Draft Guideline for Disinfection and Sterilization in Healthcare Facilities

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EXECUTIVE SUMMARY

This “Guideline for Disinfection and Sterilization in Healthcare Facilities” presents recommendations on the preferred methods for disinfection and sterilization of patient-care equipment based on the intended use of the item (i.e., critical, semicritical, and noncritical items). The chemical disinfectants recommended for patient-care equipment include alcohol, glutaraldehyde, hydrogen peroxide, iodophors, ortho-phthalaldehyde, peracetic acid, phenolics, quaternary ammonium compounds, and chlorine. The choice of disinfectant, concentration, and exposure time is based on the risk of infection associated with the use of the equipment. The sterilization methods discussed include steam sterilization, ethylene oxide (ETO), hydrogen peroxide gas plasma, and liquid peracetic acid. When properly used, these cleaning, disinfection, and sterilization processes can ensure the safe use of invasive and noninvasive medical and surgical devices. However, this requires strict adherence to current cleaning, disinfection, and sterilization recommendations.

INTRODUCTION

Each year in the United States there are approximately 27,000,000 surgical procedures and an even larger number of invasive medical procedures [1]. For example, there are at least 10 million gastrointestinal endoscopies per year. Each of these procedures involves contact by a medical device or surgical instrument with a patient’s sterile tissue or mucous membranes. A major risk of all such procedures is the introduction of infection. Failure to properly disinfect or sterilize equipment carries not only the risk associated with breach of the host barriers but the additional risk of person-to-person transmission (e.g., hepatitis B virus) and transmission of environmental pathogens (e.g., *Pseudomonas aeruginosa*).

Achieving disinfection and sterilization through the use of disinfectants and sterilization practices is essential for ensuring that medical and surgical instruments do not transmit infectious pathogens to patients. Since it is unnecessary to sterilize all patient-care items, hospital policies must identify whether cleaning, disinfection, or sterilization is indicated based primarily on the items' intended use but must consider other factors.

Multiple studies in many countries have documented lack of compliance with established guidelines for disinfection and sterilization [2-5]. Failure to comply with scientifically based guidelines has led to numerous outbreaks. In this guideline, a pragmatic approach to the judicious selection and proper use of disinfection and sterilization processes is presented, based on well-designed studies assessing the efficacy (via laboratory investigations) and effectiveness (via clinical studies) of disinfection and sterilization procedures.

Methods

This guideline is based on an exhaustive search of the literature using Medline. All articles listed under the mesh headings of disinfection or sterilization (focusing on healthcare equipment and supplies) from 1980 through September 2001 were reviewed. References listed in these articles were also reviewed. The three major peer-reviewed journals in infection control were searched by hand for relevant articles from 1990-2001. These journals are the *American Journal of Infection Control, Infection Control and Hospital Epidemiology,* and the *Journal of Hospital Infection.* Abstracts presented at the annual meetings of the Society for Healthcare Epidemiology of America (SHEA) and Association for

Professionals in Infection Control and Epidemiology (APIC), Inc. for the years 1997-2001 were also reviewed.

DEFINITION OF TERMS

Sterilization is the complete elimination or destruction of all forms of microbial life and is accomplished in healthcare facilities by either physical or chemical processes. Steam under pressure, dry heat, ETO gas, hydrogen peroxide gas plasma, and liquid chemicals are the principal sterilizing agents used in healthcare facilities. Sterilization is intended to convey an absolute meaning, not a relative one. Unfortunately, some health professionals as well as the technical and commercial literature refer to "disinfection" as "sterilization" and items as "partially sterile." When chemicals are used for the purposes of destroying all forms of microbiological life, including fungal and bacterial spores, they may be called chemical sterilants. These same germicides used for shorter exposure periods may also be part of the disinfection process (i.e., high-level disinfection).

Disinfection describes a process that eliminates many or all-pathogenic microorganisms on inanimate objects with the exception of bacterial spores. Disinfection is usually accomplished by the use of liquid chemicals or wet pasteurization in healthcare settings. The efficacy of disinfection is affected by a number of factors, each of which may nullify or limit the efficacy of the process. Some of the factors that affect both disinfection and sterilization efficacy are the prior cleaning of the object; the organic and inorganic load present; the type and level of microbial contamination; the concentration of and exposure time to the germicide; the nature of the object (e.g., crevices, hinges, and lumens); presence of biofilms; the temperature and pH of the disinfection process; and, in some cases, the relative humidity of the sterilization process (e.g., ethylene oxide).

By definition then, disinfection differs from sterilization by its lack of sporicidal property, but this is an oversimplification. A few disinfectants will kill spores with prolonged exposure times (3-12 hours) and are called chemical sterilants. At similar concentrations but with shorter exposure periods (≤45 minutes) these same disinfectants may kill all microorganisms with the exception of large numbers of bacterial spores and are called high-level disinfectants. Low-level disinfectants may kill most vegetative bacteria, some fungi, and some viruses in a practical period of time (≤10 minutes), whereas intermediate-level disinfectants may be cidal for mycobacteria, vegetative bacteria, most viruses, and most fungi but do not necessarily kill bacterial spores. The germicides differ markedly among themselves primarily in their antimicrobial spectrum and rapidity of action. Table 1 will be discussed later and consulted in this context. Table 2 lists the characteristics desired in an ideal disinfectant.

Cleaning, on the other hand, is the removal of all soil (e.g., organic and inorganic material) from objects and surfaces, and it normally is accomplished by wiping and/or using water with detergents or enzymatic products. Thorough cleaning is essential before high-level disinfection and sterilization since inorganic and organic materials that remain on the surfaces of instruments interfere with the effectiveness of these processes. Decontamination is a procedure that removes pathogenic microorganisms from objects so they are safe to handle.

Terms with a suffix “cide” or “cidal” for killing action also are commonly used. For example, a germicide is an agent that can kill microorganisms, particularly pathogenic organisms ("germs"). It is like the word disinfectant with the difference that germicide applies to compounds used on both living tissue and inanimate objects, whereas disinfectants are applied only to inanimate objects. Other words with the suffix "cide" (e.g., virucide, fungicide, bactericide, sporicide, and tuberculocide) can kill the type of microorganism identified by the prefix. For example, a bactericide is an agent that kills bacteria [6-11].

A RATIONAL APPROACH TO DISINFECTION AND STERILIZATION

Over 30 years ago, Earle H. Spaulding [7] devised a rational approach to disinfection and sterilization of patient-care items or equipment. This classification scheme is so clear and logical that it has been retained, refined, and successfully used by infection control professionals and others when planning methods for disinfection or sterilization [6, 8, 10, 12, 13]. Spaulding believed that the nature of disinfection could be understood more readily if instruments and items for patient care were divided into three categories based on the degree of risk of infection involved in the use of the items. The three categories he described were critical, semicritical, and noncritical. This terminology is employed by the 1985 Centers for Disease Control and Prevention's (CDC) "Guideline for Handwashing and Hospital Environmental Control" [14] and the CDC's "Guidelines for the Prevention of Transmission of Human Immunodeficiency Virus (HIV) and Hepatitis B Virus (HBV) to Health-Care and Public-Safety Workers" [15].

Critical Items

Critical items are so called because of the high risk of infection if such an item is contaminated with any microorganism, including bacterial spores. Thus, it is critical that objects that enter sterile tissue or the vascular system be sterile because any microbial contamination could result in disease transmission. This category includes surgical instruments, cardiac and urinary catheters, and implants. Most of the items in this category should be purchased as sterile or be sterilized by steam sterilization if possible. If heat-labile, the object may be treated with ETO, hydrogen peroxide gas plasma, or rarely by chemical sterilants if other methods are unsuitable. Table 1 lists several germicides categorized as chemical sterilants. These include ≥ 2.4% glutaraldehyde-based formulations, 0.95% glutaraldehyde with 1.64% phenol/phenate, 0.55% ortho-phthalaldehyde, 7.5% stabilized hydrogen peroxide, 7.35% hydrogen peroxide with 0.23% peracetic acid, 0.2% peracetic acid, and 0.08% peracetic acid with 1.0% hydrogen peroxide. Chemical sterilants can be relied upon to produce sterility only if cleaning, to eliminate organic and inorganic material, precedes treatment and if proper guidelines as to concentration, contact time, temperature, and pH are met.

Semicritical Items

Semicritical items are those that come in contact with mucous membranes or nonintact skin. Respiratory therapy and anesthesia equipment, endoscopes, laryngoscope blades, esophageal manometry probes, anorectal manometry catheters, and diaphragm fitting rings are included in this category. These medical devices should be free of all microorganisms, although small numbers of bacterial spores may be present. Intact mucous membranes, such as those of the lungs or the gastrointestinal tract, generally are resistant to infection by common bacterial spores but susceptible to other organisms such as bacteria, mycobacteria, and viruses. Semicritical items minimally require high-level disinfection using wet pasteurization or chemical disinfectants. Glutaraldehyde, hydrogen peroxide, ortho-phthalaldehyde, peracetic acid, peracetic acid with hydrogen peroxide, and chlorine compounds are dependable high-level disinfectants provided the factors influencing germicidal procedures are considered (Table 1). When a disinfectant is selected for use with certain patient-care items, the chemical compatibility after extended use with the items to be disinfected also must be considered. For example, while chlorine compounds are considered high-level disinfectants due to their antimicrobial spectrum, they are generally not used for disinfecting semicritical items because of their corrosive effects at high concentrations on metals.

While the complete elimination of all microorganisms in/on an instrument with the exception of small numbers of bacterial spores is the traditional definition of high-level disinfection, the Food and Drug Administration (FDA) require a more realistic endpoint. For example, the FDA accepts a 6-$\log_{10}$ reduction of microorganisms (i.e., specific strains of mycobacteria), with the exception of small numbers of bacterial

spores, as proof of high-level disinfection. This is noteworthy, as complete elimination of microorganisms (e.g., *Mycobacterium chelonae*) in a contaminated instrument will occur with a starting inoculum of $\leq 10^6$ but may not occur if the starting inoculum is $>10^6$. However, cleaning followed by high-level disinfection should eliminate sufficient pathogens to prevent transmission of infection [16].

Laparoscopes and arthroscopes entering sterile tissue ideally should be sterilized between patients. However, they sometimes undergo only high-level disinfection between patients in the United States [17, 18]. There is no evidence showing that high-level disinfection of these scopes poses an infection risk to patients [18-27].

Semicritical items should be rinsed with sterile water after high-level disinfection to prevent their contamination with organisms that may be present in tapwater, such as nontuberculous mycobacteria [28-30], *Legionella* [31-33], or gram-negative rods such as *Pseudomonas* [10, 12, 34-36]. In circumstances where rinsing with sterile water rinse is not feasible, a tapwater (or filtered water [0.2μ filter]) rinse should be followed by an alcohol rinse and forced air drying [17, 36, 37]. Forced-air drying markedly reduces bacterial contamination of stored endoscopes, most likely by removing the wet environment favorable for bacterial growth [37]. After rinsing, items should be dried and stored (e.g., packaged) in a manner that protects them from recontamination.

Some items that may come in contact with nonintact skin for a brief period of time (i.e., hydrotherapy tanks, bed side rails) are usually considered noncritical surfaces and are disinfected with intermediate-level disinfectants (i.e., phenolic, iodophor, alcohol). Since hydrotherapy tanks have been associated with cross-transmission, some facilities may chose to disinfect them with high-level disinfectants (e.g., 1000 ppm chlorine).

In the past it was recommended that mouthpieces and spirometry tubing be high-level disinfected (e.g., glutaraldehyde) and it was unnecessary to clean the interior surfaces of the spirometers [38]. This was based on a study that showed that mouthpieces and spirometry tubing become contaminated with microorganisms but there was no bacterial contamination of the surfaces inside the spirometers. More recently, filters have been used to prevent contamination of this equipment distal to the filter; such filters and the proximal mouthpiece are changed between patients.

