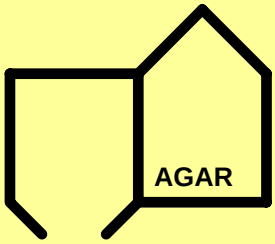

The Australian Group on Antimicrobial Resistance
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Enterococcus spp Survey
2005 Antimicrobial Susceptibility Report

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Antimicrobial Susceptibility Report of *Enterococcus* Isolates from the Australian Group on Antimicrobial Resistance (AGAR)

2005 Surveillance Report

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1 Executive Summary

Twenty two institutions around Australia conducted a point prevalence study of key resistances in isolates of *Enterococcus* species causing clinical disease amongst in- and outpatients in 2005. Each site collected up to 100 consecutive isolates and tested them for susceptibility to ampicillin, vancomycin, high-level gentamicin and/or high-level streptomycin using standardised methods. Results were compared to similar surveys conducted in 1995, 1999 and 2003. In the 2005 survey, *E. faecalis* (1987 strains) and *E. faecium* (180 strains) made up 98.6% of the 2197 isolates tested. Ampicillin resistance is now very common (77%) in *E. faecium*, but rare still in *E. faecalis* (0.2%). Resistance to vancomycin was 7.2 % in *E. faecium* and 0.2% in *E. faecalis*; the *vanB* gene was detected in all isolates. High-level resistance to gentamicin was 35.8% in *E. faecalis* and 52.2% in *E. faecium*; the figures for high-level streptomycin were 10.3% and 60.2% respectively. Compared to previous years, the proportions of vancomycin resistance and high-level gentamicin resistance in enterococci are increasing.

It is important to have an understanding of the occurrence of VRE and high level aminoglycoside resistance in Australia to guide infection control practices, antibiotic prescribing policies and drug regulatory matters.

2 Introduction

2.1 Objective of the Programme

The objective of the 2005 surveillance program was to determine the proportion of antimicrobial resistance in clinical isolates of *Enterococcus* spp throughout Australia, with particular emphasis on:

1. Assessing susceptibility to ampicillin
2. Assessing susceptibility to glycopeptides
3. Assessing changes in resistance patterns over time using data collected in previous AGAR surveys

AGAR commenced surveillance of antimicrobial resistance in *Enterococcus* spp in 1995. Similar surveys were conducted in 1995, 1999, 2003 and 2005.[1,2]

2.2 Importance of *Enterococcus* spp

Enterococci are part of the normal flora of the gastrointestinal tract. They can give rise to endogenous infections such as urinary tract infections outside of hospitals. In hospitals they can be transmitted through poor infection control practices and can give rise to a wide variety of infections usually in patients with co-morbidities. The two main species causing infections in humans are *Enterococcus faecalis* (80–90%) and *Enterococcus faecium* (5-10%) with only a very small number of other species being isolated from clinical specimens. Enterococci are recognised as significant nosocomial pathogens causing urinary tract, blood stream, sterile site and wound infections. Enterococci although resistant to many antibiotics have been generally susceptible to amoxycillin and vancomycin. *Enterococcus faecium* has become increasingly resistant to ampicillin/amoxycillin making vancomycin the treatment of choice for severe infections caused by this organism. Since 1988 resistance to vancomycin has emerged and increased worldwide and is widespread in Europe and the USA. The National Nosocomial Infections Surveillance System (NNIS) in the USA has demonstrated a rising resistance rate for enterococci causing infections in ICU patients with a 2003 rate of 28.5%.[3] The first vancomycin resistant enterococcal isolate (VRE) was reported in Australia in 1994[4] and a report on the emergence and epidemiology of VRE in Australia was described in 1998[5] when 69 isolates had been documented. Prevalence or incidence rates of VRE in Australian hospitals are not routinely collected although there have been reports of individual hospital outbreaks of VRE infections and associated colonisation of other patients.[6,7,8,9,10] The clinical impact of vancomycin resistance in enterococci has been reported to increase mortality, length of stay and hospital costs.[11,12,13] Infection control measures can be used to eradicate the organism from a hospital or to prevent it from becoming established.[6]

Enterococci cause 5-18% of all cases of endocarditis, both on prosthetic and normal heart valves.[14,15,16] Combination therapy of a ß-lactam and an aminoglycoside (gentamicin or streptomycin)[17,18,19] has been the standard treatment for at least 50 years as use of ß-lactams alone are associated with high relapse rates (30-60%). Aminoglycosides are not routinely used to treat other enterococcal infections but in endocarditis the synergy between the two agents provides a cure. Synergy does not occur if the organism has high level gentamicin or streptomycin resistance (MIC> 500mg/L).

It is important to have an understanding of the occurrence of VRE and high level aminoglycoside resistance in Australia to guide infection control practices, antibiotic prescribing policies and drug regulatory matters.

2.3 Antimicrobials Tested and Resistance

2.3.1 ß-lactams

Penicillin (IV benzylpenicillin) and ampicillin/amoxycillin (oral and IV) are the principle therapeutic agents used for the treatment of infections caused by enterococci.

Ampicillin: Testing of this agent is used to predict susceptibility to penicillin and amoxycillin. Resistance to penicillin/ampicillin most commonly results from alterations to penicillin binding proteins. Resistance is rarely mediated by a ß-lactamase.[20]

2.3.2 Glycopeptides

Vancomycin resistance is mediated by one of a number of gene clusters carried either on a transposon or on the chromosome. Organisms with a VanA phenotype are resistant to both vancomycin and teicoplanin whereas organisms with the VanB phenotype are resistant to vancomycin only. Both these phenotypes are located on transmissible genetic elements. Resistance is due to changes in the ligase gene that results in an alteration of the glycopeptide binding site. Several other genes in the cluster potentiate this alteration.
Resistance can be detected by the use of a screening plate or routine susceptibility testing. The result is confirmed by detection of the *vanA* or *vanB* genes by PCR.

