

Intrapartum Group B Streptococci Prophylaxis in Patients Reporting a Penicillin Allergy

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OBJECTIVE: To examine adherence to the 2002 Centers for Disease Control and Prevention (CDC) guidelines for group B streptococci (GBS) prophylaxis in patients who reported a penicillin allergy.

METHODS: This is a retrospective cohort study of GBS-positive, penicillin-allergic obstetric patients who delivered at our institution from 2004 through 2005 (N=233). Medical records were analyzed for type of delivery, gestational age at delivery, antimicrobial sensitivity testing, and antibiotics administered. Antimicrobial sensitivity testing and appropriate prophylactic antibiotic choice were analyzed. "Appropriate antibiotic choice" was defined using the 2002 CDC guidelines for GBS prophylaxis. Women with either a scheduled cesarean delivery or a preterm delivery were excluded from analyses. Data were analyzed using Stata 9.0.

RESULTS: Overall, 95% (95% confidence interval [CI] 91–97%) of GBS-positive, penicillin-allergic women received antibiotic prophylaxis and only 16% (95% CI 11–21%) of patients received an appropriate antibiotic. The majority of women who were given antibiotics received clindamycin (83%, 95% CI 77–87%); however,

antimicrobial sensitivity testing was performed in only 11% (95% CI 9–17%) of patients. More women received an appropriate antibiotic in 2005 than in 2004 (20% compared with 11%, $P=0.11$). Although the study was underpowered to evaluate the magnitude of increase, the overall prevalence of appropriate antibiotic administration in 2005 was still only 20% (95% CI 13–28%).

CONCLUSION: Adherence to the 2002 CDC guidelines for GBS prophylaxis in penicillin-allergic women is far from optimal. Improvements are necessary in obtaining antimicrobial sensitivity testing and choosing an appropriate antibiotic for GBS-positive women with a reported penicillin allergy.

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LEVEL OF EVIDENCE: II

Group B streptococci (GBS) is a leading cause of neonatal infection. Prophylactic antibiotics administered during labor have reduced the incidence of early-onset neonatal GBS disease by 70%.^{1,2} Although ampicillin is an acceptable alternative, penicillin is the recommended antibiotic for GBS prophylaxis because of its narrow spectrum of antimicrobial activity. No cases of GBS resistance to penicillin or ampicillin have been detected.

Approximately 10% of the population reports an allergy to penicillin.³ Traditionally, patients reporting a penicillin allergy received either clindamycin or erythromycin for GBS prophylaxis. In the United States the prevalence of GBS resistance to both clindamycin and erythromycin is increasing with rates estimated to be 3–15% for clindamycin and 7–25% for erythromycin.^{4–7} At our institution, approximately 26% of GBS isolates are clindamycin-resistant and 37% are erythromycin-resistant (Women and Infants Hospital laboratory data, Judy Struminski, Microbiology Manager, March 2005). Given this information, administering these traditional anti-

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Table 1. Recommended Regimens for Intrapartum Antimicrobial Prophylaxis for Perinatal Group B Streptococci Disease Prevention*

Status	Recommendation
Recommended*	Penicillin G, 5 million units IV initial dose, then 2.5 million units IV every 4 hours until delivery
Alternative	Ampicillin, 2 g IV initial dose, then 1 g IV every 4 hours until delivery
If penicillin allergic†	
Patients not at high risk for anaphylaxis	Cefazolin, 2 g IV initial dose, then 1 g IV every 8 hours until delivery
Patients at high risk for anaphylaxis‡	
GBS susceptible to clindamycin and erythromycin	Clindamycin, 900 mg IV every 8 hours until delivery OR Erythromycin, 500 mg IV every 6 hours until delivery
GBS resistant to clindamycin or erythromycin or susceptibility unknown§	Vancomycin 1g IV every 12 hours until delivery

IV, intravenous; GBS, group B streptococci.

* Broader-spectrum agents, including an agent active against group B streptococci, may be necessary for treatment of chorioamnionitis.

† History of penicillin allergy should be assessed to determine whether a high risk for anaphylaxis is present. Penicillin-allergic patients at high risk for anaphylaxis are those who have experienced immediate hypersensitivity to penicillin, including a history of penicillin-related anaphylaxis; other high-risk patients are those with asthma or other diseases that would make anaphylaxis more dangerous or difficult to treat, such as persons being treated with β -adrenergic–pageing agents.

