Outbreaks Associated With Contaminated Antiseptics and Disinfectants

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Running Head: Contaminated Germicides

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The Centers for Disease Control and Prevention (CDC) has estimated that healthcare-associated infections account for an estimated 2 million infections, 90,000 deaths, and $4.5 billion in excess healthcare costs annually (16). Key interventions to control healthcare-associated infections include surveillance (27,33), isolation of patients with communicable diseases (26) or multidrug-resistant pathogens (81), proper skin antisepsis prior to invasive procedures and hand hygiene by healthcare workers (12), and appropriate disinfection and sterilization of medical devices, and environmental surfaces (73,75,79).

Multiple nosocomial outbreaks have resulted from inadequate antisepsis or disinfection. Inadequate skin antisepsis may result from lack of intrinsic antimicrobial activity of the antiseptic, a resistant pathogen, over-dilution of the antiseptic, or use of a contaminated antiseptic. Inadequate disinfection of medical devices or environmental surfaces may result from lack of intrinsic antimicrobial activity of the disinfectant, incorrect choice of a disinfectant, a resistant pathogen, over-dilution of the disinfectant, inadequate duration of disinfection, lack of contact between the disinfectant and the microbes, or use of a contaminated disinfectant. Editorials have noted that contaminated antiseptics and disinfectants have been the occasional vehicles of hospital infections for more than 50 years (20,72,76). This paper will concisely review nosocomial outbreaks associated with the use of a microbiologically contaminated germicide focusing on currently recommended germicides.

DEFINITIONS

A precise understanding of terminology is important to understanding the uses of germicides in modern healthcare. Germicides are biocidal agents that inactivate microorganisms and include antiseptics, disinfectants, and preservatives. Antiseptics are antimicrobial substances that are applied to the skin or mucous membranes to reduce the microbial flora. Disinfectants are substances that are applied to inanimate objects to destroy harmful microorganisms, although they may not kill bacterial spores. Decontamination is a procedure that removes pathogenic microorganisms from objects so they are safe to handle, use, or discard. Finally, preservatives are incorporated into medications or fluids to prevent microbial growth. Germicides may become contaminated as a result of improper manufacturing techniques or during shipping (intrinsic contamination), or during manipulation or use within the healthcare facility (extrinsic contamination).
Disinfectants are further categorized by their degree of effectiveness (73,75). The choice of disinfectant agent is based on the intended use of the patient care item (Table 1).

MICROBIAL RESISTANCE TO GERMICLES

Microbial resistance to germicides has been reviewed (37,49,62,68,71). As with antibiotic resistance, resistance to germicides may be an intrinsic property or arise either by chromosomal gene mutation or the acquisition of genetic material in the form of plasmids or transposons (49-68,71). Importantly, although microbes may display intrinsic resistance to specific antiseptics, antibiotic resistant pathogens (e.g, MRSA, VRE) do not demonstrate resistance to germicides at currently used contact times and concentrations (29,66-67,69-70,92).

ANTISEPTICS

Antiseptics are used in healthcare to reduce transient microbial flora on the hands of healthcare providers, to reduce person-to-person transmission of microbes (e.g., methicillin-resistant *Staphylococcus aureus*), to prepare the skin of patients prior to invasive procedures, and to achieve surgical hand antisepsis. Products commonly used in the United States include alcohols, chlorhexidine, chloroxylenol, iodine and iodophors, quaternary ammonium compounds (e.g., benzethonium chloride), and triclosan (12). The antimicrobial spectrum of currently used antiseptics is displayed in Table 2. More than 40 outbreaks and pseudo-outbreaks due to contaminated antiseptics have been reported (Table 3) (4-5,8,10-11,13-15,17,19,20,24-25,28,30,32,34,36,38-39,43,45-47,50,52-54,58-59,61,63,78,83-86,89-91,93).

ALCOHOLS

The majority of alcohol-based hand antiseptics contain isopropanol, ethanol, or N-propanol. The latter agent, N-propanol, is not currently approved for hand hygiene in the United States. Antiseptic agents are available that combine two alcohols or alcohol solutions and another agent (e.g., hexachlorophene, quaternary ammonium compounds, povidone-iodine, triclosan, or chlorhexidine gluconate). Waterless alcohol foams, liquids and gels are now widely used in healthcare to improve compliance with hand hygiene (35,60,65). Importantly, alcohols have poor activity against bacterial spores, protozoan oocysts, and certain nonlipophilic (nonenveloped) viruses.

