Preterm labor

Osama M Warda MD

Professor of OBS/GYN – Mansoura University

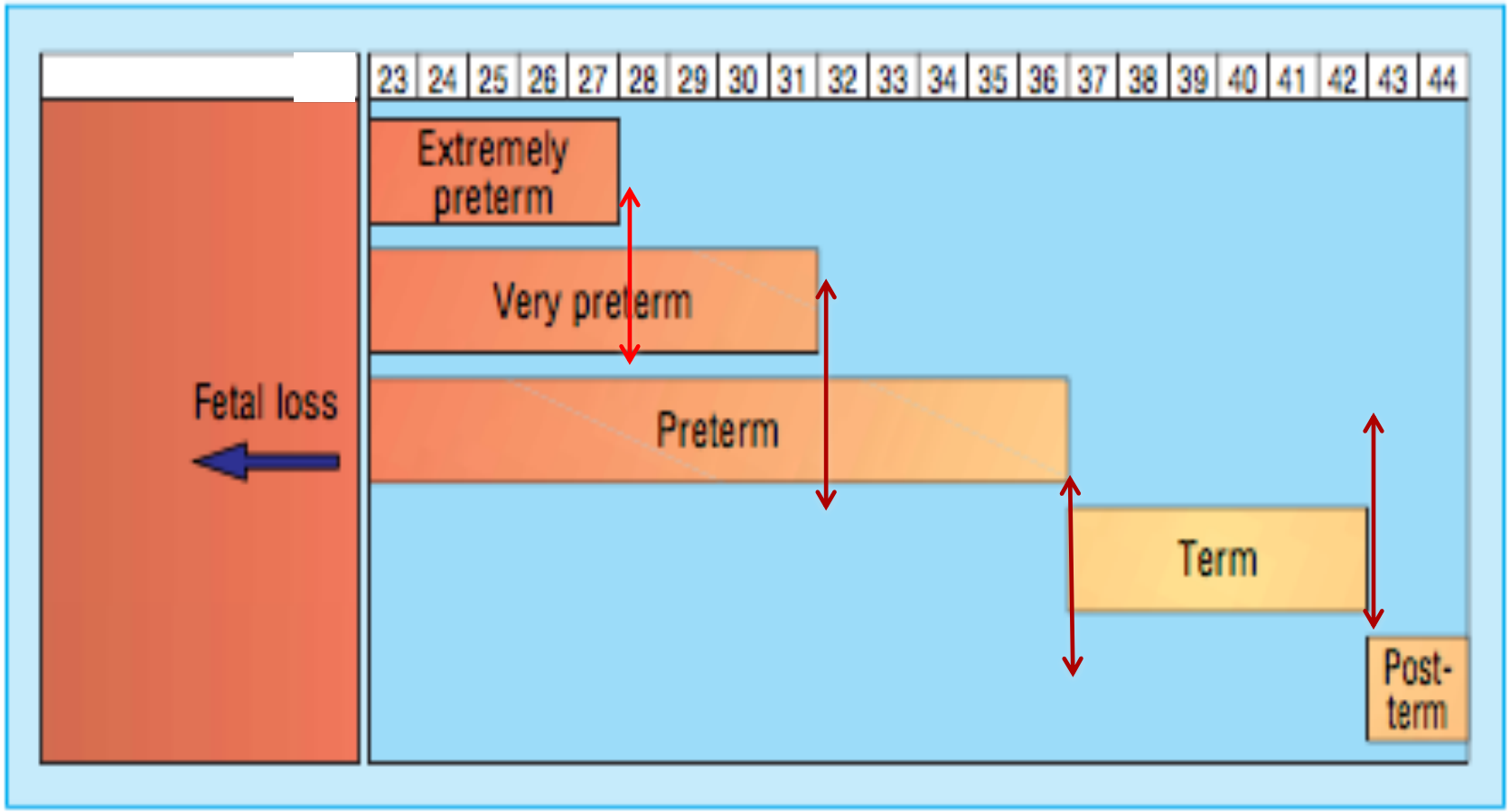
- Definitions
- Epidemiology/incidence
- Complications; neonatal-maternal
- Causes/ risk factors
- Prediction
- Prevention
- Treatment

Contents

- **Preterm** is defined as babies born alive before 37 weeks of pregnancy are completed. There are sub-categories of preterm birth, based on gestational age:

- extremely preterm (<28 weeks)
- very preterm (28 to <32 weeks)
- moderate to late preterm (32 to <37 weeks).
- Induction or caesarean birth should not be planned before 39 completed weeks unless medically indicated.

