Preterm labor management: Initial assessment & Tocolysis

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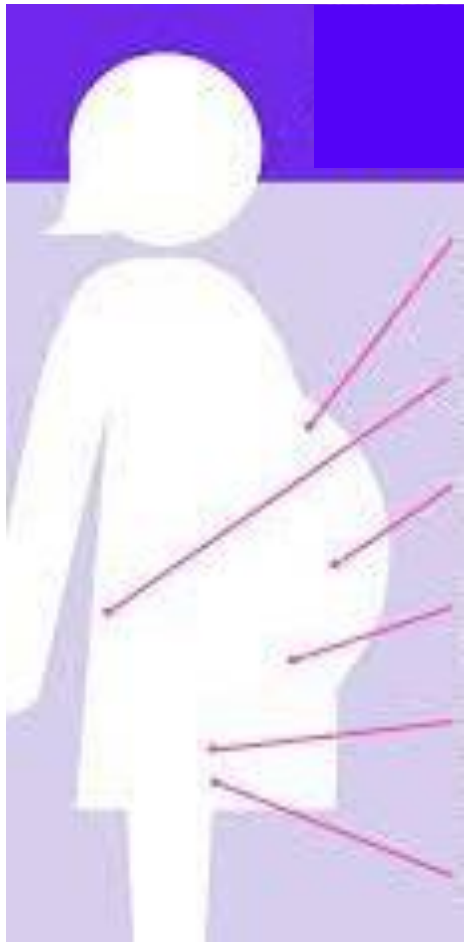
Initial assessment

- prodromal signs and symptoms: present for several hours before diagnostic criteria

Uterine contractions are the sine qua non of labor

True labor (contractions → cervical change)



