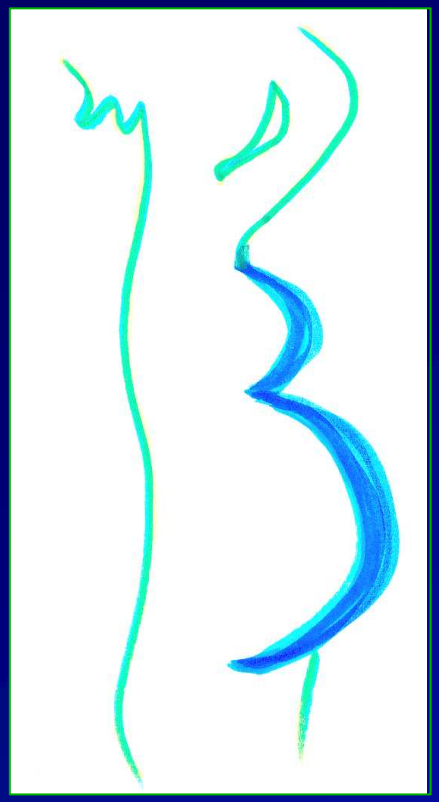


Prevention of perinatal group B streptococcal diseases

Update & Guidelines

Pierrette Melin

Medical microbiology, University hospital of Liege
Belgian reference laboratory for GBS

TRANSMISSION « Mother-Baby »

GBS colonized mothers

60 - 40 %

Non-colonized newborns

40 - 60 %

Colonized newborns

96 - 98 %
Asymptomatic

2 - 4 %
GBS EOD

sepsis
pneumonia
meningitis
long term sequelae

