Risk Factors for Carriage of *Neisseria meningitidis* during an Outbreak in Wales

Patricia E. Fitzpatrick,* Roland L. Salmon,* Paul R. Hunter,† Richard J Roberts,‡ and Stephen R. Palmer*
*PHLS Communicable Disease Surveillance Centre (Wales), Cardiff, United Kingdom; †Chester Public Health Laboratory, Chester, United Kingdom; and ‡North Wales Health Authority, Mold, United Kingdom

In a school outbreak of meningococcal disease in Wales, we compared risk factors for the carriage of *Neisseria meningitidis* B15 P1.16 with carriage of any meningococci. Students had throat swabs and completed a questionnaire. Sixty (7.9%) carried meningococci; risk for carriage was higher in those >14 years of age.

Outbreaks of meningococcal disease, although rare, may have become more common in the United Kingdom, particularly among teenagers and young adults (1-3). In an investigation of a school-based outbreak in north Wales, extensive nasopharyngeal swabbing and subtyping allowed comparison of risk factors for carriage of the epidemic strain of *Neisseria meningitidis* B15 P1.16 and carriage of other meningococci.

On consecutive days in May 1996, two cases of meningococcal disease were reported in a single year group (year 11, ages 15 to 16 years) in a large (760 students) secondary school. One case was confirmed as due to *N. meningitidis* group B, type 15 P1.16. The second involved characteristic clinical symptoms, although blood culture and polymerase chain reaction (PCR) of serum were negative. In addition, five cases of meningococcal disease from the surrounding areas (total population 8,000) had been reported in the preceding 11 months. Three of these cases were in students of the school. One had been confirmed as *N. meningitidis* B15 P1.16 and one as serogroup C. The observed incidence of notified disease in England and Wales for 1995 was 3.7 per 100,000 and of culture-confirmed disease 2.9 per 100,000 total population (4). We conducted an investigation to determine the prevalence of *N. meningitidis* B15 P1.16 carriage in the school and examine the associated risk factors.

Address for correspondence: Roland L. Salmon, PHLS Communicable Disease Surveillance Centre (Wales), Abton House, Wedal Rd, Roath, Cardiff, CF4 3QX, United Kingdom; fax: 44-1222-521-987; e-mail: roland.salmon@phls.wales.nhs.uk.

The Study

Throat swabs from students and staff were spread onto 5% Columbia blood agar containing polymyxin 25,000 units/L and vancomycin 3 mg/L. Primary incubation was conducted at 37°C for 48 hours in 10% CO_2. Plates showing preliminary growth were sent to the Meningococcal Reference Unit at Manchester Public Health Laboratory for further examination and serotyping. Rifampicin was given to students in year 11, which included all those subsequently found to be carriers of the epidemic strain.

Epidemiology

All students from whom a throat swab was taken were asked to complete a questionnaire about personal and household details, lifestyle and social behavior (including travel), and health. A household density ratio was calculated from the ratio of number of household members to the number of rooms in the house. Socioeconomic background was determined by occupation of the head of the household, according to the Office of Population Census and Surveys classification of occupations (5). As stress has been proposed as a risk factor for meningococcal disease (6), we asked about stressful events in the month before the diagnosis of the index cases (e.g., a death in the family, household move, or bad news).

Univariate analysis of risk factors for meningococcal carriage was performed by using Epi-Info (7); the chi-square test was used for statistical significance. Multivariate analysis of carriage of *N. meningitidis* was performed with

SAS (SAS Institute Inc., Cary, NC); variables from univariate analysis were entered into a forward stepwise logistic regression, and conditional odds ratios and 95% confidence intervals were calculated for the resulting significant variables.

Swabs were taken from 744 (97.8%) of 760 pupils at the school. No pupil had received prior antimicrobial chemoprophylaxis. *N. meningitidis* was cultured from throat swabs of 60 (7.9%) students; 33 (55%) were in year 11. Of 17 group B isolates, 12 were type B15P1.16 (Table 1). Of 626 students (83.4%) who completed questionnaires, *N. meningitidis* was isolated from 53 students (8.5%) (Table 1).