Contamination of alcohol-based solutions has rarely been reported. One pseudoepidemic of
bacteremia (34) and one outbreak of bacteremia (54) have been traced to contaminated alcohol used for skin antisepsis. These were traced to use of intrinsically contaminated alcohol (34) and dilution of the alcohol using contaminated water (54).

**CHLORHEXIDINE**

Chlorhexidine gluconate is widely used in the United States for hand hygiene. Its antimicrobial activity occurs more slowly than that of alcohols.

Multiple outbreaks have been linked to contaminated chlorhexidine. Most reports have been traced to the use of contaminated water to prepare diluted preparations and/or the practice of reusing bottles for dispensing chlorhexidine without adequate disinfection. Although most outbreaks have occurred with solutions containing less than 2% chlorhexidine, outbreaks have been reported with solutions of 2% to 4% chlorhexidine (90). The inappropriate use of chlorhexidine as a disinfectant has also led to outbreaks. Examples include contaminated chlorhexidine solutions used to disinfect glass reservoirs containing urinary bladder irrigants (51), plastic clamps (48) and thermometers (17). Outbreaks due to contaminated chlorhexidine/centrimide solutions have also been reported (8,13,93).

**CHLOROXYLENOL**

Chloroxylenol, also known as parachlorometaxylenol (PCMX), is a halogen-substituted phenolic compound that has been used both as a preservative and as an active agent in antimicrobial soaps. An outbreak of *Serratia marcescens* infection or colonization in a neonatal intensive care unit was traced to extrinsically contaminated 1% chloroxylenol soap (5).

**QUATERNARY AMMONIUM COMPOUNDS**

Quaternary ammonium compounds are composed of a nitrogen atom linked directly to four alkyl groups, which may vary in their structure and complexity. Of this large group of compounds, alkyl benzalkonium chlorides are the most widely used as antiseptics. Other agents include benzethonium chloride, centrimide, and cetylpyridium chloride. Benzalkonium chloride is classified by the FDA as having insufficient data to classify them as safe and effective for antiseptic hygiene.

More outbreaks have been ascribed to contaminated benzalkonium chloride than any other antiseptic (Table 3). Tiwari and colleagues in 2003, reviewed the literature and referenced multiple reports of outbreaks or pseudo-outbreaks associated with the use of benzalkonium chloride (86).
most common species were aerobic, Gram-negative bacilli including *B. cepacia*, *S. marcescens*, and *Enterobacter* spp. Most but not all outbreaks were linked to storage of benzalkonium chloride with cotton or gauze or improper dilution of the benzalkonium chloride solution. The use of benzalkonium chloride to disinfect endoscopes has also led to urinary tract and pulmonary infections (20) and the use of contaminated spray bottles for environmental disinfection led to *S. marcescens* infections complicating cardiopulmonary surgery (22). The failure of benzalkonium chloride as a preservative in multidose albuterol bottles led to respiratory tract colonization and infection (31). Contaminated benzalkonium chloride used to disinfect the septa of multidose corticosteroid bottles has led to infection site abscesses with *P. aeruginosa* (57).

**IODINE AND IODOPHORS**

Iodine has been used as an antiseptic for more than 100 years. Because iodine often causes irritation and discoloring of skin, iodophors have largely replaced iodine as the active agent in antiseptics.

Multiple outbreaks due to contaminated iodophors have been reported (Table 3). Prolonged survival of *B. cepacia* in commercially manufactured providone-iodine has been documented (3) and intrinsic contamination of a povidone-iodine solution led to both infections and pseudoinfections (10,14,36,58-59). These reports of intrinsic microbial contamination of antiseptic formulations of povidone-iodine and poloxamer-iodine caused a reappraisal of the chemistry and use of iodophors. It was found that "free" iodine (*I*₂) contributes to the bactericidal activity of iodophors and dilutions of iodophors demonstrate more rapid bactericidal action than does a full-strength povidone-iodine solution. The reason for the observation that dilution increases bactericidal activity is unclear but it has been suggested that dilution of povidone-iodine results in weakening of the iodine linkage to the carrier polymer with an accompanying increase of free iodine in solution. Therefore, iodophors must be diluted according to the manufacturers’ directions to achieve antimicrobial activity.

