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Smoking, the environment and meningococcal disease: a case control study

R. E. STANWELL-SMITH[1]*, J. M. STUART[2], A. O. HUGHES[3], P. ROBINSON[2], M. B. GRIFFIN[1] AND K. CARTWRIGHT[4]

[1] *Department of Public Health Medicine, Bristol and Weston Health Authority, Manulife House, 10 Marlborough Street, Bristol BS1 3NP*

[2] *Department of Public Health Medicine, Gloucester Health Authority, Rikenel, Montpellier, Gloucester GL1 1LY*

[3] *Department of Epidemiology, University of Bristol, Canynge Hall, Whiteladies Road, Bristol BS8 2PR*

[4] *Public Health Laboratory, Gloucestershire Royal Hospital, Great Western Road, Gloucester GL1 3NN*

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SUMMARY

This case control study investigated environmental factors in 74 confirmed cases of meningococcal disease (MD). In children aged under 5, passive smoking in the home (30 or more cigarettes daily) was associated with an odds ratio (OR) of 7·5 (95% confidence interval (CI) 1·46–38·66). ORs increased both with the numbers of cigarettes smoked and with the number of smokers in the household, suggesting a dose–response relationship. MD in this age group was also significantly associated with household overcrowding (more than 1·5 persons per room) (OR 6·0, 95% CI 1·10–32·8), with kisses on the mouth with 4 or more contacts in the previous 2 weeks (OR 2·46, 95% CI 1·09–5·56), with exposure to dust from plaster, brick or stone in the previous 2 weeks (OR 2·24, 95% CI 1·07–4·65); and with changes in residence (OR 3·0, 95% CI 1·0–8·99), marital arguments (OR 3·0, 95% CI 1·26–7·17) and legal disputes in the previous 6 months (OR 3·10, 95% CI 1·24–7·78). These associations were independent of social class. Public health measures to lower the prevalence of cigarette smoking by parents of young children may reduce the incidence of MD. The influence of building dust and stressful life events merits further investigation.

INTRODUCTION

There has been an upward trend in both notifications of meningococcal disease (MD) and laboratory isolations of meningococci in England and Wales in recent years; over 5000 cases were notified between 1 January 1988 and 31 December

* Communications to: R. E. Stanwell-Smith, PHLS Communicable Disease Surveillance Centre, 61 Colindale Avenue, London NW9 5EQ.

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1992 [1]. Vaccines against *Neisseria meningitidis* serogroup B, the most prevalent pathogenic strains in Britain, are not sufficiently developed for mass immunization programmes [2]. Antibiotic prophylaxis of close contacts is of uncertain efficacy and has not been tested by controlled trial [3].

There are few clearly established aetiological factors. Attack rates in household members of index cases are about one thousand times higher than in other members of the same community [4, 5]. Disease risk decreases with age and is inversely related to the presence of bactericidal antibodies [6]. Genetic factors may determine whether infection results in disease; in the United States and in the UK males are at higher risk than females [7–9]; inherited complement deficiencies increase susceptibility to pathogenic and non-pathogenic strains of *N. meningitidis* [10], and non-secretors of ABO blood group antigens may be more susceptible [11].

Investigation of clusters of MD sometimes reveals a mixture of serogroups and serotypes [12], suggesting the importance of environmental co-factors. Passive smoking has been strongly implicated as such a factor [13, 14]. Low socio-economic status [13, 15], mental and physical stress, preceding influenza A and other upper respiratory infections, and damp living conditions [13, 14, 16, 17] have all been associated with MD. The incidence of disease is higher in the winter in Europe and North America, while the epidemics of sub-Saharan Africa occur during the hot dry months [18].

A rise in the incidence of MD in Britain provided the opportunity to investigate possible risk factors in greater detail. Emphasis was placed on events and exposures immediately preceding the onset of disease.

