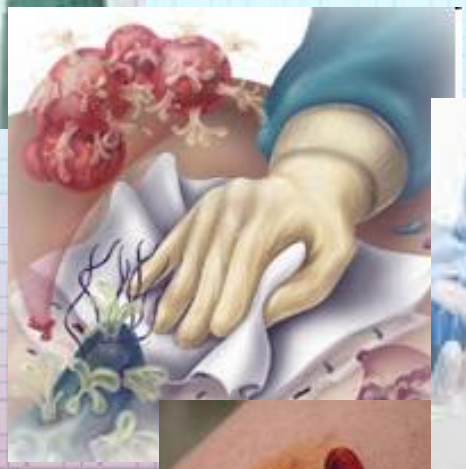
ANTISEPSIS



Lecture for general surgery

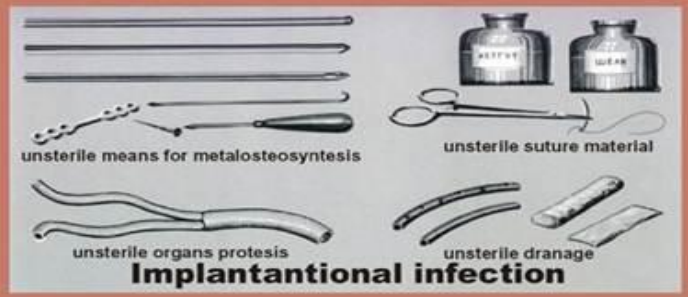
Chorna I.O.

Poltava

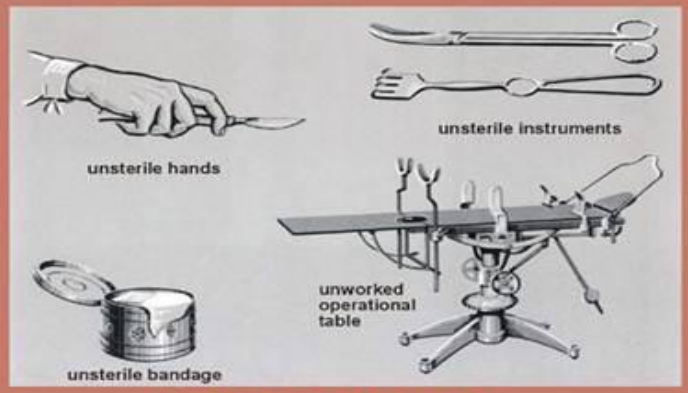
THE WAYS OF INFECTION PENETRATING INTO THE WOUND

EXOGENIC INFECTION

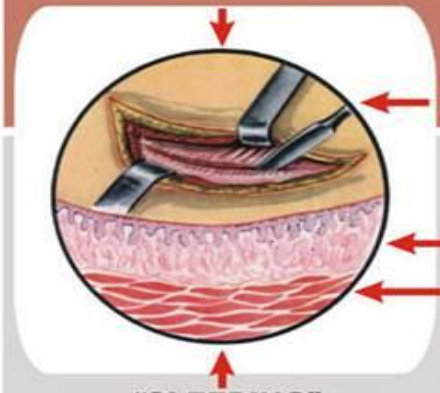
AIR-DROPING



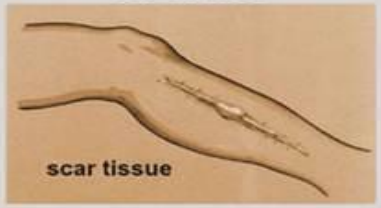
Implantantional infection



CONTACTIVE



"SLEEPING"



CONTACTIVE

HEMATOGENIC AND LYMPHOGENIC

ENDOGENIC INFECTION

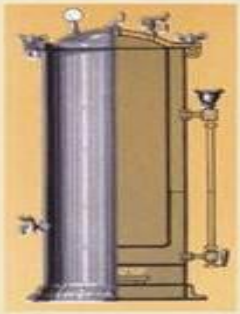
STERILIZATION OF BANDAGING MATERIAL AND UNDERWEAR

Sterilisate:

LYGNIN, NAPKINS, SHEETS, COTTON, WOOL, GAUSE, "LAYERS", SURGICAL COATS

LAYER LAY OF BIX
(HOMOGENEOUS MATERIAL)

SELECTION LAY OF BIX
(HETEROGENEOUS MATERIAL)



AUTOCLAVE

Order of the work with autoclave

- fulling of basin by the water
- lay of drum with open appertires
- hermetization of cell
- turn on of warming
- removing of air
- exposition by probebly pressure of pair
- turn off of warming
- dressing of pressure in cells and atmosphere (opening of vaive of exiting tubes)
- ezposition (5 min)
- opening of cell
- closing drum's apertures
- lay out of drum

DRY - HOT STERILIZATOR

CONTROL STERILIZATION EFFICACY

TILL STERILIZATION	AFTER STERILIZATION

1. Substances with melting temperature more then 110°C

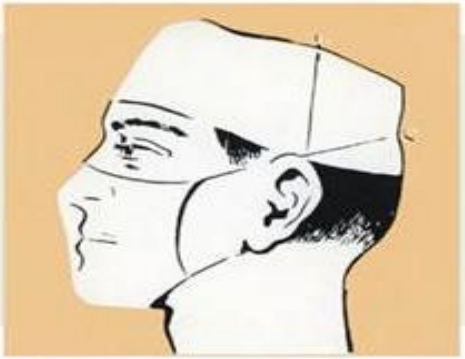
2. Bacteriological control

Growing of microflora

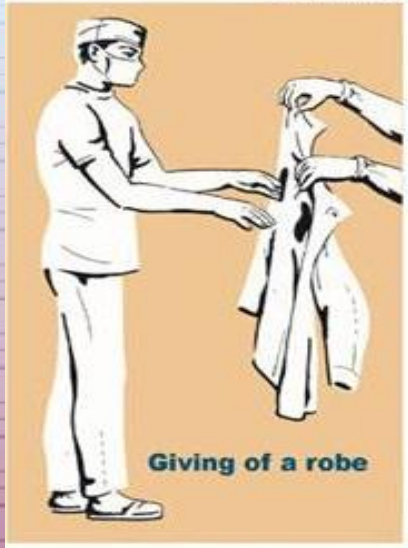
Growing of microflora is absent

GETTING THE SURGEON READY FOR THE OPERATION

PUTTING ON A MASK (AFTER CHANGING INTO SURGICAL CLOTHES).
PREPARING OF THE HANDS - NAIL TRIMMING AND CLEANING OF SUBNAIL SPACES.
WASHING HANDS WITH SOAP AND BRUSHES IN WARM RUNNING WATER
HANDS DISINFECTION

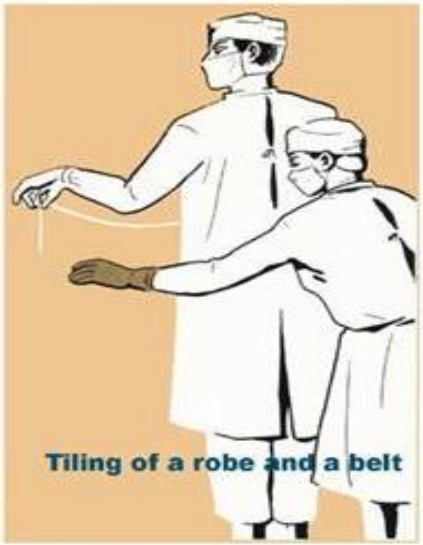


WEARING A STERILE ROBE



Giving of a robe

Tiling of a outsets



Tiling of a robe and a belt

Wearing of sterile rubber gloves

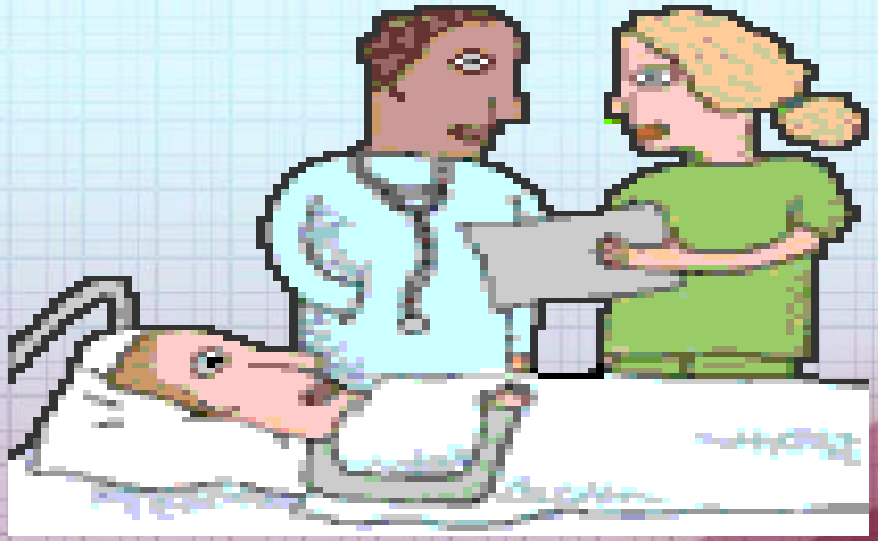
Stretching of a glove.
Disinfection of the rubber gloves with 96% alcohol (removing of the talc).

Taking off the spoilt rubber glove according to the rules of asepsis

Folding of the border of the glove.

Taking off the glove.

1) What was the "Black Period of Surgery?"



1846-70

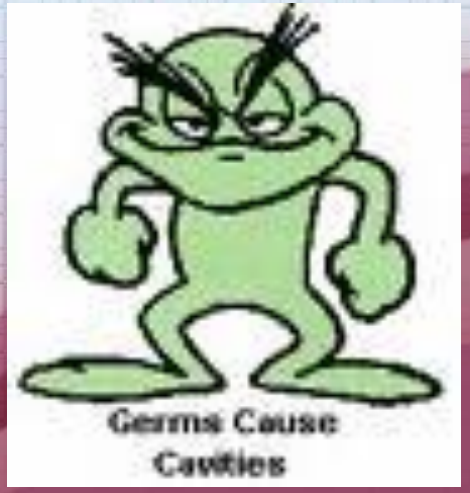
The removal of pain made doctors over confident. They took too long and infection rates went right up

2) What key discovery had to be made – including year – for the need for cleanliness to be realised?

1861

GERM

THEORY!!!



3) What did Semmelweiss do to stop doctors spreading infections?

Made doctors wash their hands (in lime chloride)

4) What were the ideas and methods of Joseph Lister?

Noticed that CARBOLIC ACID was used in sewers to kill the smell. Started to use it in operations to kill germs. It was sprayed all over the place.

5) What was the key drawback of antiseptic surgery?

Very expensive

£

✓ Very uncomfortable – acid burnt the skin

6) What was the solution to the problems of antiseptic surgery, and how did it work?

ASEPTIC SURGERY

Instead of killing germs, remove them altogether by sterilising everything

The measures to cause the exclusion or destruction of harmful microbes are generally called

antisepsis.

Antiseptics (from Greek ἀντί: anti, '"against"[1] + σηπτικός: sēptikos, "putrefactive"[2]) are antimicrobial substances that are applied to living tissue/skin to reduce the possibility of infection, sepsis, or putrefaction.

There are four types of antisepsis:

- - mechanical antisepsis - all mechanical means directed to eliminate the necrotic tissue, foreign bodies, to drain the sec-re-tion of the wound;
- - physical antisepsis - when there are developed conditions suppressing bacterial activity: cold, heat, wound dressings, drainage tubes, physiotherapy.
- - chemical antisepsis - when there are used various chemical substances with a bactericidal or bacteriostatic activity;
- - biological antisepsis - all methods that helps to raise the immune activity of the organism and helps to maintain the physiology of the wound: antibiotics, bacteriophages, serums, vaccines, immobization, rest of the patient;
-

Mechanical antisepsis

Mechanical Antisepsis ***is the mechanical removal of infected and non-viable tissue.***

- ***In essence - the primary debridement. Timely made, it turns the infected wound in aseptic operating wound healing by first intention.***
- ***Manual is used as an antiseptic surgical wound toilet, which removes foreign bodies, necrotic and nonviable tissue is performed the autopsy streaks and pockets, the washing of wounds, and other manipulations aimed at cleansing of infected wounds.***

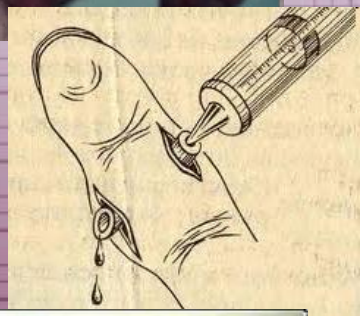
Mechanical Antisepsis

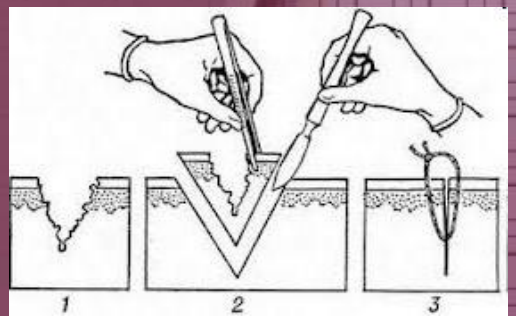
Toilet of wound

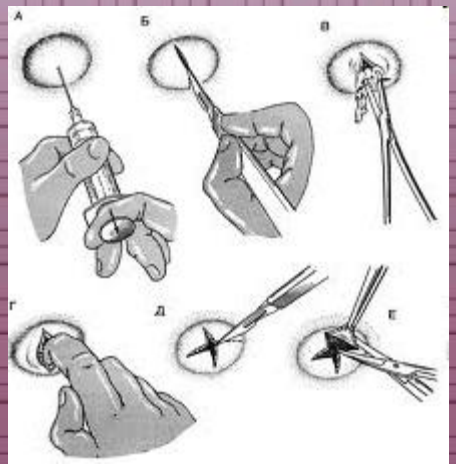
Primary debridement

Secondary debridement

Other manipulation







Physical antisepsis

Is the creation of unfavorable conditions for development of microorganisms in a wound and for suction of microbe toxins and products of tissue decay by an application of physical factors

Physical antisepsis starts from the law of capillarity, hygroscopicity, diffusion, osmosis, siphoning, heat, moist heat , dry heat , filtration, low temperature, radiation, ultrasound, laser effects and other.

