

Emergence of further serotypes of multiple drug-resistant *Streptococcus pneumoniae* in Queensland

Mike Gratten¹, Graeme Nimmo², Jane Carlisle¹, Jacqueline Schooneveldt², Erangini Seneviratne³, Robyn Kelly³, Rob Norton⁴, Chris Ashurst-Smith⁴, Kevin Love⁵, Susan Tiley⁶, Gillian Wood⁷ and Janine Fenton⁷

Abstract

We describe 27 cases of multiple drug-resistant pneumococcal infection in Queensland children (7 cases) and adults (20 cases), between February 1995 and October 1996. Seven patients had invasive disease. Serotypes were those commonly associated with paediatric infections and included types 19F (15 strains), 14 (6), 23F (4), 6A (1) and 19A (1). No rifampicin or vancomycin resistance was encountered. However, pneumococci fully resistant to cotrimoxazole, erythromycin and tetracycline were isolated from 25 of 27 cases (93%). Strains with high level resistance to penicillin and chloramphenicol were also recovered from 16 (59%) and 19 (70%) patients respectively. Twelve of 16 penicillin-resistant isolates showed intermediate resistance to ceftriaxone and two strains were fully resistant to this antibiotic. Clones of types 19F and 14 pneumococci, each with two distinctive resistance patterns, appear to be established in south-east Queensland. *Comm Dis Intell* 1997;21:133-136.

Introduction

Multiple drug resistance in pneumococci is defined as resistance to at least three

classes of antibiotics¹. The phenomenon was first recognised in 1977 in South Africa when a type 19A pneumococcus resistant to

penicillin, chloramphenicol, cotrimoxazole, erythromycin, tetracycline and clindamycin was isolated from the sputum of a child with pneumonia².

1. Acute Respiratory Infections Research and Reference Unit, Centre for Public Health Sciences, Queensland Health, GPO Box 495, Queensland 4001.
2. Princess Alexandra Hospital, Woolloongabba, Queensland.
3. Gold Coast Hospital, Southport, Queensland.
4. Townsville General Hospital, Townsville, Queensland.
5. Cairns Pathology Laboratory, Cairns, Queensland.
6. Queensland Medical Laboratory, Cairns, Queensland.
7. Prince Charles Hospital, Chermside, Queensland.

ISSN 0725-3141
Volume 21
Number 10
15 May 1997

Contents

Emergence of further serotypes of multiple drug-resistant <i>Streptococcus pneumoniae</i> in Queensland <i>Mike Gratten, Graeme Nimmo, Jane Carlisle, Jacqueline Schooneveldt, Erangini Seneviratne, Robyn Kelly, Rob Norton, Chris Ashurst-Smith, Kevin Love, Susan Tiley, Gillian Wood and Janine Fenton</i>	133
Meningitis in New South Wales	136
Communicable Diseases Surveillance	137
Overseas Briefs	144

Multiple drug-resistant pneumococci were subsequently documented in Spain, the United Kingdom, other European countries, the United States of America and Canada³. In Australia, untyped multiple drug-resistant pneumococci have been reported by both Western Australian and Queensland laboratories^{4, 5, 6, 7}. In 1992 a multiple drug-resistant clone of type 6B pneumococcus was identified in the upper respiratory tract of Aboriginal infants from a remote community in the Top End of the Northern Territory. These isolates were resistant to penicillin, chloramphenicol, cotrimoxazole, erythromycin and tetracycline⁸. In February 1995 a multiple drug-resistant type 6B pneumococcus (with an antibiogram similar to the Top End strains) caused septic arthritis in a seven month old child resident in Cairns⁹. Further multiple drug-resistant type 6B strains have been identified in north Queensland¹⁰.

Since February 1995, 27 cases of infection caused by multiple drug-resistant non-type 6B pneumococci have been identified in Queensland and are described here.

Methods

A pneumococcal surveillance program began in Queensland in 1989 and is based at the Acute Respiratory Infections Unit, Centre for Public Health Sciences, Queensland Health, Brisbane. Queensland laboratories were encouraged to refer to this unit any pneumococci isolated from normally sterile sites, as well as strains from any site which showed reduced susceptibility to one or more antibiotics. A pneumococcal transport system and referral guidelines were distributed.

