

Rapid intrapartum screening based strategy for prevention of GBS perinatal infections

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Introduction

GBS neonatal infections
Intrapartum screening

GBS neonatal infections

- In Belgium: 110 à 120000 birth/year
- EOD and LOD incidence $< 1 \text{ ‰}$
- No mandatory statement
- Estimation: around 50 EOD/year
50 LOD/year

Prevention

IAP

- First guidelines
 - 2002 USA
 - 2003 Belgique
- Vagino-rectal universal screening at 35-37 weeks' gestation
 - If positive result:
pen/cephalo/clinda/vanco
 - If unknown result:
obstetrical risk factors
- Effective on EOD

Immunoprophylaxie

- In development
- Effective on EOD and LOD

Prevention (2)

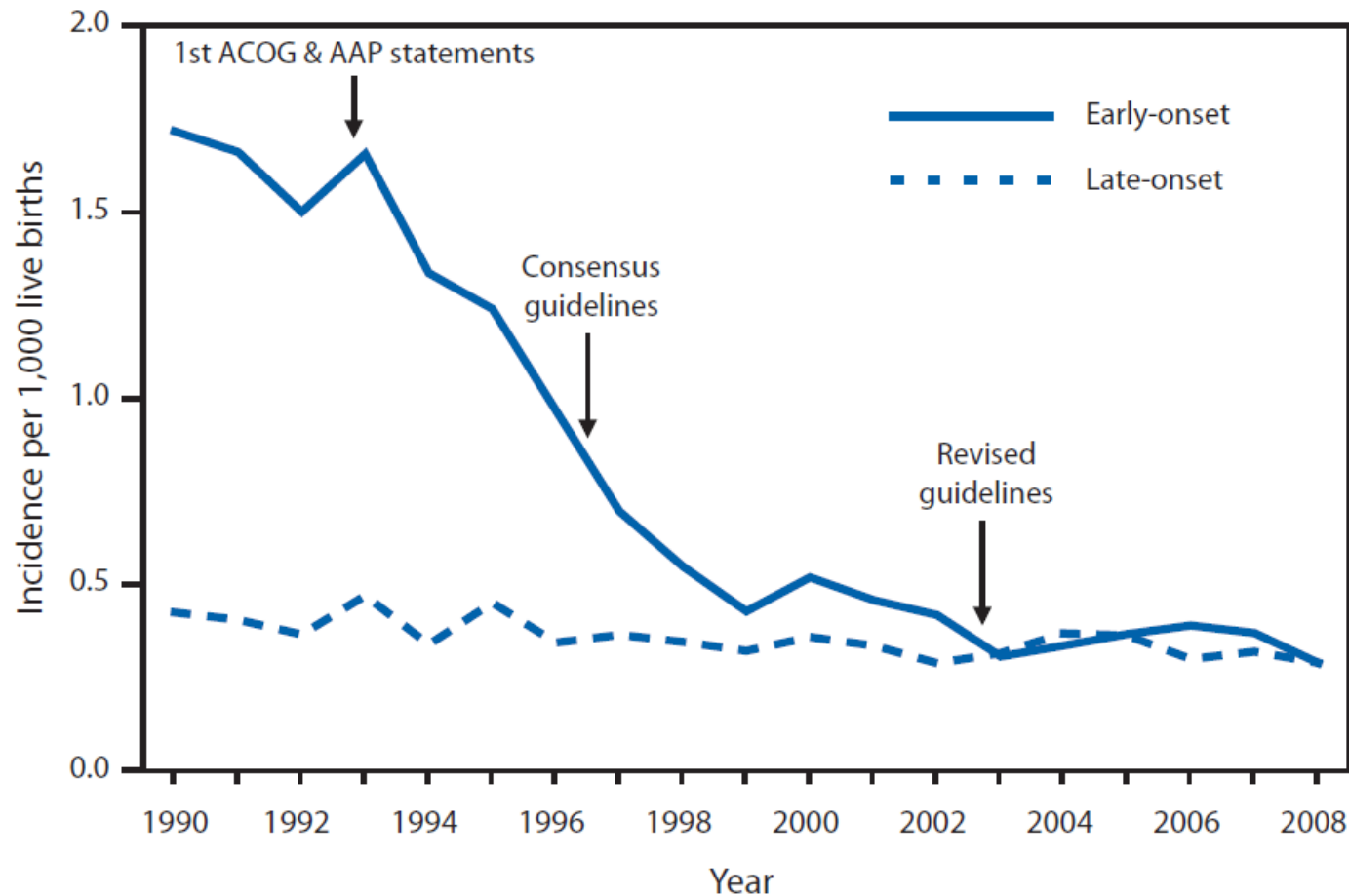


Figure 1 : EOD and LOD incidence between 1990 and 2008 (Revised Guidelines from CDC, 2010)
ACOG = American College of Obstetricians and Gynecologists et AAP = American Acad-emy of Pediatrics.

Detection of EOD risk = GBS + at delivery

Antenatal screening

- VPP 60 à 87%
- VPN 88 à 96%

- False negative: missed IAP
- False positive: unnecessary IAP

Intrapartum screening

- Expected PPV and NPV >90%

- Better targeted IAP

- No susceptibility testing

Required features for an intrapartum test (1)

- High sensitivity and specificity
- Full automation
- Easy to perform and interpret by nurses
- Time to result: maximum 1 hour
- 24/24 hours et 7/7 days available

Required features for an intrapartum test (2)

- Awaited > 20 years
- Unanimous literature

Authors	Revue	Number of included patients	Test	Site	S	Sp	PPV	NPV
Abdelazim IA	2013 Aust N Z Obstet Gynaecol	445	Xpert GBS	Lab	98.3%	99%	97.4%	99.4%
Park JS et al.	2013 Ann Lab Med	175	Xpert GBS	Lab	86.6%	95.6%	65%	98.7%
