



General Microbiology Course

Lecture 8

(Antibiotics)

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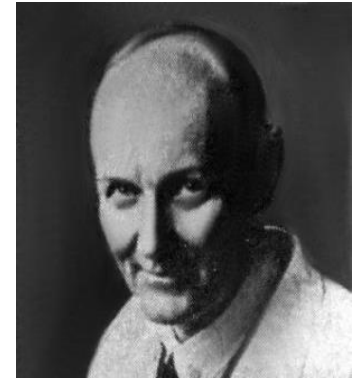
Faculty of Medicine, Mutah University

Objectives

- **Some history highlights**
- **Structure of Gram positive and negative bacteria cell wall**
- **Targets of the antibacterial drugs**
- **Mechanisms of action of antibacterial drugs**
- **The mechanisms of antibacterial resistance**

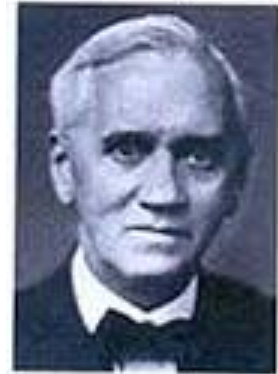
Discovery of Antimicrobial Agents

- **Dr. Gerhard Domagk**, a German chemist who **discovered** that the dye **prontosil was effective against a wide range of bacteria**.
- Sulfanilamide portion of the prontosil molecule is responsible for its antibacterial effect (sulfonamides = **sulfa drugs**).
- Won the 1939, Nobel Prize in Medicine.



Discovery of Antimicrobial Agents

Antibacterial agents which inhibit bacterial cell wall synthesis was discovered by Fleming from a fungal colony (1928)



Sir Alexander
Fleming

The product of the mold was named penicillin, after the *Penicillium* mold from which it was derived

Isolated and purified by Florey and Chain (1938)



Ernst Boris Chain



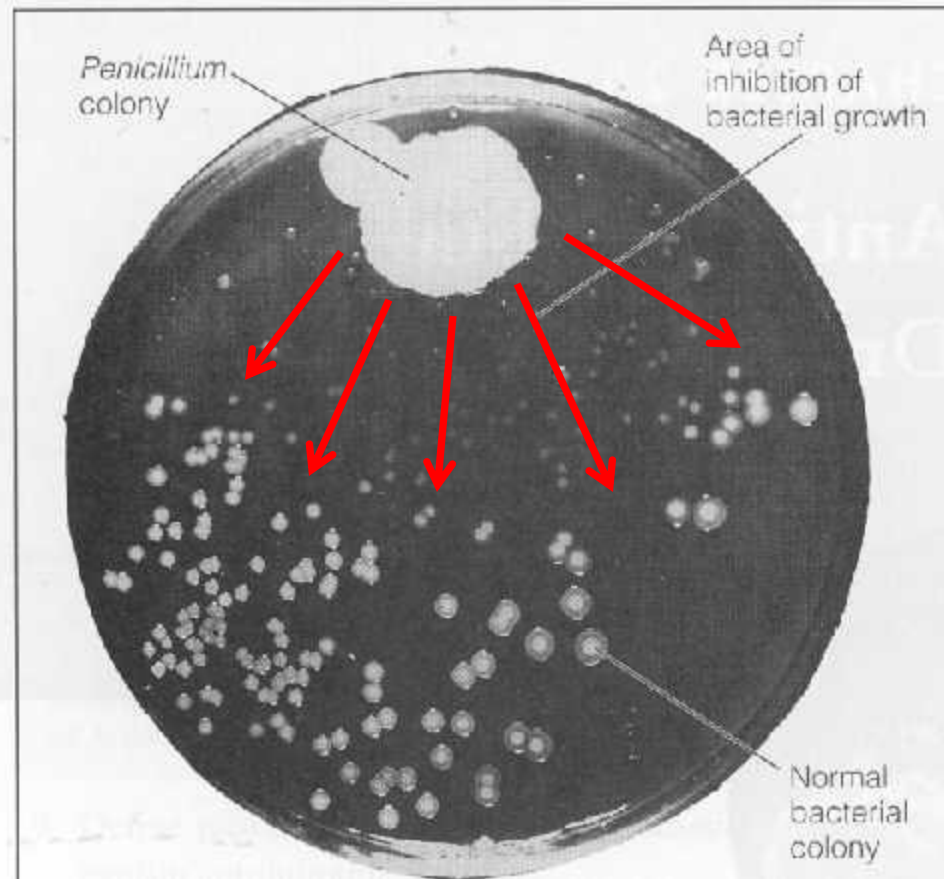
Sir Howard
Walter Florey

First successful clinical trial (1941)

Development of semi-synthetic penicillins (1958-60)

Discovery of Antimicrobial Agents

Fleming's Petri Dish

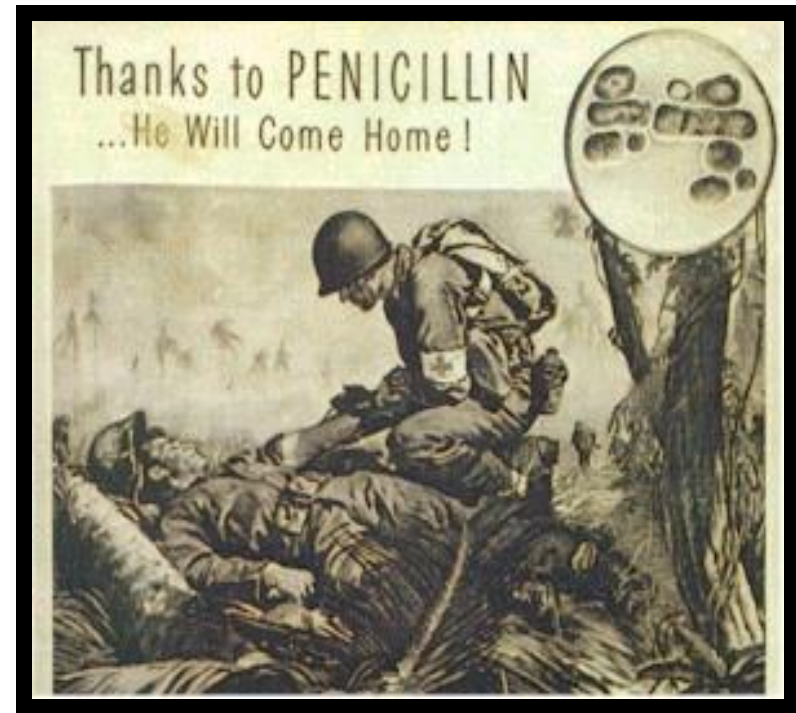


Discovery of Antimicrobial Agents

World War II

✓ Penicillin was produced by large scale fermentation (1944) and was introduced to the world just in time for World War II.

✓ It helped save many lives during the war, and has been greatly appreciated since.



Definitions

Chemotherapy: is the drug treatment pathologic microorganisms, parasites, and tumor cells.

Chemotherapy selective toxicity: kills harmful microbes without damaging the host (the selective toxicity is relative, rather than absolute).

Antibiotics: substances produced by various species of microorganisms: bacteria, fungi, to suppress the growth of other microorganisms and to destroy them

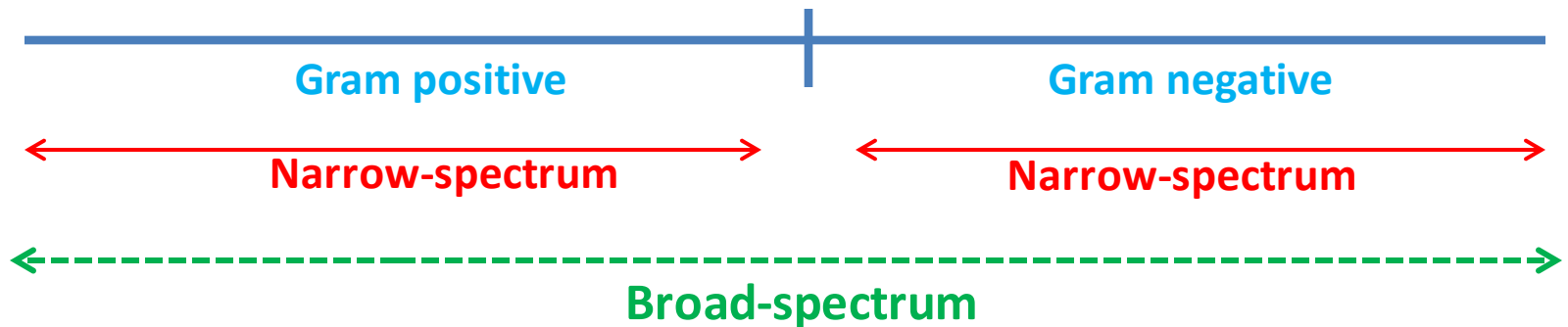
antibiosis = against life.

Definitions

Antibiotics are classified based on

1. **Target-specificity or antimicrobial spectrum:** the range that a drug kills or suppresses the growth of microorganisms.