METHODS

During a 12-month period from 1 May 1988 each new case of microbiologically confirmed MD in eight health districts in the west of England was matched to three controls. The resident population of the study area was 2·13 million on 30 June 1988 (Office of Population Censuses and Surveys (OPCS)); at least 70 new cases were expected during the year, of which it was estimated that 90% or more would be microbiologically confirmed [15]. Case confirmation comprised (i) culture of *N. meningitidis* from blood, cerebrospinal fluid (CSF), or tissue specimen, or (ii) Gram-negative diplococci in CSF, or (iii) culture-positive nasopharyngeal swab and/or a rise in meningococcal antibodies in clinically diagnosed cases in whom a characteristic haemorrhagic rash was present. Co-primary cases were defined as two or more cases in members of the same household presenting within 24 h.

Medical Officers of Environmental Health for the 20 local authority districts in the study area ascertained cases through notifications and laboratory reports. Controls of the same sex, registered with the same GP and with date of birth within 6 months were obtained from lists of National Health Service patients held by Family Practitioner Committees.

Standardized questionnaires were completed for each case and for three controls at interview by one of two trained specialist nurses within 3 weeks of the date of hospital admission (or death if before admission) of the case; a household environmental survey was conducted by an Environmental Health Officer (EHO) within 5 weeks of this date.

Apart from information relating directly to MD in cases, the same questions were addressed to cases and controls. Inquiries included: preceding illness, family health history, infant feeding, socio-economic factors, exposures to smoking, alcohol, solvents and dust, leisure activities, the number of people kissed on the cheek and/or mouth (kissing contacts) in the previous 2 weeks, and life events. Socio-economic factors on the questionnaire comprised occupation of adults and of the head of the household, home ownership, number of rooms, number of residents and sharing of bedrooms. Smoking history was obtained by quantifying average weekly and daily amounts smoked by household members, in addition to information on exposure to smoking outside the home. Exposure to the following types of dust was recorded, including the duration of exposure and the circumstances: plaster, wood, brick, metal, stone and agricultural (hay/straw). Questions on exposures and leisure activities were restricted to events in the 2 weeks prior to onset for cases and to the previous 2 weeks for controls. For life events such as bereavement, partner changes and work changes, inquiries covered the previous 6 months.

EHOs assessed the type of accommodation and recorded the presence of mould, type of heating and domestic laundry practices on a separate questionnaire; dampness was objectively assessed by 12 moisture readings of up to 4 rooms and was also allocated subjectively to 1 of 4 grades (none, slight, moderate or severe). All moisture readings were performed using a protimeter (Protimeter Plc, Meter House, Marlow, Bucks), an instrument designed to measure moisture in wood and other building materials.

Odds ratios and confidence intervals were calculated using the Mantel–Haenszel method for k controls [19]. For most tables, results are quoted for all cases, cases aged under 5 and cases aged 5 years or more. The under-5 age group included children not likely to be at school and thus possibly subject to different risk factors when compared with older age groups. Stress scores for life events were calculated using a scale developed in psychosomatic research [20, 21] and compared by non-parametric analysis of variance. Social class analyses were based on the occupation of the head of the household, using the OPCS Registrar General classification. Allowance was made for confounding for social class by also calculating odds ratios for the key variables of smoking, passive smoking, overcrowding, dust exposure and life events by conditional logistic regression [22]. Crude odds ratios calculated by this method showed small numeric differences when compared with the Mantel–Haenszel estimates, but did not change the statistical significance of the results. Unadjusted odds ratios are used throughout.

RESULTS

Seventy-four cases were ascertained during the study period; an additional 14 cases, diagnosed clinically but not confirmed, were excluded. Questionnaire interviews were completed for all 74 confirmed cases and for 232 matched controls. Four cases died.

The mother was the interviewee for approximately two thirds of cases ($n = 48$, 65%) and two thirds of the controls ($n = 140$, 64%). One third of cases and controls were old enough or sufficiently recovered to be interviewed themselves and the small proportions of interviews with the father or other relatives were similar for both case and control groups. Environmental surveys were completed for 61 cases (82%).