Definition WHO 2015



Definitions of preterm live births by completed weeks of gestation

Gestational age versus birth weight

Even in developed countries, there is often uncertainty and incomplete recording of estimates of gestation. **The categories for birth weight are:**

- **Low birth weight (< 2500 g)**
- **Very low birth weight (< 1500 g)**
- **Extremely low birth weight (< 1000 g)**

Only around **two thirds** of low birth weight infants are preterm. Term infants may be of low birth weight because they are "***small for gestational age" or "light for date" infants.***

Definition

- Every year, an estimated 15 million babies are born preterm (before 37 completed weeks of gestation), and this number is rising.
- Preterm birth complications are the leading cause of death among children under 5 years of age, responsible for nearly 1 million deaths in 2013.
- Three-quarters of them could be saved with current, cost-effective interventions.
- Across 184 countries, the rate of preterm birth ranges from 5% to 18% of babies born.

Epidemiology (Fact sheet N°363/WHO)

Extremely preterm infant born at 26 weeks' gestation

Preterm infant born at 35 weeks' gestation

- **Total incidence = 5-10%of all pregnancies**

-There is rise in incidence of preterm birth in past 20 years, however , delivery of babies <32 weeks remain constant 1-2%

-Several factors have contributed to the overall rise in the incidence of preterm birth. These factors include *increasing rates of multiple births*, *greater use of assisted reproduction techniques*, and *more obstetric intervention*.

INCIDENCE

Most of mortality and morbidity are experienced by babies born before34 weeks gestation

Major neonatal risks include:

1- Neonatal Death
2- RDS
3- Hypothermia
4- Hypoglycaemia
5- Necrotizing entero-colitis
6- Jaundice
7- Infection
8- Retinopathy of prematurity

Complications of preterm birth

In intensive care preterm infants undergo mechanical ventilation

Outcomes for infants live born before 26 weeks' gestation in British Isles*

Gestation (weeks)	Survival to discharge (%)	Survival without handicap at 30 months (%)
22	1	0.7
23	11	5
24	26	12
25	44	23

