Meningococcal carriage in close contacts of cases

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(Accepted 23 August 1990)

SUMMARY

Between 1 October 1986 and 31 March 1987, 55 cases of meningococcal disease were identified in the South-West of England, an attack rate of 1·54 per 100 000 during the study period. Antibiotics used in the treatment of the disease successfully eliminated nasopharyngeal carriage of meningococci in 13 out of 14 cases without use of rifampicin. The overall meningococcal carriage rate in 384 close contacts was 18·2% and the carriage rate of strains indistinguishable from the associated case strain was 11·1%. The carriage rate of indistinguishable strains in household contacts (16·0%) was higher than the carriage rate in contacts living at other addresses (7·0%, $P < 0\cdot05$). A 2-day course of rifampicin successfully eradicated meningococci from 46 (98%) of 47 colonized contacts.

In one third of cases groupable meningococci were isolated from at least one household contact; 92% of these isolates were of the same serogroup as the associated case strain. When a meningococcus is not isolated from a deep site in a clinical case of meningococcal disease, culture of serogroup A or C strains from nasopharyngeal swabs of the case or of household contacts is an indication that the close contact group should be offered meningococcal A + C vaccine in addition to chemoprophylaxis. The failure in this and other studies to isolate meningococci from any household contact in the majority of cases may be due either to the relative insensitivity of nasopharyngeal swabbing in detecting meningococcal carriage or to the acquisition of meningococci by most index cases from sources outside the household.

INTRODUCTION

The incidence of meningococcal disease in England and Wales rose during the 1980s and was partly attributable to an increase in serogroup B serotype 15 sulphonamide resistant (B15R) strains [1]; outbreaks due to these strains have been described in the South-West of England [2, 3]. Features characteristic of disease due to B15R meningococci include a high attack rate in teenagers, a low carriage rate (1–2%) in communities experiencing outbreaks and a relatively high incidence of disease persisting in the same community over several years [2–6].

Recommended control measures currently include rifampicin prophylaxis for household and mouth kissing contacts (PHLS, unpublished data), who run a higher risk of developing meningococcal disease in the weeks following the onset of disease in the index case [7–9]. Rifampicin is known to be effective in

eradicating meningococci from the nasopharynx of asymptomatic carriers [10,11]. It has also been suggested that index cases should be given rifampicin because they may remain nasopharyngeal carriers despite treatment with parenteral antibiotics [12].

This study was undertaken to examine patterns of carriage in close contacts of cases due to B15R and other meningococcal strains, and to examine the effectiveness of parenteral antibiotics in eliminating nasopharyngeal meningococci from cases.

METHODS

All cases of meningococcal disease notified and otherwise ascertained in residents of the 11 Districts of the South-Western Regional Health Authority and Bath Health District between 1 October 1986 and 31 March 1987, and all close contacts of cases, were included in the study.

Definitions

Case: a patient in whom either *Neisseria meningitidis* was isolated from the blood and/or cerebrospinal fluid (CSF), or Gram-negative diplococci were seen in the CSF, or clinical signs of meningitis or septicaemia were accompanied by a haemorrhagic rash.

Close contact: any person sleeping in the same household or in mouth-to-mouth contact with the case within the 10 days preceding the admission of the case to hospital (or death if before admission).

Positive swab: a nasopharyngeal swab from which any meningococcus was cultured.

Distinguishable and indistinguishable strains: strains of meningococci isolated from an index case and an associated contact were regarded as distinguishable if any of serogroup, serotype or sulphonamide sensitivity were different, e.g. B15R and B2bR, B15R and C15R, B15R and B15S; pairs of strains showing none of these differences were regarded as indistinguishable, e.g. B15R and NGntR (non-groupable, non-typable sulphonamide resistant). Capsular polysaccharide, which defines the serogroup of the organism, is not always produced by strains of the same genotype [5], and nasopharyngeal strains of meningococci are often relatively poorly endowed with capsular polysaccharide (D. M. Jones, unpublished observations). Similarly the quantitative expression of typable outer membrane proteins shows variation [5] between strains of the same genotype.

Procedures

Nasopharyngeal swabbing: the posterior wall of the nasopharynx behind the uvula was swept with a throat swab or by use of a pernasal swab in young children. Swabs were plated out directly whenever possible; otherwise the swab was placed in transport medium and plated as soon as possible but always within 24 h. Selective media were used for primary isolation (Phillips or modified New York City medium) and were incubated in CO₂ as soon as possible and always within 24 h of primary plating.