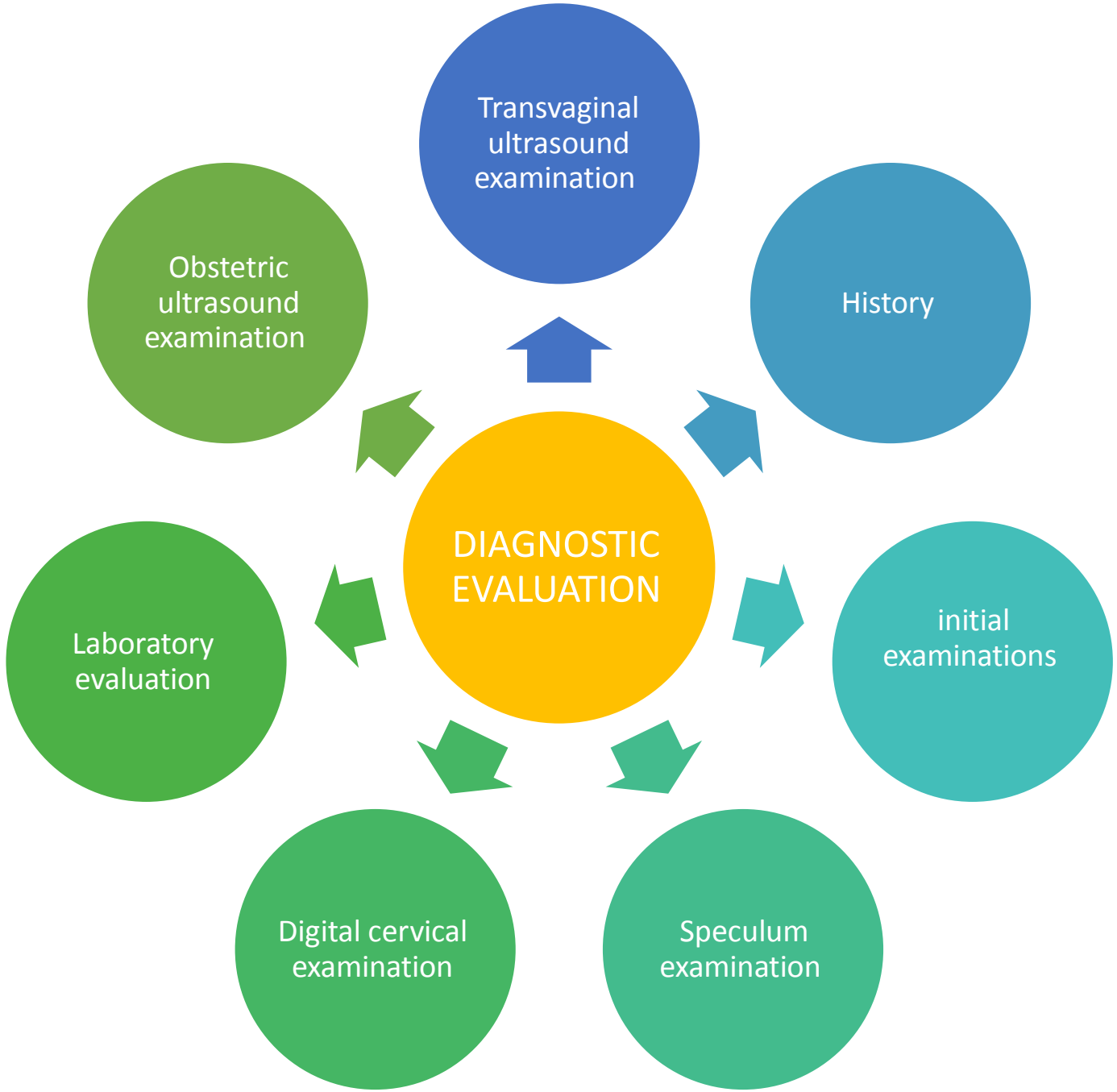
Mild, irregular contractions

Low back ache

Menstrual-like cramping

Vaginal discharge of mucus

Spotting, light bleeding


Transvaginal ultrasound examination
History
initial examinations
Speculum examination
Digital cervical examination
Laboratory evaluation
Obstetric ultrasound examination
DIAGNOSTIC EVALUATION

Diagnostic Evaluation

History :

1. Risk factors for preterm birth
2. Preterm labor may be triggered by an underlying obstetric complication or medical/surgical disorder

initial examinations:

1. Assessment of gestational age, based on the best estimate from the first ultrasound examination
2. Evaluation of signs and symptoms of preterm labor
3. Maternal vital signs
4. Fetal size, fetal position, and FHR pattern
5. Contraction frequency, duration, and intensity

Diagnostic Evaluation

Speculum examination:

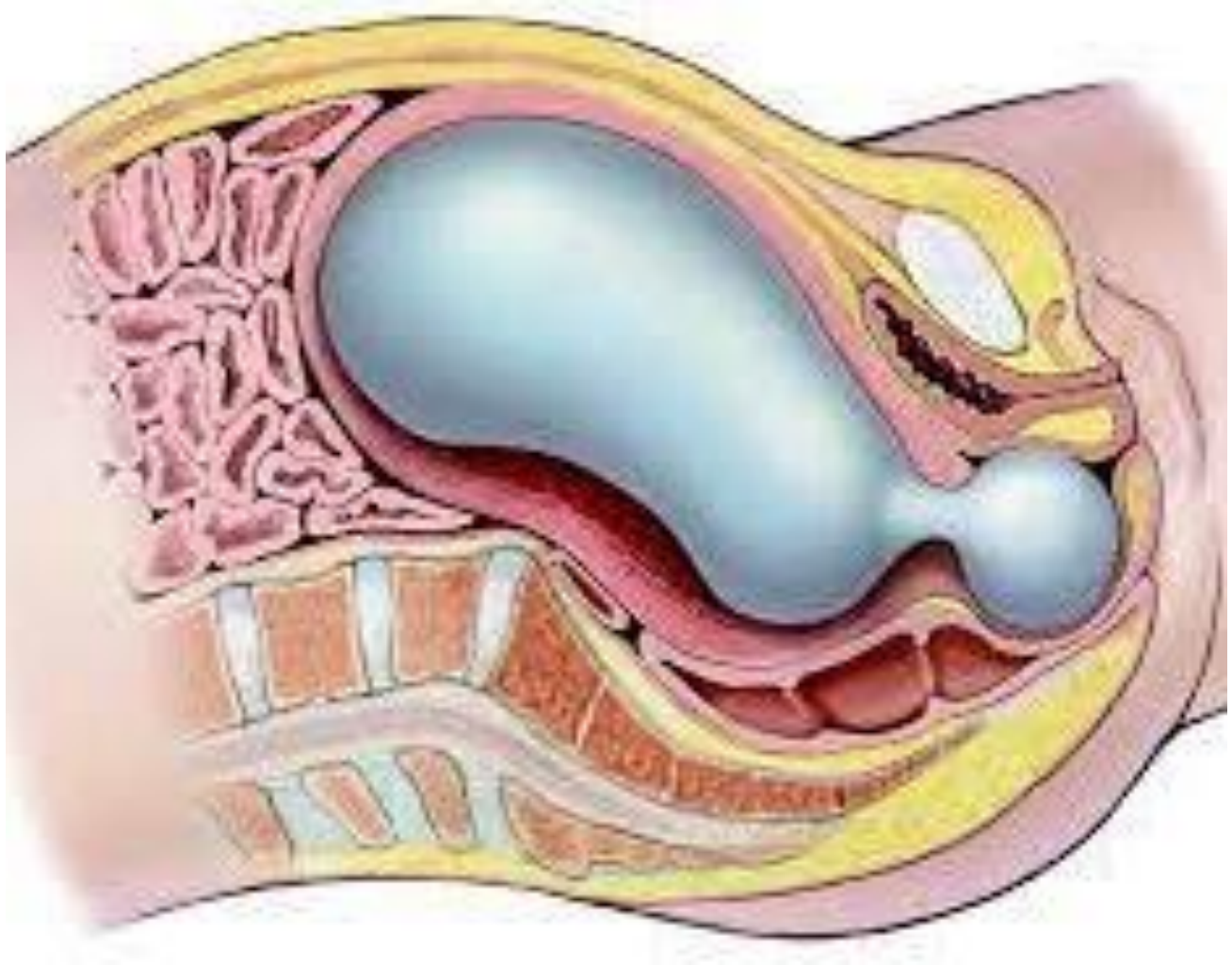
1. Speculum examination using a wet non-lubricated speculum (lubricants may interfere with tests performed on vaginal specimens)
2. Estimate cervical dilation. Cervical dilation ≥3 cm supports the diagnosis of PTL.
3. Assess the presence and amount of uterine bleeding
4. Evaluate fetal membrane status
5. fFN testing

