

Group B Streptococcus Late-Onset Disease: 2003–2010

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KEY WORDS

group B streptococcus, infant, intrapartum chemoprophylaxis, late-onset disease, sepsis

ABBREVIATIONS

CI—confidence interval
CSF—cerebrospinal fluid
EOD—early-onset disease
GBS—group B streptococcus
IAP—intrapartum antibiotic prophylaxis
IQR—interquartile range
LOD—late-onset disease
OR—odds ratio

Dr Berardi, Dr Rossi, Dr Lugli, Dr Creti, and Dr Ferrari conceptualized and designed the study and drafted the initial manuscript; Drs Bacchi Reggiani, Lanari, and Perrone conducted the initial analyses and reviewed the manuscript; Dr Memo, Dr Pedna, Dr Venturelli, Dr Ciccia, Dr Piepoli, and Dr Contiero designed the data collection instruments, coordinated and supervised data collection, and critically reviewed the manuscript; and Dr Tridapalli provided basic information, added in the current version of the article, and critically reviewed the manuscript. All authors approved the final manuscript as submitted.

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WHAT'S KNOWN ON THIS SUBJECT: A minority of infants with group B streptococcus (GBS) late-onset disease (LOD) are born to GBS-colonized mothers. Intrapartum prophylaxis does not appear to prevent late-onset GBS disease, implicating infected breast milk and nosocomial or community sources in these cases.



WHAT THIS STUDY ADDS: Most mothers of neonates with LOD are identified at diagnosis with anogenital GBS infection. Even in the absence of mastitis, GBS-infected milk may be a source of LOD. Intrapartum antibiotic prophylaxis is associated with both delayed and milder presentation of LOD.

abstract

BACKGROUND: There is insufficient population-based data on group B streptococcus (GBS) late-onset disease (LOD). Risk factors and routes of GBS transmission are poorly understood.

METHODS: A prospective, cohort study was conducted to collect incidence data on LOD and evaluate GBS infections over an 8-year period (2003–2010). Starting from January 2007, maternal rectovaginal and breast milk cultures were routinely collected on confirmation of the LOD diagnosis to assess maternal GBS culture status.

RESULTS: The incidence rate of LOD was 0.32 per 1000 live births (1.4 and 0.24 per 1000 live births for preterm and term newborns, respectively). The registered cases of LOD ($n = 100$) were classified as sepsis ($n = 57$), meningitis ($n = 36$), or focal infection ($n = 7$). Thirty neonates were preterm (2 had recurrent infection); 68 were term. Four infants died (3 early preterm, 1 term). At the time the LOD diagnosis was confirmed, 3 (6%) of 53 mothers had GBS mastitis, and 30 (64%) of 47 carried GBS at the rectovaginal site. Early (7–30 days) LOD presentation was associated with neonatal brain lesions or death (odds ratio: 0.96 [95% confidence interval: 0.93–0.99]). Intrapartum antibiotic exposure was significantly associated with mild (12 of 22) rather than severe (11 of 45; $P = .03$) LOD.

CONCLUSIONS: Preterm neonates had the highest rates of LOD and mortality. Most mothers carried GBS at the time of the LOD diagnosis, whereas 6% had mastitis. Intrapartum antibiotics were associated both with delayed presentation of symptoms and milder LOD. *Pediatrics* 2013;131:1–8

Group B streptococcus (GBS) is a leading cause of neonatal sepsis and meningitis. GBS infections present from birth to day 6 (early-onset disease [EOD]) or from day 7 to 89 (late-onset disease [LOD]).¹ EOD is the result of vertical transmission (at delivery or shortly before) from a mother who is colonized with GBS in the anorectal and vaginal sites. Routine screening for maternal GBS carriage in late pregnancy (35–37 weeks' gestation) and consequent intrapartum antibiotic prophylaxis (IAP) have substantially reduced the incidence rates of EOD.²

