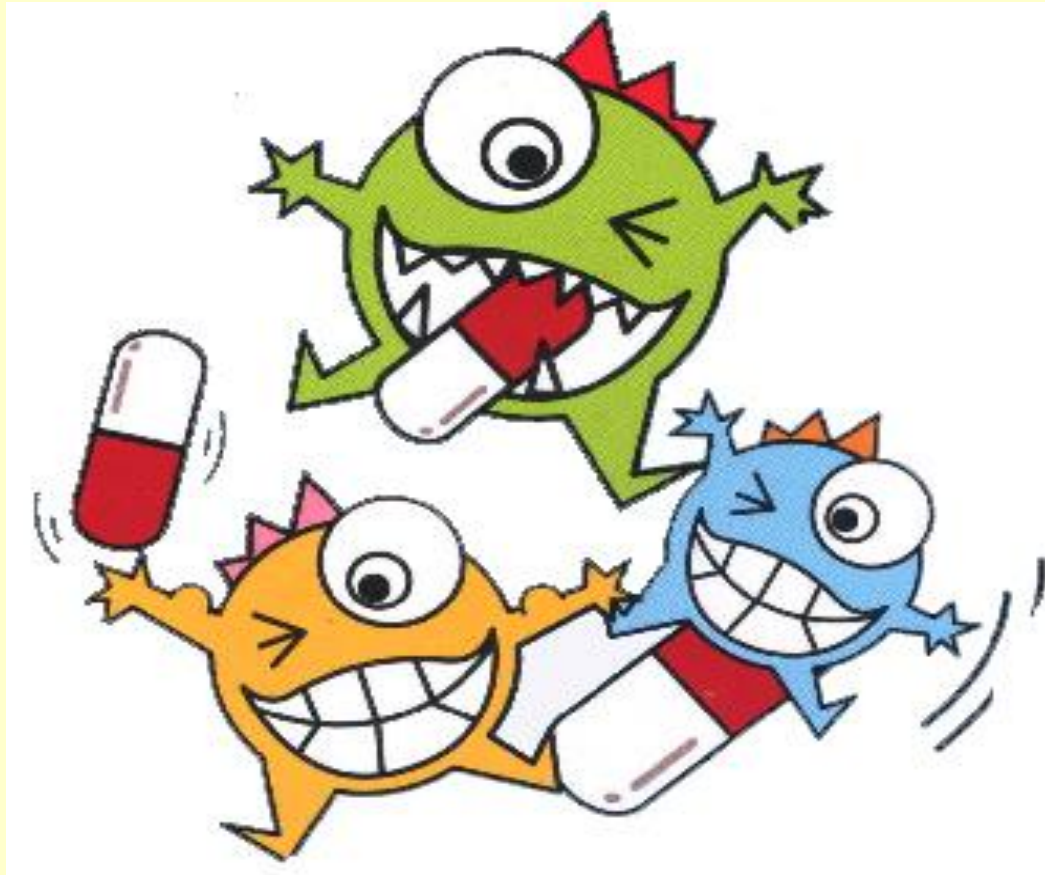


Antimicrobials



What are Antibiotics?

- Substances that kill or interfere with the growth of microorganisms, especially bacteria
- Used to treat or sometimes prevent infection.
- Apart from paracetamol and aspirin no other medicines are more widely used



The Origins of Antimicrobial Drugs

- Antibiotics are common metabolic products of aerobic bacteria and fungi
 - Bacteria: *Streptomyces* and *Bacillus*
 - Molds: *Penicillium* and *Cephalosporium*
- Chemists have created new drugs by altering the structure of naturally occurring antibiotics
- Or searching for metabolic compounds with antimicrobial effects in species other than bacteria and fungi

