DRUGS ACTING ON UTERUS

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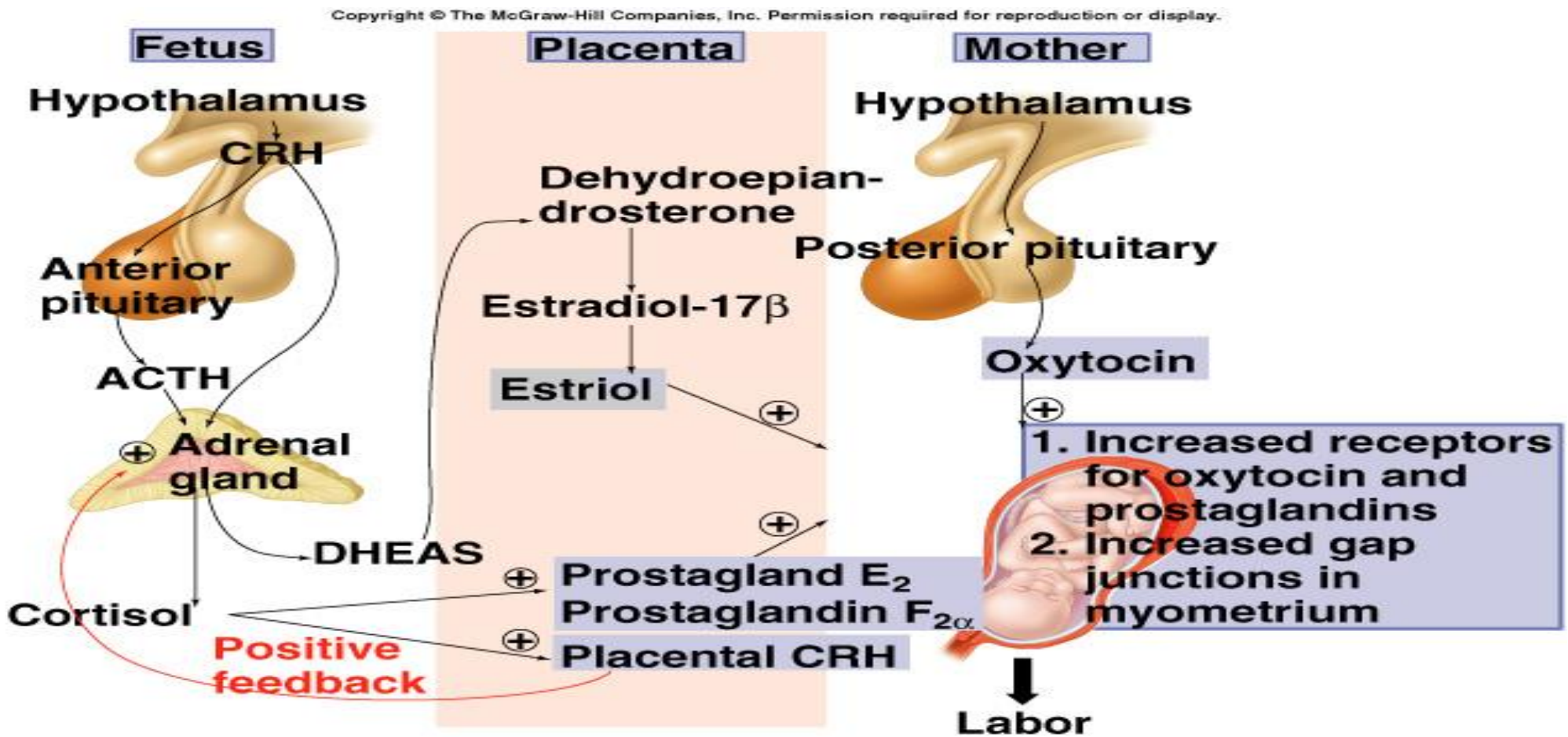
Objectives

- 1- Uterine contractions
- 2- Drugs affecting uterine contractions
- 3- Oxytocin: actins, mechanism of action, kinetics, indications, side effects , precautions and contraindications
- 4- Ergometrine: mechanism of action, uses, side effects and contraindications
- 5- Prostaglandins PGs: dinoprostone, gemeprost, misoprostol and dinoprost
- 6- Tocolytic drugs

