

## Ampicillin Susceptibilities of Vaginal and Placental Isolates of Group B Streptococcus and *Escherichia coli* Obtained between 1992 and 1994

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**Vaginal group B streptococcus (GBS) and *Escherichia coli* isolates were tested for their susceptibilities to ampicillin. All 414 GBS isolates tested were susceptible to ampicillin; the MIC at which 90% of the isolates were inhibited (MIC<sub>90</sub>) was 0.125 µg/ml, and the range was 0.06 to 0.25 µg/ml. The MIC<sub>50</sub> for the 342 *E. coli* isolates tested was 4.0 µg/ml, and 27% were resistant to ampicillin.**

The use of intrapartum ampicillin has been shown to reduce the incidence of early-onset group B streptococcus (GBS) sepsis in newborns (9). Ampicillin use for the prevention of GBS disease in women with premature rupture of membranes has been reported in association with complications in newborns attributable to ampicillin-resistant *Escherichia coli* (6). Although GBS has shown consistent susceptibility to ampicillin, a recent study reported that 8% of the clinical isolates from various sources had intermediate susceptibility to ampicillin (3).

The purpose of this study was to determine the susceptibility of GBS and *E. coli* to ampicillin in a population of women from whom vaginal cultures were obtained prior to the time of delivery at the University of Washington Medical Center. A second purpose of this study was to determine whether isolates of GBS which were near the breakpoint of intermediate susceptibility to ampicillin were susceptible to penicillin G, since some authors have suggested that penicillin G might be a better choice than ampicillin for prophylaxis against GBS (1).

Between October 1992 and December 1994, vaginal swabs were collected from women upon admission to Labor and Delivery at the University of Washington Medical Center. The swabs were placed in Amies transport media (MML Diagnostics Packaging, Inc., Troutdale, Oreg.) and then were used to inoculate Columbia agar plates containing 5% sheep blood (Prepared Media Laboratories [PML], Tualatin, Oreg.). The swabs were then placed into selective broth media (PML). Both the plates and the broths were incubated overnight in 5% CO<sub>2</sub> at 37°C. The broths were then subcultured onto other blood agar plates and incubated overnight. Placentas were cultured within 12 h of delivery by swabbing the area between the chorion and the amnion within 4 cm of the point of rupture and then directly inoculating a blood agar plate as previously described (5). These plates were incubated in 5% CO<sub>2</sub> at 37°C for 48 h. *E. coli* was identified by conventional methods. GBS was identified on the basis of colony morphology and a negative 3% catalase reaction and was confirmed by the Streptex latex agglutination system (Murex Diagnostics Limited, Dartford, England). Isolates were stored at -70°C in litmus milk (Difco Laboratories, Detroit, Mich.). In 1995, this study and

the investigators moved from Seattle to Pittsburgh, where the stocked isolates were evaluated for susceptibility. Testing of the susceptibilities of GBS and *E. coli* isolates to ampicillin and penicillin G was performed by the agar dilution method described in the National Committee for Clinical Laboratory Standards guidelines (8).

A total of 414 vaginal GBS isolates, 138 from women enrolled consecutively during October to December in each calendar year (1992 to 1994) were tested for their susceptibilities to ampicillin. This sample was selected for convenience. All isolates were susceptible to ampicillin; the MIC at which 50% of the isolates were inhibited (MIC<sub>50</sub>) and the MIC<sub>90</sub> were 0.125 µg/ml, and the range was 0.06 to 0.25 µg/ml (Table 1). Additional susceptibility testing with penicillin G on the 30 isolates of GBS that were near the breakpoint (0.125 to 0.25 µg/ml) demonstrated that all were susceptible to penicillin G, with a MIC of 0.06 µg/ml. GBS was isolated from 32 placentas during the study. All 32 isolates were susceptible to ampicillin, with a MIC of 0.125 µg/ml.

A convenience sample of 342 vaginal *E. coli* isolates, 114 from women enrolled consecutively during the same period in each calendar year, was tested for their susceptibilities to ampicillin (Table 2). The MIC<sub>50</sub> and MIC<sub>90</sub> remained at 4.0 and >128 µg/ml, respectively, for each year, with a range of 1.0 to >128 µg/ml. The proportion of *E. coli* isolates which were resistant to ampicillin (MIC ≥ 32 µg/ml) ranged from 25% in 1992 to 27% in 1993 and 28% in 1994 (not significant). Of the 13 placental *E. coli* isolates tested, 5 (39%) were resistant to ampicillin.

The results from this study do not suggest a trend toward reduced susceptibility of vaginal GBS and *E. coli* isolates to ampicillin. Selection for ampicillin resistance among strains of GBS and *E. coli* which colonize pregnant women is a concern. There are three studies which suggest that ampicillin use may be associated with an increase in *E. coli* resistance. In a study of 953 infants in 22 Swedish neonatal intensive-care units, infants treated with ampicillin had fecal carriage rates of ampicillin-resistant *E. coli* three times higher than those of untreated infants (12). However, this study focused on colonization rather than infection as an outcome. A series of four cases of adverse perinatal outcomes with resistant *Enterobacteriaceae* were reported after antibiotic usage for premature rupture of fetal membranes and carriage of GBS (6). In a third study, ampicillin-resistant strains of *E. coli* were recovered from the cerebrospinal fluid of neonates who had received ampicillin

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TABLE 1. Susceptibility of vaginal GBS isolates to ampicillin

MIC ( $\mu\text{g/ml}$ ) <sup>a</sup>	No. of isolates by yr		
	1992	1993	1994
0.06	4	18	4
0.125	133	109	128
0.25	1	11	6
Total	138	138	138

<sup>a</sup> MICs from the National Committee for Clinical Laboratory Standards (8) for isolates susceptible to ampicillin are  $\leq 0.25$   $\mu\text{g/ml}$ .

prophylaxis, who had been nursed in incubators for more than 1 week, or whose mothers had fever during labor (7).

