Annotations

Prophylaxis in bacterial meningitis

Few things cause greater anxiety in a community than a case of fulminant meningococcaemia. Once the patient with meningococcal disease (meningitis or meningococcaemia) has been started on treatment the next consideration should be the risks of disease in the contacts of the patient. We now know that children in the United States who have been close contacts of patients with invasive *Haemophilus influenzae* type B diseases are also at increased risk of developing serious haemophilus infections.¹ Chemoprophylaxis for contacts of meningococcal disease has been recommended for years, but because of the development of resistance to sulphonamides by some of the meningococci the question of which drug to use creates a dilemma. Some physicians, because of lack of knowledge about which drug to use and the proper dosage and length of treatment, avoid the whole issue of prescribing antimicrobial prophylaxis. Now with a second organism proved to spread disease the issue becomes even more complex. Fortunately, there is no evidence at the present time that contacts of patients with other types of bacterial meningitis are at substantial risk.

Meningococcal disease risks

The attack rate of meningococcal disease in Britain and the United States is about 1 case/100 000 people and in each nation the attack rate is inversely proportional to age.^{2 3}

The attack rate in household contacts of a case of meningococcal disease is about 1000 times that of the endemic attack rate shown in Table 1.⁴ During epidemic periods the secondary attack rate, defined as the rate of disease occurring in household contacts beginning 24 hours and less than 30 days after the index case is placed in hospital, may reach 15 000 times the endemic rate.⁴ In addition to the increased attack rate in young children the mortality rate is also inversely proportional to age.

Table 1 *Meningococcal meningitis attack rate/100 000 population 1979 (England and Wales)*³

Age (years)	Cases/100 000 population
≤ 1	16.9
1-4	5.95
5-14	1.3
≥ 15	0.56

Haemophilus influenzae type B risks

Five recent reports from the United States have shown that household contacts of patients with invasive haemophilus disease are at an increased risk of serious infection from this organism.^{1 5-8} For unknown reasons *H. influenzae* causes about one-third of the number of cases of meningitis in British children as in a comparable age group in the United States. The risk of secondary cases in affected households in Britain is unknown but would probably be increased. In the United States the secondary attack rate in contacts, irrespective of age, is 0.26% and therefore is about two-thirds of the secondary attack rate for meningococcal disease.⁹ However, in household contacts less than 2 years of age the risk is increased to about 3%.⁹ This risk, while highest during the first month after the index case, appears to continue at 20-25 times the endemic attack rate for at least 6 months.⁹

Strategy of antimicrobial prophylaxis

The object of chemoprophylaxis is to eradicate *Neisseria meningitidis* or *H. influenzae* from the nasopharynx of those colonised before it causes disease in them or before it can be transmitted to susceptibles. Unfortunately, most of the usual antibiotics, including those used for treatment—such as penicillin, ampicillin, chloramphenicol, tetracycline, oxytetracycline, erythromycin, and cephalixin—do not reliably eliminate these organisms from the nasopharynx.

The antimicrobials which have proved effective in eradicating susceptible strains of nasopharyngeal meningococci are rifampicin, minocycline, and sulphadiazine. Unfortunately about 50% of group A meningococci and 20-25% of the other serogroups of meningococci in the UK are resistant to the sulphonamides.¹⁰ Therefore unless one is dealing with a proved sulpha-susceptible strain, during an epidemic for instance, the previously useful sulphadiazine is a poor choice. Chemoprophylaxis should begin immediately without delaying for swabbing and susceptibility testing because 30-50% of secondary cases occur within 7 days of the index case being placed in hospital.

Chemoprophylaxis for *H. influenzae* is less clear.

We know that ampicillin, cefaclor, erythromycin, and trimethoprim-sulphamethoxazole do not reliably eliminate nasopharyngeal colonisation. We also know that carriage can reappear in the index case after treatment with either ampicillin or chloramphenicol.^{11 12} Rifampicin appears the most promising drug and it eliminated carriage in 90% of 100 treated children in four studies in the United States. These four, mostly closed, populations were treated with 20 mg/kg rifampicin once daily for 4 days.⁹ Colonisation persisted in some individuals even with good compliance and repeated treatment courses. However, a recent study using a lower dosage of rifampicin, 10 mg/kg a day, was unsuccessful.¹³ No regimen has been found that is completely effective. The more important question, which is not answered at present, is whether chemoprophylaxis for *H. influenzae* results in fewer secondary cases.

