Chemotherapy for the treatment of infections or tumoral (neoplastic) diseases caused by bacteria, protozoa, fungi, helminths or viruses ;
The chemical compounds used are called chemotherapeutics.
It is a Latin word that was first introduced by Paul Ehrlich.

What is chemotherapy?
Also called “chemo,” it’s a way to treat cancer that uses drugs to kill cancer cells.
How does chemotherapy work?
It targets cells that grow and divide quickly, as cancer cells do.

Unlike radiation or surgery, which target specific areas, chemo can work throughout your body.
But it can also affect some fast-growing healthy cells, like those of the skin, hair, intestines, and bone marrow.
That’s what causes some of the side effects from the treatment.

Chemotherapy

Chemotherapy is defined as

"treatment of disease by means of chemicals that have a specific toxic effect upon the disease producing microorganisms or that selectively destroy cancerous tissue"

According to **American Cancer Society**

"the use of medicines or drugs to treat cancer"

American Cancer Society®

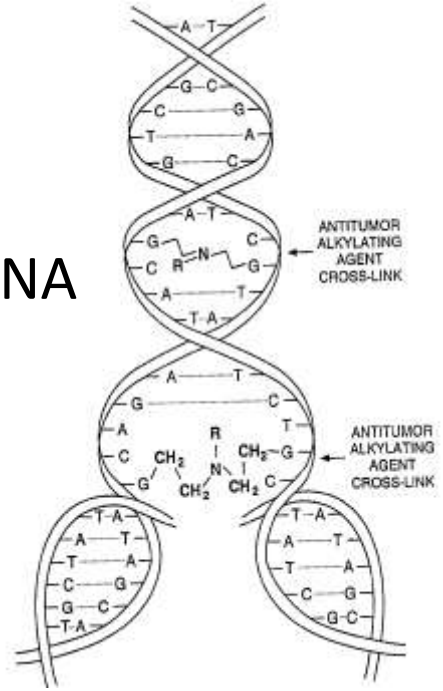
Chemotherapeutic agents

Alkylating agents

- Mode of action:

  Arrests DNA replication, Can result in DNA damage

- Examples: Carmustine, mustine



Anti-tumor antibiotics

- Mode of action:

  Alter the DNA inside cancer cells to keep them from growing and multiplying

- Examples: Daunorubicin, Actinomycin D

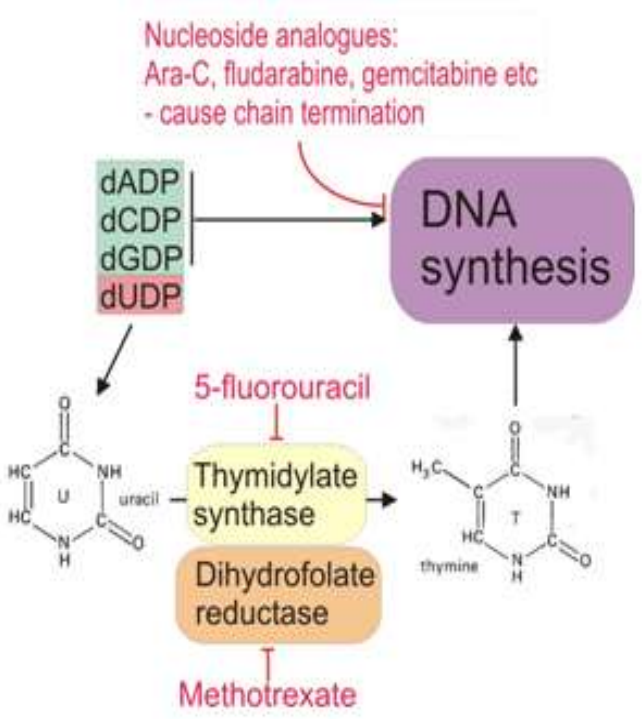
Antimetabolites

- Mode of action:

  Interfere with the availability of normal purine or pyrimidine nucleotide precursors, either by inhibiting their synthesis or by competing with them in DNA or RNA synthesis

- Examples:

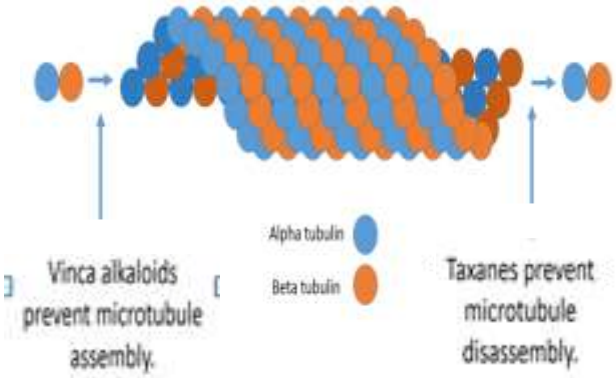
  Methotrexate, 5-FU



Antimicrotubule agents

- Mode of action:

  Block cell division by preventing microtubule function.

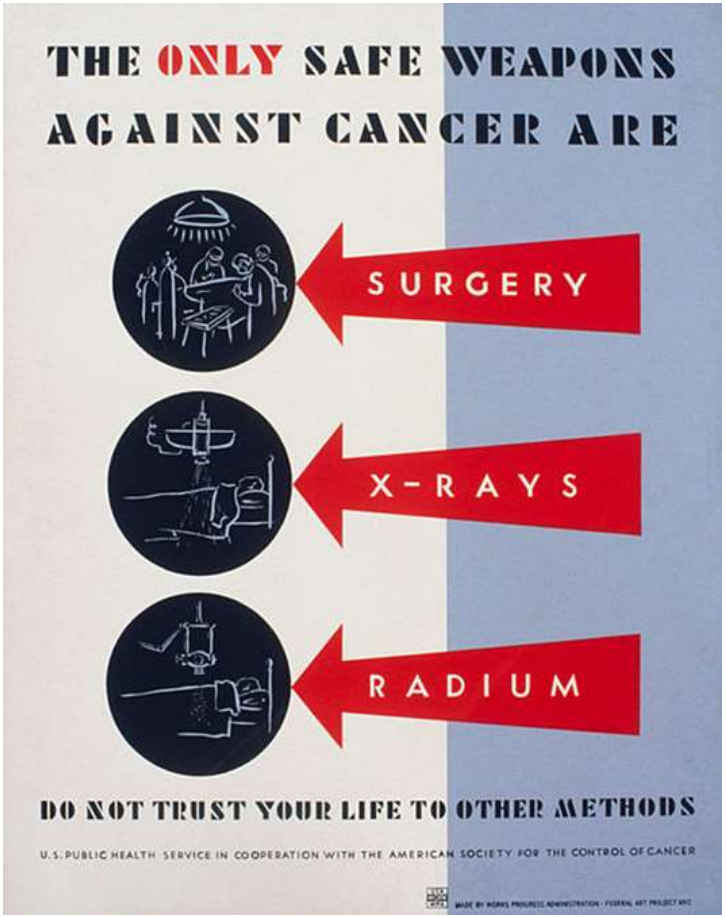


- Examples:

  vinca alkaloids prevent the formation of the microtubules

  Taxanes prevent the microtubule disassembly

History of cancer treatment



The Early Period of Cancer Drug Development(1900-1950)

- **Paul Ehrlich,** Founder of chemotherapy discovered arsphenamine for syphillis treatment(Magic Bullet)

- **Sidney Farber** worked on remission of pediatric leukemia using the drug aminopterin

- **Mustine** first chemotherapy drug (Alkylating agent,a weapon used in WWII) approved by FDA for Hodgkin's lymphoma

