Development of Putative Working Definitions of Prenatal-onset Group B Strep (POGBS) Invasive Disease Using “Internet Commons” GBS Parent and Provider Sources

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Abstract
Background: Classification of early-onset GBS disease is defined as death or birth with certain symptoms within 72 hours of delivery. Therefore, focal disease caused by GBS is not counted as early-onset group B strep disease.
Objective: To develop putative epidemiological, clinical, and laboratory definitions of prenatal-onset group B streptococcal (POGBS) invasive disease in order to inform research, advocacy, public policy, clinical care, and social support.
Methods: We used qualitative exploratory methods (including “Internet Commons” research to collect, record, and analyze GBS-related questions (FAQs) submitted to Group B Streptococcal’s website (www.pbiology.org) and to multiple professional organizations from 2000 to 2012. Questions or requests for information aimed at improving care over the world with Internet Commons” were in response to “SurveyMonkey” style surveys to professional contacts and through the internet from 2000 to 2012. Language was not restricted, but all ethical responses were in English to prompt temporality. No written consent was obtained and the process and analysis were not IRB approved.
Results: Twelve years of responses and contacts were analyzed. There were no measured differences in question types or topics among parents or providers. Of professional meetings as many as some FAQs were submitted. Making direct evidence available (JAMA) is being published along with other putative definitions of GBS-related definitions. See Table 1. Proposed Working Definitions of Prenatal-onset Group B Streptococcal Disease.

Introduction
• Group B streptococcus (GBS) was identified as a leading cause of perinatal infection in the 1970s.
• The prevalent “dogma” is that GBS exposure and subsequent infection occur only during passage through the birth canal.
• This notion is the basis of the present CDC, ACOG, and AAP guidelines to prevent early-onset GBS.
• Prenatal-onset GBS intratubine infection has been previously described by Katz, Tuleia, Bennett et al.
• Non-congenital outbreaks by Katz and more recently Tuleia, Wendel, and Sheffield suggest that GBS infection occurs often before birth, across intact fetal membranes, and causes both stillbirths and perinatal depression with depressed Aggaras as well as neonatal death.
• GBS is the commensal in the amniotic or the commonest microorganisms isolated from normally “sterile” sites after passage through the vagina, between membranes, and within the placenta, cord blood, and blood in the autopsy.
• GBS demonstrates pathophysiologic virulence capacities which can explain:
  1) intratubine infection with intact fetal membranes,
  2) premature fetal infection, and
  3) lethal factors leading to placental or fetal death.

Methods
1) Reviewed and analyzed prior observations including animal models, microbiologic findings, immunologic, and clinical experiments.
2) Used quasi-experimental and qualitative techniques to collect, record, and analyze GBS-related questions from parents and providers from 2000 to 2012.
3) Applied pathophysiologic principles including innate and acquired immunologic protection strategies, i.e., vaccination, microecologic, and clinical strategies to reduce risk of perinatal GBS infection including stillbirth (20-28 weeks gestation) and very early preterm birth and/or late miscarriage (16-20 weeks gestation), to develop and justify putative working definitions of POGBS invasive disease (see Table 1).
4) Evaluated these definitions using historical “cultural criteria,” i.e., Rock’s postulates & Bradford Hill causal criteria.

“Universal screening and intrapartum antibiotic prophylaxis have had no measurable impact on prenatal-onset disease (including stillbirths and miscarriages)”

Goals
1) Provide rationale for expanded epidemiologic studies to identify strategies which may reduce risks of pre-labor/pre-membrane rupture onset of GBS infection.
2) Provide basis for classifying cases in which GBS infection occurs prior to term labor and membrane rupture (including preterm and fullterm live births) as POGBS disease in order to better identify effective prevention strategies.

Table 1. Proposed Working Definitions of Prenatal-onset GBS Disease

<table>
<thead>
<tr>
<th>Clinical</th>
<th>Pathology</th>
<th>Microbiologic</th>
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<tbody>
<tr>
<td>Maternal fever &gt;38°C if determined</td>
<td>Visualization of microbes (3+) consistent with chorioamnionitis and/or funisitis</td>
<td>GBS positive by culture or non culture when identified from non-semisolid sources, e.g., cord blood, blood, blood, liver, placenta parenchyma</td>
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<tr>
<td>Fetal tachycardia (&gt;160) if available</td>
<td>Visualization of organisms consistent with GBS in tissue</td>
<td>Any historic evidence of inflammation in placenta</td>
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<tr>
<td>Stillborn or born with systemic evidence of infection (SIRS)</td>
<td>Abnormal WBC, neutrophilia, leukocytosis</td>
<td>Any microbiologic or nonculture evidence of GBS including surface sources</td>
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Likely
Maternal fever >38°C if determined
Perinatal depression
APGAR <4 in 5 min.
Arterial cord gas: pH ≤ 7.0, BE greater than –12 mmol
Any historic evidence of inflammation in placenta
Any microbiologic or nonculture evidence of GBS including surface sources

Possible
Nonsepticemic infection of Fetus
Pneumonitis on CXR, CT, or ultrasound site infection
0/14 microsporidial finding of chorioamnionitis or funisitis
Positive GBS surface cultures from perinatal placenta

Atypical
Evidence of maternal growth restraint
Premature labor or preterm rupture of membranes
Abnormal CXR suggestive of possible pneumonitis
GBS infection in maternal or maternal asymptomatic bacteriuria with GBS

Results
Analysis of inquiries and anecdotal cases resulted in:
1) Identifying common gaps in communication and care as well as missed opportunities for prevention, e.g., incorrect treatment for vaginal symptoms
2) Opportunity to refine educational materials and promote research topics

“The burden of prenatal-onset GBS disease has not been assessed adequately and no effective prevention tools have been identified before the intrapartum period.”
*CDC MMRWR, Nov. 19, 2010/Vol. 59/No. RR-10

Conclusions
1) Prenatal-onset GBS intratubine infection may explain GBS selective culture-based antibiochemophylaxis (IAP) failure
2) Working definitions of POGBS invasive disease can allow renewed experimentation in order to further reduce risks of GBS perinatal disease including rapid “Point of Care” microbial testing as well as adjuvant VACCINATION or other novel strategies

Recommendations
1) Implement collection of surveillance data for POGBS disease
2) Reconvene well-funded national study group to explore novel strategies to further reduce risk of GBS neonatal disease burden
3) Use these strategies separately or in combination with culture-guided (IAP)
   a) VACCINATION
   b) Microbiologic
   c) Clinical strategies – screen ASB/UTI
   d) Placental biopsy
4) Further refine microbiological screening, i.e., early in pregnancy, UTI/ASB, and in labor or after ROM
5) Improve operational procedures to enhance efficacy of IAP
6) Encourage pathology testing/autoysis which may also provide valuable information to be reviewed for subsequent pregnancies

References