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Risk factors for *Neisseria meningitidis* carriage in a school during a community outbreak of meningococcal infection

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SUMMARY

As part of the management of an outbreak of meningococcal infection, 119 school contacts of an index case were swabbed for nasopharyngeal carriage. In a cohort study, risk factors for *Neisseria meningitidis* carriage were ascertained by means of a questionnaire, completed by 114 (96%) of those swabbed.

Twenty five (21%) cultures were identified as 'neisseria positive'; of which there were 18 (15%) *Neisseria meningitidis* isolates, 2 (2%) *Neisseria lactamica* isolates and 5 (4%) showed contaminants only. Two (2%) carriers were identified as harbouring the implicated outbreak strain. Single variable analysis identified six statistically significant risk factors for meningococcal carriage; increasing age, female sex, manual social class, personal smoking, regular attendance at a discotheque and rhinorrhoea. Multivariate analysis, using logistic regression modelling, found that of these six variables only age, sex and social class remained statistically significant when the other factors were controlled for. Nevertheless the role of smoking, social events and respiratory/viral infections in nasopharyngeal carriage, and other plausible mechanisms whereby age, sex and social class might exert their effect, could usefully be investigated further.

INTRODUCTION

Since man is the only known reservoir of *Neisseria meningitidis*, factors which influence its acquisition, continued carriage and virulence are of great importance. At present, whilst infection rates are usually 1–2 per 100000 [1], the meningococcal carriage rate is approximately 5–10% in the general community [2] and this may vary enormously. During epidemics or outbreaks in closed communities the carriage rate will increase, possibly as high as 50% [3–11].

This study was performed in February 1995 during an outbreak of five cases of meningococcal infection in a rural area of Wales, during a 3-week period. Of these, three of the cases attended the same school. The two other cases had no known contact with each other or with the school cases. The school in question had a total of 650 pupils, with an age range of 11–18 years. The three school cases were all female and in different school years; aged 16, 12 and 14 years. Of the three, *N. meningitidis* was only isolated from the second case and was type B:2b:P1:10. After the second school case had occurred, a decision was made not to widely prescribe antibiotic chemoprophylaxis throughout the school, but to swab all school contacts of case 2, to determine the carriage levels of the implicated outbreak strain. These contacts consisted of those that shared a class with case 2 and those that shared the same school bus as case 2. This provided an

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opportunity to assess risk factors for *Neisseria meningitidis* carriage.

METHODS

Swabbing

Nasopharyngeal swabs were taken, on a single day by one of three doctors, by brushing the posterior nasopharynx with a throat swab and placing in a transport medium. A 'neisseria positive' was defined as any person whose swab culture yielded Gram-negative diplococci which were oxidase positive. A 'meningococcal positive' was defined as any person whose swab was 'neisseria positive' and from which *Neisseria meningitidis* was isolated. 'GCA' (New York City Formulation) selective medium was used to isolate neisseria, whilst the individual species were identified using the 'APINH' biochemical test. Serogrouping was performed at the Meningococcal Reference Laboratory for England and Wales.

The questionnaire

A questionnaire on family, household, lifestyle and medical factors was administered by a single investigator, who supervised the completion of the forms and collected them immediately afterwards.

One section of the questionnaire asked about the number of 'main rooms' in the household. For the purpose of the study, 'main room' was defined as any room in the household, excluding the following: hall, landing, toilet, garage, bathroom or attic. In addition, an overcrowding ratio was created, defined as follows: ratio = number of persons living in a household/number of main rooms in the household. The question on personal smoking was introduced as 'have you ever tried a cigarette?' After the form had been completed, social class was allocated to manual/non-manual by means of the O.P.C.S. Classification of Occupations, based on the respondent's description of their father's (or mother's) occupation.

Statistical analysis

For univariate analysis, statistical significance was calculated using 'epiinfo' [12]. Yates Corrected x^2 Analyses of 2×2 contingency tables were calculated, unless an expected cell value was less than five when Fisher's Exact Test (two tailed) was used. Relative risks were calculated by means of the Taylor Series Confidence Intervals for Relative Risk. For comparison of groups which contained non-parametric data, the Mann–Whitney test was used.

