

Use of Cefazolin for Group B Streptococci Prophylaxis in Women Reporting a Penicillin Allergy Without Anaphylaxis

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OBJECTIVE: To estimate the proportion of group B streptococci (GBS)-colonized women with a reported penicillin allergy without anaphylaxis receiving appropriate intrapartum antibiotic prophylaxis.

METHODS: We performed a retrospective cohort study of GBS-colonized, penicillin-allergic women delivering at term receiving intrapartum antibiotic prophylaxis during labor. Scheduled cesarean deliveries were excluded. The primary outcome was the proportion of women who received appropriate antibiotic coverage, defined as penicillin or cefazolin. Secondary outcomes included neonatal outcomes such as Apgar score, blood draws, antibiotic use, length of hospital stay, and composite morbidity.

RESULTS: Of 165 women reporting a penicillin allergy without anaphylaxis, 73 (44.2%) received an appropriate antibiotic and 92 (55.8%) received an inappropriate antibiotic. Of those receiving an inappropriate antibiotic, 56 (60.9%) were given clindamycin, 1 (1.1%) erythromycin, and 35 (38.0%) vancomycin. Women reporting rash as a penicillin reaction were more likely to receive cefazolin than another antibiotic (44 [60.3%] compared with 24 [26.1%], respectively; $P<.001$), whereas women whose reaction was not documented were less likely to receive cefazolin (18 [24.7%] compared with 63 [68.5%], respectively; $P<.001$). Among neonates whose mothers received appropriate compared with inappropriate

antibiotics, there were no differences in Apgar score, number of blood draws, antibiotic use, length of hospital stay, or composite morbidity.

CONCLUSION: More than half of women allergic to penicillin without anaphylaxis received an antibiotic other than penicillin or cefazolin as prophylaxis, indicating poor adherence to national guidelines.

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Group B streptococci (GBS) are bacteria that colonize the vagina or rectum in roughly 25% of healthy adult women that in pregnancy can be transmitted to the neonate.^{1,2} Intrapartum antibiotic prophylaxis for GBS-colonized women has resulted in a significant reduction in early-onset neonatal GBS infection.³

The obstetric and pediatric GBS guidelines, released in 2010 and 2011, respectively, by the Centers for Disease Control and Prevention (CDC) state that “penicillin remains the agent of choice for intrapartum antibiotic prophylaxis, with ampicillin as an acceptable alternative. Penicillin-allergic women who do not have a history of anaphylaxis, angioedema, respiratory distress or urticaria following administration of a penicillin or cephalosporin should receive cefazolin.”^{4,5} For penicillin-allergic women not at high risk for anaphylaxis, cefazolin is the preferred alternative because it achieves high intra-amniotic concentration.^{4–8} Unfortunately, several studies have demonstrated that very few penicillin-allergic women not at high risk for anaphylaxis receive cefazolin.^{9–12} These studies were performed before the release of the most recent CDC guidelines.

For women at high risk for anaphylaxis, the guidelines recommend clindamycin or vancomycin. Unlike penicillin or cefazolin, clindamycin and vancomycin have not been shown to reliably achieve high intra-amniotic concentrations and it is unknown

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whether these antibiotics are effective at preventing early-onset neonatal GBS sepsis.^{13–16} In addition, the rising resistance of GBS to these antibiotics is cause for concern.^{17–19} They are therefore deemed “inappropriate” intrapartum antibiotic prophylaxis, necessitating 48 hours of neonatal observation to rule out GBS sepsis.⁵ Additionally, inappropriate use exposes mothers to antibiotics without known benefit.

The objective of this study was to estimate the proportion of GBS-colonized women reporting a penicillin allergy who received appropriate intrapartum antibiotic prophylaxis.

MATERIALS AND METHODS

We performed a retrospective cohort study of GBS-colonized women reporting a penicillin allergy who received intrapartum antibiotic prophylaxis during labor who delivered at Women and Infants Hospital, a large tertiary care obstetric hospital, between January 2008 and December 2014. Approval was obtained from the Women and Infants’ institutional review board (#14-0019).

