

# Impact of intrapartum antibiotics on the care and evaluation of the neonate

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**Background.** Management of infants whose mothers receive intrapartum antibiotic prophylaxis (IAP) is controversial. In 1996 consensus guidelines for prevention of neonatal Group B streptococcal disease included an algorithm for management of infants whose mothers received IAP. To assess practices for testing and treatment of infants, we evaluated a population-based sample of deliveries to see whether excessive evaluation and treatment occurs after IAP.

**Methods.** Medical records for 869 deliveries in Connecticut during 1996 were sampled. IAP was administered in 96 full term deliveries. We excluded infants <37 weeks and those with intrapartum fever. We reviewed hospital records for infants born after IAP ( $n = 81$ ) and a random sample of those not exposed ( $n = 180$ ). Analyses were conducted with sample weights to account for unequal probability of selection.

**Results.** Infants whose mothers received IAP were more likely to have complete blood counts, (26% vs. 9%  $P = 0.05$ ) but were no more likely to receive antibiotics in the first week of life ( $P = 0.48$ ), have an intravenous catheter placed ( $P = 0.83$ ), or to have other invasive procedures. Mean length of hospital stay was 6 h longer for infants born by vaginal delivery to mothers who had IAP (47.0 h) than for those without IAP (41.3 h) ( $P = 0.06$ ).

**Conclusion.** Despite concerns that IAP guidelines would result in excessive neonatal evaluations, infants sampled whose mothers received IAP were not more likely to undergo invasive procedures or to receive antibiotics. Consistent

with the guidelines, collection of complete blood counts was more common among such infants.

## INTRODUCTION

Group B *Streptococcus* (GBS) is the leading cause of serious neonatal infection. In May 1996 the CDC, the American College of Obstetricians and Gynecologists and the American Academy of Pediatrics (AAP) issued consensus guidelines for prophylactic use of intrapartum antibiotics for women at risk of transmitting GBS disease to their newborns.<sup>1–3</sup> The report included recommendations and a sample algorithm for the management of neonates whose mothers had received intrapartum antimicrobial prophylaxis for prevention of early-onset GBS. This algorithm was developed on the basis of expert opinion, since limited data were available for the development of evidence-based guidelines for evaluation and treatment of neonates in this setting. With an increasing number of women receiving intrapartum antibiotics, there was concern that pediatricians, unsure how to evaluate such infants, would give more antibiotics to those infants, do more invasive procedures on them and keep them in the hospital longer. To avoid such unintended consequences, the prevention guidelines offered the management algorithm.<sup>1,2</sup> The algorithm recommended that neonates with symptoms of sepsis be given a full diagnostic workup and receive empiric antibiotics. For infants with gestational age < 35 weeks or whose mothers received their first dose of antibiotics < 4 h before delivery<sup>2</sup> (or only 1 dose instead of 2 or more),<sup>1</sup> the neonatal algorithm recommend a limited diagnostic evaluation. For all other infants whose mothers received intrapartum antibiotics, only observation for 48 h was recommended unless symptoms developed. However, results of several surveys conducted from 1990–1996 of pediatricians and neonatologists who self-reported clinical practices, suggest that clinicians were more likely to do diagnostic testing and to begin empiric antibiotic treatment of the newborn if the mother had received prophylactic intrapartum antibiotics, regardless of the infant's signs and symptoms.<sup>4–7</sup>

The goal of this study was to evaluate the actual practice of care-givers managing newborns in Connecticut in 1996. In the 30 hospitals in Connecticut where

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infants are delivered, we compared evaluation and treatment of a population-based sample of full-term infants whose mothers received intrapartum antibiotics with term infants whose mothers were not treated.

## METHODS

The project was reviewed and determined exempt from Institutional Review Board clearance at CDC. Review of medical records was approved for this evaluation by the Connecticut Hospital Association. We used the power allocation method to select a stratified random sample of 992 births.<sup>8</sup> We required a minimum sample of 20 births per hospital and included all hospitals with newborn nurseries in the state ( $n = 30$  hospitals). Strata were defined by hospital of birth and term of birth (i.e. term, preterm, or unknown term), forming 90 strata. Within each stratum, births were selected by a simple random sample. Charts of mothers and infants were abstracted for each sampled birth record. From the original 992 births, chart abstraction was completed for 869. Within each stratum, a constant weight was assigned to each sample element. The sample weight was based on the inverse probability of selection and was adjusted to account for nonresponse. The sum of the sample weights reflected the number of births in Connecticut in 1996. The sample size was designed to allow comparison of those who received intrapartum antibiotics with those who did not, not to make precise estimates. The full data from the maternal record review are the subject of a separate report focused on prenatal screening practices.<sup>9</sup>

