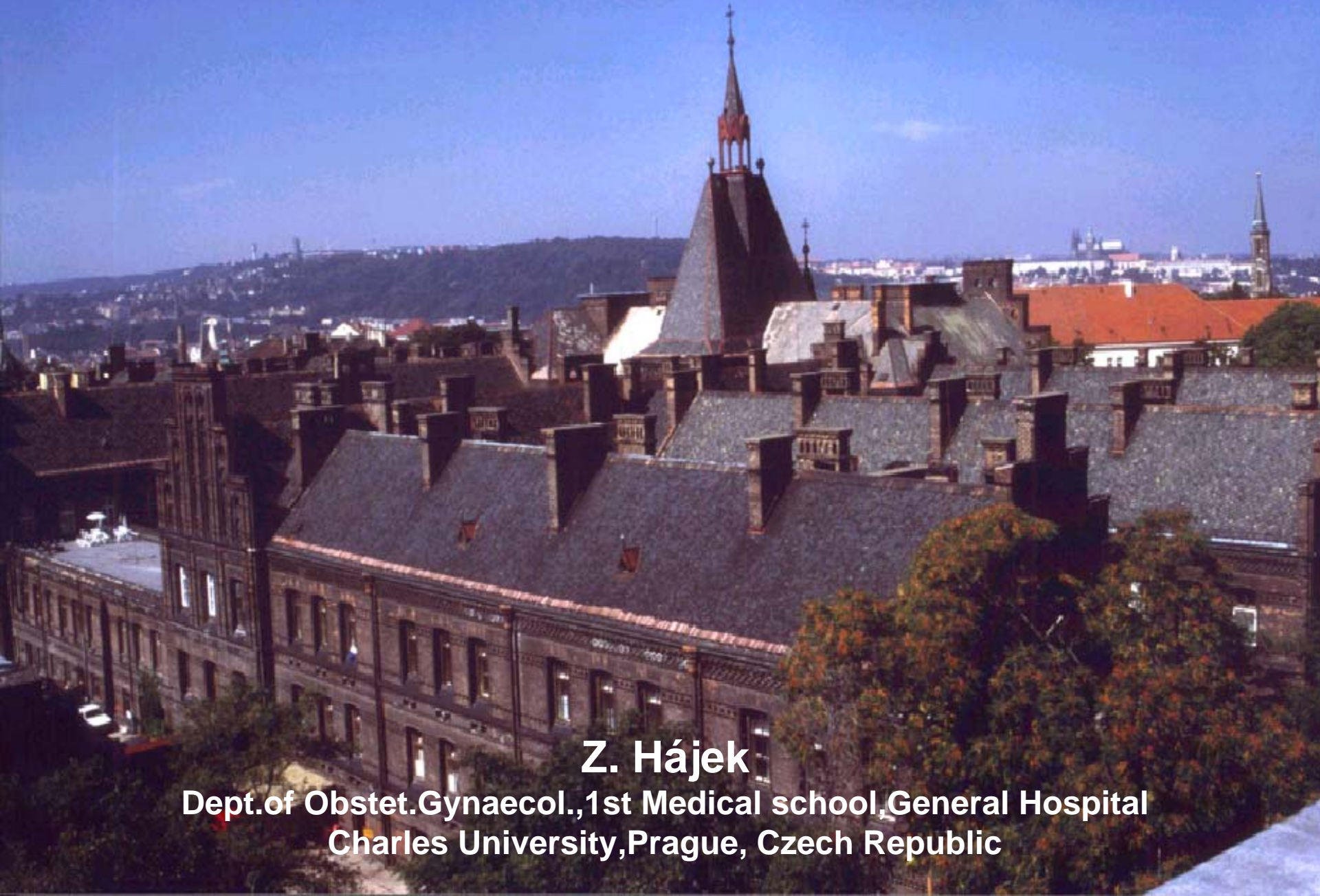


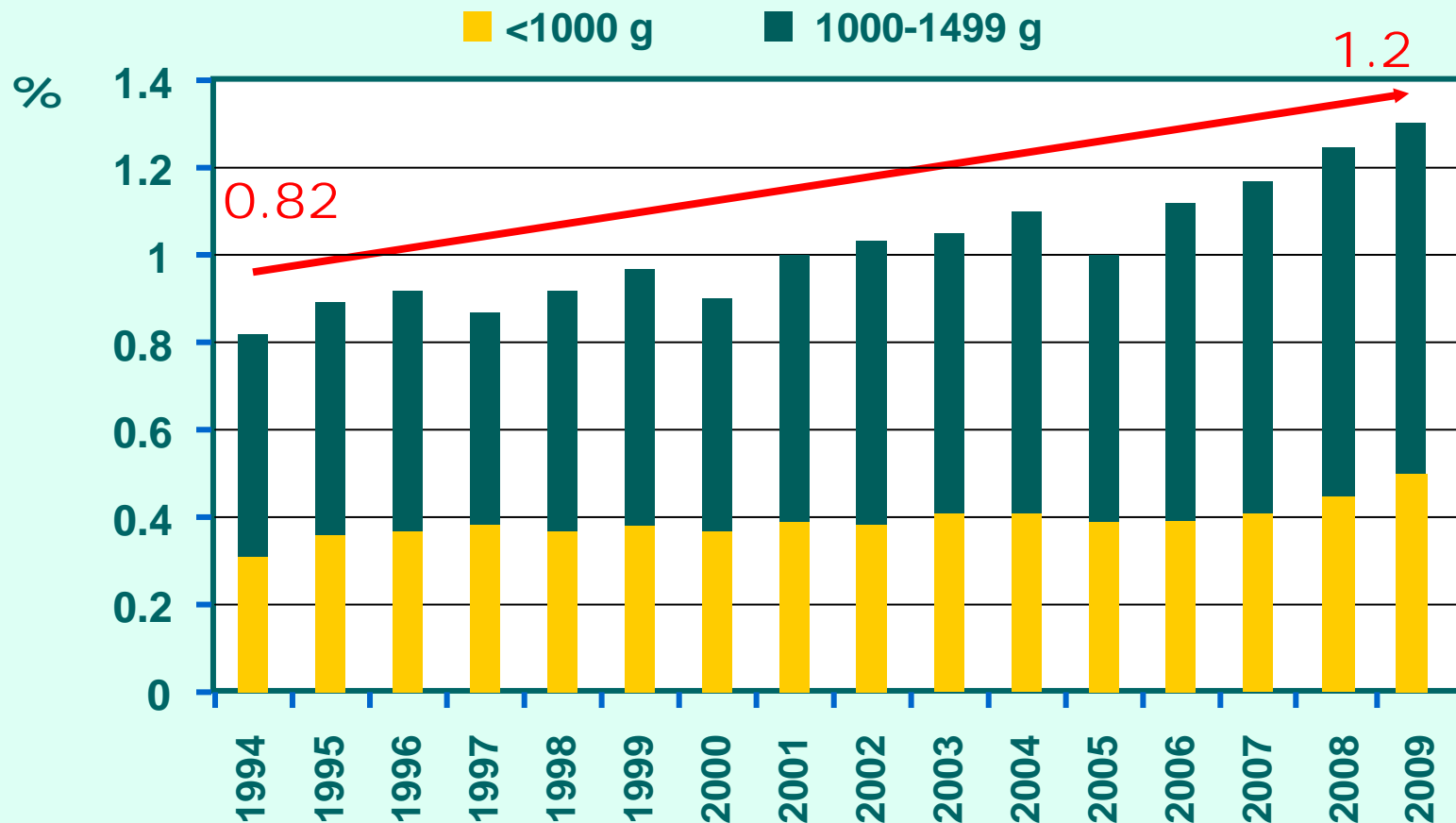
Premature labor and infection/inflammation



Z. Hájek

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Charles