Other β-lactam Antibiotics & Other Inhibitors of the Bacterial Cell Wall Synthesis

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Carbapenems
Imipenem
Meropenem
Ertapenem

- Are synthetic β -lactam antibiotics, differ in structure from the penicillins (the sulfur atom of the thiazolidine ring has been externalized and replaced by a carbon atom).
- Imipenem is compounded with cilastatin to protect it from metabolism by renal dehydropeptidase.

- Meropenem has antibacterial activity similar to that of imipenem
- Imipenem & meropenem are the broadest-spectrum β-Lactam antibiotic preparations currently available.
- Imipenem resists hydrolysis by most β- lactamases & it is active against penicillinaseproducing gram-positive and gram-negative organisms, anaerobes, and Pseudomonas aeruginosa.

Pharmacokinetics of Carbapenems

- Imipenem and meropenem are administered IV, penetrate well into CSF when the meninges are inflamed & excreted by glomerular filtration.
- Imipenem undergoes cleavage by a dehydropeptidase found in the proximal renal tubule &lead to formation of inactive nephrotoxic metabolite ,so compounding the imipenem with cilastatin prevents the formation of the toxic metabolite& allows the drug to be used in the treatment of urinary tract infections.
- Meropenem does not undergo metabolism.
- Ertapenem can be administered via IV or IM injection

Note: Doses of these agents must be adjusted in patients with renal insufficiency.

Adverse Effects of Carbapenems

1. Nausea, vomiting, and diarrhea (Imipenem/cilastatin).
2. Neutropenia are less common than with other β -lactams.
3. Seizures (with high levels of imipenem)

Monobactams

Aztreonam

- Has antimicrobial activity against the enterobacteriaceae & also acts against aerobic gram-negative rods, including P. aeruginosa.
- Its narrow antimicrobial spectrum prevents its use alone in empiric therapy
- Aztreonam is resistant to the action of β - lactamases.
- It is safe alternative for treating patients who are allergic to penicillins and/or cephalosporins

Pharmacokinetics of Monobactams

- It is administered IV or IM
- Excreted in the urine

Adverse Effects of Monobactams

1. Phlebitis, skin rash
2. Abnormal liver function tests.
3. Accumulate in patients with renal failure.

Other Inhibitors of the Bacterial Cell Wall Synthesis

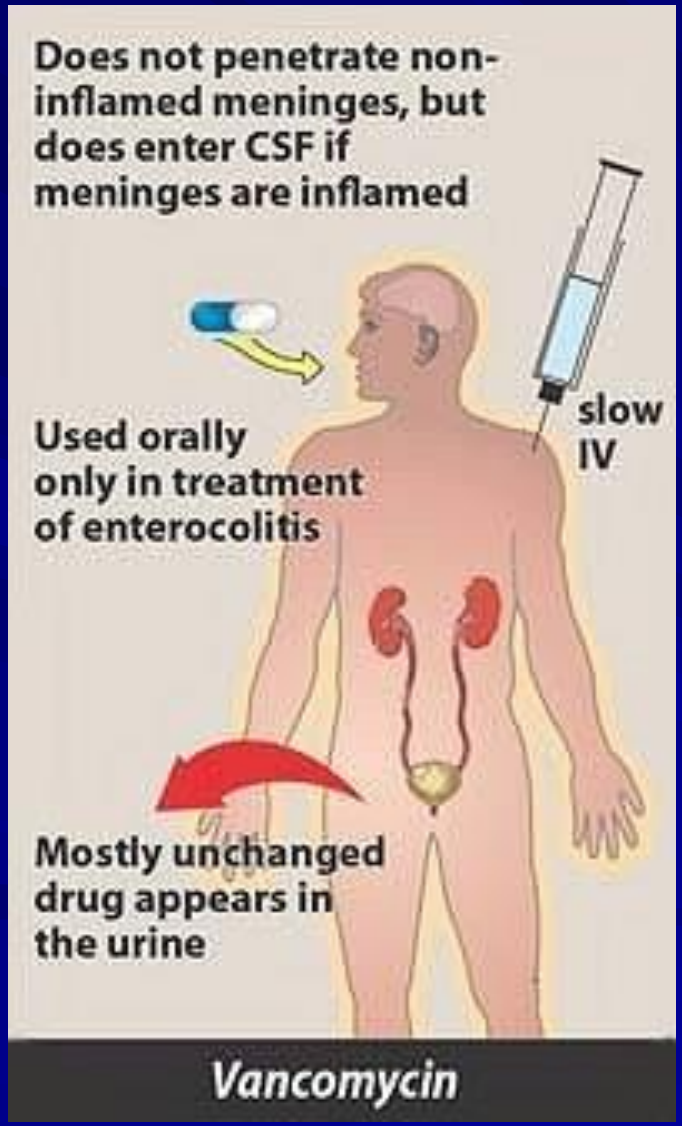
Vancomycin

- Inhibits synthesis of bacterial cell wall phospholipids & peptidoglycan polymerization, lead to weakening of the cell wall and damaging the underlying cell membrane
- Vancomycin is effective primarily against gram-positive organisms, MRSA and enterococci

Oral Vancomycin

Is limited to treatment for potentially life-threatening antibiotic-associated colitis due to C. difficile or staphylococci.

