



# GBS colonization and screening in pregnancy: how does it work in Europe?

**Pierrette Melin**

*National Reference Centre for GBS  
Medical Microbiology, University Hospital of  
Liege*

# INTRODUCTION

# Introduction

## Burden of GBS neonatal early onset diseases

Location	Incidence per 1,000 live-births	Reference
Spain	2 (1996) to 0.45 (2008)	<i>Lopez Sastre et al. ActaPediatr 2005</i>
Belgium	2 - 3	<i>Melin, Indian J Med Res 2004</i>
Eastern Europe	0.2 - 4	<i>Trijbels-Smeulders, Pediatr Infect Dis J 2004</i>
Western Europe	0.3 - 2	
The Netherlands	1.9	
Scandinavia	0.76 - 2	
Southern Europe	0.57 - 2	

- Carriage rate ?
- Ethnicity ?
- Sub-reporting?
- Systematic diagnostic approach?
- Virulence ?

*Data assessing more accurately the true burden are needed*

- **Universal prenatal screening-based strategy**
- **Risk-based strategy**
- **No guideline**

# **GUIDELINES IN EUROPEAN COUNTRIES**

# European strategies for prevention of GBS EOD

- **Intrapartumantibioprophylaxis recommended**
  - **Screening-based strategy**
    - Spain, 1998, revised 2003
    - France, 2001
    - Belgium, 2003, revision ongoing 2011
    - Germany, 1996, revised 2008
    - Switzerland, 2007
    - Italy
  - **Risk-based strategy**
    - UK, the Netherlands, Denmark
- **No guidelines**
  - Bulgaria

# MISSED OPPORTUNITIES

# Remaining burden of GBS EOD

**In spite of universal screening prevention strategy**

**In spite the great progress**

**Cases still occur**

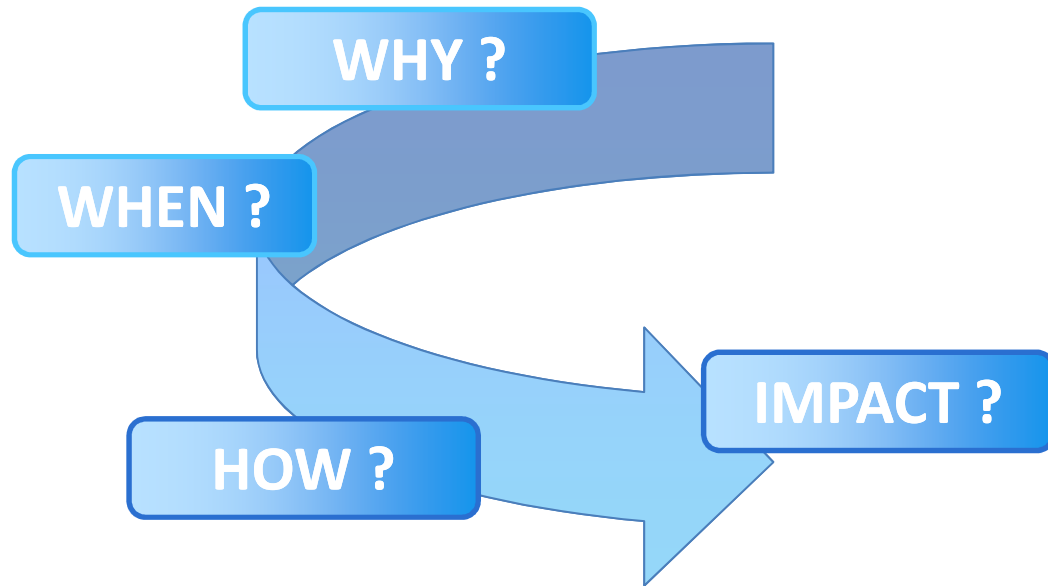
- **Among remaining cases of EOD**
  - **Some may be preventable cases**
    - Missed opportunities for (appropriate) IAP
    - False negative screening

