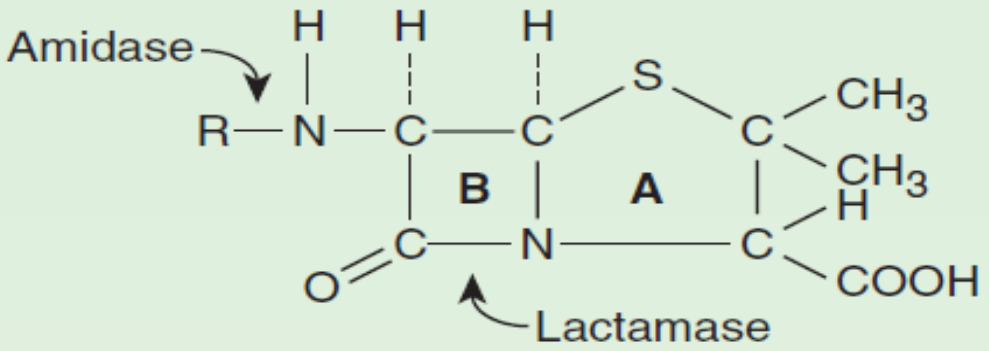
MONOBACTAMS AND CARBAPENEMS

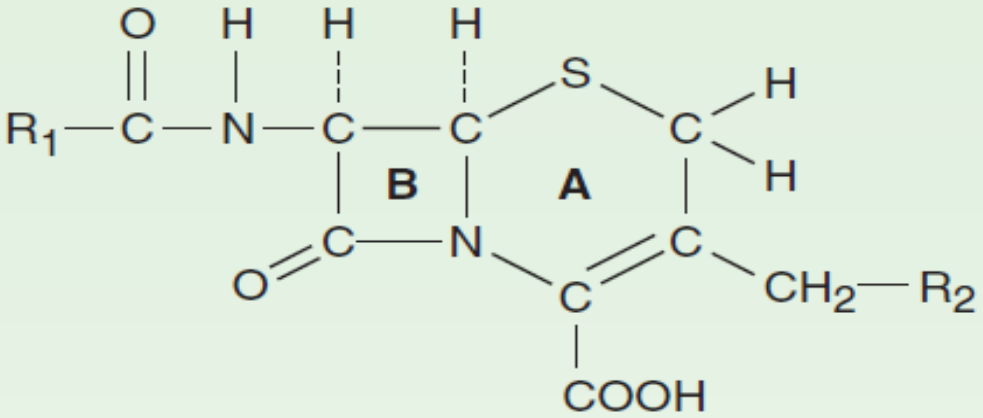
β Lactam Antibiotics

- Penicillins
- Cephalosporins
- Monobactams
- Carbapenems



Penicillin

Substituted 6-aminopenicillanic acid



Cephalosporin

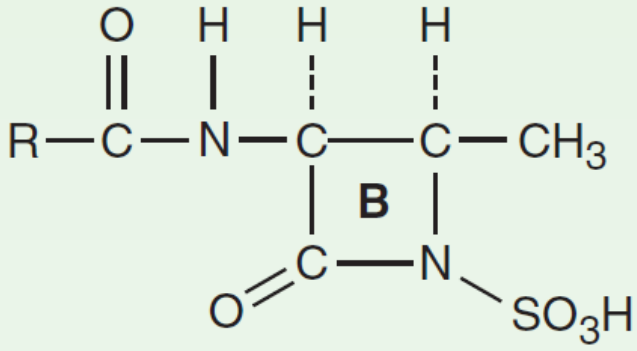
Substituted 7-aminocephalosporanic acid

MONOBACTAMS

- Monocyclic β lactam antibiotic → ∴ monobactam

- **AZTREONAM**
- **TIGEMONAM**
- **CARUMONAM**

- MOA → Binds to specific PBP → inhibits cell wall synthesis
- **Bactericidal**



Monobactam

Substituted 3-amino-4-methylmonobactamic acid
(aztreonam)

- **No cross sensitivity with other β lactam antibiotics**

→ useful in patients allergic to penicillins or cephalosporins (except Ceftazidime)

Spectrum

- **Aerobic gram –ve bacteria**
- **No activity against gram +ve bacteria or anaerobes**

- Resistant to many β lactamases except extended spectrum β lactamases

≈ AG → ∴ preferred for gram –ve infns where AG are C/I

PK

- Oral BA poor → **IM /IV**
- **Inhalational** Aztreonam –P. aeruginosa infection in Cystic fibrosis