Digital cervical examination:

1. Cervical dilation and effacement are assessed by digital examination after placenta previa and rupture of membranes have been excluded.
2. A digital examination should be performed before speculum examination if the information is urgently (eg, abnormal FHR, probable advanced phase of active labor)

cervical dilation >3 cm in the presence of uterine contractions at 20+0 to 36+6 weeks supports the diagnosis of preterm labor; inhibition of acute preterm labor is less likely to be successful as the cervix dilates beyond 3 cm.

When assessing cervical dilation and effacement in the second trimester, it is important to distinguish between patients whose membranes have hour-glassed (prolapsed) through a mildly dilated and effaced cervix (suggestive of cervical insufficiency) and those who are in active labor with advanced cervical dilation and effacement. TVUS assessment of the cervix can help distinguish between the two entities when the diagnosis is uncertain.



Diagnostic Evaluation

Transvaginal ultrasound examination:

1. A short cervix **before 34 weeks of gestation (<30 mm)** is predictive of an increased risk for preterm birth in all populations
2. A long cervix (≥30 mm) has a high negative predictive value for preterm birth.

Obstetric ultrasound examination:

1. Presence/absence of fetal, placental, and maternal anatomic abnormalities
2. Confirmation of fetal presentation
3. Assessment of amniotic fluid volume
4. Estimated fetal weight

Diagnostic Evaluation

Laboratory evaluation:

1. Rectovaginal group B streptococcal culture, if not done within the previous five weeks
2. UC
3. Drug testing in patients with risk factors for substance abuse
4. fFN in women <34 weeks of gestation with cervical dilation <3 cm and cervical length 20 to 30 mm on TVUS examination.
5. Testing for sexually transmitted infections depends on the patient's risk factors

Other laboratory tests:

1. placental alpha-microglobulin-1 (PAMG-1)
2. phosphorylated insulin-like growth factor binding protein-1 (pIGFBP-1)