*Van Dyke MK, Phares CR, Lynfield R et al. N Engl J Med 2009*

*CDC revised guidelines 2010*

*Poyart C, Reglier-Poupet H, Tazi et al. Emerg Infect Dis 2008*

*DEVANI project, unpublished data 2011*



# SCREENING FOR GBS COLONIZATION



# Antenatal GBS culture-based screening

## Goal of GBS screening

*To predict GBS vaginal (rectal) colonization at the time of delivery*

- **Critical factors influencing accuracy**
  - Swabbed anatomic sites
  - Timing of sampling
  - Screening methods
    - Culture
      - *Procedure*
      - *Media*
    - Non-culture

# Choice of the anatomic sites

## Lower vagina + rectum

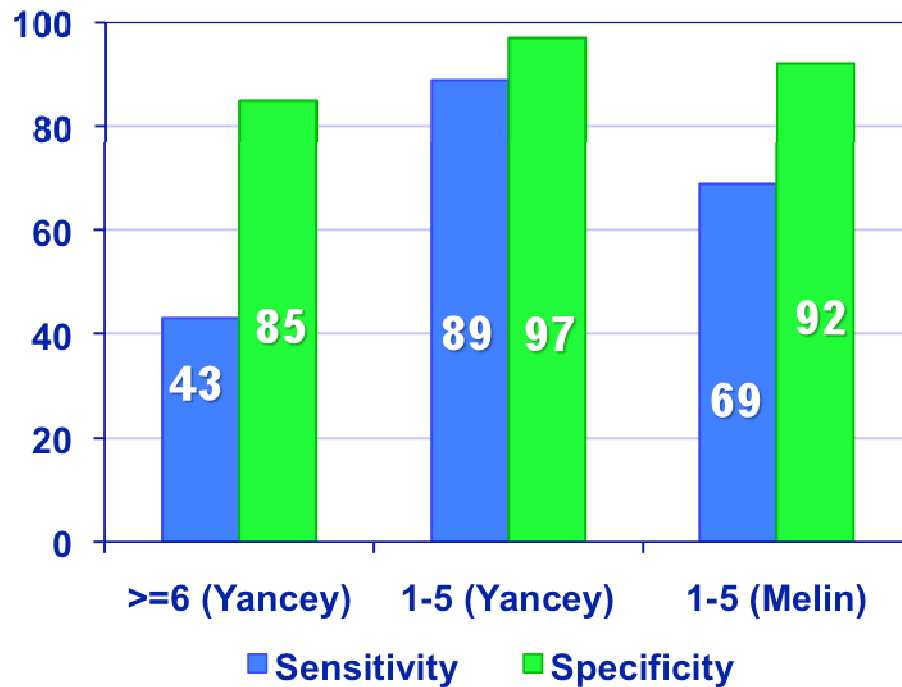
**Vagina & rectum > vagina or rectum > cervix**

*Badri et al., J Infect Dis 1977;135:308-12*

- **Lower vaginal area**
  - For collection : use of speculum out of question
- **Rectum (*through anal sphincter !*)**
  - GBS reservoir, source of vaginal colonization
  - Rectum GBS positive and vagina negative
    - 15 to 20% of GBS positive pregnant women
- **A single combined specimen**

