Molecular Epidemiology of Inducible Macrolide Resistance in *Staphylococcus aureus* in the Western Pacific: Results from SENTRY Western Pacific Plus (WP+) 1998-2000

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Abstract

Background: We have observed high rates of inducible resistance to macrolides in SAUR in the WP+. Over the observation period, 78% of oxacillin-susceptible (OSSA) and 19% of oxacillin-resistant (ORSA) erythromycin resistant (ery-R) were clindamycin susceptible (cli-S). We chose examine the molecular epidemiology macrolide resistance genes for this pattern of resistance. **Methods**: SAUR isolates from blood, respiratory, skin/ski structure and urine specimens from hospital patients with the phenotypic pattern of eryR, clin PCR were probed for methylase genes *ermA*, *ermB* and *ermC*, and the putative efflux gene *msrA* by published methods. The isolates were from 12 hospitals in 7 countries. **Results**: Macrolide resistance genes were detected in 65 of 70 strains tested. In OSSA *ermC* predominated except in Japan, while in ORSA *ermA* was the commonest genotype. *msrA* was detected in one strain from Australia. Two strains from Singapore possessed both *ermA* and *ermC*.

Conclusions: There is significant variation in the SAUR macrolide inducible phenotype between countries and institutions in our region. *ermC* is commonest mechanism in OSSA, and *ermA* in ORSA.

Introduction

Macrolide resistance in *Staphylococcus aureus* is very common in the Asia-Pacific region, and significant proportion of this resistance is inducible. Between 1998 and 2000 in the SENTRY surveillance program in our region, we found that 77% of oxacillin-susceptible strains and 17% of oxacillin-resistant strains had the inducible phenotype of erythromycin-resistant, clindamycin-susceptible. We have examined to the molecular epidemiology of this inducible phenotype in representative strains from our region

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Methods

Isolates

S. aureus isolates in the SENTRY surveillance program from a range of sources, including blood, the lower respiratory tract, skin/soft tissues and urinary tract, were collected by 17 different hospitals from eight countries or locales over defined seasonal intervals between April 1999 and December 2000. All strains were sent to a central reference laboratory (Women's and Children's Hospital, Adelaide, Australia) for testing.

Representative strains with the erythromycin-resistant, clindamycin-susceptible phenotype from 12 laboratories in 7 countries were selected for molecular analysis.

Susceptibility testing

All isolates were tested against erythromycin and clindamycin by the broth microdilution method using commercially prepared trays (TREK™ Diagnostic Systems Limited, UK), according to NCCLS standards.[1] Breakpoints for resistance were those recommended by the NCCLS.[2]

Molecular testing

Strains were PCR-probed for the following resistance genes: *ermA*, *ermB*, *ermC* methylase genes, and *msrA* putative efflux gene by published methods.[3]

Figure 1.
Clindamycin resistance in Erythromycin-resistant oxacillin-susceptible *Staphylococcus aureus*

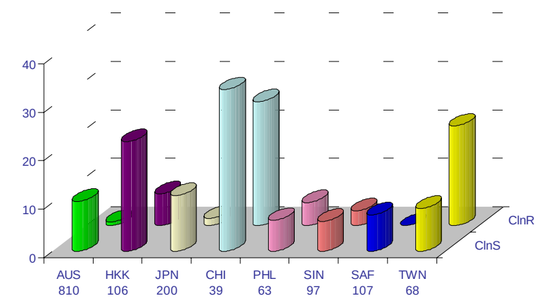

Figure 2.
Clindamycin resistance in Erythromycin-resistant oxacillin-resistant *Staphylococcus aureus*

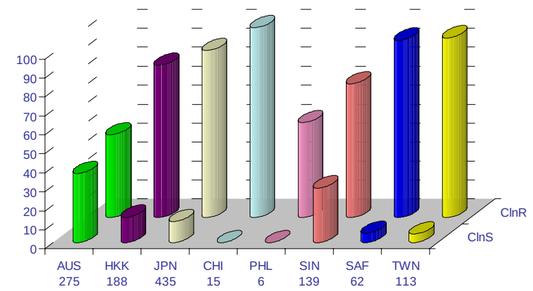

Table 1. Macrolide Genotypes vs oxacillin resistance

	Oxacillin-susceptible				Oxacillin-resistant non-multi-resistant			Oxacillin-resistant multi-resistant		
Country	-	*ermA*	*ermC*	*msrA*	-	*ermA*	*ermC*	*ermA*	*ermC*	*ermA* *ermC*
Australia	2	3	7	1		6	4	11		
Hong Kong		2	4		1		1			
Japan	1	3				1		10		
Mainland China			6							
Philippines	1		1							
South Africa									1	
Singapore								2		2

Results

- Macrolide resistance genes were detected in 65 of 70 strains tested. The gene types vs country are shown in Table 1
- For oxacillin-susceptible *S. aureus*, *ermC* predominated except in Japan, where no *ermC* strains were detected (Figure 1)
- For oxacillin-resistant *S. aureus*, *ermA* predominated (Figure 2)
- *msrA* was detected in one in one strain from Australia
- 2 strains from Singapore possessed both *ermA* and *ermC*.

Discussion and Conclusions

- **There is significant regional variation in the predominant inducible macrolide resistance genotype in our region.**
- ***ermC* predominates in oxacillin-susceptible strains, and *ermA* in oxacillin-resistant strains.**

References

1 National Committee for Clinical Laboratory Standards. Methods for Dilution Antimicrobial Susceptibility Testing for Bacteria That Grow Aerobically, 4th Ed. Approved Standard M7-A4. National Committee for Clinical Laboratory Standards, Wayne, Pa.

2 NCCLS. Performance standards for Antimicrobial Susceptibility Testing; 11th Informational Supplement. M100-S11. NCCLS 2001; Wayne, Pa

3 Martineau, F., F.J. Picard, N. Lansac, C. Menard, P.H. Roy, M. Ouellette, and M.G. Bergeron. 2000. Correlation between the Resistance Genotype Determined by Multiplex PCR Assays and the Antibiotic Susceptibility Patterns of *Staphylococcus aureus* and *Staphylococus epidermidis*. Antimicrob. Agents Chemother. 44:231-238