Microbiological results

Sixty-four cases were confirmed by positive culture of CSF or blood. Microbiological evidence for other cases included positive CSF microscopy ($n = 6$), nasopharyngeal swab culture ($n = 2$), postmortem skin culture ($n = 1$) and raised antibody titre ($n = 1$). The 67 culture-positive cases comprised 47 serogroup B, 18 serogroup C and 2 ungrouped strains (Table 1).

Demographic results

The ages of the cases ranged from 2 months to 53 years, with slightly more males (38) than females (36). Thirty-eight cases (51%) were aged under 5 years; there were 16 teenagers but no cases aged 9–14 years. Cases occurred throughout the study period, with increased incidence between December and January 1989, when a total of 22 confirmed cases was reported (Fig. 1).

Social class

Odds ratios for MD were significantly lower where the household head was in Social Class I or II and significantly raised in Social Class III households (Table 2).

Preceding illnesses and other illnesses in the household

A slight excess of reported acute non-meningococcal illness in the previous 2 weeks in cases ($n = 38$, 51%) compared with controls ($n = 89$, 40%) was not statistically significant and there was no difference in the proportion of each group seeking medical advice for these illnesses. The reported diagnoses included influenza (3 cases, 1 control), ear infection, and colds or sore-throats. Preceding 'flu-like' illness based on a combination of any 3 of 5 symptoms – sore throat, fever, headache, joint aches or dry cough – was not significantly higher in the cases (OR 1·57, 95% CI 0·63–3·93).

There was no significant difference between cases and controls in previous history of chronic illness, frequent colds or speech disorders. Neither a previous head injury requiring hospital treatment (17 cases, 23%; 33 controls, 15%), nor a recent minor head injury were significantly associated with MD ($n = 14$, 23% and $n = 56$, 30%, for cases and controls respectively who gave definite answers to these questions).

Drug therapy and type of infant feeding

Overall recent drug or medicine consumption in cases was not significantly higher than in controls (OR 1·84, 95% CI 0·96–3·67). A higher consumption of analgesics was reported in cases than controls for children aged under 5 years (OR 3·33, 95% CI 1·44–7·70). Half of the case households ($n = 37$, 50%) and nearly half of the control households ($n = 97$, 44%) reported coughs and colds in family members in the 2 weeks before onset of MD or within 2 weeks of interview in the controls. Similar proportions of cases ($n = 6$, 8%) and controls ($n = 21$, 9%) had had contact with another case of meningitis in the previous 12 months, including

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Table 1. *Serogroups and serotypes of meningococci from confirmed cases*

Serogroup	Serotype	Subtype	Sulphonamide sensitivity*	Number of cases
B	15	pl. 16	R	18
($n = 47$)	15	pl. 7	R	1
	2b	—	S	5
	2a	—	R	1
	16	pl. 15	(1R; 1S)	2
	14	pl. 15	S	1
	4	—	—	3
	1	—	—	1
	Non-typable	pl. 15	S	4
	Non-typable	pl. 2	(2R; 1S)	3
	Non-typable	—	(2R; 5S)	7
	Not typed	—	S	1
C	2a	—	(2R; 2S)	4
($n = 18$)	2a	pl. 15; pl. 2	R	4
	2b	—	(1R; 4S)	5
	2b	pl. 6	S	1
	16	pl. 15	—	1
	Non-typable	—	(2R; 1S)	3
Not grouped	Not typed	—	S	2
Total				67

* R, resistant; S, sensitive.

