Prévenir les infections périnatales à streptocoques du groupe B

Stratégie & nouveautés

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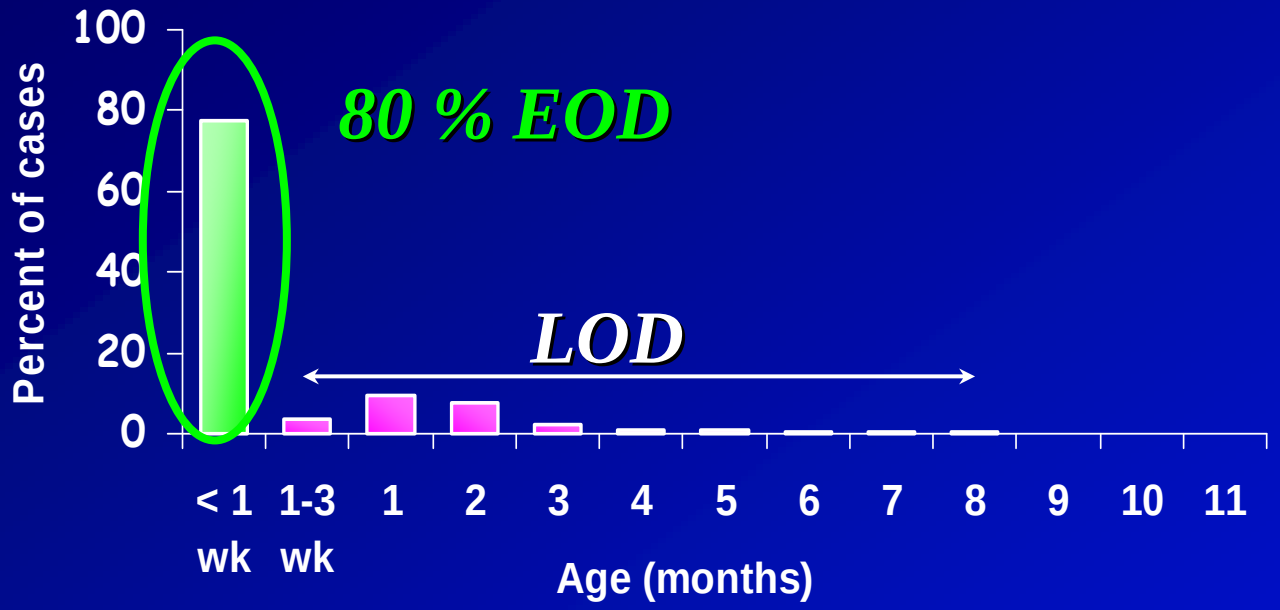
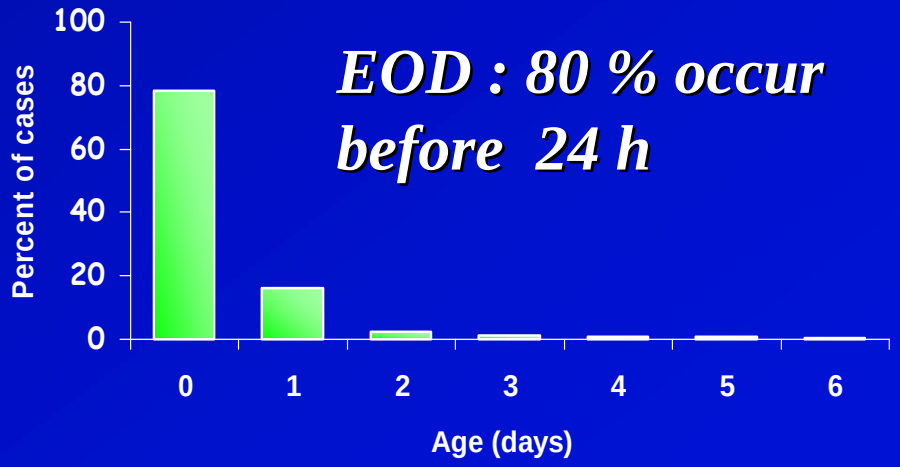
Background

- Important pathogen since the 1970s
- Perinatal GBS disease burden
  - Neonatal illness/death, long-term disability
    - Belgium : > 300 sepsis ± meningitis /year
    - 34.8% of EOD through 1991-2005
      - (No.2 = *E.coli* : 12.5%)
  - Maternal morbidity
- Neonatal direct costs

GBS Neonatal Infections

A. Schuchat, Clin Microb Rev 1998;11:497-513





EOD : 80 % occur before 24 h

"Evidence-based"

Prevention of perinatal Group B streptococcal infections

Guidelines from Belgian Council of Hygiene- July 2003

http://www.health.fgov.be/CSH_HGR

General Recommendations & Specific suggestions

WORKING GROUP :

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Gynecologists-obstetricians
Pediatrician-neonatologists
Microbiologists

