Preterm Labour

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Agenda

- Epidemiology
- Aetiology and pathophysiology
- Prediction
- Approach and Management
- Prevention
- Case discussion

What is it?

Preterm labour:

- Regular uterine contractions with cervical change (dilation, effacement, or both) before 37 weeks' gestation
  - Between 24+0 and 36+6 weeks' gestation

Preterm Birth:

- Delivery between 24 and 36+6 weeks' gestation
- Late PTB is delivery between 34 and 36+6 weeks' gestation.

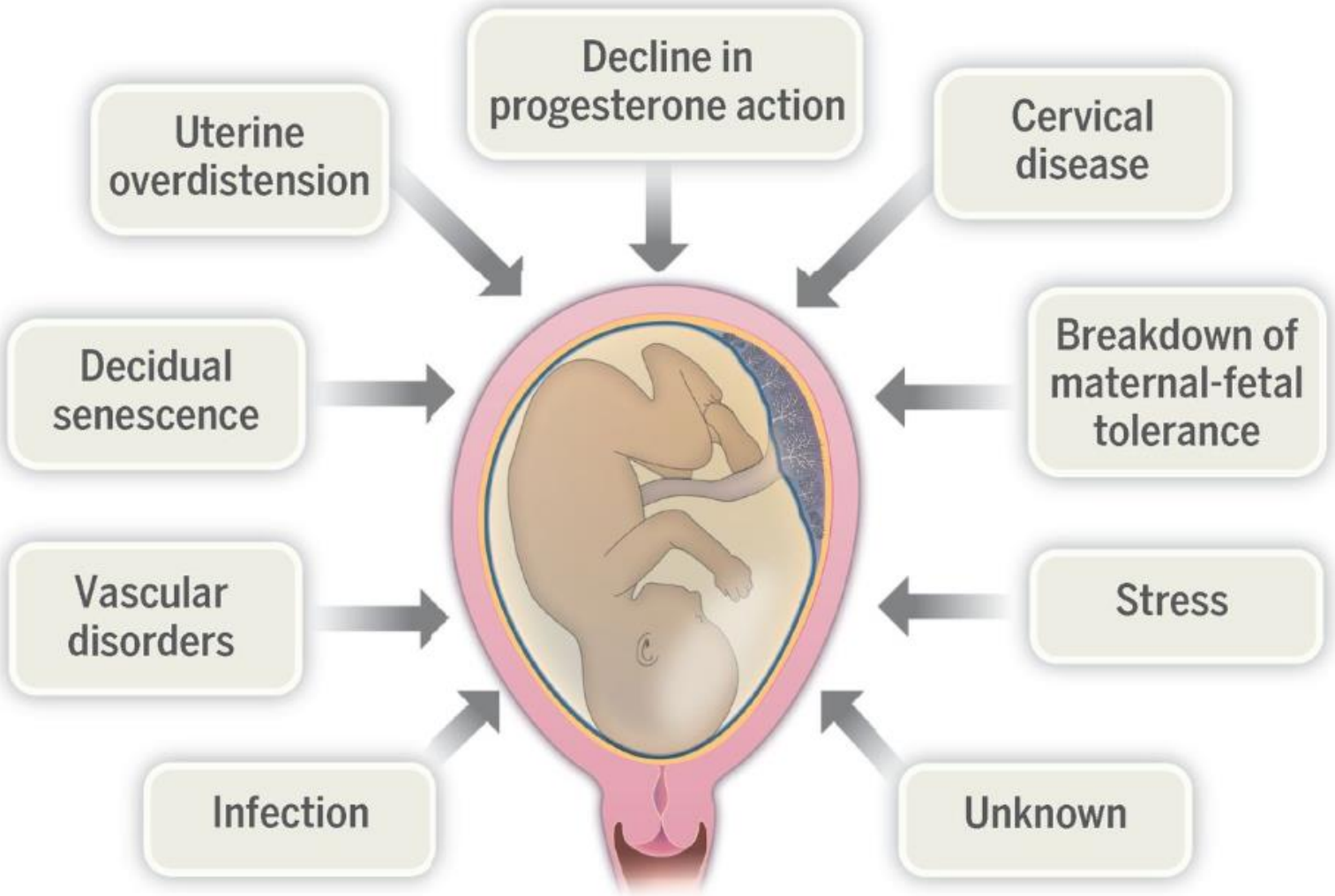
A clinical problem? YES

- Cost implications of prematurity.
- Single largest cause of neonatal mortality and morbidity
  - Determinants for the mortality and morbidity of babies born preterm are gestation at delivery and birthweight.
  - Survival rates improve considerably at lower gestational ages for each additional week gained in utero.
- Long term consequence: neurodevelopmental delay

Incidence

- 5-10% of all deliveries in developed countries and rates are on the increase

Aetiology


Decline in progesterone action
Uterine overdistension
Cervical disease
Decidual senescence
Breakdown of maternal-fetal tolerance
Vascular disorders
Stress
Infection
Unknown

