Chapter 4: antibiotics and antiseptics

Learning objectives

1/ antibiotic’s definitions and history
2/ spectrum of antimicrobial activity
3/ antimicrobial drugs modes of action
4/ survey of commonly used antimicrobial drugs
5/ which and why new antibiotics
6/ some antimicrobial chemical structures
7/ major bacterial mechanisms of drug resistance
8/ in vitro studying activities of antibiotics:
   = disk diffusion method or Kirby-Bauer test
   = broth dilution tests for MIC and MBC measurements
9/ antiseptic concept and main used antiseptics
1/ antibiotic’s definitions and history

The discovery of penicillin by Alexander FLEMING who took this photograph in 1928. The colony of *Penicillium* mold accidentally contaminated the plate and is inhibiting nearby *Staphylococcus aureus* growth.
The mold was identified as *Penicillium notatum*, and its active compound was isolated a short time later, was named *penicillin*.

Similar inhibitory reactions between colonies on solid media are commonly observed in microbiology, and the mechanism of inhibition is called *antibiosis* *(that means against live)*.

From this word comes the term *antibiotic*, a substance produce by microorganisms that in small amounts inhibits another microorganism.

More than half of our antibiotics are produced by species of *Streptomyces*, filamentous bacteria that commonly inhabit in soil. A few antibiotics are produced by bacteria of the genus *Bacillus*, and others are produced by molds, mostly of the genus *Penicillium* and *Cephalosporium*. 
Microorganisms

1/Gram + rods
= *Bacillus subtilis*
= *Bacillus polymyxa*

2/actinomycetes
= *Streptomyces nodosus*
= *Streptomyces venezuelae*
= *Streptomyces aureofaciens*
= *Streptomyces erythraeus*
= *Streptomyces fradiae*
= *Streptomyces griseus*
= *Micromonospora purpurea*

3/ fungi
= *Cephalosporium Spp.*
= *penicillium griseofulvum*
= *Penicillium notatum*

Antibiotics

> Bacitracine
> Polymyxine

> Amphotericine B
> Chloramphenical
> Chlorotetracycline et tetracycline
> Erythomycine
> Neomycine
> Streptomycine
> Gentamycine

Cephalosporines
Griseofilvine
Penicillines
In 1940, a group of scientists at Oxford University headed by Howard Florey and Ernest Chain succeeded in the first clinical trials of penicillin. They, for the first time, successfully treated a *Staphylococcus aureus* septicemia.

**Antimicrobial drugs** is the class of medication used in *chemotherapy*, the treatment of infectious diseases using chemical substances.

Drugs used in the chemotherapy of infectious diseases are classified in two groups:

- drugs that have been synthesized by chemical procedures in the laboratory are called *synthetic drugs*
- drugs produced by bacteria and fungi are called *antibiotics*
Chemotherapeutic agent act by interfering with the growth of microorganisms. However, they must often act within the host.

Therefore, their effects on the cells and tissues of the host are important. The ideal antimicrobial drug kills the harmful microorganism without damaging the host; this is the principle of selective toxicity.
Drugs’s spectrum of microbial activity is the range of different microbial types they affect.

Some drugs, such as penicillin, have a narrow spectrum of microbial activity; because penicillin affects gram-positive bacteria but very few gram-negative bacteria.

Antibiotics that affect a broad range of gram-positive and gram-negative bacteria are therefore called broad-spectrum antibiotics.

Because the identity of pathogen is not always immediately known, a broad-spectrum drug would seem to have an advantage in treating a disease by saving valuable time.
The disadvantage is that many normal microbiota of the host are destroyed by broad-spectrum drugs. The normal microbiota ordinary compete with and check the growth of pathogens and other microbes.