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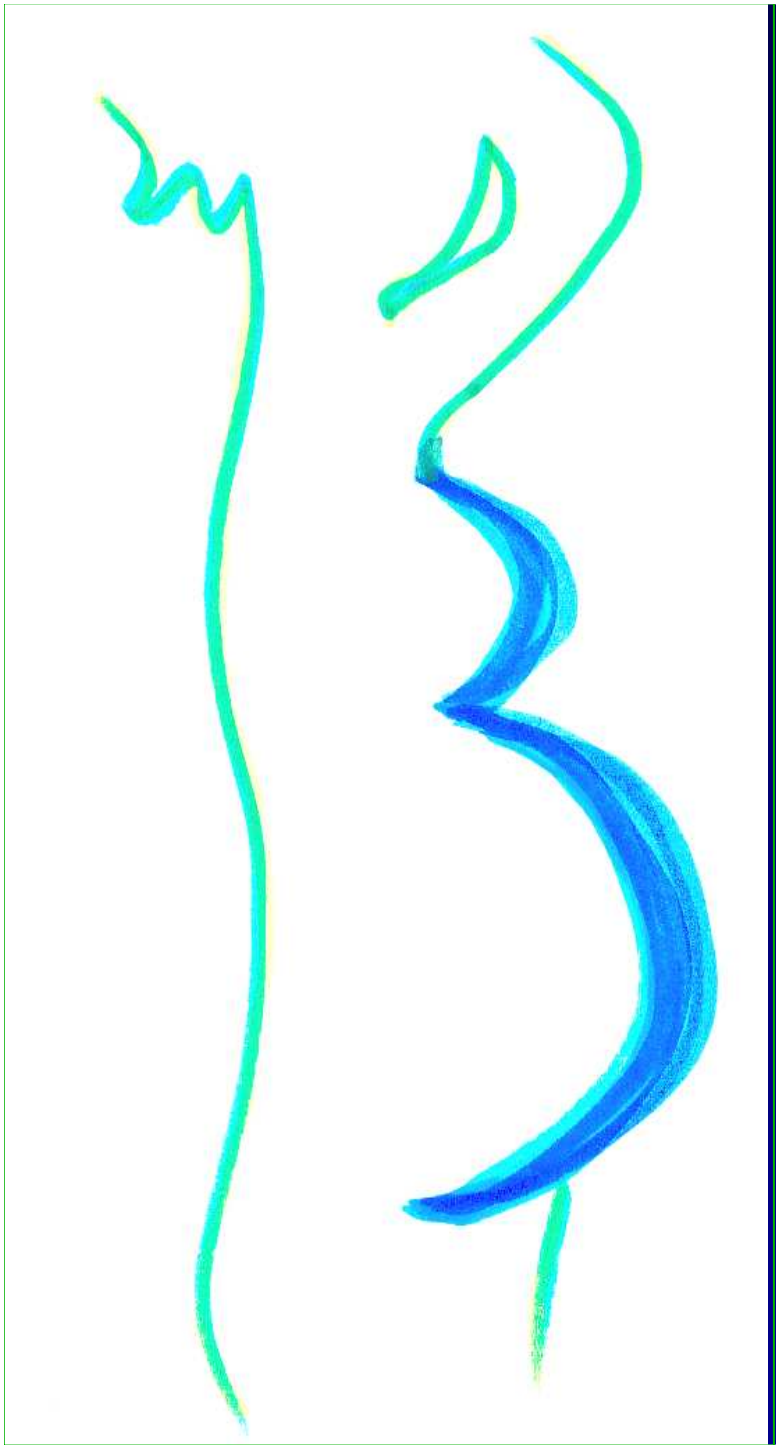
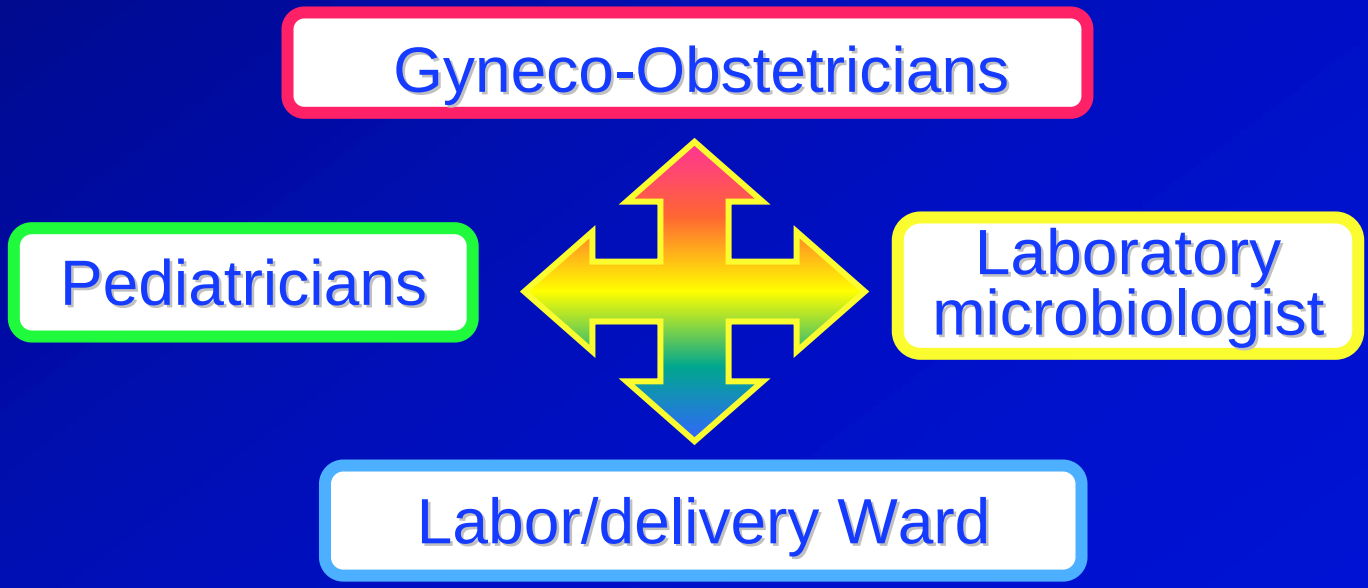


PRO SCREENING

Intrapartum antimicrobial prophylaxis-IAP

Universal prenatal screening at 35-37 weeks gestation

Risk-based approach reserved for women with unknown GBS status at time of labor.



Adhesion to a common protocol is a key of success
Multidisciplinary collaboration is mandatory

Why IAP ?
Why a Screening-based approach ?

- Risks for GBS EOD
- Goals of IAP
- Effectiveness
- Belgian choice
- Concerns about use of prophylaxis
- Belgian results

GBS VERTICAL TRANSMISSION

GBS colonized mothers

60 - 40 %

40 - 60 %

Non-colonized newborns

Colonized newborns

Risk factors

2 - 4 %
GBS EOD

96 - 98 %
Asymptomatic

sepsis
pneumonia
meningitis
long term disability

GBS maternal colonization

Risk factor for early-onset disease (EOD):

vaginal GBS colonization at delivery

- **GBS carriers**
  - **10 - 30 % of women**
  - **Clinical signs not predictive**
  - **Dynamic condition**
  - **Prenatal cultures late in pregnancy can predict delivery status**

Additional Risk Factors for Early-Onset GBS Disease

- **Obstetric factors:**
  - Prolonged rupture of membranes,
  - Preterm delivery,
  - Intrapartum fever
- **GBS bacteriuria**
- **Previous infant with GBS disease**
- **Immunologic:**
  - Low specific IgG to GBS capsular polysaccharide

No difference in occurrence either in GBS Positive or Negative women, except intrapartum fever

Lorquet S., Melin P. & al.

J Gynecol Obstet Biol Reprod 2005

GBS EOD - Belgian data

- Incidence
  - 1985: 3/1000 live births
  - 1990: 3 cases + 4 likely cases/1000 live births
  - 1999, estimation : 2/1000 live births
- Meningitis : 10 %
- Mortality > 14 %
- 60 % EOD (130 cases) : WITHOUT any maternal/obstetric risk factor
- Prenatal screening
  - Recto-vaginal cultures : 13-25 % GBS Positive

P. Melin, 2001 - Reference laboratory for GBS.

Prevention of perinatal GBS EOD

- **Intrapartum antibiotics**
  - **Highly effective at preventing EOD in women at risk of transmitting GBS to their newborns (≥ 4 h)**

INTRAPARTUM ANTIMICROBIAL PROPHYLAXIS (IAP)

- **Main goal :**
  - **To prevent 70 to 80 % of GBS EO cases**
- **Secondary :**
  - **To reduce peripartum maternal morbidity**

How best to identify women at risk ?

