Chapter 35
Disinfection Agents and Antiseptics

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Contents

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Introduction

Germicidal agents are nonspecific antimicrobial agents that are too toxic to be administered internally but are safe and effective when used topically. When applied to living tissue (e.g., the skin), they are termed *antiseptics*. When applied to inanimate objects (e.g., environmental surfaces or instruments used to perform medical procedures), they are termed *disinfectants*. All of these agents work at least by damaging microbial surfaces, often by alkylation, oxidation, or reaction with proteins. Products capable of destroying all forms of microbial life, including bacterial spores, are termed *sterilizing agents*.

Agents Used as Antiseptics

Alcohols

In 60–90 % solution in water, both ethyl alcohol and isopropyl alcohol are capable of killing vegetative (but not spore) forms of nearly all bacteria as well as fungi, and most viruses, most likely by denaturation of bacterial proteins. Long used for skin antisepsis, ethyl alcohol has more recently been combined with other agents to increase efficacy (iodine: DuraPrep®; chlorhexidine: ChloraPrep®). An important disadvantage is flammability; this happens only when the prep solution that is applied does not evaporate fully and when electrocautery is also employed. Alcoholic solutions should not be applied to mucosal surfaces and must be kept away from the eyes: even brief application may result in a requirement for corneal transplantation.

Polymer-Iodine Complex

Iodine's broad-spectrum antiseptic properties have been known since 1811. Postulated mechanisms of bactericidal action include (1) membrane destabilization, (2) inhibition of protein synthesis, (3) free electron transport inhibition, and (4) nucleic acid denaturation. Iodine's low solubility limited clinical use until Lugol combined iodine with potassium iodide salt. In 1952, Shalanski and Shalanski incorporated molecular iodine into the large polymer, polyvinylpyrrolidone to form a complex, povidone-iodine (Betadine®), that releases iodine into aqueous solution in three bactericidal forms: free molecular iodine, hypoiodous acid (HOI), and iodine cation (the most effective).

Povidone-iodine exerts its antimicrobial effects on bacteria, viruses, yeasts, fungi, and protozoa. The 10 % solution marketed for skin disinfection must be diluted before applying to the cornea or deep tissues such as open wounds.

To achieve cutaneous antisepsis prior to central venous cannulation, some studies suggest greater antibacterial efficacy if polymer-bound iodine dispersed in alcoholic solution is used, e.g., iodine acrylate copolymer (povacrylex; 0.7 % available iodine) in 74 % isopropyl alcohol (DuraPrep®). Iodophor solution from a single-use container is more reliably bacteria-free than the solution from a multidose container. A small percentage of patients will experience cutaneous reactions such as erythema, urticaria, or blistering.

Chlorhexidine Gluconate

Chlorhexidine (Chemical Structure 35.5 – see end of chapter) is a cationic bisbiguanide detergent-antiseptic that kills target organisms via membrane disruption and cytoplasmic precipitation. It is effective against all microbial organisms commonly associated with catheter-related infections and adheres to the stratum, prolonging protection after application for hours. A 4 % aqueous solution (Hibiclens®) is marketed for skin cleaning and preoperative surgical hand scrub. A 2 % solution in 70 % isopropyl alcohol (ChloraPrep®) has been approved by the US Food and Drug Administration (FDA) for preoperative skin prep. The use of a color-tinted solution can help ensure even coverage. Waiting for applied solution to dry prior to needle insertion is recommended.

Evaluations of available evidence have led task forces of several large, respected medical organizations to recommend 2 % alcoholic chlorhexidine as the best available skin prep solution prior to central venous cannulation [1] (except perhaps in neonates where povidone-iodine in alcohol may be preferred). The American Society of Regional Anesthesia accepts the use of alcoholic chlorhexidine solution prior to neuraxial blockade despite case reports and experimental evidence that clinically used concentrations are toxic when applied directly to neural tissue [1, 2]. A recent large retrospective study of its use prior to spinal anesthesia seems to confirm safety when used in this setting [3].

Agents and Techniques Used for Disinfection [4–8]

The extent of disinfection required prior to the use of medical equipment varies depending on the site of application: (1) *sterilization* if contacting deep tissues, (2) *high-level disinfection* (HLD; destruction of vegetative microbes but not spores) if contacting intact mucosa, and (3) *low-level disinfection* (LLD; destruction of most vegetative bacteria, some fungi, and some viruses in <10 min) if contacting intact skin. Standard and videolaryngoscopes and bronchoscopes are reusable anesthesia equipment most often requiring sterilization/disinfection. Anesthesia providers should also know how to perform LLD of the surfaces of an anesthesia workstation and how to decontaminate an environmental spill of blood or a disinfectant solution

used in their facility. Because of the consequences of process failure (inoculation of a patient with a pathogenic organism), all HLD and sterilization processes require monitoring (usually both chemical and biological) to verify satisfactory completion.