The rate of meningococcal carriage was significantly higher in students >14 years of age (Table 2). The proportion of carriers also increased with year in school (chi-square for linear trend 44.3; $p < 0.001$). Although having a stressful event within the previous 3 months was not associated with carriage, specifically receiving bad news was.

Table 1. Subtyping of *Neisseria meningitidis* isolates in a Welsh secondary school

Subtype	Overall	Student group: Questionnaire completed	Student group: Rate of carriage (%)
B	17[a]	14	2.2
29E	7	6	0.9
C	4	4	0.5
Y	4	4	0.5
Z	2	0	0.3
W135	1	1	0.1
Nontypable	26	24	3.5
Total	61[a]	53	8.1

[a]Including isolate from the single *N. meningitidis*-positive teacher.

Students who reported that they had smoked cigarettes or lived with a smoker were more likely to carry meningococci (Table 3). Students in the same two classerooms and the same year as the index patients were more likely to carry *N. meningitidis*. Attendance at an informal party held by year 11 students 10 days before onset of illness was associated with carriage (Table 3). This informal gathering had no list of invitees; therefore, the number of those who attended but did not have throat swabs taken is not known.

Being in a sports team or regular attendance at youth clubs, Sunday schools, cubs, scouts, brownies, or guides was not associated with carriage, nor was recent travel.

Students who had been in regular contact with one of the patients were more likely to be carriers (Table 4). On multivariate analysis, having more than two smokers in the household, being in the same year in school as the index patients, and having received bad news in the preceding 3 months remained associated with meningococcal carriage (Table 5).

For carriage of the epidemic strain, *N. meningitidis* B15 P1.16, four factors were associated: being in year 11, being older than 14, having attended the end-of-year party, and being male. Because carriage of the epidemic strain was confined to year 11 students (who were >14 years of age), multivariate analysis was not

Table 2. Personal, family, and household factors and meningococcal carriage

Variable	Exposed[a]: Meningococcal carrier	Exposed[a]: Non-carrier	Nonexposed: Meningococcal carrier	Nonexposed: Non-carrier	Odds ratio (95% CI)	Exposed: B15 P1.16 carrier	Exposed: B15 P1.16 non-carrier	Nonexposed: B15 P1.16 carrier	Nonexposed: B15 P1.16 non-carrier	Odds ratio (95% CI)
Age >14	40	201	13	372	5.69[b] (2.87-11.49)	11	230	0	384	Undef[b]
Male sex[c]	31	267	22	304	1.60 (0.88-2.95)	9	289	2	324	5.04[b] (1.01-34.07)
Low socioeconomic conditions	21	256	32	317	0.81 (0.67-2.29)	3	274	8	341	0.47 (0.10-1.95)
Shared bedroom[c]	13	106	40	466	1.43 (0.69-2.90)	4	115	7	499	2.48 (0.60-9.62)
Household ratio >0.5	39	382	14	191	1.39 (0.71-2.76)	7	414	4	201	0.85 (0.22-3.53)
≥One child <5 yrs old in same household	1	41	52	532	0.25 (0.01-1.74)	11	573	0	42	Undef
Pet animal[c]	33	408	20	161	0.65 (0.35-1.22)	6	435	5	176	0.49 (0.13-1.88)

[a]Exposure to index patient.
[b]p< 0.05.
[c]Data missing.

