Perinatal Group B Streptococcal Disease Prevention: What’s up, What’s down, What’s new

Tennessee Public Health Association Annual Meeting
November 1, 2007
Franklin, TN
Perinatal Group B Streptococcal Disease

- Emerged 1970s
- Deaths, sequelae
- Neonatal disease cost ~$300 million (1992)
Pre-prevention era: Invasive GBS Disease Incidence by Age and Race (1990)

Per 100,000 population

Age group:
- 0-90D
- 91D-14Y
- 15-24Y
- 25-34Y
- 35-44Y
- 45-54Y
- 55-64Y
- 65-74Y
- 75+Y

Whites

Blacks

MMWR Vol. 41 (No. SS-6) 1992
GBS Disease in Infants Before Prevention Efforts


Early-onset: 0-6 days of life
Late onset: 7-89 days of life
Early-onset disease: Mother to Infant Transmission

GBS colonized mother (20-25% of women)

- 50% Non-colonized newborn
- 50% Colonized newborn

- 98% Asymptomatic
- 2% Early-onset sepsis, pneumonia, meningitis
First U.S. Consensus Recommendations (CDC '96, ACOG '96, AAP '97)

Screening-based approach:
35-37 wks culture, offer intrapartum antibiotic prophylaxis (IAP) to GBS carriers and to preterm unless neg. culture result available

or

Risk-based approach:
IAP to preterm, membrane rupture $\geq 18$ hours, or intrapartum fever ($T \geq 38^\circ C$)

Both strategies also give IAP to women w/ GBS bacteriuria, or prev. infant w/ GBS disease
ABCs/ Emerging Infection Program Network for GBS surveillance

Approximately 300,000 live births annually
GBS Policies in US Hospitals Implementation by Year

% Hospitals with GBS Policies

Year


ABCs Hospitals, EIP Network
MMWR 1998; 47:665-670

1st Consensus Guidelines Issued
Change in incidence of early-onset GBS disease in hospitals w/ and w/out new policies

Rate of early- and late-onset GBS disease in the 1990s, U.S. (ABCs sites)

- Group B Strep Association formed
- 1st ACOG & AAP statements
- CDC draft guidelines published
- Consensus guidelines

Schrag, New Engl J Med 2000
Risk vs. screening

- No randomized trials comparing screening and risk-based approaches
- Observational data suggest efficacy of each approach
- Theoretical predictions suggest strategies may not be equally effective
Study design
Multistate, retrospective cohort study using infrastructure of ABCs/EIP population-based surveillance network

Study methods
Review of randomly selected labor and delivery records from births in 1998 and 1999 in 8 active surveillance areas

Included all early-onset GBS cases in these areas; births without documented GBS screening were considered exposed to risk-based approach
**Key result: Screening protective compared to risk-based approach**

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>Adjusted RR (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>GBS screening</td>
<td>0.46 (0.36-0.60)</td>
</tr>
<tr>
<td>Prolonged ROM (≥ 18 h)</td>
<td>1.41 (0.97-2.06)</td>
</tr>
<tr>
<td>Pre-term delivery</td>
<td>1.50 (1.07-2.10)</td>
</tr>
<tr>
<td>Black race</td>
<td>1.87 (1.45-2.43)</td>
</tr>
<tr>
<td>Maternal age &lt;20 y</td>
<td>2.22 (1.59-3.11)</td>
</tr>
<tr>
<td>Previous GBS infant</td>
<td>5.54 (1.71-17.94)</td>
</tr>
<tr>
<td>Intrapartum fever</td>
<td>5.36 (3.60-7.99)</td>
</tr>
</tbody>
</table>

Schrag et al. NEJM 2002, 347:233-9
Why?

Broader coverage of at-risk population

• Captures colonized women without obstetric risk factors (18% of all deliveries)

• Antibiotic effectiveness in this cohort, based on birth survey data: 89% (64-97%)

Schrag et al. NEJM 2002, 347:233-9
The 2002 Recommendations:
Universal prenatal screening; intrapartum antibiotics to colonized women

MMWR, Vol 51 (RR-11)

www.cdc.gov/groupbstrep
Areas of change

• Identification of candidates for intrapartum antimicrobial prophylaxis (IAP): A single strategy
• Second line agents for IAP
• Management of planned cesarean deliveries
• Management of threatened preterm deliveries
• More detail on specimen collection and handling
• Neonatal management
Expectations

Rapid transition to screening
Early onset incidence will decline by 32%

Hopes

Racial disparities will decrease
Intrapartum antibiotic use will remain stable
What actually happened?
Two primary sources of data
2005 GBS Participating ABCs Areas:
Live Births, 2004: 455,000