2.3.3 Aminoglycosides

High level resistance to aminoglycosides (MIC >500–2000mg/L) is mediated by plasmid borne aminoglycoside modifying enzymes (most commonly a fused 6'-acetyltransferase-2'-phosphotransferase for gentamicin, tobramycin, amikacin and a 6-adenylyltransferase for streptomycin). Possession of these enzymes eliminates synergy between the aminoglycoside and the ß-lactam.

3 Methods

Twenty two institutions from all Australian states and the Australian Capital Territory (ACT) participated in the *Enterococcus* spp survey. Commencing on the 1st January 2005 each participating laboratory collected 100 consecutive, significant, clinical isolates of enterococci. Only one isolate per patient was tested unless a different antibiogram was observed from routine susceptibility results. For each isolate the following information was obtained: date of collection, age, sex, specimen source, and inpatient or outpatient status.

3.1 Species identification

All isolates were tested for pyrrolidonyl arylamidase (PYR) and esculin hydrolysis in the presence of bile with optional testing for growth in 6.5% NaCl, Group D antigen and growth at 45°C. Isolates were identified to species level by one of the following methods: API 20S, rID32Strep, Vitek or Vitek 2, Microscan, PCR, or conventional biochemical tests. If biochemical testing was performed, the minimum tests necessary for identification were: motility, pigment production, methyl-α-D-glucopyranoside (MGP), fermentation of 1% raffinose, 1% arabinose, 1% xylose and pyruvate utilisation.

3.2 Susceptibility Testing Methodology

Participating laboratories performed antimicrobial susceptibility tests according to each laboratory's routine standardised methodology[21,22,23,24,25] (CLSI, CDS or BSAC disc diffusion, Vitek, Vitek 2, agar dilution or CLSI broth microdilution). Antimicrobials that were tested by all laboratories included ampicillin and vancomycin. In addition, all isolates were screened for high level gentamicin and 1201 (55%) isolates were screened for high level streptomycin resistance using one of the following susceptibility methods – Vitek (GPS-TA or GPS-TB), Vitek 2 (AST-P535, AST-P526 or AST-P524), CLSI, CDS or BSAC disc diffusion, agar or broth dilution.
All isolates were tested for ß-lactamase production using nitrocefin.

3.3 Quality Control

Additional quality control was not performed for this survey. As all participating laboratories are NATA accredited, routine QC testing of antimicrobial susceptibility test methods is an integral part of routine procedures. However, all isolates that were resistant to vancomycin were referred to the appropriate state NaVREN laboratory for molecular testing to confirm organism identification and resistance phenotype. All isolates were stored at -70°C for further testing if required by AGAR.

4 Demographics

4.1 Regional Source of isolates

Both public (19) and private (3) laboratories participated in this study. Participants included New South Wales (6), ACT (1), Queensland (3), Victoria (4), South Australia (3), Western Australia (4) and Tasmania (1). There were 2197 isolates from 22 institutions (Table 1). *E. faecalis* was the most frequently isolated species (90.4%) followed by *E. faecium* (8.2%) (Table 2). To ensure institutional anonymity data from NSW and ACT isolates have been combined. Similarly, data from Tasmania and Victoria have also been combined.

Table 1. Isolates by Region

Region	Participating Laboratories (n)	Isolates (n)	%
Queensland (Qld)	3	300	13.7
New South Wales/Australian Capital Territory (NSW/ACT)	7	699	31.8
Victoria/Tasmania (Vic/Tas)	5	499	22.7
South Australia (SA)	3	299	13.6
Western Australia (WA)	4	400	18.2
Total	**22**	**2197**	**100**

Table 2. Species by Region

Region	*E. faecalis*	*E. faecium*	Other Spp.	Total
Qld	286	12	2	300
NSW/ACT	619	72	8	699
Vic/Tas	449	47	3	499
SA	280	13	6	499
WA	353	36	11	400
Aus	1987 (90.4%)	180 (8.2%)	30 (1.4%)	2197

4.2 Age and Sex distribution

The age distribution of patients reflect the association of infection with other predisposing medical conditions more commonly seen in the elderly or very young. Isolation of enterococci was more common in women, in keeping with the greater incidence of urinary tract infections in

that sex. Of note however is the greater proportion of *E. faecium* (63.9%) from women compared to men (36.1%) (Table 3). 1417 (64.5%) patients were classified as hospital inpatients at time of collection and 696 (31.7%) were outpatients. Hospitalisation status was not available for 84.

Table 3. Age and Sex Distribution by Species

Age Range	***E. faecalis***	***E. faecium***	**Other Spp.**	**Total (%)**
<2	129		2	131 (6.0)
2-4	26	2	1	29 (1.3)
5-14	45	2	1	48 (2.2)
15-29	131	5	1	137 (6.2)
30-59	442	53	8	503 (22.9)
≥60	1214	118	17	1349 (61.4)
Sex				
Female	1041	115	9	1165 (53.0)
Male	946	65	21	1032 (47.0)

5 Specimen Source

The majority of isolates (73.6%) were from the urinary tract (Table 4). These were predominantly *E. faecalis* (93.7%). Invasive (primarily blood, CSF and sterile cavity) isolates comprised 10.3% of the total number collected. *E. faecium* was disproportionately represented in the invasive group (18.9%). Of the *E. faecalis* isolates, 8.7% were invasive compared to 23.9% of *E. faecium.*

Table 4. Source of Isolates

Source	***E. faecalis***	***E. faecium***	**Other Spp.**	**Total**
Urine	1514	96	6	1616 (73.6%)
Wound	157	22	9	188 (8.6%)
Blood/CSF	110	27	8	145 (6.6%)
Sterile Site	62	16	4	82 (3.7%)
Other	144	19	3	166 (7.6%)
Total	**1987**	**180**	**30**	**2197**
Invasive	172	43	12	227 (10.3%)
Non-invasive	1815	137	18	1970 (89.7%)

