



# PRETERM LABOR

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# CASE PRESENTATION

- ▶ Mt. Primo, a 24-year old African-American female G2P0100 presents to your office for prenatal care
- ▶ She is transferring prenatal care as she has recently moved, and she is currently at 23 weeks of gestational age based on an early ultrasound that is consistent with her last menstrual period

# CASE PRESENTATION

- ▶ Ms. Primo reports that she has had no difficulties with her pregnancy up to this point. She denies significant past medical or surgical history
- ▶ Her past Ob history is significant for a premature delivery. During that pregnancy, Ms. Primo started having uterine contractions at 27 weeks of gestation, which she confused for food poisoning and did not seek medical attention. When she finally started having vaginal spotting, she went to the hospital. On the way to the hospital, she began to feel vaginal pressure and delivered her baby in the parking lot of the hospital
- ▶ This baby did not survive

# CASE PRESENTATION

- ▶ She is a smoker, using 20 to 25 cigarettes daily. She recently moved in with her parents as her husband was deployed overseas with the military
- ▶ She reports that her previous Ob was giving her weekly injections with the current pregnancy; she thinks that these were vitamin shots. She denies other medication use except for prenatal vitamins. The patient reports that she has been seen regularly by her Ob/Gyn during this pregnancy and he has even sent her to a high-risk obstetrician because of her history

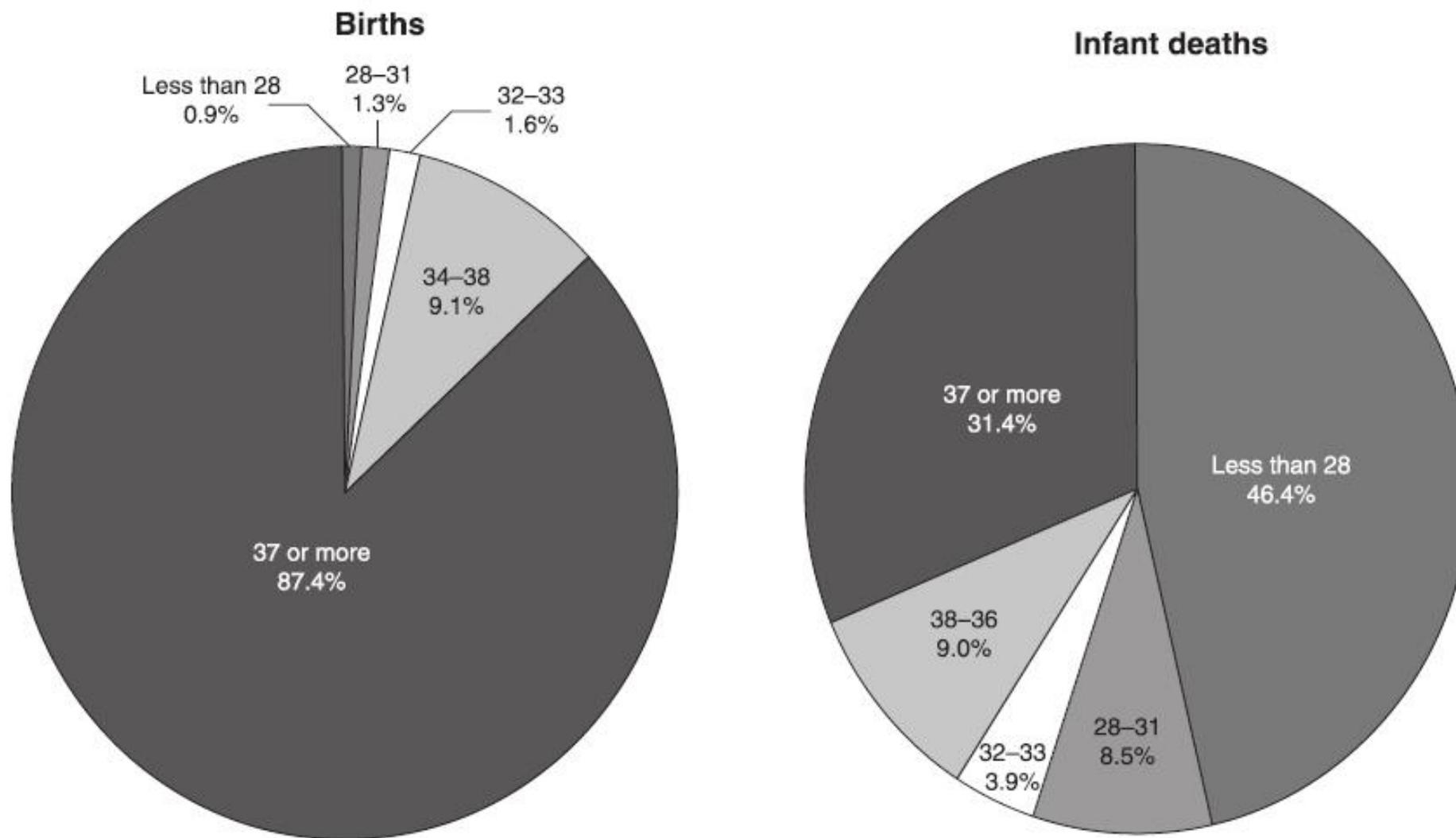
# CASE PRESENTATION

- ▶ With this pregnancy, her physician was performing regular vaginal ultrasound, and when she felt vaginal pressure at a specific visit, he "performed a test using a swab at my cervix"
- ▶ The patient reported that these tests were all normal
- ▶ She last saw her Ob/Gyn approximately 2 weeks ago

# NEED TO KNOW

## Preterm Labor and Delivery

- ▶ Preterm delivery is defined as delivery prior to 37 completed weeks of gestation.
- ▶ Preterm delivery accounts for approximately 13% of all deliveries in the United States.
  - 40% are due to spontaneous preterm labor (PTL),
  - 35% are secondary to preterm premature rupture of the membranes (pPROM)
  - 25% are obstetrically indicated
  - 70% of infant deaths
- ▶ Infants born < 2,500 g having a 10-fold higher risk of neurologic impairment as compared with infants weighing more than 2,500 g
- ▶ most of the morbidity and
- ▶ mortality associated with preterm delivery <34 weeks



**Figure 26.1** Perinatal mortality versus gestational age at delivery. Although infants born at <28 weeks of gestation are only 0.8% of total births in the United States, they account for almost half of infant deaths. (Adapted from 2005. National Vital Statistics Reports. 2006;57:2.)