LOD can be acquired from the mother (~50% of infants with LOD are colonized at birth with the same GBS serotype as the mother)³ or from environmental sources.¹ The use of IAP for the prevention of EOD has had no notable effects on the occurrence of LOD. Data from the United States have shown stable rates of LOD (~0.35 per 1000 live births), despite widespread IAP administration.⁴

The pathogenesis of LOD is less well understood than that of EOD, and in some infants, the source of infection is unclear. Nosocomial transmission of GBS through the hands of health care workers was frequent decades ago, when postparturient mothers and their infants typically remained in the hospital for ≥ 1 week.^{5–7} Anecdotal case reports have also suggested breast milk as a possible source of GBS.^{8–13} However, it is unknown whether these are currently common routes of LOD transmission.

Risk factors may differ according to the gestational age at birth. Therefore, LOD pathogenesis might be dissimilar in preterm and term neonates, and they should be studied independently.

European LOD data are limited, and the persistence of LOD after adoption of an EOD preventive strategy has yet to be investigated. A GBS prevention working group was established in Emilia-Romagna, Italy, in 2003. A screening-

based strategy was introduced,¹⁴ and the incidence rates of EOD declined from 0.29 to 0.19 per 1000 live births in the period between 2003 and 2011 (A.B., unpublished data).

The current study was designed to analyze LOD incidence and GBS-related mortality and to determine maternal culture status and clinical features in both term and preterm newborns over an 8-year period throughout an entire regional network.

METHODS

Study Design

Since 2003, a prospective, population-based study has been ongoing in Emilia-Romagna, a region in Italy with ~40 000 live births per year. The GBS active surveillance network involves all regional neonatal and pediatric departments and microbiologic laboratories. The network provides continuous information on culture-proven infections recorded in infants aged <90 days.¹⁵

A standardized form is used to collect maternal and neonatal characteristics for each GBS case; details include the results of maternal rectovaginal cultures at 35 to 37 weeks of gestation, risk factors, mode of delivery, IAP administration, neonatal symptoms, age at presentation, days of mechanical ventilation, therapies, and outcome. As of January 2007, additional information (related to maternal mastitis, milk, and rectovaginal cultures) has been requested after confirmation of the LOD diagnosis. Infections recorded from January 1, 2003, to December 31, 2010, are considered here. All standardized forms were initially analyzed by a single medical professional (A.B.), but the data were reviewed together with 2 additional medical professionals (C.R. and L.L.).

Microbiologic Methods

Blood cultures were processed by using automated systems (Bactec 9240,

Becton Dickinson, Heidelberg, Germany; Bactalert, bioMérieux, Craponne, France). Milk samples were collected by manual expression after both the breast and the nipple had been washed with soap and water and cleansed with saline solution. After the initial drops had been discarded, samples were collected in a sterile container and cultured on 5% defibrinated sheep blood, MacConkey, and Candida agar plates.¹⁶ Bacterial strain characterization was performed by using pulsed-field gel electrophoresis, according to the standard method previously reported.¹⁷

Study Definitions

GBS Case: Isolation of GBS from a normally sterile body site (eg, blood or cerebrospinal fluid [CSF]) in infants aged 7 to 89 days.

Sepsis: Growth of GBS from blood culture associated with symptoms consistent with sepsis.¹

Meningitis: Presence of clinical symptoms associated with: (1) a positive result on CSF culture; (2) a positive CSF polymerase chain reaction; (3) a positive result on blood culture and CSF pleocytosis (defined as the presence of >30 white blood cells/mm³ and <45 000 red blood cells/mm³)^{18,19}; or (4) a positive result on CSF antigen testing.

Focal Infection: GBS-positive blood culture result associated with focal signs outside the respiratory tract.

Mild Disease: Vague and short-lasting symptoms, no need for mechanical ventilation or catecholamine support, and no clinical or laboratory evidence of focal infection; infant discharged from the hospital ≤ 7 days of disease presentation.