Noncritical Items

Noncritical items are those that come in contact with intact skin but not mucous membranes. Intact skin acts as an effective barrier to most microorganisms and the sterility of items coming in contact with intact skin is "not critical." Examples of noncritical items are bedpans, blood pressure cuffs, crutches, bed rails, linens, some food utensils, bedside tables, patient furniture, and floors. In contrast to critical and some semicritical items, most noncritical reusable items may be cleaned where they are used and do not need to be transported to a central processing area. There is virtually no risk of transmitting infectious agents to patients via noncritical items [35]; however, these items could potentially contribute to secondary transmission by contaminating hands of healthcare workers or by contact with medical equipment that will subsequently come in contact with patients [6, 39-42]. Table 1 lists several low-level disinfectants that may be used for noncritical items. These products should be used according to the manufacturers' recommendations but often are not; one study showed that only 14% of sampled disinfectants had the correct concentration [43].

Although not considered noncritical items, mops and reusable cleaning cloths are regularly used to achieve low-level disinfection. However, they are commonly not kept adequately cleaned and disinfected, and if the water-disinfectant mixture is not changed regularly (e.g., after every three to four rooms), the mopping procedure may actually spread heavy microbial contamination throughout the hospital [44]. In one study, standard laundering provided acceptable decontamination of heavily contaminated mopheads but chemical disinfection with a phenolic was less effective [44]. The frequent

laundering of mops (e.g., daily) is, therefore, recommended.

Changes in Disinfection and Sterilization Since 1981 (last CDC Guideline)

The Table prepared by the CDC in 1981 as a guide to the appropriate selection and use of disinfectants has undergone several important changes (Table 1). First, formaldehyde-alcohol has been deleted as a chemical sterilant or high-level disinfectant because it is irritating and toxic and not commonly used. Second, several new chemical sterilants have been added to the Table including hydrogen peroxide, peracetic acid [45-47], and peracetic acid and hydrogen peroxide in combination. Third, 3% phenolics and iodophors have been deleted as high-level disinfectants because of their unproven efficacy against bacterial spores, *M. tuberculosis,* and/or some fungi [48]. Fourth, isopropyl alcohol and ethyl alcohol have been excluded as high-level disinfectants because of their inability to inactivate bacterial spores and because of the inability of isopropyl alcohol to inactivate hydrophilic viruses (i.e., poliovirus, coxsackie virus) [49]. Fifth, a 1:16 dilution of 2.0% glutaraldehyde-7.05% phenol-1.20% sodium phenate (which contained 0.125% glutaraldehyde, 0.440% phenol, and 0.075% sodium phenate when diluted) has been deleted as a high-level disinfectant because this product was removed from the marketplace in December 1991 because of a lack of bactericidal activity in the presence of organic matter; a lack of fungicidal, tuberculocidal and sporicidal activity; and reduced virucidal activity [48, 50-59]. Sixth, the exposure time required to achieve high-level disinfection has been changed from 10-30 minutes to 12 minutes or more depending on the scientific literature and the FDA-cleared label claim [45, 53, 54, 60-65].

In addition, many new subjects have been added to the guideline. These include inactivation of emerging pathogens, Creutzfeldt-Jakob disease (CJD) agent, and bloodborne pathogens; toxicologic and environment concerns associated with disinfection and sterilization practices; disinfection of patient-care equipment used in ambulatory and home care; inactivation of antibiotic-resistant bacteria; decontamination of bone; new sterilization processes such as hydrogen peroxide gas plasma and peracetic acid; and disinfection of complex medical instruments (e.g., endoscopes).

DISINFECTION OF HEALTHCARE EQUIPMENT

Concerns with Spaulding Scheme

One problem with the aforementioned scheme is that of oversimplification. For example, it does not consider problems with reprocessing of complicated medical equipment that often is heat-labile or problems of inactivating certain types of infectious agents (e.g., prions such as CJD agent). Thus, in some situations it is still difficult to choose a method of disinfection, even after considering the categories of risk to patients. This is especially true for a few medical devices (e.g., arthroscopes, laparoscopes) in the critical category because there is controversy about whether they should be sterilized or high-level disinfected [17, 19]. Some of these items cannot be steam sterilized because they are heat-labile; further, sterilization by using ETO which may be too time consuming for routine use between patients (new technologies, such as hydrogen peroxide gas plasma and peracetic acid reprocessor, provide faster cycle times). And although the value of sterilization of these items seems obvious, evidence is lacking that sterilization of these items improves patient care by reducing the infection risk is lacking [18, 22, 25-27, 66]. Presumably, the lack of demonstrated scientific risk is why procedures done in hospitals with arthroscopes, laparoscopes, and biopsy forceps are sometimes performed with equipment that has been processed by high-level disinfection, and not sterilization [17, 18].

Another problem in the classification system is an instrument in the semicritical category (e.g., endoscopes) that would be used with a critical instrument that would have contact with sterile body fluids. For example, is an endoscope used for upper gastrointestinal tract investigation still a semicritical item

when it is used with sterile biopsy forceps or when it is used in a patient who is bleeding heavily from esophageal varices? Provided that high-level disinfection is achieved, and all microorganisms with the exception of small numbers of bacterial spores have been removed from the endoscope, then the device should not represent an infection risk and should remain in the semicritical category [67, 68].

Among other problems in the disinfection of patient-care items are ill-defined optimal contact times, which have resulted in different strategies for disinfecting different types of semicritical items (e.g., endoscopes, applanation tonometers, endocavitary transducers, cryosurgical instruments, and diaphragm fitting rings). The impact of this variability will be discussed below. Until simpler and effective alternatives are identified for device disinfection in clinical settings, it would be prudent to follow the guidelines of CDC and the APIC[10, 12, 69, 70].

Endoscopes

Physicians use endoscopes to diagnose and treat numerous medical disorders. While endoscopes represent a valuable diagnostic and therapeutic tool in modern medicine, more healthcare-associated outbreaks have been linked to contaminated endoscopes than to any other medical device [5, 71, 72]. In order to prevent the spread of healthcare-associated infections, all heat-sensitive endoscopes (e.g., gastrointestinal endoscopes, bronchoscopes, nasopharygoscopes) must be properly cleaned and at a minimum subjected to high-level disinfection following each use. High-level disinfection can be expected to destroy all microorganisms although when high numbers of bacterial spores are present, a few spores may survive.

Flexible endoscopes, by virtue of the types of body cavities they enter, acquire high levels of microbial contamination (bioburden) during each use [73]. For example, the bioburden found on flexible gastrointestinal endoscopes following use has ranged from 10^5 colony forming units (CFU)/ml to 10^{10} CFU/ml, with the highest levels being found in the suction channels [73-75]. The average load on bronchoscopes before cleaning was 6.4×10^4 CFU/ml. Cleaning reduces the level of microbial contamination by 4 to 6 $\log_{10}$. Several investigators have shown that cleaning completely eliminates the microbial contamination on scopes [76, 77] or that ETO sterilization and high-level disinfection (soaking in 2% glutaraldehyde for 20 minutes) were effective only when the device was first properly cleaned [78].

High-level disinfectants registered by the FDA include formulations with ≥2.4% glutaraldehyde, 0.55% ortho-phthalaldehyde, 0.95% glutaraldehyde with 1.64% phenol/phenate, 7.35% hydrogen peroxide with 0.23% peracetic acid, 1.0% hydrogen peroxide with 0.08% peracetic acid, and 7.5% hydrogen peroxide [79]. Although all of these products have excellent antimicrobial activity, certain products based in oxidizing chemicals (e.g., 7.5% hydrogen peroxide and 1.0% hydrogen peroxide with 0.08% peracetic acid [latter product is no longer marketed]) have limited use because they may cause cosmetic and functional damage to endoscopes [45]. Two recently cleared formulations (i.e., 0.95% glutaraldehyde with 1.64% phenol/phenate, 7.35% hydrogen peroxide with 0.23% peracetic acid) have not been independently evaluated for antimicrobial activity or materials compatibility. ETO sterilization of flexible endoscopes is infrequent because it requires a lengthy processing and aeration time (e.g., 12 hours) and is a potential hazard to staff and patients. The two products that are most commonly used for reprocessing endoscopes in the United States are glutaraldehyde and an automated, liquid chemical sterilization process that uses peracetic acid [80]. The American Society of Gastrointestinal Endoscopy (ASGE) recommends glutaraldehyde solutions that do not contain surfactants because the soapy residues of surfactants are difficult to remove during rinsing [81]. Ortho-phthalaldehyde has begun to replace glutaraldehyde in many hospitals as it possesses several potential advantages compared to glutaraldehyde: it is nonirritating to the eyes and nasal passages, does not require activation or exposure monitoring, and has a 12-minute high-level disinfection claim in the United States. [45]. Disinfectants that are not FDA cleared and should not be used for reprocessing endoscopes include iodophors, hypochlorite solutions, alcohols, quaternary ammonium compounds, and phenolics. These solutions may still be in use outside the United States, but their use should be strongly discouraged because of lack of

proven efficacy against all microorganisms or materials incompatibility.

The FDA cleared a package label for 2.4% glutaraldehyde that requires a 45-minute immersion at 25°C to achieve high-level disinfection (i.e., 100% kill of *Mycobacterium tuberculosis*). However, available data suggest that *M. tuberculosis* levels can be reduced by at least 8 $\log_{10}$ with cleaning (4 $\log_{10}$)[63, 75, 82, 83] followed by chemical disinfection for 20 minutes at 20°C (4 to 6 $\log_{10}$)[63, 68, 84]. Based on these data, APIC [85], the Society of Gastroenterology Nurses and Associates (SGNA)[36, 86] and the American Society of Gastrointestinal Endoscopy (ASGE)[81] recommend that equipment be immersed in 2% glutaraldehyde at 20°C for at least 20 minutes for high-level disinfection [63, 81, 87]. In the absence of independently validated data regarding alternative exposure times of high-level disinfectants, the manufacturers' recommendations to achieve high-level disinfection should be followed. Currently, such data are available only for 2% glutaraldehyde solutions.

Flexible endoscopes are particularly difficult to disinfect [88] and easy to damage because of their intricate design and delicate materials [89]. Meticulous cleaning must precede any sterilization or high-level disinfection of these instruments. Failure to perform good cleaning may result in a sterilization or disinfection failure and outbreaks of infection may occur**.** Several studies have demonstrated the importance of cleaning in experimental studies with the duck hepatitis B virus [78, 90, 91] and *Helicobacter pylori* [92].

Examining healthcare-associated infections related only to endoscopes through July 1992, Spach found that 281 infections were transmitted by gastrointestinal endoscopy and 96 were transmitted by bronchoscopy. The clinical spectrum of these infections ranged from symptomatic colonization to death. *Salmonella* species and *P. aeruginosa* repeatedly were identified as causative agents of infections transmitted by gastrointestinal endoscopy, and *M. tuberculosis* (TB), atypical mycobacteria, and *P. aeruginosa* were the most common causes of infections transmitted by bronchoscopy. Major reasons for transmission were inadequate cleaning, improper selection of a disinfecting agent, or failure to follow recommended cleaning and disinfection procedures [5, 35, 71]. Failure to follow established guidelines has continued to lead to infections associated with gastrointestinal endoscopes [71] and bronchoscopes [72]. One multi-state investigation found that 23.9% of the bacterial cultures from the internal channels of 71 gastrointestinal endoscopes grew $\geq$100,000 colonies of bacteria after completion of all disinfection/sterilization procedures and before use on the next patient [93].

Automatic endoscope reprocessors (AER) offer several advantages compared to manual reprocessing: they automate and standardize several important reprocessing steps [66, 94, 95], reduce the likelihood that an essential reprocessing step will be skipped, and reduce personnel exposure to high-level disinfectants or chemical sterilants. Failure of AERs has been linked to outbreaks of infections [96] or colonization [97 72], and the AER water filtration system may not be able to reliably provide bacteria-free rinse water [98, 99]. In addition, some endoscopes (e.g., endoscopic retrograde choliagiopancreatography [ERCP], duodenoscope) contain features (e.g., elevator-wire channel) that require a flushing pressure that is not achieved by most AERs and must be reprocessed manually using a 2- to 5-ml syringe. New side-viewing duodenoscopes equipped with a wider elevator-channel that AERs can reliably reprocess are likely to be available soon [95]. Outbreaks involving endoscopic accessories [100, 101] such as suction valves and biopsy forceps emphasize the importance of cleaning to remove all foreign matter before high-level disinfection or sterilization [102].