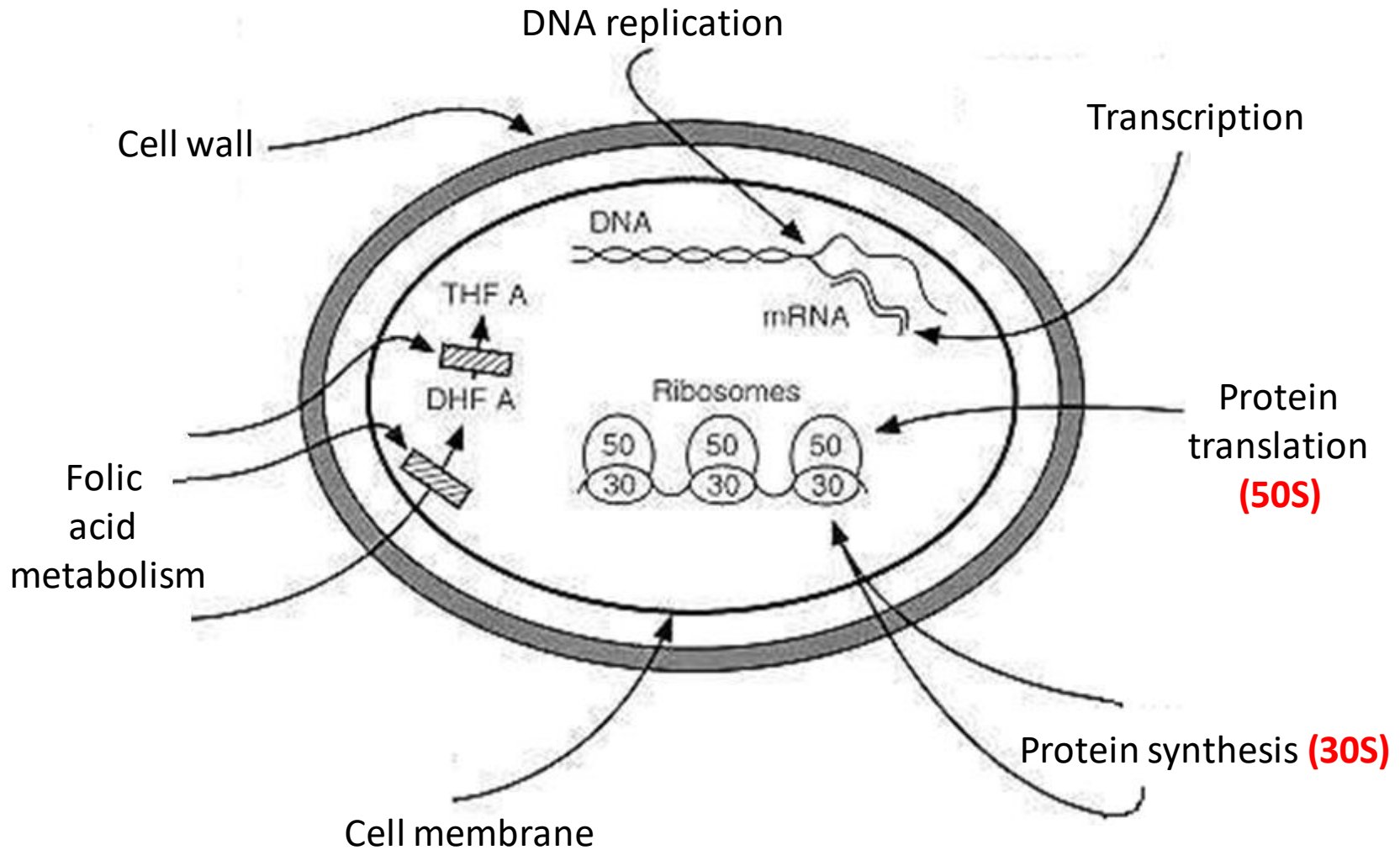
- ✓ **Narrow-spectrum:** the drugs that only act on Gram positive or Gram negative bacteria.
- ✓ **Broad-spectrum:** the drugs that have act on Gram positive & Gram negative bacteria.



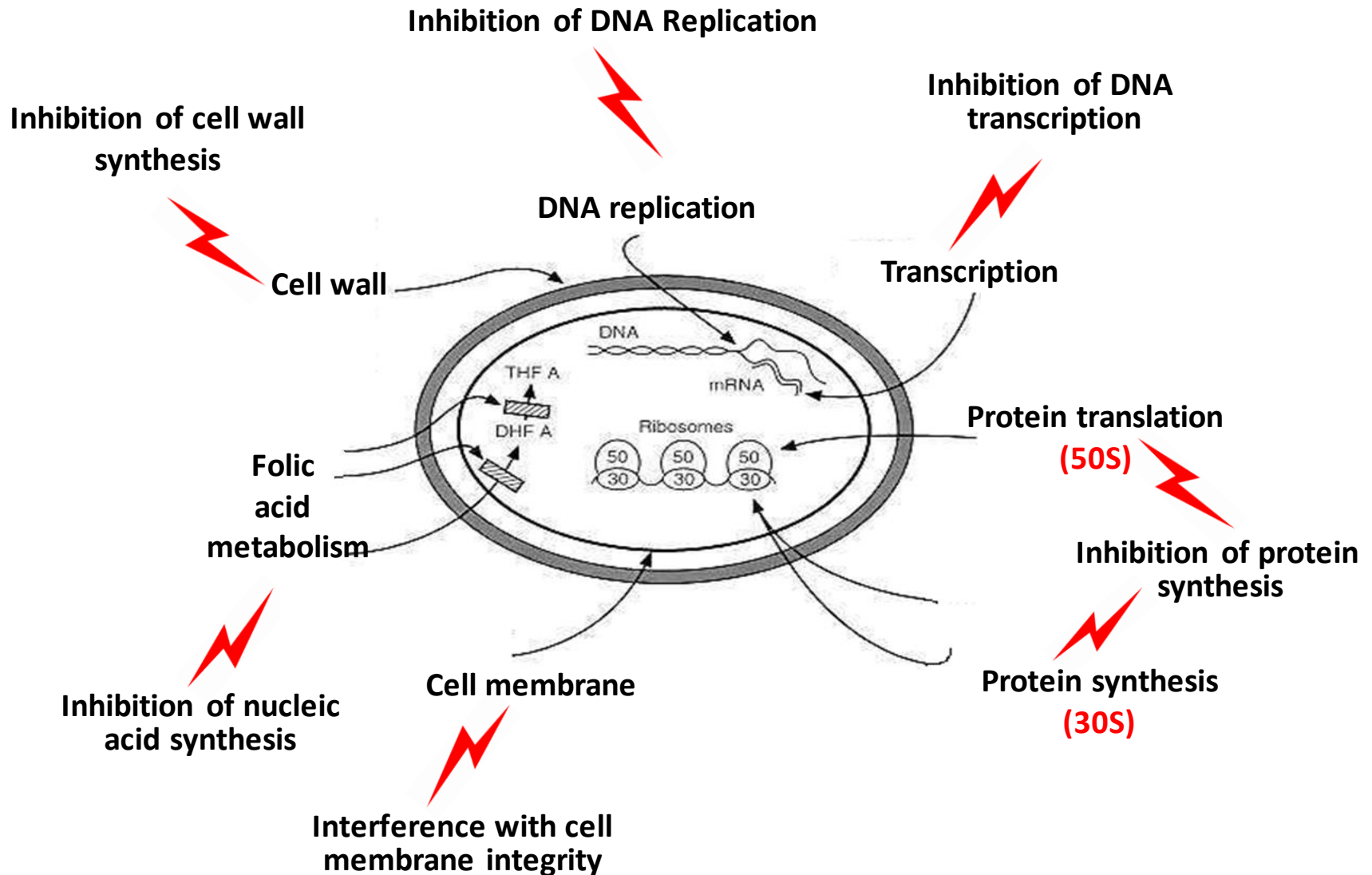
2. Killing bacteria or prevent cell division

- ✓ **Bactericidal:** antibiotic that kills bacteria
- ✓ **Bacteriostatic:** antibiotic that prevents bacterial cell division