Severe Disease: Includes any of the following: death, meningitis, seizures, brain lesions documented at hospital discharge, need for catecholamine support, or mechanical ventilation.

Early Preterm: Includes neonates born at <34 weeks' gestation.

Late Preterm: Includes neonates born at 34 to 36 6/7 weeks' gestation.

GBS Mastitis: Localized, painful inflammation of the breast occurring in conjunction with maternal flulike symptoms (eg, fever)²⁰ and yield of GBS in the milk culture.

Statistical Analyses

Analyses were performed by using Stata/SE 11.2 for Windows (Stata Corp, College Station, TX). Continuous variables were expressed as mean \pm SD or median and range; categorical data were expressed as numbers (percentages). Student's *t* test and Levene's test for assessing homoscedasticity or the Mann–Whitney rank sum test and χ^2 test or Fisher's exact test were used to compare, respectively, the continuous and categorical variables between groups.

Severe brain lesions and death were considered as the most severe complication and were studied at univariate and multivariate analyses. Mechanical ventilation or catecholamine support were not included in this composite outcome because they are risk factors for developing brain lesions or death;

furthermore, the decision to use mechanical ventilation or catecholamine support may sometimes be based on subjective rather than objective criteria.

No correlated variables reaching a *P* value <.1 in univariate analysis were included in the multivariate logistic regression model. The accuracy of the model was verified by using the Hosmer-Lemeshow goodness-of-fit test. All *P* values refer to 2-tailed tests of significance. *P* < .05 was considered significant and .10 < *P* < .05 was considered as an indication of a trend.

RESULTS

A total of 100 LOD cases (98 newborns [2 early preterm newborns had recurrent infection]) were registered across the region during the study period. The incidence was 0.32 per 1000 live births, with no significant variations occurring in the rates of infection over the 8-year study period. Table 1 presents incidence data according to gestation period for the entire region. Compared with term neonates, early preterm newborns had an increased risk of contracting LOD (odds ratio [OR]: 16.3 [confidence interval (CI): 10.2–26.2]).

Maternal Data

Sixty-one of the 98 mothers had a vaginal delivery and 37 had a cesarean delivery; in the latter group, 20 (6 preterm and 14 term births) were not in labor and had intact membranes. Twelve mothers had prolonged membrane rupture, 3 had GBS bacteriuria, and 1 had intrapartum fever ($\geq 38^\circ\text{C}$). Risk factor data were missing for 25 mothers: GBS bacteriuria (22 cases [11 preterm]), prolonged membrane rupture (2 cases), and maternal intrapartum temperature (1 case).

Table 2 provides information on antenatal screening and IAP administration for the 98 mothers included in the study. The table gives also additional information (maternal GBS carriage, milk cultures, and mastitis data) acquired after confirmation of the LOD diagnosis. This information was routinely collected starting from January 2007 and relates to 53 of the 98 mothers. Vaginal cultures taken both after the diagnosis of LOD (*n* = 47) and during antenatal screening (*n* = 40) were compared. Mothers of affected neonates were more likely to be carrying GBS at the time of the LOD diagnosis (30 of 47 cases) than at the time of antenatal screening (13 of 40 cases) (*P* < .01).

TABLE 1 Incidence and Gestation Period for LOD Cases, Contextualized With Data for the Entire Region

Regional Data ^a		
Gestation period		Live Births
Regional live births during the study period (2003–2010), <i>n</i>		
Full-term births, ≥ 37 wk' gestation, <i>n</i> (% of all regional live births)		311 893
Preterm births, <37 wk' gestation, <i>n</i> (% of all regional live births)		288 727 (92.6)
Early preterm births, <34 wk' gestation, <i>n</i> (% of all regional live births)		23 166 (7.4)
Late preterm births, 34–36 6/7 wk' gestation, <i>n</i> (% of all regional live births)		6012 (1.9)
		17 154 (5.5)
Study Data		
Neonatal LOD infections	Cases	Incidence/1000 Live Births (95% CI)
Cases, <i>n</i>	100	0.32 (0.25–0.38)
Term newborns, <i>n</i>	68	0.24 (0.18–0.29)
Preterm newborns, <i>n</i>	32 ^b	1.4 (0.9–1.8)
Early preterm newborns, <i>n</i>	23 ^b	3.8 (2.3–5.4)
Late preterm newborns, <i>n</i>	9	0.5 (0.2–0.9)