- hygroscopic bandaging material
- Hypertonic solution
- Drainage of wounds
- Sorbent
- Technical agents (means)
- environment factors

Physical antisepsis

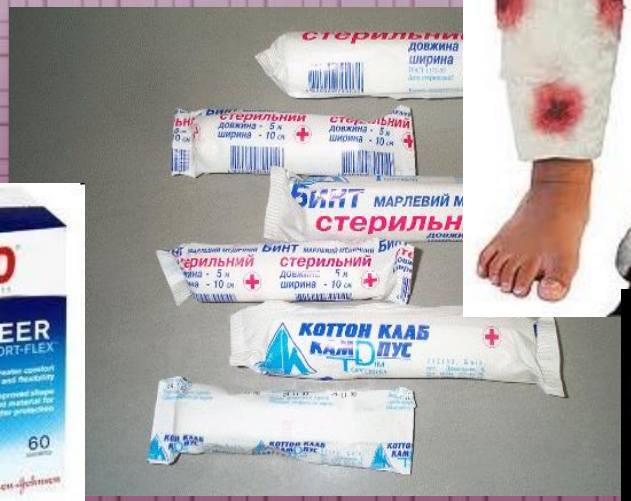
- hygroscopic bandaging material
- Hypertonic solution
- Drainage of wounds
- Sorbent
- Technical agents (means)
- environment factors

Hygroscopic bandaging (Dressing) material

Dressings materials - a material intended to protect the wound from secondary infection, they are drying, processing the operational field, stop bleeding, as well as for immobilization of organs, tissues.

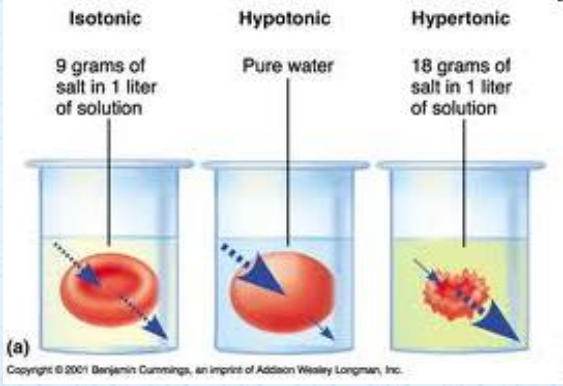
By dressing materials and finished dressing products include: cotton, gauze, alihnin, bandages, dressings packs, gauze wipes, aseptic bandages, gauze, cotton swabs, etc..

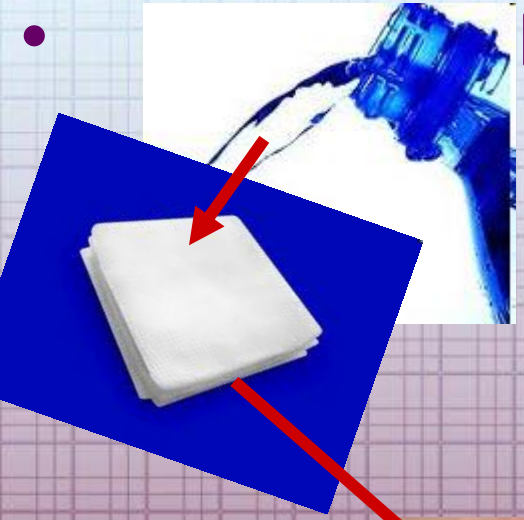
They put a number of requirements, namely: they must have good suction capacity, be flexible, should not irritate the body tissues, the application should not constitute separate fibers which can clog the wound should undergo sterilization to be cheap and accessible to a broad and wide application.

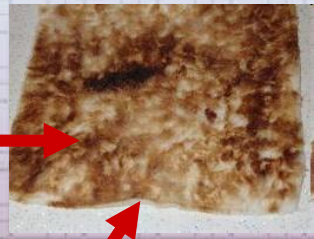


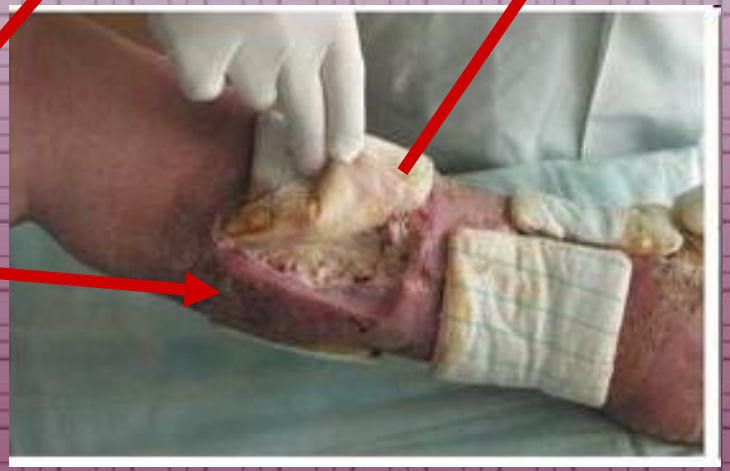
Hypertonic solution

- OSMOSIS
- NaCl 10%







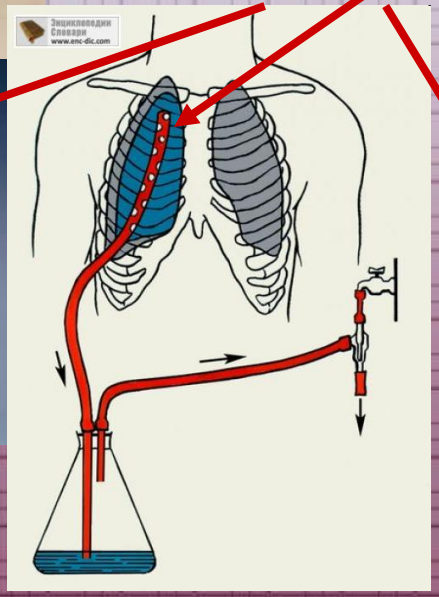


Drainage of wounds

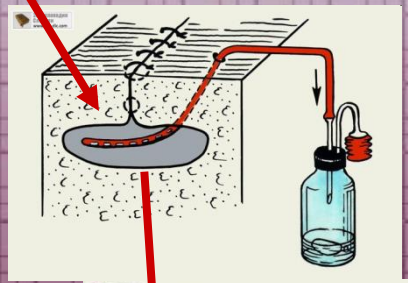
The drainage provides the outflow of wound contents and promotes the removal of toxins, microbes and products of tissue decay. Irrigation of gauze with hypertonic solutions highly increases its hydroscopic quality. But tampons with wound exudation prevent the outflow from the wound, which is why they are not good for drainage. Can be

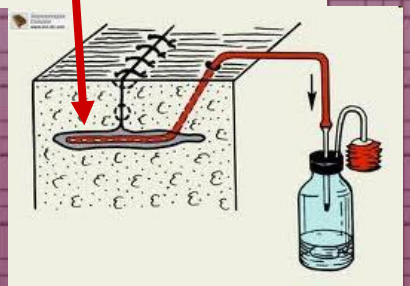
Passive

Active



Continuous irrigation drainage





Sorbent

Application sorpbents is based on the removal biological fluid, toxins, microbes from the septic wounds, ulcers, burns. The following indications for the use of sorbents in treatment of septic wounds:

Phase of inflammation

- 1. *High exuding wounds*: gelling agents based on polyvinyl alcohol - gelevin, kollavin, lizosorb, geleyodon (Russia); Melolin (UK); TenderWet, Comprigel (Germany).
- 2. *With moderate exuding wounds*: products based on carboxymethylcellulose fine - geletsel, tsellosorb (Uzbekistan) hydrogel dressings - Geliperm, Wigilon, Algoplaque, Traumasive (Germany), DermaDress (SSHA), Scarlet Red (Canada), Opragel, Hydrocoll (Germany); dextran preparations - Debrisan, (Sweden), oxidized cellulose (Oxydized cellulose) and its modifications (Belarus, Russia, SSHA, Germany); profezim, silica, Aerosil; polymethylsiloxane (Russia), carbon materials - Vaul (Belarus, Russia), SKN , AUVM "Dnepr" MN, Out M, SUMS-1 (Russia, Ukraine), polyurethane coating - SYSpur-derm (Germany).

- **Regeneration phase**
- **Sorbents based on alginates - sipralin, algimaf, algipor, teralgim (Russia), Sorbasan, Sorbalgon (SSHA), Tegagel, Kaltastat, Fibracol (UK), collagen - digispon, gentatsikol, kombutek-2 (Russia), Taurolin-Gel (UK).**

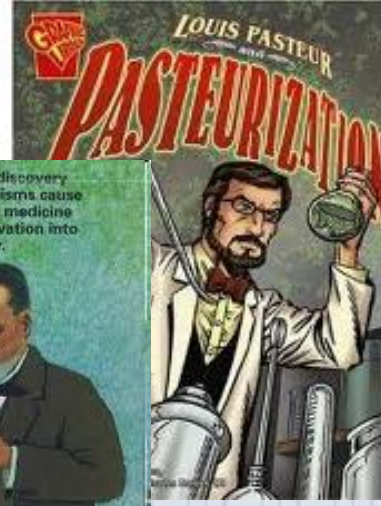
Analyzing the results of laboratory research and clinical application of medical sorbents should be noted that an active mechanism of sorption, effective conditioning outflow microflora and wound discharge from the wound provides a pronounced anti-inflammatory, nekrolitik and analgesic effects, prevents the development of super-infection in the wound, thus creating favorable conditions for course of reparative processes.

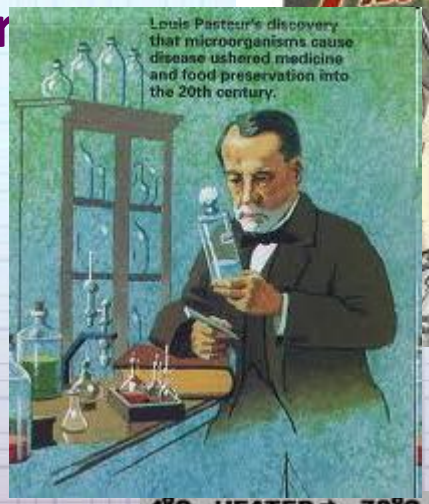
Technical agents (means)

Heat: Kills microorganisms by denaturing their enzymes and other proteins. **Heat resistance varies widely among microbes.**

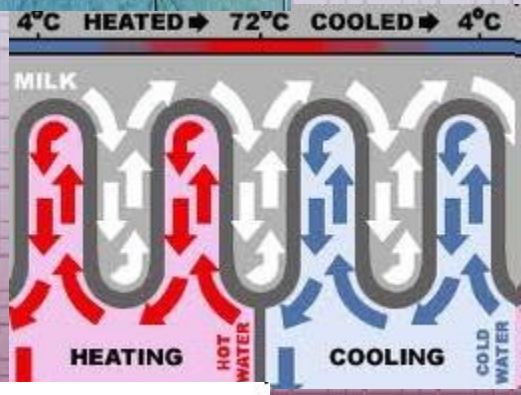
- Thermal Death Point (TDP): **Lowest temperature at which all of the microbes in a liquid suspension will be killed in ten minutes.**
- Thermal Death Time (TDT): **Minimal length of time in which all bacteria will be killed at a given temperature.**
- Decimal Reduction Time (DRT)(десятичное сокращение): **Time in minutes at which 90% of bacteria at a given temperature will be killed. Used in canning industry. (консервная)**

Moist Heat :





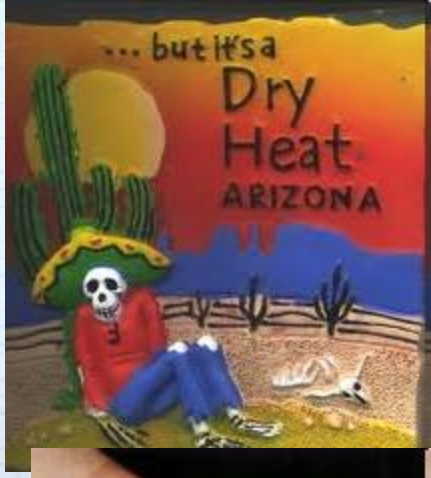
- **Pasteurization:** **Developed by Louis Pasteur to prevent the spoilage of beverages. Used to reduce microbes responsible for spoilage of beer, milk, wine, juices, etc.**
  - Classic Method of Pasteurization: **Milk was exposed to 65°C for 30 minutes.**
  - High Temperature Short Time Pasteurization (HTST): **Used today. Milk is exposed to 72°C for 15 seconds.**
  - Ultra High Temperature Pasteurization (UHT): **Milk is treated at 140°C for 3 seconds and then cooled very quickly in a vacuum chamber.**
  - Advantage: **Milk can be stored at room temperature for several months.**



Dry Heat: Kills by oxidation effects.

- Direct Flaming: **Used to sterilize inoculating loops and needles. Heat metal until it has a red glow.**
- Incineration: **Effective way to sterilize disposable items (paper cups, dressings) and biological waste.**
- Hot Air Sterilization: **Place objects in an oven. Require 2 hours at 170°C for sterilization. Dry heat is transfers heat less effectively to a cool body, than moist heat.**

The open method of treatment can be used. The wounds are dried; as a result, unfavorable conditions for development of microorganisms are created.

