Basics of Antibiotics

1. What

Basics of Antibiotics

# Physiological basis for antibiotic action

The key idea of antibiotics is the kill the pathogen with the minimum of collateral damage. To this end, identification of biochemical differences between human and bacterial cells is key:

1. **Bacteria possess a cell wall; human (eukaryotic) cells do not***This cell wall is composed of cross-linked strands of peptidoglycan, a polymer of NAM (N-actylmuramic acid) and NAG (N-acetylglucosamine)*
2. **Bacterial DNA is stored in a different way to human (eukaryotic) DNA***Bacterial DNA lies free in the cytoplasm in a single, circular chromosome; this chromosome is unpaired*
3. **Bacterial synthesis of protein is different**  
   *Bacterial ribosomes are small and different in structure to human ribosomes.*
4. **Bacteria synthesise folate; humans must absorb it from their diet**

Clearly there are many other differences; however, these four are currently exploited by common antibiotic classes.

# Classification of antibiotics by mechanism of action

## Agents acting on the cell wall

1. Beta-lactams  
   *These bind to penicillin-binding proteins which are responsible for crosslinking peptidoglycans; affected cells shed their cell wall during cell division becoming osmotically vulnerable* ***spheroplasts****Four subgroups exist:*
   1. Penicillins
   2. Cephalosporins
   3. Monobactams
   4. Carbapenems
2. Glycopeptides  
   *These bind to cell-wall precursors; once bound these precursors are then unavailable for form new cell wall  
     
   Two agents are used:*
   1. Vancomycin
   2. Teicoplanin

## Agents acting on bacterial DNA

Three groups:

1. Quinolones  
   *Inhibit topoisomerase, a key enzyme in DNA replication.  
     
   Two subgroups: (mechanism is same; spectrum is different)*
   1. Quinolones
   2. Fluoroquinolones
2. Nitroimidazoles  
   *Free radical generation leads to DNA damage.  
   Two agents are seen: metronidazole, tinidazole (anti-protazoal rather than antibacterial)*
3. Rifamycins  
   *Bind to RNA polymerase, inhibiting transcription.  
   Examples include rifampicin, rifabutin, and rifaximin*

## Agents acting on protein synthesis

These all act on the ribosome in diverse ways, but these differences are not clinically relevant.

1. Macrolides: *erythromycin, clarithromycin*
2. Lincosamides: *clindamycin*
3. Glycopetides: *gentamicin, tobramycin, neomycin, amikacin*
4. Tetracyclines: *doxycycline, tetracycline, minocycline, oxytetracycline*

## Agents acting on folate synthesis

Two classes exist, both inhibiting different enzymes in the folate synthesis pathway:

1. Trimethoprim
2. Sulfonamides  
   *Sulfamethoxazole*

# Kinetic considerations

Some antibiotics can be classified by whether

# References