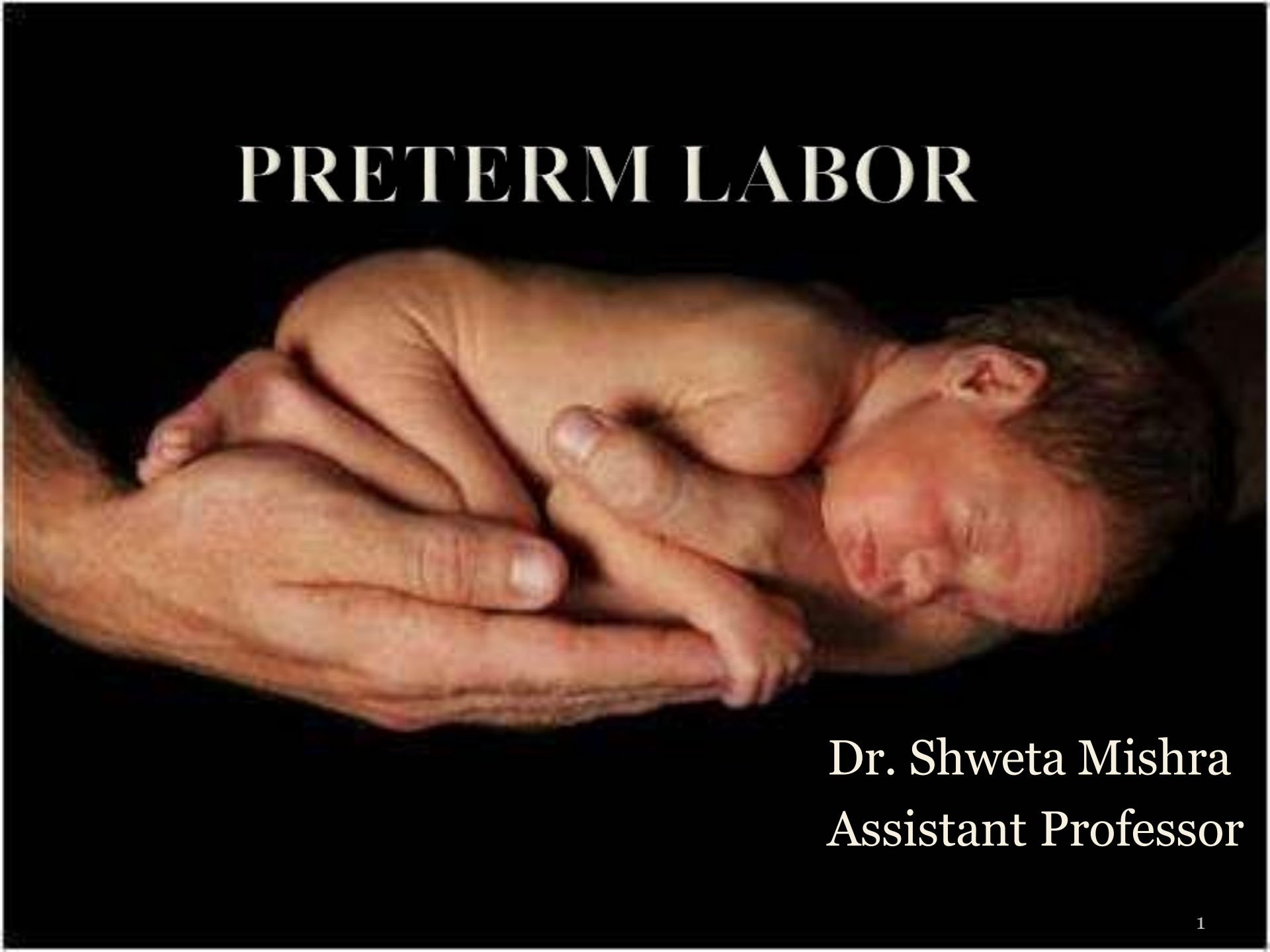
PRETERM LABOR



Dr. Shweta Mishra
Assistant Professor

- **The timing of human birth is carefully regulated event that takes place normally between 37 and 40 weeks**
- **Birth outside this timeframe has immense consequences both for the mother and the baby**
- **Still today, Prematurity is the leading cause of neonatal death***

Liu et al. 2012

DEFINITION

- **Onset of labour before 37 weeks in a pregnancy beyond 20 weeks***

  Lower limit is not clearly defined

USA (ACOG)	**20 WEEKS**
UK	24 WEEKS
BY FIGO	22 WEEKS

ACOG, Technical Bulletin No. 206; 1995

DIAGNOSIS ACOG (1997) CRITERIA

Contractions 4 in 20 minutes or 8 in 60 minutes and progressive dilatation of cervix

Cervical dilatation >= 1 cm

Cervical effacement >= 80 %

TERMINOLOGY

- **Cervix >80% and >=3 cm: Advanced PTL**
- **Cervix> 80% and 1-3 cm: Early PTL**
- **Cervix< 80% and < 1cm**

- **Cx Length >2.5 cm: False Labor**
- **Cx Length< 2.5 cm: Threatened PTL ***

Williams Obstetrics 21st edition;2001,27, 689-728

CLASSIFICATION

- **Mildly preterm birth** **32 - 36 weeks**
- **Very preterm birth** **28 - 31 weeks**
- **Extremely preterm birth** **24 - 27 weeks**

INCIDENCE

- **Accounts for 85% of all perinatal mortality and morbidity**

- **8-12%** **of all deliveries are preterm**
- **71.2%** **34-36 weeks**
- **13%** **32-33 weeks**
- **10%** **28-31 weeks**
- **6%** **<28 weeks**

WHY TO WORRY SO MUCH?!

