

Prevention of secondary cases of meningococcal disease in Denmark

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SUMMARY

Close contacts of cases of meningococcal disease are at increased risk of disease themselves. We identified household-like contacts of index cases, to investigate whether relevant target groups are informed, receive and follow recommended chemoprophylaxis and vaccination, and to ascertain the time delay for implementation of these measures. A telephone interview of 172 households of index cases and a questionnaire survey among 634 parents of contacts of cases in institutions were carried out. Results were compared with reports from Medical Officers of Health. In 21% of the cases, Medical Officers reported fewer household-like contacts than were identified in this study. Written information was effective. However, 59% of households, and 36% of parents of contacts in institutions felt a lack of information about how the disease is acquired, the risk and signs of illness. For household-like contacts the coverage rate for chemoprophylaxis with an appropriate drug was 90% and for vaccination 59%. No secondary cases occurred among those treated with chemoprophylaxis, but among those not treated, there were two secondary cases. The study design provided a useful audit methodology to evaluate the completeness of implementation and the success of prophylactic measures for meningococcal disease.

INTRODUCTION

One of the few clearly defined risk factors for developing meningococcal disease (MD) is being a close contact of an index case [1, 2]. This has been confirmed in several studies among household contacts [3–7] and in social settings such as kindergartens, boarding schools, day-care institutions and schools [5–8].

The guidelines for prevention of MD in Denmark aim to prevent the development of serious illness in secondary cases, to reduce the risk of occurrence of secondary cases and to protect against MD due to

serogroup A and C. The prophylactic measures include:

- *Information* to all relevant risk groups of close contacts about awareness of early signs of illness. The National Board of Health has developed a leaflet for that purpose for parents of contacts in schools and institutions.
- *Chemoprophylaxis* within 24 h to be offered to all persons with household-like contact with sporadic cases up to 10 days before onset of disease. If more than one case occurs within 2 months, within the same well-defined group of persons, chemoprophylaxis is recommended for that group. A single

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dose of ciprofloxacin is recommended as drug of first choice.

- *Vaccination* of the same group of persons as for chemoprophylaxis when the case is caused by serogroup A or C.

Medical Officers of Health (MOHs) are responsible for identification of the group at risk, which has to be defined on each occasion, and for implementation of the recommendations.

The overall purpose of this study was to evaluate the efficiency of the Danish guidelines for prevention of MD and to determine whether prophylactic measures and their implementation could be improved. This was done by:

- assessing who were household-like contacts of index cases through direct contact with an adult in the affected households;
- investigating whether defined target groups were sufficiently informed and offered chemoprophylaxis and vaccination;
- determining the time delay for implementation of prophylactic measures.

METHODS

Cases of suspected MD notified to the National Notification System for Communicable Diseases (NSCD) during the period 20 October 1995 to 30 April 1997 were studied. Three surveys were carried out: (i) a review of the case reports written by MOHs (the MOH survey), (ii) a telephone interview survey of an adult in households of index cases (the household survey), and (iii) a mailed questionnaire survey among parents of contacts of index cases in schools and day-care institutions (the institution survey).

A household-like contact was defined as a person sleeping in the same household or room, or a kissing or saliva-exchanging contact with the index case within 10 days of the onset of disease in the index case.

For each case, the results from both the household survey and the institution survey were compared with the recommendations given by MOHs as described in their case reports. The study was approved by all the Regional Ethics Committees and the Danish Data Protection Agency.

The MOH survey

In all, 384 reports on cases suspected of MD were reviewed. During the same period 394 cases were

notified to, and included in the NSCD, so case reports were available for 97% of notified cases.

The household survey

If written notification of the case suspected of MD was received within 22 days of the patient's admission to hospital, an adult in the household of that case was invited by letter to participate in a telephone interview. An adult was defined as the parent in the case of a child patient, and the patient himself in the case of adult patients. Adult cases with fatal outcome were excluded. A reminder was sent after 1 week. In order to reduce recall bias the interview was aimed to take place within 31 days after the patient's admission. However, for psychological and ethical reasons, the interview was carried out even if it could not be achieved within 31 days. All interviews were conducted by two medical doctors with experience in management of MD, at times convenient for the interviewed persons. The interview included questions on household-like contacts and prophylactic measures.

