

## Antimicrobial resistance in group B streptococcus: the Australian experience

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Intrapartum chemoprophylaxis for pregnant group B streptococcus (GBS) carriers reduces vertical transmission, with a resultant decrease in neonatal as well as maternal morbidity from invasive GBS infection. Current Australian guidelines recommend penicillin for intrapartum prophylaxis of GBS carriers, with erythromycin or clindamycin for those with a  $\beta$ -lactam allergy. Recent reports globally suggest that resistance to erythromycin and clindamycin may be increasing; hence, a study was undertaken to promote an evidence base for local clinical guidelines. Samples collected for standardized susceptibility testing included 1160 invasive GBS isolates (264 isolates retrospectively from 1982 to 2001 and prospectively from 2002 to 2006, plus 896 prospectively collected colonizing GBS isolates gathered over a 12 month period from 2005 to 2006) from 16 laboratories around Australia. All isolates displaying phenotypic macrolide or lincosamide resistance were subsequently genotyped. No isolates showed reduced susceptibility to penicillin or vancomycin. Of the invasive isolates, 6.4% demonstrated phenotypic erythromycin resistance and 4.2% were clindamycin resistant. Of the erythromycin-resistant isolates, 53% showed cross-resistance to clindamycin. Very similar results were found in colonizing specimens. There was no statistically significant change in macrolide-resistance rates over the two study periods 1982–2001 and 2002–2006. Genotyping for macrolide and lincosamide-resistant isolates was largely consistent with phenotype. These findings suggest that penicillin therapy remains an appropriate first-line antibiotic choice for intrapartum GBS chemoprophylaxis, with erythromycin and/or clindamycin resistance being low in the Australian population. It would, nevertheless, be appropriate for laboratories screening for GBS in obstetric patients to consider macrolide sensitivity testing, particularly for those with  $\beta$ -lactam allergy, to ensure appropriate chemoprophylaxis.

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### INTRODUCTION

*Streptococcus agalactiae*, or group B  $\beta$ -haemolytic streptococcus, is a common cause of neonatal sepsis and meningitis worldwide. The maternal genital tract is the usual source of group B streptococcus (GBS) causing early

onset neonatal infection in the first week of life (Baker & Barrett, 1973). The prevalence of GBS carriage in the vagina at the time of delivery varies from 5 to 30%, with peripartum transmission to the newborn resulting in colonization in 50–70% of cases, if no action is taken to prevent transmission (Anthony, 1982).

Early onset GBS sepsis became a notable problem in many parts of the world in the late 1970s. At the Royal Women's Hospital in Melbourne, Australia, at its peak in 1979, the rate of early onset neonatal GBS sepsis was 3.2 per 1000 births, with a mortality rate of 40% (Garland, 1991). With implementation of maternal screening and intrapartum

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Abbreviations: AEG, Antibiotic Expert Group; CDC, Centers for Disease Control and Prevention; CLSI, Clinical and Laboratory Standards Institute; GBS, group B streptococcus; MLSB, macrolide–lincosamide–streptogramin.

chemoprophylaxis during the 1980s, the rate of early onset GBS sepsis at the Royal Women's Hospital decreased to 0.5 per 1000 births (Garland & Fliegner, 1991). Similar improvements have been reported across Australia (where from 1992 to 2001 the rate of early onset GBS sepsis declined from a peak of 1.43 per 1000 live births in 1993 to 0.25 per 1000 in 2001; Daley & Garland, 2004; Daley & Isaacs, 2004), as well as worldwide (CDC, 2007; Wendel *et al.*, 2002).

Over the past decade, the practice of universal screening at 35–37 weeks gestation, with intrapartum chemoprophylaxis for colonized mothers, has been endorsed by multiple organizations, including the United States Centers for Disease Control (Schrag *et al.*, 2002), and by the Royal Australian and New Zealand College of Obstetricians and Gynaecologists (RANZCOG, 2007).

The usual recommendation for the prevention of GBS transmission from colonized women to their infants during labour is to administer intravenous penicillin every 4 h for the duration of labour (AEG, 2010). Almost all GBS isolates are highly susceptible to penicillin; there have been only a few reported instances of penicillin-resistance worldwide (Moyo *et al.*, 2001; Hsueh *et al.*, 2001). Penicillin therefore remains the first-line treatment of choice (Schrag *et al.*, 2002).

