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
  - H₂O 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 intramniontic
  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:
   \[ \text{↑ cAMP} \rightarrow \text{↓ cytoplasmic Ca}^{++} \]

* Ritodrine
  I.V infusion

Most widely used
* Terbutaline, Oral, S.C, I.V
Side Effects to $\beta$-adrenergics:
Sweating, tachycardia, chest pain…

2. Magnesium sulfate
I.V infusion
Activates adenylate cyclase and stimulates $\text{Ca}^{++}$ 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