

## DISINFECTION

Many disinfectants are used alone or in combinations (e.g., hydrogen peroxide and peracetic acid) in the health-care setting. These include alcohols, chlorine and chlorine compounds, formaldehyde, glutaraldehyde, *ortho*-phthalaldehyde, hydrogen peroxide, iodophors, peracetic acid, phenolics, and quaternary ammonium compounds. Commercial formulations based on these chemicals are considered unique products and must be registered with EPA or cleared by FDA. In most instances, a given product is designed for a specific purpose and is to be used in a certain manner. Therefore, users should read labels carefully to ensure the correct product is selected for the intended use and applied efficiently.

Disinfectants are not interchangeable, and incorrect concentrations and inappropriate disinfectants can result in excessive costs. Because occupational diseases among cleaning personnel have been associated with use of several disinfectants (e.g., formaldehyde, glutaraldehyde, and chlorine), precautions (e.g., gloves and proper ventilation) should be used to minimize exposure<sup>318, 480, 481</sup>. Asthma and reactive airway disease can occur in sensitized persons exposed to any airborne chemical, including germicides. Clinically important asthma can occur at levels below ceiling levels regulated by OSHA or recommended by NIOSH. The preferred method of control is elimination of the chemical (through engineering controls or substitution) or relocation of the worker.

The following overview of the performance characteristics of each provides users with sufficient information to select an appropriate disinfectant for any item and use it in the most efficient way.

### Chemical Disinfectants

#### Alcohol

**Overview.** In the healthcare setting, “alcohol” refers to two water-soluble chemical compounds—ethyl alcohol and isopropyl alcohol—that have generally underrated germicidal characteristics<sup>482</sup>. FDA has not cleared any liquid chemical sterilant or high-level disinfectant with alcohol as the main active ingredient. These alcohols are rapidly bactericidal rather than bacteriostatic against vegetative forms of bacteria; they also are tuberculocidal, fungicidal, and virucidal but do not destroy bacterial spores. Their cidal activity drops sharply when diluted below 50% concentration, and the optimum bactericidal concentration is 60%–90% solutions in water (volume/volume)<sup>483, 484</sup>.

**Mode of Action.** The most feasible explanation for the antimicrobial action of alcohol is denaturation of proteins. This mechanism is supported by the observation that absolute ethyl alcohol, a dehydrating agent, is less bactericidal than mixtures of alcohol and water because proteins are denatured more quickly in the presence of water<sup>484, 485</sup>. Protein denaturation also is consistent with observations that alcohol destroys the dehydrogenases of *Escherichia coli*<sup>486</sup>, and that ethyl alcohol increases the lag phase of *Enterobacter aerogenes*<sup>487</sup> and that the lag phase effect could be reversed by adding certain amino acids. The bacteriostatic action was believed caused by inhibition of the production of metabolites essential for rapid cell division.

**Microbicidal Activity.** Methyl alcohol (methanol) has the weakest bactericidal action of the alcohols and thus seldom is used in healthcare<sup>488</sup>. The bactericidal activity of various concentrations of ethyl alcohol (ethanol) was examined against a variety of microorganisms in exposure periods ranging from 10 seconds to 1 hour<sup>483</sup>. *Pseudomonas aeruginosa* was killed in 10 seconds by all concentrations of ethanol from 30% to 100% (v/v), and *Serratia marcescens*, *E. coli* and *Salmonella typhosa* were killed in 10 seconds by all concentrations of ethanol from 40% to 100%. The gram-positive organisms *Staphylococcus aureus* and *Streptococcus pyogenes* were slightly more resistant, being killed in 10 seconds by ethyl alcohol concentrations of 60%–95%. Isopropyl alcohol (isopropanol) was slightly more bactericidal than ethyl alcohol for *E. coli* and *S. aureus*<sup>489</sup>.