# Optimal time for screening 35-37 weeks gestation

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

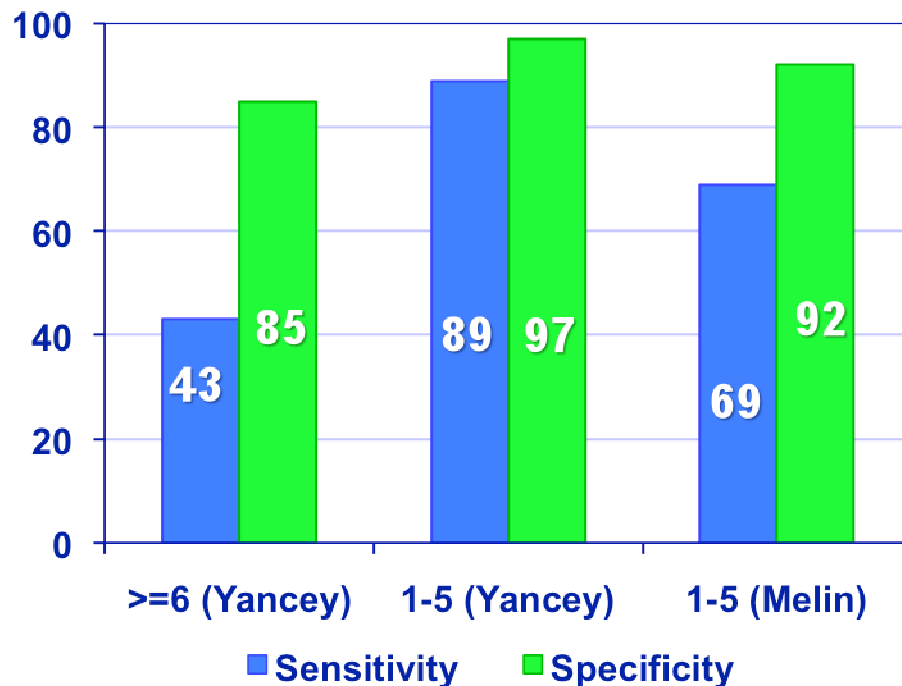


Not 100 % as  
colonization is dynamic

*Yancey MK et al. ObstetGynecol 1996;88:811-5*

# Optimal time for screening 35-37 weeks gestation

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(Yancey, 860 cases; Melin, 531 cases)



**30% of GBS pos in labor not detected with prenatal screening !**

*Melin et al. ICAAC 2000*

**Not 100 % as  
colonization is dynamic**

*Yancey MK et al. ObstetGynecol 1996;88:811-5*

From direct plating on blood agar:  
**Evolution of culture methods**  
**Use of selective enrichment broth**

- **To maximize the isolation of GBS**
- **To avoid overgrowth of other organisms**

<b>Nb women, medium</b>	<b>Direct culture 48hrs GBS+</b>	<b>Sub- culture from SEB % GBS+</b>	<b>Authors</b>
<b>200, Granada</b>	<b>88 %</b>	<b>100 %</b>	<b>Tazi A et al, 2008</b>
<b>500, Granada</b>	<b>72 %</b>	<b>99 %</b>	<b>Melin P et al, 2008</b>
<b>StrepB select</b>	<b>74 %</b>	<b>96 %</b>	
<b>288, Blood /Lim</b>	<b>52 %</b>	<b>82 %</b>	<b>Shibuya R, 2009</b>
<b>New Granada</b>	<b>52 %</b>	<b>100 %</b>	