Antibiotic Drugs

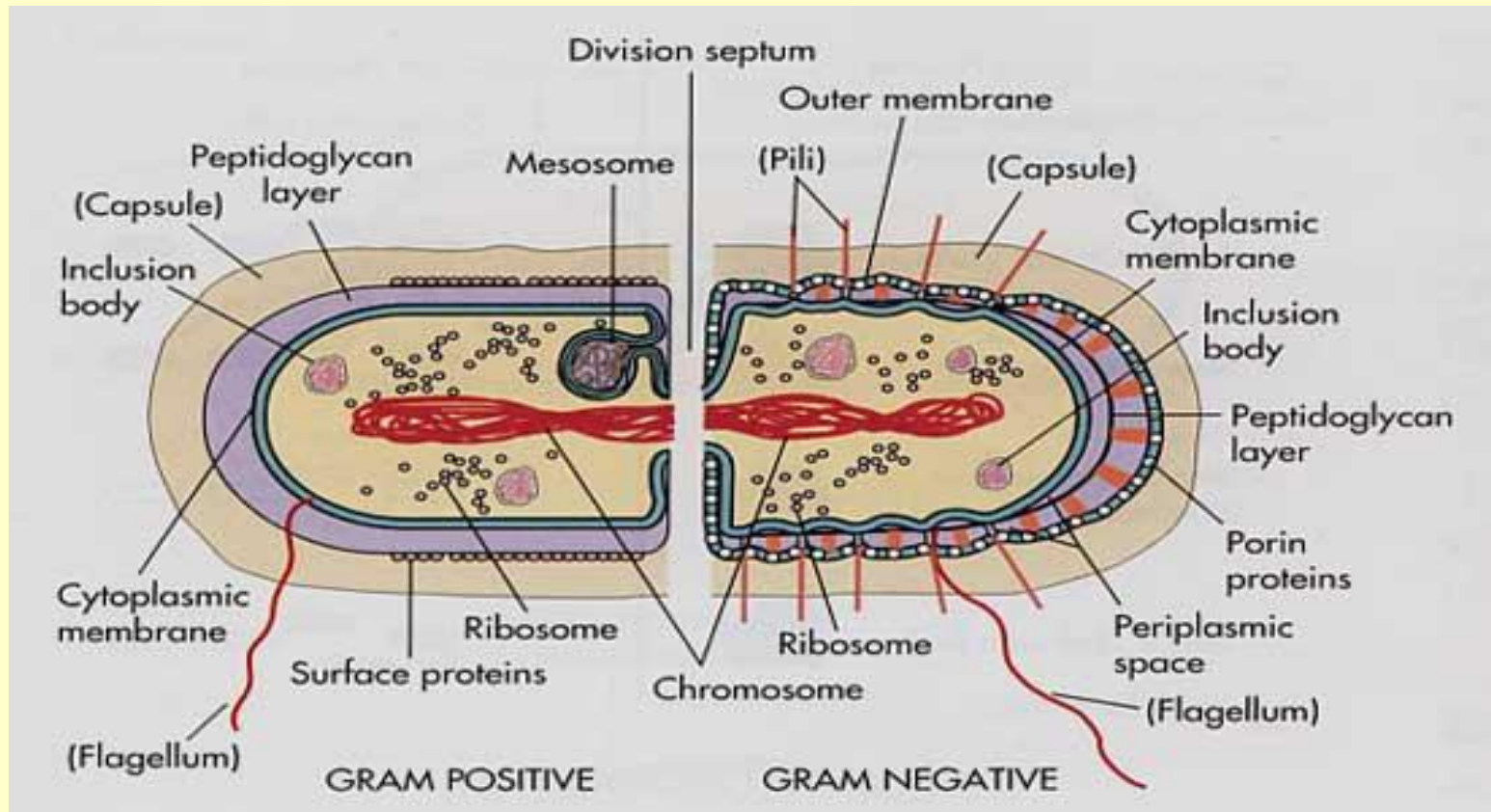
These differ, depending on the type of organism targeted...