Current recommendations

General. There should be careful questioning regarding the health of all individuals, especially children, in close or intimate contact with the index case. This includes all individuals sleeping or eating in the same household, and all preschool children in day nurseries, and room-mates in dormitories. Adults in the household or those responsible for the care of any exposed children should be instructed to seek *immediate* medical attention if any close contact develops a febrile illness.

Meningococcal infection. Chemoprophylaxis is indicated for household and other intimate contacts as defined above. Chemoprophylaxis is not generally necessary for day school classmates unless there are additional cases in the school, or for medical staff caring for the patient. Chemoprophylaxis should start immediately and if possible, simultaneously.¹⁰ After mouth-to-mouth resuscitation one should begin treatment, not chemoprophylaxis, to the exposed person.

Rifampicin is the preferred drug unless the meningococcus is known to be susceptible to sulphonamides. If sulphonamides are used sulphadiazine is the most effective. In practice, there may be difficulties in finding a local supply of the older sulphonamides, such as sulphadiazine.¹⁴ The sulphonamides are not recommended during the latter stages of pregnancy and rifampicin is not recommended in pregnancy. Since pregnancy seems to place some women in the 'therapeutic orphan' category, each physician will have to make his own decision about the importance of chemoprophylaxis.

Table 2 Dosage of drug given by mouth twice daily for 2 days

Drug	Age		
	3 months–1 year	1–12 years	> 12 years
Rifampicin	5 mg/kg	10 mg/kg	600 mg
Sulphadiazine	250 mg	500 mg	1 g

Rifampicin should also be avoided in persons wearing soft contact lenses to avoid staining the lens. The dosages shown above (Table 2) were recently recommended in the Communicable Disease Report.¹⁰ The index case should probably also receive chemoprophylaxis before leaving hospital to return home.

Haemophilus influenzae infection. Chemoprophylaxis is of unknown efficacy. If one chooses to treat families with several small children the following approach seems reasonable.⁹ (1) Chemoprophylaxis should be limited to members of households or day nurseries where there are contacts in the susceptible age group (younger than 48 months). Because of the risk of an adult harbouring the pathogen it is probably advisable to treat adults as well as the children in a household. Adults working in daycare centres have a low risk of carriage and probably do not require chemoprophylaxis. (2) Rifampicin in a dosage of 20 mg/kg per dose once daily for 4 days, with a maximum dosage of 600–900 mg daily, appears to be most likely to eliminate carriage.

A personal view

I am a firm believer in the axiom 'an ounce of prevention, . . .' and have seen too many cases in which the Rolls Royce treatment with the latest wonder antibiotic has failed miserably. As a paediatrician I have ample evidence of the risk if a child is a contact of these two infectious agents. The situation is much clearer with meningococcal disease and I strongly recommend chemoprophylaxis with rifampicin as soon as possible. If the meningococcus is proved to belong to serogroup A or C, I believe close contacts should be immunised with the appropriate monovalent meningococcal vaccine as added protection against failure of chemoprophylaxis. The meningococcus serogroup A vaccine has proved effective in epidemics in Egypt, Brazil, and Finland, and has been effective in children as young as 3 months.¹⁵ The meningococcus serogroup C vaccine gives appreciable protection in persons older than 2 years but not in younger children.¹⁶ These meningococcal vaccines are not licensed in the

UK and must be obtained from the manufacturer on a 'named patient' basis. Unfortunately, there is no effective vaccine for the meningococcus serogroup B organisms which cause the majority of infections in the UK and the United States.

I shall give rifampicin prophylaxis to contacts of my American patients with serious *H. influenzae* type B infections, as outlined, including the index case before he leaves hospital. I will use chemoprophylaxis because I believe rifampicin is reasonably safe and should eliminate carriage in most of the children. Perhaps studies will prove prophylaxis is ineffective or that another drug is preferable and cause me to change my approach. Until we have an effective vaccine against *H. influenzae* type B infections in small children, this is one approach available to me as a clinician.

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