Drugs acting on the uterus

I. Uterine stimulants

1. Oxytocin: (nonapeptide=9 a.a peptide)

- Contracts the myoepithelial cells of the breast → milk letdown; milk ejection

Major stimuli, baby cry and suckling

- Contracts the uterus → delivery

The uterus is insensitive to oxytocin in early pregnancy but its sensitivity increases with advanced pregnancy reaching maximum at time of delivery

- Has slight ADH-like activity

- Role in man ???

- **Oxytocin MOA:**

- Surface receptors → stimulation of voltage-sensitive Ca^{++} channels → depolarization of uterine muscles → contractions
- ↑ intracellular Ca^{++}
- ↑ prostaglandin release

- **Clinical uses to oxytocin:**

- Induction of labor

Drug of choice given in units in an I.V infusion

- Postpartum hemorrhage, I.M. Ergot alkaloids are better (ergonovine, methylergonovine, syntometrine= oxytocin+ ergometrine)

- Breast engorgement, intranasally

- Abortifacient, I.V infusion. ≥ 20 weeks of gestation, ineffective in early pregnancy

- **Side effects to oxytocin:**

- Rupture of the uterus

Major and most serious side effect

- H_2O intoxication and hypertension

Due to its ADH-like activity

- **Specific oxytocin antagonist**

Atosiban, effective in the management of premature delivery

2. Prostaglandins:

* Dinoprostone (PGE_2)

Vaginal pessaries, inserts and gel, tab

Abortifacient, induction of labor

* Dinoprost ($PGF_{2\alpha}$)

I.V infusion and intramniotic

Same uses as dinoprostone

* Carboprost ($PGF_{2\alpha}$)

I.M and intramniotic

Abortifacient and postpartum hemorrhage

* Gemeprost (PGE_1)

Vaginal pessaries

Used to prime the cervix

3. Ergot alkaloids:

Ergonovine, Methylergonovine

I.M, oral

- Ergot alkaloids remain the drugs of choice to manage postpartum hemorrhage
- As compared to oxytocin, ergot alkaloids are more potent, they produce more prolonged and sustained contractions of the uterus and they are less toxic
- Ergot alkaloids are contraindicated to be used as inducers to delivery (associated with high incidence of fetal distress and mortality)

II. Uterine relaxants (Tocolytics)

Major clinical use: premature delivery (weeks 20-36)
→ improve the survival of the newborn

1. β-adrenergic agonists:

↑ cAMP → ↓ cytoplasmic Ca^{++}

* Ritodrine

I.V infusion

Most widely used

* Terbutaline, Oral, S.C, I.V

Side Effects to β-adrenergics:

Sweating, tachycardia, chest pain…

2. Magnesium sulfate

I.V infusion

Activates adenylate cyclase and stimulates Ca^{++} dependent ATPase

Uses: premature delivery and convulsions of pre-eclampsia

3. Progesterone

Oral, I.M

Dydrogesterone

4. Oxytocin competitive antagonists

Atosiban

5. Prostaglandin synthesis inhibitors

Indomethacin, Meloxicam

6. Nifedipine

** Major contraindication to tocolytics: fetal distress