Our study of neonatal management practices was restricted to the sample of term births ( $n = 675$ ) based on gestational age obtained from the maternal record during the initial chart abstraction. We divided the sample of term births into two strata: 1) those whose mothers had received intrapartum antibiotics ( $n = 96$ ) and 2) those whose mothers did not receive intrapartum antibiotics ( $n = 579$ ). We defined receipt of intrapartum antibiotics as antibiotics given after the onset of labor and before the delivery of the infant. The sample size was calculated to detect with a 95% confidence limit and 80% power a difference between the two groups if the following criteria were met: at least 50% of the neonates exposed to the intervention had blood cultures or a complete blood count (CBC) done and at most 10% of neonates whose mothers did not receive the intervention had a blood culture and a CBC; at least 40% of infants exposed to intrapartum antibiotic prophylaxis (IAP) received antibiotics and at most 10% of those not exposed received antibiotics; at least 70% of infants exposed to IAP stayed in hospital longer than 48 h and at most 50% not exposed stayed longer than 48 h. To detect these differences we calculated a need for 78 case patients and 155 controls. We selected all 96 children whose mothers had received intrapar-

tum antibiotics and 190 children whose mothers did not receive intrapartum antibiotics. After excluding premature infants (i.e. among infants who were initially classified as full term), infants whose mothers had intrapartum fever (temperature,  $\geq 38.0^{\circ}\text{C}$ ) and subjects for whom we could not find both the maternal and child records, 261 children were included in our survey. Information regarding the mother's prenatal care, intrapartum treatment and the care and evaluation of the neonate was available for all children. All analyses were conducted with the use of the sample weights to account for the unequal probability of selection into the study. Data were analyzed in SAS<sup>10</sup> and SUDAAN.<sup>11</sup>

We used the following definitions: a full neonatal diagnostic evaluation consisted of a CBC with differential, a blood culture and a chest radiograph if the neonate had respiratory symptoms; and a limited evaluation was defined as CBC with differential and a blood culture. These definitions were consistent with guidance provided in algorithms included in the published prevention guidelines.<sup>1, 2</sup> To evaluate the number of hours in the hospital after birth, a natural log transformation was used.

## RESULTS

We identified 286 children for record abstraction: 96 children whose mothers had received intrapartum antibiotics and 190 children whose mothers had not received intrapartum antibiotics. On the basis of repeat abstraction, with validation of receipt of a specific antibiotic before delivery, the absence of intrapartum fever, gestational age  $>37$  weeks and location of both the mother's and infant's chart, we enrolled 261 children, 81 who exposed to maternal antibiotics and 180 who were not.

A comparison of demographic characteristics of the infants and mothers who received intrapartum antibiotics with those who did not showed the two groups to be similar with respect to Medicaid status, race of the mother, site of prenatal care, type of delivery, birth weight, sex of the infant, estimated gestational age and Apgar scores (Tables 1 and 2).

**TABLE 1.** Characteristics of mothers and infants ( $n = 261$ )

Maternal Characteristics	IAP (%)	No IAP (%)	P
Mother married	79.6	74.3	0.47
Mother on Medicaid	14.3	16.7	0.70
Maternal race black	23.8	7.5	0.42
Maternal race not specified	4.1	6.2	
Site of prenatal care			
Private clinic	32.0	36.1	0.64
Hospital clinic	25.0	29.7	0.57
Unknown	42.9	32.7	0.35
Type of delivery cesarean section	34.3	19.2	0.18
Cultures collected before delivery	70.7	36.5	0.0025
Prenatal record in chart	82.7	91.9	0.44
Male	49.1	50.15	0.92

**TABLE 2.** Infant characteristics

	IAP (Median)	No IAP (25th Quartile)	75th Quartile
Birth wt (g)			
Intrapartum antibiotics	3552	3271	3811
No intrapartum antibiotics	3481	3080	3757
5-min Apgar score			
Intrapartum antibiotics	8	8	9
No intrapartum antibiotics	8	8	9

Twenty-six percent of infants whose mothers received intrapartum antibiotics had a CBC compared with 9% of infants whose mothers did not ( $P = 0.05$ ; Table 3). Infants whose mothers received antibiotics stayed in the hospital a median of 56.8 h, whereas those whose mothers did not stayed a median of 47.0 h ( $P = 0.02$ ). Mean length of stay for both groups was longer for infants delivered by cesarean section: 81.5 h for those who received IAP and had cesarean section; and 86.5 h for those who did not receive IAP and had a cesarean section ( $P = 0.02$ ). Among infants who were delivered vaginally, the mean length of stay was 47.0 h for those who received maternal IAP and 41.3 h for those who did not receive antibiotics ( $P = 0.06$ ). There was no other significant difference in the evaluation or treatment of infants based on maternal receipt of intrapartum antibiotics (Table 3).