There is a need for further development and redesign of AERs [72, 103] and endoscopes [89, 104] so that they do not represent a potential source of infectious agents. A disposable-sheath fiberoptic endoscope that consists of three components has been developed. The reusable component is made up of the umbilicus, a control handpiece, and a D-shaped insertion tube that fits within the sheath and contains the fiberoptics. The disposable sheath contains the air-water, suction, and working channels and is discarded at the end of each procedure. A plastic cover for the control handpiece and umbilicus is discarded also after each procedure. The control dials are not covered and require removal and

disinfection between procedures [105]. Most studies report minimal differences in procedure duration, but markedly shorter reprocessing time with sheathed endoscopes. Disposable-component endoscope systems have the potential to improve the ease of cleaning and disinfection and to reduce the risk of infection. Another new technology is a swallowable camera-in-a-capsule that travels through the digestive tract and transmits color pictures of the small intestine to a receiver that is worn outside the body. At present, this capsule will not replace colonoscopies.

Recommendations for the cleaning and disinfection of endoscopic equipment have been published and should be strictly followed [36, 81, 85, 86, 106-109]. Unfortunately, audits have shown that personnel do not adhere to guidelines on disinfection [110-112] and outbreaks of infection continue to occur [113-115]. In order to ensure that reprocessing persons are properly trained, there should be initial and annual competency testing for each individual who reprocesses endoscopic instruments [36, 116].

In general, endoscope disinfection involves five steps: 1) clean - mechanically clean internal and external surfaces, including brushing internal channels and flushing each internal channel with water and a detergent or enzymatic detergent; 2) disinfect - immerse endoscope in high-level disinfectant (or chemical sterilant) and perfuse disinfectant into the suction/biopsy channel and air/water channel and expose for at least 12 minutes (or FDA-cleared exposure time)[65]; 3) rinse – rinse the endoscope and all channels with sterile water or AER filtered water; if this is not feasible use tap water; 4) dry – rinse the insertion tube and inner channels with alcohol and dry with forced air after disinfection and before storage; and 5) store -store the endoscope in a way that prevents recontamination (e.g., hung vertically). There has been no evidence of disease transmission when these practices are followed. In addition to these practices, a protocol should be developed that assures the user knows whether an endoscope has been appropriately cleaned and disinfected (e.g., placing a disposable wrap over the processed scopes, using a room or cabinet for processed endoscopes only) or has been used. Confusion can result when users leave endoscopes on movable carts and it is unclear whether the endoscope has been processed or not. While one guideline has recommended that an endoscope (e.g., a duodenoscope) should be reprocessed immediately before its use [108], other guidelines do not require this activity [36, 81] and, in general, it is not required that reprocessing be repeated so long as the original processing is done correctly. As part of a quality assurance program, healthcare facility personnel should consider random bacterial surveillance cultures of processed endoscopes to ensure high-level disinfection or sterilization. Reprocessed endoscopes should be free of microbial pathogens except for small numbers of relatively avirulent microbes that represent exogenous environmental contamination (e.g., coagulase-negative *Staphylococcus*, *Bacillus* species, diphtheroids).

Infection control professionals should ensure that institutional policies are consistent with national guidelines and conduct infection control rounds periodically (e.g., at least annually) in areas where endoscopes are reprocessed to make certain there is compliance with policy. Breaches in policy should be documented and corrective action instituted. In one incident in which endoscopes were not exposed to a high-level disinfection process, all patients were assessed for possible acquisition of human immunodeficiency virus (HIV), Hepatitis B virus (HBV), and Hepatitis C virus (HCV). This highlights the importance of rigorous infection control [117].

Laparoscopes, Arthroscopes, and Cystoscopes

While high-level disinfection appears to be the minimum standard for processing laparoscopes, arthroscopes, and cystoscopes between patients [17, 19, 20, 118], there continues to be debate of this practice [21, 26, 27]. However, neither side in the high-level disinfection versus sterilization debate has adequate data on which to base its arguments. Proponents of high-level disinfection refer to membership surveys [18] or institutional experiences [22]involving over 117,000 and 10,000 laparoscopic procedures, respectively, that cite a low risk of infection (<0.3%) when high-level disinfection is used for gynecologic laparoscopic equipment. Only one infection in the membership survey was linked to spores. In addition, studies conducted by Corson et al. demonstrated growth of common skin microorganisms (e.g., *Staphylococcus*

epidermidis, diphtheroids) from the umbilical area even after skin preparation with povidone-iodine and ethyl alcohol. Similar organisms were recovered in some instances from the pelvic serosal surfaces or from the laparoscopic telescopes, suggesting that the microorganisms probably were carried from the skin into the peritoneal cavity [23, 24]. Proponents of sterilization focus on the possibility of transmitting infection by spore-forming organisms. Researchers have proposed several reasons why sterility was not necessary for all laparoscopic equipment: only a limited number of organisms (usually ≤10) are introduced into the peritoneal cavity during laporoscopy; minimal damage is done to inner abdominal structures with little devitalized tissue; the peritoneal cavity tolerates small numbers of spore-forming bacteria; equipment is simple to clean and disinfect; surgical sterility is relative; the natural bioburden on rigid lumened devices is low[119]; and no evidence that high-level disinfection, instead of sterilization, increases the infection risk [22, 26, 27]. With the advent of laparoscopic cholecystectomy there is justifiable concern with high-level disinfection as the degree of tissue damage and bacterial contamination is greater than with laparoscopic procedures in gynecology. Data from one study suggest that disassembly, cleaning, and proper assembly of laparoscopic equipment used in gynecologic procedures before steam sterilization presents no risk of infection [120].

As with laparoscopes and other equipment that enter sterile body sites, arthroscopes ideally should be sterilized before use. However, they commonly undergo only high-level disinfection in the United States [17, 19]. Presumably this is because the incidence of infection is low and the few infections are probably unrelated to the use of high-level disinfection rather than sterilization. In a retrospective study of 12,505 arthroscopic procedures, Johnston et al. found an infection rate of 0.04% (5 infections) when arthroscopes were soaked in 2% glutaraldehyde for 15-20 minutes. Four infections were caused by *S. aureus* while the other was an anaerobic streptococcal infection [25]. Since these organisms are very susceptible to high-level disinfectants such as 2% glutaraldehyde, the origin of these infections was likely the patient's skin. There are two case reports of *Clostridium perfringens* arthritis when the arthroscope was disinfected with glutaraldehyde for an exposure time that is not effective against spores [121, 122].

Although only limited data are available, there is no evidence to demonstrate that high-level disinfection of arthroscopes, laparoscopes, or cystoscopes poses an infection risk to the patient. For example, a prospective study compared the reprocessing of arthroscopes and laparoscopes (per 1,000 procedures) with ETO sterilization and high-level disinfection with glutaraldehyde and found no statistically significant difference in infection risk between the two methods (i.e., ethylene oxide, 7.5/1000 procedures; glutaraldehyde, 2.5/1000 procedures) [26]. While the debate for high-level disinfection versus sterilization of laparoscopes and arthroscopes will go unsettled until there are published well-designed, randomized clinical trials, CDC and APIC guidelines should be followed[10, 12]. That is, laparoscopes, arthroscopes, cystoscopes, and other scopes that enter normally sterile tissue should be subjected to a sterilization procedure before each use; if this is not feasible, they should receive at least high-level disinfection.

Tonometers, Diaphragm Fitting Rings, Cryosurgical Instruments, Endocavitary Probes

Disinfection strategies for other semicritical items (e.g., applanation tonometers, rectal/vaginal probes, cryosurgical instruments, and diaphragm fitting rings) are highly variable. For example, one study revealed that no uniform technique was in use for disinfection of applanation tonometers, with disinfectant contact times varying from <15 sec to 20 minutes [17]. In view of the potential for transmission of viruses (e.g., herpes simplex virus [HSV], adenovirus 8, or HIV)[123] by tonometer tips, CDC recommends [69] that the tonometer tips be wiped clean and disinfected for 5-10 minutes with either 3% hydrogen peroxide, 5000 ppm chlorine, 70% ethyl alcohol, or 70% isopropyl alcohol. Structural damage to Schiotz tonometers has been observed with a 1:10 sodium hypochlorite (5000 ppm chlorine) and 3% hydrogen peroxide [124]. After disinfection, the tonometer should be thoroughly rinsed in tap water and dried before use. Although these disinfectants and exposure times should kill pathogens that can infect the eyes, there are no studies that provide direct support [125, 126]. The guidelines of the American Academy of Ophthalmology for preventing infections in ophthalmology focus on only one potential pathogen, HIV-1

[127]. Because a short and simple decontamination procedure is desirable in the clinical setting, swabbing the tonometer tip with a 70% isopropyl alcohol wipe is sometimes practiced [126]. Preliminary reports suggest that wiping the tonometer tip with an alcohol swab and then allowing the alcohol to evaporate may be an effective means of eliminating HSV, HIV-1, and adenovirus [126, 128, 129]. However, since these studies involved only a few replicates and were conducted in a controlled laboratory setting, further studies are needed before this technique can be recommended. In addition, two reports have found that disinfection of pneumotonometer tips between uses with a 70% isopropyl alcohol wipe contributed to outbreaks of epidemic keratoconjunctivitis caused by adenovirus type 8 [130, 131].

There are also limited studies that evaluated disinfection techniques for other items that contact mucous membranes, such as diaphragm fitting rings, cryosurgical probes, transesophageal echocardiography probes [132], or vaginal/rectal probes used in sonographic scanning. Lettau, Bond, and McDougal of CDC supported the recommendation of a diaphragm fitting ring manufacturer that involved using a soap-and-water wash followed by a 15-minute immersion in 70% alcohol [70]. This disinfection method should be adequate to inactivate HIV-1, HBV, and HSV even though alcohols are not classified as high-level disinfectants because their activity against picornaviruses is somewhat limited [49]. There are no data on the inactivation of human papillomavirus by alcohol or other disinfectants because *in vitro* replication of complete virions has not been achieved. Thus, while alcohol for 15 minutes should kill pathogens of relevance in gynecology, there are no clinical studies that provide direct support for this practice.

Vaginal probes are used in sonographic scanning. A vaginal probe and all endocavitary probes without a probe cover are semicritical devices as they have direct contact with mucous membranes. While one could argue that the use of the probe cover changes the category, this guideline proposes that a new condom/probe cover should be used to cover the probe for each patient and since condoms/probe covers may fail [132-135], high-level disinfection of the probe also should be performed. The relevance of this recommendation is reinforced with the findings that sterile transvaginal ultrasound probe covers have a very high rate of perforations even before use (0%, 25%, and 65% perforations from three suppliers)[135]. After oocyte retrieval use, Hignett and Claman found a very high rate of perforations in used endovaginal probe covers from two suppliers (75% and 81%)[135], while Amis and co-workers [136] and Milki and Fisch [133] demonstrated a lower rate of perforations after use of condoms (0.9% and 2.0%, respectively). Rooks and co-workers found that condoms were superior to commercially available probe covers for covering the ultrasound probe (1.7% for condoms versus 8.3% leakage for probe covers)[137]. These studies underscore the need for routine probe disinfection between examinations.

Although most ultrasound manufacturers recommend the use of 2% glutaraldehyde for high-level disinfection of contaminated transvaginal transducers, the use of this agent has been questioned [138] because it shortens the life of the transducer and may have toxic effects on the gametes and embryos [139]. An alternative procedure for disinfecting the vaginal transducer has been offered by Garland and deCrespigny [140]. It involves the mechanical removal of the gel from the transducer, cleaning the transducer in soap and water, wiping the transducer with 70% alcohol or soaking it for 2 minutes in 500 ppm chlorine, and rinsing with tap water and drying. The effectiveness of this and other methods [136] has not been validated in either rigorous laboratory experiments or in clinical use. High-level disinfection with a product that is not toxic to staff, patients, probes, and retrieved cells (e.g., hydrogen peroxide) should be used until such time as the effectiveness of alternative procedures against microbes of importance at the cavitary site is scientifically demonstrated. Other probes such as rectal, cryosurgical, and transesophageal probes/devices should also be subjected to high-level disinfection between patients.

