or not similar influences are exerted on the vaginal-cervical bacterial flora remains to be investigated.

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Prevention of secondary cases of meningococcal disease in household contacts by vaccination

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Summary and conclusions

Household contacts of patients with group A meningococcal infection were vaccinated with either meningococcal vaccine or tetanus toxoid. Five of the 523 subjects who received tetanus toxoid developed meningococcal meningitis and another four probably had meningococcal disease. Only one possible case of meningococcal infection occurred among 520 contacts vaccinated with meningococcal vaccine. Vaccination had no effect on nasopharyngeal carriage of meningococci.

Vaccination of household contacts of patients with group A meningococcal infections is an effective way of using limited supplies of meningococcal vaccine, though its value would be limited in an epidemic. Secondary cases of meningococcal infection often occur within a few days of the index case, and, although vaccine alone seemed to provide adequate prophylaxis in these Nigerian subjects, additional chemoprophylaxis may be needed to cover this critical period.

Introduction

Family contacts of patients with meningococcal meningitis or septicaemia have an increased chance of contracting the disease.

A recent nationwide survey in the United States showed that the attack rate among household contacts of patients with the endemic form of the infection was approximately 3 per 1000.¹ In Los Angeles during 1963-6 the attack rate among household contacts of people with sporadic infection was about 10 per 1000.² Higher secondary attack rates, however, ranging from 11 per 1000 to 59 per 1000, have been recorded in the United States during epidemics.³⁻⁶ The secondary attack rate during an epidemic of group A meningococcal disease in Chile was 25 per 1000,⁷ and during a more recent epidemic of predominantly group C infection in Brazil it was 16 per 1000.⁸ We have found no report on the incidence of secondary cases during the epidemics of meningococcal infection that often affect the savanna region of tropical Africa.

Because of their increased likelihood of contracting the infection family contacts of patients with meningococcal disease are usually given some form of chemoprophylaxis. Sulphonamides have been widely and successfully used for this purpose but they can no longer be relied on because of the emergence of sulphonamide-resistant meningococci. Minocycline and rifampicin prevent carriage in household contacts⁹ but it has yet to be definitely established that they can prevent secondary cases of the disease.⁹ We therefore studied whether vaccination could be used as an alternative form of prophylaxis for close contacts of patients with meningococcal infection.

Patients and methods

During March-May 1977 1003 patients with meningococcal disease were admitted to Ahmadu Bello University Hospital, Zaria, Nigeria. In nearly all cases the causative organism was a group A sulphonamide-resistant meningococcus.

Meningococcal infection was diagnosed when meningococci were cultured from blood or cerebrospinal fluid (CSF) or when meningococcal antigen was detected in serum or cerebrospinal fluid by counter-

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current immunoelectrophoresis or by latex test. The diagnosis was also accepted in patients with a suggestive clinical picture whose initial serum sample contained group A meningococcal haemagglutinating antibody at a titre of 1/32 or greater or in whom a rise in antibody titre of more than two doubling dilutions was observed between the acute phase and convalescent phase serum samples. A titre of 1/32 was chosen, as we have shown in population surveys that only about 1% of the population have group A meningococcal haemagglutinating antibody at a titre of 1/32 or higher.

Each evening throughout the epidemic the families of all patients admitted to hospital that day with meningococcal disease were interviewed and asked whether anyone in their compound had recently been ill. In most cases we were able to confirm histories suggestive of a previous case of meningitis by referring to our records of hospital admissions. In a few cases, however, a person with a suspicious history had not been brought to hospital or had died at home. Diagnosis was accepted in these cases only if a clear history of meningitis was obtained. At this interview families were selected for vaccination if their compound was readily accessible and if they had a co-operative compound head. The type of compound that we visited most often contained an extended family with a household head, one to four wives and their children, and a few other relatives and lodgers. In small compounds, everyone was included in the study but in large compounds only members of the immediate family group were investigated. The average number of subjects studied per compound was 17. We also studied seven Koranic schools. Pupils at these traditional schools live in the school, often under very crowded conditions with many sleeping in a single room. The average population of the Koranic schools was also 17.

On the morning after interview selected compounds were visited, their members counted, and nasopharyngeal swabs collected. Alternate compounds were vaccinated with group A and group C meningococcal vaccine (Merieux), of which only 500 doses were available, or tetanus toxoid. Tetanus is relatively common in Zaria and vaccination infrequent. Ninety-five per cent of those counted were swabbed and vaccinated but in some compounds we were not told about people who were away on the day of our visit. Compound heads were issued with a special identity card and asked to bring any member of their compound who became ill to hospital immediately.

