

Corticosteroids

- Are naturally occurring in the form of hydrocortisone
- Synthetic in the form of methylprednisolone, prednisolone and dexamethasone
- Are released naturally via the hypothalamus, pituitary, adrenal cortex axis (HPA)
- Exogenous hormones will exert negative feedback on this axis

Pharmaceutical

- Are available as IV and oral preparations

Pharmacodynamics

Mechanism

- crosses cell membranes and act on steroid receptors which then act on the nucleus
- alters gene transcription and the production of proteins

Effects / Side effects

Metabolic effects

- facilitates gluconeogenesis
- protein catabolism and lipolysis
- this causes muscle wasting and thin skin and fat redistribution (Cushingoid)
- increase bone catabolism and lead to osteoporosis
- dysregulated carbohydrate metabolism
- increased glucose release but decreased absorption from the GIT
- glycogen deposition

Anti-inflammatory effects

- lipocortin stimulation causes decreased phospholipase A2 a precursor to arachidonic acid and the prostaglandins

Immunosuppression

- via decreased inflammatory mediators, reduced IL 1-2 which decreases lymphocyte production
- alters neutrophil and macrophage function

Other side effects

- Adrenal suppression via negative feedback on the HPA
- Fluid retention - via weak mineralocorticoid activity
- Vascular reactivity - plays a permissive role in the actions of catecholamines on vessels

Potency

- is the main difference between agents
- Hydrocortisone 1, Prednisolone 4, methylprednisolone 5, dexamethasone 25

Pharmaceutical

Absorption

- All agents are rapidly and extensively absorbed when given PO or PR

Distribution

- Small volumes of distribution
- Protein binding is usually high (prednisolone is up to 90%)

Metabolism

- most corticosteroid drugs are hepatically metabolised

Elimination

- most drug half-lives are short (several hours)
- mechanism of action however means that biological half-life is usually prolonged