*Adapted from Wood NS et al. *New Engl J Med* 2000;343:378-84

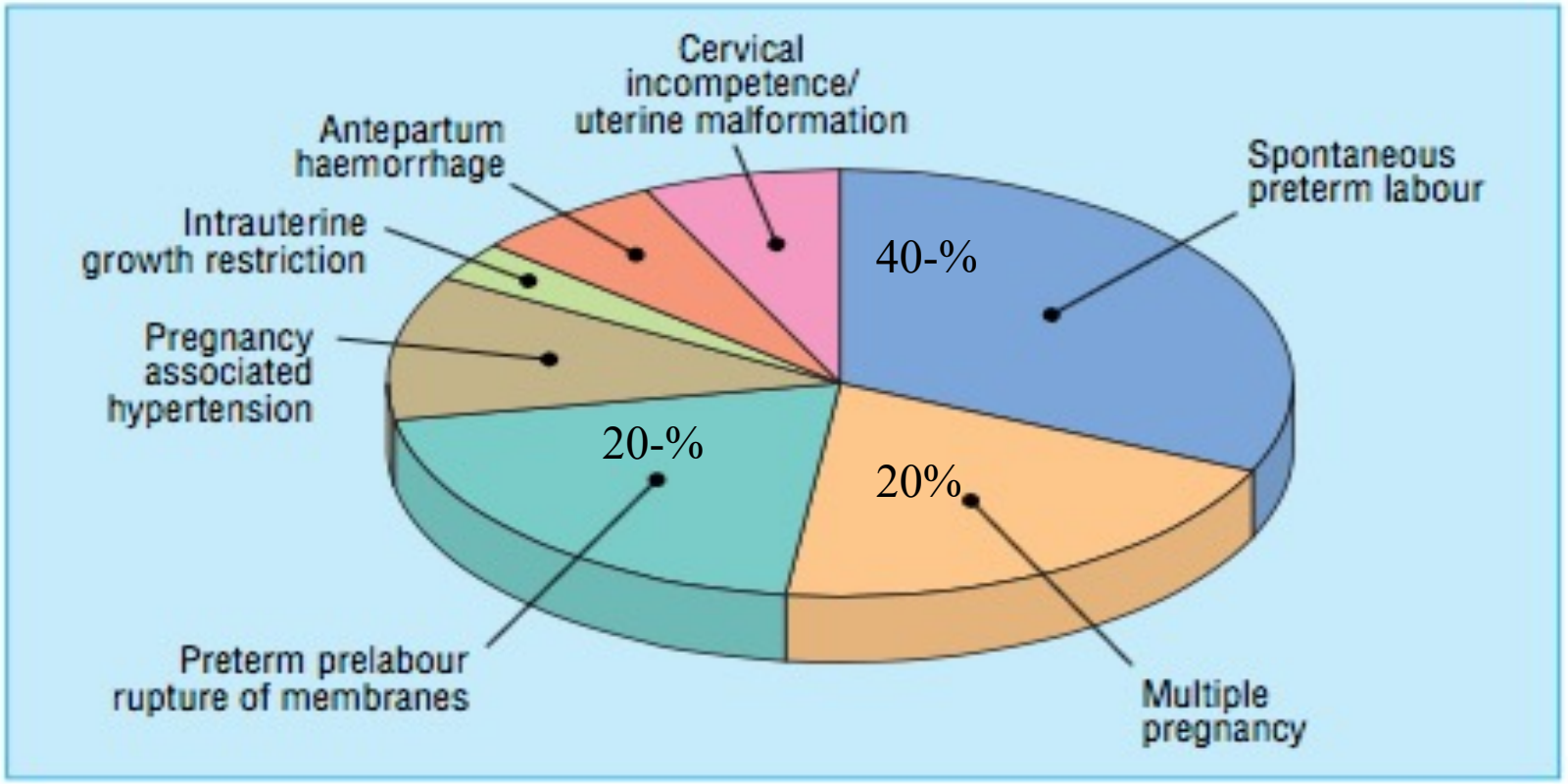
Complications PTB

1. Multiple pregnancy: risk >50%
2. Previous preterm delivery: risk 20- 40%
3. Cigarette smoking: risk 20-30%
4. Cervical incompetence
5. Uterine abnormalities
6. infection (bacterial vaginosis); 2 fold increase

Risk factors (causes)

7. Young age of mother - less than 16 years
8. Lower socioeconomic status.
9. Reduced body mass index (BMI<19kg/m^2)
10. Antiphosphlipid syndrome.
11. Obstetric complications, including PIH, Antepartum hemorrhage, polyhydramnios, fetal abnormalities.

Risk factors (causes), cont.,



Causes of preterm birth

Causes of preterm birth

1. Assessment of risk factors (history)
2. Vaginal examination to assess the cervical status
3. Ultrasound visualization of cervical length and dilatation
4. Detection of fetal fibronectin in cervico-vaginal secretions

Prediction of preterm labor

1-Assessment of risk factors

Risk factors for spontaneous preterm birth

History:

- Obstetric-gynecological history: prior spontaneous PTB (sPTB of twins is a minor risk factor for PTB when the next pregnancy is a singleton pregnancy); prior STL; prior ≥ 2 D&Es; prior cone biopsy; uterine anomalies; DES exposure; myomata; extremes of interpregnancy interval; ART
- Maternal lifestyle (smoking, drug abuse, STIs, etc.)
- Maternal pre-pregnancy weight <120 lb (<50 kg) or low BMI; poor nutritional status
- Maternal age (<19 years old; >35 years old)
- Race (especially Afro-American)
- Education (<12 grades)
- Certain medical conditions (e.g. DM, HTN)
- Low socioeconomic status
- Limited prenatal care
- Family history of spontaneous PTB (poorly studied)
- Vaginal bleeding (especially during second trimester)
- Stress (mostly related to above risks)

