Development of Putative Working Definitions of Prenatal-onset Group B Strept (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 after birth which marks fetal demise caused by GBS before birth. Therefore, fetal demise caused by GBS are not counted as being due to group B strep disease.

Objective: Develop and justify epidemiologic, clinically graded (“Proven,” “Likely,” “Possible,” or “Possible?”) case definitions of previously unclassified invasive prenatal-onset Group B streptococcal (POGBS) invasive disease in order to inform research, advocacy, public policy, clinical care, and social support.

Methods: We used quasi-experimental and qualitative techniques (“visitors” and “locum” work, provider-revised questions [FAQs] submitted to Group B Strep International’s website www.pbstotal.org) or in medical professional meetings from 2000-2012. Questions or requests for information arrived unbidden or spontaneously at the worldwide web (“Internet Commons”) or in response to “SurveyMonkey”-style requests to personal contacts made at professional meetings and through the internet from 2000 to 2012. Language was not restricted, but all analyzed responses were in English to prompt spontaneity. No written consent was obtained and the process and analysis were not IRB-approved.

Results: Twelve years of queries and contacts were analyzed. There were no measured differences in question types or topics among parents or providers. (At professional meetings as many as 500 responses were submitted daily making detailed analysis unrealistic.) Queries mainly fell into three categories: 1) clinical “anecdotal cases,” 2) procedural, e.g., how to facilitate communication of GBS status to collect, record, and analyze GBS-related queries (FAQs) submitted to Group B Strep International’s website www.pbstotal.org or in medical professional meetings from 2000-2012. Questions or requests for information arrived unbidden near the worldwide web (“Internet Commons”) or in response to “SurveyMonkey”-style inquiries to personal contacts made at professional meetings and through the internet from 2000 to 2012. Language was not restricted, but all analyzed responses were in English to prompt spontaneity. No written consent was obtained and the process and analysis were not IRB-approved.

Conclusions: Invasive Disease

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

<table>
<thead>
<tr>
<th>Proven</th>
<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>Fetal tachycardia (&gt;160) if available</td>
<td>Stillborn or born with systemic evidence of infection (SIRS)</td>
<td>Visualizations of microbes (3+) consistent with chorioamnionitis and/or funisitis</td>
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<tr>
<td>Likely</td>
<td>Maternal fever &gt;38°C if determined</td>
<td>Perinatal depression APGAR ≤ 5 @ 5 min</td>
<td>Any histologic evidence of inflammation in placenta</td>
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<tr>
<td>Possible</td>
<td>Nonsystemic finding of infection Pneumonitis on CXR, UUTI, umbilical site infection</td>
<td>Any microbiologic or non culture evidence of GBS including surface sources</td>
<td>0/1 microscopic finding of chorioamnionitis or funisitis</td>
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<tr>
<td>Atypical</td>
<td>Evidence of mastitis</td>
<td>Growth restriction Preterm labor or preterm rupture of membranes</td>
<td>Abnormal CXR suggestive of “possible pneumonitis”</td>
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| GBS infection in mother or maternal asympomatic bacteriuria with GBS |

References


“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

Introduction
• Group B streptococcus (GBS) was identified as a leading cause of neonatal infection in the 1970s.
• The prevalent “dogma” is that GBS exposure and subsequent infection occur only during passage through the GBS-colonized birth canal.
• This notion is the basis of the preterm CDC, ACOG, and AAP guidelines to prevent early-onset GBS.
• Prenatal-onset GBS intrauterine infection has been previously described by Katz, Tudela, Benirschke, etc.
• Non-consent observations by Katz and more recently Tudela, Wendel, and Sheffield suggest that GBS infection often occurs before birth, across intact fetal membranes, and causes both stillbirth and perinatal depression with depressed Apgars as well as neonatal death.
• GBS is the commonest or among the commonest microorganisms isolated from normally “sterile” sites after passage through the vagina, between membranes, and within the placenta, cord blood, heart blood or spleen at autopsy.
• GBS demonstrates pathophysiologic virulence capacities which can explain: 1) intrauterine infection with intact fetal membranes, 2) invasive fetal infection, and 3) lethal factors leading to placental or fetal death.

Methods
1) Reviewed and analyzed prior observations including animal models, microbiologic findings, microbiologic, 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 prevention 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 “causal criteria,” i.e., Kock’s postulates & Bradford Hill criteria

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

Conclusions
1) Prenatal-onset GBS intrauterine infection may explain GBS selective culture-based antibiotic chemoprophylaxis (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” diagnostic tests as well as adjunct VACCINATION or other novel strategies

Recommendations
3) Implement collection of surveillance data for POGBS disease
4) Recomend well-funded national study group to explore novel strategies to further reduce risk of GBS neonatal disease burden
5) Use these strategies separately or in combination with culture-guided iAP:
   a) VACCINATION
   b) Microecologic
   c) Clinical strategies – screen ASB/UTI
   d) Placental triage
6) Further refine microbiologic 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 pathotyping/autopsies which may also provide valuable information to be reviewed for subsequent pregnancies

“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 MMWR, Nov. 19, 2010/Vol. 59/Ro. RR-10

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