# Decision 1: Risk management

Which is a modifiable risk factor for PTL in this patient?

- ▶ A. African-American race
- ▶ B. Smoking
- ▶ C. living situation
- ▶ D. Underweight

- 
- ▶ (Answer A) African-American race is a risk factor, however, it is not modifiable
  - ▶ (Answer B) Smoking is a risk factor for PTL, and smoking cessation may help to reduce her risk
  - ▶ (Answer C) The patient's living situation may be a cause of stress, which, in some studies, may be associated with PTL
  - ▶ (Answer D) Being underweight is a risk factor for PTL, but this patient is not underweight by body mass index (BMI) criteria, having a prepregnant BMI of 20.4

**RISK FACTORS FOR PRETERM DELIVERY. THE CATEGORIZATION OF MATERNAL RISK FACTORS IS ARBITRARY IN SOME CASES, FOR EXAMPLE, AFRICAN-AMERICAN RACE IS KNOWN TO BE ASSOCIATED WITH AN INCREASED RISK OF PRETERM LABOR/DELIVERY; HOWEVER, THE REASON FOR THIS IS UNKNOWN. SOME HAVE HYPOTHESIZED THAT SOCIAL PRESSURES ARE INCREASED ON WOMEN OF COLOR, LEADING TO AN INCREASE IN PTL**

- Previous preterm delivery
- Maternal factors
  - Stress
- Anxiety
- Depression
- Life events (divorce, separation, death)
  - Social or economic stress
- Single women
- Low socioeconomic status
- African-American race
- Low level of educational achievement
- Maternal age (<18 or >40)
- Inadequate prenatal care
  - Fatigue
- Work standing
- Use of industrial machines
- Physical exertion
  - Inflammation
- Sexually transmitted infections
- Urinary tract infection
- Systemic infection
- Abdominal surgery during pregnancy
- Periodontal disease
  - Nutritional
- Poor nutrition and low body mass index
- Anemia (hemoglobin <10 g/dL)
  - Other/unexplained
- Substance abuse or smoking
- Maternal hypoxemia
- Anatomic factors
  - Cervical
- History of second trimester abortion
- History of cervical surgery
- Premature cervical dilatation or effacement
  - Uterine
- Uterine distention
- Multiple gestation
- Polyhydramnios
- Uterine anomaly
- Diethylstilbestrol
- Leiomyomata
  - Placental
- Placenta previa
- Placental abruption
- Vaginal bleeding
- Fetal factors
  - Congenital anomaly
  - Growth restriction

# CASE CONTINUES

- ▶ At 27 weeks of gestation, Ms. Primo presents to labor and delivery complaining of uterine contractions
- ▶ The patient reports that since she woke up in the morning she feels contractions that are very painful (8/10) and are occurring regularly every 5 to 10 minutes
- ▶ She denies leakage of fluid and reports that the baby is frequently moving; however, she does report that she noticed minimal vaginal spotting when she used the bathroom
- ▶ Her manual cervical examination is 1 cm dilated and 50% effaced with the fetal vertex at -2 station

# NEED TO KNOW

## Screening for Preterm Labor

### Fetal fibronectin

- ❑ Component of extracellular matrix between the chorion and decidua, is increased in cervicovaginal secretions of women who delivered early
- ❑ Clinical trials have demonstrated that the negative predictive value (if negative, the patient will not go into labor) was the most significant utility of the test.
- ❑ If a patient had a negative fetal fibronectin, she has a 99% chance that she will not deliver within 14 days
- ❑ If the test is positive, she has an increased chance of delivering early. The absolute risk depends on her a priori risk, but is <50% for most patients