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

Prevention of perinatal GBS disease

- 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

35-37 wks Screening-based strategy

Or

Risk factors-based strategy

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.

Screening for GBS

Useful or **not** ?

Effectiveness of both CDC 1996 approaches

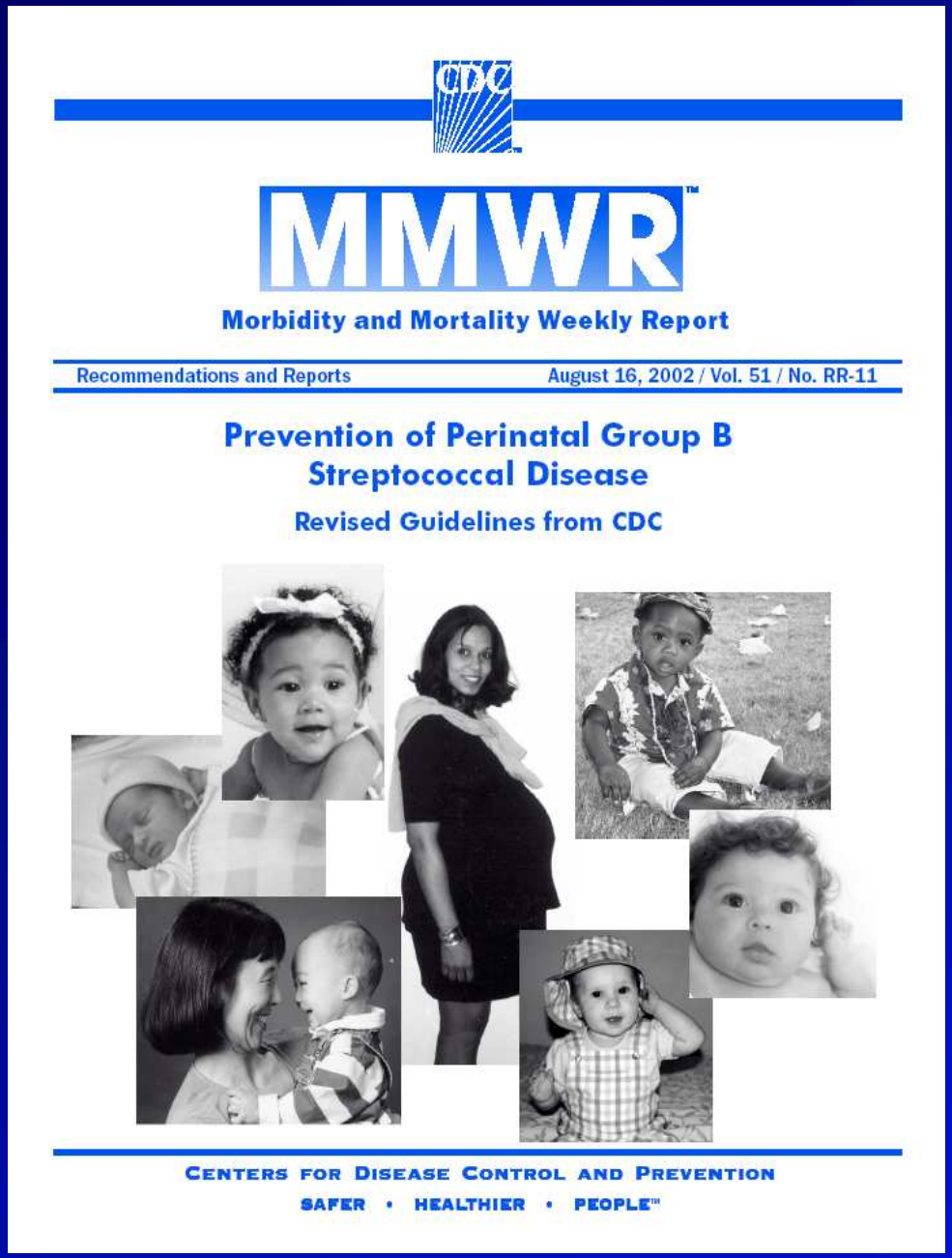
Schrag S. et al. N Engl J Med 2002; 347:233-9

