Prevalence of Antimicrobial Resistances in *Streptococcus pneumoniae* Isolates in Australia, 2005: Report from the Australian Group on Antimicrobial Resistance (AGAR)

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Introduction

Streptococcus pneumoniae is a common cause of meningitis and bacteraemia as well as community-acquired respiratory tract infections such as pneumonia, sinusitis, and otitis media. Rates of resistance to penicillins and other classes of antimicrobials have increased over the past two decades, compromising treatment efficacy particularly for meningeal infections.

The Australian Group on Antimicrobial Resistance (AGAR) performs regular multicentre period-prevalence studies to monitor changes in antimicrobial resistance. Resistance rates from this current study were compared to those from previous AGAR surveys conducted in 1989 (where only penicillin was tested), 1994, 1999 and 2002.

Methods

Twenty institutions from the 5 mainland states and the Australian Capital Territory (ACT) participated in the *S. pneumoniae* AGAR survey. Starting 1st January 2005, each laboratory collected up to 100 consecutive significant clinical isolates.

Identification: Alpha-haemolytic, optochin sensitive, and/or bile-soluble, Gram-positive cocci were identified as *S. pneumoniae*. Any strain with an optochin zone of inhibition of between 6 and 14mm in CO_2 was tested for bile solubility.

Susceptibility testing: Participating laboratories performed antimicrobial susceptibility tests according to each laboratory's routine standardised methodology (CDS, CLSI or BSAC disc diffusion, Vitek2®, agar dilution or MIC testing). Clindamycin and erythromycin discs were placed side by side to look for clindamycin inducibility. Penicillin and moxifloxacin MICs were determined for all isolates using Etest® strips. Four hundred and seventy one (95%) of the 497 isolates that were penicillin intermediate or resistant (MIC >0.064 mg/L) were also tested with either a ceftriaxone or cefotaxime Etest® strip. CLSI (2009) guidelines were used for interpretations.

Results

A total of 1,776 *S. pneumoniae* isolates were included in the study. 20% of isolates were from invasive infections (predominantly blood).

Penicillin: The new penicillin CLSI breakpoints (Table 1) were employed for this survey. Overall 497/1,776 (28%) isolates were non-susceptible to oral penicillin. All of the blood culture isolates were susceptible to the parenteral (nonmeningitis) breakpoints. One CSF isolate (MIC 0.25mg/L) was resistant by the parenteral (meningitis) breakpoint. Trend data shows that overall penicillin resistance continues to increase for invasive and non-invasive strains however since 2005 high-level resistant strains have continued to increase whereas intermediate strains have declined (Figures 2 and 3).

Ceftriaxone/cefotaxime: Cefotaxime or ceftriaxone MICs were determined on 95% of penicillin non-susceptible strains. Fourteen isolates (3.0%) were resistant to either cefotaxime or ceftriaxone.

Erythromycin and clindamycin: 404/1,776 (22.7%) isolates were erythromycin resistant. Resistance was significantly higher (P<0.001) in non-invasive (24.6%) compared with invasive strains (15.1%). 228/1,462 (15.6%) isolates were clindamycin resistant. Of 364 erythromycin resistant isolates, 222 (61%) had a MLS_B constitutive resistant phenotype and 6 (1.6%) had inducible resistance. Trend data shows that erythromycin resistance for all strains is increasing albeit slowly. A decline in resistance from 19.2% to 15.1% over the last two surveys was evident for invasive strains (Figure 4).

Results continued

Table 1 CLSI (2009) interpretive standards for penicillin

Antimicrobial agent	MIC Interpretive Standard (mg/L)		
	S	I	R
Penicillin parenteral (nonmeningitis)	≤2	4	≥8
Penicillin parenteral (meningitis)	≤0.06	-	≥0.12
Penicillin (oral penicillin V)	≤0.06	0.12-1	≥2