‡ If laboratory facilities are adequate, clindamycin and erythromycin susceptibility testing should be performed on prenatal group B streptococci isolates from penicillin-allergic women at high risk for anaphylaxis.

§ Resistance to erythromycin is often but not always associated with clindamycin resistance. If a strain is resistant to erythromycin but seems susceptible to clindamycin, it may still have inducible resistance to clindamycin.

|| Cefazolin is preferred over vancomycin for women with a history of penicillin allergy other than immediate hypersensitivity reactions, and pharmacologic data suggest it achieves effective intraamniotic concentrations. Vancomycin should be reserved for penicillin-allergic women at high risk for anaphylaxis.

Data from Schrag S, Gorwitz R, Fultz-Butts K, Schuchat A. Prevention of perinatal group B streptococcal disease. Revised guidelines from CDC. *MMWR Recomm Rep* 2002;51:1–22 and Gibbs RS, Schrag S, and Schuchat A. Perinatal infections due to group B streptococci. *Obstet Gynecol* 2004;104:1062–76.

biotics in labor as an automatic alternative to penicillin could potentially leave many infants exposed to GBS and at risk for sepsis and other complications.

The Centers for Disease Control (CDC), in collaboration with the American College of Obstetricians and Gynecologists (ACOG) and the American Association for Pediatrics (AAP), provided new guidelines for the prevention of early-onset neonatal GBS disease in 2002 (Table 1). Specific guidelines were provided for GBS prophylaxis in patients with a reported penicillin allergy.^{8–10} These guidelines recommend that practitioners obtain a detailed history of the patient's reported penicillin allergy. Patients determined to be at low risk for anaphylaxis should receive intrapartum cephalosporin for GBS prophylaxis. For all other penicillin-allergic patients, antimicrobial sensitivity testing of the GBS isolate should be performed at the time of GBS culture screening. Women with GBS isolates sensitive to both erythromycin and clindamycin should receive either clindamycin or erythromycin in labor. If antimicrobial testing demonstrates resistance to either erythromycin or clindamycin, vancomycin should be administered for GBS prophylaxis because resistance to erythromycin is often associated with clindamycin resistance. If

this testing is not performed, the patient should receive vancomycin for GBS in labor.^{8–10}

In response to these updated guidelines, Women and Infants Hospital finalized hospital guidelines in January 2004. The aim of this study was to estimate the proportion of GBS-positive, penicillin-allergic patients whose management followed the revised CDC and Women and Infants Hospital guidelines for GBS prophylaxis to improve care. We hypothesized that, among penicillin-allergic, GBS-positive patients 1) the proportion who received antimicrobial sensitivity testing increased over time; 2) compared with women who received vancomycin, women who received clindamycin were more likely to have had antimicrobial sensitivity testing; and 3) the proportion of patients who received the appropriate antibiotic increased over time.

MATERIALS AND METHODS

We performed a retrospective cohort study of GBS-positive obstetric patients who reported a penicillin allergy and delivered at Women and Infants Hospital between January 2004 and December 2005. Women and Infants Hospital, an academic tertiary medical center in Providence, Rhode Island, is the site for more than 9,000 deliveries per year. We chose 2004–



2005 because Women and Infants Hospital implemented hospital guidelines for GBS screening and prophylaxis based on the 2002 CDC Guidelines in January 2004. Before initiating the study, The Women and Infants Hospital Institutional Review Board approval was obtained (IRB #05-0094).

To select the study sample, a computerized list of obstetric patients who delivered at Women and Infants Hospital between January 2004 and December 2005 was generated. GBS-positive patients were identified using International Classification of Diseases, 9th Revision codes. Because no reliable means of identifying patients who reported a penicillin allergy was available, we reviewed antepartum and intrapartum charts of all GBS-positive patients (18.9%) in this time period to determine whether the patients also reported a penicillin allergy. Between January 2004 and December 2005, 3,595 patients were identified as GBS positive and 91% of these charts were available and reviewed. Figure 1 shows a flow chart of case identification and analyses.

Of these 3,267 patient charts, 31 were determined to be either GBS negative or GBS unknown. Of the remaining 3,236 patients, 265 charts had a recorded penicillin allergy (8.2%). Data were abstracted from medical records onto standardized data collection forms by two trained research assistants. Data abstraction included age, obstetric provider, insurance status, gestational age at delivery, type of delivery, recorded nature of the penicillin allergy, means of identifying GBS positivity, antimicrobial sensitivity testing, and antibiotics received. Data were verified for accuracy by the data management team and were maintained in a confidential computerized database. To verify data on antimicrobial sensitivity testing, computerized laboratory data were cross-checked for 20% of the sample, and no instances of misclassification were identified.

