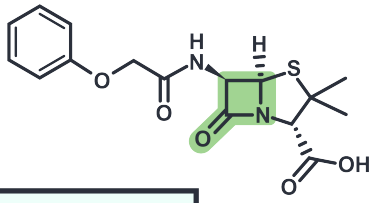
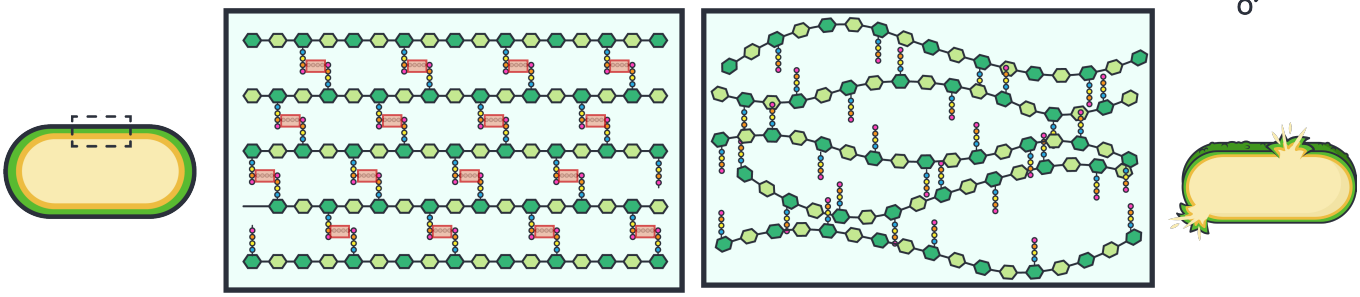
TOPIC: INHIBITORS OF CELL WALL SYNTHESIS: BETA-LACTAM & PENICILLIN

Beta-lactam Drugs



- **Beta-lactams:** bactericidal drugs that disrupt cell walls; contain a **β-lactam** ring;
- β-lactams include _____, cephalosporins, carbapenems, & monobactams.
- *Recall*: Peptidoglycan is main component of bacterial cell _____.



- β-lactams block the _____ that _____ NAM subunits.
  - As cell grows, cell walls become _____: causes cell lysis.

PRACTICE

What do all β-lactam drugs have in common?

a) They are all produced by (or derived from molecules produced by) *Penicillium* mold.
b) They all contain a β-lactam tail that is able to insert into and disrupt bacterial cell walls.
c) They all block the elongation of peptidoglycan strands, blocking the growth of bacterial cell walls.
d) They all contain a β-lactam ring structure, consisting of a ring of three carbon atoms and one nitrogen atom.

PRACTICE

Are β-Lactam drugs bactericidal or bacteriostatic? And why?

a) They are bactericidal because the lack of cross-links between NAM subunits makes the cell membrane less stable.
b) They are bactericidal because they disrupt the cell wall, leading to cell lysis due to osmotic pressure.
c) They are bacteriostatic because they prevent crosslinking between peptidoglycan strands, meaning the cell wall cannot grow.
d) They are bacteriostatic because the cross-links that are created between NAM subunits inhibit the growth of the cell wall.

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Natural Penicillins

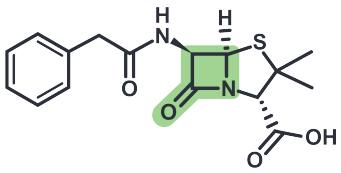
◆ **Penicillins:** group of related antibiotics (end in "-cillin") that contain a β-lactam ring → disrupt _____ _____.

- Natural penicillin: produced by *Penicillium* _____.

Penicillin ___: first antibiotic widely used.

- _____ by stomach acid

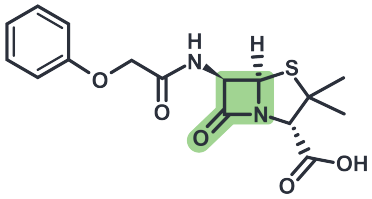
  → must be used intravenously.



Penicillin ___:

- ___ destroyed by stomach acid

  → can be taken _____.



◆ Weaknesses of natural penicillins:

- _____ spectrum: Gram ⊕ _____ Gram ⊖ _____
- Resistance is common: beta-lactam___ (penicillinase) _____ beta-lactam ring.

EXAMPLE

Which of the following patients would be a candidate for a penicillin G prescription?

1	A patient with a Gram-positive bacterial infection in their stomach lining:	_____
2	A patient with meningitis, a bacterial infection in the membranes of the brain & spinal cord caused by Gram-negative bacteria:	_____
3	A patient with strep throat, a Gram-positive infection that should be treated with drugs taken orally:	_____
4	A patient with gonorrhea, caused by a bacterial strain that produces β-lactamase:	_____
5	A patient with a Gram-positive bacterial infection in their blood:	_____

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PRACTICE

Which of the following is a major shortcoming of penicillin V and penicillin G?

a) They are only effective against Gram-negative bacteria.

b) They are susceptible to common enzymes (i.e., β-lactamase) that can inhibit them.

c) As large molecules, they cannot cross most membranes to reach the bacterial ribosomes.

d) As synthetic antibiotics, they are expensive to produce.