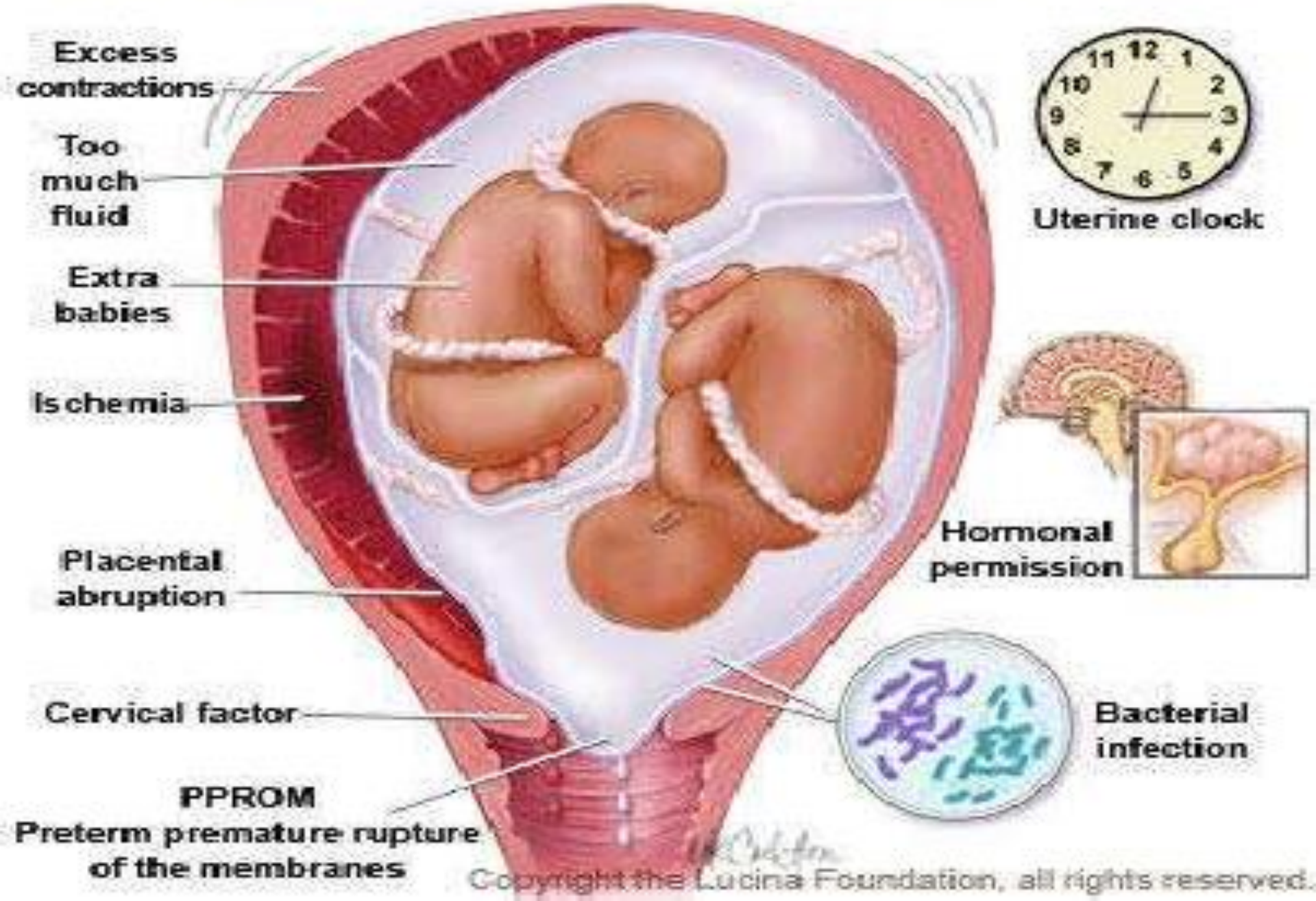
- **In spite of considerable advances in obstetrical care, all over the world the rate of preterm birth is increasing***
- **Although the survival rates have increased, the morbidity remains unaltered ($)**
- **Focus of research is now shifted on prevention of preterm labour in last few years (#)**