- Oregon
- California
- Colorado
- Minnesota
- New Mexico
- Tennessee
- Georgia
- New York
- Connecticut
- Maryland
- Connecticut

2004: 72% white, 18% black, 9% other races
Special Study: Birthnet 2

• Reviewed 7,600 L&D records, a sample of ~ 800,000 live births for 2003-2004 among residents of ABCs sites

• Objectives
  – Characterize adherence to antenatal screening recommendations
    • GBS
    • Other perinatal infections
  – Examine risk factors for failure to adhere to recommendations
### Maternal demographics

<table>
<thead>
<tr>
<th>Age &lt; 20 years</th>
<th>White</th>
<th>Black</th>
<th>Asian</th>
<th>Ethnicity</th>
</tr>
</thead>
<tbody>
<tr>
<td>3</td>
<td>71</td>
<td>21</td>
<td>7</td>
<td>Hispanic</td>
</tr>
<tr>
<td>≥1 prenatal visit</td>
<td>97</td>
<td>3</td>
<td></td>
<td>History of drug use</td>
</tr>
<tr>
<td>97</td>
<td></td>
<td></td>
<td></td>
<td>Medicaid for L&amp;D</td>
</tr>
</tbody>
</table>

### L&D History

<table>
<thead>
<tr>
<th>Cesarean delivery</th>
<th>Preterm</th>
<th>Very low birthweight</th>
<th>Previous GBS infant</th>
<th>GBS bacteriuria during pregnancy</th>
<th>Intrapartum fever</th>
<th>Membrane rupture &gt;18 h</th>
<th>Suspected chorioamnionitis</th>
</tr>
</thead>
<tbody>
<tr>
<td>24.9</td>
<td>9.3</td>
<td>2.6</td>
<td>1.3</td>
<td>5.5</td>
<td>3.3</td>
<td>7.0</td>
<td>2.9</td>
</tr>
</tbody>
</table>

† Preliminary weighted, 7,653 records representing 818,000 births
Expectation

Rapid transition to screening
GBS testing before delivery, 1998-1999: Fifty percent of births screened

Schrag et al. NEJM 2002, 347:233-9
GBS testing before delivery: 2003/2004: 86% of births screened

Birthnet project; ABCs births in 2003-4; Preliminary weighted results
GBS Prevention Implementation, 2003-4: Themes emerging from Birthnet

• Colonization rate suggests adequate specimen processing
  – 24% of screened women were GBS positive
  – Negatives among cases raise question about false negatives

• Documentation of screening date needs improvement
  – 27% had no documentation of the date
  – Among women with dates, 5% were screened at <30 weeks

• Among screened, few unknown results at delivery
  – 1.6% of screened women had no documented result at delivery
IAP implementation, 2003-4

• Strong compliance with GBS positive indication
  – 88% of GBS positive women received IAP
• Antibiotic choice for Hx PCN allergy needs improvement
  – Clindamycin still in wide use
  – Little use of cefazolin
  – Good news: Vancomycin extremely rarely used
Expectation

Early onset incidence will decline by 32%
Incidence of Early-Onset Disease (N=1020): 29% Decrease post guidelines

MMWR 2007. 56 (28)
## State-specific rates in 2005, ABCs

<table>
<thead>
<tr>
<th>State</th>
<th>No.</th>
<th>Cases/1000 live births</th>
</tr>
</thead>
<tbody>
<tr>
<td>California</td>
<td>7</td>
<td>0.16</td>
</tr>
<tr>
<td>Colorado</td>
<td>10</td>
<td>0.28</td>
</tr>
<tr>
<td>Connecticut</td>
<td>10</td>
<td>0.24</td>
</tr>
<tr>
<td>Georgia</td>
<td>30</td>
<td>0.40</td>
</tr>
<tr>
<td>Maryland</td>
<td>33</td>
<td>0.44</td>
</tr>
<tr>
<td>Minnesota</td>
<td>15</td>
<td>0.22</td>
</tr>
<tr>
<td>New Mexico</td>
<td>17</td>
<td>0.60</td>
</tr>
<tr>
<td>New York</td>
<td>7</td>
<td>0.30</td>
</tr>
<tr>
<td>Oregon</td>
<td>8</td>
<td>0.38</td>
</tr>
<tr>
<td>Tennessee</td>
<td>30</td>
<td>0.70</td>
</tr>
<tr>
<td><strong>Total</strong></td>
<td><strong>167</strong></td>
<td><strong>0.37</strong></td>
</tr>
</tbody>
</table>

*MMWR 2007. 56 (28)*
Hope

Racial disparities will decline
Incidence of Early-Onset Disease: 2000-2005

MMWR 2007. 56 (28)
Incidence of Early-Onset Disease 2000-2005

MMWR 2007. 56 (28)
Why has GBS EOD incidence increased among black infants?
Denominator artifact?