Women carrying a singleton pregnancy, who were GBS-colonized (defined by GBS found by urine or vaginal culture) and reported a penicillin allergy, delivered at term (37 weeks of gestation or greater) and received intrapartum antibiotic prophylaxis of any duration were included in the study. Patients were excluded if they reported an anaphylactic reaction to penicillin, delivered preterm (less than 37 weeks of gestation), had a multiple gestation, were GBS negative or unknown, had a prior neonate with GBS sepsis, or underwent a scheduled cesarean delivery. Anaphylaxis was defined as reporting a history of anaphylaxis, angioedema, respiratory distress, or urticaria after administration of penicillin or cephalosporin.

Data were abstracted from the electronic medical record onto a standardized data collection spreadsheet by a single investigator (V.A.B.). Double data entry was performed for 10% of the charts by a separate investigator (C.M.A.) in an effort to reduce information bias. Maternal demographic data, maternal medical history, and labor and delivery information were recorded. Newborn data, including Apgar score, birth weight, length of hospital stay, complete blood count and blood culture information, and neonatal complications (analyzed as composite morbidity), were also recorded. Composite neonatal morbidity included the need for supplemental oxygen therapy, intubation, sepsis within 72 hours, pneumonia, hypoglycemia, or meningitis.

The primary outcome was the proportion of GBS-colonized and penicillin-allergic women without

reported anaphylaxis who received appropriate antibiotic coverage for GBS prophylaxis, defined as penicillin, if the reaction was not considered a true allergy, or cefazolin, for those with a reported allergy that was not consistent with type 1 hypersensitivity in accordance with CDC guidelines. We defined appropriate intrapartum antibiotic prophylaxis as the receipt of penicillin or cefazolin because both achieve high intra-amniotic concentrations.^{4–8} Secondary outcomes included number of neonatal blood draws, neonatal length of hospital stay, and adherence to intrapartum antibiotic prophylaxis guidelines before and after 2010.

Prior literature suggests that approximately 25% of GBS-colonized, penicillin-allergic patients at low risk for anaphylaxis appropriately receive cefazolin.^{9,10,12} It was determined that a sample size of 150 was needed to detect a 10% difference in receipt of appropriate intrapartum antibiotic prophylaxis from published estimates. Secondly, this sample size was also found to be adequate to detect a doubling in adherence to guidelines before and after 2010 (from 25% to 50%).

Demographic and outcome data were compared between those who received appropriate compared with inappropriate antibiotics using χ^2 tests and Fisher exact tests for categorical variables and *t* tests and Wilcoxon rank-sum tests for continuous variables.

RESULTS

Of 345 penicillin-allergic women identified as GBS-colonized, 238 (69%) met initial inclusion criteria (Fig. 1). Of those, 73 (30.7%) reported an anaphylactic reaction to penicillin. Notably, of the 165 included, 77

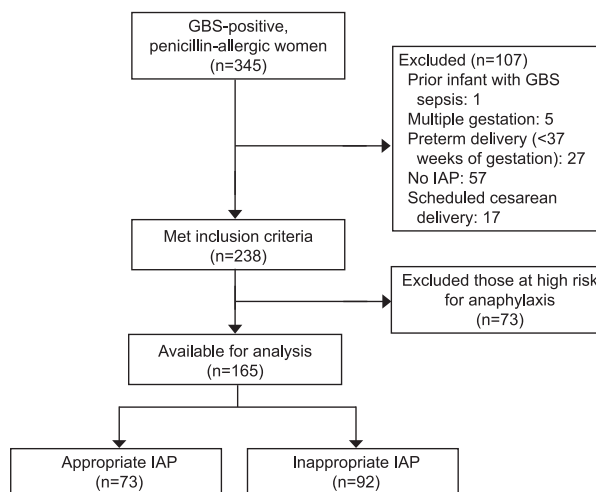


Fig. 1. Patient selection flowchart. GBS, group B streptococci; IAP, intrapartum antibiotic prophylaxis.