# NEED TO KNOW

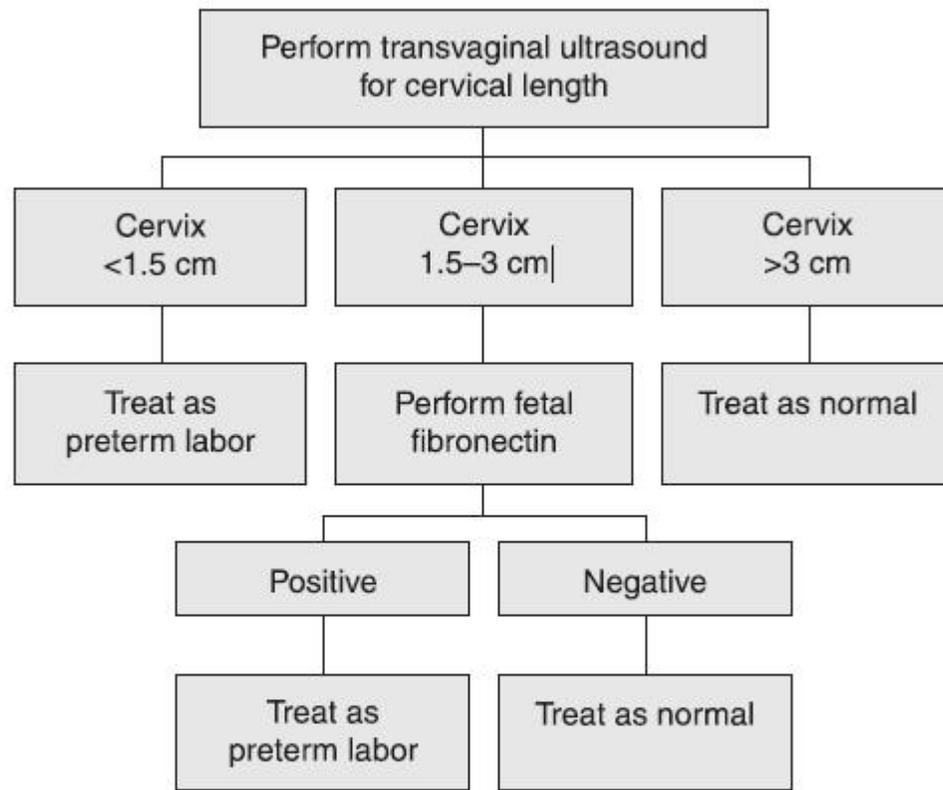
## Screening for Preterm Labor

### Vaginal ultrasound

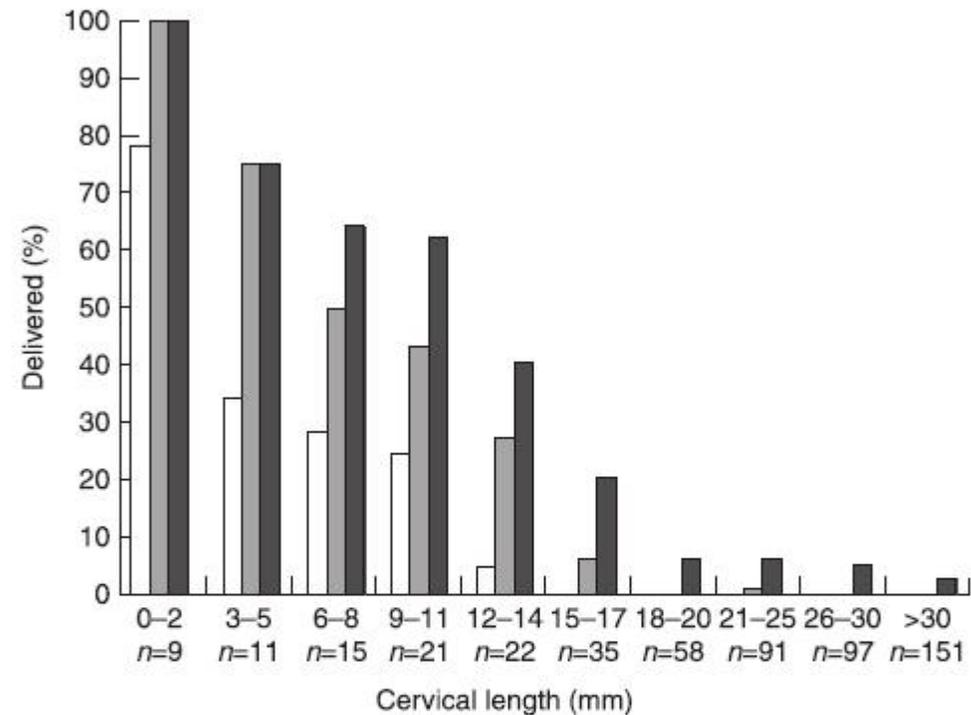
- ▶ Allows for a quantification of the cervical length
- ▶ Provides a view of entire cervical canal
- ▶ Visualization of funneling
- ▶ A short cervix <10th percentile for gestational age
- ▶ <2.5cm for the pregnancy less than 30 weeks
- ▶ The negative predictive value of this examination is similar to FFN
- ▶ Cervical length -asymptomatic women
- ▶ FFN- patients presenting with symptoms

# Ultrasound transvaginal examination of the cervix





**Figure 26.3** Triage of the symptomatic patient presenting in possible preterm labor. Initial triage is by the transvaginal ultrasound cervical length. For patients with intermediate cervical length values, fetal fibronectin is used to clarify risk status.



**Figure 26.4** Risk of delivery within 48 hours (open bars), within 7 days (gray bars) and before 35 weeks of gestation (black bars) based on cervical length at presentation among women presenting with threatened premature labor. (Adapted from Tsoi E, Fuchs IB, Rane S, et al. Sonographic measurement of cervical length in threatened preterm labor in singleton pregnancies with intact membranes. *Ultrasound Obstet Gynecol.* 2005;25:353-6.)

# Decision 2: Diagnosis

What criteria must be met to diagnose PTL?

- ▶ A. Positive fetal fibronectin
- ▶ B. Transvaginal cervical length <2.5 cm
- ▶ C. Cervical dilatation of 1 cm
- ▶ D. Regular uterine contractions and evidence of cervical change

- 
- ▶ A positive fetal fibronectin and a cervical length  $<2.5$  cm increase the risk that the patient will have PTL and delivery, but they are not diagnostic criteria for actual PTL
  - ▶ A cervical dilatation of 1 cm may be normal in this multi-gravid patient although it may also be due to PTL

#### ACOG

- ❑ Regular uterine contractions associated with cervical change or
- ❑ A cervix that is dilated on presentation

# CASE CONTINUES

- ▶ Ms. Primo has a cervical length of 1 cm and a positive fetal fibronectin
- ▶ After 2 hours of observation she is contracting every 5 minutes
- ▶ Cervical examination is 2 cm dilated
- ▶ 80% effaced
- ▶ fetal vertex at -2 station.

# Decision 3: Treatment

How should the patient be managed at this time?

- ▶ A. Continued observation
- ▶ B. Cervical cerclage
- ▶ C. Magnesium sulfate tocolysis
- ▶ D. Betamethasone intramuscular (IM) only

- 
- ▶ (Answer A) Continued observation would be inappropriate given the presumed PTL
  - ▶ (Answer B) Cervical cerclage is not appropriate in a patient with contractions
  - ▣ (Answer D) Betamethasone is administered to induce pulmonary maturity in a patient expected to deliver
  - ▣ Betamethasone is not expected to reduce uterine contractions
  - ▣ The effect of steroids wanes after 1 week
  - ▣ Multiple doses are associated with decreased fetal size

# NEED TO KNOW

## Treatment of Preterm Labor

- ▶ Once PTL is diagnosed, treatment is initiated
- ▶ Preventing newborn complications secondary to early delivery
- ▣ First tocolytics are used to try to stop or slow down the progress of labor in an attempt to administer corticosteroids and allow possible transfer to a center with experienced neonatal intensive care unit (NICU).
- ▣ Corticosteroids are administered to accelerate the maturation of the fetus, anticipating an early delivery
- ▣ Antibiotics are used as prophylaxis against possible fetal/neonatal group B streptococcus infection

# NEED TO KONW

- ▶ Most tocolytics have significant adverse side effect while evidence showing effectiveness is limited
- ▶ < 48 hours
- ▶ 40% to 60% of patients with PTL responded to placebo
- ▶ Do not recommend the use  $\geq 34$  weeks
- ▶ Contraindication-infection/fetal demise
- ▶ Four commonly used tocolytics
- ▶ magnesium sulfate, indomethacin, nifedipine, and terbutaline.