^a Data obtained from the Regional Health Agency hospital discharge charts starting from January 2008 a province outside the region (Belluno, approximately 800 live births/year) was added to the surveillance area.

^b Of 30 preterm infants, 2 early preterm infants had a single recurrent infection.

TABLE 2 Cultures of the 98 Mothers Included in the Study and Intrapartum Prophylaxis Administration

Variables	2003–2006 (<i>n</i> = 45)		2007–2010 (<i>n</i> = 53)	
	Preterm (<i>n</i> = 16)	Term (<i>n</i> = 29)	Preterm (<i>n</i> = 14)	Term (<i>n</i> = 39)
Antenatal screening, <i>n</i>	5	21	3	37
GBS culture-positive, <i>n</i>	2	3	0	13
Any indication for IAP, <i>n</i> ^a	13	4	11	14
Women exposed to IAP, <i>n</i>	6	3	6	17
Adequate prophylaxis, <i>n</i> ^b	5	3	3	8
Rectovaginal cultures (at LOD diagnosis), <i>n</i>	—	—	12	35
GBS culture-positive mothers, <i>n</i>	—	—	9	21
GBS status known, <i>n</i> ^c	—	—	2	28
Permanently culture-negative mothers, <i>n</i>	—	—	1	9
Culture-positive at least once, <i>n</i>	—	—	1	19
Breastfeeding mothers (at LOD diagnosis), <i>n</i>	—	—	11 ^d	34
Milk cultures, <i>n</i>	—	—	11	33
Culture-positive milk, <i>n</i>	—	—	2	9
GBS mastitis, <i>n</i>	—	—	1	2

^a GBS carriage or risk factors without antenatal screening.

^b Intrapartum antibiotic administration (penicillin, ampicillin, or cefazolin) at least 4 hours before delivery (according to Verani et al²).

^c GBS status was “known” if cultures were obtained both at the time of screening and after confirmation of the LOD diagnosis.

^d Milk was pump-extracted from 6 of the 11 mothers (GBS-infected milk in 2 cases).

GBS status was known both at the time of antenatal screening and at the diagnosis of LOD in 30 of the 53 mothers. Among them, 10 mothers were permanently culture-negative and 20 were culture-positive at least once.

Milk samples were taken for culture from 44 of 45 breastfeeding mothers, 3 of whom had mastitis. Of the 11 milk cultures with results positive for GBS, a bacterial count was available for 6. In the 3 cases of mastitis, the bacterial count was $\geq 1\,000\,000$ colony-forming unit/mL, and in the 3 cases without mastitis, the bacterial count was $\leq 100\,000$ colony-forming unit/mL.

Neonatal Data

Among the 98 newborns, 30 were preterm and 68 were term. Seven neonates were of African descent, 4 were Asian, and 4 were South American. The mean gestational age at delivery was 36.3 ± 4.6 weeks (range: 24–38 weeks), and the mean birth weight was 2711 ± 1000 g (range: 630–5210 g).

Of the 100 LOD cases, 57 (57.0%) were classified as sepsis, 7 (7.0%) as focal (4

arthritis, 2 cellulitis, and 1 adenitis), and 36 (36.0%) as meningitis (CSF obtained in 60 [60.0%] of 100 cases). Four infants with sepsis and 2 with meningitis also had pneumonia.

