Welcome to Gothenburg, Sweden in May 2016

2nd European Spotaneous Preterm Birth Congress
26th - 28th of May 2016

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REGISTRATION

Home

Welcome to the 2nd European Spontaneus Preterm Birth Congress in Gothenburg, Sweden in 2016.

On behalf of the Local Organizing Committee we invite you to participate in the 2nd **ESPBC** in Gothenburg, Sweden in May 2016. The European Spontaneous Preterm Birth Congress, an event held

The role of amniocentesis in the management of premature preterm labour and PPROM

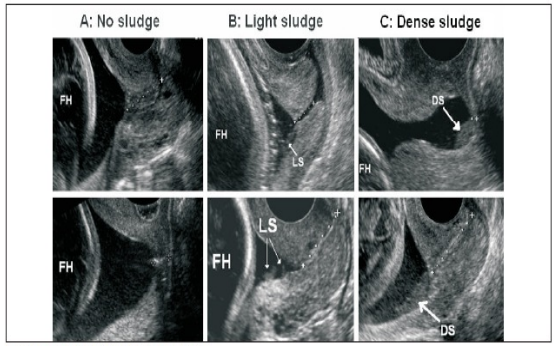
Intraamniotic infection/ inflammation (IAI)

Preterm labor with intact membranes or PPROM

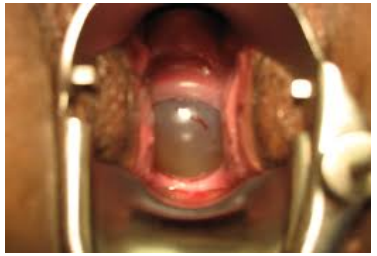
Histological chorioamniontis with/without FUNICITIS

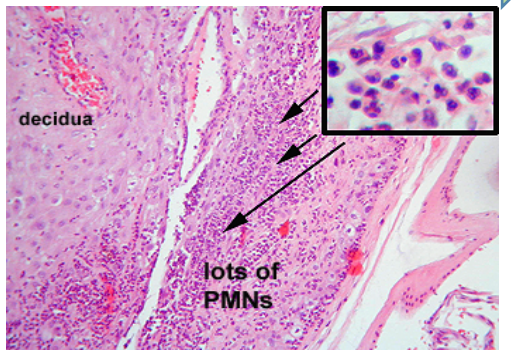
Early onset of neonatal sepsis

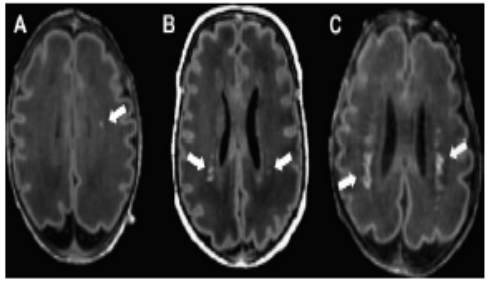
Poor neurodevelopmental outcome



FH: fetal head; LS: light sludge; DS: dense sludge.







Vedran Stefanovic,dos.
vt. os.ylilääkäri
Sikiölääketieteen keskus, HYKS,NKL

SGY, Kotka, 17.4.2015

Preterm parturition syndrome

(Romero, Science 2014)

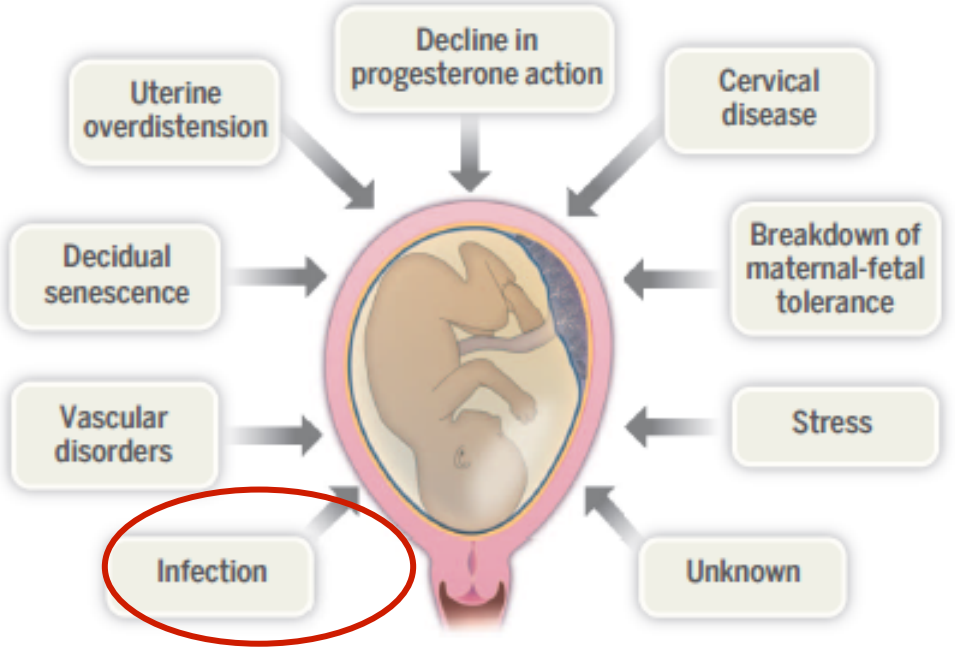


Fig. 2. Proposed mechanisms of disease implicated in spontaneous preterm labor. Genetic and environmental factors are likely contributors to each mechanism.

Finland (2009) – incidence of premature birth 5.5% (3334/60557)
0.8 % (493) born prior to 32^{+0} gestational week

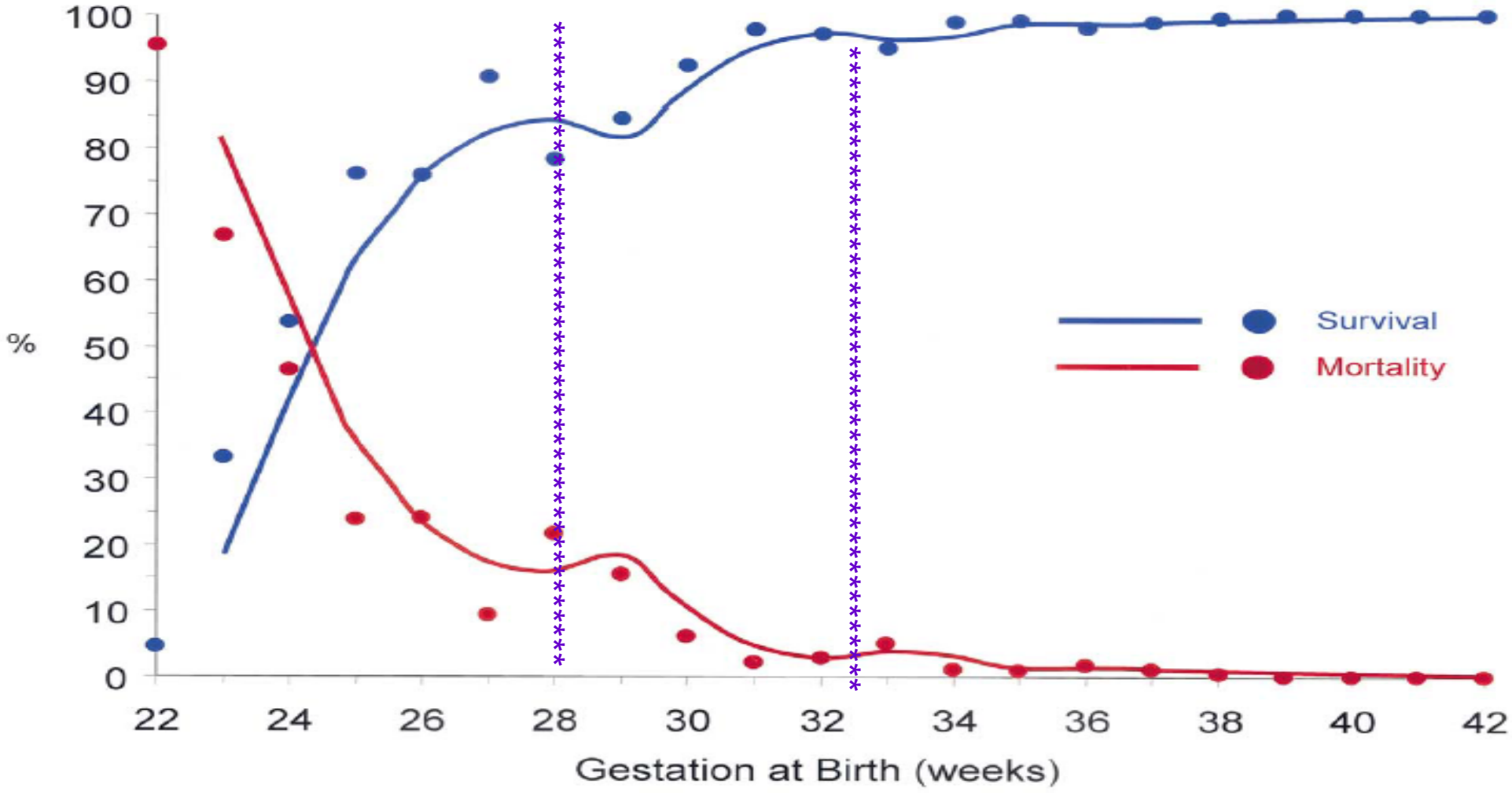


Figure 1. Survival by gestational age among live-born resuscitated infants. Results of a community-based evaluation of 8523 deliveries, 1997–1998, Shelby County, Tennessee. Curves smoothed by 2-point average.