High-Level Disinfection (HLD)

Inadequate HLD of laryngoscope blades has resulted in fatal bacterial outbreaks in neonatal intensive care units, and inadequate HLD of bronchoscopes has been proven to be the cause of many scores of reported cases of Mycobacterium and Pseudomonas infections [9, 10]. Such HLD failures require notification of patients' physicians, hospital offices of infection control and risk management, and sometimes state and federal authorities. All HLD methods described in this chapter have been approved by the US Food and Drug Administration (FDA). Not all techniques are compatible with every piece of medical equipment, however. Manufacturers of both equipment and disinfection agents are normally quite willing to make compatibility testing data and recommendations based on such data available on request, and it is often already published on the company website. All chemical solutions used for HLD are toxic if ingested or applied to the cornea. Some also require avoidance of inhalation.

Performance of HLD of a bronchoscope should typically include the following steps:

1. Immediately after use – to prevent drying of secretions which can affix and protect from cleaning a contaminated biofilm – rinsing the exterior scope and flushing suction channels with tap water, then wiping the exterior with an antiseptic-impregnated cloth or paper towel
2. Rapidly transferring the scope to a designated are where it can be leak checked, immersed in a detergent solution, and all surfaces and mechanically cleaned ports and suction channels using cylindrical brushes (very hot or hard water is not advised since excessive heat and contained minerals can inactivate enzymes, such as proteases, lipases, and amylases, often used to fortify medical-instrument-grade detergents.)
3. Disinfecting by immersion + flushing with an approved biocidal solution (glutaraldehyde, ortho-phthalaldehyde, peracetic acid/H_2O_2)
4. Rinsing with microfiltered or sterile water (failure of this step potentially later permitting residual disinfectant to contact and severely irritate airway mucosa)
5. Active drying using alcohol and/or forced air
6. Storing in a cabinet or other container that is physically separate from contaminated equipment and that permits any residual moisture to evaporate

Glutaraldehyde (Cidex®) and ortho-phthalaldehyde (Cidex OPA®) are alkylating agents, the former less expensive and the latter faster-acting and causing far less irritation to the eyes and mucous membranes. Both have excellent compatibility with most equipment and full efficacy at room temperature. Glutaraldehyde is sometimes

sold in alcoholic solution. Disadvantages include (1) a tendency for these chemicals to coagulate blood and other proteins, causing them to stick to equipment surfaces, and (2) the need to frequently monitor solution strength using color test strips. Due to environmental toxicity, some state governments have classified both agents as toxic waste and prohibit their disposal into public sewer systems without preliminary neutralization, e.g., using glycine, Na bisulfite, or dilute Na hydroxide. Federal occupational safety statues mandate low exposure limits. Large spills of either agent may require handling by a hazardous material (hazmat) response team [11].

Two peroxide solutions – hydrogen peroxide and peracetic acid – are capable of achieving HLD at low temperature (<40 °C) by oxidation. Neither have important environmental toxicity since the former breaks down into water and oxygen and the latter to these two reactants (by generating H_2O_2 in solution) plus acetic acid. Hydrogen peroxide is marketed as a concentrated solution (e.g., Steris Revital-Ox Resert XL HLD accelerated H_2O_2) and peracetic acid/hydrogen peroxide solution as either a concentrate (e.g., Rapicide™) or as dry crystals (e.g., Steris Reliance DG®). Because they react with metals and glues, peroxide solutions should not be used with some bronchoscope models. Unlike the aldehydes, neither fixes protein to equipment surfaces. H_2O_2 vapor is nonirritating to mucosa. In contrast, peracetic acid is highly irritating and is therefore normally used within a sealed automated washing/disinfecting machine.

Sterilization

A sterilization process is not required for equipment contacting intact mucosa, but should be applied to a laryngoscope that was employed in a traumatic intubation or in a patient in whom disease has compromised mucosal integrity. Unlike surgical supplies, airway equipment used in anesthesia need *not* ordinarily be stored as sterile so that HLD techniques with extended immersion times but no provision for sterile packaging are usually appropriate.

Steam autoclaving (which kills by protein coagulation and oxidation) is widely employed for sturdy metal surgical equipment. Intolerance of batteries, light bulbs, and plastic components to moist heat ordinarily discourages use of this technique on laryngoscopes and bronchoscopes.

Ethylene oxide (EtO; C_4H_2O) is a relatively inexpensive gaseous cyclic ether that kills microbes by alkylation and has excellent material compatibility. It has long been the mainstay of low-temperature sterilization of delicate equipment. Disadvantages include (1) that it is a flammable, and potentially explosive, biotoxin (carcinogenic, mutagenic) with general anesthetic properties but a (deceptively) pleasing aroma, (2) that it must be destroyed rather than released into the environment, and (3) that it has the longest cycle time of any sterilizing agent (4 h for sterilization; 12 h for dilutional aeration).

Hydrogen peroxide vapor, unlike ETO gas, is an effective agent for sterilizing laryngoscope blades but cannot diffuse sufficient distances to penetrate the full

length of bronchoscope channels. It can be used in two forms for low-temperature sterilization: (1) in high concentration (e.g., Amsco ®V-Pro™ 1 Plus) or (2) as sub-atmospheric pressurized ionized gas plasma (Sterrad®). The former kills by oxidation, the latter by oxidation-induced ultraviolet irradiation and by photodesorption (atom-by-atom erosion). Both have a relatively short cycle time, and neither emits toxic environmental waste. Polypropylene sterilization bags must be used as H_2O_2 adsorbs to paper.