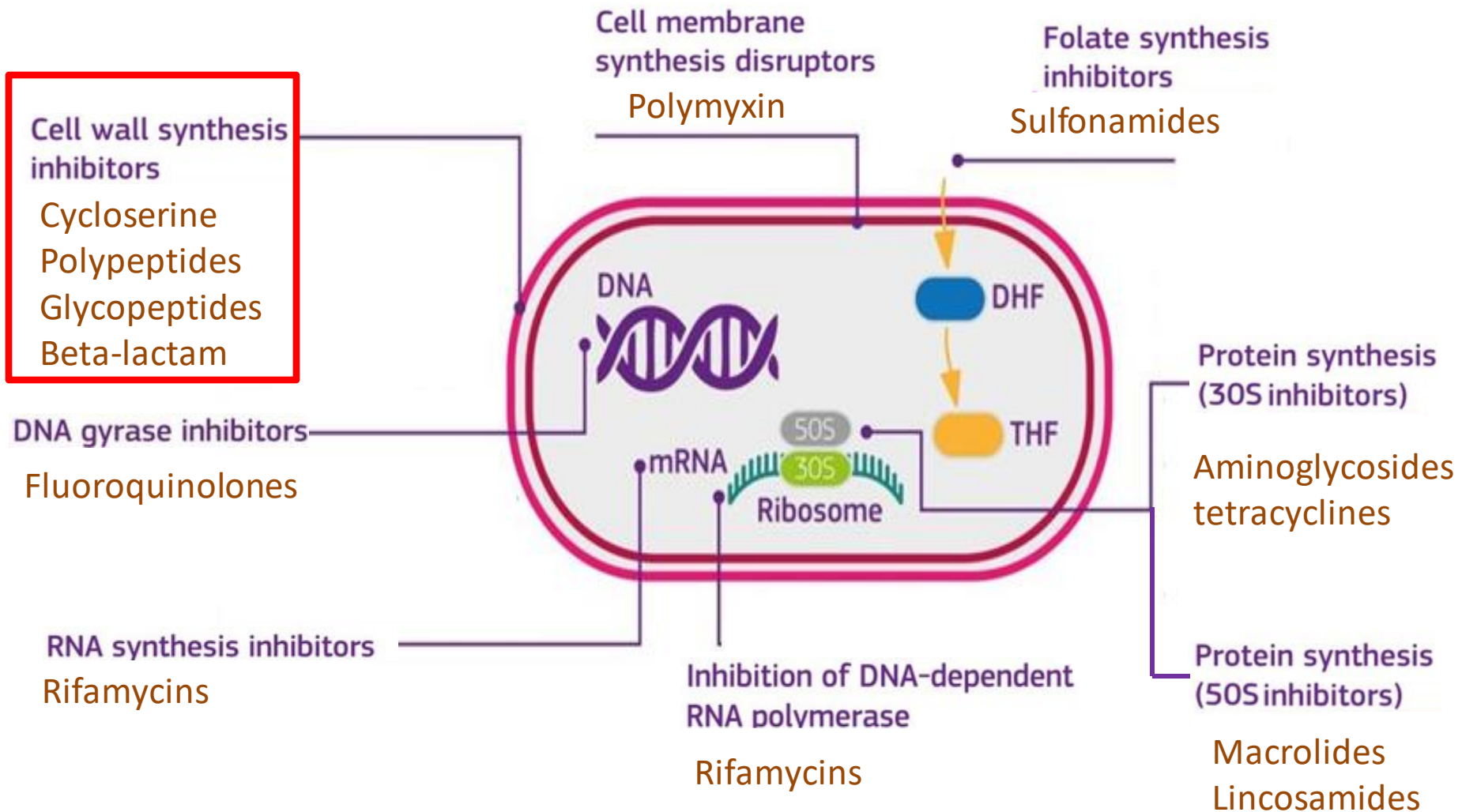
Components of bacterial cell



Mechanisms of Action of Antibacterial Drugs

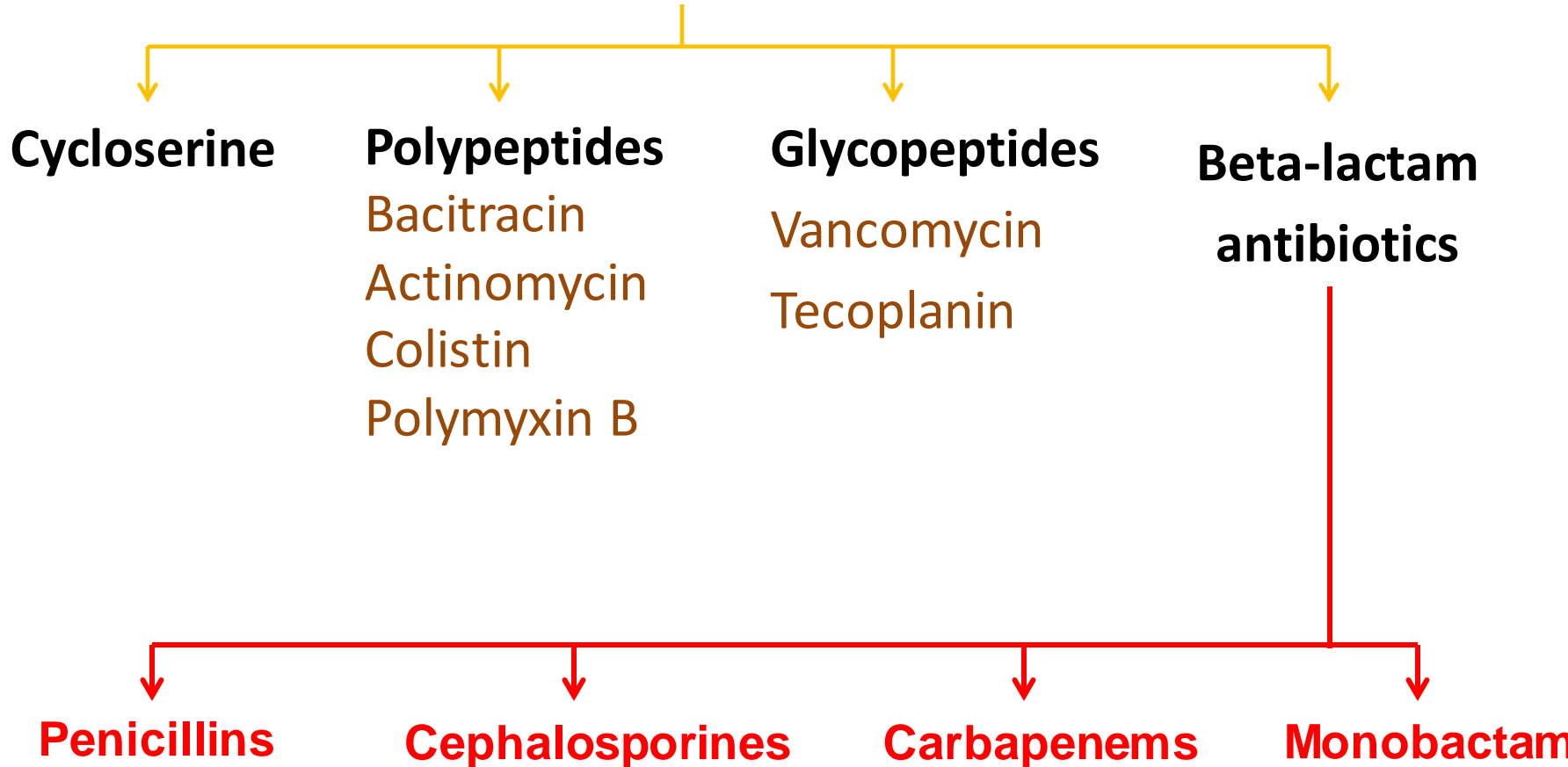


Mode of action of antibiotics



Mechanisms of Action of Antibacterial Drugs

Inhibition of cell wall synthesis



β-lactam Antibiotics

Penicillins

Penicillin G
Penicillin V
Methicillin
Nafcillin
Oxacillin
Cloxacillin
Dicloxacillin
Amoxicillin
Carbenicillin
Ticarcillin
Piperacillin
Mezlocillin
Cefoxitin
Azlocillin