Some cryosurgical probes are not fully immersible. When reprocessing these probes, the tip of the probe should be immersed in a high-level disinfectant for the appropriate time (e.g., 20 minutes exposure with 2% glutaraldehyde) and any other portion of the probe that could have mucous membrane contact could be disinfected by wrapping with a cloth soaked in a high-level disinfectant in order to allow the recommended contact time. After disinfection, the probe should be rinsed with tap water and dried before use. Healthcare facilities that use nonimmersible probes should replace them as soon as possible with

fully immersible probes.

As with other high-level disinfection procedures, proper cleaning of probes is necessary to ensure the success of the subsequent disinfection [141]. Muradali and colleagues demonstrated a reduction of vegetative bacteria inoculated on vaginal ultrasound probes when the probes were cleaned with a towel [142]. No information is available of the level of contamination of such probes by potential viral pathogens such as HBV and human papilloma virus (HPV) that may be more resistant than vegetative bacteria to disinfection procedures. Because these pathogens may be present in vaginal and rectal secretions and contaminate probes during use, high-level disinfection of the probes after such use is recommended.

Dental Instruments

Scientific articles and increased publicity about the potential for transmitting infectious agents in dentistry have focused attention on dental instruments as possible agents for pathogen transmission [143, 144]. The American Dental Association recommends that surgical and other instruments that normally penetrate soft tissue or bone (e.g., forceps, scalpels, bone chisels, scalers, and surgical burs) be classified as critical devices that should be sterilized after each use or discarded. Instruments that are not intended to penetrate oral soft tissues or bone (e.g., amalgam condensers, and air/water syringes) but may come in contact with oral tissues are classified as semicritical and should also be sterilized after each use [145]. This is consistent with recommendations from CDC and FDA [146, 147]. Handpieces that cannot be heat sterilized should be retrofitted to attain heat tolerance. Handpieces that cannot be retrofitted and thus are not able to be heat sterilized should not be used [147]. Chemical disinfection is not recommended for critical or semicritical dental instruments. Methods of sterilization that may be used for critical or semicritical dental instruments and materials that are heat-stable include steam under pressure (autoclave), chemical (formaldehyde) vapor, and dry heat (e.g., 320°F for 2 h). The steam sterilizer is the method most commonly used by dental professionals [148]. All 3 sterilization procedures can be damaging to some dental instruments, including steam sterilized handpieces [149]. ETO or hydrogen peroxide gas plasma also should be an effective means of sterilization if the instrument to be sterilized is clean and dry. Consideration must be given to the potential damage a sterilization process may have on instruments and materials.

Several studies have demonstrated variability among dental practices while trying to meet these recommendations [150]. For example, 68% of respondents believed they were sterilizing their instruments but did not use appropriate chemical sterilants or exposure times and 49% of respondents did not challenge autoclaves with biological indicators [150]. Other investigators using biological indicators have found a high portion (15-65%) of positive spore tests after assessing the efficacy of sterilizers used in dental offices. In one study of Minnesota dental offices, operator error, rather than mechanical malfunction [151], caused 87% of sterilization failures. Common factors in the improper use of sterilizers included chamber overload; low temperature setting; inadequate exposure time; failure to preheat sterilizer; and interruption of the cycle.

Mail-return sterilization monitoring services use spore strips to test sterilizers in dental clinics, but delay caused by mailing to the test laboratory could potentially cause false-negatives results. Studies revealed, however, that the post-sterilization time and temperature after a 7-day delay had no influence on the test results [152]. Miller and Sheldrake also found that delays (7 days at 27°C and 37°C, 3-day mail delay) did not cause any predictable pattern of inaccurate spore tests [153].

Uncovered operatory surfaces (e.g., countertops, chair switches, and light handles) should be disinfected between patients. This can be accomplished using products that are registered with the U.S. Environmental Protection Agency (EPA) as "hospital disinfectants." There are several categories of such products (chlorine, and phenolics) [145, 154, 155]. If waterproof surface covers are used to prevent contamination of surfaces and are carefully removed and replaced between patients, the protected surfaces do not need to be disinfected between patients but should be disinfected at the end of the day.

Decontamination of Bone

Bone is the most frequently transplanted tissue in humans with the exception of blood [156]. The risk of infections transmissible by allografts (e.g., bones, tendons, and ligaments) depends on the technique applied for procurement, preservation, and bacteriological control and also on the prevalence of infectious carriers. HIV has been transmitted by bone transplantation [157]. Despite the infection control measures employed to select the donors, the risk of infectious agents associated with the tissue obtained for transplantation cannot be ignored and a safe, dependable method of secondary sterilization without damaging the tissue or recipient is essential. Unfortunately, none of the methods for sterilization of bones, tendons, and ligaments seems ideal because they may reduce the quality of the biological graft, increase toxicity, or be ineffective in reducing contaminating microorganisms. Radiation sterilization of frozen allografts and ETO sterilization of freeze-dried allografts are the most commonly used methods.

Recently, a system to sterilize musculoskeletal tissues (e.g., bones, and tendons) for use in bone grafting was developed using various chemical solutions to remove endogenous materials (e.g., blood, and bone marrow) and inactivate infectious agents. This vacuum-pressure cleaning system uses detergent, hydrogen peroxide, and alcohol in 2 cycles. Preliminary studies have shown it is effective in eliminating *B. stearothermophilus* spores [158].

Although not often mentioned, instances have occurred in which a graft has been dropped on the operating room floor. To determine the amount of microbial contamination that occurs when the graft is dropped, surplus bone specimens from 50 procedures were dropped and submitted for culture. No positive cultures were obtained [159]. Another study evaluated the most effective method for disinfecting contaminated human bone-tendon allografts (i.e., beef muscle, cadaveric human bone-tendon allografts, and Achilles tendon-calcaneus allografts)[160]. A 2% and 4% chlorhexidine irrigation solution and 4% chlorhexidine/triple antibiotic bath completely disinfected the test tissues after an exposure time of 10 to 12 minutes.

Disinfection of HBV-, HCV-, HIV- or Tuberculosis-Contaminated Devices

Should we sterilize or high-level disinfect semicritical medical devices contaminated with blood from patients infected with HBV, HCV, or HIV or respiratory secretions from patients with pulmonary tuberculosis? The CDC recommendation for high-level disinfection is appropriate because experiments have demonstrated the effectiveness of high-level disinfectants to inactivate these and other pathogens that may contaminate semicritical devices [50, 61, 77, 91, 161-178]. Nonetheless, some hospitals modify their disinfection procedures when endoscopes are used with a patient known or suspected to be infected with HBV, HIV, or *M. tuberculosis* [17, 179]. This is inconsistent with the concept of Standard Precautions that presumes that all patients are potentially infected with bloodborne pathogens [169]. Several studies have highlighted the inability to distinguish HBV- or HIV-infected patients from noninfected patients on clinical grounds [180-182]. It also is likely that mycobacterial infection will not be clinically apparent in many patients. In most instances, hospitals that altered their disinfection procedure used ethylene oxide sterilization on the endoscopic instruments because they believed this practice reduced the risk of infection [17, 179]. ETO is not routinely used for endoscope sterilization because of the lengthy processing time. Endoscopes and other semicritical devices should be managed the same way whether or not the patient is known to be infected with HBV, HCV, HIV or *M. tuberculosis*.

An evaluation of a manual disinfection procedure to eliminate HCV from experimentally contaminated endoscopes provided some evidence that cleaning and 2% glutaraldehyde for 20 minutes should prevent transmission [183]. Using experimentally contaminated hysteroscopes, Sartor and colleagues detected HCV by polymerase chain reaction (PCR) in one (3%) of 34 samples following cleaning with a detergent, but no samples were positive following treatment with a 2% glutaraldehyde solution for 20 minutes [184]. Rey and colleagues demonstrated complete elimination of HCV (as detected by PCR) from endoscopes used on chronically infected patients following cleaning and disinfection for 3 to 5 minutes in

glutaraldehyde [185]. Similarly, Chanzy and coworkers used PCR to demonstrate complete elimination of HCV following standard disinfection of experimentally contaminated endoscopes [183]. The inhibitory activity of a phenolic and a chlorine compound on HCV showed that the phenolic inhibited the binding and replication of HCV but the chlorine was ineffective, probably due to its low concentration and its neutralization in the presence of organic matter [186].

Disinfection of Hemodialysis Machines

Hemodialysis systems (includes hemodialysis machines, water supply, water treatment systems, and distribution system) can transmit bloodborne viruses and pathogenic bacteria [187, 188]. Cleaning, disinfection, and sterilization are important components of infection control in a hemodialysis center. The procedures discussed above (i.e., low-level disinfection, high-level disinfection, and sterilization, respectively for noncritical, semicritical and critical) should be applied in the hemodialysis setting.

Disinfection on noncritical surfaces (e.g., dialysis bed or chair, countertops, external surfaces of dialysis machines, and equipment [scissors, hemostats, clamps, blood pressure cuffs, stethoscopes]) should be done with low-level disinfectants unless the item is visibly contaminated with blood in which case a tuberculocidal agent should be used. This procedure accomplishes two goals, i.e., it removes soil on a regular basis and maintains an environment that is consistent with good patient care. Disinfection of hemodialysis systems is normally accomplished by chlorine-based disinfectants (e.g., sodium hypochlorite), aqueous formaldehyde, peracetic acid, or glutaraldehyde. All products must be used according to the manufacturers' recommendations. Some dialysis systems use hot-water disinfection for the control of microbial contamination.

Since about 80% of U.S. chronic hemodialysis centers reprocess (i.e., reuse) dialyzers for the same patient, high-level disinfection or sterilization is also common in dialysis centers. Three chemical sterilants were commonly used in a 1996 survey: a peracetic acid formulation was used by 54% of centers that reused dialyzers, formaldehyde by 36%, and glutaraldehyde by 7%. A heat process [187, 188] was used by 3%. Detailed recommendations regarding disinfection and sterilization (to include the use of dedicated machines for HBsAg-positive patients) in the hemodialysis setting may be found in two reviews [187, 188].

Inactivation of *C. difficile*

The source of healthcare-associated acquisition of *C. difficile* in nonepidemic settings has not been determined. The environment and carriage on the hands of hospital personnel have been considered as possible sources of infection. Carpeted rooms occupied by a patient with *C. difficile* are more heavily contaminated with *C. difficile* than noncarpeted rooms [189]. Since *C. difficile* spores may display increased levels of spore production when exposed to disinfectants and the spores are more resistant than vegetative cells to commonly used surface disinfectants [190], some investigators have recommended the use of dilute solutions of hypochlorite (1600 ppm available chlorine) for routine environmental disinfection of rooms of patients with *C. difficile*-associated diarrhea or colitis [191] or in units with high *C. difficile* rates [192]. Mayfield and co-workers showed a marked reduction in *C. difficile*-associated diarrhea rates in the bone-marrow transplant unit (from 8.6 to 3.3 cases per 1000 patient-days) during the period of bleach disinfection (1:10 dilution) of environmental surfaces compared to cleaning with a quaternary ammonium compound (QUAT). Thus, use of a diluted hypochlorite should be considered in units with high *C. difficile* rates. However, studies have shown that asymptomatic patients constitute an important reservoir within the hospital and that person-to-person transmission is the principal means of transmission between patients. Thus, handwashing, barrier precautions, and meticulous environmental cleaning with a low-level disinfectant (e.g. germicidal detergent) should be effective in preventing the spread of the organism [193].

Contaminated medical devices such as colonoscopes can serve as vehicles for the transmission of *C. difficile* spores. For this reason, investigators have studied commonly used disinfectants and exposure times to assess whether current practices may be placing patients at risk. Data demonstrate that 2% glutaraldehyde reliably kills *C. difficile* spores using exposure times of 5 to 20 minutes [59, 194, 195].

