

Aetiology

- Spontaneous preterm labour syndrome.
- PPROM.
- Multifetal pregnancies.
- Indicated or Iatrogenic.

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Pathogenesis

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Uterine Contractions + Cervical Remodelling

(False +ve 50-90%, HUAM, premat. dilat., cerclage failures)

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Mechanisms of initiation of PTL.

A Multifactorial process.

The outcome depends on a balance of +ves & -ves.

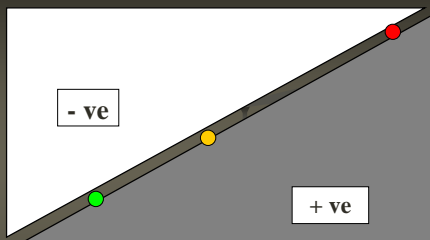
+ves

- Oxytocin receptors.
(é Gest. Age)
- Cytokines (IL-1, IL-6, TNF).
- Prostaglandins.
- Intracellular cAMP.
- Intracellular Ca⁺⁺.
- Uterine distension.
- Placental products of ischemia.
- Fetal Hypothalamopituitary axis.

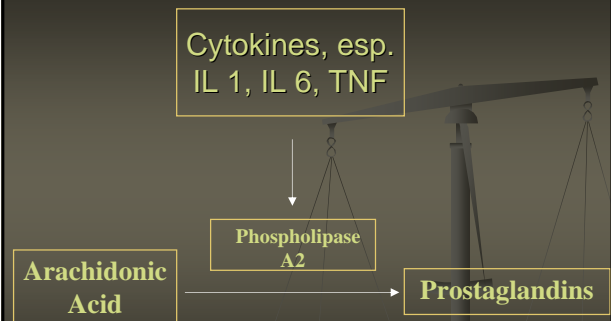
-ves

- Barriers to infection.
(BV, Chlam. Gono.,
Ureaplasma, Mycoplasma).
- Local progesterone.
- Cervical competence.

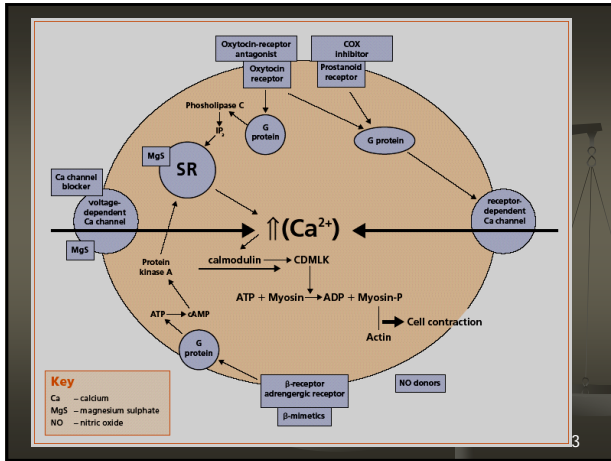
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A Model for Prevention of Risks of Prematurity

Primary Care:
 Screening & prevention in general population

Secondary Care:
 Prevention in high risk groups

Tertiary Care:
 Treatment of established cases

- Primary Care = Screening & Prevention in general population
- History.
 - Cervical Biometry.
 - Fetal Fibronectin.
 - Bacterial Vaginosis.
 - Salivary Estriol.

- ## History
1. **Obstetric:** (Lumley, 1993)
 - x 3 1st trim.= 12% / x 1 midtrimester = 15% / x 1 PTL = 30-50%
 - Recurrent indicated causes
 - last pregnancy is the most predictive
 2. **Gynecological:** malformations, trauma.
 3. **Current Pregnancy:** Low Sensitivity (Papiernik, 1984)
 - Scoring systems: (Creasy's modification of Papiernik score), (socioeconomic, physical, obstetric).
 - Warning symptoms (pressure, leucorrhoea, engagement).
 4. **Education on:**
 - Warning symptoms, STD's, induction of ovulation, Smoking, exercise, sexual activity.