CDC 1996 recommendations

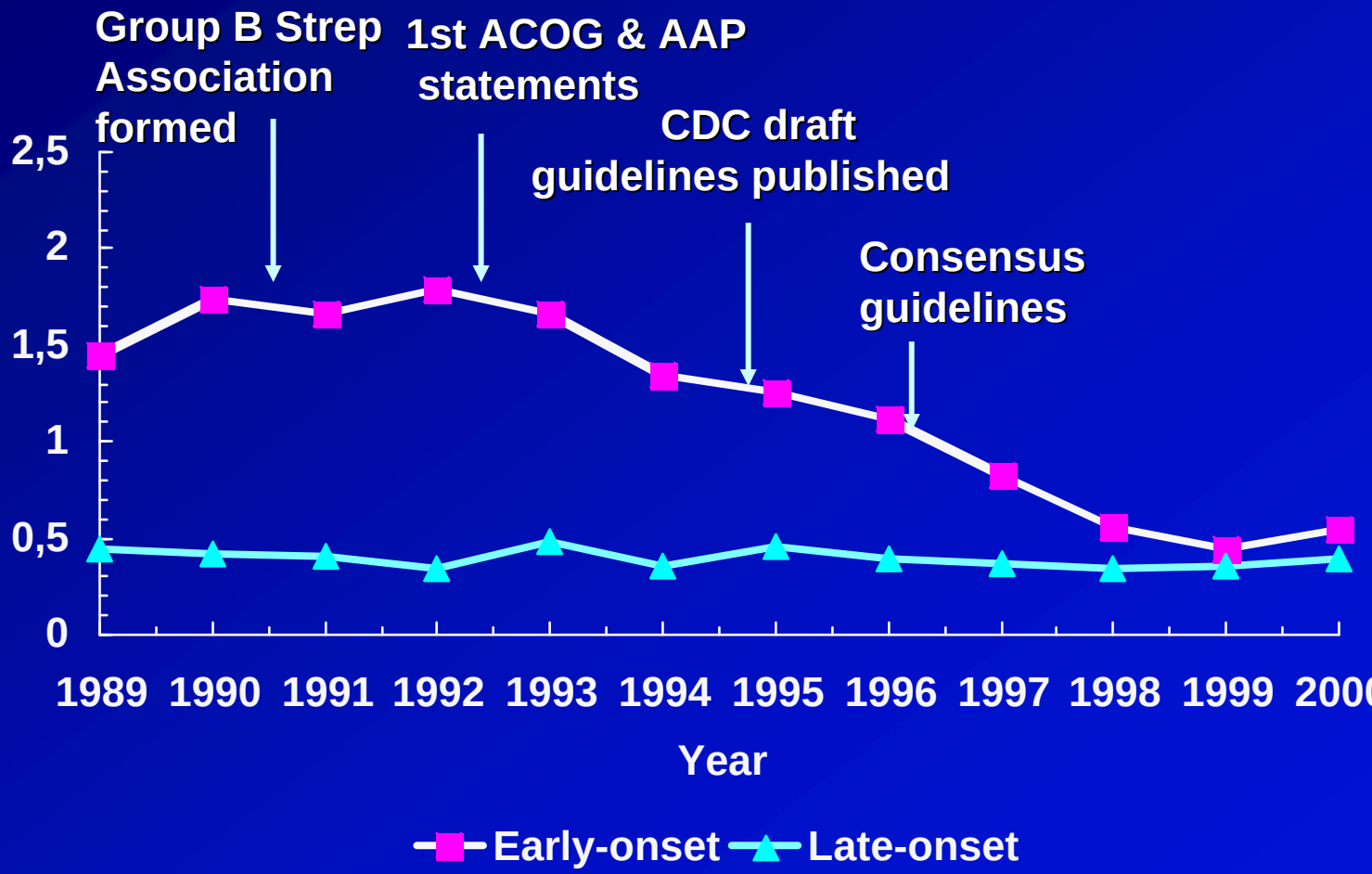
« IAP »

35-37 wks Screening-based strategy

Or

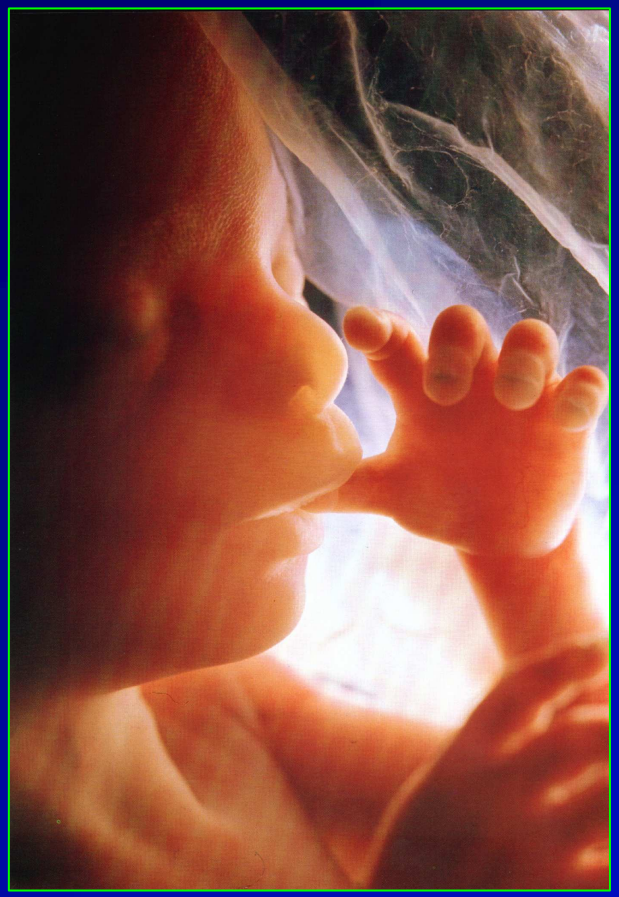
Risk factors-based strategy

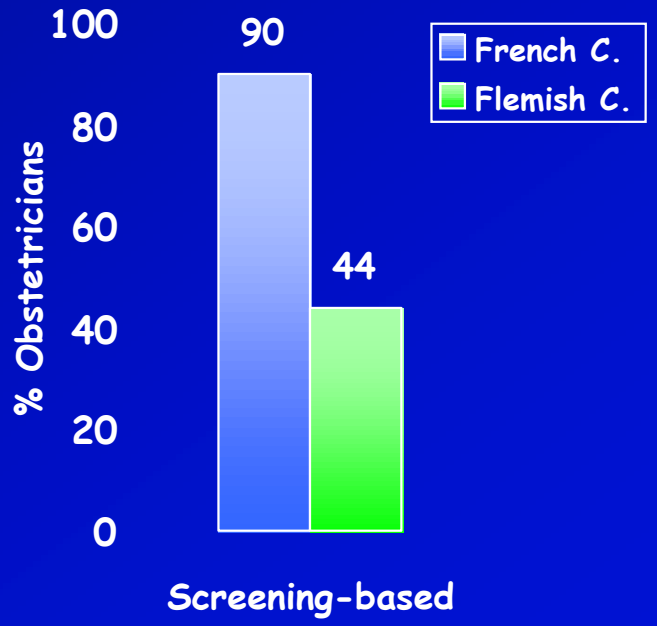
Impact of prevention practices
Rate of Early- and Late-onset GBS Disease in the 1990s, U.S.



S. Schrag, New Engl J Med 2000

Screening for GBS or risk-factors ?