# Magnesium Sulfate

- ▶ Magnesium sulfate is the most commonly used tocolytic in the United States
- ▶ Not better than other commonly used tocolytics
- ▶ Easy administration with intravenous drip and its familiarity on the delivery floor
- ▶ Inhibiting voltage-dependent calcium channels, thus reducing calcium-dependent myometrial contraction

# Magnesium Sulfate

Maternal side effect	Magnesium toxicity
nausea	loss of deep tendon reflexes
dry mouth	mental status changes
maternal flushing	respiratory depression
drowsiness	pulmonary edema
blurred vision	severe hypotension
headache	ultimately cardiac arrhythmias
	cardiac arrest

# Magnesium Sulfate

- ▶ Newborn
- ▶ Depressed (both motor and respiratory) of the newborn.
- ▶ Reduced in cerebral palsy when the infant had been exposed to magnesium in utero

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# Indomethacin

- ▶ nonselective cyclooxygenase (COX)-2 inhibitor, works by inhibiting prostaglandin synthesis at the level of the decidua
- ▶ PTL is often inflammatory and ultimately involves prostaglandin synthesis
- ▶ Contraindications
  - ❑ allergy to aspirin or other nonsteroidal anti-inflammatory medications
  - ❑ maternal coronary artery disease
  - ❑ renal failure
  - ❑ fetal cardiac lesions
  - ❑ Oligohydramnios
  - ❑ gestational age >32 weeks.

# Indomethacin

Maternal toxicity	fetal side effects
allergic reactions	constriction or premature closure of the ductus arteriosus >32weeks
stomach upset	oligohydramnios
gastrointestinal bleeding	of intraventricular hemorrhage.

The most common indomethacin dosage is a 100 mg loading dose followed by 50 mg four times daily for up to 48 hours

# Nifedipine

- ▶ calcium channel blocker
- ▶ Relax smooth muscle by decreasing calcium influx into the cell
- ▶ 10 mg PO every 20 minutes for a total of three doses, followed by 10 to 20 mg every 4 to 6 hours

Maternal side effects	fetal side effect
headache	unknow
nausea	fetal acidosis and hypoxemia in some animal studies
flushing	
hypotension	
tachycardia	
hepatotoxicity	

# Terbutaline

- ▶ Subcutaneous terbutaline (0.25 mg) is used in some centers to quiet uterine contractions in a patient who is not thought to be in PTL, or who has excess uterine activity.
- ▶ Repeated doses may be administered, though it is not utilized for long-term tocolysis
- ▶ As a betamimetic, intravenous terbutaline therapy was associated with a high risk of maternal tachycardia, hypotension, hypokalemia, hyperglycemia, and pulmonary edema. Accordingly,
- ▶ intravenous terbutaline is rarely used for tocolysis.

# Corticosteroids

- ▶ Reduce the risk of neonatal respiratory distress syndrome and intraventricular hemorrhage by approximately 50%.
- ▶ Not recommended after a gestational age of 34 weeks
- ▶ Two IM doses of 12 mg betamethasone 24 hours
- ▶ Four IM 6 mg dexamethasone doses 12 hours

# Antibiotics

- ▶ Prevent group B beta-streptococcus (GBS) infection in the neonate
- ▶ All patients in PTL are considered at high risk for neonatal GBS and thus should receive prophylactic antibiotic
- ▶ The recommended treatment is penicillin is 5 million units loading dose followed by 2.5 million units every 4 hours
- ▶ Penicillin allergic patients should get a culture and sensitivity of the GBS if possible

# CASE CONCLUSION

- ▶ You administer nifedipine for tocolysis. After an additional 2 hours, the patient continues to have contractions every 10 to 15 minutes, and you administer the first dose of betamethasone for fetal lung maturity
- ▶ Uterine contractions eventually abate, and Ms. Primo is transferred to the ward with the cervix 2 to 3 cm dilated and 80% effaced after completion of her steroid course
- ▶ On the fifth hospital day, she experiences pPROM
- ▶ She is returned to labor and delivery, where she is found to be in active labor. Two hours later she delivers a viable female infant weighing 1,076 g with the NICU team in attendance.
- ▶ She does well after the delivery and is discharged on postpartum day two

# Objectives

- ▶ Identify risk factors for preterm labor
- ▶ Know the initial evaluation and work up of preterm labor
- ▶ Understand appropriate management

