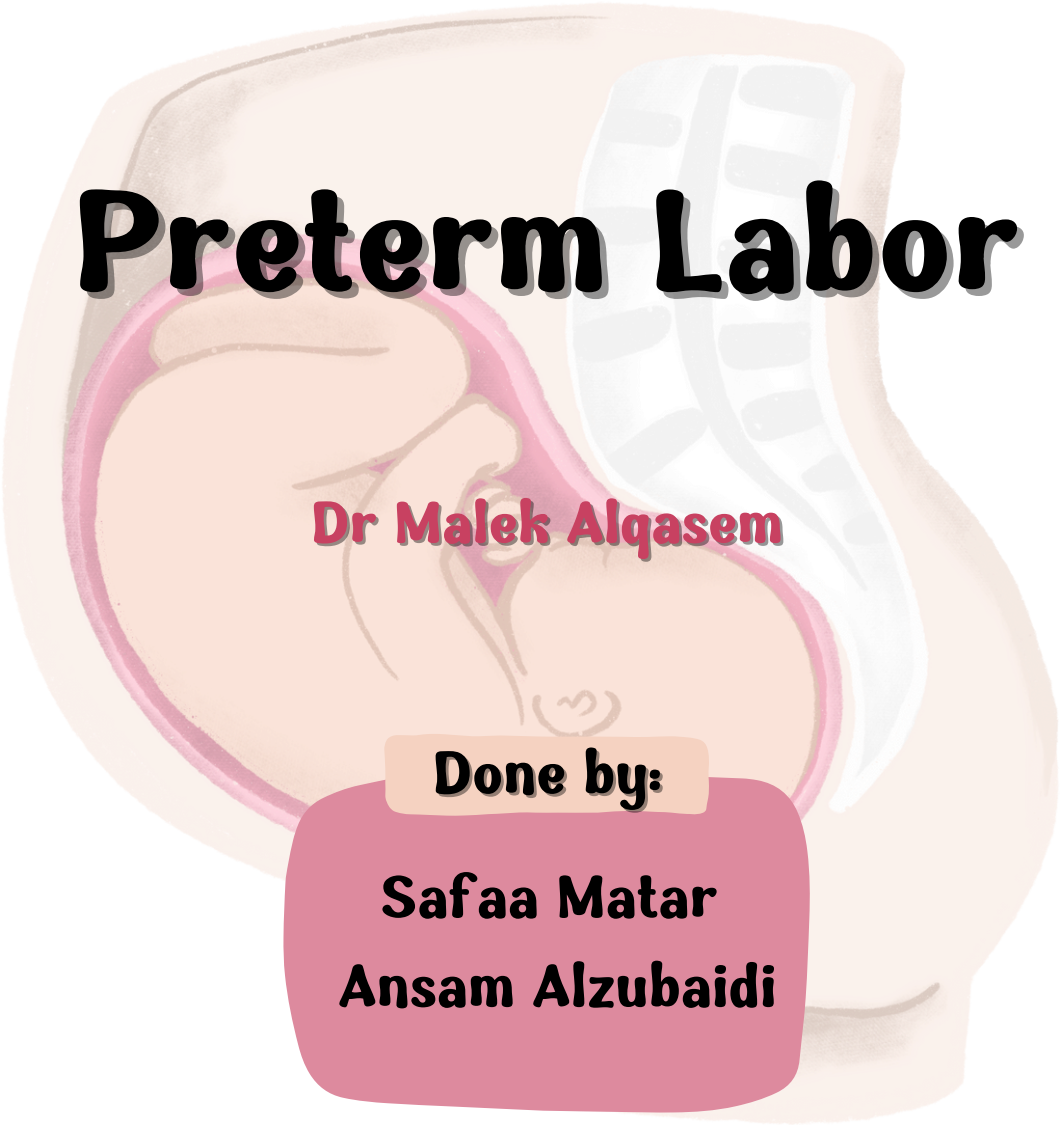
Obstetrics & Gynecology

Doctor 2019 - نبض - Medicine - MU

Preterm Labor



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This sheet contains:

- lecture slides
- Doctors notes
- additional notes and pictures from OBS & GYN books

Introduction

Preterm birth is associated with 5–18% of pregnancies
It is a leading cause of infant morbidity and mortality
Spontaneous preterm labor is a syndrome caused by multiple pathologic processes
The prevention and treatment of preterm labor have been a long-standing challenge

- as far as the baby and mother are stable, we aim to delay the delivery as much as we can
- age of viability in Jordan = 24 weeks
- the last organ to be mature is lung (after 37–38 wks)

Definition

All births before 37 weeks of gestation are defined as preterm and these are subdivided according to the gestation at delivery into:
Extreme (<28 weeks), which occurs in about 0.25% of pregnancies
Early (28–30 weeks), which occurs in about 0.25% of pregnancies
Moderate (31–33 weeks), which occurs in about 0.6% of pregnancies
Mild or late (34–36 weeks), which occurs in about 3.0% of pregnancies

- Preterm labor: The occurrence of regular uterine contraction associated with cervical changes before 37 completed weeks
- Threatened PTL (Braxton-Hicks contractions): regular uterine contractions without cervical changes

Preterm birth and neonatal complications

The leading cause of neonatal death
The second cause of childhood death below the age of 5 year
Neonates born preterm are at an increased risk of short-term complications attributed to immaturity of multiple organ systems
Neurodevelopmental disorders, such as cerebral palsy, intellectual disabilities, and vision/hearing impairments
Preterm birth is a leading cause of disability-adjusted life years, the number of years lost due to ill health, disability or early death