Inactivation of Creutzfeldt-Jakob Disease Agent

Creutzfeldt-Jakob disease is a degenerative neurologic disorder of humans with an incidence in the United States of approximately 1 case/million population/year [196, 197]. CJD is caused by a proteinaceous infectious agent or prion. CJD is similar to other human transmissible spongiform encephalopathies (TSEs) that include kuru (0 incidence, now eradicated), Gertsmann-Straussler-Sheinker syndrome (1/billion), and fatal insomnia syndrome (<1/billion). Prion diseases do not elicit an immune response, result in a noninflammatory pathologic process confined to the central nervous system, have a long incubation period, and usually are fatal within 1 year.

Recently, a new variant form of CJD (vCJD) has been recognized that is acquired from cattle with bovine spongiform encephalopathy (BSE, or mad-cow disease). A total of 105 human cases have been diagnosed (101 cases in England, 3 in France, and 1 in Ireland)[198 199] by early June 2001. Compared with CJD patients, vCJD patients are younger (29 vs. 65 years of age), have a longer duration of illness (14 vs. 4.5 months), and present with sensory and psychiatric symptoms that are uncommon with CJD. To date, variant CJD has not been reported in the United States.

The agents of CJD and other TSEs exhibit an unusual resistance to conventional chemical and physical decontamination methods. Since the CJD agent is not readily inactivated by conventional disinfection and sterilization procedures and because of the invariably fatal outcome of CJD, the procedures for disinfection and sterilization of the CJD prion have been both conservative and controversial for many years.

CJD occurs as both a sporadic and familial disease. Less than 1% of CJD episodes result from person-to-person transmission, which primarily as a results from iatrogenic exposure. Iatrogenic CJD has been described in humans in three circumstances: after use of contaminated medical equipment (2 confirmed cases); after use of extracted pituitary hormones (>100 cases); and after implant of contaminated grafts from humans (cornea-3, dura mater >110)[200, 201]. All known instances of iatrogenic CJD have resulted from exposure to infectious brain, pituitary, or eye tissue. Tissue infectivity studies in experimental animals have determined the infectiousness of different body tissues (Table 3)[202, 203]. Transmission via stereotactic electrodes is the only convincing example of transmission via a medical device. The electrodes had been implanted in a patient with known CJD and then cleaned with benzene and "sterilized" with 70% alcohol and formaldehyde vapor. Two years later, these electrodes were retrieved and implanted into a chimpanzee in which the disease developed [204]. The method used to "sterilize" these electrodes would not currently be considered an adequate method for sterilizing medical devices. The infrequent transmission of CJD via contaminated medical devices probably reflects the inefficiency of transmission unless dealing with neural tissue and the effectiveness of conventional cleaning and current disinfection and sterilization procedures [205]. Retrospective studies suggest four other episodes may have resulted from use of contaminated instruments in neurosurgical operations. All six cases of CJD associated with neurosurgical instruments occurred in Europe between 1953 and 1976 and details of the reprocessing methods for the instruments are incomplete (LM Sehulster 2000, written communication). There are no known episodes of CJD attributable to the reuse of devices contaminated with blood or via transfusion of blood products. The risk of occupational transmission of CJD to a healthcare worker is remote. Healthcare workers should use standard precautions when caring for patients with CJD.

To minimize the possibility of use of neurosurgical instruments that have been potentially contaminated during procedures performed on patients in whom CJD is later diagnosed, hospitals should consider using the sterilization guidelines outlined below for neurosurgical instruments used during brain biopsy

done on patients in whom a specific lesion has not been demonstrated (e.g., by magnetic resonance imaging and computerized tomography scans). Alternatively, neurosurgical instruments used in such patients could be disposable [205].

The inactivation of prions by disinfectant and sterilization processes has been studied by several investigators but these studies do not reflect the reprocessing procedures in a clinical setting. First, these studies have not incorporated a cleaning procedure that normally reduces microbial contamination by 4 $\log_{10}$ [10]. Second, the prion studies have been done with tissue homogenates and the protective effect of tissue may explain, in part, why the CJD agent is difficult to inactivate [206]. Brain homogenates have been shown to confer thermal stability to small subpopulations of the scrapie agent and some viruses. Third, results of inactivation studies of prions have been inconsistent due to the use of differing methodologies, which may have varied by prion strain, prion concentration, test tissue (intact brain tissue, brain homogenates, partially purified preparations), test animals, duration of follow-up of inoculated animals, exposure container, method of calculating log-reductions in infectivity, concentration of the disinfectant at the beginning and end of an experiment, cycle parameters of the sterilizer, and exposure conditions. Despite these limitations, there is some consistency in the results [205, 207].

Based on the disinfection studies many, but not all, disinfection processes fail to inactivate clinically significant numbers of prions (Table 4)[208-220]. There are four chemicals that reduce the prion titer by >3 $\log_{10}$ in 1 hour: chlorine, a phenolic, guanidine thiocyanante, and sodium hydroxide. Of these four chemical compounds, chlorine provides the most consistent prion inactivation results [205]. However, the corrosive nature of chlorine makes it unsuitable for semicritical devices such as endoscopes.

Prions also exhibit an unusual resistance to conventional physical decontamination methods (Table 5). While there is some disagreement on the ideal time and temperature cycle for autoclaving, the recommendation for 134°C for $\geq$18 minutes (prevacuum) and 121°-132°C for 60 minutes (gravity) are based on the scientific literature [210-212, 214, 220]. Some investigators also have found that combining sodium hydroxide (e.g., 0.09N for 2 hr) with steam sterilization for 1 hour at 121°C results in complete loss of infectivity [214]. However, the combination of sodium hydroxide and steam sterilization may be deleterious to surgical instruments [207] and sterilizers.

The disinfection and sterilization recommendations for CJD in this guideline are based on the belief that infection control measures should be predicated on epidemiologic evidence linking specific body tissues or fluids to transmission of CJD, infectivity assays demonstrating that body tissues or fluids are contaminated with infectious prions [6, 221](LM Sehulster, written communication, 2000), cleaning data using standard biological indicators, inactivation data of prions, the risk of disease transmission with the use of the instrument or device, and a review of other recommendations. Other CJD recommendations have been based primarily on inactivation studies [10, 207, 222]. Thus, the three parameters integrated into disinfection and sterilization processing are the risk of the patient for having a prion disease, the comparative infectivity of different body tissues, and the intended use of the medical device [6, 221, 223](LM Sehulster, written communication, 2000). High-risk patients include those with known prion disease, rapidly progressive dementia, possible prion disease, or a history of dura mater transplants or human growth hormone injection. High-risk tissues include brain, spinal cord, and eye. All other tissues are considered low or no risk (Table 3). Critical devices are defined as devices that enter sterile tissue or the vascular system (e.g. implants). Semicritical devices are defined as devices that contact nonintact skin or mucous membranes (e.g., endoscopes).

Recommendations for disinfection and sterilization of prion-contaminated medical devices are as follows. For high-risk tissues, high-risk patients, and critical or semicritical medical devices, clean the device and sterilize by autoclaving at 134°C for 18 minutes in a prevacuum sterilizer or 121-132°C for 1 hour in a gravity displacement sterilizer. Alternatively, a combination of sodium hydroxide and autoclaving could be employed as recommended by The World Health Organization (WHO)[200]. This procedure might produce a reaction that could be harmful to human health and damaging to the steam sterilizer. Persons who use this procedure should be cautious in handling hot sodium hydroxide (post autoclave) or having

potential exposure to gaseous sodium hydroxide. Prion-contaminated medical devices that are impossible or difficult to clean can be discarded. Flash sterilization should not be used for reprocessing. Environmental surfaces (noncritical) contaminated with high-risk tissues (e.g., laboratory surfaces) should be cleaned and then spot decontaminated with a 1:10 dilution of bleach.

For medium- or low-risk tissues, high-risk patients, and critical or semicritical devices, use standard conventional protocols of heat or chemical sterilization, or high-level disinfection. Environmental surfaces contaminated with medium- or low-risk tissues require only standard (i.e., blood-contaminated) disinfection [6, 205, 221]. Since noncritical surfaces are not involved in disease transmission, the normal exposure time (≤10 minutes) is recommended.

The aforementioned precautions are recommended for hospitals providing healthcare to adults (>16 years old). Children's' hospitals would not need to follow the CJD control measures as the disease in not described in this age group with the possible exception of children who received human growth hormone.

OSHA Bloodborne Pathogen Standard

In December 1991, the Occupational Safety and Health Administration (OSHA) promulgated a standard entitled "Occupational Exposure to Bloodborne Pathogens" to eliminate or minimize occupational exposure to bloodborne pathogens [224]. One component of this requirement is that all equipment and environmental and working surfaces be cleaned and decontaminated with an appropriate disinfectant after contact with blood or other potentially infectious materials. While the OSHA standard does not specify the type of disinfectant or procedure, the OSHA compliance document [225] suggests that a germicide must be tuberculocidal to kill the HBV. Thus, it suggests that a tuberculocidal agent should be used to clean blood spills on noncritical surfaces. This is inconsistent with data that demonstrate that nontuberculocidal quaternary ammonium compounds inactivate the hepatitis B virus [170]. Nonetheless, to follow the OSHA compliance document a tuberculocidal disinfectant (e.g., phenolic, and chlorine) would be needed to clean a blood spill. This caused concern among housekeeping managers who tried to find disinfectant detergents claiming to be tuberculocidal on the assumption that such products would be effective in eliminating transmission of Hepatitis B virus. This directive could be questioned on a practical level for three reasons. First, non-tuberculocidal disinfectants such as quaternary ammonium compounds inactivate the hepatitis B virus [170]. Second, noncritical surfaces are rarely, if ever, involved in disease transmission [35]. Third, the exposure times that manufacturers use in order to achieve their label claims are not employed in healthcare settings to disinfect noncritical surfaces. For example, in order to make a label claim against HBV, HIV, or TB a manufacturer must demonstrate inactivation of these organisms when exposed to a disinfectant for 10 minutes. This cannot be practically achieved for disinfection of environmental surfaces in a healthcare setting.

In February 1997, OSHA amended its policy and stated that EPA-registered disinfectants that are labeled as effective against HIV and HBV would be considered as appropriate disinfectants "...provided such surfaces have not become contaminated with agent(s) or volumes of or concentrations of agent(s) for which higher level disinfection is recommended." Thus, when bloodborne pathogens other than HBV or HIV are of concern, OSHA continues to require the use of EPA-registered tuberculocidal disinfectants or bleach solution (diluted 1:10 or 1:100 with water)[226]. Recent studies demonstrate that, in the presence of blood spills, a 1:10 final dilution of bleach should be used to inactivate bloodborne viruses [178, 227].

Emerging Pathogens (*Cryptosporidium, Helicobacter pylori, Escherichia coli* O157:H7, Human Papilloma Virus, Norwalk Virus)

Emerging pathogens are of growing concern to the general public and infection control professionals. Relevant pathogens include *Cryptosporidium parvum, Helicobacter pylori, E. coli* O157:H7, HIV, HCV, multidrug-resistant *M. tuberculosis*, and nontuberculosis mycobacteria (e.g., *M. chelonae*). The

susceptibility of each of these pathogens to chemical sterilants has been studied. With the exceptions discussed below, all of these emerging pathogens are susceptible to currently available chemical sterilants [228].

Cryptosporidium is resistant to chlorine at concentrations used in potable water. *C. parvum* is not completely inactivated by most disinfectants used in healthcare including ethyl alcohol [229], glutaraldehyde [229, 230], 5.25% hypochlorite [229], peracetic acid [229], ortho-phthalaldehyde [229], phenol [229, 230], povidone-iodine [229, 230], and quaternary ammonium compounds [229]. The only chemical disinfectants/sterilants able to inactivate greater than 3 $\log_{10}$ of *C. parvum* were 6% and 7.5% hydrogen peroxide [229]. Sterilization methods will fully inactivate *C. parvum,* including steam [229], ethylene oxide [229, 231], and hydrogen peroxide gas plasma [229]. Although most disinfectants are ineffective against *C. parvum*, current cleaning and disinfection practices appear satisfactory to prevent healthcare-associated transmission. For example, endoscopes are unlikely to represent an important vehicle for the transmission of *C. parvum* because mechanical cleaning will remove approximately 10^4 organisms and drying rapidly results in loss of *C. parvum* viability (e.g., 30 minutes, 2.9 $\log_{10}$ decrease, and 60 minutes, 3.8 $\log_{10}$ decrease)[229].