The 1950's

- **5-fluorouracil** becomes mainstay of chemotherapy for colorectal cancer

- NCI demonstrated "combination chemotherapy" for remission of acute leukemia

NATIONAL® CANCER INSTITUTE

The 1960's

- First effective chemotherapy was found for men with advanced **testicular cancer**(Actinomycin D, Methotrexate, chlorambucil)

- FDA approved two **"microtubule drugs"** vinblastine and vincristine for leukemia

- Central nervous system was treated **with radiation and intrathecal therapy** helps achieve first long term cure for the common childhood leukemia

The 1970's-Golden era

- Regarded as the age of **Adjuvant chemotherapy**
- **High-dose methotrexate /Leucovorin rescue therapy** results in significant tumor shrinkage (almost 75% of cases)
- First promising chemotherapy drug **carmustine** (cross blood-brain barrier) was reported for glioma
- **Doxorubicin** was reported active against advanced breast cancer and FDA approved it for combination chemotherapy

- **Doxorubicin** was found effective for liver cancer
- **Tamoxifen** received initial FDA approval for breast cancer but for women having tumor of estrogen and progesteron
- FDA approved the first chemotherapy drug **Cisplatin** for bladder cancer
- First effective combination chemotherapy regimen for ovarian cancer was developed but had more side effects(methotrexate, vinblastine, doxorubicin, and cisplatin)

The 1980's

- **Combination chemotherapy** was reported to improve outcomes for stomach cancer and bladder cancer
- 5-fluorouracil **Chemotherapy plus radiation** were investigated to be effective for patients of Pancreatic Cancer
- **Hormone therapy drugs** introduced slower Prostate Cancer
- **Neo- Adjuvant chemotherapy** was demonstrated to avoid amputation in children with bone cancer
- FDA approved **carboplatin** for ovarian cancer

The 1990's

- New chemotherapy **Topotecan (Hycamptin)** drug for advanced ovarian cancer

- **Gemcitabine** was found to modestly extend survival, relieve symptoms with advanced pancreatic cancer

- New **chemo-radiation therapy** offers alternative to surgery for advanced disease

- Surgery was found to cure some patients with advanced colorectal cancer

- Oral chemotherapy drug, **capecitabine**, approved for advanced breast cancer

- New oral chemotherapy drug, **temozolomide**, increases glioma survival

- FDA approved **liposomal doxorubicin** for advanced ovarian cancer

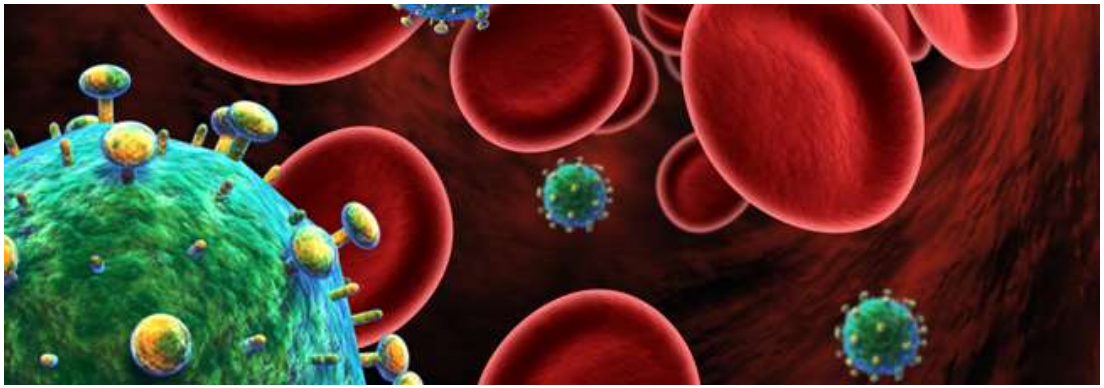
Early 21st Century

- New class of drugs **aromatase inhibitors** were introduced
- **Direct chemotherapy** approach increased the survival of cancerous patients
- Addition of an **arsenic compound** found to improve survival for rare form of leukemia
- **Taxane therapy** improves survival for several types of advanced head and neck cancers

Antimicrobial Chemotherapy

Introduction

- Clinical application of antimicrobial agents to treat infectious diseases e.g. influenza, cholera, TB.
- The antimicrobial agents may be extracted from natural substances or can be produced synthetically.
- Drugs are given in particular doses according to type and severity of infection.



Brief History

Ancient history

- Indians used **quinine** for malaria.
- Egyptians used **honey** for dressing wounds.

(Now we know it contains inhibine which convert H2and O2 into of H2O2 , an antibacterial.)

- Chinese and Greek (1550 BC) used **bread molds** to treat skin infection (They produce some raw form of antibiotic)
- Turmeric was used by indians to treat wounds.
- Onion and garlic was also used in food.

Modern era of antimicrobials

- **Paul Ehrlich** in Germany developed first antimicrobial compound Salvarsan agianst syphilis in 1910.
- **Fleming** discovered Penicillin in 1928, a breakthrough in history of medicine.

" When I woke up just after dawn on September 28, 1928, I certainly didn't plan to revolutionize all medicine by discovering the world's first antibiotic"

Penicillium notatum

antibiotic

ANTI "against"

BIOS "life"

- In 1935, German biochemist Gerhard Domagk developed the first sulfonamide, a synthetic and the first commercially available drug In name of Prontosil.

Selective toxicity

- Antimicrobials are based on concept of selective toxicity.
- Ability of a drug to injure a target cell or organism without injuring other cells or organisms that are in intimate contact .

