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# Antibiotics: mode of action and mechanisms of resistance.

By

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# What are antibiotics?

## Originally:

Naturally occurring microbial products

## Today:

Any agent used to treat infections

# Mechanisms of antibiotics

- Bacteriostatic
- Bactericidal

# Bacteriostatic antibiotics

- Tetracyclines
- Spectinomycin
- Sulphonamides
- Macrolides
- Chloramphenicol
- Trimethoprim

# Bactericidal antibiotics

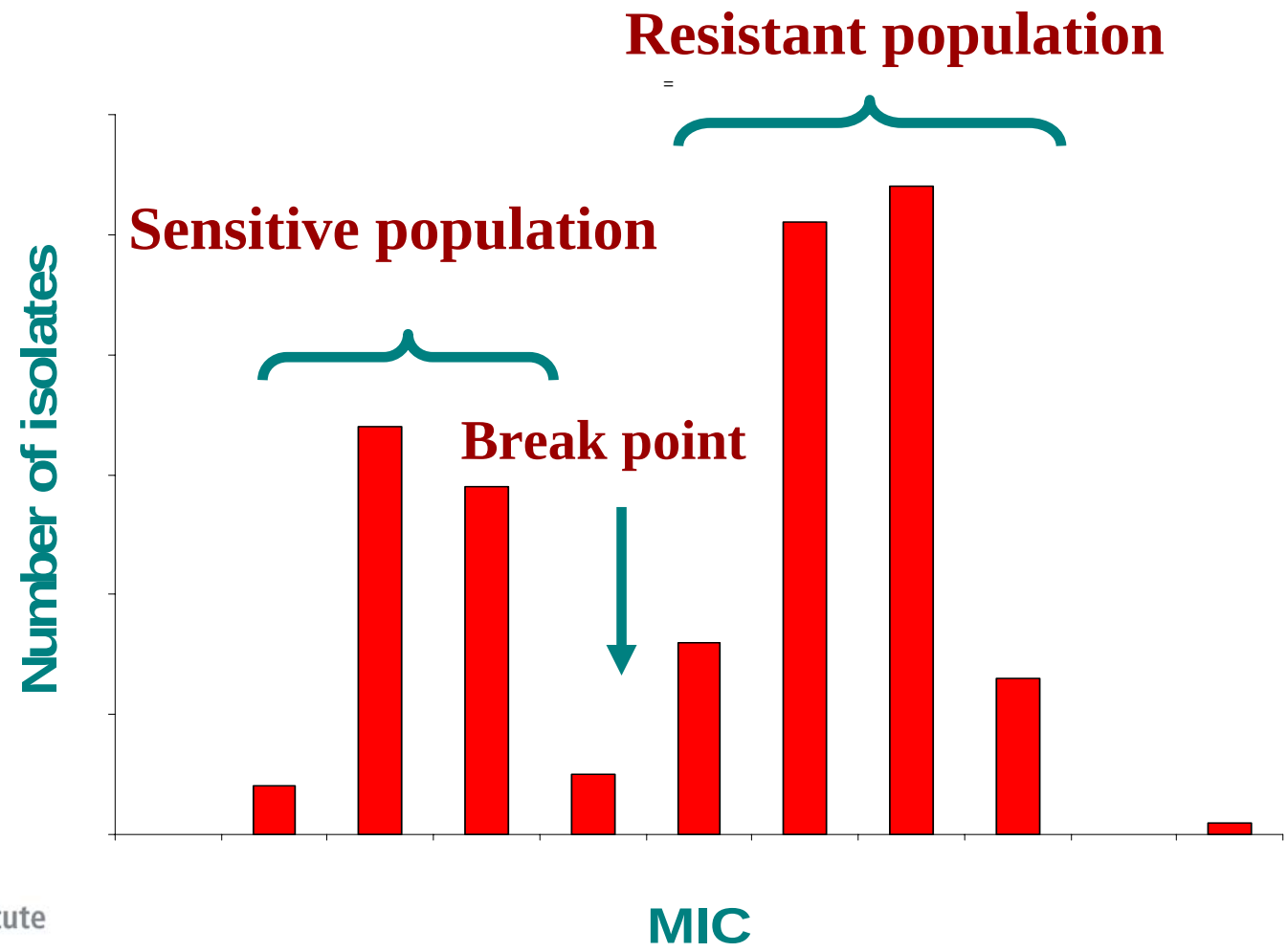
- Penicillins
- Cephalosporins
- Fluoroquinolones (Ciprofloxacin)
- Glycopeptides (Vancomycin)
- Monobactams
- Carbapenems