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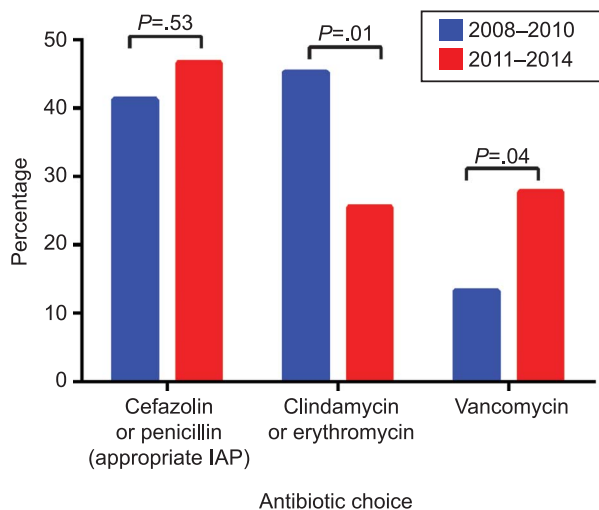


Fig. 2. Antibiotic choice before 2010 and after 2010. IAP, intrapartum antibiotic prophylaxis.

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(46.7%) did not have a reaction documented in the medical record. These patients were included in the analysis because it was thought that they likely represented a group at low risk for anaphylaxis. Additionally, none of these patients reported a cephalosporin allergy.

In the 165 pregnant women with a penicillin allergy without anaphylaxis, 73 (44.2%) received an

Table 1. Maternal Demographic Information

Variable	Appropriate Intrapartum Antibiotics (n=73)	Inappropriate Intrapartum Antibiotics (n=92)	P
Age (y)	28.5±6.3	28.2±5.9	.75*
Race			
Caucasian	60 (82.2)	65 (70.7)	.29 [†]
African American	5 (6.9)	9 (9.8)	
Asian	0 (—)	4 (4.4)	
Other	1 (1.4)	1 (1.1)	
Missing or unknown	7 (9.6)	13 (14.1)	
Ethnicity			
Hispanic	11 (15.1)	10 (10.9)	.63 [†]
Non-Hispanic	62 (84.9)	81 (88.0)	
Missing or unknown	0 (—)	1 (1.1)	
Gravidity	2.0 (1.0–9.0)	1.0 (1.0–6.0)	.26 [‡]
Parity	0 (0–4)	0 (0–4)	.88 [‡]

Data are mean±standard deviation, n (%), or median (range) unless otherwise specified.

* t test.

[†] Fisher exact test.

[‡] Wilcoxon rank-sum.

Table 2. Maternal Allergy Information

Variable	Appropriate Intrapartum Antibiotics (n=73)	Inappropriate Intrapartum Antibiotics (n=92)	P*
Type of reaction			
Nausea or vomiting	8 (10.9)	5 (5.4)	.25
Itching	1 (1.4)	1 (1.1)	1.00
Rash	44 (60.3)	24 (26.1)	<.01
Other [†]	3 (4.1)	1 (1.1)	.32
Missing or unknown	18 (24.7)	63 (68.5)	<.01

Data are n (%) unless otherwise specified.

* Fisher exact test.

[†] Includes hallucinations, intestinal bleeding, skin peeling, tachycardia, and reddened skin.

appropriate antibiotic (penicillin or cefazolin) for intrapartum antibiotic prophylaxis (95% confidence interval [CI] 36.5–52.2%) and 92 (55.8%) received an inappropriate antibiotic (95% CI 47.8–63.5%). There were seven patients who received penicillin. Two of those patients reported nausea and vomiting as the reaction to penicillin, one reported a rash, and four did not have a reaction documented. Of those who received an inappropriate antibiotic, 56 (60.9%) received clindamycin, 1 (1.1%) received erythromycin, and 35 (38.0%) received vancomycin. When evaluating the adherence to guidelines regarding appropriate intrapartum antibiotic prophylaxis before and after 2010, there was no difference with 31 (41.3%) women receiving appropriate antibiotics between 2008 and 2010 and 42 (46.7%) women receiving appropriate antibiotics between 2011 and 2014 ($P=.53$). Interestingly, of women who received an inappropriate antibiotic for intrapartum antibiotic prophylaxis, when comparing before with after 2010, more women received clindamycin or erythromycin (34 [45.3%] compared with 23 [25.6%], $P=.01$) and fewer women received vancomycin (10 [13.3%] compared with 25 [27.8%], $P=.04$) (Fig. 2).

