Prenatal-onset GBS (POGBS) Sepsis is a Distinct Cause of Stillbirth and Perinatal Mortality

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ABSTRACT

Background/Introduction
Intrauterine infection is increasingly recognized as a possible preventable cause of stillbirth (SB). (McCune, Goldenberg, Semin Fetal Neonatal Med 2009, 14(4):182-9.)

Methods
Logic model analysis:
1) Conduct an expert systematic review and analysis of group B strep (GBS) disease knowledge in order to justify recognition of prenatal-onset GBS (POGBS) as a distinct entity.
2) To correlate patient experiences, we conducted a quasi-experimental Internet commons inquiry of parent contacts who had suffered SB.
3) Computer-based national data bases were utilized to assess knowledge of GBS infections.
4) An English-language seven-queen patient survey was constructed, pretested, and disseminated to selected Group B Strept International contacts using the Internet. No written consent was obtained.

Results
Much is known about GBS disease. Despite this knowledge, preventative regimes remain inconsistently applied, and in the best of circumstances are incomparably SS-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 to support the CDC proposed (MMWR 2010, Volume: 59(5) classification of prenatal-onset GBS-EOS as a distinct entity.
2) Our limited, uncontrolled observational studies supports clinical notions that at GBS lesion is SS occurs in a bimodal gestational time distribution with the predominance of cases occurring in early term (POGBS) and b) that mothers do not reliably demonstrate fever or "febrile" findings of potential lethal intrauterine infection. Other observations are predicted by the limited, uncontrolled nature of our retrospective, self-reported sample.

BACKGROUND
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 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 experimentalizations which can justify naming "prenatal-onset of early GBS neonatal infection (POGBS-EOS)"

2) Provide rationale for expanded epidemiologic studies
3) Suggest strategies which may reduce risks of POGBS-EOS

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 criteria
3) Apply pathophysiologic principles including innate and acquired immunologic interference strategies (i.e., vaccination, microecologic, 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 most common or among the most common 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 (1979 chorioamnionitis "CAM" or intraamnion infection "IAI") can affect 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-EOS can allow renewed experimentation in order to further reduce risks of GBS neonatal disease including rapid "Point of Care" microbial testing as well as adjunct VACCINATION or other novel strategies

RECOMMENDATIONS
1) Reconvene well-funded national study group to expore 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 microbiolal screening, i.e., early in pregnancy, UTI/ASB, and in labor or after ROM
7) Improve operational procedures to enhance efficacy of IAP

REFERENCES
Levens E, Hoyt J, Arifin SF. Effectiveness of maternal influenza immunization in mothers and infants. NINR 2004;525-555-564.