Chlorine at ~1 ppm has been found capable of eliminating approximately 4 $\log_{10}$ of *E. coli* O157:H7 within 1 minute in a suspension test [232]. Electrolyzed oxidizing water at 23°C was effective in 10 minutes in producing a 5-$\log_{10}$ decrease in *E. coli* O157:H7 inoculated onto kitchen cutting boards [233]. The following disinfectants eliminated >5 $\log_{10}$ of *E. coli* O157:H7 within 30 seconds: a quaternary ammonium compound, a phenolic, a hypochlorite (1:10 dilution of 5.25% bleach), and ethanol [234]. Disinfectants including chlorine compounds are able to reduce *E. coli* O157:H7 experimentally inoculated onto alfalfa seeds or sprouts [235, 236] or beef carcass surfaces [237].

Only limited data are available on the susceptibility of *H. pylori* to disinfectants. Using a suspension test, Akamatsu and colleagues assessed the effectiveness of a variety of disinfectants against nine strains of *H. pylori* [238]. Ethanol (80%) and glutaraldehyde (0.5%) killed all strains within 15 seconds; chlorhexidine gluconate (0.05%, 1.0%), benzalkonium chloride (0.025%, 0.1%), alkyldiaminoethylglycine hydrochloride (0.1%), povidone-iodine (0.1%), and sodium hypochlorite (150 ppm) killed all strains within 30 seconds. Both ethanol (80%) and glutaraldehyde (0.5%) retained similar bactericidal activity in the presence of organic matter while the other disinfectants showed reduced bactericidal activity. In particular, the bactericidal activity of povidone-iodine (0.1%) and sodium hypochlorite (150 ppm) was markedly decreased in the presence of dried yeast solution with killing times increased to 5 to 10 minutes and 5 to 30 minutes, respectively.

Immersion of biopsy forceps in formalin before obtaining a specimen does not affect the ability to culture *H. pylori* from the biopsy specimen [239]. The following methods have been demonstrated to be ineffective for eliminating *H. pylori* from endoscopes: cleaning with soap and water [240, 241], immersion in 70% ethanol for 3 minutes [242], instillation of 70% ethanol [92], instillation of 30 ml of 83% methanol [240], and instillation of 0.2% Hyamine solution [243]. The differing results with regard to the efficacy of ethyl alcohol are unexplained. Cleaning followed by use of 2% alkaline glutaraldehyde (or automated peracetic acid) has been demonstrated by culture to be effective in eliminating *H. pylori* [240, 241, 244]. Epidemiologic investigations of patients who had undergone endoscopy with endoscopes mechanically washed and disinfected with 2.0 to 2.3% glutaraldehyde have revealed no evidence of cross-transmission of *H. pylori* [92, 245]. Disinfection of experimentally contaminated endoscopes using 2% glutaraldehyde (10 minutes, 20 minutes, 45 minutes exposure times) or the peracetic acid system (with and without active peracetic acid) has been demonstrated to be effective in eliminating *H. pylori* [241]. *H. pylori* DNA has been detected by PCR in fluid flushed from endoscope channels following cleaning and disinfection with 2% glutaraldehyde [246]. The clinical significance of this finding is unclear. *In vitro* experiments have demonstrated a >3.5-$\log_{10}$ reduction in *H. pylori* after exposure to 0.5 mg/L of free chlorine for 80 seconds [247].

There are no data on the inactivation of human papillomavirus by alcohol or other disinfectants because *in vitro* replication of complete virions has not been achieved. Similarly, little is known about the

inactivation of Norwalk virus and Norwalk virus-like particles (members of the family *Caliciviridae* and important causes of gastroenteritis in humans) as they cannot be grown in tissue culture. Inactivation studies with a closely related cultivable virus (i.e., feline calicivirus) have shown the effectiveness of chlorine, glutaraldehyde, and iodine-based products whereas the QUAT, detergent, and ethanol failed to inactivate the virus completely [248].

Toxicological and Environmental Concerns

Health hazards associated with the use of germicides in healthcare vary from mucous membrane irritation to death, with the latter to date involving accidental injection by mentally disturbed patients [249]. While variations exist in the degree of toxicity [250-252], all disinfectants should be used for the intended purpose only.

The key factors associated with assessing the health risk of a chemical exposure include the duration, intensity (i.e., how much chemical is involved), and route (e.g., skin, mucous membranes, and inhalation) of the exposure Toxicity may be acute or chronic. Acute toxicity usually results from an accidental spill of a chemical substance. The exposure of personnel is sudden and often produces an emergency situation. Chronic toxicity results from repeated exposure to low levels of the chemical over a prolonged period. The responsibility for informing workers of the chemical hazards in the workplace and implementing control measures rests with the employer. The OSHA Hazard Communication Act (29 CFR 1910.1200, 1915.99, 1917.28, 1918.90, 1926.59, and 1928.21) requires manufacturers and importers of hazardous chemicals to develop Material Safety Data Sheets (MSDSs) for each chemical or mixture of chemicals. Employers must have MSDSs readily available to employees who work with the products and thus may be exposed.

Exposure limits have been published for many chemicals used in healthcare to aid in providing a safe environment and are discussed in each section of this guideline as relevant. Exposures below the “limit” are believed to represent an insignificant hazard in the workplace. Only the exposure limits published by OSHA carry the legal force of regulations. OSHA publishes a limit as a time weighted average, that is, the average concentration for a normal 8-hour work day and a 40-hour work week to which nearly all workers may be repeatedly exposed to a chemical without adverse health effects. For example, the TWA for ethylene oxide is 1.0 ppm. Guidelines on exposure limits are also provided by the American Conference of Governmental Industrial Hygienists (ACGIH) [253].

Some states have excluded the disposal of certain chemical germicides (e.g., glutaraldehyde, formaldehyde, and phenol) or limited certain concentrations via the sewer system. These rules are intended to minimize environmental harm. If hospitals exceed the maximum allowable concentration for a chemical (e.g., ≥5.0 mg/l), they have three options. First, they can switch to alternative products. For example, they can change from glutaraldehyde to another disinfectant for high-level disinfection or from phenolics to quaternary ammonium compounds (QUAT) for low-level disinfection. Second, the hospital can collect the disinfectant and dispose of it as a hazardous chemical. Third, they can use a commercially available small-scale treatment method (e.g., neutralize glutaraldehyde with glycine).

The safe disposal of glutaraldehyde is important throughout the medical community. In the case of disposal of large volumes of spent solutions, users may decide to neutralize the microbicidal activity of glutaraldehyde prior to disposal. This can be accomplished by reaction with sodium bisulfite [254] or glycine.

European authors have suggested that disinfection by heat rather than chemicals should be used for instruments and ventilation therapy equipment. The concerns for chemical disinfection include the toxic side-effects for the patient caused by chemical residues on the instrument or object; occupational exposure to toxic chemicals; and the danger of recontamination by rinsing the disinfectant with microbially contaminated tap water [255].

Disinfection in Ambulatory Care, Home Care, and the Home

With the advent of managed healthcare, increasing numbers of patients are now being cared for in ambulatory care and in home settings. Many patients cared for in these settings may have communicable diseases, immunocompromising conditions, or invasive devices. Therefore, adequate disinfection in these settings is necessary to provide a safe patient environment. Since the ambulatory care setting (i.e., outpatient facilities) setting provides the same infection risk as the hospital setting, the Spaulding classification scheme described in this guideline should be followed (Table 1)[10].

The home environment should be a much safer setting than hospitals or ambulatory care. Epidemics should not be a problem and cross-infection should be rare. Among the products recommended for home disinfection use are bleach, alcohol, and hydrogen peroxide. It has been recommended that reusable objects (e.g., tracheostomy tubes) that touch mucous membranes be disinfected by immersion in a 1:2 dilution of household bleach (6.00%-6.15% sodium hypochlorite) for 1-3 minutes, 70% isopropyl alcohol for 5 minutes, or 3% hydrogen peroxide for 30 minutes. Noncritical items (e.g., blood pressure cuffs, crutches) can be cleaned with a detergent. Blood spills should be handled as per OSHA regulations as described in a previous section. In general, sterilization of critical items is not practical in homes but theoretically could be accomplished by chemical sterilants or boiling. Single-use disposable items can be used or reusable items sterilized in a hospital [256, 257].

Some environmental groups advocate “environmentally safe” products as alternatives to commercial germicides in the home-care setting. These alternatives (e.g., ammonia, baking soda, vinegar, Borax, liquid detergent) are not registered with the EPA and are a poor choice for disinfecting because they are ineffective against *S. aureus*. Borax, baking soda, and detergents are also ineffective against *Salmonella typhi* and *E.coli*; however, undiluted vinegar and ammonia are effective against *S. typhi* and *E.coli* [234, 258, 259]. Common commercial disinfectants designed for home use have also been found effective against selected antibiotic-resistant bacteria [234].

Public concerns have been raised that the use of antimicrobials in the home may promote the development of antibiotic-resistant bacteria [260, 261]. This issue is unresolved and needs to be considered further via scientific and clinical investigations. While the public health benefits resulting from the use of disinfectants in the home environment are unknown, it is known that many sites in the home kitchen and bathroom are microbially contaminated [262] and the use of hypochlorites results in a marked reduction of bacteria [263]. It is also known from laboratory studies that many commercially prepared household disinfectants are effective against common pathogens [234] and can interrupt surface-to-human transmission of pathogens [41]. The “targeted hygiene concept,” which means identifying situations and areas (e.g., food preparation surfaces and bathroom) where there is a risk of transmission of pathogens, may be a reasonable way to identify when disinfection may be appropriate [264].

Susceptibility of Antibiotic-Resistant Bacteria to Disinfectants

As with antibiotics, reduced susceptibility (or acquired resistance) of bacteria to disinfectants can arise by either chromosomal gene mutation or the acquisition of genetic material in the form of plasmids or transposons [265-269]. When there is a change in bacterial susceptibility that renders an antibiotic ineffective against an infection previously treatable by that antibiotic, the bacteria are referred to as “resistant.” In contrast, reduced susceptibility to disinfectants does not correlate with failure of the disinfectant because concentrations used in disinfection still greatly exceed the cidal level. Thus, the word "resistance" when applied to these changes is incorrect and the preferred term is reduced susceptibility or increased tolerance [267, 270].

Methicillin-resistant *S. aureus* (MRSA) and vancomycin-resistant *Enterococcus* (VRE) are recognized as important healthcare-associated agents. It has been known for years that some antiseptics and disinfectants are, on the basis of MICs, somewhat less inhibitory to *S. aureus* strains that contain a plasmid carrying gene encoding resistance to the antibiotic gentamicin [267]. For example, Townsend et al. found that gentamicin resistance also encodes reduced susceptibility to propamidine, quaternary ammonium compounds, and ethidium bromide [271], and Brumfitt and associates found MRSA strains less susceptible than methicillin-sensitive *S. aureus* (MSSA) strains to chlorhexidine, propamidine, and the quaternary ammonium compound cetrimide [272]. Al-Masaudi et al. found the MRSA and MSSA strains to be equally sensitive to phenols and chlorhexidine, but MRSA strains were slightly more tolerant to quaternary ammonium compounds [273]. Studies have established the involvement of two gene families (*qac*CD [now referred to as *smr*] and *qac*AB) in providing protection against agents that are components of disinfectant formulations such as quaternary ammonium compounds. Tennant and coworkers propose that staphylococci evade destruction because the protein specified by the *qac*A determinant is a cytoplasmic-membrane-associated protein involved in an efflux system that actively reduces intracellular accumulation of toxicants such as quaternary ammonium compounds to intracellular targets [274].