For the analyses, we excluded women who delivered in January, February, or March 2004 ($n=32$), because although the CDC guidelines were published in August 2002, the Women and Infants Hospital hospital guidelines were finalized on January 22, 2004. Beginning our analyses in April 2004, we permitted 2 full months for the Women and Infants Hospital guidelines to become incorporated into clinical care. Additionally, women who delivered in January and February would have been screened for GBS before the hospital guideline was finalized.

We described the age, gravidity, parity, race or ethnicity, provider type, type of insurance, gestational age at delivery, mode of delivery, means by which GBS positivity was determined, whether the nature of

the penicillin allergy was documented, and antibiotic administered for our population of GBS-positive, penicillin-allergic patients ($N=233$). We then performed two analyses in this population of GBS-positive, penicillin-allergic patients: 1) to compare patients who received antimicrobial sensitivity testing with those who did not, and 2) to compare patients who received an appropriate antibiotic with those who did not. For both of these analyses, we excluded women who had a gestational age less than 37 weeks ($n=17$) and women who had a scheduled cesarean delivery ($n=14$). We excluded women who delivered before 37 weeks of gestation because of the potential that the GBS culture results were unavailable at the time of delivery. Women with a scheduled cesarean delivery were excluded because for such patients GBS prophylaxis is not currently recommended.

Antimicrobial sensitivity testing was defined as “performed” if it was documented in the antenatal records, in the laboratory data sheets, in the intrapartum chart, in the postpartum chart, or in the electronic laboratory data files. Women who received a cephalosporin who were determined to be at low risk for anaphylaxis ($n=17$) were excluded for the analyses of antimicrobial sensitivity testing, because antimicrobial sensitivity testing is unnecessary in this population. The final sample size for these analyses was 185 women.

“Appropriate antibiotic” was defined as cephalosporin for patients at low risk for anaphylaxis, clindamycin or erythromycin if GBS was susceptible to both of these antibiotics, and vancomycin if antimicrobial sensitivity was unknown or if GBS was resistant to either clindamycin or erythromycin. Patients with missing data on the outcome (antibiotic administered) ($n=5$) were excluded from the analyses of appropriate antibiotic administration. The final sample size for these analyses was 197 women.

Within this retrospective cohort study, a nested case-control analysis was designed to compare women who received vancomycin to women who received clindamycin. These two groups were compared in terms of the prevalence of antimicrobial sensitivity testing and the proportion who received an appropriate antibiotic.

We performed a sample size and power calculation using the proportion of patients who received antimicrobial sensitivity testing as our outcome variable. These calculations were based on the assumptions that 1) 10 patients received clindamycin for every one patient who received vancomycin and 2) 75% of women who receive clindamycin had antimicrobial sensitivity testing, and half as many (anti-