But if certain organisms in the normal microbiota are not destroyed by the antibiotic and their competitors are destroyed, the survivor may flourish and become *opportunistic pathogen*

An example that sometimes occurs is overgrowth by the yeastlike fungus *Candida albicans*, which is not sensitive to bacterial antibiotics and is a intestinal microbiota
Spectrum of currently used antibiotics

<table>
<thead>
<tr>
<th>Famille</th>
<th>Antibiotique</th>
<th>Gram +</th>
<th>Gram -</th>
</tr>
</thead>
<tbody>
<tr>
<td>ß-lactamines</td>
<td>Benzylpénicilline</td>
<td>+</td>
<td>-</td>
</tr>
<tr>
<td></td>
<td>Oxacilline</td>
<td>+</td>
<td>-</td>
</tr>
<tr>
<td></td>
<td>Ampicilline</td>
<td>+</td>
<td>+</td>
</tr>
<tr>
<td></td>
<td>Imipénème</td>
<td>+</td>
<td>+</td>
</tr>
<tr>
<td>Aminosides</td>
<td>Gentamicine</td>
<td>+</td>
<td>+</td>
</tr>
<tr>
<td></td>
<td>Tobramycine</td>
<td>+</td>
<td>+</td>
</tr>
<tr>
<td>Phénicolés</td>
<td>Chloramphénicol</td>
<td>+</td>
<td>+</td>
</tr>
<tr>
<td>Tétracyclines</td>
<td>Doxycycline</td>
<td>+</td>
<td>+</td>
</tr>
<tr>
<td>Macrolides</td>
<td>Erythromycine</td>
<td>+</td>
<td>-</td>
</tr>
<tr>
<td>Glycopeptides</td>
<td>Vancomycine</td>
<td>+</td>
<td>-</td>
</tr>
<tr>
<td>Quinolones</td>
<td>Acide nalidixique</td>
<td>-</td>
<td>+</td>
</tr>
<tr>
<td>Autres</td>
<td>Acide fusidique</td>
<td>+</td>
<td>-</td>
</tr>
</tbody>
</table>
3/ the action of antimicrobial drugs

- Antimicrobial drugs are either **bactericidal** or **bacteriostatic**
- Bactericidal drugs kill microbes directly
- Bacteriostatic drugs prevent microbes for growing. In bacteriostasis, the host’s own defenses, such as phagocytosis and antibody production, thus usually destroy the microorganisms

<table>
<thead>
<tr>
<th>Drug</th>
<th>Action</th>
</tr>
</thead>
<tbody>
<tr>
<td>Penicillin</td>
<td>bactericidal</td>
</tr>
<tr>
<td>Fluoroquinolones</td>
<td>Bactericidal</td>
</tr>
<tr>
<td>Fusidic acid</td>
<td>Bacteriostatic</td>
</tr>
<tr>
<td>Chloramphenicol</td>
<td>Bacteriostatic</td>
</tr>
<tr>
<td>Cephalosporins</td>
<td>bactericidal</td>
</tr>
<tr>
<td>Aminoside</td>
<td>bactericidal</td>
</tr>
<tr>
<td>Antibacterial Class</td>
<td>Activity</td>
</tr>
<tr>
<td>---------------------------</td>
<td>--------------</td>
</tr>
<tr>
<td>Tetracyclins</td>
<td>Bacteriostatic</td>
</tr>
<tr>
<td>Macrolides</td>
<td>Bacteriostatic</td>
</tr>
<tr>
<td>Glycopeptides</td>
<td>Bactericidal</td>
</tr>
<tr>
<td>Vancomycin</td>
<td>Bactericidal</td>
</tr>
<tr>
<td>Rifampycine</td>
<td>+/- bactericidal, bacteriostatic</td>
</tr>
<tr>
<td>Lincosamides</td>
<td>Bacteriostatic</td>
</tr>
<tr>
<td>Sulfamide</td>
<td>Bacteriostatic</td>
</tr>
<tr>
<td>Synergistin</td>
<td>Bactericidal</td>
</tr>
<tr>
<td>Trimethoprimine</td>
<td>Bacteriostatic</td>
</tr>
<tr>
<td>Trimethoprimine + sulfamide</td>
<td>Bactericidal</td>
</tr>
<tr>
<td>Quinolones</td>
<td>Bactericidal</td>
</tr>
<tr>
<td>Monobactam</td>
<td>Bactericidal</td>
</tr>
<tr>
<td>Nitro-imidazole</td>
<td>Bactericidal</td>
</tr>
</tbody>
</table>
Weak concentration of an antibiotic involves generally a bacteriostatic effect; strong concentrations get bactericidal effects such as bacteriostatic chloramphénicol can act as bactericidal at high concentrations.