Although most reports of contaminated iodophors have reported Gram-negative bacilli, O’Rourke and colleagues isolated *Staphylococcus aureus* from the rims of two bottles containing an iodophor in an operating room (56). No infections were noted as a result of this contamination.

**TRICLOSAN**

Triclosan in concentrations of 0.2% to 2% has antimicrobial activity and has been incorporated
into soaps for use by healthcare workers and into a variety of commercial products. It has a broad range of antimicrobial activity, but it is often bacteriostatic.

Liquid soap bottles containing 1% triclosan used as an operating room scrub were found to be contaminated with *S. marcescens* or *Candida parapsilosis* (7). However, no infections were reported. An outbreak of newborn conjunctivitis due to *S. marcescens* was associated with the use of intrinsically contaminated 0.5% triclosan antiseptic soap (50).

**DISINFECTANTS**

A variety of chemical agents are used as disinfectants; the choice of an agent depends on its intended use (Table 1). Disinfectants have not been as commonly involved in outbreaks as antiseptics (Table 4)(6,9,18,20-23,41-42,44,55,57,64,80,82,87-88). Agents currently approved for use as high-level disinfectants (e.g., chlorine, peracetic acid, ortho-phthalaldehyde) have rarely, if ever, been implicated in outbreaks. However, outbreaks may occur when ineffective disinfectants, including iodophors, alcohols and over-diluted glutaraldehyde are used for high-level disinfection.

**Alcohols**

Alcohol is widely used for environmental disinfection of small areas (i.e., “spot” disinfection). Flammability precludes its use on large surfaces. Multiple outbreaks have resulted from the use of alcohols as “high-level” disinfectants for semi-critical medical devices. Rarely, contaminated alcohol used as a surface disinfectant has been linked to outbreaks. For example, Berger reported an epidemic of pseudobacteremia with *Bacillus cereus* that was traced to contaminated cotton pads maintained in 70 to 90% ethanol that were used to disinfect the top of blood culture bottles before inoculation (9). Alcohol is not effective as a surface disinfectant against adenovirus, and its use to disinfect tonometer tips has been associated with epidemic keratoconjunctivitis (40).

**Glutaraldehyde**

The biocidal activity of glutaraldehyde is a consequence of its alkylation of sulfydral, hydroxy, carboxyl, and amino groups of microorganisms, which alters RNA, DNA, and protein synthesis. There have been reports of microorganisms with resistance to glutaraldehyde, including some mycobacteria (e.g., *M. cheloneae, M. xenopi*), *Methyllobacterium mesophilicum*, *Trichosporon*, fungal ascospores, and *Cryptosporidium* (73). A pseudo-outbreak of *Mycobacterium cheloneae* and *Methyllobacterium*
mesophilicum was reported due to contamination of an automated endoscope washer (41). M. chelonae grew from endoscopes, the automated washers, and glutaraldehyde from the washers.

Quaternary Ammonium Compounds

The bactericidal action of the quaternaries has been attributed to the inactivation of energy-producing enzymes, denaturation of essential cell proteins, and disruption of the cell membrane. A pseudo-outbreak of B. cepacia bacteremia was traced to the use of a contaminated quaternary ammonium compound used to disinfect the rubber stopper of the blood culture bottles (21).

Formaldehyde

Formaldehyde inactivates microorganisms by alkylating the amino and sulfhydryl groups of proteins and ring nitrogen atoms of purine bases. The aqueous solution is virucidal, bactericidal, tuberculocidal, fungicidal, and sporidical. An outbreak of Klebsiella oxytoca sepsis in a neonatal and pediatric intensive care unit was traced to a contaminated solution of formaldehyde (8.0 g/dL) used for disinfection of surfaces and infusion pumps (64) while an outbreak of Pseudomonas sepsis was reported due to deficient formaldehyde mixing used to disinfect dialyzers (88).

Phenolics

Contamination of phenolics used for disinfection has been reported (Table 4).

DISCUSSION

Outbreaks and pseudo-outbreaks related to contaminated germicides have most commonly been reported with contaminated antiseptics. Outbreaks from contaminated high-level disinfectants have rarely, if ever, been reported. Outbreaks from contaminated intermediate- and low-level disinfectants have occasionally been reported. All outbreaks associated with contaminated germicides have occurred due to Gram-negative bacilli or mycobacteria. This is felt to be due to the fact that the outer membrane of Gram-negative bacteria or the complex cell wall of mycobacteria acts as a barrier to germicides (49).