# Evolution of culture methods

## Blood agar +/- CNA

### Revised guidelines from CDC (2002)

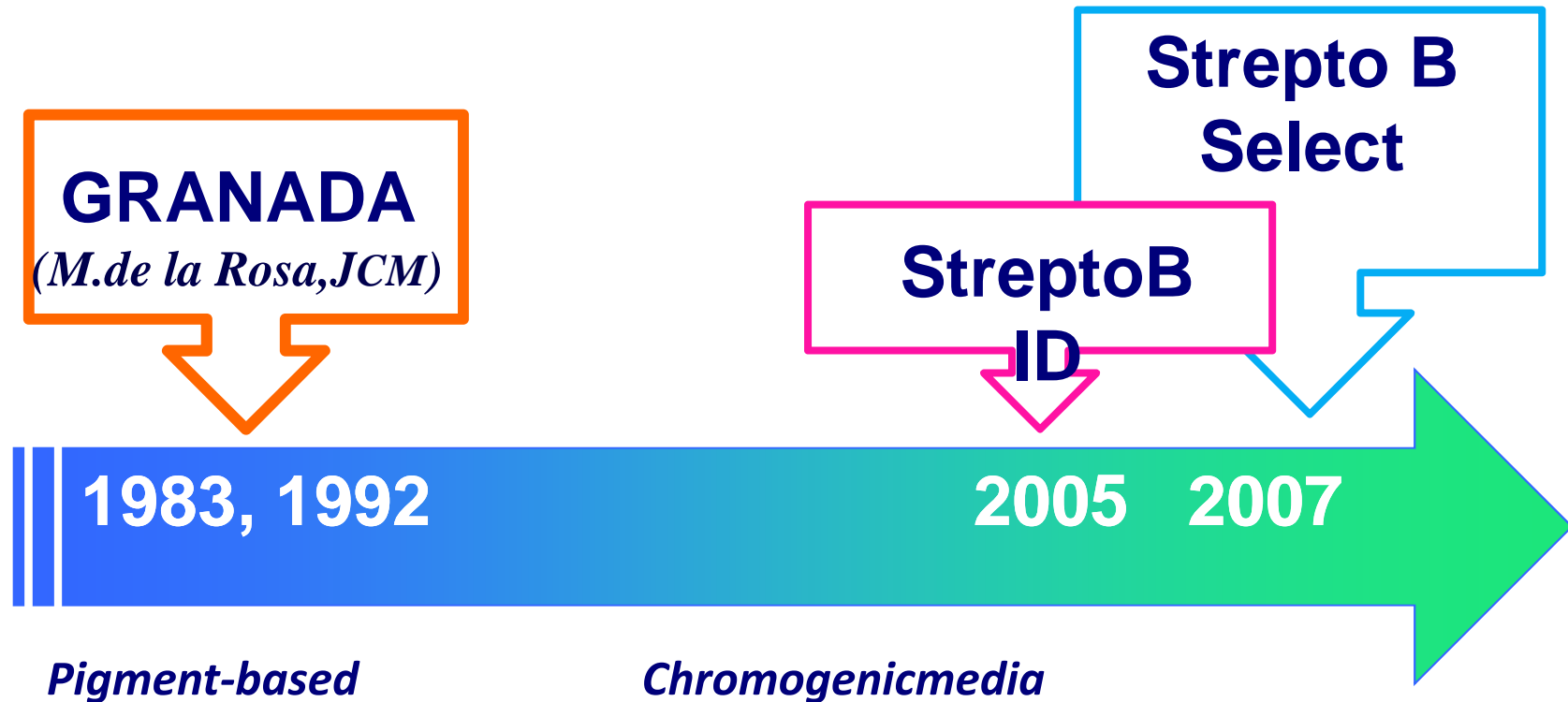
- **Sub-culture < selective enrichment broth**
  - **Blood agar +/- colistin and nalidixic acid**
    - **Advantage**
      - Growth of all GBS Isolates  $\beta$ -hemolytic or not
    - **Disadvantages**
      - Difficulty in seeing rare GBS colonies within mixed vaginal-rectal microbiota
      - Difficulty in recognizing non-hemolytic GBS in mixed microbiota

Sensitivity and specificity to be improved

# Evolution of culture methods

## Use of differential agar media

Recommended by some European guidelines (+ CDC 2010)



# Granada medium agar

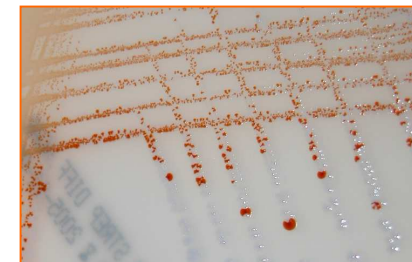
(Anaerobic incubation)

*M de la Rosa Fraile, JCM 1983 & 1992*



- Orange color: GBS pigment, Granadaene
- 100% specific for GBS //β-hemolysis

- Granada original, bioMérieux
- Group B Streptococcus Differential Modified Granada Medium™ (BD)
- Carrot Medium (Hardy)