*"RF" easier and cheaper than "screening" **BUT***

- Population-based surveillance study, U.S.
  - > 600 000 live births
    - **"Screening" > 50 % more effective than "RF"**
    - AUDIT : « IAP given when mandatory »
      - Given more often if « GBS Positive screening » than if presence of >= 1 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

"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 : **Gynecologists-obstetricians**
Pediatrician-neonatologists
Microbiologists
French/ Flemish
University/non-university

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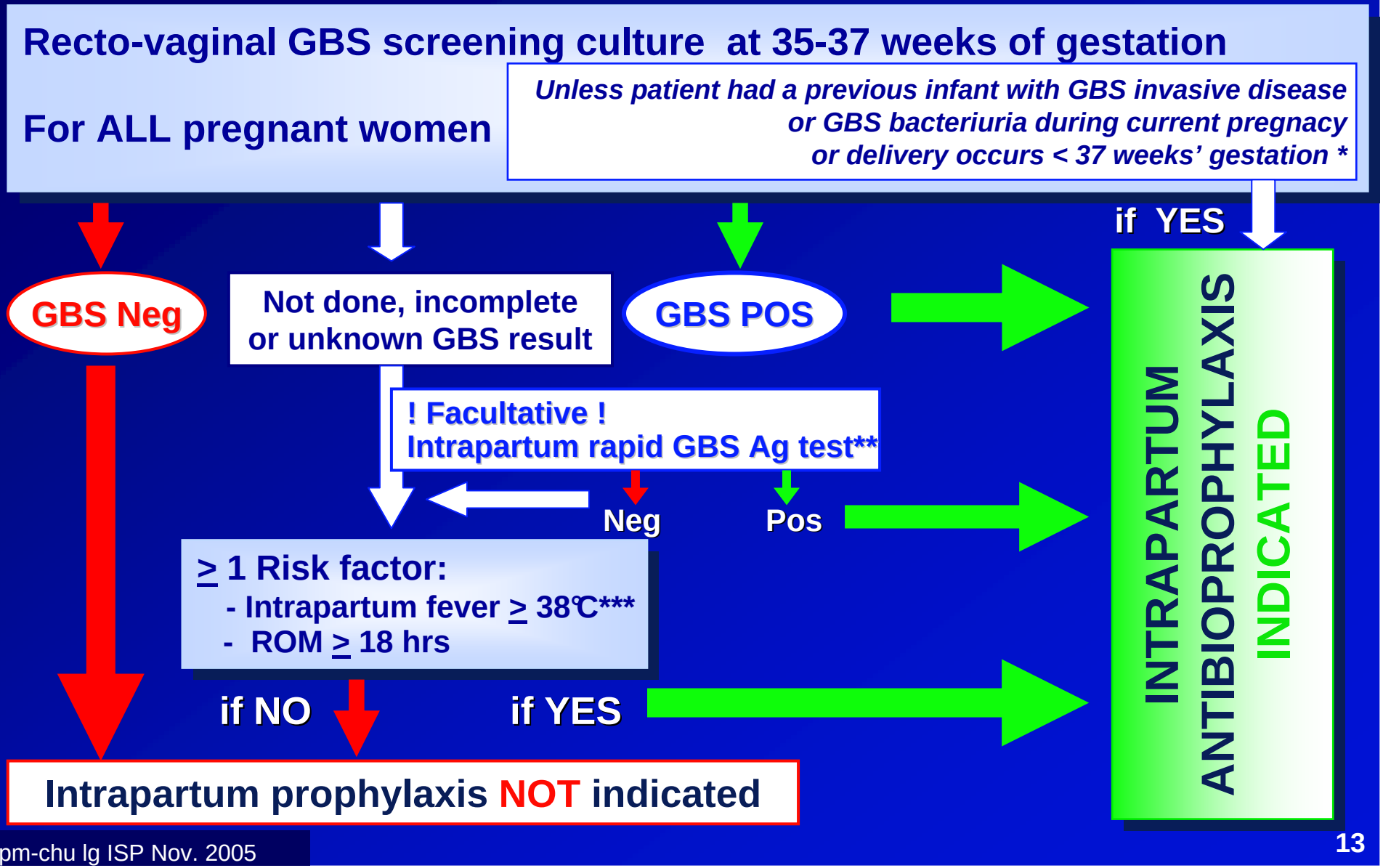
Melin P.
Naessens A.
Potvliege C.
Temmerman M.
Tuerlinckx D.
Van Eldere J.

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



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

Minimum:

V+R or V&R

↓

LIM broth

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

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

Alternative to prenatal GBS screening: intrapartum screening

Collect specimen at admision

Specimen analysis

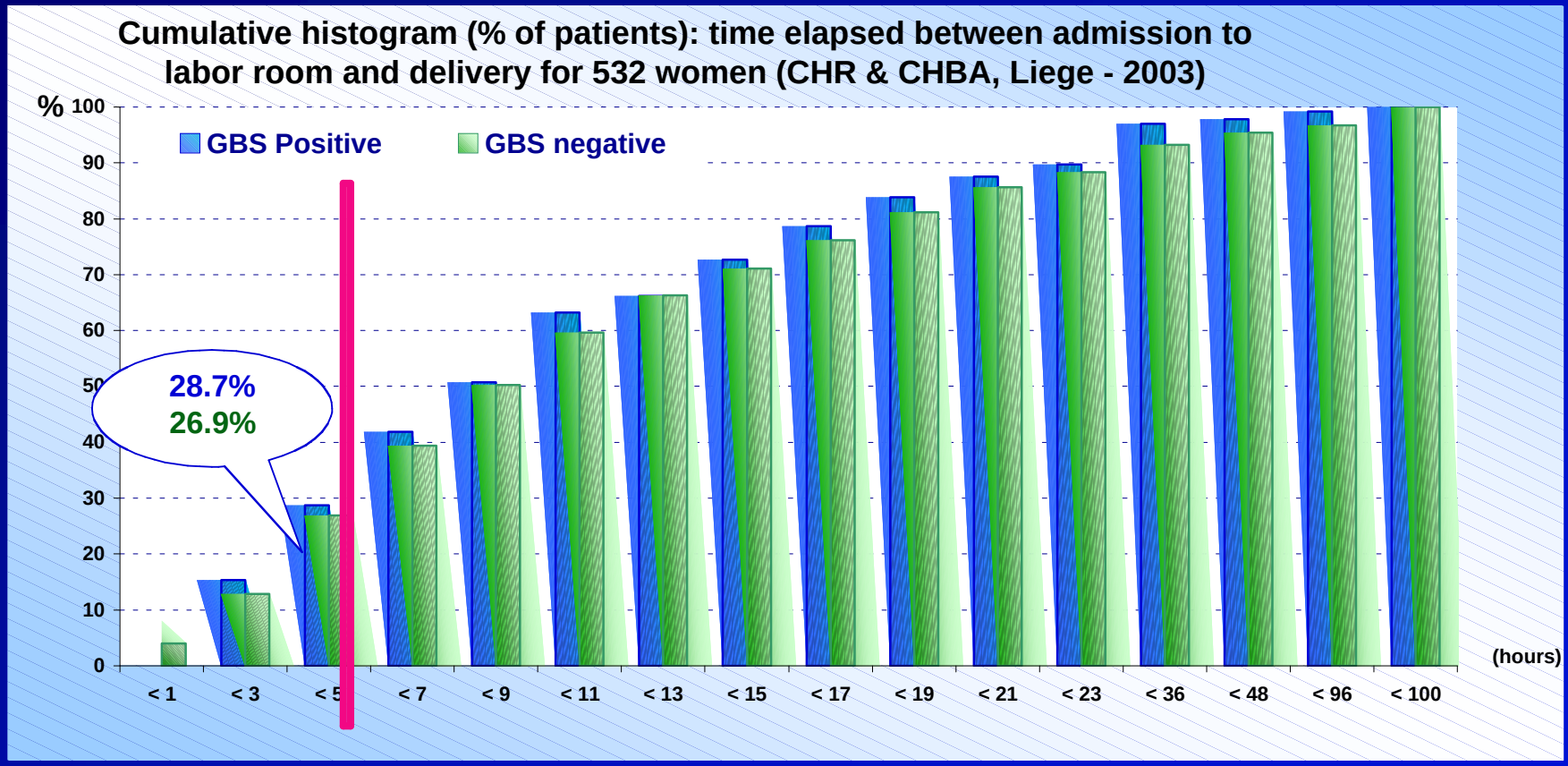
Results

Optimal management of patient

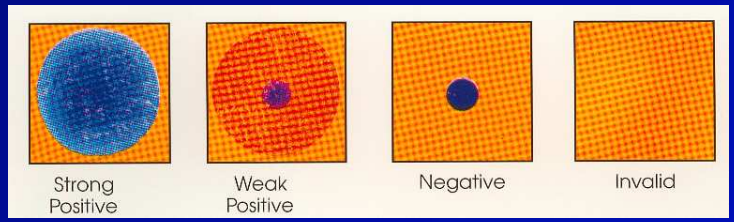
30 - 45 minutes

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

Percentage of women who could not benefit from a full IAP



Melin et al. 2004, ICAAC, Abstract G-499



Strep B OIA test

Belgian multicentric study, 2000

Detection method	Sensibility *Percentage*	Specificity	PPV	NPV
Prenatal cultures			56,3	95
Strep B OIA	62 (47-93)	99,3	93,6	94,4

2003, sensibility B OIA: 65%, Specificity ➢➢ when warm atmosphere

Melin et al. 2003, ICAAC, Abstract # ....