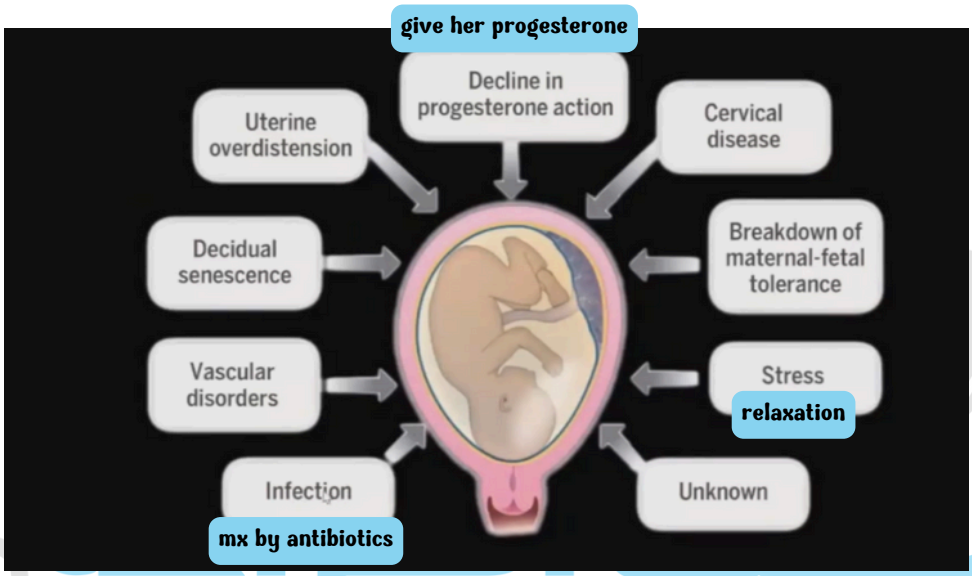
- Preterm uterine contractions are not the case of preterm labor But the clinical manifestations of the pathological insult

Risk factors

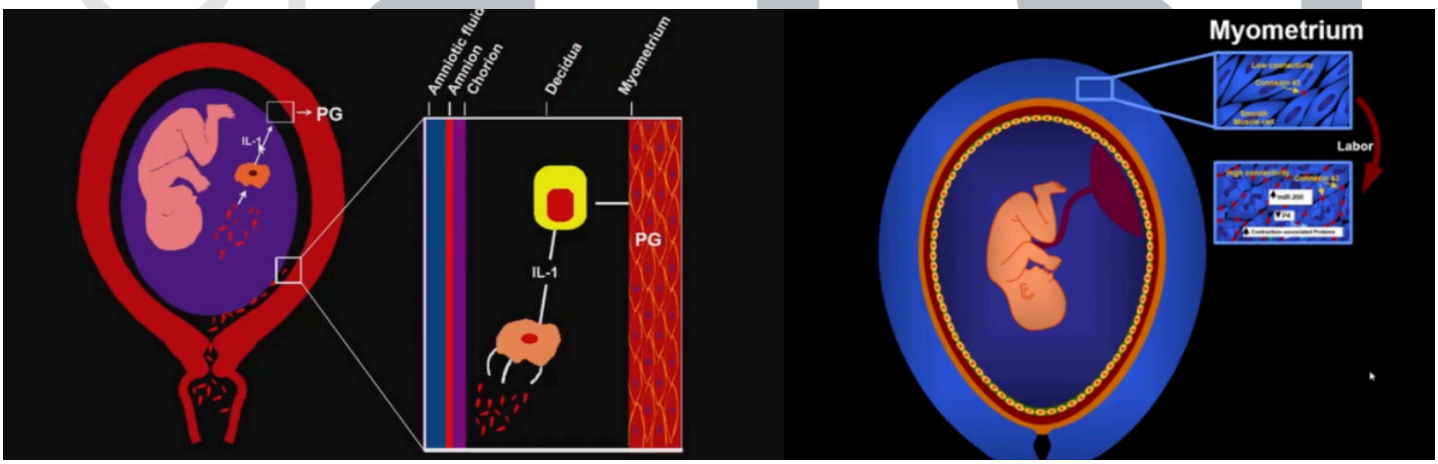
The <u>strongest predictor</u> and the most significant risk factor is previous PTL

Previous 1 PTL recurrence 15 %
Previous 2 PTL 30 %
Previous 3 PTL 45

Preterm Labor: Not Just Labor Before Term



Infection as a pathophysiology



Why does the infection cause a PTL?

the infection will induce an inflammatory reaction

>> release of cytokines & prostaglandins >>

uterine contractions

What's the difference between intra-amniotic infection and inflammation?

- **we do amniocentesis and screen for IL-6**

if > .6 >> intra-amniotic inflammation

Intra-amniotic Infection	Intra-amniotic Inflammation
• Gram stain • PCR • Culture – Aerobic / anaerobic bacteria – Genital Mycoplasmas	• Amniotic Fluid WBC • Glucose • IL-6 ≥2.6 ng/mL • MMP-8 >23 ng/mL

Amniotic fluid tests

Highlighted points

History :

Sure date and confirmation by early first trimester records

ask for risk factors esp. previous PTL

Examination: Don't forget to mention the general look!

-Vital signs(temperature>38 fever (risk for chorioamnionitis) ,hypotension with abruption)

-Abdominal pain -tenderness—localized—PTL true—(Braxton hicks)

-Assessment of presentation

-Assessment of engagement

-Sterile speculum (swab vaginal, group B strep)

-Discharge offensive and possible pooling liquor

-CTG

-Ultrasound

- start the pelvic examination by speculum, if there is ROM the PV is contraindicated !!