Ethyl alcohol, at concentrations of 60%–80%, is a potent virucidal agent inactivating all of the lipophilic viruses (e.g., herpes, vaccinia, and influenza virus) and many hydrophilic viruses (e.g.,

adenovirus, enterovirus, rhinovirus, and rotaviruses but not hepatitis A virus (HAV)<sup>58</sup> or poliovirus<sup>49</sup>. Isopropyl alcohol is not active against the nonlipid enteroviruses but is fully active against the lipid viruses<sup>72</sup>. Studies also have demonstrated the ability of ethyl and isopropyl alcohol to inactivate the hepatitis B virus (HBV)<sup>224, 225</sup> and the herpes virus,<sup>490</sup> and ethyl alcohol to inactivate human immunodeficiency virus (HIV)<sup>227</sup>, rotavirus, echovirus, and astrovirus<sup>491</sup>.

In tests of the effect of ethyl alcohol against *M. tuberculosis*, 95% ethanol killed the tubercle bacilli in sputum or water suspension within 15 seconds<sup>492</sup>. In 1964, Spaulding stated that alcohols were the germicide of choice for tuberculocidal activity, and they should be the standard by which all other tuberculocides are compared. For example, he compared the tuberculocidal activity of iodophor (450 ppm), a substituted phenol (3%), and isopropanol (70%/volume) using the mucin-loop test (10<sup>6</sup> *M. tuberculosis* per loop) and determined the contact times needed for complete destruction were 120–180 minutes, 45–60 minutes, and 5 minutes, respectively. The mucin-loop test is a severe test developed to produce long survival times. Thus, these figures should not be extrapolated to the exposure times needed when these germicides are used on medical or surgical material<sup>482</sup>.

Ethyl alcohol (70%) was the most effective concentration for killing the tissue phase of *Cryptococcus neoformans*, *Blastomyces dermatitidis*, *Coccidioides immitis*, and *Histoplasma capsulatum* and the culture phases of the latter three organisms aerosolized onto various surfaces. The culture phase was more resistant to the action of ethyl alcohol and required about 20 minutes to disinfect the contaminated surface, compared with <1 minute for the tissue phase<sup>493, 494</sup>.

Isopropyl alcohol (20%) is effective in killing the cysts of *Acanthamoeba culbertsoni* (560) as are chlorhexidine, hydrogen peroxide, and thimerosal<sup>496</sup>.

**Uses.** Alcohols are not recommended for sterilizing medical and surgical materials principally because they lack sporicidal action and they cannot penetrate protein-rich materials. Fatal postoperative wound infections with *Clostridium* have occurred when alcohols were used to sterilize surgical instruments contaminated with bacterial spores<sup>497</sup>. Alcohols have been used effectively to disinfect oral and rectal thermometers<sup>498, 499</sup>, hospital pagers<sup>500</sup>, scissors<sup>501</sup>, and stethoscopes<sup>502</sup>. Alcohols have been used to disinfect fiberoptic endoscopes<sup>503, 504</sup> but failure of this disinfectant have lead to infection<sup>280, 505</sup>. Alcohol towelettes have been used for years to disinfect small surfaces such as rubber stoppers of multiple-dose medication vials or vaccine bottles. Furthermore, alcohol occasionally is used to disinfect external surfaces of equipment (e.g., stethoscopes, ventilators, manual ventilation bags)<sup>506</sup>, CPR manikins<sup>507</sup>, ultrasound instruments<sup>508</sup> or medication preparation areas. Two studies demonstrated the effectiveness of 70% isopropyl alcohol to disinfect reusable transducer heads in a controlled environment<sup>509, 510</sup>. In contrast, three bloodstream infection outbreaks have been described when alcohol was used to disinfect transducer heads in an intensive-care setting<sup>511</sup>.

