Antimicrobial Susceptibility of *Staphylococcus aureus* in New Zealand in 1999

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by

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C O N T E N T S

SUMMARY

Staphylococcus aureus is a virulent pathogen that commonly causes community-acquired and hospital-acquired infections. The increased prevalence of methicillin-resistant *S. aureus* (MRSA) is causing a major public health problem in many countries. With many MRSA strains, vancomycin is the only effective antimicrobial agent. The recent emergence of vancomycin-intermediate *S. aureus* has raised fears about untreatable staphylococcal infections.

A national survey of the susceptibility of *S. aureus* was conducted in March 1999. A total of 583 clinically significant isolates collected by 38 hospital and community laboratories throughout New Zealand were tested for susceptibilities to a range of antimicrobial agents by an agar dilution method in ESR.

The majority of the 583 *S. aureus* were isolated from community patients (79.5%) and from wound, skin and abscesses (80.6%). The prevalence of resistance was 89% to penicillin, 28% to mupirocin, 17% to fusidic acid, 5.7% to erythromycin, 1.9% to oxacillin and gentamicin, 1.4% to clindamycin, 1.2% to ciprofloxacin, 0.9% to chloramphenicol, 0.2% to rifampicin and trimethoprim-sulphamethoxazole, 0% to vancomycin. Using a disc diffusion induction test, 13.7% of the isolates were shown to be macrolide-lincosamide (ML) resistant, the majority with inducible ML resistance. Eleven (1.9%) of the isolates, five of which were MRSA, were resistant to at least four antimicrobials.

Notably high-level mupirocin resistance accounted for 14.2% of the isolates. Mupirocin-resistant isolates occurred in all regions and in hospital and community patients. However, there were significant regional differences and mupirocin-resistant *S. aureus* were significantly more prevalent among community patients. In contrast, high-level mupirocin-resistant *S. aureus* were equally common among hospital and community patients. Fusidic acid resistance did not significantly differ between regions or between community and hospital patients.

It is reassuring that the prevalence of MRSA was less than 2%. However, the high prevalence of mupirocin and fusidic acid resistance is of concern as mupirocin is an important topical antibiotic for the eradication of MRSA and renewed interest has been shown in the use of fusidic acid for treating MRSA. The survey results indicate that a variety of antistaphylococcal agents are still effective against a large proportion of *S. aureus* in New Zealand.

RECOMMENDATIONS

- Disseminate the results obtained in this survey to all health professionals
- Examine the quantities and use patterns for mupirocin and fusidic acid in New Zealand
- Surveillance of the antimicrobial resistance among *Staphylococcus aureus* should continue and another national survey should be carried out within three to five years.

1 INTRODUCTION

Staphylococcus aureus is a virulent organism that is renown for its potential to acquire resistance to antimicrobial agents [1]. *S. aureus* is one of the most common causes of community-acquired and nosocomial infections and is a major cause of surgical wound and nosocomial bloodstream infections.

Penicillin was initially successful in treating *S. aureus* infections during and immediately after World War II but bacterial resistance to penicillin began to emerge and currently nearly 90% of *S. aureus* isolates are penicillin-resistant. Methicillin and other semisynthetic penicillins were successful in treating penicillin-resistant *S. aureus* until the 1980s, when methicillin-resistant
S. aureus (MRSA) became endemic in many hospitals. MRSA are often multiresistant and the glycopeptide vancomycin has been the only uniformly effective treatment for staphylococcal infections.

The recent emergence of vancomycin-intermediate *S. aureus* has raised fears about untreatable staphylococcal infections. Vancomycin-intermediate *S. aureus* (VISA) are still rare and has been isolated in Japan [2], United States of America, and France [3]. Recently, MRSA has been increasingly isolated from community patients and it is now accepted that MRSA is not just a hospital pathogen but is a community pathogen [4-6].

Surveillance of antimicrobial susceptibility in New Zealand in recent years has been accomplished by collating susceptibility results from hospital and clinical laboratories. The last national survey of *S. aureus* was carried out in 1982. A total of 2077 isolates were tested to ten antimicrobials and the prevalence of resistance was generally low to all the antimicrobial agents tested except penicillin [7]. Only one MRSA (0.05%) isolate was confirmed in the national survey in 1982. This national survey examines the antimicrobial susceptibility of 583 clinically significant isolates of *S. aureus* collected by 38 hospital and community laboratories.

2 METHODOLOGY

2.1 Participating Laboratories and Bacterial strains

All hospital and community laboratories in New Zealand were invited to participate in the survey. A preliminary questionnaire was completed and data on the number of *S. aureus* isolated per week were collected. Based on the isolation rates, laboratories were requested to submit between 5 and 50 clinically significant *S. aureus* isolates. Consecutive non-duplicate isolates were collected beginning in the first week of March 1999. Clinical data collected included patient name/laboratory code, gender, age, source (hospital or community), isolation site, and relevant clinical data. Laboratories were also asked for information on the number of *S. aureus* isolated in the sampling period.