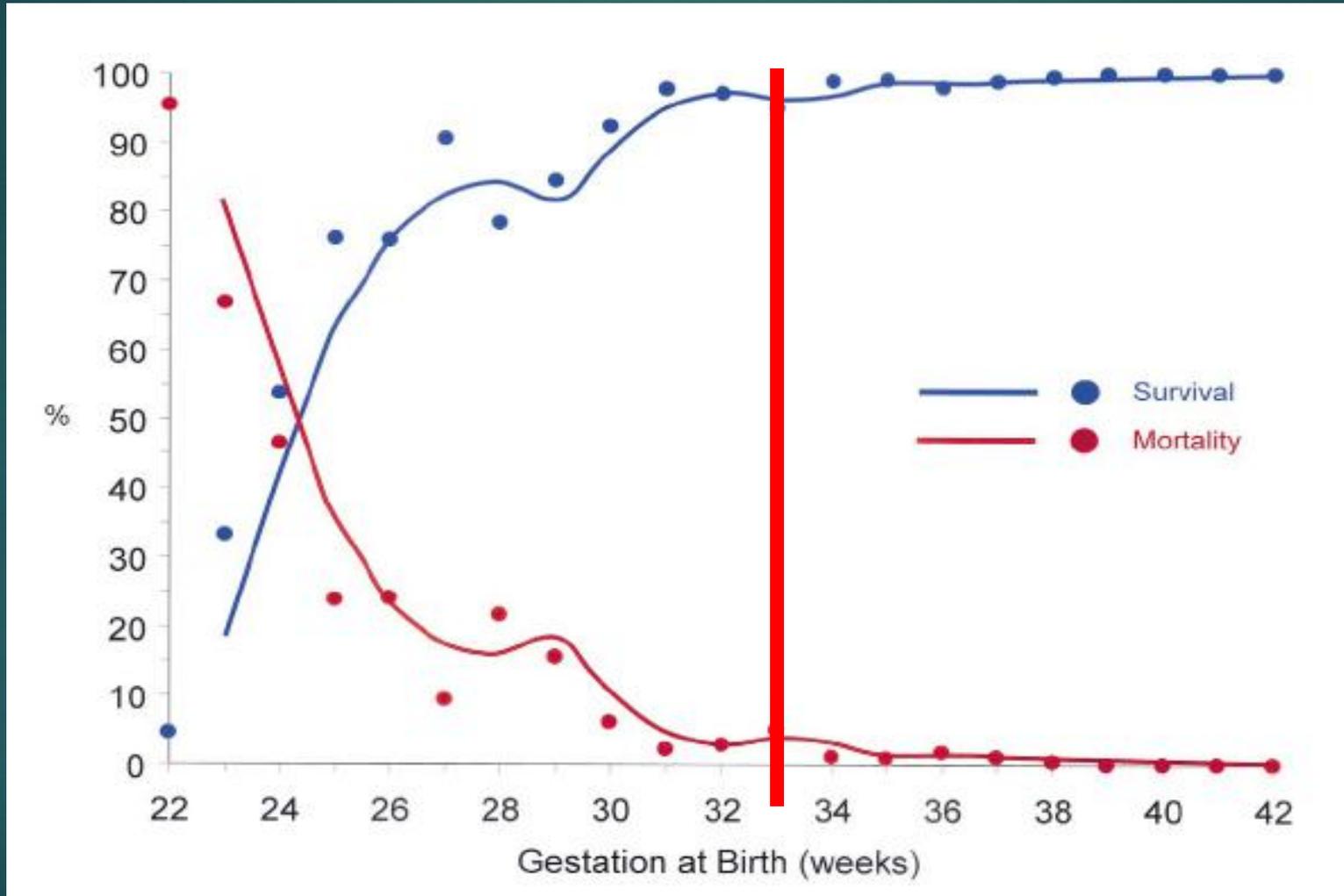
# Definition

- Frequent uterine contractions with or without cervical dilatation or effacement occurring after 20 weeks' but before 37 weeks'
  - Uterine contractions and documented cervical change
  - cervical dilatation >1cm
  - >80% effacement

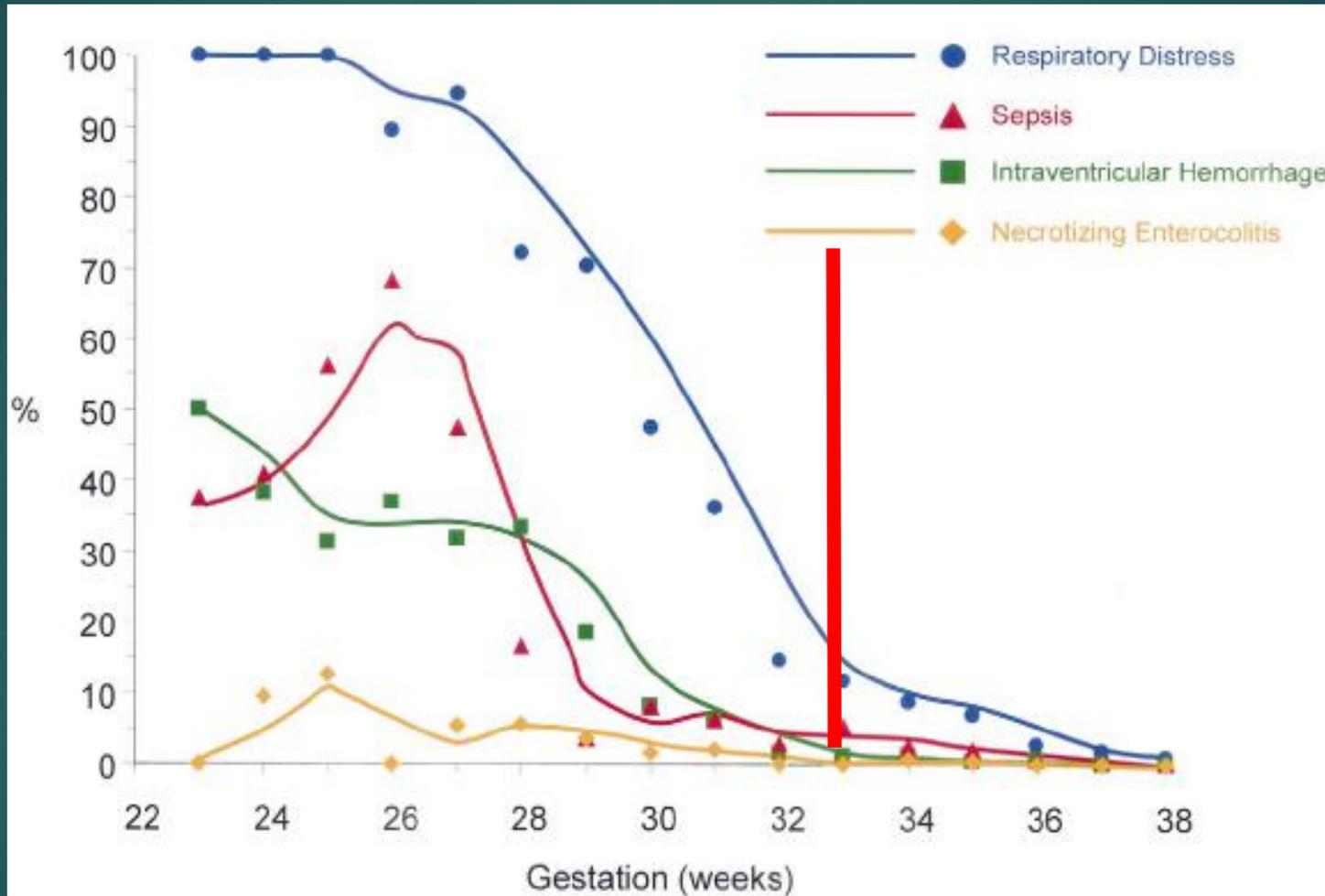
# Incidence

- PTL is the leading cause of perinatal morbidity and mortality in US
- 5%~15%
- 1/8 births in US (12%) are preterm
  - Multiple pregnancies
  - Particular higher order pregnancies
  - Use of fertility drugs
  - ART

# Survival by gestational age among live-born resuscitated infants



# Acute morbidity by gestational age among surviving infants



Results of a community-based evaluation of 8523 deliveries, 1997–1998, Shelby County, Tennessee

Mercer BM Obstet Gynecol 2003;101:178 –93.

