

## Q12 Describe the pharmacology of vancomycin (March 2012, Q16 Sept 2013)

Vancomycin is a glycopeptide antibiotic produced by streptococcus orientalis. It is active against most gram positive bacteria (including staphylococci, streptococci, enterococci, listeria monocytogenes, clostridium sp, and Bacillus sp.), with limited gram negative activity.

### PHARMACEUTICAL

Store at 2-8 degrees, clear solution. Should be given slowly due to vessel irritation (and risk of red man syndrome, see below). Monitoring required to avoid toxic levels (aiming serum concentration 15+/-3).

### PHARMACODYNAMIC

Acts by inhibiting glycopeptide synthetase and thus preventing peptidoglycan formation in the bacterial cell wall. May also alter membrane permeability and selectively inhibit RNA synthesis.

Acts synergistically with aminoglycosides, cephalosporins and rifampicin (although synergy testing required as vancomycin + cephalosporin may act antagonistically against some strains of staph epidermis)

Antimicrobial activity depends on the duration that the serum drug concentration exceeds the minimum inhibitory concentration (MIC) of the target organism and not concentration dependence.

### SIDE EFFECTS / ISSUES

Histamine release can cause 'red man' syndrome.

Neutropenia and thrombocytopenia may occur.

Ototoxicity rare, dose related.

Nephrotoxicity usually resolves on cessation of drug.

### PHARMACOKINETIC

#### ABSORPTION

Route - IV, PO, intraperitoneal

Dose - loading dose 20mg/kg, then 1-1.5g daily depending on levels

Bioavailability - PO poor (although GIT absorption can increase if mucosa inflamed), IP 40%

#### DISTRIBUTION

Vd - 1L/kg.

Protein binding 10-80%

Distributes widely in body tissue and fluids, CSF penetration improves with inflamed meninges. Bone penetration poor.

#### METABOLISM

Little to none in humans

#### ELIMINATION

Mean half life 4-6 hours, prolonged in renal failure

Excreted via kidneys unchanged

Not effectively removed by dialysis

*A commonly used drug in intensive care practice, for which a high level of understanding is required (Level A). In general answers were sufficient for a pass, but there was still a lack of sufficient breadth of knowledge, in particular to pharmacokinetics and detailed mechanism of action.*

***Outline the pharmacology of vancomycin***

*A basic and fundamental pharmacology question which required candidates to present their answer in a coherent fashion, as well as demonstrate sufficient knowledge. Candidates were expected to mention spectrum and mechanism of action, pharmacokinetics (including dose, distribution, elimination, etc) and adverse effects, activity profile e.g. time-dependent, antimicrobial activity depends on the duration that the serum drug concentration exceeds the minimum inhibitory concentration (MIC) of the target organism and not concentration dependence.*