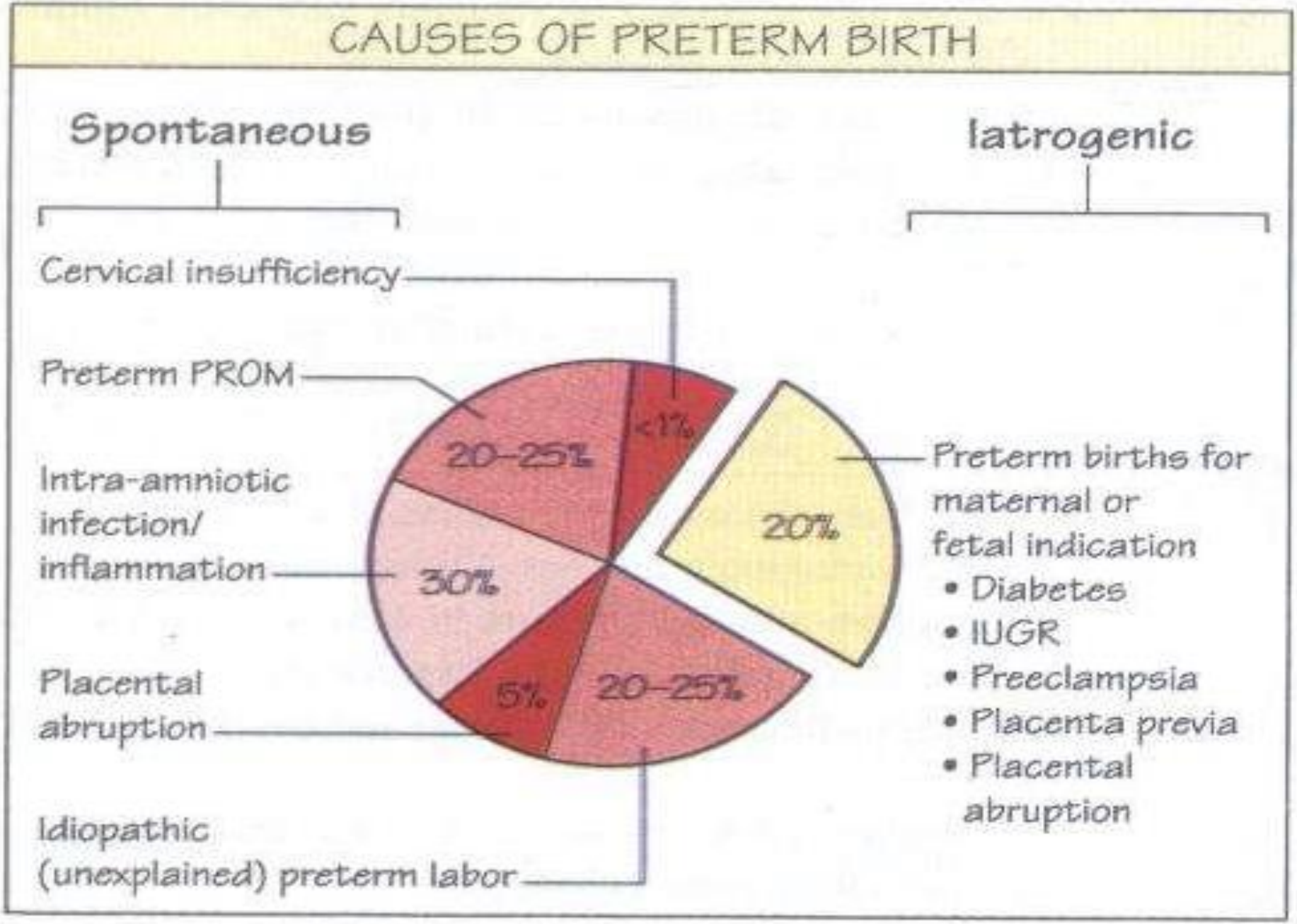
*Sykes et al. 2011, Blencowe et al. 201

$ Fanaroff et al. 2003

Howson et al. 2012

Pre-Term Labor - possible causes and risk factors

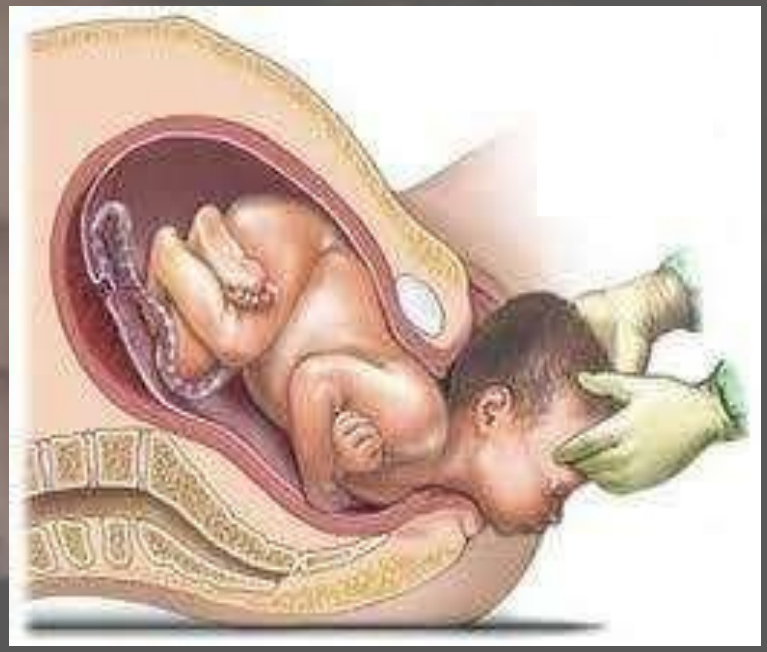



CAUSES OF PRETERM BIRTH
Spontaneous
Iatrogenic
Cervical insufficiency
Preterm PROM
Intra-amniotic infection/ inflammation
Placental abruption
Idiopathic (unexplained) preterm labor
<1%
20–25%
30%
5%
20–25%
20%
Preterm births for maternal or fetal indication
• Diabetes
• IUGR
• Preeclampsia
• Placenta previa
• Placental abruption

PATHOGENESIS

" *Premature activation of final pathway of parturition"*

A number of theories



- **Progesterone withdrawal**
- **Oxytocin stimulation**
- **Premature decidual activation**

Activation of fetal HPA Axis *or* Chorio decidual bacterial colonization *or* Enlarged Uterus

- **Uterine myometrial contraction**
- **Softening and dilatation of cervix**
- **Weakening and rupture of membranes**

PREDICTION

- **2.5 times increased incidence of SPL in women with a history of 1 abortion**
- **Assessment of risk factors**
- **Vaginal examination to assess the cervical status**
- **Ultrasound visualization of cervical length and dilatation**
- **Detection of fetal fibronectin in cervical vaginal secretions**

Spontaneous Preterm Birth is highly multi factorial so it's unlikely that a single test is sufficient to predict the same