Both outbreaks and sporadic failures of germicides may be due to user error rather than microbial contamination. Common errors include use of over-diluted solutions, use of outdated products, use of tap water to dilute the germicide, refilling small volume dispensers from large volume stock containers, and improper selection of an appropriate product (e.g., use of a low level disinfectant for disinfecting an endoscope rather than a high level disinfectant). Because multiple outbreaks have resulted from refilling
small volume dispensers from large volume stock containers, small volume containers should be used until completely empty (i.e., do not “top off” the containers), rinsed with tap water and then air-dried prior to refilling. When a potential failure of proper disinfection or sterilization occurs, we recommend the use of a standardized risk assessment for determining patient risk and the need to inform patients (74).

A critical component of disinfection is prior cleaning. Prior cleaning is necessary to remove proteinaceous material and biofilms to allow the germicide to achieve adequate microbial inactivation. Experimental studies have demonstrated that the physical thickness of cellular and extracellular material that forms on surfaces (i.e., biofilms) can protect imbedded organisms from the microbicidal actions of disinfectants and antiseptics (1-2). For example, bacteria grown in a biofilm can be up to 1500 times more resistant to germicides compared to the same bacteria grown in liquid culture (77). Failure to properly clean medical devices may lead to inadequate microbial inactivation for all chemical germicides.

With use of more effective agents and newer guidelines, the number of outbreaks due to contaminated germicides had decreased over the past 50 years. However, in order to prevent future outbreaks associated with contaminated germicides, it is critical to follow the standard recommendations (Table 5).
REFERENCES


Table 1. Classification and Uses of Chemical Disinfectants

<table>
<thead>
<tr>
<th>Disinfection Process</th>
<th>Level of Microbial Inactivation</th>
<th>Agents</th>
<th>Health Care Uses</th>
</tr>
</thead>
<tbody>
<tr>
<td>High-level (liquid immersion)</td>
<td>Destroys all microorganisms except high numbers of bacterial spores</td>
<td>&gt;2% glutaraldehyde (20-45 min), 0.55% orthophthalaldehyde (12 min), 1.12% glutaraldehyde and 1.93% phenol (20 min), 7.35% hydrogen peroxide and 0.23% paracetic acid (15 min), 7.5% hydrogen peroxide (30 min), 1.0% hydrogen peroxide and 0.08% paracetic acid (25 min), and 650-675 ppm chlorine (10 min)</td>
<td>Heat-sensitive semicritical patient-care items (GI endoscopes and bronchoscopes, tonometers, vaginal specula)</td>
</tr>
<tr>
<td>Intermediate-level (liquid contact)</td>
<td>Destroys vegetative bacteria, mycobacteria, most viruses, and most fungi but not bacterial spores</td>
<td>EPA registered hospital disinfectants with label claiming tuberculocidal activity, such as chlorine-based products and phenolics (&gt;60 sec)</td>
<td>Noncritical patient-care items (blood pressure cuffs) or surfaces (bed rails) with visible blood</td>
</tr>
<tr>
<td>Low-level (liquid contact)</td>
<td>Destroys vegetative bacteria and some fungi and viruses but not mycobacteria or spores</td>
<td>EPA registered hospital disinfectants with no tuberculocidal claim, such as chlorine-based products, phenolics, and quarternary ammonium compounds (&gt;60 sec), or 70%-90% alcohol</td>
<td>Noncritical patient-care items (blood pressure cuffs) or surfaces (bed rails) with no visible blood</td>
</tr>
</tbody>
</table>

Adapted from reference 75.
Table 2. Antimicrobial Spectrum and Characteristics of Hand Hygiene Antiseptic Agents

