Variation in Sepsis Evaluation Across a National Network of Nurseries

Sagori Mukhopadhyay, MD, MMSc,[a] James A. Taylor, MD,[b] Isabelle Von Kohorn, MD, PhD,[c] Valerie Flaherman, MD, MPH,[d] Anthony E. Burgos, MD,[e] Carrie A. Phillipi, MD, PhD,[f] Nui Dhepyasuwan, MEd,[g] Elizabeth King, MPP,[g] Miren Dhudasia, MPH,[a] Karen M. Puopolo, MD, PhD[a]

abstract

BACKGROUND AND OBJECTIVES: The extent to which clinicians use currently available guidelines for early-onset sepsis (EOS) screening has not been described. The Better Outcomes through Research for Newborns network represents 97 nurseries in 34 states across the United States. The objective of this study was to describe EOS risk management strategies across a national sample of newborn nurseries.

METHODS: A Web-based survey was sent to each Better Outcomes through Research for Newborns network nursery site representative. Nineteen questions addressed specific practices for assessing and managing well-appearing term newborns identified at risk for EOS.

RESULTS: Responses were received from 81 (83%) of 97 nurseries located in 33 states. Obstetric diagnosis of chorioamnionitis was the most common factor used to identify risk for EOS (79 of 81). Among well-appearing term infants with concern for maternal chorioamnionitis, 51 of 79 sites used American Academy of Pediatrics or Centers for Disease Control and Prevention guidelines to inform clinical care; 11 used a published sepsis risk calculator; and 2 used clinical observation alone. Complete blood cell count (94.8%) and C-reactive protein (36.4%) were the most common laboratory tests obtained and influenced duration of empirical antibiotics at 13% of the sites. Some degree of mother–infant separation was required for EOS evaluation at 95% of centers, and separation for the entire duration of antibiotic therapy was required in 40% of the sites.

CONCLUSIONS: Substantial variation exists in newborn EOS risk assessment, affecting the definition of risk, the level of medical intervention, and ultimately mother–infant separation. Identification of the optimal approach to EOS risk assessment and standardized implementation of such an approach could affect care of a large proportion of newborns.

[a]*Neonatology, Children's Hospital of Philadelphia, Philadelphia, Pennsylvania;* [b]*Pediatrics, University of Washington School of Medicine, Seattle, Washington;* [c]*Neonatology, Holy Cross Health, Silver Spring, Maryland;* [d]*Pediatrics, University of California San Francisco, San Francisco, California;* [e]*Pediatrics, Southern California Kaiser Permanente, Downey, California;* [f]*Pediatrics, Oregon Health & Science University, Portland, Oregon; and* [g]*Academic Pediatric Association, McLean, Virginia*

Dr Mukhopadhyay conceptualized and designed the study, analyzed the data and drafted the initial manuscript; Ms Dhepyasuwan and Ms King reviewed and revised the survey instrument, contributed to distribution and follow-up of the survey, and reviewed the manuscript; Mr Dhudasia contributed to data cleaning, data analysis and drafted the initial manuscript; Drs Taylor, Von Kohorn, Flaherman, Burgos, and Phillipi reviewed and revised the survey instrument, contributed to data collection, and reviewed and revised the manuscript; and Dr Puopolo designed the study, revised the survey instrument and reviewed and revised the manuscript; and all authors approved the final manuscript as submitted.

DOI: 10.1542/peds.2016-2845

Accepted for publication Dec 19, 2016

WHAT'S KNOWN ON THIS SUBJECT: A significant proportion of well-appearing newborns are evaluated for early-onset sepsis (EOS) when following national recommendations for determining EOS risk. The extent to which clinicians use such guidelines and the resulting impact on newborn care have not been described.

WHAT THIS STUDY ADDS: The present study shows that wide variation exists in many aspects of EOS risk management, affecting the frequency and intensity of patient-level intervention. Research is needed to identify the optimal approach to EOS risk management among otherwise well-appearing newborns.

