Antiseptics & Disinfectants

Antiseptics

Antiseptics and disinfectants

- Antiseptic
  - Substance used to treat a person to prevent the occurrence of infection
- Disinfectant
  - Substance used to treat materials or equipment to remove or inactivate sources of infection

- Agents used on living surfaces
- (skin, mouth) are called antiseptics while
- Those used for inanimate objects (instruments, privies, water supply) are called disinfectants
- The term germicide covers both category of drugs.

- Difference between 'disinfection’and'sterilization'.
- Sterilization means complete killing of all forms of microorganisms,
- disinfection refers to reduction in the number of viable pathogenic microbes to a level that they do not pose a risk to individuals with normal host defence.
- Thus,disinfectants do not eliminate all microbes.

Origins of antiseptics

- Ignaz Semmelweis (1818 - 1865) Hungarian physician working in Vienna
  - Realised that cross contamination was causing a high incidence of death after childbirth
  - He made doctors wash hands in chloride of lime before touching patients
  - Dramatically reduced incidence of childbed fever
  - Met much opposition from medical establishment
  - Practice stopped when he retired and deaths went up.

Origins of antiseptics

- Semmelweis was not alone in his observations
- A Scottish naval surgeon, Alexander Gordon and an American, Oliver Wendell Holmes made similar observations and proposed similar remedies
  - and there were others as well
- All were ignored and many women died unnecessarily in childbirth as a result
- It needed a parallel discovery, of micro-organisms as causative agents of disease for the basic ideas to be taken seriously.

Origins of antiseptics

- Joseph Lister (1827 - 1912)
  - Realised that deaths from operations mostly occurred from infection contracted during the operation as a result of unclean practices.
  - He started using Carbolic acid (phenol) during operations to maintain aseptic conditions with significant improvements
  - Like Semmelweiss he initially encountered opposition, but use of his methods by the Germans during the Franco-Prussian war in 1870 provided his major breakthrough and over the next 10 years, the practise of aseptic surgery became accepted.
  - For more information on Lister go to
    - http://web.ukonline.co.uk/b.gardner/Lister.html

A good antiseptic/disinfectant should be:

- (i) Chemically stable.
- (ii) Cheap.
- (iii) Nonstaining with agreeable colour and odour.
- (iv) Cidal and not merely static, destroying spores as well
- (v) Active against all pathogens-bacteria,fungi, viruses, protozoa.
- (vi) Require brief time of exposure.
- (vii) Able to spread through organic films and
- enter folds and crevices.
- (viii) Active even in the presence of blood, pus, exudates and excreta.

An antiseptic in addition should be:

- (i) Rapid in action and exert sustained protection.
- (ii) Nonirritating to tissues, should not delay healing.
- (iii) Nonabsorbable, produce minimurn toxicity if absorbed.
- (iv) Nonsensitizing (no allergy).
- (v) Compatible with soaps and other detergents.

$pectrum of aetivity of majority of antiseptics/disinfectants

- is wide, reflecting nonselectivity of action.
- However,some are rather selective, e.g. hexachlorophene, chlorhexidine, quaternary ammonium antiseptics, gentian violet and acriflavin are more active on gram-positive than gram-negative bacteria; silver nitrate is highly active against gonococci and benzoyl peroxide against P. acnes

Mechanisms of action of germicides can be grouped into:

- Oxidation of bacterial protoplasm.
- Denaturation of bacterial proteins including enzymes.
- Detergent like action increasing permeability of bacterial membrane.

Factors which modify the activity of germicides are:

- (i) Temperature and pH.
- (ii) Period of contact with the microorganism.
- (iii) Nature of microbe involved.
- (iv) Size of innoculum,
- (v) Presence of blood, pus or other organic
- matter.

- Potency of a germicide is generally expressed by its phenol cofficient or Rideal Walker coefficient,

which is the ratio of the minimum concentration of test drug required to kill a 24 hour culture of B. typhosa in 7.5 minute at 37.5'C to that of phenol under similar conditions.

- Therapeutic index of an antiseptic is defined by comparing the concentration at which it acts on microorganisms with that which produces local irritation, tissue damage or interference with healing.

