



Drugs Acting On Uterus

By

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Objectives

- 1- Uterine contractions
- 2- Drugs affecting uterine contractions
- 3- Oxytocin: actions, 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. *always present*
- It is innervated by autonomic nervous system
- Uterine contractions are muscle contractions of the uterine smooth muscle that occur during:
 - Menstrual cycle ⇒ *normally in menses* // *intensity pain in labor* *بسیار زیاد* // *pain in menstrual* → ↑PG
 - Ovulation → *weak in luteal phase* *under effect LH* *دوباره* *dysmenorrhea* *"menstrual cramps"* ↑PG
 - Pregnancy → *physiological* // *irregular* *begin in 2 trimester* *"Braxton Hicks"*
 - Labor ⇒ *intense contraction + regular periods* "5-10 min between each contraction 70s"
- Sexual stimulation & during lactation: due to oxytocin (love hormone)

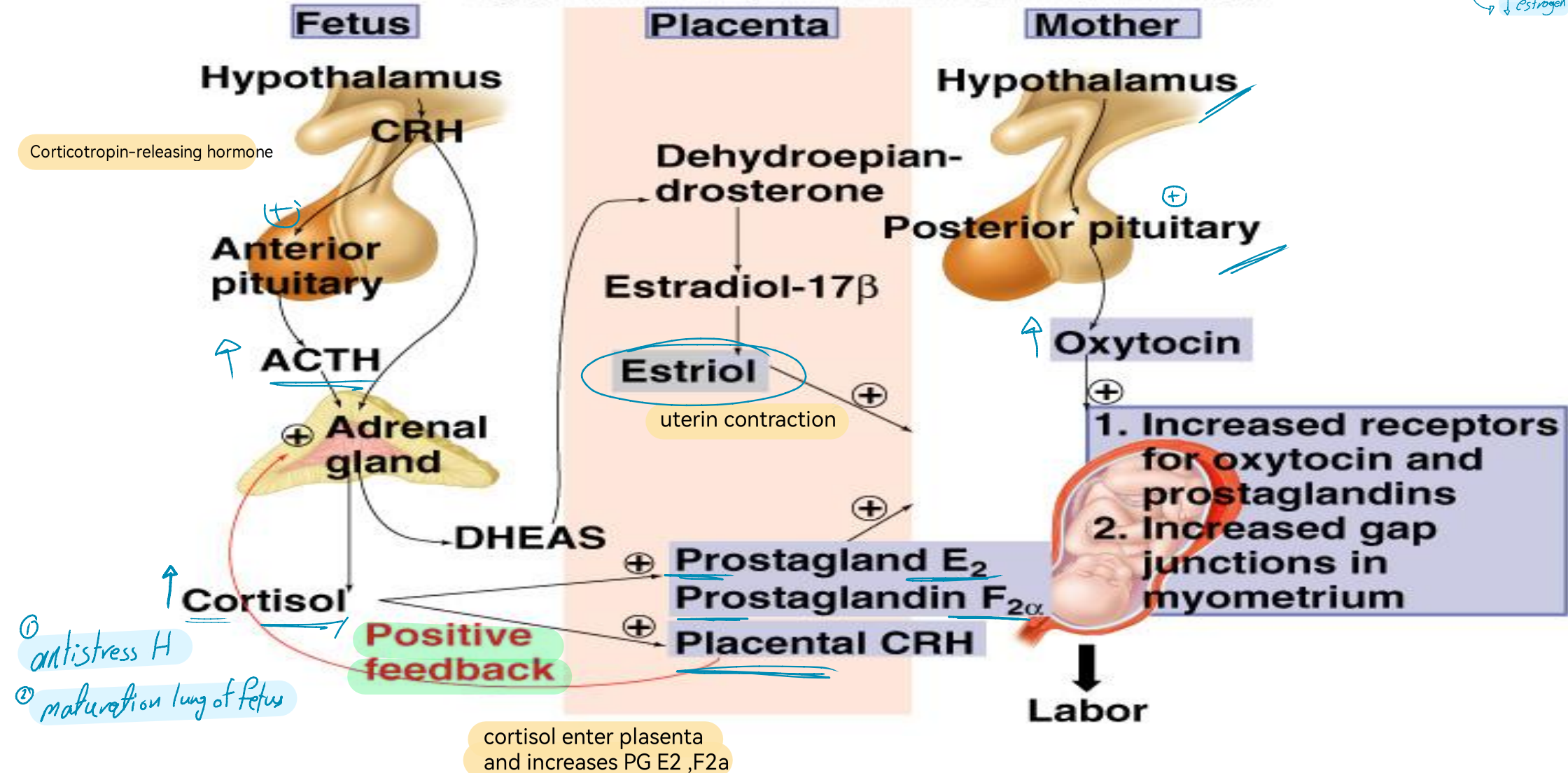
give → *NASID* ✓
↳ *spasmolytic* ✓

Parturition

The length of pregnancy is under the influence of progesterone.

uterine relaxation
↓ estrogen + ↓ PG

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Drugs affecting uterus

Stimulatory

The main drugs used clinically to increase uterine contractility:

- Oxytocin
- Alph_1 - Adrenoceptor agonists (ergot derivatives)
- PGE_2 or $\text{PGF}_{2\alpha}$

• Inhibitory

- B2- adrenoceptor agonists
- Calcium channel blockers
- Atosiban

• **Indications:**

- Prevention of preterm labor

Indications of uterine stimulants

• 1- Induce or facilitate labor:

• **Pre-term:** diabetic mother- pre-eclampsia- Rh negative fetus

↳ hypertension + protein in urine
round face + pitting edema

• **Incomplete abortion**

• **At-term:** ^{primary} uterine inertia → contraction not full stretched

"Serious condition"

• **Post-term:** delayed labor

• **2- Prevention of postpartum hemorrhage**

"to closed intramural BV"