Of the 36 cases of meningitis, 9 (25.0%) had sterile blood cultures, whereas 27 (75.0%) had both sepsis and meningitis. Thirty cases were CSF culture-proven, whereas 6 had GBS-positive blood cultures and abnormal CSF parameters (5 cases of CSF pleocytosis, 1 case of CSF-positive antigen).

Fifteen newborns (15.0%) presented with severe brain lesions at hospital discharge; 14 of them suffered from meningitis and were born at term.

Factors Associated With an Earlier LOD Presentation

Term infants were younger at LOD presentation (mean: 29.8 days; median: 23.0 days; interquartile range (IQR): 14.5–42.0) than preterm neonates (mean: 41.4 days; median: 39.0 days; IQR: 27.5–57.5; $P < .01$).

Newborns without IAP exposure were more likely to be younger at LOD pre-

sentation (mean age: 29.0 days; median: 24.0 days; IQR: 15.0–41.0; OR for early presentation: 4.3 [95% CI: 1.7–10.8]) than newborns receiving IAP for any length of time (mean age: 43.6 days; median: 40.0 days; IQR: 25.0–62.0; $P < .01$).

Considering only infants who underwent a lumbar puncture, meningitis (with or without sepsis) presented itself significantly earlier (mean: 26.6 days; median: 19.0 days; IQR: 13.0–34.5) than sepsis alone (mean: 32.87 days; median days: 29.5; IQR: 19.0–43.0; $P = .04$).

In multivariate logistic regression analysis, the presence of brain lesions or death was associated with early (7–30 days) presentation of LOD (53 cases, OR: 0.96 [95% CI: 0.93–0.99]) and an abnormal (<5000 or $>30\,000/\text{mm}^3$) white blood cell count at the time of the LOD diagnosis (23 cases, OR: 3.61 [95% CI: 1.08–2.09]).

LOD Severity

Sixty-seven LOD cases were classified as mild or severe (22 mild, 45 severe). The remaining 33 LOD cases did not meet inclusion criteria for either definition.

IAP exposure was significantly associated with mild (12 of 22) rather than severe (11 of 45; $P = .03$) LOD. Severe LOD presented itself significantly earlier (mean: 28.6 days; median: 20.0 days; IQR: 14.0–39.0) than mild disease (mean: 44.6 days; median: 45.5 days; IQR: 30.0–60.0; $P < .01$).

Infants Presenting With LOD Before Hospital Discharge

Fifteen preterm infants were still inpatients when diagnosed with LOD. Maternal GBS status at the time of the LOD diagnosis was assessed in 6 cases, and 4 of the 6 mothers were GBS culture-positive.

Inpatients were compared with outpatients born either preterm or term (Table 3). Inpatients had a lower birth

weight, younger gestational age, and were more often treated with broad-spectrum antibiotics in the postpartum period. Compared with outpatients born at term, inpatients required more catecholamine support and mechanical ventilation and were at the highest risk of mortality.

GBS Outbreak

Of the 15 inpatients, 3 were infected during a 2-week outbreak in a NICU (7 rooms, ~500 admissions per year, of which ~70 were very low birth weight newborns). The index case was an outpatient male preterm neonate (34 weeks' gestation, birth weight 1830 g) born to a culture-negative mother. Due to maternal hypertension, the infant was delivered by a cesarean delivery with intact membranes. The clinical course was uneventful, and he was discharged at day 17, but the newborn was readmitted to the NICU after 72 hours because of GBS meningitis. Results of the rectovaginal culture collected from his mother after the confirmation of LOD were negative.

The newborn was admitted to a single-bed room but placed under the care of nursing staff who were also assigned to an adjacent 6-bed room. Within the next 2 weeks, 3 inpatient preterm newborns (2 of whom were early preterm [birth weight 990 and 820 g, respectively] and

1 was late preterm [birth weight 1550 g]) presented with LOD (2 cases of sepsis, 1 of meningitis).