Due to a considerable time delay for notifications by mail, only 252 of the 394 notified cases fulfilled the criteria for being invited to participate. Of these, 232 households were invited to participate, of which 201 (87%) accepted. In all, 172 of the 232 invited households (74%) were interviewed within 31 days of the patient's admission to hospital.

Study participants

Of the 172 cases, 85 (49%) were aged 0–6 years, 55 (32%) were aged 7–19 years and 32 (19%) were above 19 years of age. Table 1 shows the relationship of the cases to the interviewed persons. Among parents of cases, 79/137 (58%) had 10 years or less school education.

Three groups of cases were compared: 201 cases where a household interview was carried out, 51 (20+31) cases of non-participants, in which the criteria for an invitation were fulfilled, and 142 cases, designated uninvited, for which the criteria for invitation were not fulfilled. There were no differences in age or geographical distribution nor in diagnostic verification such as culture of *Neisseria meningitidis*, serology, direct microscopy of cerebrospinal fluid or reliance of a clinical diagnosis between the three groups, while the proportion of cases verified by a positive meningococcal antibody test was significantly higher for the uninvited group ($P < 0.001$).

Table 1. *Study participants in the household survey and the institution survey*

Relationship to case contact	Interviewed persons (%)	Parents who completed the questionnaire (%)
Mother	118 (69)	545 (86)
Father	19 (11)	88 (14)
Partner	4 (2)	— —
Other relation	7 (4)	— —
The patient	24 (14)	— —
Unknown	— —	1 (< 1)
Total	172 (100)	634

Table 2. *Numbers and types of institutions and schools, numbers of returned questionnaires and participation rates in the institution survey*

No.	Types of institution	Returned questionnaires	Participation rate (%)
5	Day care/day nurseries	32	72
11	Kindergartens	477	67
6	Primary schools	74	61
2	Secondary schools	34	71
1	Business school	17	63
25		634	68

The institution survey

This survey was carried out from October 1996 to April 1997. Heads of institutions were contacted by telephone when the written notification of the case suspected of MD was received within 22 days of the patient's admission to hospital. Heads were asked to deliver a letter and the questionnaire to parents of contacts of the index case. Since the survey was anonymous, 2 weeks later the institution delivered a reminder to all the same parents. All questionnaires returned with an identifiable school or institution were included in the analysis. The questionnaire included questions on prophylactic measures.

Of 26 invited institutions, 25 agreed to participate. The types of institutions participating are shown in Table 2. In all, 928 questionnaires were distributed, and 634 of these were included in the survey. The overall participation rate was thus 68% with a range of 45–100% between different institutions. The participation rate for different types of institutions varied from 61–72% (Table 2).

Study participants

Of the 634 included 'contact children' 494 (78%) were aged 0–6 years and 139 (22%) were aged

7–19 years; Table 1 shows the distribution of the parents who completed the questionnaire. Among those parents, 248/623 (40%) had 10 years or less school education.

Statistical analyses

Data were analysed using Epi-Info version 6. Differences in proportions were tested by the χ^2 test and with Fisher's exact test where the number of observations was less than 5. The effects of receiving the information leaflet were assessed by calculating odds ratios (ORs). Trends in proportions were analysed by the χ^2 test for trend; 95% confidence intervals (CIs) were used.

RESULTS

The term 'household' refers to results from the household survey and the term 'institution' includes all day-care institutions and schools and refers to results from the institution survey.