The major modes of action of antimicrobial drugs are:

- inhibition of cell wall synthesis
- inhibition of nucleic acid replication and transcription
- inhibition of protein synthesis
- injury to plasma membrane
- inhibition of synthesis of essential metabolisms

Antimicrobial drugs destroy constant bacterial structures or impair main metabolism pathways.
**Figure 20.2** A summary of the major modes of action of antimicrobial drugs.

- Inhibition of cell wall synthesis: Penicillins, cephalosporins, bacitracin, vancomycin
- Inhibition of protein synthesis: Chloramphenicol, erythromycin, tetracyclines, streptomycin
- Inhibition of nucleic acid replication and transcription: Quinolones, rifampin
- Injury to plasma membrane: Polymyxin B
- Inhibition of synthesis of essential metabolites: Sulfanilamide, trimethoprim

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The inhibition of protein synthesis by antibiotics. The black arrows indicate the specific points at which different antibiotics interfere with the process.
4/survey of commonly used antimicrobial drugs

Principal families of antibiotics

- Sulfonamides 1936
- ß lactamines 1940
- Tetracyclines 1949
- Phenicoles 1949
- Aminoglycosides 1950
- Macrolides 1952
- Glycopeptides 1958
- Polymyxin 1959
- Quinolones 1962 and Fluoroquinolone 1990
- Nitro-imidazoles 1971
- Anti-mycobacteria such as Isoniacid (INH), Ethambutol, and Rifampicine 1966
- Fosfomycine 1980
- Trimethoprim 1980
- Cephalosporin 1980
5/ New antibiotics

>LEVOFLOXACINE  1990
( fluoroquinolone)
>MOXIFLOXACINE  1990
( fluoroquinolone)
>LINOZOLIDINES 2005
( oxazolidinone)
>TELITHROMYCINE 2005
( ketolide)
>ERTAPENEM 2005 ( carbapenem)
>DALFOPRISTINE/QUINUPRISTINE 2005 (synergistine)
>DAPTOMYCINE 2006
( glycyclycline)
Why new antibiotics?

- In 1952 vancomycin was isolated from Streptomyces orientalis, a filamentous mold.
- This new drug was extremely bactericidal against *Staphylococcus* species.
- Since, vancomycin is reserved for multiresistant staphylococci and enterococci strains.
- In 1987 some bacteria (*Staphylococcus aureus* Methicillin Resistant or SAMR and multiresistant enterococci) which was the main bacteria involved in nosocomial infectious, became resistant to vancomycin.
And researchs revealed that, in GB, Ireland and Italy hospitals, 36 to 50% of isolated staphylococcus species were SAMRS.

In 1999 in USA, one isolates a *Staphylococcus* strain which resists to all known antibiotics.

According to the FDA, multiresistant bacteria are responsible of at least to 20% of nosocomial infectious.

All those epidemiologic situations require to find new antibiotics and to study new targets of the antibiotics.
## 6/ Drugs by mode of actions