The documented shortcomings of alcohols on equipment are that they damage the shellac mountings of lensed instruments, tend to swell and harden rubber and certain plastic tubing after prolonged and repeated use, bleach rubber and plastic tiles<sup>482</sup> and damage tonometer tips (by deterioration of the glue) after the equivalent of 1 working year of routine use<sup>512</sup>. Tonometer biprisms soaked in alcohol for 4 days developed rough front surfaces that potentially could cause corneal damage; this appeared to be caused by weakening of the cementing substances used to fabricate the biprisms<sup>513</sup>. Corneal opacification has been reported when tonometer tips were swabbed with alcohol immediately before measurement of intraocular pressure<sup>514</sup>. Alcohols are flammable and consequently must be stored in a cool, well-ventilated area. They also evaporate rapidly, making extended exposure time difficult to achieve unless the items are immersed.

## Chlorine and Chlorine Compounds

**Overview.** Hypochlorites, the most widely used of the chlorine disinfectants, are available as liquid (e.g., sodium hypochlorite) or solid (e.g., calcium hypochlorite). The most prevalent chlorine

products in the United States are aqueous solutions of 5.25%–6.15% sodium hypochlorite (see glossary), usually called household bleach. They have a broad spectrum of antimicrobial activity, do not leave toxic residues, are unaffected by water hardness, are inexpensive and fast acting<sup>328</sup>, remove dried or fixed organisms and biofilms from surfaces<sup>465</sup>, and have a low incidence of serious toxicity<sup>515-517</sup>. Sodium hypochlorite at the concentration used in household bleach (5.25-6.15%) can produce ocular irritation or oropharyngeal, esophageal, and gastric burns<sup>318, 518-522</sup>. Other disadvantages of hypochlorites include corrosiveness to metals in high concentrations (>500 ppm), inactivation by organic matter, discoloring or “bleaching” of fabrics, release of toxic chlorine gas when mixed with ammonia or acid (e.g., household cleaning agents)<sup>523-525</sup>, and relative stability<sup>327</sup>. The microbicidal activity of chlorine is attributed largely to undissociated hypochlorous acid (HOCl). The dissociation of HOCl to the less microbicidal form (hypochlorite ion OCl<sup>-</sup>) depends on pH. The disinfecting efficacy of chlorine decreases with an increase in pH that parallels the conversion of undissociated HOCl to OCl<sup>-</sup><sup>329, 526</sup>. A potential hazard is production of the carcinogen bis(chloromethyl) ether when hypochlorite solutions contact formaldehyde<sup>527</sup> and the production of the animal carcinogen trihalomethane when hot water is hyperchlorinated<sup>528</sup>. After reviewing environmental fate and ecologic data, EPA has determined the currently registered uses of hypochlorites will not result in unreasonable adverse effects to the environment<sup>529</sup>.

Alternative compounds that release chlorine and are used in the health-care setting include demand-release chlorine dioxide, sodium dichloroisocyanurate, and chloramine-T. The advantage of these compounds over the hypochlorites is that they retain chlorine longer and so exert a more prolonged bactericidal effect. Sodium dichloroisocyanurate tablets are stable, and for two reasons, the microbicidal activity of solutions prepared from sodium dichloroisocyanurate tablets might be greater than that of sodium hypochlorite solutions containing the same total available chlorine. First, with sodium dichloroisocyanurate, only 50% of the total available chlorine is free (HOCl and OCl<sup>-</sup>), whereas the remainder is combined (monochloroisocyanurate or dichloroisocyanurate), and as free available chlorine is used up, the latter is released to restore the equilibrium. Second, solutions of sodium dichloroisocyanurate are acidic, whereas sodium hypochlorite solutions are alkaline, and the more microbicidal type of chlorine (HOCl) is believed to predominate<sup>530-533</sup>. Chlorine dioxide-based disinfectants are prepared fresh as required by mixing the two components (base solution [citric acid with preservatives and corrosion inhibitors] and the activator solution [sodium chlorite]). In vitro suspension tests showed that solutions containing about 140 ppm chlorine dioxide achieved a reduction factor exceeding 10<sup>6</sup> of *S. aureus* in 1 minute and of *Bacillus atrophaeus* spores in 2.5 minutes in the presence of 3 g/L bovine albumin. The potential for damaging equipment requires consideration because long-term use can damage the outer plastic coat of the insertion tube<sup>534</sup>. In another study, chlorine dioxide solutions at either 600 ppm or 30 ppm killed *Mycobacterium avium-intracellulare* within 60 seconds after contact but contamination by organic material significantly affected the microbicidal properties<sup>535</sup>.