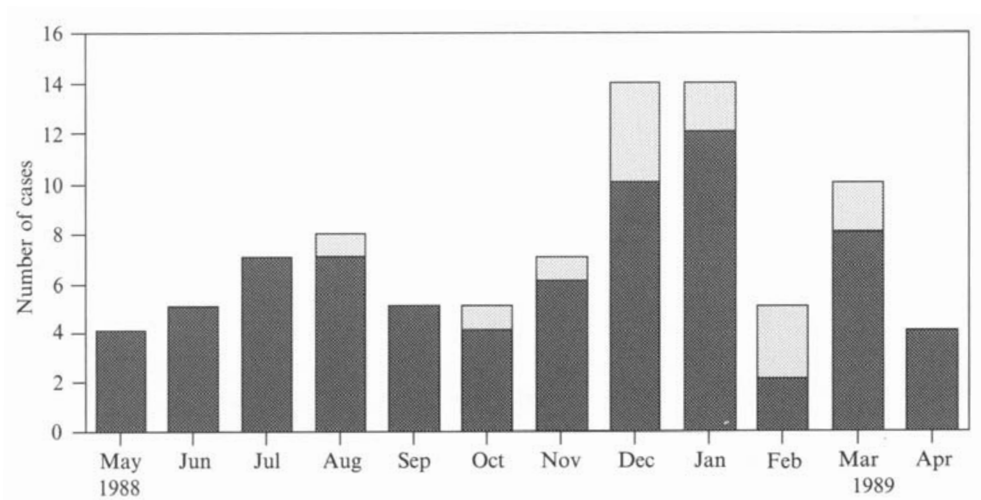

Fig. 1. Date of onset of cases. ■, Confirmed cases; □, clinical cases.

two brothers who were co-primary cases. While a slightly higher proportion of cases ($n = 16$, 22%) than controls ($n = 38$, 17%) gave a definite family history of meningitis, this difference was not significant.

There was no association of MD with type of infant feeding; a similar proportion of cases (49%) and controls (53%) were breast fed. The same proportions (8% of cases and of controls) were not weaned at the time of illness or interview. In the small number of infants for whom difficulty in sucking was reported, this was significantly less likely for cases (OR 0·11, 95% CI 0·01–0·98).

Table 2. *Association between meningococcal disease and household size, close contacts, and kissing and nights away from home in the previous 2 weeks*

	Confirmed cases					
	All ages ($n = 74$)		Under 5 ($n = 38$)		5 and over ($n = 36$)	
Risk factor	Odds ratio	95% CI†	Odds ratio	95% CI	Odds ratio	95% CI
Social class						
(Head of Household)						
I & II	**0·39**	**0·20–0·77**	**0·12**	**0·03–0·51**	0·70	0·31–1·58
IIINM & M	**1·89**	**1·08–3·31**	2·12	0·96–4·65	1·68	0·76–3·75
IV & V	0·88	0·34–2·31	0·70	0·18–2·74	1·14	0·29–4·50
Number residents in home						
6 or more	1·78	0·94–3·35	**2·50**	**1·14–5·48**	1·00	0·34–2·97
Persons per room						
0·5 or less	0·93	0·46–1·90	0·33	0·06–1·73	1·33	0·57–3·13
0·51–1·100	**0·45**	**0·25–0·80**	0·61	0·28–1·32	**0·29**	**0·12–0·72**
1·01–1·50	**2·53**	**1·16–5·55**	1·73	0·64–4·69	**4·75**	**1·21–18·6**
Greater than 1·50	**3·75**	**1·01–14·0**	**6·00**	**1·10–32·8**	1·50	0·14–16·5
Mouth kissing contacts						
1 or less	**0·43**	**0·24–0·76**	0·56	0·26–1·18	**0·29**	**0·12–0·71**
2–3	1·81	0·83–3·95	1·00	0·31–3·26	**3·17**	**1·04–9·62**
4 or more	**2·47**	**1·27–4·83**	**2·46**	**1·09–5·56**	2·50	0·77–8·09
Nights away from home	**2·23**	**1·26–3·92**	1·56	0·68–3·34	**3·15**	**1·40–7·12**
Away in UK	**2·46**	**1·37–4·43**	2·00	0·85–4·72	**2·93**	**1·29–6·62**
Away overseas	6·00	0·54–66·2	*	—	6·00	0·54–66·2

*, No cases; no controls.
† CI, Confidence interval.
Figures in bold type indicate a statistically significant difference between case and control groups.

