No Change in the Incidence of Ampicillin-Resistant, Neonatal, Early-Onset Sepsis Over 18 Years

OBJECTIVE: The objective of this study was to assess the effect of maternal antibiotic exposure on neonatal early-onset sepsis (EOS) rates over an 18-year period.

METHODS: A review was performed of infant and maternal records for all culture-proven cases of EOS in infants delivered at the Brigham and Women’s Hospital (Boston, MA) in 1990–2007.

RESULTS: Data were analyzed from 335 EOS cases over periods that differed with respect to hospital policy for intrapartum antibiotic prophylaxis against group B Streptococcus (GBS): 1990–1992 (no prophylaxis); 1993–1996 (risk-based); and 1997–2007 (screening-based). The overall incidence of EOS decreased over these periods (3.70 vs 2.23 vs 1.59 cases per 1000 live births; \( P < .0001 \)). No change in the incidence of infection with ampicillin-resistant organisms was observed overall or among very low birth weight infants. However, an increased proportion of infections were caused by ampicillin-resistant organisms. Mothers of infants with ampicillin-resistant infections were more likely to have been treated with ampicillin \( (P = .0001) \). Overall peripartum antibiotic use increased during the study period primarily because of increased use of penicillin G and clindamycin, with no significant change in the use of ampicillin.

CONCLUSIONS: Predominant use of penicillin G for GBS prophylaxis resulted in decreased incidence of EOS. No change in the incidence of ampicillin-resistant EOS was observed, but resistant cases were associated with peripartum ampicillin exposure. These findings suggest that obstetricians should consider preferential use of penicillin G for GBS prophylaxis. *Pediatrics* 2010;125:e1031–e1038
The incidence of neonatal early-onset sepsis (EOS) resulting from group B Streptococcus (GBS) has decreased dramatically with widespread use of intrapartum antibiotic prophylaxis (IAP). Whether greater antibiotic use in the peripartum period affects the incidence and antibiotic resistance profiles of other perinatally acquired infections remains unclear. Concerns have been raised regarding unintended consequences of the use of IAP, including potential increases in non-GBS and antimicrobial agent-resistant cases of sepsis. A review by the Centers for Disease Control and Prevention (CDC) assessed 23 articles reporting on trends in EOS. Eight of the reviewed articles specifically studied the association of IAP with antibiotic-resistant neonatal infections, reporting trends (some nonsignificant) toward increased incidences of ampicillin-resistant infections after exposure to IAP. Those studies were heterogeneous with respect to population site (multicenter or single-center), population type (all newborns or preterm infants), and the information on intrapartum antibiotic use available. The authors concluded that, to assess the true potential for unintended consequences of IAP, ongoing research is needed to assess changes in both overall EOS and antibiotic-resistant EOS, in both term and preterm populations, with the use of time periods and populations large enough to detect significant changes.

We reported previously on significant decreases in the incidence of EOS attributable to GBS in both term and preterm infants coincident with the implementation of IAP at our large maternity center. However, the combination of IAP to prevent neonatal GBS disease and the use of intrapartum antibiotic therapy for other obstetric indications has resulted in large increases in the number of mothers exposed to antibiotics in the peripartum period; in our center in 2006–2007, 40% of births had some peripartum antibiotic exposure. The objective of this study was to assess whether increased peripartum antibiotic exposure has changed the overall incidence and microbiologic features of EOS in our center since the implementation of a screening-based policy for GBS prevention in 1997.

METHODS
Case Ascertainment and Chart Review
This was a retrospective cohort study of all infants born at the Brigham and Women’s Hospital (BWH) (Boston, MA) between January 1, 1990, and December 31, 2007. Cases of EOS were identified through querying of the microbiology laboratory electronic database for any blood culture that was positive for a bacterial species and was obtained from an infant before 72 hours of age. To eliminate positive cultures considered to reflect contaminants, a culture was considered to represent a case of EOS if the attending neonatologist considered the infant to be infected and surviving infants were treated with an appropriate course of antibiotics (≥7 days). Cases were analyzed for 3 time periods, which were distinguished by the hospital protocol for the administration of IAP against neonatal GBS disease. Before 1993, IAP was not used routinely. In 1993–1996, a risk-based protocol was in place at this hospital. In 1997, a screening-based policy was universally implemented at this hospital. Data on EOS cases from 1990–1996 were published previously; that work defined EOS cases as those occurring before 7 days of life and did not include full data for 1992.