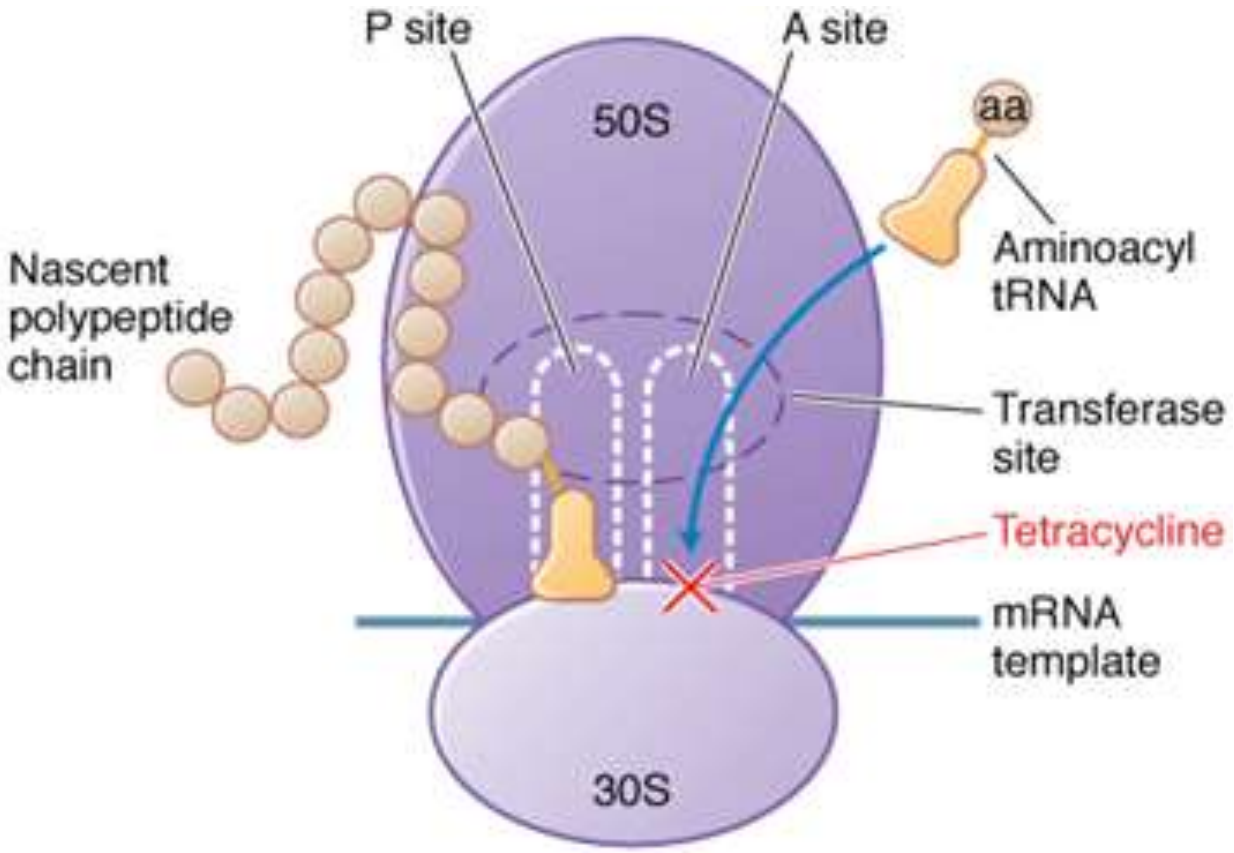
Reasons of selective toxicity

1- Drug accumulates in microbe more than in human cells.

2- Drug is targeted against particular feature of microbe not present in host.

- E.g penicillin inhibits peptidoglycan synthesis in the cell wall. Humans don’t have a cell wall nor peptidoglycan
- Streptomycin target bacterial protein synthesis because bacterial ribosomes (70S) are different from the ribosomes (80S) of humans and other eukaryotic organisms.

Tetracycline is used to treat acne and cholera.



Types of antimicrobial chemotherapy

Antibacterial chemotherapy

Antiprotozoal chemotherapy

Four types

Antifungal chemotherapy

Antiviral chemotherapy

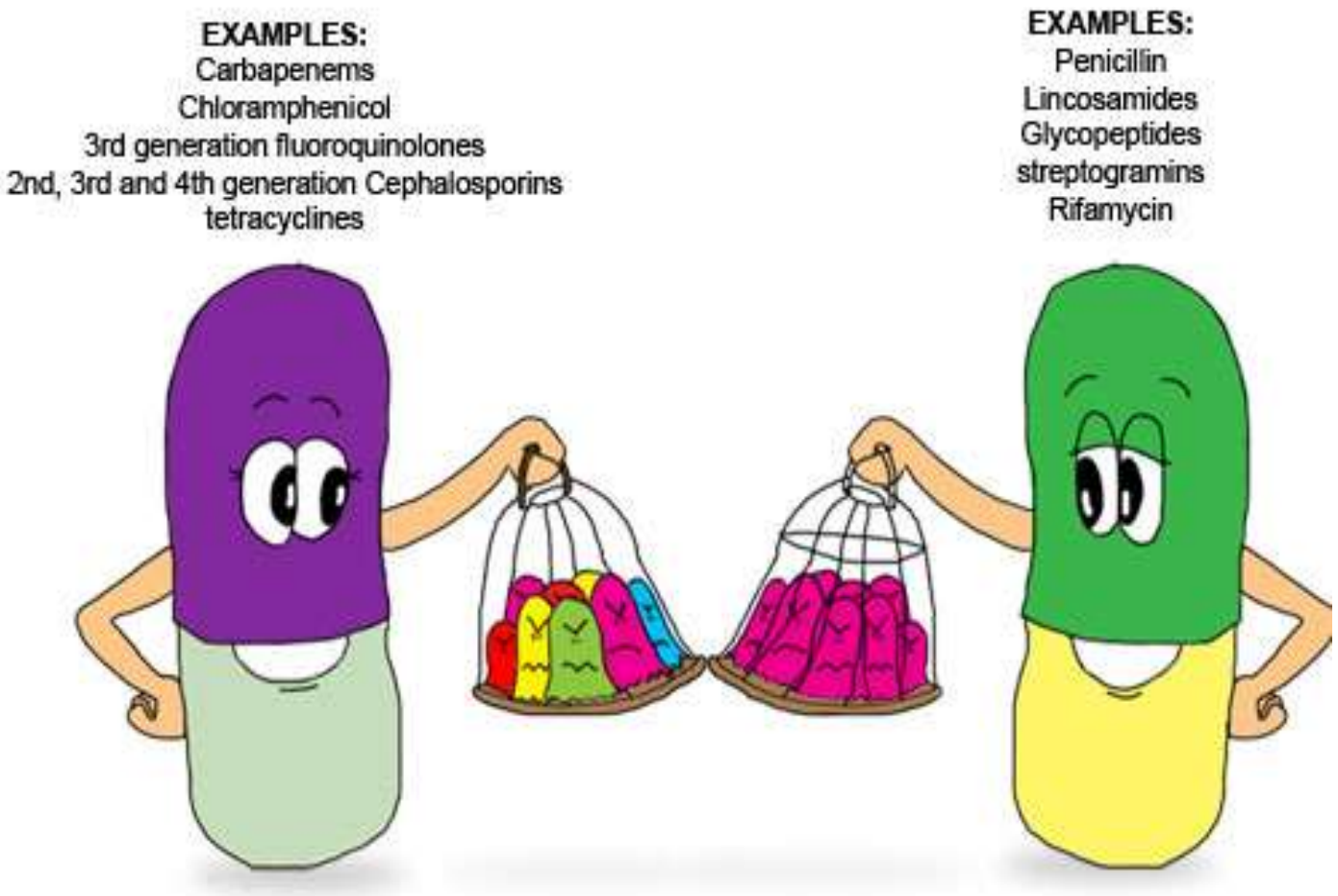
Antibacterial drugs

- Used to treat bacterial infections e.g. tuberculosis
- **Broad spectrum antibacterial** are active against both Gram +ve and Gram -ve.

E.g: tetracyclines, phenicols

- **Narrow spectrum antibacterial** have limited activity and are only useful against particular species.

- For example, glycopeptides and bacitracin are only effective against gram +ve bacteria, whereas polymixins are usually only effective against Gram -ve bacteria.