PREDICTION OF PRETERM LABOUR

warning signals

Though not very specific , should not be overlooked

- **menstrual like cramps (pains)**
- **low dull backache**
- **abdominal cramps**
- **feeling of pressure or heaviness in vagina**
- **increase or change in vaginal discharge- bloody fluid leaking per vagina**
- **uterine contractions less than 10 minutes apart ,even if painless**
- **vaginal infections**

PREDICTION OF PRETERM LABOUR

Risk scoring system

- **Socioeconomic factors**
- **Previous medical history**
- **Daily habits**
- **Condition in present pregnancy**
-

Not found very useful

Half of the preterm deliveries occur in low risk patients also

PREDICTION OF PRETERM LABOUR

Routine per vaginal examination **to assess the cervix at each antenatal visit is advocated by some**

Position

Length

Consistency of cervix and

Formation of lower segment are checked

This is advisable in high risk patients only

All patients do not prefer this

P/V examination itself may increase the risk of preterm labour

PREDICTION OF PRETERM LABOUR

Transvaginal sonography

- **Cervical changes in absence of uterine contractions**
- **Funneling(Internal Os diameter >5 mm)**

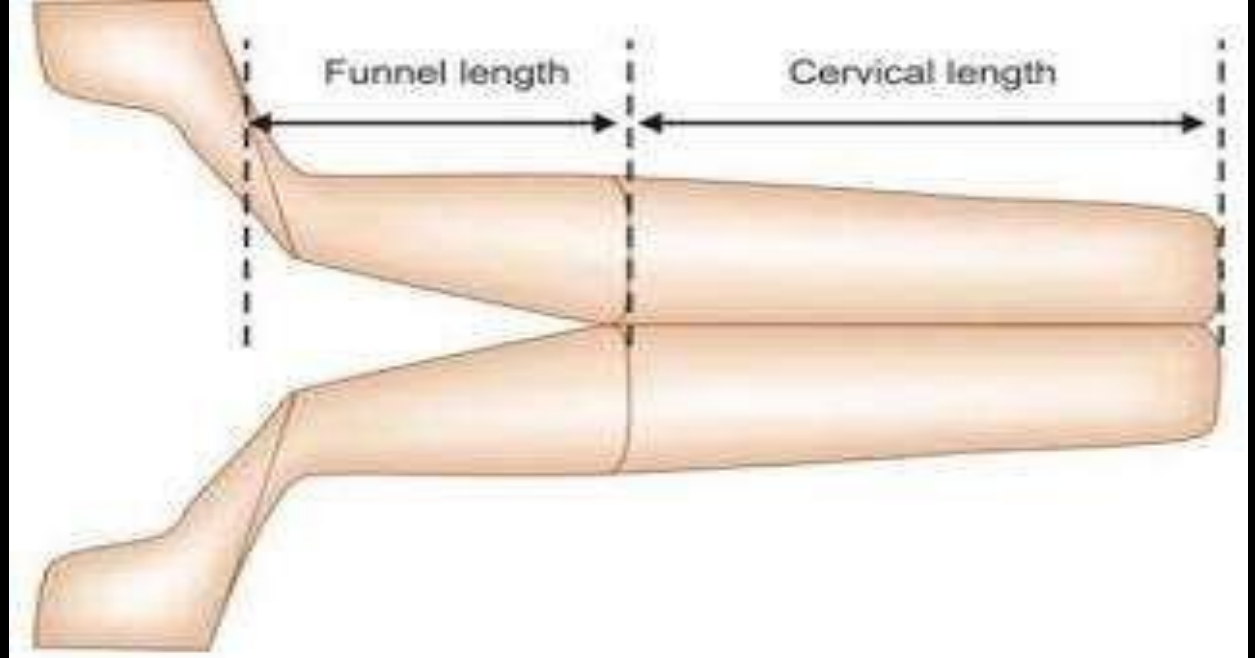
80-100% of women who deliver early have cervix <25 mm
50% delivery rate within one week have cervix < 15 mm