6 Susceptibility Testing Results: 2005 Study and Trend Data Surveys 1995, 1999, 2003, 2005

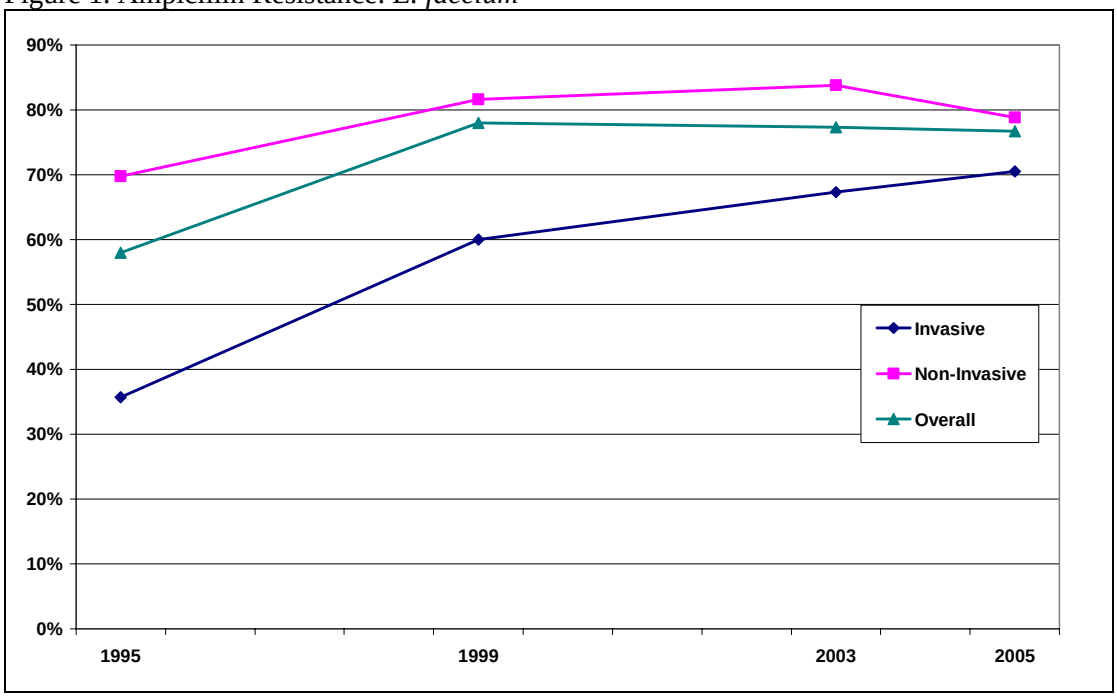
6.1 Ampicillin

Resistance to ampicillin was predominantly in the *E. faecium* isolates where the proportion of resistance was similar across all the states except Queensland where the rate was lower (Table 5). Resistance in all species was due to penicillin binding protein changes. 2077 (94.5%) of the isolates were tested for ß-lactamase; none were positive. Trend data for *E. faecium* show an initial increase in ampicillin resistance between 1995 and 1999 with a plateau from 1999 to 2005 (Figure 1).

Table 5. Ampicillin Resistance. Number Resistant/Total (%)

	QLD	NSW/ACT	VIC/TAS	SA	WA	AUS
E. faecalis	0/286 (0)	1/619 (0.2)	0/449 (0)	0/280 (0)	2/353 (0.6)	3/1987 (0.2)
invasive	0/22 (0)	0/76 (0)	0/35 (0)	0/8 (0)	0/31 (0)	0/172 (0)
E. faecium	7/12 (58.3)	57/72 (79.2)	36/47 (76.6)	10/13 (76.9)	28/36 (77.8)	138/180 (76.7)
invasive	2/4 (50.0)	18/20 (80.0)	8/12 (66.7)	0/0 (0)	4/7 (57.1)	30/43 (69.8)

Figure 1. Ampicillin Resistance: *E. faecium*



6.2 Vancomycin

Vancomycin resistance was uncommon in *E. faecalis* (0.2%). A total of 7.2% of *E. faecium* were vancomycin resistant with a greater proportion isolated from invasive infections. Resistant organisms were detected in three of the five regions (Table 6). The sixteen vancomycin resistant enterococci were all confirmed by PCR and were of the *vanB* genotype. 13 (81.2%) were *E. faecium* (Table 7). Trend data for *E. faecium* show that after no vancomycin resistance was detected in 1995 there has been a marked increase, particularly for the invasive category (Figure 2) during the study periods. Vancomycin resistant *E. faecium* have occurred in all 5 regions over the four survey periods, with Vic/Tas showing the greatest increases in VRE over time.

Table 6. Vancomycin Resistance. Number Resistant/Total (%)

	QLD	NSW/ACT	VIC/TAS	SA	WA	AUS
E. faecalis	0/286 (0)	1/619 (0.2)	1/449 (0.2)	0/280 (0)	1/353 (0.3)	3/1987 (0.2)
invasive	0/22 (0)	0/76 (0)	0/35 (0)	0/8 (0)	0/31 (0)	0/172 (0)
E. faecium	0/12 (0)	1/72 (1.4)	10/47 (21.3)	0/13 (0)	2/36 (5.6)	13/180 (7.2)
invasive	0/4 (0)	1/20 (5.0)	3/12 (25.0)	0/0 (0)	0/7 (0)	4/43 (9.3)

Table 7. Vancomycin Resistant Enterococci

	E. faecalis	*E. faecium*	Genotype
Specimen source			
Urine	3	5	*vanB*
Wound		3	*vanB*
Blood		1	*vanB*
Sterile site		3	*vanB*
other		1	*vanB*
Total	**3**	**13**	