2.2 Health Funding Authorities (HFA) Localities

Based on the location of the referring laboratory, isolates were grouped according to HFA localities (Table 1).

Table 1. Sub-regions included in HFA localities

HFA Locality	Sub-regions
Northland (NL)	Northland
Auckland (AK)	North Harbour, West Auckland, Central Auckland, South Auckland
Waikato (WK)	Thames, Central & Northern Waikato, Hamilton, South & Eastern Waikato, King Country
Bay Of Plenty (BP)	Western & Eastern Bay of Plenty, Lakes (Taupo & Rotorua)
Tairawhiti/Hawke's Bay (HB)	Tairawhiti, Hawke's Bay
Taranaki (TN)	Taranaki
Wanganui/Manawatu (MW)	Wanganui, Manawatu
Wellington (WN)	Porirua-Kapiti, Hutt, Wellington, Wairarapa
Nelson/Marlborough (NM)	Nelson-Marlborough
Canterbury/West Coast (CW)	West Coast, North Canterbury, Canterbury, Christchurch, Mid Canterbury, South Canterbury
Otago/Southland (OS)	Waitaki, Central Otago & Queenstown, Dunedin, Clutha, Southland, Invercargill

2.3 Definition of Community and Hospital Isolates

For the purposes of this study, hospital-acquired isolates were defined as isolates from in-patients who had been admitted at least 48 hours earlier. Community-acquired isolates were defined as isolates from specimens referred from general practitioners, rest homes, hospital outpatient clinics, accident and emergency units, or from hospital patients within 48 hours of admission.

2.4 Antimicrobial Susceptibility Tests

The susceptibility of the isolates was tested by an agar dilution method following NCCLS guidelines [8] to the following antimicrobial agents: chloramphenicol (Cm), ciprofloxacin (Cx), clindamycin (Cl), erythromycin (Em), fusidic acid (Fa), gentamicin (Gm), mupirocin (Mu), oxacillin (Ox), penicillin (Pe), rifampicin (Rf), trimethoprim-suphamethoxazole (TS), vancomycin (Vm). As currently recommended, oxacillin was used preferentially to methicillin for confirming MRSA. Mueller-Hinton agar was used to test for all the antimicrobial agents except for oxacillin and trimethoprim-sulphamethoxazole. Mueller-Hinton agar supplemented with 2% NaCl was used for testing oxacillin and Mueller-Hinton agar supplemented with 5% lysed horse blood was used for trimethoprim-sulphamethoxazole. An inoculum of 10^4 cfu/spot was applied to plates using a multipoint inoculator. The plates were incubated at 35°C for 18 hours. MIC endpoints were read as recommended by NCCLS and interpreted according to NCCLS recommendations [9] except for mupirocin and fusidic acid. Mupirocin and fusidic acid results were interpreted as recommended by Cookson [10] and the British Society for Antimicrobial Chemotherapy [11], respectively.

The following controls were included in the survey:

- *Staphylococcus aureus* NZRM Acc 2243 (ATCC 29213), sensitive control
- *Staphylococcus aureus* NZRM Acc 3388, borderline oxacillin-resistant control
- *Staphylococcus aureus* NZRM Acc 1056, oxacillin-resistant control
- *Staphylococcus aureus* NZRM Acc 3673, high-level mupirocin-resistant control

2.5 Determination of *mecA* Gene by PCR

Isolates with borderline oxacillin MICs of 1 - 4 mg/L were tested for the *mecA* gene by PCR using the method described by Geha et al. [12]

2.6 Determination of Erythromycin Resistance Phenotypes

Macrolide, lincosamide and streptogramin B (MLS_B) antibiotics are chemically distinct inhibitors of protein synthesis. Three major mechanisms of macrolide resistance have been described. A common mechanism mediated by an rRNA erm methylase confers cross resistance to macrolides, lincosamides and streptogramin B antibiotics (MLS_B phenotype). Expression of MLS_B resistance may be constitutive or inducible.

Isolates that were resistant or intermediate to erythromycin (MIC ≥ 1 mg/L) or clindamycin (MIC ≥ 1 mg/L) were tested for inducible or constitutive macrolide-lincosamide (ML) phenotype by disc diffusion induction tests [13]. Clindamycin discs were used to represent lincosamides. Disc tests were set up following NCCLS guidelines and erythromycin 15 μg (inducer) and clindamycin 2 μg discs were placed 20 mm apart. The zone diameters were measured and the presence of blunting of clindamycin zones near the erythromycin disc was noted. The phenotype was considered to be constitutive ML if there were no inhibition zones around both the erythromycin and clindamycin discs and inducible ML if the clindamycin zone was blunted near the erythromycin disc.