The microbicidal activity of a new disinfectant, “superoxidized water,” has been examined. The concept of electrolyzing saline to create a disinfectant or antiseptics is appealing because the basic materials of saline and electricity are inexpensive and the end product (i.e., water) does not damage the environment. The main products of this water are hypochlorous acid (e.g., at a concentration of about 144 mg/L) and chlorine. As with any germicide, the antimicrobial activity of superoxidized water is strongly affected by the concentration of the active ingredient (available free chlorine)<sup>536</sup>. One manufacturer generates the disinfectant at the point of use by passing a saline solution over coated titanium electrodes at 9 amps. The product generated has a pH of 5.0–6.5 and an oxidation-reduction potential (redox) of >950 mV. Although superoxidized water is intended to be generated fresh at the point of use, when tested under clean conditions the disinfectant was effective within 5 minutes when 48 hours old<sup>537</sup>. Unfortunately, the equipment required to produce the product can be expensive because parameters such as pH, current, and redox potential must be closely monitored. The solution is nontoxic to biologic tissues. Although the United Kingdom manufacturer claims the solution is noncorrosive and nondamaging to endoscopes and processing equipment, one flexible endoscope manufacturer (Olympus Key-Med, United Kingdom) has voided the warranty on the endoscopes if superoxidized water is used to disinfect them<sup>538</sup>. As with any germicide formulation, the user should check with the device manufacturer for

compatibility with the germicide. Additional studies are needed to determine whether this solution could be used as an alternative to other disinfectants or antiseptics for hand washing, skin antiseptics, room cleaning, or equipment disinfection (e.g., endoscopes, dialyzers)<sup>400, 539, 540</sup>. In October 2002, the FDA cleared superoxidized water as a high-level disinfectant (FDA, personal communication, September 18, 2002).

**Mode of Action.** The exact mechanism by which free chlorine destroys microorganisms has not been elucidated. Inactivation by chlorine can result from a number of factors: oxidation of sulfhydryl enzymes and amino acids; ring chlorination of amino acids; loss of intracellular contents; decreased uptake of nutrients; inhibition of protein synthesis; decreased oxygen uptake; oxidation of respiratory components; decreased adenosine triphosphate production; breaks in DNA; and depressed DNA synthesis<sup>329, 347</sup>. The actual microbicidal mechanism of chlorine might involve a combination of these factors or the effect of chlorine on critical sites<sup>347</sup>.

**Microbicidal Activity.** Low concentrations of free available chlorine (e.g., HOCl, OCl<sup>-</sup>, and elemental chlorine-Cl<sub>2</sub>) have a biocidal effect on mycoplasma (25 ppm) and vegetative bacteria (<5 ppm) in seconds in the absence of an organic load<sup>329, 418</sup>. Higher concentrations (1,000 ppm) of chlorine are required to kill *M. tuberculosis* using the Association of Official Analytical Chemists (AOAC) tuberculocidal test<sup>73</sup>. A concentration of 100 ppm will kill ≥99.9% of *B. atrophaeus* spores within 5 minutes<sup>541, 542</sup> and destroy mycotic agents in <1 hour<sup>329</sup>. Acidified bleach and regular bleach (5,000 ppm chlorine) can inactivate 10<sup>6</sup> *Clostridium difficile* spores in <10 minutes<sup>262</sup>. One study reported that 25 different viruses were inactivated in 10 minutes with 200 ppm available chlorine<sup>72</sup>. Several studies have demonstrated the effectiveness of diluted sodium hypochlorite and other disinfectants to inactivate HIV<sup>61</sup>. Chlorine (500 ppm) showed inhibition of *Candida* after 30 seconds of exposure<sup>54</sup>. In experiments using the AOAC Use-Dilution Method, 100 ppm of free chlorine killed 10<sup>6</sup>–10<sup>7</sup> *S. aureus*, *Salmonella choleraesuis*, and *P. aeruginosa* in <10 minutes<sup>327</sup>. Because household bleach contains 5.25%–6.15% sodium hypochlorite, or 52,500–61,500 ppm available chlorine, a 1:1,000 dilution provides about 53–62 ppm available chlorine, and a 1:10 dilution of household bleach provides about 5250–6150 ppm.

