




Disinfectants In Interventional Practices

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Abstract

Purpose of Review This review aims to provide relevant, aggregate information about a variety of disinfectants and antiseptics, along with potential utility and limitations. While not exhaustive, this review's goal is to add to the body of literature available on this topic and give interventional providers and practitioners an additional resource to consider when performing procedures.

Recent Findings In the current SARS-CoV2 epidemiological environment, infection control and costs associated with healthcare-associated infections (HAIs) are of paramount importance. Even before the onset of SARS-CoV2, HAIs affected nearly 2million patients a year in the USA and resulted in nearly 90,000 deaths, all of which resulted in a cost to hospitals ranging from US\$28 billion to 45 billion. The onset SARS-CoV2, though not spread by an airborne route, has heightened infection control protocols in hospitals and, as such, cast a renewed focus on disinfectants and their utility across different settings and organisms.

Summary The aim of this review is to provide a comprehensive overview of disinfectants used in the inpatient setting.

Keywords Disinfectants · SARS-COV2 · Inpatient · Healthcare-associated infections · Interventional practices

Introduction

Disinfectants can be broadly defined as chemical agents used on inanimate objects to neutralize most known pathogenic microorganisms—though not all known microbial forms (i.e., endospores) [1••]. Although often used interchangeably with antiseptics, the key difference between disinfectants and antiseptics is that the latter typically refers to substances applied to living tissues as opposed to inanimate objects—for infection control [2••, 3•]. On a more granular level, disinfectants and antiseptics can be further broken down by the mechanism of action, typical medical use, efficacy, and safety of

their active chemical agents (biocides) [1••, 3•]. Antiseptics and disinfectants are used routinely in an effort to prevent nosocomial (hospital-acquired) infections, particularly so in interventional practices.

In the current SARS-CoV2 epidemiological environment, infection control and costs associated with healthcare-associated infections (HAIs) are of paramount importance. Even before the onset of SARS-CoV2, HAIs affected nearly 2 million patients a year in the USA and resulted in nearly 90,000 deaths, all of which resulted in a cost to hospitals ranging from US\$28 billion to 45 billion [4•]. The onset SARS-CoV2, though not spread by an airborne route, has

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heightened infection control protocols in hospitals and, as such, cast a renewed focus on disinfectants and their utility across different settings and organisms [5•].

This review aims to provide relevant, aggregate information about a variety of disinfectants and antiseptics, along with potential utility and limitations. While not exhaustive, this review's goal is to add to the body of literature available on this topic and give interventional providers and practitioners an additional resource to consider when performing procedures.

Alcohol

Alcohol has been used as a disinfectant for several decades and possibly as early as the 1800s. In the healthcare setting, ethyl-alcohol (ethanol) or isopropyl-alcohol are considered the two most effective disinfectants, with 70% ethanol considered generally superior to isopropyl alcohol [6•]. Alcohols work as disinfectants primarily through the denaturation of microbial proteins. This mechanism of action is supported by a variety of studies, including work done with *E. Coli* dehydrogenases, *Enterobacter Aerogenes*, and the influenza virus [6•, 7•, 8•].

Alcohols, at 60–70% concentration, have several decades of data and studies accounting for their bactericidal, viricidal, tuberculocidal, and fungicidal properties. As such, they are commonly used for surface and hand disinfection, both in and out of healthcare settings [9•, 10•, 11•, 12•, 13•, 14••] However, alcohols do not contain sufficient sporicidal activity for the sterilization of surgical and procedural tools [15•]. For this reason, alcohols are not useful as disinfectants for sterile and invasive procedures, or in the intensive care unit—where alcohol-based disinfection has been associated with an increased rate of bloodstream infections [16•].

Besides its limitations in sterile procedure, alcohol is also a known corrosive material and can damage tubes, lines, lenses, and other components of medical equipment over time and prolonged exposure—rubber and plastic tubing, glass lenses, and shellac lens coatings are particularly susceptible to damage from prolonged disinfection with alcohol [14••]. Additionally, it is a known fact that alcohols are flammable, and care must be taken to ensure proper storage and ventilation while using them as disinfectants.

Chlorine and Chlorine Compounds

Sodium Hypochlorite

Sodium hypochlorite, also known as bleach, has been in use for many years. Its mechanism of action involves the ion hypochlorite, formed when dissolved into an aqueous solution.