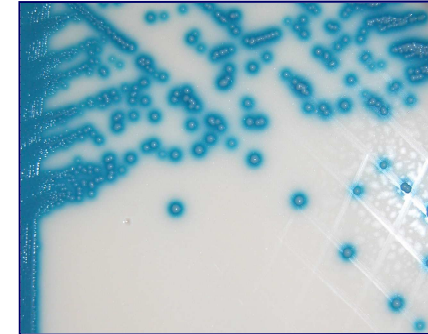
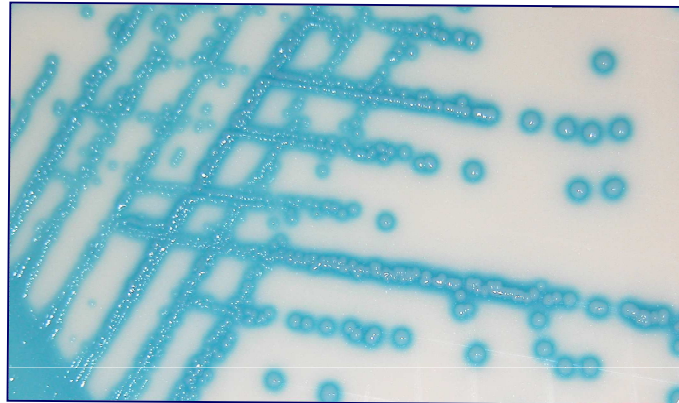
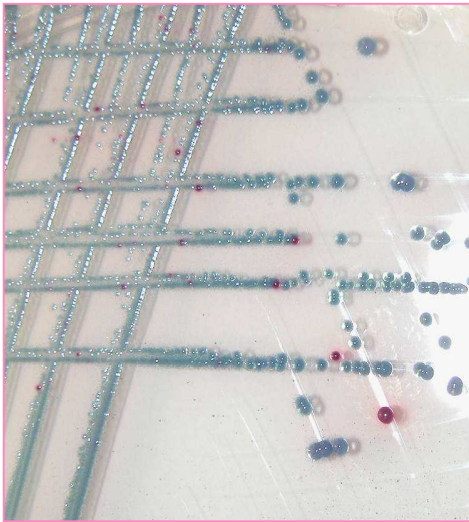


**Does not show non-hemolytic strain !**  
( < 4% of invasive isolates ??)



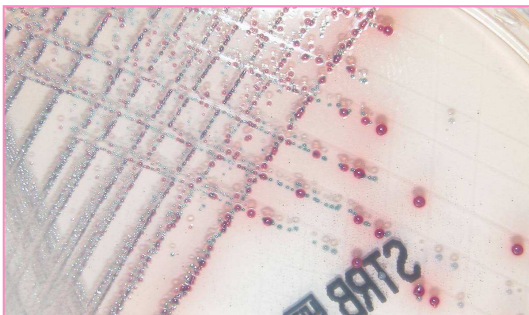
# Strepto B ID agar (BioMérieux)

## Strep B Select agar (BioRad)



### High sensitivity for growth of GBS

- pink to red colonies (bioM)
- or pale to darkblue-turquoise colonies (BioR)



### Chromogenic media

Not 100 % specific for GBS: Id to confirm(latex)  
(GAS, GCS, Staphylococci, alpha-hemolytic colonies, etc.)

# Which agar or which combination?

+/- Blood agar



**Workload - costs - extra-testing - non  $\beta$ -hemolytic GBS detection to be considered**

# Crucial conditions to optimize SCREENING

- **WHEN** 35-37 weeks
- **WHO** ALL the pregnantwomen
- **Specimen** Vaginal + rectal swab(s)
- **Collection** WITHOUT speculum
- **Transport** Transport/collection device /condition  
(non nutritive medium: Amies/Stuart or Granada like tube)(Length and T°)
- **Requestform** To specify prenatal « GBS » screening  
*+expected address for delivery*
- **Laboratory procedure**