Two of three preterm mothers were culture-negative at delivery, whereas the placental culture of the third mother yielded GBS. These 3 infants plus the index case were culture-negative at birth; 2 of them were exposed to adequate IAP and broad-spectrum antibiotics in the postpartum period. Pulsed-field gel electrophoresis analysis was performed for the index case and 3 inpatient preterm newborns. The analysis demonstrated that the GBS strains were indistinguishable.

Of the 38 newborns subsequently admitted to the NICU and screened in the next 4 weeks, 5 preterm neonates were identified as asymptomatic and GBS colonized.

Further GBS transmission was successfully prevented through control measures such as surveillance cultures of infants, cohorting of all colonized and infected newborns, reliance on dedicated nursing staff, careful hand-washing, and infection control practices.

DISCUSSION

Population-based LOD data in the literature varies greatly.²¹ LOD incidence in Europe ranges from 0.10 to 0.24 per

1000 live births (an incidence 1.5–4 times lower than that associated with EOD), and LOD case fatality rates range from 2% to 8%.^{21–28}

In the available literature, low birth weight has been associated with an increased risk of GBS infection. The underrepresentation of low birth weight neonates (<20%) in a study sample can lead to a substantial underestimation of the disease.²⁴

The current study included a high percentage of preterm newborns. The relatively high LOD incidence rate (0.32 per 1000 live births) is comparable to that reported in the Active Bacterial Core surveillance areas of the United States (0.32–0.36 per 1000 live births) during the era of universal screening.⁴

GBS status was most commonly known in mothers who delivered term infants; <30% of them had positive culture results at the time of antenatal screening, but higher rates of GBS carriage were found after the diagnosis of LOD. The authors have previously reported that GBS strains cultured from both mothers and infants at the time of the LOD diagnosis were indistinguishable according to molecular typing in all examined cases.¹⁷ False-negative screening results and a change of maternal culture status after screening may explain the higher rates

TABLE 3 Comparison of Infants Presenting With LOD Before (Inpatients) or After (Outpatients) Hospital Discharge

Characteristic	Inpatients (<i>n</i> = 15)	Outpatients, Born Preterm (<i>n</i> = 15)	Outpatients, Born Term (<i>n</i> = 68)	<i>P</i> ^a	<i>P</i> ^b
Birth weight, median, g (IQ)	980 (860–1190)	1860 (1602–2175)	3195 (2932–3570)	<.01	<.01
Gestational age at delivery, median, wk (IQ)	27 (26.0–29.7)	33 (31.0–34.0)	39 (38.0–40.0)	<.01	<.01
Age at LOD diagnosis, median, d (IQ)	39 (21.7–47.0)	39 (30.5–58.7)	23 (14.5–42.0)	.57	.08
IAP exposure, <i>n</i> (%)	5 (33.3)	7 (46.7)	20 (29.4)	.71	.99
Postpartum antibiotics, median, d (IQ) ^c	7 (4.2–7.7)	0 (0.0–6.5)	0 (0.0–0.0)	.03	<.01
Meningitis (± sepsis), <i>n</i> (%) ^d	3 (50.0)	4 (36.4)	29 (67.4)	.98	.70
Catecholamine support, <i>n</i> (%)	4 (36.4)	2 (13.3)	3 (4.4)	.66	.02
Mechanical ventilation, <i>n</i> (%)	8 (53.3)	2 (13.3)	5 (7.4)	.05	<.01
Brain lesions at hospital discharge, <i>n</i> (%) ^e	0	1 (6.7)	14 (20.6)	.46	.12
Mortality, <i>n</i> (%)	3 (20.0)	0	1 (1.5)	.22	.02

^a Comparison between inpatients and preterm outpatients.

^b Comparison between inpatients and term outpatients.

^c All infants administered broad-spectrum antibiotics in the postpartum period before LOD presentation.

^d Comparison includes only newborns who had a lumbar puncture (6 inpatient and 54 outpatient neonates, of whom 11 were preterm and 43 were term).