Cases were swabbed at least 2 days after completion of the course of antibiotics prescribed for treatment of the invasive disease; if this swab was positive a 2-day course of rifampicin was prescribed (600 mg b.d. for adults, 10 mg/kg b.d. for children aged 1–12 years, and 5 mg/kg b.d. for infants).

Close contacts were swabbed and were prescribed rifampicin as above, as soon as possible after the hospitalization of the index case. Those with positive swabs were swabbed again 2–4 days after completing the rifampicin course; if still positive, the rifampicin course was repeated.

All meningococcal isolates were sent to the PHLS Meningococcal Reference Laboratory, Manchester for serogrouping, serotyping, subtyping and sulphonamide and rifampicin sensitivity testing.

Co-ordinators were nominated in each district to ensure that paediatricians and physicians were familiar with the study, to request their co-operation in following the study protocols, and to return completed record sheets to Gloucester.

The data were entered into a microcomputer, cross-checked and analysed using a relational database. The Chi-square test with Yates' correction or the Mantel Haenszel summary Chi-square test as appropriate was used in the statistical analysis of data.

Meningococcal carriage rates in contacts were compared with rates obtained using similar methods in Stonehouse, a community within the South-Western Region, during a protracted outbreak of meningococcal disease due principally to B15R strains [5,13].

RESULTS

In the study population of 3·57 million, 55 cases were identified of whom 42 (76%) were notified and 13 were otherwise ascertained. The overall attack rate was 1·54/100 000 (Table 1) and the notification rate was 1·16/100 000 over the 6-month study period. Twenty-six (47%) of the index cases were male and 29 female. Thirty-four (62%) were aged under 10 years, 13 (24%) were aged between 10 and 19, and 8 (14%) were over 19 years old. The geographical distribution of cases was uneven (Table 1). Nineteen cases occurred in the first 3 months of the study (October–December 1986) and 36 in the second three months (January–March 1987).

Neisseria meningitidis was isolated from culture of CSF, blood and/or nasopharyngeal swab in 46 (84%) of the 55 cases (three cases having clinical disease and a positive nasopharyngeal swab only); Gram-negative diplococci were seen in the CSF of a further four cases (7%); five cases (9%) were diagnosed solely on clinical criteria. Of the 46 isolates 26 (57%) were B15R, 9 were serogroup B sulphonamide sensitive and 8 were serogroup C sulphonamide sensitive; 3 other strains were identified. The age distribution of cases was similar in disease due to B15R and other strains.

All 55 cases were treated with penicillin (benzyl penicillin with or without subsequent penicillin V) for a minimum of 7 days; in addition 32 received chloramphenicol for varying periods and 2 others received cefotaxime. Two were given a 2-day course of rifampicin at the end of treatment. Of the 53 cases not given rifampicin, 14 had a nasopharyngeal swab after the course of treatment. The mean interval between the completion of antibiotic treatment and subsequent

Table 1. *Geographical distribution of meningococcal attack rates 1 October 1986–31 March 1987*

Health Authority (West → East)	Population (× 1000)	No. of cases	Attack rate per 100000 (6 months)
Cornwall and Isles of Scilly	448.2	2	0.45
Plymouth	327.9	12	3.66
Exeter	302.6	1	0.33
Torbay	237.0	3	1.27
North Devon	131.5	0	0.00
Somerset	396.4	1	0.25
Bristol and Weston	364.8	10	2.74
Bath	396.4	13	3.28
Frenchay	219.7	1	0.46
Southmead	232.3	2	0.86
Gloucester	308.0	10	3.25
Cheltenham and district	209.1	0	0.00
Total	3573.9	55	1.54

nasopharyngeal swabbing was 12.8 days (range 3–39 days). Thirteen of these 14 swabs (93 %, 95 % CI 78.6–100 %) were negative.

Three hundred and ninety-six close contacts were identified from the 51 cases in whom contact sheets were completed, a mean of 7.8 contacts per case (range 1–21). Of the 384 contacts whose first throat swab result was recorded, 70 (18.2 %) were found to be carrying meningococci of any serogroup or serotype. After a 2-day course of rifampicin, meningococci were successfully eliminated in 46 of the 47 (98 %, 95 % CI 93.8–100 %) who had a second swab. The one documented failure was due to the development of rifampicin resistance during treatment and ciprofloxacin 100 mg b.d. for 2 days successfully eradicated carriage. The mean interval between first and second swabs was 8.3 days (range 3–26).