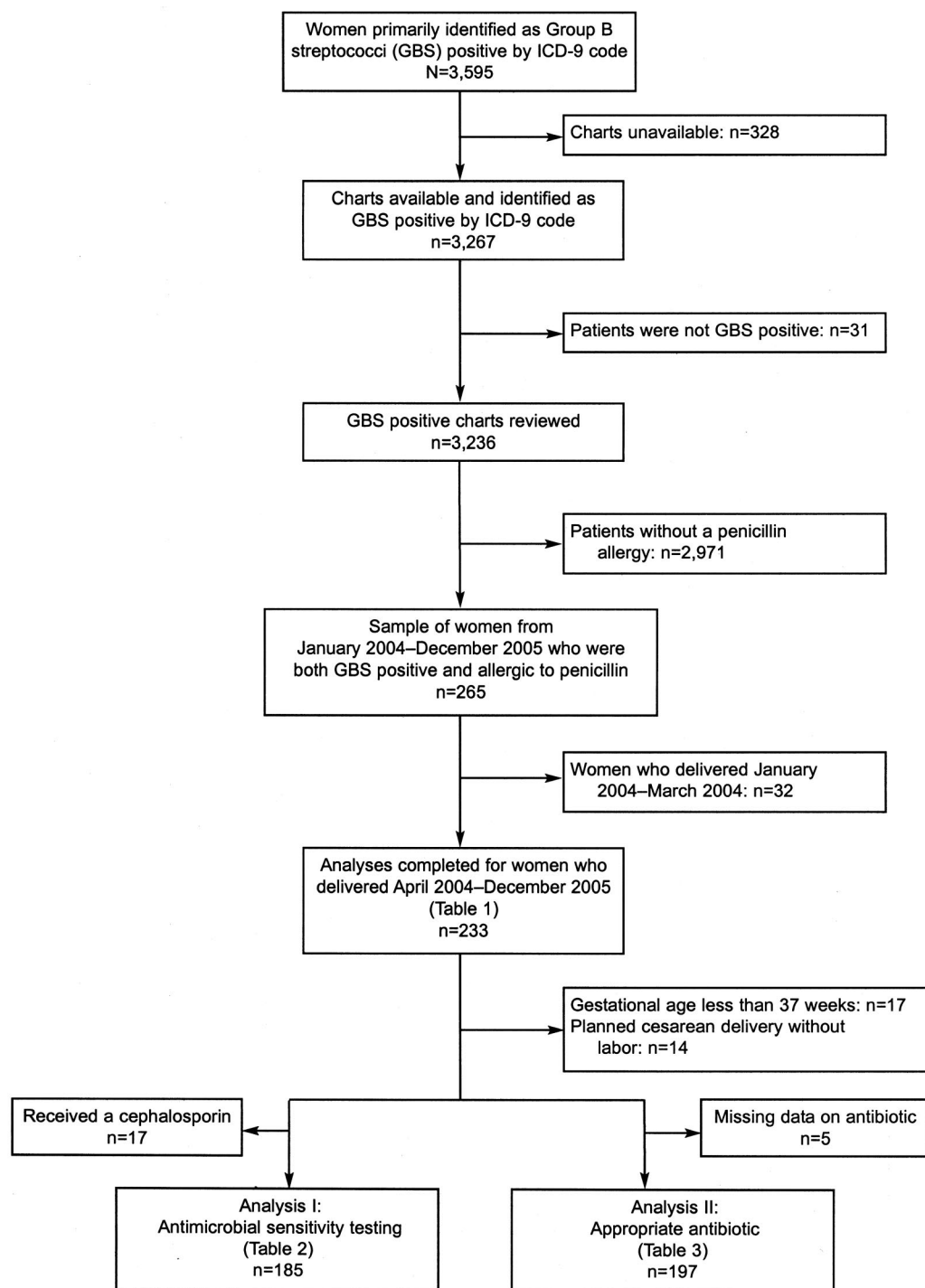


Fig. 1. Flow chart of patient selection.

Matteson. Group B Streptococci and Penicillin Allergy. *Obstet Gynecol* 2008.

pated difference=37.5%) women who received vancomycin had antimicrobial sensitivity testing. Based on these assumptions and setting $\alpha=0.05$ and $\beta=0.20$ (power=80%), we needed 176 women for the analy-

ses. Data were analyzed using Stata 9.0 (StataCorp, College Station, TX). Categorical variables were compared using Fisher exact test, medians were compared using the Wilcoxon rank sum test, and 95% confi-



Table 2. Characteristics of the Group B Streptococci-Positive, Penicillin-Allergic Patients Who Delivered at Women and Infants Hospital between April 1, 2004, and December 31, 2005

Characteristics	Number	Percentage*
Total N	233	
Median age (y)	33 (16–45)	
Median gravidity	2 (1–9)	
Median parity	1 (0–6)	
Race/ethnicity		
Non-Hispanic white	178	76.4 (70.5–81.4)
Non-Hispanic African American	12	5.1 (2.9–8.9)
Hispanic	29	12.5 (8.8–17.3)
Other	4	1.7 (0.5–4.5)
Unknown	10	4.3 (2.2–7.8)
Provider type		
Private physician	158	67.8 (61.6–73.5)
Maternal–fetal medicine	14	6.0 (3.5–9.9)
Resident clinic	33	14.2 (10.2–19.3)
Certified nurse-midwife	9	3.8 (1.9–7.3)
Community health center	17	7.3 (4.5–11.4)
Unknown	2	0.9 (0.03–3.3)
Gestational age at delivery (wk)		
Less than 37	17	7.3 (4.5–11.4)
37 or more	216	92.7 (88.6–95.5)
Type of delivery		
Vaginal	168	72.1 (66.0–77.5)
Cesarean after labor	50	21.5 (16.7–27.2)
Planned cesarean	15	6.4 (3.9–10.4)
Method of identification of GBS positivity		
Rectovaginal culture	157	67.4 (61.1–73.1)
GBS bacteruria	44	18.9 (14.4–24.4)
Previous neonate with GBS sepsis	3	1.3 (0.3–3.9)
Screening method not documented	28	12.0 (8.4–16.9)
Unknown	1	0.4 (0–2.6)
Patient documentation of nature of the penicillin allergy	144	61.8 (55.4–67.8)
Patients with documentation that they received any antibiotics	221	94.9 (91.1–97.1)
Type of antibiotics received		
Cephalosporin	18	8.1 (5.1–12.6)
Clindamycin	183	82.8 (77.3–87.2)
Erythromycin	4	1.8 (0.5–4.7)
Vancomycin	16	7.2 (4.4–11.5)