- **Antiviral drugs**

To stop development of virus in host. E.g. HIV, influenza, herpes simplex

Acyclovir, amantadine

- **Antifungal drugs**

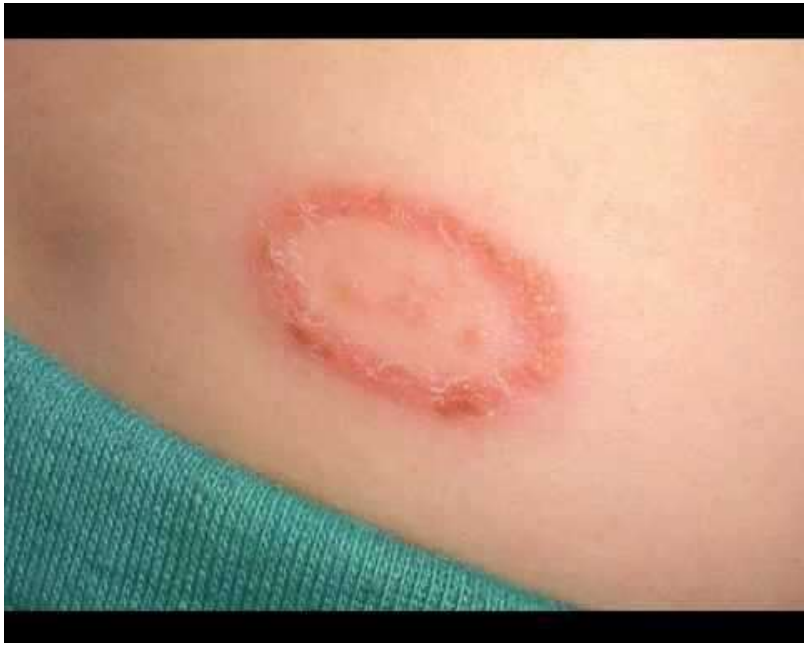
To treat fungal infections

such as athlete's foot, ringworm,

candidiasis (thrush),serious

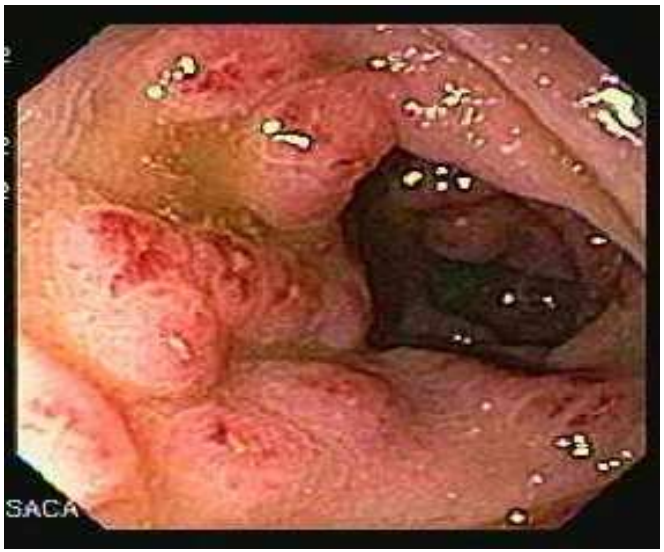
cryptococcal meningitis

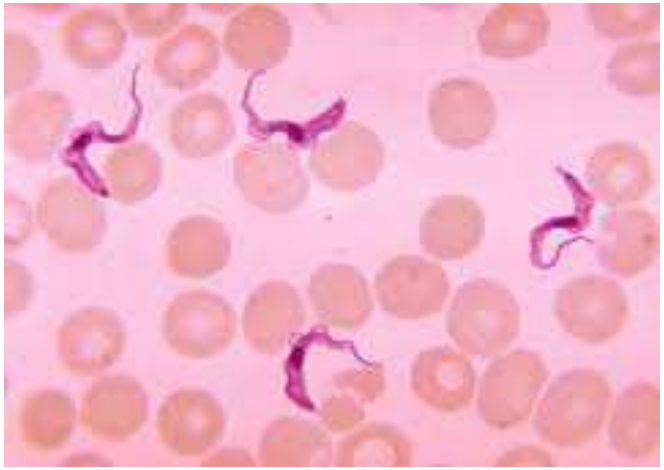
-Amphotericin, ketoconazole



- **Antiprozoal**

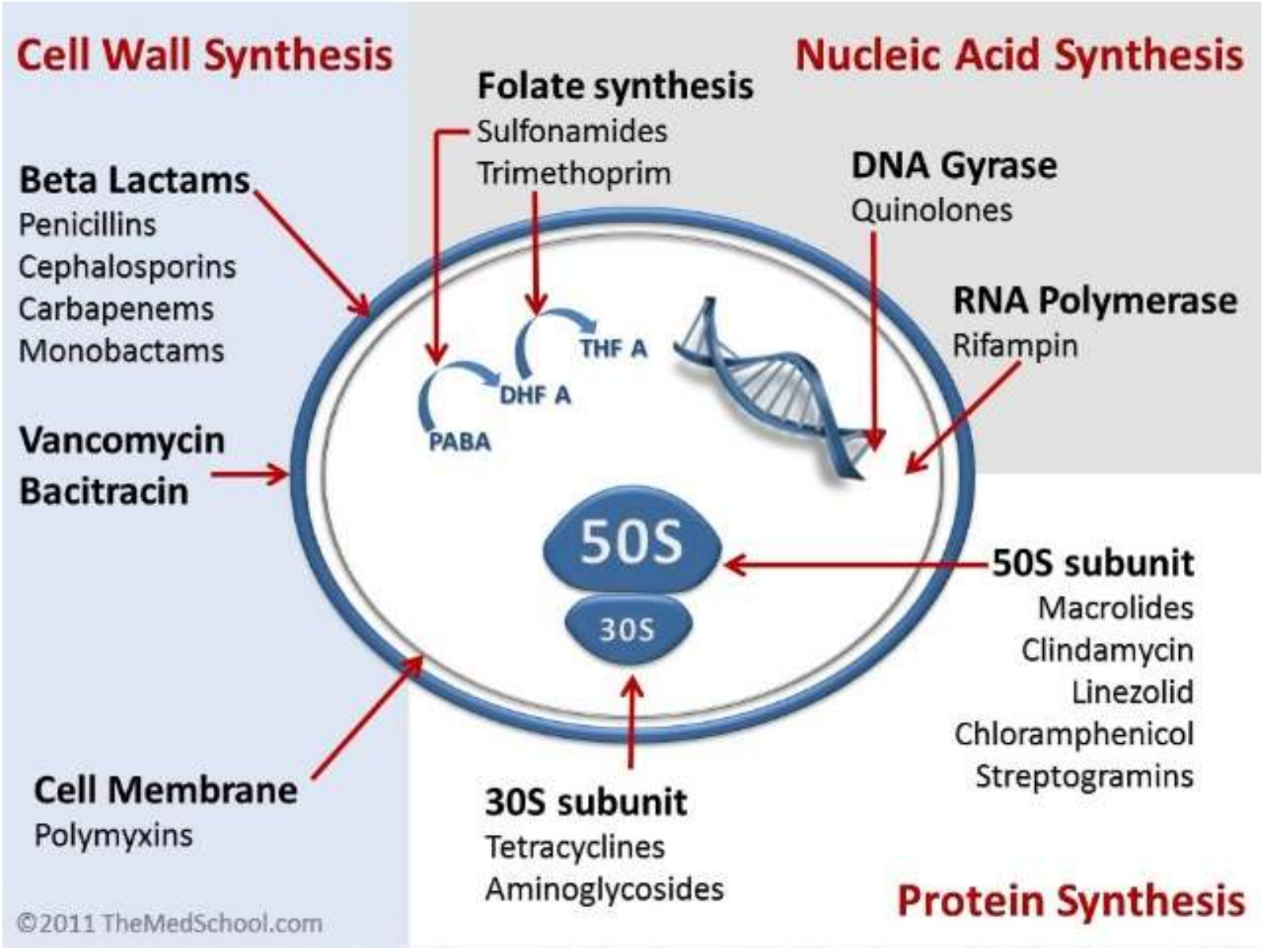
To kill single cell infective protozoans like Entamoeba histolytica(Ulcer of intestins) Plasmodium (malaria) Trypanosoma brucei (sleeping sickness).