Figure 2 Vancomycin Resistance: *E. faecium*

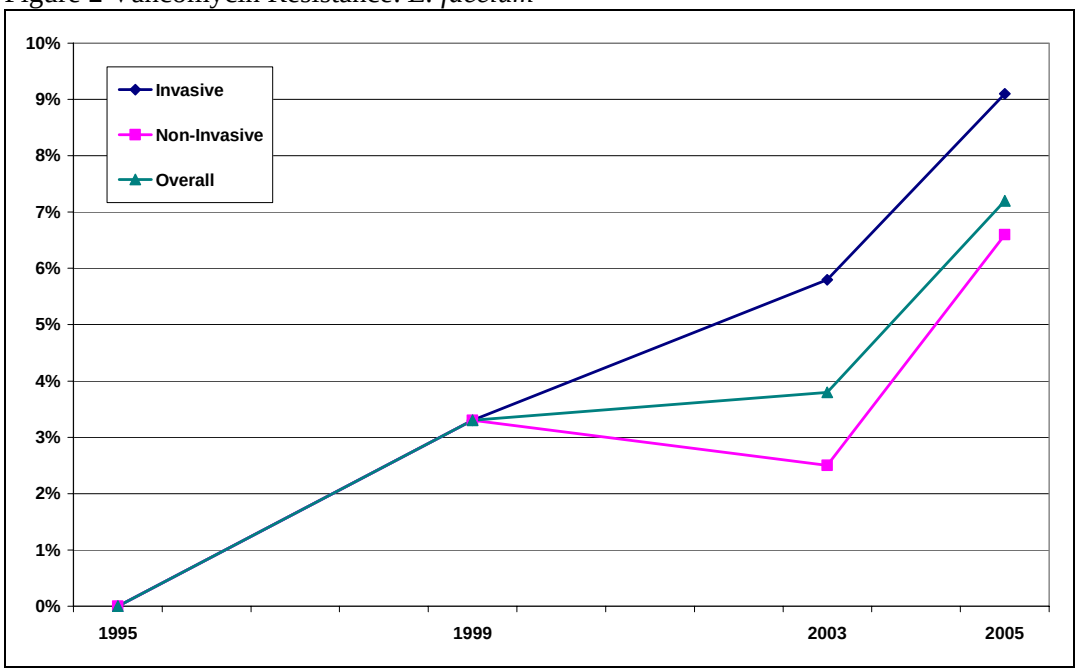
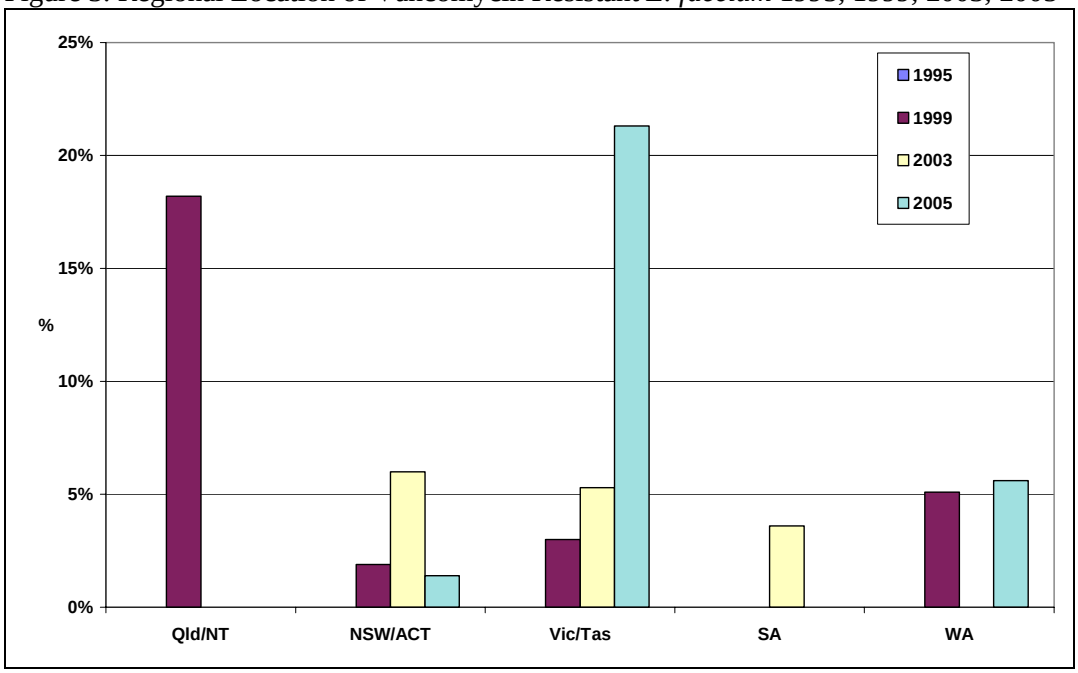


Figure 3. Regional Location of Vancomycin Resistant *E. faecium* 1995, 1999, 2003, 2005



6.3 Aminoglycosides

6.3.1 Gentamicin

High level gentamicin (HLG) resistance was seen in both *E. faecalis* (35.8%) and *E. faecium* (52.2%) with comparable proportions in most regions (Table 8). Trend data for 1995 to 2005 (Figures 4 and 5) show an increase in HLG resistance over the last 10 years. However, in *E. faecium*, HLG has reached a plateau whilst in *E. faecalis* resistance is continuing to increase.

Table 8. High Level Gentamicin Resistance

	QLD	NSW/ACT	VIC/TAS	SA	WA	AUS
E. faecalis	101/286 (35.3)	243/619 (39.4)	145/448 (32.4)	58/280 (20.7)	163/353 (46.2)	710/1986 (35.8)
invasive	7/22 (31.8)	34/76 (44.7)	10/35 (28.6)	2/8 (25.0)	15/31 (48.4)	68/172 (39.5)
E. faecium	7/12 (58.3)	48/72 (66.2)	12/47 (25.5)	9/13 (69.2)	18/36 (50.0)	94/180 (52.2)
invasive	2/4 (50.0)	16/20 (80.0)	2/12 (16.7)	0/0 (0)	5/7 (71.4)	25/43 (58.1)