<table>
<thead>
<tr>
<th>Group</th>
<th>Gram-positive bacteria</th>
<th>Gram-negative bacteria</th>
<th>Mycobacteria</th>
<th>Fungi</th>
<th>Viruses</th>
<th>Speed of Action</th>
<th>Comments</th>
</tr>
</thead>
<tbody>
<tr>
<td>Alcohols</td>
<td>+++</td>
<td>+++</td>
<td>+++</td>
<td>+++</td>
<td>+++</td>
<td>Fast</td>
<td>Optimum concentration 60%-95%; no persistent activity</td>
</tr>
<tr>
<td>Chlorhexidine (2% and 4% aqueous)</td>
<td>+++</td>
<td>++</td>
<td>+</td>
<td>+</td>
<td>+++</td>
<td>Intermediate</td>
<td>Persistent activity; rare allergic reactions</td>
</tr>
<tr>
<td>Iodine compounds</td>
<td>+++</td>
<td>+++</td>
<td>+++</td>
<td>++</td>
<td>+++</td>
<td>Intermediate</td>
<td>Causes skin burns; usually too irritating for hand hygiene</td>
</tr>
<tr>
<td>Iodophors</td>
<td>+++</td>
<td>+++</td>
<td>+</td>
<td>++</td>
<td>++</td>
<td>Intermediate</td>
<td>Less irritating than iodine; acceptance varies</td>
</tr>
<tr>
<td>Phenol derivatives</td>
<td>+++</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>Intermediate</td>
<td>Activity neutralized by nonionic surfactants</td>
</tr>
<tr>
<td>Triclosan</td>
<td>+++</td>
<td>++</td>
<td>+</td>
<td>-</td>
<td>+++</td>
<td>Intermediate</td>
<td>Acceptability on hands varies</td>
</tr>
<tr>
<td>Quaternary ammonium compounds</td>
<td>+</td>
<td>++</td>
<td>-</td>
<td>-</td>
<td>+</td>
<td>Slow</td>
<td>Used only in combination with alcohols; ecologic concerns</td>
</tr>
</tbody>
</table>

Key: +++ = excellent, ++ = good but does not include entire microbial spectrum; + = fair; - = no activity or not sufficient. Hexachlorophene not included because it is no longer an accepted ingredient of hand disinfectants.

Reference 12
Table 3. Outbreaks and Pseudo-outbreaks Due to Contaminated Antiseptics