Mercer. Treatment of Preterm PROM. Obstet Gynecol 2003.

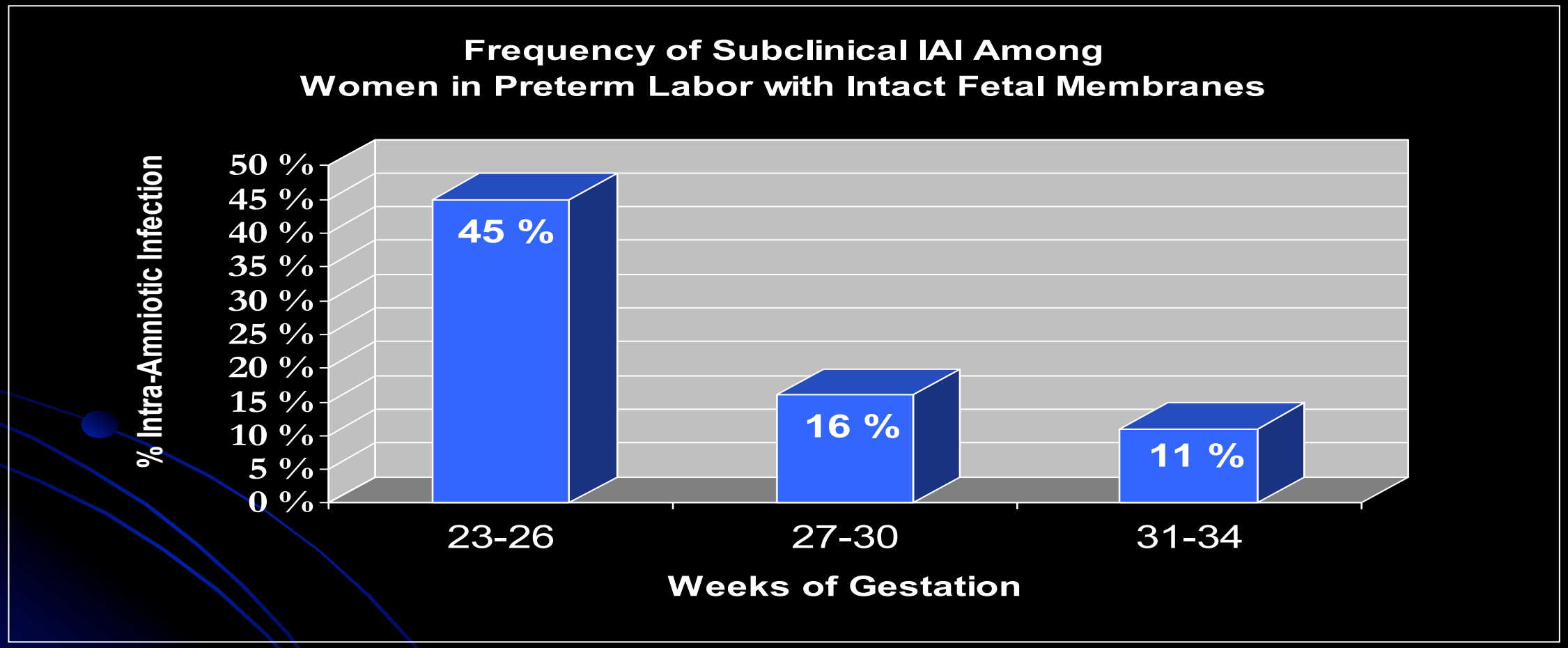
Why this presentation?

- Wrong perception on ”what´s more harmful: preterm labour or PPROM?”
- Wrong optimal delivery time determination (away from the stone-age)

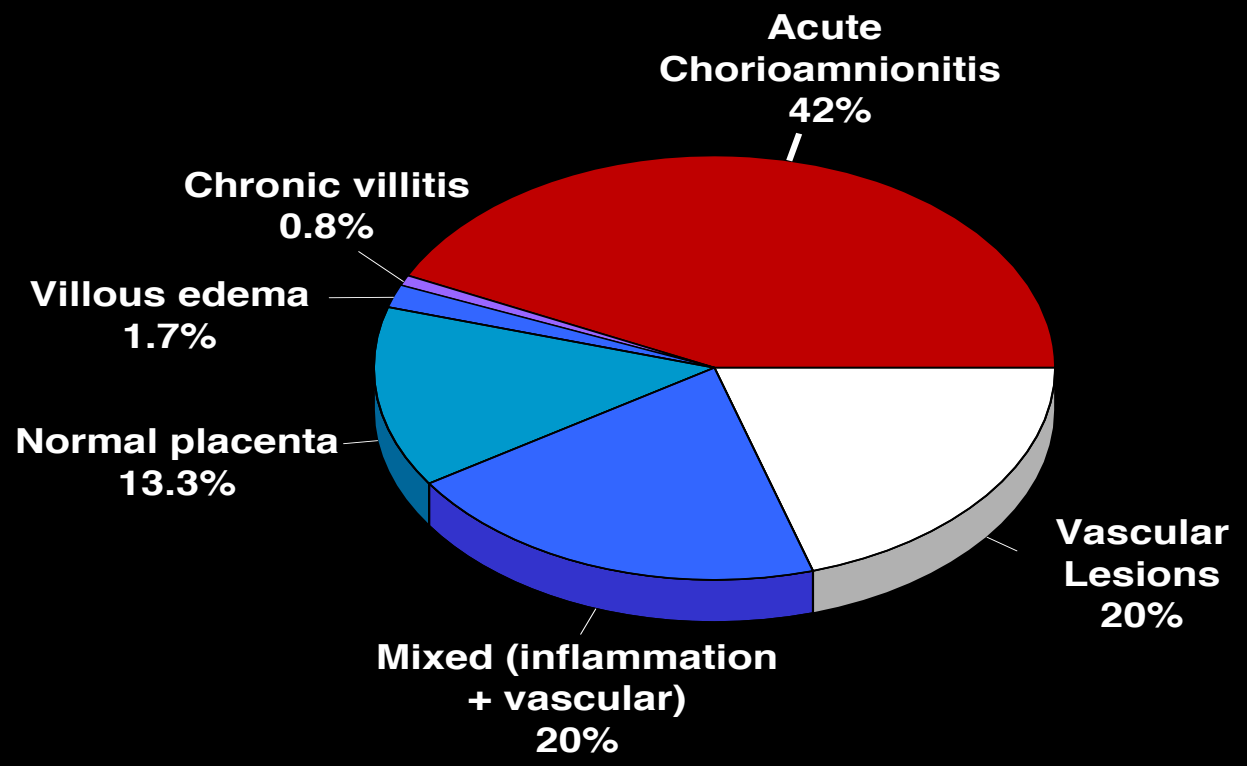
- Wrong antibiotics
- Wrong management of patients with PPROM
- Wrong attitude towards the whole problem

- Right audience

Increased Risk of IAI at Lower Gestational Ages



Modified from Watts, et al. 1992



Arias et al. Obstet Gynecol 1997

What are we talking about?