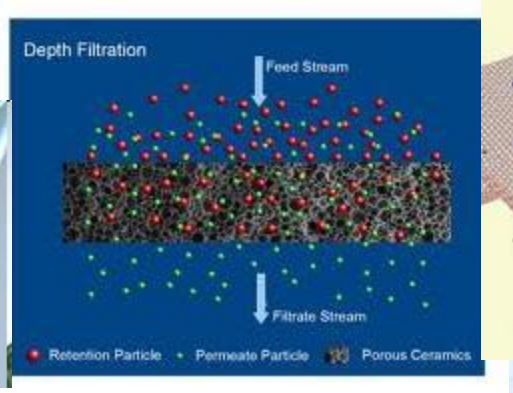


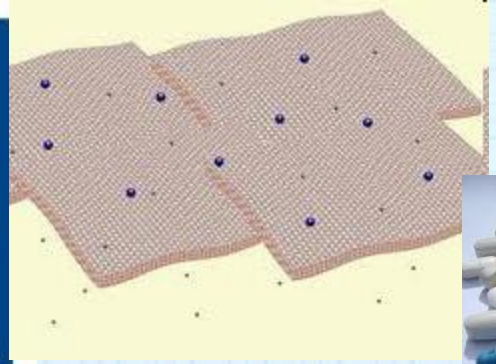
Laser Therapy

Light photons from the laser penetrate deep into targeted tissues and accelerate cellular reproduction and growth. Laser light also increases cellular energy and ATP levels allowing injured cells to utilize nutrients better and remove waste faster. As a result, all types of cells, including skin, tendons, ligaments and muscles, heal quicker. Even better, research proves that laser light stimulates fibroblast formation. Fibroblasts are the building blocks of collagen, the cells responsible for closing wounds and repairing injured tissues. Laser treatment has proven especially helpful in treating open wounds and burns.

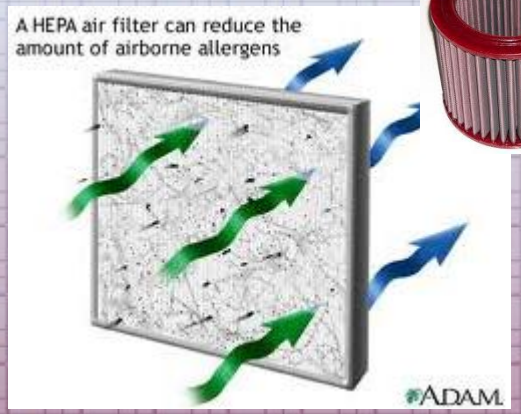
In surgery laser scalpel very widely used

Filtration:

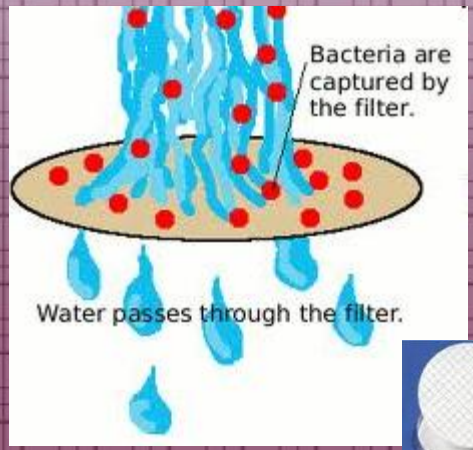




Removal of microbes by passage of a liquid or gas through a screen like material with small pores. Used to sterilize heat sensitive materials like vaccines, enzymes, antibiotics, and some culture media.



- **High Efficiency Particulate Air Filters (HEPA):** Used in operating rooms and burn units to remove bacteria from air.
- **Membrane Filters:** Uniform pore size. Used in industry and research. Different sizes:
  - **0.22 and 0.45um Pores:** Used to filter most bacteria. Don't retain spirochetes, mycoplasmas and viruses.
  - **0.01 um Pores:** Retain all viruses and some large proteins.

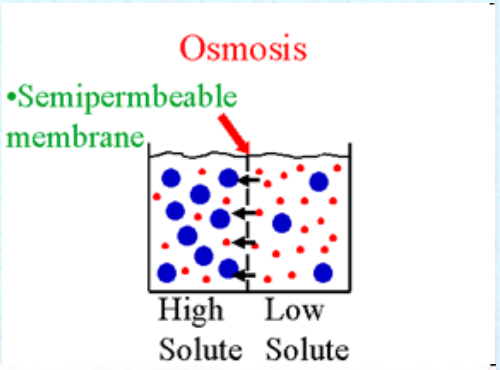


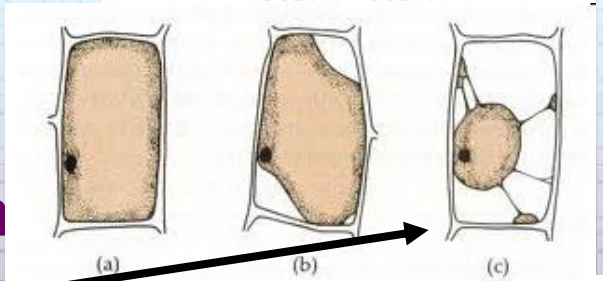
Low Temperature: Effect depends on microbe and treatment applied.

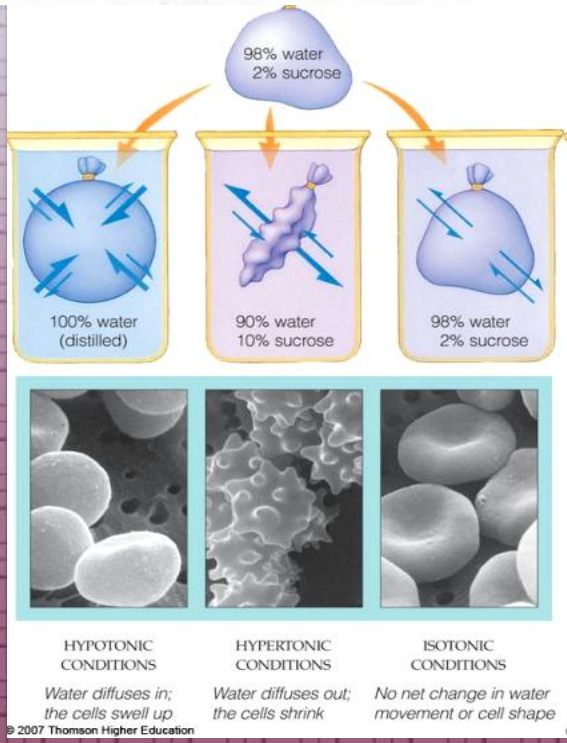
- **Refrigeration: Temperatures from 0 to 7°C.** Bacteriostatic effect. **Reduces metabolic rate o microbes so they cannot reproduce or produce toxins.**
- **Freezing: Temperatures below 0°C.**
  - Flash Freezing: **Does not kill most microbes.**
  - Slow Freezing: **More harmful because ice crystals disrupt cell structure.**
  - **Over a third of vegetative bacteria may survive 1 year.**
  - **Most parasites are killed by a few days of freezing.**

Osmotic Pressure: The use of high concentrations of salts and sugars in foods is used to increase the osmotic pressure and create a hypertonic environment.

Plasmolysis: As water leaves the cell, plasma membrane shrinks away from cell wall. Cell may not die, but usually stops growing.







- Yeasts and molds: **More resistant to high osmotic pressures.**
- *Staphylococci spp.* **that live on skin are fairly resistant to high osmotic pressure.**

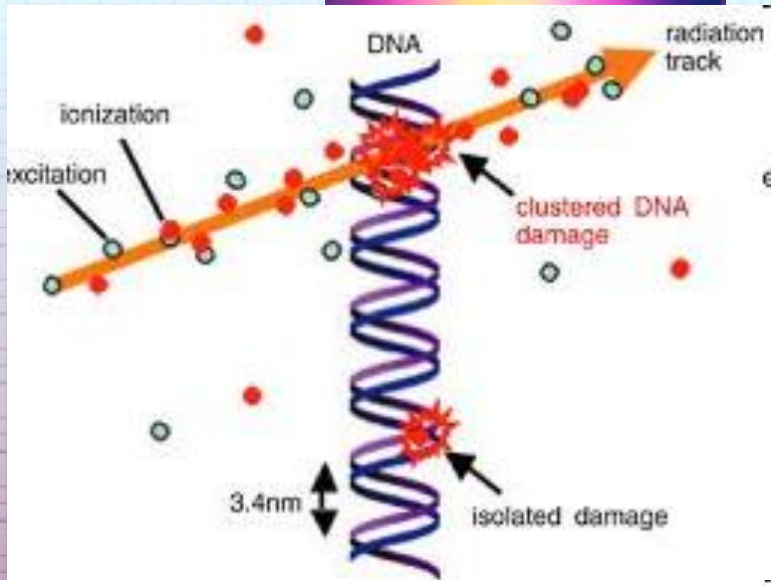
Radiation: **Three types of radiation kill microbes:**

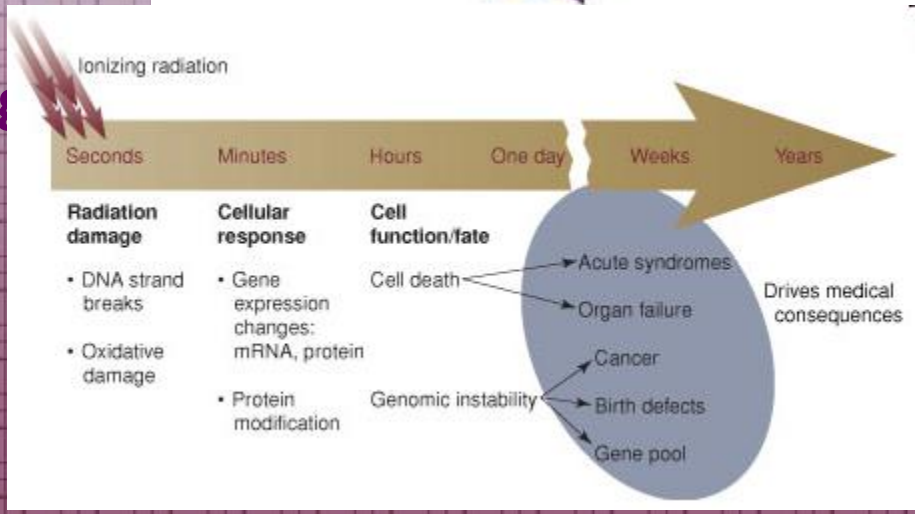
1. Ionizing Radiation: Gamma rays, X rays, electron beams, or higher energy rays. Have short wavelengths (less than 1 nanometer).

Dislodge electrons from atoms and form ions. Cause mutations in DNA and produce peroxides.

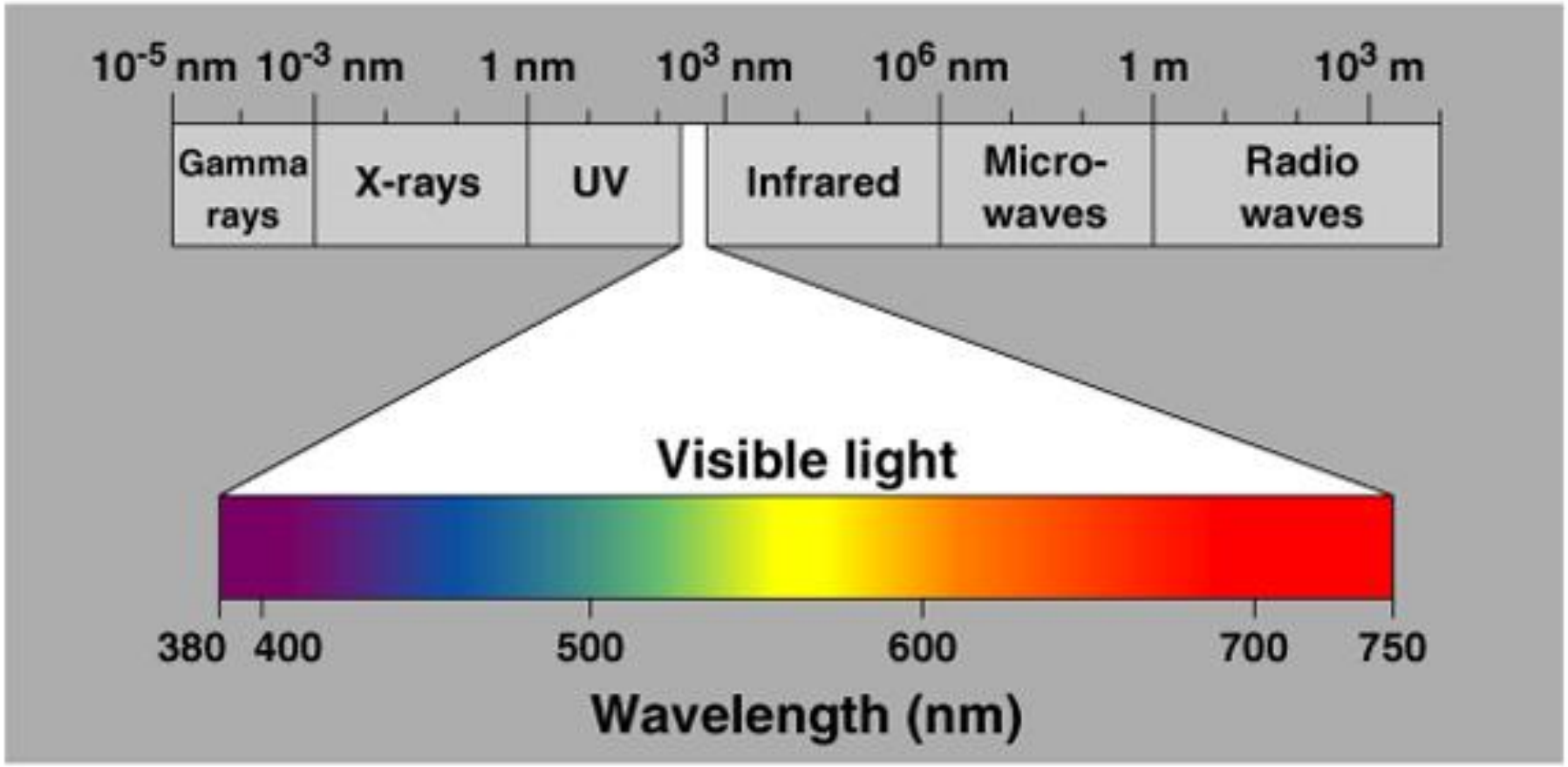
Used to sterilize pharmaceuticals and disposable medical supplies. Food industry is interested in using ionizing radiation.