A number of women will, however, report a penicillin or cephalosporin allergy. Under these circumstances, the alternative antibiotic choices have traditionally been erythromycin or clindamycin. Current Australian antibiotic therapeutic guidelines (AEG, 2010) and Australasian Society for Infectious Diseases guidelines (Palasanthiran *et al.*, 2002) recommend the use of clindamycin for second-line intrapartum prophylaxis in GBS-colonized mothers with  $\beta$ -lactam antibiotic allergy.

Recent reports from around the world have, however, raised concerns about the rising rates of macrolide resistance in GBS (Andrews *et al.*, 2000; Desjardins *et al.*, 2004; Janapatla *et al.*, 2008). Cross-resistance (either inducible or constitutive) to lincosamides such as clindamycin may exist (Castor *et al.*, 2008). There are two major mechanisms of macrolide resistance and each genetic mechanism manifests a different resistance phenotype. In general, resistance to macrolides in GBS is conferred either by methylases encoded by *erm* genes (B, A/TR or C), giving rise to the macrolide–lincosamide–streptogramin (MLS<sub>B</sub>) resistance phenotype, or by membrane-bound pumps that cause efflux of macrolide antibiotics, encoded by *mef* genes (A or E), and giving rise to the M phenotype (Marimón *et al.*, 2005). Erythromycin-resistant isolates with the MLS<sub>B</sub> phenotype will usually display cross-resistance to clindamycin, whereas isolates with the M phenotype usually display only erythromycin resistance.

Worldwide, resistance rates of up to 54 % for erythromycin (DiPersio & DiPersio, 2006) and 39 % for clindamycin

have been described (Janapatla *et al.*, 2008). In light of the high levels of resistance reported worldwide, some experts have recommended that vancomycin (rather than macrolides or lincosamides) should constitute the second-line intrapartum chemoprophylaxis for GBS prevention (Peláez *et al.*, 2009; Schrag *et al.*, 2002).

To date, there have been no data to suggest that such a change to guidelines would be necessary in Australia. A small study performed on 250 colonizing GBS isolates at a single institution in Melbourne in 2001 showed that only 2.8 % of isolates were resistant to erythromycin (Stylianopoulos *et al.*, 2002). This study was limited by its size, its inclusion of only colonizing isolates and the fact that it was not population based.

The purpose of this national survey was to obtain a more comprehensive understanding of rates of macrolide resistance in GBS around Australia. Another objective was to determine if there has been a change in resistance patterns amongst invasive GBS isolates over the past decade. This should provide a better evidence base for future antimicrobial recommendations for GBS intrapartum prophylaxis, particularly for women who report a  $\beta$ -lactam allergy.

## METHODS

**Study population.** In 2004, an invitation to participate in a nationwide survey of GBS isolates was publicized through the Australasian Group for Antimicrobial Resistance. Sixteen public and private laboratories, servicing obstetric and neonatal patients across most of the States and Territories in Australia, participated in the study.

Both invasive (blood and cerebrospinal fluid specimens) and colonizing GBS isolates were requested and supplied. Participants were asked to submit the first ten colonizing anogenital isolates received by the laboratory each month over a period of 24 months from October 2004 to September 2006. In addition, stored invasive GBS isolates collected between 1982 and 2001 were requested, as well as prospectively collected invasive GBS isolates from 2002–2006. Specimens were submitted to a central bacteriology laboratory at the Royal Children's Hospital in Melbourne and stored at  $-70^{\circ}\text{C}$  until needed for further testing.

**Confirmation of GBS identification and susceptibility testing.** All submitted isolates had their identification confirmed by standardized methods at the central bacteriology laboratory. Test and control organisms were subcultured onto horse blood agar (Oxoid) and incubated at  $35^{\circ}\text{C}$  in 5 %  $\text{CO}_2$  for 24 h. To confirm identification of each isolate, a CAMP (Christie–Atkins–Munch–Petersen) test was performed (Gerhardt *et al.*, 1994) on whole blood Mueller–Hinton agar (Oxoid). A positive control, *Streptococcus agalactiae* ATCC 13813, and two negative control organisms, *Enterococcus faecalis* ATCC 29212 and *Streptococcus pyogenes* ATCC 19615, were employed, along with *Staphylococcus aureus* ATCC 25923. Any referred isolates with a negative CAMP test had the test repeated. If the isolate failed the repeat test or produced equivocal results, a latex agglutination test was performed using the Streptex kit (Remel). If no agglutination occurred, the isolate was discarded.

