

# VANCOMYCIN



# OUTLINE

- History
- Introduction
- Mechanism of action
- Basis of selectivity
- Mechanisms of resistance
- Pharmacokinetics
- Clinical uses
- Adverse effects

# VANCOMYCIN: HISTORY

- From the organism *Amycolatopsis orientalis*
- Derived from the word “vanquish”
- The original indication – treatment of penicillin resistant *staph. aureus*

# VANCOMYCIN : INTRODUCTION

- Glycopeptide / Peptolide antibiotic

# VANCOMYCIN:

## MECHANISM OF ACTION 1/2

Inhibitor of cell wall synthesis

- Vancomycin binds with high affinity to a cell wall precursor unit: D-alanyl-D-alanine
- Prevents release of the building block for peptidoglycan synthesis
- BACTERIOCIDAL

Basis of selectivity

Eukaryotic cells do not have a peptidoglycan cell wall

# VANCOMYCIN: MECHANISM OF ACTION 2/2

## Mechanism of resistance

- Expression of a unique enzyme that modifies the D-alanyl-D-alanine precursor to prevent binding of vancomycin
- Plasmid transferable resistance in Enterococcal spp can be spread to other gram +ve organisms

# VANCOMYCIN: PHARMACOKINETICS

- Poorly absorbed after oral administration
  - Used to treat pseudomembranous colitis
- Use is intravenous, never im
- Widely distributed, including CSF
- 90% excreted by glomerular filtration
  - Must reduce dose with decreased GFR

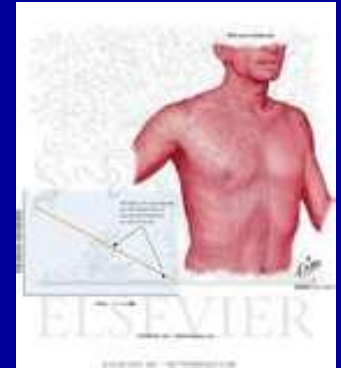
# VANCOMYCIN: CLINICAL USES

Main use against gram +ve cocci:

- Used where penicillin resistance is suspected e.g. severe pneumococcal pneumonia or meningitis, or proved e.g. MRSA
- In penicillin allergy for severe staphylococcal infection or *S.viridans* endocarditis
- Combined with aminoglycoside for enterococcal endocarditis



# VANCOMYCIN: ADVERSE EFFECTS



- Hypersensitivity reactions
  - Occasionally extreme maculopapular rash: 'red man syndrome'
- Ototoxicity and nephrotoxicity
  - Associated with excessively high plasma levels, so therapeutic drug monitoring is useful
  - **Avoid** co-administration with aminoglycosides

# CLINDAMYCIN



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# CLINDAMYCIN:INTRODUCTION

- Lincosamide antibiotic

# CLINDAMYCIN: MECHANISM OF ACTION 1/2

Suppresses protein synthesis by binding to the 50 S sub-unit of bacterial ribosomes

- Prevents elongation of the polypeptide chain
- Similar site of action to macrolides and chloramphenicol, though structurally unrelated

# CLINDAMYCIN: MECHANISM OF ACTION 2/2

## Basis of selectivity

- Prokaryotic cells have a 50 S ribosomal sub-unit; eukaryotes a 80 S sub-unit one

## Mechanism of resistance

- Methylation of the 50 S ribosome
- Transferable by plasmid

# CLINDAMYCIN: PHARMACOKINETICS

- Well absorbed orally, also iv & im
- Widely distributed including across the placenta, but not the meninges
- Metabolised in the liver to inactive metabolites



# CLINDAMYCIN: ADVERSE EFFECTS 1/2

High incidence of antibiotic induced diarrhoea (0.2 – 20 %)

- Pseudomembranous colitis caused by the toxin from *Clostridium difficile*
- Abdominal pain , fever, diarrhoea with blood & mucus

Can be fatal



# CLINDAMYCIN: ADVERSE EFFECTS 2/2

Treatment of pseudomembranous colitis

- Stop clindamycin
- Rehydrate
- Oral metronidazole or vancomycin

Hypersensitivity reactions: skin rashes,  
hepatitis

# CLINDAMYCIN: CLINICAL USES

Limited by adverse effects

- Wide spectrum against aerobic gram +ve cocci
- Less sensitive against anaerobic gram – ve cocci e.g. clostridial species
- Used in combination therapy against toxoplasma and pneumocystis

# FUSDIC ACID



# FUSIDIC ACID

- Mode of action
- Indications
- Adverse effects

# FUSIDIC ACID : MODE OF ACTION

- Protein synthesis inhibitor
- **Bacteriostatic**
- Acts on gr.(+) ve bacteria (staph., corynebacterium species)

# FUSIDIC ACID : INDICATIONS

- Staph. aureus infections (not used on it's own)
- Coagulase (-)ve staph
- MRSA (may need combination with rifampicin for serious infections)
- Corynebacterium
- Most clostridium species



# FUSIDIC ACID : ADVERSE EFFECTS

- Jaundice
- Nausea , vomiting, diarrhoea
- Phlebitis (I.V.preperations)