Disadvantages: **Penetrates human tissues. May cause genetic mutations in humans.**





Forms of Radiation



Radiation: **Three types of radiation kill microbes:**

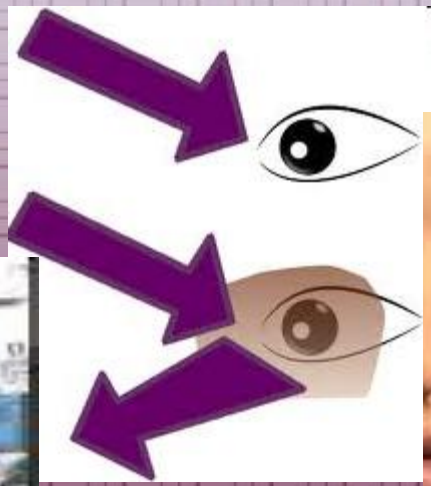
2. **Ultraviolet light** (Nonionizing Radiation

Wavelength is longer than 1 nanometer.

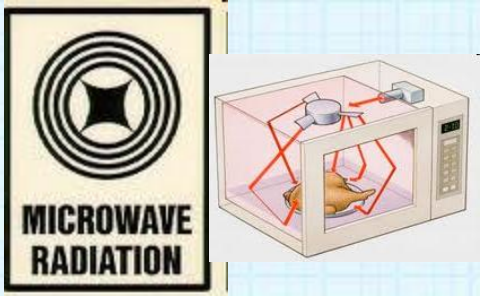
Damages DNA by producing thymine dimers, which cause mutations.

Used to disinfect operating rooms, nurseries, cafeterias.

Disadvantages: **Damages skin, eyes. Doesn't penetrate paper, glass, and cloth.**



Radiation: **Three types of radiation kill microbes:**



3. **Microwave Radiation:** **Wavelength ranges from 1 millimeter to 1 meter.**

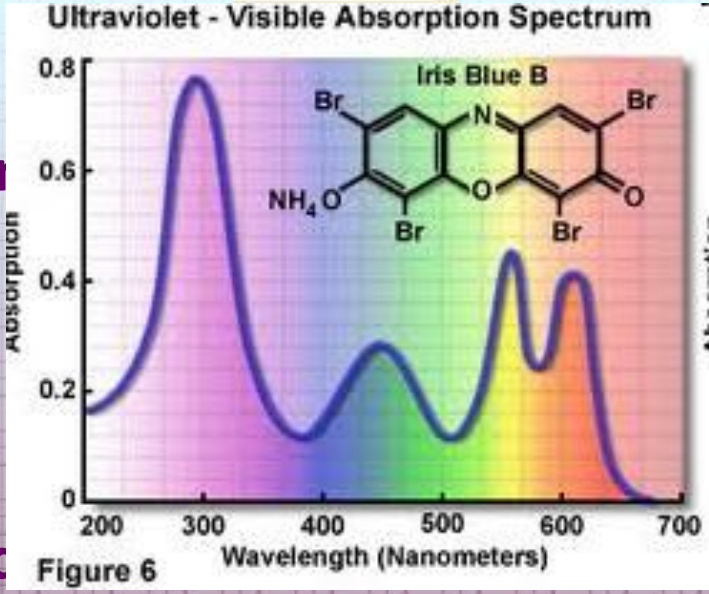
Heat is absorbed by water molecules.

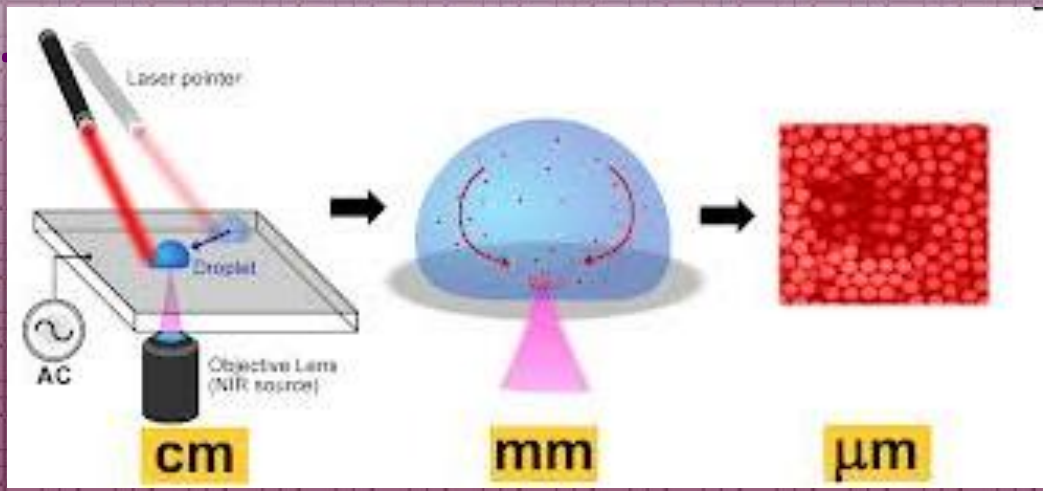
May kill vegetative cells in moist foods.

Bacterial endospores, which do not contain water, are not damaged by microwave radiation.

Solid foods are unevenly penetrated by microwaves.

Trichinosis outbreaks have been associated with pork cooked in microwaves.





Environment factors

Washing the wound. To avoid the development of septic complications wound should be cleaned

Dessication(высушивание):

In the absence of water, microbes cannot grow or reproduce, but some may remain viable for years. After water becomes available, they start growing again.

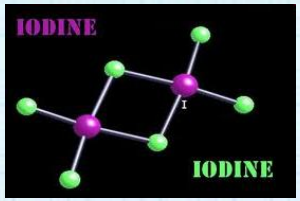
Susceptibility to dessication varies widely:

- *Neisseria gonnorrhea*: Only survives about one ho
- *Mycobacterium tuberculosis*: May survive several months.
- Viruses are fairly resistant to dessication.
- *Clostridium spp*. and *Bacillus spp*.: May survive decades.

Chemical antysepsis

- Synthetic antibacterial agents are used to combat bacterial infection in the wound or inflammatory foci. These are both effective for therapy and prophylaxis and help achieve antibacterial effect inside the human body.
- There are many chemical antiseptics; they are section into the following groups:

1. Halogens: Effective alone or in compounds.



A. Iodine:

- **Tincture of iodine** (alcohol solution) was one of first antiseptics used.
- Combines with amino acid tyrosine in proteins and denatures proteins.
- Stains skin and clothes, somewhat irritating.
- **Iodophors**: Compounds with iodine that are slow releasing, take several minutes to act. Used as skin antiseptic in surgery. ***Not effective against bacterial endospores.***
  - Drags of an iodine: Iodonatum of 1% sol., Iodinolum of 1% sol., 1% iodopironi sol , iodobak, iodoskin, Betadine, Isodine

1. Halogens: **Effective alone or in compounds.**

B. Chlorine:

- **When mixed in water forms hypochlorous acid:**

$Cl_2 + H_2O$ ------> H+ + Cl- + HOCl

Hypochlorous acid

- **Used to disinfect drinking water, pools, and sewage.**
- **Chlorine is easily inactivated by organic materials.**
- **Sodium hypochlorite (NaOCl): Is active ingredient of bleach.**
- **Chloramines: Consist of chlorine and ammonia. Less effective as germicides.**

Degerming in preparation for surgery

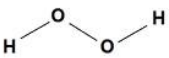
2. Oxidants = Peroxygens (Oxidizing Agents):

- Oxidize cellular components of treated microbes.
- Disrupt membranes and proteins.

A. Ozone:

- Used along with chlorine to disinfect water.
- Helps neutralize unpleasant tastes and odors.
- More effective killing agent than chlorine, but less stable and more expensive.
- Highly reactive form of oxygen.
- Made by exposing oxygen to electricity or UV light.

2. Peroxygens (Oxidizing Agents):



HYDROGEN PEROXIDE

B. Hydrogen Peroxide

- It is an oxidizing agent that attacks sulfhydryl groups, thereby inhibiting enzymatic activity.
- Used as antiseptic 3% sol to clean wounds.
- Used to disinfect contact lenses.
- Its effectiveness is limited because bacteria and body tissues contain enzymes (catalase) that inactivate hydrogen peroxide.
- Sterilization can also be achieved after 6 hrs of exposure to a 6% solution.
- Effective in disinfection of inanimate objects as an antiseptic 6% sol.
- Sporicidal at higher temperatures.
- Used by food industry .

2. Peroxygens (Oxidizing Agents):

C. Benzoyl Peroxide:

- Used in acne medications.

D. Peracetic Acid:

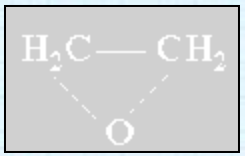
- One of the most effective liquid sporicides available.
- Sterilant :
  - Kills bacteria and fungi in less than 5 minutes.
  - Kills endospores and viruses within 30 minutes.
- Used widely in disinfection of food and medical instruments because it does not leave toxic residues.

E. Perhydrolum, contains about 33 % of peroxide of Hydrogenous, is used for preparation of a solution pervomur;

F. Permanganate of a potassium (potassium permanganate) - apply to a lavage of the wounds - 0,1 % sol., for a lavage of an oral cavity and a stomach - 0,01 sol.;

- Oxidizers are especially effective at anaerobic and putrefactive diseases.

2. Peroxygens (Oxidizing Agents):



G. ETHYLENE OXIDE

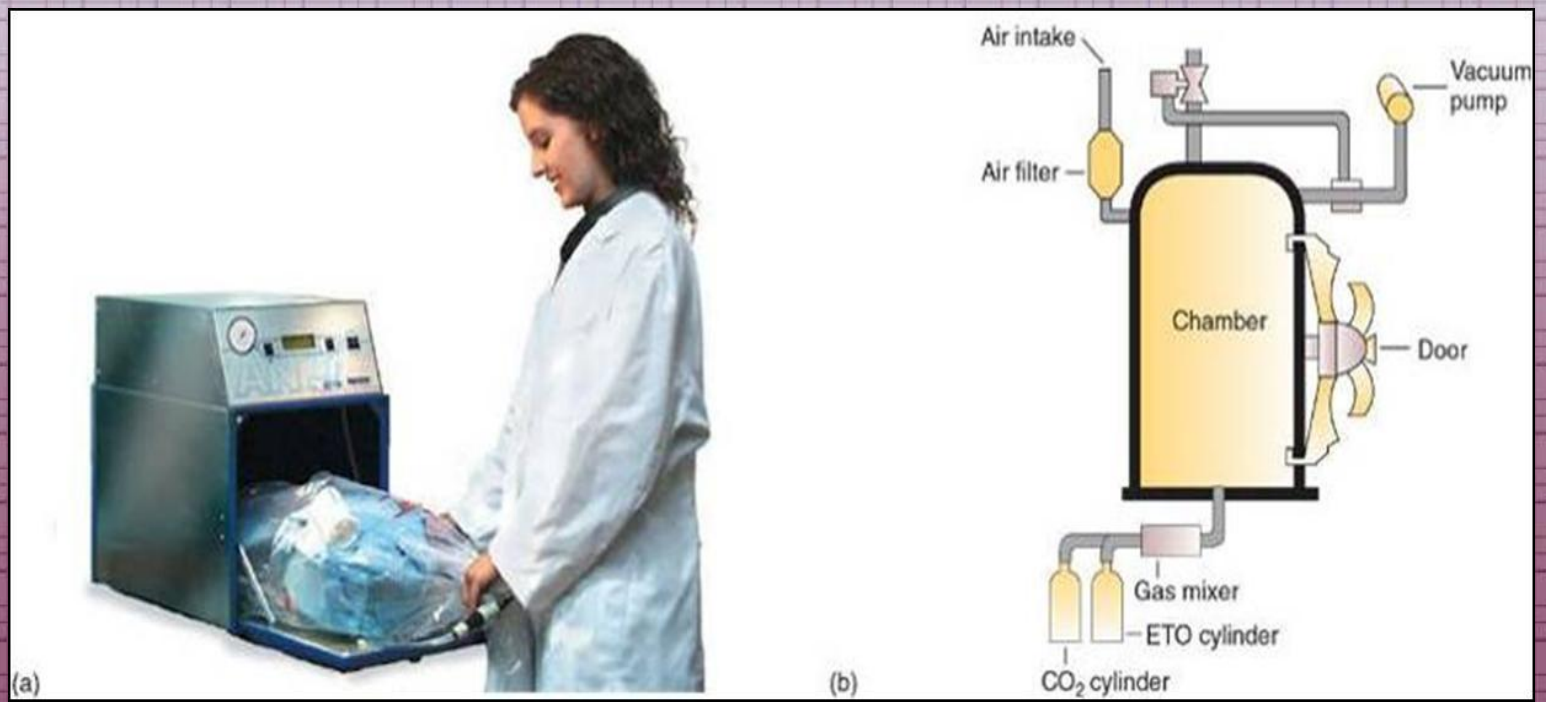
- **Mode of action: It is an alkylating agent. Denature proteins, by replacing functional groups with alkyl groups.**
- **It acts by alkylating sulfydryl-, amino-, carboxyl- and hydroxyl- groups.**
- **EtO is liquid at temp below 10.8^{o}C. Above this temp. , it vaporizes rapidly.**
- **Excellent penetration capacity & sporicidal activity.**
- **Toxic & highly explosive.**
- **Since it is highly flammable, it is usually combined with CO_2 (10% CO_2+ 90% EO)**