- IAI (Intraamniotic inflammation or/and infection)
- MIAC (Microbial invasion of the amniotic cavity)
- HCA (Histological chorioamnionitis)
- EONS (Early onset of neonatal sepsis)

A) Intraamniotic colonization (the evidence of MIAC by culture or molecular microbiology)

B) Intraamniotic inflammation (MMP-8, IL-6, cathelicidine etc)

Intraamniotic infection = A+B

- IAI (Intraamniotic inflammation/infection)

Sludge (möhnä, mönjä, mömmö)

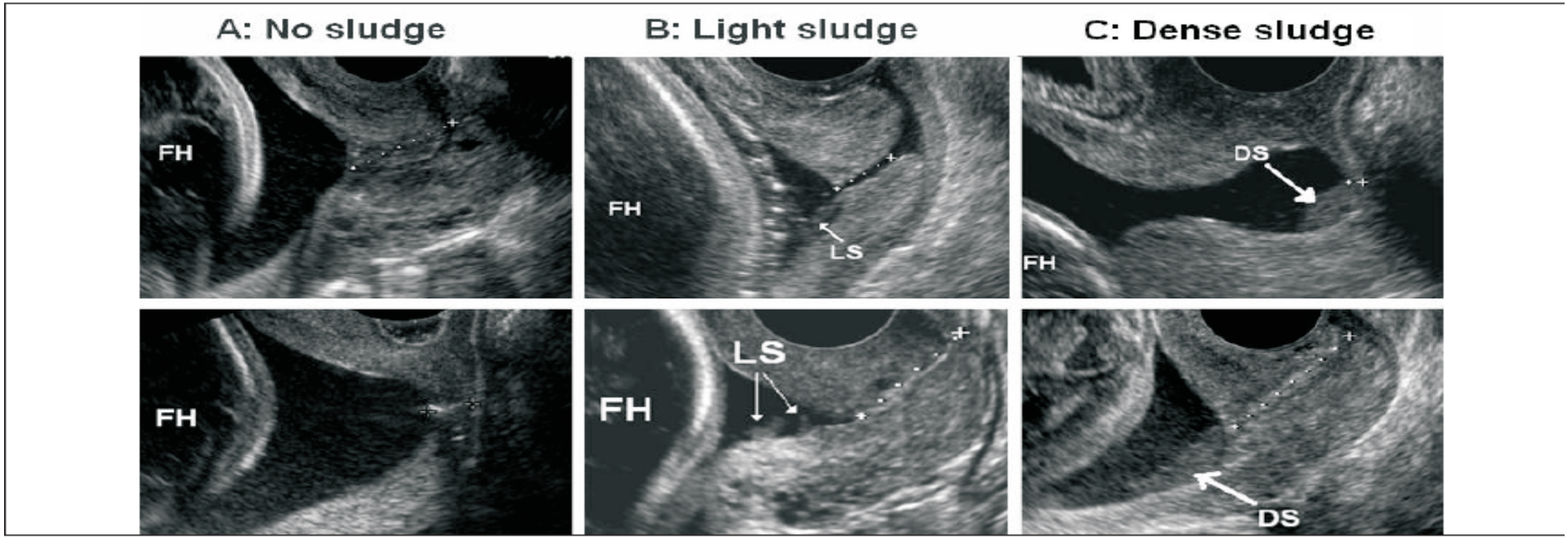
sludge.avi

- Light, dense
- Intraamniotic free-floating ”biofilm” containing mostly embedded white blood cells and bacteria
- Sludge in the early second trimester associated with the PPROM and preterm delivery
- Sludge in women with cervical changes, symptomes of preterm labour is even more associated with preterm delivery shortly after admission
- Not all IAI cases have sludge
- Not all sludges are IAI
- Evidence that antibiotic treatment in cases with sludge results in later delivery
- Recommendations of amniocentesis in
  - *A) women with intention of elective or emergency cerclage*
  - *B) women with PTL , intact membranes and sludge*

Sludge

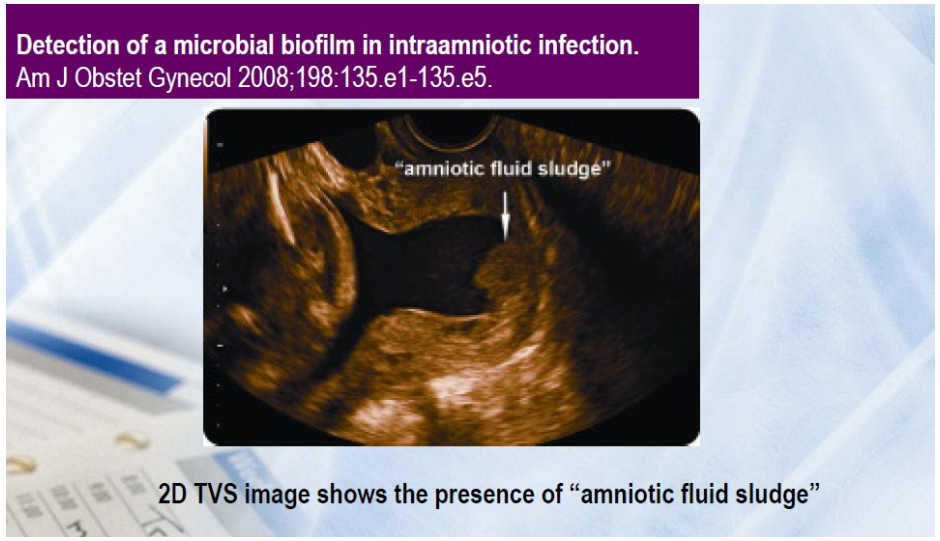
Bujold et al.

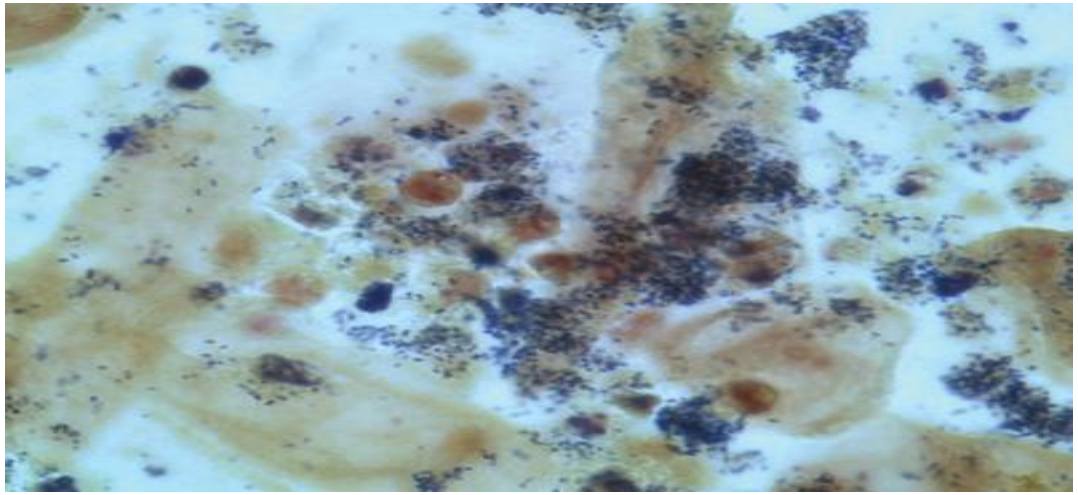
J Obstet Gynaecol Can 2006;28(3):198–202



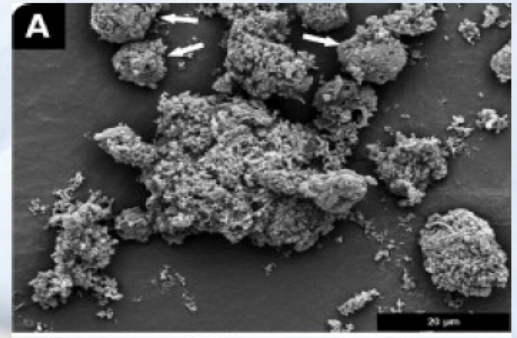
FH: fetal head; LS: light sludge; DS: dense sludge.

