Haemophilus influenzae infections in siblings: the need for prophylaxis

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Abstract
An 8 month old child developed Haemophilus influenzae meningitis 12 days after his elder brother had developed epiglottitis. There is not at present in the United Kingdom a recognised policy for prophylactic treatment of contacts of patients with H influenzae infection. Variations in clinical practice were confirmed by the result of a survey of paediatricians in the Northern region.

Haemophilus influenzae type b is an important cause of severe bacterial infection in childhood and is associated with appreciable mortality. During recent years there has been a large increase in the incidence of such infections throughout the world, and a recent study from Oxford reported a current incidence of 33/4/100 000 children under 5 years old. The two cases described here illustrate different presentations of the infection and highlight the question of prophylactic medication for contacts of such patients. Following our experience we carried out a survey of paediatricians in the Northern region about their use of antibiotics in the prophylaxis of H influenzae type b infections.

Case reports
CASE 1
In November 1988 a 33 month old boy was admitted with a six hour history of inspiratory stridor. A clinical diagnosis of epiglottitis was made, and this was confirmed on intubation. Swabs from the trachea and blood were cultured and grew H influenzae type b that was resistant to erythromycin and ampicillin, but sensitive to chloramphenicol. He was intubated for 48 hours and treated with chloramphenicol intravenously. He made an uneventful recovery and was discharged having completed a seven day course of treatment.

CASE 2
Twelve days after the admission of case 1, his 8 month old brother was admitted to hospital with a 24 hour history of a febrile illness, irritability, and vomiting. Results of a lumbar puncture confirmed the diagnosis of meningitis, and the cerebrospinal fluid grew H influenzae type b on culture, with identical sensitivities to those of the organism cultured from his sibling’s tracheal secretions and blood. The identical nature of the organism was also confirmed by serotyping. He was treated with chloramphenicol intravenously and made a gradual recovery complicated by anaemia and thrombocytosis. He has remained well since.

Recognising that guidelines for prophylaxis do exist and that we had missed an opportunity of possibly preventing a life threatening infection, we assessed the practice of consultant paediatricians in the Northern region.

Results
The results are shown in the table.

<table>
<thead>
<tr>
<th>Responses of 29 paediatricians to questions about their use of prophylaxis for contacts of patients with H influenzae infection</th>
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<tbody>
<tr>
<td>No who use prophylaxis for contacts</td>
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<tr>
<td>Of those:</td>
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<tr>
<td>Include parents</td>
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<td>Include all children</td>
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<td>Include only children &lt;6 years</td>
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<td>Include only children &lt;3 years</td>
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Discussion
No vaccine against H influenzae is in regular use in the United Kingdom, nor is there a consistent practice of prophylaxis for contacts. This is in contrast to the United States, where guidelines have already been produced. Fifteen of paediatricians in the Northern region said they would use prophylaxis, and all said their drug of choice would be rifampicin.

Currently the only common infection for which prophylaxis for contacts is considered routinely is meningococcal infection, because of the increased risk of secondary cases. Studies have also shown, however, that for 30 days after H influenzae meningitis the risk in household contacts is 585 times greater than the age adjusted risk in the general population. This increased risk is especially pronounced in those under 2 years old and is associated with a rise in the nasopharyngeal carriage of H influenzae.

In 1984 the American Committee of Infectious Diseases produced recommendations on the use of rifampicin as prophylaxis for contacts of patients with H influenzae infection. They suggested that rifampicin (20 mg/kg) should be given to all household contacts including those adults who had at least one contact under 49 months old including the patient. The data on which their recommendations were based were collected from a number of clinical trials including a multicentre trial in which the rates of nasopharyngeal carriage of H influenzae in contacts were studied. Rifampicin given to the contacts eradicated the organism in 96%, compared with 29% in those given placebo.
Despite a suggestion that *H. influenzae* infection in the United Kingdom may behave differently, four half the paediatricians questioned in our study were already following the American example in offering prophylaxis to siblings of contacts; we also now intend to follow this practice.

We thank Dr S Hudson, consultant bacteriologist, for help in serotyping the organism, and Dr R Nelson for permission to present case 1.

7 Glode M, Daum RS, Boles EG. Effect of rifampicin chemoprophylaxis on carriage eradication and new acquisition of *H. influenzae* type b in contacts. *Pediatrics* 1985;76:537-42.

Commentary

This case report describes the unusual, but well documented, occurrence of a case of systemic *Haemophilus influenzae* type b infection secondary to *H. influenzae* type b meningitis in an older sibling. It stimulates discussion of several points. Glode et al were among the first to document the contagiousness of these infections. Their data and that of others in North America have indicated a substantially increased likelihood that household contacts of a child with *H. influenzae* type b meningitis will also contract invasive infection with the same organism. A crucial point is that the risk of secondary disease is strongly correlated with the age of the household contact, being greatest in those aged ≤2 years. Subsequent clinical studies showed that rifampicin could eradicate nasopharyngeal colonisation with *H. influenzae* type b and also, but less convincingly, the strategy could decrease the risk of secondary disease. As a consequence, the advice of the American Academy of Paediatrics is that ‘. . . prophylaxis is recommended for all household contacts, including adults, in those households with at least one contact younger than 49 months old. . .’

Two additional points should be emphasised. Firstly, the data resulting in this recommendation were obtained in North America. It should not be assumed that the epidemiology of *H. influenzae* type b disease in North America is necessarily an appropriate basis for recommendations for the United Kingdom. *H. influenzae* type b strains (carrier or disease isolates) show genotypic and phenotypic differences depending on their geographical origin. Therefore the epidemiological behaviour of different bacterial clones may be dissimilar owing to variation in virulence factors that are important to transmission and invasive potential. Secondly, the issue of what constitutes a secondary case is not straightforward. A reasonable, but arbitrary, definition has included contacts contracting invasive disease within 30 days of exposure to the index case. Furthermore, this definition does not allow a distinction between coprimary and secondary infection.

Condemnably, the authors draw attention to the disparate advice tended by paediatricians. The questionnaire, however, did not secure the answer to the following pertinent question: in a household with at least one child aged <4 years (other than the index case), how many paediatricians would recommend rifampicin for all household contacts and the index case? Those responding ‘yes’ would be following the advice of the American Academy of Pediatrics. The advice is sensible and the recommendation cited in the BPA Manual on Infections and Immunisations in Children says that: ‘When there is another pre-school child in the house of a case of invasive type b infection, rifampicin prophylaxis is recommended for all household contacts. The index case should also receive rifampicin since standard treatment does not eradicate nasopharyngeal carriage’.

Finally, the ‘bottom line’ is that even if this policy were implemented, it has the potential to prevent only a minority of invasive *H. influenzae* type b infections. Furthermore, there are documented instances in which rifampicin has apparently failed to prevent secondary cases. The controversy is likely to become academic as active immunisation should soon consign invasive *H. influenzae* type b infections to the list of preventable communicable diseases and render rifampicin prophylaxis redundant.