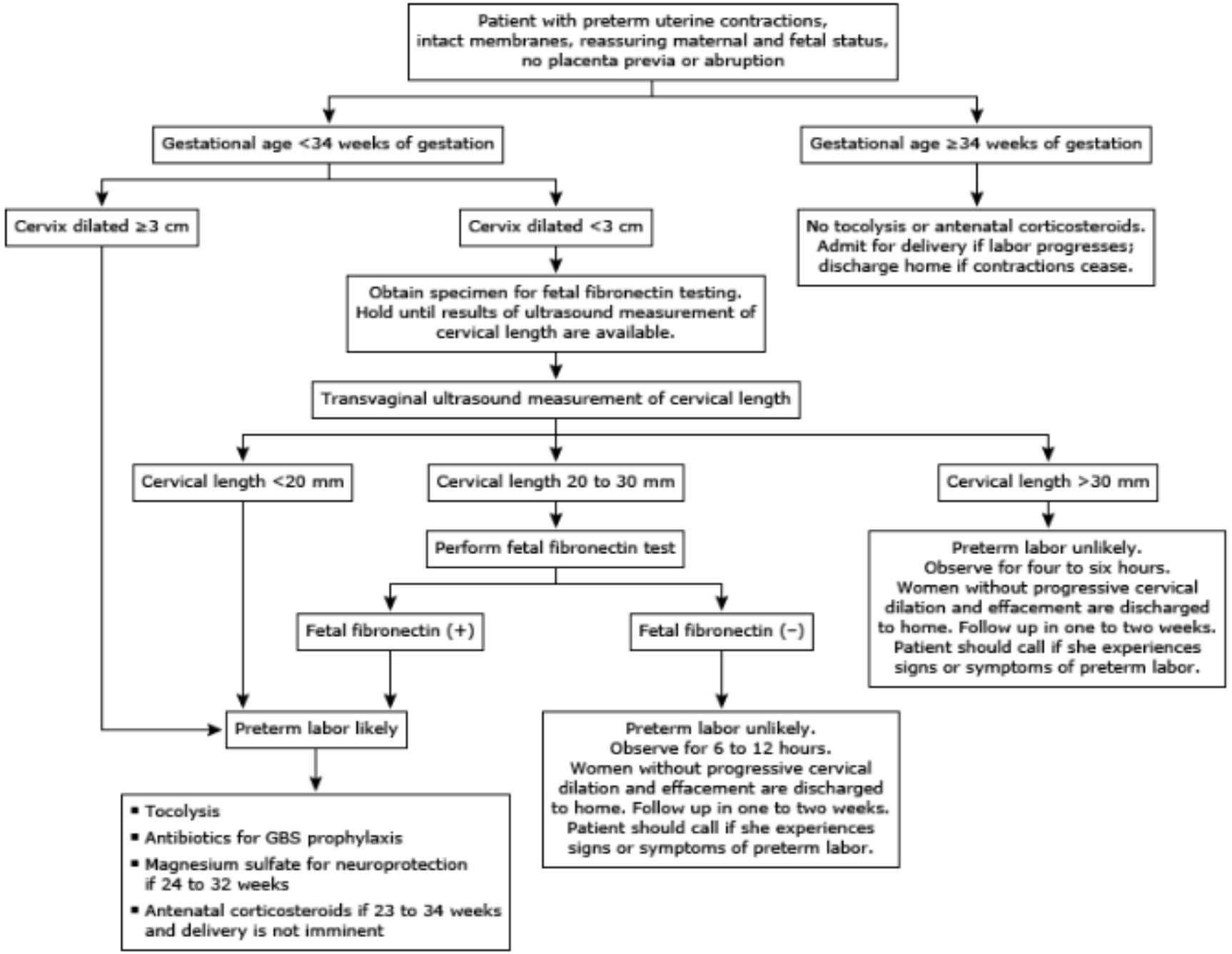
Diagnosis

- The diagnosis of preterm labor based upon clinical criteria of regular painful uterine contractions + cervical change
- Vaginal bleeding and/or ruptured membranes in this setting increase diagnostic certainty

Uterine contractions (≥4 every 20 minutes or ≥8 in 60 minutes) **plus**		
Cervical dilation ≥3 cm **or**	Cervical length <20 mm on TVS **or**	Cervical length 20 to <30 mm on TVS and positive fFN