Age-specific carriage rates in close contacts varied between 16 % and 22 % except in those aged over 65 years of whom 6 % (1/17) were carriers (Fig. 1). Carriage rates were significantly higher in close contacts ($P < 0.01$) than in the comparable age groups in the Stonehouse population. This difference was greatest in children aged under 5 years where there was a carriage rate of 16.7 % in contacts compared to 2.1 % in Stonehouse ($P < 0.001$).

Of the 384 close contacts, 315 were contacts of the 42 culture-positive index cases for whom contact sheets were completed. Meningococci were isolated from 54 (17.1 %) of these 315 close contacts; 4 strains failed to survive subculture, and 35/50 (70 %) were indistinguishable from the associated case strains (Fig. 2). The carriage rate of indistinguishable strains was 11.1 % (35/315), this rate being higher amongst contacts living at the same address (household contacts) than in close contacts at other addresses (16.0 *v.* 7.0 %, $P < 0.05$) (Table 2). When meningococci were isolated from household contacts 23/28 (82 %, 95 % CI 67.3–96.9 %) were indistinguishable from the associated index strain. This proportion rose to 21/23 (91 %, 95 % CI 79.1–100 %) in relatives living at the same address (i.e. excluding student contacts in lodgings) whereas in close contacts

Fig. 1. Age distribution of meningococcal carriage. ■, Contacts; ▨, Stonehouse.

Fig. 2 Flow chart showing carriage patterns in close contacts of cases.

living at other addresses 12/22 (55 %, 95 % CI 32.5–76.5 %) of contact strains were indistinguishable.

The carriage rate of indistinguishable strains was significantly lower in close contacts of B15R cases than in contacts of cases due to other meningococcal strains (6.0 *v.* 16.9 % $P < 0.01$) (Table 3).

Household contacts of cases aged less than 15 years were more likely to carry indistinguishable strains than household contacts of older cases (19.0 *v.* 10.4 %). This difference was not statistically significant.

Of the 46 culture-positive cases 37 had contacts living at the same address who were all swabbed and whose swab results were all recorded. In 22 (60 %) of these 37 groups no carriers were identified amongst 68 contacts. Of the 15 groups which

Table 2. *Meningococci isolated from nasopharyngeal swabs of close contacts according to address*

Address	No. of contacts	Indistinguishable strains	Distinguishable strains
Same as index case	144	23	5
Different from index case	171	12	10
Total	315	35	15

Table 3. *Meningococci isolated from nasopharyngeal swabs of close contacts according to case strain*

Case strain	No. of contacts	Indistinguishable strains	Distinguishable strains
B15/16R	167	10	8
Other	148	25	7
Total	315	35	15

Table 4. *Contact groups living at same address as the case*

Serogroup	
Same as index	11
Non-groupable only	3
Same and other	1
No organism isolated	22
	37

contained at least one colonized person, 11 carried only strains of the same serogroup as the index case organism. In three groups there were only carriers of non-groupable strains and in the remaining group both B and C serogroup carriers were identified (Table 4).

DISCUSSION

The notification rate observed in this study (1.16/100 000) was similar to the rate for England and Wales during the same period (1.24/100 000) and the age distribution of cases was similar to that observed in England and Wales between 1984 and 1988 (D. M. Jones, unpublished observations). The failure to demonstrate a difference between the age distribution of cases of disease due to B15R and other meningococci was unexpected, though in Gloucestershire, where an outbreak due mainly to B15R strains has persisted since 1982, the proportion of teenagers affected by B15R organisms has decreased as the outbreak has progressed.

Abramson and colleagues [12] found 4 of 14 meningococcal cases still harbouring meningococci in the nasopharynx 1 week after the cessation of parenteral antibiotic treatment and concluded that index cases should receive rifampicin prior to discharge from hospital to prevent spread of organisms to susceptible close contacts. We found post-treatment nasopharyngeal colonization in 1 out of 14 cases who had not received rifampicin. These results suggest that

parenteral antibiotics used in the treatment of meningococcal disease can be effective in eliminating nasopharyngeal meningococci. Nevertheless the small numbers of cases in both studies are insufficient to warrant any change in the current advice to give rifampicin to index cases. In this study rifampicin was again shown to be highly effective (98 %) in eradicating nasopharyngeal meningococcal carriage in close contacts of cases.