Cephalosporins

1st Generation

Ampicillin
Cefadroxil
Cephalexin
Cephalothin
Cephapirin
Cephradine

2nd Generation

Cefazolin
Cefamandole
Cefonicid
Cefmetazole
Cefotetan
Cefuroxime

3rd Generation

Cefaclor
Cefoperazone
Ceftizoxime
Ceftazidime
Ceftriaxone
Cefixime
Moxalactam

4th&5th Generation

Cefepime
Cefozopran
Cefpirome
Cefquinome
Ceftobiprole
Ceftaroline
Fosamil

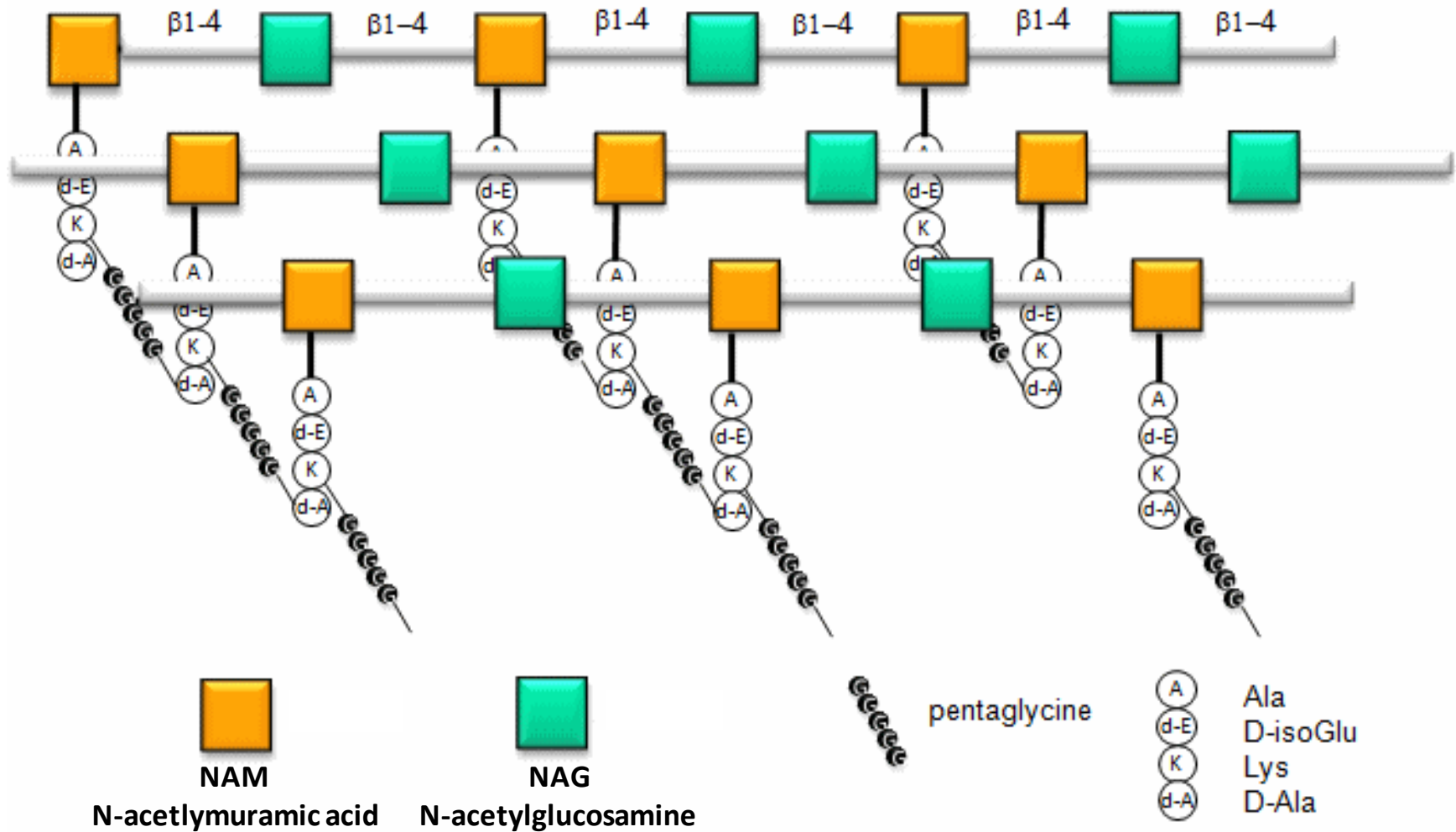
Carbapenems

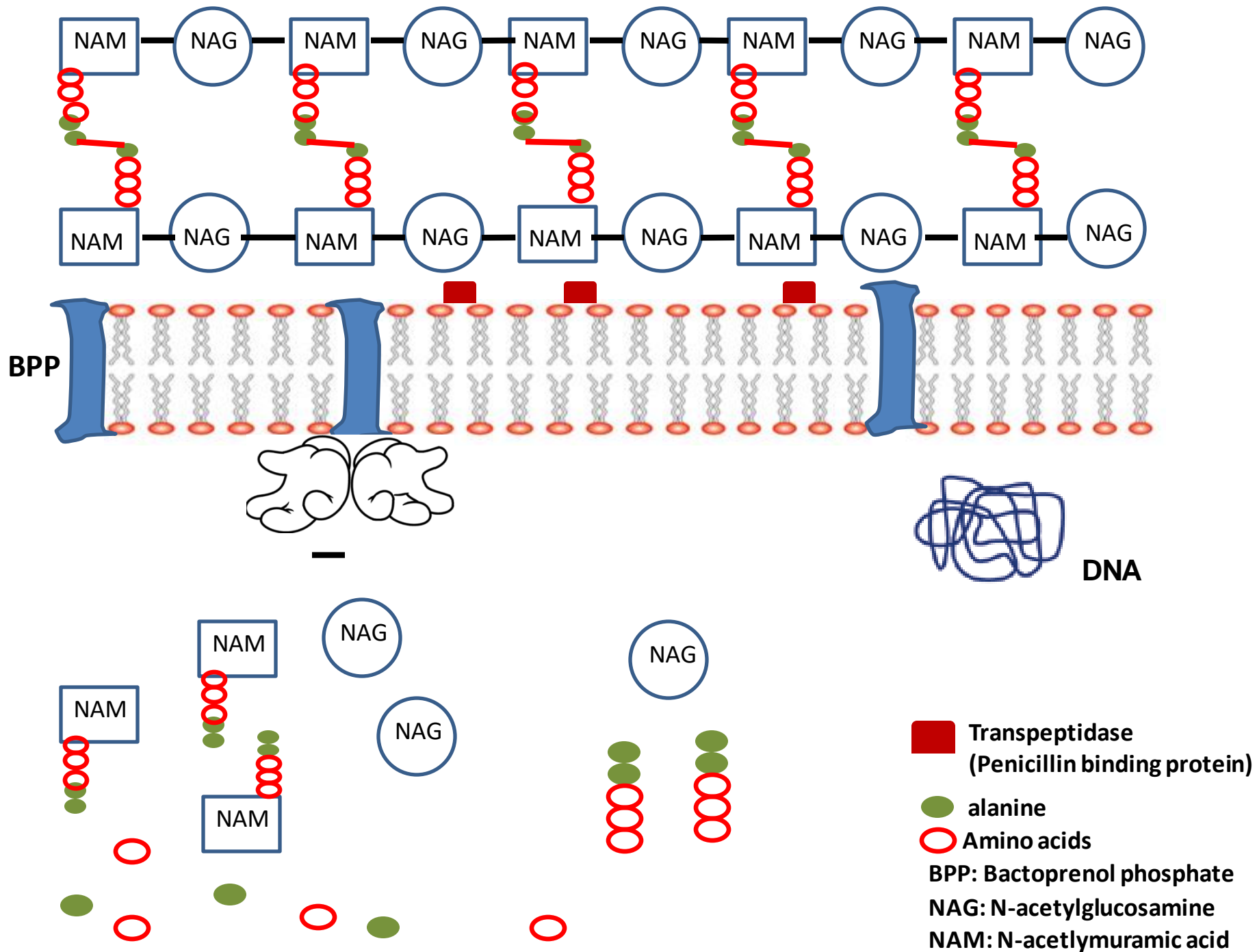
Biapenem
Ertapenem
Doripenem
Imipenem
Panipenem

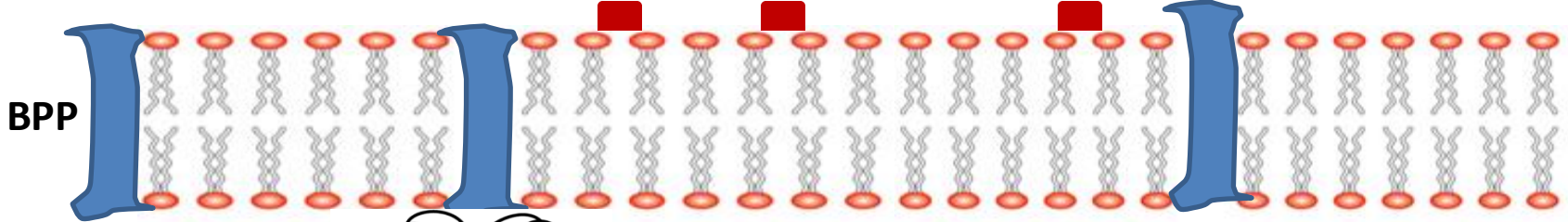
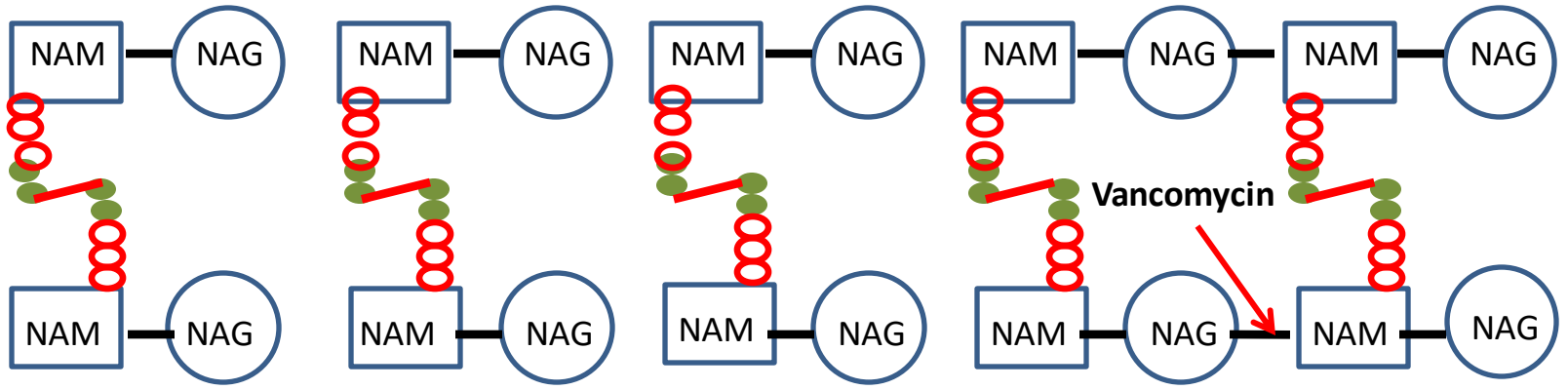
Monobactams