2.7 Statistical Analysis

The results obtained were analysed using SAS. χ^2 and two-tailed Fisher's exact tests were used to calculate probabilities.

3 RESULTS

3.1 Isolates Collected

A total of 583 *S. aureus* isolates were submitted by 38 hospital and clinical laboratories for the survey. Appendix 1 details the participating laboratories, the number of isolates contributed to the survey, their estimate of the number of *S. aureus* isolated per week and the actual isolation rate during the sampling period. The distribution of the isolates among the 11 HFA localities is shown in Figure 1. Information on the source of the isolates was known for 567 (97.4%). Of the 567 *S. aureus*, 79.5% were community isolates and 20.5% were hospital isolates.

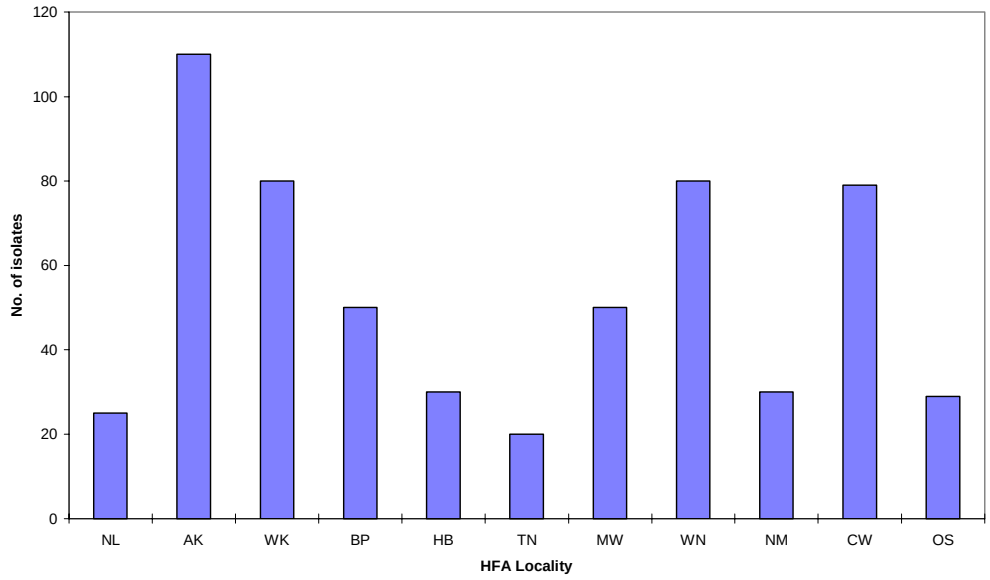

Figure 1. Distribution of S. aureus isolates by HFA locality

The isolation sites of the *S. aureus* are shown in Table 2. The majority of isolates (80.6%) were from wound swabs, skin swabs and abscesses.

Table 2. Isolation sites of S. aureus

Source of isolate	Number	%
Wound, abscess, skin	470	80.6
Ear	44	7.5
Nose, sputum, throat, tracheal aspirates	25	4.3
Eye	21	3.6
Urine, genital, urethra	10	1.7
Blood, sterile aspirates	7	1.2
Unknown	6	1.0

The distribution of the isolates by age groups is shown in Figure 2. Isolates were obtained from all age groups. Notably, 25% were from children aged below 11 years.

