Epidemiology of invasive meningococcal disease in North Queensland, 1995 to 1999

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Abstract

This study describes all episodes of invasive meningococcal disease (n=120) acquired in north Queensland over the 5 year period 1995 to 1999. Indigenous people had a 3-fold greater risk than others of acquiring invasive meningococcal disease. There were 7 deaths, six in non-indigenous people. The majority (72.4%) of identified isolates were serogroup B. We found no evidence of significant resistance to the antibiotics recommended for treatment or chemoprophylaxis. Two outbreaks of disease were identified, one serogroup B and one serogroup C. Compared to the previous 5 years (1990 to 1994) there were far fewer cases of serogroup C disease and a lower incidence and risk of invasive meningococcal disease among indigenous people. *Commun Dis Intell* 2002;26:44-50.

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Introduction

The epidemiology of invasive meningococcal disease in north Queensland from 1990 to 1994 has been reviewed previously.[1] In that period there were 69 cases with invasive meningococcal disease, giving an annual incidence of 3.3 per 100,000 population.[1] The incidence rate in indigenous people was 12.6 times that of non-indigenous people. From 1990 to 1994 seventy per cent of cases were caused by serogroup C *Neisseria meningitidis*, and there were 5 group C outbreaks. There were 3 deaths, all of indigenous people and all caused by group C organisms. In this paper we review the epidemiology of invasive meningococcal disease in north Queensland for the period 1995 to 1999, and make comparisons with the earlier study.[1]

Materials and methods

Case definition

Only cases of invasive meningococcal disease diagnosed and acquired in north Queensland between the beginning of 1995 and the end of 1999 were included in the study.

A confirmed case of invasive meningococcal disease was defined as a clinically compatible illness and at least one of the following:

- isolation of *N. meningitidis* from a normally sterile site;
- a positive PCR test for meningococcal DNA in a specimen from a normally sterile site;
- detection of Gram-negative intracellular diplococci in a specimen from a normally sterile site; or
- the detection of meningococcal antigen in CSF.

The PCR test became available in Queensland for the first time in 1999; a serological test for detecting meningococcal IgM did not become available until 2000.

A probable case of invasive meningococcal disease was defined as a clinically compatible illness with at least one of the following:

- a haemorrhagic rash;
- isolation of *N. meningitidis* from a throat swab; or
- close recent contact with a confirmed case.

Probable cases were notified for the first time in Queensland in 1999.

Since 1995, the geographical area included in the surveillance jurisdiction of north Queensland has been expanded to include the Mackay and Moranbah Health Service Districts (Figure 1). In 1996, the total population of north Queensland was 592,000, of whom approximately 48,000 (8%) were Indigenous.[2]

Figure 1. The Northern Public Health Zone of Queensland showing the 11 Health Service District jurisdictions

Case ascertainment

All cases of invasive meningococcal disease notified to The Tropical Public Health Unit in Cairns during the period 1 January 1995 to 31 December 1999 were collated. These data were supplemented with a search of the state-wide computerised notifiable diseases database for invasive meningococcal disease; one additional case was ascertained in this way. Information on indigenous status, clinical presentation and mortality for this case was also collected from these sources, and supplemented from hospital medical records.

Bacteriological data and methods

All laboratory data on meningococcal isolates examined by the Public Health Microbiology Laboratory, Queensland Health Scientific Services, Brisbane, were accessed. These data were searched and information on serogroup, serotype, serosubtype and antibiotic sensitivities was

collated. Serogrouping was performed on each isolate using commercially available antisera (Murex Biotech, England). Monoclonal reagents for sero/subtyping were obtained from the National Institute of Public Health and the Environment, Netherlands. Antibiotic sensitivities were determined using an agar plate dilution method as part of the set methodology adopted by the National *Neisseria* Network around Australia.[3]

Analysis

Data were entered into a MS Access database and analysed using MS Excel, the Statistical Package for the Social Sciences (SPSS) and Epi Info (Version 6.04b).

Incidence rates were calculated for each year for defined age groups, and for each Health Service District. Denominator populations were calculated from annual estimated resident populations. To compare risks in different age groups the incidence rate ratio (IRR), the ratio of the incidence in the age cohort of interest to the incidence in the reference age cohort (40+ years) was calculated[4] using Epi Info. The IRR was also calculated for indigenous people relative to non-indigenous people based on 1996 census data.[2]

Results

During the study period there were 120 notifications, 113 confirmed and 7 probable cases. Two notified cases were tourists, both of whom had been in north Queensland for at least 2 weeks before symptom onset, and therefore it was assumed that they had acquired their disease in the region.

The annual incidence of invasive meningococcal disease for the north Queensland zone varied between 2.9 and 5.0 cases per 100,000 population (Table 1). The incidence in 1999 when probable cases first became notifiable was 3.8 cases per 100,000 population for confirmed cases only.