Identifiable by screening:

- Anemia
- Periodontal disease
- TVU CL <25 mm (especially <30 weeks)
- fFN positive (>50 ng/mL)

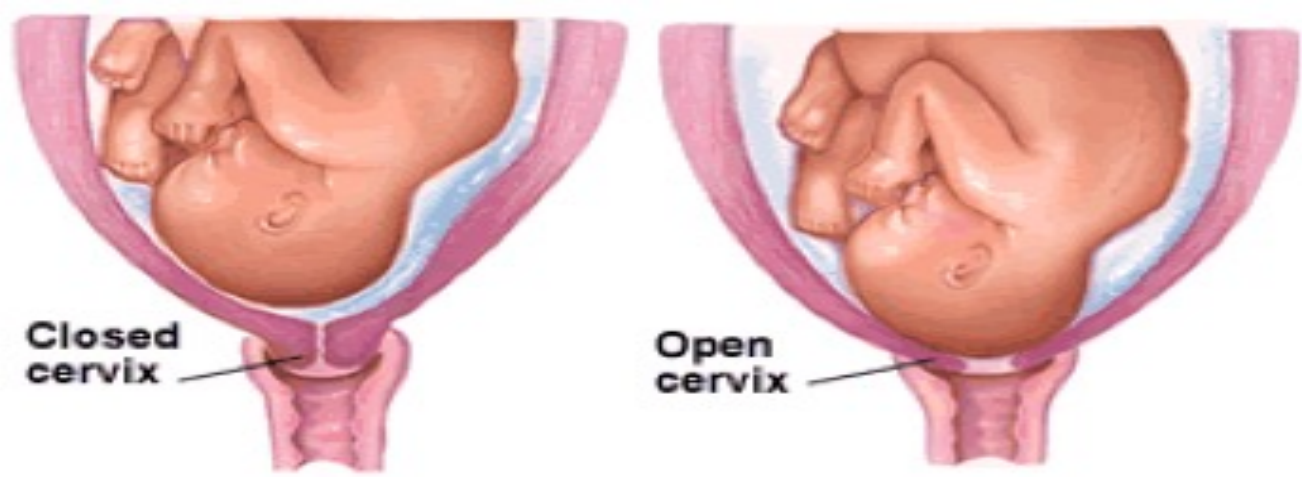
Usually symptomatic:

- Uterine contractions

Not spontaneous (indicated/iatrogenic):

- Fetal demise/major anomaly/compromise/ polyhydramnios
- Placenta previa
- Placental abruption
- Major maternal disease (HTN complications, DM, etc.)

- Digital examination is the traditional method used to detect cervical maturation, but quantifying these changes is often difficult.



2- Vaginal examination

- ***Vaginal ultrasonography allows a more objective approach to examination of the cervix.***

Cervical Length	RR of PTD
<35mm	2.35
<30mm	3.79
<26mm	6.19
<22mm	9.49
<13mm	13.99

3- TVS cervicometry

Cervicovaginal fetal fibronectin test

Fibronectin is:

- Glycoprotein in amniotic fluid or placental tissue
- Released because of damage to membrane of placenta
- Measured from cervical or vaginal swabs

-If -ve FFN → Negative predictive value of 99% (good –ve)

-If +ve FFN → Positive predictive value of 13-30%

- 99.5% of symptomatic women with **negative FFN** are undelivered at *7 days*

- 99.2% of symptomatic women with **negative FFN** are undelivered at *14 days*

4- FETAL FIBRONECTIN TESTING

- Primary prevention for PTB aimed at the general population has been insufficiently studied. It includes family planning, avoidance of lifestyle risks, and proper nutrition.
- Management for prevention of PTB is therefore mostly based on *identification and treatment of risk factors* (secondary prevention) or *treatment of symptomatic women with preterm labor (PTL) or premature preterm rupture of membranes (PPROM)* (tertiary prevention).

