Australian Government

Department of Health and Ageing

Australia and New Zealand Horizon Scanning Network

ANZHSN

AN INITIATIVE OF THE NATIONAL, STATE AND TERRITORY GOVERNMENTS OF AUSTRALIA AND THE GOVERNMENT OF NEW ZEALAND

National Horizon Scanning Unit
Horizon scanning prioritising summary

Volume 14, Number 6:

Pre-hospital administration of antibiotics by paramedics for suspected cases of meningococcal disease

September 2006

AHTA

Adelaide Health Technology Assessment

[add ISSN]
[add Publications Approval Number]

Electronic copies can be obtained from http://www.horizonscanning.gov.au

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The production of this *Horizon scanning prioritising summary* was overseen by the Health Policy Advisory Committee on Technology (HealthPACT), a sub-committee of the Medical Services Advisory Committee (MSAC). HealthPACT comprises representatives from health departments in all states and territories, the Australia and New Zealand governments; MSAC and ASERNIP-S. The Australian Health Ministers' Advisory Council (AHMAC) supports HealthPACT through funding.

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PRIORITISING SUMMARY

REGISTER ID: **000229**

NAME OF TECHNOLOGY: **PRE-HOSPITAL ADMINISTRATION OF ANTIBIOTICS BY PARAMEDICS**

PURPOSE AND TARGET GROUP: **FOR SUSPECTED CASES OF MENINGOCOCCAL INFECTION**

STAGE OF DEVELOPMENT (IN AUSTRALIA):

☐	Yet to emerge	☐	Established
☐	Experimental	☒	Established *but* changed indication or modification of technique
☐	Investigational	☐	Should be taken out of use
☐	Nearly established		

AUSTRALIAN THERAPEUTIC GOODS ADMINISTRATION APPROVAL

☐	Yes	ARTG number
☐	No	
☒	Not applicable	

INTERNATIONAL UTILISATION:

COUNTRY	LEVEL OF USE		
	Trials Underway or Completed	Limited Use	Widely Diffused
United Kingdom			✓
Australia		✓	

IMPACT SUMMARY:

Meningococcal disease is a notifiable disease in Australia and New Zealand. In order to reduce the risk of death associated with the disease, guidelines for the management of meningococcal recommend the immediate administration of benzylpenicillin to suspected cases (DoHA 2001).

BACKGROUND

The causative agent of meningococcal disease is the bacteria *Neisseria meningitidis*. There are 13 serotypes of *N. meningitidis*, with A, B and C the serotypes most commonly isolated in Australia. There is no vaccine available that is effective against all *N. meningitidis* serotypes (Patel et al 1997). Similarly, there is no vaccine available for the subtype of serotype B that is prevalent in Australia, however there is an effective vaccine available for the subtype of serotype B that is prevalent in New Zealand (Dyet et al 2005). Since 2003, the Australian Immunisation Schedule has made vaccination against meningococcal C available free of charge to all infants turning 12 months, as well as to children and young adults <19 years from 2003-June 2006 (DoHA 2005). The New Zealand Ministry of Health are providing a free vaccine (MeNZB) against the serotype B that is in epidemic proportions in New Zealand to all individuals under the age of 20 years, until December 2006. The vaccine will continue

to be made available for New Zealand infants and children aged six weeks to five years until the end of 2009 (MoH 2006).

Clinical symptoms of meningococcal disease include fever, vomiting and drowsiness in association with a petechial rash. Many patients will present with a non-distinctive rash or no rash at all, which may lead to misdiagnosis (Patel et al 1997). In 2005, serotype B represented the majority of confirmed laboratory tests (73%) in Australia (Tapsall 2006). Patients infected with *N. meningitides* may deteriorate rapidly as the bacteria undergo exponential growth, releasing large amounts of bacterial endotoxin, and resulting in meningococcal septicaemia. Meningococcal septicaemia is associated with significant mortality and morbidity. Symptoms of septicaemia include shock, vasomotor collapse, multiple organ failure and disseminated intravascular coagulation, which may result in the loss of limbs and ultimately death (Walker 2005). Morbidity and mortality as a consequence of meningococcal septicaemia is dependent on serotype of the infection, the patient's age and general health, and the severity of the illness before first line treatment was sought (Tippett & Bonham 2005).