- Achieves therapeutic conc. in CSF in the presence of inflamed meninges → alternative to cephalosporins in the Rx of meningitis caused by gram –ve bacilli

- Excreted in the urine

Adverse effects

Skin rashes

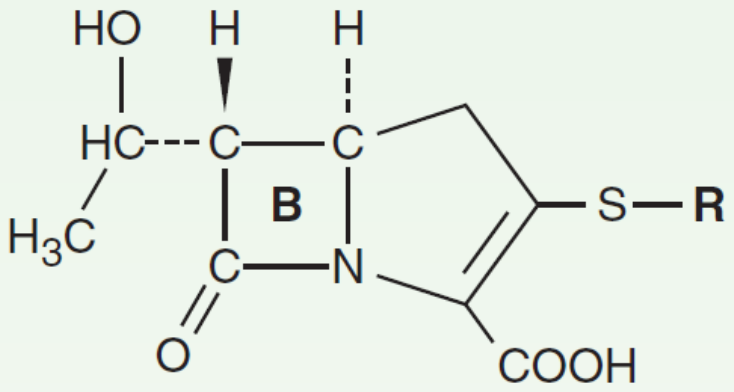
Rise in serum Amino transferases

AZTREONAM

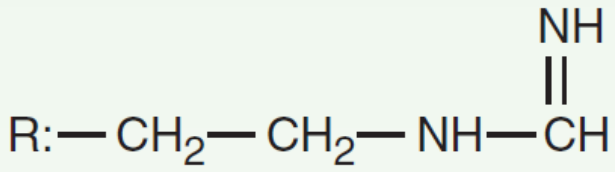
- **Aerobic gram –ve bacteria**
- ≈ AG → ∴ preferred for gram –ve infns where AG are C/I
- **No cross sensitivity with other β lactam antibiotics → useful in patients allergic to penicillins or cephalosporins**

CARBAPENEMS

CARBAPENEMS



Carbapenem



Substituted 3-hydroxyethylcarbapenemic acid (imipenem)

- **Broader spectrum of activity**

- **MOA** - binds to PBPs → disrupts bacterial cell wall synthesis → bacterial death
- **Bactericidal**

- Resistant to hydrolysis by most β lactamases except Carbapenemases or metallo-β-lactamases

Imipenem
Meropenem
Doripenem
Ertapenem
Faropenem
Razupenem

IMIPENEM

- Spectrum

:wide spectrum with good activity against many **gram-negative rods**, including P.aeruginosa, **gram-positive organisms** and **anaerobes**

