2009b(6)/MAKEUP: Discuss the pharmacodynamics of drugs that affect uterine tone

General: Drugs can be used to ↑uterine tone (induction / acceleration of labour, treatment of postpartum haemorrhage), or ↓uterine tone (prevent / slow down labour)

↑Uterine Tone
1. Oxytocics

Oxytocin
- Endogenous nonapeptide hormone produced in hypothalamus and stored in post pituitary
  o Exhibits some analogy with ADH
  o Synthetic syntocinon doesn't exhibit ADH action
- Preparations: 5/10 IU/ml for IV infusion / IMI
- Use:
  o Accelerate / induce labour
  o Rx PPH
  o Aid in lactation
- MOA: Oestrogen during pregnancy ↑number of oxytocin receptors in the myometrium
  o ↑K⁺ conductance → ↑membrane excitability
  o Dose related ↑amplitude, frequency of contractions with complete relaxation in between
- Pharmacodynamics:
  o CVS:
    ▪ ↓MAP 2° vasodilation
    ▪ Reflex ↑HR
    ▪ ECG: ↑QT, T-wave flattening (2° ↓perfusion coronary aa)
  o Renal: Endogenous oxytocin → V₂ receptor stimulation CD → aquaporin insertion → ↑H₂O reabsorption
  o Side Effects/Toxicity: water intoxication / uterine spasm / rupture (2° fetal asphyxia)

Ergometrine
- Ergot alkaloid
- Presentation: 500μg IMI
- Uses: Rx PPH
- MOA: Unknown ?partial agonist α adrenoceptor / 5-HT
  o Uterine contraction with ↑basal tone → activity dependent (i.e. >effect on quiescent uterus)
- Pharmacodynamics
  o CVS:
    ▪ ↑MAP 2° vasoconstriction
    ▪ ↓Coronary aa perfusion → angina pain
    ▪ ↑PVR
  o CNS:
    ▪ N&V 2° D₂R stimulation of CTZ
    ▪ Blurred vision / headache 2° vasoconstriction

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- Seizures
  - Side Effect: Uterine spasm

2. Prostaglandins
   F type (PGF$_{2\alpha}$): Dinoprost
   - Do NOT give IVI → PGs metabolised in pulmonary circuit → causes
     ↑↑↑PVR, ↑↑bronchoconstriction →→ DEATH. Myometrial injection only
   E type (PGE$_2$): Dinoprostone
   - Presentation: Tablets, pessaries
   - Uses: Induction of labour, ripening of cervix
   - MOA: Promote series of coordinated contractions of body of pregnant
     uterus with ↑basal tone and relaxation of cervix

Side Effects: Uterine pain, N&V

↓Uterine Tone (Tocolytics)
3. Mg$^{2+}$
4. $\beta_2$ adrenoceptor agonists → Salbutamol, terbutaline
5. VA (except N$_2$O)
6. Nitrates → GTN, amylnitrate
7. NSAIDS
8. Atosiban (anti-oxytocin)
9. Ca$^{2+}$ antagonists → Nifedipine, felodipine