To cite: Mukhopadhyay S, Taylor JA, Von Kohorn I, et al. Variation in Sepsis Evaluation Across a National Network of Nurseries. *Pediatrics.* 2017;139(3): e20162845

Evaluating term infants for risk of neonatal early-onset sepsis (EOS) is one of the most common clinical tasks performed by neonatal clinicians. National guidelines have been published by the Centers for Disease Control and Prevention (CDC) and the American Academy of Pediatrics (AAP) that address evaluation of newborns at risk for EOS.[1–3] Clinical implementation of such guidelines is complicated by ambiguities in the definition of specific perinatal risk factors, as well as poor test performance of common screening laboratory tests recommended for use in the management of at-risk newborns. Some experts question the resulting widespread use of antibiotic therapy among infants who are ultimately found to be uninfected.[4–7] In the era of group B streptococcus (GBS) screening and intrapartum antibiotic prophylaxis (IAP), the incidence of EOS among term infants has declined to ~1 case in every 2000 live births.[8,9] The risk/benefit balance of empirical antibiotic treatment is therefore of particular concern among this low-incidence population. For example, we previously reported that ~7% of infants born at ≥36 weeks' gestation were evaluated for EOS in a single center following the CDC 2010 guidelines, despite being well at birth.[9] None of these infants was ultimately found to be infected. Another center following the current AAP guidelines reported that 554 (4.6%) of 12 121 infants born at ≥35 weeks' gestation were evaluated solely based on the diagnosis of maternal chorioamnionitis.[4] Although 4 (0.7%) of these infants had culture-confirmed EOS, 112 (20.2%) received antibiotics for ≥7 days (due to abnormal laboratory test values) despite negative culture findings.

Alternate approaches to EOS risk assessment have been proposed. A multivariate model of sepsis risk based on objective data has been developed; this model uses established risk factors for EOS as categorical or continuous variables and separately considers newborn clinical condition.[10,11] Recommended clinical actions for specific risk estimates have been published, but individual care settings can set locally appropriate guidelines.[11] In another approach, serial observation without empirical therapy or screening laboratory tests is recommended for those with a normal physical examination.[12,13]

The extent to which clinicians use any of these approaches has not been described, and understanding such variation may inform the optimal approach to sepsis evaluation. The Better Outcomes through Research for Newborns (BORN) network represents 97 nurseries in 34 states across the United States.[14] The participating members are primarily general pediatricians and represent the provider group that most commonly cares for well term newborns during the birth hospitalization. Clinicians in this network were surveyed to determine the extent of clinical practice variation in the approach to sepsis screening and management among well-appearing term newborns.

METHODS

The study was conducted by the BORN network, a national group of researchers and clinicians who provide care for term and late-preterm neonates at academic and community medical centers. The network was established in 2010 and was sponsored by the American Pediatric Association; it has been described previously.[14] At the time of the survey, the network included an estimated 360 members from 97 newborn nursery sites located in 34 states. Cumulatively, these sites had an annual birth rate of >400 000 infants.

The present study was determined to be exempt from human subjects research review by the institutional review board at the University of Pennsylvania.

Survey Methods

A 19-question survey was constructed by using the University of Pennsylvania–maintained REDCap system, a secure Web application for survey design and database management.[15] The questions were designed with input from pediatric and neonatal care providers; the goal was to target the primary issues clinicians consider when assessing sepsis risk for a well-appearing infant born at ≥37 weeks' gestation. Questions required either yes/no or multiple choice responses. The option of responding "other" was provided for most questions, which opened a text field to allow narrative comments. The survey was sent to the designated site representative at each BORN center between October 2015 and January 2016. A site representative from each BORN nursery was instructed to complete the survey describing EOS evaluation and management as they apply to well-appearing infants born at ≥37 weeks' gestation and as practiced by the majority of clinicians at their institution.

The primary goal of the study was to determine the newborn management approach after birth to a mother with an obstetric concern for chorioamnionitis. Responses were categorized as follows: (1) approach aligned with CDC 2010 perinatal GBS guidelines[1]; (2) approach aligned with AAP Committee on the Fetus and Newborn statements[2,3]; (3) approach incorporating use of the Web-based sepsis risk calculator[10,11]; or (4) other locally derived approaches. Secondary goals were to identify the following: (1) the management approach after birth to a GBS-positive mother with inadequate indicated IAP; (2) specific perinatal factors used to identify newborns at increased risk of EOS;

TABLE 1 Background Information for Responding Sites ($N = 81$)

Variable	Value
Annual births	3000 (2023–4200)
Maternal insurance[a]	
>50% private	29 (41.4)
>50% public	26 (37.1)
Newborn nursery providers	
General pediatricians	79 (97.5)
Family physicians	43 (53.1)
Neonatologists	19 (23.5)
Trainees (pediatric/family medicine residents)	60 (74.1)
Nurse practitioners or physician assistants	40 (49.4)
Youngest gestational age cared for by newborn nursery[a]	
32–33 wk	4 (5)
34–35 wk	68 (85)
≥36 wk	8 (10)
Medical care provided in newborn nursery	
Intravenous antibiotics	48 (59.3)
Isolette care	42 (51.9)
Supplemental oxygen	20 (24.7)
Intravenous fluids	20 (24.7)
Nasogastric/orogastric tube feeding	19 (23.5)

Data are presented as median (interquartile range) or *n* (%).