Clinical and microbiologic information was obtained through review of the medical records for the infants and mothers. Maternal antibiotic exposure was assessed for the hospital admission leading to delivery. Annual live birth, birth weight, and NICU admission data were obtained from hospital summary statistics. Data on the overall use of antibiotics during admissions leading to delivery were obtained from the hospital research database that links pharmacy records with discharge diagnoses.

Blood Culture Methods and Antibiotic Susceptibility
Blood cultures were performed in the BWH microbiology laboratory with an automated Bactec system (BD Diagnostics, Franklin Lakes, NJ). Both aerobic and anaerobic bottles were used for routine infant cultures. Antibiotic susceptibility testing was performed by the microbiology laboratory, using standard methods for disk diffusion testing.

Statistical Methods
Bivariate analyses of categorical data were performed with Fisher’s exact test or χ² tests. Multivariate analyses were performed through logistic regression, by using SAS 9.1 (SAS Institute, Cary, NC).

RESULTS
Incidence and Microbiologic Features of EOS During Study Periods
We identified 335 cases of culture-proven EOS among infants born at the BWH in 1990–2007 (Table 1). Infants born with birth weights of <1500 g (very low birth weight [VLBW]) accounted for 2.5% of all live births at our institution during this period and 29.9% (100 of 335 cases) of all infections (Table 2). The overall incidence of EOS during the study period was 2.07 cases per 1000 live births; the VLBW incidence was 24.35 cases per 1000
TABLE 1 Distribution of Organisms Causing EOS in All Infants

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<tbody>
<tr>
<td>GBS</td>
<td>56</td>
<td>39</td>
<td>44</td>
<td>139</td>
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<tr>
<td>Enterococci</td>
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<td>4</td>
<td>6</td>
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<td>3.9</td>
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<tr>
<td>Other streptococci</td>
<td>13</td>
<td>3</td>
<td>23</td>
<td>39</td>
<td>11.6</td>
</tr>
<tr>
<td><em>Staphylococcus aureus</em></td>
<td>2</td>
<td>5</td>
<td>6</td>
<td>13</td>
<td>3.9</td>
</tr>
<tr>
<td>Coagulase-negative staphylococci</td>
<td>2</td>
<td>2</td>
<td>10</td>
<td>14</td>
<td>4.2</td>
</tr>
<tr>
<td>Listeria</td>
<td>0</td>
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<td>2</td>
<td>2</td>
<td>0.6</td>
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<tr>
<td>Other Gram-positive species</td>
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<tr>
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<td>5</td>
<td>7</td>
<td>26</td>
<td>38</td>
<td>11.6</td>
</tr>
</tbody>
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Gram-negative

<table>
<thead>
<tr>
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<tr>
<td><em>Escherichia coli</em></td>
<td>15</td>
<td>16</td>
<td>40</td>
<td>71</td>
<td>20.2</td>
</tr>
<tr>
<td><em>Bacteroides</em> spp</td>
<td>1</td>
<td>4</td>
<td>10</td>
<td>15</td>
<td>4.5</td>
</tr>
<tr>
<td>Klebsiella spp</td>
<td>0</td>
<td>1</td>
<td>3</td>
<td>4</td>
<td>1.3</td>
</tr>
<tr>
<td><em>Haemophilus influenza</em></td>
<td>0</td>
<td>2</td>
<td>4</td>
<td>6</td>
<td>1.9</td>
</tr>
<tr>
<td>Other Gram-negative species</td>
<td>3</td>
<td>1</td>
<td>4</td>
<td>8</td>
<td>2.6</td>
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<tr>
<td>Ampicillin-resistant, Gram-negative species</td>
<td>12</td>
<td>12</td>
<td>38</td>
<td>62</td>
<td>18.5</td>
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<tr>
<td>Fungi</td>
<td>0</td>
<td>1</td>
<td>2</td>
<td>3</td>
<td>0.9</td>
</tr>
<tr>
<td>Total ampicillin-resistant species</td>
<td>17</td>
<td>20</td>
<td>68</td>
<td>103</td>
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</tr>
<tr>
<td>Total</td>
<td>96</td>
<td>78</td>
<td>161</td>
<td>335</td>
<td>100</td>
</tr>
</tbody>
</table>