<table>
<thead>
<tr>
<th>Antiseptic</th>
<th>Contaminant(s)</th>
<th>Sites of Microbes</th>
<th>Mechanism of Contamination/Source</th>
<th>Reference</th>
</tr>
</thead>
<tbody>
<tr>
<td>Alcohols</td>
<td><em>Bacillus cereus</em></td>
<td>Blood (pseudobacteremia), pleural fluid</td>
<td>Intrinsic contamination</td>
<td>Hsueh et al., 1999 (34)</td>
</tr>
<tr>
<td>Alcohols</td>
<td><em>Burkholderia cepacia</em></td>
<td>Blood (catheter-related)</td>
<td>Contaminated tap water used to dilute alcohol for skin antisepsis</td>
<td>Nasser et al., 2004 (54)</td>
</tr>
<tr>
<td>Chlorhexidine</td>
<td><em>Pseudomonas spp.</em></td>
<td>Not stated</td>
<td>Refilling contaminated bottles; washing used bottles using cold tap water; contaminated washing apparatus; low concentration (0.05%)</td>
<td>Burdon and Whitby, 1967 (13)</td>
</tr>
<tr>
<td>Chlorhexidine</td>
<td><em>Burkholderia cepacia</em></td>
<td>Blood, urinary, wounds</td>
<td>Not determined</td>
<td>Speller et al., 1971 (84)</td>
</tr>
<tr>
<td>Chlorhexidine</td>
<td><em>Flavobacterium meningosepticum</em></td>
<td>Blood, CSF, wounds, skin</td>
<td>Not determined but possibly due to contaminated water and/or topping off of stock solution; or low concentration (1:1000-1:5000)</td>
<td>Coyle-Gilchrist et al., 1976 (17)</td>
</tr>
<tr>
<td>Chlorhexidine</td>
<td><em>Pseudomonas sp., Serratia marcescens, Flavobacterium sp.</em>,</td>
<td>Not stated</td>
<td>Not determined but authors speculate due to over-dilution or refilling contaminated bottles</td>
<td>Marrie and Costerton, 1981 (47)</td>
</tr>
<tr>
<td>Chlorhexidine</td>
<td><em>Pseudomonas aeruginosa</em></td>
<td>Wounds</td>
<td>Tap water used to dilute stock solutions; low concentration (0.05%)</td>
<td>Anyiwo et al., 1982 (4)</td>
</tr>
<tr>
<td>Chlorhexidine</td>
<td><em>Burkholderia cepacia</em></td>
<td>Blood, wounds, urine, mouth, vagina</td>
<td>Metal pipe and rubber tubing in pharmacy through which deionized water passed during dilution of chlorhexidine; low concentration</td>
<td>Sobel et al., 1982 (83)</td>
</tr>
<tr>
<td>Antiseptic</td>
<td>Pathogen</td>
<td>Site(s)</td>
<td>Dilution Method and Concentration</td>
<td>Reference(s)</td>
</tr>
<tr>
<td>---------------------</td>
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</tr>
<tr>
<td>Chlorhexidine</td>
<td>Ralstonia pickettii</td>
<td>Blood</td>
<td>Contaminated bidistilled water; low concentration (0.05%)</td>
<td>Kahan et al., 1983 (38)</td>
</tr>
<tr>
<td>Chlorhexidine</td>
<td>Ralstonia pickettii</td>
<td>Blood</td>
<td>Contaminated deionized water; low concentration (0.05%)</td>
<td>Poty et al., 1987 (63)</td>
</tr>
<tr>
<td>Chlorhexidine</td>
<td>Ralstonia pickettii</td>
<td>Blood (pseudobacteremia)</td>
<td>Distilled water used to dilute chlorhexidine; low concentration (0.05%)</td>
<td>Verschraegen et al., 1985 (89)</td>
</tr>
<tr>
<td>Chlorhexidine</td>
<td>Ralstonia pickettii</td>
<td>Blood (pseudobacteremia)</td>
<td>Distilled water used to dilute chlorhexidine; low concentration (0.05%)</td>
<td>Maroye et al., 2000 (46)</td>
</tr>
<tr>
<td>Chlorhexidine</td>
<td>Achromobacter xylosoxidans</td>
<td>Blood, wounds</td>
<td>Atomizer (low concentration, 600 mg/L)</td>
<td>Vu-Thien et al., 1998 (91)</td>
</tr>
<tr>
<td>Chlorhexidine</td>
<td>Achromobacter xylosoxidans</td>
<td>Blood</td>
<td>Atomizer</td>
<td>Tena et al., 2005 (85)</td>
</tr>
<tr>
<td>Chlorhexidine</td>
<td>Serratia marcescens</td>
<td>Blood, urine, wounds, sputum, others</td>
<td>Not determined but use of nonsterile water for dilution to 2% and distribution in reusable nonsterile containers</td>
<td>Vigeant et al., 1998 (90)</td>
</tr>
<tr>
<td>Chlorhexidine plus centrimide</td>
<td>Pseudomonas multivorans</td>
<td>Wounds</td>
<td>Tap water used to prepare stock solutions; low concentration (0.05% and 0.5%, respectively)</td>
<td>Bassett, 1970 (8)</td>
</tr>
<tr>
<td>Chlorhexidine plus centrimide</td>
<td>Stenotrophomonas maltophilia</td>
<td>Urine, umbilical swabs, catheter tips, others</td>
<td>Deionized water used to prepare solutions; failure to disinfect contaminated bottles between use</td>
<td>Wishart et al., 1976 (93)</td>
</tr>
<tr>
<td>Chloroxylenol</td>
<td>Serratia marcescens</td>
<td>Multiple sites</td>
<td>Contaminated (extrinsic) 1% chloroxylenol soap; sink</td>
<td>Archibald et al., 1997 (5)</td>
</tr>
</tbody>
</table>
Table 3 (continued). Outbreaks and Pseudo-outbreaks Due to Contaminated Antiseptics