Aztreonam
Tigemonam
Carumonam
Nocardicin A

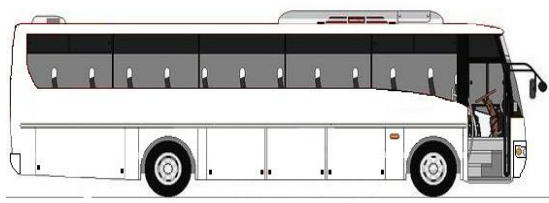
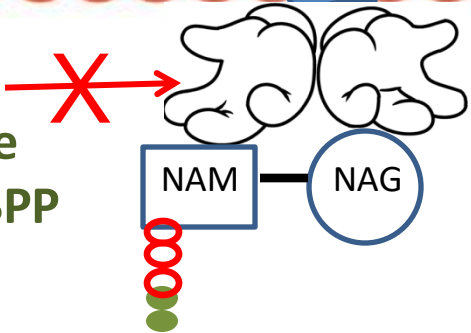
bacterial cell wall synthesis



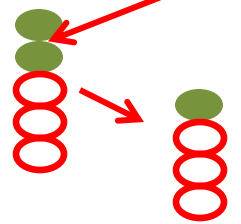




Bacitracin
Inhibits the
action of BPP



Cycloserine: inhibits the alanine alanine peptide bond formation

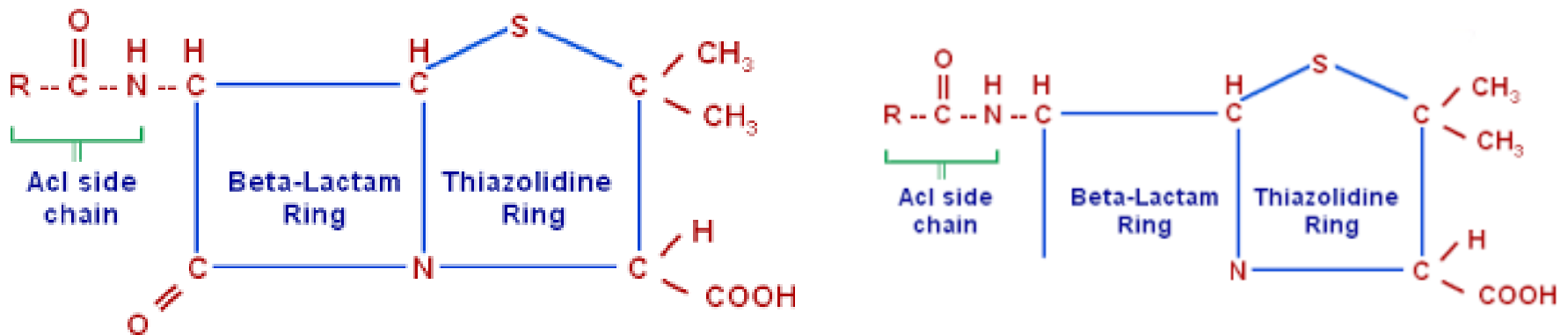


Vancomycin: inhibits the formation of glycosidic bonds between the NAM-NAG repeat unites



Penicillins

- Penicillins contain a β -lactam ring which inhibits the formation of peptidoglycan crosslinks in bacterial cell walls (especially in Gram-positive organisms)
- Penicillins are bactericidal but can act only on dividing cells
- They are not toxic to animal cells which have no cell wall