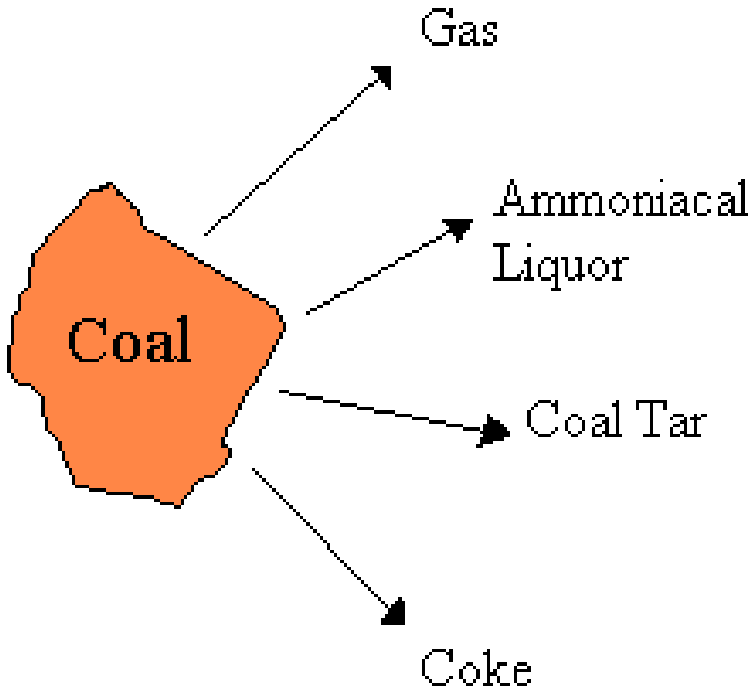
- CLASSIFICATION
- 1. Phenol derivatives- Phenol, Cresol, Hexylresorcinol, Chloroxylenol, Hexachlorophene.
- 2. Oxidizing agents: Pot. Permanganate,Hydrogen peroxide, Benzoyl peroxide.
- 3. Halogens: Iodine, Iodophores, Chlorine,Chlorophores.
- 4. Biguanide: Chlorhexidine.
- 5. Quaternary ammonium (Cationic): Cetrimide,
- Benzalkonium chloride, Dequalinium chloride.
- 6. Soaps: of Sod. And Pot.
- 7. Alcohols: Ethanol, Isopropanol.

- 8. Aldehydes: Formaldehyde,Glutaraldehyde.
- 9. Acids: Boric acid, Acetic acid.

- 10. Metallic salts: Merbromin, Silver nitrate, Silver sulfadiazine, Mild silver protein, Zinc sulfate, Calamine, Zinc oxide.
- 11. Dyes: Gentian violet, Acriflavine, Proflavine.
- 12.Furan derivative: Nitrofurazone.

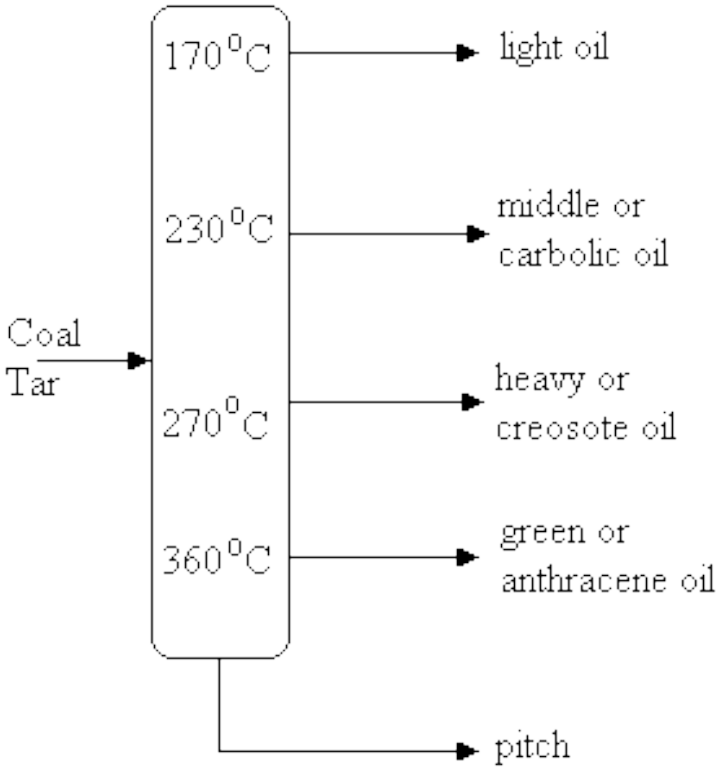
Sources of antiseptics

- Early antiseptics were probably vegetable extracts
  - Many spices contain antibacterial agents
- Essential oils extracted from plants often have antibacterial properties
- Lister used carbolic acid which chemically is a solution of phenol
  - Phenol was originally extracted from coal tar.
  - Coal tar preparations are still used today in therapeutic soaps and shampoos.