<table>
<thead>
<tr>
<th>Antiseptic</th>
<th>Pathogen</th>
<th>Site</th>
<th>Description</th>
<th>Reference</th>
</tr>
</thead>
<tbody>
<tr>
<td>Benzalkonium chloride</td>
<td><em>Pseudomonas species</em></td>
<td>Blood</td>
<td>Storage of benzalkonium chloride (0.1%) with cotton/gauze</td>
<td>Plotkin, 1958 (61)</td>
</tr>
<tr>
<td>Benzalkonium chloride</td>
<td><em>Pseudomonas-Achromobacteriaceae group</em></td>
<td>Blood, urine</td>
<td>Storage of benzalkonium chloride (0.1%) with cotton/gauze; dilution with nonsterile water</td>
<td>Lee et al., 1961 (43)</td>
</tr>
<tr>
<td>Benzalkonium chloride</td>
<td><em>Enterobacter aerogenes</em></td>
<td>Blood, sinus tract</td>
<td>Storage of benzalkonium chloride (0.13%) with cotton/gauze</td>
<td>Malizia et al., 1960 (45)</td>
</tr>
<tr>
<td>Benzalkonium chloride</td>
<td><em>Pseudomonas kingii</em></td>
<td>Urine</td>
<td>Contamination (intrinsic) of antiseptic</td>
<td>CDC, 1969 (15)</td>
</tr>
<tr>
<td>Benzalkonium chloride</td>
<td><em>Pseudomonas EO-1</em></td>
<td>Urine</td>
<td>Contaminated (intrinsic) cleansing-germicide solution</td>
<td>Hardy et al., 1970 (32)</td>
</tr>
<tr>
<td>Benzenethonium chloride</td>
<td><em>Pseudomonas species</em></td>
<td>Blood (pseudobacteremia)</td>
<td>Contaminated (intrinsic solution) (0.2%)</td>
<td>Dixon et al., 1976 (20)</td>
</tr>
<tr>
<td>Benzalkonium chloride</td>
<td><em>Bulkholderia cepacia</em>, <em>Enterobacter species</em></td>
<td>Blood (pseudobacteremia)</td>
<td>Storage of benzalkonium chloride with cotton/gauze; improper dilution; storage bottles infrequently sterilized</td>
<td>Kaslow et al., 1976 (39)</td>
</tr>
<tr>
<td>Benzalkonium chloride</td>
<td><em>Bulkholderia cepacia</em></td>
<td>Bacteremia</td>
<td>Storage of BC with rayon balls; failure to disinfect squeeze bottles</td>
<td>Frank and Schaffner, 1976 (25)</td>
</tr>
</tbody>
</table>
Table 3 (continued). Outbreaks and Pseudo-outbreaks Due to Contaminated Antiseptics