Household-like contacts

In the household survey 802 contacts were reported as household-like contacts of index cases within 10 days

Table 3. Agreement between numbers and types of household-like contacts of cases of meningococcal disease reported by households and by Medical Officers of Health (MOHs) respectively

	No. of households (%)
Complete agreement (both for persons and number)	88 (55)
MOHs reported more contacts	31 (19)
MOHs reported fewer contacts	33 (21)
Same number (different persons)	5 (3)
Unknown	3 (2)
Total	160 (100)

Table 4. Effect of receiving the leaflet developed by the National Board of Health for parents of contacts in institutions and schools

	Received leaflet		Odds ratio	95% CI
	Yes	No		
Felt lack of information (<i>n</i> = 608)				
Yes	170	45		
No	324	69	0.8	0.5–1.3
Sought further information (<i>n</i> = 600)				
Yes	201	48		
No	288	63	0.9	0.6–1.4
Felt calmed in relation to their child (<i>n</i> = 576)				
Yes	415	60		
No	66	35	3.7	2.2–6.2
Felt sufficiently informed about early signs of illness (<i>n</i> = 577)				
Yes	415	57		
No	54	51	6.9	4.2–11.3
Felt sufficiently informed about how meningococcal disease is acquired (<i>n</i> = 569)				
Yes	317	39		
No	143	70	4.0	2.5–6.3
Felt sufficiently informed about the risk of contracting the infection (<i>n</i> = 558)				
Yes	279	38		
No	170	71	3.1	1.9–4.9

of admission to hospital. Table 3 shows the extent of agreement between the numbers and types of persons reported as household-like contacts by the households and by MOHs. In 21% of cases, MOHs reported fewer contacts than were identified in this study.

Information

Of 568 parents who should have received the leaflet developed by the National Board of Health, 494 (87%) had done so. Table 4 shows the effect of

receiving the leaflet on parents of contacts in institutions. Almost all (99%) parents of contacts in institutions had received information about the case in their child's institution.

A total of 71 out of 172 households (41%) had received information about awareness of early signs of illness, 67 (39%) about what to do if someone fell ill, and 79 (46%) were informed about factors associated with an increased risk of infection.

Parents of contacts in institutions felt significantly more often than households that they were sufficiently informed about early signs of MD (78 *vs.* 52%), about

Table 5. *Self-reported information about meningococcal disease (MD) in households and among parents of contacts in institutions and schools*

Felt sufficiently informed about	Households	Institutions
Early signs of MD	52% (90/172)	78% (486/624)
How MD is acquired	37% (63/172)	59% (370/624)
The risk of contracting MD	36% (61/172)	52% (326/624)

Table 6. *Time delay for implementation of prophylactic measures in households and schools and institutions*

Time delay for information		
From the admission of the case to hospital until the household received information:		
At the admission	41/172	(24%)
Within 3 days	23/172	(13%)
Later than 3 days	7/172	(4%)
Continuously during the admission	24/172	(14%)
From telephone notification to the MOHs until they informed the institutions:		
less than 1 day	18/25	(72%)
1 day	3/25	(12%)
2 days due to weekends	2/25	(8%)
6 and 8 days due to holiday	2/25	(8%)
From the time the institution received information until parents were informed:		
less than 1 day	22/25	(88%)
1 day	3/25	(12%)
Time delay for chemoprophylaxis		
Within 24 h after the admission of the case to hospital	128/163	(79%)
Between 24 h and 4 days	21/163	(13%)
Between 5 days and 8 days	3/163	(2%)
More than 10 days	1/163	(< 1%)
Time delay for vaccination		
Within the first week after the admission of the case to hospital	10/22	(45%)
Within the second week	5/22	(23%)
Within the third week	6/22	(27%)
Within the fourth week	1/22	(5%)

how MD is acquired (59 *vs.* 37%) and about the risk of contracting MD (52 *vs.* 36%), $P < 0.0001$, (Table 5). Parents of contacts in institutions were less likely than household contacts to feel a lack of information, 230/634 (36%) *vs.* 102/172 (59%), $P < 0.001$. Both groups lacked information about how the disease is acquired, and about the risk and signs of MD. A total of 86/172 (50%) of the households had worried about themselves and/or the rest of their families, while 463/628 (74%) of parents of contacts in the institutions had worried about their child. Eighty percent (490/611) of parents of contacts in institutions felt calmed in relation to their child as a result of receiving information.

A significantly higher proportion of parents of cases had 10 years or less school education than parents of contacts in institutions, 58 *vs.* 40%, $P < 0.001$.