Regarding sensitivity testing, only 7 (28.0%) women who had GBS bacteriuria had sensitivity testing performed compared with 85 (58.2%) who had vaginal colonization ($P<.001$). Of the 57 women who received clindamycin or erythromycin, 20 (35.1%) did not have sensitivities performed. Of the 37 women who received clindamycin or erythromycin and had sensitivity testing performed, 7 (18.9%) were resistant to either or both clindamycin and erythromycin and therefore should not have received either drug. When evaluating performance of



Table 3. Labor and Delivery Data

Variable	Appropriate Intrapartum Antibiotics (n=73)	Inappropriate Intrapartum Antibiotics (n=92)	P
Gestational age (wk)	39.6±1.2	39.9±0.9	.08*
Duration of membrane rupture (h)	9.1±7.3	8.2±7.8	.25 [†]
Mode of delivery			
Vaginal	57 (78.1)	73 (79.3)	.85 [‡]
Cesarean	16 (21.9)	19 (20.7)	
Maternal fever	7 (9.6)	7 (7.6)	.78 [‡]
Pathologic chorioamnionitis	5 (6.9)	9 (9.8)	.79 [‡]
Antibiotic received for chorioamnionitis	6 (8.2)	3 (3.3)	.19 [‡]
Postpartum endometritis	0	0	—

Data are mean±standard deviation or n (%) unless otherwise specified.

* *t* test.

[†] Wilcoxon rank-sum.

[‡] Fisher exact test.

sensitivity testing, either vaginal or urinary, before and after 2010, there were again no differences (42 [56.0%] compared with 49 [54.4%], *P*=.27).

In comparing women who received appropriate compared with inappropriate intrapartum antibiotic prophylaxis, there were no differences in age, race, ethnicity, or pregnancy history (Table 1). When evaluating the type of reaction, more women who received appropriate compared with inappropriate intrapartum antibiotic prophylaxis reported a rash compared with other types of reactions, 60.3% compared with 26.1%. Conversely, fewer women who received appropriate compared with inappropriate intrapartum antibiotic prophylaxis had a reaction that was missing or unknown, 24.7 compared with 68.5% (Table 2). Women who had sensitivity testing performed on a vaginal culture were less likely to receive appropriate

compared with inappropriate intrapartum antibiotic prophylaxis (29 [45.3%] compared with 56 [68.3%], *P*=.01). In those with sensitivities from a urine culture, there was no difference in receipt of appropriate compared with inappropriate intrapartum antibiotic prophylaxis (two [15.4%] compared with [41.7%], *P*=.12).

When evaluating labor and delivery variables, there were no differences between those who received appropriate compared with inappropriate antibiotics in mean gestational age, duration of membrane rupture, mode of delivery, maternal fever, receipt of antibiotics for chorioamnionitis, pathologic chorioamnionitis, or postpartum endometritis (Table 3). Of note, no postpartum endometritis was documented in either group.

Among neonates whose mothers received appropriate compared with inappropriate intrapartum

Table 4. Neonatal Outcomes

Variable	Appropriate Intrapartum Antibiotics (n=73)	Inappropriate Intrapartum Antibiotics (n=92)	P
5-min Apgar score	9.0 (5.0–10.0)	9.0 (3.0–10.0)	.24*
Birth weight (g)	3,414±428	3,492±469	.28 [†]
Length of hospital stay (d)	2.7±1.2	3.0±4.4	.13*
Longer than 2	25 (34.3)	22 (23.9)	.17 [‡]
Longer than 3	15 (20.6)	16 (17.4)	.69 [‡]
Blood culture performed	2 (2.7)	9 (9.9)	.11 [‡]
Neonate placed on antibiotics	3 (4.1)	4 (4.4)	1.00 [‡]
Composite neonatal morbidity [§]	2 (2.7)	7 (7.6)	.30 [‡]
Composite neonatal outcome	20 (27.4)	21 (22.8)	.59 [‡]

Data are median (range), mean±standard deviation, or n (%) unless otherwise specified.

* Wilcoxon rank-sum.

[†] *t* test.

[‡] Fisher exact test.