As there is no effective vaccine against serotype B (in Australia), the main method of controlling invasive meningococcal disease is the timely and effective administration of antibiotics (Hall 2002). All meningococcal serotypes respond to early treatment with penicillin. Antibiotics should be administered intravenously. However, if access to a vein is problematic, then antibiotics should be administered intramuscularly. Shock and hypotension associated with meningococcal disease may, however, impair the absorption of the drug via this route (Hall 2002; Patel et al 1997). In the majority of cases the administration of penicillin will cause no harm to patients; however some patients may have a penicillin allergy and in these cases antibiotics should not be administered and the patient should be hospitalised immediately (Todd 2004).

Cefotaxime or ceftriaxone are the recommended drugs to treat meningococcal disease but are not available routinely as an emergency "doctors bag" medicine in Australia (Patel et al 1997). The Australian and New Zealand guidelines for the management of meningococcal disease recommend that general practitioners (GP) stock benzylpenicillin in their surgeries and emergency bags for immediate administration to suspected cases. This should be followed by the immediate transfer of the patient to hospital where cefotaxime or ceftriaxone can be administered (Baker et al 2001; DoHA 2001; Patel et al 1997).

CLINICAL NEED AND BURDEN OF DISEASE

In Australia, meningococcal disease is rare. During the period 2005, there were 345 laboratory confirmed cases of invasive meningococcal. Using the 2004 population as an estimate, this equates to a population rate of 1.7 per 100,000[1]. Of these confirmed cases, 251 (73%) were serotype B, 50 (14.5%) were serotype C and the remaining cases were a mix of serotypes A, Y, W135 or not typable. The majority of these cases occurred in New South Wales (32%), Victoria (23%) and Queensland (17%). The highest proportion of cases occurred in the younger age groups (13.6% in infants less than 1 year and 18.2% in children 1-4 years), with a secondary peak of cases in the 15-19 years age bracket (13.9%). The

[1] The population in 2004 was 20,091,500 ABS (2006). *Population Projections, Australia, 2004 to 2101* [Internet]. Australian Bureau of Statistics. Available from: http://www.abs.gov.au/ausstats/abs@.nsf/mf/3222.0 [Accessed 15th September 2006].

remaining cases were evenly spread across all age groups. Cases in very young children (< 4 years) were overwhelmingly of serotype B (90%), with serotype C affecting those more in the older age group (>25 years 50% serotype B and 27% serotype C). Outcome data were only available for 163/345 (47%) of confirmed cases. Of these cases, the case fatality rate was 9.2 per cent (15/163). The majority of deaths occurred in patients infected with serotype B (10/15, 66.7%) with three deaths (20%) in patients infected with serotype C (Tapsall 2006).

New Zealand has been experiencing an epidemic of meningococcal disease since 1991, caused by a different strain of the serotype B bacteria than that found in Australia. The number of notified cases has risen from 53 (population rate 1.5 per 100,000) in 1990 to peaks of 613 (16.9 per 100,000) and 650 (17.4 per 100,000) in 1997 and 2001, respectively. The age-specific rates for infants < 1 year was 124.4 per 100,000 and in children aged 1-4 years was 59.7 per 100,000. During the period 1991-2003, there was an average case fatality rate of 4.1 per cent. Interestingly, data collected during 1999-2003, indicated that the case fatality rate was highest in those aged over 40 years (10.9%). Overall, mortality was highest for patients infected with serotype C (10.4%) compared to serotype B (3.8%) (Baker et al 2001; Dyet et al 2005).

The number of suspected meningococcal patients transported by ambulance in Australia could not be ascertained.

