

High prevalence of Macrolide-Lincosamide Resistance in *Streptococcus agalactiae* in the Asia-Pacific Region; a SENTRY Antimicrobial Surveillance Program Report

J. M. Bell, J. D. Turnidge, and R. N. Jones

SA Pathology, Women's and Children's Hospital, Adelaide, Australia
JMI Laboratories, North Liberty, IA, USA



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Background

Streptococcus agalactiae (group B streptococcus) is a major cause of invasive infection in neonates and pregnant women. Macrolide and lincosamides are frequently recommended for the treatment and prophylaxis of group B streptococcal infections. Reports of resistance to these drug classes has been increasing. We examined the prevalence of resistance to these drug classes in the Asia-Pacific region between 1998 and 2008.

Methods

Isolates

S. agalactiae from infected hospitalized patients in 10 countries (39 laboratory centres) collected since 1998 were examined. Isolates came from patients with bacteraemia, complicated skin and skin structure infections, and other infections. All strains were referred to the Women's and Children's Hospital, Adelaide, Australia for testing.

Susceptibility testing

We examined the macrolide (erythromycin - ERY) and lincosamide (clindamycin - CLN) susceptibility using custom made dry-form broth microdilution panels (TREK Diagnostic Systems). A wide range of other antimicrobials, including quinupristin/dalfopristin (QD) was also tested according to CLSI standards.¹ Breakpoints for resistance to other antimicrobial agents were those recommended by the CLSI.²

Quality control strains utilized included *Staphylococcus aureus* ATCC 29213, *Enterococcus faecalis* ATCC 29212, and *Streptococcus pneumoniae* ATCC 49619; all MIC results were within CLSI specified ranges.

On-scale MIC values for selected isolates was obtained using Etest® strips.

Phenotype

M Ery^R, CLN^S; macrolide-lincosamide-streptogramin (MLS_B); MLS-CR (Ery^R, CLN^R)

Figure 2. QD MIC Distribution by MLS Phenotype

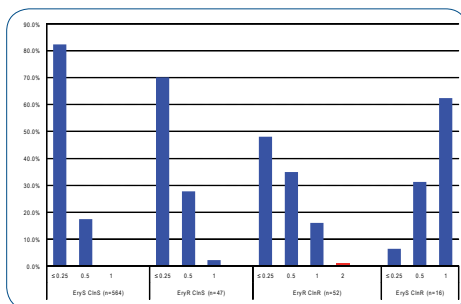


Table 1. Resistance Rates by Year

Year	N	Resistance(%):		Phenotype (%)		
		Ery	Cln	EryR ClnR	EryR ClnS	EryS ClnR
1998	35	2.9	5.7	2.9	0.0	2.9
1999	38	7.9	5.3	5.3	2.6	0.0
2000	57	17.5	10.5	8.8	8.8	1.8
2001	207	18.8	12.1	12.1	6.8	0.0
2002	60	16.7	5.0	5.0	11.7	0.0
2003	61	21.3	16.4	16.4	4.9	0.0
2004	50	20.0	12.0	12.0	8.0	0.0
2006	78	37.2	38.5	30.8	6.4	7.7
2007	58	27.6	27.6	24.1	3.4	3.4
2008	83	20.5	21.7	12.0	8.4	9.6

Results and Discussion

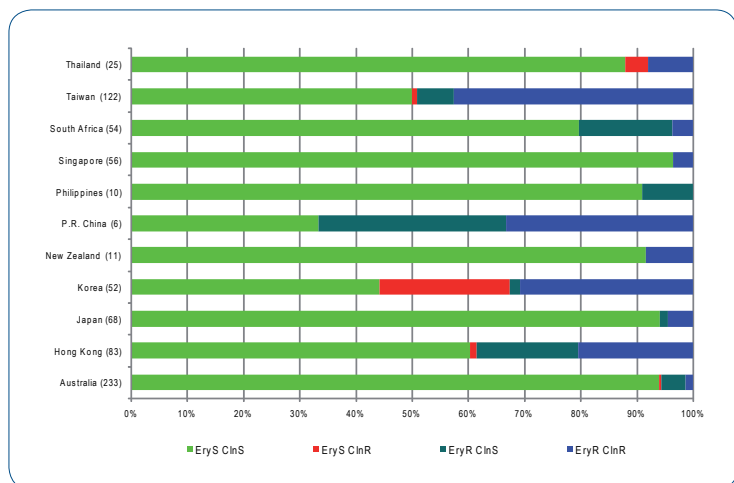
- A total of 727 *S. agalactiae* were examined. No isolates were collected in 2005. The MLS resistance phenotypes observed for each country are shown in Figure 1
- There was a significant increase in the resistance rates for both ERY and CLN over the 10 year period (Table 1). MLS_B constitutive was the dominant phenotype.
- Starting in 2006, strains resistant to CLN but susceptible to ERY began to emerge in Korea. Four other countries have also had sporadic occurrences of this particular MLS phenotype.
- All isolates contained group B antigen, and MIC results were reproducible.
- Although QD MICs were elevated, no resistant strains were detected. One strain from Hong Kong had a QD MIC = 2 mg/L (Figure 2). The MICs to other agents are shown in Table 2.
- CLN resistance was low-level (MICs 4-6 mg/L). Lincomycin MICs are unknown at present.
- These strains are being investigated for the presence of *erm(A)*, *erm(TR)*, *erm(B)* and *erm(C)* genes encoding ribosomal methylases; and for the *lnu(A)* and *lnu(C)* genes encoding lincosamide nucleotidyltransferases. The recent emergence of this phenotype may indicate the presence of a novel resistance gene.

Table 2. MICs of Isolates with EryS and ClnR phenotypes

Year	Country	N	MIC (mg/L) to ^a :						
			CLN	ERY	LEV	LIN	PEN	QD	VAN
1998	Hong Kong	204	1	≤0.25	≤0.5		0.06	1	0.5
2000	Australia	201	1	≤0.06	0.5	1	0.06	0.5	0.5
2006	Korea	224	1	≤0.25	≤0.5	1	0.06	0.5	0.5
2006	Korea	224	1	≤0.25	≤0.5	1	0.06	0.5	0.5
2006	Korea	225	1	≤0.25	≤0.5	1	0.06	0.5	0.5
2006	Korea	225	>2	≤0.25	≤0.5	1	0.06	1	0.5
2006	Taiwan	215	>2	≤0.25	≤0.5	1	0.06	1	0.5
2007	Korea	219	>2	≤0.25	≤0.5	1	0.06	1	0.5
2007	Korea	219	>2	≤0.25	1	1	0.06	1	0.5
2008	Korea	219	>2	≤0.25	1	1	0.06	1	0.5
2008	Korea	219	6	0.094	≤0.5	1	0.06	1	0.5
2008	Korea	219	6	0.094	1	1	0.06	1	0.5
2008	Korea	219	4	0.094	1	1	0.06	1	0.5
2008	Korea	225	6	0.125	1	1	0.03	≤0.25	0.5
2008	Thailand	226	1	≤0.25	≤0.5	1	0.06	0.5	0.5

^a CLN, clindamycin; LEV, levofloxacin; LIN, linezolid; PEN, penicillin; VAN, vancomycin

Figure 1. MLS Phenotype Distribution by Country



REFERENCES

- CLSI. 2009. M7-A8. Wayne, PA.
- CLSI. 2009. M100-S19. Wayne, PA.

CONCLUSIONS

- Resistance to macrolides and/or lincosamides is now a major problem in the Asia-Pacific region.
- Isolates are undergoing investigation for known MLS genes, including *lnu(B)* and *lnu(C)*.