Administration and Fate of Vancomycin



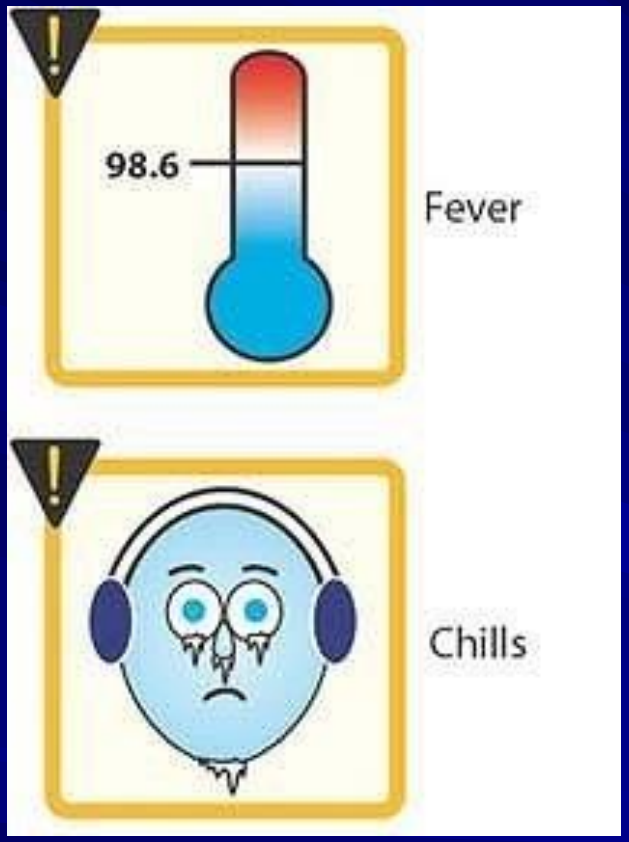
Adverse Effects of With Vancomycin

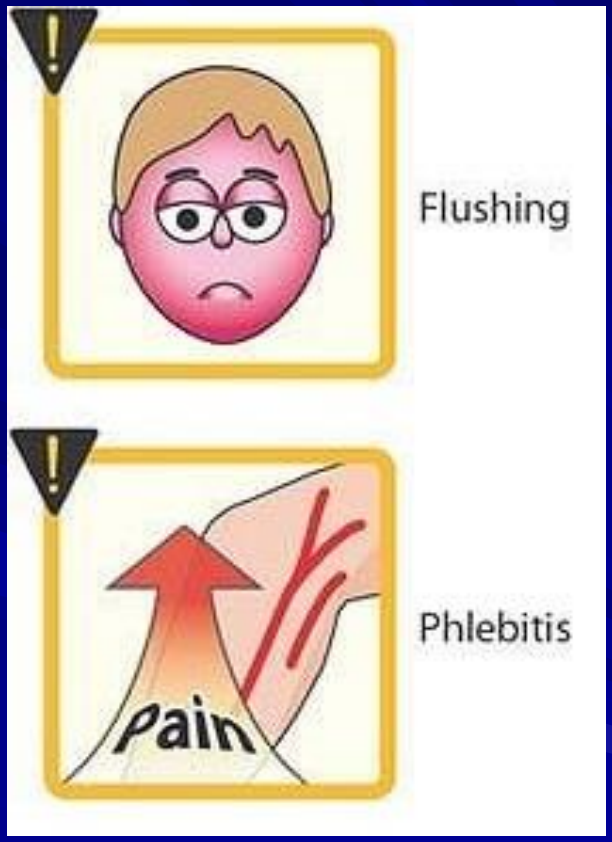
1. Infusion-related reaction :fever, chills
   Flushing (red man syndrome) and shock results from histamine release associated with a rapid infusion
2. phlebitis at the infusion site

Note: If an infusion-related reaction occurs, slow the infusion rate to administer vancomycin over 2 hours, increase the dilution volume, or pretreat with an antihistamine 1 hour prior to administration. Additionally, reactions can be treated with antihistamines and steroids

3. Ototoxicity and nephrotoxicity
   - Hearing loss (Dose-related) has occurred in patients with renal failure
   - Ototoxicity and nephrotoxicity are more common when vancomycin is administered with another drug (for example, an aminoglycoside)

Some Adverse Effects of Vancomycin





Bacitracin

- Its inhibits bacterial cell wall synthesis.
- It is active against a wide variety of gram-positive organisms.
- Only used topically (because of nephrotoxicity)