GBS, group B streptococci.

Data are n, median (range), or percentage (95% confidence interval for proportion).

* May not add up to 100% because of rounding.

dence intervals (CIs) were calculated for binomial proportions using the Agresti-Coull method. Spearman rank correlation was performed to assess the

improvement of antimicrobial sensitivity testing and administration of an appropriate antibiotic over time.

RESULTS

Between 2004 and 2005, there were 18,831 deliveries at our institution with a GBS-positive prevalence of 18.9% (95% CI 18.4–19.5%). The prevalence of patient-reported penicillin allergy among GBS-positive women was 8.2% (95% CI 7.3–9.2%).

After applying the detailed exclusion and inclusion criteria to the sample, 233 charts were eligible for review (Fig. 1). First, the characteristics of this population were described (Table 2). Sixty-two percent of these women had some documentation of the nature of their penicillin allergy. Ninety-three percent of women delivered at 37 or more weeks of gestation, and 72% of women delivered vaginally. Overall, 95% (95% CI 91–97%) of women received antibiotic prophylaxis, and the majority of these women were given clindamycin (83%).

Next, we analyzed data from 185 women to compare the GBS-positive, penicillin-allergic women who did and did not have antimicrobial sensitivity testing and to determine trends over time in antimicrobial sensitivity testing (Table 3). Eleven percent (95% CI 8.5–16.8%) of the sample received antimicrobial sensitivity testing. There was no difference between groups in terms of age, race or ethnicity, provider type, gravidity, parity, and whether they received any antibiotics. The majority of women in this sample received clindamycin. Comparing these women who received clindamycin with women who received vancomycin, we found that women who received clindamycin were more likely to have unknown antimicrobial susceptibilities than women who received vancomycin (91% compared with 54%, $P<.01$). We performed analyses for correlation between date of delivery and whether antimicrobial testing was performed and found that there was no change over time ($r=-0.06$, 95% CI -0.48 to 0.38). Because antimicrobial sensitivity testing in the setting of GBS bacteruria is less clear, we performed all of the above analyses, excluding these women, and there was no change in results (data not shown).

We then compared women who did and did not receive an appropriate antibiotic (Table 4). Of the 197 patients included in these analyses, only 16% (95% CI 11–21%) received an appropriate antibiotic. More women received an appropriate antibiotic in 2005 than in 2004 (20% compared with 11%, $P=.11$); however, this increase in appropriate antibiotic over time was not statistically significant. Similar to what we found for antimicrobial sensitivity testing, there



Table 3. Group B Streptococci-Positive, Penicillin-Allergic Patients Who Delivered at Women and Infants Hospital Between April 2004 and January 2006: Comparisons Between Women Who Had Antimicrobial Sensitivity Testing and Women Who Did Not Have Antimicrobial Sensitivity Testing