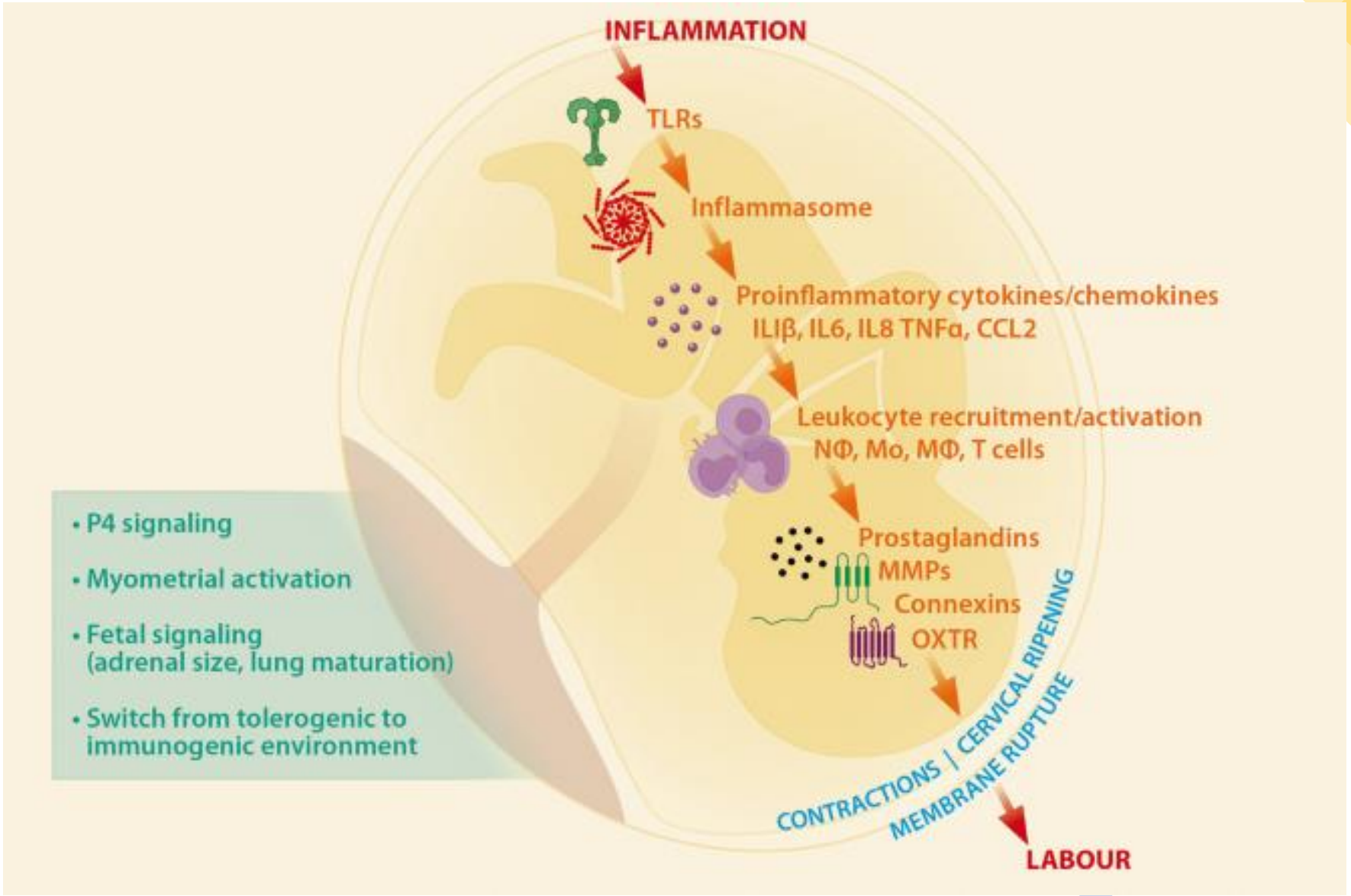
Pathophysiology

- Infection/inflammation
- Activation of the maternal/fetal hypothalamic-pituitary-adrenal axis
- Decidual haemorrhage
- Pathologic uterine distension

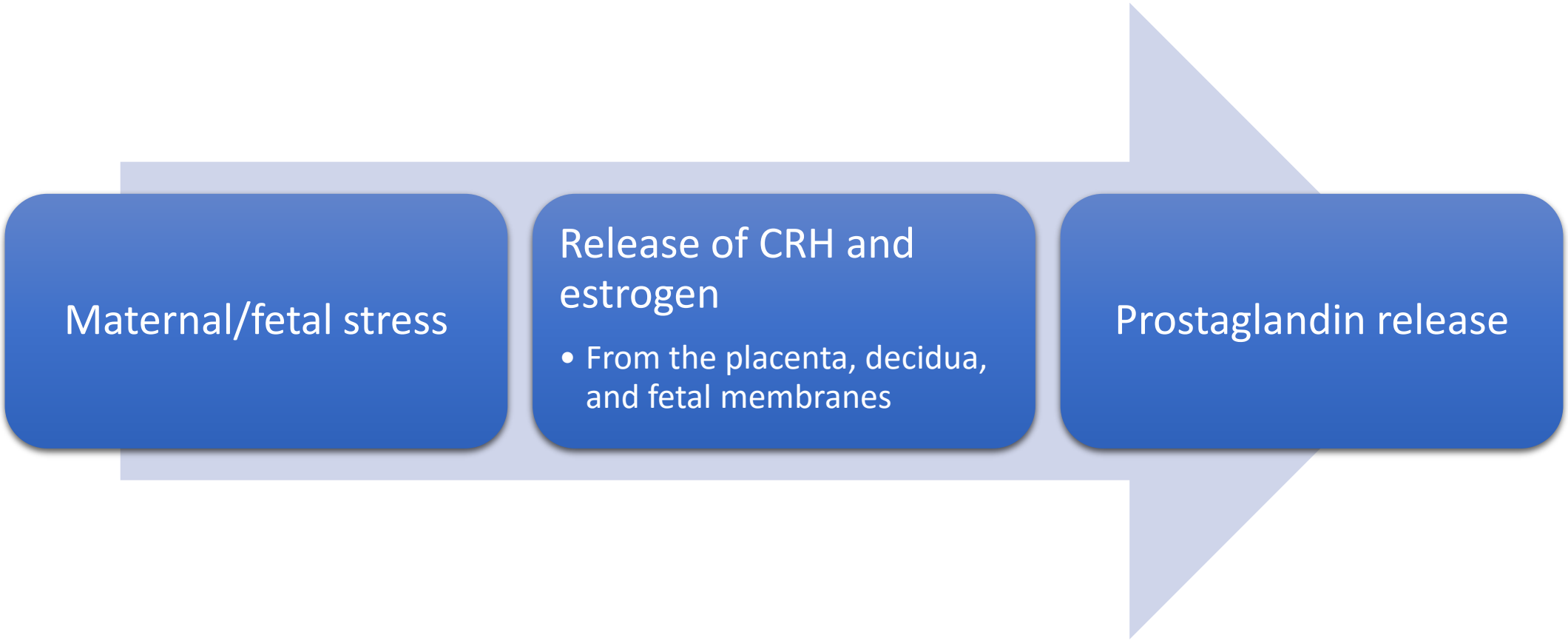
- All activate a final common pathway leading to the onset of labour which seems to involve an inflammatory reaction with upregulation of prostaglandins, cytokines and other inflammatory mediators within the cervix, myometrium and fetal membranes.