Table 3. Risk factors for meningococcal carriage in a Welsh secondary school

	Exposed[a]		Nonexposed			Exposed		Nonexposed		
Variable	Meningococcal carrier	Noncarrier	Meningococcal carrier	Noncarrier	Odds ratio (95% CI)	B15 P1.16 carrier	B15 P1.16 noncarrier	B15 P1.16 carrier	B15 P1.16 noncarrier	Odds ratio (95% CI)
Year 11[a]	33	96	20	477	8.20[b] (4.34-15.56)	11	118	0	497	Undef[b]
Same classes as index cases[c]	10	42	43	530	2.93[b] (1.28-6.58)	1	121	10	494	0.41 (0.02-3.13)
Smoker	21	136	32	437	2.11[b] (1.12-3.94)	3	154	8	461	1.12 (0.23-4.71)
Other smoker in household	26	202	27	371	1.77[b] (0.99-3.24)	4	224	7	391	1.00 (0.24-3.84)
Student smoker and other in household	12	70	41	503	2.10[b] (1.00-4.41)	2	80	9	535	1.49 (0.00-7.54)
>2 smokers in household[c]	9	37	44	535	2.96[b] (1.24-6.89)	1	45	10	567	1.26 (0.00-12.81)
Football team[c]	6	88	47	415	0.60 (0.22-1.54)	3	91	8	454	1.87 (0.38-8.02)
Rugby team[c]	3	29	50	466	0.96 (0.22-3.51)	1	31	10	506	1.63 (0.00-13.27)
Hockey team[c]	3	29	50	467	0.97 (0.22-3.52)	1	31	10	507	1.64 (0.00-13.30)
Netball team[c]	1	54	52	452	0.16 (0.01-1.13)	0	55	11	493	0.00 (0.00-4.46)
Any sport	10	172	43	401	0.54 (0.25-1.16)	3	179	8	436	0.91 (0.19-3.83)
Regular youth club[c]	21	180	32	341	1.24 (0.67-2.31)	3	198	8	365	0.69 (0.14-2.93)
Regular disco[b]	30	279	23	248	1.16 (0.63-2.14)	4	305	7	264	0.49 (0.12-1.92)
Attendance at party[c]	23	111	29	461	3.29[b,c] (1.75-6.18)	8	126	3	487	10.31[b] (2.42-50.34)
Cubs/brownies/ scouts/guides	1	42	52	531	0.24 (0.01-1.72)	0	43	11	572	0.00 0.00-0.00
Life event	18	146	35	427	1.50 (0.79-2.86)	2	162	9	453	0.62 (0.00-3.15)
Death in family[c]	4	56	49	516	0.75 (0.22-2.30)	0	60	11	554	0.00 (0.00-4.58)
Change of house[c]	5	33	48	539	1.70 (0.55-4.89)	0	38	11	576	0.00 (0.00-7.63)
Received bad news[c]	15	79	38	493	2.46* (1.22-4.91)	2	92	9	522	1.26 (0.00-6.46)
Travel[c]	6	107	47	464	0.55 (0.21-1.40)	1	112	10	501	0.45 (0.02-3.48)

[a]Same school year as index case.
[b] $p < 0.05$.
[c]Data missing.

Table 4. Medical factors associated with meningococcal carriage in a Welsh secondary school

	Exposed[a]		Nonexposed			Exposed		Nonexposed		
Variable	Meningococcal carrier	Noncarrier	Meningococcal carrier	Noncarrier	Odds ratio (95% CI)	B15 P1.16 carrier	B15 P1.16 noncarrier	B15 P1.16 carrier	B15 P1.16 noncarrier	Odds ratio (95%CI)
Recent illness	43	482	10	91	0.81 (0.37-1.80)	7	518	4	97	0.33 (0.08-1.37)
Recent injury	10	127	43	446	0.82 (0.37-1.75)	0	137	11	478	0.00 (0.00-1.71)
History of tonsillectomy/ adenoidectomy[a]	8	60	45	511	1.51 (0.62-3.56)	3	65	8	548	3.16 (0.64-13.68)
Close contact with case of meningococcal disease[a]	12	72	40	496	2.07[b] (0.99-4.34)	3	81	8	528	2.44 (0.50-10.51)

[a]Data missing.
[b] $p < 0.05$.