All isolates were sero and factor typed with antisera from the Statens Seruminstitut, Copenhagen, Denmark. The minimal inhibitory concentrations (MIC) of eight antibiotics (penicillin, chloramphenicol, cotrimoxazole, erythromycin, tetracycline, ceftriaxone, rifampicin and vancomycin) were determined by the Etest (AB Biodisk, Sweden). MIC values were interpreted according to National Committee for Clinical Laboratory Standards (NCCLS) performance standards¹¹.

Results

Between February 1995 and October 1996, 430 pneumococcal isolates were referred to the Acute Respiratory Infections Unit from 14 Queensland laboratories. Of these, 286 (67%) were invasive isolates, and 144 (34%) were from non-sterile sites.

Multiple drug-resistant pneumococci were isolated from 20 adults aged 21 to 90 years and seven children aged two to 55 months. Seven patients had invasive disease; six were identified in two hospitals in south-east Queensland and one in north Queensland. Their isolates represented 3.9 per cent of 181 invasive pneumococci referred from the three hospitals during the study period. Six patients were bacteraemic and one had bacteraemic meningitis. Five were adults aged between 30 and 80 years and two were children aged less than two years. All survived.

Other samples or sites from which multiple drug-resistant pneumococci were isolated included sputum (14), upper respiratory tract secretions (4), bronchial washings (1) and conjunctivae (2). The same organism was recovered from two patients on separate occasions; from blood and CSF in one case and twice from sputum in the other.

Multiple drug-resistant pneumococci are detailed in the Table. No resistance to rifampicin and vancomycin was encountered. However, isolates from all cases were either fully (25 strains) or intermediately resistant (2) to cotrimoxazole. Nineteen strains (70%) were fully resistant to chloramphenicol, 25 (93%) to erythromycin and 25 (93%) to tetracycline. Penicillin-resistant pneumococci (MIC \geq 2.0 mg/L) were isolated from 16 patients (59%) and intermediately resistant strains (MIC = 0.1 - 1.0 mg/L) from a further two cases. Twelve of 16 penicillin-resistant isolates showed intermediate resistance to ceftriaxone (MIC = 1.0 mg/L) and two strains were fully resistant to this antibiotic (MIC = 2.0 mg/L).

The type distribution of multiple drug-resistant pneumococci included type 19F (15 isolates), type 14 (6), type 23F (4), type 6A (1) and type 19A (1). Twelve type 19F strains from

south-east Queensland possessed two distinctive resistance antibiograms which differed from those of three isolates from north Queensland. Of five type 14 isolates identified in south-east Queensland, one of two resistance patterns resembled that of the single north Queensland isolate. Each of the four type 23F pneumococci exhibited unique resistance profiles, with two differing only in the MIC of erythromycin (= 2.0 mg/L versus \geq 256 mg/L).

Discussion

This report describes the emergence of a further five multiple drug-resistant pneumococcal serotypes (6A, 14, 19F, 19A and 23F) in Queensland. Multiple drug-resistant type 6B infections have been previously reported^{9,10}. Because the surveillance of non-invasive pneumococci in Queensland is currently limited to strains showing antibiotic resistance, the overall incidence of resistant pneumococcal infections is unknown. Although one-quarter of our multiple drug-resistant isolates came from patients with invasive disease in three hospitals, these strains represented less than 4% of invasive pneumococci referred from these hospitals during the study period.

Since the first report of a multiple drug-resistant pneumococcus in South Africa in 1977, broad spectrum antibiotic resistance among pneumococci has become a global problem¹. Multiple drug-resistant pneumococci are confined largely to paediatric groups and types such as 6, 14, 19 and 23 which colonise the upper respiratory tract of young children and cause invasive disease in both children and adults. A study of upper respiratory tract carriage in young Aboriginal children hospitalised in Alice Springs with acute lower respiratory infection showed that 64% of 136 colonised subjects carried pneumococcal types 6A, 6B, 14, 19F, 19A and 23F¹². More recently, 17% of 95 adults in north Queensland and 46% of 89 Aboriginal children in central Australia with invasive disease were infected with pneumococcal types normally associated with paediatric infection^{13, 14}. Immunisation of young children with conjugate pneumococcal vaccine may not only

Table. Multiple drug-resistant *Streptococcus pneumoniae* serotypes by resistance pattern, region and isolation site/source