- ## Cervical Sonography
- Competence is Mechanical / bacteriological barrier.
 - Process of effacement.
 - Categorical Vs. Continuous variable (ε age & size & contractions).
 - Once Vs. Dynamic Vs. Serial.
 - The earlier it starts, the earlier she delivers.
 - Clinical exam Vs. TAS Vs. TVS.
 - Length Vs. Width Vs. Funnel Vs. SCORE. (FUNNEL+1 / ENDOCX) (>0.52) (Gomez et al., 1994)
 - Cutoff depends on Contractions & Gest. Age (diagnosis & prediction)
 - Population based charts needed.
 - Twins and polyhydramnios. (Iams et al, 1994)

At 24 weeks				
75%	50%	10%	5%	1%
40 mm	35 mm	25 mm	20 mm	15 mm
	X 3	X 6	X 9	X 20

At 18 weeks			
30 mm	20 mm	+ Funnel 5mm	+ Obst Hx
X 8	X 20	X 30	X 20

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Diagnosis of PTL

15 mm has a NPV 98%
& a PPV 50%

(Fuchs et al., 2004)

Prediction of PTL

25 mm has a PPV 15-20%

15 mm has a PPV 20-30%

NPV 90-98%

(Alfirevic et al., 2004)

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Fetal Fibronectin

The GLUE of choriodecidual space,
< 22 wks and > 37 wks.

Diagnosis in next 7 dys:

PPV=80% NPV=97%.

Prediction at 24 wks to next 4 wks:

PPV = 60 % (high&low risk groups).

(Peaceman et al., 1996; Goldenburg et al., 1996)

100 Pts kit for 700 LE

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Ffn state	Short Cx	Result
+ ve	+ ve	Imminent labor
- ve	- ve	No pathology
+ ve	- ve	Pathology on, no effect yet
- ve	+ ve	No pathology, but can Progress easily if it starts

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Bacterial Vaginosis

- The earlier it's treated, the more effective it is. (< 16 weeks) (Rosenstein et al., 2000).
- Flagyl/clindamycin/penicillin/erythromycin/azithromycin.
- Safety: Class B (FDA).
- 1ry care = 25% 2ry care = 60% (Iams, 2000).
- Other genital colonization:
(Chlam., Gono., Ureaplasma, Mycoplasma).

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Combinations
logically better

Selective Vs.
Routine

Research Vs.
Practice

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Secondary Care = Prevention in High Risk Asymptomatic Patients

- Proper Gynaecology is prophylactic Obstetrics.
- Corticosteroids (Vs TRH).
- Counsel on NICU & Surfactant therapy.
- Physical and Social factors.
- Cerclage.
- Progesterone supplementation.
- Antibiotics for B.V. previously discussed
- Antibiotics for PPROM.
- ? Phenobarbitone , ? Vitamin K
- At risk of Indicated Prematurity.
- In Multifetal pregnancy.

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Elective Cerclage

- On typical history.
- At 12-14 weeks.
- 3 RCT's: benefits observed in 1:25 of mixed risk groups

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Urgent Cerclage = On USS evidence.

- **Elective Vs. Urgent Cerclage:**
 - Same obstetric outcome with lower need for surgery.
(*Berghella et al., 2002; Higgins et al., 2004; Groom et al., 2004*).
- **Urgent Vs. No Cerclage:**
 - No difference (*Alfirevic et al., 2004; Berghella et al., 2002*)
 - Up to 87% success (*Rust et al., 2002*)
- **Differences due to:**
 - * Fibronectin state & level of risk were both unaccounted for.
 - * Associated variables, e.g infection, contractions, social.
 - * Cutoff at which centile (1st, 3rd, 5th, 10th)?
 - * Timing of screening: once, 16, 22 or 24wks?

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Emergency Cerclage

- **Advanced cervical dilatation > 2 cm**
- **Without contractions or after stopping contractions.**

- Lower success reported 20-40 %
(*Latta & McKenna, 1996*)
- Risky, must exclude contractions, infection, placental insufficiency.
- Not advisable at > 24-26 wks
(*Depending on NICU*).

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Progesterone supplementation

- Between 24-34 wks
 - 100 mg vaginally/day
- Brazilian RCT on 134 pts,
- Statistically significant at 34 and 37 wks.
(*da Fonseca et al., 2003*)

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Antibiotics for PPROM

ORACLE

“Overview on the Role of Antibiotics in Curtailing labor and Early delivery”

- Erythromycin 250 mg x4 x10
 - Augmentin → NEC
 - Swabs to follow up.

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- ? Phenobarbitone , ? Vitamin K (*Thorp et al., 1995*)

- At risk of **“Indicated Prematurity”**:

- Prevent PET, Placental insufficiency, etc...

- In **Multifetal pregnancy**:

- Cervical sonography predictive but with different charts. (*Fuchs et al., 2004*)
 - Cerclage and bed rest both currently unproven. (*Strauss et al., 2001*)

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To prevent preterm labour, further interest should be focussed on scoring systems combining ultrasound with biochemical and maybe molecular cell methods such as measurement of fetal DNA in maternal blood.