Nearly three quarters of the infections were acquired within the Health Service Districts containing major population centres: Cairns, Townsville and Mackay. There was no significant difference in risk between the different Health Service Districts, except Cape York, which had no cases (Table 2).

Almost half the notified cases were females (58, 48.3%). The largest number of cases and the highest risk occurred in the 0-4 year age group, which had about 15 times the risk of those aged over 40 years (Table 3).

Table 1. Incidence rates for invasive meningococcal disease, north Queensland, 1995 to 1999, by year

Year	Number of cases	Incidence per 100,000 per annum
1995	27	4.9
1996	16	2.9
1997	21	3.7
1998	27	4.7
1999*	29	5.0
Total	**120**	**4.2**

* includes probable as well as confirmed cases. The rate in confirmed cases only was 3.8 cases per 100,000 population.

Twenty-five (20.8%) cases were in Aboriginal or Torres Strait Islander people yielding an incidence of 10.4 cases per 100,000 population. The incidence for non-indigenous people was 3.5 cases per 100,000 population. Indigenous people were three times more likely to develop invasive meningococcal disease than non-indigenous people (IRR = 3.0, 95% CI = 1.9-4.7).

There were 15 cases for which the serogroup was not determined; 7 of these were probable cases. During the study period a single case was diagnosed using PCR. At this time serogrouping using PCR was not being performed. Of the remaining seven, six had Gram-negative diplococci seen in cerebral spinal fluid (CSF), and one had *N. meningitidis* cultured in a district hospital laboratory, but the isolate was neither serogrouped nor forwarded to the reference laboratory. Ninety-two per cent of the 105 isolates that were serogrouped were caused by serogroup B (72.4%, 76) and serogroup C organisms (20.0%, 21). In all 5 years the majority of isolates were serogroup B *N. meningitidis*. There were no serogroup A isolates (Figure 2). Twenty-two isolates from the 25 indigenous cases were serogrouped; the majority (17, 77.3%) were serogroup B and three (13.6%) were serogroup C.

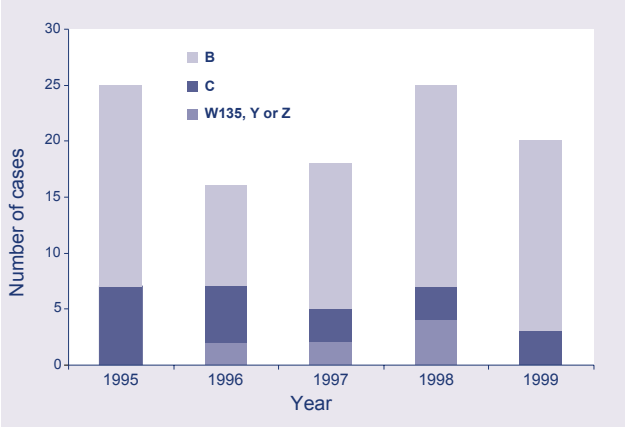
Table 2. Invasive meningococcal disease, north Queensland, 1995 to 1999, by Health Service District of acquisition

Health Service District	Number of cases	Per cent	Incidence per 100,000 per annum
Cairns	37	30.8	5.7
Townsville	28	23.3	3.7
Mackay	23	19.2	4.5
Bowen	7	5.8	4.4
Mount Isa	6	5.0	3.8
Moranbah	5	4.2	4.7
Charters Towers	4	3.3	5.0
Innisfail	4	3.3	2.5
Tablelands	4	3.3	2.2
Torres and northern peninsula area	2	1.7	4.5
Cape York	0	0.0	0.0

Table 3. Invasive meningococcal disease, north Queensland, 1995 to 1999, by age group

Age group	Number of cases	Incidence per 100,000 per annum	IRR and 95% CI	
0-4	48	21.1	15.4	8.5-28.0
5-9	17	7.5	5.5	2.7-11.1
10-14	7	3.2	2.3	0.9-5.8
15-19	14	6.8	4.9	2.4-10.4
20-29	16	3.4	2.5	1.2-5.1
30-39	4	0.8	0.6	0.2-1.9
40+	14	1.4	1.0	(Reference)

Figure 2. Invasive meningococcal disease, north Queensland, 1995 to 1999, by serogroup and year



Full serogroup, serotype and serosubtype could not be determined for all isolates. In part, this was because serotyping and subtyping was not performed during 1995 and 1996, but also because 41 isolates were non-typeable when serotyped and/or serosubtyped. Among the isolates there were three of the phenotype B:4:P1.4, however, these were tested using pulse-field gel electrophoresis, and were not genotypically of the New Zealand epidemic strain.[5] There were no isolates of the 'outbreak' virulent C strain C:2a:P1.5,[6] but there were 3 isolates with the C:2b:P1.2 phenotype,[1] all from non-indigenous cases.