Other streptococci included *Streptococcus mitis*, *Streptococcus mitis*, *Streptococcus morgilli*, *Streptococcus murti*, *Streptococcus oralis*, *Streptococcus pneumoniae*, *Streptococcus salivarius*, *Streptococcus sanguinis*, and *Streptococcus virdans*. Other Gram-positive species included *Clostridium perfringens*, *Corynebacterium*, *Bacillus*, and *Micrococcus* species. Other Gram-negative species included *Brevundimonas vesicularis*, *Citrobacter diversus*, *Citrobacter freundii*, *Fusobacterium nucleatum*, *Morganella morganii*, and *Proteus mirabilis*.

TABLE 2 Distribution of Organisms Causing EOS in VLBW Infants

<table>
<thead>
<tr>
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<tr>
<td>GBS</td>
<td>9</td>
<td>3</td>
<td>9</td>
<td>21</td>
<td>21.0</td>
</tr>
<tr>
<td>Enterococci</td>
<td>0</td>
<td>1</td>
<td>0</td>
<td>1</td>
<td>1.0</td>
</tr>
<tr>
<td>Other streptococci</td>
<td>7</td>
<td>1</td>
<td>4</td>
<td>12</td>
<td>12.0</td>
</tr>
<tr>
<td><em>Staphylococcus aureus</em></td>
<td>0</td>
<td>1</td>
<td>2</td>
<td>3</td>
<td>3.0</td>
</tr>
<tr>
<td>Coagulase-negative staphylococci</td>
<td>1</td>
<td>0</td>
<td>4</td>
<td>5</td>
<td>10.0</td>
</tr>
<tr>
<td>Listeria</td>
<td>0</td>
<td>0</td>
<td>1</td>
<td>1</td>
<td>1.0</td>
</tr>
<tr>
<td>Other Gram-positive species</td>
<td>1</td>
<td>0</td>
<td>2</td>
<td>3</td>
<td>3.0</td>
</tr>
<tr>
<td>Ampicillin-resistant, Gram-positive species</td>
<td>1</td>
<td>1</td>
<td>8</td>
<td>10</td>
<td>10.0</td>
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</tbody>
</table>

Gram-negative

<table>
<thead>
<tr>
<th></th>
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</thead>
<tbody>
<tr>
<td><em>Escherichia coli</em></td>
<td>8</td>
<td>7</td>
<td>19</td>
<td>34</td>
<td>34.0</td>
</tr>
<tr>
<td><em>Bacteroides</em> spp</td>
<td>0</td>
<td>4</td>
<td>6</td>
<td>10</td>
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</tr>
<tr>
<td>Klebsiella spp</td>
<td>0</td>
<td>0</td>
<td>1</td>
<td>1</td>
<td>1.0</td>
</tr>
<tr>
<td><em>Haemophilus influenza</em></td>
<td>0</td>
<td>1</td>
<td>1</td>
<td>2</td>
<td>2.0</td>
</tr>
<tr>
<td>Other Gram-negative species</td>
<td>3</td>
<td>1</td>
<td>1</td>
<td>5</td>
<td>5.0</td>
</tr>
<tr>
<td>Ampicillin-resistant, Gram-negative species</td>
<td>8</td>
<td>8</td>
<td>16</td>
<td>32</td>
<td>32.0</td>
</tr>
<tr>
<td>Fungi</td>
<td>0</td>
<td>0</td>
<td>2</td>
<td>2</td>
<td>2.0</td>
</tr>
<tr>
<td>Total ampicillin-resistant species</td>
<td>9</td>
<td>9</td>
<td>24</td>
<td>42</td>
<td>42.0</td>
</tr>
<tr>
<td>Total</td>
<td>29</td>
<td>19</td>
<td>52</td>
<td>100</td>
<td>100</td>
</tr>
</tbody>
</table>