Characteristics	Did Not Undergo Sensitivity Testing		Underwent Sensitivity Testing		P
	Number	Percent*	Number	Percent*	
Total (N=185)	164		21		
Median age (y)	33 (16–45)		34 (20–45)		.23
Median gravidity	2 (1–9)		2 (1–7)		.51
Median parity	1 (0–5)		0 (0–2)		.79
Race/ethnicity					.82
Non-Hispanic white	130	79.3 (72.4–84.8)	16	76.2 (54.5–89.8)	
Non-Hispanic African American	9	5.5 (2.8–10.2)	2	9.5 (1.4–30.1)	
Non-Hispanic other	3	1.8 (0.4–5.5)	0	0.0 (0–18.2)	
Hispanic	17	10.4 (6.5–16.1)	3	14.3 (4.1–35.5)	
Unknown	5	3.0 (1.1–7.1)	0	0.0 (0–18.2)	
Provider type					.29
Private physician	121	73.8 (66.5–79.9)	14	66.7 (45.1–83.0)	
Maternal–fetal medicine	4	2.4 (0.7–6.3)	2	9.5 (1.4–30.1)	
Resident clinic	16	9.8 (6.0–15.3)	4	19.0 (7.1–40.6)	
Certified nurse-midwife	9	5.5 (2.8–10.2)	0	0.0 (0–18.2)	
Community health center	12	7.3 (4.1–12.5)	1	4.8 (0–24.4)	
Unknown	2	1.2 (0.05–4.6)	0	0.0 (0–18.2)	
Method of identification of GBS positivity					.23
Rectovaginal culture	117	71.3 (64.0–77.7)	13	61.9 (40.8–79.3)	
GBS bacteruria	32	19.5 (14.1–26.3)	3	14.3 (4.1–35.5)	
Method not documented	14	8.5 (5.1–13.9)	5	23.8 (10.2–45.5)	
Unknown	1	0.6 (0.02–3.4)	0	0.0 (0–18.0)	
Patients who received any antibiotics	159	97.0 (92.9–98.9)	21	100.0 (81.8–100)	1.0
Type of antibiotics received (%)					.001
Clindamycin	149	91.4 (86.0–94.9)	14	8.6 (5.1–14.0)	
Erythromycin	3	75.0 (28.9–96.6)	1	25.0 (3.4–71.1)	
Vancomycin	7	53.9 (29.1–76.8)	6	46.1 (23.2–70.9)	
Missing	5	100 (51.1–100)	0	0.0 (0–52.2)	
Year of delivery (%)					.25
2004	64	85.3 (75.4–91.8)	11	14.7 (8.2–24.6)	
2005	100	90.9 (83.9–95.2)	10	9.1 (4.8–16.1)	

GBS, group B streptococci.

Data are n, median (range), or percentage (95% confidence interval).

* May not add up to 100% because of rounding.

was not a significant correlation between date of delivery and whether an appropriate antibiotic was administered ($r=0.35$, 95% CI -0.09 to 0.68).

DISCUSSION

Most cases of early onset neonatal GBS disease can be prevented by administering appropriate intrapartum antimicrobial prophylaxis to women who are at risk for transmitting GBS to their newborn (Table 1). Although the implementation of active prevention strategies has significantly decreased the incidence of GBS disease over the past two decades, GBS is still a leading cause of neonatal morbidity and mortality. In our study we found that 95% of GBS-positive, penicillin-allergic patients received antibiotics for the pre-

vention of GBS disease. However, an important aspect of the 2002 published guidelines, requesting antimicrobial sensitivity testing and prescribing an appropriate antibiotic, was not consistently followed.

National guidelines for the prevention of GBS disease were first published in 1996 and were revised in 2002.^{9,11} One major difference between the 1996 and 2002 guidelines is the recommended algorithm and antibiotic regimens for women with a penicillin allergy. In 1996, clindamycin or erythromycin was recommended for chemoprophylaxis in all women who reported a penicillin allergy. Because of the increasing prevalence of GBS resistance to these antibiotics, the 2002 guidelines outlined a new strategy for treating penicillin-allergic women.



Table 4. Group B Streptococci-Positive, Penicillin-Allergic Patients Who Delivered at Women and Infants Hospital Between April 2004 and January 2006: Comparisons Between Women Who Received an Appropriate Antibiotic and Women Who Did Not Receive an Appropriate Antibiotic