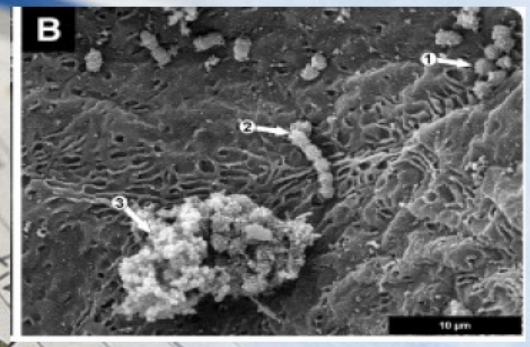
Amniotic fluid sludge



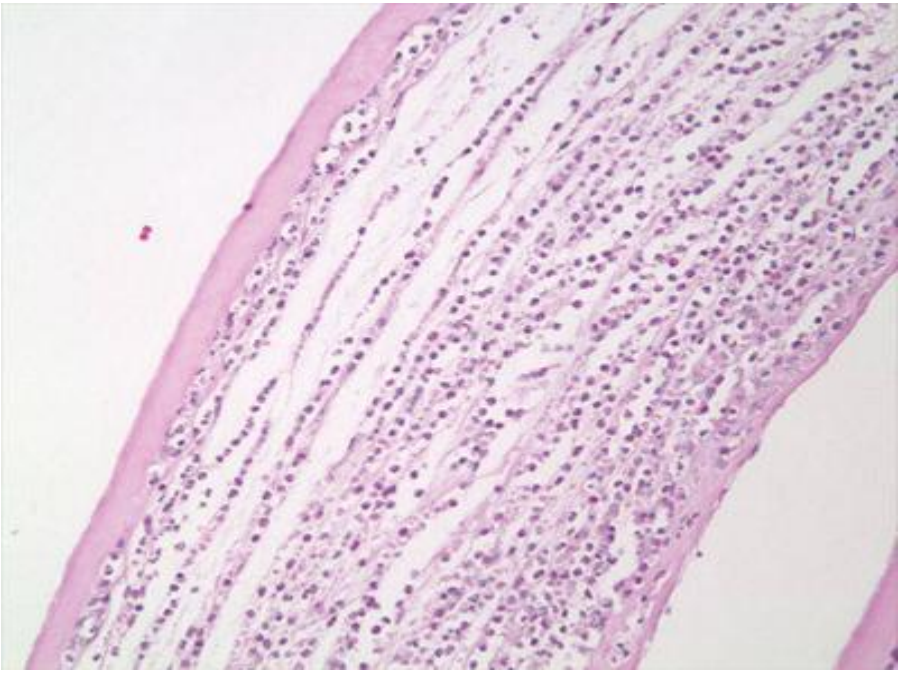


Detection of a microbial biofilm in intraamniotic infection.
Am J Obstet Gynecol 2008;198:135.e1-135.e5.





- **A**, The biofilm, in the center, and several neutrophils.
- **B**, The coccoid bacteria are on the surface of a fetal epithelial cell in a form of
  - individual cells,
  - chain of cocci,
  - biofilm aggregate in which they are partially “buried” in amorphous slime



ORIGINAL ARTICLE

Prevalence and Diversity of Microbes in the Amniotic Fluid, the Fetal Inflammatory Response, and Pregnancy Outcome in Women with Preterm Pre-Labor Rupture of Membranes

Daniel B. DiGiulio[1,2], Roberto Romero[3,4,5], Juan Pedro Kusanovic[3,5], Ricardo Gómez[6,7], Chong Jai Kim[3,8], Kimberley S. Seok[2], Francesca Gotsch[3], Shali Mazaki-Tovi[3,5], Edi Vaisbuch[3,5], Katherine Sanders[2,9], Elisabeth M. Bik[2,9], Tinnakorn Chaiworapongsa[3,5], Enrique Oyarzún[7], David A. Relman[1,2,9]

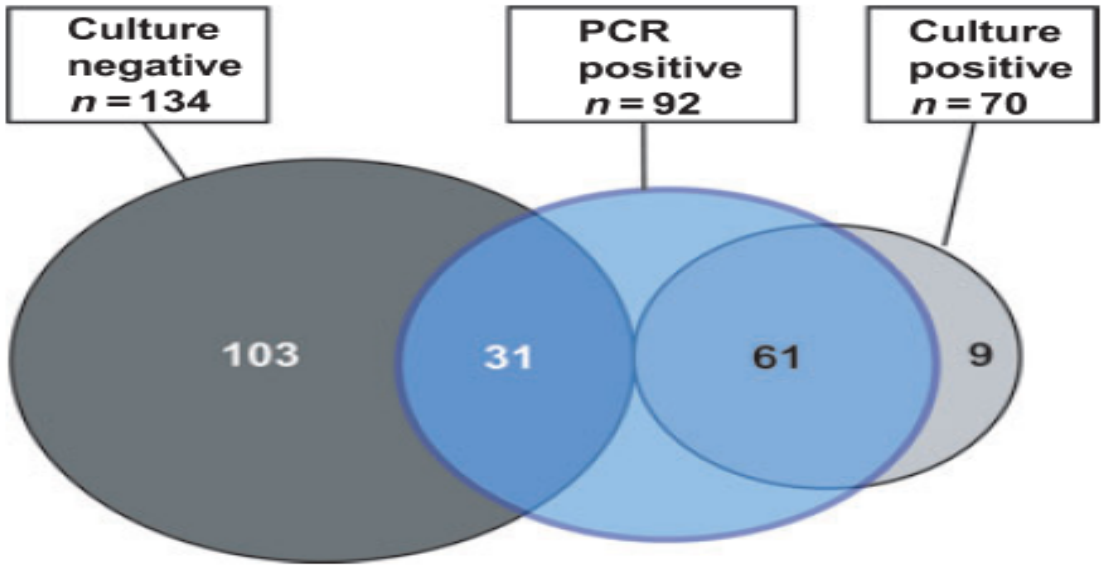


Fig. 1 Distribution of subjects ($n = 204$) according to results of polymerase chain reaction (PCR) and culture of amniotic fluid. Data are from amniocentesis at presentation of 204 subjects for whom results from all culture assays were available. Culture refers to the aggregate results from routine cultivation methods for bacteria (aerobes, anaerobes, and genital mycoplasmas) and for fungi. PCR refers to the aggregate results from end-point or real-time PCR targeting domain *Bacteria*, domain *Archaea*, genus *Candida*, and five specific bacterial groups (see Methods). Circle areas are not to scale.

Broad bacterial 16s and 18s PCR from the amniotic fluid samples are rarely analysed

The best correlation of prenatal *IAI and EONS* would be the triple sample (amniotic fluid-cord blood and neonatal blood for molecular microbiology)

Am J Reprod Immunol 2010;

Science Translational Medicine
AAAS

The Placenta Harbors a Unique Microbiome

Kjersti Aagaard *et al.*

Sci Transl Med **6**, 237ra65 (2014);
DOI: 10.1126/scitranslmed.3008599

Downloaded from stm.scien

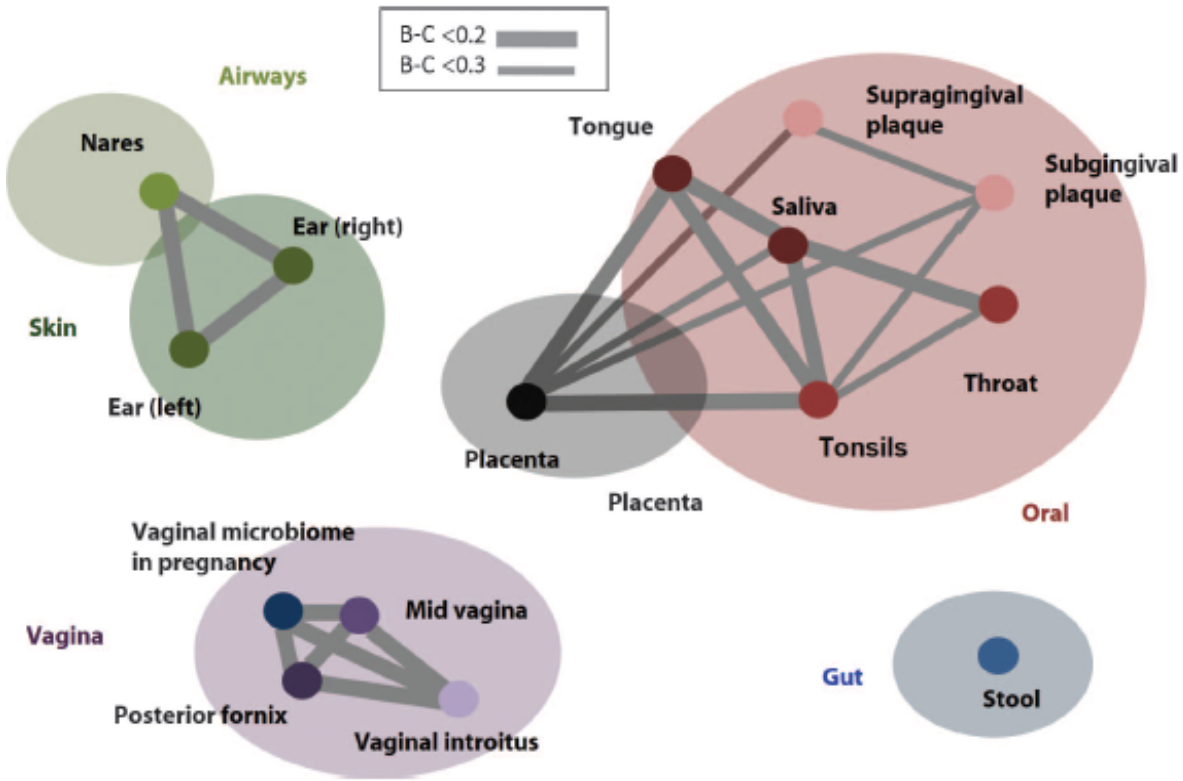


Fig. 1. The placental microbiome has a taxonomic profile that is similar to the oral microbiome. Bray-Curtis (B-C) dissimilarity was calculated using WGS-generated phylum-level abundance of bacteria from each body site, including placental data from this study; gut, vagina, posterior auricular skin, and nasal airways data from the HMP; and vaginal data from previously published gravidae (*1–4*). The thicker the connecting line, the greater the similarity of the taxonomic profile (Bray-Curtis <0.2). Strong phylum-level similarity was observed between the placenta and tongue, tonsils, saliva, and subgingival plaque taxonomic profiles. The colors of dots reflect the vicinity of the body sites.

