Q22 Outline the mechanism of action of ampicillin, gentamicin, vancomycin and ciprofloxacin. How does resistance develop to each of these antibiotics? (Sept 2011)

	Mechanism of action	Development of resistance
Ampicillin	Contains a beta lactam ring structure. Beta-lactam antibiotics inhibit the growth of sensitive bacteria by inactivating transpeptidase enzymes located in the bacterial cell membrane, inhibiting crosslinkage of peptidoglycans and thus impairing cell wall synthesis	- Bacteria produce beta lactamases, which hydrolyse and inactivate the antibiotic
Gentamicin	Binds to the bacterial 30R ribosomal subunit to inhibit protein synthesis and thus bacterial growth	- Alteration in access to target site – membrane impermeability / transport defect in the active transport of gentamicin - Multiple enzymes have been identified which block gentamicin (acetytransferases, adenyltransferases, phosphotransferases)
Vancomycin	A glycopeptide antibiotic which inhibits glycopeptide synthetase and thus preventing peptidogolycan formation in the bacterial cell wall, hence impairing cell wall synthesis and bacterial growth.	- VanA resistance – gene mutation leading to decreased affinity of peptidoglycan precursors for vancomycin. Induced by exposure to vanc / teicoplanin - Van B resistance – similar but only induced by vancomycin; strains may remain susceptible to teicoplanin
Ciprofloxacin	Quinolone antibiotic, binds to bacterial DNA supergyrase thus inhibiting supercoiling of bacteria DNA	- Alteration in target enzyme – changes to the DNA-bidning surface of DNA supergyrase infers resistance - Alteration in drug entry – altered expression of outer membrane porin proteins that form channels for passive diffusion of ciprofloxacin - Increase in efflux of drug – expression of nonspecific energy dependent efflux pumps which remove drug