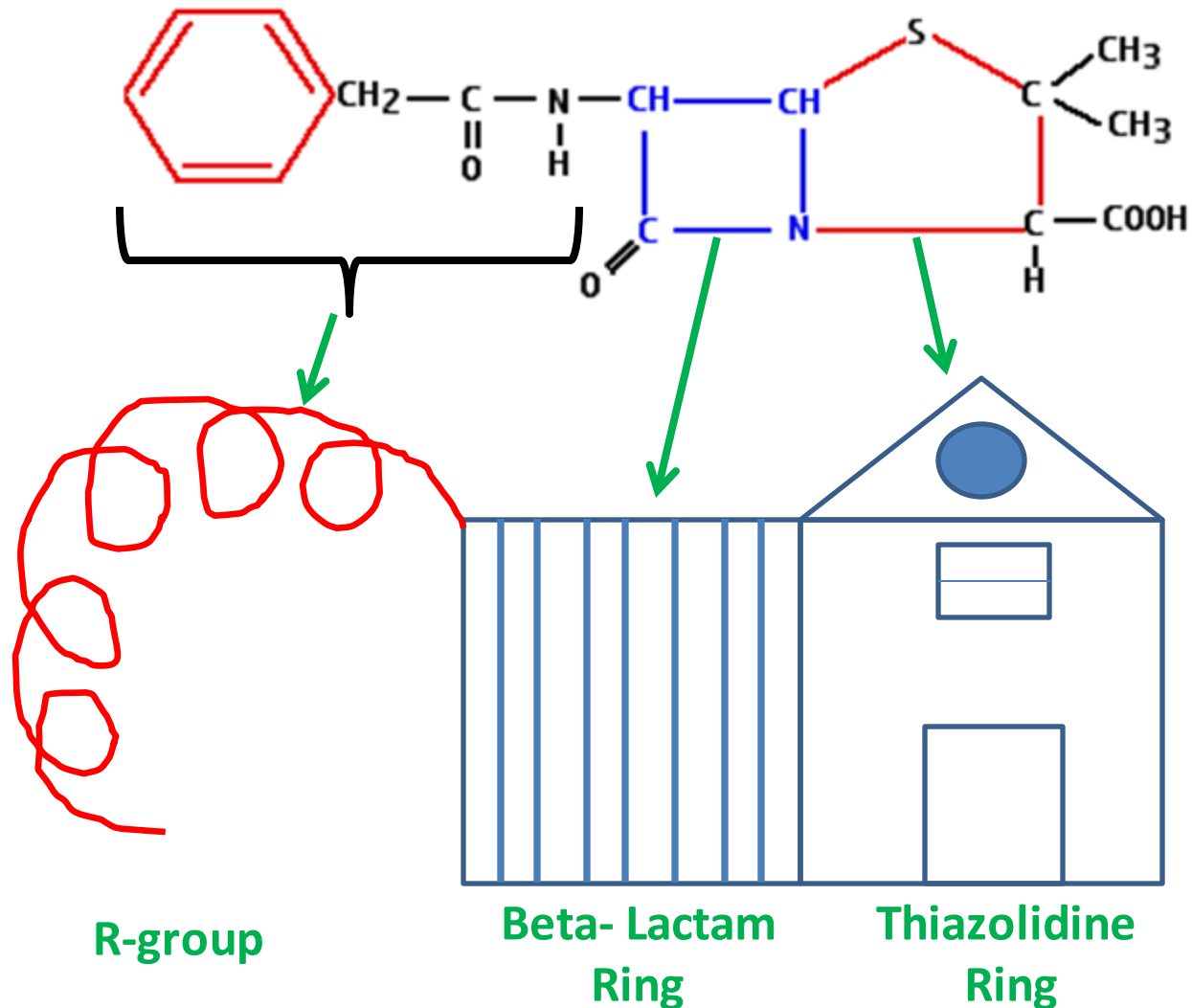
General Structure of Penicillins


 β -Lactamase

Mechanisms of Action of Antibacterial Drugs

Inhibition of cell wall synthesis

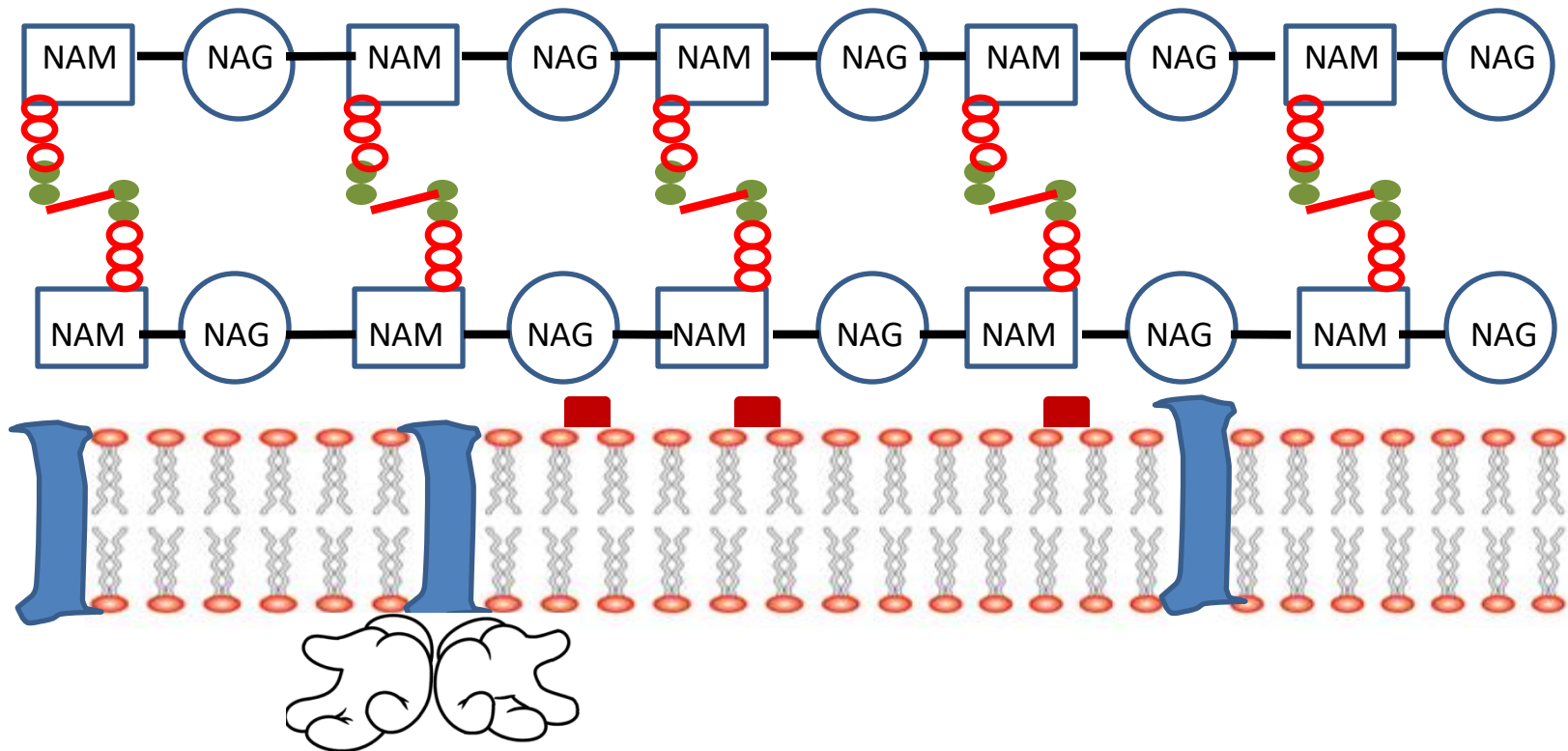
Structure of penicillin



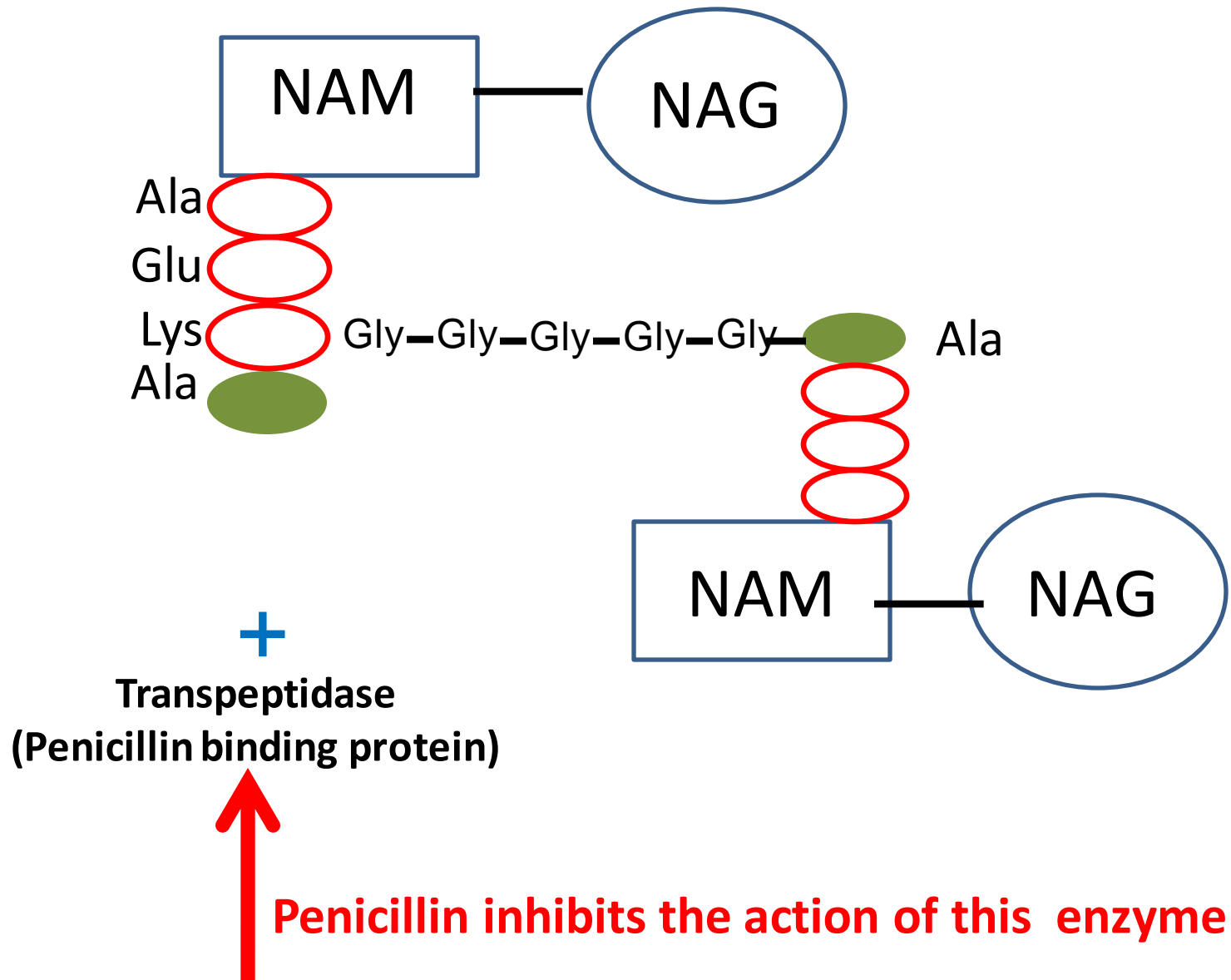
Mechanisms of Action of Antibacterial Drugs

Inhibition of cell wall synthesis

Mode of action of Penicillins: they interfere with the function of the Transpeptidase enzyme

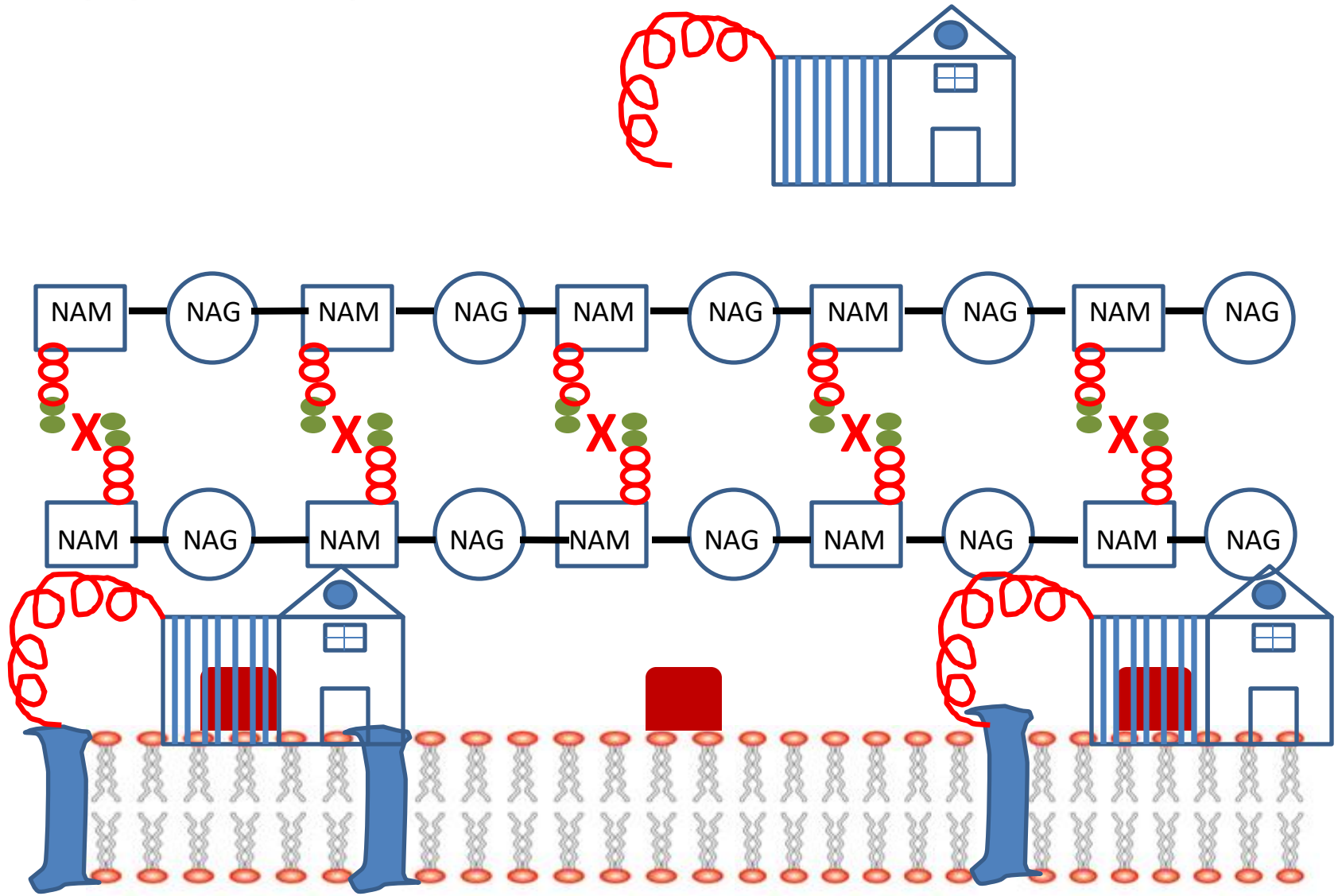


Mechanism of action - bacterial cell wall synthesis



Mechanisms of Action of Antibacterial Drugs

Mode of action of Penicillins: they interfere with the function of the transpeptidase enzyme