Figure 4. High level Gentamicin Resistance: *E. faecium*

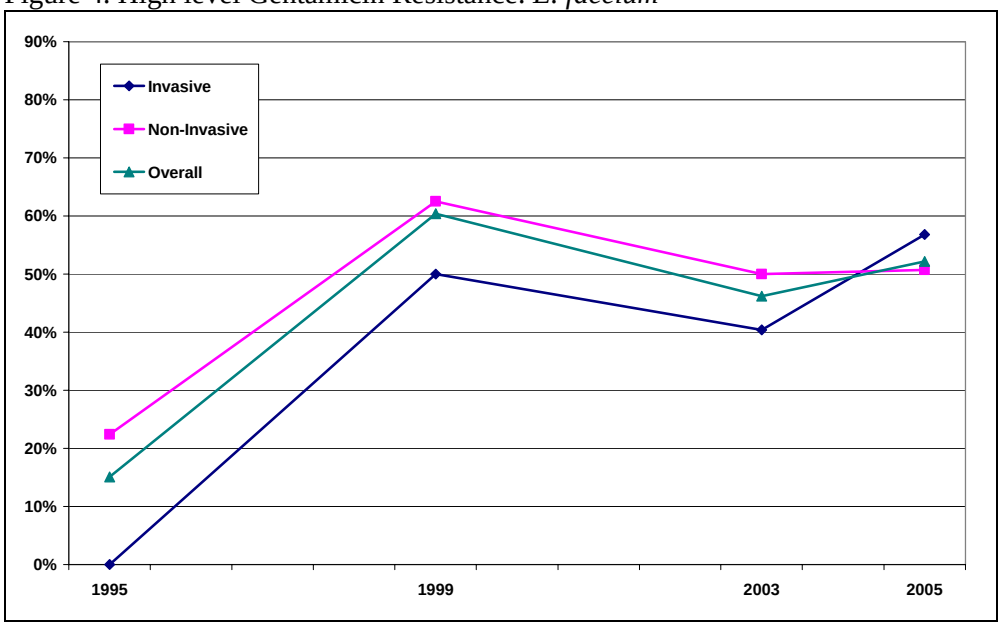
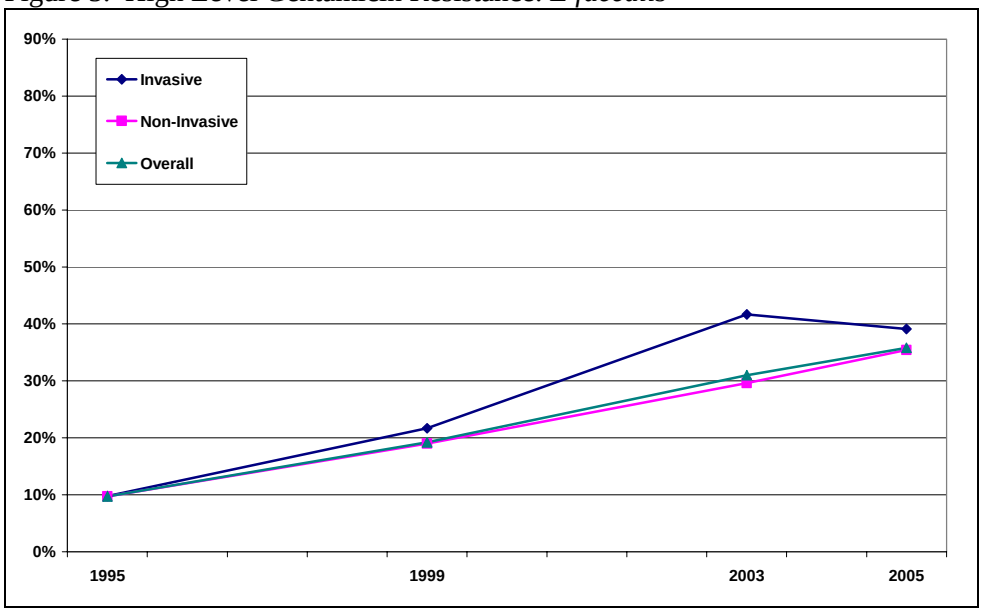


Figure 5. High Level Gentamicin Resistance: *E faecalis*



6.3.2 Streptomycin

High level streptomycin resistance (HLS) as with HLG resistance is more common for *E. faecium* than *E. faecalis* (Table 9). The trend since 1995 is for increasing resistance particularly for invasive isolates of *E. faecium* (Figures 6 and 7). The rate of increase in HLS is similar to that for HLG for *E faecium*. In *E faecalis*, the HLS is relatively stable with lower rates of expression than HLG.

Table 9. High Level Streptomycin Resistance

	QLD	NSW/ACT	VIC/TAS	SA	WA	AUS
E. faecalis	40/286 (14.0)	32/348 (9.2)	11/90 (12.2)	22/280 (7.9)	8/88 (9.1)	113/1092 (10.3)
invasive	2/22 (9.1)	5/36 (13.9)	1/9 (11.1)	0/8 (0)	1/5 (20.0)	9/80 (11.2)
E. faecium	6/12 (50.0)	25/50 (50.0)	7/8 (87.5)	9/13 (69.2)	9/11 (81.8)	56/94 (60.2)
invasive	3/4 (75.0)	8/13 (61.5)	2/2 (100)	0/0 (0)	2/3 (66.7)	15/22 (68.2)