When age-specific nasopharyngeal carriage rates of meningococci amongst close contacts of cases were compared with carriage rates found in a Gloucestershire village experiencing a high attack rate of meningococcal disease a higher mean carriage rate was seen in the contact groups. High carriage rates of meningococci in contacts of cases have been demonstrated before [14–18]. The lower carriage rate of indistinguishable strains in close contacts of B15R cases when compared with the carriage rate in close contacts of cases due to other strains of meningococci is in accord with the hypothesis that B15R meningococci are less transmissible and/or more virulent than other pathogenic strains.

The identification of the organism in cases of meningococcal disease has assumed increasing importance in the last 2 years with the introduction of meningococcal vaccines capable of protecting against disease due to strains of serogroups A and C. It is now recommended that close contacts of cases due to these serogroups should be immunized in addition to receiving rifampicin prophylaxis [19]. Vaccines are not available for protection against disease due to serogroup B strains. It is therefore important that the strain causing disease should be isolated and serogrouped as the management of contacts will vary according to the serogroup of the case organism. Further important epidemiological information results from serotyping, subtyping and antibiotic sensitivity testing of these strains. While the need to identify the causative organism has been increasing, the recommendation to general practitioners to administer penicillin promptly to suspected cases of meningococcal disease prior to admission to hospital renders blood cultures sterile in almost all cases [20]. Even after parenteral penicillin treatment by the general practitioner an organism can often be grown from the CSF, but the dangers of lumbar puncture, though never prospectively established, may be perceived by clinicians as a reason not to undertake this important diagnostic procedure [21].

A nasopharyngeal swab obtained promptly from the index case yields an organism in about 50 % of cases (K. A. V. Cartwright, unpublished observations) which is almost always indistinguishable from isolates obtained from blood or CSF [12]. Provided the clinical picture is characteristic of meningococcal disease, a positive nasopharyngeal swab from the index case, even if unsupported by an isolate from a deep site, therefore provides reliable information on the serogroup, serotype and subtype of the probable causative organism.

Nasopharyngeal swabbing of contacts is not generally recommended on the grounds that any meningococcus isolated may be of a different serogroup or serotype from that causing disease in the index case [22]. However we found that when groupable meningococci were isolated from household contacts they were highly likely (11/12, 92 %) to be all of the same serogroup as the index case strain. Olcen and colleagues, studying defined groups of close contacts, recorded similar results [17]. For a given index case, at least 30 % of household contacts are likely

to be carrying a groupable meningococcus and approximately 90 % of isolates will be of the same serogroup as the associated case. In view of the good protection which is likely to be available through immunization of contacts of serogroup C (or A) cases, we suggest that nasopharyngeal swabbing of household contacts may be of value when the index case has received parenteral penicillin prior to hospital admission and/or a lumbar puncture is not undertaken. Meningococcal isolates from contacts outside the household are not reliable indicators of the index case strain.

Munford and colleagues [14], investigating a serogroup C meningococcal outbreak in Brazil, found meningococcal carriage rates in household contacts inversely proportional to the age of the index case. A similar (but non-significant) trend was observed in our study. Munford and others have proposed that meningococci are usually introduced into the household by adult members, spreading secondarily to susceptible children and infants [14, 23]. The lower likelihood of isolating indistinguishable meningococci from household contacts of older cases suggests that these cases may acquire meningococci more frequently from social contacts outside the immediate family.

Meningococci were not isolated from any member of most close contact groups in this and other studies [14-16, 18]. This may be due to the relative insensitivity of a single nasopharyngeal swab in identifying meningococcal carriers [6, 17] or to the possibility that the source of infection in most cases of meningococcal disease is the wider contact network and not the immediate family group. If the first hypothesis is correct the observed delay in onset of secondary cases following chemoprophylaxis of close contacts [11] would be explained (by the time taken for meningococci to re-enter the close contact group). Either hypothesis is consistent with the failure of rifampicin prophylaxis to prevent some secondary cases.

ACKNOWLEDGEMENTS

We are very grateful to the study co-ordinators: Dr A. Dawson (Plymouth), Dr R. Grainger (Cornwall), Dr P. M. Green (Torbay), Dr D. Hagen (Cheltenham), Dr R. J. C. Hart (Exeter), Dr N. F. Lightfoot (Somerset), Dr W. J. Poulson (Frenchay & Southmead), Dr P. T. Regester (North Devon), Dr R. Stanwell-Smith (Bristol & Weston), Dr D. G. White (Bath) and their colleagues, to the staff of the microbiology laboratories, and for the helpful comments of Dr D. M. Jones, Dr J. W. G. Smith, Dr S. Reilly and Professor N. D. Noah on this paper.

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