PCR IDI Strep B

IDI-Strep B	GBS Positive culture								GBS neg culture
	From primary culture on Granada I						CDC protocol & Granada II	TOTAL	
	Overall	Density							
		4+	3+	2+	1+	Very Rare			
	(N=154)	*(54)*	*(28)*	*(18)*	*(30)*	*(24)*	*(N=60)*	*(N=214)*	*(N=705)*
GBS Positive	133	54	27	16	23	13	26	159	6*
SENSITIVITY %	86.4	100	96.4	88.9	76.7	54.1	43.3	74.3	
SPECIFICITY :		99.1 %							
Positive Predictive Value :		96.4 %							
Negative Predictive Value :		92.7 %							

23.6% (16.8 + 6.8%) Vaginal culture GBS +
****: 3/6 positive by an Ag method***

P.Melin et al, ICAAC 2004

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 everye 4 h until delivery.*
  - **Acceptable** alternative , **but** broader spectrum, potential selection of R bacteria

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

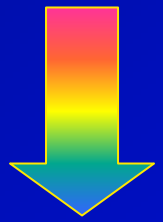
- *Patients at low risk for anaphylaxis*
  - Céfazolin
    - 2 g IV initial dose, then 1g IV every 8 h until delivery.
- *Patients at high risk for anaphylaxis*
  - Clindamycin
    - 900 mg IV every 8 hours until delivery.
    - *If GBS resistant to clindamycin : ask for infectiologist opinion*