Figure 6. High Level Streptomycin: *E. faecium*

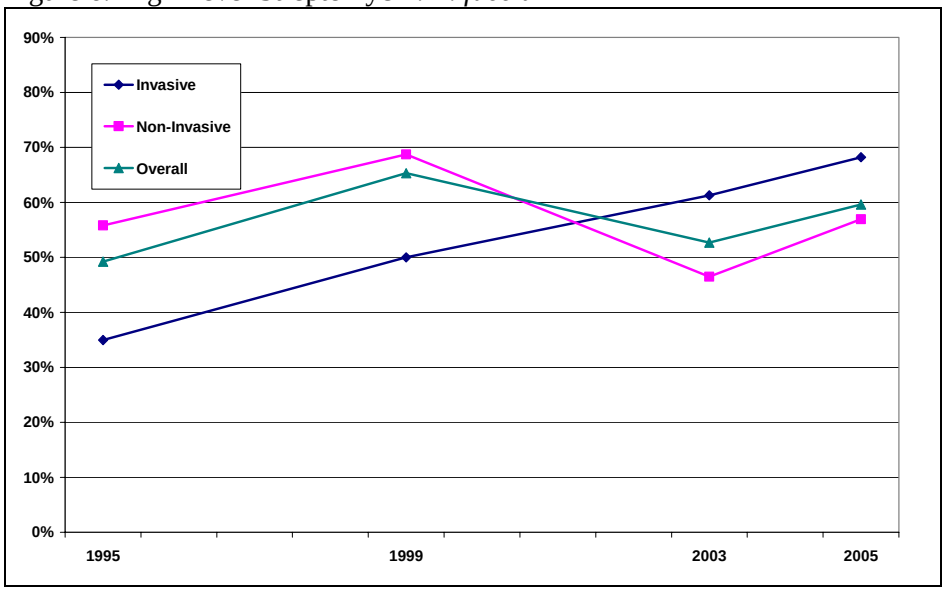
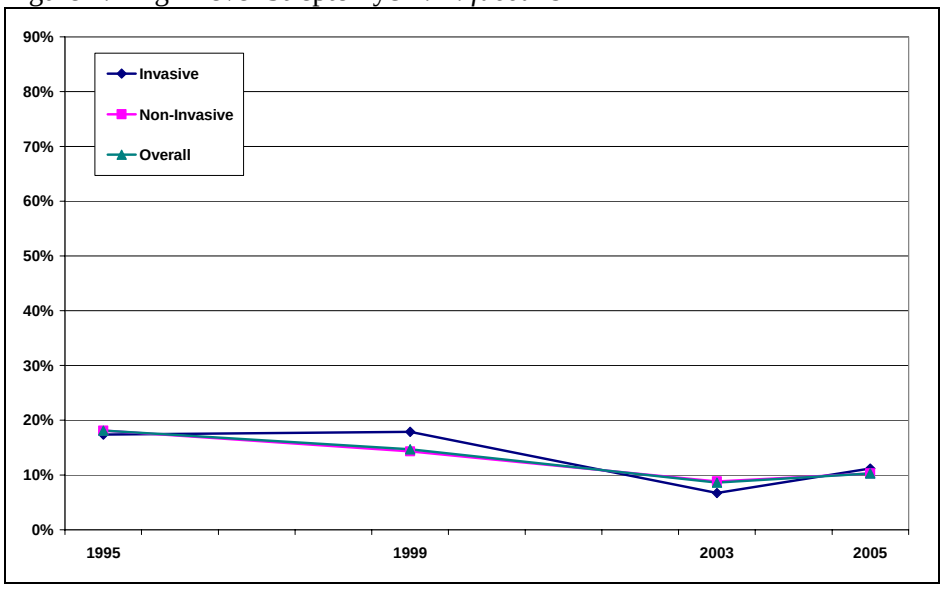


Figure 7. High Level Streptomycin: *E. faecalis*



6.3.3 Relationship between HLG and HLS resistance by location

E. faecalis: High level gentamicin resistance for all regions was the predominant feature for aminoglycosides (Figure 8).
E. faecium: The proportion of resistance varied between the states with HLS being higher than HLG in Vic/Tas and WA. There is a reversal of this finding in NSW/ACT and Qld (Figure 9).

Figure 8 *E. faecalis* Aminoglycoside (HLG, HLS) Resistance by Region

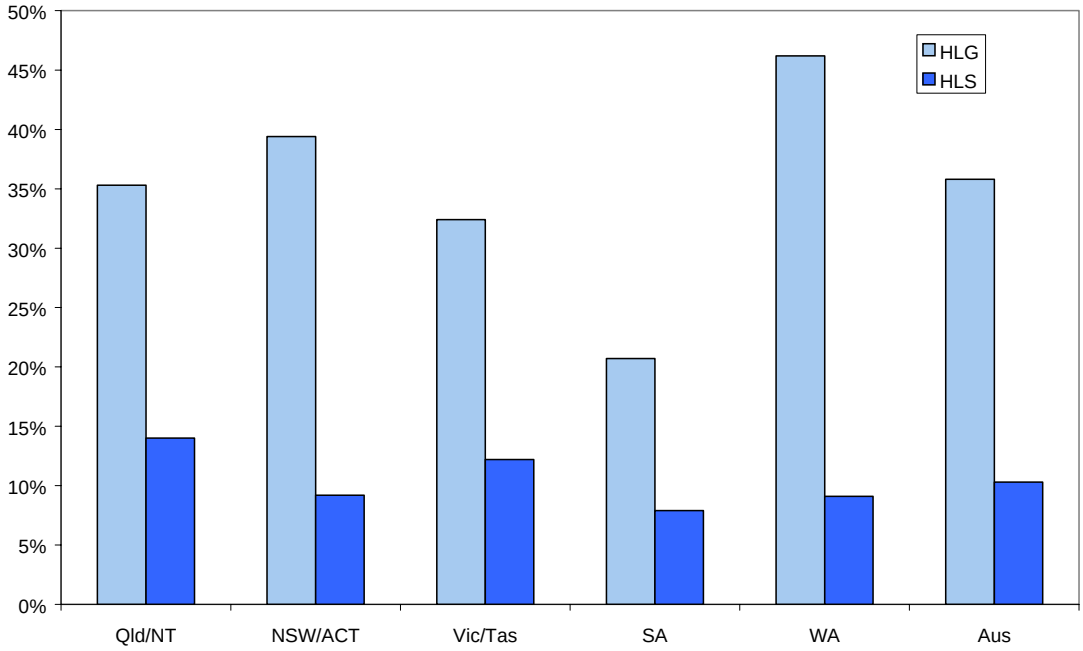
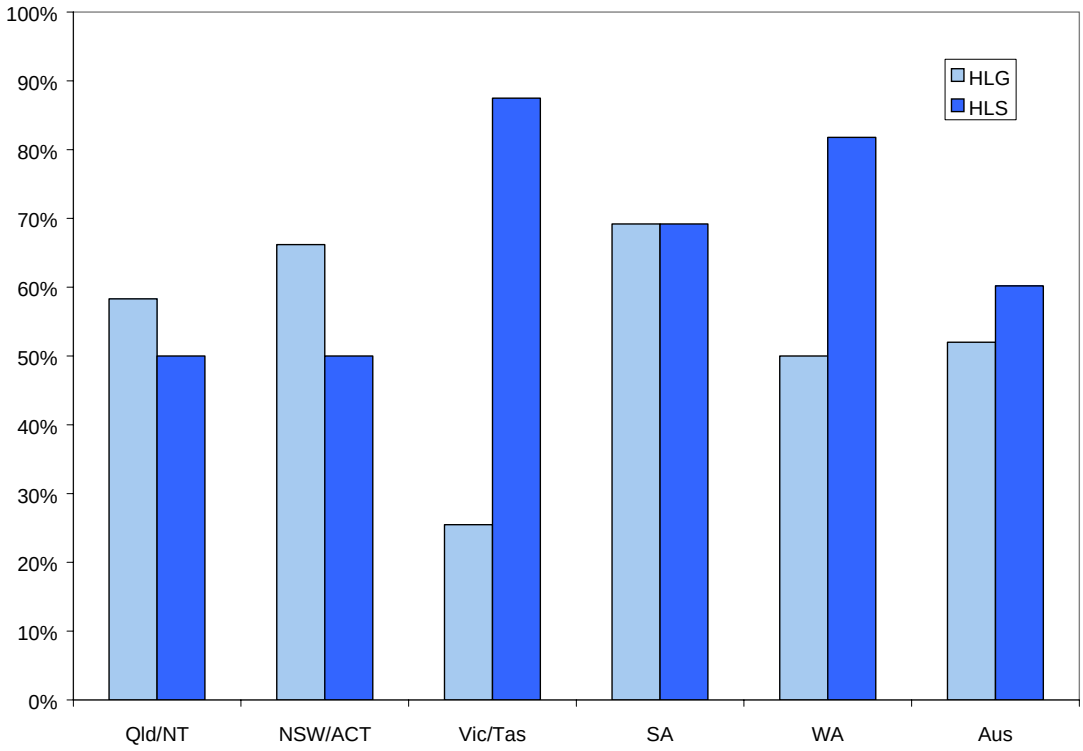