Screening

The two most important predictors of spontaneous preterm birth are:

Sonographic short cervix in the mid-trimester

Spontaneous preterm birth in a prior pregnancy

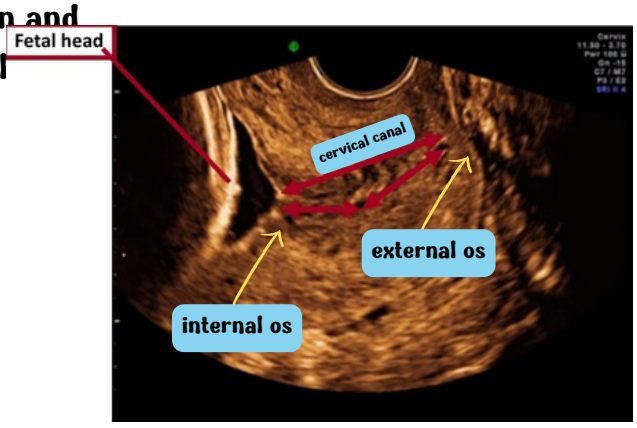
Cervical length:

Cervical length at 18–22 weeks in pregnancies that deliver at term is normally distributed with a mean of 34 mm

In pregnancies with sPTB at <34 weeks there is a bimodal distribution in cervical length. The cervical length is <15 mm in 1% of the population and this group contains 20% of cases of sPTB at <34 weeks.

The cervical length is <25 mm in 10% of the population and this group contains 40% of cases of sPTB at <34 weel

< 2.5 cm cervical length is a big risk factor for PTL



Cervico-vaginal fetal fibronectin

Fetal fibronectin is an extracellular matrix glycoprotein produced by amniocytes and by cytotrophoblast

It is localized between chorion and decidua and acts as a 'glue' between the pregnancy and the uterus

if we didn't find it >> the patient is stable

if we find it >> it doesn'tmean that the patient has a risk for PTL

Cell-free Fetal DNA Done after the 10th week

A role for cell-free fetal (cff) DNA as a signal for the onset of labor has recently been proposed

In pregnant women, cff DNA is normally present in the plasma, and concentrations increase as a function of gestational age - peaking at the end of pregnancy just prior to the onset of labor

cff DNA (in contrast with adult cell-free DNA) is hypomethylated and induce an inflammatory response

The downstream consequences could include activating the common pathway of labor

Patients who have an elevation of cff DNA in the midtrimester are at increased risk for spontaneous preterm delivery later in gestation

Patients with preterm labor and high plasma concentrations of cff DNA are also at increased risk for preterm delivery

Management

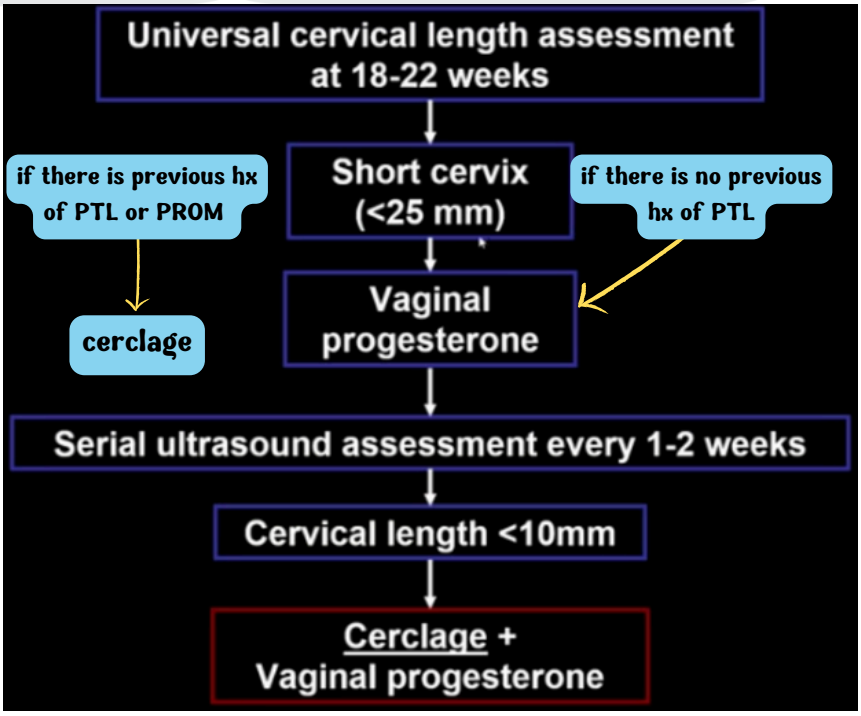
Goals :