Management of neonates at risk for GBS EOD

Rem.: 95 % of GBS EOD are symptomatic < 24 h of live

Neonates born to women who received IAP

Symptomatic NN / asymptomatic NN



To minimize unnecessary evaluation and antimicrobial treatment

Management of symptomatic newborns at risk for GBS EOD

Clinical signs of sepsis

1- Full diagnostic evaluation *

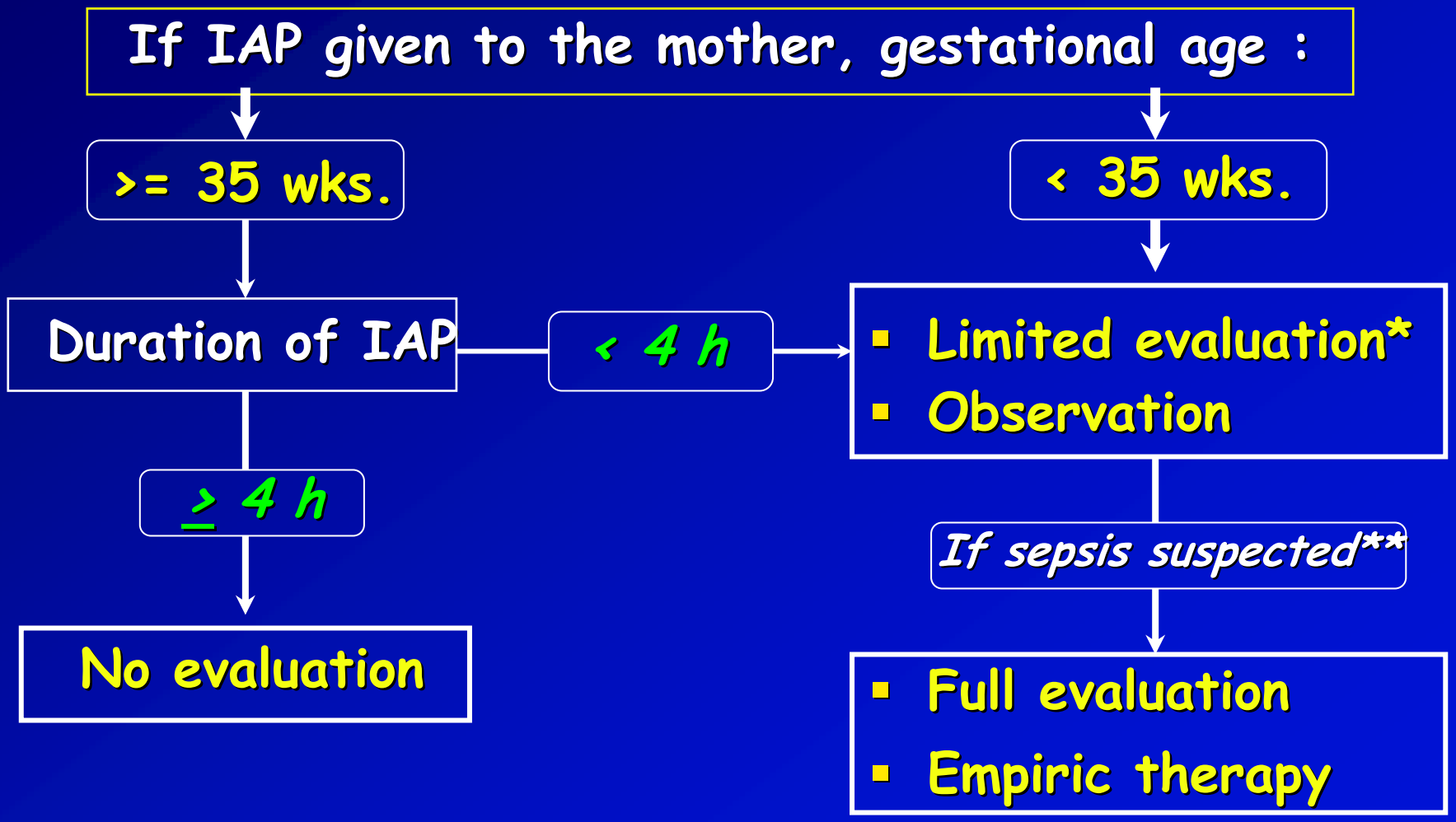
2- Empiric antibiotherapy

(Ampicilline + 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 low risk* » for GBS EOD



