Routes of Elimination

1. What organ systems can eliminate drugs?
   1. What pathways exist within these organs?
2. What is ion-trapping?
   1. Where does it occur?
   2. Why is it relevant?
3. What is enterohepatic circulation?
   1. Where and when does it occur?
   2. Why is it relevant?

Routes of Elimination

Three topics are important for a basic understanding:

1. The routes of elimination
2. How those routes are affected by disease
3. Rates of elimination

# Routes of Elimination

Three routes are important:

1. Renal excretion
2. Biliary excretion
3. Pulmonary excretion  
   *Only relevant for anaesthetic gasses; not considered further here*

## Renal Excretion

Two broad renal pathways are seen:

|  |  |
| --- | --- |
| Filtration in the glomerulus | This is a passive process. To be filtered a molecule must be:   * Small (*so as not to be blocked by the podocytes*) * Non-protein bound (*protein is not filtered*) * Water soluble (*lipid soluble drugs, if there are filtered, will tend to be reabsorbed*) |
| Secretion in the tubules | This is mostly an active process. The transporters tend to be specific for classes of molecule, rather than specific to a single molecule. For example, there are transporters for:   * Acidic drugs * Basic drugs |

### Ion trapping

As a general rule, ionic or otherwise charged drugs are not able to cross lipid membranes so are not reabsorbed. Some drugs are weak acids or bases and thus charged and uncharged species exist in equilibrium:

For weak acids:

H-A ⇆ H+ + A-

For weak bases:

B-OH ⇆ B+ + OH-

This means that:

1. Acidic urine tends to trap basic drugs
2. Alkaline urine tends to trap acidic drugs

## Biliary Excretion

Substances must be actively secreted into bile.

Other key differences when compared to the kidney include:

1. There is no equivalent of filtration
2. It does not depend on solubility or phase 2 reactions  
   *But the precise form in which secretion occurs is specific to the drug in question and some forms may not be secreted at all*

### Enterohepatic circulation

Substances secreted in bile are exposed to the contents of the bowel.

Some bacteria in the bowel produce glucuronidase. If a normally lipid-soluble substance had been rendered insoluble by glucuronide conjugation, it may be reabsorbed after bacterial exposure.

In general, this is not a controllable process – it is either important or it isn’t. However, antibiotic treatment the gut flora may be reduced and glucuronidase levels may fall.

This may mean that the excretion of some drugs may rise unexpectedly.

# References

1. Pharmacology for Anaesthesia and Intensive Care (4th Edition); Peck TE & Hill SA; Cambridge University Press