Household factors

Case households tended to have more residents, although this difference was only significant for cases under 5 in households of six or more people (Table 2). The number of rooms in the households did not differ significantly between cases and controls. However, the mean number of residents per room was higher (0·92) for cases than for control households (0·80). For all ages, odds ratios increased with the mean number of persons per room (Table 2). The odds ratios remained significant after adjustment for the potentially confounding effect of social class.

Cases were more likely than controls to share a bedroom (OR 3·64, 95% CI 1·42–9·28), although actually sharing a bed was not significantly associated with the disease. Cases under the age of 5 were also significantly more likely to live in local authority rented properties than other types of home (OR 4·75, 95% CI 1·86–12·14). Home ownership was significantly less common for families of cases under 5 years than for controls (OR 0·27, 95% CI 0·12–0·61).

Kissing and regular contact with others

The numbers of regular close contacts or of cheek kissing contacts were not associated with illness. However mouth kisses with four or more contacts in the previous 2 weeks was significantly more frequent in cases under the age of 5 years

Table 3. *Exposure to cigarette smoke and smokers in confirmed cases and controls*

	Confirmed cases					
	All ages (n = 74)		Under 5 (n = 38)		5 and over (n = 36)	
Type of exposure	Odds ratio	95% CI*	Odds ratio	95% CI	Odds ratio	95% CI
Any household smoker	**1·84**	**1·04–3·26**	**4·09**	**1·59–10·70**	0·93	0·43–1·99
Smoking at home	**2·13**	**1·18–3·83**	**4·67**	**1·63–13·40**	1·09	0·50–2·39
Smoking on visits	**2·86**	**1·48–5·51**	**3·00**	**1·31–6·88**	2·67	0·91–7·81
Cigarettes smoked per day in home						
None	0·72	0·33–1·55	**0·16**	**0·03–0·85**	2·50	0·81–7·71
1–9	1·14	0·57–2·27	0·79	0·30–2·09	1·08	0·67–4·81
10–19	1·58	0·82–3·03	**3·00**	**1·19–7·56**	0·69	0·22–2·11
20–29	1·71	0·76–3·85	2·86	0·89–9·17	0·90	0·27–3·04
30 or more	1·91	0·69–5·30	**7·50**	**1·46–38·7**	0·67	0·13–3·47
Number of smokers in household						
None	0·57	0·33–1·00	**0·30**	**0·12–0·73**	1·04	0·48–2·23
One	0·98	0·56–1·70	0·96	0·46–2·02	1·00	0·43–2·31
Two	**1·91**	**1·09–3·34**	**2·53**	**1·19–5·39**	1·35	0·58–3·15
Three or more	1·13	0·42–3·03	4·00	0·90–17·9	0·46	0·10–2·09

* CI, Confidence interval.

Figures in bold type indicate a statistically significant difference between case and control groups.

(Table 2). Cases over the age of 5 were significantly more likely to have spent nights away from home, particularly to stay with friends (Table 2).

Exposure to cigarette smoke and smokers

Fifty-four case households (73%), and 130 control households (59%) reported at least one regular cigarette smoker. This was significantly associated with MD in those aged under 5 years (Table 3). Cases under the age of 5 years were also more likely than controls to be exposed to cigarette smoke in the home and in visits away from home. These differences remained statistically significant after adjustment for social class.

For cases under 5 years, odds ratios rose with increasing numbers of cigarettes smoked daily in the home, and also with the number of smokers in the household (Table 3). A similar pattern of rising odds ratios for both variables was observed after removal of the confounding effect of social class. For cases aged 5 or more years a reversed dose–response relationship was observed, though this was not statistically significant. Eight cases (11%) and 25 controls (19%) were themselves smokers.