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

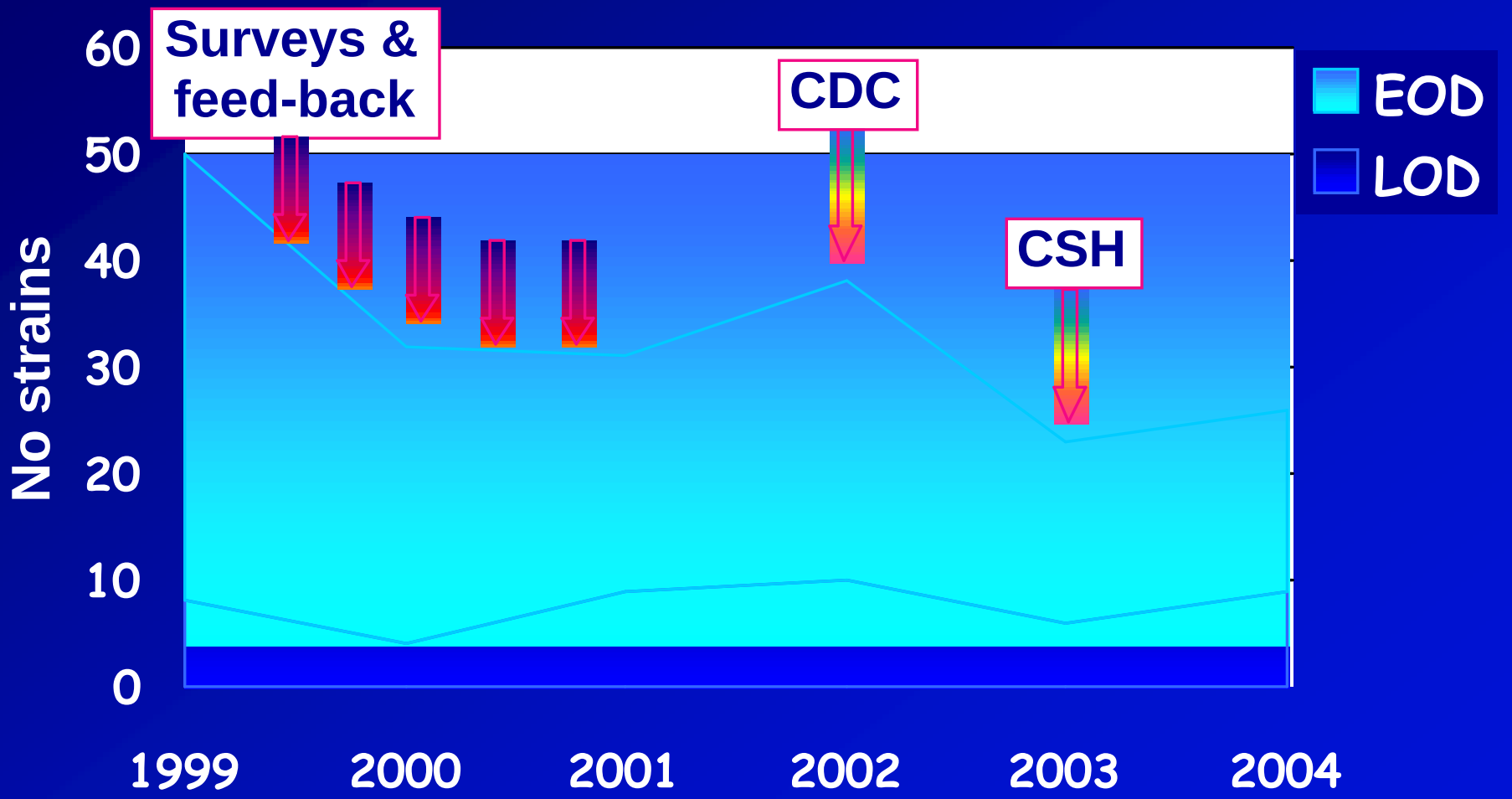
Empiric therapy

Duration of antibiotherapy

Threatened preterm delivery

Planned caesarean delivery for GBS colonized women

Strains isolated from neonatal EOD or LOD and sent to the Belgian ref. Lab. for GBS



Summary

IAP

Universal prenatal screening at 35-37 weeks gestation

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

Conclusions & perspectives

- Not the ideal strategy :
  - Temporary, waiting for vaccines
- Other approaches are investigated
    - Vaginal douching with antiseptic solution
    - Real time PCR for intrapartum screening
- To implement in the daily practice
- Screening method
  - V+R culture
    - Necessary
- !! Transmission of results !!

Rough cost-effective « analysis »
for 1.000 women

	Screening option	RF options
Criteria for IAP	GBS +	PRM >= 18 h, T°>=38°C
Patients treated/1000 births	+/- 250	+/- 250
GBS cases prevented (%)	75 %	<< 50 %
Patients treated/prevented case	111	166
Lab cost /prevented case	2,200 €	/
IAP cost /prevented case	N € x 111	N € x 166
Min.cost /case (8 d, ICU/NN)	+/- 3,300 €	+/- 3,300 €
Indirect cost, sequelae, etc	not estimated	not estimated