-Delay delivery

-Identification etiology

-Administration of steroids

-GBs prophylaxis

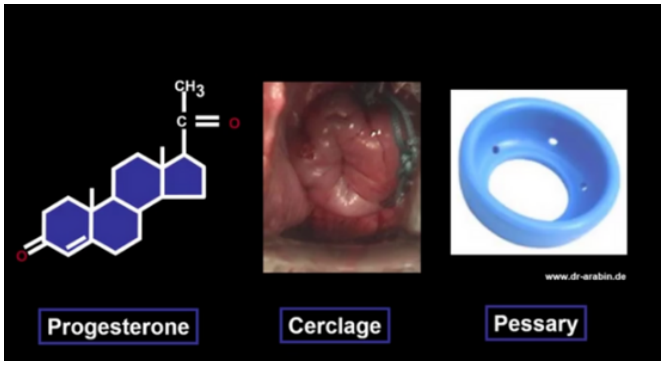


1 oclock >> 11 >> 7 >> 5 >> 1

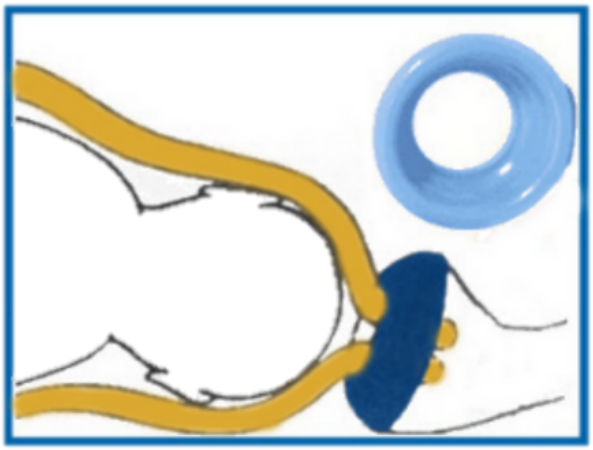
Types of cerclage stiches

- McDonald (at the external os)
- Shirodkor procedure
- abdominal cerclage
- laproscopic cerclage

Prevention PTB in short cervix



Cervical pessary (Weak evidence)



Preventions

Bed rest in a hospital or at home is widely recommended for the prevention of preterm birth but there is no scientific evidence to support this practice
Bed rest may also have some adverse effects on women, including an increased likelihood of venous thrombosis, muscle atrophy, and stress

Betamimetics is given prophylactically

Lifestyle interventions include decreased manual labor, increased visits to antenatal clinics, psychological support, or diet supplementation with iron, folate, calcium, zinc .magnesium, vitamins, or fish oil

According to obstetric history Studies investigating the value of preventative measures have essentially focused on two groups of women:

Women with a previous preterm birth

Women with no previous preterm delivery but found through a screening test in pregnancy to be at increased risk of preterm birth

Women with a previous preterm birth

No benefit from bed rest, prophylactic tocolytics, or lifestyle interventions
Vaginal progesterone every night from 20 to 34 weeks reduces PTB by 25%
Measurement of cervical length every 2 weeks between 14 and 24 weeks and cervical cerclage if the cervix becomes less than 25 mm reduces PTB by 25%

women with no previous preterm birth but positive screening test

Short cervix at 20–24 weeks consider Cervical cerclage it may reduce PTB at <34 weeks by 15%
Vaginal progesterone every night from 20 to 34 weeks reduces PTB at <34 weeks by 35–40%
In women with asymptomatic bacteruria the risk of PTB and pyelonephritis is increased

Threatened preterm labor

Management Women presenting with threatened preterm labor are often with:

Hospitalization in a unit with facilities for neonatal intensive care
Administration of tocolytics to prevent preterm birth
Administration of steroids to improve fetal lung maturit

Fetal Lung Maturity

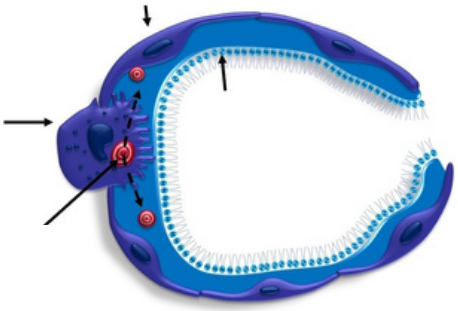
Respiratory distress syndrome of the newborn infant is caused by immaturity of the fetal lung
Measurement of pulmonary surfactant production is the most effective way to evaluate pulmonary maturity

As the lung develops, significant quantities of surfactant are washed out of the fetal lung and accumulate into the amniotic fluid

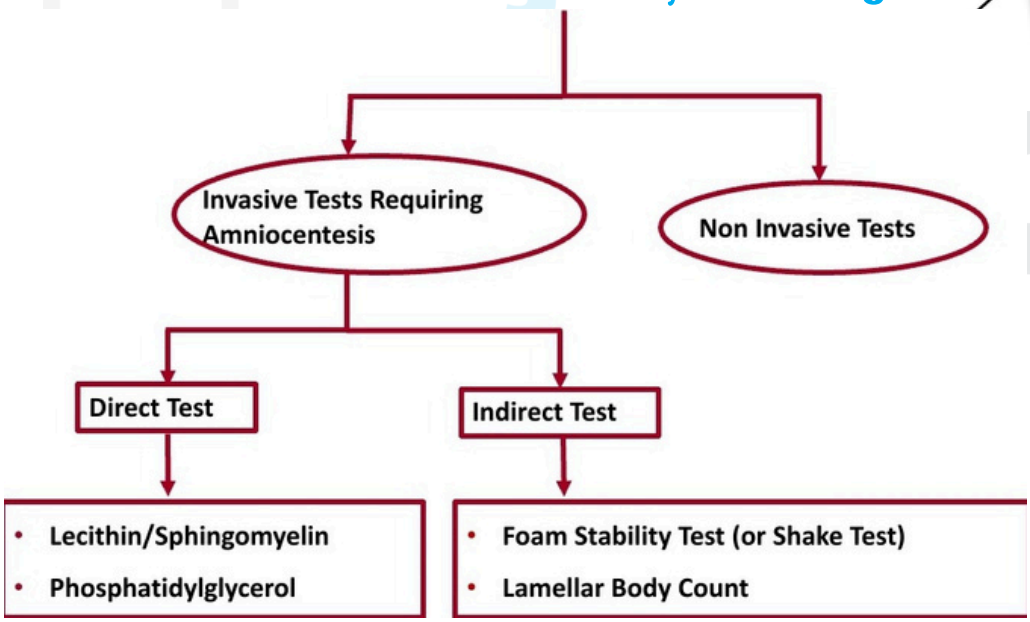
What are the benefits of performing a lung maturity test?