The reasons noted in the chart for maternal intrapartum antibiotics were as follows: a positive maternal GBS culture, 43%; prevention of GBS not otherwise specified, 11%; GBS bacteriuria during pregnancy, 4%; other reasons, 39%. Six percent were also reported to have received intrapartum antibiotics because of maternal fever, although elevated temperature was not documented in the chart. All patients in this study survived. No infant or mother developed group B streptococcal infections after birth, nor were they readmitted for GBS infection. We did not review outpatient charts.

**TABLE 3.** Procedures and outcomes among infants by maternal exposure to intrapartum antibiotics\*

Variable	IAP (%) (n = 81)	No IAP (%) (n = 180)	P
CBC done	26.3	9.4	0.05
Blood culture drawn (%)	12.9	5.8	0.14
Urine culture collected by bladder catheterization	2.7	0.8	0.37
Any urine culture done	4.8	1.1	0.13
Chest radiograph	3.6	4.2	0.84
Infant treated with antibiotics in first 7 days	7.0	4.3	0.48
Infant given intravenous catheter	5.0	4.2	0.83
Infant in neonatal intensive care unit	3.7	3.9	0.94
Mechanical ventilation	1.5	0.00	0.09
Supplemental oxygen	6.1	5.1	0.78
Hospitalized $\geq 48$ h	16.8	6.6	0.01
Hospitalized $>72$ h	16.8	9.7	0.25

\* Percentages are based on weighted calculations.

**CBC.** Among the 14 infants with signs of sepsis whose mothers received intrapartum antibiotics, 67% had a CBC compared with 66% of the 13 infants with signs of sepsis whose mothers did not receive intrapartum antibiotics ( $P = 0.97$ ). However, among infants with no signs of sepsis, 20% of those whose mothers received intrapartum antibiotics had a CBC, compared with 4% of infants whose mothers did not receive intrapartum antibiotics ( $P = 0.06$ ).

**Full diagnostic evaluation.** The neonatal algorithm in the AAP and CDC guidelines also recommended that infants who had signs of sepsis and whose mothers received intrapartum antibiotics receive a full diagnostic evaluation and empiric antibiotics. We found that 66% of infants whose mothers received intrapartum antibiotics and who had signs of sepsis (including fever, hypothermia, grunting, poor color, hypotension, acidosis, tachypnea, poor tone, apnea or hypoglycemia) received a full diagnostic evaluation, and all received empiric antibiotics. Among infants with symptoms of sepsis whose mothers did not receive intrapartum antibiotics, 25% received a full diagnostic evaluation (the difference was not significantly different from those who were exposed to IAP,  $P = 0.08$ ), and 100% received empiric antibiotics.

**Limited diagnostic workup.** The guidelines also called for infants whose mothers had received intrapartum antibiotics  $<4$  h before delivery to receive a limited diagnostic workup and to be observed for 48 h. In our study 4.3% of infants born to mothers who received antibiotics  $<4$  h before delivery received a limited diagnostic workup, and 86% remained in the hospital for at least 48 h. Among infants whose mothers received intrapartum antibiotics at least 4 h before delivery, 3.6% ( $P = 0.89$ ) had a limited diagnostic workup and 48% ( $P = 0.01$ ) were observed for at least 48 h. Among infants whose mothers received only one dose of antibiotics, 6.9% received a limited diagnostic workup, and 80.4% were observed for  $>48$  h; whereas among those whose mothers received two or more doses of antibiotics, 1.7% ( $P = 0.32$ ) received a limited diagnostic workup and 58% ( $P = 0.17$ ) were observed for  $>48$  h. These differences were not statistically significant. However, among infants whose mothers received IAP  $\geq 4$  h before delivery and who did not have signs and symptoms of sepsis, 19.3% had a CBC although the algorithm recommended that such infants only be observed. Use of maternal intrapartum antibiotics had no impact on use of antibiotics for infants in the setting of prolonged rupture of membranes. Among infants whose mother had prolonged rupture of membranes for  $\geq 18$  h and whose mothers received IAP, 20.8% received antibiotics in the first 7 days of life; whereas among infants not exposed to IAP, 31.5% received antibiotics in the first 7 days ( $P = 0.67$ ).