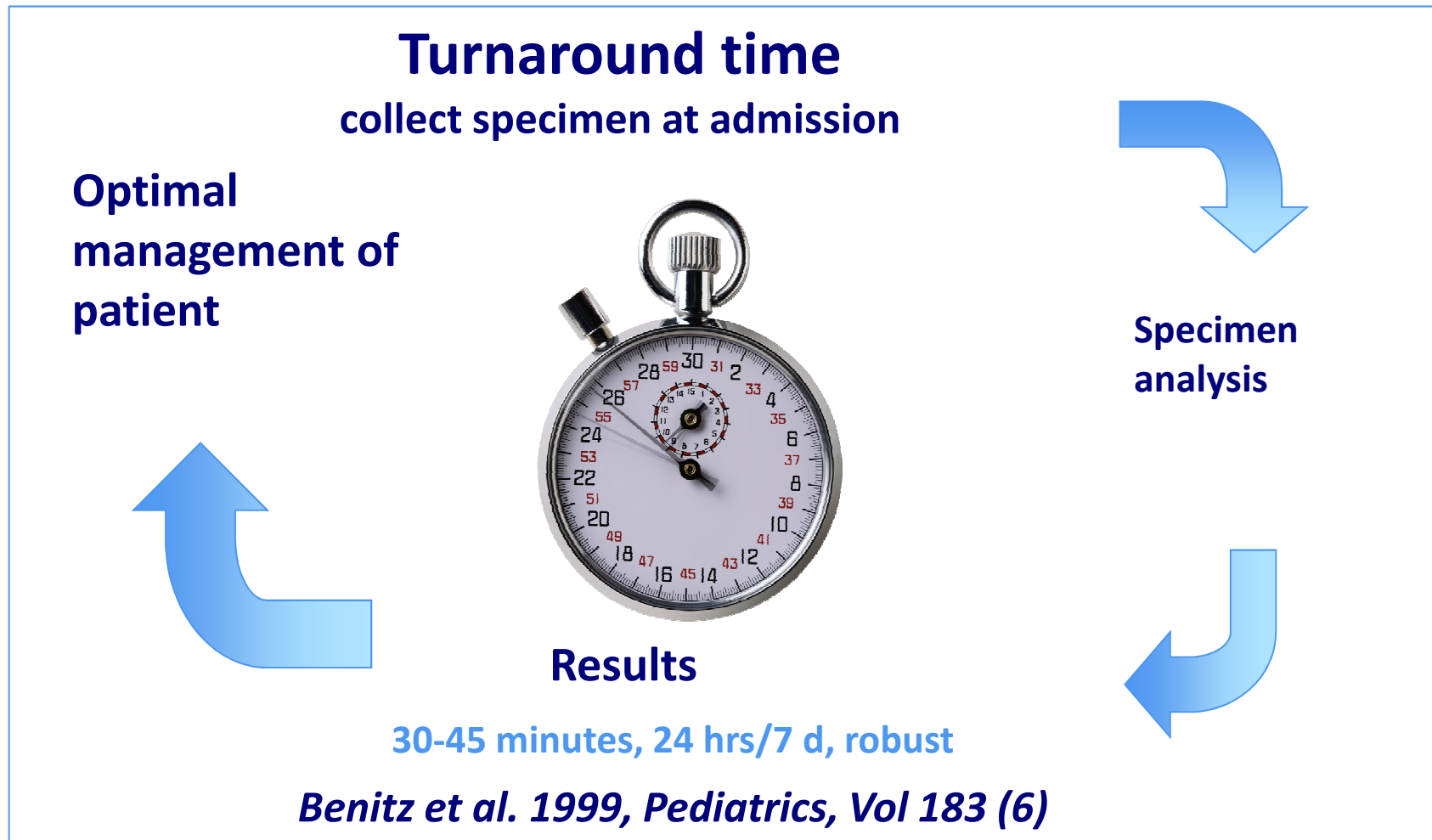
*(CDC 2010 - Belgian SCH 2003)*

# Prenatal culture-based screening: Limiting factors

- **Positive and negative predictive values**
  - **False-negative results**
    - Failure of GBS culture (oral ATB, feminine hygiene) or new acquisition
    - Up to 1/3 of GBS positive women at time of delivery
    - Continuing occurrence of EO GBS cases
  - **False-positive**
    - Unnecessary IAP