(*Hoesli et al., 2003*)

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Tertiary Care = Diagnosis and Treatment of established PTL

- Diagnosis.
- Tocolysis Vs Delivery.
- Tocolytics.
- Other Supportive Measures.
- Delivery

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Threatened Vs Established

(Not to early & Not to late!)

- False + ve: 50-90%
- False – ve: 20%
- Cause of misleading results with tocolysis and possibly Abio.
- Cx USS: Cutoff at 15-30 mm
- Fetal Fibronectin : PPV 80%, NPV 97%

(*Fuchs et al., 2004; Gomez et al., 1994*)

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REMEMBER !!

- Exclude maturity (?NICU) and Fetal or maternal indications to deliver.
- Steroids.
- IUT.
- Pdf e.g UTI.
- GBS prophylaxis (*RCOG Guideline No. 36, 2003*).
- ORACLE.

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DELIVERY

- MODE
- ? EPISIOTOMY
- ? PROPHYLACTIC FORCEPS
(*Schwartz et al., 1981; O'Driscoll et al., 1983*)
- Delay cord clamping x 30 seconds.

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TOCOLYTICS

- NO ENOUGH SUPPORT FROM RCT's
- NO APPARENT FETAL BENEFIT UNLESS STEROIDS/IUT.
- SOME HAVE SEVERE SIDE EFFECTS.
- NO BENEFIT FROM ORAL MAINTENANCE
Tachyphylaxis + Low Bioavailability.

(Leveno et al., 1990; Groom et al, 2004)
(RCOG GUIDELINE No. 1B, 2002)
(Cochrane review articles)

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	Rito-drine	Nife-dipine	Indo-methacin	Atosiban	Mg So4
Delay 27	Signif.	Signif	Signif	Signif	NS
Delay 77	Signif	Signif	Signif	Signif	NS
Birth Wt < 2500g	NS	Trend	Signif	NS	NS
Fetal benefit	NS	Less RDS& PNMR	NS	NS	Less CP
Fet. SE	Rare	Rare		NS	NS
Mat. SE	CVS, RBS, K Placenta	Lower Than B-stimul	GIT Pladlets	Lower Than B-timul	Mg
Contra-Indications	Heart, K, DM, TFT	Rare	> 32/40 > 48 h Anti-PG	Rare	?renal
Dose	50 - 350 ug/min = 1-7ml/h	10 mg x 4-5 /15min then 60-160 per day	100mg/h x2 then 200/dy	6.75mg x 1min → 18mg/h x 18 h → 6mg/h x 15 h	6 gm then 2-4 g / h

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NIFEDIPINE

- Considered 1st Choice.
 - Cheap and easy.
 - Fetal benefit.
- Less placent. Insufficiency
- Hypotension 15-20%, asymptomatic.

NO donors, AntiCOX-II, Sulindac ???

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Maintenance or Failure

- Wrong diagnosis. (False Alarm)
- ?Abrupton, distress, infection.
- Combinations should be properly chosen (? Ca++).

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Only when the factors underlying prematurity are fully understood can any intelligent attempt at prevention be made. (Eastman, 1947)

This is a multifactorial process; the only successful way to approach it is a multifaceted one.

Individualized treatment and global understanding are two faces of the same coin.

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Take Home Messages (1)

1. The main factors that reduced thePNMR were the corticosteroids and the NICU services, not the obstetric interventions.
2. Definition of PTL is contractions + Cx changes.
3. False +ve 50-90% (False - ve 20%)
4. A Multifactorial process, the outcome α on a balance.
5. Most PTL are in low risk groups.
6. History of last preg. is the most predictor of next one.
7. Cx-competance is Dynamic + time-limited →

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Take Home Messages (2)

9. Flagyl/Clindamycin/Azithromycin: FDA Class B.
10. Elective cerclage is controversial but probably beneficial. Urgent & Emergency cerclage so far not properly studied, but of potential benefit.
11. Warning symptoms must not be ignored.
12. Progesterone, antioxidants, reassurance all have a role.
13. ORACLE.
14. Vit. K and Phenobarbitone.

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- Cx length in Diagnosis of PTL
(15 mm) has a PPV 50% & a NPV 98%.
- While in Prediction of PTL
(25 mm) has a PPV 15-20% and
(15 mm) has a PPV 20-30%
NPV 90-98%.
- Fibronectin power in Diagnosis in next 7 dys PPV=80% NPV=97%.
- While its predictive power at 24 w. to next 4 wks: PPV = 60 %
- BV diagnosis & treatment <16 wks can differ by:
25%(1ry care) to 60% (2ry care)

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fFn state	Short Cx	Result
+ ve	+ ve	Imminent labor
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