Coal tar distillation

- Coal tar is a complex mixture rich in aromatic compounds
- These are first separated by distillation
- Phenol is found in the carbolic oil and is recovered by further distillation and washing with slaked lime (calcium hydroxide) solution
- Nowadays phenol is produced by chemical synthesis.

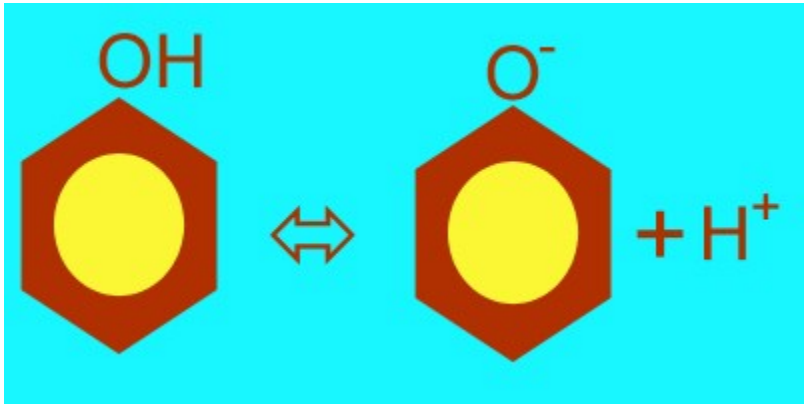


Phenol

- Phenol, or carbolic acid was one of the first antiseptics
- it contains a six-membered ring of carbon and hydrogen atoms
- Such compounds are known as *aromatic*
- The other important part of the phenol molecule is the OH group attached to the ring.
- Such Compounds are known as alcohols
- Thus Phenol is an aromatic alcohol

Properties of phenol

- Although phenol is technically an alcohol, it behaves differently from other alcohols
- It is able to ionise when dissolved in water
- This gives it some of the properties of an acid
- Hence its old name “Carbolic acid”



Phenol as an antiseptic

- The phenol molecule comprises an ionisable part and a hydrocarbon part
- In other words, the molecule resembles those of detergents with hydrophyllic and hydrophobic parts
- This is the key to phenol's action as an antiseptic.

- The OH is the hydrophyllic part and the hydrocarbon ring the hydrophobic part

Phenol as an antiseptic

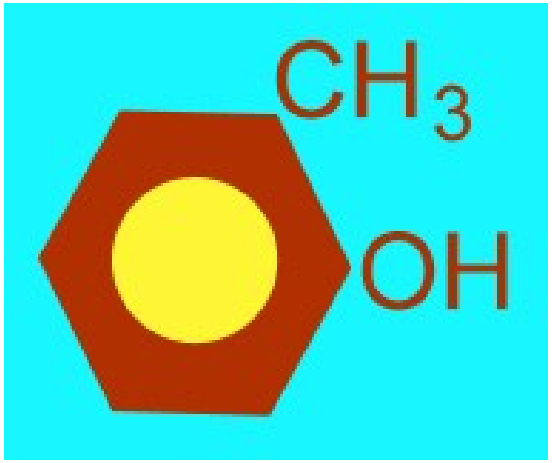
- Phenol acts as an antiseptic, at least in part, because of its detergent properties
- It solubilises the materials that make up the cell membrane, thus disrupting the cell membrane.
- Its action is similar to that of cationic surfactants
  - It is able to replace phospholipids in the cell wall, thus disrupting them

Problems with phenol

- Phenol is a caustic substance and reacts with tissue causing damage.
- The maximum concentration permitted in proprietary preparations is 1%
- At these concentrations, phenol acts as a *bacteriostat* i.e. it reduces bacterial growth, but does not kill the bacteria
- A substance that kills bacteria is a *bacteriocide*

Alternatives to phenol

- A number of other phenolic compounds exist which can act as effectively, if not more so than phenol but are less hazardous
- One of the simplest is catechol which contains an extra CH_3 group



- Others include
  - Derivatives of resorcinol (has two OH groups)
  - thymol
  - Various chlorinated compounds

It is a relatively weak agent ,poor action on bacterial spores).

- **It is a general protoplasmic poison, injuring microbes and tissue cells alike-at higher concentrations**
- **causes skin burns and is a caustic**
- **It acts by disrupting bacterial membranes and denaturing bacterial proteins.**
- **Organic matter diminishes its action slightly while alkalies and soaps do so profoundly (carbolic soaps are not more germicidal than soap itself).**
- **It is now seldom employed as an antiseptic, but being cheap, it is used to disinfect urine, faeces, pus, sputum of patients and is sometimes included in antipruritic**
- **preparations because of its mild local anaesthetic**
- **action.**

- Cresol: It is methyl-phenol; more active (3-10
- times) and less damaging to tissues.
- Used for disinfection of utensils, excreta and for washing hands.
- Hexylresorcinol :It is a more potent derivative of the phenolic compound resorcinol that is odourless and nonstaining; used as mouthwash, lozenge and as antifungal.