Life events analysis

There was no evidence for an association between MD and the total score for life changes in families of cases and controls over the previous 6 months (mean score for cases 156·0; mean score for all controls 149·7). Scores were neither age nor social class related. Nevertheless, certain life events were significantly more common in cases and their families than in those of controls (Table 4). These comprised marital problems, including changes of partner (reported for 28 cases

Table 4. *Associations between life events in household in previous 6 months and meningococcal disease*

	Confirmed cases					
	All ages (n = 74)		Under 5 (n = 38)		5 and over (n = 36)	
Type of event	Odds ratio	95% CI†	Odds ratio	95% CI	Odds ratio	95% CI
Marital arguments	**2·50**	**1·20–5·20**	**3·00**	**1·26–7·17**	1·67	0·43–6·49
Other marriage difficulties	**5·67**	**1·39–23·2**	*	—	**5·67**	**1·39–23·1**
Other events						
Change in living conditions	1·86	0·92–3·76	**3·00**	**1·09–8·25**	1·15	0·41–3·22
Change in residence	2·08	0·87–4·97	**3·00**	**1·00–8·99**	1·00	0·20–4·95
Holidays in last 6 months	**0·35**	**0·16–0·79**	**0·24**	**0·07–0·79**	0·53	0·17–1·68
Legal disputes	1·61	0·85–3·05	**3·10**	**1·24–7·78**	0·78	0·28–2·16

*, No cases, no controls.
† CI, Confidence interval.
Figures in bold type indicate a statistically significant difference between case and control groups.

(38%) compared with an average of 16 (22%) for the 3 controls (n = 48)), and marital arguments (reported for 15 (20%) cases and an average of 7 (9%) controls). In addition, the families of cases in the under-5 age group tended to experience more legal problems (17 cases (23%), average of 11 controls (15%)), changes in living conditions (18 cases (24%), average of 12 controls (16%)) or place of residence (12 cases, average of 7 controls). The life events for which odds ratios were raised remained significant after controlling for social class. A holiday in the previous 6 months was significantly less common in case households (n = 18, 24%) than those of controls (n = average 25, 34%) (Table 4).

Exposure to dust

Forty-five cases (61%) had been exposed to dust within 2 weeks of onset, compared with 81 controls (36%) in the 2 weeks before interview. Of the six different types of dust specified on the questionnaire, only plaster, brick or stone dust exposure was significantly associated with acquiring MD. This type of exposure was significant for each dust and for combinations of the three types (Table 5); the associations remained significant after controlling for social class and smoking. The occupation of the case or household head of a case was more likely to be in the building trade than control household heads; when combined with building and decorating as a hobby, this excess was significant for the age group aged 5 or more. There was no evidence of an association with exposure to chemicals, including six commonly used types of solvent.

Environmental survey

EHOs were more likely to grade the homes of cases as being moderately or severely damp. However dampness was not reported more frequently by interviewees in homes of cases and there was no significant difference between the instrumental measurement of dampness of homes of cases and controls. The age

Table 5. *Matched case control analyses for association between domestic and environmental exposures and meningococcal disease*

	Confirmed cases					
	All ages (*n* = 74)		Under 5 (*n* = 38)		5 and over (*n* = 36)	
Type of exposure	Odds ratio	95% CI*	Odds ratio	95% CI	Odds ratio	95% CI
Dust (all types)	**2·46**	**1·44–4·20**	**2·79**	**1·35–5·76**	2·11	0·96–4·67
Plaster, brick or stone	**2·81**	**1·59–4·97**	**2·24**	**1·07–4·65**	**3·89**	**1·52–9·95**
Any two of plaster, brick or stone	**3·67**	**1·68–8·02**	**4·80**	**1·55–14·89**	2·86	0·96–8·55
Combination of plaster, brick and stone	**7·00**	**1·04–47·03**	(1)	—	1·00	0·06–16·0
Reported damp in the home	1·43	0·72–2·83	2·00	0·81–4·93	0·86	0·29–2·56
Damp grade 3+ (moderate)	**2·50**	**1·01–6·21**	**4·00**	**1·23–13·0**	1·00	0·19–5·32
Damp grade 4+ (severe)	**11·0**	**1·14–106·0**	3·67	0·33–40·7	3·00	0·19–48·0
Coal or wood heating in living room	**0·22**	**0·05–0·98**	0·15	0·02–1·50	0·30	0·04–2·31
Contact with pets anywhere	1·64	0·75–3·56	2·40	0·86–6·70	1·00	0·31–3·26
Contact with pets in home	0·91	0·50–1·67	1·33	0·59–3·01	1·11	0·24–1·38
Father a builder or active D.I.Y.	**2·04**	**1·08–3·86**	1·67	0·72–3·85	**2·88**	**1·08–7·68**