For multivariate analysis 'MULTLR' software [13] was used. A model was developed which included all those variables statistically significant ($P < 0{\cdot}05$) on single variable analysis. To assess the contribution of each variable in this model, a backward stepwise regression technique was used [14].

RESULTS

Microbiological

Of 119 eligible contacts, all 119 (100%) were swabbed. Seventy (59%) were male, whilst 49 (41%) were female. The neisseria carriage rate was 25/119 (21%), of which 18 were confirmed as *N. meningitidis*, giving a meningococcal carriage rate of 18/119 (15%). In addition, 2 isolates of *N. lactamica* were obtained, whilst 5 grew 'contaminants only'. Two (2%) were found to carry the outbreak strain (B:2b:P1.10). The remainder were B (5: 4%), W135 (2: 2%), Y (1: 1%) or non-groupable (8: 7%). The meningococcal carriage rate for bus contacts was 12/49 (24%) and class contacts 7/78 (9%). There was a small amount of overlap, with one of the meningococcal carriers being a bus and class contact.

Epidemiological

From the 119 contacts, 114 (96%) completed questionnaires were obtained. Of the five that didn't complete the questionnaire; all were male, one of which was 'neisseria positive' (but not 'meningococcal positive').

The single variable analysis

None of the household and family factors were statistically associated with meningococcal carriage (Table 1). In addition, non-parametric analysis found that there was no significant difference in the overcrowding ratio of the meningococcal positives, compared to the ratio for meningococcal negatives (Mann–Whitney P value = $0{\cdot}50$). Lifestyle factors which had statistically significant associations with carriage included manual social class, personal smoking and regularly attending a disco (Table 2). Whilst 'a smoker in the household' gave a 3% increase in carriage rate, there was a larger increase in rates (6%) if there was a smoker in the household who smoked more than 20 cigarettes per day (i.e. a dose-response relationship). Among the medical and biological factors, being female and a history of rhinorrhoea in the previous month were statistically significant (Table

Table 1. *Risk factors for meningococcal carriage – household and family factors. Wales rural school study, February 1995*

Risk factor	Exposed			Unexposed			Attributable risk per cent	Relative risk (95% CI)	*P* value
	Carriers	Non-carriers	Carriage rate (%)	Carriers	Non-carriers	Carriage rate (%)			
More than 4 persons in household	9	45	9/54 (17)	9	51	9/60 (15)	+2	1·11 (0·48, 2·59)	0·99
More than 2 adults in household	6	25	6/31 (19)	12	71	12/83 (14)	+5	1·34 (0·55, 3·26)	0·57
More than 2 persons under 18 in household	6	33	6/39 (15)	12	63	12/75 (16)	−1	0·96 (0·39, 2·37)	0·85
1 or more persons under 5 in household	3	8	3/11 (27)	15	88	15/103 (15)	+12	1·87 (0·64, 5·47)	0·38
6 or less main rooms in household	11	40	11/51 (22)	7	56	7/63 (11)	+11	1·94 (0·81, 4·65)	0·21
Share a bedroom	3	14	3/17 (18)	15	82	15/97 (15)	+3	1·14 (0·37, 3·52)	0·73
Exposed to damp	7	26	7/33 (21)	11	70	11/81 (14)	+7	1·56 (0·66, 3·68)	0·47
Exposed to recent building work (i.e. dust)	4	18	4/22 (18)	14	78	14/92 (15)	+3	1·19 (0·44, 3·28)	0·75
Birth order – first born	9	41	9/50 (18)	9	55	9/64 (14)	+4	1·28 (0·55, 2·98)	0·75

Table 2. *Risk factors for meningococcal carriage – lifestyle factors. Wales rural school study, February 1995*

