Screening for GBS colonization

OLD & NEW TOOLS

Pierrette Melin
Belgian National Reference Centre for Group B Streptococci
Clinical Microbiology, University Hospital of Liege, University of Liege

WHY?
WHEN?
HOW?
IMPACT?

Stages in the pathogenesis of GBS neonatal EOD: Bacterial & individual factors

COLONIZATION:
- adhesion to epithelial cells different virulence factors (pili, scpB, ...)

GBS pathogenesis

Brain barrier
Pili, III ST-17
β-hemolysin, ...

Sepsis
- IL1, IL6, TNF α, PGE2, TxA2,
- β-hemolysin, ...

- Resistance to phagocytose
  - Capsule
  - CsA peptidase
  - ...

- Phagocytes cells, CPS Antibodies, Complement

β-hemolysin, invasins (pneumonia)

β-hemolysin, (amnionitis)

Intrapartum antibioprophylaxis

> 4 (2) hours before delivery

Highly effective in preventing GBS EOD (1st clinical trials in late 80s)

OBJECTIVES

To provide a comprehensive picture of current and coming practices for GBS screening

Culture methods versus NAAT
Antenatal versus intrapartum

- To emphasize critical criteria for success
- To identify some possibilities for improvement
- To point out advantages and drawbacks
Impact of prevention practices
Early- and Late-onset GBS Diseases, U.S.

Resistance to macrolides/lincosamides
Wide geographical variation of rates

Resistance to clindamycin: Constitutive or Inducible R
D-Test recommended
Resistance to macrolides/lincosamides
Wide geographical variation of rates

Resistance to clindamycin: Constitutive or Inducible R
→ D-Test recommended

Screening for GBS colonization
Goal of GBS screening
To predict GBS vaginal (rectal) colonization at the time of delivery

Expected high predictive values
- False negative
  → Missed IAP
- “False” positive
  → Unnecessary IAP

Critical factors influencing accuracy
- Swabbed anatomic sites (distal vagina + rectum)
- Timing of sampling
- Screening methods
  - Culture
  - Procedure
  - Media
  - Nucleic Acid Amplification Test (NAAT)

Crucial conditions to optimize universal antenatal SCREENING
- WHEN 35-37 weeks
- WHO ALL the pregnant women
- Specimen Vaginal + rectal swab(s)
- Collection WITHOUT speculum
- Transport Transport/collection device/condition
  (non nutritive medium: Amies/Stuart or Granada like tube) (type of swab)(Length and T°°°°
- Request form To specify prenatal « GBS » screening
- Laboratory procedure

(CDC 2010 - Belgian SCH 2003)
Culture-based screening done 1 to 5 or > 6 weeks before delivery
(Yancey, 860 cases; Melin, 531 cases)

Not 100% as colonization is dynamic


Culture-based screening done 1 to 5 or > 6 weeks before delivery
(Yancey, 860 cases; Melin, 531 cases)

Melin, 13-16% GBS Pos
PPV= 56%
NPV= 95%
or 5% False negative
or 30% of GBS pos in labor not detected with antenatal screening!


Remaining burden of GBS EOD
Missed opportunities

In spite of universal screening prevention strategy
In spite the great progress
Cases still occur

- Among remaining cases of EOD
  - Some may be preventable cases
    - Missed opportunities for (appropriate) IAP
  - False negative screening

CDC revised guidelines 2010
DEVANI project, unpublished data 2011

From direct plating on blood agar
Evolution of culture methods

Use of selective enrichment broth (Lim broth, e.g.)
- To maximize the isolation of GBS
- To avoid overgrowth of other organisms

Use of differential agar media
Recommended by some European guidelines (+ CDC 2010)

GRANADA (M.de la Rosa, JCM)
Strepto B Select
StreptoB ID
Brilliance StrepB

Pigment-based Chromogenic media
Which agar or which combination?