Placental microbiome is most similar to the oral microbiome !

Intrauterine cavity is NOT sterile

OBSTETRICS

Amniotic fluid infection, inflammation, and colonization in preterm labor with intact membranes

C. Andrew Combs, MD, PhD; Michael Gravett, MD; Thomas J. Garite, MD; Durlin E. Hickok, MD, MPH; Jodi Lapidus, PhD; Richard Porreco, MD; Julie Rael, RN; Thomas Grove, PhD; Terry K. Morgan, MD, PhD; William Clewell, MD; Hugh Miller, MD; David Luthy, MD; Leonardo Pereira, MD; Michael Nageotte, MD; Peter A. Robilio, MD; Stephen Fortunato, MD; Hyagriv Simhan, MD; Jason K. Baxter, MD; Erol Amon, MD; Albert Franco, MD; Kenneth Trofatter, MD; Kent Heyborne, MD; for the ProteoGenix/Obstetrix Collaborative Research Network

2014

CONCLUSION: We confirmed previous reports that intraamniotic inflammation is associated with adverse perinatal outcomes whether or not intraamniotic microbes are detected. Colonization without inflammation appears relatively benign. Intraamniotic inflammation is not simply present or absent but also has degrees of severity that correlate with adverse outcomes. We propose the designation amniotic inflammatory response syndrome to denote the adverse outcomes that are associated with intraamniotic inflammation.

TABLE 3

Clinical characteristics at enrollment

Variable	Group: Amniotic fluid interleukin-6, ≥11.3 ng/mL: Infection (n = 27)	Amniotic fluid interleukin-6, ≥11.3 ng/mL: Severe inflammation (n = 36)	Amniotic fluid interleukin-6, 2.6-11.2 ng/mL: Mild inflammation (n = 47)	Amniotic fluid interleukin-6, <2.6 ng/mL: Colonization (n = 4)	Amniotic fluid interleukin-6, <2.6 ng/mL: Negative (n = 191)	*P* value[a]
Demographics						
Maternal age, y[b]	25.8 ± 5.4	26.6 ± 4.9	26.5 ± 5.2	25.5 ±5.2	25.8 ±5.6	.92
Nulliparous, n (%)[c]	10 (37)	11 (31)	19 (41)	2 (50)	48 (25)	.17
Presentation						
Gestational age, wk[b]	27.5 ± 3.9	26.8 ± 3.5	29.9 ± 3.9	30.3 ± 4.7	31.1 ± 3.6	< .0001
Cervical dilation, cm[b,d]	3.0 ± 1.6	3.2 ± 1.4	3.3 ± 1.5	2.0 ± 1.4	2.7 ± 1.4	.05
Cervical dilation ≥2 cm, n (%)[d]	21 (88)	27 (90)	39 (85)	2 (50)	134 (80)	.27
Maternal signs, n (%)						
Uterine tenderness	2 (7)	5 (14)	2 (4)	1 (25)	10 (5)	.13
Fever ≥100.4°F	1 (4)	0	0	1 (25)	8 (4)	.10
White blood cell count >15,000/mm^3	13 (48)	14 (39)	5 (11)	2 (50)	22 (12)	< .001
Baseline fetal heart rate >160 beats/min	1 (4)	0	0	0	4 (2)	.54
Amniotic fluid markers						
Glucose <20 mg/dL, n (%)[e]	25 (96)	9 (25)	6 (13)	1 (33)	17 (9)	< .0001
Gram stain positive, n (%)	14 (52)	0	0	0	1 (<1)	< .0001
Amniotic fluid interleukin-6, ng/dL[f]	41.4 ± 2.5	23.0 ± 1.7	4.4 ± 16	0.8 ± 1.9	1.0 ± 2.4	N/A

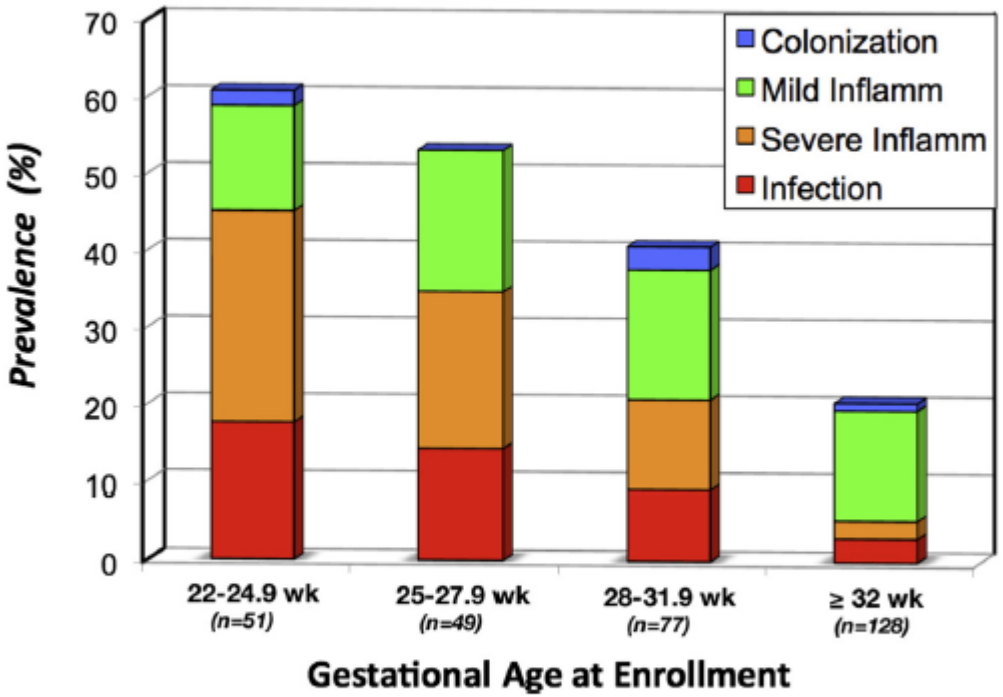
N/A, analysis of variance was not performed because amniotic fluid interleukin-6 was used to define the groups; the difference between the infection and severe inflammation groups was significant at $P = .002$ (*t* test on log-transformed values).

[a] Comparison of subjects across all 5 groups with analysis of variance or χ^2 test; Fisher exact test was used in lieu of χ^2 for clinical signs of infection because of the small counts; [b] Data are given as mean ± SD; [c] N = 27, 35, 46, 4, and 191 for the 5 groups, respectively, because of missing values; [d] N = 24, 30, 46, 4, and 167 for the 5 groups, respectively, because of missing values; [e] N = 3 for the colonization group and n = 190 for the negative fluid group because of missing values; [f] Data are given as geometric mean and SD.

Combs. Inflammation, infection, preterm labor. Am J Obstet Gynecol 2014.