• **3- Induction of abortion**

1. Oxytocin

9 amino acid

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.

to be efficient // divide into periods

2. Induction of intermittent uterine contractions and maintenance of labor:

↳ continuous may cause rupture + fetal distress

- It contributes to initiation of parturition.
- Reaches **peak** during **pushing phase of labor**
- **Oxytocin-induced contractions can be inhibited by:**
- B₂-adrenoceptor agonists or by general anesthetics.

3. Uterine involution

حجم الرحم - ما رجع الحجم الطبيعي
60g

4. Oxytocin has weak antidiuretic or pressor activity.

بسبب التناوب مع
Action of Vasopressin
تؤثر في same side

appear in high dose

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). *peptide*
- It is **NOT** bound to plasma proteins
- Eliminated by liver and kidney (plasma $t_{1/2} \sim 5$ min): IV infusion.

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-immunization
- 2- Primary uterine inertia, and to enhance uterine contractions in **incomplete abortion** and **full-term labor**
- 3- **Delayed onset of labor at term: post-maturity**

Postpartum hemorrhage

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

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

N.B. Clinically oxytocin is given only when uterine cervix is soft and dilated → 10 cm

if give before soft + dilated
↓
rupture

↳ by PG
"repinning"

↳ by oxytocin
"efficient uterine contraction"

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

الطبيعي "30-70" contraction

عزل "90-100" without interval

جنين مضطرب

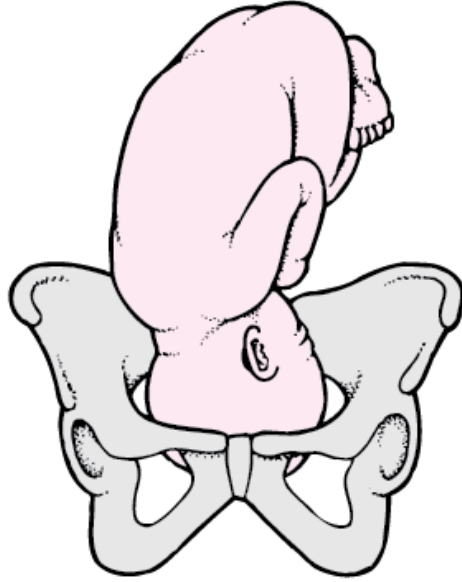
upper Antidiuretic affect

- 3- **Water intoxication** can rarely occur due to **large volume of IV infused fluid**.
(may be fatal) *↪ dilussional hyponatremia ~ disorientation, coma then death*
- 4- **Increased incidence of neonatal jaundice:** due to increased osmotic fragility of RBC