<table>
<thead>
<tr>
<th>Inhibitors of Cell Wall Synthesis</th>
<th>Comments</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Natural penicillins</strong></td>
<td>Gram-positive bacteria, injected. Bactericidal.</td>
</tr>
<tr>
<td>Penicillin V</td>
<td>Broad spectrum. Bactericidal.</td>
</tr>
<tr>
<td>Semisynthetic penicillins</td>
<td>Resistant to penicillinase. Bactericidal.</td>
</tr>
<tr>
<td>Ampicillin</td>
<td>Gram-negative bacteria, including <em>Pseudomonas</em> spp. Bactericidal.</td>
</tr>
<tr>
<td>Methicillin</td>
<td>Resistant to penicillinase; gram-negative bacteria with a broad spectrum of activity. Bactericidal.</td>
</tr>
<tr>
<td>Monobactams</td>
<td>$\beta$-lactam type, very broad spectrum. Bactericidal.</td>
</tr>
<tr>
<td>Cephalosporins</td>
<td>Glycopeptide type, penicillin-resistant gram-positive bacteria. Bactericidal.</td>
</tr>
<tr>
<td>Carbapenems (imipenem)</td>
<td>Mycobacteria (tuberculosis); inhibits synthesis of mycolic acid component of mycobacterial cell wall. Bacteriostatic.</td>
</tr>
<tr>
<td>Bacitracin</td>
<td>Mycobacteria (tuberculosis); inhibits incorporation of mycolic acid into mycobacterial cell wall. Bacteriostatic.</td>
</tr>
<tr>
<td>Vancomycin</td>
<td>Isoniazid (INH)</td>
</tr>
</tbody>
</table>
### Inhibitors of Protein Synthesis

<table>
<thead>
<tr>
<th>Class</th>
<th>Effect</th>
</tr>
</thead>
<tbody>
<tr>
<td>Streptomycin</td>
<td>Topical use, broad spectrum. Bactericidal.</td>
</tr>
<tr>
<td>Neomycin</td>
<td>Broad spectrum, including <em>Pseudomonas</em> spp. Bactericidal.</td>
</tr>
<tr>
<td>Gentamicin</td>
<td></td>
</tr>
<tr>
<td>Tetracyclines</td>
<td>Broad spectrum, including chlamydas and rickettsias; animal feed additives. Bacteriostatic.</td>
</tr>
<tr>
<td>Tetracycline, oxytetracycline, chlorotetacycline</td>
<td></td>
</tr>
<tr>
<td>Chloramphenicol</td>
<td>Broad spectrum, potentially toxic. Bacteriostatic.</td>
</tr>
<tr>
<td>Macrolides</td>
<td></td>
</tr>
<tr>
<td>Erythromycin</td>
<td>Alternative to penicillin. Bacteriostatic.</td>
</tr>
</tbody>
</table>

### Injury to the Plasma Membrane

<table>
<thead>
<tr>
<th>Agent</th>
<th>Effect</th>
</tr>
</thead>
<tbody>
<tr>
<td>Polymyxin B</td>
<td>Topical use, gram-negative bacteria, including <em>Pseudomonas</em> spp. Bactericidal.</td>
</tr>
</tbody>
</table>

### Inhibitors of Nucleic Acid Synthesis

<table>
<thead>
<tr>
<th>Class</th>
<th>Effect</th>
</tr>
</thead>
<tbody>
<tr>
<td>Rifampin</td>
<td></td>
</tr>
<tr>
<td>Quinolones and fluoroquinolones</td>
<td>Inhibits DNA synthesis; broad spectrum; urinary tract infections. Bactericidal.</td>
</tr>
<tr>
<td>Nalidixic acid, norfloxacin, ciprofloxacin</td>
<td></td>
</tr>
</tbody>
</table>

### Competitive Inhibitors of the Synthesis of Essential Metabolites

<table>
<thead>
<tr>
<th>Agent</th>
<th>Effect</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sulfonamides</td>
<td>Broad spectrum; combination is widely used. Bacteriostatic.</td>
</tr>
<tr>
<td>Trimethoprim-sulfamethoxazole</td>
<td></td>
</tr>
</tbody>
</table>
7/ Some chemical structures

Vancomycin

Tretracyclines
acide nalidixique
Quinolone

Fluoroquino lone

5-nitro-imidazoles

R

-CH₂-CH₂-OH
-CH₂-CHOH-CH₂-Cl
-CH₂-CH₂-SO₂-CH₂-CH₃

nom:
Métronidazole
Ornidazole
Tinidazole

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Figure 20.6 A comparison of the structures of PABA and sulfanilamide, a sulfa drug that inhibits the synthesis of essential metabolites. Sulfanilamide’s structural resemblance to PABA allows it to act as a competitive inhibitor, stopping the synthesis of folic acid, a compound necessary for microorganisms to grow.