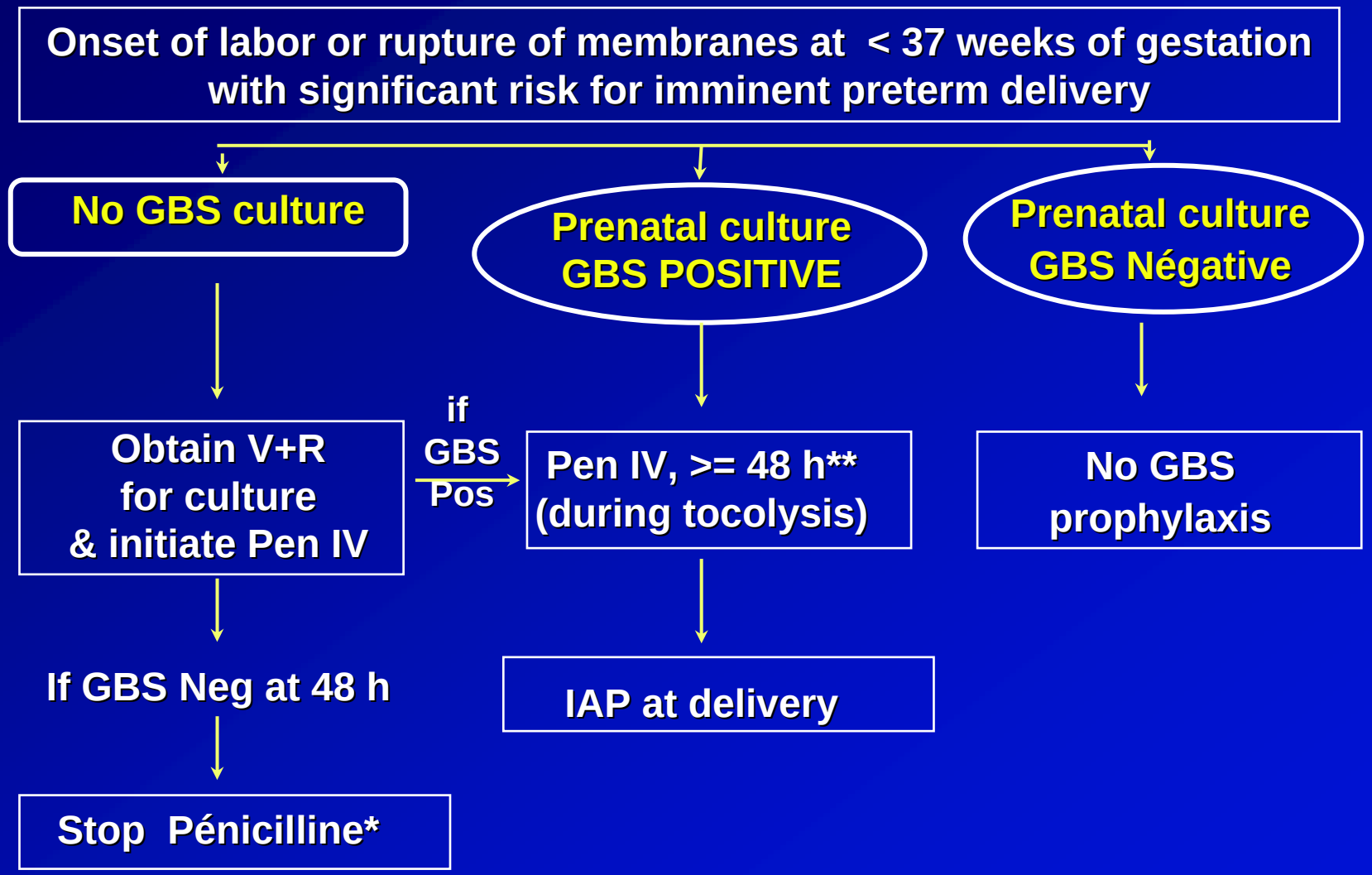
Hypothesis: GBS prevalence in women: 20% ; Natural incidence of GBS EOD: 3/1000 ; prevalence of RF as in our study in Liege in 2002

Duration of antibiotherapy

Focus of infection	Duration
- Suspected sepsis but not confirmed by clinical, biological or bactériological	48 hours
- Proven sepsis	10 days
- Meningitis	minimum 14 days
- Ventriculitis/osteomyelitis	28 days

If GBS confirmed: switch to penicillin, aminoside 3-5 d

Threatened preterm delivery



Planned caesarean delivery for GBS colonized women

C-section performed before

- Rupture of amniotic membrane
- Onset of labor

= very low risk for GBS EOD

⬇

NO specific IAP

(if indicated, regular caesarean-prophylaxis after clamping the umbilical cord.)

Concerns about the number of women who is given IAP

Prevalence of factors inducing the decision of IAP (CHR Liege, 2002, 1350 consecutive deliveries)

FACTORS	« SREENING » OPTION	« RISK FACTORS » OPTION
Prematurity	17 %	
GBS bacteriuria	1.2 %	
GBS Positive	15-25 %	/
ROM >= 18 h	/	19 %
T° >= 38°C	/	1.6 %

Lorquet, Melin, Foidart, J Gynecol Obstet Biol Reprod 2005

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

Vaccination pour la prévention des infections à GBS

- Vaccins polysaccharidiques (Ag de type) :
  - Non conjugué
    - Peu immunogénique
    - Immunité à court terme
  - Conjugué
    - Différentes protéines porteuses
    - Bien toléré
    - Immunité à plus long terme
    - Améliore opsono-phagocytose
- Vaccins protéiques
  - Le plus efficace de tous: protéine de surface Sip de GBS