## DISCUSSION

Management of newborns in the setting of maternal exposure to antibiotics has challenged pediatricians because antibiotics may mask signs of neonatal illness, resulting in subclinical infection. Guidelines for prevention of neonatal GBS infection have predictably increased use of intrapartum antibiotics, but their effect on management of newborns is not yet clear. With the adoption of the prevention guidelines for group B streptococcal disease in newborns,<sup>1-3</sup> rates of early onset GBS disease have declined >65%.<sup>12, 13</sup> In 1997 a survey of hospitals in Connecticut revealed that 25 of 30 (85%) had a policy regarding prevention of neonatal GBS disease. The same survey indicated that hospitals with neonatal GBS prevention policies had a 56% decrease in the number of cases of early onset GBS disease.<sup>12, 14</sup>

Three studies evaluated recent practices regarding the care and evaluation of neonates whose mothers received intrapartum antibiotics. In one, published in 1990, questionnaires were sent to all fellowship program directors in neonatology and infectious diseases in the United States<sup>6</sup>; in the other two, published in 1995 and 1996, questionnaires were sent to US pediatricians who were members of the AAP.<sup>5, 7</sup> These surveys suggested that physicians would begin antibiotic treatment of newborns whose mothers had received intrapartum antibiotics regardless of symptoms. Unnecessary use of empiric antibiotic therapy is particularly concerning because of the potential impact on antibiotic resistance.

In our study the practices of pediatricians were examined through chart abstraction. Infants whose mothers received intrapartum antibiotics were no more likely to receive empiric antibiotic treatment in the first 7 days of life than those whose mothers had not. Although the infants whose mothers received intrapartum antibiotics were more likely to have a specimen collected for complete blood count, they were no more likely to have any other procedure performed.

In addition to the impact of the guidelines on the care and evaluation of neonates, there has also been concern about their cost, particularly regarding increased length of stay for asymptomatic neonates whose mothers received intrapartum antibiotics. A study at a health maintenance organization in Northern California concluded that implementation of the guidelines could be cost-saving unless the length of hospital stay was extended for well, term infants whose mothers received intrapartum antibiotics.<sup>15</sup> Another study concluded that pediatric costs varied with the length of stay for term infants and the cost of a hospital day.<sup>16</sup> This latter study considered only asymptomatic infants of mothers who received intrapartum antibiotics. In the analysis no additional costs were generated

among infants born by cesarean section, given that those infants generally stay longer than 48 h.<sup>16</sup>

In our study the average length of stay for infants whose mothers received intrapartum antibiotics was ~10 h longer than the average length of stay for those whose mothers did not. Infants whose mothers received IAP were more likely to be hospitalized for  $\geq 48$  h than those whose mothers did not ( $P = 0.01$ ; Table 3). With the passage of a federal law requiring insurers to cover up to 48 h of hospitalization after a vaginal delivery,<sup>17</sup> it is unlikely that the prevention guidelines would cause a substantial increase in pediatric costs related to extended length of stay. New economic analyses should take this legislation into account.

Despite concerns about the impact of the prevention guidelines for intrapartum antibiotics on the care and evaluation of the neonate, our study shows that although infants exposed to maternal intrapartum antibiotics are more likely to have a CBC and longer hospital stay, they are not more likely to receive antibiotics or to have more invasive procedures. This study underscores the importance of studying actual clinical practice rather than physician reports through surveys and provides population-based data that could be used in future economic models.

This study was limited by small numbers. We may not have had the power to detect small differences between the two groups. It was conducted in a single year (1996) in a single state (Connecticut). Practices identified in this population may not be representative of physicians nationally or of practices in 2003. We did not evaluate optimal management of neonates born to mothers with IAP, so we cannot determine whether certain testing can be eliminated. Such a study would require examination of clinical outcomes for extremely large numbers of infants. Some work is now being done to create algorithms for the workup of infants at risk for neonatal sepsis<sup>18, 19</sup>; however, more research is needed into how to manage infants at risk for sepsis. New guidelines for perinatal GBS prevention issued by the CDC in August 2002 include an updated neonatal care algorithm.<sup>20</sup>

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## Substantial variability in community respiratory syncytial virus season timing

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**Background.** Respiratory syncytial virus (RSV) is the major cause of bronchiolitis and pneumonia in young children. Prevention of RSV disease in children in certain high risk groups through use of immunoglobulin preparations has been recommended by the American Academy of Pediatrics since 1998. A more precise understanding of the timing of annual RSV epidemics should assist providers in maximizing the benefit of

these preventive therapies. The objective of this study was to determine whether current national RSV surveillance data could be used to define the timing of seasonal outbreaks

**Methods.** Weekly RSV testing data from the National Respiratory and Enteric Viruses Surveillance System for the period July 1990 through June 2000 were analyzed. RSV season onset week, peak week and duration were calculated for the entire United States, Census regions and select local laboratories. Season variability was estimated by comparing calculations for individual RSV seasons to median measurements for the entire surveillance period

**Results.** RSV seasons in the South region began significantly earlier ( $P < 0.05$ ) and lasted longer ( $P < 0.05$ ) than seasons for the rest of the nation.

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