Other studies demonstrated that plasmid-mediated formaldehyde resistance is transferable from *Serratia marcescens* to *E. coli* [275] and plasmid-mediated quaternary ammonium resistance is transferable from *S. aureus* to *E. coli* [276]. Tolerance to mercury and silver is also plasmid borne [265-269].

Since the concentrations of disinfectants used in practice are much higher than the MICs observed, even for the more tolerant strains, the clinical relevance of these observations is questionable. Several studies have found antibiotic-resistant hospital strains of common healthcare-associated pathogens (i.e., *Enterococcus, P. aeruginosa, Klebsiella pneumoniae, E. coli*, *S. aureus,* and *S. epidermidis*) to be equally susceptible to disinfectants as antibiotic-sensitive strains [234, 277, 278]. The susceptibility of glycopeptide-intermediate *S. aureus* was similar to vancomycin-susceptible, methicillin-resistant *S. aureus* [279]. Based on these data, routine disinfection and housekeeping protocols do not need to be altered because of antibiotic resistance provided the disinfection method is effective [280, 281]. A recent study that evaluated the efficacy of selected cleaning methods (e.g., QUAT-sprayed cloth, and QUAT-immersed cloth) for eliminating VRE found that currently used disinfection processes are likely highly effective in eliminating VRE. However, surface disinfection must involve contact with all contaminated surfaces [280].

Lastly, does the use of antiseptics or disinfectants facilitate the development of disinfectant-tolerant organisms? Based on current evidence and reviews [260, 261, 269, 270, 282], the development of enhanced tolerance to disinfectants in response to disinfectant exposure can occur. However, it is not important in clinical terms since the level of tolerance is low and unlikely to compromise the effectiveness of disinfectants where much higher concentrations are used [270].

The issue of whether low-level tolerance to germicides selects for antibiotic-resistant strains is unsettled but may depend on the mechanism by which tolerance is attained. For example, changes in the permeability barrier or efflux mechanisms may affect susceptibility to antibiotics and germicides but specific changes to a target site may not. Some researchers have suggested that the use of disinfectants or antiseptics (e.g., triclosan) could facilitate the development of antibiotic-resistant microorganisms [260, 261, 283]. While there is evidence in laboratory studies of low-level resistance to triclosan, the concentrations of triclosan in these studies were low (generally <1 ug/ml) and dissimilar from the higher levels used in antimicrobial products (2,000-20,000 ug/ml)[284, 285]. Thus, researchers can create laboratory-derived mutants that demonstrate reduced susceptibility to antiseptics or disinfectants. In some experiments, such bacteria have demonstrated reduced susceptibility to certain antibiotics [261]. There is no evidence that using antiseptics/disinfectants selects for antibiotic-resistant organisms in nature or that mutants survive in nature [286]. In addition, there are fundamental differences between the action of antibiotics and disinfectants. Antibiotics are selectively toxic and generally have a single target site in bacteria, thereby inhibiting a specific biosynthetic process. Germicides generally are considered to be nonspecific antimicrobials because of a multiplicity of toxic effect mechanisms or target sites and are

broader spectrum in the types of microorganisms against which they are effective [267, 270].

The rotational use of disinfectants in some environments (e.g., pharmacy production units) has been recommended in an attempt to prevent the development of resistant microbes. Currently, there appears to be no evidence that appropriately used disinfectants have resulted in a clinical problem arising from the selection or development of nonsusceptible microorganisms [287].

Surface Disinfection: Should We Do It?

The effective use of disinfectants constitutes an important factor in preventing healthcare-associated infections. Surfaces are considered noncritical items as they come in contact with intact skin. Use of noncritical items or contact with noncritical surfaces carries little risk of transmitting a pathogen to patients or staff. Thus, the routine use of germicidal chemicals to disinfect hospital floors and other noncritical items is controversial. In 1991, Favero and Bond provided a useful expansion of the Spaulding scheme by dividing the noncritical environmental surfaces into housekeeping surfaces and medical equipment surfaces [288]. Medical equipment surfaces (e.g., blood pressure cuffs, stethoscopes, hemodialysis machines, and x-ray machines) may become contaminated with infectious agents and have been incriminated in the spread of healthcare-associated infections. For this reason noncritical medical equipment surfaces should be disinfected with a low- or intermediate-level disinfectant. Use of a disinfectant will provide antimicrobial activity that is likely to be achieved with minimal additional cost or work.

Environmental surfaces also may potentially contribute to cross-transmission by hand contamination of healthcare personnel due to contact with contaminated surfaces, medical equipment, or patients [289, 290]. A recent paper reviews the epidemiological and microbiological data (see Table 6) regarding the use of disinfectants on noncritical surfaces [291].

Table 6 lists seven reasons for using a disinfectant on noncritical surfaces. Four of these are particularly noteworthy and support the use of a germicidal detergent. First, hospital floors become contaminated with microorganisms by settling of airborne bacteria: by contact with shoes, wheels, and other objects; and occasionally by spills. The removal of microbes is a component in the control of healthcare-associated infections. In an investigation on the cleaning of hospital floors, the use of soap and water (80% reduction) was less effective in reducing the numbers of bacteria than was a phenolic disinfectant (90% reduction)[292]. However, a few hours after floor disinfection the bacterial count was nearly back to the pretreatment level. Second, detergents become contaminated and result in seeding the patient's environment with bacteria. Investigators have shown that mop water becomes increasingly dirty during cleaning, and mop water becomes contaminated if soap and water is used rather than a disinfectant. For example, Ayliffe and co-workers found that bacterial contamination in soap and water without a disinfectant increased from 10 CFU/ml to 34,000 CFU/ml after cleaning a ward while the contamination in a disinfectant solution did not change (20 CFU/ml)[293]. Dharan and associates also found that the use of detergents on floors and patient room furniture increased the bacterial contamination in the patients' environmental surfaces after cleaning (average increase = 103.6 CFU/24cm^2)[294]. Third, CDC recommends in their Isolation Guideline that noncritical equipment contaminated with blood, body fluids, secretions, or excretions be cleaned and disinfected after use. The same guideline recommends that, in addition to cleaning, disinfection of the bedside equipment and environmental surfaces (e.g., bedrails, bedside tables, carts, commodes, door-knobs, and faucet handles) is indicated for certain pathogens, especially enterococci, which can survive in the inanimate environment for prolonged periods [295]. Fourth, using a single product throughout the facility may simplify both training and appropriate practice.

There also are reasons for using a detergent alone on floors since noncritical surfaces contribute minimally to endemic healthcare-associated infections [296], and there are no differences in healthcare-

associated infections rates when floors are cleaned with detergent versus disinfectant [294, 297, 298].

Since housekeeping surfaces are associated with the lowest risk of disease transmission, some have suggested that either detergents or a disinfectant detergent could be used [288]. While there are no data that demonstrate a reduction in healthcare-associated infection rates with the use of surface disinfection of floors, there are data that demonstrate a reduction in microbial load associated with the use of disinfectants. Given this information and that environmental surfaces (e.g., bedside table, bed rails) in close proximity to the patient and in outpatient settings [299] have been demonstrated to become contaminated with epidemiologically important microbes such as VRE and MRSA [40, 299-301] and these organisms survive on various hospital surfaces [302, 303], these surfaces should be disinfected on a regularly scheduled basis. Spot contamination on fabrics that remain in hospitals or clinic rooms while patients move in and out (e.g., privacy curtains) also should be considered. One study demonstrated the effectiveness of spraying the fabric with 3% hydrogen peroxide [304]. Future studies should evaluate the level of contamination on noncritical environmental surfaces as a function of high and low hand contact and whether some surfaces (e.g., bedrails) near the patient with high contact frequencies require more frequent disinfection. Regardless of whether a detergent or disinfectant is used on surfaces in a healthcare facility, cleaning should be undertaken on a routine basis and when environmental surfaces are dirty or soiled in order to provide an aesthetically pleasing environment and to prevent potentially contaminated objects from serving as a source for healthcare-associated infections [305]. The value of designing surfaces (e.g. hexyl-polyvinylpyridine) that kill bacteria on contact or have sustained antimicrobial activity [306] should be further evaluated [307].

Heavy microbial contamination of wet mops and cleaning cloths and the potential for spread of such contamination have been recognized by several investigators [44, 308]. They have shown that wiping hard surfaces with contaminated cloths may result in contamination of hands, equipment, and other surfaces [44, 309]. Data have been published that can be used to formulate effective policies for decontamination and maintenance of reusable cleaning cloths. For example, heat was the most reliable treatment of cleaning cloths as a detergent washing followed by drying at 80°C for 2 hours produced elimination of contamination. Alternatively, immersing the cloth in hypochlorite (4000 ppm) for 2 minutes produced no detectable survivors in 10 of 13 cloths [310]. If reusable cleaning cloths or mops are used, decontamination should occur regularly to prevent surface contamination during cleaning with subsequent transfer of organisms from these surfaces to patients or equipment via the hands of healthcare workers.

Air Disinfection

The use of a disinfectant spray-fog technique for antimicrobial control of hospital rooms has been used. This technique of spraying of disinfectants is an unsatisfactory method of decontaminating air and surfaces and is not recommended for general infection control in routine patient-care areas [295]. Disinfectant fogging is rarely, if ever, used in United States healthcare facilities for air and surface disinfection in patient-care areas.

Microbial Contamination of Disinfectants

Contaminated disinfectants and antiseptics have been occasional vehicles of hospital infections and pseudoepidemics for more than 50 years. A summary of the published reports describing contaminated disinfectants and antiseptic solutions leading to healthcare-associated infections has been published [311]. Since this summary additional reports have been published [312-314]. When examining the reports of disinfectants found contaminated with microorganisms there are several noteworthy observations. Perhaps most importantly, members of the genus *Pseudomonas* (e.g., *P. aeruginosa*) are the most frequent isolates from contaminated disinfectants, being the agents recovered from 80% of the contaminated products. Their ability to remain viable or grow in use-dilutions of disinfectants is unparalleled. This survival advantage for *Pseudomonas* is presumably due to their nutritional versatility,

their unique outer membrane that constitutes an effective barrier to the passage of germicides, and/or efflux systems. While the concentrated solutions of the disinfectants have not been demonstrated to be contaminated at the point of manufacture, Newman et al. found that an undiluted phenolic may be contaminated by a *Pseudomonas* sp. during use [315]. In most of the reports that describe illness associated with contaminated disinfectants, the product was used to disinfect patient-care equipment such as cystoscopes, cardiac catheters, and thermometers. The germicides used as disinfectants that were reported contaminated include chlorhexidine, quaternary ammonium compounds, phenolic, and pine.

The following control measures should be instituted to reduce the frequency of bacterial growth in disinfectants and the threat of serious healthcare-associated infections from the use of such contaminated products. First, some disinfectants should not be diluted and those that are must be prepared correctly to achieve the manufacturer's recommended use-dilution. Second, we must learn from the literature what inappropriate activities result in extrinsic contamination (i.e., at the point of use) of germicides and prevent their recurrence. Common sources of extrinsic contamination of germicides in the reviewed literature are the water to make working dilutions, contaminated containers, and general contamination of the hospital areas where the germicides are prepared and/or used. Third, stock solutions of germicides must be stored as indicated on the product label. Fourth, independent laboratories or the EPA should verify manufacturers' efficacy claims against microorganisms. This should provide assurance that products that meet the EPA registration requirements are capable of achieving a certain level of antimicrobial activity when used as directed.

FACTORS AFFECTING THE EFFICACY OF DISINFECTION AND STERILIZATION

The activity of germicides against microorganisms depends on a number of factors, some of which are intrinsic qualities of the organism, while others depend on the chemical and external physical environment. An awareness of these factors should lead to a better utilization of disinfection and sterilization processes; thus they will be briefly reviewed. More extensive consideration of these and other factors may be found in the references for this section [6, 7, 9, 316, 317].