1- Infection/inflammation:

- 20-40% of spontaneous PTL
- Cytokines stimulate production of uterotonics (**prostaglandins**, leukotrienes, endothelins) and proteases (**matrix metalloproteinases**) within the membranes, myometrium and cervix


INFLAMMATION
TLRs
Inflammasome
Proinflammatory cytokines/chemokines
ILIβ, IL6, IL8 TNFα, CCL2
Leukocyte recruitment/activation
NΦ, Mo, MΦ, T cells
Prostaglandins
MMPs
Connexins
OXTR
CONTRACTIONS | CERVICAL RIPENING
MEMBRANE RUPTURE
LABOUR
• P4 signaling
• Myometrial activation
• Fetal signaling
(adrenal size, lung maturation)
• Switch from tolerogenic to
immunogenic environment

2- Activation of Maternal/fetal hypothalamic-pituitary-adrenal axis:



3- Decidual hemorrhage:

- Abruption
- Bleeding at the choriodecidual interface leads to generation of **thrombin**, which enhances protease and prostaglandin production and activates the myometrium

4- Pathologic uterine distension:

- Polyhydramnios
- Multiple pregnancy
- Uterine abnormalities restricting normal uterine expansion (congenital mullerian anomalies?)

- How?

- Pathological stretching of the myometrium & fetal membranes
- Myometrial activation & enhanced gap junction formation between myometrial cells
- Increases oxytocin receptors & synthesis of prostaglandins

Prediction

- Obstetric strategies to reduce perinatal morbidity and mortality associated with PTB should ideally involve the **early identification of women at risk and the use of prophylactic therapies**

- Aim is to predict:
  - Women at risk of preterm labour
  - Imminent delivery in women with preterm labour

1- History: screening by history alone can identify up to 10% of women at risk

- Previous PTB (GA of prior event often correlates with subsequent PTB)
- Previous Preterm Prelabour Rupture Of Membranes (P-PROM)
- Mid-trimester pregnancy loss
- Congenital uterine anomalies
- Multiple pregnancy
- History of vaginal bleeding
- Cervical procedures (LLETZ, cone)
- Smoking
- Extremes of age

2- Cervical length assessment:

- **Transvaginal** US used for screening of cervical length in women at high risk.
- Abdominal US is unreliable as it needs full bladder for assessment which may lead to false lengthening of the cervix

Women at high risk include:

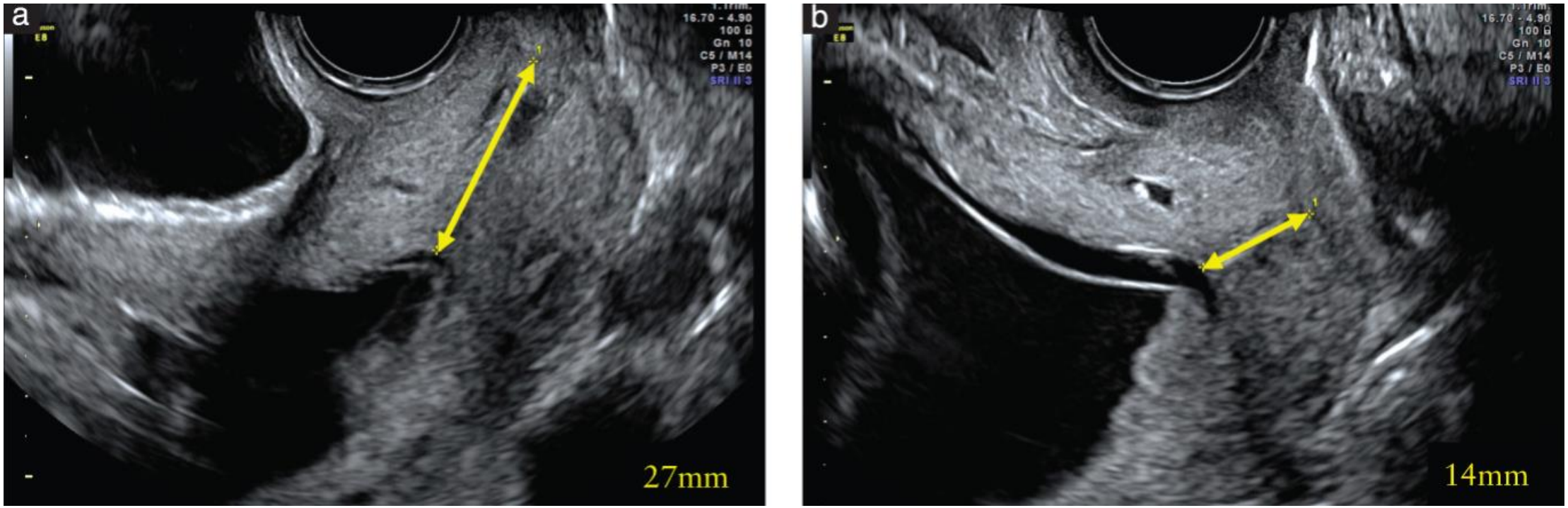
- Those with a previous spontaneous preterm birth or second trimester loss
- Previous preterm prelabour rupture of membranes (PPROM)
- Previous use of cervical cerclage
- Known uterine variant
- Intrauterine adhesions
- History of trachelectomy

- Women at **high** risk are offered:
  - **Ultrasound surveillance of cervical length every 2-4 weeks between 16-24 weeks, if it falls < 25 mm management is offered**