Hypochlorite works against both viruses and bacteria but is less efficacious against endospore-forming bacteria and fungi [17•]. Both the acidity of the solution, along with the concentration of the hypochlorite are important in its germicidal action and cleaning efficiency [18•]. Clinically, it is used in healthcare settings for decontaminating water systems. It can be used directly to disinfect surfaces, laundry, blood spills, and directly on equipment. It is also strong enough to decontaminate medical waste [17•]. More recently, it has been paired with UV light to turn over hospital rooms [19•]. Bleach paired with UV light has increased efficacy against *Clostridium difficile* and its spores. As a sole agent, sodium hypochlorite has shown effective bactericidal action against *Staphylococcus aureus* and *Pseudomonas aeruginosa* [20•]. More importantly, evidence suggests that sodium hypochlorite is able to eliminate the biofilms formed by *Pseudomonas aeruginosa*. *Escherichia coli* and Ebola virus from patient bodily fluids/feces were also found to be completely interrupted by exposure to .5% hypochlorite exposure [21•].

Safety precautions when using sodium hypochlorite include avoiding direct contact, as irritation can occur, which can range from mild dermatitis to necrosis of the skin [17•]. It can also cause severe irritation with mucus membranes, gastrointestinal tract, and conjunctiva. However, the incidence of injury secondary to sodium hypochlorite in the healthcare setting is deemed to be low [17•].

Sodium Dichloroisocyanurate

Sodium dichloroisocyanurate is another chlorine-containing compound that ionizes into an oxidizing bactericidal and cytotoxic agent [22•]. While sodium hypochlorite has been used for over two centuries as a disinfectant, sodium dichloroisocyanurate was introduced in the past 50 years as a synthetic disinfectant, similar to sodium hypochlorite in the mechanism, but heralded as more effective in bactericidal activity [23•]. Its medical uses include purifying drinking water, irrigating in endodontic procedures, and disinfecting surfaces [21•, 24•, 25•, 26•]. It can be dissolved from its tablet form into a solution or hydrolyzed into a gaseous chlorine compound [27•]. Sodium dichloroisocyanurate has shown efficacy against human immunodeficiency virus (HIV), mycobacterium tuberculosis, human corona virus 229e, *Staphylococcus aureus*, and *Pseudomonas aeruginosa* [28•, 29•, 30•].

For safety, a color additive can be added to sodium dichloroisocyanurate, which turns the solution blue, which then turns colorless as the compound evaporates to enhance safety [30•]. Much like sodium hypochlorite, sodium dichloroisocyanurate is a mild irritant to skin and mucus membranes.

Chlorine Dioxide

Chlorine dioxide works as a strong oxidant that is bactericidal and antimicrobial [31•]. In the medical field, it is used in the liquid form typically. Evidence has shown that chlorine dioxide gas solutions are strongly antiviral and even stronger than a standard sodium hypochlorite solution [32•]. It can also be used to purify hospital water systems, with bactericidal activity against non-tuberculosis mycobacterium, legionella, and gram-negative rods [33•, 34•]. Additionally, chlorine dioxide can safely be used to decontaminate medical waste, showing efficacy against human immunodeficiency virus [35•]. Chlorine dioxide has also been traditionally used to sterilize medical equipment [36•]. This sterilization process can be precluded with heating or an autoclaving process.

For safety, as a gas, chlorine dioxide can cause irritation to the respiratory tract and with direct contact as a solution, is an irritant to skin and eyes [37•]. There is also a concern when chlorine dioxide is used to purify water systems; it leaves behind carcinogenic by-products [38•].

Super-Oxidized Water

Super-oxidized water is a more novel disinfectant, produced by running sodium chloride through regular tap water while running an electric current, causing electrolysis. This produces a high concentration of chlorine and oxygen reactive species [39•]. Super-oxidized water has been utilized for its antimicrobial properties as it is both bactericidal and antiviral [40•, 41•]. Although it is not as commonly used as sodium hypochlorite, super-oxidized water is used medically as a disinfectant for simple surfaces, root canals, wounds, and reusable medical devices [39•, 42•, 43•]. In the order of minutes, super-oxidized water is proposed to be effective against human immunodeficiency virus, Mycobacterium tuberculosis, Candida albicans, and Pseudomonas aeruginosa [40•].

For safety, super-oxidized water is an irritant to the skin for some [44•]. However, it is safe enough to be used in wound care, as mentioned above.

