokers as among nonsmokers (OR = 3.30; $P < 0.001$) (Table 7), but no association between the number of cigarettes smoked daily and carriage was detected (data not shown). Individuals were assumed to be exposed to passive smoking at home when at least one of the family members was a smoker. The carriage rate was more than doubled for individuals subjected to passive smoking, even considering only nonsmokers (OR = 2.30; P = 0.006) (Table 7).

Multivariate analyses. To estimate the independent contributions to meningococcal carriage of significant variables identified by the univariate analyses, a logistic regression analysis was carried out (Table 8). Thirty-four cases were rejected because of missing data; thus, 912 subjects were

TABLE 6. Meningococcal carriage rate in relation to conditions of habitation

Factor	No.[a] (%)	OR (95% confidence interval)	P
Age of dwelling			
Less than 10 yr	17/260 (6.5)	1.00	
10 yr or more	70/654 (10.7)	1.71 (0.96–3.09)	0.053
Type of dwelling			
Apartment house	21/203 (10.3)	1.00	
Other	70/739 (9.5)	0.91 (0.53–1.57)	0.709
Size of dwelling			
Less than 100 m^2	29/281 (10.3)	1.00	
100 to 149 m^2	26/224 (11.6)	1.14 (0.63–2.07)	0.665
150 m^2 or more	31/297 (10.4)	0.90 (0.46–1.78)	0.755
No. of rooms			
Less than 4	17/184 (9.2)	1.00	
4 or 5	34/420 (8.1)	0.87 (0.45–1.67)	0.642
6 or more	29/308 (9.4)	1.02 (0.52–2.01)	0.948
Heating system			
Electric	75/756 (9.9)	1.00	
Central (oil)	12/105 (11.4)	1.17 (0.58–2.32)	0.631
Wood	46/464 (9.9)	1.00 (0.67–1.50)	0.997
Size of the household (no. of persons)			
1	6/68 (8.8)	1.00	
2 or 3	41/449 (9.1)	1.14 (0.44–3.11)	0.775
4 or more	44/414 (10.6)	1.35 (0.52–3.67)	0.510

[a] Number of carriers/total number of participants.

included in the analysis. Age was the most important factor. Being between 15 to 24 years old increased the risk of being a carrier more than 13 times compared with the reference category of being under 15 years old. After the age of 24, the adjusted OR was 3.6. Sex was also significant, with the risk of carriage being more than twice as high in males as in females. When corrected for age and sex, the probability of carriage was 2.8 times higher for smokers than for nonsmokers, and passive smoking also increased the probability of carriage. The use of antibiotics and the reporting of disease other than influenza-like illness were not significant when the data were corrected for age, sex, and active and passive smoking.

TABLE 7. Meningococcal carriage rate in relation to active and passive smoking

Factor	No.[a] (%)	OR (95% confidence interval)	P
Smoking habits			
Nonsmoker	46/698 (6.6)	1.00	
Smoker	45/238 (18.9)	3.30 (2.08–5.26)	<0.001
Passive smoking, including smokers			
Nonexposed	41/610 (6.7)	1.00	
Exposed	50/333 (15.0)	2.45 (1.55–3.88)	<0.001
Passive smoking, nonsmokers only			
Nonexposed	24/490 (4.9)	1.00	
Exposed	22/208 (10.6)	2.30 (1.21–4.37)	0.006

[a] Number of carriers/total number of participants.

TABLE 8. Logistic regression analysis of factors associated with meningococcal carriage

Variable[a]	Adjusted OR	95% Confidence interval	P
Age (yr)			
15–24	13.55	4.52–40.58	<0.001
>24	3.56	1.21–10.42	0.021
Sex	2.18	1.34–3.54	0.002
Active smoking	2.79	1.67–4.64	<0.001
Passive smoking	1.66	1.01–2.71	0.044
Having a disease other than influenza	0.49	0.19–1.29	0.153
Recent use of antibiotics	0.52	0.18–1.53	0.237

[a] Reference categories: age, 0 to 14 years old; sex, female; active smoking, nonsmoker; passive smoking, no smoker at home; disease, no disease other than influenza-like illness; antibiotic use, no antibiotic taken in the past 3 months.

DISCUSSION

With the exception of the Stonehouse survey (32), which was performed in connection with an outbreak and in which the whole population was sampled, carriage rates have only been estimated for selected population groups, such as military recruits and schoolchildren. In 1984, a large carrier survey including various age groups was performed in Norway (20). However, the individuals were not randomly selected but were sampled at day-care centers, schools, and workplaces, etc. In the present study, we wanted to estimate the overall carriage rate in Norway by performing an unbiased selection of individuals.

The 1,500 individuals randomly selected from the population register lived in a municipality of 27,000 inhabitants outside Oslo. This area has both urban and rural parts, representing the variety of living conditions found in the country. No case of meningococcal disease had occurred in the municipality in the 14 weeks prior to the survey, and one case of serogroup C disease occurred 4 weeks after the end of the collection of the samples (1).

The survey was performed in the late winter, the period of the year during which most cases of meningococcal disease occur in Norway (5). While it could thus be assumed that this is the period with the highest carriage rate in Norway, no data have yet shown a seasonal variation in carriage rate.

Of the 943 individuals who agreed to participate in the study, 9.6% were meningococcal carriers. From the nonparticipants, only age and sex distributions were available. When corrected for the difference in participation according to sex and age, the carriage rate in the population can be estimated to be 10.9%. The difference results from the low participation (probably because of compulsory military service and education outside the home) of 20- to 24-year-old males, who had the highest carriage rate (42.1%).