	Exposed			Unexposed					
Risk factor	Carriers	Non-carriers	Carriage rate (%)	Carriers	Non-carriers	Carriage rate (%)	Attributable risk per cent	Relative risk (95% CI)	*P* value
Social class – manual	10	22	10/32 (31)	8	66	8/74 (11)	+20	2·89 (1·26, 6·64)	0·02*
Personal smoking	10	24	10/34 (29)	8	72	8/80 (10)	+19	2·94 (1·27, 6·80)	0·02*
A smoker in household	7	32	7/39 (18)	11	64	11/75 (15)	+3	1·22 (0·52, 2·91)	0·85
A smoker in household who smokes > 20 a day	3	11	3/14 (21)	15	85	15/100 (15)	+6	1·43 (0·47, 4·32)	0·46
Regularly attend a Youth Club	7	41	7/48 (15)	11	55	11/66 (17)	−2	0·88 (0·37, 2·09)	0·97
Regularly attend a disco	12	29	12/41 (29)	6	67	6/73 (8)	+21	3·56 (1·44, 8·78)	0·01*
Regularly play football/rugby/netball/hockey	5	30	5/35 (14)	13	66	13/79 (16)	−2	0·87 (0·34, 2·25)	0·99
Regularly attend Sunday School	1	3	1/4 (25)	17	93	17/110 (15)	+10	1·62 (0·28, 9·33)	0·50
Regularly attend cubs/scouts/brownies/guides	1	8	1/9 (11)	17	88	17/105 (16)	−5	0·69 (0·10, 4·58)	1·00
Any of the above social events	15	58	15/73 (21)	3	38	3/41 (7)	+14	2·81 (0·86, 9·13)	0·11
An animal in the house	13	70	13/83 (16)	5	26	5/31 (16)	0	0·97 (0·38, 2·50)	1·00
Travelled abroad in last 3 months	1	10	1/11 (9)	17	86	17/103 (17)	−8	0·55 (0·08, 3·75)	1·00
A recent stressful life event	6	19	6/25 (24)	12	77	12/89 (13)	+11	1·78 (0·74, 4·26)	0·22

* Statistically significant at the 0·05 level.

Table 3. Risk factors for meningococcal carriage – medical and biological factors. Wales rural school study, February *1995*

Risk factor	Exposed Carriers	Exposed Non-carriers	Exposed Carriage rate (%)	Unexposed Carriers	Unexposed Non-carriers	Unexposed Carriage rate (%)	Attributable risk per cent	Relative risk (95% CI)	*P* value
Aged under 13	5	39	5/44 (11)	13	57	13/70 (19)	−8	0·61 (0·23, 1·60)	0·45
Sex – male	5	65	5/70 (7)	13	36	13/49 (27)	−20	0·27 (0·10, 0·71)	0·01*
A cough in the last month	13	57	13/70 (19)	5	39	5/44 (11)	+8	1·63 (0·63, 4·27)	0·45
A runny nose in the last month	15	52	15/67 (22)	3	44	3/47 (6)	+16	3·51 (1·08, 11·44)	0·04*
Wheezing in the last month	3	10	3/13 (23)	15	86	15/101 (15)	+8	1·55 (0·52, 4·65)	0·43
Sore throat in the last month	13	53	13/66 (20)	5	43	5/48 (10)	+10	1·89 (0·72, 4·95)	0·28
Earache in the last month	7	17	7/24 (29)	11	79	11/90 (12)	+17	2·39 (1·04, 5·49)	0·06
Hoarse voice in the last month	4	17	4/21 (19)	14	79	14/93 (15)	+4	1·27 (0·46, 3·46)	0·74
Flu-like illness in the last month	11	39	11/50 (22)	7	57	7/64 (11)	+11	2·01 (0·84, 4·81)	0·18
Any of the above URTI symptoms in the last month	18	84	18/102 (18)	0	12	0/12 (0)	+18	Not calculable	0·21
A physical injury in the last month	4	15	4/19 (21)	14	81	14/95 (15)	+6	1·43 (0·53, 3·87)	0·50
Ever had an operation to remove tonsils/adenoids/both	2	7	2/9 (22)	16	89	16/105 (15)	+7	1·46 (0·40, 5·37)	0·63

* Statistically significant at the 0·05 level.

Table 4. *Multiple logistic regression – final model. Wales rural school study, February 1995*

Risk factor	Coefficient	Standard error	Z-Score	*P* value	Odds ratio (unadjusted)
Age (in years)	0·77	0·22	3·57	0·0004	2·2 (1·8)
Sex (m = 0, f = 1)	1·85	0·70	2·67	0·01	6·4 (4·3)
Social class (non-manual = 0, manual = 1)	1·78	0·65	2·74	0·01	5·9 (3·8)
Constant	−13·78	3·28			

3). The median age of meningococcal carriers was 13·5, compared with 13·0 for non-carriers (Mann–Whitney *P* value = 0·02).