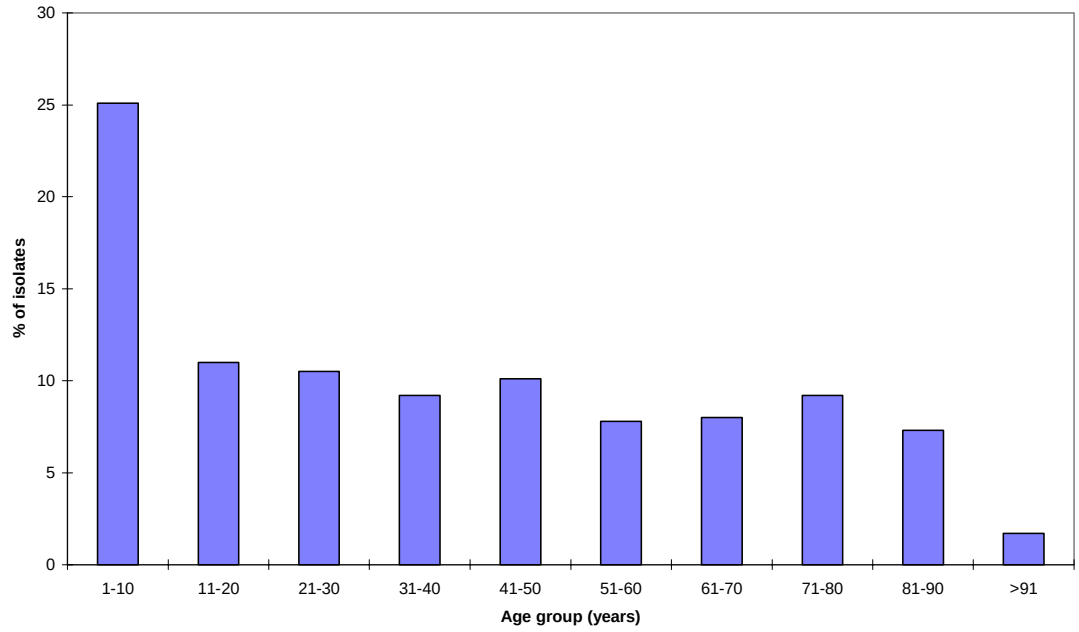

Figure 2. Distribution of S. aureus isolates by age groups

3.2 Antimicrobial Susceptibilities of *S. aureus*

The ranges, MIC_{50}, MIC_{90} and percent resistance of each antimicrobial tested are shown in Table 3. The most prevalent resistance was penicillin resistance (89%). The next most prevalent resistances were mupirocin (28%), fusidic acid (17%) and erythromycin (5.7%). Resistances to ciprofloxacin, chloramphenicol, clindamycin, gentamicin, oxacillin, rifampicin and trimethoprim-sulphamethoxazole were below 2%. No vancomycin resistance or intermediate vancomycin (MIC 8-16 mg/L) resistance was found.

Table 3. Ranges, MIC_{50}, MIC_{90} of 583 Staphylococcus aureus isolates

Antimicrobial agent	MIC (mg/L)			% resistant
	range	MIC_{50}	MIC_{90}	
Chloramphenicol	2-64	4.0	8.0	0.9
Ciprofloxacin	0.06-32	0.25	0.5	1.2
Clindamycin	0.03-128	0.12	0.12	1.4
Erythromycin	0.12-128	0.5	4.0	5.7
Fusidic acid	0.016-16	0.06	4.0	17.0
Gentamicin	0.06-128	0.25	0.5	1.9
Mupirocin	0.12-1024	0.12	1024	28.0
Oxacillin	0.25-128	0.25	0.5	1.9
Penicillin	0.06-64	1.0	4.0	89.0
Rifampicin	0.004-4	0.008	0.008	0.2
Trimethoprim-sulphamethoxazole	0.03/0.6-8/152	0.03/0.6	0.03/0.6	0.2
Vancomycin	0.25-2	0.5	1	0

3.3 Mupirocin-Resistant *S. aureus*

Of the 583 isolates, 28% (163) were mupirocin-resistant; 14.2% (83) with high-level resistance (MIC ≥ 512 mg/L) and 13.8% (80) with low-level resistance (MIC 8-256 mg/L). Mupirocin resistance occurred in all eleven HFA localities and in all age groups. High-level mupirocin-resistant *S. aureus* occurred in all eleven HFA localities and in all age groups; 53.1% of the isolates were from patients aged below 21 years. The high-level mupirocin-resistant *S. aureus* were isolated from a variety of sites: wound, abscess and skin (82%, 68), ear (9.6%, 8), eye (3.6%, 3), nose (2.4%, 2) and vagina (1.2%, 1). The commonest resistance pattern (antibiogram) exhibited by the high-level mupirocin-resistant isolates was Mu^{HL}Fa Pe (51.8%, 43) and Mu^{HL}Pe (37.3%, 31).

3.4 Fusidic Acid-Resistant *S. aureus*

Fusidic acid-resistant *S. aureus* (17%, 98) occurred in all eleven HFA localities and in all age groups. The fusidic acid-resistant *S. aureus* were isolated from a variety of sites: wound, abscess and skin (83.8%, 83), ear (7.1%, 7), nose/sputum/trachea (5.1%, 5), eye (3.1%, 3), and unknown (1.0%, 1). The commonest antibiograms exhibited by the fusidic acid-resistant isolates were Mu Fa Pe (49.5%, 49) and Fa Pe (33.3%, 33). Two MRSA isolates were fusidic acid-resistant, one was resistant to five and the other to seven antimicrobials.

3.5 *MecA* Gene

Oxacillin MICs of the eleven MRSA isolates ranged from 16 - >128 mg/L. Ten isolates with oxacillin MIC 1 or 2 mg/L were tested for the *mecA* gene. All were negative for the *mecA* gene by PCR showing the correlation of the genotypic results with the phenotypic results.

3.6 Erythromycin Resistance Phenotypes

A total of 33 isolates were erythromycin-resistant (MIC ≥ 8 mg/L) and 56 isolates were erythromycin-intermediate resistant (MIC 1-4 mg/L). Of the erythromycin-resistant isolates, eight were clindamycin-resistant and demonstrated constitutive ML resistance. The remaining 25 isolates comprised 24 with inducible ML resistance and one that was macrolide-resistant and clindamycin-sensitive.