Formaldehyde

Formaldehyde is a chemical that is well known to cause direct DNA damage and hampers DNA repair, which is why formaldehyde has been implicated as a chemical that is both mutagenic and carcinogenic [45•, 46•]. For this reason, direct contact with skin is avoided, and it is used more for disinfection of spillages, heat-sensitive hospital equipment, and hemodialysis machinery [36•, 47•, 48•]. Formaldehyde is usually administered in liquid form but is known to aerosolize, as evidenced by the concern for its indoor pollution of anatomy

labs [49•]. However, it is a powerful agent with efficacy against gonorrhea, HIV, hepatitis B virus, chlamydia, and mycoplasma.

For safety, there is a concern for the reproductive harm that comes with exposure with formaldehyde, including infertility, seen in animal studies [50•, 51•]. Formaldehyde is also an irritant to skin, putting users at risk for dermatitis and urticaria [52•, 53•].

Glutaraldehyde

Glutaraldehyde is widely used in the chemistry world to immobilize and fix proteins [54•]. The chemical accomplishes this by cross-linking proteins causing them to gel. In the medical world, glutaraldehyde is used to disinfect hospital instruments and dialysis systems [28•, 48•, 55•]. Typically, a 2% solution of glutaraldehyde works well to eliminate microbes, soaking for about 5–10 min. Efficacy has been shown against Mycobacterium, Pseudomonas, Staphylococcus aureus, severe acute respiratory syndrome coronavirus, human immunodeficiency virus, and hepatitis B [55•, 56•, 57•].

For safety, a barrier is recommended when handling glutaraldehyde, as contact dermatitis is a common reaction observed among healthcare workers who handle the chemical [58•, 59•]. A study found that healthcare workers tend to have eight times more allergic reactions to glutaraldehyde than their non-healthcare worker counterparts. Glutaraldehyde can also be toxic to the respiratory system, increasing the potential risk of bronchitis and nasal symptoms [60•]. However, no evidence exists of the carcinogenic or genetic toxicity of glutaraldehyde in animal studies. Caution is still recommended as small amounts of glutaraldehyde can cause adverse effects.

Hydrogen Peroxide

Hydrogen peroxide works as an oxidizing agent when used as a disinfectant [61•]. It has a strong appeal in that it eventually decomposes to non-toxic compounds, oxygen, and water. It is also popular in its lack of strong odor and reduced surface corrosiveness. Hydrogen peroxide can be used in both as a liquid, aerosolized gas, or topical wipe [62•, 63•, 64•]. In the medical field, it is used for cleaning surfaces, turning over hospital rooms, and disinfecting ambulances. Hydrogen peroxide has shown efficacy against spore and biofilm-forming bacteria and both DNA and RNA viruses, including coronavirus [20•, 24•, 65•, 66•].

For safety, gloves should be used when handling hydrogen peroxide, as it can cause allergic dermatitis [67•]. It is an irritant to human tissue and can cause a direct cytotoxic effect, especially if ingested [68•]. However, once hydrogen peroxide decomposes, with exposure to sunlight, it becomes inert.

Iodophors

Iodophors, e.g., povidone-iodine (PVP-I), are widely used as an antiseptic to prevent and treat wounds. PVP-I, or “Betadine,” is an iodophor solution containing water-soluble iodine (the microbicidal element) and polyvinylpyrrolidone (PVP). This complex works by slowly releasing free iodine upon contact with tissues. Through the iodination of lipids and oxidation of cytoplasmic and membrane compounds, this agent effectively kills bacteria, fungi, protozoa, and viruses [69•]. The PVP component itself has no bactericidal properties, but its affinity for cell membranes allows it to deliver the iodine to the target [70•]. Then the gradual release of iodine minimizes toxicity to mammalian tissues while preserving the agent’s germicidal activity [69•].

Iodophor preparations are most commonly used to disinfect skin prior to injections, invasive procedures, and surgery. It is an extremely effective broad-spectrum microbicidal agent with no known bacterial resistance, which makes it an ideal agent for broader use. Interestingly, low concentrations of PVP-I have been demonstrated to be more effective antimicrobials in chemistry literature [70•]. This paradoxical effect is likely due to the increased free-iodine available in more dilute solutions [71•]. Lower concentrations of PVP-I have a variety of alternative applications as disinfectants and as topical therapeutic agents. For example, a diluted ophthalmic formulation is used before most invasive ocular procedures [70•]. There is also an established utility of these preparations as prophylactic and therapeutic agents in neonatal and pediatric conjunctivitis [72•, 73•]. Several studies demonstrate the use of dilute PVP-I in otitis media, otitis externa, and even chronic otomycosis [74•, 75•]. Investigators have also shown iodophor preparations to safely and effectively prevent respiratory infections and treat sinusitis [76•, 77•]. A variety of studies support dilute Betadine use in chronic, non-healing wounds (e.g., diabetic foot ulcers) to reduce bacterial colonization [70•].

