



Pre-hospital antibiotic treatment of meningococcal disease: scope for improvement

Tania Riddell and Chris Bullen

Abstract

Aim To determine the extent to which Auckland general practitioners (GPs) follow Ministry of Health guidelines recommending the administration of pre-hospital antibiotic treatment to suspected cases of meningococcal disease.

Methods Retrospective audit of notified cases of meningococcal disease referred by Auckland GPs from 1 May 2001 to 30 April 2002.

Results Of 142 meningococcal disease cases that were referred to hospital by GPs, 111 (78%) were 'eligible' or met Ministry of Health guideline criteria for pre-hospital antibiotic treatment. Of these, only 33 (30%) were given parenteral antibiotics. Those with a rash were twice as likely as those without a rash to receive antibiotics (RR 2.1; 95% CI 1.7–2.7). There was no difference in antibiotic administration by age, sex, ethnicity, or where there was an estimated delay of greater than 30 minutes to assessment in hospital.

Conclusions The findings of this audit reinforce the need for GPs to have a higher index of suspicion and lower threshold for treatment for suspected cases of meningococcal disease and to give antibiotics more often than they do at present.

New Zealand is in its twelfth year of a serogroup B meningococcal disease epidemic. In 2002, the epidemic showed no sign of abating and trials aimed at controlling it by using a strain-specific vaccine began. However, it could be another two years before national mass vaccination begins. Even with a vaccine, pre-hospital antibiotic treatment of suspected cases of meningococcal disease is essential. The case fatality rate for patients seen by a doctor and given antibiotic treatment prior to hospitalisation is significantly lower than for patients who do not see a doctor and do not receive parenteral antibiotics.^{1–3} In New Zealand, pre-hospital antibiotic treatment is given to only about one quarter of suspected meningococcal disease cases.⁴ This study aimed to determine the extent to which Auckland GPs follow Ministry of Health guidelines that advise them to administer parenteral antibiotics to:

- all suspected cases of meningococcal disease in whom there is any haemorrhagic rash; or
- all other suspected cases in whom the delay in reaching hospital is likely to be greater than 30 minutes.

Methods

Retrospective audit of all cases of meningococcal disease in Auckland for the 12-month period 1 May 2001 to 30 April 2002.

Cases were identified through EpiSurv – the national database for notifiable diseases.

Figure 1 gives the case definition for meningococcal disease.

Figure 1. Definition of case of meningococcal disease

The case definition given in the Ministry of Health Communicable Disease Control Manual⁶ states: 'Meningococcal disease presents as meningitis or meningococcal septicaemia. The disease presents as acute fever, nausea, vomiting and headache, that may progress rapidly to shock and death. Petechial rash is seen in about 50 per cent.' Cases with a clinically compatible illness are classified as confirmed or probable as follows:

Confirmed case: A clinically compatible illness with at least one of the following:

1. isolation of *Neisseria meningitidis* from a sterile body site; or
2. a positive nucleic acid test using PCR on CSF, blood, serum, or aspirate; or
3. detection of gram-negative intracellular diplococci in CSF, aspirate, or skin biopsy; or
4. positive meningococcal antigen test on CSF.

Probable case:

1. a clinically compatible illness and isolation of *Neisseria meningitidis* from throat; or
2. a clinically compatible illness.

PCR = polymerase chain reaction; CSF = cerebrospinal fluid

All notified Auckland meningococcal disease cases (both confirmed and probable) were included in the study. The audit included those cases who were referred by a GP to hospital and subsequently diagnosed with meningococcal disease. Cases were classified as 'eligible' to have received pre-hospital parenteral antibiotics if they met with Ministry of Health guideline criteria.

Auckland Regional Public Health Service records were used to obtain case details. Permission to review records was obtained from supervising consultants and the Auckland Ethics Committee determined that ethics approval was not required.

A standard 'proforma' was used to extract the following information:

- whether the attending GP had administered parenteral antibiotics before patient admission to hospital; and
- what factors influenced the use of antibiotics (age, gender, ethnicity, presence of a rash, distance of general practice from hospital).

Practice nurses were contacted by telephone and asked if the travel time from their practice to the nearest appropriate hospital was greater than 30 minutes.