Multivariate analysis

The main effects model is shown in Table 4. Thus after adjusting for age, sex and social class, neither personal smoking, nor regular disco attendance, nor rhinorrhoea remained statistically significant at the 0·05 level. The final column in Table 4 gives the odds ratio for each variable, both before the backward stepwise regression (unadjusted) and after.

DISCUSSION

In this study, age, sex and social class were independently related to *Neisseria meningitidis* carriage. This agrees with other research, which has found that carriage rates are maximal in teenagers and young adults [1, 2, 11, 15]. By contrast, the finding of a higher rate of carriage in females contradicts a number of studies which have detected higher rates in males [2, 16, 17]. This could be due to the fact that all three cases were female. However, only two carriers were found to have the implicated strain.

Those factors that were statistically significant during the single variable analysis may help to determine the mechanisms whereby age, sex and social class influence meningococcal carriage. For example, personal and passive smoking have previously been implicated in meningococcal carriage [16, 18–21]. Within this study, the personal smoking variable was found to be statistically significant, thus possibly explaining the higher carriage rates in older girls from social classes IV and V. The initial question on personal smoking, which was phrased as 'have you ever tried a cigarette?', was thought to act as a proxy for personal smoking whilst not formally admitting the habit (despite assurances to the contrary, some children may have had concerns that the school-teachers had access to the questionnaire forms). The lack of specificity in this question may explain why the variable dropped out of the final model. The number and nature of social contacts may have a large impact on nasopharyngeal carriage [22]. Regular attendance at a discotheque is a plausible example of this and may have played a role in this outbreak. Their behaviour is likely to vary between age groups, sexes and social class groups.

It has been argued that an upper respiratory tract infection (URTI) or flu-like illness can increase the risk of carriage [7, 11, 22–28]. This is supported by the analysis, since all of the respiratory/viral/ENT categories had higher rates in those exposed, compared to the non-exposed (with rhinorrhoea being statistically significant). Unfortunately the summary variable ('any of the above URTI symptoms in the last month') may have been too broad, since 102 persons (out of 114) claimed to have had one of the symptoms in the previous month.

A number of studies have claimed that overcrowding may be a risk factor for meningococcal carriage [18, 20]. This study found no evidence for such an association. However, it may be that a threshold level exists, such that only extreme overcrowding influences nasopharyngeal carriage. Also, it has been claimed that humidity or dust may be a factor in carriage [20] but, again, no relationship was detected. Other factors which have been claimed to increase carriage rates are physical injury, previous tonsillectomy [29], contact with animals, travel abroad or a recent stressful life event [20, 21]. They were not found to be important. For all those variables failing to achieve significance, it could be argued that the relative insensitivity of a single throat swab [5, 7] reduced the investigators' ability to detect an association or that the questions asked were not sufficiently specific to implicate the variable.

Because there were high levels of concern, the motivation to participate was good. Consequently, the questionnaire uptake rate was very high (96%).

During a normal school week, the composition of the classes varied for each subject, thus accounting for the large number of class contacts in this investigation. At the time the questionnaire forms were completed, the respondents were blind to their carrier status thus minimizing any response bias.

Of the 18 people that carried meningococci, 8 (44%) had non-groupable strains. However, this should not affect the conclusions since: (i) the aim of the study was to identify risk factors for the carriage of all types of meningococci strains, both groupable and non-groupable, (ii) no significant differences were observed when risk factors were analysed for groupable and non-groupable strains separately, albeit based on small numbers, and (iii) whilst groupable meningococcal strains are more virulent than non-groupable strains, the authors are unaware of any evidence of differences in risk factors for carriage.

The management of more than one case of meningococcal meningitis in a school setting is often problematic. However, the swabbing of a large sample of the school population proved to be useful in the management of this outbreak. Thus, the extremely low carriage rate for the implicated epidemic strain supported the decision not to widely prescribe chemoprophylaxis. It also corroborated the view that the school was not the setting for transmission, which meant that the study on risk factors for carriage within the school may not necessarily identify the risk factors for the community outbreak. On the other hand, many aspects of the questionnaire concentrated on social and lifestyle factors that were outside of the school setting. Also, by exploring the risk factors for meningococcal carriage in general, it provided useful information for the management of future outbreaks.

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