PVP-I is one of the rare topical microbicidal agents shown to be effective against viruses, fungi, spores, protozoa, amoebic cysts, and bacteria, including strains known to cause nosocomial infections (i.e., methicillin-resistant *Staphylococcus aureus*) within 20–30 seconds of exposure ([78•]). In contrast, comparators such as chlorhexidine require much longer exposure times [79•]. However, one study determined that the sequential application of povidone-iodine-alcohol (PVI) followed by chlorhexidine gluconate-alcohol reduces surgical wound contamination more effectively than PVI applied twice [80•]. There is also increasing evidence of bacterial resistance to comparable antiseptics, including chlorhexidine, quaternary ammonium salts, silver, and triclosan. Remarkably, there have been no confirmed reports of resistance to PVP-I, likely due to its multiple mechanisms of action [78•, 81•].

PVP-I is generally well-tolerated by most patients, especially when used as a topical. In contrast to chlorhexidine,

PVP-I is scarcely associated with allergic contact dermatitis, with urticarial or anaphylactic reactions exceedingly rare. An EU Safety Assessment Report included data involving 6.9 g of PVP-I applied to the hands and forearms and concluded that the use of iodine for hand disinfection is suitable for human health [81•]. Although generally safe, cases of thyroid dysfunction have been reported with long-term use. For that reason, PVP-I product labeling includes general warnings against patients with thyroid disorders, very low birth weight infants, and the patient receiving radio-iodine therapy [78•].

Peracetic Acid and Hydrogen Peroxide:

Peracetic acid (PAA) is an emerging disinfectant with a low potential to form carcinogenic disinfection by-products and no persistent residues in the environment [82•, 83•]. PAA (CH_3COOOH) is a mixture of acetic acid (CH_3COOH) and hydrogen peroxide (H_2O_2) in a watery solution. PAA acts as a disinfectant by oxidizing the outer cell membranes of microorganisms [84•]. PAA preparations are registered Environmental Protection Agency disinfectants with rapid activity against bacterial, fungi, viruses, mycobacteria, and spores [85•].

This hydrogen peroxide based-liquid is mainly used as a surface disinfectant for environmental cleaning to prevent healthcare-associated infections. PAA is most commonly used in automated machines designed to sterilize medical equipment (e.g., endoscopes, dental instruments), and in a formulation with hydrogen peroxide to disinfect hemodialyzers [85•].

PAA and hydrogen peroxide are strong oxidants widely used in cleaning and disinfectant products; however, their mixture is a recognized asthmagen. Hospital cleaning staff using these products report work-related aggravation of the eye, upper airway, lower airway, and contact dermatitis symptoms. Acute eye and nasal irritation and shortness of breath are associated with increased exposure to this oxidant mixture [86•]. However, there is no evidence of any endocrine disruption potential of PAA in human health or in ecotoxicological studies [82•].

Phenolics

Phenol (carbolic acid) is the first widely used antiseptic in surgery. In 1865, British surgeon Joseph Lister used phenol to sterilize his operating field, and his mortality rate for surgical amputations dropped by about 38% [87•]. Phenolic compounds work by targeting the cell membrane.

At high concentrations, phenol acts as a gross protoplasmic poison to denature bacterial proteins and lyse the cell membrane [88•]. Low concentrations of phenol and high molecular weight phenol derivatives kill bacteria by inactivating essential enzyme systems, resulting in the leakage of key metabolites from the cell wall [89•].

Phenol is active against a wide variety of microorganisms, including some fungi and viruses, but is only slowly effective against some spores [90•]. It is bacteriostatic at concentrations of 0.1–1% and considered bactericidal, tuberculocidal, fungicidal, virucidal for enveloped viruses at their recommended use-dilution in commercial products [91•, 92•]. Many phenolic germicides are EPA-registered disinfectants for environmental surfaces (e.g., exam tables, bedrails) and noncritical medical devices. However, phenolic compounds are not approved by the Federal Drug Administration (FDA) as high-level disinfectants for use on semi-critical devices. Though, phenolics could be used to preclean or decontaminate critical and semi critical equipment prior to high-level sterilization [89•].