P.Melin, 40th ICAAC, 2000
L.Mahieu, 2000, J Obst Gyn;5:460-4

Effectiveness of both CDC 1996 approaches

Schrag S. et al. N Engl J Med 2002; 347:233-9

"RF" easier and cheaper than "screening" BUT

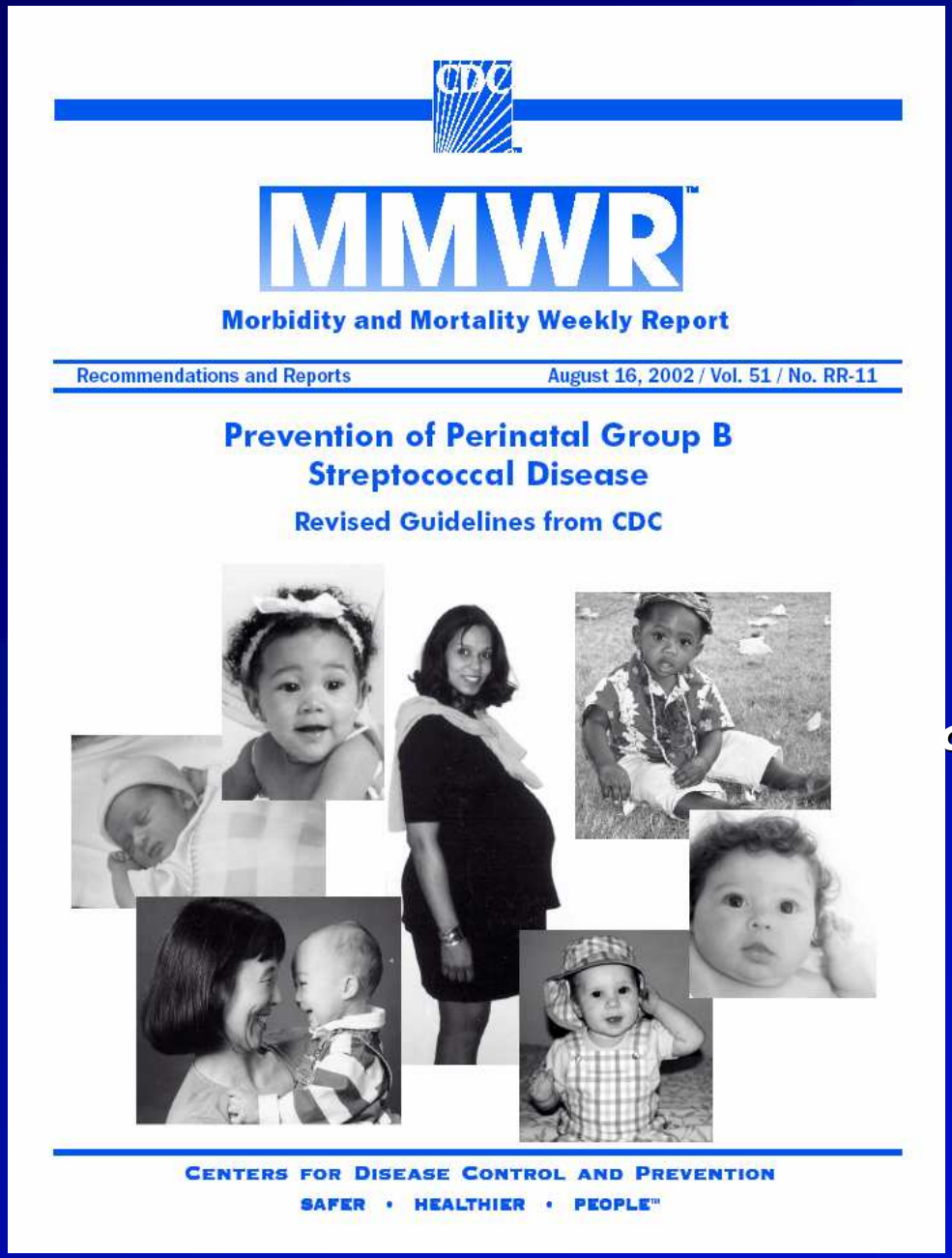
- **Population-based surveillance study, U.S.**
  - **312 GBS EOD ; ± 600 000 live births**
    - **AUDIT (5144 files): « IAP given when mandatory »**
      - **52 % of all deliveries had screening**
      - **IAP given more often if « GBS Positive screening » than if presence of >= 1 RF**

"Screening" > 50 % more effective than "RF"

Why is Screening more protective than the risk-based approach ?

Broader coverage of « at-risk » population

- **Captures colonized women without obstetric RF**
- **High level of compliance with recommendations**
- **Enhanced compliance with risk-based approach cannot prevent as many cases as universal screening**