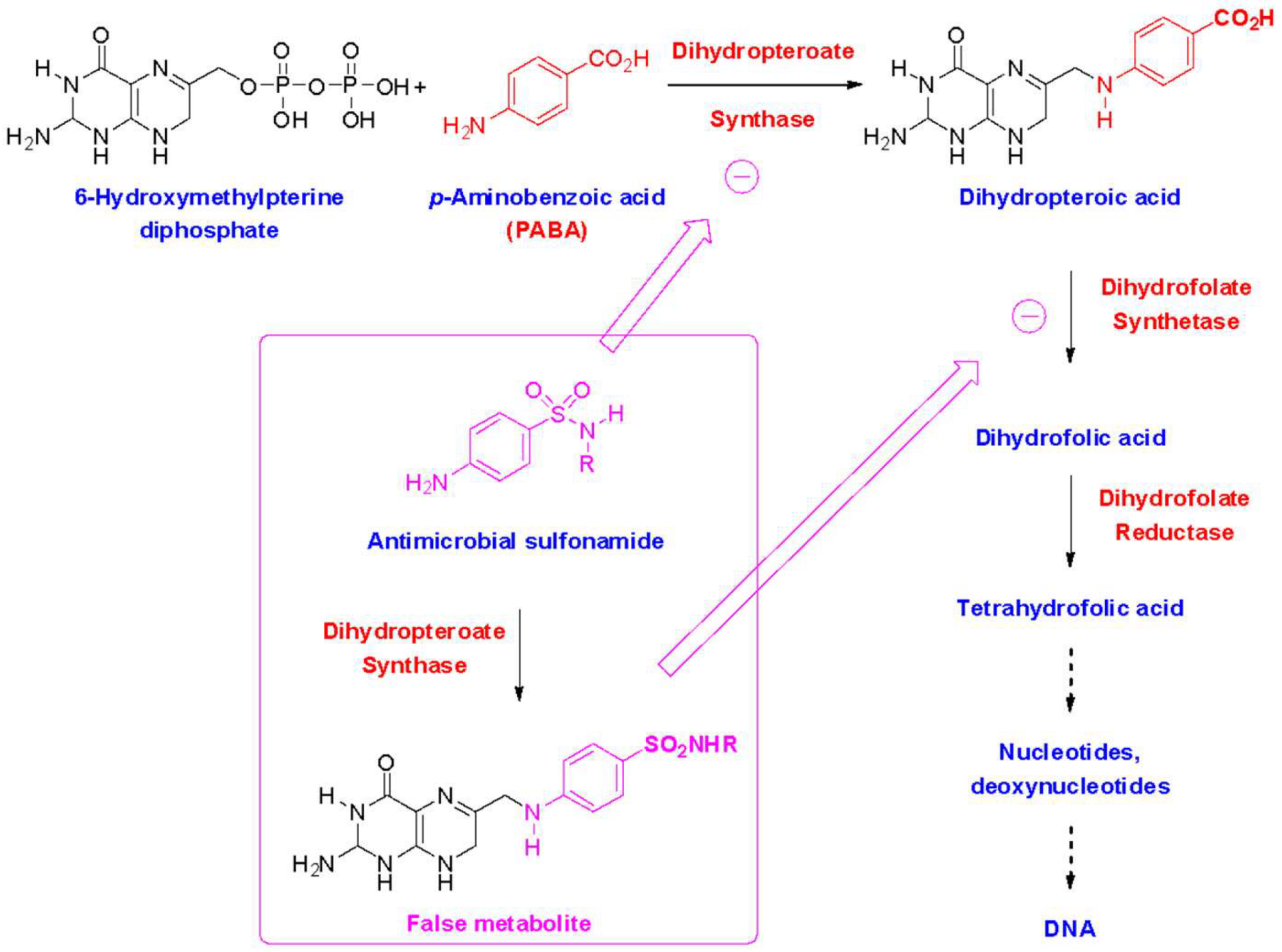




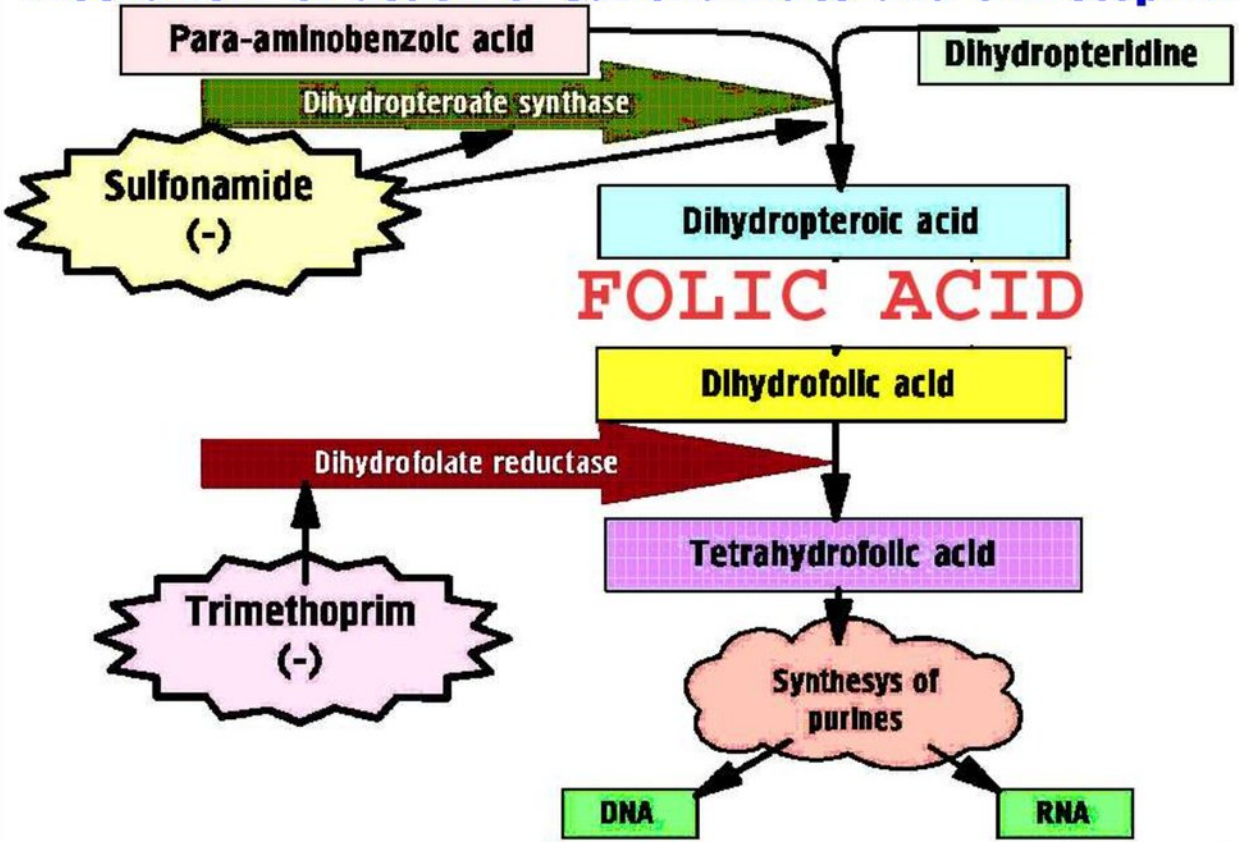
- Tinidazole
- Nifursemizone

Mechanism of action




6-Hydroxymethylpterine diphosphate
p-Aminobenzoic acid (PABA)
Dihydropteroate Synthase
Dihydropteroic acid
Dihydrofolate Synthetase
Dihydrofolic acid
Dihydrofolate Reductase
Tetrahydrofolic acid
Nucleotides, deoxynucleotides
DNA
Antimicrobial sulfonamide
Dihydropteroate Synthase
False metabolite

Mechanism of action of sulfonamides and trimetoprim



Co-trimoxazole: the combination of

Sulfamethoxazole and **Trimethoprim**:

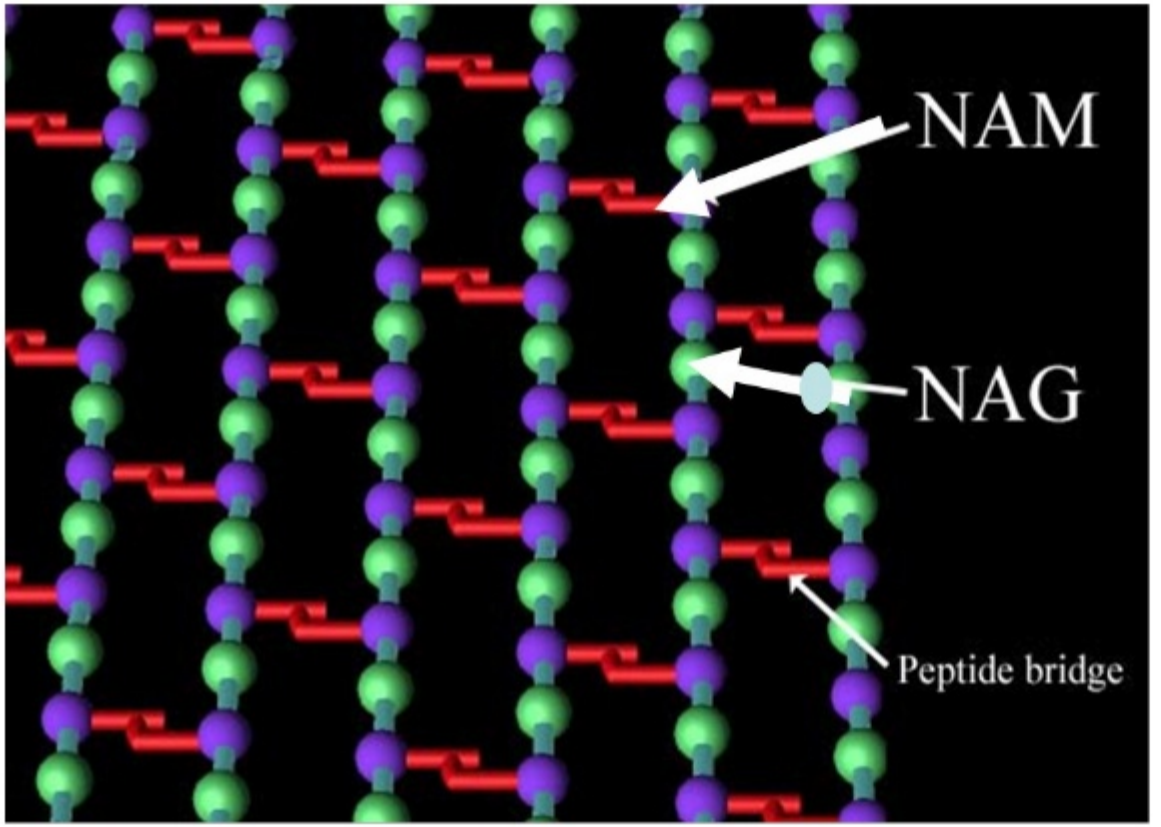
is generally bactericidal

- acts by sequential blockade of **folic acid enzymes** in the synthesis pathway:

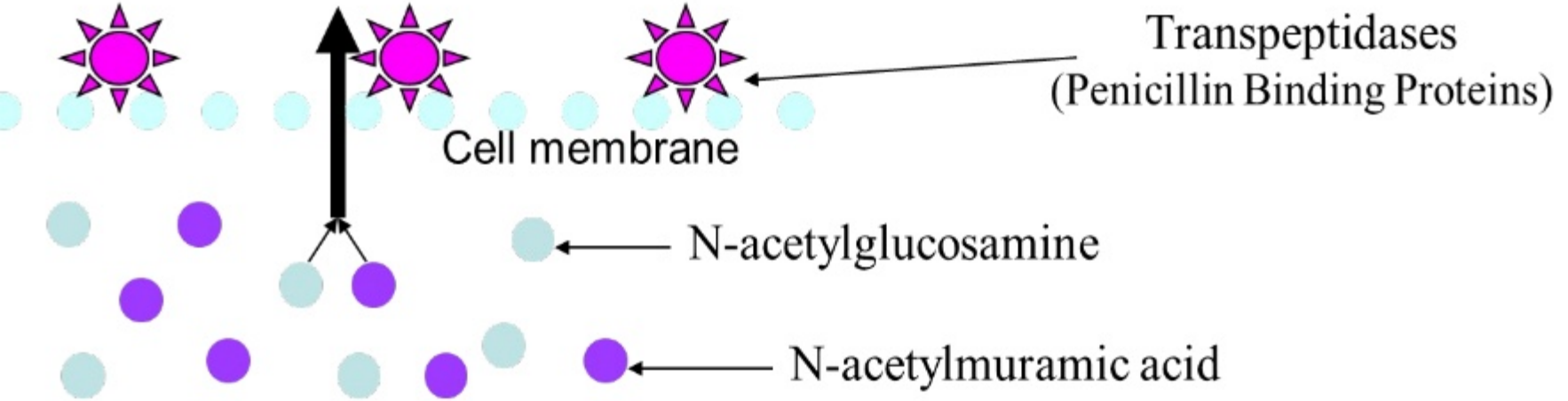
Sulfamethoxazole inhibits formation of dihydrofolic acid from PABA,

Trimethoprim inhibits dihydrofolate reductase responsible for formation of tetrahydrofolic acid from dihydrofolic acid

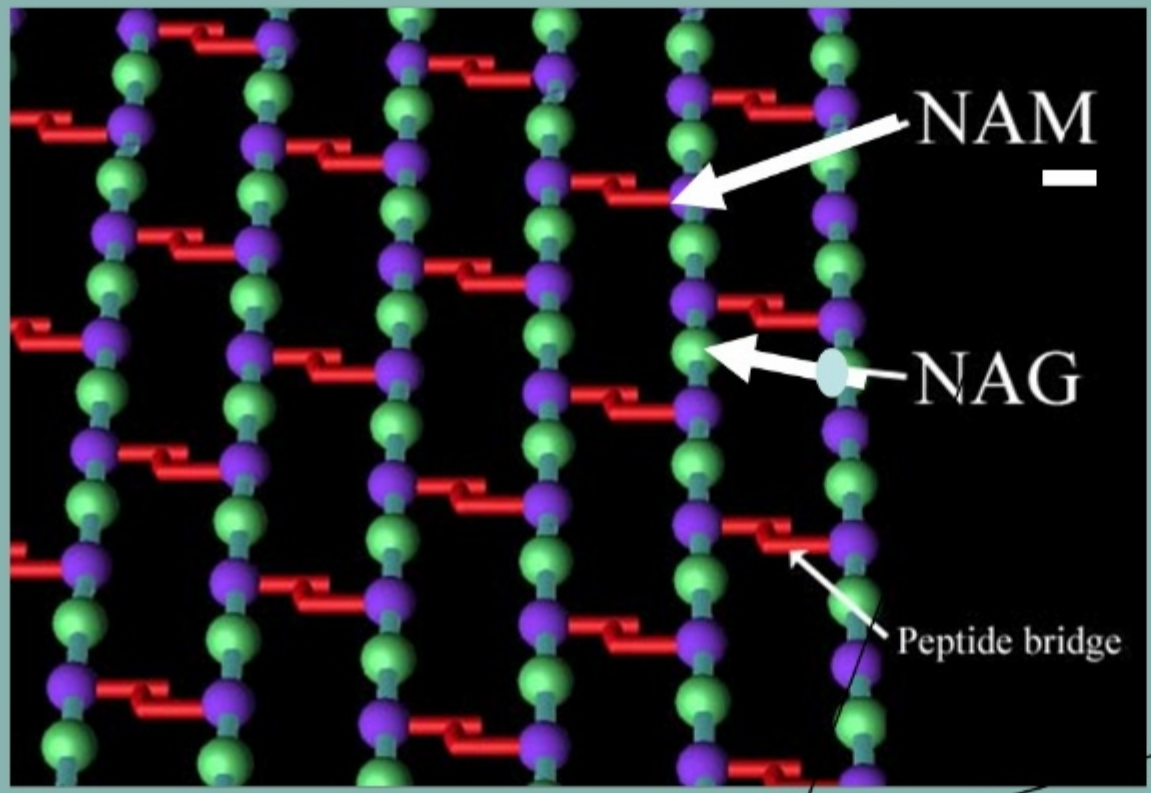
(Peptidoglycan cell wall)



- Transpeptidases located with in the cell membrane are responsible for cross linking the Peptidoglycan chains
- In order to make the rigid grid, There is an enzyme called Transpeptidase,which connects the Little peptide strings perpendicular to the NAM and NAG chains.