Data are available for chlorine dioxide that support manufacturers' bactericidal, fungicidal, sporicidal, tuberculocidal, and virucidal label claims<sup>543-546</sup>. A chlorine dioxide generator has been shown effective for decontaminating flexible endoscopes<sup>534</sup> but it is not currently FDA-cleared for use as a high-level disinfectant<sup>85</sup>. Chlorine dioxide can be produced by mixing solutions, such as a solution of chlorine with a solution of sodium chlorite<sup>329</sup>. In 1986, a chlorine dioxide product was voluntarily removed from the market when its use caused leakage of cellulose-based dialyzer membranes, which allowed bacteria to migrate from the dialysis fluid side of the dialyzer to the blood side<sup>547</sup>.

Sodium dichloroisocyanurate at 2,500 ppm available chlorine is effective against bacteria in the presence of up to 20% plasma, compared with 10% plasma for sodium hypochlorite at 2,500 ppm<sup>548</sup>.

“Superoxidized water” has been tested against bacteria, mycobacteria, viruses, fungi, and spores<sup>537, 539, 549</sup>. Freshly generated superoxidized water is rapidly effective (<2 minutes) in achieving a 5-log<sub>10</sub> reduction of pathogenic microorganisms (i.e., *M. tuberculosis*, *M. chelonae*, poliovirus, HIV, multidrug-resistant *S. aureus*, *E. coli*, *Candida albicans*, *Enterococcus faecalis*, *P. aeruginosa*) in the absence of organic loading. However, the biocidal activity of this disinfectant decreased substantially in the presence of organic material (e.g., 5% horse serum)<sup>537, 549, 550</sup>. No bacteria or viruses were detected on artificially contaminated endoscopes after a 5-minute exposure to superoxidized water<sup>551</sup> and HBV-DNA was not detected from any endoscope experimentally contaminated with HBV-positive mixed sera after a disinfectant exposure time of 7 minutes<sup>552</sup>.

**Uses.** Hypochlorites are widely used in healthcare facilities in a variety of settings.<sup>328</sup> Inorganic chlorine solution is used for disinfecting tonometer heads<sup>188</sup> and for spot-disinfection of countertops and floors. A 1:10–1:100 dilution of 5.25%–6.15% sodium hypochlorite (i.e., household bleach)<sup>22, 228, 553, 554</sup> or