^e Lesions were: hydrocephalous (*n* = 3), white matter damage (*n* = 3), white matter and cortex damage (*n* = 6), white matter and basal ganglia damage (*n* = 2), and unspecified lesions (*n* = 1).

of maternal GBS carriage at the time of the LOD diagnosis.

More than one-half of the women who were culture-positive at the time of antenatal screening received IAP. However, GBS may persist for many weeks after antibiotic therapy,²⁹ and mothers therefore remain an important source of transmission.

Only one-third of mothers whose culture status was examined both during antenatal screening and at the time of the LOD diagnosis were permanently culture-negative. Transmission from a nosocomial or community source may be suspected.

Case reports have implicated infected breast milk as a possible cause of LOD, with^{8–10} or without the occurrence of mastitis.^{11–13} Mastitis results in a massive GBS milk inoculum, which may lead to heavy neonatal colonization, a known risk factor for invasive GBS infections.¹ In the current study, 6% of mothers had mastitis, and they had the highest bacterial counts. Most GBS-infected milk samples were obtained from mothers without mastitis, who had the lowest bacterial counts.

The most common clinical presentation of LOD was sepsis, followed by meningitis and focal infection. Meningitis was the main cause of brain lesions in term infants.

The earlier LOD presented itself, the higher was the risk for meningitis and death. Furthermore, IAP administration was found to be associated both with delayed LOD presentation and with milder LOD. The reason for this association is unclear. However, IAP exposure might change the routes of GBS transmission (ie, from vertical to horizontal), leading to less heavy neonatal colonization and less severe LOD.

One-half of the preterm newborns were inpatients at the time they were diagnosed with LOD. A few mothers had cultures; most of them were found to

carry GBS at the vaginal site at the time the diagnosis of LOD was confirmed. Thus, the source of GBS for inpatients may not necessarily be nosocomial.

Newborns who were inpatients at the time of onset had a lower birth weight, younger gestational age, and more severe disease. Possible reasons for increased susceptibility to severe LOD include immature immune responses and the many invasive devices used to provide life-supporting care. The newborns were also more likely to receive broad-spectrum antibiotics in the postpartum period. Antibiotics may alter infant bacterial flora,³⁰ and an association between late-onset sepsis and broad-spectrum antibiotics after day 3 in very low birth weight newborns has been documented previously.³¹

Reports of GBS outbreaks have recently become uncommon.^{32,33} Vertical transmission from culture-positive carrier women is less common after the introduction of IAP; therefore, the occurrence of cross-transmission in the obstetrics ward is likely to be rarer than in the past.

In this study, the index case of the GBS outbreak was infected by a non-maternal source (before or soon after hospital discharge). After GBS was introduced into the NICU, 3 inpatient preterm newborns (who had negative culture results at birth) were infected with the same strain. The infection was probably transmitted through the hands of health care workers and was brought successfully to a halt through the implementation of adequate disease control measures. Clinicians and nurses must be aware of the potential nosocomial spread of invasive pathogens within NICUs, and hospital infection control recommendations must be rigorously followed.

This study has a number of limitations. Although information on maternal GBS carriage and mastitis at the time of LOD diagnosis was routinely obtained start-

ing from 2007, bacterial counts of milk cultures were available for few mothers without mastitis. The extent to which milk contamination could be a risk factor for LOD therefore cannot be quantified.

Furthermore, most mothers who delivered preterm had unknown GBS status before delivery. As a result, the source of GBS was unclear for most infected infants who were still inpatients when diagnosed with LOD.

CONCLUSIONS

The main source of neonatal infection was the mothers themselves, and IAP exposure was insufficient to prevent the transmission of GBS to the newborn. Conjugate vaccines, currently at advanced stages of testing, may be the most attractive strategy for future prevention.

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Group B Streptococcus Late-Onset Disease: 2003–2010

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