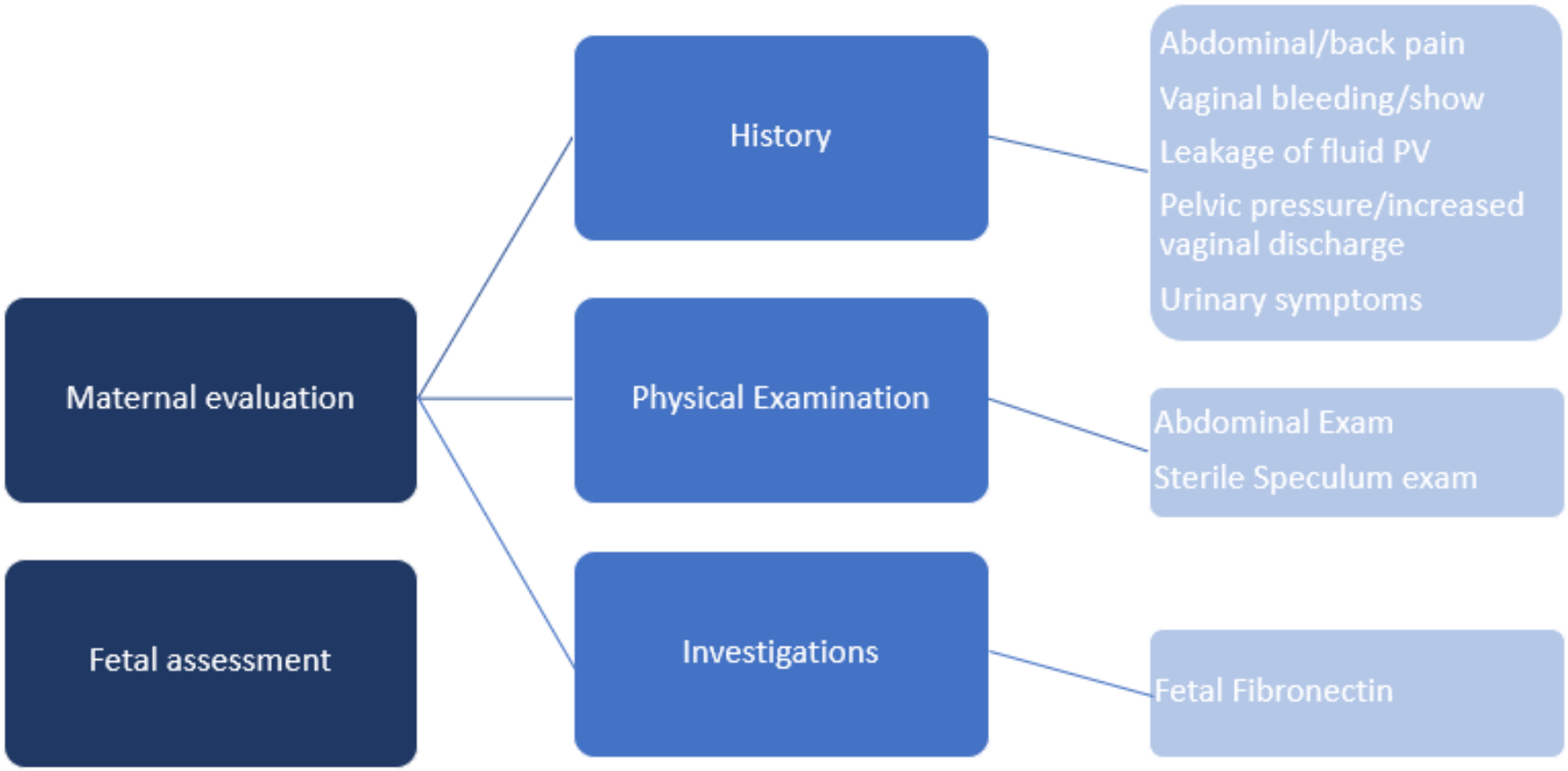
- Women at intermediate risk:

- Those who have a history of a previous second stage C-section
- Significant cervical excisional surgery i.e. large loop excision of the transformation zone (LLETZ) with an excision depth greater than 1 cm, more than one procedure or a cone biopsy

- Women at **intermediate** risk:
  - These women should undergo a **single transvaginal cervix scan no later than 18–22 weeks as a minimum, management is individualized**


a
16.70 - 4.90
100
Gn 10
C5 / M14
P3 / E0
27mm
b
16.70 - 4.90
100
Gn 10
C5 / M14
P3 / E0
14mm

Approach


Maternal evaluation
Fetal assessment
History
Physical Examination
Investigations
Abdominal/back pain
Vaginal bleeding/show
Leakage of fluid PV
Pelvic pressure/increased vaginal discharge
Urinary symptoms
Abdominal Exam
Sterile Speculum exam
Fetal Fibronectin

- Abdominal exam:
  - SFH
  - Lie and presentation
  - Uterine tenderness: abruption, chorioamnionitis

- Sterile Speculum exam:
  - Pooling of amniotic fluid, blood and/or abnormal discharge
  - Visual assessment of cervical dilatation
    - Digital vaginal exam should be limited (stimulates prostaglandin production and may introduce organisms into cervical canal)

- Fetal fibronectin:

- An extracellular glycoprotein, found in high concentrations in cervicovaginal secretions, mainly before fusion of the membranes at around 21 weeks of gestation.

- It’s mainly used for it’s **high Negative Predictive Value**
    - Negative fFN result indicates that 96.7% of the patients will not deliver within 7 days
    - Positive test indicates that 12.7% might deliver within next 7 days.