There were 2 clusters in north Queensland during the study period, one each caused by serogroup B and serogroup C organisms. These have been described elsewhere.[7,8] Neither of these clusters occurred in indigenous communities.

There were 7 deaths due to invasive meningococcal disease. Three deaths occurred in patients with meningitis and four in patients with septicaemia. The case fatality rate for disease caused by serogroup C organisms was 9.5 per cent (2/21) and 6.6 per cent (5/76) for cases with serogroup B infections. Only one of the deaths occurred in an indigenous person, a one-year-old male who became unwell in Mt Isa in August 1998. The other 6 deaths were of 3 females aged between 3 months and 18 years, and 3 males aged between two and 20 years. One death occurred in 1995, two in 1998 and four in 1999.

Penicillin sensitivity was available for 83 (69.2%) of the 120 notified cases. None of these were 'relatively resistant' (MIC ≥ 1 mg/L). Nineteen (22.9%) were 'sensitive' (MIC ≤ 0.03 mg/L) and 64 (77.1%) were 'less sensitive' (MIC 0.06-0.5 mg/L).[9] Eighty-three isolates were tested for sensitivity to tetracycline; all were inhibited at 8 µg/ml. These isolates were also all inhibited at 5 µg/ml of spectinomycin, 0.008 µg/ml of ceftriaxone and 0.03 µg/ml of ciprofloxacin. Eighty isolates were tested for their sensitivity to rifampicin. Ten of these were not inhibited at the standard breakpoint of 0.125 µg/ml.

Discussion

This study and the earlier one by Hanna *et al*[1] describe relatively large numbers of cases of a rare disease over a considerable period of observation. Therefore, it is possible to make meaningful comparisons regarding changes in the epidemiology of invasive meningococcal disease in north Queensland over a decade. Two of the major changes observed are:

1. a decline in the proportion of cases caused by serogroup C *N. meningitidis* with a concomitant decline in the number of serogroup C clusters; and
2. a decline in risk for indigenous people in the second relative to the first period, manifest both as a lower IRR and fewer deaths (3.1 versus 12.6 and 1 versus 3, respectively). The differences between 1990 to 1994 and 1995 to 1999 are summarised in Table 4.

In Australia 63 per cent[9] and in Queensland 70 per cent[8] of *N. meningitidis* isolates obtained during 1999 were serogroup B. Our findings on serogroup are therefore consistent with the epidemiology of meningococcal disease in the State and the nation. The relative disappearance of serogroup C *N. meningitidis* is intriguing but fortunate because it resulted in relatively fewer outbreaks.

Considering the poor living conditions for indigenous people in Cape York and the high prevalence of cigarette smoking by indigenous adults in this area (65.2%, Well Person's Health Check, unpublished report, Tropical Public Health Unit, Cairns), the absence of cases of invasive meningococcal disease from Cape York was surprising. However, there was a marked decline in the overall incidence of invasive meningococcal disease in indigenous people in north Queensland in 1995 to 1999 compared to the previous 5 years (Table 4). A large proportion (43.8%) of people living in Cape York in 1996 were Indigenous.[2] Therefore, the causes of the reduced incidence of invasive meningococcal disease in indigenous

Table 4. Invasive meningococcal disease, north Queensland, 1990 to 1994 and 1995 to 1999

Parameter	1990 to 1994	1995 to 1999
Incidence (per 100,000 per annum)	3.3	4.2
Indigenous incidence (per 100,000 per annum)	20.2	10.4
IRR for indigenous people relative to others	12.6	3.0
Serogroup B (%)	26	72
Serogroup C (%)	70	20
Number of clusters	5	2
Number of serogroup C clusters	5	1
Number of serogroup C clusters in indigenous communities	3	0
Case fatality rate (%)	4.3	5.8
Case fatality rate for serogroup C (%)	6.3	9.5

people in north Queensland are likely, at least in part, to account for the absence of cases from Cape York. It should also be noted however, that the population of Cape York Health Service District was only 8,387 (1.4% of the North Queensland Health Zone)[2] and therefore one would not expect many cases from this area. The remoteness of much of the district may lead to under-reporting. No comparison with 1990 to 1994 is possible as cases were not reported by the Health Service District in the earlier study.[1]