Contra-indications:

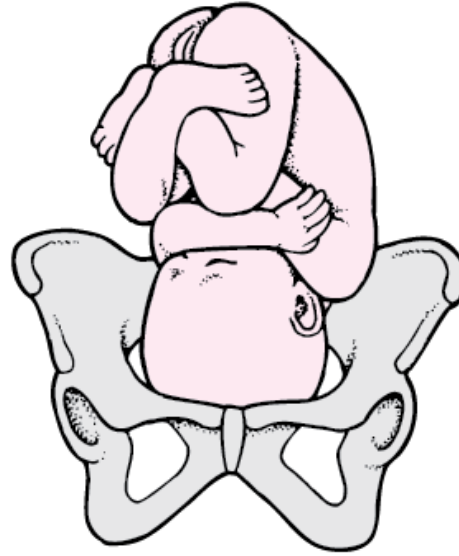
- 1- **Fetal distress** *مقاومة تقلب في تقلصات قوية*
- 2- **Prematurity** of fetus *↗*
- 3- **Fetal-malpresentation** e.g. breech presentation & **Cephalopelvic** *narrow pelvic ↗*
disproportion i.e. contracted pelvis: both predispose to uterine rupture.
- 4- **Prolapse of umbilical cord** following rupture of fetal membranes.

Facing Backward
Head First



Normal Position and
Presentation

Facing Forward



Abnormal
Position

Frank Breech



Complete Breech



Footling Breech



Precautions to oxytocin use

- Multiple pregnancy → weak uterine muscle
- Previous c- section → scarred fibrous tissue
- Hypertension
⇒ Antidiuretic side effect

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-HT₂, α_1 -adrenoceptor agonist actions).

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

prevent in labor

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)

- **Mechanism of action as uterine stimulants:**
- 1- **Direct action:** via receptors
- 2- **Indirect action:** upregulation of oxytocin receptors

❑ **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 hours 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**: PGE1 analogue

only oral

❑ oral or vaginal supp.:

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

PGF_{2α} (Dinoprost) : less commonly used

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

Intra-amniotic PGF_{2α} has up to 100% success rate with fewer and less severe adverse effects than IV.

Side effects:

PGF_{2α} causes more G.I. side effects (vomiting, diarrhea) than PGE₂.

Tocolytics

What are tocolytic drugs?

- Drugs that inhibit uterine contractions

Indications:

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

- **Clinical hint:**

before use drugs

- 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. B₂ - adrenoceptor agonists

- Ritodrine, Terbutaline, salbutamol
- **Mechanism of action:** increasing cAMP in myometrium
- **Route of administration:**
- oral or IV infusion in 5% dextrose
- **Side effects:**
 1. Tachycardia
 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
- **Mechanism of action**: inhibition of Ca influx in myometrium
- **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