All confirmed GBS isolates were tested for susceptibility to penicillin, erythromycin, clindamycin and vancomycin using a 0.5 McFarland

**Table 1.** Phenotypic resistance patterns amongst invasive GBS isolates over two study periods 1981–2001 and 2002–2006

Invasive	Total	1981–2001	2002–2006
Total no. of GBS isolates	264	117	147
Erythromycin resistance only	8	5	3
Clindamycin resistance only	2	0	2
Combined erythromycin and clindamycin resistance	9	1	8
Total no. of isolates with either erythromycin or clindamycin resistance	19	6	13

standard suspension in 2.0 ml Mueller–Hinton broth. Suspension turbidity was determined using a Vitek colorimeter (bioMérieux). Isolates were tested by agar disc diffusion, with manual reading of zone diameters analysed according to the interpretive criteria recommended by the Clinical and Laboratory Standards Institute (CLSI) guidelines (supplement M100-S16) (CLSI, 2006).

All isolates had their penicillin MIC confirmed by Etest (bioMérieux) according to CLSI guidelines. In addition, all erythromycin and/or clindamycin-resistant isolates had their MICs for erythromycin and clindamycin determined by Etest.

For the detection of a 'D zone' indicating inducible clindamycin-resistant, erythromycin-resistant, clindamycin-sensitive strains were tested with erythromycin (15 µg) and clindamycin (2 µg) discs, with the inner edges 25 mm apart. Strains with D shaped (or flattened) clindamycin zones were classified as having inducible resistance to clindamycin (CLSI, 2006).

**PCR and DNA sequencing.** All erythromycin- and/or clindamycin-resistant strains were genotyped using a genotype specific PCR and/or sequencing of: a portion of the *cps* gene cluster; surface protein antigens, including *Cx*, *Rib*,  $\alpha$ -like proteins 2-4 and *Cβ*; and 3–7 mobile genetic elements – *IS861*, *IS1548*, *IS1381*, *ISSa4*, *ISSag1*, *ISSag2* and *GBSi1*, as described by Zeng *et al.* (2006).

**Statistical analysis.** The Pearson's  $\chi^2$  test was used to assess the non-parametric data. The test of significance was two-tailed and a  $P < 0.05$  was considered significant. The test was performed with SPSS version 12 software (SPSS).

## RESULTS AND DISCUSSION

In total, 1302 isolates were received from 16 independent laboratories around Australia. Of these, 142 were excluded for the following reasons: 98 were non-viable, 22 were not confirmed as GBS, 21 could not be identified as colonizing or invasive specimens by the submitting laboratory and 1

was sent in duplicate. Of the remaining 1160 isolates included in this survey, 264 were invasive isolates and 896 were colonizing isolates.

### Antibiotic susceptibility

All isolates were susceptible to penicillin and vancomycin. There was no evidence of an increase in penicillin MICs over the study period (maximum penicillin MIC penicillin in this study 0.125 µg ml<sup>-1</sup>).

This study found that rates of erythromycin and clindamycin resistance remain relatively low in GBS isolates across Australia, in both invasive and colonizing isolates. Of the invasive isolates, 17/264 (6.4%) showed erythromycin resistance (with MICs between 6 and 12 µg ml<sup>-1</sup>), whilst 11/264 (4.2%) showed clindamycin resistance. Of the erythromycin-resistant isolates, 9/17 (53%) showed cross-resistance to clindamycin. The macrolide and lincosamide resistance rates amongst invasive isolates are shown in Table 1.

Of note, there was no statistically significant ( $P = 0.43$ ) increase in the rate of macrolide resistance in invasive specimens between the two study periods 1982–2001 (5.1%) and 2002–2006 (7.5%), although there was a significant increase in the number of macrolide-resistant isolates that exhibited cross-resistance to clindamycin from 17 to 73% ( $P = 0.03$ ). Interestingly, rates of macrolide resistance reported in this study are somewhat higher than those reported in a 2002 single centre study in Melbourne (Stylianopoulos *et al.*, 2002). No invasive isolates collected in the period 1981–2002 showed only clindamycin resistance, but from 2002 to 2006 there were two invasive isolates that demonstrated such resistance.