Serotype (number)	Resistance pattern	South-east Queensland (n=21)			North Queensland (n=6)			Site/source
		PAH	GCH	PCH	TGH	CP	QML	
19F(15)	Cotrimoxazole, Erythromycin, Tetracycline.	2						Upper respiratory tract
	Chloramphenicol, Cotrimoxazole, Erythromycin, Tetracycline.	6						Blood (2), conjunctivae, Sputum (2), upper respiratory tract
	Penicillin, Chloramphenicol, Cotrimoxazole, Erythromycin, Tetracycline.	2	2					Sputum
	Penicillin, Chloramphenicol, Cotrimoxazole, Tetracycline.					1		Upper respiratory tract
	Penicillin, Cotrimoxazole, Erythromycin, Tetracycline.				1	1		Blood and cerebrospinal fluid, sputum
14(6)	Penicillin, Cotrimoxazole, Tetracycline.	1						Blood
	Penicillin, Chloramphenicol, Cotrimoxazole, Erythromycin, Tetracycline.	3		1			1	Blood (2), sputum (2), upper respiratory tract
23F(4)	Cotrimoxazole, Erythromycin, Tetracycline.	1						Blood
	Penicillin, Chloramphenicol, Cotrimoxazole, Erythromycin.	1						Conjunctivae
	Penicillin, Chloramphenicol, Cotrimoxazole, Erythromycin ¹ , Tetracycline.	1						Sputum
	Penicillin, Chloramphenicol, Cotrimoxazole, Erythromycin ² , Tetracycline.						1	Bronchial washing
6A(1)	Penicillin, Cotrimoxazole, Erythromycin, Tetracycline.				1			Sputum
19A(1)	Penicillin, Cotrimoxazole, Erythromycin.	1						Sputum

PAH Princess Alexandra Hospital
GCH Gold Coast Hospital
PCH Prince Charles Hospital
TGH Townsville General Hospital
CP Cairns Pathology
QML Queensland Medical Laboratory

1. Erythromycin MIC = 2.0 mg/L
2. Erythromycin MIC ≥ 256 mg/L

reduce invasive disease, but also eradicate upper respiratory tract carriage of serotypes associated with antibiotic resistance^{15,16}.

The epidemiology of multiple drug-resistant pneumococci has been associated with hospitalised children and adults receiving antibiotics¹. In our study only two of five cases of bacteraemia diagnosed at Princess Alexandra Hospital were nosocomial infections. In the wider community however, the carriage and transmission of multiple drug-resistant pneumococci among young children may increase the distribution of multiple drug-resistant types in adults. Two American studies of community acquired multiple drug-resistant pneumococcal infection in day care centres found that, in addition to children occupying the same room as the index cases, staff and parents also became colonised with the multiple drug-resistant strain^{17,18}.

The most common resistance patterns encountered in the current study included those of strains resistant to four or more antibiotics. Fifteen of 17 such isolates belonged to types 19F (10 strains) and 14 (5). Analysis of resistance patterns suggests that several clones, distinct from those in north Queensland, exist in south-east Queensland and that one has caused two cases of bacteraemia. Two clones of multiple drug-resistant type 14 pneumococci, both responsible for invasive disease, have also been identified. The resistance profiles of four type 23F isolates differ significantly. The genomic DNA of all multiple drug-resistant pneumococci will be examined to determine their type-specific genetic relatedness.

The emergence of multiple drug-resistant pneumococcal clones in Queensland is in keeping with a recently published national survey and further highlights the need for increased awareness and vigilance by diagnostic laboratories and

clinicians¹⁹. The occurrence of multiple drug-resistant strains with high level resistance to both penicillin and third generation cephalosporins in invasive infection, particularly meningitis, will create a real dilemma in the choice of antibiotic therapy for these conditions.

The true prevalence of multiple drug-resistant pneumococci in Queensland is unknown since a number of hospitals in central and south-east Queensland are not linked to the surveillance network. A laboratory-based monitoring system is required which ensures that all pneumococci isolated from normally sterile sites are submitted for typing and antibiotic susceptibility testing. In addition, cross sectional studies incorporating longitudinal upper respiratory tract sampling of at-risk populations such as children in day care centres, inpatients of paediatric wards and children residing in Aboriginal communities are needed to determine the prevalence of, and increase in, drug-resistant pneumococci in upper respiratory sites.