DIFFUSION

Currently only ambulance and mobile intensive care paramedics in the Australian Capital Territory, Victoria, South Australia (SA) and Tasmania have approval to carry and administer parenteral benzylpenicillin, cefotaxime or ceftriaxone to patients suspected of being infected with meningococcal disease (7:30 Report 2006; Walker 2005). Clinical practice guidelines for the United Kingdom ambulance service give approval and instructions to paramedics for the intravenous administration of benzylpenicillin (Todd 2004). The administration of medicines is viewed as a value judgment that should only be made by medical personnel. Therefore, in SA, paramedics contact the Medical Director of the Ambulance service by phone to describe the patient's symptoms. The Director makes the final decision whether to administer antibiotics based on the described symptoms, current demographic data (i.e. prevalence of meningococcal disease) and distance from the nearest hospital. When benzylpenicillin is administered in SA, paramedics are also instructed to prepare an adrenalin solution in case of anaphylactic shock (personal communication, Medical Director South Australian Ambulance Service, 15th September 2006)[2].

COMPARATORS

The only treatment option available for patients suspected of meningococcal disease is the administration of intravenous antibiotics. The condition of the patients may deteriorate so rapidly that antibiotics should be administered before laboratory confirmation of infection is obtained. There is a large body of evidence pointing to successful patient outcomes (survival) when patients are administered antibiotics prior to hospital admission, usually by their GP (Harnden et al 2006; Tippett & Bonham 2005; Walker 2005). However, not all symptomatic

[2] The Medical Director of the South Australian Ambulance Service is also the Chair of the Clinical Committee for the Council of Ambulance Authorities

patients present to GPs. Data from New Zealand indicated that 60 per cent of patients were seen by their GP, and of these patients only 39 per cent were administered antibiotics (Baker et al 2001). A recent systematic review on the effectiveness of parenteral antibiotics for meningococcal infection reported that the risk of death was reduced when patients were treated before hospital admission (p= 0.04) (level III-2 Intervention evidence) [3] (Hahne et al 2006).

EFFECTIVENESS AND SAFETY ISSUES

The New Zealand cohort study by Baker et al (2001) reported the case fatality rate of patients seen by a general practitioner and administered intravenous antibiotics prior to admission to hospital to be 1.5 per cent. The case fatality rate for patients seen by a GP but *not* administered antibiotics was 4.1 per cent (level IV Intervention evidence).

The Victorian Ambulance Service introduced the policy for administration of antibiotics to suspected meningococcal patients by paramedics in 2004. An audit of this policy revealed that in the 12-months since December 2004, four patients were administered antibiotics by ambulance staff; two children (8 and 12 years old), a female in her mid-20s and a 58 year old male. Each case was in excess of 30 minutes away from the nearest medical facility. The 58 year old male was in a small rural community at least 50 minutes from hospital and was found in a critical condition: unconscious with a Glasgow Coma Score of 6, tachycardia (120 beats per minute), no recordable blood pressure and a purpuric rash. All patients were administered ceftriaxone en-route to hospital and received further treatment upon arrival. All patients were found to have been positive for meningococcal. All made a full recovery and were discharged without sequale (Walker 2005). Since the end of this audit in December 2005, an additional two children (9-months and 3-years old) were treated for suspected meningococcal disease. Only one of these patients were confirmed positive by the laboratory (personal communication, 15th September 2006).

The administration of antibiotics (benzylpenicillin) by paramedics was approved in the United Kingdom in November 2000. Of the 31 ambulance services in the UK only 19 had introduced this practice at the beginning of 2003. A 12-month audit was established during 2003 to monitor the appropriateness of the administration of benzylpenicillin for suspected meningococcal cases. UK Guidelines advise that benzylpenicillin should only be administered in the presence of the characteristic purpuric rash. During this time frame 69 patients had antibiotics administered by paramedics. The majority of these patients (39%) were young (0-5 years). Of the 69 cases, 81.2 per cent were deemed to have antibiotics administered appropriately, whereas 18.8 per cent of patients either did not have a rash present or a rash was not documented by the ambulance officer. In one case (1.5%) a sub-optimal dose of antibiotic was administered. Two of the "non-compliant" cases (2.9%) had come into contact with an individual who had recently died from meningococcal disease and were therefore considered to be at risk. Unfortunately no mortality outcome data were available from this audit (Cooke 2005).