- Do **not** use fetal fibronectin in:

- Estimated GA <24 weeks or >34 weeks
- Preterm PROM
- Multiple pregnancy
- Cervix >3 cm dilated
- Active vaginal bleeding
- Vaginal exam/ intercourse within 24 hours
- Use of lubricant gel

- Fetal assessment:

- US: presentation, EFW, AFI
- NST

Management

- Hydration
- Rest
- Maternal corticosteroids
- +/- Tocolytics
- +/- $MgSO_4$
- +/- Antibiotics

1- Rest and rehydration:

- On left lateral side
- Dehydration increases ADH, which may in turn cross react with oxytocin receptors leading to uterine contractions

2- Corticosteroids:

- Use: decreases RDS, neonatal mortality, and intraventricular hemorrhage
- Stimulates type II pneumocytes to produce surfactant which reduces alveolar surface tension
- Corticosteroids should be offered to women at **24+0 to 34+6** weeks' gestation in suspected/diagnosed PTL
    - Women at 35 to 36+6 weeks: balance risks vs. benefits and individualize

- Formulae used: Betamethasone or Dexamethasone
- Route: Intramuscular
- Dose:
  - Betamethasone: two divided doses of 12 mg 24 hours apart
  - Dexamethasone: 24 mg given in: two divided doses of 12 mg 24 hours apart OR four divided doses of 6 mg 12 hours apart
- Maximal benefit: when course is completed between one day and seven days before birth

- Risks of corticosteroids:

- Women: Increased maternal blood glucose levels (shortly after injection and up to 5 days)
  - Caution should be exercised in diabetics

- Babies:
  - Might affect growth (lower birthweights)
  - Neonatal hypoglycemia

- Contraindications of corticosteroids:

  - Systemic infection
  - Delivery need to be expedited as soon as possible

3- Tocolytics:

- Indications:
  - Buying time until steroids are effective
  - In utero transfer

- Contraindications:
  - Established labour
  - Contraindication to prolonging pregnancy/ need for urgent delivery

- Offer tocolytics in cases of PTL -if indicated- between 26- and 33+6-weeks' gestation (may consider between 24-25+6 weeks)

- Options:
  - Nifidipine: first line, but can't be given with MgSO4
  - Atosiban: oxytocin antagonist

4- Magnesium Sulphate ($MgSO_4$):

- The RCOG Specialist Advisory Committee Opinion Paper(29) concluded that magnesium sulphate given to mothers shortly before delivery **reduces the risk of cerebral palsy and protects gross motor function** in those infants born preterm.
- The effect may be greatest at early gestations and is not associated with adverse long-term fetal or maternal outcome

5- Antibiotics

- Only in:
  - PROM
  - GBS carrier
  - Known infection

Mode of delivery

- Individualized
- According to obstetric factors and patient preference

Outcomes

- Maternal:
  - Risks associated with tocolytic use, underlying causes of PTL (e.g. abruption, sepsis) with a CS (PPH & classical CS).
  - Risk of postnatal depression
  - A postnatal follow-up appointment should be offered so that events surrounding the preterm birth (PTB) are discussed in full and a plan formulated for future pregnancies

- Neonatal:
  - RDS, NEC, and IVH
  - Cerebral palsy
  - PDA can lead to congestive cardiac failure
  - Jaundice secondary to liver immaturity, brain is more susceptible to neurotoxic effects of unconjugated bilirubin (immature BBB)
  - Hypothermia
  - Difficulty in feeding
  - Chronic lung disease
  - Retinopathy

Prevention

- Minimize risk factors, e.g. stop smoking, reduce alcohol intake, normalize BMI, improve diet
- Treat any vaginal infections, asymptomatic bacteriuria
- Transvaginal cervical length
  - If cervical shortening is detected, a cervical cerclage can be considered.
- No role for prophylactic tocolytics

- Progesterone supplementation:
  - 2 RCT in singleton pregnancies with a hx of previous PTB, showed reduction in the risk of delivery < 37 weeks
  - Improved perinatal outcomes not demonstrated
  - Not in multiple pregnancies