- Antibacterial drugs
- Antifungal drugs
- Antiviral drugs
- Antiprotozoal drugs

These are all microbes (except viruses) but they are very different and require different drugs

Gram positive and Gram negative bacteria

Bacteria can be classified by their cell wall structure



Gram positive and Gram negative bacteria

Escherichia coli - Gram negative

Staphylococcus aureus – Gram positive

Salmonella species - Gram positive

Helicobacter pylori – Gram negative

Clostridium difficile – Gram positive

Pseudomonas aeruginosa - Gram negative

Acinetobacter baumannii – Gram negative

Gram negative bacteria are innately more resistant to anti-bacterial drugs – especially those that target the synthesis of peptidoglycan

Classification of bacteria - shape

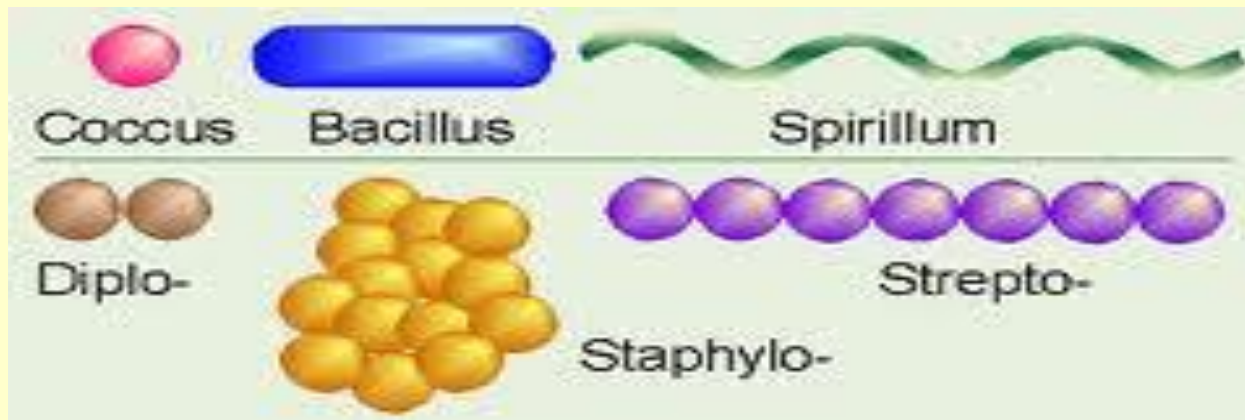
Bacteria come in various shapes and these are used in classification:

Bacilli are rod shaped – *Escherichia coli*

Cocci are spherical– *Staphylococcus aureus*

Spirochaetes are helical – *Helicobacter pylori*

Vibrio are comma shaped– *Vibrio cholerae*



Antibacterial Drugs

The general principle of antibiotic drugs is to target differences between the pathogen's cells and our cells

Otherwise the drug will damage human cells

Mechanisms of Drug Action:

- Inhibition of cell wall synthesis
- Breakdown of cell membrane structure or function
- Inhibition of nucleic acid synthesis, structure or function
- Inhibition of protein synthesis
- Blocks on key metabolic pathways

Best Choice of Drug

Best to choose the drug with high selective toxicity for the infectious agent and low human toxicity

- **Therapeutic index (TI):** the ratio of the dose of the drug that is toxic to humans as compared to its minimum effective dose
- The smaller the ratio, the greater the potential for toxic drug reactions

Interactions Between Drug and Microbe

- Goal of antimicrobial drugs
 - Disrupt the cell processes or structures of bacteria, fungi, and protozoa
 - Or inhibit virus replication
- Most interfere with the function of enzymes required to synthesize or assemble macromolecules or destroy structures already formed in the cell
- Drugs should be **selectively toxic**- they kill or inhibit microbial cells without damaging host tissues

Antibacterial Drug Targets

Target	Example drugs	Effects
Bacterial Cell Wall	Penicillin and Cephalosporin	Target peptidoglycan in bacteria cell wall - prevents reproduction
Biosynthesis of folic acid	Sulphonamides and trimethoprim	block the action of enzymes involved in biosynthesis of folic acid - cells cannot divide and grow
Protein Synthesis - bacterial ribosomes	Tetracyclines and aminoglycosides	Smaller than eukaryotes and so can be targeted
Protein Synthesis - bacterial enzymes	Rifampicin and ciprofloxacin	
Uncertain action	Nitrofurantoin and metronidazole	