Uterine contractions

- Uterine smooth muscle is characterized by high level of spontaneous contractile activity.
- It is innervated by autonomic nervous system
- Uterine contractions are muscle contractions of the uterine smooth muscle that occur during:
- Menstrual cycle
- Ovulation
- Pregnancy
- Labor

Parturition



Drugs affecting uterus

Stimulatory

- Muscarinic agonists
- $Alph_1$- Adrenoceptor agonists (ergot derivatives)
- Oxytocin
- PGE_2 or $PGF_{2\alpha}$
- 5-HT_2 agonists

Inhibitory

- B_2- adrenoceptor agonists
- Calcium channel blockers
- Atosiban

1. Oxytocin

The main drugs used *clinically* to increase uterine contractility include Oxytocin, PGs, and Ergot derivatives (Ergonovine)

1. **Oxytocin (Pitocin, Syntocinon) :** Oxytocin and vasopressin are nonapeptide hormones, synthesized in hypothalamus, then transported to posterior pituitary where they are stored and released.

Pharmacological actions of oxytocin :

1. **Contraction of myoepithelial cells** surrounding secretory alveoli of breast leading to **milk ejection in lactating females**.

2. Induction of intermittent uterine contractions and maintains labor:

Reaches peak during pushing phase of labor and it contributes to initiation of parturition.

These contractions can be inhibited by B_2-adrenoceptor agonists or by general anesthetics.

3. Uterine involution

4. Oxytocin has weak antidiuretic or pressor activity.

Mechanism of action:

1. Stimulation of oxytocin receptors
2. Increasing PGs levels intrauterine

PKs of oxytocin

- **It is not given orally** since it is destroyed by proteolytic enzymes of stomach and intestine (trypsin and chymotrypsin).
- It is not bound to plasma proteins
- Eliminated by liver and kidney (plasma t½~ 5 min).

Therapeutic uses of oxytocin:

Induction of labor: given by IV infusion in:

1- Conditions requiring early vaginal delivery at 37-38 weeks: maternal diabetes, pre-eclampsia, Rh-isoimmunization

2- Delayed onset of labor at term: post-maturity

3- Primary uterine inertia, and to enhance uterine contractions in incomplete abortion and full-term labor

4- Control of post-partum hemorrhage (PPH): (by IV infusion or IM injection with ergonovine)

5- To induce milk let-down after labor: by nasal spray.

N.B. Clinically oxytocin is given only when uterine cervix is soft and dilated

Adverse effects:

rare with proper supervision

1- With **large IV infusion doses, tetanic uterine contractions can occur which obstructs intramural uterine blood flow causing:**

- **fetal distress or death**.

- **Uterine rupture may occur esp. with obstructed labor.**

2- **with large doses , blood pressure increases** due to vasoconstriction

3- Water intoxication can rarely occur due to large volume of IV infused fluid. (may be fatal)

4- Increased incidence of neonatal jaundice: due to increased osmotic fragility of RBC

Contra-indications:

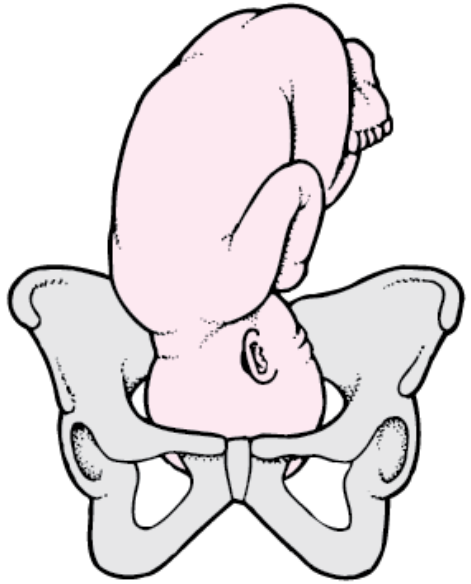
1- **Fetal distress**

2- Prematurity of fetus

3-Fetal malpresentation e.g. breech presentation & **Cephalopelvic disproportion** i.e. contracted pelvis: both predispose to uterine rupture.