Infrequently used (though approved) methods of sterilization include:

- Immersion in peracetic acid solution – limited because sterilized items are wet, and therefore, cannot be stored as sterile
- Dry heat in a convection oven – non-rusting, but limited by requirement for higher temperatures, longer cycle times, and more uneven penetration with a sealed package
- Gamma irradiation (often from ^{60}Co) – limited by need for expensive equipment, dangerous supplies (and so extensive regulatory supervision), and unreliable sterilization of surfaces lying behind thick or metallic portions of an irradiated item, thus mainly employed by manufacturers of disposable cloth or plastic surgical supplies and implants

Low-Level Disinfection (LLD)

Present recommendations are for performing LLD of the anesthesia work area and laryngoscope handle, i.e., killing such vegetative (nonspore) pathogens as Pseudomonas sp., methicillin-resistant *Staphylococcus aureus* (MRSA), vancomycin-resistant Enterococcus (VRE), many fungi, and hepatitis, immunodeficiency, and SARS coronaviruses within one to a few minutes. Surfaces should be wiped with an aqueous or alcoholic solution of one of several approved agents.

Quaternary ammonium solutions (active molecules being ammonium compounds in which there are four nitrogenous bonds to alkyl or heterocyclic radicals and a fifth to a halide, sulfate, or similar anion) have detergent as well as disinfectant properties. They are often supplied in squirt bottles or saturated disposable towelettes. Such is the active ingredient of Lysol®, Dettol®, Bactine®, and Sani-Wipes (0.0175 benzyl ammonium chloride + 5.5 % isopropyl alcohol). These compounds are inactivated by soaps, inhibited by calcium and magnesium ions and cotton, and ineffective against some strains of Pseudomonas and some non-enveloped viruses. These agents are *not* approved for HLD.

Aqueous ethyl and isopropyl alcohol 70–90 % solutions – both more rapidly dissipating than aqueous solutions used for LLD – are preferred agents when there is a possibility of the presence of Mycobacterium tuberculosis. These solutions, however, penetrate proteinaceous material poorly and have limited efficacy against a few hydrophilic viruses (notably polio and Coxsackie). Alcoholic solutions are not approved for HLD.

Sodium hypochlorite solution 5.25–6.15 % (household bleach) is a powerful oxidizing agent. In 1:10–1:100 dilution, it is an effective LLD agent and (at 1:10 dilution) may be the preferred agent to use to disinfect areas of blood spill after initial (gloved) cleaning because of its effectiveness against hepatitis viruses, HIV, and *Clostridium difficile*. It has long-term stability when stored away from light. Disadvantages include odor, eye irritation, corrosive effects on metals, bleaching effect on fabric, release of toxic fumes in the event of contact with ammonia or acid (e.g., vinegar), and greatly reduced effectiveness in the presence of organic material. Na hypochlorite is approved for HLD in Great Britain but not the USA.

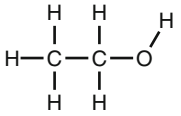
Hydrogen peroxide 3–6 %, available as spray and wipes, is also a powerful oxidizing agent but decomposes to only oxygen and water (no environmental toxicity). HLD is achievable using H_2O_2 but only at high concentrations or together with peracetic acid (see above).

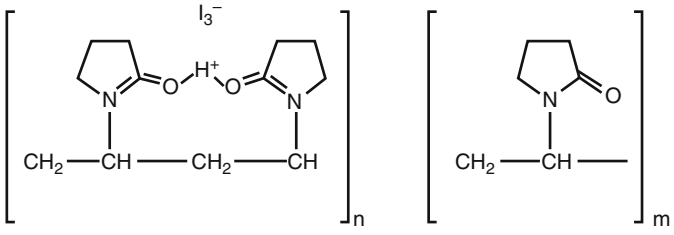
Summary

Recent recommendations for pre-procedural skin antisepsis favor alcoholic solutions of iodophors and chlorhexidine, but these should be allowed to dry before skin puncture, especially for neuraxial regional anesthesia. Approved agents and techniques for sterilization and high-level disinfection of medical devices have increased in number and complexity, but newer methods are more efficient and environmentally friendly.

Chemical Structures

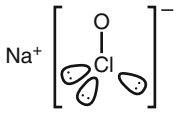
Chemical Structure
35.1 Ethyl alcohol/ethanol



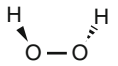


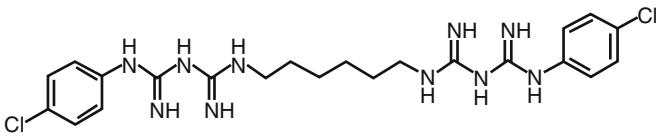
Chemical Structure 35.2 Povidone-iodine

Chemical Structure
35.3 Sodium hypochlorite



Chemical Structure
35.4 Hydrogen peroxide





Chemical Structure 35.5 Chlorhexidine

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