March 2009
QUESTION 23

Describe the mechanism of action, antibacterial spectrum and pharmacokinetics of aminoglycosides

- Aminoglycoside
  - prototype is gentamicin
  - complex chemical structure

- Pharmaceutical
  - water soluble
  - available as an IV preparation only

- Pharmacodynamics
  - Mechanism of action
    - irreversible inhibitor of protien synthesis via the 30S subunit
    - diffuse across outer membranes via porins
    - actively transported by oxygen dependent process across cell membrane to cytoplasm
      - low O2 and extracellular pH prevent this process
  - Mechanisms of resistance
    - production of a transenzyme inactivates aminoglycosides by adenylylation
    - impaired entry into the cell (blocked porins or the O2 dependent process)
    - mutated ribosomal 30S subunit
  - Spectrum of activity
    - provide good gram negative coverage and some gram positive
    - most often used against enteric infections and in sepsis
    - usually used in combination with a beta lactam
  - Side effects
    - ototoxicity
    - nephrotoxicity (worse with loop diuretics ore pre-existing renal disease)
    - can cause paralysis if used in combination with neuromuscular blockers

- Pharmacokinetics
  - Absorption
    - poorly absorbed orally, usually given IV, IM or topical
  - Distribution
    - highly polar drug
    - does not cross the BBB
    - small volume of distribution (increased in oedema, overload)
    - minimally protien bound
  - Metabolism
    - not metabolised
  - Excretion
    - half life
      - greatly dependent on renal function
      - several hours to days
    - excreted in urine unchanged