**Table 2.** Selected antimicrobial resistance patterns for GBS in published studies worldwide

Country	Reference	Year	Erythromycin resistance (%)	Clindamycin resistance (%)
United States	DiPersio & DiPersio (2006)		54	33
Taiwan	Janapatla <i>et al.</i> (2008)	2001–2007	44	39
Korea	Uh <i>et al.</i> (2007)	2003–2004	37	43
Norway	Bergseng <i>et al.</i> (2008)	2006	25	25
France	Fitoussi <i>et al.</i> (2001)	2000	18	12
Portugal	Figueira-Coelho <i>et al.</i> (2004)	1999–2002	11	10
Japan	Matsubara <i>et al.</i> (2001)	1999–2000	3	1

**Table 3.** Phenotypic resistance patterns amongst 19 invasive GBS isolates displaying phenotypic macrolide or lincosamide resistance, with the genotype correlates

Invasive GBS	Total	<i>ermA</i>	<i>ermB</i>	<i>mefA</i>
Erythromycin resistance only	8	6	–	8
Clindamycin resistance only	2	2	–	–
Both erythromycin and clindamycin resistance	9	4	8	9

Amongst the colonizing isolates, 55/896 (6.1%) were resistant to erythromycin (MICs 4–16  $\mu\text{g ml}^{-1}$ , except for 2 isolates with MICs  $>256 \mu\text{g ml}^{-1}$ ) and 60/896 (6.7%) were clindamycin resistant. Of the erythromycin-resistant isolates 38/55 (69%) showed cross-resistance to clindamycin; of these 19 demonstrated inducible resistance (based on a positive D test) and 19 demonstrated constitutive resistance (based on CLSI zone of inhibition interpretation). Of note, rates of erythromycin resistance did not vary significantly between invasive and colonizing isolates (6.4% versus 6.1%;  $P=0.86$ ).

This situation in Australia differs from other parts of the world, where rates of erythromycin resistance appear to be rising rapidly. Resistant rates of up to 54% for erythromycin and 43% for clindamycin have been described in international studies (DiPersio & DiPersio, 2006) (Table 2). In one series, 71% of erythromycin-resistant strains were also resistant to clindamycin (Bergseng *et al.*, 2008).

### Correlation of phenotype and genotype

All isolates with phenotypic macrolide or lincosamide resistance were further investigated by genotyping, comprising a total of 19 invasive and 77 colonizing isolates. In general, genotypes were largely consistent with phenotype.

Amongst the invasive isolates, all 8 of the erythromycin-only resistant isolates contained the *mefA* gene and 6/8 (75%) additionally carried the *ermA* gene. The two clindamycin-only resistant isolates carried only the *mefA* gene. Amongst the 9 isolates with a phenotype of combined macrolide and lincosamide resistance, all 9 carried the *mefA* gene and 8/9 (89%) additionally carried the *ermB* gene (Table 3), as might be expected for the MLSB phenotype.

Amongst the colonizing isolates, 16/17 (94%) of the erythromycin-only resistant isolates carried the *mefA* gene.

Amongst those that demonstrated phenotypic macrolide-lincosamide cross-resistance, 18/38 (47%) carried the *ermB* gene and 22/38 (58%) carried the *ermA* gene; 15/38 (39%) additionally carried the *mefA* gene. Of note, in 16 isolates (14 of which demonstrated constitutive clindamycin resistance only), no genotypic resistance mechanism could be determined. Most of these isolates displayed only constitutive lincosamide resistance, similar to the LSA phenotype reported in New Zealand (Malbruny *et al.*, 2004). The macrolide and lincosamide resistance rates amongst colonizing isolates, with associated genotyping, are shown in Table 4.

### Limitations

This study was limited by the non-randomized nature of laboratory participation and may therefore not adequately represent the true geographical spread of GBS phenotypes across all of Australia. In addition, samples prior to 2002 were collected based upon available stored samples, which may not have been randomly chosen for storage and may potentially bias results.

### Conclusion

In the Australian context, penicillin remains the antibiotic of choice for intrapartum GBS chemoprophylaxis, and erythromycin and clindamycin remain appropriate alternatives for  $\beta$ -lactam allergic patients requiring prophylaxis. In light of the possibility of macrolide and lincosamide resistance, however, it is advisable that laboratories should perform macrolide and lincosamide susceptibility testing, particularly for those women with  $\beta$ -lactam allergy, to ensure appropriate chemoprophylaxis. If GBS susceptibility is unknown at the time of delivery, consideration should be given to the use of vancomycin for second-line chemoprophylaxis (Schrag *et al.*, 2002).