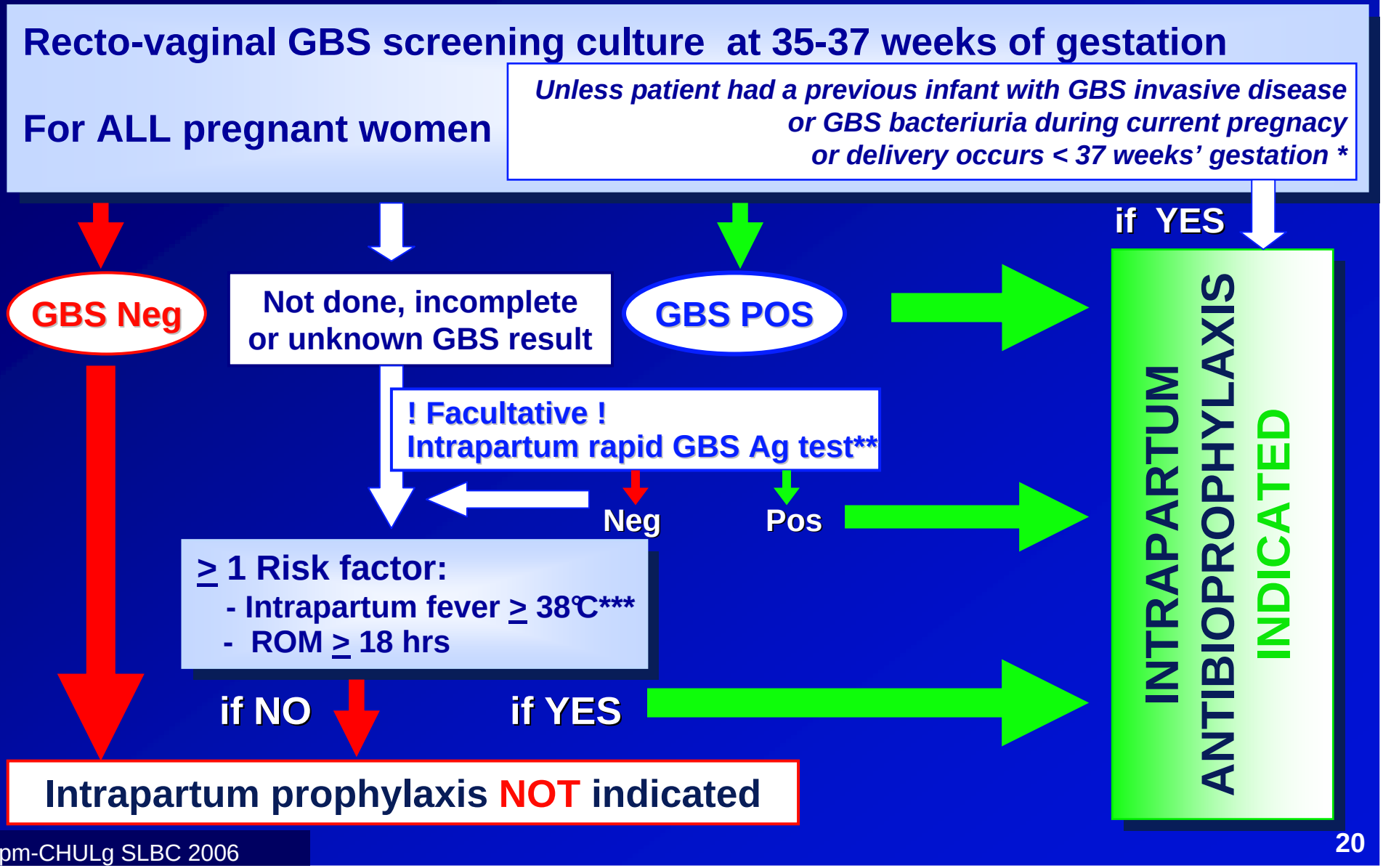
CDC
The Recommendations

MMWR, Vol 51
(RR-11) August 2002

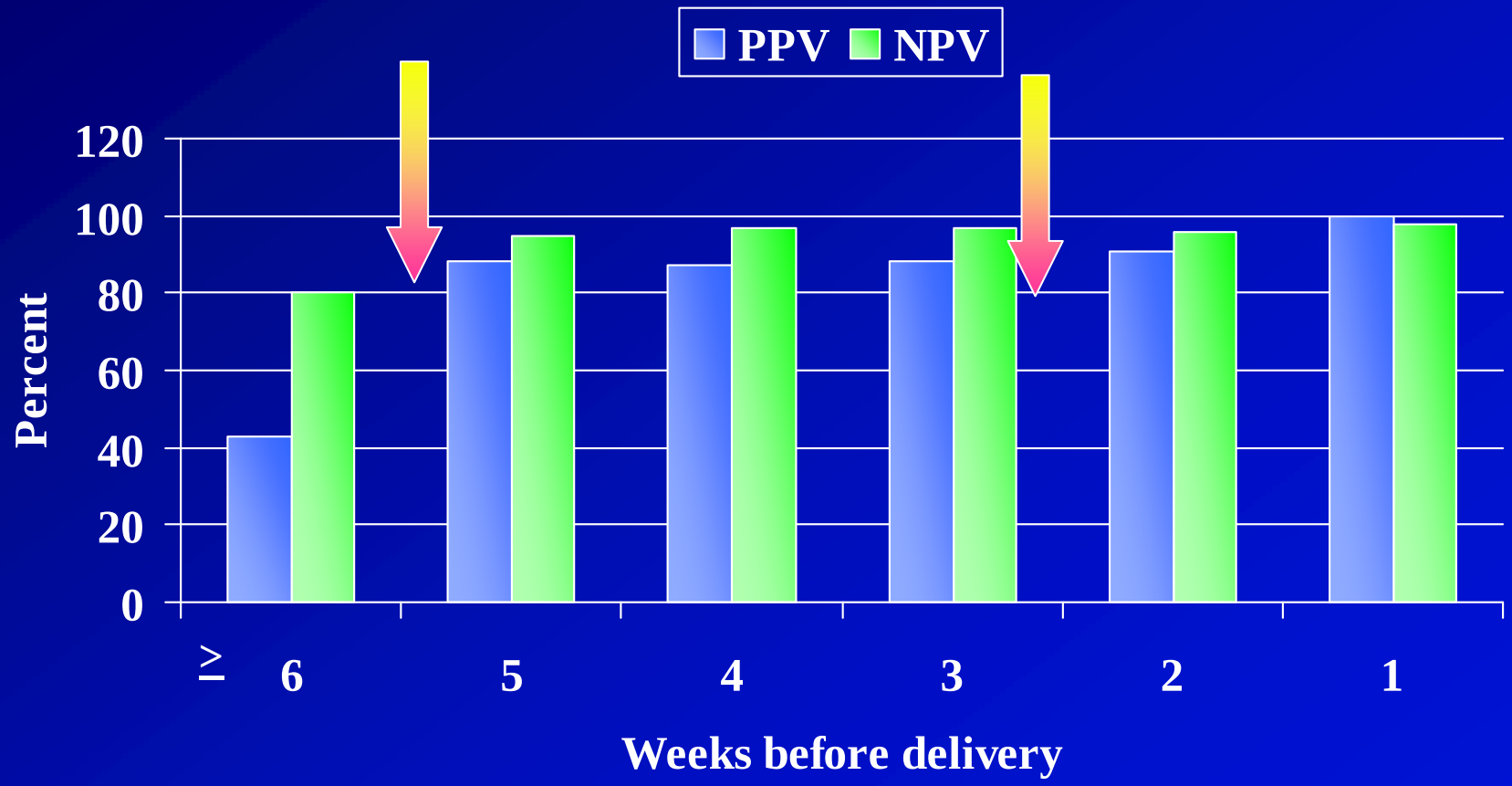
Universal prenatal screening
& RF reserved for unknown GBS culture results

Endorsed by AAP and by ACOG in 2002

Screening-based strategy for prevention of GBS perinatal disease *(Belgian CH, 2003)*



GBS Screening: Predictive Value of Antenatal Cultures by Interval to Delivery



N=826; 26.5% GBS carriers

Yancey et al., OB GYN 1996;88:811-5.

Crucial conditions to optimize SCREENING

❖ **WHEN**	**35-37 weeks**
❖ **WHO**	**ALL the pregnant women**
❖ **Specimen**	**Vaginal + rectal swab(s)**
❖ **Collection**	**WITHOUT speculum**
❖ **Transport**	**Transport/collection device** (non nutritive medium: Amies/Stuart)
❖ **Request form**	**To specify prenatal « GBS » screening + *expected address for delivery***

(CDC 2002 - Belgian HC 2003)

Prenatal GBS screening : Laboratory procedure *(Belgian HC, 2003)*

Minimum:

35-37 wks V+R

↓

Selective enrichment broth (eg.LIM)

Overnight, 35-37°C

↓

Sub-culture onto "Granada" agar

Overnight, 35-37°C anaerobically

Presence of orange colonies = GBS

Absence of orange colonies

POSITIVE screening

Negative screening

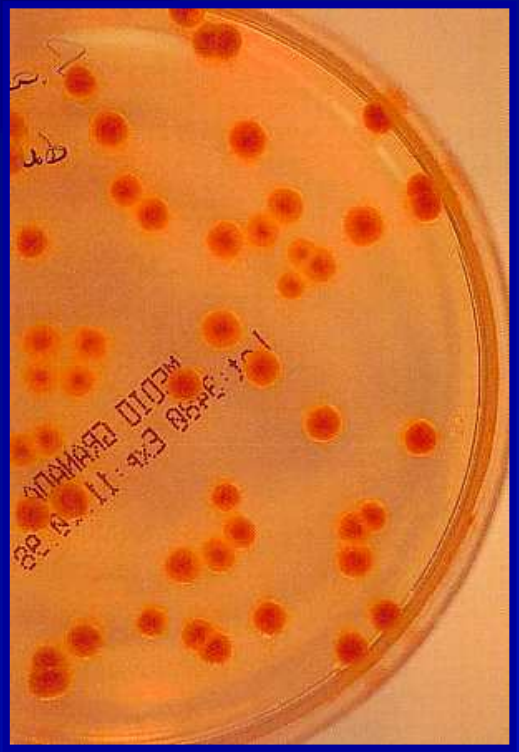
Selective enrichment broth

Lim Broth =

Todd Hewitt broth + colistin (15 µg/ml) + nalidixic acid (10 µg/ml)

Overnight at 37°C and sub-cultured onto « Granada » (and/or BA ou BA+CNA)

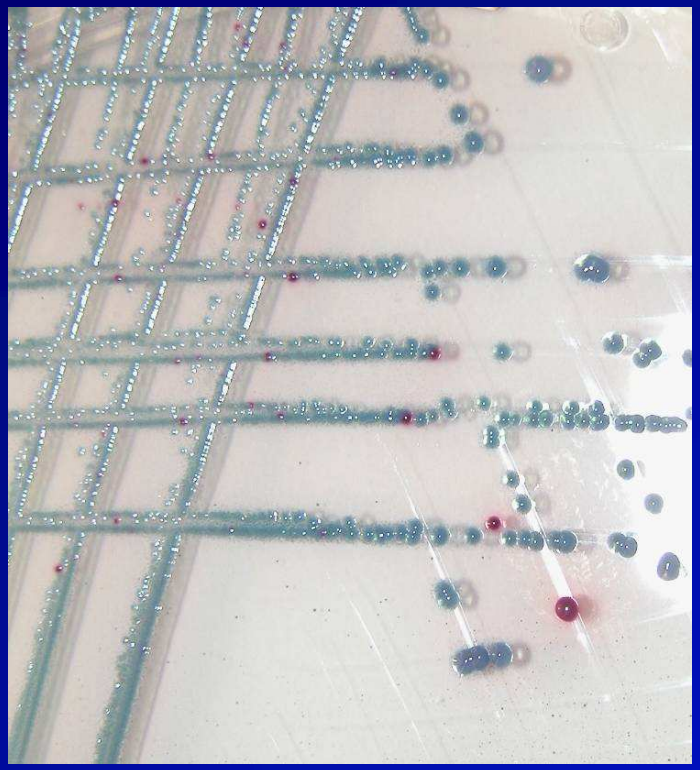
Granada medium agar or BD™ Group B Streptococcus Differential Medium