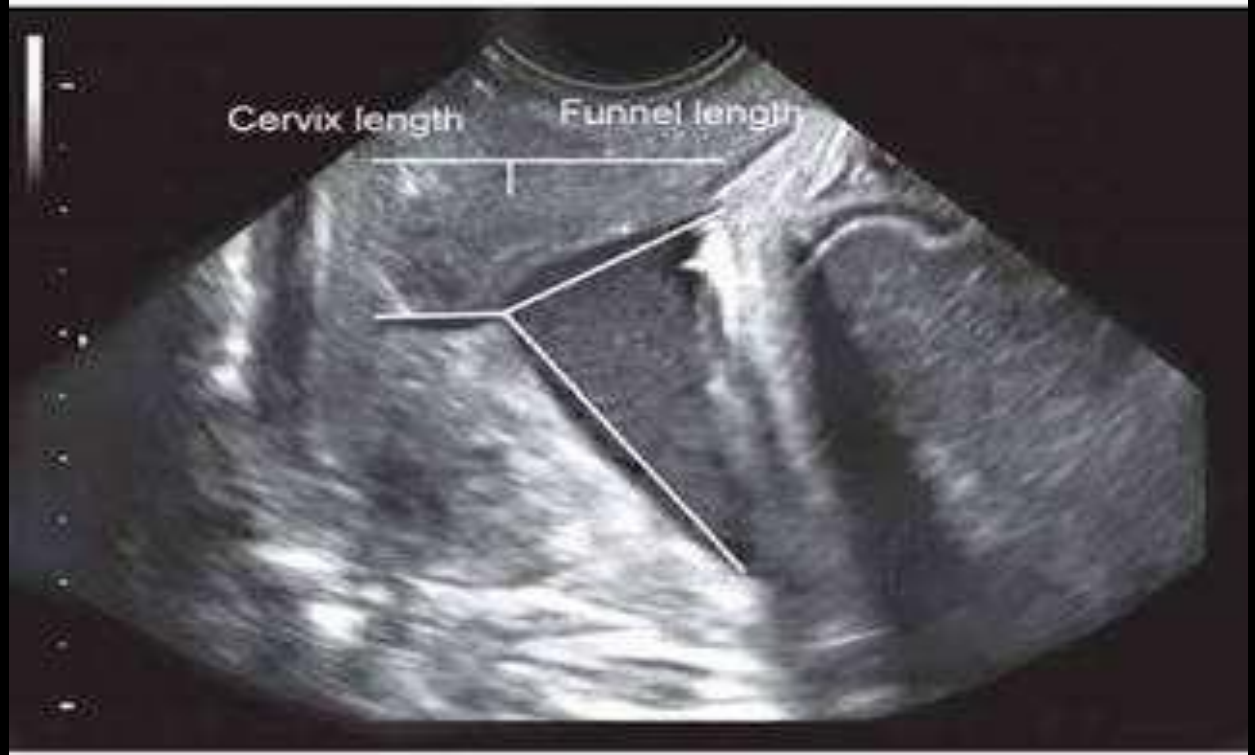
Infections

- **If CRP >1.6 mg/dl ⇒ Amniocentesis**

- **If amniocentesis suggests infection-Deliver ASAP**
- **If amniocentesis is negative-Expectant Mx**
- **If CRP <0.8 Expectant Mx**
- **If CRP 0.8-1.6 ⇒ Repeat in 24 hours**

Amniocentesis itself can cause PTL?!


Funnel length
Cervical length


Cervix length
Funnel length

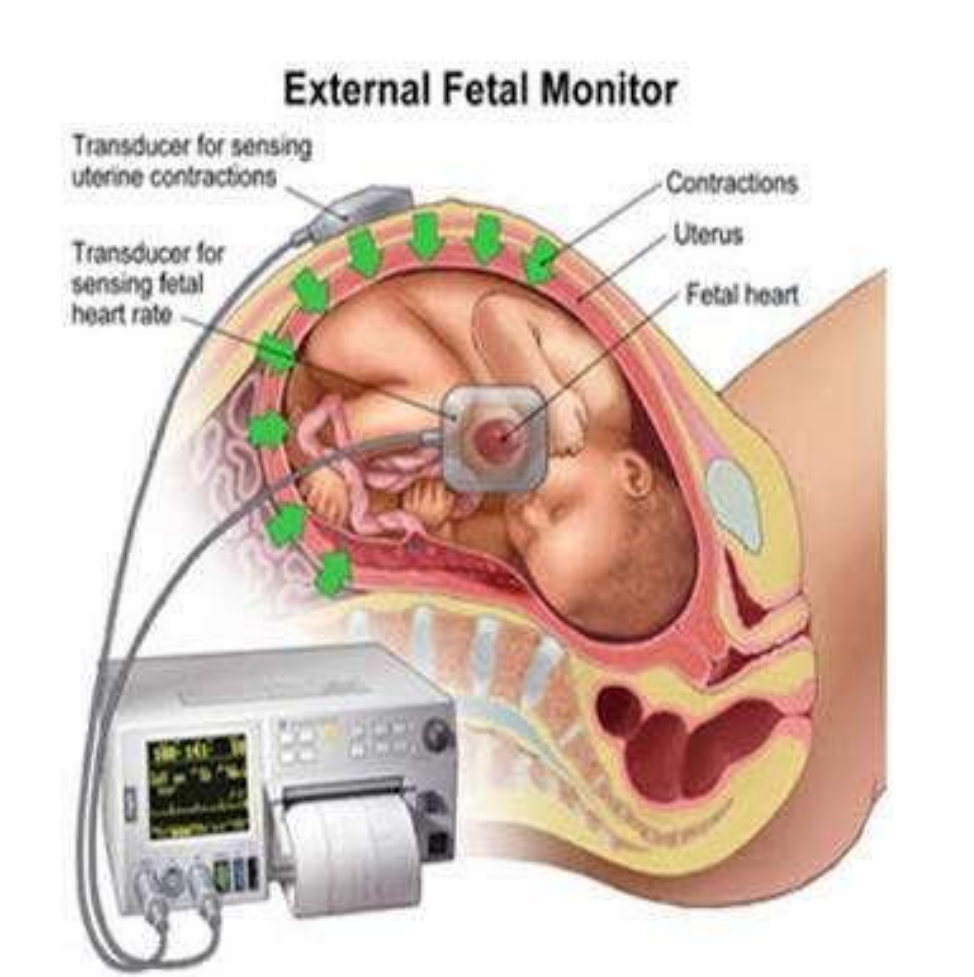
PREDICTION OF PRETERM LABOUR

Home uterine activity monitoring (HUAM)