# Survival in Premature Infants



- 26 wks – 80%
- 27 wks – 90%
- 28-31 wks – 90 to 95%
- 32-33 wks – 95%
- 34-36 wks – approaches term survival rates

# Risk factors for preterm birth

- Epidemiological Factors

- Maternal age
- Smoking
- Low socioeconomic status
- Nutrition and BMI

- Psychosocial Factors

- Stress
- Depression
- Occupational hazards

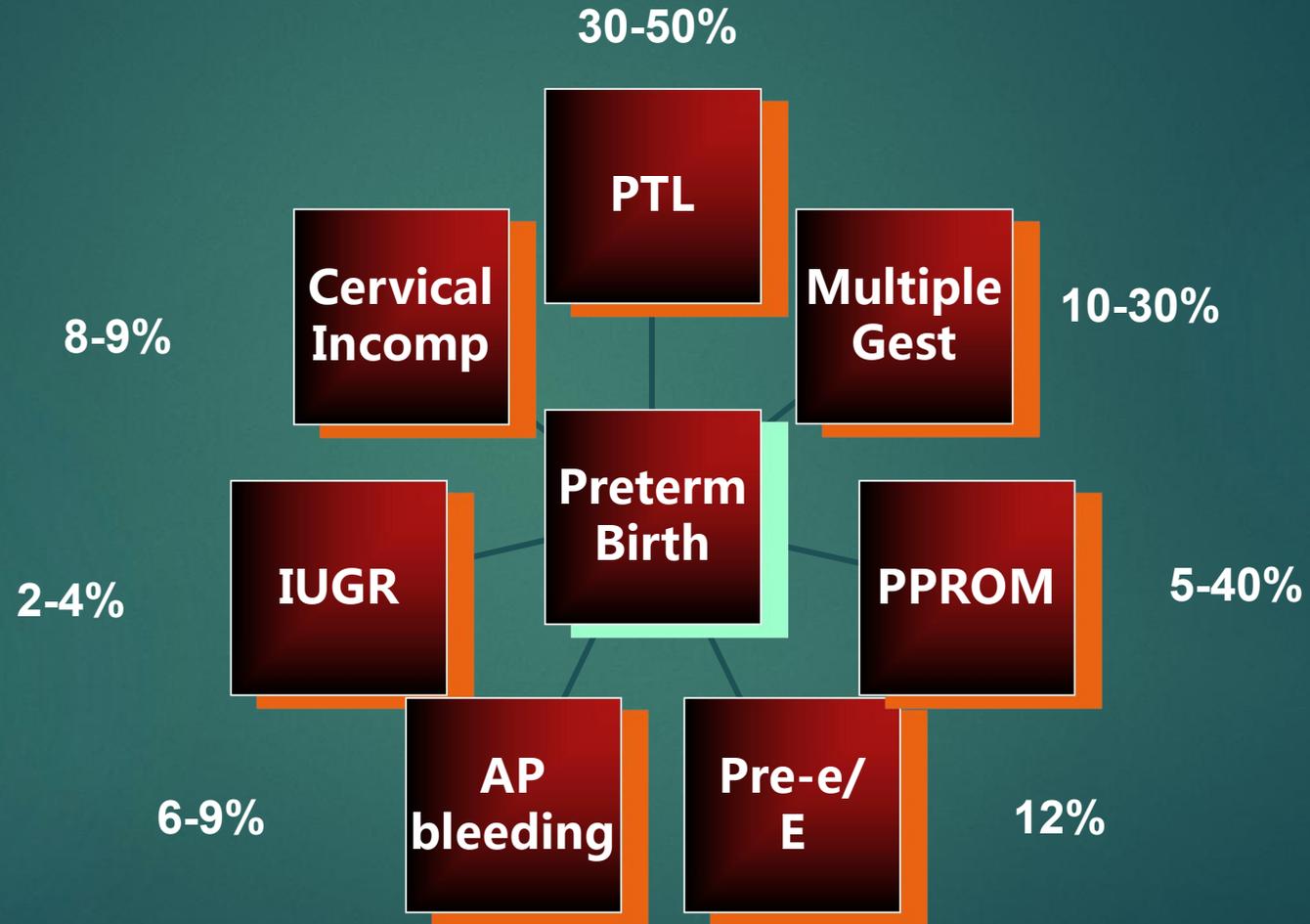
- Obstetrical Factors

- History
- Complications

# Risk factors for preterm birth

- ▶ Fetal factors
  - ▶ Congenital anomaly
  - ▶ Growth restriction
- ▶ Placental factors
  - ▶ Placenta previa
  - ▶ Placenta abruption
- ▶ Iatrogenic
- Idiopathic

# Causes for preterm birth





# Pathogenesis

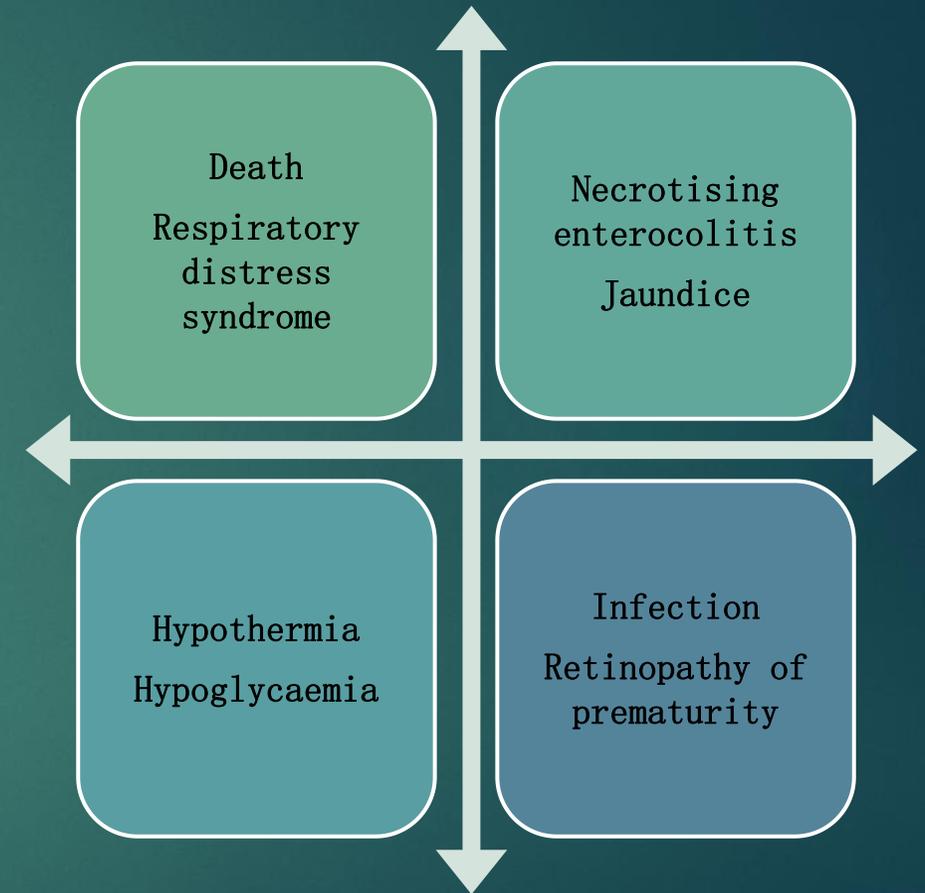
- Obstetric
- Medical
- Anatomic
- 50% of PTL is idiopathic