**Need for more accurate predictor of  
intrapartum GBS vaginal colonization**

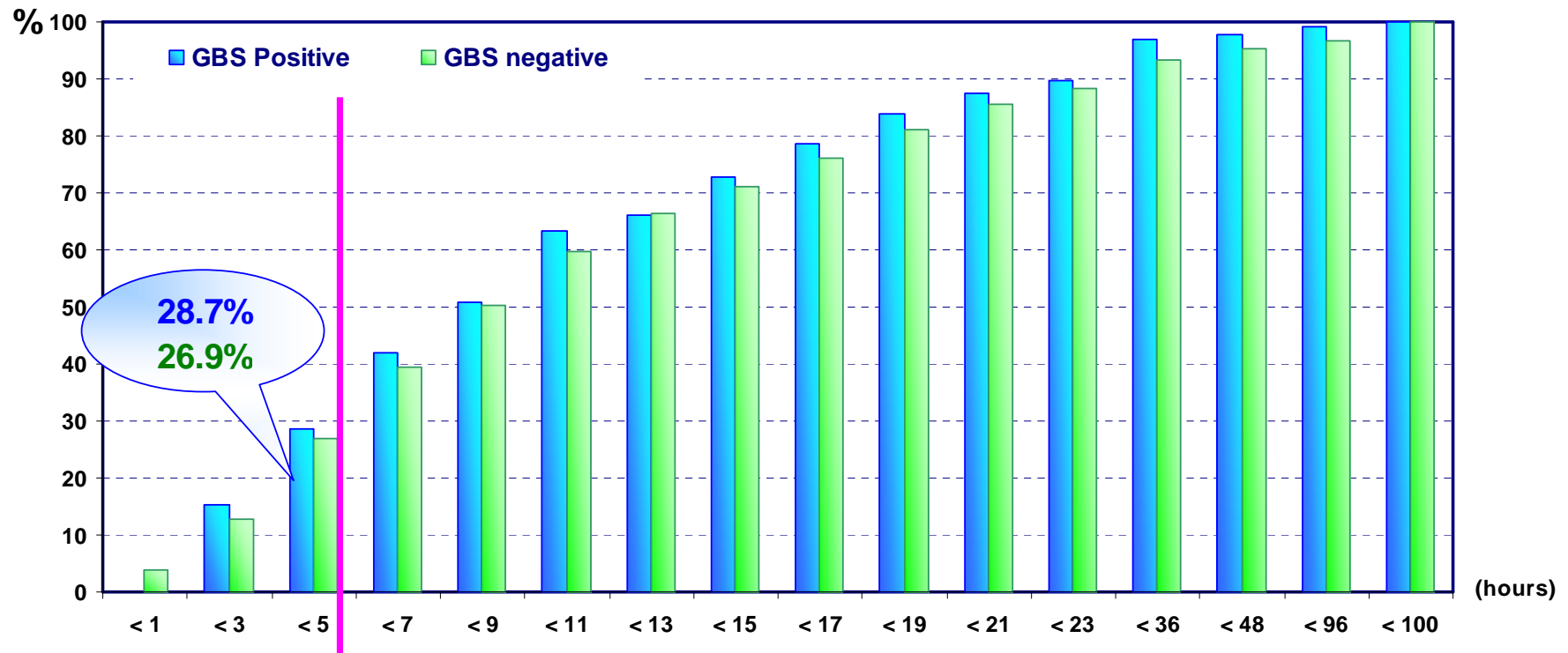
# Alternative to GBS prenatal screening: intrapartum screening



# Time between admission and delivery

Optimal time for IAP efficiency  $\geq 4$  hour

Cumulative histogram (% of patients) of time elapsed between admission to labor room and delivery for 532 women (sites CHR & CHBA)