FIGURE 2

Prevalence of infection, inflammation, and colonization vs gestational age



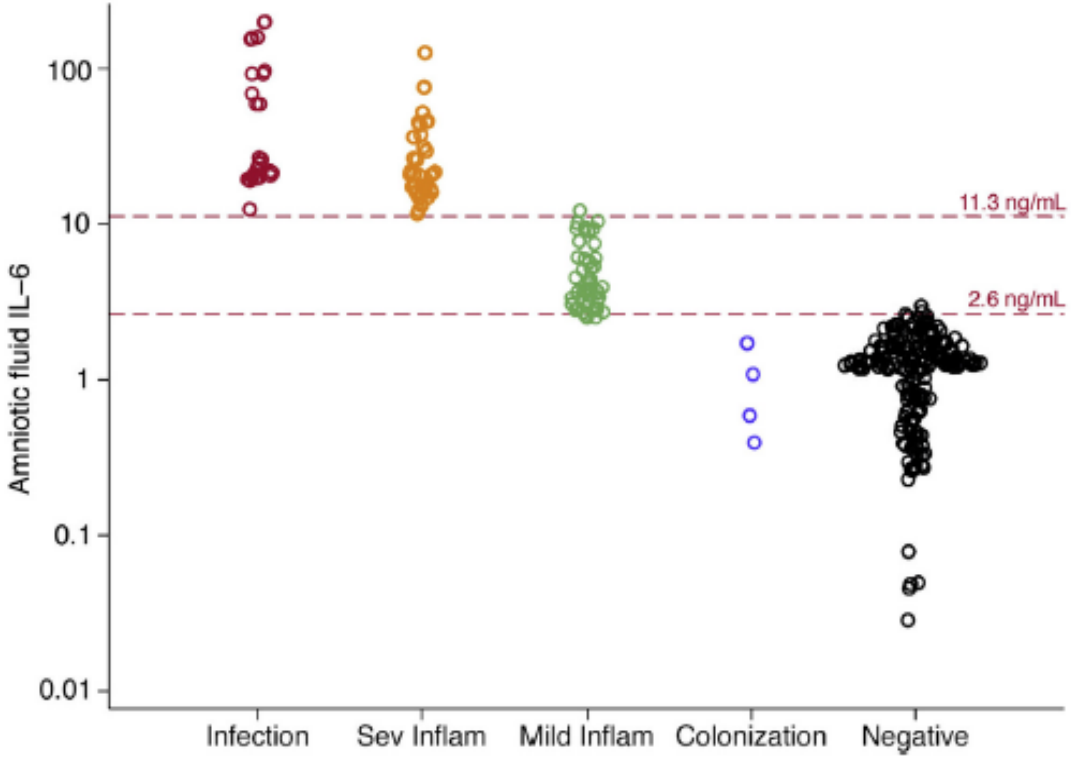
$P < .0001$ for χ^2 test across 5 groups (including the negative group, not shown).

Inflam, inflammation.

Combs. Inflammation, infection, preterm labor. Am J Obstet Gynecol 2014.

FIGURE 1

Dot-plot of amniotic fluid IL-6 levels in the 5 groups (log scale)



IL-6, interleukin 6; *Inflam*, inflammation; *Sev*, severe.

Combs. Inflammation, infection, preterm labor. Am J Obstet Gynecol 2014.

TABLE 4

Pregnancy outcomes

Variable	Group: Amniotic fluid interleukin-6, ≥11.3 ng/mL		Amniotic fluid interleukin-6, 2.6-11.2 ng/mL	Amniotic fluid interleukin-6, <2.6 ng/mL		*P* value[a]
	Infection (n = 27)	Severe inflammation (n = 36)	Mild inflammation (n = 47)	Colonization (n = 4)	Negative (n = 191)	
Gestational age at delivery, wk[b]	27.6 ± 3.9	27.9 ± 3.9	32.3 ± 4.7	33.6 ± 4.4	35.5 ± 3.3	< .0001
Median latency, d[c,d]	<1 (0–1)	2 (0–7)	7 (2–24)	23.5 (11.5–33)	25 (6–48)	< .0001
Latency <72 h, n (%)[c]	23 (88)	20 (56)	16 (34)	1 (25)	32 (17)	< .0001
Latency <7 d, n (%)[c]	26 (100)	25 (69)	23 (49)	1 (25)	48 (25)	< .0001
Birth <37 wk, n (%)[c]	26 (100)	35 (97)	39 (83)	3 (75)	122 (64)	< .0001
Clinical chorioamnionitis, n (%)	4 (15)	2 (6)	2 (4)	1 (25)	11 (6)	.17
Histologic chorioamnionitis, n (%)[e]	22 (85)	13 (38)	7 (19)	0	10 (8)	< .0001
Funisitis, n (%)[e]	19 (73)	7 (20)	7 (19)	0	13 (11)	< .0001
Postpartum endometritis, n (%)	1 (4)	1 (3)	1 (2)	1 (25)	6 (3)	.26

[a] Comparison of subjects across all 5 groups with analysis of variance (gestational age), nonparametric analysis of variance (latency), or χ^2 test for other outcomes; for histologic chorioamnionitis, funisitis, and postpartum endometritis, the Fisher exact test was used because of small sample sizes; [b] Data are given as mean ± SD; [c] N = 26 in the infection group because of missing data; [d] Data are given as median (interquartile range) for latency; [e] N = 26, 34, 37, 1, and 120 for the 5 groups, respectively, because of missing data.

Combs. Inflammation, infection, preterm labor. Am J Obstet Gynecol 2014.

TABLE 5

Perinatal outcomes

Variable	Group: Amniotic fluid interleukin-6, ≥11.3 ng/mL: Infection (n = 27)	Amniotic fluid interleukin-6, ≥11.3 ng/mL: Severe inflammation (n = 36)	Amniotic fluid interleukin-6, 2.6-11.2 ng/mL: Mild inflammation (n = 47)	Amniotic fluid interleukin-6, <2.6 ng/mL: Colonization (n = 4)	Amniotic fluid interleukin-6, <2.6 ng/mL: Negative (n = 191)	*P* value[a]
Birthweight, g[b]	1165 ± 614	1335 ± 839	2083 ± 858	2206 ± 1102	2725 ± 772	< .0001
Composite perinatal morbidity and death: ≥1 of the following, n (%)	22 (81)	26 (72)	25 (53)	1 (25)	41 (21)	< .0001
Perinatal death	5 (19)	7 (19)	3 (6)	0	3 (2)	< .0001
Stillbirth	0	3	1		2	
Neonatal death	5	4	2		1	
Respiratory distress syndrome, n (%)	17 (63)	20 (56)	23 (49)	1 (25)	37 (19)	< .0001
Intraventricular hemorrhage, grade 3 or 4, n (%)	2 (7)	3 (8)	2 (4)	0	4 (2)	.15
Necrotizing enterocolitis, n (%)	1 (4)	2 (6)	0	0	0	.02
Culture proven neonatal sepsis, n (%)	6 (22)	6 (17)	4 (9)	0	6 (3)	.001

[a] Comparison of the subjects in the 5 groups by analysis of variance (birthweight) or Fisher exact test (morbidities); [b] Data are given as mean ± SD.

Combs. Inflammation, infection, preterm labor. Am J Obstet Gynecol 2014.

DOI: 10.1111/j.1471-0528.2007.01385.x
www.blackwellpublishing.com/bjog

Systematic review

Use of C-reactive protein as a predictor of chorioamnionitis in preterm prelabour rupture of membranes: a systematic review

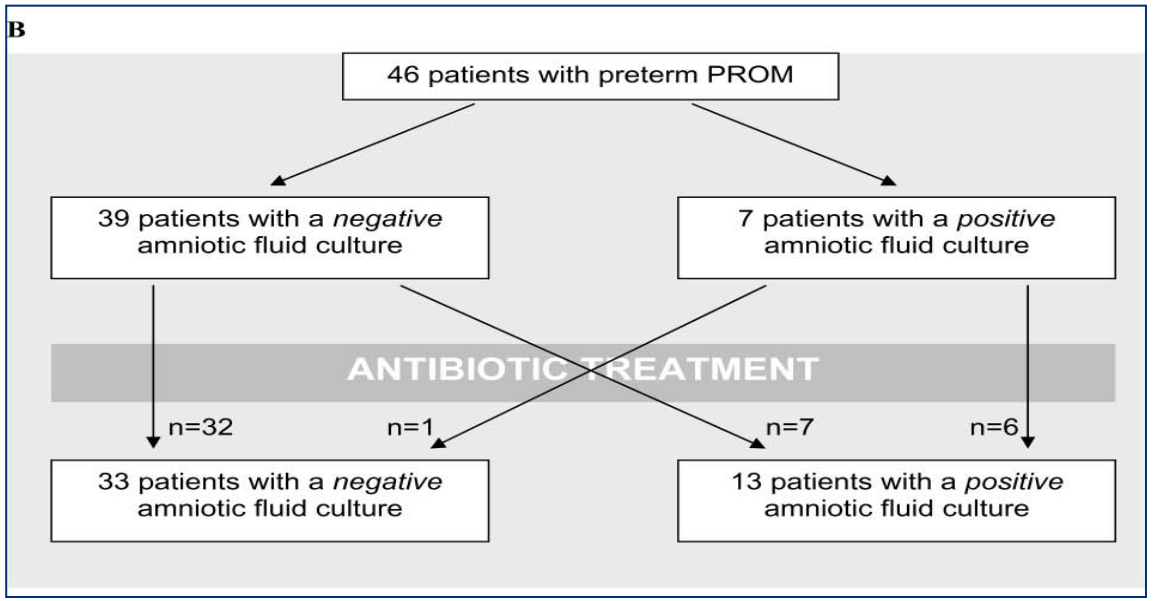
RD Trochez-Martinez,[a] P Smith,[b] RF Lamont[c]

[a]Women and Children Division, Gynaecology and Obstetrics Directorate, Torbay Hospital, Devon, UK [b]The Chilterns, Women & Children's Health, Southmead Hospital, Bristol, UK [c]Women and Children Division, Northwick Park Hospital, Middlesex, UK
Correspondence: Dr RD Trochez-Martinez, Level 4 Maternity Unit, Torbay Hospital, Lawes Bridge, Torquay, Devon TQ2 7AA, UK.
Email ruben.trochez-martinez@nhs.net

Accepted 29 March 2007.