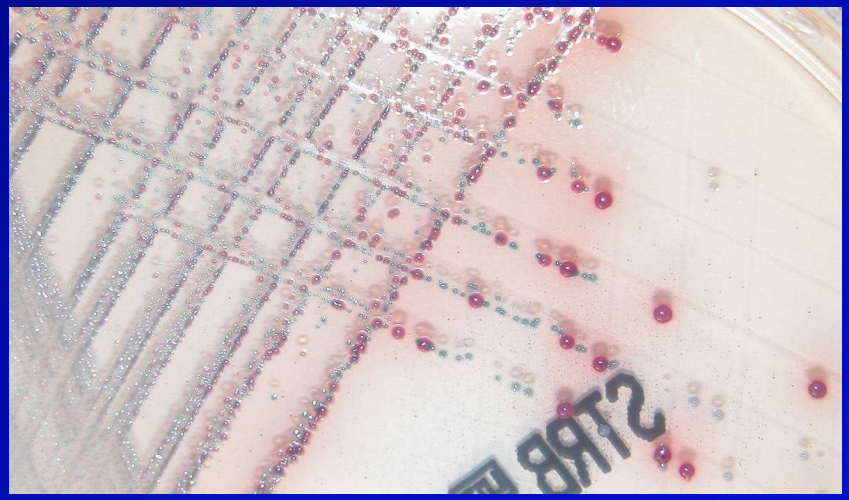


Orange color:

Specific for GBS // β-hemolysis

Strepto B ID agar - BioMérieux



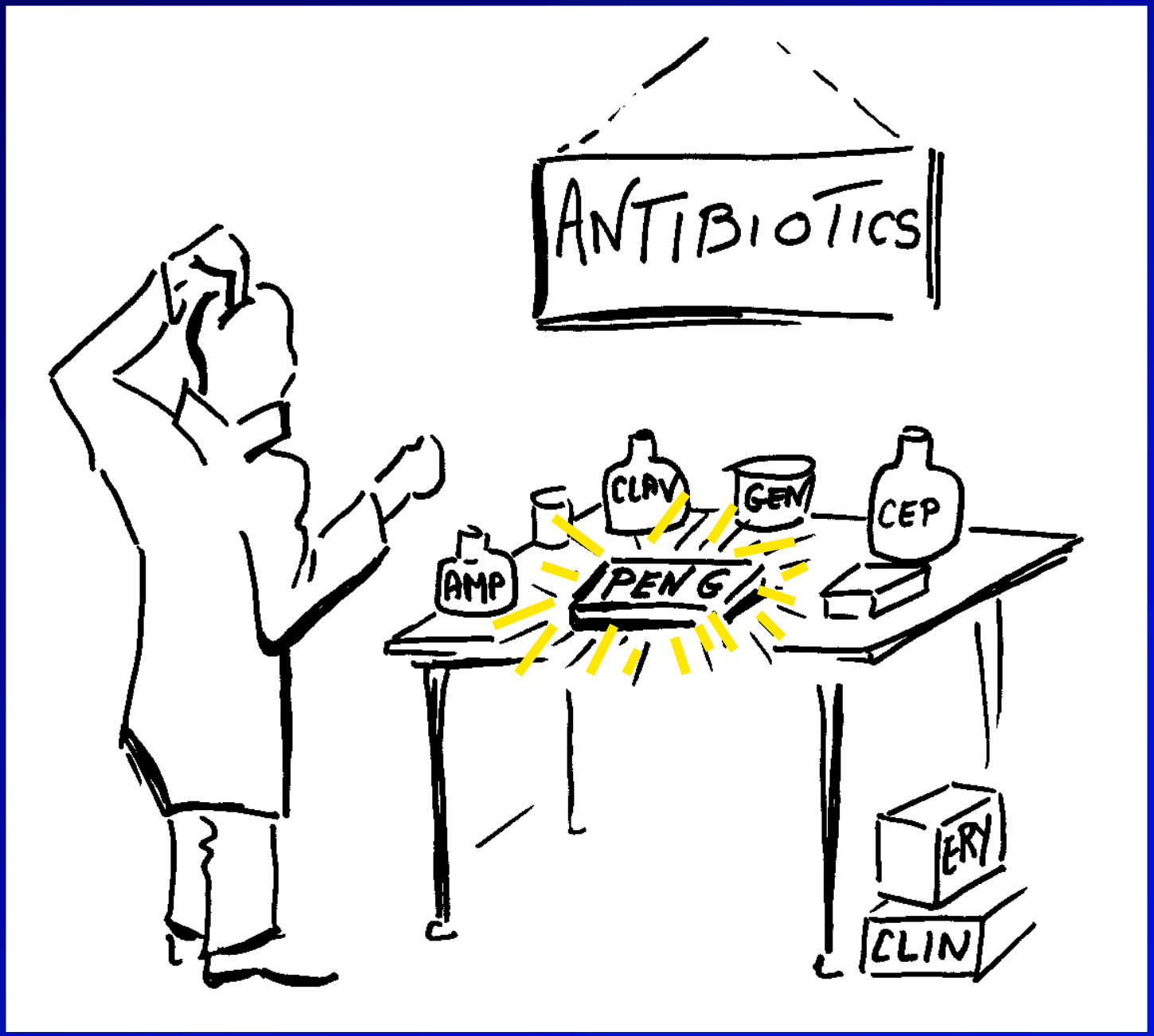


High sensitivity
for growth of GBS
GBS = pink to red colonies

Not 100 % specific for GBS: Id to confirm (latex)

What to do in case of Positive GBS screening ?

- Send results to requesting doctor ***and a copy to expected site for delivery***
- DO NOT treat during pregnancy if asymptomatic
  - *(! To treat if GBS bacteriuria !)*
- To schedule IAP


ANTIBIOTICS
AMP
CLAV
GEN
PEN G
CEP
ERY
CLIN

Intrapartum Antibio-Prophylaxis

(Belgian HC 2003)

- **Penicillin G**
  - *5 millions U, IV initial dose, then 2,5 millions U IV every 4 hours until delivery.*

- **Ampicilline**
  - *2 g IV initial dose, then 1 g IV every 4 h until delivery.*
  - **Acceptable** alternative , **but** broader spectrum, potential selection of R bacteria

Intrapartum Antibio-Prophylaxis
If penicillin allergy *(Belgian HC 2003)*

- *Patients at low risk for anaphylaxis*
  - Cefazolin
    - 2 g IV initial dose, then 1g IV every 8 h until delivery.
- *Patients at high risk for anaphylaxis*
  - Clindamycin
    - 900 mg IV every 8 hours until delivery.
    - *If GBS resistant to clindamycin : ask for infectiologist opinion*