*P. Melin, 2004 ICAAC #G499*

# Real Time PCR for intrapartumscreening

- Advance in PCR techniques & development of platforms
  - BD GeneOhm™ Strep B Assay (+/- 1 hr) (in laboratory)
  - Xpert GBS, Cepheid (35-75 min) (can be performed as a POCT)



# Rapid non-cultural GBS screening

## Real-time PCR

- **IDI Strep B (BD GeneOhm)**
  - Sensitivity : 94 %
  - Specificity : 96 %
  - PPV : 84 % and NPV : 98.6 %

*HD Davies et al., CID 2004 .*

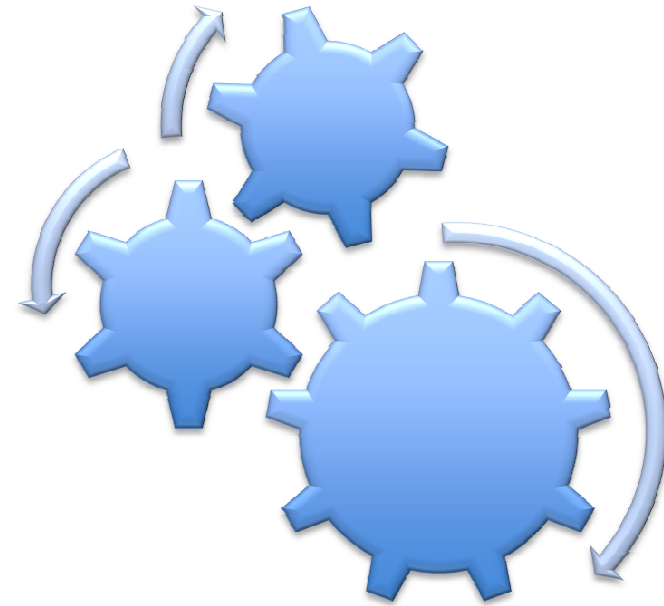
- **Xpert™ GBS**
  - Sensitivity : 92 %
  - Specificity : 95.6 %
  - PPV : 86.7 % and NPV : 97.4 %

**Intrapartum RT-PCRs surpass sensitivity of antenatal cultures**  
**Sensitivity // inoculum density = real time risk**



# Real-time PCR, very promising, but ...

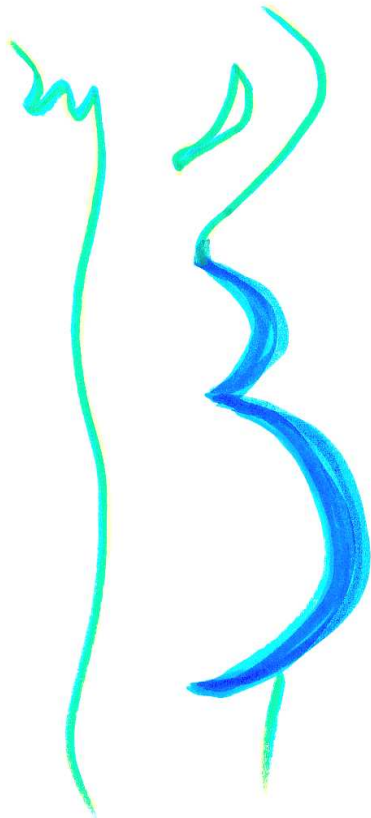
- **Still an expensive technology**
- **Logistic**
  - 24 hours 7 days
  - In the lab?
  - In the obstetrical department ?
- **In combination with prenatal screening strategy ?**
  - CDC 2010
- **No antimicrobial result**
  - In the future detection of R genes, but mixed microbiota !



**Coordination - Interaction**

# **CONCLUSION**

# In Europe, as globally



- **Neonatal GBS diseases**
  - EOD and LOD, a public health concern
  - IAP efficient for prevention of EOD
    - Best strategy still a matter of debate
    - Not 100% efficient
  - IAP not widely recommended
  - Need better data assessing more accurately the true burden
- **GBS vaccine eagerly expected**