*CI, confidence interval.

Figures in bold type indicate a statistically significant difference between case and control groups.

and construction material of the home, adequacy of ventilation, use of tumble dryers and other domestic practices did not differ significantly between cases and controls. While no specific type of home heating was implicated as a risk factor, cases were significantly less likely to live in a home heated by wood or coal fires (Table 5).

Other exposures

There was no evidence of an association between MD and leisure activities, including contact with pets, physical exercise or recently increased physical activity, sports and visits to public places, swimming pools, religious ceremonies, parties or clubs. Visits to smoky places in the preceding 2 weeks were not associated with meningococcal infection. Alcohol consumption, including gripe water in infants, was not significantly increased in cases.

DISCUSSION

This is the first incident case-control study in the UK to examine events and exposures associated with the onset of meningococcal disease. The study confirmed some previously suspected risk factors and identified others not previously reported.

Passive smoking

A link between exposure to cigarette smoke and MD in young children is strongly supported by this study. This association has been demonstrated previously [13, 14], but our results demonstrate a high level of association and for the first time, a dose–response relationship between cigarette smoking in the home and risk of disease. The association was not abolished by adjustment for social class, an important observation in British studies as prevalence of smoking varies considerably between social classes [23]. These results add to the evidence for the adverse effects of passive smoking on children's health [24, 25] and underlines the importance of measures aimed at reducing smoking. An association between passive smoking and general susceptibility to serious infection was demonstrated in a recent case-control study of American children attending day-care groups [26], though there were only small numbers of cases of MD in the study.

One explanation of our findings is that cigarette smoking reduces nasopharyngeal mucosal defences against meningococcal invasion [13, 14]. However, as the data do not support such an effect on older children and adults, this would imply that any effect diminishes with age.

Alternatively, since cigarette smokers are more likely to be meningococcal carriers [27–29], young children living in households with smokers would have higher contact with carriers, higher chances of acquiring pathogenic meningococci, and hence higher attack rates. Also, greater exposure to non-pathogenic meningococci in the early years of life would be expected to confer higher levels of immunity through the development of cross-protective antibodies [30]. Thus children brought up in smoking families might be less susceptible to MD in later years than children raised in non-smoking households. This hypothesis is supported by the reversed dose–response relationship in the older age group in the present study.

Close contact and overcrowding

Although overcrowding was not found to be a significant factor in a previous English study [13], our results support the findings of Glover's classical work on military recruits in the First World War [31] and of more recent research in civilian populations [32]. Chemoprophylaxis for contacts may be more important in overcrowded households [3], as well as adding to the evidence for an association between overcrowding and ill health [33].

Exposure to dust

The association between MD and recent dust exposure (mainly plaster, brick or stone) and 'dusty' occupations (building or do-it-yourself (DIY) home improvements) in the older age group has not been previously reported. Epidemics of group A disease in Africa are known to occur during the season when the Harmattan winds are blowing dust off the Sahara and when absolute humidity is very low [18]. No similar climatic conditions occur in Europe, although associations with dust exposure at new building sites have been observed in Norway and Spain (Dr T. Gedde-Dahl, pers. comm.). Dust particles may act as a co-factor for meningococcal invasion by lowering mucosal resistance in the nasopharynx. Inhalation of fine silica particles increases the multiplication rate of

Mycobacterium tuberculosis [34], possibly due to overloading of macrophages [35]. Further research quantifying the amount and nature of dust exposure is needed to investigate this association with MD.