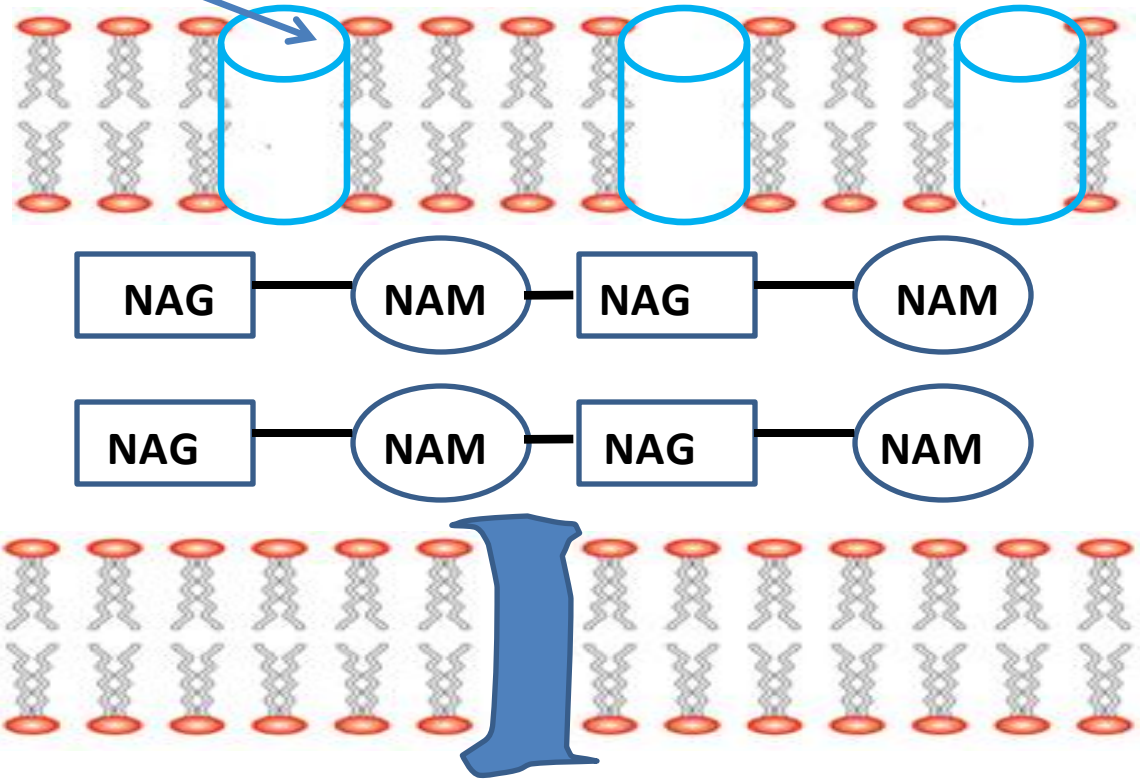
Mechanisms of Action of Antibacterial Drugs

Mode of action of Penicillins

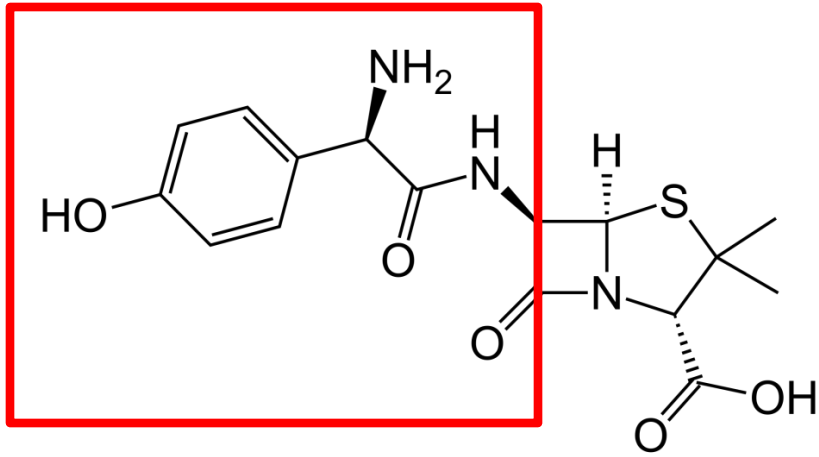
1. The β -lactam binds to Penicillin Binding Protein (PBP)
2. PBP is unable to crosslink peptidoglycan chains
3. The bacteria is unable to synthesize a stable cell wall
4. The bacteria is lysed

Gram negative bacterial cell wall structure

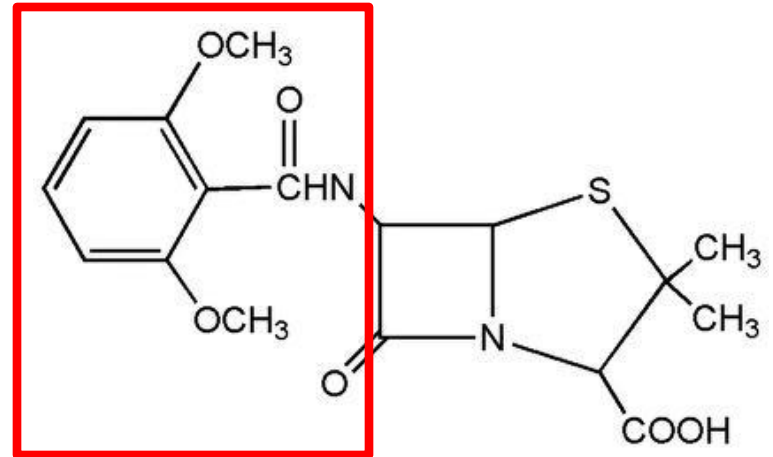
Porins



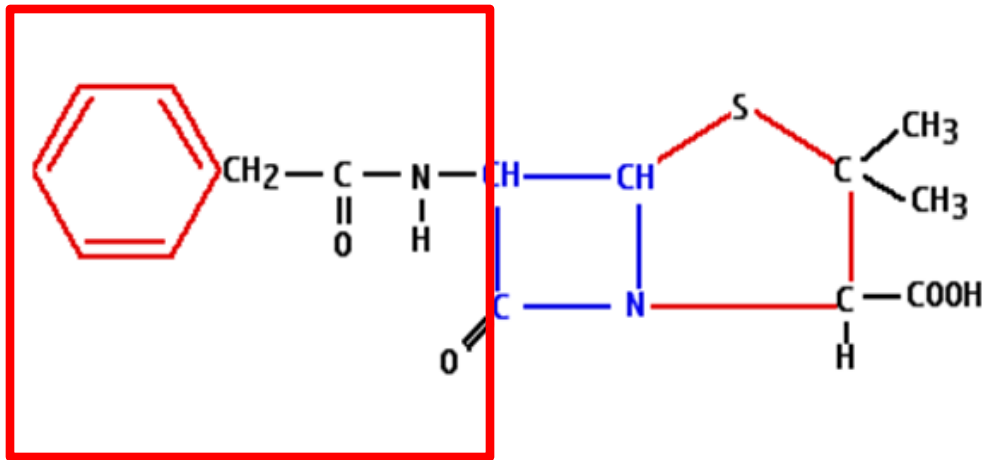
Mechanisms of Action of Antibacterial Drugs