USFDA Approved

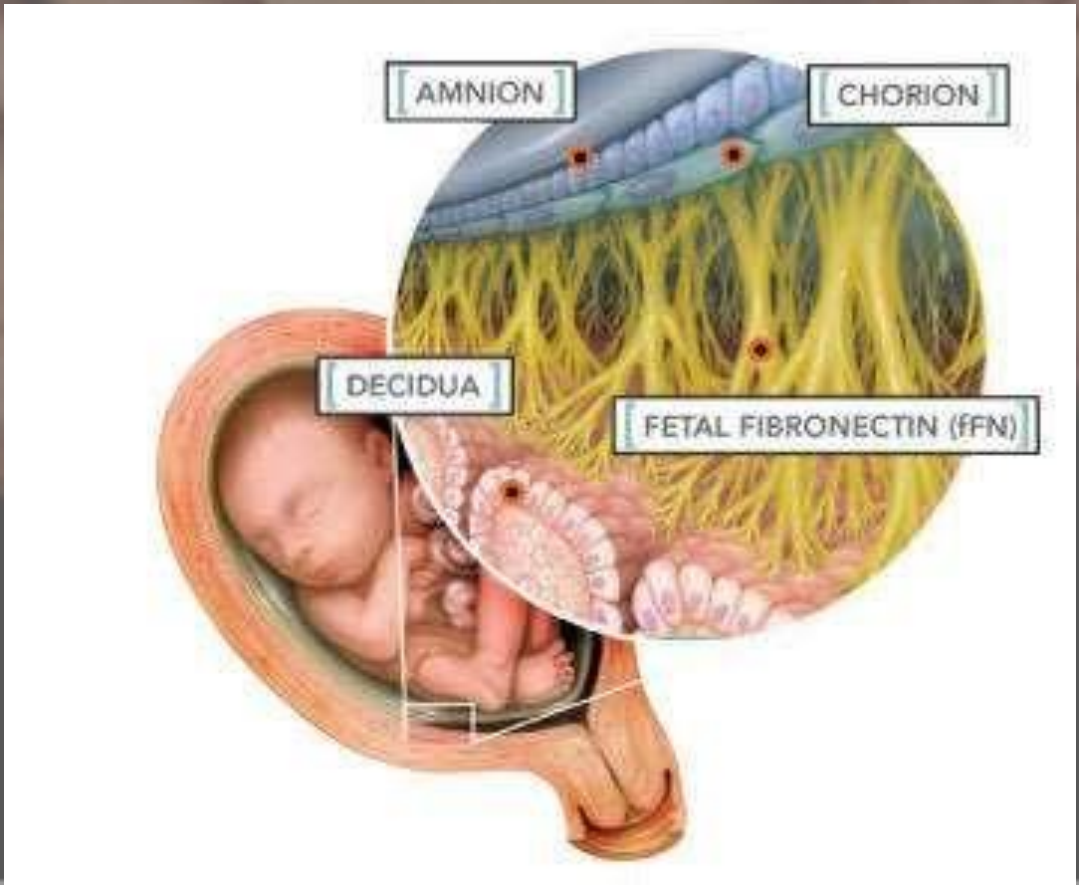
- **By special external tocodynamometer**
- **Contractions are recorded twice a day**
- **Costly**
- **Not easily available**
- **Increased contractions predicts preterm labour**

Not useful in reducing PTL



Biochemical markers

- Fibronectin is a protein that binds the fetal membrane to the decidua
- 'Biological Glue'
- Normally found in the cervicovaginal discharge before 22 Weeks and again after 37 weeks



Presence of fetal fibronectin in cervicovaginal secretions prior to rupture of membranes is a specific predictor

> 50 ng /ml is positive & Chances of PTL are 35% higher

Owing to high negative predictive value of fFN, a negative fFN value is helpful in reducing unnecessary patient intervention and management protocols*

- ***Increased salivary estriol***
- ***High levels of Non esterified fatty acids(NEFA) in serum at 9-20 weeks have higher chances of PTL before 34 weeks ($)***
- ***Elevated albumin and Vitamin D levels in cervicovaginal secretions***

- ***FETAL BREATHING MOVEMENTS***

  Absence of fetal breathing movements detected on real rime USG suggest that patients are likely to go in preterm labour within 48 hours

Foster C, Biomark Med. April2014

$ Catov JM Am J Epidermol, May 2014

PREDICTION OF PRETERM LABOUR

Combined measurements

Positive fFN and Cx length < 1.5 cm before 32 weeks

90% chances of PTL *

** Vidaeff AC et al, Am J of Perinatol 2006;Jan*

In short , a number of factors in combination which can predict PTL positively are

- ***Symptoms*** **of preterm labour**
- ***H/O*** **prior preterm birth**
- **Uterine contractions** ***>/= 4*** **per hour**
- **Cervical length** ***</= 2.5*** **cms**
- **Cervical dilatation** ***> 1 cm*** **and effacement** ***>80 %***
- **Vaginal bleeding**
- **Presence of** ***fibronectin*** **in cervicovaginal discharge between 24 and 34 weeks**

PREVENTION OF PTB

- ***Primary Prevention*: Eliminate high risk factors**

  e.g. Infections, abstinence, bed rest

- ***Secondary Prevention*: Screening tests for early detection and Prophylactic Rx**