**Table 4.** Phenotypic resistance patterns amongst colonizing GBS isolates, with genotype correlates

Colonizing GBS	Total	Inducible	Constitutive	<i>ermA</i>	<i>ermB</i>	<i>mef</i>	None
Erythromycin resistance only	17	–	–	–	–	16	1
Clindamycin resistance only	22	3	19	7	1	–	14
Both erythromycin and clindamycin resistance	38	19	19	22	18	15	1
Total	77	22	38	29	19	31	16

In view of the global situation, where macrolide and lincosamide resistance is rising sharply in some regions, together with concerns about the clonal spread of resistance, rates of GBS resistance in Australia require ongoing close surveillance to ensure that antibiotic recommendations for GBS prophylaxis remain appropriate and safe.

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## REFERENCES

- AEG (2010).** *Therapeutic Guidelines: Antibiotic*, version 14. Melbourne: Therapeutic Guidelines Limited.
- Andrews, J. I., Diekema, D. J., Hunter, S. K., Rhomberg, P. R., Pfaller, M. A., Jones, R. N. & Doern, G. V. (2000).** Group B streptococci causing neonatal bloodstream infection: antimicrobial susceptibility and serotyping results from SENTRY centers in the western hemisphere. *Am J Obstet Gynecol* **183**, 859–862.
- Anthony, B. F. (1982).** Carriage of group B streptococci during pregnancy: a puzzler. *J Infect Dis* **145**, 789–793.
- Baker, C. J. & Barrett, F. F. (1973).** Transmission of group B streptococci among parturient women and their neonates. *J Pediatr* **83**, 919–925.
- Bergseng, H., Rygg, M., Bevanger, L. & Bergh, K. (2008).** Invasive group B streptococcus (GBS) disease in Norway 1996–2006. *Eur J Clin Microbiol Infect Dis* **27**, 1193–1199.
- Castor, M. L., Whitney, C. G., Como-Sabetti, K., Facklam, R. R., Ferrieri, P., Bartkus, J. M., Juni, B. A., Cieslak, P. R., Farley, M. M. & other authors (2008).** Antibiotic resistance patterns in invasive group B streptococcal isolates. *Infect Dis Obstet Gynecol* **2008**, 727505.
- CDC (2007).** Perinatal group B streptococcal disease after universal screening recommendations – United States, 2003–2005. *MMWR Morb Mortal Wkly Rep* **56**, 701–705.
- CLSI (2006).** *Performance Standards for Antimicrobial Susceptibility Testing*, supplement M100-S16. Wayne, PA: Clinical and Laboratory Standards Institute.
- Daley, A. J. & Garland, S. M. (2004).** Prevention of neonatal group B streptococcal disease: progress, challenges and dilemmas. *J Paediatr Child Health* **40**, 664–668.
- Daley, A. J. & Isaacs, D. (2004).** Ten-year study on the effect of intrapartum antibiotic prophylaxis on early onset group B streptococcal and *Escherichia coli* neonatal sepsis in Australasia. *Pediatr Infect Dis J* **23**, 630–634.
- Desjardins, M., Delgaty, K. L., Ramotar, K., Seetaram, C. & Toye, B. (2004).** Prevalence and mechanisms of erythromycin resistance in group A and group B streptococcus: implications for reporting susceptibility results. *J Clin Microbiol* **42**, 5620–5623.
- DiPersio, L. P. & DiPersio, J. R. (2006).** High rates of erythromycin and clindamycin resistance among OBGYN isolates of group B streptococcus. *Diagn Microbiol Infect Dis* **54**, 79–82.
- Figueira-Coelho, J., Ramirez, M., Salgado, M. J. & Melo-Cristino, J. (2004).** *Streptococcus agalactiae* in a large Portuguese teaching hospital: antimicrobial susceptibility, serotype distribution, and clonal analysis of macrolide-resistant isolates. *Microb Drug Resist* **10**, 31–36.
- Fitoussi, F., Loukil, C., Gros, I., Clermont, O., Mariani, P., Bonacorsi, S., Le Thomas, I., Deforche, D. & Bingen, E. (2001).** Mechanisms of macrolide resistance in clinical group B streptococci isolated in France. *Antimicrob Agents Chemother* **45**, 1889–1891.