References

1. Klugman KD. Pneumococcal resistance to antibiotics. *Clin Microbiol Rev* 1990;3:171-196.
2. Jacobs MR, Koornhof HJ, Robins-Browne M *et al*. Emergence of multiple resistant pneumococci. *N Engl J Med* 1978;299:735-740.
3. Appelbaum PC. Antimicrobial resistance in *Streptococcus pneumoniae*: An overview. *Clin Infect Dis* 1992;15:77-83.
4. Byrnes P. Multiple resistant *Streptococcus pneumoniae* infection. *Med J Aust* 1993;159:427-428.
5. Cooper G, Tandy M, Bielenberg P. Increased incidence of antibiotic resistant pneumococci in a Queensland pathology practice. *Comm Dis Intell* 1994;18:90-91.
6. Leung M, Stingmore N, McGechie DB. Prevalence of penicillin resistant *Streptococcus pneumoniae*. *Med J Aust* 1994;160:449-450.
7. Cooper G, McDougall R. High level penicillin resistant pneumococcus in Australia: report of an isolate. *Comm Dis Intell* 1994;18:474.

8. Leach AJ, Shelby-James T, Mayo M *et al*. Report of a multidrug resistant clone of *Streptococcus pneumoniae* (MRSPN) in Aboriginal infants in the Northern Territory. *Comm Dis Intell* 1995;19:134-137.
9. Hanna J, Brookes D, Muscio P *et al*. A multiple antibiotic-resistant pneumococcus in Cairns: case report and investigation. *Comm Dis Intell* 1995;19:261-264.
10. Gratten M, Tiley S. Multi-drug resistant pneumococci in North Queensland. *Trop Public Health Unit North Queensland Newsletter* 1996;No.17:4-5.
11. Performance standards for antimicrobial susceptibility testing. Sixth informational supplement M100-S6. Villanova: National Committee for Clinical Laboratory Standards, 1995.
12. Gratten M, Manning K, Dixon J *et al*. Upper airway carriage by *Haemophilus influenzae* and *Streptococcus pneumoniae* in Australian Aboriginal children hospitalised with acute lower respiratory infection. *Southeast Asian J Trop Med Public Health* 1994;25:123-131.
13. Hanna J, Gratten M, Tiley S *et al*. Pneumococcal vaccination: an important strategy to prevent pneumonia in Aboriginal and Torres Strait Island adults. *Aust NZ J Public Health* (in press).
14. Gratten M, Torzillo P, Morey F *et al*. Distribution of capsular types and antibiotic susceptibility of invasive *Streptococcus pneumoniae* isolated from Aborigines in central Australia. *J Clin Microbiol* 1996;34:338-341.
15. Dagan R, Melamed R, Muallem M *et al*. Reduction of nasopharyngeal carriage of pneumococci during the second year of life by a heptavalent conjugate pneumococcal vaccine. *J Infect Dis* 1996;174:1271-1278.
16. Obaro SK, Adegbola RA, Banya WAS *et al*. Carriage of pneumococci after pneumococcal vaccination [letter]. *Lancet* 1996; 348:271-272.
17. Radetsky M, Istre G, Johansen TL *et al*. Multiple resistant pneumococcus causing meningitis: its epidemiology within a day-care centre. *Lancet* 1981;iii:771-773.
18. Reichler M, Allphin AA, Breiman RF *et al*. The spread of multiple resistant *Streptococcus pneumoniae* at a day care centre in Ohio. *J Infect Dis* 1992;166:1346-1353.
19. Collignon PJ, Bell JM. Drug-resistant *Streptococcus pneumoniae*: the beginning of the end for many antibiotics? *Med J Aust* 1996; 164:64-67.

Meningitis in New South Wales

Fifteen cases of meningococcal disease were reported from western Sydney between January and May 1997. Seven cases were aged under five years and five were aged 15 - 24 years. Of the 15 cases, six were due to serogroup C, four serogroup B (two untypable, one B:4:P1.4 and one B:2b:P1.10) and five were based on a clinical diagnosis. The Western Sector Public Health Unit has not established an epidemiological link between cases, however five isolates were phenotype C:2a:P1.5, which was the phenotype identified in a western Sydney outbreak in 1996. Thirty-six cases of meningococcal disease have been reported in New South Wales during 1997. A total of 165 cases was reported during 1996.