# What is antimicrobial resistance I?

***The ability of a microorganism to survive at a given concentration of an antimicrobial agent at which the normal <u>population</u> of the microorganism would be killed***

**This is called the "Epidemiological breakpoint".**

# Population distribution



# What is antimicrobial resistance II?

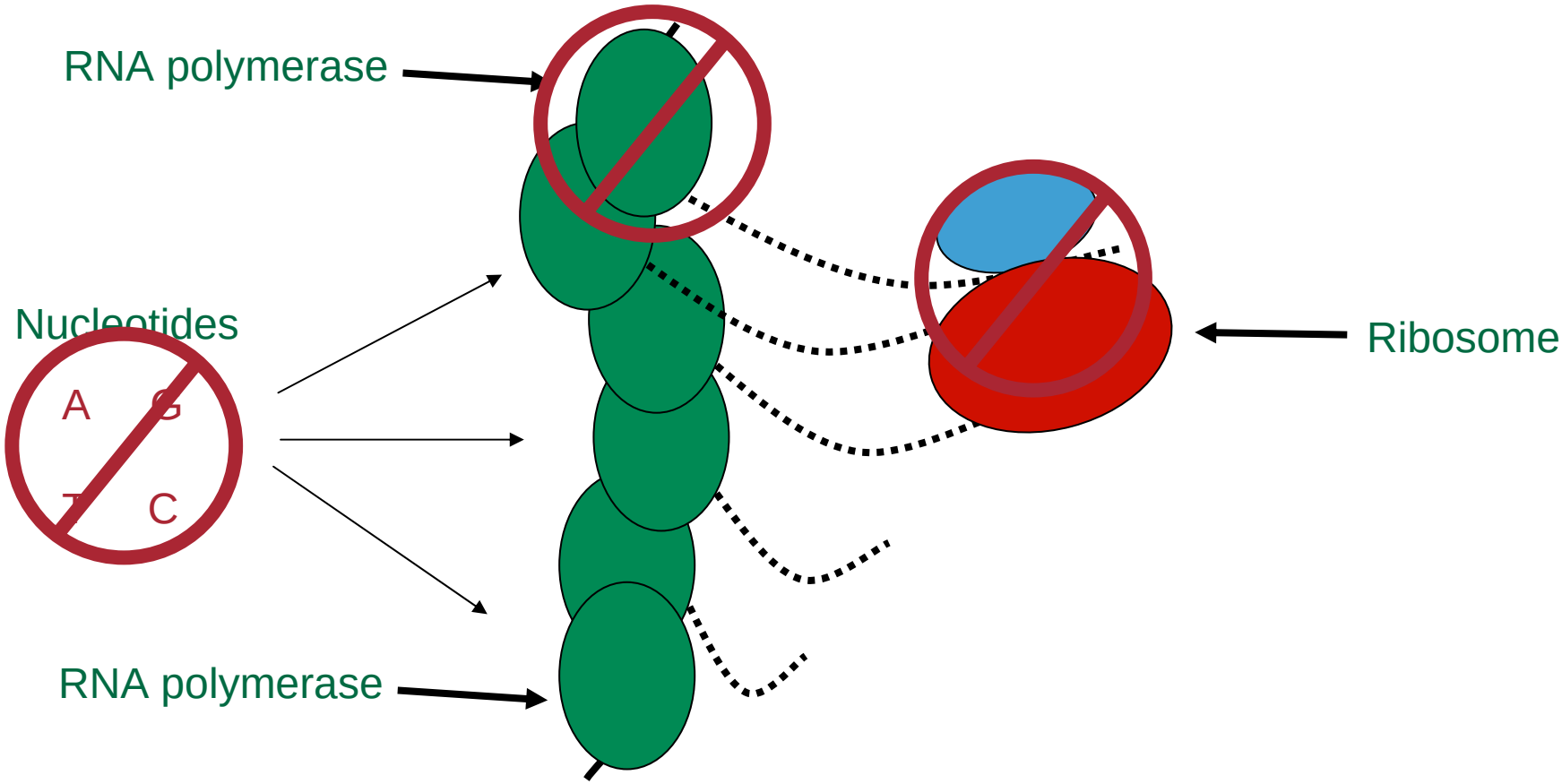
***The ability of a microorganism to survive treatment with a clinical concentration of an antimicrobial agent in the body.***