Vincenzo Berghella (2007)

Prevention of preterm labor 20

Secondary prevention of PTB has been effective in the following groups for the following interventions:

- ***In women who smoke, smoking cessation counseling/ support programs.***
- ***In women with ≥ 1 prior spontaneous PTBs, now carrying a singleton gestation, for the following interventions:***
  - **17α-hydroxyprogesterone caproate 250 mg IM every week starting at 16–20 weeks until 36 weeks**
  - **Cerclage if the cervical length is < 25 mm between 14 and 23 6/7 weeks**
  - **Omega-3 fatty acids.**
- ***In women with ≥3 prior PTBs or second trimester losses, history-indicated cerclage.***
- **In women with asymptomatic bacteriuria of > 100 000 bacteria/ml, appropriate antibiotics.**
- In women with **asymptomatic group B streptococcus (GBS) bacteriuria of any colony count, appropriate antibiotics (usually penicillin).**

PREVENTION OF PTB

Supplemental progesterone:

- Progesterone im injection (100 mg amp)
- 17 hydroxy progesterone im depot form
- Vaginal progesterone pessaries & creams
- Oral micronized progesterone or dydrogesterone

- Start 2nd trimester, continue until 36 weeks if prior delivery before 34 wks

- 17OHP use in high risk women reduced PTB by 15-70%

Prevention of preterm labor 22

3 criteria to document PTL(20-37w):

1-Regular uterine contractions occur at 4/20 min. or 8/60 min. Plus:

progressive change in the cervix.

2- Cervical dilatation > 1 cm
3- Cervical Effacement ±80%.

Diagnosis of preterm labor

- **Women with PTL but negative fetal fibronectin (fFN) and transvaginal ultrasound (TVU) cervical length (CL) ≥ 30 mm have a ≤ 2% chance of delivering within 1 week, and a > 95% chance of delivering ≥ 35weeks without therapy and should therefore not receive any treatment.**

Diagnosis of preterm labor; cont,

- **Tocolysis** – *inhibit myometrial contractility*
  1. **Magnesium salt**
  2. **Terbutaline (beta agonist)**
  3. **Indomethacine (PG synthetase inhibitor)**
  4. **Nifedipine (calcium channel blocker)**
  5. **Atosiban (oxytocin receptor inhibitor)**

- ***Contraindications to tocolysis*:**
  - ***IUFD, lethal fetal anomalies, NRFHT***
  - ***Severe IUGR, chorioamnionitis, antepartum hage.***
  - ***Severe pre-/eclampsia***

Treatment of preterm labor

	MgSO4	Terbutaline	Indocin	Nifedipine
Class		B -agonist	Cox inhibitors	CCB
Action	Competes for Ca	↑ cAMP ↓ intracellular Ca	↓ PGD production	Block Ca influx
Side Effect	Pulm edema, ? ↑ ped M&M	Tachy, ↓ BP, palp, ↓ K, pulm edema	N/V, gastritis, narrowing of DA, oligo	↓ BP, reflex tachy, ? ↓ of blood flow
Efficacy	Not very good!	No ↓ of PTB @ 7 days, sx relief	Appears to be more effective than placebo	↓ # of women giving birth at 7 days

- *Tocolytics should **not** be used without concomitant use of corticosteroids for fetal lung maturity.*
- ***No tocolytic** has been shown to improve perinatal mortality.*
- There is no tocolytic agent that is most safe and efficacious.

TOCOLYSIS ...(EBM)

- **Cyclo-oxygenase (COX) inhibitors** are the only class of primary tocolytics shown to **decrease PTB < 37 weeks** compared with placebo.
- **COX inhibitors, beta- mimetics, and oxytocin receptor antagonists** (ORA) have been shown to significantly **prolong pregnancy at 48 hours and 7 days** compared with placebo.
- COX inhibitors, **calcium channel blockers (CCB), and oxytocin receptor agonists (ORAs)** have significantly **less side effects than β-mimetics.**

TOCOLYSIS…(EBM)

- There is **no maintenance tocolytic that prevents PTB or perinatal morbidity/mortality**.
- There is insufficient evidence to evaluate multiple tocolytic agents for primary tocolysis, refractory (primary agent is failing, so another is started) tocolysis, or repeated (after successful primary tocolysis) tocolysis.