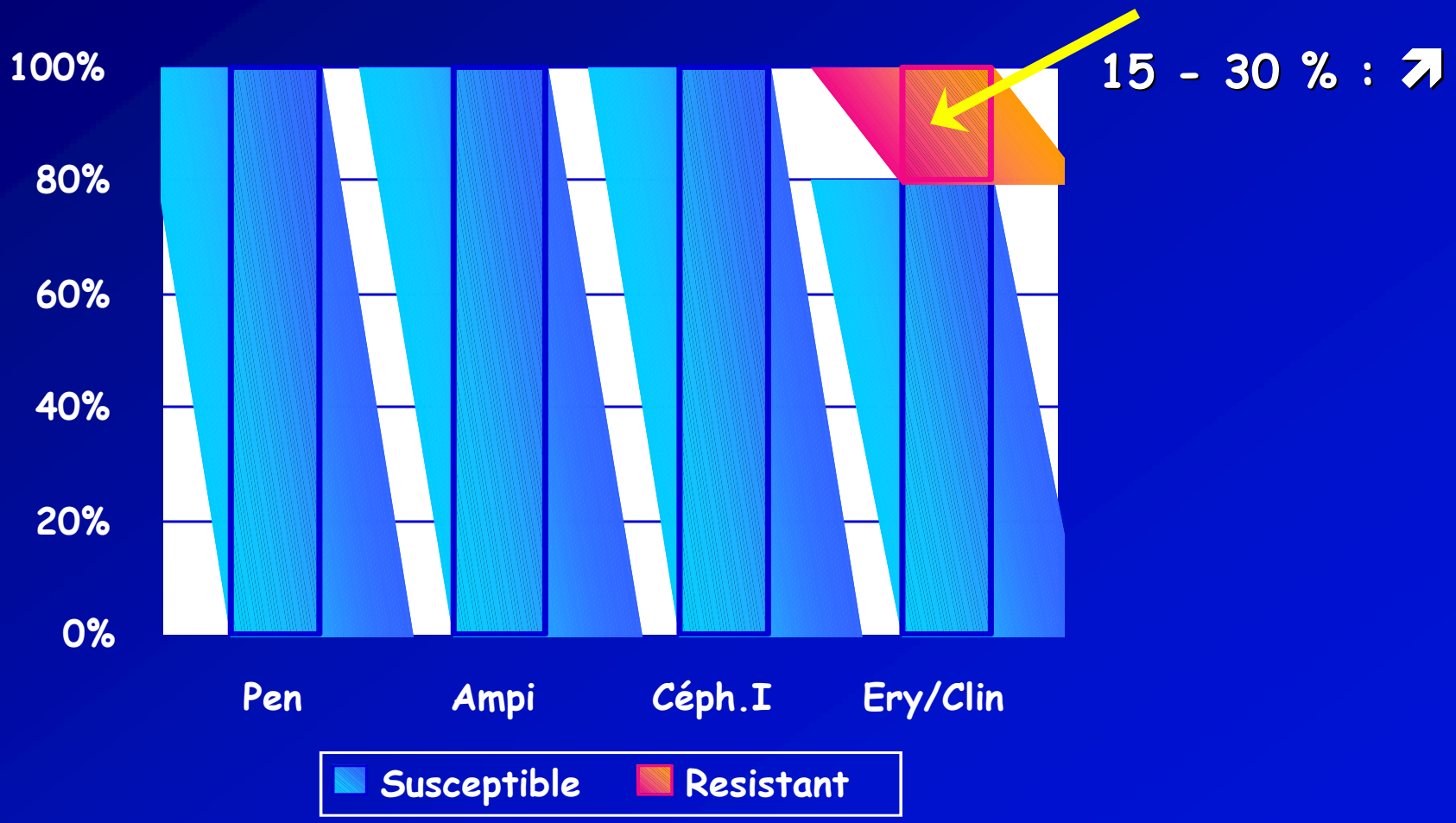
Feasibility in Belgium

- Screening
  - Follow-up visit already scheduled around 35-37 wks gestation
  - Accessability to laboratories
- IAP (*intra-venous*)
  - Most of deliveries occur at hospital

Concerns about potential adverse / unintended consequences of prophylaxis

- Allergies
  - Anaphylaxis occurs but rarely
- Changes in incidence or resistance of other pathogens causing EOD
  - Data are complex …
  - BUT Most studies: stable rates of « other » sepsis
- Changes in GBS antimicrobial resistance profile

Susceptibility pattern of GBS



Melin et al. 2002, ICAAC, Abstract ...

Interpretation criterian *(MH with blood)*

(CLSI 2006)

	Zone Diameter (mm)			MIC (mg/L)		
	S	I	R	S	I	R
Penicillin	**≥ 24**	**-**	**-**	**≤ 0.12**	**--**	
Erythromycin	**≥ 21**	**16-20**	**≤ 15**	**≤ 0.25**	**0.5**	**≥ 1**
Clindamycin	**≥ 19**	**16-18**	**≤ 15**	**≤ 0.25**	**0.5**	**≥ 1**

Phenotypes of resistance to macrolide - lincosamide : Dtest

cMLS Erythro R & Clinda R

iMLS Erythro R & Clinda S/I/R with Dtest +

M Erythro R & Clinda S with Dtest -

Concerns about potential adverse / unintended consequences of prophylaxis

- Management of neonates
  - Increase of unecessary evaluation
  - Increase of unecessary antimicrobial treatments

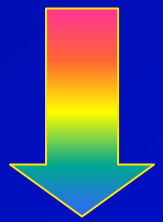
Management of neonates at risk for GBS EOD

***Rem.*: 90% of GBS EOD are symptomatic < 24 h of live**

Neonates born to women who received IAP

Symptomatic NN / asymptomatic NN

At low/at high risk



To minimize unnecessary evaluation and antimicrobial treatment

Management of symptomatic newborns at risk for GBS EOD

Clinical signs of sepsis

1- Full diagnostic evaluation *

2- Empiric antibiotherapy

(Ampicillin + aminoside)

*:- Full blood cell count (FBC) + differential
- CRP
- Bloodculture
- (Lumbar P.)
- Chest Xray
- Endotracheal culture (if intubated or if resp.distress. or Rx infiltrate)