No attempt was made to determine whether the nonparticipants differed from the participants in other characteristics. The daily smoking habits of the participants, however, were close to those of the whole Norwegian population in 1991: 31.5 and 34.5% of the male and female participants, respectively, between the ages of 16 and 74 years were smokers; the percentages in that age range for the whole

population were 36% for the males and 33% for the females. The average numbers of cigarettes smoked per day were 12.2 for the smokers among the participants and 13.5 for the smokers in the whole country (23).

The 91 individuals who harbored *N. meningitidis* in their throat all belonged to different households. The meningococcal strains were assigned to 77 ETs, and strains of 7 ETs only were recovered from more than one carrier. No relationship between carriers of strains of the same ET was determined from the questionnaire, suggesting that these clones are commonly found among carriers. ET-38, the most frequently isolated clone, has been repeatedly recovered in carrier surveys performed in Norway since the beginning of the 1980s (10, 11). Only two strains (of ET-56 and ET-57) belonged to the group of ETs designated cluster D (12), which has been frequently recovered from Norwegian carriers in other surveys (10–12).

Six and two isolates, respectively, belonged to the two groups of clones, the ET-5 complex and the ET-37 complex, which together were responsible for nearly 75% of the systemic meningococcal disease in Norway in 1991. The carriers of these eight possibly virulent strains were between the ages of 11 and 69; three were female and five were male. Five of them were smokers, and six were exposed to passive smoking at home. Another one was found to have a boyfriend who was a smoker; this discovery was made during sampling from close contacts before antibiotic treatment of carriers of potentially virulent strains. The boyfriend was also a carrier but harbored a different clone.

While many analyses of risk factors associated with meningococcal carriage have been performed recently, the relative importance of multiple factors has not been documented. We found that the most significant risk factor was age, with the probability of being a carrier increasing by a factor of 13 in the age group of 15 to 24 years, compared with that for individuals less than 15 years old. A significant difference between our results and those of the Stonehouse study (8), as well as several other carrier surveys (4, 13, 25), is the very low carriage rate that we observed for children up to 14 years of age. In the Stonehouse survey, the relatively high carriage rate in children seemed to be related to the high rate of carriage of the outbreak strain among 5- to 9-year-old children.

Males were twice as likely as females to be carriers. The higher carriage rate in males was seen in nearly all age groups. The male/female ratio for carriage (1.9) was much higher than that for meningococcal patients (1.1) in Norway (5). While the higher risk for meningococcal disease in males occurs in the first 3 years of life (5), the difference in carriage between the sexes is constant throughout life. While the second peak of disease in Norway occurred among teenagers 2 years earlier in females than males (5), no such difference was seen for carriage (data not shown).

Active smoking appeared as the second most important factor next to age and was independently associated with meningococcal carriage. The association of smoking with carriage in our study was even stronger than that reported by other investigators (2, 3, 33). However, in contrast to the Stonehouse study (33) and studies of military recruits in Greece (2), there was no increase in carriage rate with the number of cigarettes consumed per day. This discrepancy may be a consequence of the low number of heavy smokers in the Norwegian population, as less than 1% of the smokers reported smoking more than 25 cigarettes daily.

Passive smoking has been shown to influence the occurrence of meningococcal disease in persons under the age of 12 years (17). We also confirmed here the results of Stuart et al. (33), who found that exposure to cigarette smoke at home, as judged by the presence of at least one smoker within the household is, independently of active smoking, a risk factor for meningococcal carriage. However, it was not determined in our study whether passive smoking had a direct causal effect on colonization of the nasopharynx or whether having a smoker in the household, who was more likely to be a carrier, increased the chance of acquiring *N. meningitidis*. The study of Stuart et al. (33) supported the second hypothesis, but a direct effect of tobacco smoke on mucosa has been suggested (18), and further studies are clearly warranted.

We did not find any association of the dwelling conditions, the education of the individuals themselves or their parents, or the health conditions with carriage. While viral infections have been shown to predispose persons to meningococcal disease (7, 22, 26, 36), there was no evidence that anamnestic influenza-like illness in the month prior to the throat sampling influenced the carriage rate. Similar results were found by Stuart et al. (33), but their questionnaires were sent 6 months after the throat samples were taken.

In individuals over 17 years old, being single or being separated or divorced (OR = 1.96; $P = 0.05$), working outside the home (OR = 3.74; $P = 0.01$), and having an occupation in transportation or industry (OR = 1.94; $P = 0.03$) were found to be independently associated with meningococcal carriage, when corrections for gender and smoking were made. These results suggest that the frequency of social contacts is an important factor associated with meningococcal carriage.

If the population sampled is representative of the whole Norwegian population, we can estimate that in 1991 nearly 40,000 healthy people in Norway were carriers of virulent strains, about 30,000 carrying ET-5 complex strains and 10,000 carrying ET-37 complex strains. That same year, there was a total of 163 notified cases of systemic meningococcal disease. By the results of Kristiansen et al., who identified 16 carriers of the disease-causing strain among close contacts of 13 patients (21), sampling of close contacts of all the patients in Norway in 1991, and subsequent eradication of carriage among them would have led to the elimination of less than 1% of the carriage of virulent strains in the Norwegian population. While it has not yet been established whether carriage eradication in household contacts of patients prevents the occurrence of secondary cases (34), our study clearly shows that this measure is unlikely to significantly influence the overall epidemiological situation.

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