Among the 56 erythromycin-intermediate isolates, the majority (83.9%, 47) possessed inducible ML resistance. The remaining nine isolates, eight with erythromycin MIC 1 mg/L and one with MIC 2 mg/L, did not exhibit inducible ML resistance. In the disc diffusion induction test, colonies were observed within the inhibition zones around the erythromycin disc of all the

isolates with inducible ML resistance and erythromycin MICs of 1-4 mg/L.

Taking into account the disc diffusion induction tests, overall, 13.7 % (80) of the isolates can be considered to be erythromycin-resistant; 1.4% (8) with constitutive ML resistance, 12.2% (71) with inducible ML resistance and 0.2% (1) with the erythromycin-resistant, clindamycin-sensitive phenotype.

3.7 Antibiograms and Multiresistance

The prevalence of multiresistance and distribution of antibiograms is shown in Table 4. The commonest antibiogram was Pe which accounted for 50.6% of the isolates. The antibiograms Pe Mu, Pe Mu Fa, Pe Fa and Pe Mu Em occurred in 14.9, 8.4, 5.7 and 2.2% of the isolates respectively. Each of the remaining 24 antibiograms accounted for less than 10 isolates. Eleven (1.9%) isolates were multiresistant to at least four antimicrobial agents; five were MRSA isolates. Only 8.9% of the isolates were fully sensitive.

Table 4. Prevalence of multiresistance and antibiograms among 583 S. aureus in 1999

	%	(Number)	Antibiogram	Number with each pattern
Fully sensitive	8.9	(52)		
Resistant to 1 agent	52.3	(305)	Pe	295
			Fa	4
			Mu	3
			Cx	1
			Cm	1
			Em	1
Resistant to 2 agents	24.7	(144)	Pe Mu	87
			Pe Fa	33
			Pe Em	9
			Pe Ox	6
			Pe Cx	4
			Mu Fa	2
			Pe TS	1
			Pe Cm	1
			Pe Gm	1
Resistant to 3 agents	12.2	(71)	Pe Mu Fa	49
			Pe Mu Em	13
			Pe Mu Gm	3
			Pe Em Fa	2
			Pe Em Cl	2
			Pe Cm Gm	1
			Pe Cx Fa	1
Resistant to 4 agents	1.2	(7)	Pe Mu Fa Gm	4
			Pe Fa Em Cl	2
			Pe Mu Ox Gm	1
Resistant to 5 agents	0.3	(2)	Pe Ox Cm Em Cl	1
			Pe Ox Fa Em Cl	1
Resistant to 7 agents	0.3	(2)	Pe Ox Cm Em Cl Cx Gm	1
			Pe Ox Em Cl Mu Fa Rf	1

Cm = chloramphenicol, Cx = ciprofloxacin, Cl = clindamycin,
Fa = fusidic acid, Gm = gentamicin, Mu = mupirocin, Ox = oxacillin, Pe = penicillin,
Rf = rifampicin, TS = trimethoprim-sulphamethoxazole.

3.8 Distribution of Resistant *S. aureus* by HFA Localities

The prevalence of resistance to penicillin, mupirocin, fusidic acid, and erythromycin by HFA localities is shown in Figure 3. There was a significant relationship (χ^2 test, p value = 0.009) between the prevalence of mupirocin resistance and HLA locality. The prevalence of mupirocin resistance ranged from 41.3% in Waikato and 40.0% in Northland to 10.3% in Otago/Southland. While not significant (χ^2 test, p value = 0.054), there was an association between the prevalence of fusidic acid resistance and HLA locality. The prevalence of fusidic acid resistance ranged from 36% in Northland to 3.4% in Otago/Southland. There were no significant associations between the HFA locality and the prevalence of penicillin (p value = 0.308) and erythromycin (p value = 0.234).