[§] Sepsis within 72 hours, pneumonia, meningitis, need for supplemental oxygen, intubation, hypoglycemia, death.

^{||} Hospital stay longer than 3 days, having complete blood count drawn, having blood culture drawn, having antibiotics started, or neonatal sepsis.



antibiotic prophylaxis, there were no differences in Apgar score, number of blood draws, antibiotic use, length of hospital stay, or composite morbidity (Table 4). Nine (9.9%) neonates born to mothers who did not receive appropriate antibiotics underwent blood cultures compared with two (2.7%) who were born to mothers who did receive appropriate antibiotics ($P=.11$).

Finally, we stratified neonates based on receipt of 4 or more or less than 4 hours of antibiotics because this is the cutoff offered by neonatal guidelines when assessing for adequacy of GBS prophylaxis. When looking at only those neonates who received 4 hours or more of antibiotics, there were again no differences in Apgar score, number of blood draws, antibiotic use, length of hospital stay, or composite morbidity (Table 5).

DISCUSSION

More than half of women allergic to penicillin without anaphylaxis (55.8%) received an “inappropriate” antibiotic for GBS prophylaxis. Although this is an improvement over the previously reported 25%, the majority of women continue to receive an inappropriate antibiotic and, concerning, more are receiving vancomycin. Women reporting a rash as a penicillin allergy are more likely to receive cefazolin than clindamycin or vancomycin, whereas women whose allergy was not recorded (either the patient did not know or it was not asked) are less likely to receive cefazolin. Finally, women without a history of anaphylaxis to penicillin do not need sensitivity testing

performed on a GBS culture. Interestingly, when these women had sensitivity testing performed on a vaginal sample, they were more likely to receive inappropriate intrapartum antibiotic prophylaxis.

No differences were found when comparing neonatal outcomes in women who received appropriate compared with inappropriate intrapartum antibiotic prophylaxis, although our sample size was not large enough to adequately test for differences. Future studies should evaluate potential adverse neonatal outcomes resulting from inappropriate GBS prophylaxis such as neonatal testing for infection, prolonged hospitalization, or neonatal antibiotics. Although not able to be evaluated in the current study, it is clear that some cases of early-onset GBS disease could be avoided with appropriate antibiotic use.^{20,21}

A 2011 retrospective study performed at the same institution found that, after the implementation of interventions to improve adherence to the CDC guidelines, the proportion of GBS-colonized, penicillin-allergic women receiving appropriate antibiotics increased from 16.2% in 2004–2006 to 76% in 2008.¹² Our study found many fewer women received appropriate intrapartum antibiotic prophylaxis over a similar timeframe. This study by Critchfield et al,¹² however, looked at all women with a reported penicillin allergy and did not categorize women into high and low risk for anaphylaxis to penicillin. They do note in their discussion that although they did not clearly determine which patients were high and low risk, they believed that cephalosporins were underutilized.

Table 5. Neonatal Outcomes Among Neonates Receiving 4 Hours or More of Intrapartum Antibiotic Prophylaxis

Variable	Appropriate Intrapartum Antibiotics (n=62)	Inappropriate Intrapartum Antibiotics (n=72)	P
5-min Apgar score	9.0 (5.0–10.0)	9.0 (3.0–10.0)	.43*
Birth weight (g)	3,421±451	3,495±479	.36 [†]
Length of hospital stay (d)	2.5±0.9	2.9±4.8	.18*
Longer than 2	19 (30.7)	16 (22.2)	.33 [†]
Longer than 3	12 (19.4)	11 (15.3)	.65 [†]
Complete blood count performed	6 (9.7)	9 (12.5)	.79 [†]
Blood culture performed	1 (1.6)	6 (8.5)	.12 [†]
Neonate placed on antibiotics	2 (3.2)	4 (5.6)	.69 [†]
Composite neonatal morbidity [§]	1 (1.6)	5 (6.9)	.22 [†]
Composite neonatal outcome	17 (27.4)	15 (20.8)	.42 [†]

Data are median (range), mean±standard deviation, or n (%) unless otherwise specified.

* Wilcoxon rank-sum.

[†] t test.

[‡] Fisher exact test.

[§] Sepsis within 72 hours, pneumonia, meningitis, need for supplemental oxygen, intubation, hypoglycemia, death.

