Q24 Describe the mechanism of action, and side effects of THREE (3) classes of drugs that are used to increase uterine tone and THREE (3) classes of drugs used to decrease uterine tone (March 2013)

Drugs which increase uterine tone (oxytocics)

- Oxytocin analogues
  - Mechanism → Syntocinin is a synthetic analogue of oxytocin. Acts by binding to the Gq-protein coupled oxytocin receptor in the myometrium to increase the frequency and amplitude of uterine contractions (with return to normal resting tone in between contractions)
  - Side effects → may have CVS effects (vasodilatation or arrhythmia), GI (nausea/vomiting) and renal effects (water retention via actions on renal V2 receptors). May also cause uterine rupture.

- Ergot alkaloids
  - Mechanism → ergometrine's mechanism is not entirely understood; it may act via partial alpha, 5HT and/or dopamine agonism as well as inhibition of NO release to cause an increase in uterine contractions with an increase in basal tone
  - Side effects → Hypertension (due to alpha agonism), coronary artery spasm, gangrene, nausea/vomiting, headache, tinnitus and seizures. May also cause uterine rupture

- Prostaglandins
  - Mechanism → dinoprostone may be administered via pessary. Releases PGE2 to the cervical tissue to enable cervical ripening. Dinoprost contains PGF2 which induces uterine contractions
  - Side effects → uterine rupture, DIC

Drugs which decrease uterine tone (tocolytics)

- B2 agonists
  - Mechanism → eg, salbutamol. Act via G-S protein coupled receptors resulting in an increase in cAMP, a reduction in intracellular Ca and thus myometrial relaxation.
  - Side effects → tachycardia, headache, hypokalaemia, hyperglycaemia

- Calcium channel blockers
  - Mechanism → eg, nifedipine. Act via binding to the D-binding site of the L-type calcium channel to cause a reduction in intracellular Ca levels and thus uterine smooth muscle relaxation
  - Side effects → hypotension, nausea, flushing, palpitations

- NSAIDs
  - Mechanism → eg, indomethacin. Inhibits cyclooxygenase to prevent the production of prostaglandins required for uterine contraction.
  - Side effects → gastritis, platelet dysfunction, renal dysfunction. Concern for premature closure of the ductus arteriosus.