Approach to Triage: Singleton pregnancies

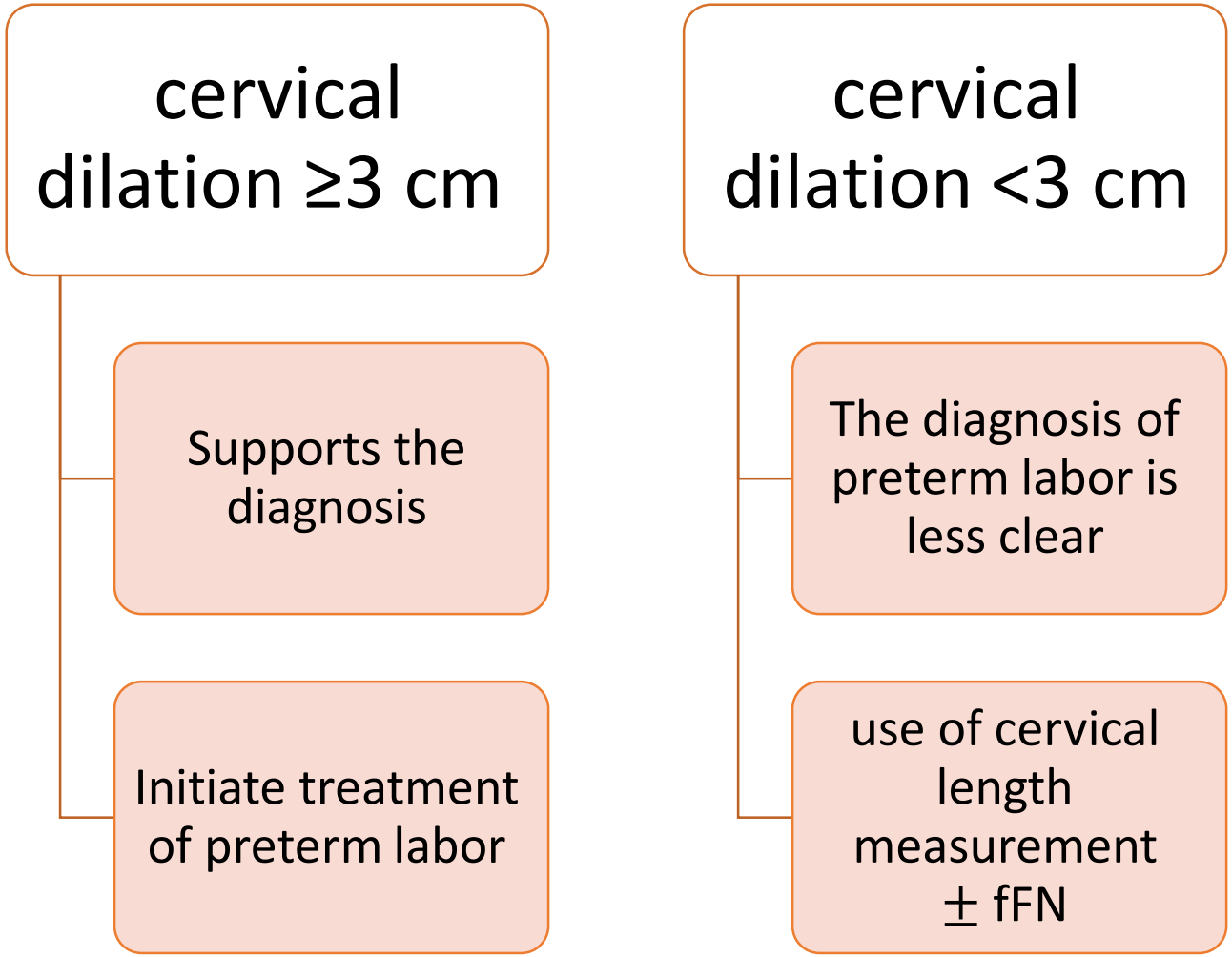
Suggested approach to management of suspected preterm labor



≥34 weeks of gestation

- observation period of **four to six hours**
- without progressive cervical dilation and effacement are discharged to home, as long as fetal well-being is confirmed (NST)
- arrange **follow-up in one to two weeks**
- generally do not administer antenatal corticosteroids after 34 weeks

<34 weeks of gestation



<34 weeks of gestation + cervical dilation <3 cm

Cervical length 20 to <30 mm

- cervicovaginal sample for **fFN** testing
- fFN test is positive → interventions
- fFN test is negative → discharge the patient after **6 -12** hours of observation