Table 5. Factors remaining significant for meningitidis carriage in final model

Variable	Odds ratio (95% CI) unadjusted	Odds ratio (95% CI) adjusted[a]
Year 11[b]	8.20 (4.34-15.56)	8.61 (4.66-15.91)
>2 smokers in household	2.96 (1.24-6.89)	2.99 (1.25-7.15)
Received bad news	2.46 (1.22-4.91)	2.67 (1.32-5.40)

[a]adjusted for other significant variables.
[b]same school year as index case.

performed. Within year 11, no single factor was associated with carriage of *N. meningitidis* B15 P1.16.

Conclusions

In February 1995, we investigated risk factors for the carriage of any meningococci among the contacts of three ill students at another Welsh secondary school (8). These index patients were students in different school years, and 2 (1.7%) of 119 contacts carried the epidemic strain (type B2b P1.10). In the current outbreak, we identified 11 (1.5%) of 744 students with the epidemic strain (type B15 P1.16). In contrast, outbreaks of disease associated with serogroup C disease are typically accompanied by lower rates of carriage in populations at risk. However, outbreaks of group C disease involving higher carriage rates are occasionally described. In an outbreak at an agricultural college in England, carriage of the epidemic strain of serogroup C organisms among students and staff was 6.2% (9). In the current outbreak, the fact that all carriers of the epidemic strain were in the same school year as the two index patients enabled us to examine risk factors for carriage of the epidemic strain. Risk factors for the carriage of any meningococci may differ. For example, in an outbreak of six cases among first-year students at Southampton University (United Kingdom) in 1997, 0.9% of students surveyed carried serogroup C strains; however, no first year students were carriers (10).

Better knowledge of risk factors for carriage of epidemic meningococci may help identify close contacts who are candidates for antimicrobial therapy to eliminate nasal carriage and prevent spread of disease (11). Carriers of an epidemic strain with the potential to infect others may be missed, and a number of people may receive unnecessary antibiotics, which has implications for the spread of antibiotic resistance.

Carriage of any meningococci was associated in the univariate analysis with the well-described risk factors of increasing age and smoking (active and passive) (12-14). Smoking may predispose to colonization by inhibiting bronchial ciliary action (12). We also found increasing age and active smoking to be associated with carriage in our previous study (8). In the current study, receipt of bad news was associated. No obvious biological mechanism exists to explain what may be a chance finding, although recent stress has been described as a risk factor for meningococcal disease (6). Being in the same year as the index patients and attending the end-of-year party were risk factors for carriage of any strain of meningococci in this outbreak, mainly because these were the only two risk factors associated with carriage of the epidemic strain. These two factors reflect the kinds of social contacts among teenagers and young adults that may permit spread of meningococci. In a review of 22 school-based clusters between 1989 and 1993, the patients in nine of the clusters had contact through extracurricular activities; these activities in four clusters were parties or dances (15). Patronage of a particular bar was implicated in the university outbreak in Illinois (16), and a particular discotheque in an outbreak among eight adults (five of whom were teenagers) in Corrientes, Argentina (17). Such social settings differ from the residential settings, of outbreaks among military recruits and prisoners, where over-crowding and proximity of beds may permit transmission (18).

Attendance at the party may have been the critical factor in carriage of the epidemic strain among year 11 students. However, another hypothesis may account for our observations. Young adults who socialize frequently at discotheques and parties may, particularly if they smoke, be at higher risk for carriage of meningococci of all types. This increased long-term risk for disease may have a protective effect against a virulent outbreak strain (19). In contrast, those who participate infrequently in social events such as the end-of-year party may be at higher risk. This hypothesis may explain some of the risk for first-year university students. In addition to longitudinal studies, combining the results of surveys during outbreaks may help provide a more scientific basis for the management of future outbreaks.

Dr. Fitzpatrick is a lecturer in the department of Public Health Medicine and Epidemiology, University College, Dublin, Ireland. Her areas of expertise and research interests include epidemiology of prostate cancer and infectious and chronic diseases and health services research.