Characteristics	Did Not Receive an Appropriate Antibiotic		Received an Appropriate Antibiotic		P
	Number	Percent*	Number	Percent*	
Total (N=197)	165		32		
Median age (y)	33 (16–45)		30 (19–45)		.52
Median gravidity	2 (1–9)		3 (1–8)		.18
Median parity	1 (0–5)		1 (0–3)		.42
Race/ethnicity					.34
Non-Hispanic white	130	78.8 (71.9–84.3)	22	68.8 (51.3–82.2)	
Non-Hispanic African American	8	4.9 (2.3–9.4)	3	9.4 (2.5–25.0)	
Hispanic	20	12.1 (7.9–18.1)	4	12.5 (4.4–28.7)	
Non-Hispanic other	2	1.2 (0.05–4.6)	1	3.1 (0–17.1)	
Unknown	5	3.0 (1.1–7.1)	2	6.3 (0.7–21.2)	
Provider type					.09
Private physician	117	70.9 (63.6–77.3)	18	56.3 (39.3–71.8)	
Maternal–fetal medicine	6	3.6 (1.5–7.9)	1	3.1 (0–17.1)	
Resident clinic/healthcenter	32	19.4 (14.0–26.1)	13	40.6 (25.5–57.8)	
Certified nurse-midwife	9	5.5 (2.8–10.2)	0	0.0 (0–12.7)	
Unknown	1	0.6 (0–3.7)	0	0.0 (0–12.7)	
Method of identification GBS positivity					.03
Rectovaginal culture	115	69.7 (62.3–76.2)	25 (78.1)	78.1 (61.0–89.3)	
GBS bacteruria	31	18.8 (13.5–25.5)	2	6.2 (0.7–21.2)	
Previous neonate with GBS sepsis	0	0.0 (0–2.7)	2	6.2 (0.7–21.2)	
Not documented	18	10.9 (6.9–16.7)	3	9.4 (2.5–25.0)	
Unknown	1	0.6 (0–3.7)	0	0.0 (0–12.7)	
Patients who received any antibiotics	93	56.4 (48.7–63.7)	24	75.0 (57.7–87.0)	.05
Type of antibiotics received (%)					.001
Cephalosporin	4	25.0 (9.7–50.0)	12	75.0 (50.0–90.3)	
Clindamycin	157	95.7 (91.3–98.1)	7	4.3 (1.9–8.7)	
Erythromycin	4	100.0 (45.4–100)	0	0.0 (0–54.6)	
Vancomycin	0	0.0 (0–26.6)	13	100 (73.4–100)	
Year of delivery (%)					.11
2004	66	89.2 (79.8–94.7)	8	10.8 (5.3–20.2)	
2005	99	80.5 (72.5–86.6)	24	19.5 (13.4–27.5)	

GBS, group B streptococci.

Data are n, median (range), or percentage (95% confidence interval).

* May not add up to 100% because of rounding.

The 2002 CDC guidelines and experts on infectious diseases and clinical pharmacology advocate that by taking a detailed clinical history of the penicillin allergy, the practitioner can determine the likelihood that the patient had a type I/anaphylactic reaction to penicillin in the past. The practitioner can then use his or her judgment to determine the appropriateness of administration of a cephalosporin. The true incidence of cephalosporin cross-reactivity in penicillin-allergic patients is a controversial topic. Although some studies have shown that allergic reactions to cephalosporins are greater in the population of penicillin-allergic individuals than in non-penicillin-allergic individuals, the overall incidence of anaphylaxis

to cephalosporins is less than 0.001%.^{12–14} In our study, only 8% of women received a cephalosporin.

Women who did not receive cephalosporins should have received antimicrobial sensitivity testing of their GBS isolates; however, only 11% received this testing. Clindamycin is an appropriate antibiotic only for GBS isolates that have known antimicrobial sensitivity to both clindamycin and erythromycin. Women with GBS isolates that have unknown susceptibilities or resistance to either clindamycin or erythromycin should receive vancomycin. Contrary to these guidelines, we found that almost all patients who received clindamycin did not have antimicrobial sensitivity testing and that women who received



vancomycin were actually more likely to have had sensitivity testing.

Not surprising given our low rates of antimicrobial sensitivity testing, only 16% of our population received a guideline-appropriate antibiotic. Administration of appropriate antibiotic trended toward increasing over time, although the overall prevalence in 2005 was still only 20% (95% CI 13–28%). Given our institutional estimate that 26% of GBS isolates are resistant to clindamycin, it is possible that up to 41 patients received inadequate prophylaxis for the prevention of neonatal GBS disease.

Change in medical culture takes time. It is likely that the use of clindamycin in this study population reflects health care providers practicing according to the 1996 guidelines. We hypothesized that adherence to the 2002 guidelines would improve over time. Although appropriate antibiotic use seemed to increase over time, the study was underpowered to evaluate the magnitude of the increase. No correlation was present between date of delivery and either the proportion of women who had antimicrobial sensitivity testing or received an appropriate antibiotic.