[a] Data for youngest gestational cared for by a nursery was missing for 1 site and for details of maternal insurance was missing for 11 sites.

(3) laboratory tests used; (4) use of empirical antibiotic treatment; and (5) whether mothers and newborns are separated for EOS evaluation and/or empirical treatment.

Analysis

Respondents were provided the option of uploading a copy of their local institutional sepsis risk protocol. Information from institutional protocols was used only when directly referred to by a respondent or when a respondent left a survey question incomplete yet provided a protocol. Answers for such questions were coded by one of the authors (S.M.) and reviewed by another (K.M.P.). This scenario occurred for 3 institutions in response to 1 question each. Information from written protocols was not otherwise analyzed. Demographic data for participating nurseries were obtained from BORN membership enrollment surveys.

RESULTS

We received responses from 81 (83.5%) of 97 BORN sites with a cumulative annual delivery rate of 277 239 infants; characteristics of the 81 participants are summarized in Table 1. Most participants provided Level 1 or Level 2 neonatal care per the AAP classification.[16] Written institutional newborn sepsis risk protocols were reported by 49 (60%) of 81 respondents, and 20 (40.8%) of 49 provided the protocols. Respondents at 27 (33.3%) of 81 centers stated that their center had no written policy, and 5 (6.2%) were unsure if such a policy existed at their institution.

Perinatal Factors Used to Identify Well-appearing Term Infants at Risk for EOS

The most frequently cited factors for designating a well-appearing newborn as being at increased risk for EOS were the obstetric diagnosis of chorioamnionitis and prolonged rupture of membranes (PROM), both cited by 79 (97.5%) of 81 respondents. The 2 respondents who did not consider chorioamnionitis a risk factor used the sepsis risk calculator as a means for determining infant risk. Other factors used to flag well-appearing infants as at increased risk included inadequate GBS IAP even in the absence of PROM (74 of 80 [92.5%]), fetal tachycardia (55 of 81 [67.9%]), and maternal fever without a diagnosis of chorioamnionitis (64 of 81 [79.0%]).

Management of Infants With Maternal Chorioamnionitis

Table 2 provides the specific management scenarios used in the survey and the distribution of responses. Although nearly one-half of respondents indicated that their management is guided by the CDC GBS prevention guidelines, the remaining respondents took a variety of approaches, including adherence to AAP guidelines, use of the sepsis risk calculator, use of a locally derived protocol, or allowing for individual provider discretion. Two respondents noted that their site practice is to provide observation and routine newborn care to all well-appearing infants, without consideration to perinatal sepsis risk factors. The sepsis risk calculator does not consider the clinical diagnosis of chorioamnionitis but uses objective data, including highest maternal intrapartum temperature. Despite this approach, 9 of 11 sites reporting use of the sepsis risk calculator also identified chorioamnionitis as an independent factor for identifying at-risk infants when responding to a separate question.

Inadequate GBS IAP

Less variation was noted when presented with a scenario involving inadequate GBS IAP without PROM. CDC GBS prevention guidelines would recommend routine care for this newborn with in-hospital observation for at least 48 hours. Most respondents (61 of 80 [76.3%]) provided responses consistent with this recommendation, although 6 sites also increased the frequency of newborn vital signs monitoring (Table 2). However, when asked about the reasons respondents had for performing laboratory tests, 17