+/- Blood agar

Workload - costs - extra-testing - non β-hemolytic GBS detection to be considered

Crucial conditions to optimize SCREENING

- WHEN 35-37 weeks
- WHO ALL the pregnant women
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- Laboratory procedure

(CDC 2010 - Belgian SCH 2003)

Improvement of transport condition of swabs for Group B streptococcal (GBS) screening


National Reference Centre for GBS, University Hospital of Liège, Liège, Belgium

To sustain viability Whatever is storage T°°° for a few days

Use of a selective enrichment Lim broth as transport media
**Results:**
Recovery of GBS in Lim BD at 4° C, RT and 35° C  
*Clinical studies ongoing*

- **Continuous decrease**

<table>
<thead>
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<th>Recovery (CFU)</th>
<th>0 h</th>
<th>24 h</th>
<th>48 h</th>
<th>72 h</th>
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<td>35°C</td>
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</tbody>
</table>

- **Granada tube: not shown, dramatic drop at 48-72h**

**Antenatal culture-based screening combined with amplification molecular test**

- **NAAT performed from Lim enrichment broth Broth**
  - The Xpert GBS LB assay
  - The LAMP Illumigene GBS Assay

**Clinical evaluations**
- **Speed:** time to result minus one day
- **Accuracy:** good comparison to reference culture
- **Cost, logistic, training:** very important to consider

**Antenatal culture-based screening: Limiting factors**

- **Positive and negative predictive values**
  - False-negative results
    - Failure of GBS culture *reduced viability during transport, oral ATB, feminine hygiene* or new acquisition
    - Up to 1/3 of GBS positive women at time of delivery
  - Eagerly expected, a more accurate predictor
    - For intrapartum GBS vaginal colonization
Alternative to GBS antenatal screening: intrapartum screening
Theranostic approach

- **Turnaround time**
  - Collect specimen at admission
- **Results**
  - Sensitivity > 90%
  - Specificity > 95%
  - 30-45 minutes, 24 hrs/7 days robust

Inclusion of women without prenatal screening/care
Identification of women with change of GBS status after 35-37 wks gestation (new acquisition, false negative)
Increased accuracy of vaginal GBS colonization status at time of labor & delivery
Drawback: no antimicrobial susceptibility result

**Expected advantages: pro & con**
- IAP addressed to right target
  - Reduction of inappropriate/unnecessary IAP
  - Broader coverage of « at GBS risk women »
- Improvement of prevention

**Real Time PCR for intrapartum screening**
- **Advance in PCR techniques & development of platforms & to be used as a POCT**
- **Xpert® GBS, Cepheid (35-45 min)**
  - Already recommended by CDC for women with no prenatal care, …

**Xpert® GBS for intrapartum screening**
*(selected paper amongst many others)*

**Diagnostic Accuracy of a Rapid Real-Time Polymerase Chain Reaction Assay for Universal Intrapartum Group B Streptococcus Screening**
Najoua El Helali, Jean-Claude Nguyen, Aïcha Ly, Yves Giovangrandi and Ludovic Trinquart
*Clinical Infectious Diseases* 2009;49:417–23

- **968 Pregnant women**
- **Intrapartum Xpert GBS, Cepheid** *(performed in lab)*
  - vs intrapartum culture
    - **antenatal culture (French recom.)** *(vaginal swab/CNA-BA)*
    - Sensitivity 98.5%
    - Specificity 99.6%
    - PPV 97.8%
    - NPV 99.7%
**Xpert® GBS for intrapartum screening**

*Selected paper amongst many others*

Cost and effectiveness of intrapartum group B streptococcus polymerase chain reaction screening for term deliveries.


*Obstet Gynecol 2012 Apr;119 (4):822-9*

<table>
<thead>
<tr>
<th>Year</th>
<th>Authors</th>
<th>Journal</th>
<th>Nb patients</th>
<th>Site</th>
<th>Sensitivity</th>
<th>Specificity</th>
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<td>2009</td>
<td>Mueller et al</td>
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**Real Time PCR for intrapartum screening**

- Advance in PCR techniques & development of platforms & to be used as a POCT
- Xpert® GBS, Cepheid (35-45 min)
  
  Already recommended by CDC for women with no prenatal care, …

- Easy BUT …
- Midwives teams: numbers, turn-over
- TRAINING is essential
  - Sample preparation
  - Proper breaking the swab into the cartridge
  - Loading the instrument
- To be used under lab control

**Xpert® GBS for intrapartum screening**

*Main papers*

**Take-home messages**

- Acknowledged need for improvement of predictive values & logistics
- GBS screening
- Identified possibilities for improvement of culture method
- NAAT on enrichment broth as an alternative approach
  - NAAT available (but no clindamycin susceptibility result)
  - Some evidence of cost-effectiveness
  - Additional studies needed for validation as a POCT