◆ **Kills all microbes and endospores, but requires exposure of 4 to 18 hours.**

◆ **Chemicals that sterilize in a chamber similar to an autoclave**

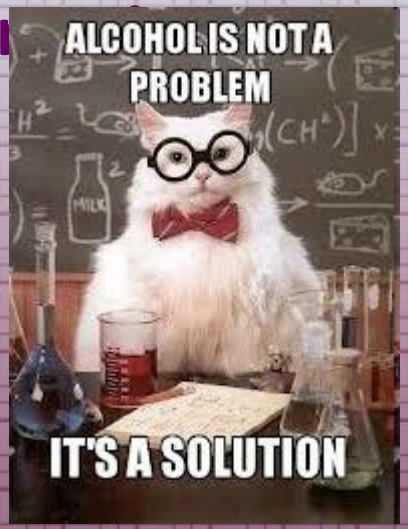
Continue…

- **It is an effective sterilizing agent for heat & moisture sensitive materials.**
- **EtO is used to sterilize papers, leather, wood, metal and rubber products as well as plastics.**
- **In hospitals, it is used to sterilize catheters, artificial heart valves, heart-lung machine components & other optical equipment.**



3. Alcohols:

- Kill bacteria, fungi, but not endospores or naked viruses.
- Act by denaturing proteins and disrupting cell membranes.
- Evaporate, leaving no residue.
- Used to mechanically wipe microbes off skin before injections or blood drawing.
- Not good for open wounds, because cause pr to coagulate.



- Ethanol: Drinking alcohol.
- Isopropanol: Rubbing alcohol. Better disinfectant

than ethanol. Also cheaper and less volatile.

Optimum concentration is 70% and 96 % sol .

4. Aldehydes:

- Include some of the most effective antimicrobials.
- Inactivate proteins by forming covalent crosslinks with several functional groups.

A. Formaldehyde gas:

- Excellent disinfectant.
- Commonly used as formalin, a 37% aqueous solution.
- Formalin was used extensively to preserve biological specimens and inactivate viruses and bacteria in vaccines.
- Irritates mucous membranes, strong odor.
- Also used in mortuaries for embalming.

4. Aldehydes:

B. Glutaraldehyde:

- **Less irritating and more effective than formaldehyde.**
- **One of the few chemical disinfectants that is a sterilizing agent.**
- **A 2% solution of glutaraldehyde (Cidex) is:**

- **Bactericidal, tuberculocidal, and viricidal in 10 minutes.**
  - **Sporicidal in 3 to 10 hours.**
- **Commonly used to disinfect hospital instruments.**
- **Also used in mortuaries for embalming.**

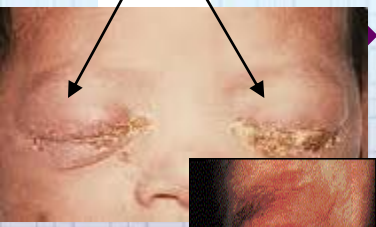
5. Phenols and Phenolics:

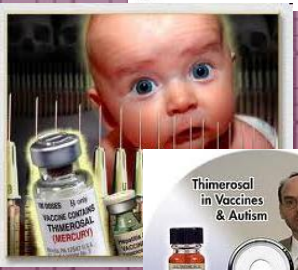
- **Phenol (carbolic acid) was first used by Lister as a disinfectant.**
  - Rarely used today because it is a skin irritant and ha strong odor.
  - Used in some throat sprays and lozenges.
  - Acts as local anesthetic.
- **Phenolics are chemical derivatives of phenol**
  - Cresols: Derived from coal tar (Lysol).
  - Biphenols (pHisoHex): Effective against gram-positive staphylococci and streptococci. Used in nurseries. Excessive use in infants may cause neurological damage.
- **Destroy plasma membranes and denature proteins.**
- Advantages: **Stable, persist for long times after applied, and remain active in the presence of organic compounds.**

6. Dyes

- — ***Brilliant green*** is used as a 1—2% alcohol solution for superficial wounds, abrasions and suppurative skin infections.
- — ***Methylene blue*** is used for superficial wounds and abrasions (3% alcohol solution), burns (1-2% alcohol solution) and for washing purulent cavities (0,02% aqueous solution).

7. Heavy Metals:





Include copper, selenium, mercury, silver, and zinc.

- Oligodynamic action: **Very tiny amounts are effective.**

A. Silver:

- **1% silver nitrate used to protect infants against gonorrheal eye infections until recently. Salts of silver: a colloid silver and Protargolum**

. Mercury

Mercury compounds exert antibacterial action by reversible binding to sulfhidryl enzymes in microorganisms. However, they are highly toxic to tissues, and penetrate poorly. Organic mercury compounds like merthiolate and mercurochrome are used to disinfect skin wounds. Mercuric oxide ointment 1%, amoniated mercury ointment, thimerosal, nitromersol and merbromin.

THIMEROSAL (mercury derv.), previously used as a preservative in vaccine

4. Heavy Metals:

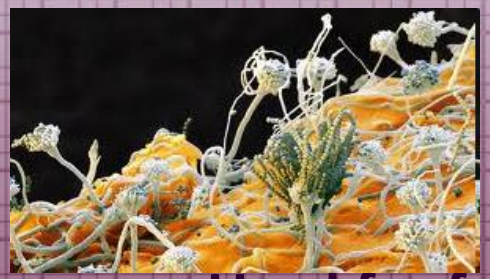
C. Copper

- Copper sulfate is used to kill algae in pools and fish tanks, to control the growth of fungi.

D. Zinc

Treatment and prevention of foot-rot and foot scald. Treatment and prevention of dermatophilosis (mycotic dermatitis or lumpy wool)

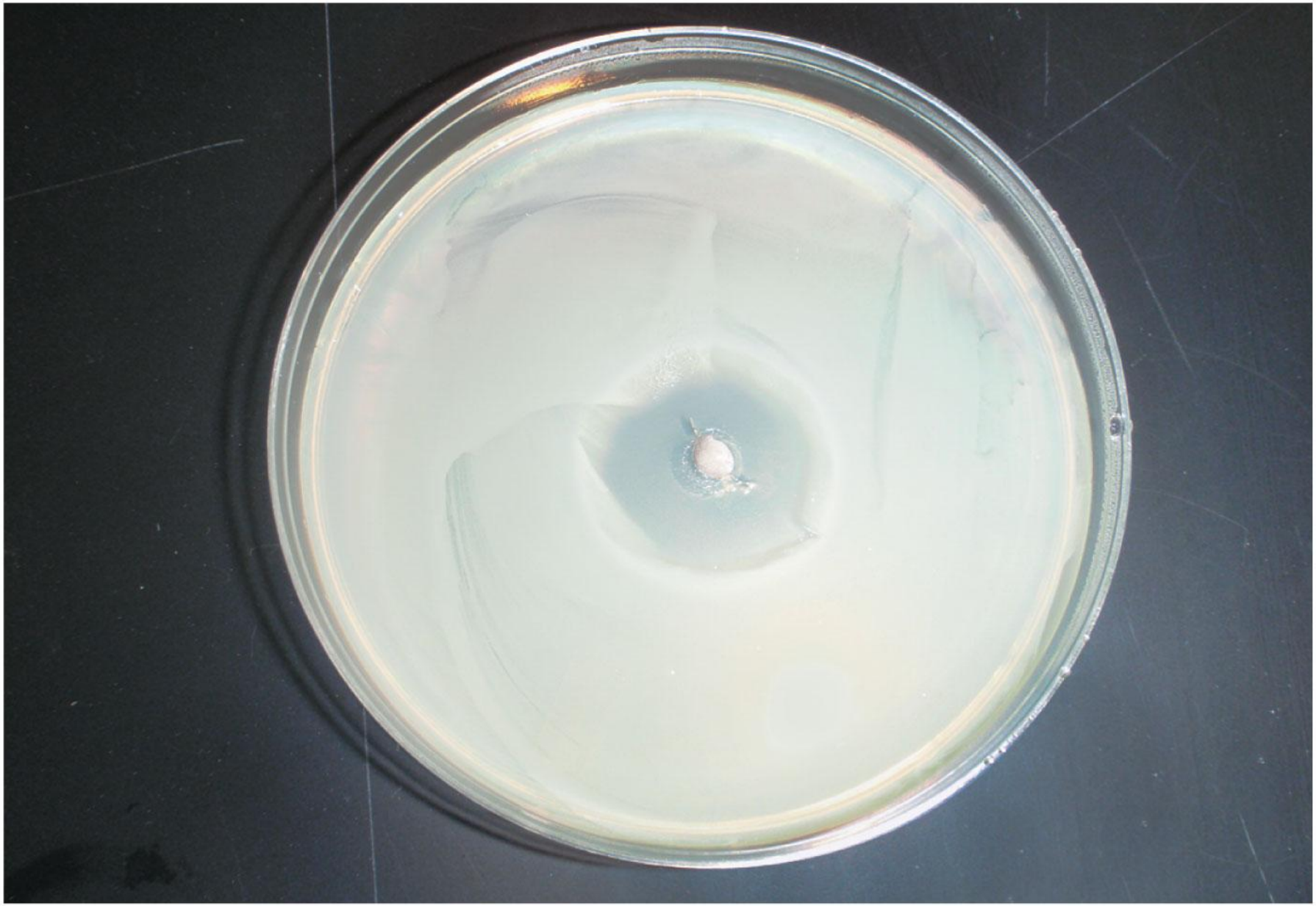
- Zinc chloride is used in mouthwashes.
- Zinc oxide is used as antifungal agent in paints.



E. Selenium

- Kills fungi and their spores. Used for fungal infections.
- Also used in dandruff (перхоть) shampoos.

The effect of heavy-metal ions on bacterial growth



8. Detergents:

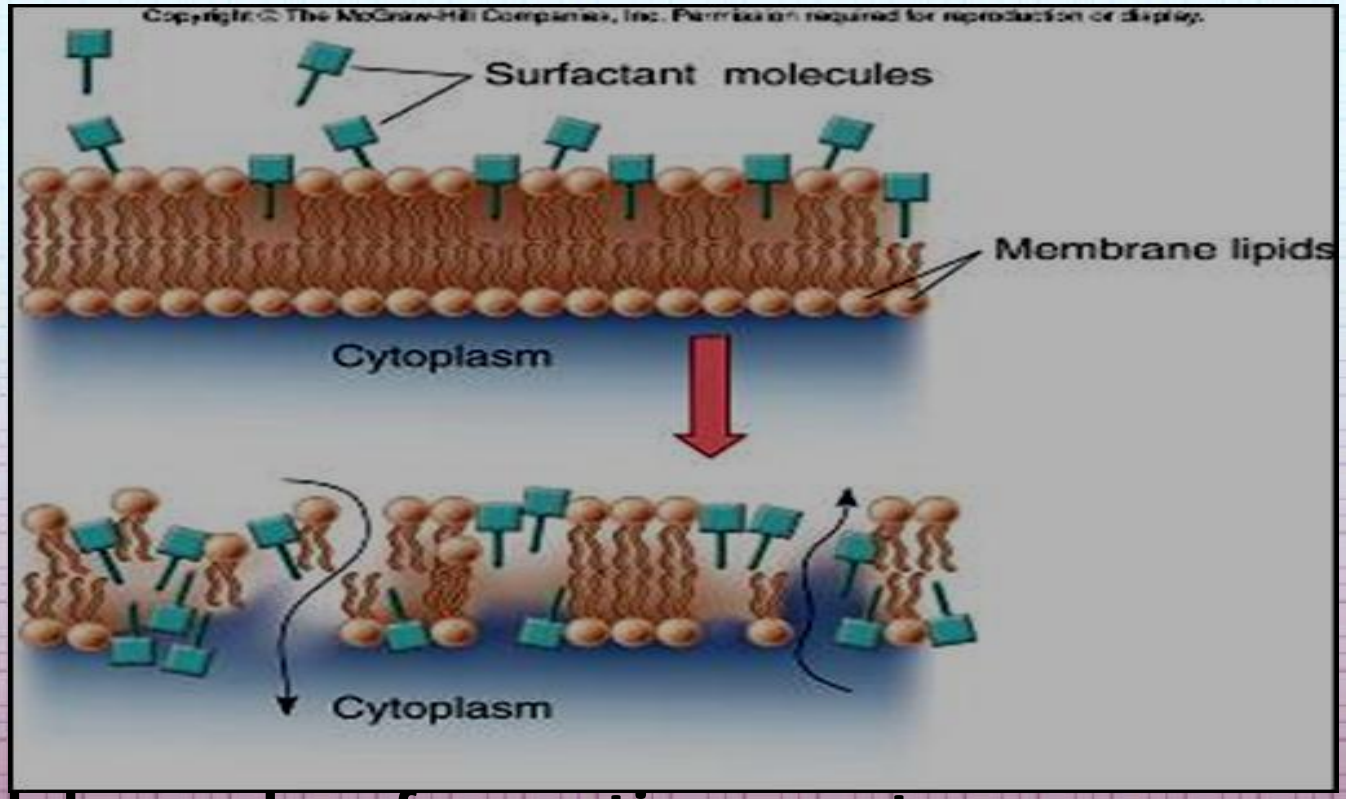
- Detergents are synthetic chemicals acting as strong wetting agent & surface tension reducers.
- While soaps are always negatively charged, some detergents are negatively charged while others are positively charged.
- One example of a positively charged detergent are quaternary ammonium compounds (also known as quats)

Chlorhexidine begluconat. The main aqueous solution contains 20% of chlorhexidine bigluconate. For cleaning wounds, a 1:400 solution is available, for washing infected body's cavities a 1:1,000 may be used. These are strong surface-active compound.