Why are sulfonamides specific for bacteria?
Bacteria become resistant to chemotherapeutic agents by three major mechanisms:

1. **Destruction or inactivation** of the drug for example by β-lactamase enzyme which inactive antibiotics of the β-lactamines family.

*Figure 20.9* The effect of penicillinase on penicillins. Bacterial production of this enzyme, which is shown breaking the β-lactam ring, is by far the most common form of resistance to penicillins. R is an abbreviation for the chemical side groups that differentiate similar or otherwise identical compounds.
Gram-negative bacilli excreted penicillinases which hydrolyze β lactaman core of penicillins. One counts more than 400 currently different β lactamases (penillinases, cephalosporinases ect...)

Also gram-negative multiresistant bacteria produce BLSE or β-lactamases with largest spectrum
2) **Prevention of penetration** to the target sites within the microbe (a frequent mechanism for tetracycline resistance) = Impermeability of bacterial cell wall can occur:
   a) by modifications of the porine that became tiny or disappear.
   b) by efflux; such as act *Pseudomonas* that by a metabolic pump drive back antibiotics outside of the bacterium
3) **Alteration of the drug’s target sites.** For example, a single amino acid change in the ribosome may be enough to make the microbe resistant to certain macrolide antibiotics. 

*Staphylococcus aureus* has modified the PBP or penicillin binding proteins, targets of β-lactamases. So appear, one year after methicillin using, MRSA strains or Methicillin resisting *Saphylococcus aureus*.

Modified PBP, penicillin binding protein by certain *Staphylococcus aureus* strains; that confer resistance to methicillin.
> There are two types of antibiotic resistance:

1) *natural resistance*: that’s an innate resistance to one or more antibiotics before bacteria encounter those chemotherapeutic agents. It is present in all strains of the considered specie and pre exists to the use of antibiotics. **That it is a genetic characteristic which delimits the spectrum of antibiotics’s activity**

As all gram-negative bacilli, species of genus *Serratia* express natural resistance to colistine.
2)- **acquired resistance**: that’s a new bacterial resistance to an antibiotic by species usually sensitive; it’s acquired by a modification of species genetic capital.

This modification can be due to a chromosomal mutation or more frequently to acquired plasmids of resistance.

![Image of bacterial plates](image1.png)

**Strains of E. Coli** before acquired resistance

![Image of bacterial plates](image2.png)

**Acquired resistance to amoxicillin and ticarcillin**
3) More than 90% of antibiotic’s resistances occur by transferred plasmids of resistance.

4) The evolution of a bacterium toward the resistance is not an uniform phenomenon, it is a discontinuous phenomenon. The intensity of this resistance varies with the places, that’s at the hospital that this phenomenon of resistance appears the most frequently.

5) That’s not the antibiotic that induces the resistance. It only acts as selector agent. Strains resistant are going to be encouraged in its presence.
As soon as we use a new antibiotic we will rapidly expect to observe appearance of resistance against it.

The dissemination of resistance, bound to the circulation of the genes between the bacteria, is more important than one imagined it. These transferable genes can have an epidemic dissemination within bacterial world.
Like this gene coding for the β TEM lactamase (enzyme deactivating the β lactamines) identified in *Escherichia coli and Proteus mirabilis* strains (two enteric bacteria) two years after ampicilline introduction, one of first synthetic penicillin with larger spectrum.
Plasmids of resistance can be transferred from one bacterium to another from different genus. This contributes to the spread of resistance among bacteria.
9/ *In vitro* studying activities of antibiotics