Assessment of the risk/benefit ratio in case of elective delivery in late pregnancy complications (iatrogenic preterm delivery)

Decision on the administration of corticosteroids



Tests for fetal lung maturity



Direct Tests

Lecithin/Sphingomyelin Ratio

The most popular test was reported in 1971 using a thin-layer chromatography procedure

3-4ml amniotic fluid centrifuged at low speed mixed with methanol

Lipid extraction and then application to thin layer chromatography plate vs controls

Visualization of phospholipid components

L/S ratio of <u>2.0 or greater indicates maturity</u>

Phosphatidylglycerol (PG)

It can be detected by two-dimensional thin-layer chromatography or polyclonal antibodies

The detection decreases the rate of false immature results

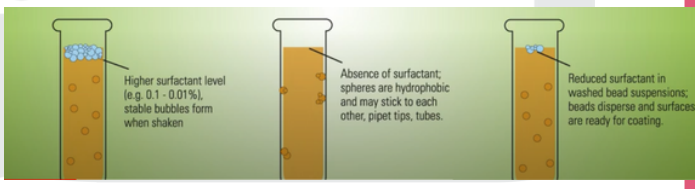
The presence of PG in amniotic fluid specimens contaminated with blood or meconium remained a valid finding even when the results of the L/S ratio were called into .question

Presence indicates a more advanced state of fetal pulmonary maturity

But the disadvantage they are late appearance in pregnancy

Indirect tests

Foam Stability (Shaking test)



https://www.youtube.com/watch?v=t_HLlbPNCuM

The principle:

Addition of amniotic fluid to different concentrations of 95% ethanol solution followed by shaking and observing the meniscus for the presence of a ring of bubbles

Lamellar Body Count

Phospholipids are packaged into multi-layered lamellar bodies

They are similar in size to platelets

Therefore they can be counted with an automated cell counter

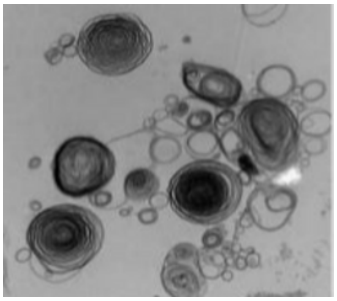
The lamellar body count method is an indirect reflection of surfactant concentration

If the count :

<= 8.000 immature no further testing

9.000-32.000 transitional perform L/S and PG

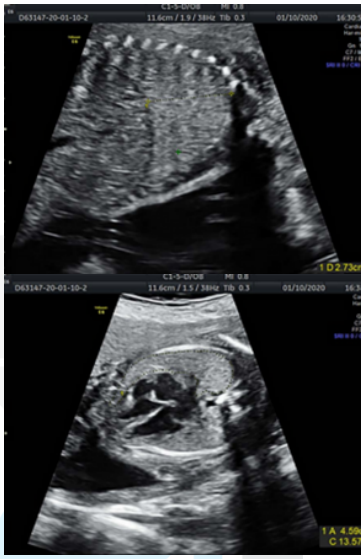
>32.000 mature no further testing



Non invasive tests

Ultrasound

Ultrasound can evaluate the development of fetal pulmonary parenchyma by measuring the diameter and area of fetal lungs
Color Doppler can show the distribution of fetal pulmonary vessels, helping to understand the development of fetal pulmonary circulation, as well as the fetal pulmonary maturity



Ultrasound features for fetal lung maturity detection:

Gray-Scale Measurements
Lung Tissue Motion
Relationship Between Image Features of Fetal Lung vs Placental or Liver Tissue
Doppler ultrasound

Neonates delivered at 36–38 weeks after confirmed fetal lung maturity are at higher risk of adverse outcomes than those delivered at 39– 40 weeks

Antenatal corticosteroid consists of
2 doses of 12 mg of betamethasone, given intramuscularly 24hours apart, or 4 doses of 6 mg of dexamethasone given intramuscularly 12 hours apart

Maternal corticosteroid administration with:

- Preterm labor likely to deliver in next 7 days
- Preterm prelabor rupture of membranes (PPROM)
- Severe preeclampsia
- Severe IUGR with umbilical artery Dopplers with absent or reversed end diastolic flow
- Patient at <37 weeks with high risk of delivery in next 7 days

Treatment

Patients with following complications are not candidate for tocolysis:

Infections advanced labour active phase PROM APH

Contraindications to tocolysis:

BAD CUP

- **B**leeding (severe) from any cause
- **A**bruptio placentae
- **D**eath of fetus
- **C**horioamnionitis
- **U**nstable **P**atient hemodynamics

Tocolytics:

B -mimetics

- Ritodrine and salbutamol & terbutaline
- Stimulate B2 receptors and relax smooth muscle (uterus)
- Highly side effects : tremor ,nausea, hyperglycemia, pulmonary edema

Calcium channel blockers

- Nifedipine ---inhibit myometrial contractions
- Effective -reduce PTD within 7 days and decreased RDS
- Fewer side effects comparing B-agonist
- Inexpensive and easy to use
- Side effects: hypotension, flushing. diarrhea, constipation , headaches.