TOCOLYSIS…[EBM]

- ***Tocolytic drugs should be used in:***

1-women with suspected preterm labor with otherwise uncomplicated pregnancy. [B]

2- women with preterm labor needing transfer to hospital that provide neonatal intensive care, or those who have no yet completed a full course of corticosteroids [✓]

Tocolysis (EBM)

- ***Effectiveness of tocolytic drugs:***

- **Nifedipine and atosiban have comparable effectiveness in delaying birth for up to 7 days.[A]**
- **Compared with beta- agonists, nifedipine is associated with improvement in neonatal outcome, although there are no long-term data. [A]**

- ***Adverse effects of tocolytic drugs :***
- **Beta-agonists have a high ferquency of adverse effects. Nifedipine, atosiban and COX inhibitors have fewer types of adverse effects. [A]**
- **Using multiple tocolytic drugs appears to be associated with a higher risk of adverse effects and so should be avoided . [B]**

Recommended doses regimen for nifedipine & atosiban:

- **Nifedipine; initial oral dose of 20mg followed by 10-20mg (three or four times daily), adjusted according to uterine activity for up to 48 hours. A total dose > 60mg is associated with 3-4 fold increase in adverse effects. [✓]**

- **Atosiban; an initial bolus dose of 6.75mg over 1 minute, followed by infusion of 18mg/hour for 3 hours , then 6mg/hour for up to 45 hours (to maximum of 330 mg) [✓]**

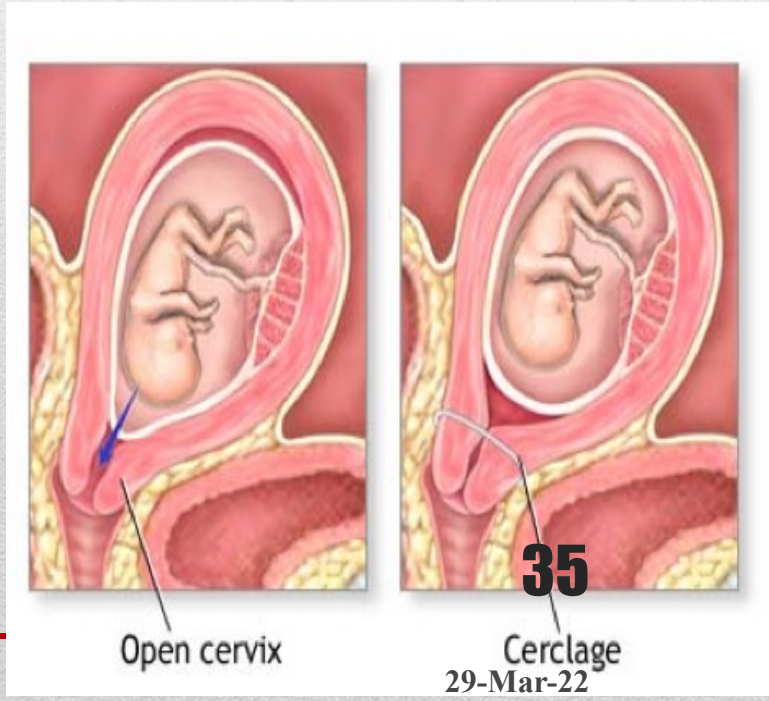
- **Corticosteroids (betamethasone 12mg IM every 24 hours × 2 doses between 24 and 33 6/7 weeks** is preferred if available) given to the mother prior to preterm birth (either spontaneous or indicated) are **effective in preventing respiratory distress syndrome, intraventricular hemorrhage (IVH), and neonatal mortality.**
- **Dexamethazone 24 mg IM in divided doses is a second choice if betamethazone is not available**
- **maximum benefit if the woman delivered after 24hrous to 7 days after treatment.**

Glucocorticoids rule!