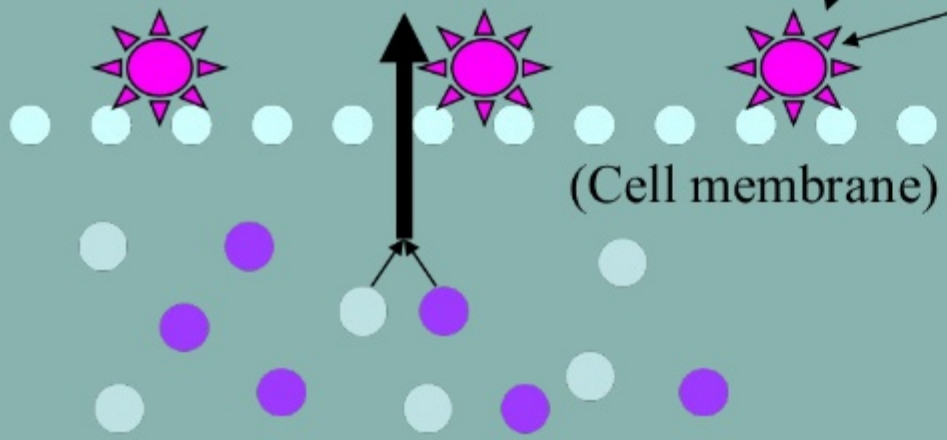
(Peptidoglycan cell wall)

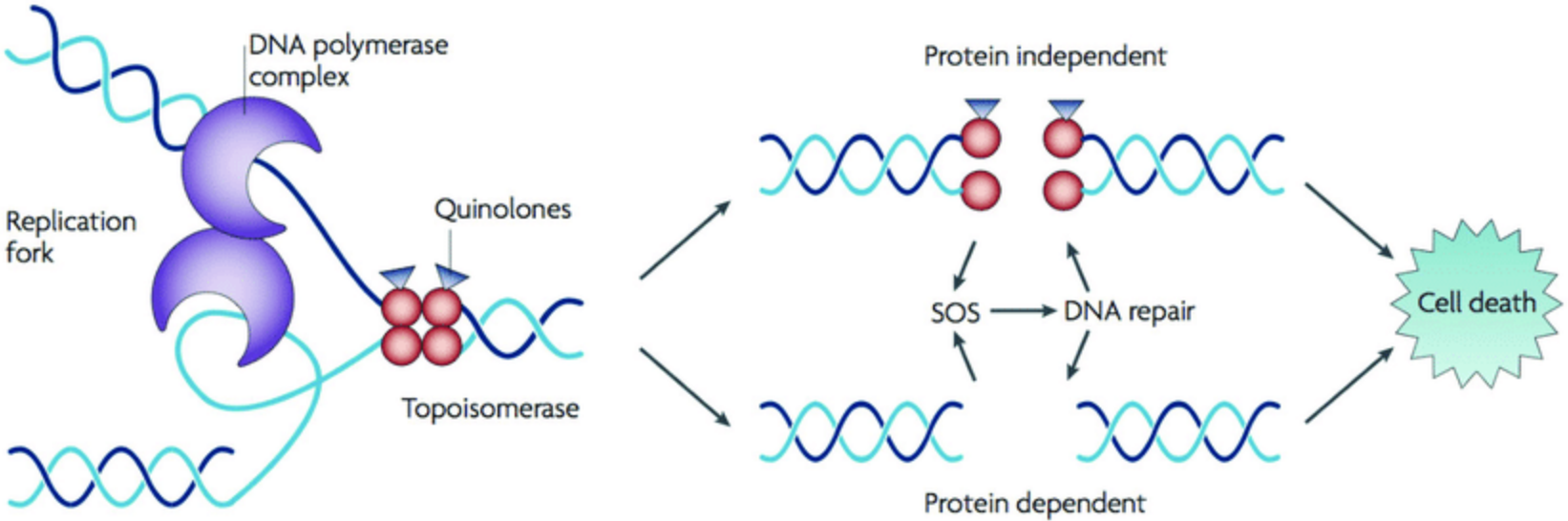


Penicillin's inactivate the transpeptidase enzyme by covalently bonding to the serine residues within the active site.

Bonding is by acetylation

Transpeptidases
(Penicillin Binding Proteins)




DNA polymerase complex
Replication fork
Quinolones
Topoisomerase
Protein independent
SOS
DNA repair
Cell death
Protein dependent

Antimicrobial resistance

- Loss of efficacy of antimicrobial agent
- Resistance against penicillin was first reported in 1965
- Caused because of overuse or insufficient dose

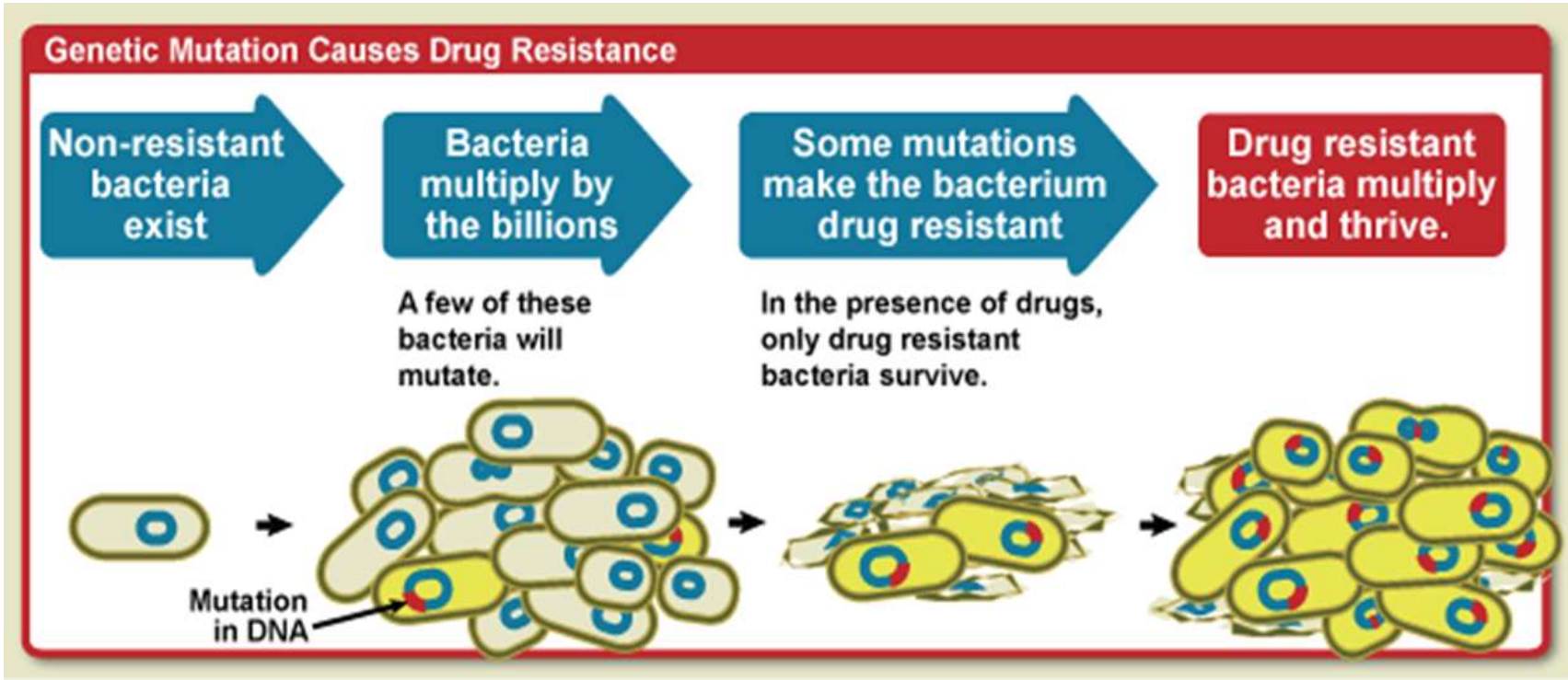
Mechanisms

(1) Due to drug inactivation , destruction

(2) target site alteration

(3) Increased removal from the cell (efflux resistance)