Penicillin G is an alternative to intravenous ampicillin for antibiotic prophylaxis against early-onset GBS disease in the newborn. Amstey and Gibbs consider penicillin G to be a better choice since it has a narrower spectrum of activity, which may reduce the possibility of selecting for resistant organisms in the mother or neonate (1). Penicillin G is also currently recommended by the Centers for Disease Control for GBS prophylaxis during labor (4). Penicillin G was shown to be effective in vitro against 30 GBS isolates.

In this study, all 414 GBS isolates were susceptible to ampicillin. These results are similar to those of a 1989 study of 156 genital isolates of GBS (2). Our results differ from those of a Spanish study of 100 GBS urogenital tract isolates which found

TABLE 2. Susceptibility of vaginal *E. coli* isolates to ampicillin

MIC ( $\mu\text{g/ml}$ ) <sup>a</sup>	No. of isolates by yr		
	1992	1993	1994
1.0	3	3	2
2.0	17	34	24
4.0	61	42	51
8.0	4	3	4
16.0	0	1	1
64.0	2	1	3
128.0	1	0	0
>128	26	30	29
Total	114	114	114

<sup>a</sup> MICs from the National Committee for Clinical Laboratory Standards (8) for susceptible, intermediate, and resistant isolates, respectively, are as follows:  $\leq 8.0$ , 16.0, and  $\geq 32.0$   $\mu\text{g/ml}$ .

that 8% of strains had intermediate susceptibility to ampicillin and 2% had intermediate susceptibility to penicillin (3).

Prevention of GBS sepsis through intrapartum prophylaxis will require that an estimated 27% of women be treated with intravenous antibiotics during labor (4, 10). This level of antibiotic exposure has the potential to increase GBS resistance to beta-lactams. Screening pregnant women antepartum and treating intrapartum is a good interim prevention strategy. However, for the long term, a vaccine against GBS which would offer immunity to invasive infection may be a preferable strategy (11).

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## REFERENCES

- Amstey, M. S., and R. S. Gibbs. 1994. Is penicillin G a better choice than ampicillin for prophylaxis of neonatal group B streptococcal infections? *Obstet. Gynecol.* **84**:1058-1059.
- Berkowitz, K., J. A. Regan, and E. Greenberg. 1990. Antibiotic resistance patterns of group B streptococci in pregnant women. *J. Clin. Microbiol.* **28**:5-7.
- Betriu, C., M. Gomez, A. Sanchez, A. Cruceyra, J. Romero, and J. J. Picazo. 1994. Antibiotic resistance and penicillin tolerance in clinical isolates of group B streptococci. *Antimicrob. Agents Chemother.* **38**:2183-2186.
- Centers for Disease Control and Prevention. 1996. Prevention of perinatal group B streptococcal disease: a public health perspective. *Morbid. Mortal. Weekly Rep.* **45**(No. RR-7):1-27.
- Hillier, S. L., M. A. Krohn, N. B. Kiviat, D. H. Watts, and D. A. Eschenbach. 1991. Microbiologic causes of neonatal outcomes associated with chorioamnion infection. *Am. J. Obstet. Gynecol.* **165**:955-961.
- McDuffie, R. S., Jr., J. A. McGregor, and R. S. Gibbs. 1993. Adverse perinatal outcome and resistant *Enterobacteriaceae* after antibiotic usage for premature rupture of the membranes and group B *Streptococcus* carriage. *Obstet. Gynecol.* **82**:487-489.
- Mulder, C. J. J., P. Bol, A. J. J. M. Nabbe, and H. C. Zanen. 1985. Susceptibility of 126 isolates of *Escherichia coli* from the cerebrospinal fluid of neonates to five antibiotics. *J. Antimicrob. Chemother.* **15**:115-118.
- National Committee for Clinical Laboratory Standards. 1997. Methods for dilution antimicrobial susceptibility tests for bacteria that grow aerobically, 4th ed. Approved standard M7-A4. National Committee for Clinical Laboratory Standards, Wayne, Pa.
- Pylypow, M., M. Gaddis, and J. S. Kinney. 1994. Selective intrapartum prophylaxis for group B *Streptococcus* colonization: management and outcome of newborns. *Pediatrics* **93**:631-635.
- Rouse, D. J., R. L. Goldenberg, S. P. Oliver, G. R. Cutter, S. T. Mennenmeyer, and C. A. Fargason, Jr. 1994. Strategies for the prevention of early-onset neonatal group B streptococcal sepsis: a decision analysis. *Obstet. Gynecol.* **83**:483-494.
- Schuchat, A., and J. D. Wenger. 1994. Epidemiology of group B streptococcal disease: risk factors, prevention strategies, and vaccine development. *Epidemiol. Rev.* **16**:374-402.
- Tullus, K., B. Berglund, and L. G. Burman. 1990. Emergence of cross-resistance to  $\beta$ -lactam antibiotics in fecal *Escherichia coli* and *Klebsiella* strains from neonates treated with ampicillin or cefuroxime. *Antimicrob. Agents Chemother.* **34**:361-362.