

The Penicillins

■ Ampicillin:

- Broad-spectrum penicillin, can cause diarrhea, due to overgrowth of normal flora, and incomplete absorption.
- Frequently administered with a β -lactamase inhibitor

The Penicillins

■ Amoxicillin:

- Same, but more completely absorbed than ampicillin.
- So, less diarrhea, and longer acting than ampicillin.

■ Azlocillin, Piperacillin, and Ticarcillin: Have extended spectrum, e.g. Proteus, Pseudomonas, Klebsiella, and certain other gram-negative microorganisms

The Penicillins

■ Adverse Effects:

Relativley very safe drugs; except:

- Pain of injection.
- Abscess formation.
- Allergic reactions:
 - Skin rash.
 - Urticaria.
 - Anaphylaxis.
 - rash,
 - fever, bronchospasm,
 - dermatitis, Stevens–Johnson syndrome

Anaphylaxis is a serious allergic reaction that is rapid in onset and may cause death.

Stevens–Johnson syndrome, a form of toxic epidermal necrolysis, is a life-threatening skin condition, in which cell death causes the epidermis to separate from the dermis.

Management of the Patient Potentially Allergic to Penicillin.

Evaluation of the patient's history is the most practical way.

Most patients who give a history of allergy to penicillin should be treated with a different type of antibiotic

Antistaphylococcal (penicillinaseresistant) Penicillins

- including Nafcillin, oxacillin, cloxacillin, and dicloxacillin which are more resistant to bacterial B-lactamases than is penicillin G.
- Consequently, these antibiotics are effective against for MRSA and methicillin-resistant *Staphylococcus epidermidis* (MRSE).

Methicillin, is no longer marketed in the United States, is another penicillinase-resistant antibiotic similar to nafcillin and oxacillin.

- Many hospitals are reservoirs for MRSA and methicillin-resistant *Staphylococcus epidermidis* (MRSE). These pathogens are resistant in vitro to all B-lactam antibiotics.
- For parenteral therapy, nafcillin and oxacillin offer comparable efficacy and antimicrobial spectra of activity.
- Indications for nafcillin or oxacillin include severe staphylococcal infections like cellulitis, empyema, endocarditis, osteomyelitis, pneumonia, septic arthritis, and toxic shock syndrome

B-Lactamase Inhibitor Combinations

Several formulations combine a B-lactam antibiotic with a B-lactamase inhibitor such as

- (ampicillin-sulbactam [Unasyn],
- ticarcillin-clavulanic acid [Timentin],
- piperacillin-tazobactam [Zosyn],
- and amoxicillin–clavulanic acid [Augmentin]).

All of the B-lactamase inhibitor combinations except amoxicillin-clavulanic acid are parenteral formulations.

- Elimination of the combination drugs occurs primarily by renal excretion.

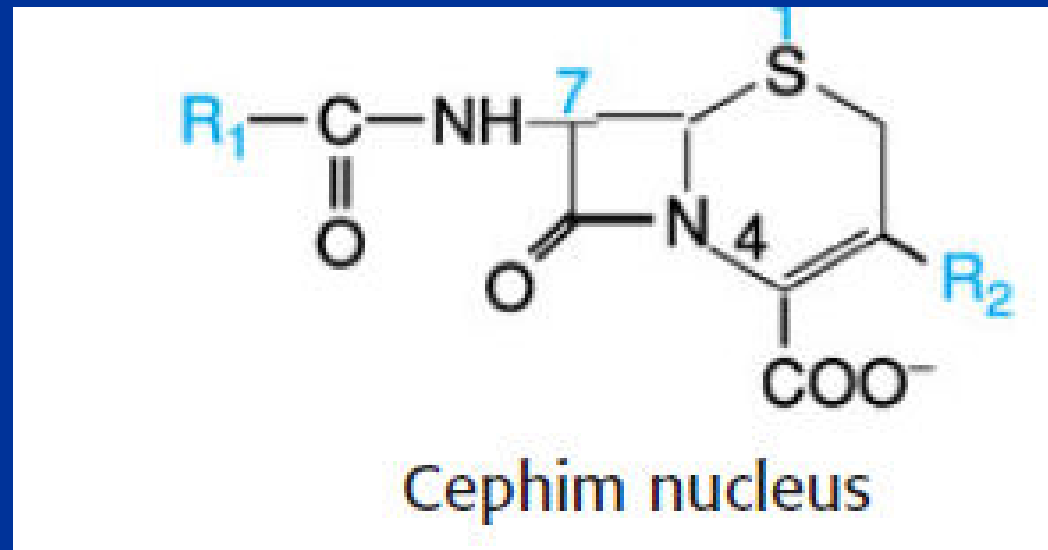
- all of the B-lactamase inhibitor combinations require dose adjustments in patients with renal insufficiency.
- The addition of the B- lactamase inhibitor significantly broadens the spectrum of antibacterial activity against B-lactamase-producing organisms.
- Consequently, these drugs have clinical use in treating infections with known or suspected mixed bacterial flora, such as biliary infections, diabetic foot ulcers, endomyometritis, and peritonitis.

- Gram-positive bacteria are bacteria that give a positive result in the Gram stain test. They then appear to be purple-coloured. This is because the thick peptidoglycan layer in the bacterial cell wall retains the stain after it is washed away from the rest of the sample.
- Gram-negative bacteria cannot retain the violet stain after the decolorization step; Their peptidoglycan layer is much thinner and sandwiched between an inner cell membrane and a bacterial outer membrane, causing them to take up the counterstain and appear red or pink.

The Cephalosporins

- Came one decade later after the penicillins.
- Rarely the drugs of first choice for any infection.
- Mainly used for surgical prophylaxis.
- Expensive, especially the newer generations.
- Same toxicity as penicillins.
- Cross allergic with the penicillins.
- Activity differs among the generations.

The generations differ in modifications in the R1 and R2 groups and is based on general features of antimicrobial activity



The Cephalosporins

■ **First Generation:** good activity against gram-positive bacteria and relatively modest activity against gram negative microorganisms.

- **Cephalothin**

- **Cefazolin**

The Cephalosporins

■ Second Generation:

somewhat increased activity
against gram-negative
microorganisms

■ Cefamandole.

■ Cefoxitine.

The Cephalosporins

- **Third Generation:** more active against the Enterobacteriaceae, including β -lactamase-producing strains
 - Cefoperazone.
 - Cefotaxime.
 - Ceftriaxone.

The Cephalosporins

- Fourth-generation extended spectrum of activity and stability from hydrolysis

- Cefepime