Two weeks after vaccination a second nasopharyngeal swab was collected, an 85% completion rate being obtained. All compounds were visited a third time at the end of the epidemic to check whether any illness had occurred in the compound since the time of vaccination.

Laboratory methods—Nasopharyngeal swabs were collected using charcoal-coated swabs. These were plated directly on to sheep blood agar plates containing vancomycin 2 mg/l and polymyxin 3 mg/l. Likely colonies were subcultured on to Mueller-Hinton medium and meningococci identified by Gram stain, oxidase test, ONPG, and

sugar reactions. Serotyping was performed by agglutination in Perspex trays using rabbit antisera. Meningococcal antibodies were measured by haemagglutination using vaccine-coated human red cells.

Results

Incidence of secondary cases—The families of 905 patients with meningococcal disease were interviewed. In 101 cases a history of a recent illness, which was probably meningococcal disease, in a member of the same household or Koranic school as the patient was obtained. Given a compound size of 17, the figure obtained in the prospective part of the study, this indicates a secondary attack rate of approximately 7 per 1000. In a further 12 cases a history of a previous case in the same State primary or secondary school as the patient was obtained. Three members of the hospital staff (rough number 700) developed meningitis—a staff nurse, a maid working in the children's emergency room, and a student technologist. Table I shows the time interval between the onset of illness in index and in secondary cases. In five cases both patients became ill on the same day.

Effect of vaccination on incidence of secondary cases—Seven of the 523 household contacts of patients with group A meningococcal infection who were given tetanus vaccine developed pyogenic meningitis, proved by lumbar puncture, during the epidemic. In five cases the meningitis was shown to be due to a group A meningococcal infection, and meningococcal infection was probable in the remaining two patients (table II). In addition two other household contacts developed a septicaemic illness which was associated with serological evidence of group A meningococcal infection. None of the 520 household contacts given meningococcal vaccine developed meningitis.

TABLE III—Effects of meningococcal and tetanus vaccines on incidence of secondary cases in household contacts of patients with meningococcal disease

	Cases of meningococcal disease		
	Proved	Probable or possible	Total
Tetanus vaccine (n = 523)	5	4	9
Meningococcal vaccine (n = 520)	0	1	1
χ^2	3.2		5.0
P	<0.1		<0.05

* χ^2 with Yates's correction.

A 10-year-old girl developed an acute febrile illness, which might have been meningococcaemia, 10 days after vaccination but she died on the way to hospital and was not seen by a doctor. Two cases of proved group A meningococcal meningitis (not shown in the table) occurred in members of compounds where people had received meningococcal vaccine. Both of these patients had been away on the day that their compound was visited and they had not been vaccinated. Early vaccination with meningococcal vaccine thus reduced the incidence of secondary meningococcal infection in household contacts (table III).

Meningococcal carriage in household contacts—The overall nasopharyngeal carriage rate of group A meningococci in 1016 household

TABLE I—Time interval between onset of illness in index and secondary cases of meningococcal disease

Time (days):	≤4	5-14	15-27	≥28	Total
Family contacts	36	31	8	4	79
Koranic school contacts	4	7	2	4	17
State school contacts	8	3	1	0	12
Total	48	41	11	8	108

TABLE II—Episodes of serious illness in household contacts of patients with meningococcal disease receiving tetanus toxoid or meningococcal vaccine during an epidemic

Case No	Age (years)	Interval since index case (days)	Relationship to index case	Clinical features	CSF		Antibody	Other features
					Culture	Antigen		
Tetanus vaccine (n = 523)								
1	6	12	Not related	Meningitis	+	+	Rise in A Rise in A A	Carrier of group A meningococci. 2 sibs with proved group A meningitis
2	6	10	Co-pupil	Meningitis	+	+		
3	4	14	Cousin	Meningitis	—	+		
4	5	35	Brother	Meningitis	—	—		
5	5	10	Brother	Meningitis	—	—		
6	3	7	Sister	Meningitis	—	—		
7	10	12	Co-pupil	Meningitis	—	—	A	Petechiae
8	15	14	Co-pupil	Septicaemia			Rise in A	WBC 14·8 × 10 ⁹ /l
9	7	2	Brother	Septicaemia			Rise in A	WBC 22·8 × 10 ⁹ /l
Meningococcal vaccine (n = 520)								
1	10	10	Not related	Fever				Died on way to hospital

contacts of patients with group A meningococcal disease was only 3.7%. A higher carriage rate of 7.7% was, however, found among 220 members of the immediate family group (parents, children, or siblings). The carriage rate among those who received meningococcal vaccine was 4.3% and among those who received tetanus toxoid 3.1%.