- Garland, S. M. (1991).** Early onset neonatal group B streptococcus (GBS) infection: associated obstetric risk factors. *Aust N Z J Obstet Gynaecol* **31**, 117–118.
- Garland, S. M. & Fliegner, J. R. (1991).** Group B streptococcus (GBS) and neonatal infections: the case for intrapartum chemoprophylaxis. *Aust N Z J Obstet Gynaecol* **31**, 119–122.
- Gerhardt, P., Krieg, N. & Murray, R. (1994).** *Methods for General and Molecular Bacteriology*. Washington, DC: American Society for Microbiology.
- Hsueh, P. R., Teng, L. J., Lee, L. N., Ho, S. W., Yang, P. C. & Luh, K. T. (2001).** High incidence of erythromycin resistance among clinical isolates of *Streptococcus agalactiae* in Taiwan. *Antimicrob Agents Chemother* **45**, 3205–3208.
- Janapatla, R. P., Ho, Y. R., Yan, J. J., Wu, H. M. & Wu, J. J. (2008).** The prevalence of erythromycin resistance in group B streptococcal isolates at a University Hospital in Taiwan. *Microb Drug Resist* **14**, 293–297.
- Malbruny, B., Werno, A. M., Anderson, T. P., Murdoch, D. R. & Leclercq, R. (2004).** A new phenotype of resistance to lincosamide and streptogramin A-type antibiotics in *Streptococcus agalactiae* in New Zealand. *J Antimicrob Chemother* **54**, 1040–1044.
- Marimón, J. M., Valiente, A., Ercibengoa, M., García-Arenzana, J. M. & Pérez-Trallero, E. (2005).** Erythromycin resistance and genetic elements carrying macrolide efflux genes in *Streptococcus agalactiae*. *Antimicrob Agents Chemother* **49**, 5069–5074.
- Matsubara, K., Nishiyama, Y., Katayama, K., Yamamoto, G., Sugiyama, M., Murai, T. & Baba, K. (2001).** Change of antimicrobial susceptibility of group B streptococci over 15 years in Japan. *J Antimicrob Chemother* **48**, 579–582.
- Moyo, S. R., Maeland, J. A. & Munemo, E. S. (2001).** Susceptibility of Zimbabwean *Streptococcus agalactiae* (group B streptococcus; GBS) isolates to four different antibiotics. *Cent Afr J Med* **47**, 226–229.
- Palasanthiran, P., Starr, M. & Jones, C. (editors) (2002).** *Management of Perinatal Infections*. Sydney: Australasian Society for Infectious Diseases.
- Peláez, L. M., Gelber, S. E., Fox, N. S. & Chasen, S. T. (2009).** Inappropriate use of vancomycin for preventing perinatal group B streptococcal (GBS) disease in laboring patients. *J Perinat Med* **37**, 487–489.
- RANZCOG (2007).** *Screening and Treatment for Group B Streptococcus in Pregnancy*, RANZCOG statement C-Obs 19. Melbourne: Royal Australian and New Zealand College of Obstetricians and Gynaecologists.
- Schrag, S., Gorwitz, R., Fultz-Butts, K. & Schuchat, A. (2002).** Prevention of perinatal group B streptococcal disease. Revised guidelines from CDC. *MMWR Recomm Rep* **51**, 1–22.

**Stylianopoulos, A., Kelly, N. & Garland, S. (2002).** Is penicillin and/or erythromycin resistance present in clinical isolates of group B streptococcus in our community? *Aust N Z J Obstet Gynaecol* **42**, 543–544.

**Uh, Y., Hwang, G. Y., Jang, I. H., Kwon, O., Kim, H. Y. & Yoon, K. J. (2007).** Antimicrobial susceptibility patterns and macrolide resistance genes of  $\beta$ -hemolytic viridans group streptococci in a tertiary Korean hospital. *J Korean Med Sci* **22**, 791–794.

**Wendel, G. D., Jr, Leveno, K. J., Sanchez, P. J., Jackson, G. L., McIntire, D. D. & Siegel, J. D. (2002).** Prevention of neonatal group B streptococcal disease: a combined intrapartum and neonatal protocol. *Am J Obstet Gynecol* **186**, 618–626.

**Zeng, X., Kong, F., Wang, H., Darbar, A. & Gilbert, G. L. (2006).** Simultaneous detection of nine antibiotic resistance-related genes in *Streptococcus agalactiae* using multiplex PCR and reverse line blot hybridization assay. *Antimicrob Agents Chemother* **50**, 204–209.