Author's conclusions There is no clear evidence to support the use of CRP for the early diagnosis of chorioamnionitis. Further research is required to address the contradictory findings of diagnostic accuracy.

Antibiotic administration to patients with preterm premature rupture of membranes does not eradicate intra-amniotic infection
Gomez et al, 2007



(1) Antibiotic administration rarely eradicates intra-amniotic infection in patients with preterm PROM

(2) Intra-amniotic inflammation developed in one-third of patients who did not have inflammation at admission, despite antibiotic administration

(3) A sub-group of patients with documented inflammation of the amniotic cavity demonstrated a decrease in the intensity of the inflammatory process after antibiotics

NKL 2011

tullut	am-gluk	am-LD	PCR	partus		
22 sludge, bulging membranes	<0.5	559	negat	23+1	chorio	induktio 23+1
28+5 LVM	<0.5	1253	Ureaplasma urealyticum	29+3	chorio	induktio 29+3
23+4, aeimmin konisaatio	<0.5	EO	Mycoplasma hominis	25+6	chorio	
24+6, LVM	0.7	1941	Candida species	25+0	chorio	
24+5	0.7	452	Ureaplasma urealyticum	29+2	chorio	perätilasektio
30	0.6	1692	negat	32+2	chorio	
28+1 LVM	*01.40	338	Paracoccus	30+4	chorio	punktoitu kahdesti
28+3	alle 0.6	1770	negat	28+4	chorio	vesi sektion yhteydessa
19+5 lvm	*1.1	1314	negat	27+4	ablaatio	
30+0	0.9	494	Ureaplasma urealyticum	31+1	chorio	
26+3	alle 0.5	2044	negat	26+4	chorio	
35+3 sup ja jomottelu	alle 0.5	EO	Haemophilus	35+4	abskessi	
27+1 LVM (langa aiemmin)	alle 0.5	1453	urea+candida	27+2	chorio	
23+0 LVM	alle 0.5	7178	EO	24+4	chorio	
25+	*1.3	566	FUSOBACT.NUCLEATUM	27+	tulematta	
28+4 pprom	*3.6	1219	Ureaplasma urealyticum	29+2		
	<0.5	3241	BACTEROID.UREOLyt,fusobact		chorioamnionitis,funicitis	
	<0.5	4834	Bacteroides,ureaplasma,candida		chorioamnionitis	

NKL, 10/2011

Lapsivesipunktio ja epäily intra-amniaalisesta infektiosta ≤H32

Indikaatiot: tapauskohtaisesti, pääosin potilaat:

1. joilla lapsivedenmeno ja lievästi nousut CRP, lämpö alle 37.5
2. potilaat, joilla kalvo pullottaa ja vaginaalisessa ultraäänessä selkeä sludge-löydös kliinisen tilanteen mukaan tapauskohtaisesti
3. ennen hätälankaa jos vaginaalisella uä:llä todetaan sludge-löydös

tutk.nro	tutkimus	poikkeava arvo
1. 1460	Am-Gluk	alle 0.8 mmol/L
2. 8667	-LD (MAININTA:LAPSIVESI!)	yli 419 U/L , suspekti jo yli 250 U/L
3. 4381 (bakt PCR)	-BaktNhO (maininta:lapsivesi!)	
4. 3491	Pu-BaktVil (maininta:lapsivesi!)	
5. 4594	P-CRP (maininta: lapsivesi!)	

Am-Epo ja Am-Iam lääkärin harkinnan mukaan, ei "automaatisesti"

-Jos LV runsaasti , otetaan kaikki ao. tutkimukset.
-Jos niukasti, otetaan ainakin ensimmäiset kolme tutkimusta ao. listasta.
-Kätilö laittaa potilaan tarran LVP vihkoon,joka on os 42 kansliassa.

Istukka lähetetään PAD:ksi synnytyksen jälkeen. Punktion yhteydessä tästä maininta Obstetrixin "Huomiot" osaan !

Current Clinical Management of Suspected IAI

Clinically SILENT in majority of cases

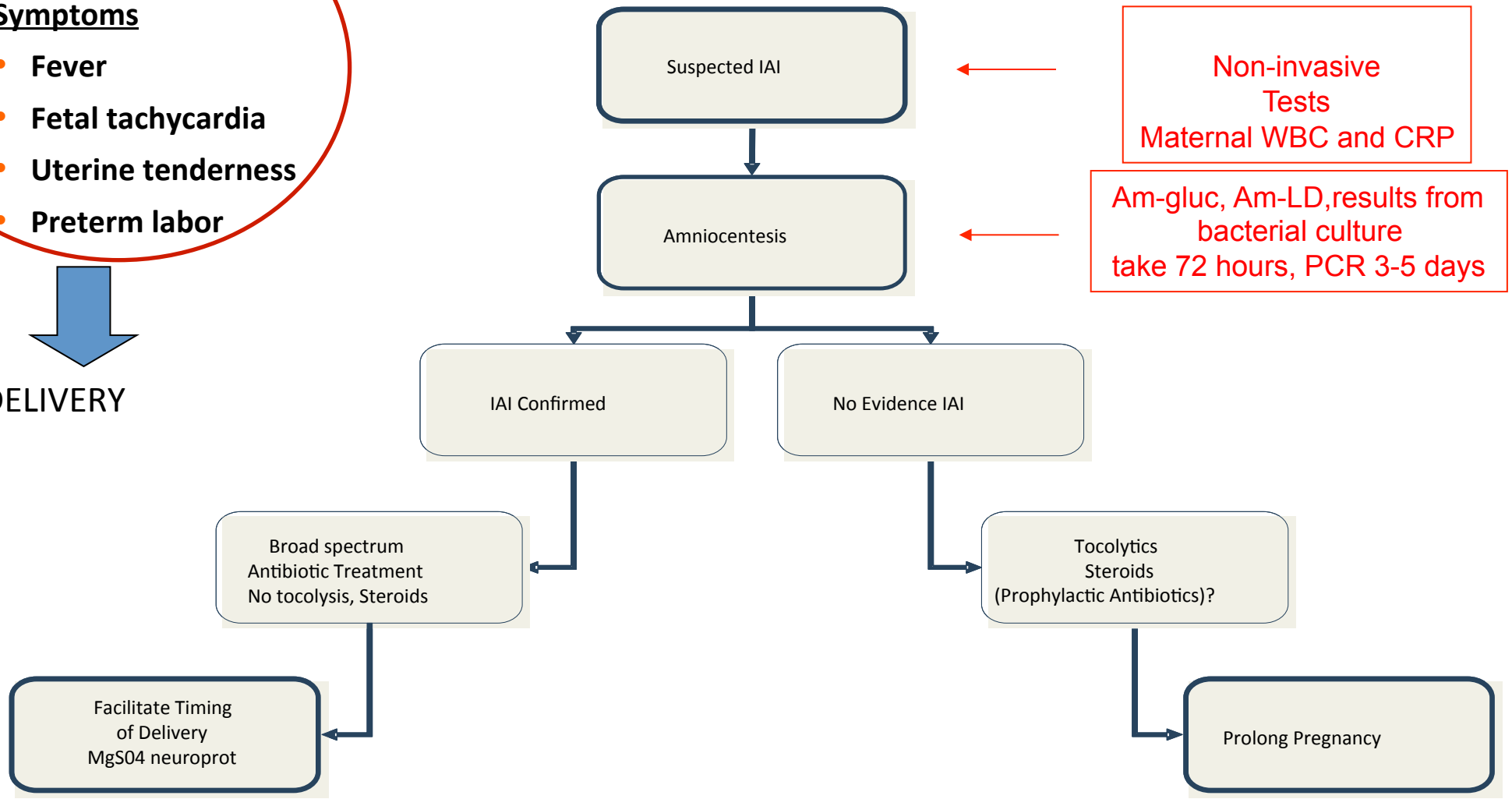
5-17%

Symptoms

- **Fever**
- **Fetal tachycardia**
- **Uterine tenderness**
- **Preterm labor**

DELIVERY

Bulging membranes, and/or PPROM



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SOMANZ

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Amniotic fluid glucose, lactate dehydrogenase and matrix-metalloproteinase-8* concentrations predict positive bacterial PCR and histological chorioamnionitis in women with clinically asymptomatic PPROM