  e.g. fFN, Cx Length, Tocolytics

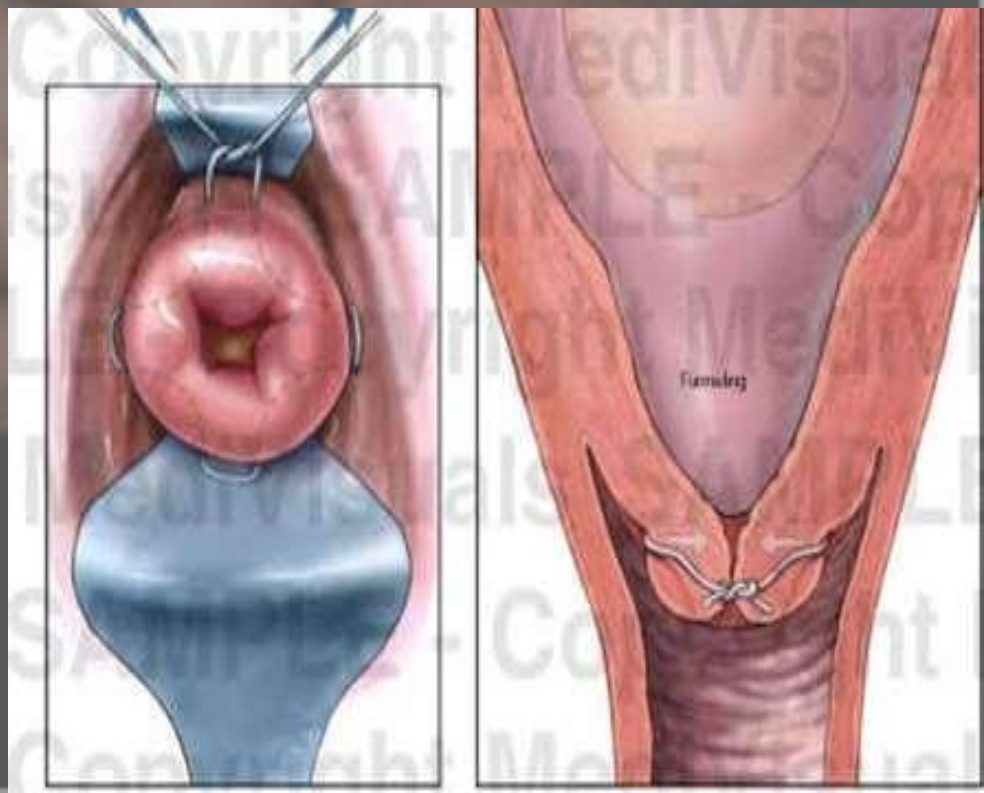
- ***Tertiary Prevention:* Decreasing Perinatal morbidity and mortality**

  e.g. Steroids

CERVICAL ENCIRCLAGE

- **Provides a mechanical barrier to prevent untimely cervical dilation**
- **Routine measurement of cervical length in low risk women and performing encirclage on incidentally detected short cervix does not reduce SPL***
- **Routine cervical assessment in low risk–not indicated**

Alfirevic z et al, Lancet 2004; 363



PREVENTION OF PTB

- ***The main challenge lies in the fact the majority of the causes are heterogeneous and so need to develop a single strategy that prevents activation of pathway for preterm labour or cervical remodeling or PROM ****

Villar et al. 2012

MANAGEMENT

- Is the patient in labor?

- Are the membranes ruptured?
- Is the fetus preterm?

- What risk factors are present?

HISTORY AND PHYSICAL EXAMINATION

- **Maternal vitals: signs of infection**
- **General physical exam**
- **No digitals cervical exam if membrane rupture suspected**
- **Sterile Speculum exam**
- **GBS culture**

ADDITIONAL TESTS

- **CBC, Urinalysis**
- **Amniocentesis**
- **Ultrasound**
- **Cervicovaginal swab for fetal fibronectin**

ANTIBIOTICS

1. **Cover sub-clinical and clinical infections**
2. **Prevent ascending infections**
3. **Delays clinical chorio amnionitis in PROM**

Overall effect is prolongation of pregnancy

SINGLE DOSE STEROIDS

Between 24 and 34 weeks – for RDS, IVH, NEC, Sepsis

Stimulates type II pneumocyctes to produce surfactant & Structural development of lungs

- **Accelerated maturation of fetal intestines**

  (Prevent NEC)

- **Effect on myocardium (Prevent IVH)***

- ***Morgan A ; Arch Dis Child Fetal NeonatalEd 2014***

TOCOLYSIS

- **Reasonable not to use, as there is *no clear evidence* that they improve outcome**
- **Consider if the few days gained for completing a course of corticosteroids or in utero transfer**
- **No single agent has a clear therapeutic advantage**
- **Maintenance tocolysis beyond 48 hours is not recommended**
- **Not recommend at or after 34 weeks**
- **No consensus on a lower gestational age**

CANDIDATES FOR TOCOLYSIS

- **No contraindications to drug**
- **Fetus currently healthy**
- **Clear diagnosis of preterm labor**
- **Cervix < 4cm dilatation**
- **Gestational age between 24 and 34 weeks**

CONTRAINDICATION OF TOCOLYSIS

- **Severe pregnancy induced hypertension**
- **Uncontrolled diabetes mellitus**
- **Placental abruption**
- **Cardio-pulmonary diseases**
- **Maternal hyperthyroidism**
- **Rhesus iso-immunisation**
- **Sickle cell disease**
- **Severe anaemia**

Tocolytic agents

- **Betamimetics –(beta adrenergic agonists) Isoxsuprine , Ritodrine ,Terbutaline , Salbutamol**
- **Magnesium sulfate**
- **Calcium channel blockers- Nifedipine**
- **PG synthatase inhibitors – Indomethacine Mefenamic acid**
- **Nitric oxide donors- Nitroglycerine patch**
- **Ethanol – not used today for its toxic effects**
- **Progesterone – weak tocolytic agent**
- **Newer drugs under trial**
  - ✓ **a. Atosiban – oxytocin antagonist**
  - ✓ **b. Aprikalim , Pinacidil-Potassium channel openers**

1. BETAMIMETICS

- **There are two types of Beta adrenergic receptors**
  - **Beta 1 are mainly found in heart , intestines and adipose tissues**
  - **Beta 2 are present in myometrium , blood vessels and bronchioles**

Mechanism of action

- **These drugs bind to B2 receptors on uterine smooth muscle activating the enzyme adenyl cyclase which leads to increase in CAMP**