Acknowledgment

The authors thank the Meningococcal Reference Unit, Manchester PHL, for further examination and serogrouping of isolates.

References

1. Ramsay M, Kaczmarski E, Rush M, Mallard R, Farrington P, White J. Changing pattern of case ascertainment in meningococcal disease in England and Wales. Communicable Disease Report Review 1997;7:R49-54.
2. PHLS Meningococcal Working Group and Public Health Medicine Environment Group. Control of meningococcal disease: guidance for consultants in communicable disease control. Communicable Disease Report Review 1995;5:R189-95.
3. Stuart JM, Monk PN, Lewis DA, Constantine C, Kaczmarski EB, Cartwright KAV, et al. Management of clusters of meningococcal disease. Communicable Disease Report Review 1997;7:R3-5.
4. Kaczmarski EB. Meningococcal disease in England and Wales. Communicable Disease Report Review 1997;7:R55-9.
5. Office of Population Census and Surveys. Occupation and social class. London: The Office; 1990.
6. Haneberg B, Tonjum T, Rodahl K, Gedde-Dahl T. Factors preceding the onset of meningoccoal disease, with special emphasis on passive smoking, stressful events, physical fitness and general symptoms of ill-health. Symposium "Causes and control of meningococcal disease," Oslo 1982.
7. Dean AD, Dean JA, Burton JH, Dicker RC. Epi-Info, version 5. Centers for Disease Control, Atlanta 1990.
8. Davies AL, O'Flanagan D, Salmon RL, Coleman TJ. Risk factors for *Neisseria meningitidis* carriage in a school during a community outbreak of meningococcal infection. Epidemiol Infect 1996;117:259-66.
9. Riordan T. A college outbreak of group C meningococcal infection: how widely should investigation and prophylaxis extend? Communicable Disease Report Review 1997;7:R5-9.
10. Gilmore A, Jones G, Barker M, Soltanpoor N, Stuart JM. Meningococcal disease at the University of Southampton: outbreak investigation. Epidemiol Infect 1999;123:185-92.
11. Kristiansen B-E, Tveten Y, Jenkins A. Which contacts of patients with meningococcal disease carry the pathogenic strain of *Neisseria meningitidis*? A population based study. BMJ 1998;317:621-5.
12. Stuart JM, Cartwright KAV, Robinson PM, Noah ND. Effect of smoking on meningococcal carriage. Lancet 1989;ii:723-5.
13. Stanwell Smith R, Stuart J, Hughes A, Robinson P, Griffin M, Cartwright K. Smoking, the environment and meningococcal disease: a case control study. Epidemiol Infect 1994;112:315-28.
14. Cartwright KAV, Stuart JM, Jones DM, Noah ND. The Stonehouse survey: carriage of meningococci and *Neisseria lactamica*. Epidemiol Infect 1987;99:591-601.
15. Zangwill KM, Schuchat A, Riedo FX, Pinner RW, Koo DT, Reeves MW, et al. School-based clusters of meningococcal disease in the United States; descriptive epidemiology and case-control analysis. JAMA 1997;277:389-95.
16. Imrey PB, Jackson LA, Ludwinski PH, England AC, Fella GA, Fox BC, et al. Outbreak of serogroup C meningococcal disease associated with campus bar patronage. Am J Epidemiol 1996;143:624-30.
17. Cookson ST, Corrales JL, Lotero JO, Regueira M, Binsztein N, Reeves MW, et al. Disco fever: epidemic meningococcal disease in Northeastern Argentina associated with disco patronage. J Infect Dis 1998;178:266-9.
18. Tappero JW, Reporter R, Wenger JD, Ward BA, Reeves MW, Missbach TS, et al. Meningococcal disease in Los Angeles County, California, and among men in the county jails. N Engl J Med 1996;335:833-9.
19. Kristiansen BE, Knapskog AB. Secondary prevention of meningococcal disease. BMJ 1996;312:591-2.