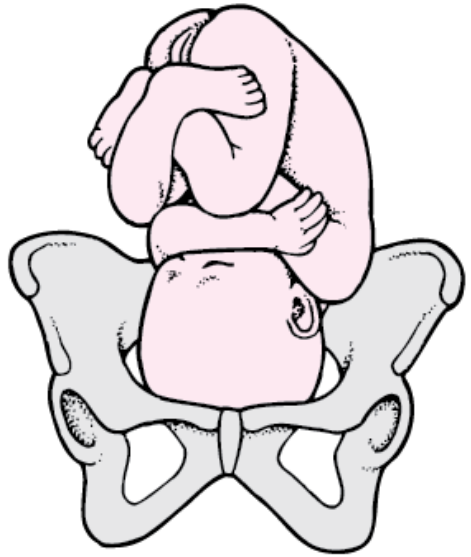
4- Prolapse of umbilical cord following rupture of fetal membranes.

Facing Backward
Head First

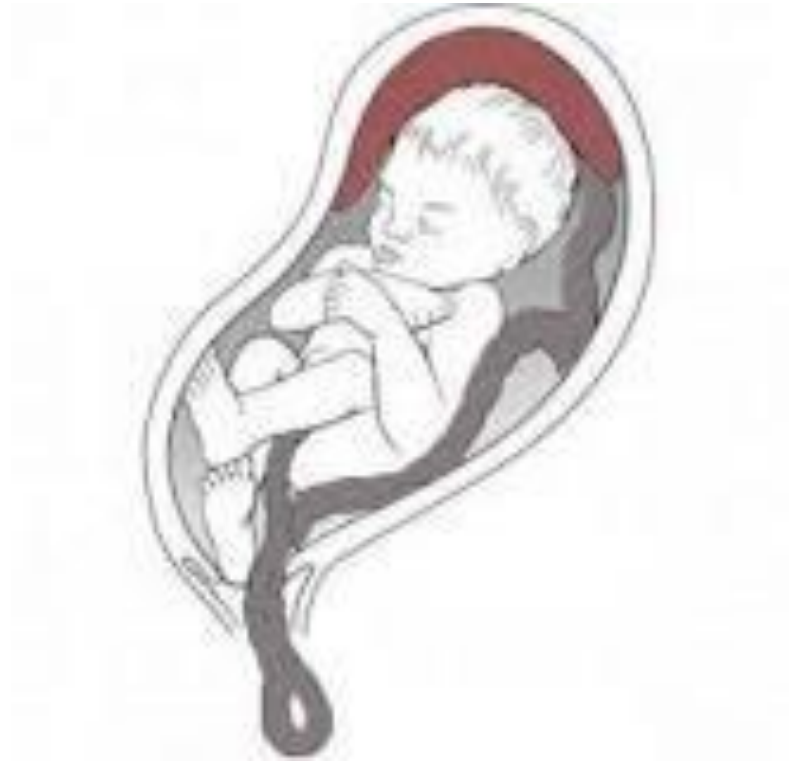


Normal Position and Presentation

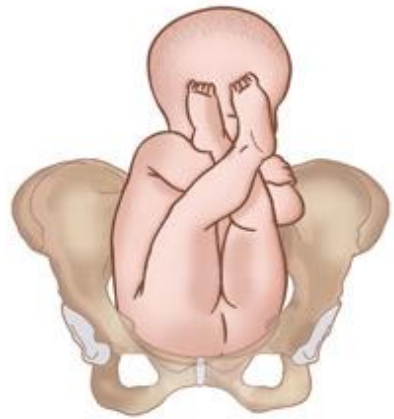
Facing Forward



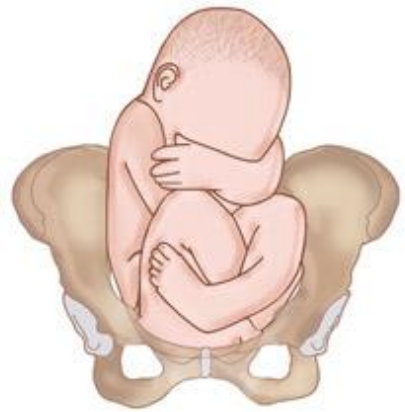
Abnormal Position



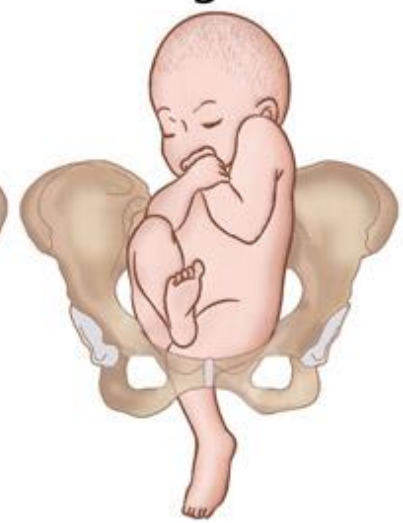
Frank Breech



Complete Breech



Footling Breech



Precautions

- Multiple pregnancy
- Previous c- section
- Hypertension

2. Ergonovine (Ergometrine) and methylergonovine

More selective than other ergot alkaloids in stimulating the uterus and **is the ergot alkaloid of choice in obstetrics.**

Mechanism of action:

1. Powerful direct action on uterine muscles
2. Possibly other actions (5-HT_2 + $\alpha lpha_1$-adrenoceptor agonist actions).

It helps to prevent postpartum hemorrhage by causing powerful , sustained uterine contraction.

Route of administration:

IV or IM at time of delivery of placenta or after delivery of fetus but never before.

Side effects: Increased B.P

Contraindications

1. Hypertension as in pre-eclampsia
2. Peripheral vascular disease
3. Angina

3. Prostaglandins (PGs)

PGE2 (Dinoprostone): It is commonly used vaginal

A. To stimulate uterine contractions for:

Induction of labor given as vaginal gel or insert

Note: If oxytocin is needed for induction of labor, it is given after 6 hs have passed after PG use to avoid excessive uterine contractions.

Induction of abortion: vaginal suppository is used.

B. For softening the cervix at term: This shortens time to onset of labor and labor time. PGE2 **directly affects collagenase of cervix that breaks down the collagen network and softens it.**

Gemeprost: PGE1 analogue