University,Prague, Czech Republic**

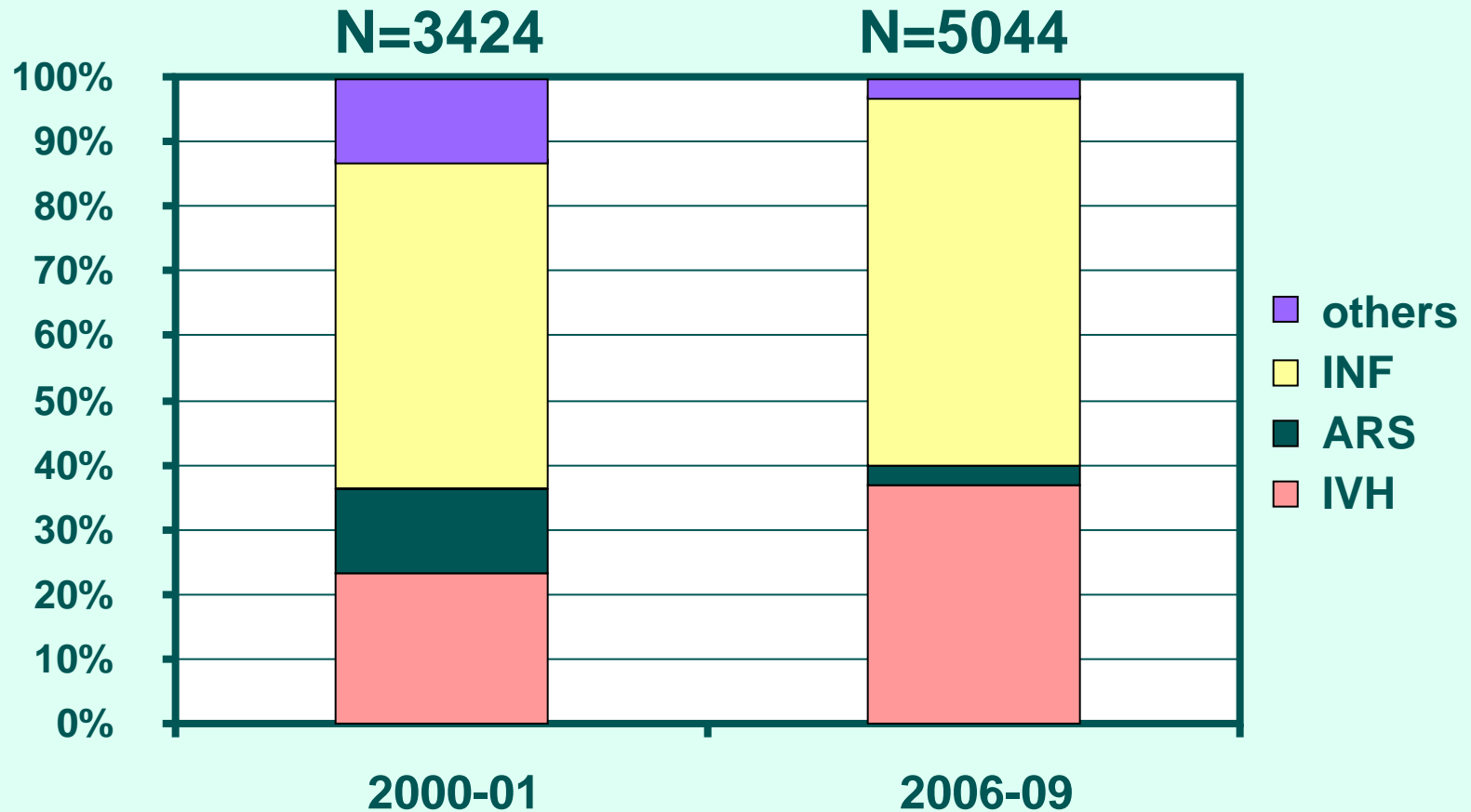
Incidence of VLBWI in the CR



viability border 24th week

Main causes of death in LBWI

BW 1000-1999g (proportional)



