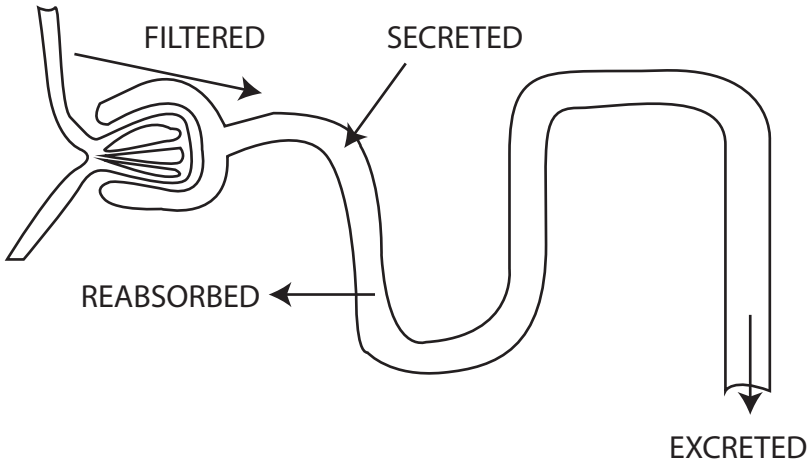
March 2010
QUESTION 08

Describe the role of the kidney in drug excretion and the factors affecting this (80% marks). Briefly outline how you would alter the dosing of a drug with high renal excretion in a patient with renal impairment (20% marks).

Drug excretion is the removal of a drug from the body either unchanged or as a metabolite
- the kidney (via urine) is the most important method in the body for excretion
- the GIT (faeces) and the lungs (exhaled) are other methods



In the kidney drugs may be
- Filtered
  - dependent on the glomerular filtration rate / renal blood flow
    - determined by the filtration coefficient and the net starling force
  - smaller molecules more freely filtered (protien bound drugs are filtered less)
  - there is a slight negative charge to the glomerulus which favours positive ion filtration
- Secreted
  - occurs primarily at the proximal tubules
  - pencillin is an example
  - may be passive (if the drug is able to cross membranes) down a concentration gradient
  - or actively secreted via cotransporters or ATP dependent processes
- Reabsorbed
  - drugs able to cross lipid membranes may be reabsorbed (passive)
    - non-ionised compounds are lipophilic and may be reabsorbed
    - the pH of the urine is therefore important in determining degree of ionisation (pKa)

Points
- hepatic metabolism generally increases water solubility (phase 1 - removing, phase 2 adding)
- this increases filtration and decreases reabsorption
- drugs excreted unchanged or as active metabolite are GFR dependent

Gentamicin
- aminoglycoside antibiotic
- normal dose is 2-6mg/kg
- dose related nephrotoxicity and ototoxicity
- excreted unchanged in urine
- dose is adjusted according to creatinine clearance or eGFR
- narrow therapeutic window - needs monitoring of levels to ensure MIC and safety
- consider alternative antimicrobial, avoid co-administration of other nephrotoxins