NSAIDs

- Indomethacin: Prostaglandin inhibitor (PGf2a)—50-100 mg orally
- Side effects ---oligohydramnios, constriction of the ducts arteriosus, renal effect

Magnesium sulfate

RESEARCH ARTICLE

Assessing the neuroprotective benefits for babies of antenatal magnesium sulphate: An individual participant data meta-analysis

uses in pregnancy for :

- For managing preeclampsia-eclampsia

As tocolytics agent

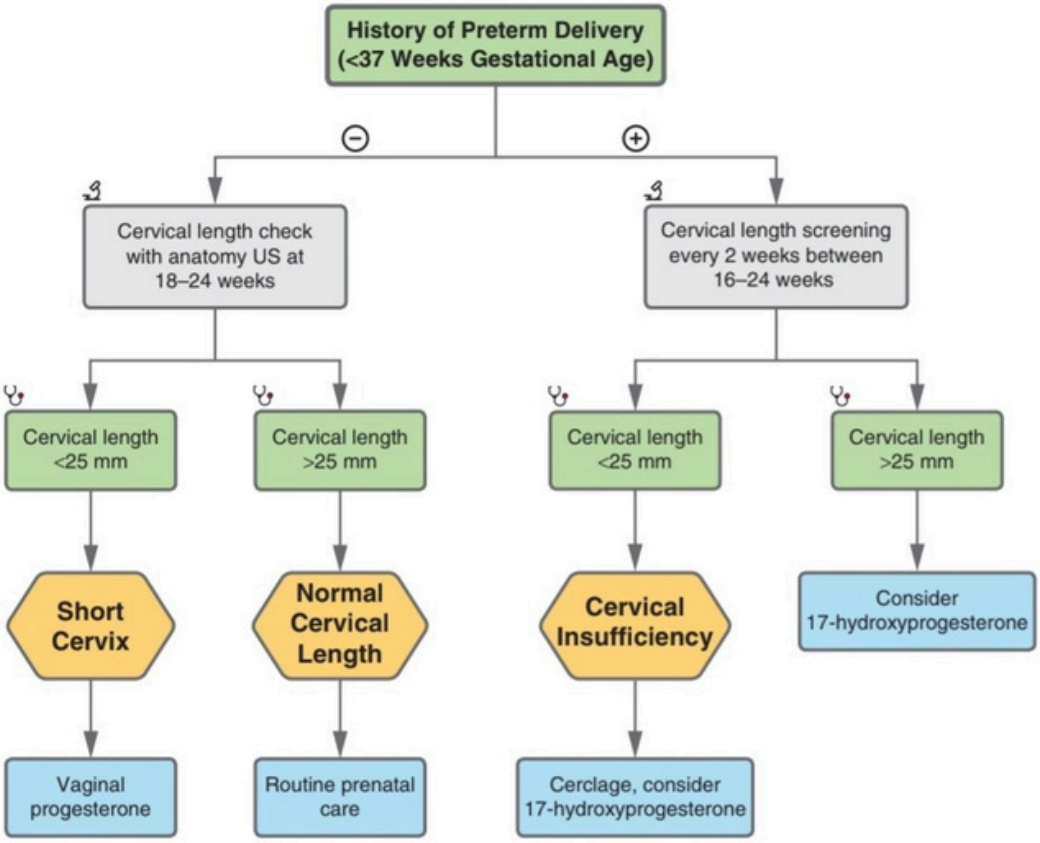
As a fetal-neonatal neuroprotective agent

- Use 4 g, the smallest effective dose, with or without a 1 g/hour maintenance dose

Atosiban (tractocile)

- Oxytocin-vasopressin antagonist
- Fewer side effects
- The most common side effect with Tractocile is nausea
- Reported cases of fetal demise
- Expensive

Summary



Management of Preterm Labor

High-Yield

Management of preterm labor involves several steps.

Step 1: Confirm labor using the three criteria listed earlier—gestational age, contraction frequency, cervical exam.

Step 2: Rule out contraindications to tocolysis. Do not try to prolong pregnancy if obstetric, fetal, maternal complications are present.

Step 3: Start IV $MgSO_4$ if <32 weeks for fetal neuroprotection of cerebral palsy. Administer at least four hours before anticipated birth.

Step 4: Administer IM betamethasone if <34 weeks to stimulate fetal type II pneumocyte surfactant production. A 48-hr course is needed for full effect to take place.

Step 5: Start tocolytic therapy if <34 weeks to prolong pregnancy to allow for antenatal steroid effect. There is no benefit exceeding 48 hours. **$MgSO_4$, terbutaline**, or **nifedipine** can be used up to 34 weeks. **Indomethacin** should not be used after 32 weeks due to concerns regarding in-utero closure of the PDA.

Step 6: Start IV penicillin G if <36 weeks for GBS sepsis prophylaxis (use vancomycin if allergic to penicillin G). First obtain recto-vaginal cultures.