Effect of vaccination on meningococcal carriage—The effects of tetanus toxoid and meningococcal vaccine on the nasopharyngeal carriage of group A and group C meningococci in household contacts are shown in table IV. Meningococcal vaccination did not lower the carriage rate.

TABLE IV—Number of family contacts carrying group A or group C meningococci at time of vaccination with group A plus group C meningococcal vaccine or tetanus toxoid and at two weeks after vaccination

	Group A		Group C	
	1st swab	2nd swab	1st swab	2nd swab
Meningococcal vaccine (n = 431)	19	29	3	6
Tetanus vaccine (n = 450)	15	15	4	6

Discussion

During an epidemic of group A meningococcal infection in an area within the African meningitis belt¹⁰ we observed a secondary attack rate of 18 per 1000 among household contacts of patients with the disease who were given tetanus toxoid and carefully followed throughout the epidemic. Less precise data obtained by interviewing families of patients suggested a secondary attack rate of about 7 per 1000; this figure is probably an underestimate because of the difficulty of establishing a diagnosis retrospectively. These secondary attack rates are comparable with those recorded in other parts of the world during epidemics of group A meningococcal infection.³⁻⁷ The risk of infection was greatest among close family contacts, especially among siblings of the index case. As found in Brazil,¹¹ little spread occurred in day schools but several secondary cases occurred among pupils in Koranic schools, where contact between the boarders is often as close as in small family groups.

Meningococcal vaccine successfully prevented secondary infections in household contacts when given on the day after admission of the index case to hospital. Vaccination of household contacts is an effective way of using this vaccine when only limited amounts are available, but it cannot be expected to control an epidemic, for only about 10% of cases occur in the families of affected patients. Our results suggest that all household contacts of patients with group A or group C meningococcal infection should be vaccinated as soon as possible. It is less certain whether other contacts need protection. Contacts at day schools are probably not at risk¹¹ and do not require prophylaxis. Non-family contacts living in close contact with a patient—for example, in a lodging house¹² or, as in our study, Koranic schools—should probably be vaccinated. The risk of hospital infection is thought to be low but three members of the hospital staff contracted the infection during this epidemic and another hospital infection has recently been reported in Finland.¹² Vaccination of medical, nursing, and laboratory staff likely to be in frequent contact with patients with meningococcal disease or with infected samples is therefore probably advisable, especially in tropical Africa, where adults are affected more often than in Europe and America.

Many secondary cases of meningococcal infection occur within a few days of the onset of illness in the index case. It has therefore been suggested that vaccination of household contacts would be unlikely to be an effective form of prophylaxis.¹³ This did not prove to be the case in this study. Low titres of serum antibody to group A meningococci, perhaps acquired as a result

of infection with cross-reacting organisms, are found in most healthy subjects living in Zaria and the surrounding areas. In these circumstances vaccination may induce a rapid secondary immune response which, within two or three days, results in the production of enough antibody to prevent systemic invasion by meningococci. Nevertheless, the absence of secondary cases during the first few days after vaccination in this study may have been a chance phenomenon and some additional prophylaxis may be needed to cover this critical period. This may be especially important in Europe and America, where secondary cases occur more often in young children than in Nigeria, for young children are relatively poor responders to vaccination.^{14 15} Sulphonamides can no longer be relied on, particularly in Africa, as most meningococci are now resistant (M Hassan-King, unpublished). Rifampicin is probably the best choice for an additional chemotherapeutic agent but its extensive use is likely to lead to widespread resistance and the drug is expensive. Penicillin is a possible alternative for developing countries with limited budgets but it needs to be given in a full therapeutic dose to be effective (M Hassan-King).¹⁶

Vaccination with group A plus group C vaccine had no effect on the nasopharyngeal carriage of group A or group C meningococci in household contacts, again suggesting that vaccination may have to be combined with some chemoprophylaxis. Our results differ from those found in military camps, where meningococcal vaccines have been moderately effective in reducing carriage rates.^{17 18} In these camps, however, a very high proportion of recruits become carriers, while carriage is much less common among contacts of civilian cases. Perhaps household contacts who become carriers are a special group who have difficulty in eliminating meningococci after either natural infection or vaccination.

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