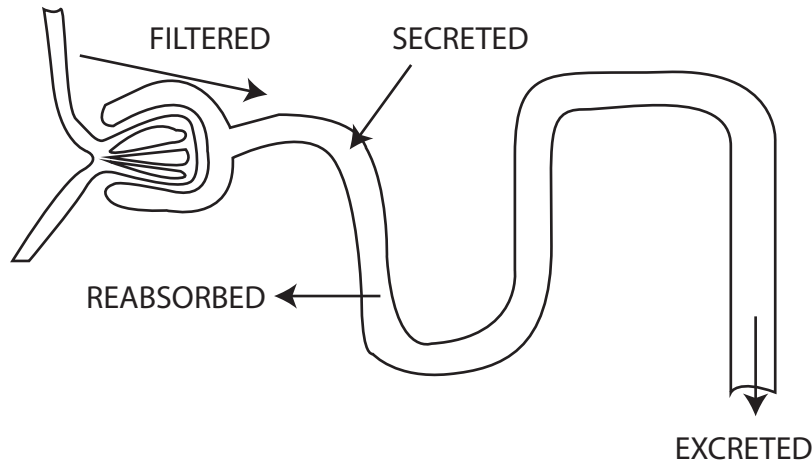


FEB 2008
QUESTION 17

Describe the role of the kidney in drug excretion, and the factors affecting this. Briefly outline how you would alter the dosing of gentamicin in a patient with renal impairment

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
- normal filtration is 180L/day (20% of renal plasma flow)
- smaller molecules more freely filtered (protein 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
- penicillin 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
- pinocytosis, solute drag

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

Dosing adjustment

- required if the drug is filtered and excreted with active metabolites or unchanged (aminoglycosides)
- dose is adjusted according to creatinine clearance or eGFR
- plasma monitoring of levels may be warranted (such as with aminoglycosides)
- dosing intervals and dose adjusted accordingly
- effort should be made to avoid or limit nephrotoxins