Progesterone withdrawal--- Initiation

Intra-amniotic inflammatory--- Trigger contraction

## Major Risks of Preterm Delivery

**PRETERM LABOR →  
Most mortality and  
morbidity is  
experienced by babies  
born before 34 weeks**



# Preterm Birth

How do we identify who is at Risk?

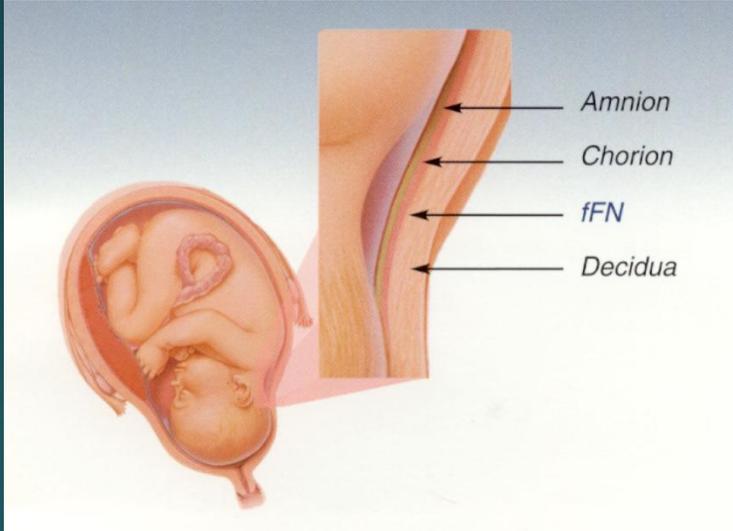
Risk  
Factors

Fetal  
Fibronectin

Cervical  
Length

Symptoms  
of PTL

# Fetal Fibronectin (fFN)



- Glycoprotein found in extracellular matrix of amniotic membranes
- Binds chorion to decidua
- Normally found in cervico-vaginal secretions until 22 weeks gestation and again near the time of labour
- Presence of  $>50$  ng/mL considered positive

# Biologic markers for predicting preterm birth

- ▶ Fetal fibronectin- need intact membranes, less than 3 cm dilated, not useful before 20 weeks or after 34 weeks 6 days
- ▶ Negative fetal fibronectin gives about a 95% chance of the pregnancy continuing 14 days or more. A positive test is not as predictive.