Increasing disparity for late-onset GBS disease
Artifact of gestational age?
White Infants, 2000-2005

Cases per 1000 live births

Year

2000 2001 2002 2003 2004 2005

Preterm
Term
Incidence of EOD in Black Infants by Gestational Age, 2000-2005

Year

Cases per 1000 live births

Preterm

Term

2000 2001 2002 2003 2004 2005
## Racial disparities in GBS screening?

<table>
<thead>
<tr>
<th>Screened</th>
<th>Black</th>
<th>Non-black</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>All births</td>
<td>82%</td>
<td>87%</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Term births</td>
<td>87%</td>
<td>90%</td>
<td>&lt;0.004</td>
</tr>
<tr>
<td>EOD cases</td>
<td>64%</td>
<td>77%</td>
<td>0.04</td>
</tr>
<tr>
<td>Screen date</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>&lt; 5 weeks before</td>
<td>57%</td>
<td>61%</td>
<td>NS</td>
</tr>
<tr>
<td>birth</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Unknown</td>
<td>27%</td>
<td>26%</td>
<td>NS</td>
</tr>
<tr>
<td>Result</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>GBS positive</td>
<td>32%</td>
<td>22%</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Unknown</td>
<td>2.1%</td>
<td>1.4%</td>
<td>NS</td>
</tr>
</tbody>
</table>

Birthnet project; ABCs births in 2003-4; Preliminary weighted results
Racial disparities in IAP administration?

<table>
<thead>
<tr>
<th>Received IAP</th>
<th>GBS positive</th>
<th>88%</th>
<th>88%</th>
<th>NS</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>GBS unknown</td>
<td>73%</td>
<td>66%</td>
<td>NS</td>
</tr>
<tr>
<td></td>
<td>with indication</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>EOD cases</td>
<td>29%</td>
<td>32%</td>
<td></td>
<td>NS</td>
</tr>
<tr>
<td>≥4 hrs IAP</td>
<td>63%</td>
<td>58%</td>
<td></td>
<td>NS</td>
</tr>
</tbody>
</table>

Birthnet project; ABCs births in 2003-4; Preliminary weighted results
Intrapartum antibiotic use will remain stable
Increase in intrapartum antibiotic exposure, US

Schrag et al., 2002. NEJM 347:233-9
Increase in intrapartum antibiotic exposure, US

Birthnet project; ABCs births in 2003-4; Preliminary weighted results
Deliveries exposed to intrapartum antibiotics by state, 2003/4

Birthnet project; ABCs births in 2003-4; Preliminary weighted results
Unintended consequences of intrapartum prophylaxis: What we know at this point

- Allergies: anaphylaxis occurs but rarely
- Resistance: Clinda & erythromycin resistance now more common in GBS
- Health services: no major increases in newborn management
- Other pathogens: data are complex…
Central concern

Does IAP replace a bad problem (GBS) with a worse problem (e.g., ampicillin-resistant *E. coli*)?
What we know about trends in nonGBS pathogens

- Most studies: stable rates of ‘other’ sepsis
- A few hospitals reported increased rates or #s of *E.coli*, all gram negs, or amp R infxs
- One multicenter study of very LBW infants found increase in *E.coli* rates (Stoll et al)
- Pop-based (multicenter) studies find stable rates of total nonGBS and *E.coli*
- % of *E. coli* sepsis w/ amp resistance may be increasing
- Increases restricted to low birth weight or preterm deliveries
GBS and *E. coli*, very low birthweight infants

Incidence (per 1000 live births)

Invasive neonatal sepsis incidence, ABCs, 2005-2006

Overall Incidence: 0.8/1000 live births

Incidence (per 1,000)

<table>
<thead>
<tr>
<th>ABCs Site</th>
<th>CA</th>
<th>CT</th>
<th>GA</th>
<th>MN</th>
</tr>
</thead>
<tbody>
<tr>
<td>Incidence</td>
<td>0.6</td>
<td>0.7</td>
<td>1.0</td>
<td>0.6</td>
</tr>
</tbody>
</table>
Neonatal sepsis etiologies, 2005-2006

- GBS: 38%
- E. coli: 23%
- S. aureus: 5%
- S. viridans: 17%
- H. flu: 4%
- Other: 13%
Neonatal Group B Streptococcal Disease (GBS)

