Sept 2010
QUESTION 11

Compare and contrast hydrocortisone, methylprednisolone and dexamethasone

- Corticosteroids
  - Are naturally occuring in the form of hydrocortisone
  - Are released naturally via the hypothalamus, pituitary, (adrenal cortex) axis (HPA)
  - Synthetic in the form of metylprednisolone, prednisolone and dexamtheasone
  - Exogenous hormones will exert negative feed back on the HPA

- Pharmaceutical
  - Are available as IV and oral preparations

- Pharmacodynamics
  - Mechanism
    - crosses cell membranes and bind to steroid receptors which then act on the nucleus
    - alters gene transcription and the production of protiens
  - Effects / Side effects
    - Metabolic effects
      - facilitates gluconeogensis
        - protien 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
    - Immunosupression
      - via decreased inflammatory mediators, reduced IL 1-2 which decreases lymphocyte prod
      - alters neutrophil and macrophage function
    - Other side effects
      - Adrenal supression via negative feedback on the HPA
      - Fluid retention - via weak mineralcorticoid 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
    - Protien binding is usually high (prednisolone is up to 90%)
  - Metabolism
    - most corticosteroid drugs are hepatically metabolised
  - Elimination
    - mostly in urine
    - most drug half lives are short (several hours)
    - mechanism of action however means that biological half life is usually prolonged