TABLE 2 Management of Well-Appearing Term Infants Considered at Risk for EOS

Scenario	N (%)
An infant is born to a mother who is diagnosed with chorioamnionitis by her obstetrician. Management of this infant at your institution by most care providers would be most closely aligned with which of the following[a]:	
CDC GBS prevention guidelines (2010)	36 (45.5)
AAP, Committee of Fetus and Newborn Statement (2013, 2014)	12 (15.2)
Sepsis risk calculator[b]	11 (13.9)
Locally derived management protocol[c]	10 (12.7)
No site-specific protocol; management per provider discretion	10 (12.7)
A well-appearing infant is born at 38 wk of gestation via spontaneous vaginal delivery to a mother colonized with GBS. Rupture of membrane was for 10 h, and the mother did not receive any antibiotic prophylaxis before delivery. Which of the following approaches to newborn management would be most consistent with the general practice at your site?[d]	
Routine care for the infant	6 (7.5)
Routine care for infant but not eligible for discharge <48 h age	55 (68.7)
Laboratory tests at birth or later in newborn admission	11 (13.8)
Laboratory tests and empirical antibiotic treatment at birth	0
Enhanced vital signs monitoring for 24–48 h	6 (7.5)
Management is provider-dependent	2 (2.5)

[a] Seventy-nine of 81 sites provided responses to this scenario.
[b] As per Escobar et al[11] and Cantoni et al.[12]
[c] Three sites used a local protocol modified from CDC/AAP.
[d] Eighty of 81 sites provided responses to this scenario.

TABLE 3 Perinatal Factors Prompting Laboratory Tests and Empirical Antibiotic Therapy for EOS Among Well-Appearing Term Infants

Factor	Laboratory Tests (n = 71)	Empirical Antibiotics (n = 66)
Which perinatal risk factor, in isolation, would result in the following intervention?		
Obstetric diagnosis of chorioamnionitis	61 (85.9%)	56 (84.8%)
Maternal fever >38.3°C (no chorioamnionitis)	22 (31.0%)	10 (14.1%)
Maternal fever 38°C –38.3°C (no chorioamnionitis)	17 (23.9%)	4 (6.1%)
Rupture of membranes >24 h	15 (21.1%)	2 (3.0%)
Inadequate indicated GBS prophylaxis	17 (23.9%)	2 (3.0%)
None of the above, if present in isolation	7 (9.9%)	6 (9.1%)

(23.9%) of 71 cited inadequate GBS IAP alone and 2 (3.0%) of 66 cited inadequate GBS IAP alone as the reason for administering empirical antibiotics (Table 3).

Laboratory Testing and Empirical Antibiotic Administration

Perinatal factors prompted laboratory testing to screen for EOS in 71 (88.6%) of 80 sites and resulted in initiation of empirical antibiotic therapy in 66 (82.5%) sites. Table 3 presents the perinatal factors for which sites would perform these interventions for a well-appearing term infant. Of the 14 respondents who said they would not initiate antibiotics based on a single perinatal risk factor alone, 5 made antibiotic decisions using the sepsis risk calculator, 4 relied on laboratory test results for antibiotic decisions, 3 treated only if symptoms consistent with sepsis were present, and 2 gave no additional information. Laboratory tests used to determine the need for further interventions included complete blood cell count (CBC) with differential (69 of 71 [97.2%]), blood culture (57 of 71 [80.3%]), C-reactive protein (CRP) (21 of 71 [29.6%]), and blood glucose (8 of 71 [11.3%]). The 2 sites that do not send CBC samples sent only screening blood culture specimens. These tests were used in different combinations: CBC with blood culture (44 of 71 [62.0%]); CBC, CRP, and blood culture (11 of 71 [15.5%]); and CBC with CRP (10 of 71 [14.1%]). When asked what laboratory tests would be sent after a decision was made to administer empirical antibiotics, 80 sites responded. Excluding the 3 sites that neither evaluated nor treated asymptomatic infants, all the remaining 77 respondents send blood culture specimens, followed by CBC (73 of 77 [94.8%]), CRP (28 of 77 [36.4%]), and blood glucose (15 of 77 [19.5%]) specimens before initiating antibiotic therapy. Few sites reported using cerebrospinal fluid analysis (3 of 77 [3.9%]) or urine culture (2 of 77 [2.6%]). Antibiotics were discontinued after 36 to 48 hours of treatment based on blood culture results at 60 (77.9%) of 77 sites, but the other 17 sites combined blood culture results with other laboratory test results (10 of 17 [13%]), the perceived severity of clinical risk factors (3 of 17 [3.9%]), or provider judgment (3 of 17 [3.9%]) to determine length of antibiotic treatment. One site did not clarify their criteria for discontinuing antibiotics.