Intrauterine infection

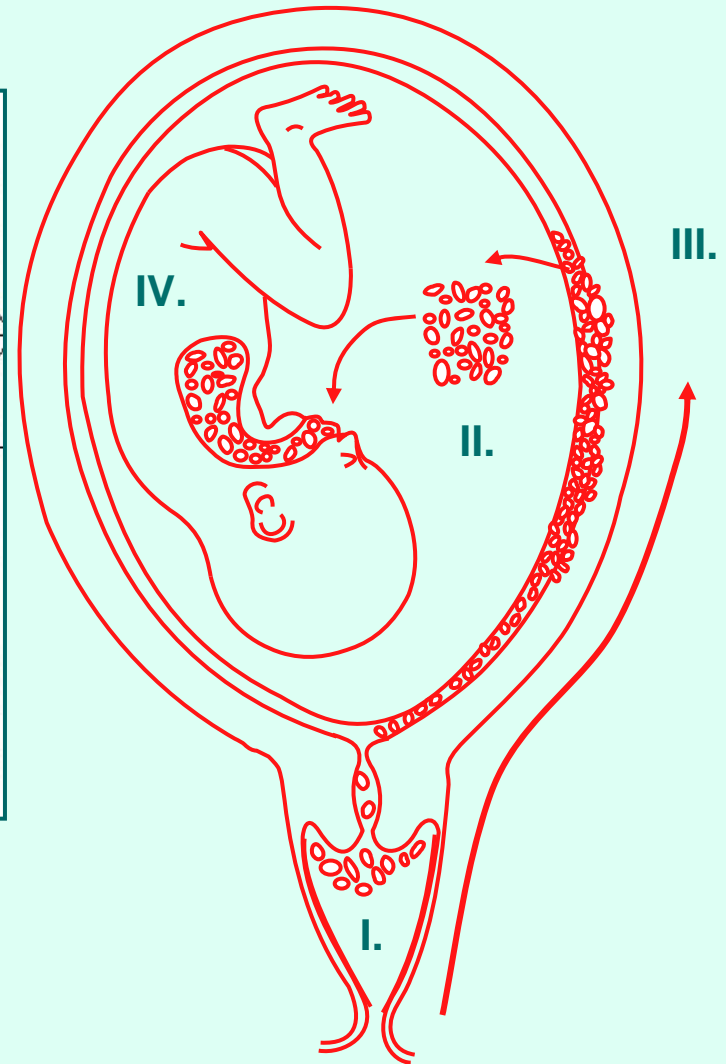
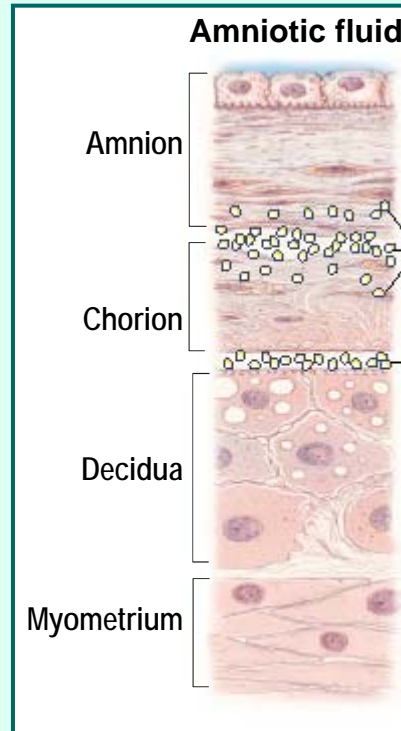
Microbial invasion of the amniotic cavity

Access of microorganisms to the:

- decidua
- membranes
- amniotic fluid

Microbial invasion of the fetus

FIRS – fetal inflammatory response syndrome



Fetal risk by PPRROM

- **Main cause**
of preterm labour
- **Infection**
30% before PROM
75% during labour after PROM
- **Abruption of placenta**
- **Compression of umbilical cord**