Figure 9 *E. faecium* Aminoglycoside (HLG, HLS) Resistance by Region



7 Cross Resistance

Cross resistance to other agents was examined in vancomycin resistant strains of enterococci (Table 9). Resistance to ampicillin and high levels of gentamicin and streptomycin was more common in VRE, except for high-level gentamicin resistance in *E. faecium*.

Table 9. Cross Resistance in VRE

Species	Agent	Ampicillin NS (%)	Gentamicin NS (%)	Streptomycin NS (%)
E. faecalis	**Vancomycin S**	3/1984 (0.2%)	707/1983 (36%)	113/1092 (10%)
	Vancomycin R	0/3 (0%)	3/3 (100%)	NT
E. faecium	**Vancomycin S**	127/167 (76%)	89/167 (53%)	52/90 (58%)
	Vancomycin R	11/13 (85%)	5/13 (38%)	9/13 (69%)

NS = Non Susceptible NT = Not Tested

8 Limitations of the Study

The enterococci in this study were tested against a limited range of antimicrobials. In part this was driven by the presence of intrinsic resistances in this genus. Enterococci are intrinsically resistant to cephalosporins, macrolides, lincosamides and conventional therapeutic levels of aminoglycosides when used alone. A number of newer reserve agents are active against enterococci: quinupristin-dalfopristin (a streptogramin combination), which is active against most species except *E. faecalis*, and linezolid (an oxazolidinone). These two agents could be included in future surveys. Other agents which are usually active against enterococci in urinary tract infection, including fluoroquinolones and nitrofurantoin, were also not examined largely because few clinical treatment problems have been encountered up to now with enterococcal UTI.

It is likely that the number of wound isolates in this study is under-represented, as it is common for microbiology laboratories not to proceed with identification of enterococci when they are found in mixed cultures from wound infections.

As only a maximum of 100 isolates were collected per institution only a portion of actual clinical isolates are represented.

There have been changes in participating laboratories in the AGAR *Enterococcus* surveys over time from 1995 through to 2005 with the more recent inclusion of a number of private pathology laboratories. This may have influenced trend data.

9 Discussion

It is clear from this study and the examination of trends over the last 10 years that resistance problems are increasing significantly in *E. faecium*. Furthermore, this species is accounting for an increasing proportion of invasive disease. Treatment options for this species are becoming ever more limited as resistance to ampicillin and other penicillins is now very high, and glycopeptide resistance is increasing (7% across Australia, range 0-21% in 2005). In some instances only expensive and/or potentially toxic treatment options such as linezolid, quinupristin-dalfopristin or tigecycline are available.

In *E. faecium*, ampicillin resistance is the result of changes in penicillin-binding proteins. This is also true for most strains of *E. faecalis*, although ß-lactamase production has been seen rarely (3 known instances in Australia in the last decade).[20] No ß-lactamase-producing strains of enterococci were detected in this survey. This survey has shown that ampicillin resistance is now the norm in *E. faecium* but is still uncommon in *E. faecalis*. Ampicillin resistance in enterococci presents considerable challenges when infections are serious, as the strains will not be susceptible to any ß-lactam, and the drug of choice becomes vancomycin, which is only slowly bactericidal. Further, for endocarditis the combination of vancomycin with an aminoglycoside creates significant toxicity problems.

Unfortunately vancomycin resistance in enterococci is slowly increasing in Australia. It has been seen in all states and territories although rates in each region seem to vary considerably. It is widely recognised that rates of colonisation far exceed the rates of infection with VRE, and thus the amount of VRE seen in our survey do not truly reflect the size of the VRE reservoir. The survey results are also consistent with the previous Australian experience that the dominant type of resistance is encoded by the *vanB* complex[26], in contrast with the situation in Europe and the USA where *vanA* dominates. Vancomycin-resistant strains causing serious infection are very challenging to treat. The choices are linezolid, quinupristin-dalfopristin and the recently released tigecycline. Each of these agents presents its own challenges for treatment as well.
The increasing rates of high-level resistance to aminoglycosides (except for streptomycin resistance in *E. faecalis*) is surprising. It is not clear what is driving this increase. For *E. faecium* it may well be the increase in resistant clones which are becoming established in some hospitals. Loss of susceptibility to high levels of aminoglycosides greatly compromises the ability to effectively treat enterococcal endocarditis.