Chemoprophylaxis and vaccination

Among household-like contacts, 724/802 (90%) had received chemoprophylaxis and no secondary cases occurred among them, whereas there were 2 secondary cases amongst the 72/802 (9%) of the contacts who had not received chemoprophylaxis. These secondary cases occurred 2 and 3 days respectively after the primary cases. Both secondary cases were related to

the primary cases as playmates or friends and in both cases they had slept in the same room.

In all, 163 out of 172 cases (95%) had at least one household-like contact. Of these households 114 (70%) were unaware of which kind of medicine they had been offered, 21 (13%) knew that they had been offered ciprofloxacin, 24 (15%) that it was an antibiotic and for 4 (2%) there was no clear answer. Of the same households, 159 (98%) reported that they had taken the chemoprophylaxis as a single dose; in the remaining 4 households, contacts were pregnant women.

The households reported about 149 persons, who had received chemoprophylaxis without fulfilling the criteria for a household-like contact. The mean 'over-treatment' was thus $149/172 = 0.9$ person/case and the mean 'under-treatment' was $72/172 = 0.4$ contact/case.

A total of 143 individuals were identified as household-like contacts of 36 cases of serogroup C meningococcal disease and 85 (59%) of these contacts were vaccinated. MOHs had recommended vaccination in 28/36 (78%) of the cases, but according to the households, only 23/36 (64%) of these had been offered vaccination. Thirteen households, evenly distributed across the country, had not been recommended vaccination even though 11 of these households had been offered chemoprophylaxis.

The households reported about 35 persons who were vaccinated without fulfilling the criteria for a household-like contact. Mean 'over-vaccination' was thus $35/36 = 1.0$ person/case and mean 'under-vaccination' was $51/36 = 1.4$ contact/case.

Time delay

Table 6 shows an overview of the registered time delays. In all, 24% of the households received information about factors concerning MD at the time of the patient's admission to hospital. MOHs informed 72% of institutions about the case on the same day as the case was notified by telephone. Most (88%) of the institutions passed the information on to the parents of contacts on the same day as they were informed by the MOH.

Most (79%) of households received chemoprophylaxis within 24 h of the patient's admission to hospital. Only 45% of vaccinated households were vaccinated within the first week of the patient's admission to hospital.

DISCUSSION

This study showed that our design constituted a useful audit methodology to compare prophylactic measures reported through a combined interview and questionnaire study with reports from the MOHs. In Denmark, written information given as a prophylactic measure seems to be efficient among parents of contacts of cases of meningococcal disease occurring in institutions. Chemoprophylaxis to household-like contacts fulfilled the official recommendation of an optimal regimen and was largely given in a timely manner.

Participation rates in our study were relatively high, 87% in the household survey and 68% in the institution survey. Similar high participation rates, about 85% [9, 10], have been achieved in comparable studies. Time delay for a notification by mail was crucial for an invitation to participate in this study. Consequently, cases verified by a positive meningococcal antibody test were over-represented in the group not invited to participate, because the result of this test is available only 2–3 weeks after the onset of illness. However, since diagnostic verification is not thought to influence the implementation of prophylactic measures, participants were considered to be representative of the invited households, except for adult cases with fatal outcome.

There was a discrepancy between the households and the MOHs in numbers of reported household-like contacts at the level of individual contacts. Numbers of contacts reported by households through a direct contact were probably more precise than reports from the MOHs. MOHs are not in direct contact with households, since contact is usually through the clinical doctors at the hospital admitting the index case. The lack of direct contact might explain why not all household-like contacts are identified. It is important to identify all contacts, since two secondary cases occurred among those who had not received chemoprophylaxis, whereas there were no secondary cases among those who had not received chemoprophylaxis. Some uncertainty about the time interval for contact with a case to be considered as a household-like contact could also be of importance since the limit of 10 days is not mentioned in the official guidelines.