Journal of Perinatology, 23, 2003: 235-239

**Perinatal
Asphyxia**

**Perinatal
Infection
Damaged
or stress cells**

TLRs activation

NF - κ B activation

**Immune response induction
of proinflammatory Cytokines/Chemokines**

Brain Damage

Systemic Inflammation

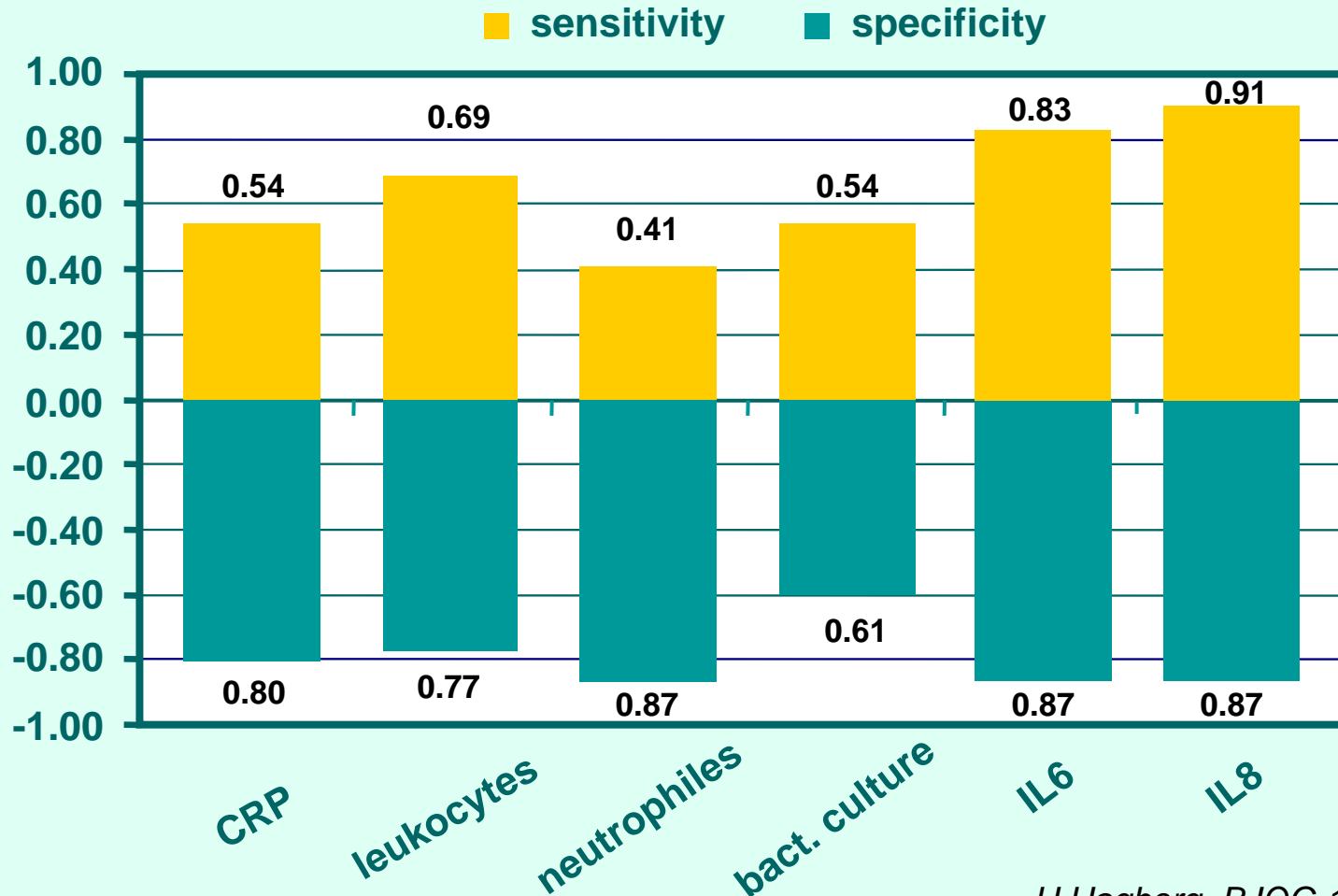
Maternal monitoring during PPRROM

- **Signs of intrauterine infection**
 - **laboratory markers**
 - **Leucocytes + neutrophils(I/T ratio)**
 - **CRP**
 - **temperature $>38^{\circ}\text{C}$**
 - **maternal,fetal tachycardia**
 - **vaginal culture**
 - **fundal tenderness**
- **Contractions**
- **Changes of Bishop score**
- **Doppler velocimetry, biophysical profile**

Sensitivity and specificity of basic markers of infection

Premature labour < 7 days

N = 101 (median 28 ± 0.6)



Diagnosis of intrauterine infection

➤ Direct examination

➤ Confirmed intrauterine infection

- Amniocentesis (AC) – culture/PCR; cytokines
- Cordocentesis (CC) - fetal blood cytokines

➤ Indirect evaluation

➤ Suspected intrauterine infection

- Presence of clinical signs or biomarkers

Novel markers in detection of infection/inflammation

- **Pattern recognition receptors (PRR)**
- **Toll-like receptors (TLR)**
- **RAGE-receptor for advanced glycation end products**
- **Calcium binding proteins (A-C)**
- **Proteomic biomarkers (neutrophil defensin-1, 2, Calgranulins A, C)**
- **Vaginal AF glucose measurement**
- **CCL20 (Exodus 1, MIP-3, LAR)**
- **MCP 1-3 monocyte chemotactic protein**
- **CRF and CRF-BP, CD 14**
- **MMP-8 bedside rapid test**
- **Procalcitonin**

Detection of feto-maternal infection/inflammation by the soluble receptor for advanced glycation end products (sRAGE): results of a pilot study*

Zdeněk Hájek^{1,**}, Anna Germanová², Michal Koucký¹, Tomáš Zima², Pavel Kopecký¹, Marie Vítková³, Antonín Pařízek¹ and Marta Kalousová²