Other streptococci included *Streptococcus mitis*, *Streptococcus morgilli*, *Streptococcus pneumoniae*, *Streptococcus sanguinis*, and *Streptococcus virdans*. Other Gram-positive species included *Clostridium perfringens*, *Corynebacterium*, *Bacillus*, and *Bacillus* species. Other Gram-negative species included *Citrobacter diversus*, *Citrobacter freundii*, *Fusobacterium nucleatum*, *Morganella morganii*, and *Proteus mirabilis*.

VLBW live births (Table 3). Gram-positive species accounted for 68.1% of all infections. Only 3 cases of early-onset fungal infections were documented during the 18-year period. Nearly 5% of infections were caused by strictly anaerobic *Bacteroides* species.

Changes in EOS Incidence With Changes in GBS IAP Policy

To determine the impact of IAP during the study period, we divided the cases into those that occurred in 1990–1992, a period during which IAP was not used, in 1993–1996, a period during which the hospital enforced a screening-based approach to IAP, and in 1997–2007, a period during which the hospital endorsed a risk factor–based approach to IAP. The overall incidence of EOS decreased significantly across these periods, from 3.70 cases per 1000 live births in 1990–1992 to 1.59 cases per 1000 live births in 1997–2007 (*P < .0001*) (Table 3 and Fig 1A). The overall decrease in EOS rates was driven by significant decreases in rates of EOS caused by GBS (*P < .0001*) and other streptococci (*P = .030*). The overall incidence of EOS in VLBW infants decreased from 1990–1992 to 1993–1996, but there was no further decrease in 1997–2007 (Table 3 and Fig 1B). The EOS incidence among VLBW infants decreased in 1990–1992 versus 1997–2007, but this finding was of borderline significance (*P = .13*).

EOs Caused by Ampicillin-Resistant Organisms

We observed no change in the incidence of EOS caused by ampicillin-resistant *Escherichia coli* or by any ampicillin-resistant organism, among all infants or among VLBW infants (Table 3 and Fig 2). Trends toward decreases in the incidence of EOS caused by ampicillin-resistant *E coli* were observed among all infants and among VLBW infants (Table 3). However, with the decrease in the incidence of EOS caused by ampicillin-sensitive organisms, the proportion of EOS cases caused by ampicillin-resistant organisms increased between the 1990–1992 and 1997–2007 periods. Among all infants, 17 (18%) of 96 EOS cases were caused by ampicillin-resistant organisms in 1990–1992, compared with 66 (41%) of 161 in 1997–2007 (*P = .0001*). Among VLBW infants, 9 (31%) of 29 EOS cases were caused by ampicillin-resistant organisms in 1990–1992, compared with 24 (46%) of 52 in 1997–2007 (*P = .24*). Ampicillin-resistant *E coli* accounted for 9 (53%) of 17 ampicillin-resistant infections, and other streptococci accounted for 13 (72%) of 18 infections.
resistant EOS cases in 1990–1992 and 22 (33%) of 66 ampicillin-resistant EOS cases in 1997–2007 (P = .17). Ampicillin-resistant E coli accounted for a decreasing proportion of ampicillin-resistant, VLBW cases, that is, 6 (67%) of 9 ampicillin-resistant, VLBW cases in 1990–1992 and 8 (33%) of 24 ampicillin-resistant, VLBW cases in 1997–2007 (P = .12).