Logistics of EOS Evaluation in Asymptomatic Term Infants

Timing and location of EOS testing and antibiotic administration are shown in Table 4. Some mother/infant separation was required by

TABLE 4 Hospital Logistics of EOS Interventions ($N = 77$)

Logistics	*N* (%)
How soon after birth do you initiate EOS antibiotics for a well-appearing term infant?	
0–1 h after birth	23 (29.9)
2–6 h after birth/post-breastfeeding	26 (33.7)
No time specification	28 (36.4)
Are EOS procedures (eg, laboratory tests, IV insertion) conducted in a location separate from the mother's room?	
Yes	59 (76.6)
No	4 (5.2)
Partly/occasionally	14 (18.2)
If IV antibiotics are started on a well-appearing newborn, can newborn room-in with mother?	
Yes	40 (51.9)
No	31 (40.3)
Case specific	6 (7.8)
If IV antibiotics are started on a well-appearing newborn and newborn cannot room-in with mother, where is the newborn cared for? ($n = 37$)	
NICU/special care nursery	28 (75.7)
In NICU 6–24 h, then room-in	5 (13.5)
Only separated for antibiotic administration	2 (5.4)
No response	2 (5.4)

Table data exclude 3 centers that do not ever administer antibiotics to well-appearing infants and 1 site with missing data. IV, intravenous.

73 (94.5%) of 77 sites, and only 40 (51.9%) of these 77 centers allowed well-appearing newborns to room-in with the mother if receiving antibiotics. One center that reported neither testing nor empirical treatment of well-appearing infants with perinatal risk factors required that such infants be monitored for 24 hours at a location separate from the mother.

DISCUSSION

We focused our survey on well-appearing term infants, reasoning that such infants are at the lowest risk among all newborns at danger for EOS and, potentially, the most straightforward for whom to provide care. However, our results found substantial variation in risk identification, evaluation, and empirical antibiotic treatment. Depending on the delivering BORN hospital, the same well-appearing term infant may be considered at different risk and treated differently. In practice, this scenario means the same infant may have no evaluation or NICU admission; no laboratory testing or multiple tests; no antibiotics or prolonged antibiotics; and discharge after 24 hours or at 1 week of age. Although it is important to tailor practice to account for local resources and structures of care, variations in decisions to start and stop antibiotics among newborns under the same clinical circumstances likely represent unnecessary deviations in management.

Despite guidelines provided by national professional organizations such as the CDC and AAP, we found no consistent overall standard of care for EOS evaluation and treatment. Only ∼60% of centers reported informing their local care with these national guidelines, whereas others reported adopting locally derived guidelines, using the validated sepsis risk calculator, or allowing individual provider management. Reported management varied in the direction of both doing more and doing less than national recommendations. For example, despite CDC 2010 perinatal GBS prevention guidelines advocating for observation only when low-risk term infants are born without adequate indicated GBS IAP,[1] ∼20% of centers reported using laboratory tests or additional monitoring for such infants (Table 2). The change in CDC recommendations was made based on the lower risk for GBS disease in these infants and aimed at reducing unnecessary evaluations.[1,17] We speculate that some providers are uneasy with "not doing anything" for a clinical factor that in previous recommendations triggered an EOS evaluation. Similarly, although not advocated by the CDC, AAP, or the sepsis risk calculator, two-thirds of centers considered fetal tachycardia to be an independent risk factor for EOS. Nine of 11 centers that reported using the sepsis risk calculator approach also considered chorioamnionitis an additional consideration, despite the clear intent of the sepsis risk calculator to provide risk estimates independent of that diagnosis.[10] Finally, 3 centers clearly communicated that newborn clinical status was their most important consideration, and made no risk distinction and no intervention among infants if their physical examination was normal. The predictive value of clinical status is considerable:

Escobar et al[11,18] found that good clinical status decreased an infant's probability of EOS based on perinatal presentation by a factor of ~0.40 in 2 separate studies, but in neither study was there zero risk of EOS among such infants. We speculate that the reported variations in care derive from differences in risk perception, as well as from basing risk estimates on dichotomous determinations (eg, chorioamnionitis versus no chorioamnionitis, PROM versus no PROM) that do not inform individual risk estimates.