Demographic changes are unlikely to account for the observed change in indigenous incidence. The 1991 census recorded only 7.5 per cent of the population in the North Queensland Health Zone as indigenous people (Fiona Tulip, data manager, Tropical Public Health Unit, Cairns, personal communication, 2001). In the 1996 census it was 8.1 per cent.[2] The major cause for the decline in the indigenous incidence is likely to be the decline in serogroup C disease, due to the decline or disappearance of clones that have a propensity to cause outbreaks. In the period 1990 to 1994, three of 5 outbreaks involved indigenous people, and two of these outbreaks involved C:2b:P1.2 *N. meningitidis*. These 2 outbreaks accounted for 13 (33.3%) of the 39 indigenous cases of invasive meningococcal disease.[1] By contrast, in 1995 to 1999 only 3 cases involved C:2b:P1.2 *N. meningitidis*, and none of these were in indigenous people. Of 22 people involved in 5 outbreaks caused by serogroup C organisms during 1990 to 1994, 16 (72.7%) were Indigenous. During 1995 to 1999, 2 outbreaks (one serogroup B and serogroup C) involved 6 people,[7,8] none of whom were Indigenous.

The incidence rate for invasive meningococcal disease in north Queensland during 1995 to 1999 (4.2 per 100,000 per annum) was higher than that reported for Sydney (2.3 per 100,000 per annum)[10] and other New South Wales areas (2.8 per 100,000 per annum)[10] in 1991 to 1999, and for Queensland during 1999 (2.8 per 100,000 per annum).[8] Indeed, for 1999 the incidence rate for north Queensland (5.0 per 100,000 per annum) was much higher than that for Queensland, and the rates both include probable cases and hence can be compared.

During the course of this study Queensland Health was using monoclonal antibodies to perform serosubyping and this resulted in many isolates being only partially typeable or non-typeable. This has also been seen by other researchers.[11] Queensland Health is currently introducing molecular serosubtyping, and this will reduce the non-typeable rate.

The prevalence of reduced sensitivity to penicillin (77%) was similar to that for Australia as a whole (74%) in 1999.[9] No north Queensland isolates were resistant (MIC ≥ 1 mg/L) to penicillin. All 83 isolates were fully sensitive to ceftriaxone and ciprofloxacin. Only one isolate had a raised MIC to rifampicin (MIC ≥ 1 mg/L). Our findings on

sensitivity to penicillin and ceftriaxone mean that current recommendations on treatment (benzylpenicillin with ceftriaxone or cefotaxime initially for bacterial meningitis, benzylpenicillin once penicillin sensitive *N. menigitidis* is isolated, ceftriaxone or cefotaxime if the patient is allergic to penicillin)[12] remain appropriate for north Queensland. The rarity of significant resistance to rifampicin and universal sensitivity to ceftriaxone and ciprofloxacin means that these antibiotics can all be safely recommended for chemoprophylaxis in north Queensland, as in current guidelines.[12]

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References

1. Hanna J, McCall B, Murphy D. Invasive meningococcal disease in north Queensland, 1990-1994. *Commun Dis Intell* 1996;20:320-324.
2. Tropical Public Health Unit Network. North Queensland District Health Services selected demography ABS census 1996. Cairns: Tropical Public Health Unit Network.
3. Australian Gonococcal Surveillance Programme, 1984. Penicillin sensitivity of gonococci in Australia: development of an Australian Gonococcal Surveillance Programme. *British Journal of Venereology* 60:226-230.
4. Rothman KJ. Modern Epidemiology. Boston/Toronto: Little, Brown and Company 1986.
5. Martin DR, Walker SJ, Baker MG, Lennon DR. New Zealand epidemic of meningococcal disease identified by a strain with phenotype B:4:P1.4. *J Infect Dis* 1998;177:497-500.
6. Whalen AM, Hockin JC, Ryan A, Ashton F. The changing epidemiology of invasive meningococcal disease in Canada, 1985 through 1992. *JAMA* 1995;273:2390-2394.
7. Brookes D, Richards A, Smith H. Tracking a meningococcal disease cluster: carriage on a train. Communicable Diseases Control Conference 2001. Canberra.
8. Ward J, Hanna JN, Bates JR, Selvey LA. Enhanced surveillance for meningococcal disease in Queensland in 1999. *Commun Dis Intell* 2000;24: 332-336.
9. Australian Meningococcal Surveillance Programme. Annual report of the Australian Meningococcal Surveillance Programme, 1999. *Commun Dis Intell* 2000;24:181-189.
10. McAnulty J, Habib M, Muscatello D. EpiReview: Meningococcal disease in NSW 1991-1999. NSW *Public Health Bulletin* 2000;11:128-130.
11. Jelfs J, Munro M, Wedege E, Caugaunt DA. Sequence variation in the porA gene of a clone of *Neisseria meningitidis* during epidemic spread. *Clin Diagn Immunol* 2000;7:390-395.
12. Spicer J, Christiansen K, Currie B, Fairley C, Ferguson J, Glasziou P et al. *Therapeutic Guidelines Antibiotic* 2000. North Melbourne: Therapeutic Guidelines Limited.