### Risk Factors for Ampicillin-Resistant Infections

To determine whether specific factors might place infants at risk for an ampicillin-resistant infection, we compared the clinical characteristics of the births of infants infected with ampicillin-sensitive or ampicillin-resistant organisms (Table 4). In bivariate analyses, infants infected with ampicillin-resistant organisms, compared with ampicillin-sensitive organisms, were of significantly lower gestational age and birth weight (Table 4). Mothers of infants with ampicillin-resistant EOS were more likely to have deliveries complicated by preterm labor and/or premature rupture of membranes and were less likely to exhibit colonization with GBS. Mothers of infants with ampicillin-resistant EOS were more likely to have been treated with any antibiotic in the intrapartum period; the strongest association was with the receipt of ampicillin. In addition, they were more likely to have been treated with intrapartum antibiotic therapy for prolonged periods. Each of these factors (preterm labor, premature rupture of membranes, intrapartum antibiotic therapy, and longer duration of antibiotic treatment) tracked with lower gestational age and birth weight, however, and a significantly greater proportion of mothers treated with ampicillin tested GBS-negative, compared with all other mothers (63%...
vs 31%; \( P = .006 \). In logistic regression analyses controlling for gestational age and birth weight, intrapartum ampicillin exposure remained significantly associated with ampicillin-resistant infections (ampicillin exposure, odds ratio: 2.18 [95% confidence interval: 1.25–3.82]; \( P = .006 \)).

**Ampicillin Exposure and E coli Infections**

To address specifically the relationship between E coli EOS and ampicillin exposure in the era of GBS prophylaxis, we identified 40 cases of E coli EOS that occurred during the 1997–2007 period; 19 of 40 involved VLBW infants. Overall, ampicillin was administered to the mothers of 10 of 22 infants with ampicillin-resistant infections and 6 of 18 infants with ampicillin-sensitive infections (\( P = .53 \)). Among the VLBW infants, however, ampicillin administration was significantly associated with ampicillin-resistant E coli infections (7 of 8 ampicillin-resistant cases versus 3 of 11 ampicillin-sensitive cases; \( P = .02 \)).

**Overall Intrapartum Antibiotic Use at BWH**

Obstetric policy at BWH has recommended the use of penicillin G for GBS IAP since the screening-based approach was introduced in 1997. To determine what type of intrapartum antibiotic therapy was administered, we used the hospital data registry to link pharmacy records to all obstetric admissions that resulted in a vaginal delivery in 1997–2007. We restricted this analysis to vaginal deliveries to avoid confounding factors in the use of antibiotics for cesarean sections, including surgical antibiotic prophylaxis and the increased likelihood of labor complicated by chorioamnionitis resulting in operative delivery. The proportion of vaginal deliveries with antibiotic exposure increased from 19.7% in 1997 to 41.5% in 2007 (\( P < .0001 \)). The use of

![Figure 2](image-url)

**FIGURE 2**

Incidences of ampicillin-sensitive and ampicillin-resistant EOS in 1990–2007. The decrease in all-cause EOS incidence was driven by decreases in ampicillin-sensitive (AmpS) EOS rates, with no changes in ampicillin-resistant (AmpR) EOS rates, among all infants (A) and among VLBW infants (B).
We observed no significant changes in the use of ampicillin (7.1% of all vaginal deliveries in 1997 and 7.7% in 2007; $P = .23$) except for a period in 1999–2000 during which there was a national shortage of penicillin G.14,15 We observed significant increases in the use of penicillin G (4.6% of all vaginal deliveries in 1997 and 22.9% in 2007; $P < .0001$) and the other antibiotics recommended for IAP among women who are allergic to penicillin (clindamycin, 0.8% vs 5.5%; erythromycin, 0.2% vs 0.7%; cefazolin, 1% vs 4%; vancomycin, 0.05% vs 0.7%; $P < .0001$ for each comparison). We also observed a relative decrease in the use of erythromycin and increases in the use of cefazolin and vancomycin after 2002, when the revised CDC guidelines alerted clinicians to increasing erythromycin resistance among GBS isolates.16 To determine whether the use of ampicillin changed in higher-risk deliveries, we also examined the proportions of all deliveries (vaginal and cesarean) in which the mother received ampicillin in 1997 versus 2007; ampicillin use remained static over this time period (8.1% vs 8.7%; $P = .19$).