Uncertainty about risk seems to drive a significant amount of laboratory testing for EOS. Nearly 90% of centers use variable combinations of CBC, CRP, and blood glucose values to "screen" infants for EOS risk. Several studies have shown the poor predictive value of the white blood cell count, differential, and platelet count for EOS among both term and preterm infants.[19–22] Although serial CRPs have been reported to have better negative predictive value than blood counts, there are reports of culture-confirmed infection without increases in CRP levels.[4,23] Blood glucose levels have been associated with mortality among both infected and uninfected newborns,[24–26] but no study has demonstrated any utility of using blood glucose level to evaluate well-appearing term infants for EOS. Despite this evidence, not only did our survey report widespread use of these tests to determine the need to initiate antibiotics, 13% of centers used these laboratory test results to make the decision to discontinue antibiotics among well-appearing infants with negative blood cultures. Such use has been shown to increase the proportion of infants receiving antibiotics and length of stay and should be balanced against the growing body of harm from unnecessary antibiotic exposure.[4,27] Variation in use of laboratory testing has also been demonstrated in a recent international survey of EOS practices.[28]

One area of consistency among survey respondents was the use of the obstetric diagnosis of chorioamnionitis as a perinatal risk factor for EOS. Much has been written about the uncertainties in this diagnosis.[5,7] A recent conference sponsored by the National Institutes of Health and attended by neonatal and obstetric leaders urged alternate definitions for this entity, as well as alternate approaches to neonatal management.[29] The sepsis risk calculator approach specifically eliminates use of this obstetric diagnosis, using objective data on intrapartum characteristics to predict EOS risk.[10] The National Institutes of Health conference experts urged clinical observation for initially well-appearing term infants, although multiple studies demonstrate the low but not-zero rate of EOS among such infants.[18,30] Our survey strongly suggests that resolution of the "conundrum" of chorioamnionitis could have a significant impact on EOS practices.

Other consistencies in practice were also noted. Duration of membrane rupture was used to identify at-risk neonates at most sites. All respondents send blood culture specimens before the initiation of antibiotics, and the majority (78%) discontinued antibiotics in asymptomatic infants if the blood culture results were negative. Most centers (85%) practiced some form of observation for well infants with inadequate maternal GBS prophylaxis. We also noted similarities in the logistics of EOS evaluation, with most sites requiring separation for the initial evaluation and many requiring separation for the entire duration of antibiotic therapy.

EOS practices have a significant impact on the well nursery care provided to the mother and her newborn. Approximately 280 000 infants are delivered annually at the BORN centers participating in this survey. We previously evaluated the impact of a local EOS algorithm based on CDC 2010 guidelines and found that ~7% of well-appearing infants were evaluated for EOS and ~5% received empirical antibiotics. In our survey birth population, such a CDC based EOS management protocol would translate to evaluation of ~19 600 infants and empirical treatment of 14 000. With a term population EOS incidence of 0.5 case per 1000 live births, and accounting for good clinical status, we estimate ~60 infants would develop culture-confirmed EOS.[8] Therefore, we estimated that at a minimum, ~300 infants undergo some form of evaluation and empirical treatment of EOS for every identified case of infection. Our survey revealed that nearly all of those evaluated and all of those treated will be separated from the mother, events we have previously associated with late initiation of breastfeeding and increased formula supplementation.[31] An increasing number of studies implicate early-life antibiotic exposures with negative impacts on subsequent childhood health; both dysbiosis mediated by antibiotic exposures and decreased rates of exclusive breastfeeding could contribute to these findings.[32,33] EOS practices are conducted to ensure newborn safety, but our understanding of the true risk/benefit balance of our current approaches is still evolving.

Our study has several limitations. Only 1 person at each institution was asked to respond to our survey, and provider variation that may exist within a center would not be captured. We did not receive written protocols from each center, making it difficult to address differences between

survey responses and the center's stated policy. We did not query respondents regarding definitions of chorioamnionitis or cutoff values for diagnostic tests, and we cannot comment on variation in these important areas. Finally, survey questions are susceptible to interpretive differences that may impact responses.

CONCLUSIONS

There was substantial variation in the management of newborns at risk for EOS at BORN nursery sites, which directly affects laboratory testing, empirical antibiotic administration, and mother/infant separation at birth. Our survey findings suggest that there is a lack of consensus about EOS risk assessment in the United States, and national efforts to optimize practice are warranted.

ACKNOWLEDGMENTS

The authors thank all BORN members for their participation in this study.

ABBREVIATIONS

AAP: American Academy of Pediatrics
BORN: Better Outcomes through Research for Newborns
CBC: complete blood cell count
CDC: Centers for Disease Control and Prevention
CRP: C-reactive protein
EOS: early-onset sepsis
GBS: group B streptococcus
IAP: intrapartum antibiotic prophylaxis
PROM: prolonged rupture of membranes

Address correspondence to Sagori Mukhopadhyay, MD, MMSc, The Children's Hospital of Philadelphia, Newborn Care at Pennsylvania Hospital, 800 Spruce St, 2nd Floor, Cathcart Building, Philadelphia, PA 19107. E-mail: mukhopadhs@email.chop.edu

PEDIATRICS (ISSN Numbers: Print, 0031-4005; Online, 1098-4275).