There was a significant difference in the perceived level of information between the two principal target groups, namely households and parents of contacts in institutions. These differences were illustrated by the

answers to three different questions (Table 5) and were supported by the fact that the reported lack of information also was significantly higher for households than for parents of contacts in institutions. Both groups felt a lack of information about how the disease is acquired, the risk of disease and signs of illness. The considerable differences must be interpreted with caution. Data from the two surveys were collected by two different methods (although questions and pre-coded answers were identical when results were compared). The two target groups were not identical since households included persons other than parents of cases and were thus a more heterogeneous group. In addition, parents of cases had significantly shorter school education than parents of contacts in institutions. A further potential confounder is the fact that the target groups received the information in different ways. Most parents of contacts in institutions received the same leaflet, whereas households received information individually from many different doctors and nurses at the hospitals. The answers from the households do not necessarily reflect the information actually given at the hospital, but rather what the interviewed person remembered of it, illustrated by a patient's mother, who said: 'You cannot understand the information provided because you are in a crisis.' Furthermore, parents of contacts in institutions worried primarily about their child and households about the patient, which could have made a difference in their immediate motivation for information about factors concerning MD. Nevertheless, the study identified a lack of information in both target groups. The need for further information in those two target groups is probably impossible to satisfy completely due to the anxiety created by MD, but especially the households have an unmet need for information given as a prophylactic measure.

The risk and the attack rate for MD among household contacts is higher than for the population in general [1, 3–7]. Secondary cases generally arise within the first month after the index case [5–8]. Chemoprophylactic eradication of nasopharyngeal carriage of meningococci has been seen as one approach to prevent MD. Rifampicin given in 2 doses for 2 days eradicates the carriage state in 80–90% of those treated [1, 11–13] and a single dose of ciprofloxacin eradicates the carriage state in more than 90% of those treated [14–16]. Most households reported that they had received their chemoprophylaxis as single doses within 24 h, thereby fulfilling the

official recommendation for an optimal regimen and also for timely implementation. In England and Wales contacts of only 6/16 index cases (38%) received their chemoprophylaxis within the recommended 24 h [17]; in another study 85% of household contact groups received chemoprophylaxis on the day of admission of the index case [6].

The overall coverage rate for chemoprophylaxis with an appropriate drug to household-like contacts was high, 90%, and higher than the 46–84% reported elsewhere [1, 3, 17–19]. In this study, coverage rates were estimated on the basis of individual household-like contacts identified through a direct contact in the household, which makes the data more valid than results based on the group of contacts related to each index case [6, 18].

The two secondary cases among those not treated with chemoprophylaxis had both slept in the same room as the primary cases. In a Danish study among military recruits, transmission of meningococci occurred with high frequency between recruits within the semi-closed community and when a case of MD appeared, it was most likely that the invasive strain had been transmitted from asymptomatic carriers among the room-mates [20].

'Over-treatment' with chemoprophylaxis is well-known [18, 21] and to be expected in view of anxiety. It was estimated to constitute about 200–250 persons per year in this study. Up to the present time, resistance to ciprofloxacin has not been a problem in Denmark. A part of this use of chemoprophylaxis is beyond the control of the MOHs.

Vaccination was not offered to contacts in about one third of those households who were deemed eligible. The majority of contacts in those households had been identified as household-like contacts since they had been offered chemoprophylaxis. The low coverage rate for vaccination was primarily due to the lack of a recommendation from the MOHs. MOHs have different routines for relaying recommendations of vaccination to relevant contacts. A tightening of these routines might increase the coverage rates and perhaps also shorten the time delay for vaccination.

Written information given as a prophylactic measure was effective. We therefore recommend that in addition to institutional contacts, household contacts should also receive this form of information. The leaflet in current use would be suitable. Since household-like contacts are assessed individually in every case, the identification of such contacts is explicit. The coverage rate for chemoprophylaxis and

vaccination could be improved to nearly 100% if households were asked more carefully about possible contacts and (in the case of serogroup A or C disease) all received the offer of vaccination in addition to chemoprophylaxis. Our study showed that considerable efforts are being made to prevent secondary cases of MD in Denmark, and that many persons are involved in each case. Therefore, coordinated, timely, clear and relevant information and actions are needed to avoid unnecessary anxiety in close contacts as well as in the public.

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