**This is called the "Clinical breakpoint".**

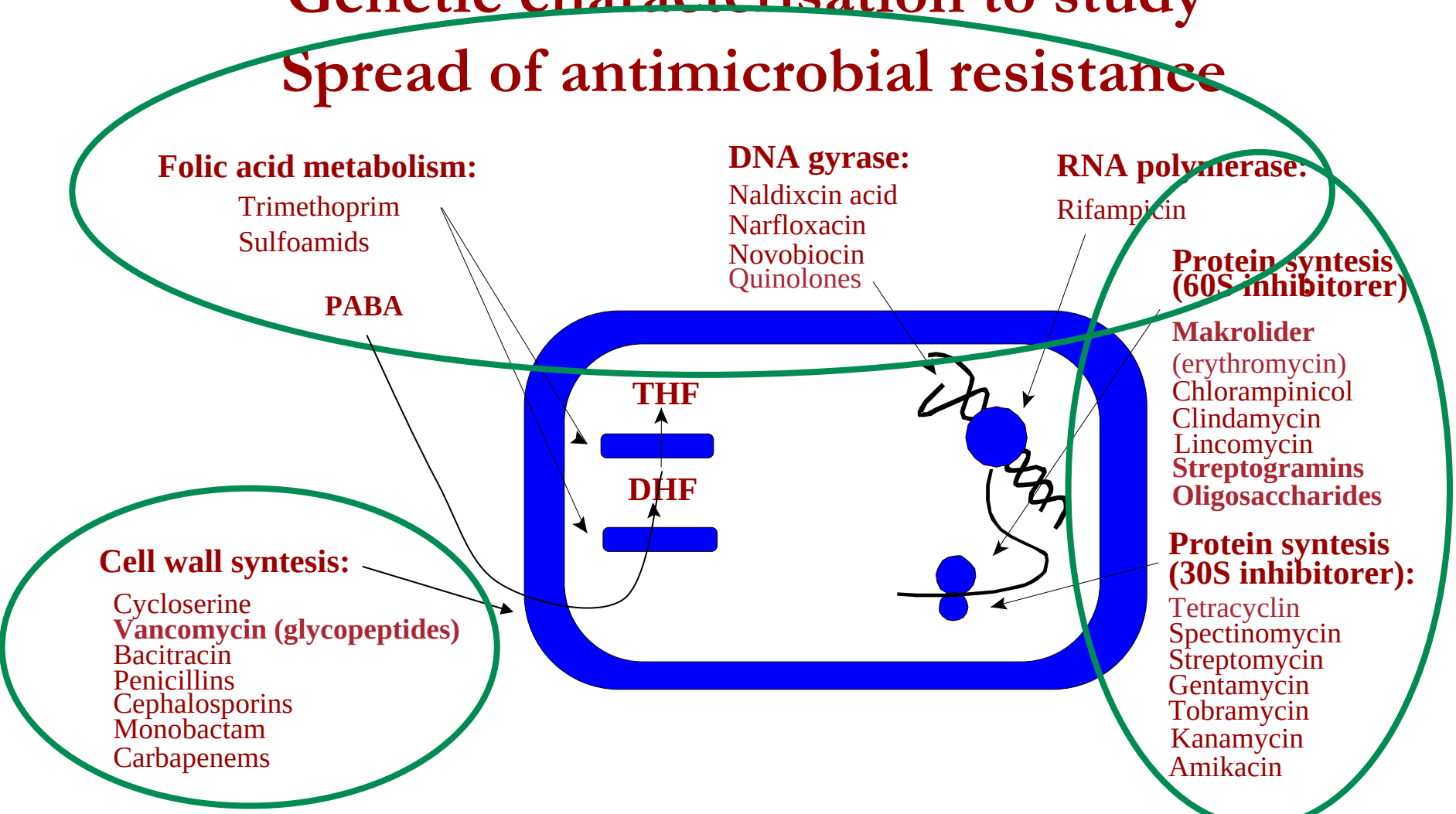
# Antibiotics: Modes of action

- Inhibitors of DNA synthesis
- Inhibitors of bacterial protein synthesis
- Inhibitors of bacterial cell wall synthesis