- Chloroxylenol: It has a phenol coefficient of 70;
- does not coagulate proteins, is noncorrosive,
- nonirritating to intact skin
- It is poorly water soluble; the commercial 4.8% solution (Dettol) is prepared in 9% terpinol and 13% alcohol; used for surgical antisepsis.
- A 0.8% skin cream and soap, 1.4% lubricating obstetric cream (for vaginal examination, use on forceps, etc.), and a mouthwash (Dettolin1%) are also available.
- These preparations lose activity if diluted with water and kept for a time.

- Hexachlorophene :
- This chlorinated phenol acts by inhibiting bacterial enzymes and (in high concentration) causing bacterial lysis.
- It is odourless, nonirritating and does not stain.
- Its activity is reduced by organic matter but not by soap.
- It is commonly incorporated in soap and other cleansing antiseptics for surgical scrub, patient's skin, etc., but is narrow spectrum; kills gram-positive but not gram-negative bacteria or spores.

2. OXIDIZING AGENTS

- **Potassium permanganate- It occurs as purple crystals, highly water soluble, liberates oxygen which oxidizes bacterial protoplasm.**

- **The available oxygen and germicidal capacity is used up if much organic matter is present-the solution gets decolourised.**
- **A 1:4000 to 1:10,000 solution (Condy's lotion) is used for gargling, douching, irrigating cavities, urethra and wounds.**
- **The action is rather slow and higher concentrations cause bums and blistering-popularity therefore has declined.**
- **It has also been used to disinfect water (wells, ponds) and for stomach wash in alkaloidal poisoning (except atropine and cocaine which are not efficiently oxidized).**
- **It promotes rusting and is not good for surgical instruments.**

Benzoyl peroxide -It is specifically active against P. acnes and used on acne vulgaris

- **Hydrogen peroxide -It liberates nascent oxygen which**
- **oxidizes necrotic matter and bacteria.**
- **A 30% solution produces 10 volumes of oxygen much of which escapes in the molecular form.**
- **Hydrogen peroxide has poor penetrability and a weak, transient action. It loses potency on keeping.**
- **Use therefore is much restricted.**

Disinfectants

Chlorine

- Discovered 1774 by a Swede, C.W. Scheele
- It is a pale green, toxic, reactive gas
- It is a powerful irritant and toxin
  - Used as a gas warfare agent in WWI
  - very nasty, inflicting lifelong damage on those who survived
  - The damaged lungs were possibly a factor in the 1918 flu pandemic
- Solution of chlorine in water is both a powerful bleach and disinfectant
  - Semmelweis had used chloride of lime as his antiseptic

Chlorine disinfectants

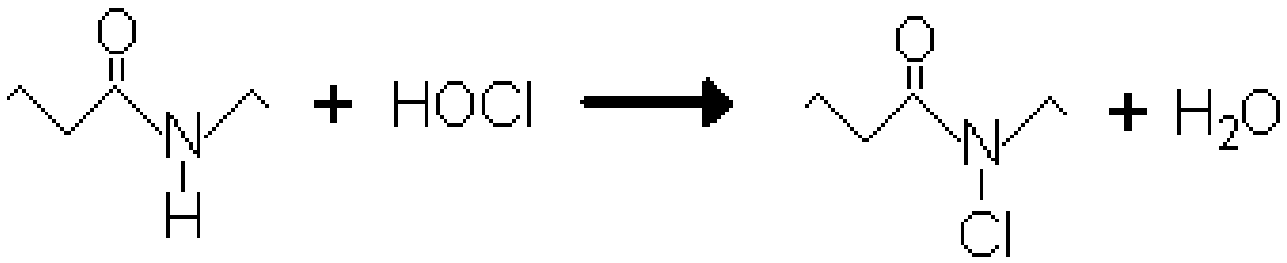
- Chlorine is soluble in water forming a weak acid
  - $Cl_2 + H_2O \Leftrightarrow HOCl + Cl^- + H^+$
- Resulting solution is an effective bleaching agent and disinfectant
- The active agent is the HOCl (hypochlorous acid)
  - Solution not particularly stable & Gradually loses Cl_2
  - HOCl is attacked by UV

Chlorine disinfectants

- Dissolve Chlorine in NaOH or KOH, and the solution is more stable
  - $Cl_2 + 2OH^- \Leftrightarrow OCl^- + Cl^- + H_2O$
- Most bleach based disinfectants are solutions of sodium hypochlorite
- If dissolved in acid, sodium hypochlorite liberates chlorine gas
  - $H^+ + HOCl + Cl^- \Leftrightarrow Cl_2 + H_2O$

Action of hypochlorite

- HOCl is said to be an “active” chlorine compound
  - It will chlorinate organic compounds
- HOCl attacks the peptide bond which joins together amino acids in proteins
  - This weakens the bond and destroys the protein.