- for processings of an abdominal cavity at a peritonitis - 1 % an aqueous solution.
- Apply to processing hands of the surgeon - 0,5 % alcogol solution
- **Cerygel -** apply to processing hands of the surgeon.

Roccalum - 10 % and 1 % an aqueous solution.

8. Detergents. Quaternary Ammonium Compounds (Quats):



- **Widely used surface active agents.**
- **Cationic (positively charge) detergents.**
- **Effective against gram positive bacteria, less effective against gram-negative bacteria.**
- **Also destroy fungi, amoebas, and enveloped viruses.**

8. Detergents. Quaternary Ammonium Compounds (Quats):

- **Zephiran, Cepacol, also found in our lab spray bottles.**
- ***Pseudomonas* strains that are resistant and can grow in presence of Quats are a big concern in hospitals.**
- Advantages: **Strong antimicrobial action, colorless, odorless, tasteless, stable, and nontoxic.**
- Diasadvantages: **Form foam(пена). Organic matter interferes with effectiveness. Neutralized by soaps and anionic detergents. Quats do not kill endospores, *Mycobacteria* spp., nor non-enveloped viruses**

9. 5-Nitroimidazole derivatives

- **Metronidazole is a synthetic, nitroimidazole-derivative antibacterial and antiprotozoal (**Amebiasis, Giardiasis, Trichomoniasis**) agent trade names — trichopol, Trichazol, Clont,Danizol, Flagyl, Gineflavir, Metric, Metrodzhil, MetroGel, Metrogyl, Trichopol**
- Bacterial Infections
  - **Metronidazole has potent antibacterial activity against anaerobes, including bacteroides and clostridium species**
  - **Metronidazole is indicated for treatment of anaerobic or mixed intra-abdominal infections, vaginitis (bacterial vaginosis), antibiotic-associated enterocolitis, acute gingivitis and other dental infections**
  - **Metronidazole is indicated for treatment of vaginitis due to bacterial Gardnerella or Mycoplasma hominis infection in symptomatic patients**
  - **Helicobacter pylori eradication therapy, as part of a multi-drug regimen in peptic ulcer disease**
  - **It is effective against non-clostridial anaerobes and can be given intravenously (0,5 g in 100 ml of solvent).**

10. Dioxydin. **This is a derivative of oxychinolin. 0,1 — 1% aqueous solutions are indicated for purulent wounds, for washing the urinary bladder, empyema or abscess cavities, and purulent fistulae. It is available as 10 ml ampoules with 1 % solutions of the drug. In severe purulent infections (sepsis, purulent peritonitis), it can be infused intravenously as much as 60—90 ml 2—3 times a day (30 ml of the solution diluted in 500 ml of 5% glucose solution). It should be avoided in patients with impaired renal function.**

11. Sulphonamides or Sulfonamides is the basis of several groups of drugs. The original antibacterial sulfonamides (sometimes called sulfa drugs or sulpha drugs) are synthetic antimicrobial agents that contain the sulfonamide group. (streptocide, ethazol, sulfacyl)

- Derivatives of sulfacyl with prolonged activity (sulfadimethoxin, sulfalen, sulfapiridazin, streptocidum) are available as tablets, pudres.
- Short-acting - (5-11 hours) Sulfadiazine (Microsulfon)

Sulfamethizole (Thiosulfil), Sulfisoxazole (Gantrisin)

Sulfamethoxazole, Sulfisomidine

Intermediate-acting (11-12 hours)

Sulfacetamide,Sulfadoxine,

Sulfamethoxazole (Gantanol)

Sulfasalazine (Azulfidine) ,

Trimethoprim sulfamethoxazole

TRIPRIM

Description

Sulfadimidine 200mg

Trimethoprim 40mg/100mL

TRIPRIM ***is a sterile, aqueous injectable solution of trimethoprim and a sulfadimethylpyrimidine compound. The*** *aqueous solution* ***is unique and is*** *far better tolerated,* ***locally and generally, than injectable solutions made with the more conventional organic solvents***

TRIPRIM *is a* ***broad spectrum bactericidal agent*** *which is* ***rapidly absorbed*** *from blood into sites of infection!*

12.Soaps

- A soap is a chemical compound of fatty acids combined with potassium or hydrogen peroxide.
- The pH of the compound is usually about 8.0 & some microbial destruction is therefore due to the alkaline conditions established on the skin.
- However, the major activity of the soap is as a degerming agent for the mechanical removal of m.org. from the skin surface.
- Soaps are ‘wetting agents’, i.e. they emulsify & solubilize particles clinging to a surface.

13. ACIDS

- Benzoic acid
- Salicylic acid
- Boric acid is weekly germicidal and nonirritating. But it is readily absorbed if applied to large denuded areas, and can cause severe systemic toxicity with gastrointestinal disorders, hypothermia, renal impairment, vascular collapse, shock and death. It can be limitedly used only in ophthalmology.
- Organic acids are particularly valuable as food preservative.
- Lactic & acetic acid e.g. are important preservatives in sour foods such as cheese & pickled products.
- Propionic acid is added to bakery products to keep microbial population low.

14. Hypertonic solutions –

- Sol Natrii chloride 10-20%
- A hypertonic salt solution - 10 % Sodium chloridum sol.
- 30 % ureas sol.
- 40 % glucoses sol.
- Disadvantage of the hypertonic solutions is the fast inactivation due to delution the wound's exudates.

15. Derivatives of nitrofuran. These agents are effective against purulent cocci. Nitrofurazone is bactericidal against many gram-negative and positive microorganisms in dilutions up to 1:75000. It is clinically useful as topical antiseptic on surgical wounds and superficial skin lesions including burns, ulcers, but systemic toxicity may result from absorption from large wound areas.

- *- Furacilin* - Aqueous solution *1:5000 kills only gram-positive bacteria.* It is used for washing out purulent wounds during dressing, washing out abscess cavities and empyemas through the drainage tube (e.g. in purulent pleurisy and purulent fistula of osteomyelitis).
- *- Soluble Furagin (Furagin K- or Furagin-potassium, Solafur).* The indications of its 0,1% solution are similar to those of furacilin. It can also be given intrave-nously in a dose of 300 ml. Orally, furazolidon is taken as 50 mg tablets.
- Derivatives of nitrofuran may also be ingredients of the membranous compound lifusol manufactured as an aerosol and used to treat superficial wounds and burns. It forms a defensive membrane that causes antimicrobial effect on the wound's surface. Effect of this membrane lasts for 5—7 days.

16. Myramistinum

- «Miramistin» is Russian new generation antiseptic drug. It has a wide scope of action and can be most efficient in prevention and treatment of infections – bacterial (profound antibacterial effect on gram-positive and gram-negative, aerobic and anaerobic bacteria in the form of monocultures and microbe associations, including hospital strains with multiresistance to antibiotics), mycotic and viral infections.
- Method of issuance : 0.01% solution for local applications in bottles of 100 ml and 500; 0.5% ointment in the box on 15, 20 and 30 grams

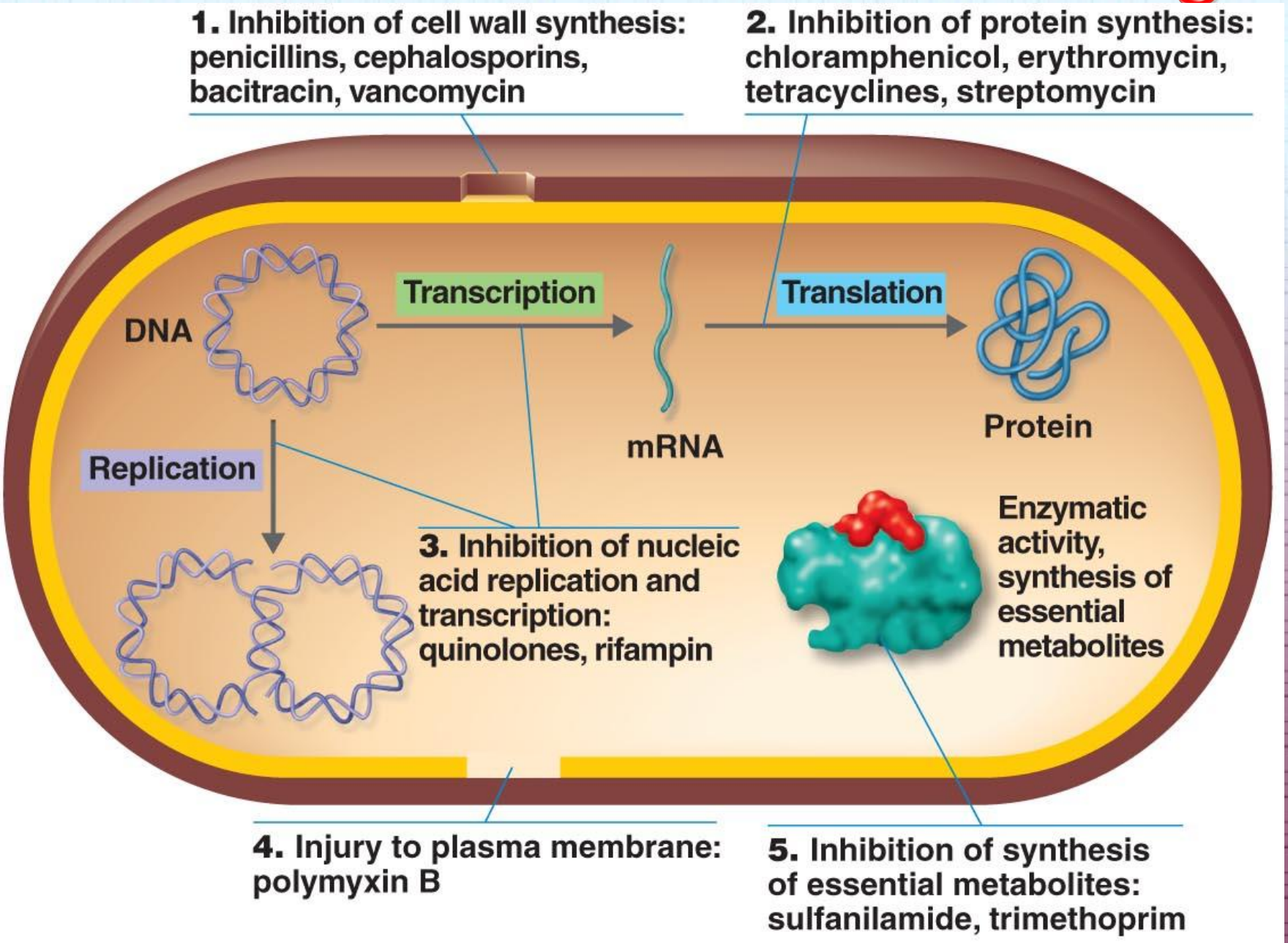
and banks to 30, 100, 1000 and 2000.

Biological antysepsis

- Biological antibacterial agents are used to combat bacterial infection in the wound or inflammatory foci. These are both effective for therapy and prophylaxis and help achieve antibacterial effect inside the human body.
- There are many biological antiseptics; they are section into the following groups:

1. Antibiotics
2. Enzymes
3. Bacteriophages
4. Serums
5. Immunoglobulin

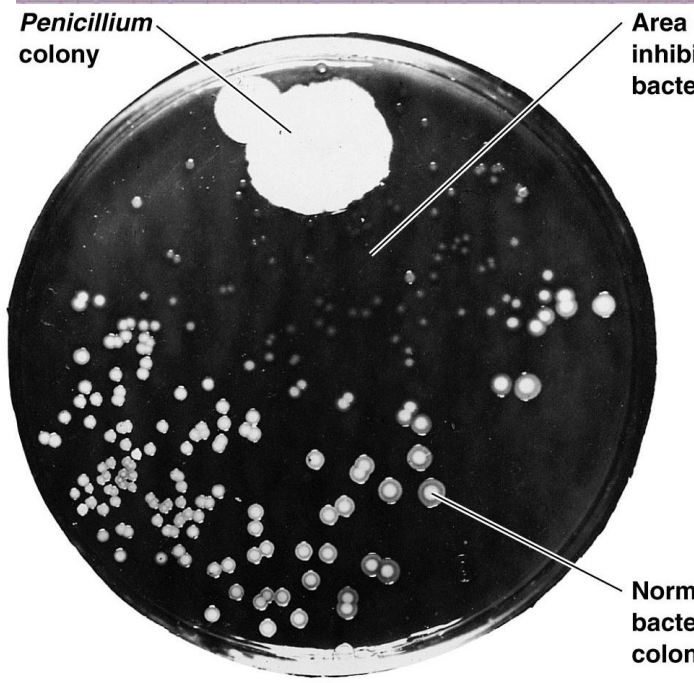
The Action of Antimicrobial Drugs



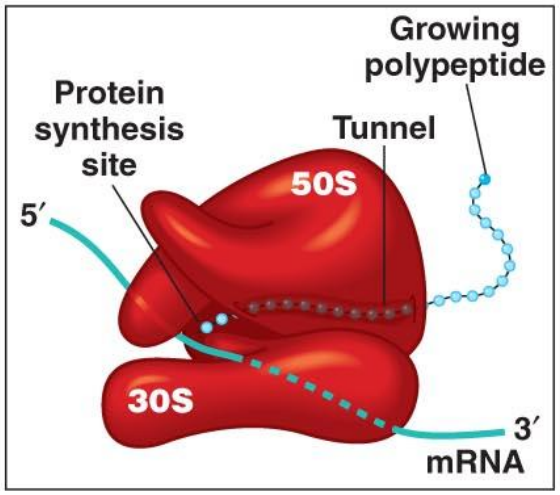
- **1. Antibiotics (AB) are known to be of greatest importance as far as antibacterial therapy is concerned. Currently, the use of antibiotics has been facing a multitude of problems associated with changes in biology of target microorganisms, i.e. quite a number of drug-resistant strains have emerged**

1928: **Fleming** discovered penicillin

1940: Howard **Florey** and Ernst **Chain** performed first clinical trials of penicillin.