Church DL et al.	2011 Diag Microbiol Infect Dis	231	Xpert GBS	Lab	100%	100%	100%	100%
De Tejada BM et al.	2011 Clin Microbiol Infect	695	Xpert GBS	Obstetrics facility	85%	96.6%	85.7%	96.3%
Young BC et al.	2011 Am J Obstet Gynecol	559	Xpert GBS	Lab	90.8%	97.6%	92.2%	97.1%
El Helali N et al.	2009 Clin Infect Dis	968	Xpert GBS	Lab	98.6%	99.6%	97.8%	99.7%

* Intrapartum GBS screening and antibiotic prophylaxis : a European consensus conference. J Matern Fetal Neonatal Med 2014;27:1-17.

Test Xpert GBS

- Real Time PCR on GeneXpert system (Cepheid).
 - Amplification of a conserved region adjacent to the *cfb* gene of GBS
- On vaginal or vagino/rectal swab
- Fully automated
- Easy handling
- Result in 45 minutes



Ongoing study in CHU Liège / UZ Antwerp: Aims

1. To assess the practical and analytical aspects of the implementation of the PCR test Xpert GBS® in Belgium
 - Performed by midwives
 - For all women at onset of labor
 2. To evaluate the cost-effectiveness of the intrapartum screening strategy
- **To consolidate the proposal of the European Expert Group**

Material and methods

Population

Specimen collection

Test Xpert GBS

Population

- Prospective study in 2 Belgian hospitals: CHU Liège and UZ Antwerp
- Sample size in CHU Liège: 500
- ALL women at onset of labor included
- Case-report form
 - Demographic and obstetric data
 - Result of the antenatal screening at 35-37 weeks' gestation

Specimen collection

Prenatal screening

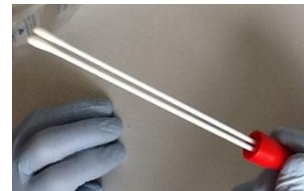
- vagino/rectal specimen collected at 35-37 weeks' gestation

Intrapartum screening

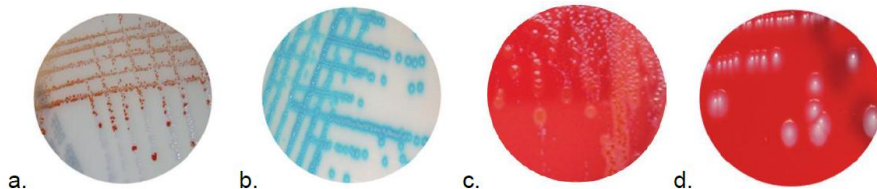
- vaginal specimen using a double swab
- From ALL women at onset of labor