FINANCIAL DISCLOSURE: The authors have indicated they have no financial relationships relevant to this article to disclose.

FUNDING: No external funding.

POTENTIAL CONFLICT OF INTEREST: The authors have indicated they have no potential conflicts of interest to disclose.

COMPANION PAPER: A companion to this article can be found online at www.pediatrics.org/cgi/doi/10.1542/peds.2016-4211.

REFERENCES

1. 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(RR-10):1–36
2. Polin RA; Committee on Fetus and Newborn. Management of neonates with suspected or proven early-onset bacterial sepsis. *Pediatrics*. 2012;129(5):1006–1015
3. Brady MT, Polin RA. Prevention and management of infants with suspected or proven neonatal sepsis. *Pediatrics*. 2013;132(1):166–168
4. Kiser C, Nawab U, McKenna K, Aghai ZH. Role of guidelines on length of therapy in chorioamnionitis and neonatal sepsis. *Pediatrics*. 2014;133(6):992–998
5. Benitz WE, Wynn JL, Polin RA. Reappraisal of guidelines for management of neonates with suspected early-onset sepsis. *J Pediatr*. 2015;166(4):1070–1074
6. Cotten CM, Taylor S, Stoll B, et al; NICHD Neonatal Research Network. Prolonged duration of initial empirical antibiotic treatment is associated with increased rates of necrotizing enterocolitis and death for extremely low birth weight infants. *Pediatrics*. 2009;123(1):58–66
7. Taylor JA, Opel DJ. Choriophobia: a 1-act play. *Pediatrics*. 2012;130(2):342–346
8. Weston EJ, Pondo T, Lewis MM, et al. The burden of invasive early-onset neonatal sepsis in the United States, 2005-2008. *Pediatr Infect Dis J*. 2011;30(11):937–941
9. Mukhopadhyay S, Dukhovny D, Mao W, Eichenwald EC, Puopolo KM. 2010 Perinatal GBS prevention guideline and resource utilization. *Pediatrics*. 2014;133(2):196–203
10. Puopolo KM, Draper D, Wi S, et al. Estimating the probability of neonatal early-onset infection on the basis of maternal risk factors. *Pediatrics*. 2011;128(5). Available at www.pediatrics.org/cgi/content/full/128/5/e1155
11. Escobar GJ, Puopolo KM, Wi S, et al. Stratification of risk of early-onset sepsis in newborns ≥34 weeks' gestation. *Pediatrics*. 2014;133(1):30–36
12. Cantoni L, Ronfani L, Da Riol R, Demarini S; Perinatal Study Group of the Region Friuli-Venezia Giulia. Physical examination instead of laboratory tests for most infants born to mothers colonized with group B streptococcus: support for the Centers for Disease Control and Prevention's 2010 recommendations. *J Pediatr*. 2013;163(2):568–573
13. Berardi A, Fornaciari S, Rossi C, et al. Safety of physical examination alone

for managing well-appearing neonates ≥ 35 weeks' gestation at risk for early-onset sepsis. *J Matern Fetal Neonatal Med*. 2015;28(10):1123–1127