### DISCUSSION

Thirteen years after the first CDC guideline endorsed the use of IAP to prevent neonatal EOS, the incidence of GBS EOS has decreased markedly on a national basis.1 However, the overall impact of IAP practices on the incidence and microbiologic features of EOS remains uncertain, particularly among VLBW infants.2,17–22 Our study of EOS over an 18-year period at a single, large, maternity center reveals decreases in all-cause EOS rates for both term and VLBW infants, with no change in the incidence of ampicillin-resistant infections. In addition, the implementation of a screening-based approach to GBS IAP in our institution resulted in a significant increase in the proportion of deliveries with exposure to antibiotics predominantly active against Gram-positive organisms but no change in the use of ampicillin. Although it is effective for prevention of early-onset GBS disease, broad use of IAP could be associated with untoward consequences because of the significant increase in peripartum antibiotic exposure. Specifically, questions have been raised regarding whether IAP results in higher incidences of EOS attributable to organisms other than GBS and whether it is associated with changes in rates of EOS caused by ampicillin-resistant organisms, particularly in VLBW infants.2,17–22 Our study is the largest single-center study of exclusively inborn neonates to address these questions. We found that the overall incidence of neonatal EOS decreased in the era of GBS IAP, among all newborns and among VLBW infants. The primary reason for this change was the decreased incidence of EOS caused by GBS and by other streptococcal species. The significant decrease in the incidence of EOS caused by other streptococcal species coincident with IAP has not been reported previously and provides evidence that infections caused by non-GBS streptococcal organisms also may be susceptible to the strategy of IAP.

We observed no increases in Gram-negative infection, ampicillin-resistant infection, *E coli* infection, or ampicillin-resistant *E coli* infection rates among all infants or among VLBW infants examined separately. In contrast to
these findings, the multicenter National Institute of Child Health and Human Development Neonatal Network previously reported a sustained increase in *E. coli* EOS incidence among VLBW infants since 1998 in their hospitals, with ~80% of the reported infections being caused by ampicillin-resistant *E. coli*. In those reports, the overall EOS incidence in VLBW infants was unchanged over the study period, because the decrease in the incidence of GBS-related EOS was countered by an increase in the incidence of *E. coli* infections. Bizzarro et al reported an increase in the overall incidence of EOS infections among VLBW infants cared for at Yale-New Haven Hospital between 1979 and 2006, which was driven by an increase in *E. coli* infections. That study used a denominator of VLBW NICU admissions in a mixed inborn/outborn population, with significant trends toward the admission of gestationally younger and smaller infants over the study period, which likely influenced their findings. Current CDC recommendations for GBS prophylaxis include use of either ampicillin or penicillin G for women without allergies. Over our study period, we observed an increase in peripartum exposure to antibiotics primarily effective against Gram-positive organisms (penicillin G, vancomycin, and clindamycin) and no change in the use of ampicillin. Although data on overall peripartum antibiotic use were not available from the National Institute of Child Health and Human Development Neonatal Network or from the referring centers in the Yale-New Haven study, we speculate that differences in the microbiologic features of EOS we observed in our center might be attributable to differences in peripartum antibiotic use, particularly our strict adherence to the use of narrower-spectrum antibiotics for IAP.

The influence of ampicillin exposure alone on the microbiologic features of EOS and whether different effects may be observed for VLBW infants, compared with gestationally older infants, remain unclear. The Neonatal Network and the Yale-New Haven study reported that VLBW infants with ampicillin-resistant *E. coli* infections were more likely to have been exposed to ampicillin in the peripartum period, compared with those with ampicillin-sensitive *E. coli* infections. In contrast, a multistate, surveillance, case-control study performed by the CDC demonstrated no association between intrapartum antibiotic exposure of any type and ampicillin-resistant infection rates when the analysis was controlled for gestational age and birth weight. We found that ampicillin exposure was significantly associated with ampicillin-resistant infection rates when the analysis was controlled for gestational age and birth weight. The difference between our findings and those of the CDC study may be attributable to differences in study design. The CDC study focused only on *E. coli* infections and evaluated the effect of intrapartum exposure to ampicillin or penicillin as one variable. We considered all ampicillin-resistant infections (not just *E. coli* infections) and evaluated the effect of intrapartum antibiotic exposure by categorizing antibiotics as 3 separate variables, that is, antibiotics with predominantly Gram-positive spectra (penicillin, clindamycin, erythromycin, and vancomycin), ampicillin, and antibiotics with broad Gram-negative spectra (cephalosporins). Although the association of intrapartum antibiotic use with ampicillin-resistant infection rates is confounded by the increased use of these antibiotics in high-risk, preterm delivery settings, the design of our study allowed us to examine specifically the effect of the use of ampicillin on the overall risk of infection with ampicillin-resistant organisms.