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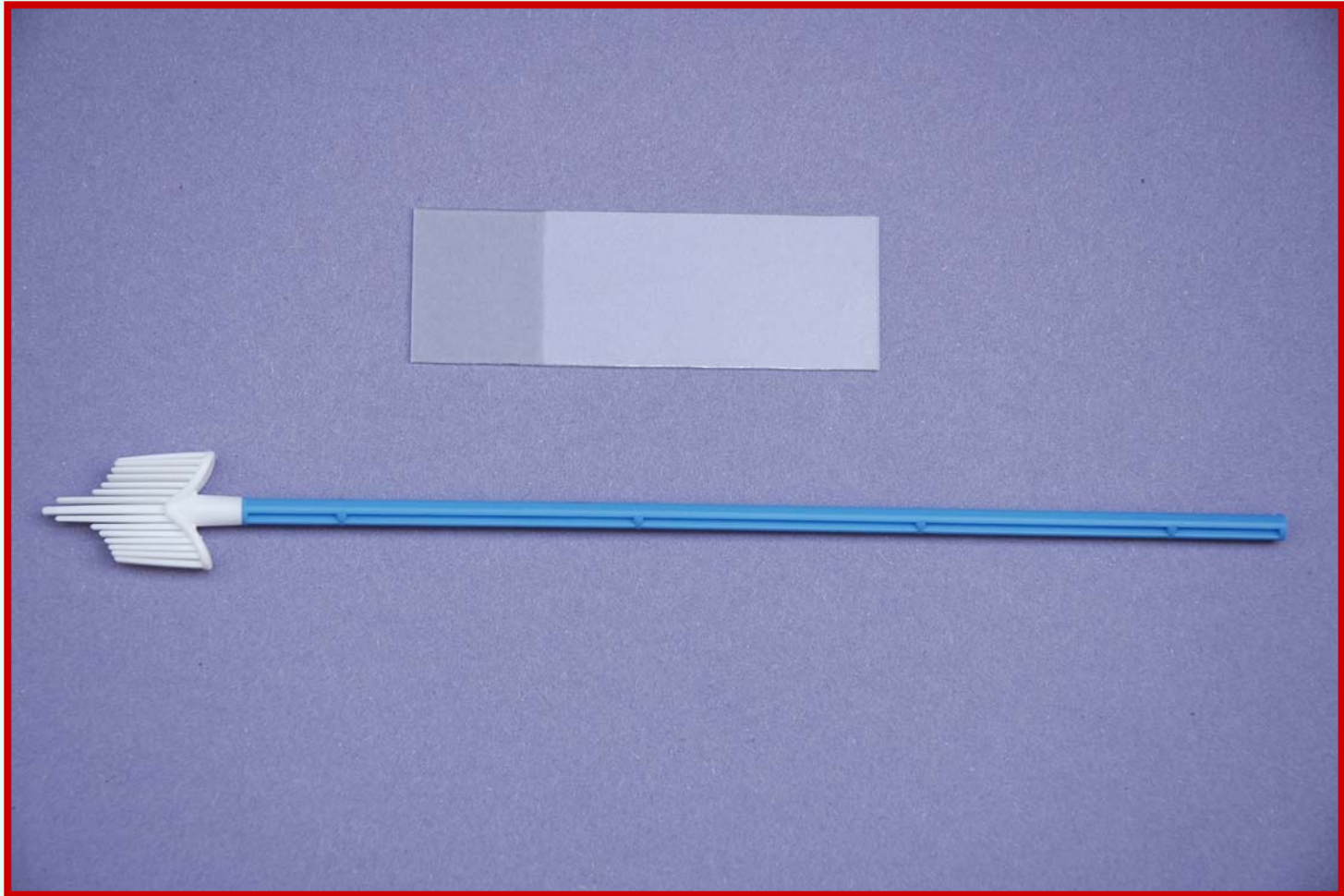
significantly lower levels of sRAGE compared with patients with threatening premature labor (600 ± 324 pg/mL, $P < 0.05$). sRAGE correlated negatively with leukocyte counts ($r = -0.325$, $P < 0.05$).

Conclusions: sRAGE might be a new and promising marker of premature labor, especially with the symptoms of PPRM.

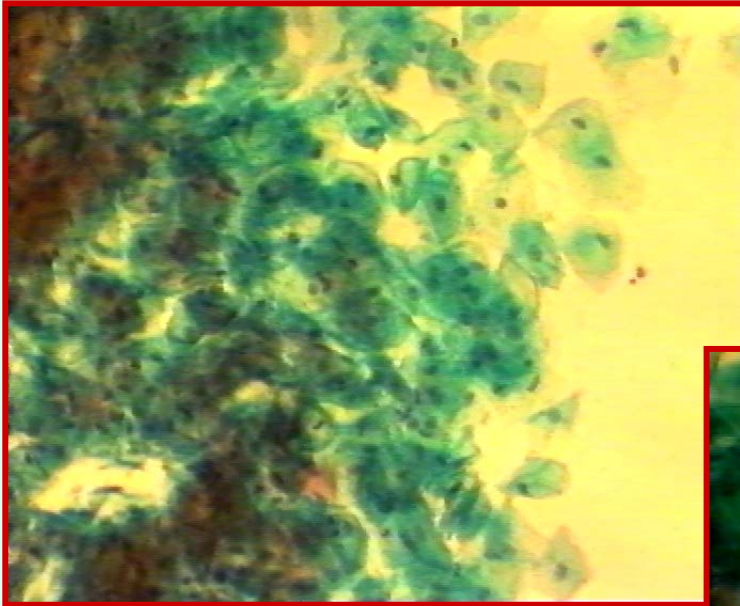
Keywords: Fetal inflammation; PPRM; preterm labor; soluble receptor for advanced glycation end products; sRAGE.

Women with PPRM had lower s-RAGE level 600.09 ± 324.41 pg/ml $p < 0.005$ compared to women with contractions, vaginal bleeding or cervical dilatation 890.91 ± 257.06 pg/ml, 820.99 ± 257.06 , 869.35 ± 373.98

