Prenatal-onset GBS (POGBS) Disease as a Cause of Perinatal Morbidity and Mortality

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ABSTRACT

Background
Intrauterine infection is increasingly recognized as a possibly preventable cause of stillbirth (SB). The objective of this review/analysis is to justify recognition of prenatal-onset group B strep (POGBS) sepsis, distinct from early-onset (EO) and late-onset (LO) infections from group B strep (GBS) and other microorganisms.

Methods
Logic model analysis:
1) Conduct an expert systematic review and analysis of group B strep disease knowledge in order to justify recognition of POGBS sepsis, distinct from EO and LO infections from GBS and other microorganisms.
2) To correlate patient experiences, we conducted a quasi-experimental "internet commons" inquiry of parent contacts who had suffered GBS SB.
3) Computer-based national data bases were utilized to assess knowledge of GBS infectious disease.

Results
Much is known about GBS disease. Despite this knowledge, preventative regimes remain inconsistently applied, and in the best of circumstances are incompletely (85-90%) successful in reducing early-onset GBS infection and do not address late-onset or prenatal-onset GBS infections.

Conclusion
1) There is sufficient knowledge supporting the Centers for Disease Control & Prevention (CDC) (MMWR 2010, Volume 59/RR-10) use of the term "prenatal-onset GBS disease" as a distinct entity.
2) Our limited, uncontrolled investigation supports clinical notions that a) GBS loss or SB occurs in a bimodal gestational time distribution with the preponderance of cases occurring near term (POGBS); and b) that mothers do not reliably demonstrate fever or "textbook" findings of potentially lethal intrauterine infection.

BACKGROUND

Group B streptococcus (GBS) was identified as a leading cause of perinatal infection in the 1970s. Intrauterine infection is increasingly recognized as a possibly preventable cause of stillbirth (SB). (McClure, Goldenberg. Semin Fetal Neonatal Med 2009, 14(4):182-9.)

The prevalent "dogma" is that GBS exposure and subsequent infection occurs only during passage through the GBS colonized birth canal. This notion is the basis of the present CDC, ACOG and AAP guidelines to prevent GBS Early-onset Sepsis (EOS).

Non-congruent observations by Katz and more recently Tudela, Wendel, and Sheffield suggest that GBS infection also occurs before birth across intact fetal membranes and causes both stillbirth (SB) and perinatal depression (PD) with depressed Apgars and neonatal death.

Systematic epidemiologic investigations may allow for investigations to possibly reduce risks of pre-labor onset of GBS infections.

GOALS

1) Review and Analyze prior observations including:
   a) Animal models
   b) Microbiologic findings
   c) Microbiologic
   d) Immunologic
   e) Clinical experimentations which can justify naming "prenatal-onset" GBS disease
2) Provide rationale for expanded epidemiologic studies
3) Suggest strategies which may reduce risks of POGBS disease

METHODS

1) Review/Analyze available information justifying "official" designation of prenatal-onset GBS infections
2) Evaluate this proposal using historical "causal criteria," i.e., Kock's postulates & Bradford Hill causal criteria
3) Apply pathophysiologic principles including innate and acquired immunologic prevention strategies (i.e., vaccination, microecological, and clinical strategies to reduce risk of perinatal GBS infection including SB (20-28 weeks) and very early PTB and/or late miscarriage (16-20 weeks)

RESULTS

1) Prenatal-onset GBS intrauterine infection has been previously described (Katz, Tudela, Benirschke, others)
2) GBS is the commonest or among the commonest microorganisms isolated from normally "sterile" sites after passage through the vagina, between membranes, within placenta, cord blood, heart blood or spleen at autopsy.
3) GBS demonstrates pathophysiologic virulence capacities which can explain:
   a) Intrauterine infection with intact fetal membranes
   b) Invasive fetal infection
   c) Lethal factors (toxins, NETs, others) leading to placental or fetal death
   d) Multiple studies/analysis demonstrate feasibility and practicability of **ACTIVE GBS VACCINATION**

CONCLUSIONS

1) GBS, similar to other "perinatal pathogens," is an apparent cause of intrauterine infection (1° chorioamnionitis "CAM" or intraamniotic infection "IAI" can cause SB and very early PTB and possibly LM
2) Intrauterine infection or prenatal-onset GBS may explain GBS selective culture-based antibiotic chemoprophylaxis (IAP)
3) Recognition of POGBS 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) Reconvene well-funded national study group to explore novel strategies to further reduce risk of GBS neonatal disease burden
2) These strategies can be separate or in combination with culture-guided IAP:
3) VACCINATION
4) Microecologic
5) Clinical Strategies - screen UTI/ASB
6) Further refine microbials screening, i.e., early in pregnancy, UTI/ASB, and in labor or after ROM
7) Improve operational procedures to enhance efficacy of IAP

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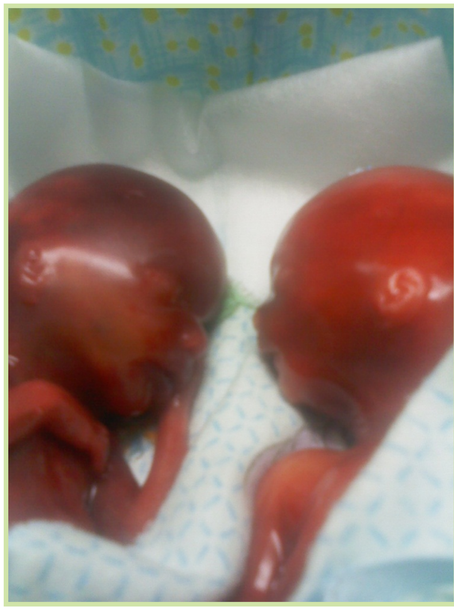

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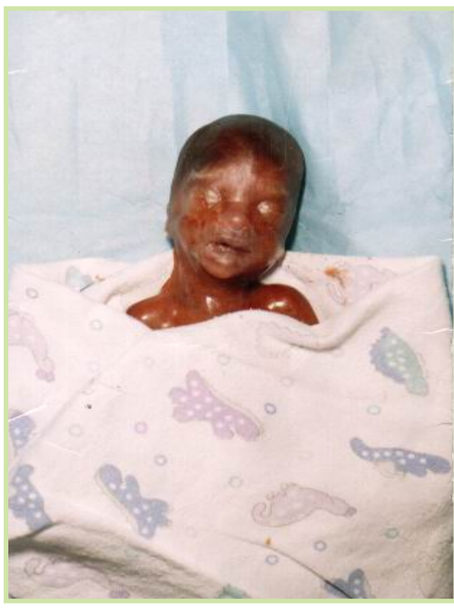

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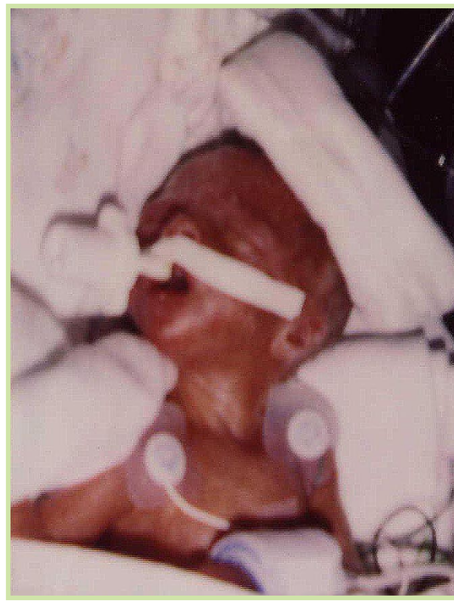

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