- used as **vaginal suppository to induce early medical abortion during first trimester.**

Misoprostol: oral or vaginal supp.:

used for induction of medical abortion in second trimester or when gemeprost is not available.

$PGF_{2\alpha}$ (Dinoprost) : less commonly used

May be **given vaginally**, **intra-amniotically, or IV** for **induction of abortion in second trimester**.

Intra-amniotic $PGF_{2\alpha}$ has up to 100% success rate with fewer and less severe S.Es than IV.

Side effects:

$PGF_{2\alpha}$ causes more G.I. side effects (vomiting, diarrhea) than PGE_2.

Tocolytics

What are tocolytic drugs?

- Drugs that inhibit uterine contractions

Indications:

Delay, inhibit or prevent premature labor (< 37 weeks of pregnancy).

Clinical hint:

Usually, regular uterine contractions can stabilize on bed rest & local warmth. When this is insufficient, then a tocolytic drug is used.

N.B. Betamethasone is given IV to mother or into cord blood to stimulate maturation of fetal lung (by enhancing surfactant formation); it is preferred to dexamethasone because it is bound less to plasma proteins.

1. B_2 - adrenoceptor agonists

- **Ritodrine, Terbutaline, salbutamol**
- **Route of administration:**
- oral or IV infusion in 5% dextrose
- **Side effects:**
- 1. Tachycardia and increased cardiac output
- 2. Sometimes acute left ventricular failure in mother occurs due to overload of infusion fluid and marked tachycardia.
- 3. Hypokalemia
- 4. Hyperglycemia

2. Calcium channel blocker

- The short acting Nifedipine or Nicardipine
- **Route of administration**: oral
- **Side effects**: hypotension

3- Atosiban

- analogue of oxytocin that act as competitive antagonist, inhibiting oxytocin binding to its receptor.
- Given IV

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THANK YOU