^{||} Hospital stay longer than 3 days, having complete blood count drawn, having blood culture drawn, having antibiotics started, or neonatal sepsis.



A large percentage of women did not have sensitivity testing performed, contrary to the recommended guidelines. This is especially true with positive GBS bacteriuria results (58.2% of women with vaginal GBS colonization had testing performed compared with 28.0% of women with GBS bacteriuria). These findings are similar to those found by Critchfield et al.¹²

Strengths of this study include that it was performed at a large institution and is one of few studies that has looked specifically at GBS prophylaxis in women with a penicillin allergy without reported anaphylaxis.

Limitations of the study include that it was retrospective in nature and performed at a single institution. Additionally, to obtain our predetermined sample size, a large timeframe was needed and during that timeframe, new guidelines were introduced that could have changed practice patterns. However, by evaluating our data before and after 2010, we documented that there likely was not a large change.

Although 10% of patients in the United States report a penicillin allergy,^{22,23} when further evaluated, only approximately 3% have an IgE-mediated allergy (which would put them at high risk for anaphylaxis) confirmed with skin testing, oral testing, or both.²⁴ Furthermore, and contrary to general belief, there is only 1–3% crossreactivity between penicillins and cephalosporins.²⁵ Therefore, in women who cannot clearly provide a history consistent with an IgE-mediated reaction to a penicillin or cephalosporin, it is likely safe to administer cefazolin. Although there is a theoretical risk of anaphylaxis when given a cephalosporin in women with an unknown reaction to penicillin, the current recommendations support that these women should receive a cephalosporin.^{24,25}

Group B streptococci prophylaxis is an example of a perinatal maternal therapy given solely for neonatal benefit. Appropriate use of antibiotics can limit the development of maternal antibiotic resistance. Use of the appropriate drugs, which have been shown to achieve effective neonatal blood levels to prevent GBS infection, will potentially avoid unnecessary neonatal monitoring and prolonged hospitalization.

Future hospital initiatives to improve allergy documentation in the electronic medical record are overdue. These should include education regarding what constitutes a history of anaphylaxis and also which patients are at high risk for anaphylaxis if administered a cephalosporin. This type of initiative, tied to quality improvement protocols, is likely the most important first step to improve adherence to

guidelines. Finally, research evaluating the adequacy of second-line antibiotics for the treatment of GBS is needed to better guide our use of these antibiotics and also our neonatology colleagues in the treatment of these neonates.