A rate ratio was calculated for the variables: age, sex, ethnicity, presence of a rash and general practice greater than 30 minutes away from the admitting hospital. Adjustment for possible confounding factors was carried out using the Mantel-Haenszel method. Cases for which the relevant data were unknown were excluded from analysis. Statistical analysis was carried out using EpiInfo 2000.⁵

Results

Over the 12-month study period, 214 cases were recorded on EpiSurv as having been admitted to Auckland hospitals with meningococcal disease. About two thirds of these cases ($n = 142$) were referred to hospital by a GP. One hundred and eleven (78%) cases were eligible for pre-hospital antibiotics according to Ministry of Health guideline criteria.

The median age of the GP-referred cases was six years (range 28 days to 67 years) with over half of cases (55%) under five years old. Eighty three cases (58%) were male. There were 58 (41%) Pacific Islands people, 40 (28%) Europeans, 36 (25%) Maori, and eight (6%) of 'Other' ethnic groups.

Of the 111 eligible cases, 33 (30%) were given parenteral antibiotics by their attending GP. Of the 79 cases (56% of all the cases referred) reported to have a rash, only 31 (39%) received antibiotic treatment. Thirty two (28%) of the eligible cases were referred from practices where the delay to assessment in hospital was estimated

to be greater than 30 minutes. Of these, only nine (28%) received pre-hospital antibiotic treatment.

Cases with a rash were twice as likely as those without a rash to have received pre-hospital antibiotic treatment (RR 2.1; 95% CI 1.7–2.7). In fact, of the 33 cases overall who were administered antibiotics, 31 (94%) had a rash. There was no difference in antibiotic administration by age, sex, ethnicity or distance of general practice from hospital.

Discussion

This study suggests there is scope for improvement to the pre-hospital management of suspected cases of meningococcal disease in Auckland. Despite regular advice urging the administration of parenteral antibiotics prior to hospital admission,^{7–9} this study found that in Auckland only one third of eligible patients were given treatment by an attending GP. Furthermore, parenteral antibiotics were rarely given in the absence of a rash, even for those in whom the delay to assessment in hospital was likely to be greater than 30 minutes.

A number of reasons have been postulated to explain the failure to start early treatment for suspected meningococcal disease in the primary care setting. These include diagnostic uncertainty, concern about interference with hospital tests, the belief that patients will be treated promptly once in hospital, fears of administering unnecessary treatment or causing an anaphylactic reaction, and unproven benefit.¹⁰

Diagnostic uncertainty is common in general practice where many diseases are encountered at early stages when signs and symptoms are often non-specific.¹¹ The diagnosis of meningococcal disease is largely a clinical one as highlighted by the case definition (Figure 1). The petechial or purpuric rash of meningococcal septicaemia is a physical sign that can assist early suspicion of infection.¹² In this study, the presence of a rash was the most important factor that led to administration of antibiotic treatment prior to hospital admission. This supports the findings of other studies.^{11–13} However, as only about half of the patients in this study were reported to have a rash, the tendency to focus on overt physical signs may be inappropriate. General practitioners who suspect meningococcal infection should not be deterred from starting antibiotic treatment,¹¹ particularly when there are early signs and symptoms of septic shock such as excessive tachycardia.

Interference with hospital tests and fear of rendering cultures sterile is misguided if the consequence of delayed treatment is death.¹³ Treating a potentially fatal condition is more important than eliciting a precise diagnosis. Importantly, species-specific polymerase chain reaction (PCR) testing is now available and is a powerful diagnostic tool that is more sensitive than culture and less affected by antibiotics. PCR tests may prove positive three days after initiating treatment.⁴

General practitioners cannot assume that patients will be treated quickly once admitted to hospital. Patients suspected of having meningococcal disease may wait some considerable time in hospital before treatment is started.¹⁴ Since parenteral antibiotics interrupt growth of meningococci, and the build up of endotoxins and cytokines in the plasma, the management of meningococcal disease cases is time critical. How quickly treatment is initiated is the key issue, not who initiates it.