Phenol is an antiseptic and disinfectant with variable actions and adverse effects dependent on the concentration. Concentrations > 0.5% have a local anesthetic effect and are used in products such as Chloraseptic throat spray and lozenges to treat pharyngitis [90•]. Phenol is used to topically treat pruritis, stings, and burns because its local anesthetic and antibacterial properties relieve itching and decrease infections [91•].

Phenol penetrates organic matter effectively; however, at higher concentrations (i.e., 5% solution), phenol is strongly irritating and corrosive to tissues. Thus, it is mainly used to disinfect equipment or organic materials that will be destroyed (i.e., contaminated food or excrement). Due to its irritant and corrosive properties at higher concentrations, phenol is no longer commonly used as an antiseptic, except to cauterize infected areas—such as infected umbilicus in neonates [91•]. Phenol is also used in the surgical treatment of ingrown toenails to permanently destroy the problematic nail edge [90•].

Phenol in concentrated solutions is toxic. During World War II, the Nazis used phenol injections to execute prisoners [90•]. Oral ingestion or extensive cutaneous application can devastate the central nervous and cardiovascular systems to result in systemic toxicity and death [91•]. Phenol vapors are corrosive to the skin, eyes, and respiratory tract. Exposure to phenol and its related compounds is also associated with spontaneous abortion [90•]. Phenol disinfectants may cause skin irritation, skin depigmentation, local burns, headaches, vomiting, diarrhea, and kidney damage in severe cases [89•, 92•].

The use of phenolics is especially cautioned in nurseries due to its association with hyperbilirubinemia when infants were placed in bassinets cleaned with phenolic detergents. If phenolics are used to clean nursery floors, they must be diluted to the recommended concentration by the manufacturer. Phenolics are now contraindicated in cleaning infant bassinets and incubators while occupied. If the phenolics are used to terminally disinfect bassinets and incubators, these surfaces must be thoroughly rinsed with water and dried prior to reuse [89•].

Quaternary Ammonium Compounds

Quaternary Ammonium Compounds (QACs) are cationic surface-active agents with a permanent positive charge that allows them to readily bind to the negatively charged surface of most microbes [93•]. The bactericidal properties of quaternaries are due to the inactivation of energy-producing enzymes, denaturation of essential cell proteins, and disruption of the cell membrane [89•]. There are numerous commercially available products and formulations of QACs. Some examples of chemical names of QACs used in healthcare include alkyl dimethyl benzyl ammonium chloride, alkyl didecyl dimethyl ammonium chloride, and dialkyl dimethyl ammonium chloride [89•].

Quaternaries sold as hospital disinfectants are generally fungicidal, bactericidal, and viricidal against lipophilic (enveloped) viruses given that their primary mechanism of action is via disruption of cell membranes [89•]. Only limited formulations have claimed activity against mycobacteria, and QACs are generally not sporicidal or viricidal against hydrophilic (nonenveloped) viruses [94•]. Manufacturer data and published scientific literature indicates that QACs effectively remove an/or inactivate > 95% contaminants, including multidrug-resistant *Staphylococcus aureus*, vancomycin-resistant *Enterococcus*, *Pseudomonas aeruginosa*, from computer keyboards with a 5-s application time without any functional or cosmetic damage to the computer keyboards, even after 300 applications of the disinfectant [89•].

Nosocomial infections have resulted from using contaminated QACs to disinfect procedural medical equipment, such as cystoscopes or cardiac catheters [89•]. Additionally, cotton and gauze pads can absorb the active ingredients of quaternaries, and decrease the microbicidal properties. Case reports have recognized occupational asthma as a result of exposure to benzalkonium chloride, a QAC [89•].

Quaternaries are commonly used in the environmental sanitization of noncritical surfaces (i.e., floors, furniture, and walls). EPA-registered QACs are appropriate to use for disinfecting medical equipment that contacts intact skin (e.g., blood pressure cuffs), according to the Center for Disease Control and Prevention [89•].

Discussion and Conclusion

Acutely understanding the difference between various disinfectants is paramount for optimizing patient safety and lowering hospital infection rates. In 2020, more so than otherwise, the importance of proper disinfection technique and use has been at the forefront of the healthcare landscape. Our review of the multiple modalities used for disinfection and sanitization, particularly for invasive,

inpatient procedures, aims to elucidate the mechanisms, uses, and in some cases, drawbacks of multiple chemical disinfectants. We hope that adding a comprehensive, topical ledger of disinfectants to the existing body of literature is timely, judicious, and ultimately, helpful to the healthcare community as reference resource.

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