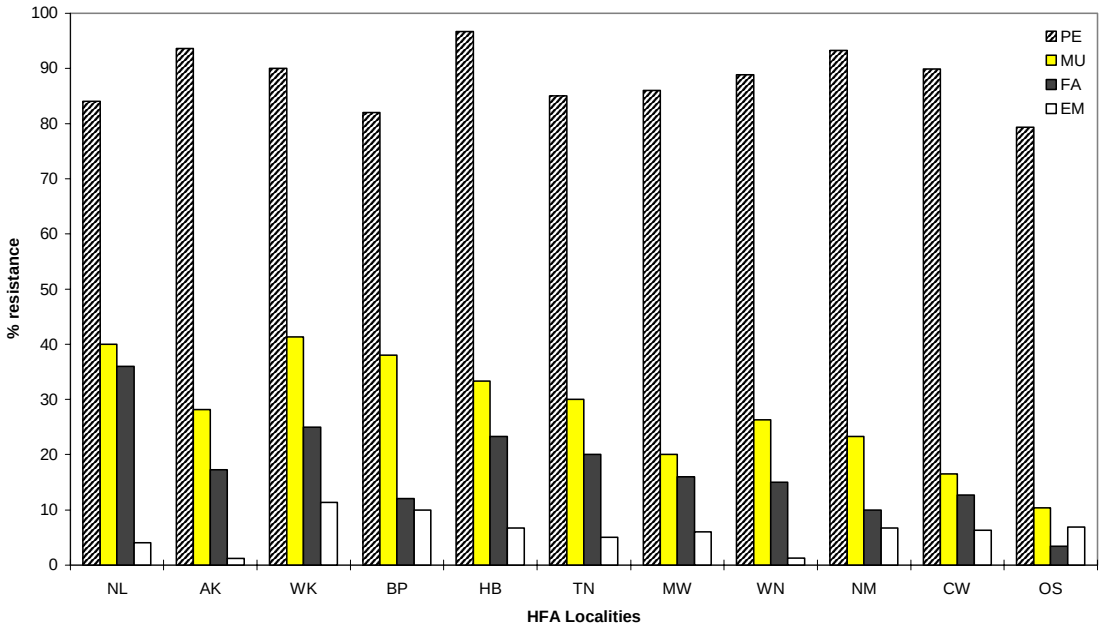

Figure 3. Distribution of resistance prevalence by HFA localities

3.9 Community vs Hospital Isolates

The prevalence of resistance among the 567 community and hospital isolates was compared for each antimicrobial agent by χ^2 or the two-tailed Fisher's exact test (Table 5). Mupirocin and penicillin resistance were significantly ($p > 0.05$) more prevalent among community isolates than hospital isolates. In contrast, the prevalence of high-level mupirocin resistance was not significantly different among community and hospital isolates. There were no significant differences between the prevalence of resistance among community and hospital isolates for the other antimicrobial agents..

Table 5. Antimicrobial resistances(%) of 567 S. aureus, by specimen source

	Community isolates n=451	**Hospital isolates n=116**	**p-value***
	% Resistant (Number)		
Chloramphenicol	0.9 (4)	0.9 (1)	1.0
Ciprofloxacin	0.9 (4)	2.6 (3)	0.16
Clindamycin	1.3 (6)	1.7 (2)	0.67
Erythromycin	6.2 (28)	3.4 (4)	0.25
Fusidic acid	16.4 (74)	18.1 (21)	0.66
Gentamicin	2.2 (10)	0.9 (1)	0.48
Mupirocin	30.2 (136)	19.8 (23)	0.03
High-level mupirocin	14.2 (64)	13.8 (16)	0.91
Oxacillin	1.8 (8)	2.6 (3)	0.70
Penicillin	90.7 (409)	82.8 (96)	0.02
Rifampicin	0 (0)	0.9 (1)	0.21
Trimethoprim-sulphamethoxazole	0.2 (1)	0 (0)	1.0

* Two-tailed Fisher's exact test was used for all antimicrobial agents except mupirocin, fusidic acid, erythromycin and penicillin. Isolates were categorised as either resistant or susceptible, the intermediate category was included in the susceptible category.

3.10 Comparison with Previous Survey in 1982

The MIC range and MIC_{90} values for the antimicrobials that were tested in 1982 and 1999 are shown in Table 6. Notably, the MIC_{90} value of fusidic acid has increased to 4 mg/L in 1999 from 0.12 mg/L in 1982.

Table 6. Comparison of MIC ranges and MIC_{90} (mg/L) in 1982 and 1999

	1982 Survey n=2077		**1999 Survey n=583**	
	Range	**MIC_{90}**	**Range**	**MIC_{90}**
Chloramphenicol	2-64	8	2-64	8
Clindamycin	0.06->128	0.12	0.03->128	0.12
Erythromycin	0.12->128	2	0.12->128	4
Fusidic acid	0.06->128	0.12	0.016-16	4
Gentamicin	0.06->128	0.5	0.06-128	0.5
Penicillin	0.03->128	8	0.06-64	4
Vancomycin	0.25-2	1	0.25-2	1

4 DISCUSSION

Analysis of the patient information showed that clinically significant *S. aureus* were mainly isolated from wound, skin and abscess swabs from community patients. Almost 80% of the specimens were from community patients and 80.6% were from wound swabs, skin swabs and abscesses. While specimens were isolated from all patients ranging in age from neonates to the elderly, nearly one quarter of the specimens were from children aged below 11 years.

As expected, penicillin resistance was very prevalent and occurred in 89% of the isolates. This continuing upward trend has been noted in most other studies [14] [15-17]. Earlier surveys in New Zealand have shown an increase in penicillin resistance from 58.7% in 1972 to 81.5% in 1982 [7].