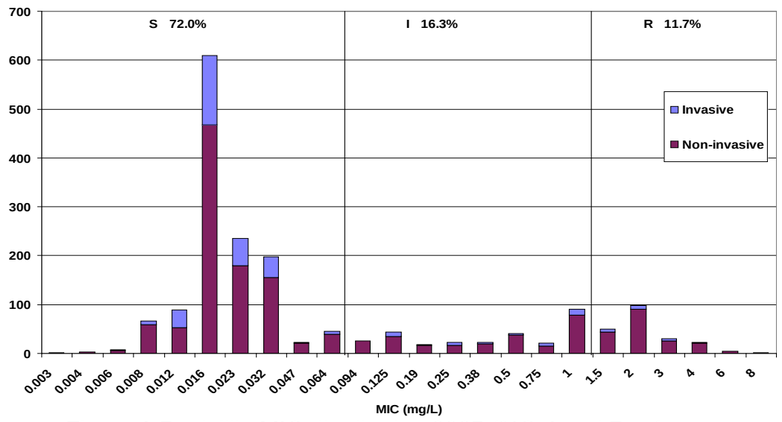

Figure 1 Penicillin MIC distribution 2005 (%S, I and R refer to oral penicillin breakpoints)

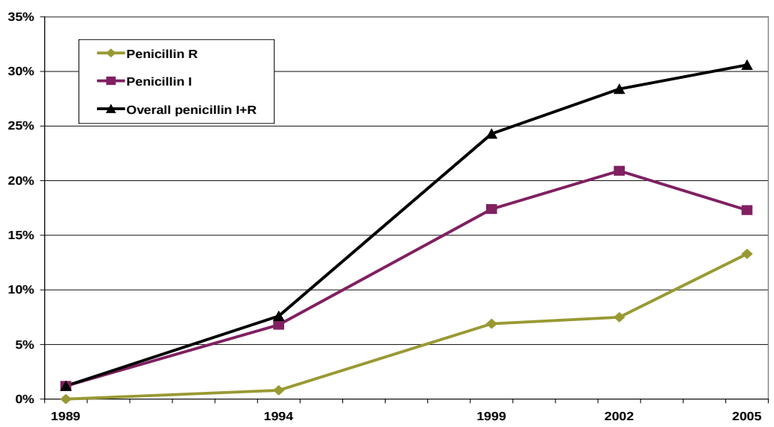

Figure 2 Trends in penicillin for non-invasive isolates 1989-2005

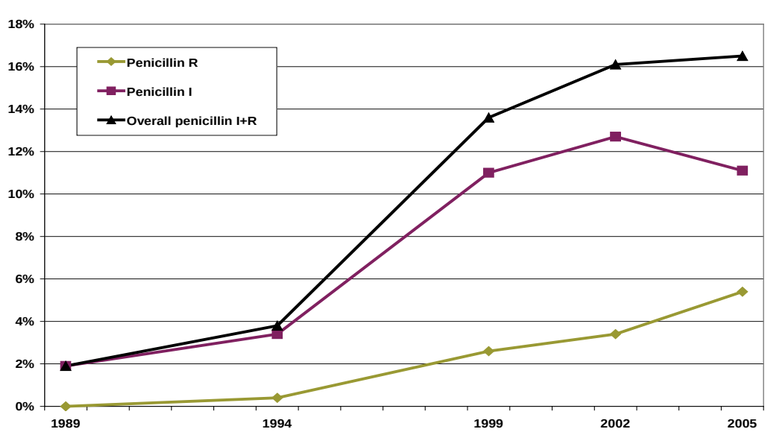

Figure 3 Trends in penicillin for invasive isolates 1989-2005

Tetracycline: 326/1,775 (18.4%) isolates were tetracycline resistant. There was a significant difference (P<0.001) in tetracycline resistance among non-invasive (21.3%) and invasive (6.3%) strains. Trend data shows that after an increase in resistance in non-invasive isolates from 1994 to 1999, overall resistance has remained relatively steady from 1999 to 2005 (Figure 5).

Co-trimoxazole: 550/1,775 (31.0%) isolates were co-trimoxazole resistant. Resistance was significantly higher (P<0.05) in non-invasive (32.2%) compared with invasive (25.6%) strains. Trend data shows decreasing rates of resistance in invasive isolates from 1994 to 2005 and a decrease for non-invasive strains from 2002 to 2005 (Figure 6).

Levofloxacin and moxifloxacin: Levofloxacin resistance was detected in only four of 1,775 (0.2%) isolates tested. Intermediate resistance to levofloxacin was detected in another four isolates. Moxifloxacin resistance was present in two isolates with MICs of 3 mg/L and 4 mg/L.