The fear of administering inappropriate antibiotics should not discourage pre-hospital treatment. Minimal harm can be expected if an antibiotic is given and meningococcal disease is not confirmed.¹³ It has been recommended in New Zealand that any patient with a known allergy to penicillin is urgently transferred to hospital without antibiotics.¹⁵ However, it is known that only a minority of those with a history of penicillin allergy are subsequently confirmed as genuinely allergic.¹⁶

Finally, despite the use of pre-hospital antibiotic treatment in meningococcal disease being questioned,¹⁷ it is generally agreed that meningococcal infection should be treated with parenteral antibiotics as soon as is possible.¹⁰ The current consensus is that it is the most effective way of controlling life-threatening infection from meningococcal disease.¹⁸ A reduction in case fatality rates from the administration of pre-hospital antibiotics has been observed in New Zealand³ and elsewhere.^{1,2,13}

There are a number of limitations to this study. First, information regarding preliminary diagnosis, as assessed by the attending GP, was unavailable. Second, some of the case notes were incomplete, which hindered determination of the estimated distance of general practice from hospital. Third, clinical condition of the patient at presentation was a potential confounding factor. We could not exclude the possibility that cases who presented to a GP with a rash were already well advanced in their illness and were therefore more likely to receive antibiotics before being transferred to hospital. Finally, differences by ethnicity, for example, may have remained undetected due to small numbers. Similarly, some cases in this study died, but we did not analyse outcome data because numbers were too small to make unbiased comment. A prospective study that is large enough to stratify by known confounders, and have adequate explanatory power to compare risk factors and outcome data, is needed.

It is with great hope that we look to mass immunisation to terminate the current and prolonged serogroup B epidemic in New Zealand. In the interim, early and aggressive treatment of suspected cases of meningococcal disease by GPs in the community setting is essential. A higher index of suspicion and lower threshold for treatment are needed. Further effort to encourage early diagnosis and treatment is necessary.

Author information: Tania Riddell, Public Health Registrar; Chris Bullen, Public Health Physician, Auckland Regional Public Health Service, Auckland

Acknowledgements: This study was funded by the Auckland Regional Public Health Service, Auckland District Health Board. Phillip Hill assisted with the original concept of the study and its design.

Correspondence: Dr Tania Riddell, P O Box 147 094, Ponsonby, Auckland. Fax: (09) 376 3238; email: taniar@nhf.org.nz

References:

1. Wylie PA, Stevens D, Drake W 3rd, et al. Epidemiology and clinical management of meningococcal disease in west Gloucestershire: retrospective, population based study. *BMJ* 1997;315:774-9.
2. Cartwright K, Levin M, Begg N. Initial management of suspected meningococcal infection. Parenteral benzylpenicillin is vital. *BMJ* 1994;309:1660-1.
3. Martin D, McDowell R, Garrett N, Baker M. The epidemiology of meningococcal disease in New Zealand in 2001. Report prepared for the Ministry of Health by the Institute of Environmental Science and Research Limited. Wellington: Ministry of Health; 2002.

4. Ministry of Health. Meningococcal vaccine strategy: background information. Wellington: Ministry of Health; 2002.
5. Dean A, et al. EpiInfo 2000. A database and statistics program for public health professionals for use on Windows 95, 98, NT and 2000 computers. Atlanta, GA: Centres for Disease Control and Prevention; 2000.
6. Ministry of Health. Communicable disease control manual. Wellington: Ministry of Health; 1998
7. Ministry of Health. Immunisation handbook 1996 (reprint). Wellington: Ministry of Health; 1996
8. Ministry of Health. Meningococcal disease circular letter. Wellington: Ministry of Health; 1998.
9. Ministry of Health. Immunisation handbook 2002. Wellington: Ministry of Health; 2002
10. Wood AL, O'Brien SJ. A primary care perspective of meningococcal disease. *J Public Health Med* 1998;20:382-5.
11. Granier S, Owen P, Pill R, Jacobson L. Recognising meningococcal disease in primary care: qualitative study of how general practitioners process clinical and contextual information. *BMJ* 1998;316:276-9.
12. Riordan FA, Thomson AP, Sills JA, Hart CA. Who spots the spots? Diagnosis and treatment of early meningococcal disease in children. *BMJ* 1996;313:1255-6.
13. Cartwright K, Reilly S, White D, Stuart J. Early treatment with parenteral penicillin in meningococcal disease. *BMJ* 1992;305:143-7.
14. Wood AL, O'Brien SJ. How long is too long? Determining the early management of meningococcal disease in Birmingham. *Public Health* 1996;110:237-9.
15. Auckland Healthcare. *Public Health Advice* 1998;4:1
16. Surtees SJ, Stockton MG, Gietzin TW. Allergy to penicillin: fable or fact? *BMJ* 1991;302:1051-2.
17. Peltola H. Early meningococcal disease: advising the public and the profession. *Lancet* 1993;342:509-10.
18. Van Deuren M, Brandtzaeg P. Parents' and GPs' key role in diagnosis of meningococcal septicaemia. *Lancet* 2000;356:954-5.