Bethesda system 2001 „Cervex“



Normal pregnancy

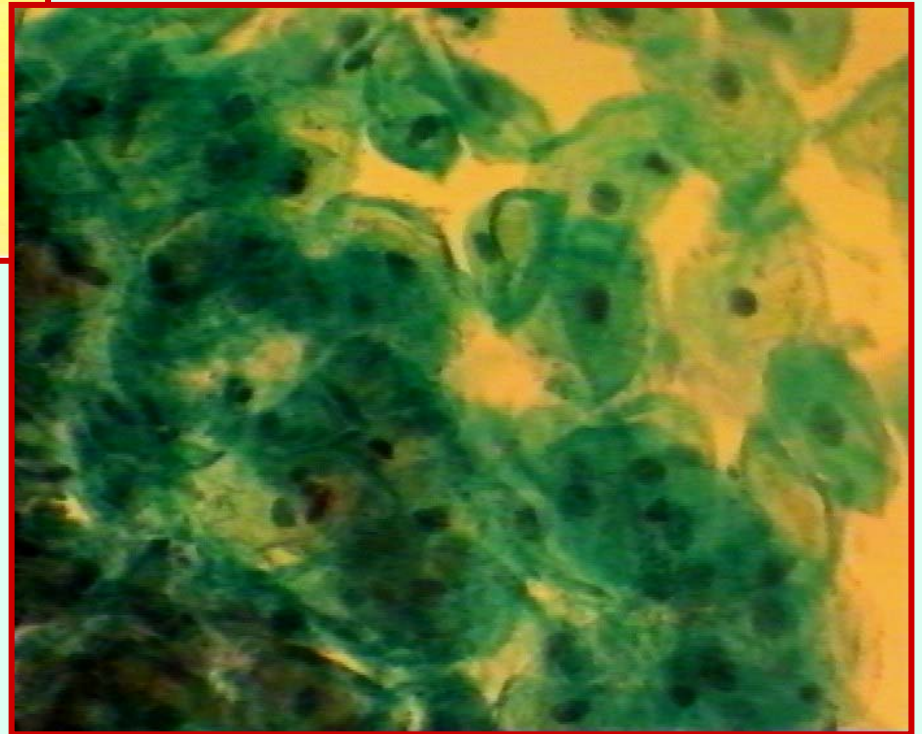


High crowded index

High folded index

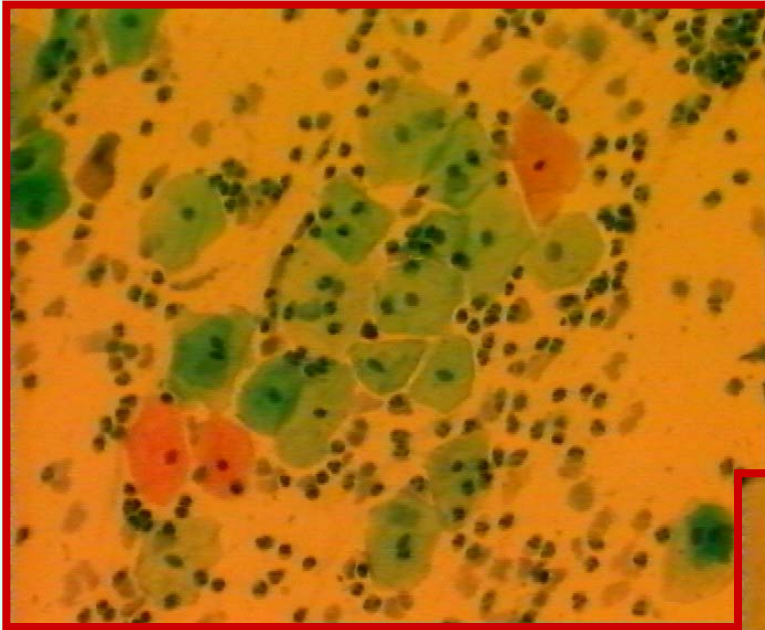
Navicular cells

Progesteron influence



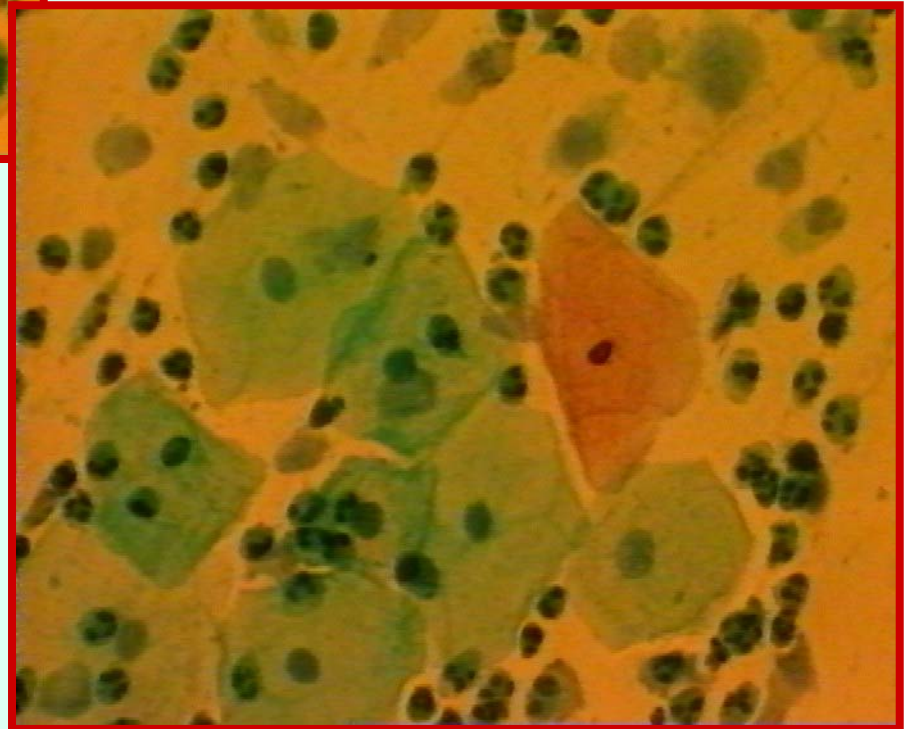
Preterm birth (30th week)