The next most prevalent resistance was to mupirocin. Twenty eight percent of the isolates were mupirocin-resistant; 14.2% with high-level resistance. While the clinical significance of low-level resistance is dubious the general consensus is that staphylococci with high-level mupirocin resistance cannot be eradicated with mupirocin [10]. Globally, high-level mupirocin-resistant *S. aureus* are still rare [10, 18-21]. Mupirocin has been widely used in Europe for the eradication of nasal carriage of MRSA in patients and staff. Indiscriminate and widespread use of mupirocin has been shown to encourage the emergence of mupirocin-resistant *S. aureus*. Miller et al. [22] described the increase in mupirocin resistance among MRSA in a hospital from 2.7% to 65% associated with increased use of mupirocin ointment as an adjunct to infection control measures.

Mupirocin was introduced into clinical use in New Zealand in November 1986 and was made available over-the-counter in October 1991. Susceptibility data from Auckland has shown a high prevalence of mupirocin-resistant *S. aureus* among community patients [23, 24]. The authors report an increase in the prevalence of mupirocin-resistance from 3.7% (170/4544) in 1991-1992 to 16% (1550/9700) in 1996-1997. The results obtained in this survey showed that high-level mupirocin resistance occurred in all regions and in hospital and community patients. There were significant regional differences in the prevalence of mupirocin resistance, and mupirocin-resistant *S. aureus* were significantly more prevalent in the community patients than in the hospital patients. However, high-level mupirocin resistant *S. aureus* were equally prevalent among community and hospital patients. Unfortunately no data are available on the mupirocin susceptibility of community *S. aureus* prior to the publication by Lang et al [23] in 1992. Mupirocin susceptibility has been monitored among MRSA in New Zealand from 1987. Among MRSA, mupirocin resistance first emerged in 1988 and remained at below 3% until 1993. Mupirocin resistance increased to 5.6% in 1994 and has ranged from 5% to 7.7% between 1995 and 1998. The overall high prevalence of mupirocin resistance among *S. aureus* in New Zealand should be a cause for concern as mupirocin is an important topical antimicrobial agent and has been shown to be efficacious in eradicating MRSA colonisation [10, 25].

Notably, this survey also showed that 17% of the isolates were resistant to fusidic acid. Fusidic acid resistance has increased from 2.4% in the 1982 survey to 17% in 1999. In contrast to mupirocin resistance, there were no significant regional differences in the occurrence of fusidic acid resistance. Fusidic acid resistance was also equally prevalent among community and hospital patients. Fusidic acid has been in clinical use since 1962 [26]. Early reports of emerging resistance led to the use of fusidic acid in combination with another antimicrobial agents [27]. The rising incidence of MRSA has renewed interest in the use of fusidic acid as an alternative to vancomycin. The high prevalence noted in this survey contrasts with results obtained in other countries [19, 28, 29]. Shanson reviewed two decades of fusidic acid use in the management of staphylococcal infection and reported that resistance has remained at 1-2% [30]. In Denmark, the use of fusidic acid has not been accompanied by the development of resistance in Danish *S. aureus* strains [31]. A similar experience has also been noted in Canada [32]. Of concern too was the observation that approximately 50% of the *S. aureus* isolates in this survey with high-level mupirocin resistance were also fusidic acid-resistant.

With the exception of penicillin, mupirocin and fusidic acid resistance, the prevalence of antimicrobial resistances among *S. aureus* remains low. In the 1982 survey, only one of 2077 isolates (0.05%) was an MRSA [7]. In 1999, 1.9% (11/583) of the isolates were MRSA. In contrast to the 1999 survey results, data obtained from the collation of routine susceptibility testing results of hospital and community laboratories show comparatively higher prevalences for several antimicrobial agents. According to the collated national data for 1998, resistance to oxacillin, erythromycin, fluoroquinolone, mupirocin occurred in 4.7%, 10.3%, 4.6% and 18.5% respectively. There are many possible reasons for the discrepancies. One possibility is that with MRSA patients, there could be replicate sampling (for different sites) for clearance monitoring. Another reason is that the time period chosen for the survey coincided by chance with a time of lower resistance prevalence. The discrepancies could also be due to the fact that the 1999 survey was conducted in one centre using agar dilution methodology while the 1998 collated data were sourced from 18 laboratories using a mixture of methodologies.

The low prevalence of MRSA contrasts with recent observations in other countries. In the United Kingdom, the prevalence of MRSA among *S. aureus* isolated from blood culture or CSF has increased from about 1.5% in 1989-1991 to 13.2% in 1995 [14]. In the United States, MRSA is a major problem in hospitals and long-term care facilities [33-35]. However other studies have shown a similar low prevalence of antimicrobial resistance among *S. aureus*. In the Netherlands methicillin resistance accounted for 0.3% of *S. aureus* tested between 1989 and 1995 [28]. Similarly in Denmark, only 0.2% of *S. aureus* isolated from blood cultures between 1981 and 1995 were methicillin-resistant [36]. MRSA are similarly uncommon in Norway [37].