14. Simpson E, Goyal NK, Dhepyasuwan N, et al. Prioritizing a research agenda: a Delphi study of the better outcomes through research for newborns (BORN) network. *Hosp Pediatr*. 2014;4(4):195–202
15. Harris PA, Taylor R, Thielke R, Payne J, Gonzalez N, Conde JG. Research electronic data capture (REDCap)—a metadata-driven methodology and workflow process for providing translational research informatics support. *J Biomed Inform*. 2009;42(2):377–381
16. American Academy of Pediatrics Committee on Fetus and Newborn. Levels of neonatal care. *Pediatrics*. 2012;130(3):587–597
17. Centers for Disease Control and Prevention. Overview of 2010 guidelines. Available at: www.cdc.gov/groupbstrep/guidelines/new-differences.html. Accessed October 18, 2016
18. Escobar GJ, Li DK, Armstrong MA, et al. Neonatal sepsis workups in infants >/=2000 grams at birth: a population-based study. *Pediatrics*. 2000;106(2 pt 1):256–263
19. Mukhopadhyay S, Eichenwald EC, Puopolo KM. Neonatal early-onset sepsis evaluations among well-appearing infants: projected impact of changes in CDC GBS guidelines. *J Perinatol*. 2013;33(3):198–205
20. Newman TB, Puopolo KM, Wi S, Draper D, Escobar GJ. Interpreting complete blood counts soon after birth in newborns at risk for sepsis. *Pediatrics*. 2010;126(5):903–909
21. Ottolini MC, Lundgren K, Mirkinson LJ, Cason S, Ottolini MG. Utility of complete blood count and blood culture screening to diagnose neonatal sepsis in the asymptomatic at risk newborn. *Pediatr Infect Dis J*. 2003;22(5):430–434
22. Hornik CP, Benjamin DK, Becker KC, et al. Use of the complete blood cell count in early-onset neonatal sepsis. *Pediatr Infect Dis J*. 2012;31(8):799–802
23. Benitz WE, Han MY, Madan A, Ramachandra P. Serial serum C-reactive protein levels in the diagnosis of neonatal infection. *Pediatrics*. 1998;102(4):E41
24. Preissig CM, Rigby MR. Pediatric critical illness hyperglycemia: risk factors associated with development and severity of hyperglycemia in critically ill children. *J Pediatr*. 2009;155(5):734–739
25. McGowan JE. Neonatal hypoglycemia. *NeoReviews*. 1999;20(7):e6–e15
26. Hays SP, Smith EO, Sunehag AL. Hyperglycemia is a risk factor for early death and morbidity in extremely low birth-weight infants. *Pediatrics*. 2006;118(5):1811–1818
27. Mukherjee A, Davidson L, Anguvaa L, Duffy DA, Kennea N. NICE neonatal early onset sepsis guidance: greater consistency, but more investigations, and greater length of stay. *Arch Dis Child Fetal Neonatal Ed*. 2015;100(3):F248–F249
28. van Herk W, el Helou S, Janota J, et al. Variation in current management of term and late-preterm neonates at risk for early-onset sepsis: an international survey and review of guidelines. *Pediatr Infect Dis J*. 2016;35(5):494–500
29. Higgins RD, Saade G, Polin RA, et al; Chorioamnionitis Workshop Participants. Evaluation and management of women and newborns with a maternal diagnosis of chorioamnionitis: summary of a workshop. *Obstet Gynecol*. 2016;127(3):426–436
30. Wortham JM, Hansen NI, Schrag SJ, et al; Eunice Kennedy Shriver NICHD Neonatal Research Network. Chorioamnionitis and culture-confirmed, early-onset neonatal infections. *Pediatrics*. 2016;137(1)
31. Mukhopadhyay S, Lieberman ES, Puopolo KM, Riley LE, Johnson LC. Effect of early-onset sepsis evaluations on in-hospital breastfeeding practices among asymptomatic term neonates. *Hosp Pediatr*. 2015;5(4):203–210
32. Corvaglia L, Tonti G, Martini S, et al. Influence of intrapartum antibiotic prophylaxis for group B streptococcus on gut microbiota in the first month of life. *J Pediatr Gastroenterol Nutr*. 2016;62(2):304–308
33. Vangay P, Ward T, Gerber JS, Knights D. Antibiotics, pediatric dysbiosis, and disease. *Cell Host Microbe*. 2015;17(5):553–564

Variation in Sepsis Evaluation Across a National Network of Nurseries

Sagori Mukhopadhyay, James A. Taylor, Isabelle Von Kohorn, Valerie Flaherman, Anthony E. Burgos, Carrie A. Phillipi, Nui Dhepyasuwan, Elizabeth King, Miren Dhudasia and Karen M. Puopolo

Pediatrics 2017;139;
DOI: 10.1542/peds.2016-2845 originally published online February 8, 2017;

PEDIATRICS®
OFFICIAL JOURNAL OF THE AMERICAN ACADEMY OF PEDIATRICS

Variation in Sepsis Evaluation Across a National Network of Nurseries

Sagori Mukhopadhyay, James A. Taylor, Isabelle Von Kohorn, Valerie Flaherman, Anthony E. Burgos, Carrie A. Phillipi, Nui Dhepyasuwan, Elizabeth King, Miren Dhudasia and Karen M. Puopolo

Pediatrics 2017;139;
DOI: 10.1542/peds.2016-2845 originally published online February 8, 2017;