- Before using an antibiotic, it would be necessary to determine the action spectrum of it, that means to determine the intensity of antibiotic activity on isolated bacteria.
- Because different species and strains have different degrees of susceptibility to different chemotherapeutic agents, thus, a physician must know the sensitivities of the pathogen before treatment can be started.
- However, physician often cannot wait for sensitivity test and must begin treatment based on their « best-guess » estimation of the most likely pathogen causing the illness.
- If the organisms have been identified certain drug can be selected without specific testing for susceptibility.
- Tests are necessary only when susceptibility is not predictable, or when antibiotic resistance problems develop.
a) the diffusion methods

- Probably the most widely used method of testing is the *disk-diffusion method*, also called the *Kirby-Bauer test*

- A Petri plate is inoculated over his entire surface with a standardized amount of a test organism. This plate contains *Muller-Hinton agar medium* in which antibiotics have a good diffusion

- Next, filter papers disks impregnated with known concentration of chemotherapeutic agents are placed on the solidified agar surface

- Normally those disks contain chemotherapeutic agent on concentration near the *MIC OR MINIMAL INHIBITORY CONCENTRATION*, the lowest concentration that prevents visible bacteria growth
- Usually 8 or 9 antibiotic disks are tested
- During incubation, the chemotherapeutic agents diffuse from the disks into agar.

Box of impregnated paper disks

Inoculated agar medium with disks after incubation
If the antibiotic is effective, a **zone of inhibition** forms, after incubation time, around the disk. The diameter of the zone can be measured.

The zone diameter is compared to a standard table for that drug and concentration. The result report that the organism is **sensitive, intermediate or resistant**
The disk-diffusion test is simple and inexpensive and is most often used when more sophisticated laboratory facilities are not available.

Resistant strain to ticarcillin and amoxicillin by synthesizing of penicillinases.

Sensitive strain to β-lactamines.
b) Broth dilution tests

- A weakness of the diffusion method is that it does not determine whether a drug is *bactericidal* and not just *bacteriostatic*.

- A *broth dilution test* is often used in the determination of the *minimal inhibitory concentration or MIC* and the *minimal bactericidal concentration MBC* of an antimicrobial drug.

- MIC is the lowest concentration of a chemotherapeutic agent that will prevent the growth of the test microorganism.

- MBC is the lowest concentration of a chemotherapeutic agent that will kill test microorganism. This concentration must kill at least 99.9% of test microorganism.

- Determining of MIC and MBC is important because it avoids the excessive or erroneous use of expensive antibiotics, and minimizes the chance of toxic reaction that larger-than-necessary doses may be cause.
The MIC is determined by making a sequence of decreasing concentration of the drug in a broth, which is then inoculated with the test bacteria.

Sequence of decreasing concentrations of the drug

MIC measurement of 4mg/l
MBC measurement of 16 mg/l

**E-test** is performed on a plastic-coated strip contains a gradient of antibiotic concentrations, on it the MIC can be read from a scale printed on the strip.
Antiseptics are substances of very different chemical nature.

They act on bacteria that they destroy more or less to a constant speed fast.

Globally, the antiseptics act directly on the bacterial structures by physico-chemical processes.

And all living cells in which the antiseptics can penetrate are sensitive; whereas the antibiotics only interest the bacteria.

The antiseptics are little specific.
In spite of new antiseptic discovery, more specific, the efficient doses of those are often little distant of the poisonous dose.

Thus, their action is generally bactericidal; and they must be used locally.

The conditions of use are function of concentration, solubility of the product, ambient temperature and time of contact.

As regards to the convenient use, they possess a certain aggressiveness that exercises themselves in general on all living cell.