- **Enterococcus faecium, MRSA, C.difficile,Corynbacterium are resistant**

Gram (+) cocci

- Staph. aureus*
- Enterococcus faecalis
- S. pneumoniae

Gram (–) cocci

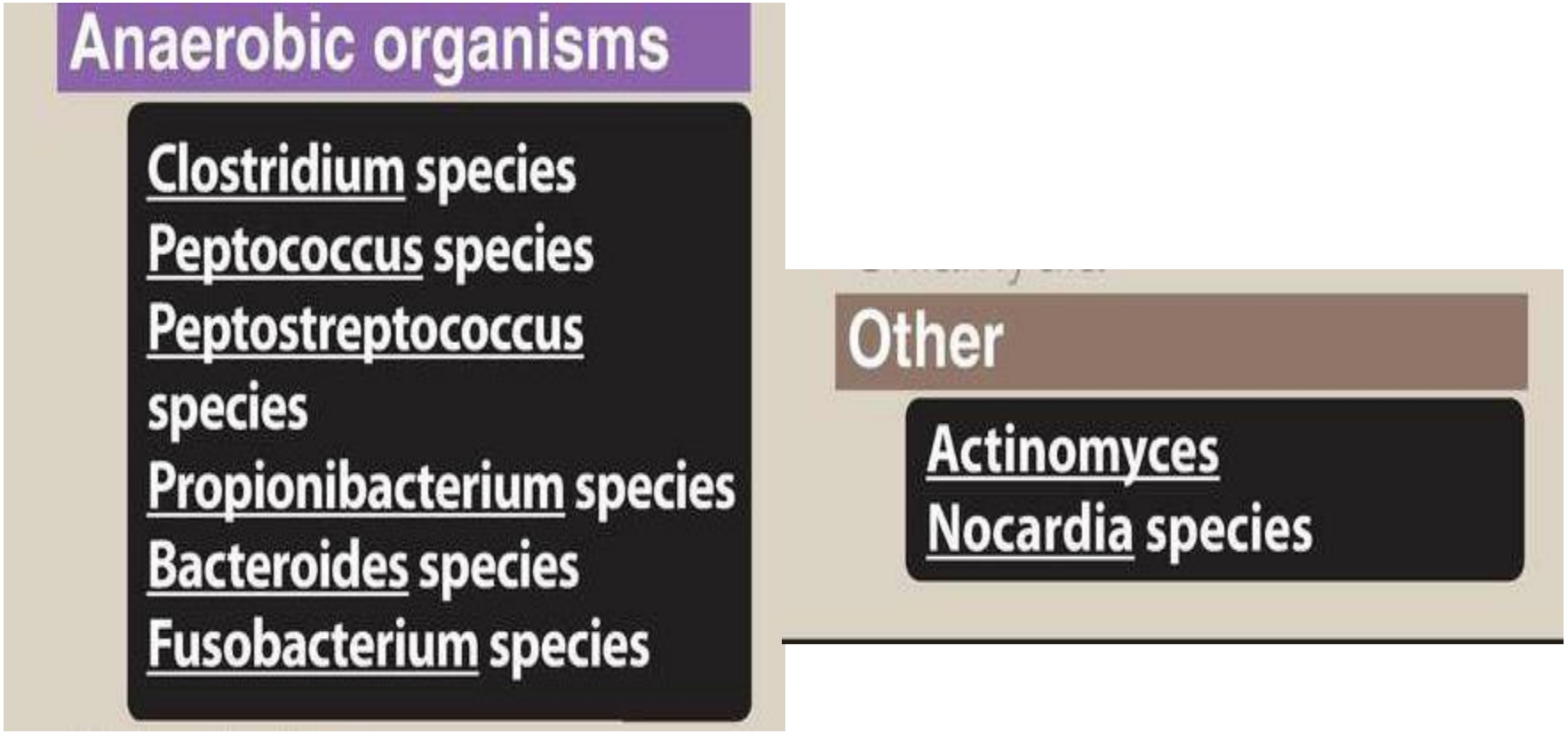
- N. gonorrhoeae
- N. meningitidis

Gram (–) rods

- Acinetobacter
- Enterobacter
- E. coli
- Gardnella vaginalis
- H. influenzae
- Klebsiella
- Proteus
- Pseudomonas aeruginosa
- Salmonella
- Serratia