No vancomycin intermediate resistant *S. aureus* were isolated in the survey. In the 1999 and the 1982 surveys, vancomycin MICs ranged from 0.25 to 2 mg/L and the MIC_{90} was 1 mg/L. Similarly, the vancomycin ranges among New Zealand isolates of MRSA have consistently been between 0.25 to 2 mg/L with MIC_{90} values of 0.5-1 mg/L.

There have been several recent reports on heterogenous intermediate vancomycin resistant *S. aureus* (hetero-VISA) detected by population analysis [38-40]. Hetero-VISA has been defined as a strain that is susceptible to vancomycin, i.e. MIC ≤ 4 mg/L by NCCLS breakpoints, but which contains subpopulations of cells that exhibit intermediate susceptibility (MICs 8-16 mg/L). Geisel et al. [39] reported that 8.2% (7/85) of MRSA in the Dusseldorf area were hetero-VISA. The vancomycin MIC of the seven strains was 1 mg/L. It has been postulated that hetero-VISA may swiftly evolve into homogeneous VISA during exposure to glycopeptide therapy. However, Ariza et al. [40] did not observe any selection for homogeneous resistance in their MRSA patients after vancomycin therapy but commented that the presence of heterogeneous resistance may have contributed to some of the failed therapeutic outcomes.

In staphylococci erythromycin resistance is predominantly caused by erm methylases resulting in the macrolide-lincosamide-streptogramin B (MLS) phenotype which can be either constitutive or inducible. The results obtained in this survey showed that inducible erythromycin resistance was more common in New Zealand isolates than constitutive resistance. Notably the difficulties of testing for erythromycin and clindamycin resistance were highlighted by results obtained when the agar dilution tests were supplemented with disc diffusion induction tests. Use of the agar dilution methodology and NCCLS interpretive standards indicated that 5.6% were erythromycin-resistant, 9.6% were erythromycin-intermediate and 1.2% were clindamycin-resistant. Supplementation with disc diffusion induction tests further revealed that a total of 13.7% were ML-resistant (1.4% were constitutive ML resistant and 12.2% were inducible ML resistant). The majority of isolates that were intermediate erythromycin-resistant by NCCLS interpretive guidelines possessed inducible ML resistance despite low clindamycin MICs. The results obtained in this survey indicate that disc diffusion induction tests should be carried out to detect inducible MLS resistance. This is consistent with the recommendations of Sanchez et al. [13].

In conclusion, data obtained in this survey indicate that a variety of antistaphylococcal agents are still effective against a large proportion of *S. aureus* in New Zealand.

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A P P E N D I X

Participating Laboratory*	No. of isolates in survey	Estimated No. per week	Actual isolation rate
Medlab Auckland	50	250	85/day
Diagnostic Laboratory, Auckland	40	>200	-
Green Lane Hospital, Auckland	10	15	-
Middlemore Hospital, Auckland	10	35	-
Wairau Hospital, Blenheim	10	25	23/week
Canterbury Health Laboratories, Christchurch	20	50	-
Medlab South, Christchurch	30	130	200/week
Southern Community Laboratories, Christchurch	29	100	-
Dargaville Hospital, Dargaville	5	6	12/week
Dunedin Hospital, Dunedin	9	20	21/week
Southern Community Laboratories, Dunedin	10	40	84/week
Gisborne Hospital, Gisborne	10	15	16/week
Medlab Hamilton	30	100	113/week
Waikato Hospital, Hamilton	20	65	46/week
Waikato Pathology, Hamilton	20	80	18/day
Memorial Hospital, Hastings	10	20-50	6-10/day
Southern Community, Hastings	10	10-15	15/week
Medlab Kew, Invercargill	10	10-20	-
Kaitaia Hospital, Kaitaia	10	30	12/week
Hutt Hospital, Lower Hutt	20	50	-
Valley Diagnostic, Lower Hutt	20	70	80/week
Diagnostic Laboratory, Nelson	10	40	10/day
Nelson Hospital, Nelson	10	10	-
Medlab, New Plymouth	10	30	30/week
Taranaki Hospital, New Plymouth	10	20	-
Medlab Central, Palmerston North	30	140	31/day
Rotorua Diagnostic, Rotorua	10	15	-
Rotorua, Rotorua	10	13	-
Medlab Bay of Plenty, Tauranga	20	60	62/week
Thames Hospital, Thames	5	7	5/week
Te Kuiti Hospital, Te Kuiti	5	5	1/week
Taumaranui Hospital, Taumaranui	5	5	2/week
Diagnostic Laboratory, Wanganui	10	20	39/week
Wanganui Hospital, Wanganui	5	5	9/week
Whakatane Hospital, Whakatane	10	40	-
Medlab, Wellington	30	125	-
Wellington Hospital, Wellington	10	-	-
Northland Hospital, Whangarei	10	15	11/week

* Isolates were submitted by Auckland Hospital but were lost in transit.