an EPA-registered tuberculocidal disinfectant<sup>17</sup> has been recommended for decontaminating blood spills. For small spills of blood (i.e., drops of blood) on noncritical surfaces, the area can be disinfected with a 1:100 dilution of 5.25%–6.15% sodium hypochlorite or an EPA-registered tuberculocidal disinfectant. Because hypochlorites and other germicides are substantially inactivated in the presence of blood<sup>63, 548, 555, 556</sup>, large spills of blood require that the surface be cleaned before an EPA-registered disinfectant or a 1:10 (final concentration) solution of household bleach is applied<sup>557</sup>. If a sharps injury is possible, the surface initially should be decontaminated<sup>69, 318</sup>, then cleaned and disinfected (1:10 final concentration)<sup>63</sup>. Extreme care always should be taken to prevent percutaneous injury. At least 500 ppm available chlorine for 10 minutes is recommended for decontaminating CPR training manikins<sup>558</sup>. Full-strength bleach has been recommended for self-disinfection of needles and syringes used for illicit-drug injection when needle-exchange programs are not available. The difference in the recommended concentrations of bleach reflects the difficulty of cleaning the interior of needles and syringes and the use of needles and syringes for parenteral injection<sup>559</sup>. Clinicians should not alter their use of chlorine on environmental surfaces on the basis of testing methodologies that do not simulate actual disinfection practices<sup>560, 561</sup>. Other uses in healthcare include as an irrigating agent in endodontic treatment<sup>562</sup> and as a disinfectant for manikins, laundry, dental appliances, hydrotherapy tanks<sup>23, 41</sup>, regulated medical waste before disposal<sup>328</sup>, and the water distribution system in hemodialysis centers and hemodialysis machines<sup>563</sup>.

Chlorine long has been used as the disinfectant in water treatment. Hyperchlorination of a *Legionella*-contaminated hospital water system<sup>23</sup> resulted in a dramatic decrease (from 30% to 1.5%) in the isolation of *L. pneumophila* from water outlets and a cessation of healthcare-associated Legionnaires' disease in an affected unit<sup>528, 564</sup>. Water disinfection with monochloramine by municipal water-treatment plants substantially reduced the risk for healthcare-associated Legionnaires disease<sup>565, 566</sup>. Chlorine dioxide also has been used to control *Legionella* in a hospital water supply.<sup>567</sup> Chloramine T<sup>568</sup> and hypochlorites<sup>41</sup> have been used to disinfect hydrotherapy equipment.

Hypochlorite solutions in tap water at a pH >8 stored at room temperature (23°C) in closed, opaque plastic containers can lose up to 40%–50% of their free available chlorine level over 1 month. Thus, if a user wished to have a solution containing 500 ppm of available chlorine at day 30, he or she should prepare a solution containing 1,000 ppm of chlorine at time 0. Sodium hypochlorite solution does not decompose after 30 days when stored in a closed brown bottle<sup>327</sup>.

The use of powders, composed of a mixture of a chlorine-releasing agent with highly absorbent resin, for disinfecting spills of body fluids has been evaluated by laboratory tests and hospital ward trials. The inclusion of acrylic resin particles in formulations markedly increases the volume of fluid that can be soaked up because the resin can absorb 200–300 times its own weight of fluid, depending on the fluid consistency. When experimental formulations containing 1%, 5%, and 10% available chlorine were evaluated by a standardized surface test, those containing 10% demonstrated bactericidal activity. One problem with chlorine-releasing granules is that they can generate chlorine fumes when applied to urine<sup>569</sup>.

## Formaldehyde

**Overview.** Formaldehyde is used as a disinfectant and sterilant in both its liquid and gaseous states. Liquid formaldehyde will be considered briefly in this section, and the gaseous form is reviewed elsewhere<sup>570</sup>. Formaldehyde is sold and used principally as a water-based solution called formalin, which is 37% formaldehyde by weight. The aqueous solution is a bactericide, tuberculocide, fungicide, virucide and sporicide<sup>72, 82, 571-573</sup>. OSHA indicated that formaldehyde should be handled in the workplace as a potential carcinogen and set an employee exposure standard for formaldehyde that limits an 8-hour time-weighted average exposure concentration of 0.75 ppm<sup>574, 575</sup>. The standard includes a second permissible exposure limit in the form of a short-term exposure limit (STEL) of 2 ppm that is the maximum exposure allowed during a 15-minute period<sup>576</sup>. Ingestion of formaldehyde can be fatal, and long-term exposure to low levels in the air or on the skin can cause asthma-like respiratory problems and skin irritation, such as dermatitis and itching. For these reasons, employees should have limited direct contact