Demographic factors

The age, sex and seasonality of cases reflected national patterns at the time (Dr D. M. Jones: unpublished observations). Geographical variation in disease incidence [36, 37] may be due to underlying differences in the prevalence of virulent strains circulating, the level of population immunity and differences in exposure. Historically, increases in MD have been associated with periods of high population mobility, such as in Britain and the USA during World War II and in Brazil in the 1970s [38]. This would be consistent with the increased risk associated with nights away from home observed in the present study.

Preceding illness and previous health history

Previous studies have implicated viral upper respiratory tract infections as co-factors; in one study isolations of viruses and *Mycoplasma hominis* were more frequent in cases of MD due to strains of serogroup A than in controls [39], and an association between influenza A infection and MD has now been documented [40]. Our study was conducted during a period of low influenza activity and although preceding illness was reported more frequently in cases, the difference was not significant. Symptoms of minor illness are unreliable indicators of viral infection [16], and the possibility of cases of long prodromal meningococcal illness cannot be excluded [41]. The hypothesis that viral or other upper respiratory infections predispose to MD needs to be tested more thoroughly.

Carriers in the household of a case have been reported to have upper respiratory tract symptoms more frequently than non-carriers [42], and it has been suggested that such infections may increase transmission of meningococci. The similar frequency of coughs and colds in household members of cases and controls in this study does not support this hypothesis.

This study produced no evidence of an association between MD and any type of head injury, nor of a protective effect from breast milk, although studies in the sub-Saharan 'Meningitis Belt' [43] have suggested that breast feeding may protect infants from meningococcal disease.

Exposure to damp

The significant association between MD and damp housing in the EHO assessment was not confirmed by protimeter readings. A disparity between reports of damp and that measured by whirling hydrometer and air samples was also found in a study in East London [44], suggesting the need to examine critically the subjective and objective methods for assessing the degree of dampness in the home. A previous case-control study in Gloucestershire and Plymouth suggesting an association with damp housing did not include objective measurements [13].

Influence of live events

Stress, whether in the form of increased physical activity or the psychological effects of traumatic life events, has been suspected to increase susceptibility to disease, including MD [14] and other infectious diseases [45–48]. The ability of the host to cope with stress is probably an important factor; speed of recovery from infectious mononucleosis has been observed to correlate with high 'ego strength' scores [46]. Social support has been shown to affect both health status and host resistance, particularly in women [49]. In our study, half the cases were under 5 years and host factors would necessarily include the adults on whom the child was dependent. The association between MD and recent marital disputes or changes of home supports this; an association between childhood respiratory tract illness and changes in routine or disruptive life events has been reported previously [50].

This study has helped to define environmental co-factors in the aetiology of MD. In the associations between passive smoking, overcrowding, bed sharing, mouth kissing and nights away from home, the common factor is the likelihood of greater exposure to meningococci. Cigarette smoke and dust may enhance invasion via the nasopharynx; stressful life events also appear to increase susceptibility.

However, attack rates in Britain are low and attributable risks for these factors would be relatively small. Acquisition of either immunity or disease depends mainly on the prevalence of both pathogenic and non-pathogenic strains of meningococci and on genetic factors in the host. The development of a safe, cheap vaccine effective against all invasive serogroups would be the best means of prevention. Nevertheless, the expectation of future improvements in vaccines and treatment should not be a cause for complacency about contributory environmental factors. In an era of increased concern about the various harmful exposures and stresses in the environment, this study has identified possible interventions and further avenues for research. Meanwhile, increased awareness of cigarette smoking and overcrowding in the home might reduce the toll of this serious disease.

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