Culture



Test Xpert GBS



a/Granada, b/StrepB Select, c,d/GS-CNA

Test Xpert GBS: Procedure

Mettre des gants



9. Remettre un écouvillon dans le système de transport (à envoyer au labo). Utiliser l'autre pour le GeneXpert



13. Si l'écouvillon ne tombe pas au fond de la chambre, poussez-le avec votre doigt.



6. Se procurer la cartouche et ouvrir le couvercle



10. Rouler l'écouvillon du GeneXpert délicatement sur du papier Kleenex



14. Fermer la cartouche



7. Retirer les écouvillons du système de transport



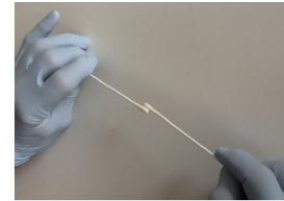
11. Localiser le marquage de cassure sur l'écouvillon



Retirer les gants



8. Frotter doucement les écouvillons l'un sur l'autre



12. Casser l'écouvillon dans la cartouche (ouverture en bas à droite) au niveau du marquage



 **Cepheid.**
A better way.



- Procedure performed by midwives
- GeneXpert system installed at the Obstetrics facility

Test Xpert GBS: Results

Assay Information

Assay	Assay Version	Assay Type
Xpert GBS G3	3	In Vitro Diagnostic

Test Result:

POSITIVE

Presence of GBS

Test and Analyte Result

Analyte Name	Ct	EndPt	Analyte Result	Probe Check Result
SPC	34.4	108.0	NA	PASS
GBS	34.1	188.0	POS	PASS
IC	31.0	149.0	NA	PASS

Test Result:

NEGATIVE

Negative for GBS

Test Result:

ERROR

Indeterminate status for GBS

Test Result:

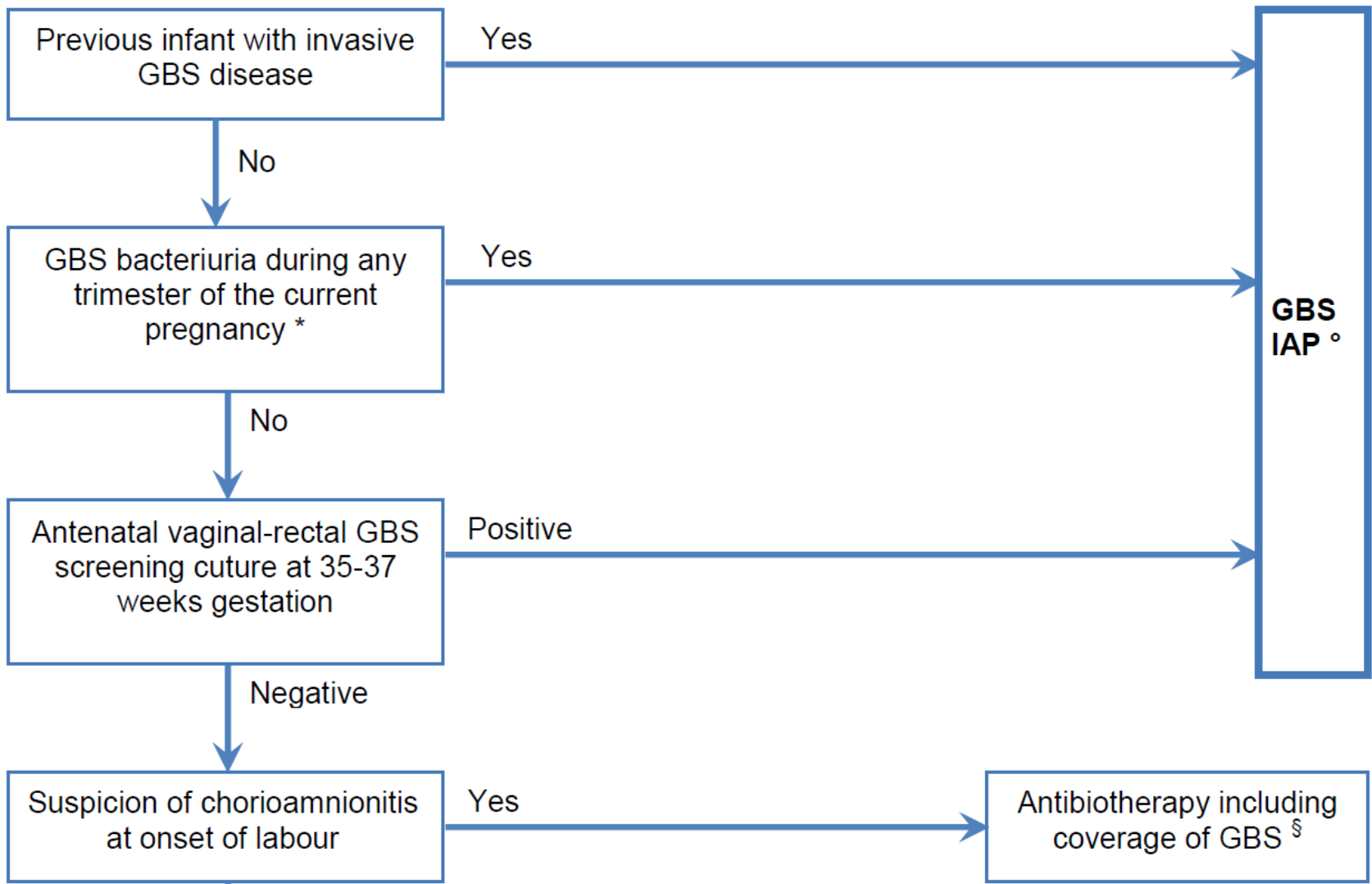
NO RESULT

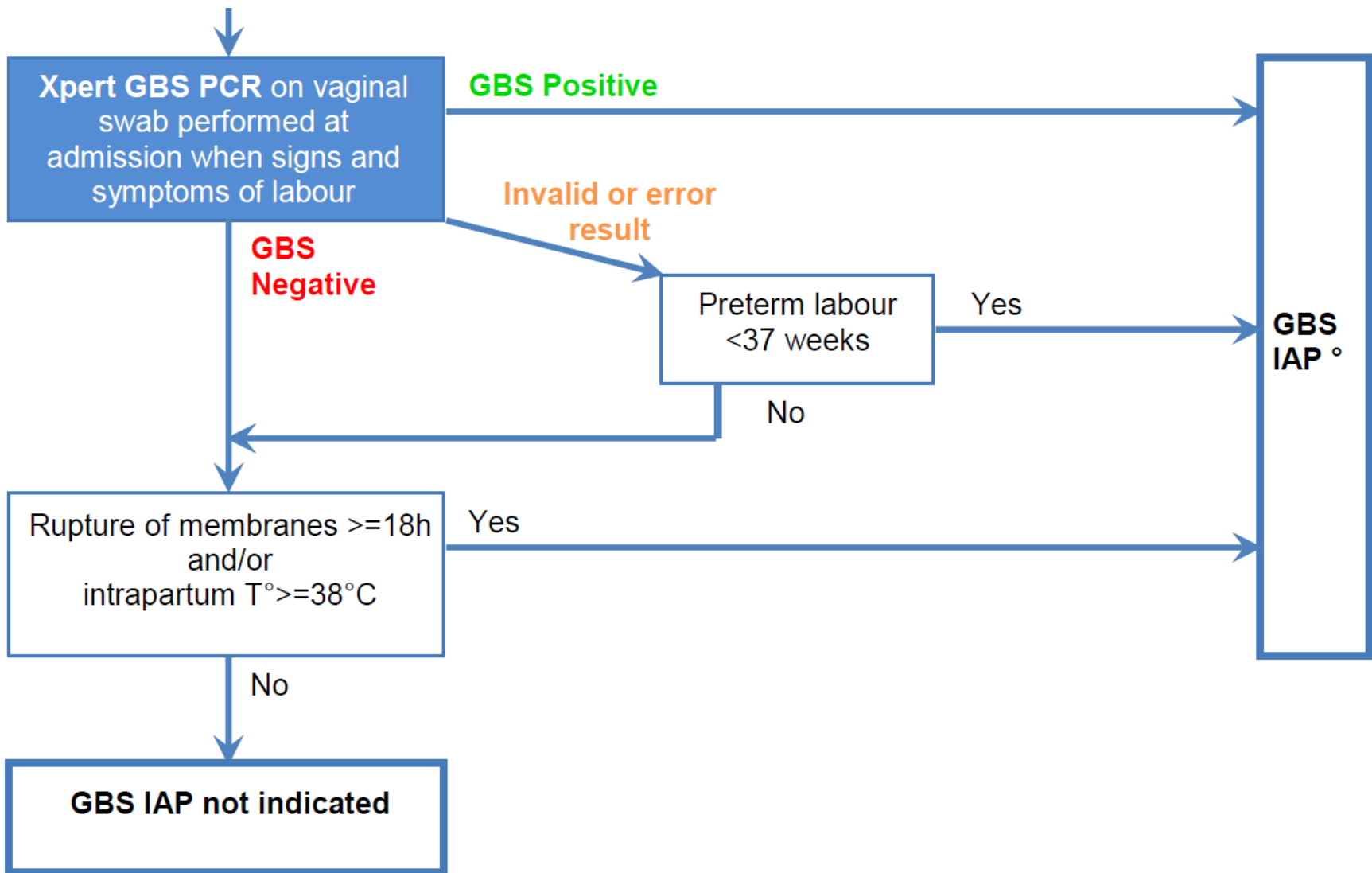
Test Xpert GBS: Results (2)

