



High Rates of Macrolide Resistance and Emerging Quinolone Resistance in *Streptococcus agalactiae* in the Asia-Pacific Region

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Introduction

Streptococcus agalactiae (SAGA) is an important cause of neonatal and maternal sepsis and some other invasive diseases. Macrolides are considered the drugs of choice for penicillin-allergic patients. We have monitored resistance patterns in this species in the Asia-Pacific region from 1998-2002.

Methods

Isolates

All strains of SAGA from 17 laboratories in 8 countries were sent to a central reference laboratory (Women's and Children's Hospital, Adelaide, Australia) for testing.

Susceptibility testing

All isolates were tested by broth microdilution using custom made panels (TREK™ Diagnostic Systems), according to NCCLS standards,¹ to a wide range of antimicrobials. Breakpoints for resistance were those recommended by the NCCLS.² Strains were considered resistant if their MIC was above the susceptible breakpoint.

Genotype

Erythromycin non-susceptible strains were examined for erythromycin resistance genes using PCR and ELISA with primers specific for *erm(A)*, *erm(B)*, *erm(C)*, *erm(A)* subclass *erm(TR)* and *mef(A/E)* as described by Farrell³

Results

- A total of 397 isolates were received from 7 countries over the collection period. In most countries the majority of isolates were recovered from blood or wounds (Table 1)
- Results of the pooled data for the 5 years for erythromycin (ERY), clindamycin (CLN), tetracycline (TET), chloramphenicol (CHL) and ciprofloxacin (CIP) are shown in Table 2
- TET resistance was prevalent everywhere as expected, although in Japanese strains the level was lower
- M-phenotype strains were common in South Africa and Hong Kong (Figure 2)
- MLS-phenotypes were common in Taiwan, while macrolide resistance was infrequent in other countries
- Half of the ERY-resistant strains were examined for resistance genes; *erm(B)* was dominant (Table 3)
- CIP^R rates were significant in Japan and Hong Kong China (Table 4). Six isolates had high level CIP resistance (MIC >32 mg/L); the QRDR is being examined for amino acid substitutions
- Although multi-drug resistance was common in Taiwan, no strains were ciprofloxacin-resistant (Figure 3)

Table 1. Source of Isolates

Source	N (%)	AUS	HKC	JPN	PHL	SIN	SAF	TWN
Blood	169 (43)	86 (56)	18 (37)	13 (22)	1	12 (31)	29 (64)	10 (20)
Wounds	109 (27)	39 (25)	21 (43)	12 (20)		22 (56)	8 (18)	7 (14)
Urine	62 (16)	16 (10)	1 (2)	12 (20)		5 (13)	1 (2)	27 (55)
LRT	28 (7)	8 (5)		15 (25)			1 (2)	4 (8)
URT	13 (3)	1 (1)	7 (14)	5 (8)				
Other	13 (3)	3 (2)	2 (4)	3 (5)			4 (9)	1 (2)
Unknown	3 (1)				1		2 (4)	
Total	397	153	49	60	2	39	45	49

Table 2. Resistance in *Streptococcus agalactiae*

Antimicrobial	N	Number (%) of isolates resistant to:				
		ERY	CLN	TET	CHL	CIP
		>0.5	>0.5	>4	>8	>1
Australia	153	6 (3.9)	2 (1.3)	130 (85.0)	1 (0.7)	1 (0.7)
Hong Kong	49	15 (30.6)	6 (12.2)	43 (87.8)	9 (18.4)	2 (4.1)
Japan	60	4 (6.7)	3 (5.0)	19 (31.7)	2 (3.3)	6 (10.0)
Philippines	2	0	0	1	0	0
Singapore	39	1 (2.6)	1 (2.6)	26 (66.7)	0	0
South Africa	45	11 (24.4)	2 (4.4)	44 (97.8)	0	0
Taiwan	49	26 (53.1)	24 (49.0)	44 (89.8)	3 (6.1)	0

Table 3. Genotype vs Macrolide Phenotype (n=31)

Species	Genotype	Total	M	MLSs-IR	MLSs-CR
<i>S. agalactiae</i>	<i>mef(A)</i>	4	3	1	
	<i>erm(TR)</i>	3		1	2
	<i>erm(B)</i>	10		1	9
	- ^a	14	1		13

^a no gene detected

Acknowledgments

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Figure 1. Erythromycin Resistance and Phenotype (all strains)

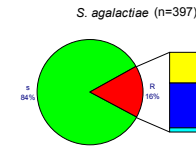


Figure 2. Erythromycin Phenotype vs Country

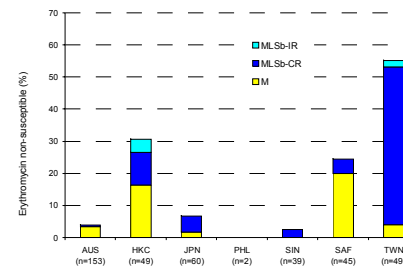
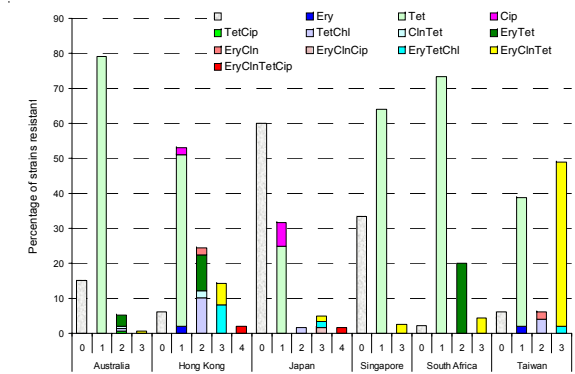


Table 4. Ciprofloxacin >2 mg/L

Country	Site	Source	Cip MIC	Co-resistances	MLS _B	erm
Japan	205	LRT	> 32 mg/L			
Japan	205	LRT	3 mg/L			
Japan	205	Urine	> 32 mg/L			
Japan	206	LRT	6 mg/L	EryClnTet	CR	
Japan	207	LRT	> 32 mg/L	EryCln	CR	
Japan	207	LRT	> 32 mg/L			
Hong Kong	204	Wound	3 mg/L	EryCln	CR	erm(TR)
Hong Kong	204	Wound	> 32 mg/L			
Australia	203	Wound	> 32 mg/L			

Figure 3. Resistance to Drug Classes and Phenotypes vs Country



Conclusions

- Macrolide resistance is very common in some countries in the Asia-Pacific region, with different phenotypes predominating
- Ciprofloxacin resistance is an emerging problem in Japan and Hong Kong China
- More than 50% of isolates from Taiwan were resistant to erythromycin, clindamycin and tetracycline
- No resistance to penicillin was seen

References

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