REFERENCES

1. Regan JA, Klebanoff MA, Nugent RP. The epidemiology of group B streptococcal colonization in pregnancy. *Vaginal Infections and Prematurity Study Group. Obstet Gynecol* 1991; 77:604–10.
2. Haberland CA, Benitz WE, Sanders GD, Pietzsch JB, Yamada S, Nguyen L, et al. Perinatal screening for group B streptococci: cost-benefit analysis of rapid polymerase chain reaction. *Pediatrics* 2002;110:471–80.
3. Ohlsson A, Shah VS. Intrapartum antibiotics for known maternal Group B streptococcal colonization. The Cochrane Database of Systematic Reviews 2014, Issue 6. Art. No.: CD007467. DOI: 10.1002/14651858.CD007467.pub4.
4. Verani JR, McGee L, Schrag SJ. Division of Bacterial Diseases, National Center for Immunization and Respiratory Diseases, Centers for Disease Control and Prevention (CDC). Prevention of perinatal group B streptococcal disease—revised guidelines from CDC, 2010. *MMWR Recomm Rep* 2010;59:1–36.
5. Committee on Infectious Diseases; Committee on Fetus and Newborn, Baker CJ, Byington CL, Polin RA. Policy statement—Recommendations for the prevention of perinatal group B streptococcal (GBS) disease. *Pediatrics* 2011;128:611–6.
6. Fiore Mitchell T, Pearlman MD, Chapman RL, Bhatt-Mehta V, Faix RG. Maternal and transplacental pharmacokinetics of cefazolin. *Obstet Gynecol* 2001;98:1075–9.
7. Allegaert K, van Mieghem T, Verbesselt R, de Hoon J, Rayyan M, Devlieger R, et al. Cefazolin pharmacokinetics in maternal plasma and amniotic fluid during pregnancy. *Am J Obstet Gynecol* 2009;200:170.e1–7.
8. Popović J, Grujić Z, Sabo A. Influence of pregnancy on ceftriaxone, cefazolin and gentamicin pharmacokinetics in caesarean vs. non-pregnant sectioned women. *J Clin Pharm Ther* 2007;32:595–602.
9. Van Dyke MK, Phares CR, Lynfield R, Thomas AR, Arnold KE, Craig AS, et al. Evaluation of universal antenatal screening for group B streptococcus. *N Engl J Med* 2009;360:2626–36.
10. Paccione KA, Wiesenfeld HC. Guideline adherence for intrapartum group B streptococci prophylaxis in penicillin-allergic patients. *Infect Dis Obstet Gynecol* 2013;2013:917304.
11. Peláez LM, Gelber SE, Fox NS, Chasen ST. Inappropriate use of vancomycin for preventing perinatal group B streptococcal (GBS) disease in laboring patients. *J Perinat Med* 2009;37:487–9.
12. Critchfield AS, Lievense SP, Raker CA, Matteson KA. Group B Streptococcus prophylaxis in patients who report a penicillin allergy: a follow-up study. *Am J Obstet Gynecol* 2011;204:150.e1–8.
13. Pacifici GM. Placental transfer of antibiotics administered to the mother: a review. *Int J Clin Pharmacol Ther* 2006;44:57–63.
14. Laiprasert J, Klein K, Mueller BA, Pearlman MD. Transplacental passage of vancomycin in noninfected term pregnant women. *Obstet Gynecol* 2007;109:1105–10.
15. Philipson A, Sabath LD, Charles D. Transplacental passage of erythromycin and clindamycin. *N Engl J Med* 1973;288:1219–21.



16. Muller AE, Mouton JW, Oostvogel PM, Dörr PJ, Voskuyl RA, DeJongh J, et al. Pharmacokinetics of clindamycin in pregnant women in the peripartum period. *Antimicrob Agents Chemother* 2010;54:2175–81.
17. Ferrieri P, Lynfield R, Creti R, Flores AE. Serotype IV and invasive group B *Streptococcus* disease in neonates, Minnesota, USA, 2000–2010. *Emerg Infect Dis* 2013;19:551–8.
18. Lambiase A, Agangi A, Del Pezzo M, Quaglia F, Testa A, Rossano F, et al. In vitro resistance to macrolides and clindamycin by Group B *Streptococcus* isolated from pregnant and nonpregnant women. *Infect Dis Obstet Gynecol* 2012;2012: 913603.
19. Back EE, O'Grady EJ, Back JD. High rates of perinatal group B *Streptococcus* clindamycin and erythromycin resistance in an upstate New York hospital. *Antimicrob Agents Chemother* 2012;56:739–42.
20. Blaschke AJ, Pulver LS, Korgenski EK, Savitz LA, Daly JA, Byington CL. Clindamycin-resistant group B *Streptococcus* and failure of intrapartum prophylaxis to prevent early-onset disease. *J Pediatr* 2010;156:501–3.
21. Puopolo KM, Madoff LC, Eichenwald EC. Early-onset group B streptococcal disease in the era of maternal screening. *Pediatrics* 2005;115:1240–6.
22. Salkind AR, Cuddy PG, Foxworth JW. The rational clinical examination. Is this patient allergic to penicillin? An evidence-based analysis of the likelihood of penicillin allergy. *JAMA* 2001;285:2498–505.
23. Wong BB, Keith PK, Wasserman S. Clinical history as a predictor of penicillin skin test outcome. *Ann Allergy Asthma Immunol* 2006;97:169–74.
24. Macy E, Ngor EW. Safely diagnosing clinically significant penicillin allergy using only penicilloyl-poly-lysine, penicillin, and oral amoxicillin. *J Allergy Clin Immunol Pract* 2013;1:258–63.
25. Campagna JD, Bond MC, Schabelman E, Hayes BD. The use of cephalosporins in penicillin-allergic patients: a literature review. *J Emerg Med* 2012;42:612–20.

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