Inhibition of Protein Synthesis by Antibiotics



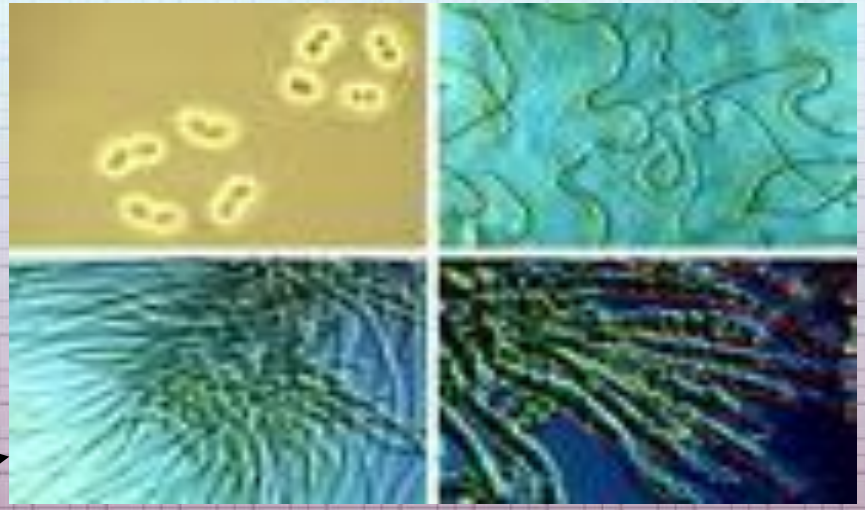
(a) Three-dimensional detail of the protein synthesis site showing the 30S and 50S subunit portions of the 70S prokaryotic ribosome

(b) Diagram indicating the different points at which chloramphenicol, the tetracyclines, and streptomycin exert their activities

Figure 20.4

Sources Of Antibiotics

1. Cyanobacteria
2. Bacteria
3. Actinomycetes
4. Fungi
5. Higher Organisms



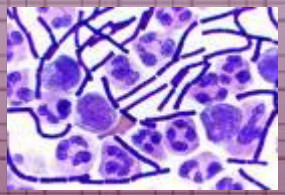
Cyanobacteria

- Mostly produce toxins that kill higher organisms.
- Malingolide is an antibiotic produced by a cyanobacteria.

Bacteria

- **Out of the 19 different principal groups into which bacterias can be divided (Bergey's Classification) the following groups mostly are source of antibiotics**

Bacterial group number	Bacterial type
2	Gliding bacteria
7	Gram –ve aerobic rods & cocci
8	Gram –ve facultatively anaerobic rods
14	Gram +ve cocci
15	Bacillus
16	Gram +ve ,asporogenous rods
17	Actinomycetes & related organisms
12	Mycoplasmas

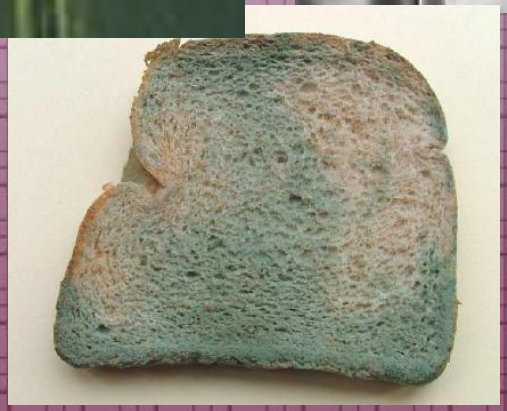


Actinomycetes

- It is the largest source of antibiotics.
- 90%-95% of which is produced by the genus “Streptomyces”(soil bacteria).
- Another genus important for antibiotics production is Micromonospora

Fungi

- Richest source is the genera “penicillium” and “aspergillus”



Higher organisms

- Such as algae, lichens, higher plants , protozoa, insects, molluscs, sponges, worms and vertebrates.

SPECTRUM OF AB EFFECTS

1. **Narrow spectrum antibiotics (NSAB)**

   Main effect : sensitive for gram positive bacteria and bacil

   e.g. : Pen. G, Pen. Resistent penicillinase semisynthetics, bacitracin, macrolides, lincomycin, vancomycin

2. **Broad Spectrum Antibiotics (BSAB)**

   Main effect : sensitive for gram positive and gram negative bacteriae

   e.g. : Pen. (ampicillin and amoxycillin), cefalosporins, tetracyclins, chloramphenicol, trimetroprim and sulfonamides

Method of action – bactericidal/bacteriostatic

• The penicillins

- ***One of the first antibiotics*** **was a natural antibiotic**
- **Bactericidal agents,**
- **Contain a β-lactam ring in structure.**
- **They inhibit synthesis of the bacterium cell wall by affecting synthesis of peptidoglycan.**
- **Peptidoglycan cell wall surrounds certain bacteria and is essential for their survival.**
- ***benzylpenicillin*** **still used nowadays in selected cases. The main advantage of benzylpenicillin is low toxicity.**

Semisynthetic penicillins fall into the next groups:

- **I) stable penicillins (*oxacillin, metycillin, dicloxacillin*), which are active against gram-positive bacteria. They are indicated for staphylococcal infections of various localization (pneumonia, lung abscess, pleural empyema, osteomyelitis, abscess or phlegmon of soft tissues, wounds)**

- **2) broad-spectrum semisynthetic penicillins (*ampicillin; ampiox* — a combination of ampicillin and oxacillin; carbenicillin). These are effective in burns, peritonitis, infected wounds caused by *Pseudomonas* and *Proteus spp.***

- *Co-amoxiclav* - Consists of amoxicillin combined with a beta-lactamase inhibitor clavulanic acid

Spectrum: - Active against Gram-ve rods resistant to amoxicillin due to beta-lactamases

- **E.g. resistant strains of *E.coli*, *S. aureus* and *H. influenzae*.**
- **Clavulanic acid has no antibacterial activity**

- *Flucloxacillin* - Bactericidal antibiotic, A beta-lactamase-resistant penicillin, Used for penicillin-resistant staphylococci. IV dose: 0.25-2g every 6 hours

Can be less effective against bacterium that does not produce beta-lactamase

It is less active against *Streptococcus pneumoniae* and *Str. pyogenes* than penicillin.

Su Siccu, near the harbor of Cagliari, the site where cephalosporin was discovered

Cephalosporins

Fungi of genus
Cephalosporium
⇒ 4 Generations of cephalosporins


Giuseppe Brotzu

1. First-generation: Narrow spectrum, gram-positive (kefzol, cefazolin)
2. Second-generation: Extended spectrum includes gram-negative (cephalothin, cephuroxim)
3. Third-generation: Includes pseudomonads; mostly injected, some oral (cephalexin; cephataxime, cefotaxim, ceftriaxon).
4. Fourth-generation: Most extended spectrum cephalothin

Aminoglycosides

- These include gentamicin, kanamycin, streptomyocin, neomycin, tobramycin and semisynthetic aminoglycoside (amikacin).
- They resemble each other in:
  - Antibacterial activity
  - Pharmacokinetic properties
  - Toxicity
- Mechanism:
  - Bactericidal activity
  - Inhibit bacterial protein synthesis
  - They do this by binding to the 30S ribosomal subunit.
  - They stop the translation of mRNA into the proteins.

Aminoglycosides (cont..)

- Spectrum:
  - Many Gram-ve (Including *Pseudomonas*)
  - Some Gram+ve
  - Inactive against anaerobes
  - Used in serious Gram –ve infections in combination with agents that disrupt cell wall synthesis (e.g. penicillin)
  - Synergistic effect with penicillin
  - Not absorbed orally so only given IM or IV.
- Elimination:
  - Renally by glomerular filtration
  - In renal impairment accumulation occurs rapidly
  - Result is an increase in toxicity (ototoxicity and nephrotoxicity)
  - Dose adjustment is essential in renal impairment

Macrolides

These include erythromycin, oleandomycin, azithromycin, clarithromycin.

- **Similar antibacterial spectrum to penicillins**
- **Mechanism: inhibit bacterial protein synthesis by binding to bacterial ribosome.**
- **Bacteriostatic**
- **Can be effective against unusual organisms**
- **Generally safe drugs**
- ***Erythromycin* can cause gastrointestinal problems which are less common with other agents.**
- ***Azithromycin* has a long half life**
- **Macrolides can inhibit cytochrome P450 leading to accumulation of drugs.**

- **Fluorquinolones - Quinolones (bactericidal)** (***ofloxacin, pefloxacin, cipro-floxacin, lomefloxacin nalidixic acid, ciprofloxacin, ofloxacin, norfloxacin, levofloxacin, lomefloxacin, sparfloxacin***)
- Mode of action **- These antimicrobials bind to the A subunit of DNA gyrase (topoisomerase) and prevent supercoiling of DNA, thereby inhibiting DNA synthesis.**
- Spectrum of activity **- broad spectrum of activity covers numerous gram-negative and gram-positive microorganisms (e.g. *E. coli, Enterobacteriaceae, Klebsiella* and *Staphylococcus spp)***
- Resistance **- Common for nalidixic acid; developing for ciprofloxacin.**

Tetracyclines

- These include tetracycline, oxytetracycline and semisynthetic tetracyclines (metacycline or rondo-mycin), doxycycline (vibramycin).
- Mechanism inhibit protein synthesis
- Absorption of tetracyclines is affected by calcium and magnesium ions, food and iron preparations.
- Broad spectrum antibiotics
- Bacteriostatic
- Should be avoided in pregnancy, breast feeding and children under 12 years as they bind to calcium in growing bones and teeth causing discoloration.

Carbapenems

- Similar mode of action to other β-lactams
- Greater affinity for PBP-2
  - Faster bacterial death
  - Extremely broad spectrum
- E.g. imipenem / meropenem
- Used for severe hospital acquired infections
- carbopinems (imipenem, pleropenem, tienam (a combination of imipenem + sodium celastatin).

Glycopeptides

- Prevent bacterial cell wall synthesis
  - Bind to amino acids in cell wall
- Active against Gram positive bacteria.
  - Don't penetrate outer membrane of Gram neg bacteria (polar molecules)
- E.g. Teicoplanin, vancomycin Used in severe Gram pos infection
- Vancomycin
  - Needs levels monitoring (after 3-4 doses in normal renal function)
  - "red man syndrome"
  - Glycopeptide from *Streptomyce*
  - Inhibition of cell wall synthesis
  - Used to kill MRSA
  - Emerging Vancomycin resistance: VRE and VRSA

Other groups of antibiotics used to combat purulent infections are Chloramphenicol, Lincomycin, Clindamycin (bacteriostatic)

- Mode of action **- These antimicrobials bind to the 50S ribosome and inhibit peptidyl transferase activity.**
- Spectrum of activity **- Chloramphenicol - Broad range;Lincomycin and clindamycin - Restricted range**
- Resistance **- Common**
- Adverse effects **- Chloramphenicol is toxic (bone marrow suppression) but is used in the treatment of bacterial meningitis.**

Fusidic acid (bacteriostatic)

- Mode of action **- Fusidic acid binds to elongation factor G (EF-G) and inhibits release of EF-G from the EF-G/GDP complex.**
- Spectrum of activity **- Gram-positive cocci**

Rifampin, Rifamycin, Rifampicin, Rifabutin (bactericidal)

- Mode of action - **These antimicrobials bind to DNA-dependent RNA polymerase and inhibit initiation of mRNA synthesis.**
- Spectrum of activity - **Wide spectrum but is used most commonly in the treatment of tuberculosis**
- Resistance - **Common**
- Combination therapy - **Since resistance is common, rifampin is usually used in combination therapy.**

Antibiotic Assays to Guide Chemotherapy

Agar Disk Diffusion Method **determines susceptibility of an organism to a series of antibiotics:** Kirby-Bauer test