<table>
<thead>
<tr>
<th>Antiseptic</th>
<th>Pathogen</th>
<th>Site/Contamination</th>
<th>Details</th>
<th>Reference</th>
</tr>
</thead>
<tbody>
<tr>
<td>Benzalkonium chloride</td>
<td><em>Serratia marcescens</em></td>
<td>Intravenous catheters (dogs and cats), other sites</td>
<td>Storage of benzalkonium chloride (0.025%) with cotton/gauze</td>
<td>Fox et al., 1981 (24)</td>
</tr>
<tr>
<td>Benzalkonium chloride</td>
<td><em>Serratia marcescens</em></td>
<td>Joint</td>
<td>Storage of benzalkonium chloride with cotton/gauze</td>
<td>Nakashima et al., 1987 (53)</td>
</tr>
<tr>
<td>Benzalkonium chloride</td>
<td><em>Serratia marcescens</em></td>
<td>Cerebrospinal fluid</td>
<td>Contamination (extrinsic) of stock bottle</td>
<td>Sautter et al., 1984 (78)</td>
</tr>
<tr>
<td>Benzalkonium chloride</td>
<td><em>Mycobacterium chelonae</em></td>
<td>Skin abscesses</td>
<td>Storage of benzalkonium chloride with cotton/gauze, improper dilution</td>
<td>Georgia Division of Public Health, 1990 (28)</td>
</tr>
<tr>
<td>Benzalkonium chloride</td>
<td><em>Mycobacterium abscessus</em></td>
<td>Joint</td>
<td>Storage of benzalkonium chloride with cotton/gauze, dilution using probable contaminated tap water</td>
<td>Tiwari et al., 2003 (86)</td>
</tr>
<tr>
<td>Benzalkonium chloride/picloxydine</td>
<td><em>Burkholderia cepacia</em></td>
<td>Blood, urine, wound, sputum</td>
<td>Water used to dilute the antiseptic</td>
<td>Guinness and Levey, 1976 (30)</td>
</tr>
<tr>
<td>Benzalkonium chloride/picloxydine</td>
<td><em>Burkholderia cepacia</em></td>
<td>Blood</td>
<td>Water used to dilute the antiseptic</td>
<td>Morris et al., 1976 (52)</td>
</tr>
<tr>
<td>Povidone-iodine</td>
<td><em>Burkholderia cepacia</em></td>
<td>Blood (pseudobacteremia)</td>
<td>Intrinsic contamination, 10% povidone-iodine (probable B. cepacia proliferating on the deionizing resin in the water system)</td>
<td>Berkelman et al., 1981 (10)</td>
</tr>
<tr>
<td>Povidone-iodine</td>
<td><em>Burkholderia cepacia</em></td>
<td>Blood (pseudobacteremia)</td>
<td>Intrinsic contamination</td>
<td>Craven et al., 1981 (19)</td>
</tr>
<tr>
<td>Antiseptic</td>
<td>Bacterial Species</td>
<td>Site(s)</td>
<td>Mode of Contamination</td>
<td>Reference</td>
</tr>
<tr>
<td>---------------------</td>
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<td>----------------------------------</td>
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<td>------------------------------------</td>
</tr>
<tr>
<td>Poloxamer-iodine</td>
<td><em>Pseudomonas aeruginosa</em></td>
<td>Peritoneal fluid, wound</td>
<td>Intrinsic contamination</td>
<td>Parrott et al., 1982 (59)</td>
</tr>
<tr>
<td>Povidone-iodine</td>
<td><em>Burkholderia cepacia</em></td>
<td>Blood (pseudobacteremia),</td>
<td>Intrinsic contamination</td>
<td>CDC 1989 (14), Jarvis 1991 (36),</td>
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<td></td>
<td></td>
<td>peritoneal fluid</td>
<td></td>
<td>Panlilio et al., 1992 (58)</td>
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<tr>
<td>Povidone-iodine</td>
<td><em>Pseudomonas putida</em></td>
<td>Blood, catheter tips</td>
<td>Not determined</td>
<td>Bouallegue et al., 2004 (11)</td>
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<tr>
<td>Triclosan</td>
<td><em>Serratia marcescens</em></td>
<td>Conjunctiva</td>
<td>Intrinsic contamination</td>
<td>McNaughton et al., 1995 (50)</td>
</tr>
<tr>
<td>Disinfectant</td>
<td>Contaminating Microbes</td>
<td></td>
<td></td>
<td></td>
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<td>------------------------</td>
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<td></td>
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</tr>
<tr>
<td>Ethanol</td>
<td><em>Bacillus cereus</em> (9)*</td>
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<tr>
<td>Glutaraldehyde</td>
<td><em>Mycobacterium cheloneae</em> (41)<em>, <em>Methylobacterium mesophilicum</em> (41)</em>, <em>Mycobacterium species</em> (42,87)</td>
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<tr>
<td>Formaldehyde</td>
<td><em>Pseudomonas aeruginosa</em> (88)<em>, <em>Stenotrophomonas maltophilia</em> (88), <em>Klebsiella oxytoca</em> (64)</em></td>
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<tr>
<td>Quaternary ammonium compounds</td>
<td><em>Burkholderia cepacia</em> (20,21)<em>, <em>Serratia marcescens</em> (22)</em>, <em>Achromobacter xylosoxydans</em> (44)*,</td>
<td></td>
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<td></td>
<td><em>Pseudomonas aeruginosa</em> (57,80)*</td>
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<td>Phenolics</td>
<td><em>Pseudomonas species</em> (18,23,55), <em>Pseudomonas aeruginosa</em> (6*,55), <em>Alcaligenes faecalis</em> (82)</td>
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</tr>
</tbody>
</table>

* Outbreak or pseudo-outbreak
Table 5. Recommendations to Prevent Outbreaks Associated with Germicides

1. Use only CDC recommended and FDA cleared antiseptics.
2. Use only CDC recommended, and EPA registered or FDA cleared disinfectants.
3. Use all germicides at their recommended use dilution. Do not over dilute products.
4. Use sterile water for diluting antiseptics.
5. Use all germicides at recommended contact times.
6. Do not use germicides labeled only as antiseptics for disinfecting medical devices or surface disinfection.
7. Follow recommended procedures in preparation of products to prevent extrinsic contamination.
8. Small volume dispensers that are refilled from large volume stock containers should be used until entirely empty and then prior to refilling, they should be rinsed with tap water and then air-dried.
9. Store stock solutions of germicides as indicated on their product label.