Vedran Stefanovic [1]

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Introduction

Chorioamnionitis may be devastating pregnancy complication. Ascending infection is a key pathway in the etiology of early preterm births. The most challenging group of patients are those with very preterm premature rupture of membranes (PPROM) without clinical symptoms suggesting intraamniotic infection (IAI).Optimal delivery time in cases of subclinical IAI is essential to avoid adverse long-term outcome. Many biochemical markers have been proposed as useful in IAI detection, but in most publications the end-point was delivery within 72 hours, not "intention-to-treat/deliver".

Material and methods

Retrospective analysis of 29 women with clinically asymptomatic PPROM (gestational age 24+2 – 31+6) .All women received broad spectrum antibiotics after confirmed PPROM. Amniocentesis was performed to evaluate amniotic fluid glucose (Am-gluc), lactate dehydrogenase (Am-LD), matrix metalloproteinase 8 (MMP-8) and bacterial PCR. The diagnosis of IAI was established and delivery decision was made if Am-gluc concentration was ≤ 0.8 mmol/l or/and Am-LD concentration was ≥ 419 IU/L or in presence of positive PCR. MMP-8 analysis was performed after delivery.

Results

Nineteen samples were PCR positive for presence of bacteria in the amniotic fluid. Am-gluk and Am-LD concentrations correlated with positive amniotic fluid PCR and histological chorioamnionitis ($p=0.037$ and $p=0.042$, respectively). MMP-8 concentrations showed the best performance in predicting positive amniotic fluid bacterial PCR and histological chorioamnionitis ($p< 0.001$).Both Am-gluc and Am-LD highly correlated with MMP-8 concentrations ($p<0.01$)

Conclusions

Amniocentesis is a safe and useful in asymptomatic patients with PPROM. Simple and rapid markers of IAI in the amniotic fluid (glucose and lactate dehydrogenase) have very good performance in predicting amniotic fluid positive bacterial PCR and histological chorioamnionitis. By adding MMP-8 determination in the amniotic fluid, the performance of these markers is clearly improved. In cases of PPROM , determination of Am-gluc, Am-LD and MMP-8 levels may improve IAI diagnostic and optimize delivery time.

Table 2. Amniotic fluid and maternal serum biomarkers in women with or without HCA

T.Myntti et al, unpublished

	HCA n=49		No HCA n=17		p-value
am-LD, median (range)	1355	(83-9698)	296	(62-3170)	<0.001
am-Gluc, median (range)	0.4	(0-6.0)	1.1	(0-4.5)	0.011
Positive bacterial PCR* n (%)	23	(47)	0	(0)	0.001
Positive bacterial culture** n (%)	13	(27)	1	(6)	0.137
Either PCR or culture positive*** n (%)	27	(55)	1	(6)	<0.001
Maternal P-CRP mg/l at delivery date	35.5	(3-97)	19	(0-104)	0.32
Maternal WBC 109/l at the delivery date	14.5	(9-28.1)	12.3	(6.7-22.8)	0.015

*missing n= 10 (HCA n= 6, no HCA n=4)

**missing n=21 (HCA n= 14, NO HCA n=7)

***missing n=3 (HCA n= 2, No HCA n=1)

am-LD= amniotic fluid lactate dehydrogenase; am-Gluc = amniotic fluid glucose; PCR= 16-S-r-RNA sequencing; WBC = white blood cell; CRP=c-reactive protein

Table 5. Am-LD and am-Gluc association with PPROM in patients with or without HCA

	HCA			No HCA		
	PPROM+ n=29	PPROM- n=20	p-value	PPROM+ n=10	PPROM- n=7	p-value
am-LD IU/L, median (range)	1253 (83-9698)	1417 (247-6385)	0.416	323 (62-3170)	222 (125-1728)	0.669
am-Gluc mmol/l, median (range)	0.7 (0-6.0)	0.05 (0-3.4)	0.396	1.1 (0-4.5)	1.6 (0.6-1.9)	0.887
bacterial PCR positive*, n(%)	13 (44.8)	10 (50)	0.571	0	0	
bacterial culture positive** , n (%)	8 (27.6)	5(25)	0.726	0	1 (14.3)	

*missing HCA: PPROM+ n=3 ; PPROM- n=3, missing No HCA PPROM+ n=2; PPROM- n=2

**missing HCA: PPROM+ n=6; PPROM- n=8, missing No HCA PPROM+ n=4, PPROM- n=4

am-LD= amniotic fluid lactate dehydrogenase; am-Gluc = amniotic fluid glucose; PCR= 16-S-r-RNA sequencing; PPROM= preterm prelabor rupture of membranes; HCA= histologic chorioamnionitis; CRP=c-reactive protein

Table 4. Microbial findings in am-PCR or bacterial culture N=32

	Microbes in amniotic fluid	N	am-LD IU/L	(range)	am-Gluc mmol/l	(range)	PCR / culture	early sepsis n(%)	aerobic / anaerobic
1	Ureaplasma urealyticum	11	1253	(91-9698)	0	(0-3.4)	PCR	2 (18)	
2	Candida albicans	6	1834.5	(1453-4834	0.05	(0-0.9)	culture	2 (33)	
3	E coli	1	5276		0		culture	0	anaerobic
4	Fusobacterium nucleatum	3	3241	(292-5276)	0	(0-0.7)	PCR	1 (33)	anaerobic
5	Hemofilus influenzae	1	671		1.5		PCR	1 (100)	aerobic
6	Gardnerella vaginalis	3	1785	(912-4426)	0	(0-2.8)	culture	1 (33)	anaerobic
7	Str viridans	2	842.5	(330-1355)	0.9	(0-1.8)	PCR	1 (50)	aerobic
8	Str pneumoniae	1	438		0		PCR and culture	0	anaerobic
9	Bacteroides ureolyticus	2	4350	(3241-5459	0.3	(0-0.6)	PCR	1 (50)	anaerobic
10	Peptostreptococcus anaerobius & anginosus	2	2340	(1911-2769	0.1	(0.1-0.1)	PCR and culture	1 (50)	anaerobic

Data shown as median (range)

Does incorporation of amniocentesis in the management of PTL and PPROM **improves neonatal outcome?**

- Yes it DOES
- 2 randomized studies (”clinical treatment” vs. amniocentesis)
- *Porreco, 2008*
- *Shinjo, 2012*
- Less composite neonatal morbidity in groups with amniocentesis incorporated in the management

Conclusions

1. Majority of patients with severe IAI are asymptomatic

2. Antibiotics policy should be changed

3. Tocolysis in patients with PPROM should be discouraged unless IAI is ruled out

4. Amniocentesis is safe and useful in asymptomatic patients with both intact membranes PPROM, by this approach SAFE pregnancy prolongation is possible

5. Simple and rapid markers of IAI (amniotic fluid gluc and LD) have good performance in predicting positive cultures/PCR and histological chorioamnionitis

6. Determination of MMP-8 and other matkers of imflammation adds an additional value, especially in cases with discrepancy between Am-gluc and Am-LD

7. Both cultures and molecular microbiology techniques should be used

Conclusions

- There is ENOUGH evidence that amniocentesis in PPROM and/or PTL cases in useful to :

1. Rule out IAI
2. Prolong pregnancy and improve neonatal outcome
3. Enable time-window for Mg-neuroprophylaxis
4. It is cost-effective

Conclusions

8. Patients´ counselling and involvement of neonatologist are essential

9. Placenta should always be sent for PAD

10. Early diagnosis of PPROM, ”appropriate” antibiotic and MgS04 administration is benefitial for many premature babies

11. Future possible ”anti-inflammatory treatment might safely prolong pregnancy and decrease neonatal morbidity/mortality

12. Feed-back