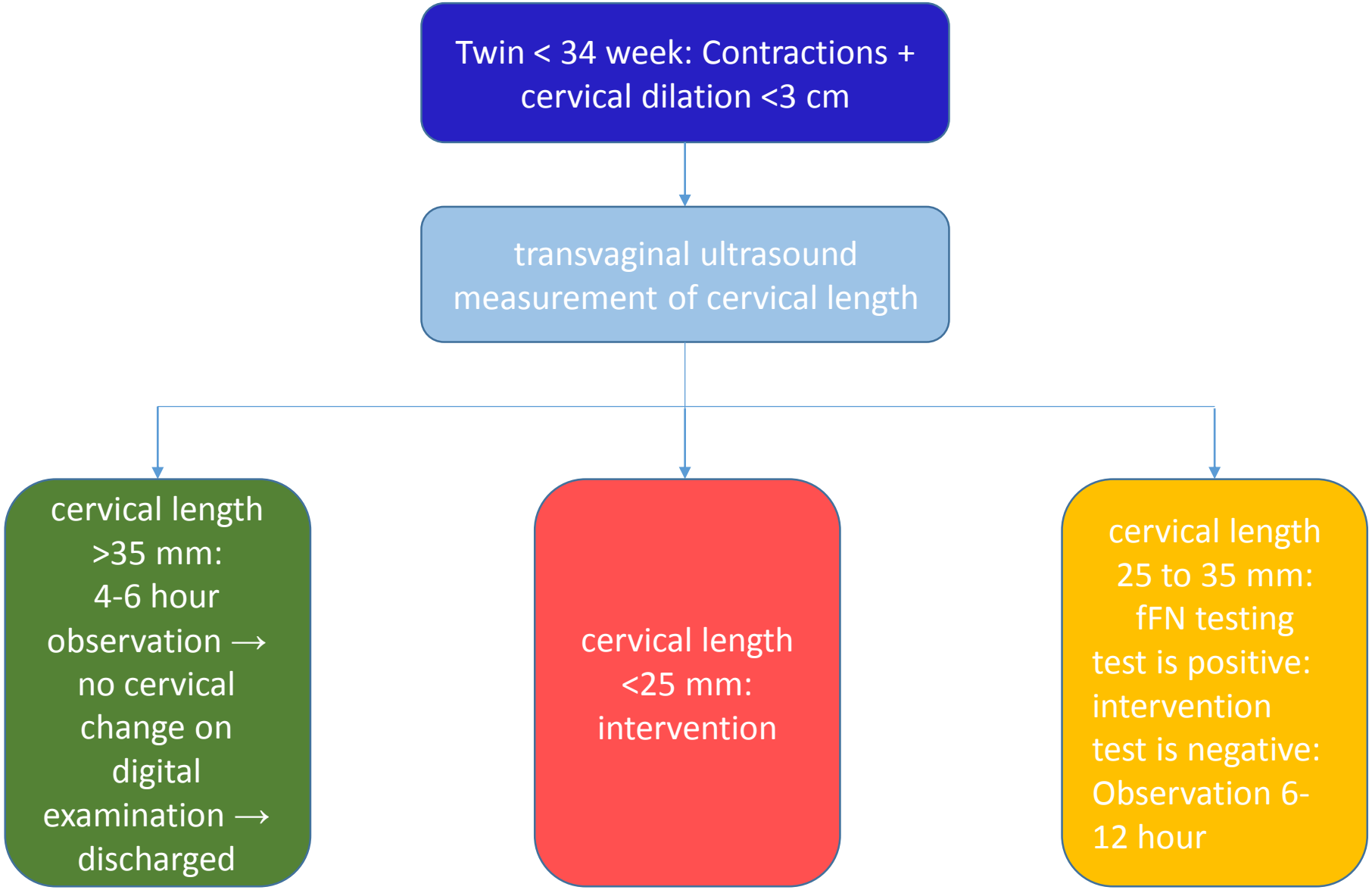
Cervical length <20 mm

- high risk (>25%) of delivery within seven days
- begin interventions

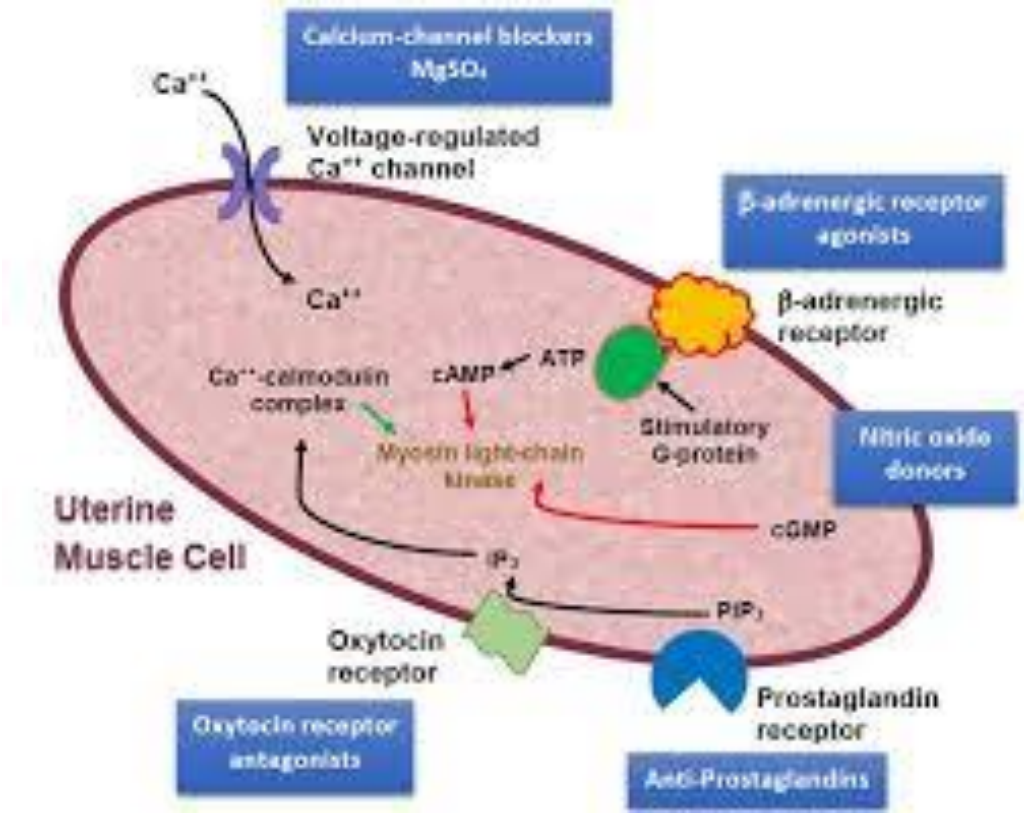
Cervical length ≥30 mm

- low risk (<5%) of delivery within seven days
- observation period of 4- 6 hours & arrange follow-up in 1-2 weeks