This study had several strengths. First, we reviewed the charts of the entire population of GBS-positive pregnant women who delivered in 2004 and 2005 to determine penicillin allergy and establish our study sample. Second, these medical records were thoroughly reviewed; we reviewed separate data sources (antepartum charts, an electronic laboratory database, and intrapartum charts) to determine the outcomes, antimicrobial sensitivity testing and appropriate antibiotic choice. This approach increased the accuracy of our classification of the outcome and decreased our risk of misclassification of outcome.

One limitation of our study is that the most recent data are from 2005. Some improvements in adherence to the guidelines may have occurred since the time of study. Also, this study was a retrospective review of medical records. Therefore, our data were limited by what was actually recorded in the medical record. For example, it is possible that providers asked patients about their penicillin allergy but did not document it in the chart. Additionally, we do not know who completed the individual laboratory request forms for the GBS testing and antimicrobial sensitivity testing. These are sometimes completed by the physician and often completed by nurses and medical assistants in private offices under the direction of the physician. Because of institutional adherence to the guidelines, it will be important to educate physicians and all individuals who may order labora-

tory tests for the physicians about the 2002 CDC guidelines. Last, although the CDC guidelines recommend taking a detailed patient history to determine risk of anaphylaxis to penicillin, this approach does have some limitations. Some studies suggest that skin testing (which has an extremely low risk of anaphylaxis) is preferable over a detailed history to determine who is at risk for penicillin-anaphylaxis, because clinical history of the nature of the penicillin reaction may be a poor predictor of positive skin testing.^{13,15,16} We used patient history alone to define penicillin allergy for this study.

Although this study includes one institution and does not provide information about adherence at other institutions or nationally, it is an example for other institutions to investigate their adherence to the 2002 guidelines for GBS chemoprophylaxis in penicillin-allergic women. It is possible that the nature of our institution, an academic and teaching hospital, may have influenced our results. Our adherence to the guidelines could be positively affected by increased opportunities to attend lectures and the emphasis placed on evidence-based medicine. Conversely, our adherence could be negatively affected, because information on new guidelines may be disseminated less efficiently due to the large numbers of providers of obstetric care. Regardless, the results from this study will lead to the development of specific institutional strategies and protocols to facilitate antimicrobial sensitivity testing and appropriate selection of antibiotics. One strategy is to educate practitioners about the 2002 CDC guidelines by presenting the study results and the 2002 prevention guidelines to all hospital medical staff. To facilitate adherence to the guidelines, we are working with laboratory services to more consistently identify penicillin-allergic patients for both GBS screening and urine cultures so that antimicrobial sensitivity will be performed automatically for all GBS isolates from penicillin-allergic women. To evaluate the effect of this intervention, we plan to repeat this study to measure adherence to the GBS prophylaxis guidelines in the future.

Just as it is important to evaluate adherence to established guidelines, it is important to evaluate the effect of implemented guidelines. Future directions in research should include evaluating these revised 2002 CDC guidelines for the prevention of neonatal GBS disease in terms of incidence of neonatal GBS disease and incidence of non-GBS infections in the era of GBS chemoprophylaxis. Additionally, very limited data are available on the effects of vancomycin administration during pregnancy.¹⁷ The incidence of



adverse effects of vancomycin administration, including infusion reactions, gastrointestinal symptoms, ototoxicity, and nephrotoxicity, on both mother and neonate should continue to be evaluated.

Improving the use of appropriate antibiotics could further reduce the incidence of early-onset GBS disease. Appropriate antepartum and intrapartum management of penicillin-allergic, GBS-positive women could have a significant effect on GBS disease. Using a prevalence of GBS colonization of 20% and a prevalence of reported penicillin allergy of 10%, we estimate that 2% of the pregnant population is both GBS colonized and reportedly penicillin allergic. Managing this 2% of patients appropriately could affect the outcomes of 80,000 neonates annually (using the estimated 4 million U.S. births in 2005).

The administration of prophylactic antibiotics during labor has greatly reduced the incidence of early-onset neonatal GBS disease. This strategy will continue to be effective for reducing the burden of neonatal GBS disease if appropriate antibiotics are chosen. The antibiotics that are appropriate for GBS prophylaxis have changed as a result of antimicrobial resistance of GBS. Adherence to the 2002 CDC Guidelines for GBS prophylaxis in penicillin-allergic women is far from optimal at our institution. Other institutions should consider evaluating their adherence to these practice guidelines. Significant improvements are necessary in obtaining antimicrobial sensitivity testing and choosing an appropriate antibiotic for GBS-positive women with a reported penicillin allergy.

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