Pathological preparation for labour

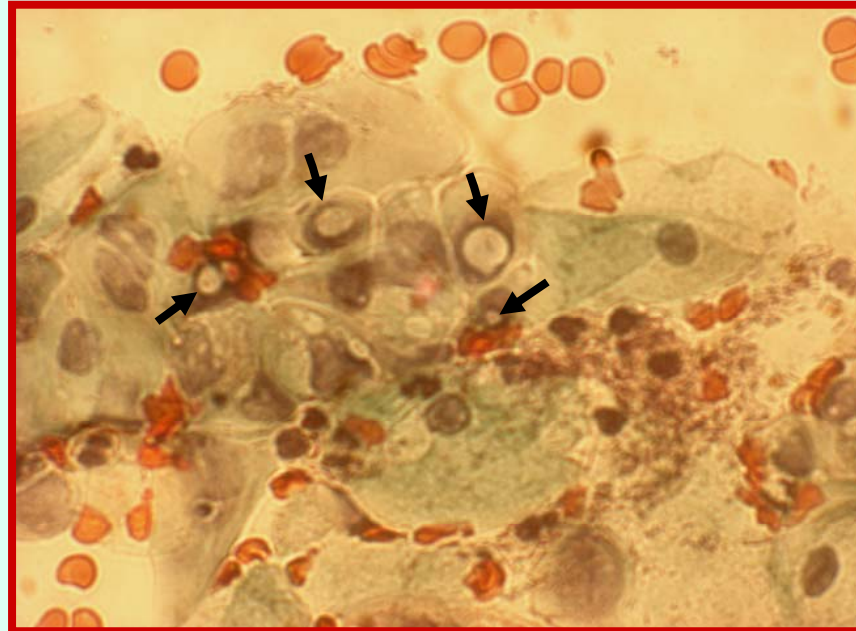


Leucocytes, histiocytes

cervical inflammation



Diagnosics of STD (Chlamydia infections)



Frequency of genital infection serotypes D-K 2 – 10%

| | Sensitivity | Specificity |
|-----------------|--------------------|--------------------|
| DFA, EIA | 60 – 75 % | 97.0 % |
| PCR, TMA | 98 – 99 % | 99.7 % |

Timing of delivery -PPROM

in pregnancies with compromised very preterm fetuses is one of the most difficult decision for the obstetrician.



Extremely preterm delivery on fetal indication

Considerations before the decision:

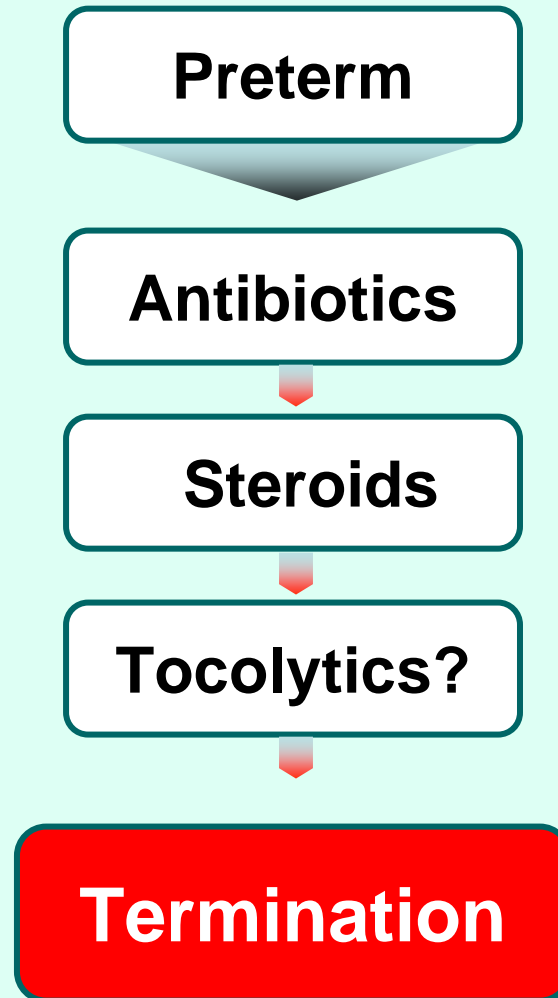
- ▶ **parents' attitude**
- ▶ **knowledge about the prognosis *in utero***
- ▶ **knowledge about the neonatal outcome
(survival, morbidity) in the local NICU**

Viability border of the infants in Europe

| | 22+0-22+6 | 23+0-23+6 | 24+0-24+6 | 25+0-25+6 |
|-------------|------------|------------|------------|-----------|
| Germany | Individual | Individual | CPR | CPR |
| Norway | Individual | Individual | Individual | CPR |
| Switzerland | paliative | paliative | individual | CPR |
| Nederlands | paliative | paliative | paliative | CPR |
| Ireland | paliative | paliative | CPR | CPR |
| Czech R. | paliative | individual | CPR | CPR |

CRP-cardiopulmonary resuscitation

Obstetric interventions for intrauterine infection



Advantage of expectant management

| | A | B | C | D | Avs B | Bvs C | Bvs D |
|----------------|----------------|----------------|-----------|-----------|----------|----------|----------|
| | PROM <48hrs | PROM >7days | 24th g.a. | 25th g.a. | p | p | p |
| N | 66 | 51 | 24 | 41 | | | |
| PROM (hrs) | 103.8 | 522h = 3.1wks | 15.5 | 103.3 | | | |
| g.a. (mean) | 28 | 28.1 | 24 | 25 | | | |
| brtw. (mean),g | 1036 | 1151g | 659.1 | 726 | | | |
| mortality | 1.5% | 5.8% | 21% | 19.5% | 0.2 | 0.05 | 0.050 |
| BPD | 11% | 16.6% | 33% | 30.0% | 0.5 | 0.10 | 0.200 |
| ROP | 0% | 0.0% | 15% | 18.0% | 0 | 0.01 | 0.005 |
| IVH | 3% | 2.1% | 15% | 3.0% | 0.5 | 0.05 | 0.500 |
| PVL | 6% | 2.1% | 0% | 3.0% | 0.5 | 0.50 | 0.500 |