APPROACH TO TRIAGE: TWIN PREGNANCIES


Twin < 34 week: Contractions + cervical dilation <3 cm
transvaginal ultrasound measurement of cervical length
cervical length >35 mm: 4-6 hour observation → no cervical change on digital examination → discharged
cervical length <25 mm: intervention
cervical length 25 to 35 mm: fFN testing
test is positive: intervention
test is negative: Observation 6-12 hour

Tocolysis


Calcium-channel blockers
$MgSO_4$
Ca^{++}
Voltage-regulated
Ca^{++} channel
β-adrenergic receptor agonists
β-adrenergic receptor
Ca^{++}
Ca^{++}-calmodulin complex
cAMP
ATP
Stimulatory G-protein
Myosin light-chain kinase
Nitric oxide donors
Uterine Muscle Cell
cGMP
IP_3
PIP_2
Oxytocin receptor
Prostaglandin receptor
Oxytocin receptor antagonists
Anti-Prostaglandins

Treatment Goals

Delay delivery by at least 48 hours (when safe to do so) so that antenatal corticosteroids (primary or rescue) administered to the mother have time to achieve their maximum fetal/neonatal effects.

Provide time for safe transport of the mother, if indicated, to a facility that has an appropriate level of neonatal care if she delivers preterm (In utero transport)

Prolong pregnancy (when safe to do so) when underlying, self-limited conditions that can cause labor, such as pyelonephritis or abdominal surgery, are present but unlikely to cause recurrent preterm labor.

PATIENT SELECTION

ACOG pointed: "Interventions to reduce the likelihood of delivery should be reserved for women with preterm labor at a gestational age at which a delay in delivery will provide benefit to the newborn. Because tocolytic therapy is generally effective for up to 48 hours, only women with fetuses that would benefit from a 48 hour delay in delivery should receive tocolytic treatment"	Inhibition of acute preterm labor is less likely to be successful as labor advances to the point that cervical dilation is greater than 3 cm.	**Lower gestational age limit:** ACOG and SMFM recommend not administering tocolysis before 24 weeks of gestation **Upper gestational age limit:** ACOG and SMFM define that 34 weeks of gestation the threshold at which perinatal morbidity and mortality are sufficiently low.

Contraindications

Intrauterine fetal demise
Lethal fetal anomaly
Nonreassuring fetal status
Preeclampsia with severe features or eclampsia
Maternal hemorrhage with hemodynamic instability
Intraamniotic infection
Preterm prelabor rupture of membranes, except in the absence of infection when needed for maternal transport, steroid administration, or both
Medical contraindications to the tocolytic drug

Which tocolytic is the best?

Choice of first-line therapy

- 24 to 32 weeks: indomethacin
- 32 to 34 weeks: nifedipine

- Do not use indomethacin for more than 72 hours
- Use nifedipine as a first-line agent for women who have a contraindication to indomethacin (maternal platelet dysfunction or bleeding disorder, hepatic dysfunction, GI ulcerative disease, renal dysfunction, or asthma or hypersensitivity to aspirin)

Choice of second-line therapy

- 24 to 32 weeks: nifedipine
- 32 to 34 weeks: terbutaline

For those who received nifedipine as a first-line agent at 24 to 32 weeks, we switch to terbutaline

Duration of tocolysis

Discontinue tocolytics 48 hours after administration of the first corticosteroid dose.

Retreatment: If a second episode of acute preterm labor occurs, our indications for retreatment are the same as for a primary episode (i.e, delay delivery for corticosteroid administration [primary or rescue] and/or maternal transfer). There are no data on the role of repeated courses of tocolytics for treatment of recurrent preterm labor.