لسا ضايل نص المحاضرة :)

Preterm pre-labor rupture of membranes (PPROM)

Rupture of the membrane before the onset of labor <37 weeks
PPROM complicates 2-4% of all births and 30-40 of all preterm births.
Associated with inflammatory reaction +- infection.

look for the gestational age: if <24 wks >> pre-viable ROM
if >24 wks & there is no labor >> prelabor, preterm ROM (PPROM)
if >24 wks & there is labor >> preterm ROM (PROM)

PPROM and complications

-Prolonged maternal hospitalization
-Early onset neonatal sepsis
-Fetal Pulmonary hypoplasia depending on gestational age
-Higher neonatal morbidity and mortality
-Inflammation-related adverse neurodevelopmental outcomes
-Infection includes chorioamnionitis
-Retained placenta
-Placental abruption

Risk factors

-Prior PPROM or PTL of any cause
-Bleeding in any trimester
-Genital tract infections
-Tobacco exposure
-Collagen disease
-Psychosocial stressors

Fetal membranes

-•Surface area of 1500 cm2

•200-300 um thick at term

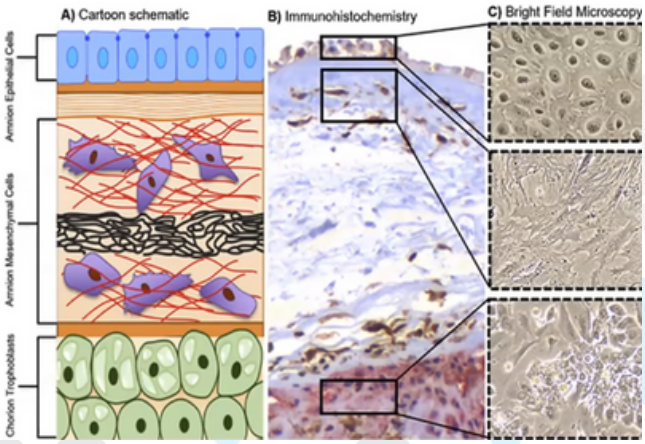
•Resistant and elastic mechanical barrier

•Rich source of functionally relevant biochemicals

•Fetal membrane matrix is maintained by progesterone

•Provide mechanical ,structural ,immune ,antimicrobial and endocrine functions

Protection mechanism reduced in inflammation

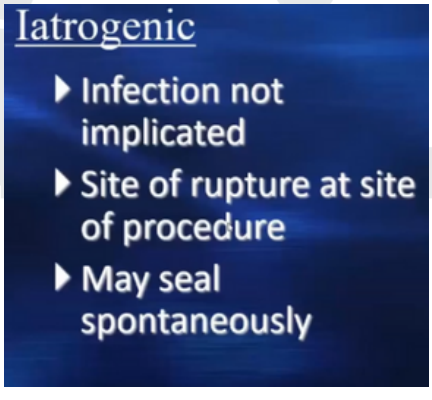


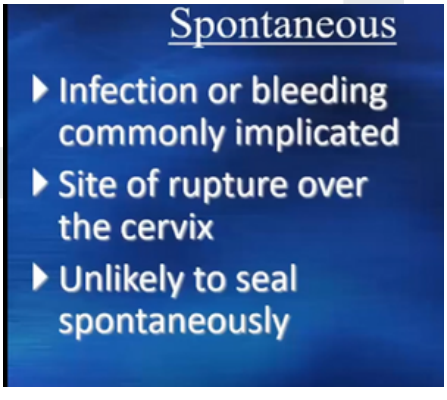
Etiology

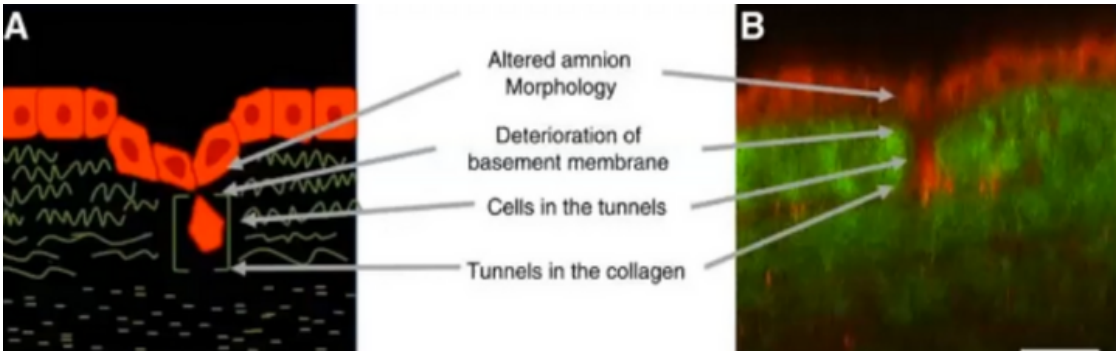
Inflammation

Microfractures

Fetal membrane aging







Clinical evaluation

History

sudden gush of fluid, soaking clothes, dampness of underwear mistaken)

urinary incontinence

Odder and color (green color or bleeding(APH) or clear)

Abdominal pain, contractions

Mild pyrexia, feeling unwell, abnormal vaginal discharge

Vaginal bleeding

Dysuria

Cord prolapse

OB Triad

Ruptured Membranes

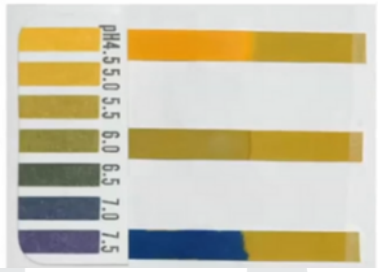
- Posterior fornix pooling
- Fluid is nitrazine (phenaphthazine) (+)
- Glass slide drying: fern (+)

Diagnosis

Ferning

sample of vaginal fluid, if we detect crystals this mean that this fluid is amniotic fluid