# Cervical Length Assessment

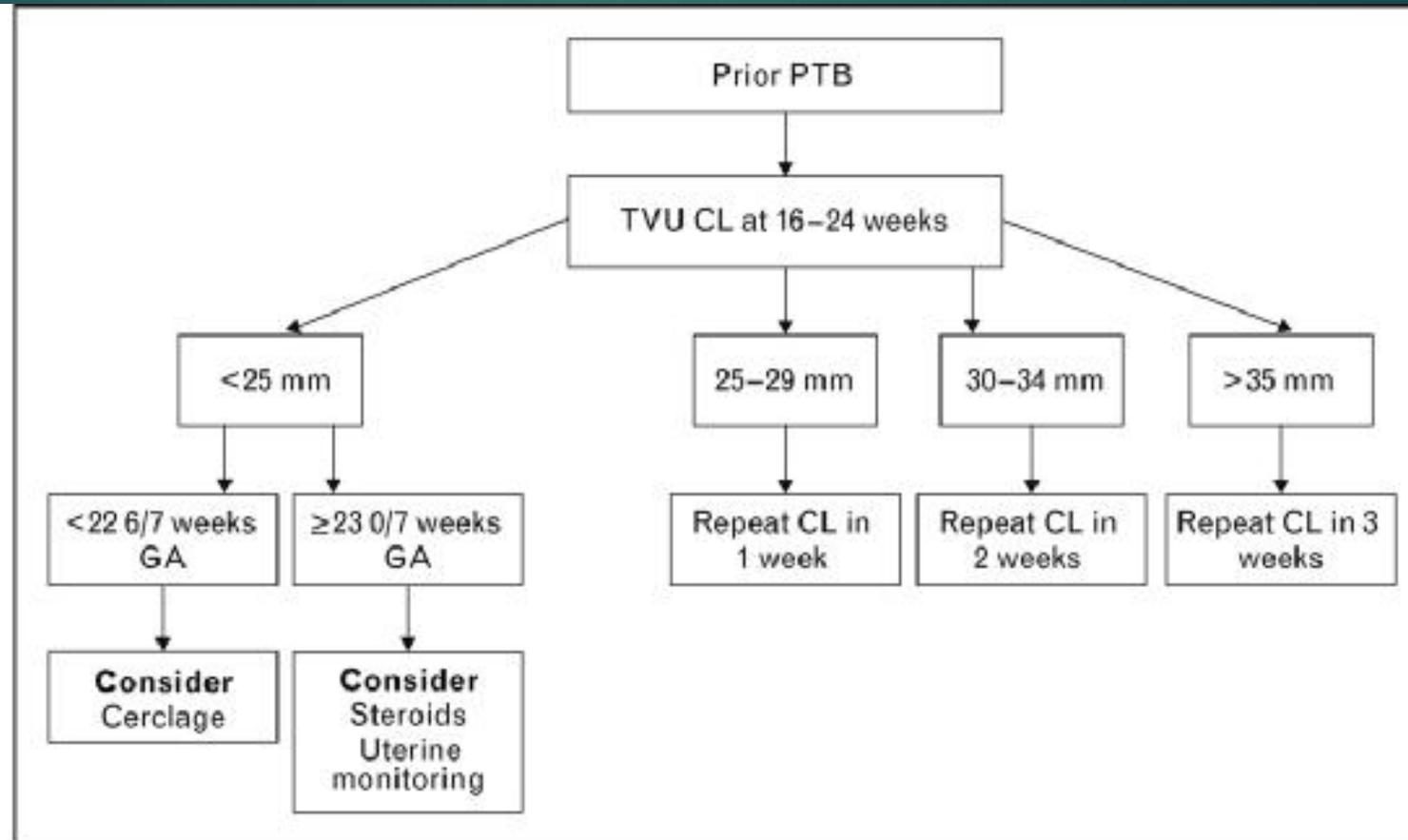


## Method

- Digital <2.5cm
- TAU
- TVU
- Funneling Internal os 5mm

- 
- True cervical length: 30-50 mm at 14-30 wks
  - Cannot measure CL before 14 weeks
  - Most studies use a length <25-35mm as abnormal

# Timing of TVU cervical length screening prior preterm birth



GA, gestational age.

## Summarize of predicting preterm birth

- Use history, cervical length less than 2.5 cm (some authors 3.0 cm)
- Fetal fibronectin positive
- Cervix 80% effaced
- dilation above 2cm
- 1 cm change in cervical dilation

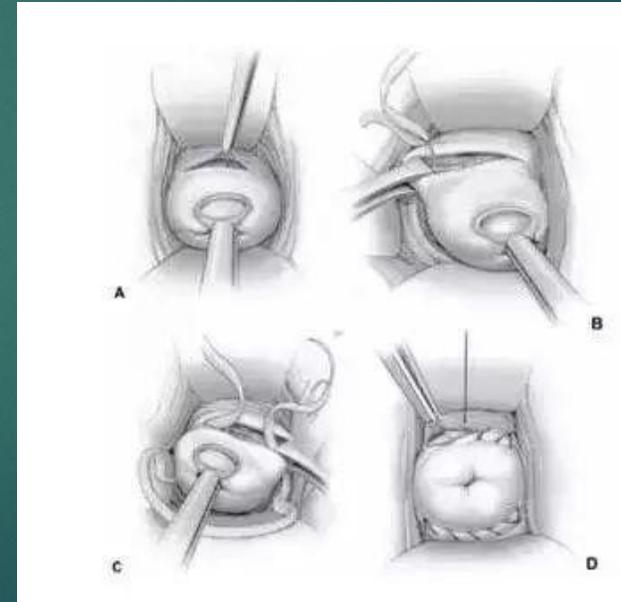
# Complications of Prematurity

- RDS
- IVH
- Feeding difficulties
- Apnea
- Infection
- Jaundice
- Hypothermia
- Neurobehavioral
- Anemia



# Prevention

- Antenatal care
- Cervical circlage
- Bed rest
- Hydration
- Antibiotics
- Preogesterone



# Diagnosis and Evaluation

- Baseline History
- Symptoms and signs
- Evaluation
- Laboratory

# History

- Pregnancy complications
- Gestational age
- Infection
- Hydration status
- Risk factors

# Symptoms of preterm labor

- None
- Contractions (painless or painful)
- Dilatation and effacement of cervix
- Vaginal bleeding

# Clinical Findings

## *Symptoms and Signs*

### Uterine Contractions

Two 30-second contractions within 10 minutes over a 30 minute observation period

# Clinical Findings

## *Symptoms and Signs*

### Dilatation and Effacement of Cervix

Cervical dilation or effacement that is progressive over a 30 to 60 minute interval or a cervix that is well effaced and dilated (at least 2 cm) on admission is considered diagnostic

# Clinical Findings

## *Symptoms and Signs*

### Vaginal Bleeding

- Many patients present with bloody mucous vaginal discharge or bloody show
- More significant vaginal bleeding should be evaluated for placenta abruption or placenta previa

# Evaluation

## Gestational Age

Gestational age must be between 20 and 37 weeks' estimated gestational age (EGA)

- LMP
- Date of conception
- Previous sonographic

# Evaluation

Fetal Weight: Care must be taken to determine fetal size by ultrasonography

Presenting Part: The presenting part must be noted because abnormal presentation is more common in earlier stages of gestation

Fetal Monitoring: Continuous fetal monitoring should be performed to ascertain fetal well-being.

# Laboratory Studies

- Complete blood count with differential.
- Urine obtained by catheter for urinalysis
- Cervical culture for Group B streptococcus
- fFN assay
- Amniocentesis

# Management

- First determine if it is truly labor
- Monitor contraction and assess cervical change
- If fetal fibronectin is negative no treatment needed, unless the cervix is less than 2.5cm
- Once a patient contracts regularly consider bed rest

# Some cases in which preterm labor should not be suppressed

## Maternal factors

- Severe hypertensive disease
- Pulmonary or cardiac disease
- Advanced cervical dilation(>4cm)
- Maternal hemorrhage

## Fetal factors

- Fetal death or lethal anomaly
- Fetal distress
- Intrauterine infection
- Estimated fetal weight>2500g
- Severe intrauterine growth retardation

# Management

- Treat infections
- Treat asymptomatic bacturia
- Decrease activity
- Decrease or eliminate smoking or drugs
- Because of unknown group B strep status give penicillin until cultures are back

# Newer tocolytics

- Atosiban: Oxytocin antagonist
- NO donors
- Progesterone

# Prognosis

- Weighing 2000-2500 g usually have survival rates of more than 97%;
- Weighing 1500-2000 g, more than 90%;
- Weighing 1000-1500 g, 65%-80%;
- Mortality and morbidity rates are much higher in smaller fetuses.



# Summary for PTL

- Does the patient have PTL?
  - Cervical exam
  - Document advanced dilation or change
  - Toco monitor
- Is the patient a candidate for tocolysis?
  - <34 weeks
  - Viable
  - No contraindications

# Summary for PTL

- ▶ What method should be used?
  - ▶ Use magnesium if not contraindicated
    - ▶ Best tolerated
    - ▶ Easiest dosing to control
  - ▶ Retodrine generally considered second line, then Indomethacin
- ▶ What else should be given?
  - ▶ Steroids (ALWAYS)
  - ▶ Antibiotics