- Algorithm proposed to clinicians:

Integration of the intrapartum Xpert result in addition to :

- patient's clinical data
- Result of the antenatal screening at 35-37 weeks' gestation





Preliminary results



Culture results

PCR results

Global overview

- Study period : 8/4 au 03/10/2014 (still ongoing)
- 658 deliveries
- Included patients : 486 Xpert® GBS tests performed (74%)
 - Inclusion rate lower among antenatally positive screened patients.

Culture results

- Colonization rate (35-37 weeks): 19.4%
- Performances of the antenatal culture screening

Sensitivity	Specificity	PPV	NPV
67.3 %	94.2 %	68.8 %	93.8 %

- intrapartum culture as gold standard

PCR results

- Not yet available for presentation

- Difficulties encountered:

- Low inclusion rate
- Wrong manipulations
- Invalid results



- Study still ongoing, with a revised protocol

Discussion



Intrapartum PCR: Inclusion rate

- Lower than expected
- **Bias linked to low inclusion of antenatally positive detected women**
- 100% inclusion rate is utopian:
 - Delay before delivery too short, high workload
 - Technical problems, lack of involvement in the study.

Intrapartum PCR: Handling

- Test easy to perform « a priori » BUT...
- Many difficulties encountered by midwives :
 - Sample preparation
 - Proper breaking into the cartridge
 - Loading in the instrument
- Large team, high turn-over

→ Continuous training required

Conclusion (1)

- **Intrapartum screening:**
 - Proven clinical value
 - Recommended by new European directives
 - Cost-effectiveness remains to be demonstrated in Belgium
 - **Test Xpert GBS :**
 - Sensible et specific
 - Fully automated
 - Fast result
 - Feasible in point-of-care, 24h/24
 - Easy to perform...
- BUT...**

Conclusion (2)

Necessary supervision by the lab :

- Careful training of operators
- Verification of test performance before routine implementation
- Daily technical supervision
- Involvement of gynecologists:
 - ensure adequate inclusion rates
 - integrate the result of the rapid test in the care of the patient

Conclusion (3)

Is the Xpert® GBS test enough robust to be universally recommended as a POCT ?

Desired developments at Cepheid :

- Internal control checking for human cells
- Simplifying the interface of the GeneXpert system

Thank you !

A decorative graphic consisting of a solid teal horizontal bar that spans the width of the slide. Below this bar, on the right side, there are several horizontal lines of varying lengths and colors, including teal and white, creating a layered, stepped effect.