Our study strongly supports the use of GBS IAP as providing a net positive impact on neonatal health with respect to infection, but it does so in the setting of a maternity center that has primarily used penicillin G for prophylaxis. We speculate that the use of ampicillin for IAP may not yield such uniformly positive results, particularly for VLBW infants. Finally, it should be noted that, with decreases in the rates of GBS and other (primarily ampicillin-sensitive) streptococcal infections, the proportion of EOS cases caused by ampicillin-resistant organisms did increase during our study period. Since 1997, we have observed that EOS cases are enriched for ampicillin-resistant organisms. Our center routinely uses empiric ampicillin and gentamicin treatment for infants at risk for EOS. In the era of GBS prophylaxis, when physicians are faced with critically ill infants and have a strong suspicion of EOS, consideration should be given to the use of antibiotics other than ampicillin until culture results are available.

One limitation of our study is that we assessed the impact of intrapartum ampicillin use by performing a comparison of ampicillin-sensitive cases and ampicillin-resistant cases and not a case-control study. Our study has several strengths, however, including the large birth cohort from a single maternity center, the long period of study, and particularly the 10-year period of study with strict implementation of a screening-based approach to GBS prophylaxis. Although a variety of obstetricians deliver infants at our center (including practitioners in private group practices, solo practices, a midwife group, a resident-dominated hospital practice, and a large, high-risk, maternal-fetal medicine practice), this study allowed for evaluation of GBS prophylaxis policies in a center.
where obstetric policies are uniformly determined and enforced by the academic obstetric administration. In addition, the availability of information on bacterial isolate antibiotic susceptibility, peripartum antibiotic use, and complications of delivery for >300 cases of EOS and information on intrapartum antibiotic use for all deliveries during the 10-year period of screening-based GBS prophylaxis strengthens our data.

CONCLUSIONS
Short-term use of narrow-spectrum antibiotics primarily active against Gram-positive organisms for GBS IAP resulted in decreases in the incidence of EOS in all infants and in VLBW infants, with no change in the incidence of ampicillin-resistant EOS. The association of peripartum ampicillin exposure with the development of ampicillin-resistant infections suggests that obstetricians should be encouraged to use penicillin G preferentially for routine GBS IAP.

ACKNOWLEDGMENTS
This work was supported in part by National Institutes of Health grants M01-RR00635-210718 and M01-RR002635-225344 (to Dr Puopolo).

We thank Andrew Onderdonk, PhD, Nancy Jeffery-Harrison, and the technical staff of the BWH microbiology laboratory for microbiologic database support, isolate identification, and minimal inhibitory concentration testing; Caryn Douma, BSN, MSN, for maternal and infant data abstraction; Katherine T. Chen, MD, MPH, and Ruth Tuomala, MD, for provision of maternal clinical data; Ellice Lieberman, ORPH, MD, Mary Lucia Gregory, MD, MMSc, and Steven J. Melly, MS, for assistance with statistical analyses; Paul Hughes, MBA, for provision of hospital demographic information; and Stella Kourembana, MD, Ann R. Stark, MD, Steven A. Ringer, MD, PhD, and Dennis L. Kasper, MD, for ongoing support of our work.

REFERENCES
No Change in the Incidence of Ampicillin-Resistant, Neonatal, Early-Onset Sepsis Over 18 Years

Karen M. Puopolo and Eric C. Eichenwald

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