The Spectrum of an Antimicrobial Drug

Spectrum – range of activity of a drug

- **Narrow-spectrum** – effective on a small range of microbes
 - Target a specific cell component that is found only in certain microbes
- **Broad-spectrum** – greatest range of activity
 - Target cell components common to most pathogens (ribosomes)

Broad spectrum antibacterials

Ampicillin - effective against G+ and G- bacteria but susceptible to penicillinases such as those produced by resistant *S aureus* and *E coli*.

Amoxicillin - a derivative of ampicillin and similar in character but better absorbed.

Co-amoxiclav - a compound mixture of amoxicillin and clavulanic acid, an inhibitor of beta-lactamases produced by many resistant bacteria.

Cephalosporins - similar in structure and action to penicillins but with certain differences in selectivity and susceptibility to beta-lactamases.

Carbapenems - a class of beta-lactam antibiotics with a structure that renders them resistant to beta-lactamases. Includes aztreonam, imipenem and meropenam

Unwanted effects

- Hypersensitivity
- Digestive disturbances
- Antibiotic –associated colitis
- Aminoglycosides -can result in vestibular and auditory damage as well as nephro-toxicity
- Rifampicin is a potent inducer of hepatic enzymes that can degrade other drugs including oral contraceptives

Bacterial resistance



Superinfection

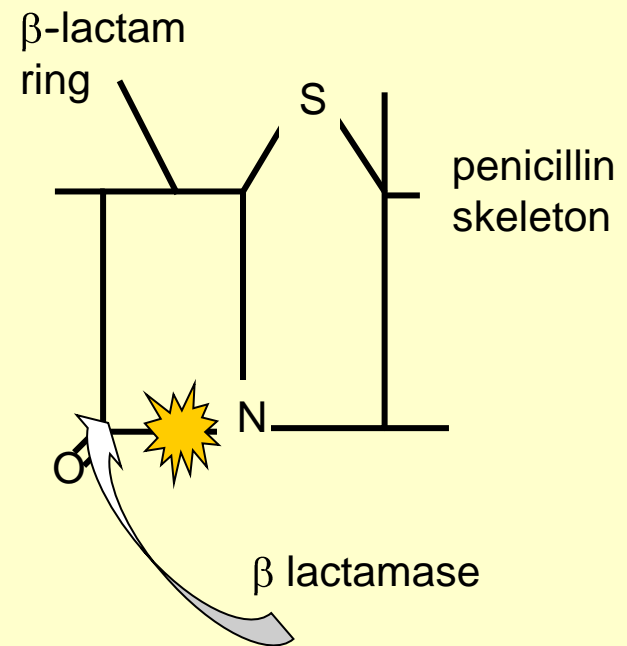
- When beneficial species are destroyed, microbes that were once kept in small numbers can begin to overgrow and cause disease—a **super infection**
 - Using a broad-spectrum cephalosporin for a urinary tract infection; destroys lactobacilli in the vagina; without the lactobacilli *Candida albicans* can proliferate and cause a yeast infection
 - Oral therapy with tetracyclines, clindamycin, and broad-spectrum penicillins and cephalosporins is associated with antibiotic-associated colitis

Extended -Spectrum Beta-Lactamase producing E.coli (ESBL)