RITODRINE

- Started i v in 5% glucose drip 0.05 mg /min dose
- Dose is increased 0.05 mg every 10 -15 minutes until uterine contractions have ceased or side effects appear
- Do not exceed dose > 0.35 mg/min
- I.V. therapy is continued for 12- 48 hours after contractions stop
- Oral therapy is then started by 1 tab (10mg) every 2 hourly for the first day starting 20 minutes before iv infusion is stopped
- Thereafter 1-2 tab. are given 4-6 hourly till 37 weeks

- **Usually well tolerated**
- **Side effects are due to its effects on extra uterine beta receptors**
- **Tachycardia, palpitations, nausea, vomitting, headache, tremor, restlessness, anxiety, hypotension, hyperglycemia, and hypokalemia**
- **Cardiac arrhythmia , myocardial ischaemia, pulmonary edema , and death**
- **Pulmonary edema occurs when the mother is anemic, severe tachycardia is there and IV fluid is administered in excess along with concomittent steroids administration**

ISOXUSPRINE

- **Maximally used drug in our country**
- **Nonselective betamimetic**
- **Dose**

  I.V. in drip 5% glucose /R.L

  Starting dose is 0.2 mg / min

  increased slowly to maximum 0.8 mg /min for 24 hours

  followed by IM 10 mg 6 hourly for 24 - 48 hours

  then orally 10 mg 6- 8 hourly up to 37 weeks

TERBUTALINE

I V - 5 mg / min in increasing by 5 mg every 10 min till contractions cease or a dose of 30 n g / min is reached

ORAL - initially 5 mg every 4 hourly for 24 hours then 2.5 to 5 mg every 4-6 hourly

S.C. – 0.25 mg repeated hourly till adequate tocolysis occurs

MAGNESIUM SULFATE

- **Used in PIH, Diabetes and Hyperthyroidism cases where betamimetics are contraindicated**
- **Success rate varies 65- 90 %**
- **Serum levels of magnesium 5- 8 ng/ml is needed for myometrial inhibition**
- ***The BEAM trial-Beneficial Effects of Antenatal MgSO4****

Institute of Ob/Gy and Royal College of Ireland-2015

NIFEDIPINE*(Preferable)*

- **Works by blocking the influx of Ca into the cell**
- **Dose – 30 mg orally , followed by 20 mg four times a day**
- **May cause severe hypotension and fetal death***

- **It is smooth muscle relaxant**
- **It also inhibits placental CRH (corticotrophin releasing hormone) secretion**
- **10- 20 mg patch is applied over abdominal skin every 24 hours**

Elvira OG; BMC Pregnancy Childbirth,2014

INDOMETHACINE

- **PG synthatase inhibitor**
- **Loading dose is 100- 200 mg rectally or 50 -100 mg orally ,followed by 250 mg 4 to 6 hourly**
- **Contraindicated in hepatic disease , renal disease , peptic ulcer and coagulation disorder .**
- **Useful for polyhydramnios - decreases liquor**
- **Drawback –Premature closure of DA, NEC**
- **Given for < 48 hours < 32 weeks gestation, 200 mg/day**

- **Can be used as a second-line agent**

OTHERS

ATOSIBAN

- **it is oxytocin antagonist**
- **used as 300 mg /min iv infusion**
- **under trial**

Dosage and administration- a three-step procedure

The initial bolus dose is 6.75 mg over one minute, followed by an infusion of 18 mg/hour for three hours and then 6 mg/hour for up to 45 hours

Duration of treatment should not exceed 48 hours and the total dose given during a full course should preferably not exceed 330 mg of Atosiban*

Cost is very high

Cochrane 2014 Jun

POTASSIUM CHANNEL OPENERS

Under research

PROGESTERONE

- **Weak tocolytic agent**
- **Not effective in active PTL**
- **Large dose may required, Costly**
- ***USFDA approves weekly progesterone in PTL***

ARABIN CERVICAL PASSARY

Cheap, easy to insert in conjunction with intravaginal progesterone*

Zimmerman AL ,2014 Feb

GENERAL PREVENTION

- **Improvement of socio-economic condition**
- **Patient education – pre pregnancy counseling in HRP**
- **Identification and correction of risk factors**
- **Proper assessment of fetal maturity before induction to avoid iatrogenic prematurity**
- **Treatment of vaginal and cervical infections and asymptomatic bacteriuria**
- **Avoidance of coitus in in late pregnancy**

- **Role of LSCS - Controversial**
- **By expelling the fluid from chest during delivery and facilitating lung expansion***

Jones HA et al, 1997

MANAGEMENT OF PROGRESSIVE PTL

FIRST STAGE

1. rest in bed to preserve membrane
2. electronic fetal monitoring if available
3. avoid strong sedatives – mild
4. epidural analgesia is best if can provide
5. minimum P/V examinations
6. adequate hydration should be maintained
7. prophylactic oxygen is advised

SECOND STAGE

1. liberal episiotomy traditionally (No evidence)*
2. no instrumentation as far as possible
3. forceps application if fetal distress develops
4. immediate clamping of cord – to prevent blood overload

THIRD STAGE

1. More chances of delay in separation and delivery of placenta in preterm delivery
2. Wait and watch
3. Do not pull cord – thin and fragile
4. IV methargin only after placental delivery

Expert neonatologist should be present for immediate resuscitation of preterm neonates at time of delivery

****ACOG, April 2006***

- **Asymptomatic bacteriuria - antibiotics**
- **Screen for GBS colonization- antibiotics**
- **Historical factors - cervical Circlage improves outcomes only in women with three or more PTL**
- **Tocolytics- Not much useful**
- **Steroids- Useful**


THANK
YOU!