

# Development of Putative Working Definitions of Prenatal-onset Group B Streptococcal (P-OGBS) Invasive Disease Using "Internet Commons" GBS Parent and Provider Sources

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## ABSTRACT

**Background**  
Develop and justify epidemiologic, clinically graded ("Proven," "Likely," "Possible," or "Atypical") case definitions of previously unclassified invasive prenatal-onset group B streptococcal (P-OGBS) invasive disease in order to inform research, advocacy, public policy, clinical care, and social support.

**Methods**  
We used quasi-experimental and qualitative techniques ("gedanken" research) to collect, record, and analyze GBS-related questions (FAQ's) submitted to Group B Strep International's website ([www.gbs-intl.org](http://www.gbs-intl.org)) or at medical professional meetings from 2000-2012. Questions or requests for information arrived unbidden over the worldwide web ("Internet Commons") or in response to "Survey Monkey" 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.

**Results**  
Twelve years of inquiries 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 questions were submitted daily making detailed analysis unreliable.) Queries mainly fell into three categories:  
1) clinical "anecdotal cases,"  
2) procedural, e.g., how to facilitate communication of GBS status cards, and  
3) informal non-evidence-based advice for uncommon or unstudied clinical circumstances, e.g., severe penicillin allergy, prior GBS-associated stillbirth.

Table 1) Proposed Working Classifications of Prenatal-onset GBS Invasive Disease

	Clinical	Pathology	Microbiologic
<b>Proven</b>	Maternal fever >38°C if determined Fetal tachycardia (>160) if available Stillborn or born with systemic evidence of infection (SIRS)	Visualization of microbes (3-4+) consistent with chorioamnionitis and/or funisitis Visualization of organisms consistent with GBS in tissue Abnormal WBC: neutropenia, leukocytosis	GBS positive by culture or non culture when identified from non surface sources, e.g., cord blood, heart blood, spleen, liver, placenta parenchyma
<b>Likely</b>	Maternal fever >38°C if determined Perinatal depression APGAR <4 @ 5min. Arterial cord gas: pH less than 7.1, BE greater than 12 mmol	Any histologic evidence of inflammation in placenta	Any microbiologic or nonculture evidence of GBS including surface sources
<b>Possible</b>	Nonsystemic finding of infection Pneumonitis on CXR, UTI, umbilical site infection	0/+1 microscopic finding of chorioamnionitis or funisitis	Positive GBS surface cultures from perinate placenta
<b>Atypical</b>	Evidence of mastitis Growth restriction Preterm labor or preterm rupture of membranes	Abnormal CXR suggestive of "possible pneumonitis"	GBS infection in mother or maternal asymptomatic bacteriuria with GBS

**Conclusions**  
We utilized "internet commons" and other contacts to post putative working case definitions of "Proven," "Likely," "Possible," or "Atypical" prenatal-onset GBS invasive disease. These proposed definitions may facilitate study of the epidemiology, pathophysiology, and means to further prevent occurrences of prenatal-onset GBS invasive 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 GBS-colonized birth canal
- This notion is the basis of the present CDC-P, ACOG, and AAP guidelines to prevent GBS Early-onset Sepsis (E-OS)
- Prenatal-onset GBS intrauterine infection has been previously described (Katz, Tudela, Benirshke, others)
- Non-congruent 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

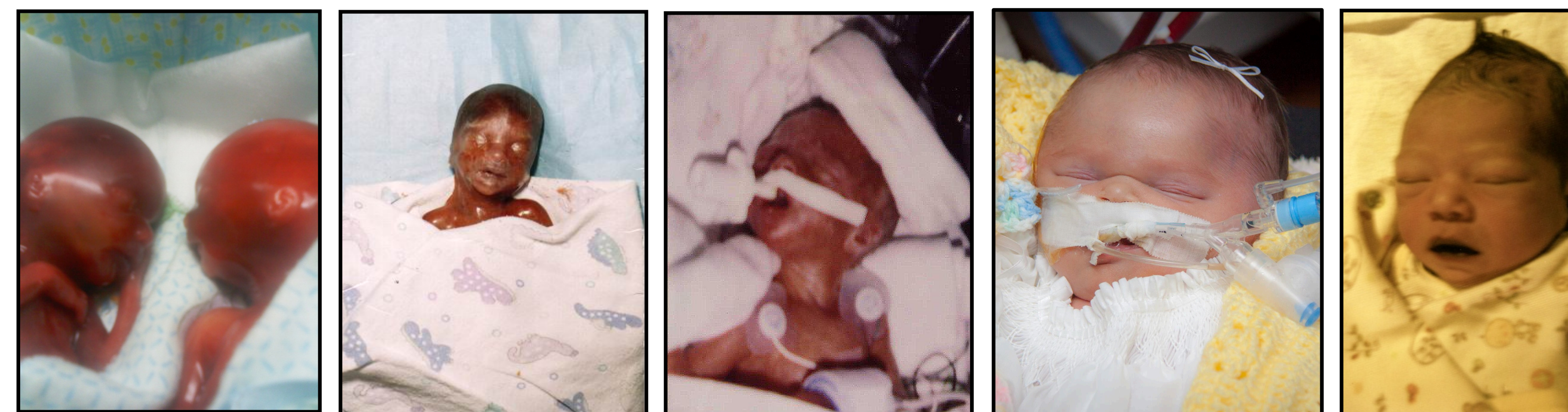
## INTRODUCTION (continued)

- 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:
  - Intrauterine infection with intact fetal membranes
  - Invasive fetal infection
  - Lethal factors leading to placental or fetal death

"Universal screening and intrapartum antibiotic prophylaxis have had no measurable impact on ...prenatal-onset disease (including stillbirths and miscarriages)...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/No. RR-10

## GOALS

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



## METHODS

- Reviewed and analyzed prior observations including animal models, microbiologic findings, immunologic, and clinical experimentations
- Used quasi-experimental and qualitative techniques to collect, record, and analyze GBS-related questions from parents and providers from 2000 to 2012
- 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 case definitions of P-OGBS invasive disease (see Table 1 of Abstract box)
- Evaluated these definitions using historical "causal criteria," i.e., Kock's postulates & Bradford Hill causal criteria

## RESULTS

Analysis of inquiries and anecdotal cases resulted in:

- Identifying common gaps in care and communication as well as missed opportunities for prevention, e.g., incorrect treatment for vaginitis symptoms
- Opportunity to refine educational materials and promote research topics

## CONCLUSIONS

- Prenatal-onset GBS intrauterine infection may explain GBS selective culture-based antibiotic chemoprophylaxis (IAP) failure
- Working definitions of P-OGBS 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

- Implement collection of surveillance data for P-OGBS disease
- Reconvene well-funded national study group to explore novel strategies to further reduce risk of GBS neonatal disease burden
- Use these strategies separately or in combination with culture-guided IAP:
  - VACCINATION
  - Microecologic
  - Clinical strategies - screen UTI/ASB
  - Placental triage
- Further refine microbials screening, i.e., early in pregnancy, UTI/ASB, and in labor or after ROM
- Improve operational procedures to enhance efficacy of IAP
- Encourage pathology testing/autopsies which may also provide valuable information to be reviewed for subsequent pregnancies

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