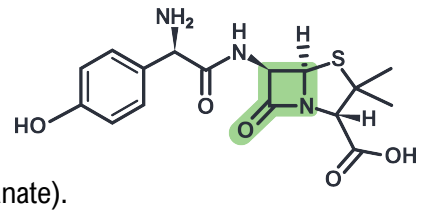
Semisynthetic Penicillins

◆ **Semisynthetic Penicillin:** chemically modified to give _____ spectrum ___ β-lactamase resistance.

_____ **Spectrum Penicillins** Gram⊕ ____ Gram⊖ ____ → ____ β-lactamase resistant.

Ampicillin & **Amoxicillin:**

- Chemically modified to pass through Gram ____ outer membrane.
- Often given with a beta-lactam___ inhibitor (e.g. clavulanate).



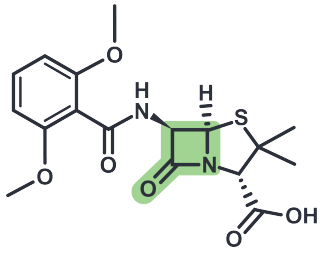
β-lactamase _____ **Penicillins**→ _____ Spectrum Gram⊕ ____ Gram⊖ ____

Methicillin:

- Use discontinued due to other resistance.
  - MRSA: _____ Resistant *S. aureus*.

Oxacillin:

- Used against beta-lactamase-producing bacteria.



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EXAMPLE

Match the following penicillin-type antibiotics with their description:

1	Narrow-spectrum drug that can be given to combat penicillinase resistant bacteria:	____
2	Effective against Gram-negative bacteria; often given alongside β-lactamase inhibitor:	____
3	Natural penicillin that is destroyed by stomach acid; must be taken intravenously:	____
4	β-lactamase-resistant, but now discontinued due to widespread resistance by other mechanisms:	____

Penicillins

a) Amoxicillin
b) Methicillin
c) Oxacillin
d) Penicillin G

PRACTICE

Amoxicillin is often prescribed as a combination drug that includes clavulanic acid. Clavulanic acid is a small molecule that contains a beta-lactam ring. Based on your knowledge, which mechanism below could best explain how clavulanic acid works synergistically with amoxicillin?

a) Clavulanic acid allows amoxicillin to enter the Gram-negative outer membrane, giving it a broader spectrum.
b) Clavulanic acid is a beta-lactamase enzyme, allowing the beta-lactam ring to be cleaved more easily.
c) Clavulanic acid binds to the active site of beta-lactamase, and in doing so, deactivates the enzyme.
d) Clavulanic acid also binds to the peptidoglycan cell wall, increasing the toxicity of both drugs.

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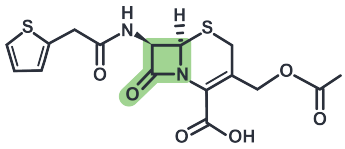
Other Beta-lactam Antibiotics

◆ Some classes of antibiotics contain β-lactam ring but are _____ different than penicillin.

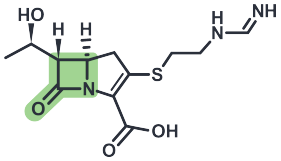
Cephalosporins: start with "ceph" or "cef" (e.g. cefalotin).

- _____ spectrum. Gram ⊕ ____ Gram ⊖ ____
- Many generations increasing spectrum.
- ____ generation used against MRSA.



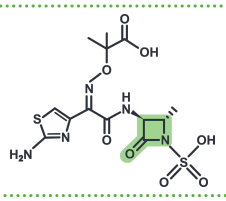
Carbapenems: end in "enem" (e.g. impenem).

- Very broad spectrum. Gram ⊕ ____ Gram ⊖ ____
- Reserved for _____ resistant infections.



Monobactams: (e.g. aztreonam).

- β-lactam ring is a _____ ring structure.
- _____ spectrum. Gram ⊕ ____ Gram ⊖ ____



EXAMPLE

For each statement below, write "T" if the statement is true and write "F" if the statement is false. On the line below, correct each false statement.

1	Monobactams contain a single ring in their β-lactam structure: _____ _____
2	All narrow-spectrum β-lactam antibiotics are effective against gram-positive bacteria, but not gram-negative. _____ _____
3	Cephalosporins are reserved for multidrug resistant infections: _____ _____
4	Carbapenems are considered fist-line of defense drugs because they are so broad spectrum: _____ _____

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PRACTICE

Why are carbapenems typically reserved for severe, multi-drug-resistant infections, instead of being used as first-line antibiotics?

a) Carbapenems are completely synthetic and therefore cause more side effects than natural antimicrobials.

b) Carbapenems are extremely narrow-spectrum, so they are only used against very specific bacterial strains.

c) Carbapenems are difficult to produce, so they are only available in limited amounts.

d) Overuse of carbapenems could promote widespread resistance.

PRACTICE

Based on your knowledge of beta-lactam drugs, which of the following antibiotics likely has the broadest spectrum?

a) Cephalexin, a first generation cephalosporin. b) Meropenem. c) Oxacillin. d) Aztreonam.