<table>
<thead>
<tr>
<th></th>
<th>Early-Onset</th>
<th>Late-Onset</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Definition</strong></td>
<td>Day 0-6 of life</td>
<td>Day 7-89 of life</td>
</tr>
<tr>
<td><strong>Transmission</strong></td>
<td>Vertical</td>
<td>Unknown</td>
</tr>
<tr>
<td><strong>Risk factors</strong></td>
<td>Well-described</td>
<td>Poorly-understood</td>
</tr>
<tr>
<td><strong>Prevention Strategy</strong></td>
<td>Established in 1990s</td>
<td>None</td>
</tr>
</tbody>
</table>
Incidence of Early- and Late-Onset GBS, 1990-2005

Cases / 1,000 live births

Early-onset GBS

Late-onset GBS

Before national prevention policy
Transition
Universal screening
Proportion of Neonatal Disease Accounted for by Late-Onset GBS

- 1990-1995 (Before national prevention)
- 1996-2002 (Transition period)
- 2003-2005 (Universal screening)

Legend:
- Late onset
- Early onset
Late onset disease burden, 2003-5

- Projected US cases: 1250-1300 cases/yr
- Case fatality rate: 4%
- Proportion of cases with meningitis: 19%
- Gestational age <37 weeks at birth: 54%
- Median age of onset: 37 days

US serotype distribution, 2005

EOD (n=98)

Remaining types: VI, NT

LOD (n=111)

Remaining types: Ib, IV, NT

*ABCs, unpublished. Data from 7 surveillance areas; 80% cases have isolates available
Steps you can take:
Laboratory-specific issues

– Plan how to report GBS from prenatal urine cultures (any concentration of GBS should be reported to provider)

– Plan how to perform susceptibility testing of GBS if Pen allergy

– Facilitate timely communication of results

– Explore ways to document GBS test dates or include lab slips in prenatal record forwarded to hospital
Infection control contributions

– System for flagging GBS + results, Pen allergy
– Education around pen allergy recs
– Standing orders (eg. GBS carriers, GBS bacteriuria, previous GBS invasive disease, or unknown carriage and a RF)
– Patient education materials
– Evaluation of implementation indicators (eg, proportion of deliveries getting IAP, proportion of women GBS+, proportion of GBS+ getting IAP)
– Evaluation of early-onset cases for missed opportunities for prevention
Key GBS Resources

- 2002 GBS guidelines
  - http://www.cdc.gov/mmwr/preview/mmwrhtml/rr5111a1.htm
- American College of Obstetricians and Gynecologists
  - http://www.acog.org
- American Academy of Pediatrics
  - http://www.aap.org
- Public Health Foundation
  - http://www.phf.org
- CDC's GBS Internet page
  - http://www.cdc.gov/groupbstrep
Extra Slides
Clinical Neonatal Sepsis Rates, National Hospital Discharge Data, 1990-2002

Lukacs, 2004. SPER.
Early-onset *E. coli* sepsis, Preterm Infants, CA and GA, 1998-2000

N=37, p=0.02, linear trend
Hyde, 2002 Pediatrics 110;690-5
# Early-Onset GBS 2000-2005 (N=1020)

<table>
<thead>
<tr>
<th>Race</th>
<th>Percentage</th>
</tr>
</thead>
<tbody>
<tr>
<td>White</td>
<td>54%</td>
</tr>
<tr>
<td>Black</td>
<td>34%</td>
</tr>
<tr>
<td>Other</td>
<td>7%</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Term</th>
<th>75%</th>
</tr>
</thead>
<tbody>
<tr>
<td>Case Fatality Ratio</td>
<td>7%</td>
</tr>
</tbody>
</table>
GBS Early-onset Disease – Projections to the US, 2005*

• 1275 cases & 75-80 deaths occurred
• Proportion of preterm cases increasing
  (2000: 20%; 2004: 29%; P<0.01)
• Stable incidence, 2003-2005
• Still a leading infectious cause of newborn illness and death

*Provisional ABCs/EIP Network 2005 data
Concern 1. GBS antimicrobial resistance

- So far, no resistance to penicillins
- Emerging resistance to second line agents

Castor, M. et al., Submitted 2006. ABCs
N=2939 invasive GBS isolates; all ages
Pre-IAP: Rates of Early-Onset GBS Disease by Prenatal Colonization & Risk Factors

Col: prenatal vag/rect culture
RF: risk factors (gest. <37 wks, ROM >12 hr, fever > 37.5 C)

Era of universal screening:
Rates of Early-Onset GBS Disease by Prenatal Colonization & Risk Factors

Col: prenatal vag/rect culture
RF: risk factors (gest. <37 wks, ROM >18 hr, fever >38 C)

2003/2004 birthnet preliminary results; 7653 records representing 818,000 births