Anecdotal evidence from the Medical Director of South Australian Ambulance Service suggests that approval has been given for the administration of benzylpenicillin 10 times since

[3] The level of evidence assigned to the systematic review must reflect the level of evidence of the studies included in it

the introduction of this policy three years ago. One patient was treated by volunteer ambulance officers in a rural town south of Broken Hill where no other medical assistance was available. The most recent case was September 7th of this year, when an 18 month old infant was administered benzylpenicillin while developing a purpuric rash en-route to hospital. Outcome data based on positive laboratory confirmation may be difficult to obtain as once treated with large doses of antibiotics a positive specimen may not be possible (personal communication, Medical Director South Australian Ambulance Service, 15th September 2006).

Safety issues include the risk of analphylatic shock; however there have been no reports of this occurring (Walker 2005).

COST IMPACT

The Pharmaceutical Benefits Scheme lists the price of ceftriaxone as $20.85 (5 ampoules, 250 mg each), $27.80 (5 ampoules, 500 mg each) and $40.65 (5 ampoules, 1 gm each). Cefotaxime is listed as $26.40 (10 ampoules, 1 gm each) and $48.60 (10 ampoules, 2 gm each). Benzylpenicillin is listed as costing $22.09 (10 ampoules, 600 mg each) (DoHA 2006). The Victorian Ambulance service estimates to supply the antibiotics to all ambulance vehicles, the total additional outlay would be $3,800 every three years (personal communication, 15th September 2006). The recommended dosage for these intravenous antibiotics is 300 mgs for infants less than 1 year, 600 mgs for children aged between 1-9 years and 1200 mgs for adults and children over the age of 10 years (DoHA 2001). In their powdered form these antibiotics have an estimated shelf life of 36-months (Tippett & Bonham 2005). There would be costs associated with training paramedics on the recognition and management of meningococcal symptoms, and in maintaining these skills. The Clinical and Education Services Department of Rural Ambulance Victoria have developed a training program that involves a workbook, a 2-hour training session with case studies and post-training competency assessment with a clinical educator. This program was designed for established paramedics and has also been incorporated into the paramedic undergraduate curriculum. All paramedics are trained in adult and paediatric intravenous cannulation (Walker 2005).

ETHICAL, CULTURAL OR RELIGIOUS CONSIDERATIONS

A randomised controlled trial is unlikely to be conducted into the pre-hospital administration of antibiotics by paramedics for suspected cases of meningococcal disease due to ethical reasons. Ambulance services may be an important link in the early treatment of suspected meningococcal patients in rural and remote areas, where there is the prospect of long transport times and varied access to healthcare (Walker 2005).

OTHER ISSUES:

A review of the evidence for pre-hospital administration of antibiotics by paramedics in Queensland was conducted in 2005. This review acknowledged that there was strong evidence for improved outcomes for patients infected with *N. meningitides* when antibiotics were administered prior to hospital admission. However, the review concluded that "…for the small number of cases in which Queensland Ambulance Service would be likely to be the primary provider, the cost-benefit of securing the drug for administration by ambulance officers; shelf-life of the agent (once reconstituted these agents must be used immediately and

in dry form would be expected to have a shelf life of up to 36-months); and development and delivery of an education package to support implementation, makes introduction of antibiotics in Queensland contraindicated at this time" (Tippett & Bonham 2005).

CONCLUSION:

The supply of antibiotics in ambulances for administration by paramedics would appear to be a simple and relatively cheap program that has the potential to save lives. There is good evidence to support the pre-hospital parenteral administration of antibiotics to patients suspected of having meningococcal disease. The level of evidence supporting the introduction of such a policy however is poor as only anecdotal evidence suggests that this policy is effective. The potential risk of anaphylactic shock would need to be considered, along with the availability of adrenalin to prevent such sequelae.

HEALTHPACT ACTION:

A policy of antibiotic administration by paramedics is being implemented by the majority of jurisdictions in Australia. As a result, it is recommended that the technology be archived.