# From DNA to protein



# Genetic characterisation to study Spread of antimicrobial resistance

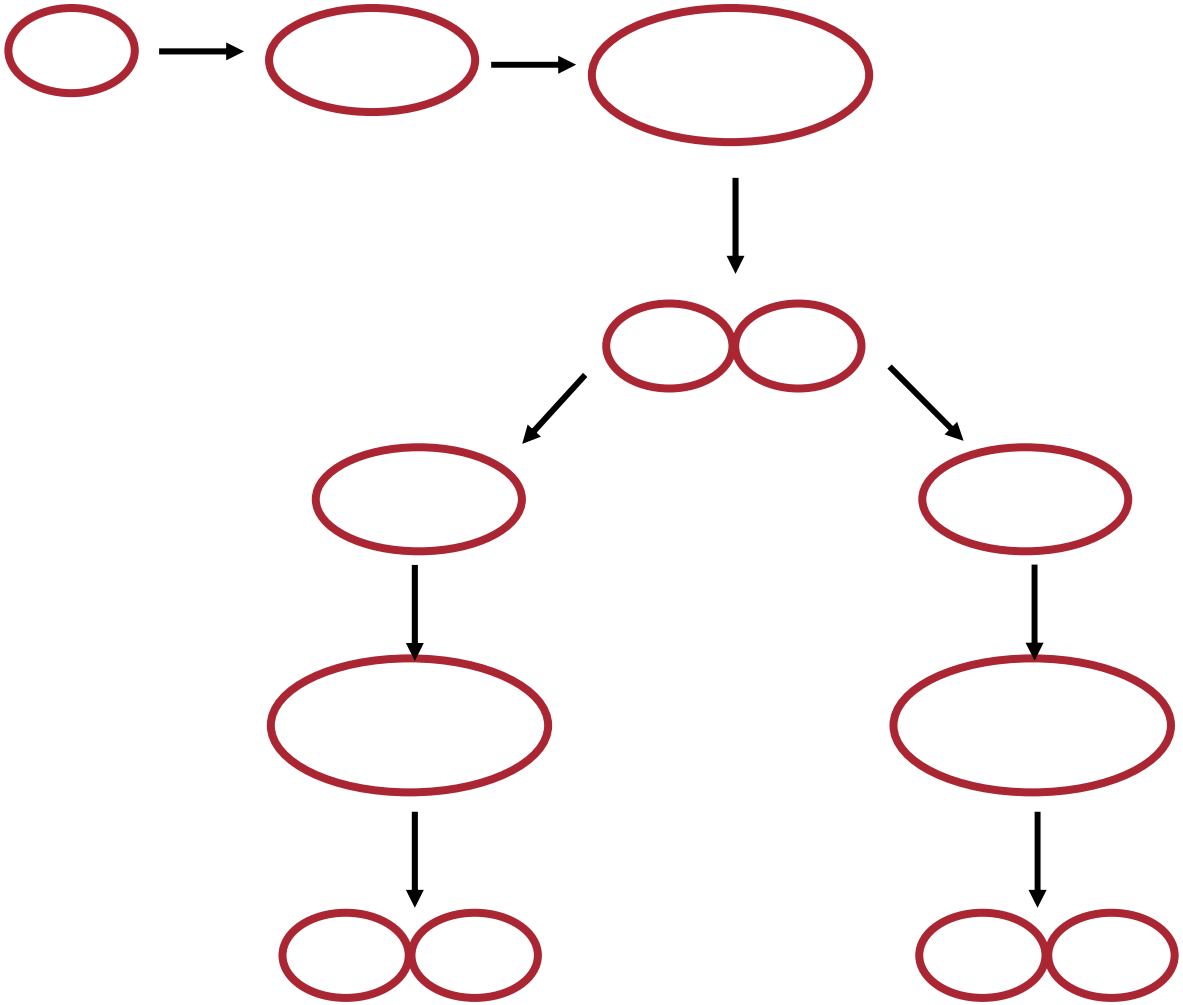



(**PABA=** p-aminobenzocis acid, **DHF=** dihydrofolate, **THF=** tetrahydrofolate (essential for growth of bacteria))