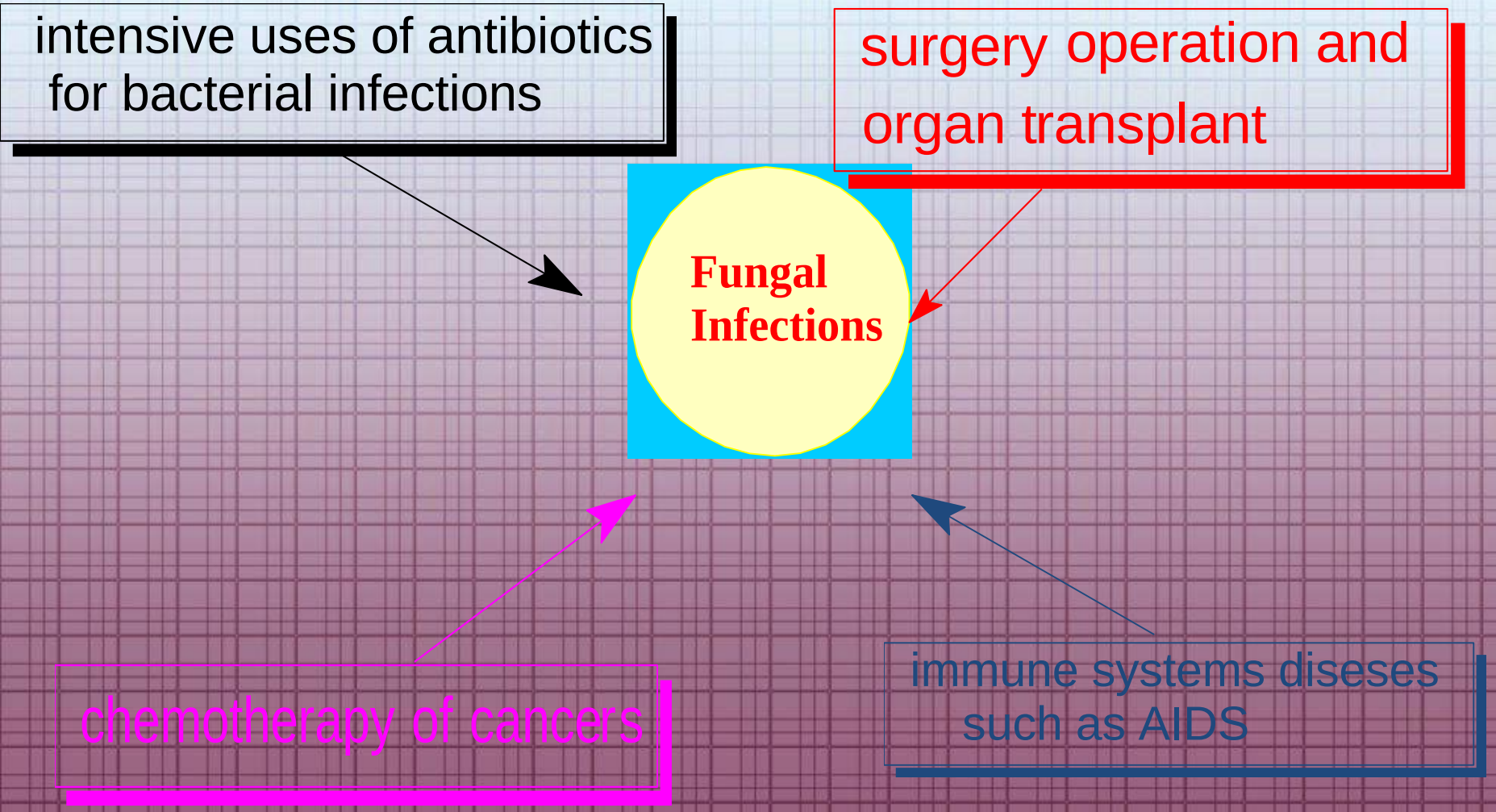
More sophisticated methods available for clinical labs

Antifungal Agents

- Fungi are plant-like, eukaryotic organisms. Most fungi live as saprophytes in soil or on dead plant materials and are important in the mineralization of organic matter.
- There are 300,000 kinds of fungi, but only 270 of which cause disease in humans and animals. These fungi are divided into two classes according to mycotic illnesses in humans they caused.
- Mucocutaneous Fungi : cause skin and hair infections (shallow infections)
- Systemic Fungi : cause visceral infections (deep infections)

Fungal infections

In recent year, the incidence of fungal infections has reached alarming proportions. This duo to a number of factors .



The classification of antifungal agents

Antimycotic antibiotics: Polyenes (Amphotericin B)

Others (Griseofulvin)

Synthetic antifungal Agents:

Fluorinated pyrimidines (Fluorocytosine)

Azoles

Imidazoles (ketoconazole)

Triazoles (Fluoconazole)

Allyamines (Terbinafine)

Thioureas (Tolnafate)

Others (Ciclopirox)

Antimycotic antibiotics

- Polyenes**, such as** nystatin **and** amphotericin B, **for systemic fungal infections. Inhibition of ergosterol synthesis ⇒ fungicidal. Nephrotoxic**
- Griseofulvin **from *Penicillium*. Systemic/oral. Binds to tubulin ⇒ For *Tineae***

Antiviral Drugs

Nucleoside analogs inhibit DNA synthesis

Acyclovir and newer derivatives: Selective inhibition of herpes virus replication. Acyclovir conversion to nucleotide analog only in virus infected cells ⇒ very little harm to uninfected cells!

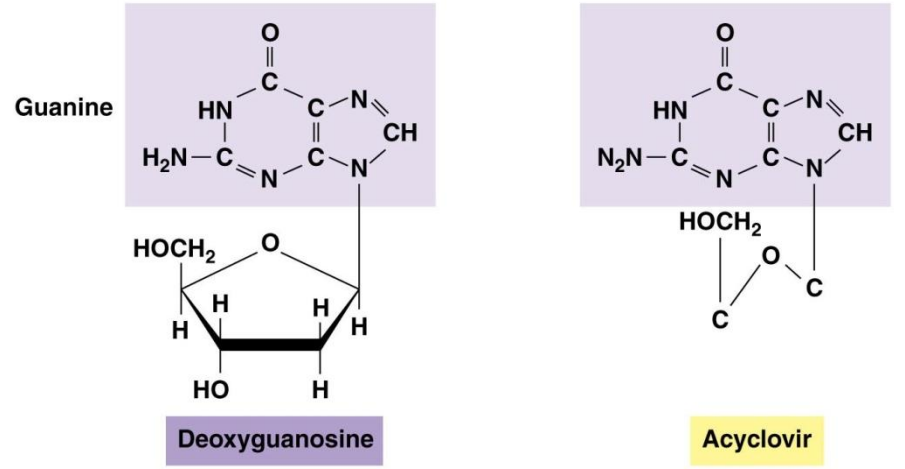


Fig 20.16

(a) Acyclovir structurally resembles the nucleoside deoxyguanosine.

- **Enzymes**
  - Antimicrobial enzymes act against microorganisms
  - Human tears contain lysozyme
    - Digests peptidoglycan cell wall of bacteria
  - Enzymes to control microbes in the environment
    - Lysozyme used to reduce the number of bacteria in cheese
    - Prionzyme can remove prions on medical instruments

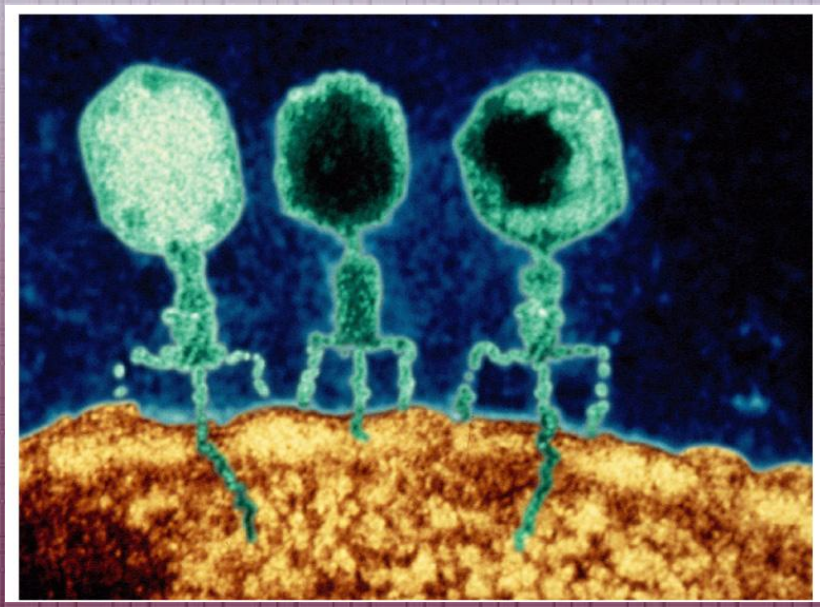
  As anti-inflammatory agents proteolytic enzymes (trypsin, chemotrypsin) are given intramuscularly or intravenously in doses of 0,07 mg/kg.

Bacteriophages

- Bacteriophages are viruses that can infect and destroy bacteria.
- They have been referred to as bacterial parasites, with each phage type depending on a single strain of bacteria to act as host.
- Two basic types of bacterial viruses

Lytic viruses – infect cells, multiply rapidly,lyse cells

Lysogenic viruses – infect cells, can integrate into genome and go dormant (a prophage). - at some point, can excise, multiply and lyse cells.

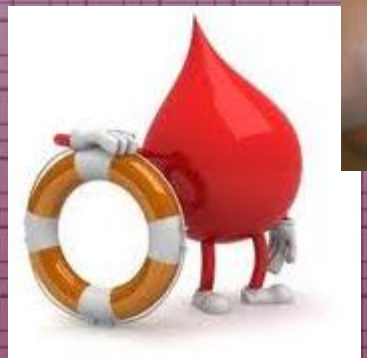


Anatoxins

- ***Staphylococcal anatoxins*** **are given subcutaneosly in doses of 0,1 ml at the scapular area, and repeated each 2—3 days, with an increase in the dose by 0,1 ml each time up to a maximum of 1 ml. In emergency, 0,5 ml can be given preoperatively.**
- ***Tetanus antitoxin*** **is used for both scheduled and emergent prophylaxis against tetanus. Injection of the drug in emergency is combined with prophylactic doses of antitetanus serum.**

Immunoglobulin

- *Antibodies are substances made by the body's immune system in response to bacteria, viruses, fungus, animal dander, or cancer cells. Antibodies attach to the foreign substances so the immune system can destroy them.*
- *Antistaphylococcal gamma globulin*
- *Antitetanus gamma globulin*



Immune Serum

immune serum is a serum containing naturally or artificially produced antibodies to a given antigen, obtained from human or animal sources.

- **Antitetanus serum**
- **Antigangrene serum**
- ***polyvalent serum*** - *antiserum containing antibody to more than one kind of antigen.*
- ***antilymphocyte serum*** *(ALS) antiserum derived from animals immunized against human lymphocytes; a powerful nonspecific immunosuppressive agent that causes destruction of circulating lymphocytes.*
- ***antirabies serum*** *antiserum obtained from the blood serum or plasma of animals immunized with rabies vaccine; used for postexposure prophylaxis against rabies if rabies immune globulin is unavailable.*

Prebiotics

- A prebiotic is a nondigestible component which beneficially affects the host by selectively stimulating the growth and/or activity of one or a limited number of colonic bacteria, thereby improving the health of the host

***In other words, prebiotics are nutrients that the bacteria use as a fuel source; these include dietary fiber and carbohydrates*

Not absorbed or degraded

- Alter the balance of intestinal flora and by acting as substrates stimulate the growth of beneficial bacteria (i.e., Lactobacillus and Bifidobacteria)

- Must not be hydrolyzed nor absorbed in the upper gastrointestinal tract
- Must be a substrate for growth or activity of one or a limited number of beneficial colonic bacteria
- Must therefore be able to alter the colonic microflora towards a healthier composition and to induce luminal or systemic effects which are beneficial to the health of the host
- Fructooligosaccharide (aka oligofructose)
- Isomaltooligosaccharide
- Xylooligosaccharide
- Inulin
- Fiber
- Oligomate
- Palatinose
- Pyrodextrin
- Raftiline

Prebiotics- examples

- Inulin
- Garlic
- Onions
- Chicory root
- Asparagus
- Whole wheat
- Rye
- Barley

Probiotics

- Probiotics defined as microorganisms that have a beneficial effect on the host intestinal microbial balance
- Probiotics, which means “for life” was meant to contrast “antibiotics”, popularly prescribed and known to also destroy beneficial organisms and impact the immune system.

Probiotics

- Non-pathogenic live microbial food supplements
- Organisms that, when administered in adequate amounts, exert a positive influence on the health of the host animal
- Live organisms that benefit the host animal by improving intestinal microbial balance
- Usually administered in yogurt or capsules

A Brief History of Probiotics

- Metchnikoff – 1907 – ingesting yogurt with Lactobacilli reduces toxic bacteria of the gut and prolongs life
- Kipeloff – 1926 – stressed importance of Lactobacillus acidophilus for good health
- Rettger – 1930's – early clinical application of Lactobacillus
- Parker – 1974 – 1st to use the term probiotics
- Fuller – 1989 – defined probiotics

Probiotics

- Lactobacilli – anerobic, gram (+) rods
  - casei
  - plantarum
  - acidophilus
  - reuteri
- Bifidobacteria – anerobic, gram (+) rods
- VSL #3 (8 separate organisms: 3 Bifidobacteria, 1 Streptococcus, 4 Lactobacilli)
- Enterococcus
- Streptococcus salivarius
- Saccharomyces

How is normal mucosal immune function maintained?

- GI secretions (saliva, acid, bile)
- Mucus
- Normal peristalsis (presence of MMC)
- Barrier function (tight junctions)
- Intestinal proteolysis
- Intestinal immune cells
- IgA production and secretion

Intestinal Flora: A symbiotic relationship with the host

- Human GI tract contains 10x more bacteria (10^{14}) than eukaryotic cells in the body
- Protects the host
  - Stimulates immune function
  - Produces antimicrobial substances
- Trophic effect on intestinal epithelium
- Maintains the enterohepatic circulation of bile acids
- Involved in metabolic processes (i.e., fermentation) in the colon

Probiotics: Mechanism of Action

- Competitive inhibition
- Barrier protection
- Immune effects
- Anti-inflammatory effects
- Production of various substances (enzymes, SCFA, bacteriocidal agents)
- Ability to alter local pH and physiology
- Provides nutrition to colonocytes

Thanks for your attention!!!