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**Distinctive patterns of macrolides, lincosamides, and streptogramins resistance
phenotypes and determinants among *Staphylococcus aureus* populations in Hong Kong**

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Sir,

In staphylococci, resistance to macrolides, lincosamides, and streptogramin B antibiotics (MLS phenotype) is caused by a ribosomal methylase encoded by the *erm* genes. Expression of resistance to clindamycin can be either inducible or constitutive. The inducible phenotype is expressed only in the presence of macrolides, and these strains appear to be susceptible to clindamycin in vitro. However, reports of treatment failures have led to concerns about the efficacy of clindamycin for strains with inducible (iMLS) phenotypes [1], especially when oral clindamycin may be used for outpatient treatment of infections caused by community-associated methicillin-resistant *Staphylococcus aureus* (CA-MRSA). In Hong Kong, studies have showed that multiple lineages of CA-MRSA are emerging [2]. Here, we determine the prevalence of MLS phenotypes and their resistance determinants among our CA-MRSA isolates and compared them with methicillin-sensitive *S. aureus* (MSSA) and healthcare-associated (HA)-MRSA.

Susceptibility of the isolates to erythromycin and clindamycin were determined by the disc diffusion method. The D-test was used to detect inducible resistance to clindamycin. Quality control strains were included on each day of testing. The relatedness of the strains were characterized by *spa* typing and/or multilocus sequencing. MRSA strains were additionally tested by SCCmec multiplex PCR [2,3]. Multiplex PCR assays for the *erm A*, *ermB*, *ermC*, *mef* and *msrA* genes were performed using previously described primers [4].

A total of 422 *S. aureus* isolates including 185 MSSA group, 107 HA-MRSA and 130 CA-MRSA isolates collected in Hong Kong during 2004-2007 from diverse sources were tested [2,3]. Overall, the erythromycin resistance rate was 36.7% (155/422) including 60.7% (65/107) for HA-MRSA, 26.9% (35/130) for CA-MRSA and 29.7% (55/185) for MSSA. Among erythromycin-resistant (ery-R) isolates, 24.5% (38/155) and 67.1% (104/155) had constitutive (cMLS phenotype) and inducible (iMLS phenotype) resistance to clindamycin, respectively. The remaining 13 erythromycin-resistant isolates (11 CA-MRSA and 2 MSSA) had the M phenotype (i.e. resistant to erythromycin only). Another four isolates (all CA-MRSA) were resistant to clindamycin alone (L phenotype). The iMLS phenotype predominated among MSSA (78.1%, 43/55) and HA-MRSA (93.8%, 61/65), while the cMLS phenotype was prevalent among CA-MRSA (68.6%, 24/35).

The 155 ery-R isolates were tested for the presence of MLS resistance genes (Table 1). At least one *erm* gene was detected in 98.6% (140/142) of the isolates with cMLS or iMLS phenotype. Among ery-R MSSA isolates, *ermA* gene (67.3%, 37/55) predominated, followed by *ermC* (18.2%, 10/55) and *ermB* (10.9%, 6/55). By comparison, 56.9% and 44.6% of the ery-R HA-MRSA were found to possess *ermC* and *ermA*, respectively. In CA-MRSA, the MLS phenotype was largely attributed to *ermB* and the M phenotype to *msrA* genes.

In MRSA, the MLS determinants were largely distributed among clonally related strains. Thirty-one (86.1%) of the 36 *ermC* positive HA-MRSA isolates were of the

CC45/SCCmec IV/V clone (t1081 or related spa types). The remaining five *ermC* HA-MRSA isolates belonged to CC7/SCCmec V lineage (n=2, t1081), EMRSA-15 (n=2, ST22, t032) and ST188 (n=1, t198). Similarly, 86.2% (25/29) of the *ermA* positive and the singleton *ermA* + *ermC* positive HA-MRSA isolates were of the CC5/SCCmec II clone (t002). For CA-MRSA, all of the 20 *ermB* positive and two *ermB* + *ermC* positive isolates were of the CC59/SCCmec V clone. All the 11 *msrA* positive CA-MRSA isolates belonged to the ST8/SCCmec IV clone (i.e. USA300) and they have spa types t008 (n=9) or t2196 (n=2). Conversely, the MSSA strains with *ermA*, *ermB* or *ermC* genes were genetically diverse. Analysis of 28 ery-R MSSA isolates showed that they fell into 17 different spa types. Types with >1 isolates included t338 (n=7), t437 (n=3), t002 (n=2), t091 (n=2) and t127 (n=2). The following spa types had one isolate each: t012, t034, t1244, t1399, t2421, t337, t3485, t363, t732, t899 and t930.

This study revealed distinctive patterns of *erm* and *msrA* genes among *S. aureus* populations. The majority of ery-R MSSA and HA-MRSA had the iMLS phenotype encoded by either the *ermA* or *ermC* genes. In contrast, ery-R CA-MRSA isolates often had the cMLS phenotype and *ermB*. The findings indicate both independent acquisitions of the *erm* genes as well as spread of specific resistant clones. As observed previously, *ermA* is usually inducible while *ermB* is expressed constitutively, and the expression of *ermC* may be either inducible or constitutive [5]. A small proportion of the *ermA* positive strains had the cMLS phenotype.

Such change from inducible to constitutive expression could possibly be due to gene duplication, deletion or point mutation in the *erm* regulatory regions [4]. With the exception of the CA-MRSA isolates related to the USA300 clone, the *msrA* was rare among the other *S. aureus* populations; suggesting that the gene may have been recently introduced to our community. In conclusion, our findings demonstrate that emergence of CA-MRSA in our locality was associated with emergence of the *ermB* and *msrA* genes that were uncommon among the MSSA and HA-MRSA populations.

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Ethical approval: not required.

Table 1

Prevalence of macrolide resistance genes among 155 erythromycin-resistant *Staphylococcus aureus* isolates, 2004-2007

<i>S. aureus</i> group	No (% by <i>S. aureus</i> group)				
	<i>ermA</i>	<i>ermB</i>	<i>ermC</i>	<i>msrA</i>	none
MSSA (n=55)					
cMLS	0	6 (10.9)	4 (7.3)		
iMLS	37 (67.3)	0	6 (10.9)		
M	0	0	0	1	1
HA-MRSA (n=65)					
cMLS	2 (3.1)	0	2 (3.1)		
iMLS	27 (41.5)	0	35 (53.8) ^a		
CA-MRSA (n=35)					
cMLS	0	22 (62.9)	2 (5.7) ^b		2
M	0	0	0	11	

^a One isolate positive for both *ermA* and *ermC* genes.

^b Two isolates positive for both *ermB* and *ermC*

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