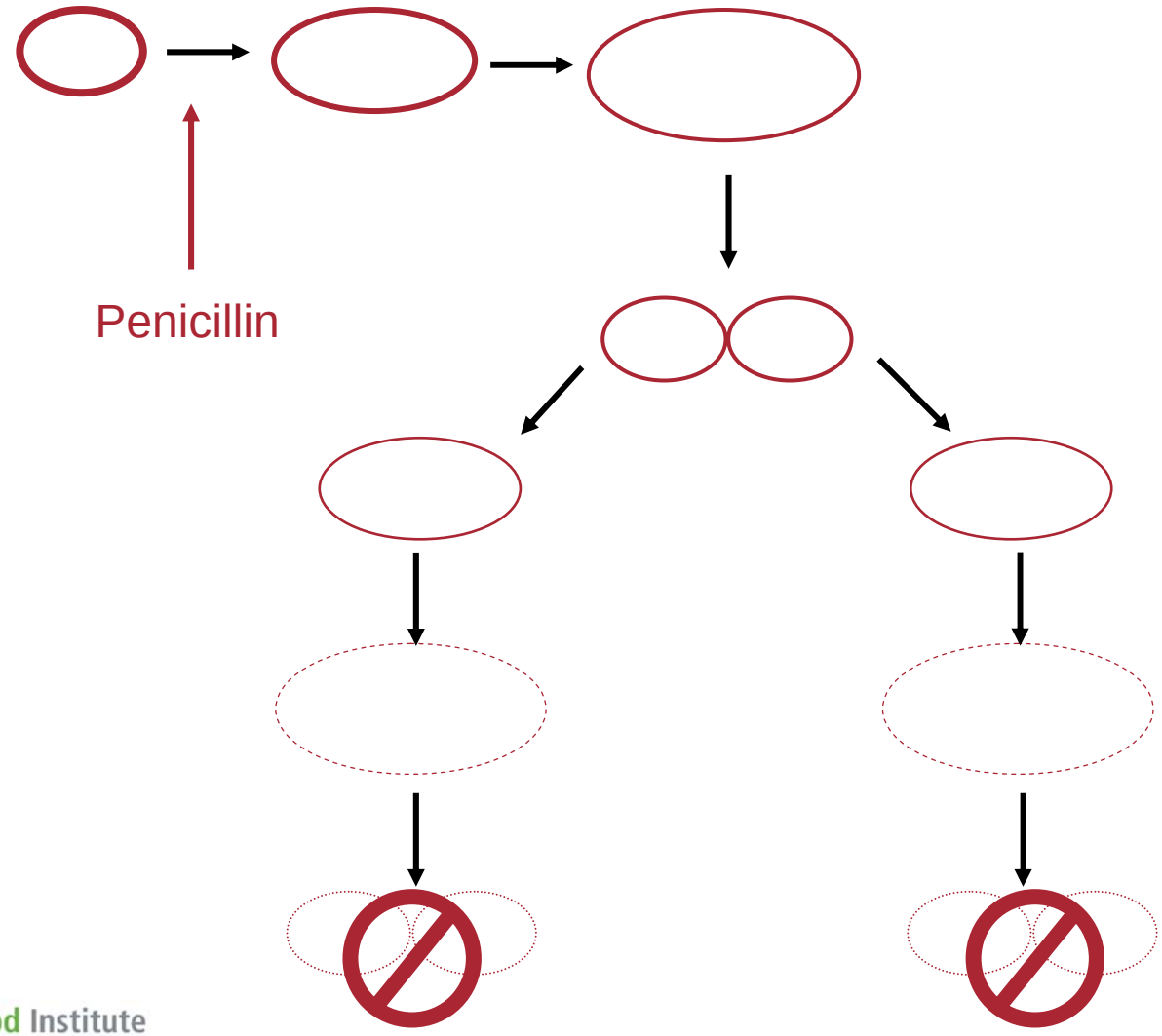


## Targets in the bacterium

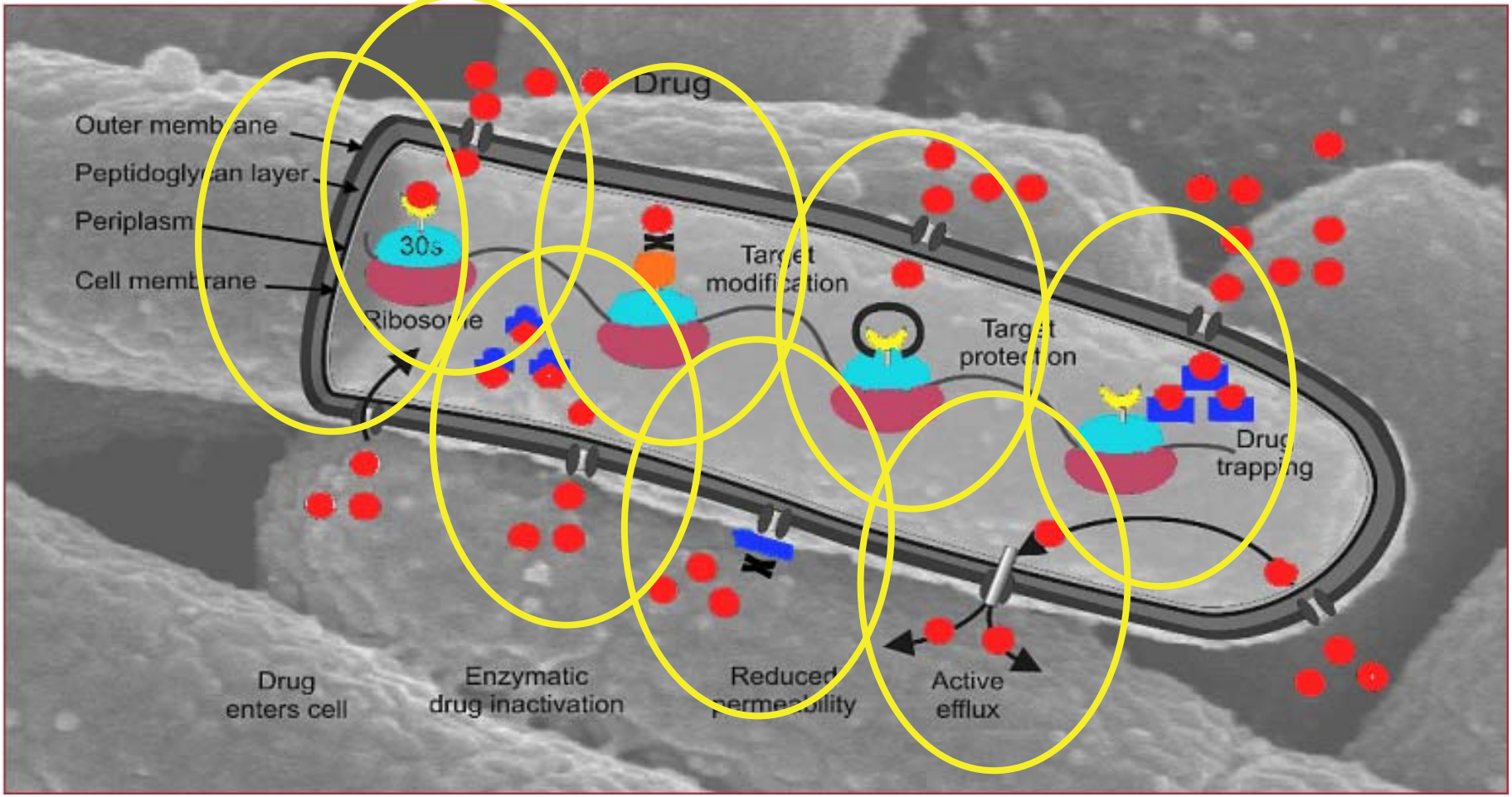
# Bacterial growth



# Inhibition of cell wall synthesis

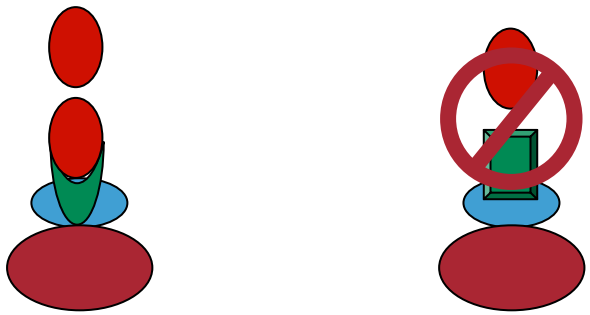


# Antibiotics: Modes of resistance



# Resistance mechanisms I

- Point mutations in target genes/influx pumps



# Genetic variations/Point mutations

## DNA gyrase –quinolone resistance

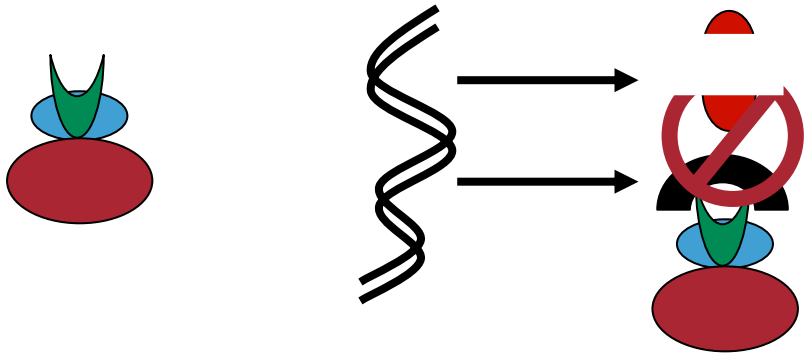