SOURCES OF FURTHER INFORMATION:

7:30 Report (2006). *Lack of funds stall meningococcal vaccine trials* [Internet]. Australian Broadcast Corporation. Available from: http://www.abc.net.au/7.30/content/2006/s1740471.htm [Accessed 14th September 2006].

ABS (2006). *Population Projections, Australia, 2004 to 2101* [Internet]. Australian Bureau of Statistics. Available from: http://www.abs.gov.au/ausstats/abs@.nsf/mf/3222.0 [Accessed 15th September 2006].

Baker, M. G., Martin, D. R. et al (2001). 'A 10-year serogroup B meningococcal disease epidemic in New Zealand: descriptive epidemiology, 1991-2000', *J Paediatr Child Health*, 37 (5), S13-19.

Cooke, M. E. (2005). 'Prehospital Administration of Benzyl Penicillin by Paramedics in the UK', *Journal of Emergency Primary Health Care*, 3 (1-2).

DoHA (2001). *Guidelines for the early clinical and public health management of meningococcal disease in Australia*, Deaprtment of Health and Ageing, Communicable Diseases Network Australia, Canberra.

DoHA (2005). *Childhood meningococcal C vaccination program* [Internet]. Australian Government. Available from: http://www.immunise.health.gov.au/internet/immunise/publishing.nsf/content/meningocv-child [Accessed 14th September 2006].

DoHA (2006). *Schedule of Pharmaceutical Benefits* [Internet]. Australian Government, Department of Health and Ageing. Available from: http://www9.health.gov.au/pbs/scripts/search. [Accessed 14th September 2006].

Dyet, K., Devoy, A. et al (2005). 'New Zealand's epidemic of meningococcal disease described using molecular analysis: implications for vaccine delivery', *Vaccine*, 23 (17-18), 2228-2230.

Hahne, S. J., Charlett, A. et al (2006). 'Effectiveness of antibiotics given before admission in reducing mortality from meningococcal disease: systematic review', *BMJ*, 332 (7553), 1299-1303.

Hall, R. G. (2002). 'The control of meningococcal disease', *Med J Aust*, 176 (12), 573-574.

Harnden, A., Ninis, N. et al (2006). 'Parenteral penicillin for children with meningococcal disease before hospital admission: case-control study', *BMJ*, 332 (7553), 1295-1298.

MoH (2006). *Meningococcal B Immunisation Programme* [Internet]. Ministry of Health, New Zealand. Available from: http://www.immunise.moh.govt.nz/ [Accessed 14th September 2006].

Patel, M. S., Collignon, P. J. et al (1997). 'New guidelines for management and prevention of meningococcal disease in Australia. Meningococcal Disease Working Party of the National Health and Medical Research Council', *Med J Aust*, 166 (11), 598-601.

Tapsall, J. (2006). 'Annual report of the Australian Meningococcal Surveillance Programme, 2005', *Communicable Diseases Intelligence*, 30 (2).

Tippett, V. & Bonham, R. (2005). 'Review of the evidence for prehospital administration of benzyl penicillin in meningococcal septicaemia - experience in Queensland', *Journal of Emergency Primary Health Care*, 3 (1-2).

Todd, I. (2004). *Clinical Practice Guidelines for use in U.K. Ambulance Services*, Joint Royal Colleges Ambulance Liason Committee, London.

Walker, T. (2005). 'Pre-hospital paramedic administration of Ceftriaxone for suspected meningococcal septicaemia in Victoria, Australia', *Journal of Emergency Primary Health Care*, 3 (1-2).

LIST OF STUDIES INCLUDED

Total number of studies	
Level III-2 Intervention evidence	1
Level IV Intervention evidence	1

SEARCH CRITERIA TO BE USED:

Anti-Bacterial Agents/therapeutic use
Australia/epidemiology
Bacterial Vaccines
Disease Outbreaks/ prevention & control
Meningococcal Infections/diagnosis/ epidemiology/prevention & control/ therapy