When using antiseptics, it is necessary to protect himself.
The main antiseptics are:

- acids and bases;
- halogens: iodine, fluorine and chlore;
- mineral salts, such as Hgs and Cus;
- the oxidizers such as hypochlorite of soude, (or Javel water) permanganate of potassium, oxygenated water, formalin and phénol;
- solvents such as ether and toluene;
- some stains such as methylene blue, mercurochrome,
- some tensioactive substances such as ammonium quaternary or absolute alcohol.
SECTION 4 RECALLING

- Antibiotics are substances produced by microorganisms that in small amount inhibit others microorganisms; such as *penicillins* produced by *Penicillium notatum* a mold

- Antimicrobial drugs are used in chemotherapy of infectious diseases. They can be classified in two groups:
  - synthetic drugs as ampicillin or methicillin
  - Antibiotics as natural penicillin G and V

- Antimicrobial drug’s spectrum is the range of different microbial types that are affected

- Penicillins have a narrow spectrum affecting Gram-positive bacteria but very few Gram-negative ones

- Imipenem synthesized penicillins are broad spectrum antibiotics that affect a broad range of Gram-positive and Gram-negative bacteria
Antimicrobial drugs are either bactericidal or bacteriostatic
- Bactericidal drugs kill microbes
- Bacteriostatic drugs prevent microbes for growing

*Penicillins, Vancomycin, Fluoroquinolones* are bactericidal; while *Chloramphenicols, Tetracyclines and Trimethoprim* are bacteriostatic

Major modes of action of antimicrobial drugs are:

a) Inhibition of cell wall synthesis by $\beta$-lactamines, *Vancomycin*

b) Inhibition of nucleic acids replication and transcription as act *Quinolones and Rifampicin*

c) Inhibition of protein synthesis by *Chloramphenicols, Tetracyclins and Streptomycin*

d) Injury of plasma membrane by *Polymyxin B*

e) Inhibition of synthesis of essential metabolism by *Sulfanilamide, Trimethoprim*
Common used antibiotic families are:
- β-lactamines, Phenicols, Quinolones and Fluoroquinolones,
  antimycobacteria such as Isoniacid (IHH)Rifampicin and streptomycin,
  Trimethoprim, sulfamides, Macrolides, Glycolipids including
  Vancomycin

Since 30 years epidemiological situations of multiresistant bacteria spreading that cause nosocomial infections must be taken in account

Studies are attended to find new antibiotics with new targets

Resistance of antibiotics involves in two kinds:

a) Natural resistance which:
- is present in all strains of considered specie
- pre-exist to the use of antibiotic
- is a genetic characteristic included in identification of species
- delimits the spectrum of antibiotic’s activity
b) Acquired resistance by genetic transfer from resistant bacteria to a sensitive ones which so becomes resistant:
- that’s a acquired modification of species genetic capital
- it occurs by chromosomal mutation and mainly in more than 90% cases acquiring of plasmids of resistance to antibiotics

- Antibiotics don’t induce resistance, but act as selector agents
- As soon as we use a new antibiotic we will rapidly expect to observe appearance of resistance against it
- That’s at the hospital that resistance appear most frequently
- Plasmids of resistance to antibiotics can be transferred from one bactrium to an other from different genus so spread resistance to a great population of bacteria

- How in vitro studying activity of antibiotics?

  a) Disk diffusion method or Kirby-Bauer test which is performed on a inoculated test microorganism Petri plate of Mueller-Hinton agar on which paper disks impregnated with antibiotic are placed
b) broth diffusion test using a sequence of decreasing concentration of the antibiotic in broth that are then inoculate with test microorganism

- The disk diffusion method determine a zone of inhibition around the antibiotic disk (when it’s sensitive!) And according with zone of inhibition diameter, tested microorganism will be reported as sensitive, intermediate or resistant to impregnated antibiotic

- Broth diffusion test is often used in determination of MIC and/or MBC

- MIC for minimal inhibition concentration is the lowest concentration of the antibiotic that prevent growth of test microorganism

- MBC for minimal bactericidal concentration of an antibiotic will kill the test microorganism, at least 99.9% of strains.

- Antiseptics globally act directly on bacterial structures by physico-chemical processes; and also on all sensitive cells in which they can penetrate

- They are substances of very different chemical nature with little specificity such as bases or acids, halogen, oxiders, mineral salts and some stains (mercurochrome ect...)
They differ from antibiotics which only interest bacteria, have specific action modes with few side effects or toxicity.

Efficient doses of antiseptics are little distant of poisonous dose

Therefore when using antiseptic, it’s necessary to protect himself