Cervical cerclage

- For cervical insufficiency which complicates 0.1-2% of all pregnancies and is responsible for 20% of late 2nd trimester losses.
- Prophylactic cerclage – 12-14wks
- Rescue cerclage – when cervical changes already detected

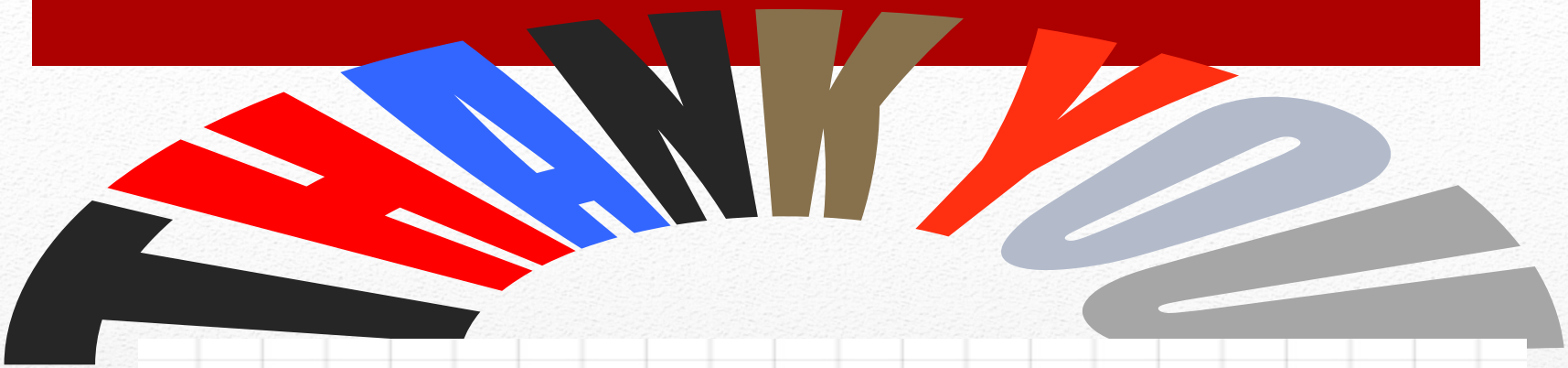
- ***Various techniques; shirodkar, MacDonald, Caspi, and Abdominal cerclage***



- **All decisions about cerclage are difficult and should be made with senior involvement. A doctor with the necessary skills and expertise to perform cerclage should carry out the procedure. [✓]**
- **TYPES (definitions): cerclage terminology according to indication:**

- **History –indicated cerclage at (12-14 weeks)**
- **Ultrasound -indicated cerclage at (14-24weeks) inserted as a salvage measure in case of premature cervical dilation with exposed fetal membranes in vagina.**

Cervical Cerclage: (GTG60)



Osama Warda, MD
Prof. OBS/GYN

THANK YOU

Grades of recommendation

A	At least one meta-analysis, systematic review or randomised controlled trial rated as 1++ and directly applicable to the target population; or A systematic review of randomised controlled trials or a body of evidence consisting principally of studies rated as 1+ directly applicable to the target population and demonstrating overall consistency of results.
B	A body of evidence including studies rated as 2++ directly applicable to the target population and demonstrating overall consistency of results; or Extrapolated evidence from studies rated as 1++ or 1+.
C	A body of evidence including studies rated as 2+ directly applicable to the target population and demonstrating overall consistency of results; or Extrapolated evidence from studies rated as 2++.
D	Evidence level 3 or 4; or Extrapolated evidence from studies rated as 2+.
✔	Good practice point: recommended best practice based on the clinical experience of the guideline development group.

- 1- Preterm birth is defined as……
  ……
  .
- 2-what are the WHO sub-categories of preterm birth based on the gestational age
- In a woman with uncertain dates, how can you diagnose preterm birth based on birth weight?
- The following are causes of preterm birth:

a) Bacterial vaginosis
b) Cervical insufficiency
c) Placental calcification
d) Rupture of fetal membranes

- Regarding prediction of preterm labor (T or F):

a) Vaginal digital evaluation of the cervix is most reliable method

b)Endovaginal ultrasound measurement of the cervical canal length is a reliable method.

c) Transvaginal estimation of internal os diameter is the most important ultrasound predictor

d) Fetal fibronectin testing in cervico-vaginal secretions has a good positive predictive value