Cyclooxygenase inhibitors (indomethacin)

Nonspecific COX inhibitor

The most commonly used

Maternal side effects:

1) Nausea & emesis
2) Reflux
3) Gastritis
4) Platelet dysfunction

Fetal side effects:

1) Constriction of the ductus arteriosus
2) Oligohydramnios

Contraindication:

platelet dysfunction or bleeding diathesis

hepatic dysfunction gastrointestinal ulcerative disease

renal dysfunction

asthma hypersensitivity to aspirin

Cyclooxygenase inhibitors (indomethacin)

Dose:

- loading dose: 50 to 100 mg (PO, rectal)
- followed by 25 mg orally every 4-6 hours

Monitoring:

- If indomethacin is continued for longer than 48 hours, sonographic evaluation warranted at least weekly .
- Evidence of oligohydramnios or ductal constriction should prompt discontinuation of this therapy.

Calcium channel blockers (Nifedipine)

Peripheral vasodilator

The relative safety

Maternal tolerance

Ease of administration

Reduction in adverse neonatal outcomes →

Support use of nifedipine rather than beta-agonists for inhibition of acute preterm labor.

Maternal side effects:

Nausea

Flushing

Headache

Dizziness

Palpitations

hypotension

Contraindications:

known hypersensitivity to the drugs

Hypotension

preload-dependent cardiac lesions → should be used with caution in women with heart failure with reduced ejection fraction.

The concomitant use of a CCB and magnesium sulfate could act synergistically to suppress muscular contractility, which could result in respiratory depression

Calcium channel blockers (Nifedipine)

Dose:

- loading dose of 20-30 mg PO, followed by an additional 10 to 20 mg PO every 3-8 hours for up to 48 hours, with a maximum dose of 180 mg/day

The half-life of nifedipine: 2-3 hours

duration of action of a single orally administered dose: up to six hours.

Plasma concentrations peak: 30 to 60 minutes.

Nifedipine is almost completely metabolized in the liver and excreted by the kidney.

Beta-agonists (Terbutaline)

Only drug approved by FDA for the treatment of preterm labor

Maternal side effects:

↑maternal HR & SV

lower blood pressure

shortness of breath

Pulmonary edema is uncommon results from several additive factors

Hypokalemia

Hyperglycemia

lipolysis

Myocardial ischemia is a rare complication.

Fetal side effects :

fetal tachycardia

Neonatal hypoglycemia

Contraindications:

relatively in tachycardia-sensitive cardiac disease

poorly controlled hyperthyroidism

diabetes mellitus

Beta-agonists (Terbutaline)

glucose and potassium concentrations are closely monitored

Should be used with caution in women at risk for massive hemorrhage

should not be used in pregnant women for prolonged (beyond 48 to 72 hours) treatment of preterm due to potential for serious maternal heart problems and death

FDA: oral terbutaline should not be used for prevention or any treatment of preterm labor

Dose:0.25 mg SC every 20 to 30 minutes for up to 4 doses or until tocolysis is achieved. Then, 0.25 mg can be administered SC every 3-4 hours until the uterus is quiescent for 24 hours.

Infusion :2.5 to 5 mcg/min and increasing by 2.5 to 5 mcg/min every 20 to 30 minutes to a maximum of 25 mcg/min, or until the contractions have abated

Magnesium Sulfate

- Efficacy: In a 2014 meta-analysis of randomized trials comparing magnesium sulfate with no treatment/placebo control, magnesium sulfate administration did not result in a statistical reduction in birth <48 hours after trial entry or improvement in neonatal and maternal outcomes.
- In 33 comparative trials, magnesium sulfate was neither more nor less effective than other tocolytics (betamimetics, calcium channel blockers, COX inhibitors, prostaglandin inhibitors, or human chorionic gonadotropin).

The American College of Obstetricians and Gynecologists (ACOG) and the Society for Maternal-Fetal Medicine consider magnesium sulfate an option for short-term prolongation of pregnancy (up to 48 hours) to allow administration of antenatal corticosteroids to pregnant women at risk for preterm delivery within 7 days .

Magnesium Sulfate

- Maternal and fetal side effect:

1. Diaphoresis and flushing are the most common
2. Slight decrease in baseline fetal heart rate and fetal heart rate variability
3. Significant increase in radiographic bone abnormalities in neonates with in utero exposure for more than 7 days, and a significant difference in the serum Mg, ca, phosphorus, and osteocalcin.

Contraindications:

1. MG
2. known myocardial compromise or cardiac conduction defects

- Neuroprotective effects:

If tocolysis is indicated because of persistent preterm labor in a patient receiving magnesium sulfate for neuroprotection, the most effective tocolytic with the most favorable side-effect profile should be used.

Dose:

6 g IV load over 20 minutes, followed by a continuous infusion of 2 g/hour

Less Effective Tocolytic Drugs

1. Oxytocin receptor antagonists (eg, Atosiban)
2. Nitric oxide donors (eg, Nitroglycerin)

thanks