**Codon 83:** TCC → Ser

TTC → Phe

TAC → Tyr

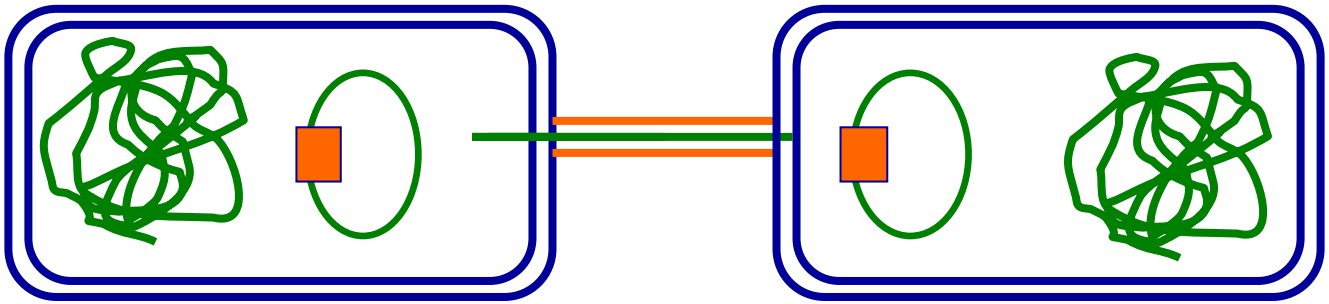
# Resistance mechanisms II

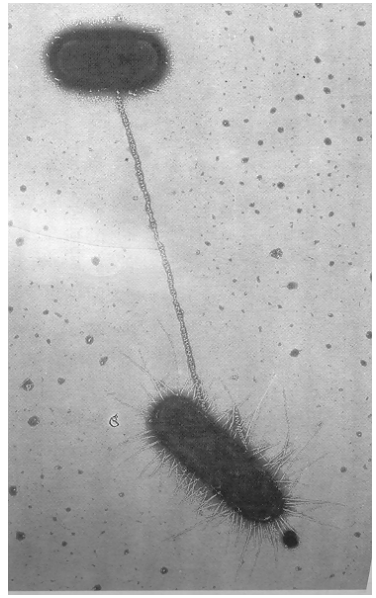
- Acquired genes



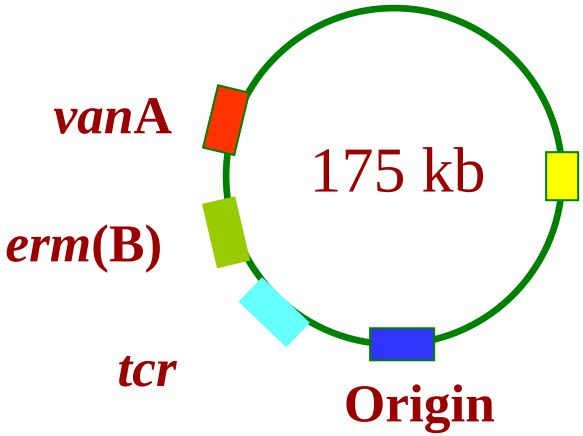
# Acquisition of resistance

## *E. coli/ salmonella*





# Co-selection of resistance




*tcr*=Transferable copper resistance

**Usage of copper or erythromycin selects for presence of vancomycin resistance**

# Antimicrobials and resistance problems

## Emerging problems

- Fluoroquinolones-resistant *Salmonella*
- 3rd gen. Cephalosporin-resistant *Salmonella (ESBL)*
- Fluoroquinolone- and macrolide-resistant *Campylobacter*
- Vancomycin resistant enterococci (VRE)
- (Multiresistant *E. coli*)
- MRSA in animals (report of high prevalence of MR*SA* in pigs in the Netherlands - now also found in Danish animals).