

Penicillins

Introduction

- Penicillins are β -lactam antibiotics, among the earliest discovered and widely used antimicrobial agents.
- They are bactericidal, meaning they kill bacteria by inhibiting cell wall synthesis.
- Penicillins are especially effective against gram-positive bacteria and have been extensively used in the treatment of various bacterial infections.
- They are generally safe, but resistance, especially due to β -lactamase (penicillinase) production by bacteria, is a significant challenge in clinical use.

Classification of Penicillins



Natural Penicillins



Penicillinase-Resistant



Aminopenicillins



Extended-Spectrum



β -lactamase Inhibitors

A. Natural Penicillins

- **Penicillin G (Benzylpenicillin)** – given parenterally
- **Penicillin V (Phenoxymethylpenicillin)** – given orally

B. Penicillinase-Resistant Penicillins (Anti-staphylococcal)

- Methicillin (no longer used clinically due to toxicity)
- Nafcillin
- Oxacillin
- Cloxacillin
- Dicloxacillin

C. Aminopenicillins (Broad-spectrum)

- Ampicillin
- Amoxicillin

D. Extended-Spectrum Penicillins (Anti-pseudomonal)

- **Carboxypenicillins:** Carbenicillin, Ticarcillin
- **Ureidopenicillins:** Piperacillin, Azlocillin

E. β -lactamase Inhibitor Combinations

- Used to overcome resistance caused by β -lactamase enzymes:

- Amoxicillin + Clavulanic acid
- Ampicillin + Sulbactam
- Piperacillin + Tazobactam
- Ticarcillin + Clavulanic acid

Mechanism of Action

- Penicillins inhibit bacterial cell wall synthesis by:
 - Binding to **Penicillin-Binding Proteins (PBPs)** on the bacterial cell membrane
 - Blocking the **transpeptidation reaction** that links peptidoglycan chains
 - Leading to **weakening of the cell wall**, cell lysis, and bacterial death
- This action is bactericidal and time-dependent.

Pharmacokinetics (ADME)

Absorption:

- **Penicillin G:** Poor oral absorption; given IM or IV
- **Penicillin V, Amoxicillin:** Well absorbed orally
- Food interferes with absorption of some penicillins (e.g., ampicillin)

Distribution:

- Widely distributed in body fluids
- Poor penetration into CSF unless meninges are inflamed
- Crosses placenta (but not teratogenic)

Metabolism:

- Minimal hepatic metabolism for most penicillins

Excretion:

- Primarily excreted unchanged by the kidneys via tubular secretion
- Dose adjustment needed in renal impairment
- Nafcillin and oxacillin are excreted mainly in bile

Pharmacodynamics

- **Time-dependent killing:** Efficacy depends on duration the drug concentration remains above MIC (minimum inhibitory concentration)
- **Bactericidal action**
- Selective toxicity due to absence of peptidoglycan cell wall in human cells

Spectrum of Activity

Natural Penicillins:

- Gram-positive cocci: *Streptococcus pyogenes*, *S. pneumoniae*
- Gram-negative cocci: *Neisseria meningitidis*
- Anaerobes: *Clostridium spp.*, *Actinomyces*
- Spirochetes: *Treponema pallidum* (syphilis)

Penicillinase-Resistant Penicillins:

- Effective against penicillinase-producing *Staphylococcus aureus*

Aminopenicillins:

- Broader spectrum: Includes some gram-negative bacteria like *E. coli*, *H. influenzae*, *Salmonella*, *Shigella*

Anti-pseudomonal Penicillins:

- Active against *Pseudomonas aeruginosa*, *Klebsiella*, and other gram-negative rods

Adverse Effects

1. Hypersensitivity Reactions

- Rash, urticaria
- Anaphylaxis (rare but life-threatening)
- Serum sickness, drug fever

2. Gastrointestinal Effects

- Diarrhea, especially with ampicillin
- Nausea, vomiting

3. Neurotoxicity

- High doses can cause seizures, especially in renal impairment

4. Hematologic Effects

- Hemolytic anemia, neutropenia (rare)

5. Electrolyte Imbalance

- High-dose penicillin G (sodium salt) may cause hypernatremia, hypokalemia

6. Jarisch-Herxheimer Reaction

- Seen in syphilis treatment: acute febrile reaction due to rapid lysis of spirochetes

Contraindications

- Known allergy to penicillins (cross-reactivity with cephalosporins ~5–10%)
- Caution in patients with renal impairment – dose adjustment required

- Avoid methicillin (not used clinically due to nephrotoxicity and interstitial nephritis)

Drug Interactions

- **Probenecid:** Inhibits renal excretion, increases penicillin levels
- **Oral contraceptives:** May reduce effectiveness (controversial, but caution advised)
- **Aminoglycosides:** Synergistic when used together against enterococci or *Pseudomonas* (must be given separately due to inactivation in mixture)
- **Methotrexate:** Toxicity increased due to reduced renal clearance

Therapeutic Uses

Penicillin G and V

- Streptococcal infections (pharyngitis, endocarditis)
- Syphilis (*T. pallidum*)
- Meningococcal infections
- Clostridial infections (tetanus, gas gangrene)

Penicillinase-resistant Penicillins

- Mild to moderate *Staphylococcus aureus* infections (excluding MRSA)

Aminopenicillins

- Respiratory tract infections (*S. pneumoniae*, *H. influenzae*)
- UTIs
- Enteric infections (*Salmonella*, *Shigella*)
- *Listeria monocytogenes* (especially ampicillin)

Anti-pseudomonal Penicillins

- Nosocomial infections caused by *P. aeruginosa*, *Klebsiella*, etc.
- Often used in combination with β -lactamase inhibitors

Dose and Route of Administration

Drug	Route	Dose
Penicillin G	IM or IV	2–4 million units IV every 4–6 hours
Penicillin V	Oral	250–500 mg every 6–8 hours
Amoxicillin	Oral	250–500 mg every 8 hours or 875 mg twice daily
Ampicillin	Oral	250–500 mg every 6 hours
	IV	1–2 g every 4–6 hours
Piperacillin + Tazobactam	IV only	3.375–4.5 g IV every 6–8 hours

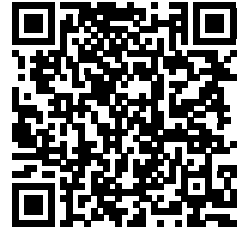


FREE PREVIEW

[Click here to visit our website](#)

PHARMACY PREMIUM NOTES

Complete subject
and semesters are
available on
FirstHope app only.



[Scan or click here](#)

Click here to get the app



Available on Google Play

JOIN THE FIRSTHOPE COMMUNITY

Join our Telegram channel

Click here to join Telegram



[Scan or click here](#)

@FirstHopeNotes

Instagram

@firsthope.official

[Click here to follow >](#)

YouTube channel

FirstHope-Pharmacy / Live streams

[Click here to watch >](#)

WhatsApp channel

Follow FirstHope on WhatsApp

[Click here to join >](#)

FirstHope website

firsthopenotes.com

[Click here to visit >](#)

B.Pharm / D.Pharm / M.Pharm / Pharm.D

Preview notes. Complete subjects and semesters in the FirstHope app.