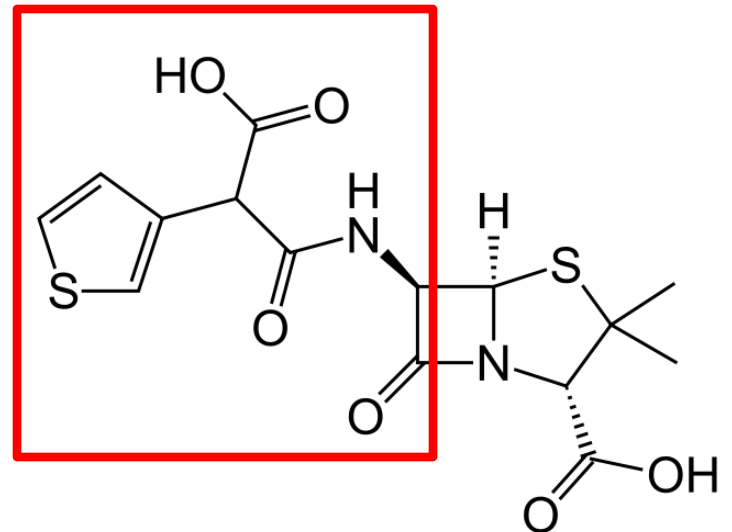
Amoxicillin



Methicillin



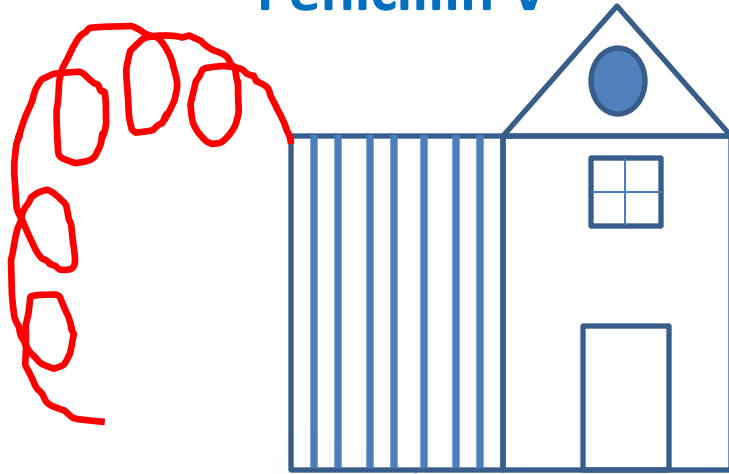
Penicillin G



Ticarcillin

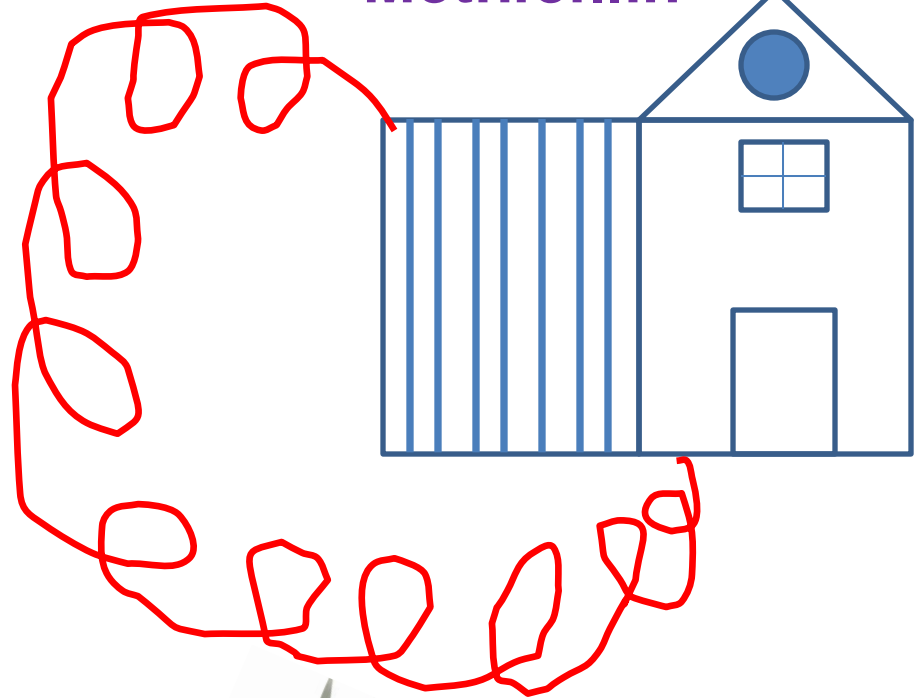
Inhibition of protein synthesis

Penicillin V



Penicillinase

Methicillin



Inactive

Penicillinase

Mechanisms of Action of Antibacterial Drugs

Inhibition of cell wall synthesis

Penicillins

Narrow spectrum

Wide spectrum

Narrow spectrum

Very very narrow spectrum

Smart wide spectrum

Very Smart wide spectrum

Penicillin G
Penicillin V

Methicillin
Nafcillin
Cloxacillin
Dicloxacillin
Flucloxacillin

Amoxicillin
Ampicillin

Mezlocillin
Piperacillin
Ticarcillin
Carbenicillin

Mechanisms of Action of Antibacterial Drugs

Q: Why penicillins vary in their range against Gram positive and negative bacteria?
This depends on the penicillin molecular size which is determined by the R-group

Penicillins

Narrow spectrum

Wide spectrum

Narrow spectrum

Very very narrow spectrum

Smart wide spectrum

Very Smart wide spectrum

bulky (moderately large R group): they go only through Gram positive bacteria

Developed to overcome the staphylococcal resistant to the natural penicillin due the production of penicillinase. They are very bulky and they can only penetrate the peptidoglycan *Staphylococci* and therefore they are called anti-staphylococcal antibiotics

Against all bacteria except *Pseudomonas*

Developed against *Pseudomonas* Because *Pseudomonas* porins are vey narrow

Mechanisms of Action of Antibacterial Drugs

Q: Why do penicillins vary in their range against Gram positive and negative bacteria?

This depends on the penicillin molecular size which is determined by the R-group

Penicillins

Narrow spectrum

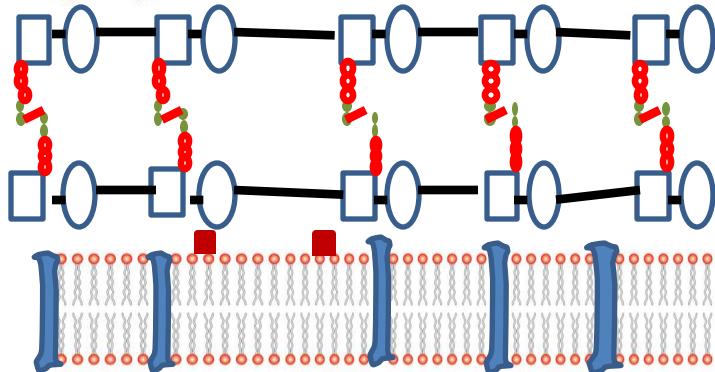
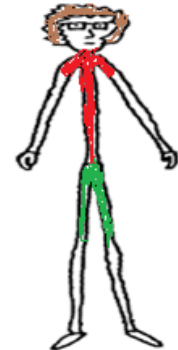
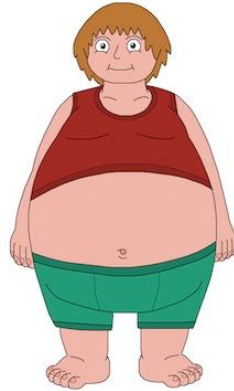
Wide spectrum

Narrow spectrum

Very very narrow spectrum

Smart wide spectrum

Very smart wide spectrum



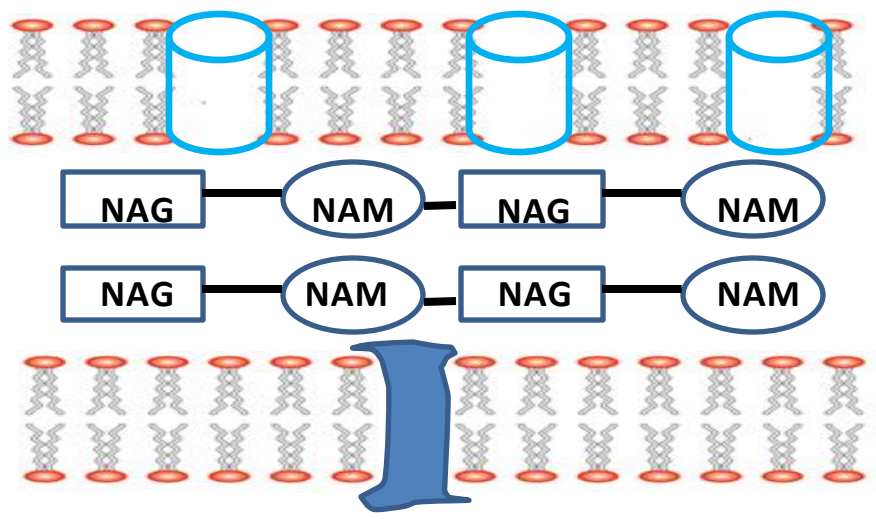
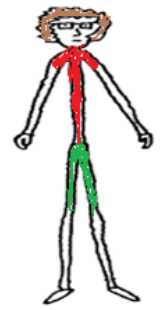
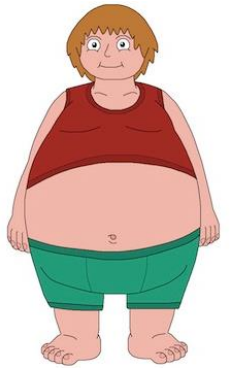
Staphylococcal Cell wall

Narrow spectrum

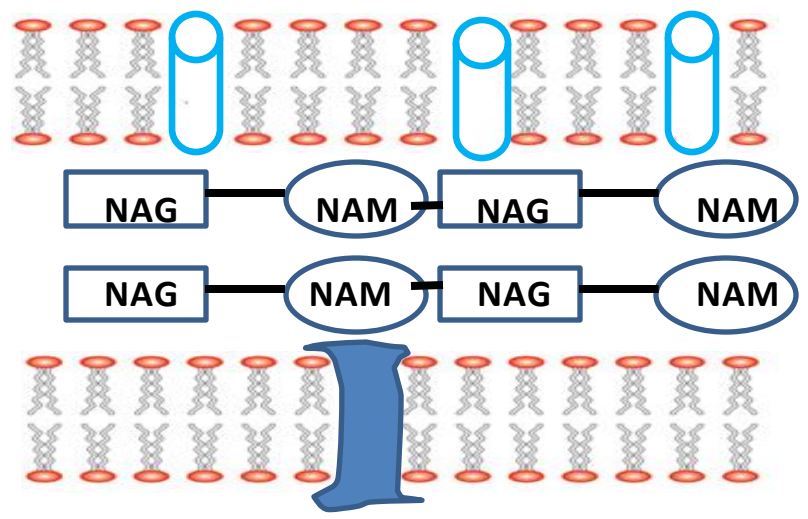
Very very narrow spectrum

Smart wide spectrum

Smart wide spectrum



Gram negative bacteria



Pseudomonas species