Rem. ! NOT recommanded :
1- Urinary GBS Ag
2- « Monitoring » cultures

Management of asymptomatic newborns « *at high risk* » for GBS EOD

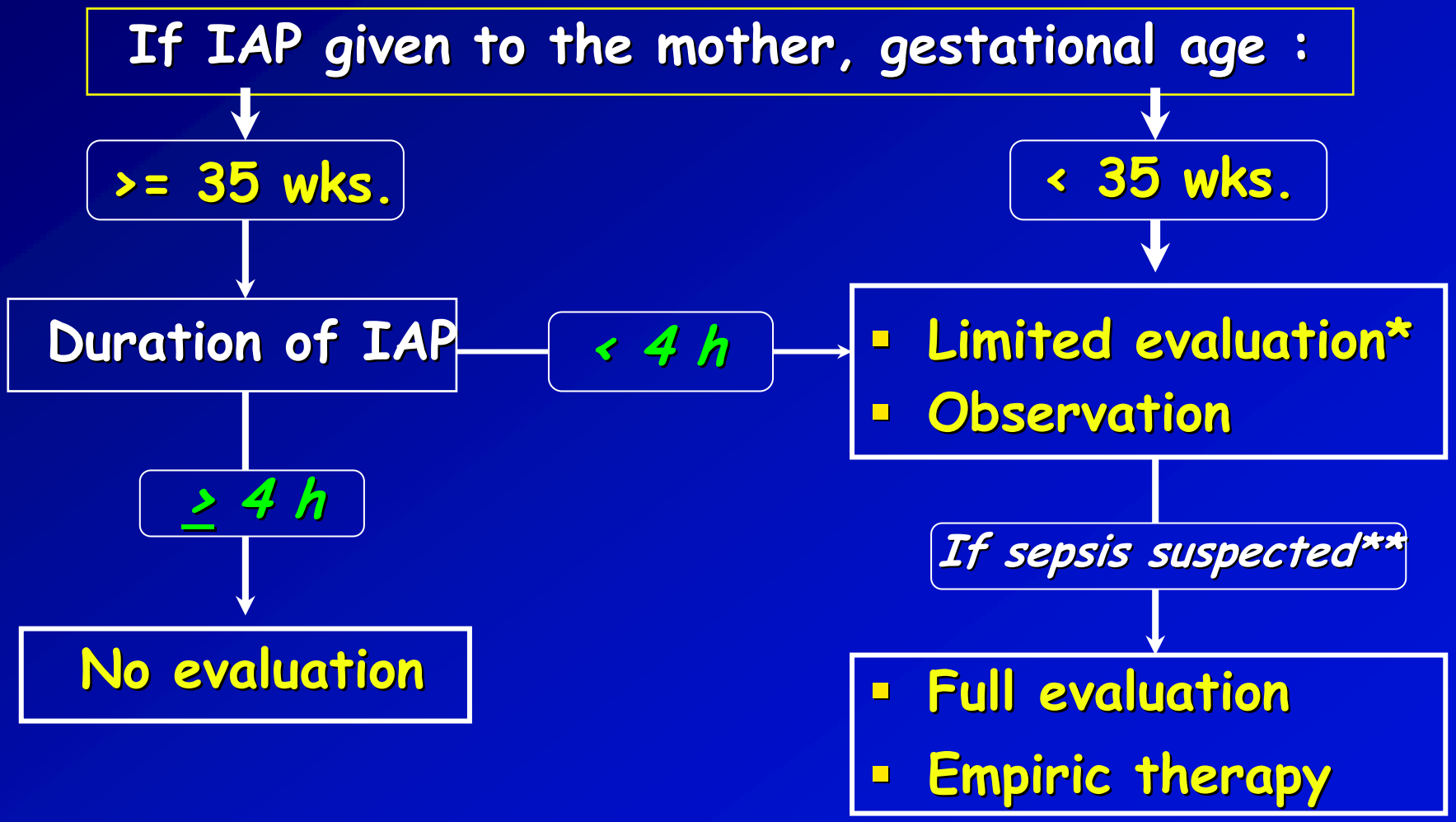
If antibiotherapy given to mother for

- Suspicion of chorioamnionitis or
- Premature AND prolonged rupture of membranes

Full evaluation

Empiric therapy

Management of asymptomatic newborns « *at low risk* » for GBS EOD

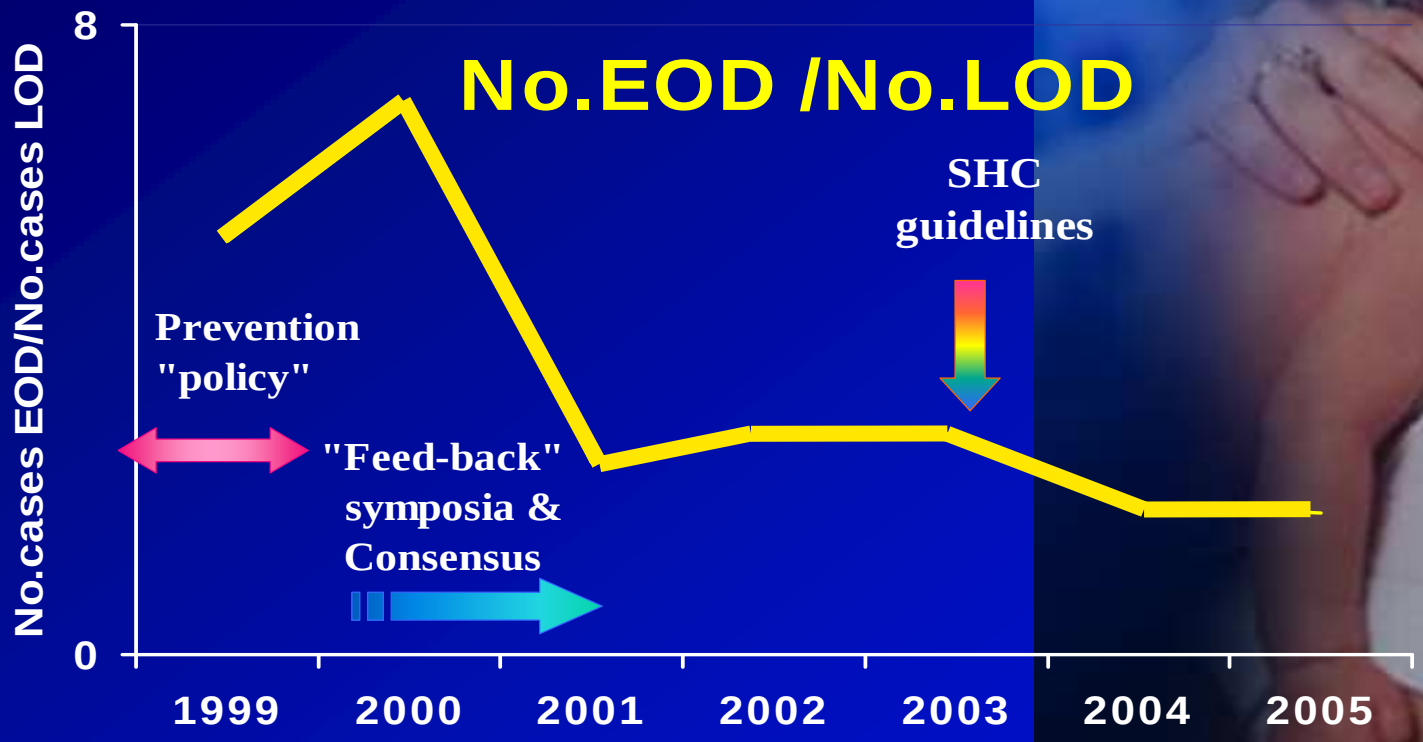


Duration of antibiotherapy

Threatened preterm delivery

Planned caesarean delivery for GBS colonized women

Preventive strategies
Current Belgian benefits



Melin P. et al. Belgian GBS Ref.Lab, ICAAC2006, Abstract #G-0864

Conclusions & perspectives

Prevention of GBS perinatal Diseases
PRO-SCREENING

Currently the best choice but NOT the ideal strategy

Temporary, waiting for vaccines, other approach

- To implement in the daily practice
- V+R Screening method
- !! Transmission of results !!
- Epidemiological surveillance

Alternative to prenatal GBS screening: intrapartum screening

Collect specimen at admision

Specimen analysis

Results

Optimal management of patient

30 - 45 minutes

Benitz et al. 1999, Pediatrics, Vol 183 (6)

Perspectives

- Other investigated approaches
  - Real time PCR for intrapartum screening

(GenExpert - Cepheid)

Belgian Challenge =
To prevent annually > 200 cases of neonatal GBS EOD

GDLux Challenge =
To prevent annually > 10 cases
of neonatal GBS EOD

Key GBS Resources

- MMWR : August 16, 2002 / 51(RR11); 1-22
- ACOG Comm Opin 2002, N°279
  - Obstet Gynecol, 2002;100:1405-12
- CDC 's GBS Internet page
  - http://www.cdc.gov/groupBstrep/
- Conseil supérieur d'hygiène *(brochure strep B)*
  - http://www.health.fgov.be/CSH_HGR