Results continued

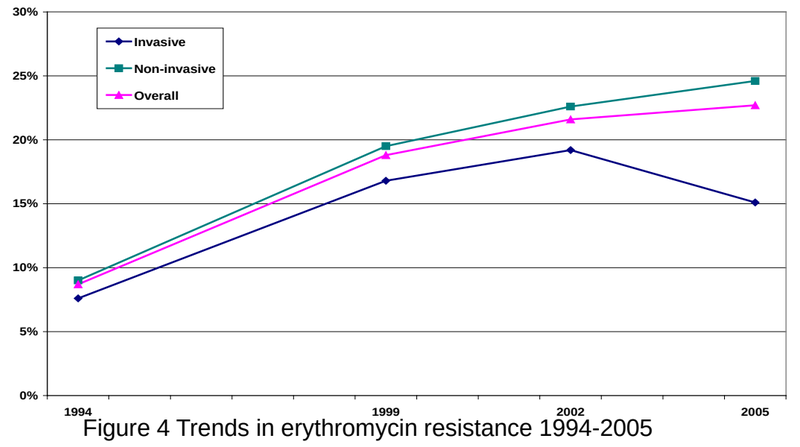

Figure 4 Trends in erythromycin resistance 1994-2005

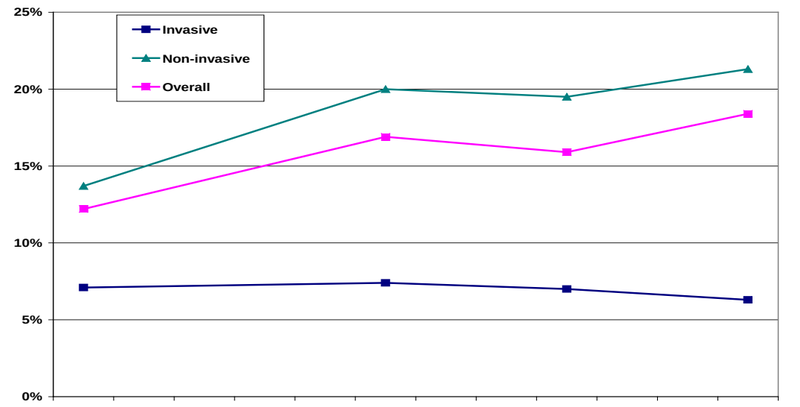

Figure 5 Trends in tetracycline resistance 1994-2005

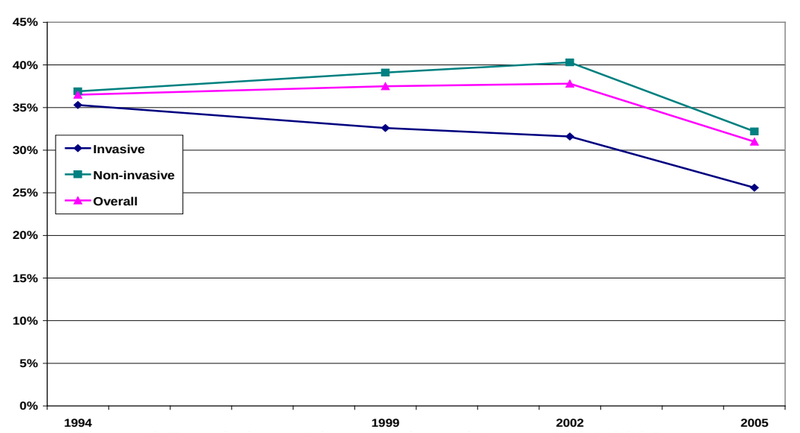

Figure 6 Trends in co-trimoxazole resistance 1994-2005

Table 2 Multi-resistance in *S. pneumoniae*, 2005

		Non-multiresistant				Multi-resistant		
Source	No.	0	1	2	%	3	4	%
Invasive	351	216	77	37	94.0	12	9	6.0
Non-invasive	1425	789	213	136	79.9	75	212	20.1
Total	1776	1005	290	173	82.7	87	221	17.3

Multi-resistance: 17.3% of isolates were multi-resistant (acquired resistance to >2 drug classes) (Table 2). Multi-resistance was significantly higher (P<0.001) in non-invasive strains (20.1%) compared with invasive strains (6.0%).

Conclusions

Penicillin non-susceptibility continues to rise, mainly due to the increase of high-level resistant strains in invasive and non-invasive infections. Macrolide resistance continues to increase with current rates at 23%. Of concern is the high proportion of multi-resistant strains with almost one in five strains resistant to three or more antimicrobial classes.

Acknowledgements

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