Antibiotic resistant strains of E.coli

Produce an enzyme - ESBL

Only 2 oral antibiotics and a very limited IV antibiotics remain effective



Prevalance

Emerging problem

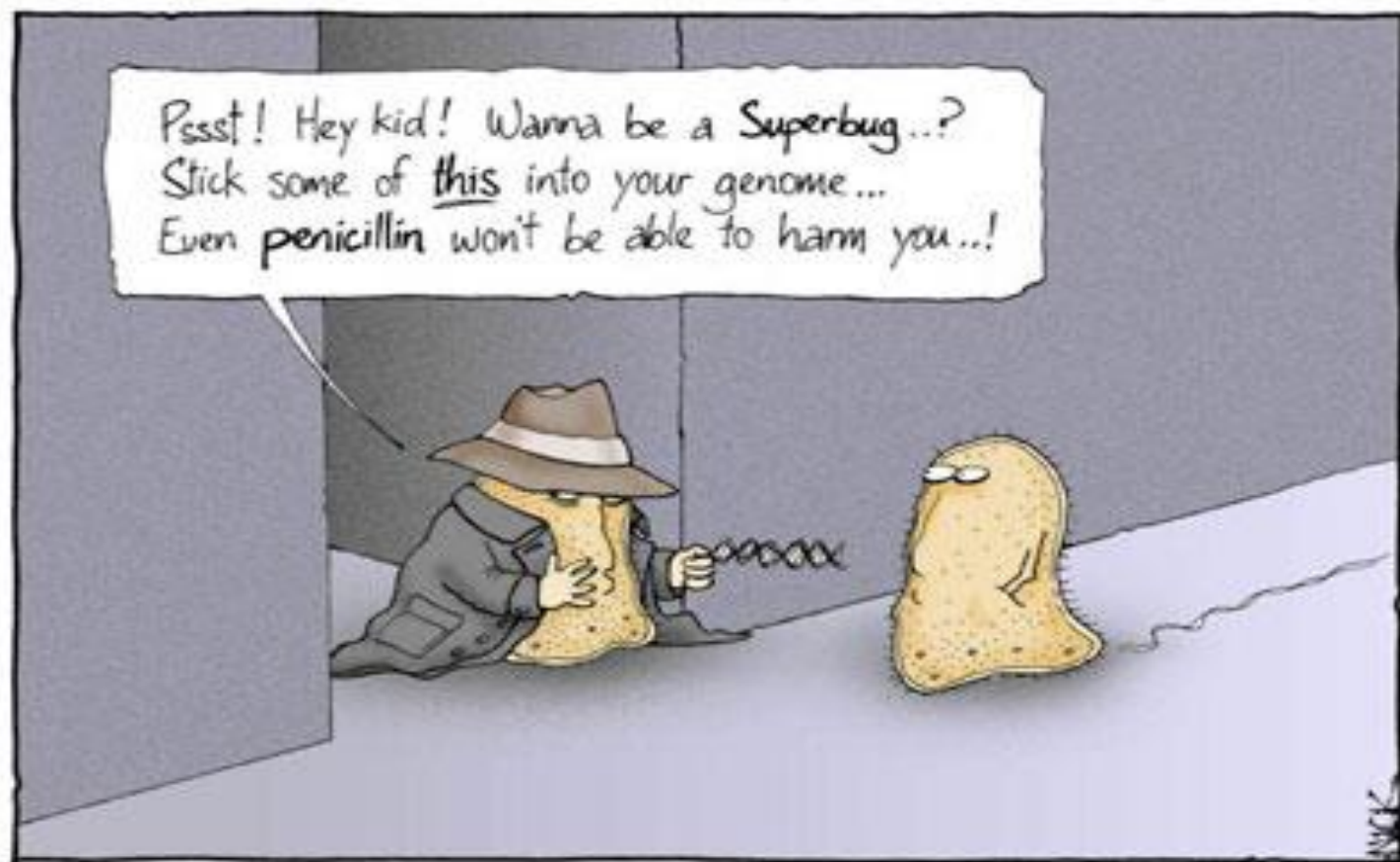
Surveillance requires adaption

Current information for E.coli bacteraemia indicate:

1994 -2004 year on year increase

Total numbers have doubled in last decade to 17,416 cases

Percentage multi-resistant and therefore likely ESBL – associated is 4% in 2003



It was on a short-cut through the hospital kitchens that Albert was first approached by a member of the Antibiotic Resistance.