Gram (+) bacilli

- Listeria monocytogenes

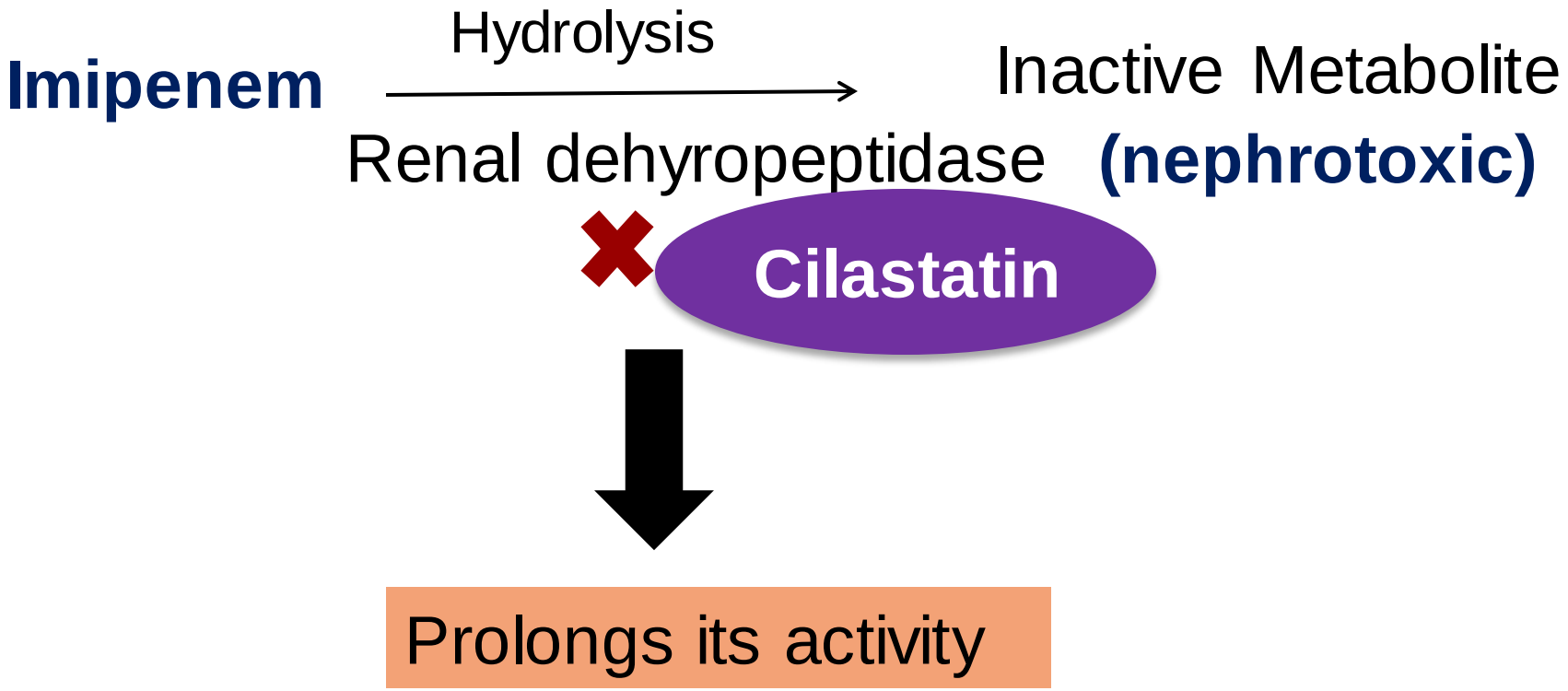

Anaerobic organisms
Clostridium species
Peptococcus species
Peptostreptococcus species
Propionibacterium species
Bacteroides species
Fusobacterium species
Other
Actinomyces
Nocardia species

PK

- Not absorbed orally ,Given iv/im→IV preferred
- Faropenem can be given orally

- Excretion – renal - dose adjustment needed in renal insufficiency

Rationale of combining imipenem with cilastatin



Ertapenem,Doripenem and Meropenem are not degraded by renal dehydropeptidases.

Adverse effects

Imipenem

- **Nausea , vomiting**
- **Diarrhoea**
- **Skin rash**
- **Seizures at higher doses**

Meropenem,Ertapenem & Doripenem donot cause seizures & are safer than Imipenem

- Patients who are allergic to other beta-lactam antibiotics- hypersensitivity reactions

Uses

- **Severe RTI, UTI**
- **Meningitis**
- **Skin & soft tissue infections**
- **Bone & joint infections**
- **Abd & gynecological sepsis with MDR org**
- **Serious hospital acquired infection in Neutropenics**
- **MDR infections in Cancer & AIDS patients**

Doripenem : more active against pseudomonas

- **Should not be used as monotherapy for pseudomonas infns : risk of developing resistance during therapy**

A carbapenem is indicated for infections caused by susceptible organisms that are resistant to other available drugs, eg, P aeruginosa , and for treatment of mixed aerobic and anaerobic infections.

	Imipenem	Meropenem / doripenem	Ertapenem
Spectrum	Gram neg rods, gram +ve organisms, anerobes	More potent on gram neg aerobes	Less active against Pseudomonas & Acinetobacter
Hydrolysis by renal peptidase	+	-	-
Cilastatin	+	-	-
Seizures	+++	+	+

Carbapenems

- β-lactam antibiotics with broader spectrum of activity
- Coadministration with Cilastatin – Imipenem
- Reserve drugs

Previous questions

- Rationale of combining cilastatin with imipenem
- Useful spectrum of Aztreonam

Previous questions

- Enumerate the antibiotics which act by inhibiting cell wall synthesis. Mention the detailed MOA of any one of them on bacterial cell wall synthesis. Add a note on beta lactamase inhibitors

- Classify cephalosporins. Describe the MOA and uses of ceftriaxone.

- Classify cephalosporins. Mention the mechanism of action, adverse effects and uses of third generation cephalosporin.

- Classify beta lactam antibiotics. Explain the mechanism of action, uses and adverse effects of ceftriaxone.

- 2nd generation cephalosporins & uses.

Two drugs

- Burns infected with pseudomonas
- Typhoid fever
- 4th generation cephalosporins
- Drugs effective against both gram positive & gram negative organisms

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- Mention different group of penicillins with examples
- Explain mechanism of action
- Describe uses and adverse effects of Amoxycillin(5+3+4+3)