The data provided by this survey will be useful in informing microbiologists, infectious diseases physicians and infection control practitioners about the increasing importance of VRE in Australia. It will help to guide prescribers treating presumptive enterococcal infections in empirical choices; e.g. ampicillin/amoxycillin still being active against the vast majority of strains of *E. faecalis* when treating infections caused by this organism. Finally, the data will assist regulators and the pharmaceutical industry on the growing importance of VRE in Australia, and guide decision makers about controls that might be required on reserve antibiotics.

10 References

1. Bell J, Fernandes L, Coombs G, Fernandes C. Prevalence of antimicrobial resistance in enterococci in Australian teaching hospitals. 11th European Congress of Clinical Microbiology and Infectious Diseases. *Clin Micr Infect* 2001;S1:24.
2. Nimmo G, Bell J, Collignon P, on behalf of the Australian Group for Antimicrobial Resistance (AGAR). Fifteen years of surveillance by the Australian Group for Antimicrobial Resistance (AGAR). *Commun Dis Intell* 2003;27:547-54.
3. National Nosocomial Infections Surveillance (NNIS) System Report, data summary from January 1992 through June 2004, issued October 2004. *Am J Infect Control* 2004;32:470-85.
4. Kamarulzaman, A, Tosolini FA, Boquest AL, Geddes JE, Richards MJ. Vancomycin-resistant *Enterococcus faecium* in a liver transplant patient. *Aust NZ J Med* 1995;25:560.
5. Bell J, Turnidge J, Coombs G, O'Brien F. Emergence and epidemiology of vancomycin-resistant enterococci in Australia. *Commun Dis Intell* 1998;22:249-52.
6. Christiansen KJ, Tibbett PA, Beresford B, Pearman J, Lee R, *et al*. Eradication of a large outbreak of a single strain of vanB vancomycin-resistant *Enterococcus faecium* at a major Australian teaching hospital. *Infect Control Hosp Epidemiol* 2004;25:384-90.
7. Cooper E, Paull A, O'Reilly M. Characteristics of a large cluster of vancomycin-resistant enterococci in an Australian hospital. Infect *Control Hosp Epidemiol* 2002;23:151-3.
8. Bartley PB, Schooneveldt JM, Looke DF, Morton A, Johnson DW, Nimmo GR. The relationship of a clonal outbreak of *Enterococcus faecium vanA* to methicillin-resistant *Staphylococcus aureus* incidence in an Australian hospital. *J Hosp Infect* 2001;48:43-54.
9. MacIntyre C, Empson M, Boardman C, Sindhusake D, Lokan J, Brown G. Risk factors for colonisation with vancomycin-resistant enterococci in a Melbourne hospital. *Infect Control Hosp Epidemiol* 2001;22:624-9.
10. Padiglione A, Grabsch E, Olden D, Hellard M, Sinclair M, Fairley C, Grayson M. Fecal colonization with vancomycin-resistant enterococci in Australia. *Emerg Infect Dis* 2000;6:534-6.
11. Joels C, Matthews B, Sigmon L, Hasan R, Lohr C *et al*. Clinical characteristics and outcomes of surgical patients with vancomycin-resistant enterococcal infections. *Am Surg* 2003;69:514-9.
12. DiazGranados C, Zimmer S, Klein M, Jernigan J. Comparison of mortality associated with vancomycin-resistant and vancomycin susceptible enterococcal bloodstream infections: A meta-analysis. *Clin Infect Dis* 2005;41:327-33.

13. DiazGranados C, Jernigan J. Impact of vancomycin resistance on mortality among patients with neutropenia and enterococcal bloodstream infection. *J Infect Dis* 2005;191:588-95.
14. Kazanjian P. Infective endocarditis: Review of 60 cases treated in community hospitals. *Infect Dis Clin Pract* 1993;5:41.
15. Serra P, Brandimarte C, Martino P *et al.* Synergistic treatment of enterococcal endocarditis. *Arc Intern Med* 1977;137:1562.
16. Mergran D. Enterococcal endocarditis. *Clin Infect Dis* 1992;15:63.
17. Pelletier L, Petersdorf R,. Infective endocarditis: a review of 125 cases from the University of Washington Hospitals, 1963-72. *Medicine (Baltimore)* 1997;56:287-313.
18. Murray B. The life and times of the enterococcus. *Clin Microbiol Rev* 1990;3:46-65.
19. Eliopoulos G, Eliopoulis C. Therapy of enterococcal infections. *Eur J Clin Microbiol Infect Dis* 1990;9:118-26.
20. McAlister T, George N, Faoagali J, Bell J. Isolation of a β-lactamase positive vancomycin resistant *Enterococcus faecalis*; first case in Australia. *Commun Dis Intell* 1999:23:237-239.
21. Bell S, Gatus B, Pham J, Rafferty D. Antibiotic susceptibility testing by the CDS method: A manual for medical and veterinary laboratories. Third edition 2004. www.med.unsw.edu.au/pathology-cds
22. BSAC disc diffusion method for antimicrobial testing. Version 3.1 2004. www.bsac.org.uk
23. Clinical and Laboratory Standards Institute (2006). Performance standards for antimicrobial susceptibility testing; Sixteenth Informational Supplement. M100-S16. CLSI, Villanova, PA, USA.
24. Clinical and Laboratory Standards Institute (2006). Methods for dilution antimicrobial susceptibility tests for bacteria that grow aerobically. Approved standard – seventh edition. M7-A7. CLSI, Villanova, PA, USA.
25. National Committee on Clinical Laboratory Standards (2003). Performance standards for antimicrobial disk susceptibility tests: approved standard – eighth edition. M2-A8. NCCLS, Wayne, PA, USA.
26. Bell J, Paton JC, Turnidge J. Emergence of vancomycin-resistant enterococci in Australia: phenotypic and genotypic characteristics of the isolates. *J Clin Microbiol* 1998;2187-90.