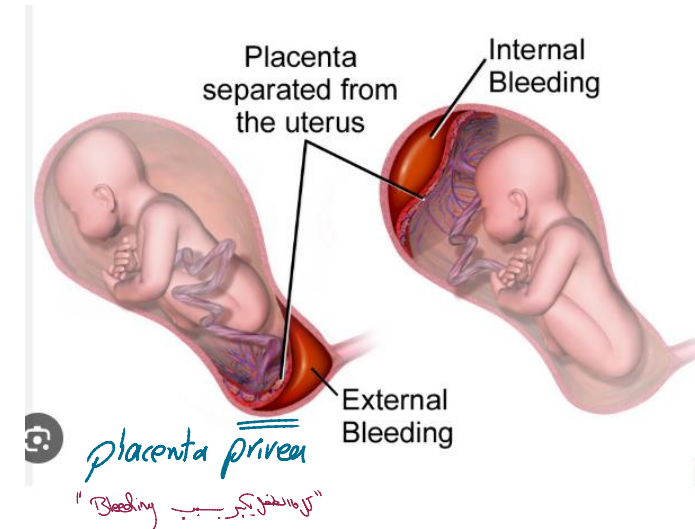
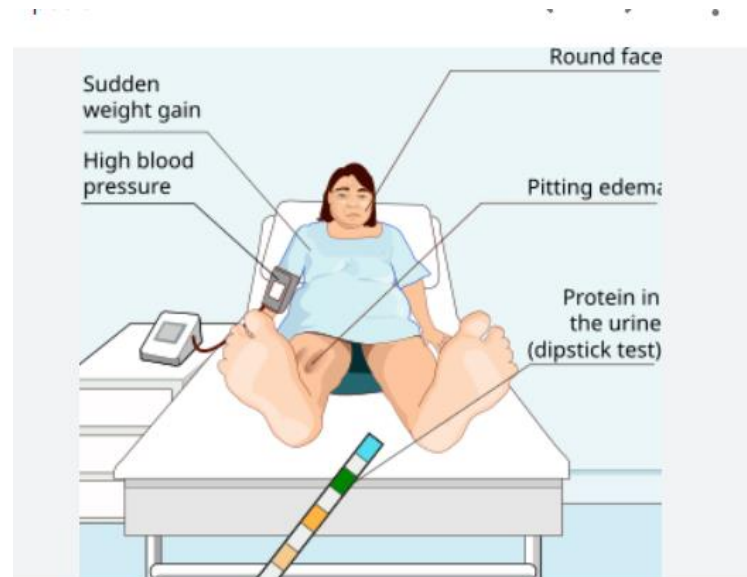
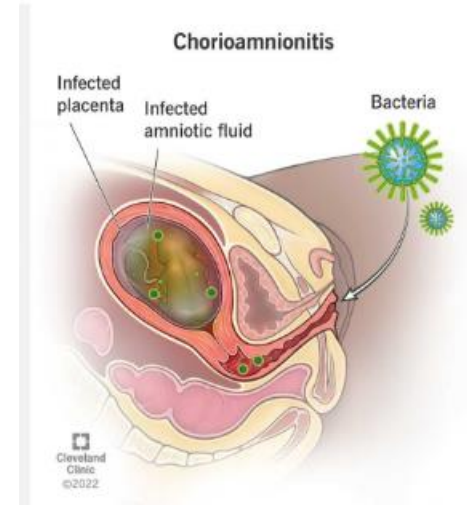
4- Miscellaneous drugs

- Progesterone
- Halothane
- Nitroglycerine: NO donor: increasing cGMP in myometrium *→ relaxation*
- Indomethacin: COX inhibitor

Contraindications of tocolytics

- 1- Chorioamnionitis: infection of fetal membranes
- 2- Congenital anomalies
- 3- Late pregnancy: more than 34 weeks
- 4- Placenta abruption
- 6- Pre-eclampsia

▷ Separated placenta from uterus.



دعواتكم، وسامعونا في التفسير.

الحمد لله

THANK YOU

“اللَّهُمَّ وَا بَعَثْ فِيْنَا هِمَّةً مُخْتَلِفَةً،
وَنَصْرًا صَادِقًا لَأُمَّتِكَ، لَا يَقْتُلُنَا
فِيهِ سَوَالُ الْعِجْزِ، وَلَا يَأْخُذُنَا بِهِ
فِتْوَرٌ وَلَا ذُبُولٌ، وَارْزُقْنَا صِدْقًا
بِمَا نَطْلُبُ وَإِخْلَاصًا بِمَا نَفْعَلُ،
وَاجْعَلْ حُرْقَةَ صَدُورِنَا فِعْلًا لَا
عِجْسَرًا، وَقُوَّةً لَا ضَعْفًا، وَاخْتَرْنَا
حِينَ تَتَّخِذُ مِنَ الْأُمَّةِ شُهَدَاءَ!”

-قصي العسيلي