Other chlorine disinfectants

- React hypochlorite with ammonia gives chloramine
  - $NH_3 + HOCl \Leftrightarrow NH_2Cl + H_2O$
  - This is unstable, but replaced a hydrogen by an organic group, R; R-NHCl gives a series of useful disinfectants
  - When dissolved in water, will liberate HOCl fairly slowly making them controllable and more useful for medical applications.
  - Note: If the Cl is attached directly to the carbon atom, the chlorine is not active, but produces useful solvents.

Other disinfectants

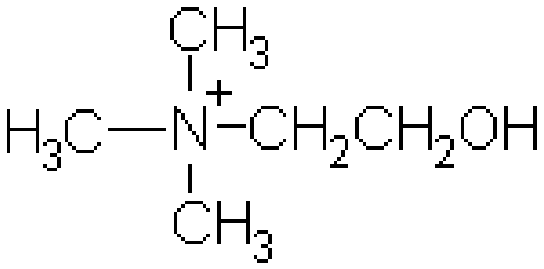
- Chlorine gas is used to disinfect drinking water
  - Contentious, but safe in suitable doses
  - Can cause taint of the water
- Iodine is chemically related to chlorine and has proved a useful antiseptic.
  - Generally best as KI in alcohol solution (tincture of iodine)
  - HOI is more active than HOCl, so alcohol solution reduces activity.

Quaternary ammonium compounds

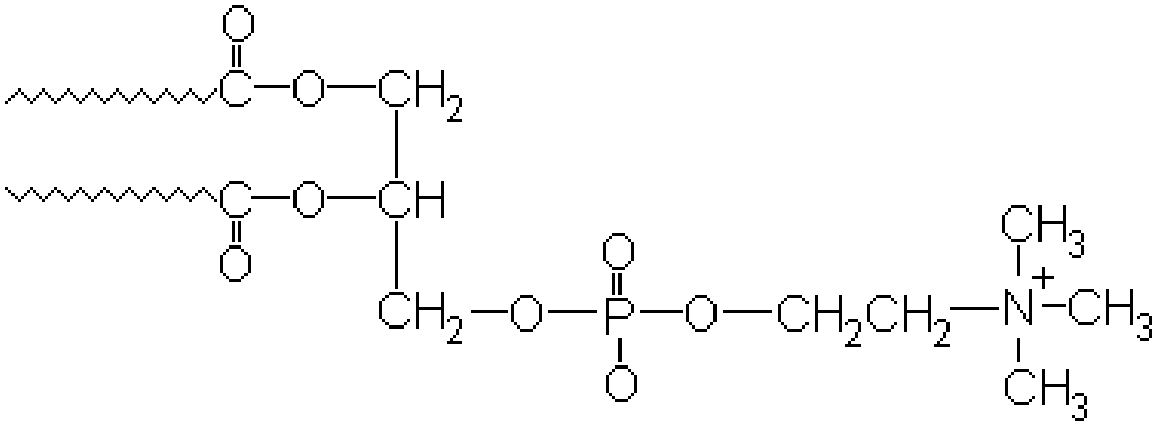
- These are cationic surfactants
  - do not have particularly powerful cleaning properties,
  - though are be used as fabric softeners
- Structurally similar to phospholipids in cell membranes
  - Natural quat is choline which is found in phospholipids
  - Quats disrupt the cell membrane
- Useful antiseptics, but cannot be taken internally
  - disrupt blood cell membranes
- Widely used in the food industry

Choline & Phospholipids

- Choline



- Phospholipid



Activity

- Phenol is a hazardous substance
  - Find out what hazards phenol poses and how these may be avoided or dealt with
- Other phenolic compound effective as antiseptics include thymol, hexachlorophane, chloroxylenol, and trichlorophenol
  - Find the chemical formula of these
  - How effective are these as antiseptics?
  - Some are the basis of proprietary antiseptics. Can you find their names?