PPROM - Acute labor & expectant management < 34 weeks

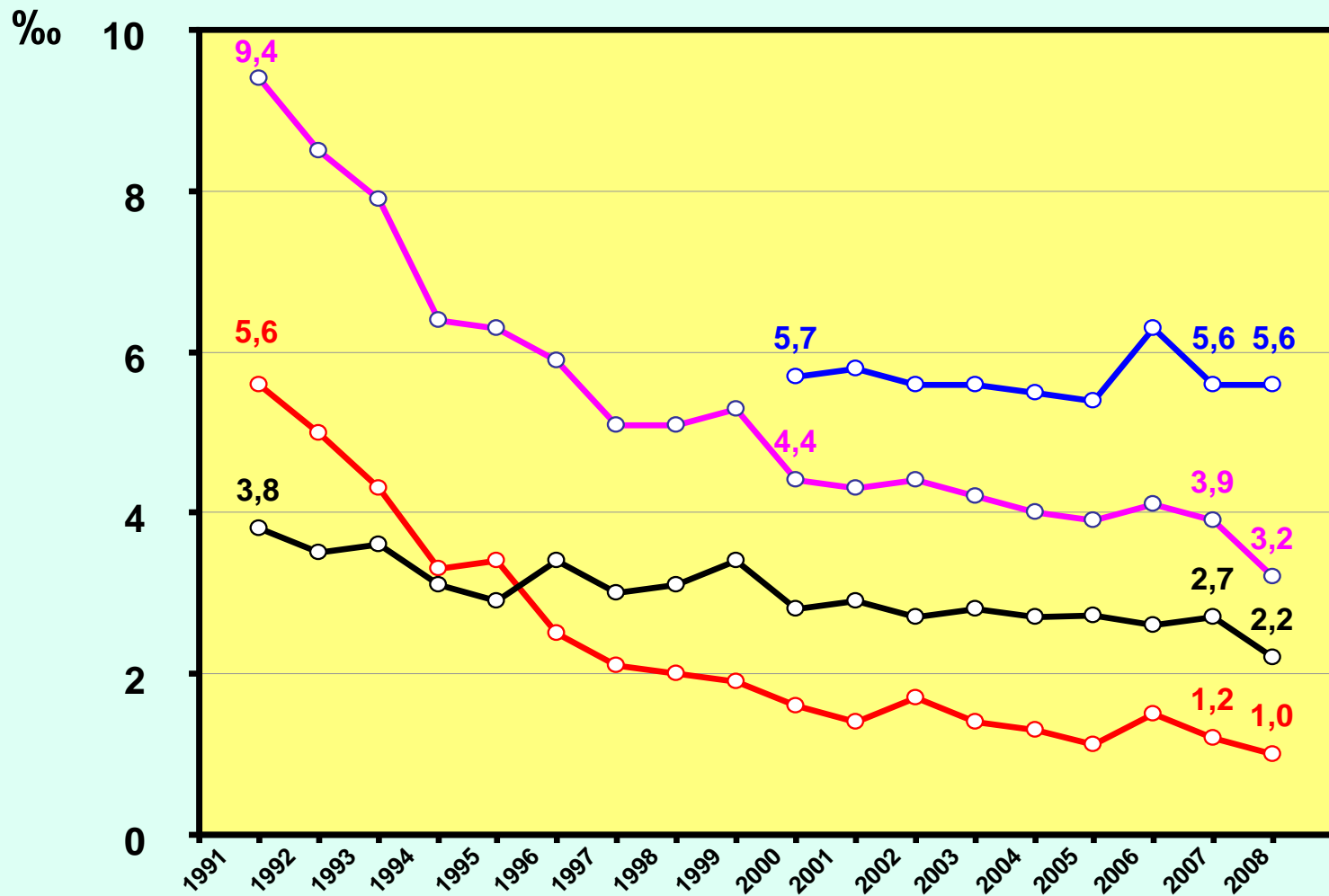
| Complications | N | Acute labor (%) | Expectant management (%) | RR (95% CI) |
|---------------------|-----|-----------------|--------------------------|------------------|
| CS | 140 | 11.1% | 8.8% | 1.21 (0.45-3.28) |
| Chorioamnionitis | 260 | 6.28% | 23.6% | 0.25 (0.12-0.53) |
| Neonat. sepsis | 257 | 7.0% | 6.2% | 1.00 (0.41-2.45) |
| RDS | 257 | 3.97% | 2.3% | 1.59 (0.41-5.97) |
| Perinatal mortality | 260 | 1.6% | 1.5% | 1.24 (0.19-8.06) |

Mode of delivery and neonatal morbidity/mortality (< 750 g)

| | VD (%) | SC (%) | OR |
|------------|--------|--------|------|
| Severe IVH | 41 | 22 | 2.79 |
| PVL | 5 | 3 | NS |
| Mortality | 55 | 35 | NS |
| Combined | 67 | 41 | 2.95 |

After multiple logistic regression analysis, in this subgroup, severe IVH and combined poor short term outcome were significantly correlated with vaginal delivery.

Perinatal mortality rate (PMR), stillbirths (SBR) and early neonatal mortality (ENMR) in the CR from 1991



Conclusion

- **In management of preterm birth is a clear trend to favor CS, especially below 750 g, because the prevalence of IVH and PVL in vaginal delivery**
- **The indication for CS has been indicated especially in breech presentation**
- **ATB ,corticosteroids and tocolytics have been used routinely, even if the markers of infection are elevated**
- **The outcome of infants delivered after 27th week of gestation was better than infants delivered 3-4 weeks earlier**
- **Some infants can profit from expectant management of PPRM if the infection/inflammation of mother is under control**



Thank you for your attention