Nitrazine



high false positive ratio so its not used any more

ROM Plus

Sensitivity 99%

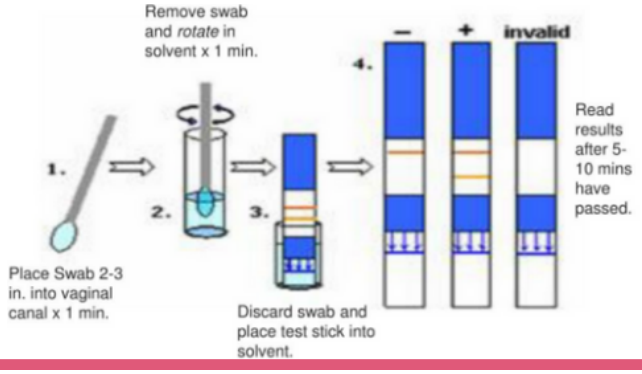
specificity 91%

Detect IGFBP-1 and AFP

Amnisure

sensitivity 94-99% specificity 87-100%

non-invasive strip test for the detection of the placental alphamicroglobulin-1 protein



Actim-PPROM

sensitivity 95-100%

Specificity 93-98%

rapid test that reliably detects PROM, even before any visible signs can be detected

Differential diagnosis

-Urinary incontinence: leakage of small amounts of urine is common in the last part of pregnancy

-Normal vaginal secretions of pregnancy.

Increased sweat or moisture around the perineum.

-Increased cervical discharge.

-Semen.

-Douching

Investigation (CBC Urinalysis High vaginal swab CRP US)

Management

Screening for infection including GBS

Antenatal corticosteroids

Tocolysis only to achieve the benefit of corticosteroids

Antibiotics prolong latency based on numerous trials (penicillin plus macrolide)

Fetal monitoring NST, AFV, and fetal growth

Maternal monitoring for infection or labor

Timing of delivery -dependent on NICU capability

Malpresentation may require cesarean delivery

The risk of cord prolapse should be evaluated

Delivery at 34 weeks or sooner if indicated

Majority of pregnancies with PPROM deliver within one week of rupture

Mgso4 is an important drug in early PPROM

Antenatal corticosteroids potent drugs with potent side effects:

Reduced placental weight

Reduced fetal weight and height

Reduced head circumference

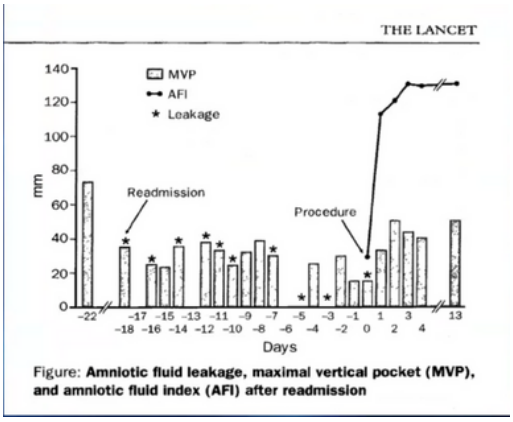


Figure: Amniotic fluid leakage, maximal vertical pocket (MVP), and amniotic fluid index (AFI) after readmission

Chorioamnionitis

Acute chorioamnionitis is the most frequent diagnosis in placental pathology reports, and is generally considered to represent the presence of intra-amniotic infection or "amniotic fluid infection syndrome"

Diagnosed by the presence of maternal fever (temperature ≥37.8°C) plus two or more of the five following clinical signs:

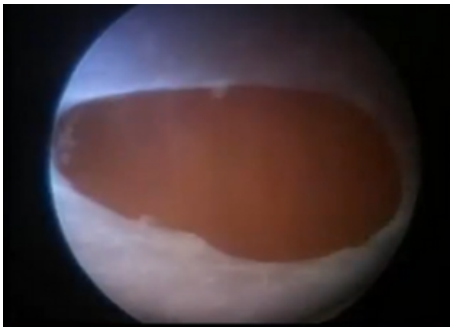
-Maternal tachycardia (heart rate >100 beats/min)
-Fetal tachycardia (heart rate >160 beats/min)
-Uterine tenderness
-Purulent or foul-smelling amniotic fluid or vaginal discharge
-Maternal leukocytosis (white blood cell count >15,000/mm3)

The most frequent microorganisms identified in the amniotic fluid of women with clinical chorioamnionitis include Ureaplasma (most common) urealyticum, Gardnerella vaginalis, Mycoplasma hominis, Streptococcus agalactiae, Lactobacillus species, and Bacteroides species

The standard treatment for clinical chorioamnionitis has been administration of antibiotics and antipyretics and expedited delivery

Surgical treatment of rupture of membrane

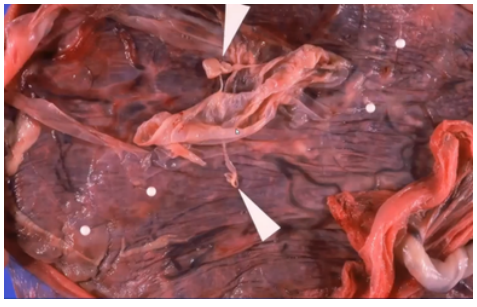
Amniograft
Amniotic patch



The procedure can seal membrane defects up to 4 mm in diameter

Amniopatch technique

22- gauge needle
Injection into an available pocket of fluid
½unit of platelets
one unit of cryoprecipitate



Summary

PROM Management by GA

	>37	34/0–36/6	23/0–33/6	<23/0
Expectant management?	No—delivery indicated	Consider with shared decision making	Yes	Consider with shared decision making
Steroids	No	Yes	Yes	No
Antibiotics for latency	No	No	Yes	Consider with shared decision making
Magnesium for neuroprotection?	No	No	Yes if <32 weeks	No