(4) Inhibition as a result of metabolic byproducts


Genetic Mutation Causes Drug Resistance
Non-resistant bacteria exist
Bacteria multiply by the billions
Some mutations make the bacterium drug resistant
Drug resistant bacteria multiply and thrive.
A few of these bacteria will mutate.
In the presence of drugs, only drug resistant bacteria survive.
Mutation in DNA

Side effect of chemotheraupetics

1. **Allergic reactions (Especially anaphylactic shock,** Penicillines**)**

2. **Neurological disorders (Ototoxicity) :** Gentamicin, Streptomycin, Tobramycin

3. **Gastrointestinal disorders : Nausea, vomiting, diarrhea, loss of appetite.**

4. **Common organisms in Superinfections include :** The definition of a superinfection is an additional infection that happens during or immediately after an existing infection.

- ***Clostridium difficile***
- **MDR gram-negative rods** (Multidrug-resistant Gram-negative bacteria)
- **MRSA**
- **Candida** or other fungi

5. **Nephrotoxicity :** Neomycin, kanamycin, paromomycin, bacitracin, the polymyxins (polymyxin B, and colistin), and amphotericin B.

6. **Hepatotoxicity :** Amoxicillin – Clavunate
   Sulfametoksazole - Trimethoprim
   Floroquinolones

7. **Myelotoxicity** : Bone marrow suppression.

Chloramphenicol and most of the antineoplastic drugs.

Pancytopenia is a condition that occurs when a person has low counts for all three types of blood cells:

red blood cells = Anemia

white blood cells = leukopenia

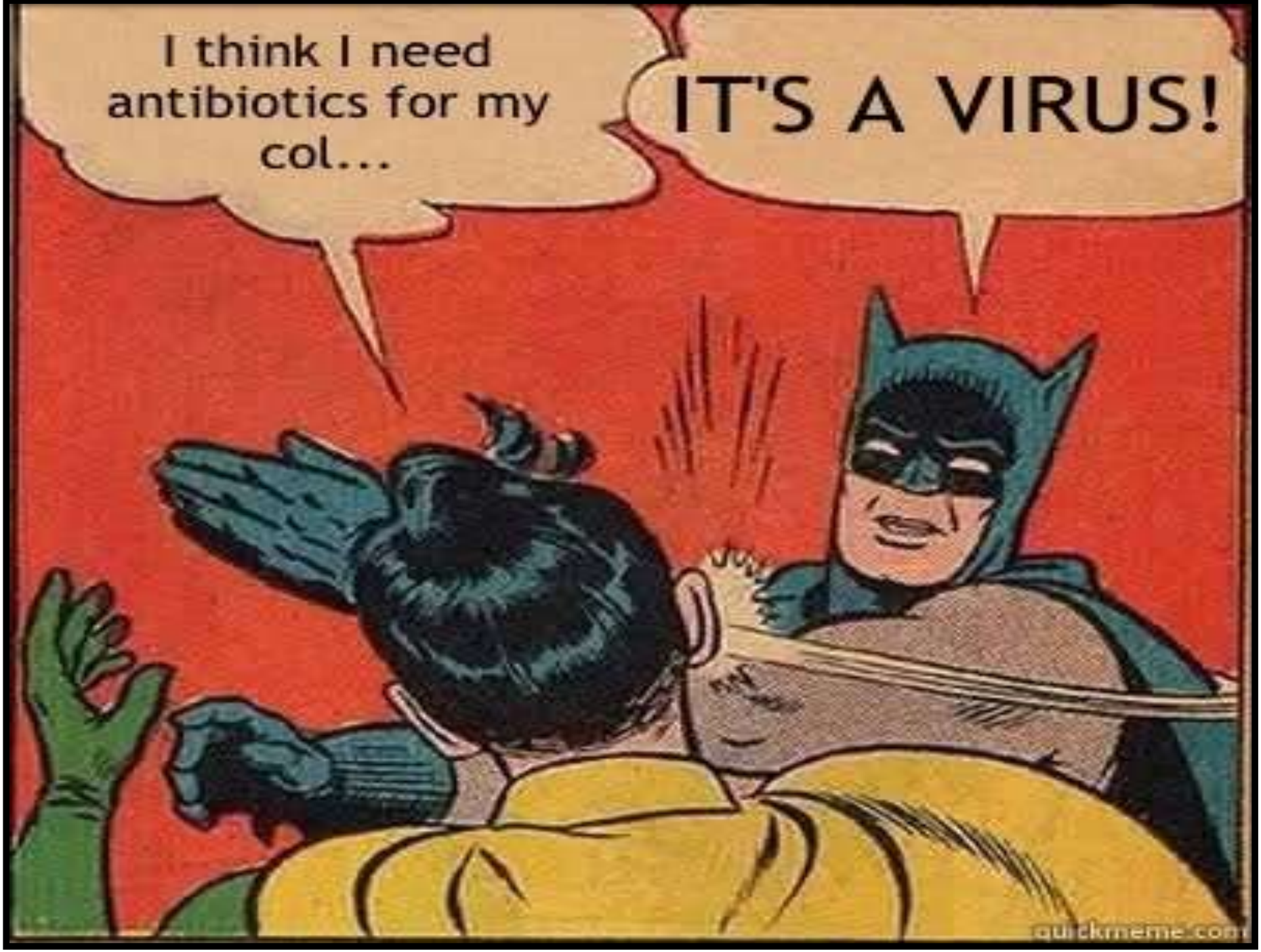
platelets = thrombocytopenia

Opportunistic infection

An **opportunistic infection** is an infection caused by pathogens (bacteria, viruses, fungi, or protozoa) that take advantage of an opportunity not normally available, such as a host with a weakened immune system, an altered microbiota (such as a disrupted gut microbiota), or breached integumentary barriers. Many of these pathogens do not cause disease in a healthy host that has a normal immune system.

Types of infections

- *Aspergillus* sp.
- *Candida albicans*
- *Cryptococcus neoformans*
- *Cytomegalovirus*
- *Histoplasma capsulatum*
- *Kaposi's Sarcoma* *caused by* *Human herpesvirus 8* *(HHV8)*, also called Kaposi's sarcoma-associated herpesvirus (KSHV)
- *Mycobacterium avium complex* *(MAC) (Nontuberculosis Mycobacterium)*
- *Mycobacterium tuberculosis*
- *Pneumocystis jirovecii*, previously known as *Pneumocystis carinii* f. *hominis*
- *Pseudomonas aeruginosa*
- *Salmonella*
- *Staphylococcus aureus*
- *Streptococcus pneumoniae*
- *Streptococcus pyogenes*
- *Toxoplasma gondii*


I think I need antibiotics for my col...
IT'S A VIRUS!
quickmeme.com