Number and Location of Microorganisms

All other conditions remaining constant, the larger the number of microbes present, the longer it takes for a germicide to destroy all of them. This relationship was illustrated by Spaulding when he employed identical test conditions and demonstrated that it took 30 minutes to kill 10 *B. subtilis* spores but 3 hours to kill 100,000 *B. subtilis* spores. This reinforces the need for scrupulous cleaning of medical instruments before disinfection and sterilization. By reducing the number of microorganisms that must be inactivated, one correspondingly shortens the exposure time required to kill the entire microbial load. Researchers have also shown that aggregated or clumped cells are more difficult to inactivate than monodispersed cells [318].

The location of microorganisms also must be considered when assessing factors affecting the efficacy of germicides. Medical instruments with multiple pieces must be disassembled and equipment such as endoscopes that have crevices, joints, and channels are more difficult to disinfect than a flat- surface equipment because it is more difficult to penetrate all parts of the equipment with a disinfectant. Only surfaces in direct contact with the germicide will be disinfected so there must be no air pockets and the equipment must be completely immersed for the entire exposure period. Manufacturers should be encouraged to produce equipment that is engineered so cleaning and disinfection may be accomplished with ease.

Innate Resistance of Microorganisms

Microorganisms vary greatly in their resistance to chemical germicides and sterilization processes (Figure 1). Intrinsic resistance mechanisms in microorganisms to disinfectants varies. For example, spores are resistant to disinfectants because the spore coat and cortex act as a barrier, mycobacteria have a waxy cell wall that prevents disinfectant entry, and gram-negative bacteria possess an outer membrane that acts as a barrier to the uptake of disinfectants [265-268]. Implicit in all disinfection strategies is the consideration that the most resistant microbial subpopulation controls the sterilization or disinfection time. That is, in order to destroy the most resistant types of microorganisms-bacterial spores, the user needs to employ exposure times and a concentration of germicide needed to achieve complete destruction. With the exception of prions, bacterial spores possess the highest innate resistance to chemical germicides, followed by mycobacteria (e.g., *M. tuberculosis*), nonlipid or small viruses (e.g., poliovirus, and coxsackievirus), fungi (e.g., *Aspergillus,* and *Candida*), lipid or medium-size viruses (e.g., herpes, and HIV), and vegetative bacteria (e.g., *Staphylococcus,* and *Pseudomonas*). The germicidal resistance exhibited by the gram-positive and gram-negative bacteria is similar with the exception of *P. aeruginosa* which shows greater resistance to some disinfectants [319, 320]. *P. aeruginosa* have also been shown to be significantly more resistant to a variety of disinfectants in their "naturally occurring" state as compared to cells subcultured on laboratory media. Rickettsiae, chlamydiae, and mycoplasma cannot be placed in this scale of relative resistance because information on the efficacy of germicides against these agents is limited [321]. Since these microorganisms contain lipid and are similar in structure and composition to other bacteria, it might be predicted that they would be inactivated by the same germicides that destroy lipid viruses and vegetative bacteria. A known exception to this supposition is *Coxiella burnetii* which has demonstrated resistance to disinfectants [322].

Concentration and Potency of Disinfectants

With other variables constant, and with one exception (i.e., iodophors), the more concentrated the disinfectant, the greater its efficacy and the shorter the time necessary to achieve microbial kill. Generally not recognized, however, is that all disinfectants are not similarly affected by concentration adjustments. For example, quaternary ammonium compounds and phenol have a concentration exponent of 1 and 6, respectively; thus halving the concentration of a quaternary ammonium compound requires a doubling of its disinfecting time, but halving the concentration of a phenol solution requires a 64-fold (i.e., 2^6) increase in its disinfecting time [285, 323].

It is also important to consider the length of the disinfection time, which is dependent upon the potency of the germicide. This was illustrated by Spaulding who demonstrated using the mucin-loop test that 70% isopropyl alcohol destroyed 10^4 *M. tuberculosis* in 5 minutes, whereas a simultaneous test with 3% phenolic required 2 to 3 hours to achieve the same level of microbial kill [7].

Physical and Chemical Factors

Several physical and chemical factors also influence disinfectant procedures temperature, pH, relative humidity, and water hardness. For example, the activity of most disinfectants increases as the temperature increases but there are exceptions (e.g., sodium hydroxide). Further, too great an increase in temperature will cause the disinfectant to degrade, weaken its germicidal activity, and produce a potential health hazard.

An increase in pH improves the antimicrobial activity of some disinfectants (e.g. glutaraldehyde, quaternary ammonium compounds) but decreases the antimicrobial activity of others (phenols, hypochlorites, and iodine). The pH influences the antimicrobial activity by altering the disinfectant molecule or the cell surface.

Relative humidity is the single most important factor influencing the activity of gaseous disinfectants such as ethylene oxide and formaldehyde.

Water hardness (i.e., high concentration of divalent cations) reduces the rate of kill of certain disinfectants. This occurs because divalent cations (e.g., magnesium, and calcium) interact with soap to form insoluble precipitates.

Organic and Inorganic Matter

Organic matter in the form of serum, blood, pus, fecal, or lubricant material may interfere with the antimicrobial activity of disinfectants in at least two ways. Most commonly the interference occurs by a chemical reaction between the germicide and the organic matter resulting in a complex that is less germicidal or nongermicidal, leaving less of the active germicide available for attacking microorganisms. Chlorine and iodine disinfectants, in particular, are prone to such interaction. Alternatively, organic material may protect microorganisms from attack by acting as a physical barrier [324].

The effects of inorganic contaminants on the sterilization process were studied in the 1950's and 1960's [325, 326]. These studies and more recent studies show the protection of microorganisms due to occlusion in salt crystals to all sterilization processes [327, 328]. This further emphasizes the importance of meticulous cleaning of medical devices before any sterilization or disinfection procedure since both organic and inorganic soils are easily removed by washing [327].

Duration of Exposure

Items must be exposed to the appropriate germicide for certain minimum contact times to be disinfected. All lumens and channels of endoscopic instruments must come in contact with the disinfectant. Air pockets will interfere with the disinfection process and items floating in the disinfectant will not be disinfected. The disinfectant must be introduced reliably into the internal channels of the device. The exact times for disinfecting medical items are somewhat elusive because of the effect of the aforementioned factors on disinfection efficacy. Contact times that have proved reliable are presented in Table 1, but, in general, the longer contact times are more effective than shorter ones.

Biofilms

Microorganisms may be protected from disinfectants due to the production of thick masses of cells [329] and extracellular materials or biofilms [330-334]. Biofilms are microbial masses attached to surfaces that are immersed in liquids. Once these masses are formed, disinfectants must saturate or penetrate them before they can kill the microorganisms within the biofilm. Investigators have hypothesized that the glycocalyx-like cellular masses on the interior walls of polyvinyl chloride pipe would protect embedded organisms from some disinfectants and serve as a reservoir for continuous contamination [330, 331, 335]. Biofilms have been found in whirlpools [336], dental unit waterlines [337], and numerous medical devices (e.g., contact lenses, pacemakers, urinary catheters, central venous catheters)[338]. Their presence may have serious implications for immunocompromised patients and patients with indwelling medical devices. Enzymes can be used for the degradation of biofilms [339].

CLEANING

Cleaning is the removal of all foreign material (e.g., soil, and organic material) from objects, and it is normally accomplished using water with detergents or enzymatic products. Thorough cleaning is required before high-level disinfection and sterilization since inorganic and organic materials that remain

on the surfaces of instruments interfere with the effectiveness of these processes. Also, if the soiled materials become dried or baked onto the instruments the removal process becomes more difficult and the disinfection or sterilization process less effective or ineffective. Surgical instruments should be presoaked to prevent drying of blood and to soften or remove blood from the instruments.

Cleaning is done manually when the use area does not have a mechanical unit (ultrasonic cleaner or washer-decontaminator/washer-sterilizer) or for fragile or difficult-to-clean instruments. If cleaning is done manually the two essential components are friction and fluidics. Using friction (e.g., rubbing/scrubbing the soiled area with a brush) is an old and dependable method. Fluidics (i.e., fluids under pressure) is used to remove soil and debris from internal channels after brushing and when the design does not allow the passage of a brush through a channel [340].

The three most common types of mechanical or automatic cleaners are ultrasonic cleaners, washer-decontaminators, and washer-sterilizers. Ultrasonic cleaning removes soil by a process called cavitation in which waves of acoustic energy are propagated in aqueous solutions to disrupt the bonds that hold particulate matter to surfaces. Bacterial contamination may be present in used ultrasonic cleaning solutions as these solutions generally do not make antibacterial label claims [341]. Washer-sterilizers are modified steam sterilizers that clean by filling the chamber with water and detergent through which steam is passed to provide agitation. Instruments are subsequently rinsed and subjected to a short steam sterilization cycle. Another washer-sterilizer employs rotating spray arms for a wash cycle followed by a steam sterilization cycle at 285°F [342, 343]. Washer-decontaminators act like a dishwasher that uses a combination of water circulation and detergents to remove soil. These units sometimes have a cycle that subjects the instruments to a heat process (e.g., 93°C for 10 minutes)[344]. Detailed information on cleaning and preparation of supplies for terminal sterilization is provided by professional organizations [345, 346] and books [347]. Studies have shown that manual and mechanical cleaning of endoscopes achieves approximately a 4-$\log_{10}$ reduction of contaminating organisms [63, 76, 348]. Thus, cleaning alone is very effective in reducing the number of microorganisms present on contaminated equipment.

The best choice for instrument cleaning is neutral or near-neutral pH detergent solutions, as these solutions generally provide the best material compatibility profile and good soil removal. Enzymes, usually proteases, are sometimes added to neutral pH detergent solutions to assist in the removal of organic material. Enzymes in these formulations attack proteins that make up a large portion of common soil (e.g., blood, pus). Cleaning solution also can contain lipases (enzymes active on fats) and amylases (enzymes active on starches). Enzymatic detergents are cleaners and not disinfectants and proteinaceous enzymes may be inactivated by germicides. Like all chemicals, enzymes must be rinsed from the equipment or adverse reactions (e.g., fever) could result [349]. Neutral pH detergent solutions that contain enzymes are compatible with metals and other materials used in medical instruments and are the best choice for cleaning delicate medical instruments, especially flexible endoscopes [350]. Some data demonstrate that enzymatic detergents are more effective cleaners that neutral detergents [351, 352]. A new nonenzyme, hydrogen peroxide-based formulation was as effective as enzymatic detergents in removing protein, blood, carbohydrate, and endotoxin from surface test carriers. In addition, this product was able to effect a 5-$\log_{10}$ reduction in microbial loads with a 3-minute exposure at room temperature [353].

Although the effectiveness of high-level disinfection and sterilization mandates effective cleaning, there are no “real-time” tests that can be employed in a clinical setting to validate cleaning. If such tests were available they could be used to ensure that an adequate level of cleaning has been done [354-357]. The only way to ensure adequate cleaning is to conduct a reprocessing validation test (e.g., microbiologic sampling) but this is not routinely recommended. Monitoring of the cleaning processes in a laboratory setting is possible by microorganism detection, chemical detection for organic contaminants, radionuclide tagging, and chemical detection for specific ions [327, 356].

DISINFECTION

A great number of disinfectants are used alone or in various combinations in the healthcare setting. These include alcohols, chlorine and chlorine compounds, formaldehyde, glutaraldehyde, ortho-phthalaldehyde, hydrogen peroxide, iodophors, peracetic acid, phenolics, and quaternary ammonium compounds. With some exceptions (e.g., ethanol or bleach), commercial formulations based on these chemicals are considered unique products and must be registered with the EPA or FDA. In most instances, a given product is designed for a specific purpose and is to be used in a certain manner. Therefore, the label should be read carefully to ensure that the right product is selected for the intended use and applied in an efficient manner.

Disinfectants are not interchangeable and an overview of the performance characteristics of each is provided below so the user has sufficient information to select an appropriate disinfectant for any item and use it in the most efficient way. It should be recognized that excessive costs may be attributed to incorrect concentrations and inappropriate disinfectants. Finally, occupational diseases among cleaning personnel have been associated with the use of several disinfectants such as formaldehyde, glutaraldehyde, chlorine, and others and precautions (e.g., gloves, proper ventilation) should be used to minimize exposure [251, 358, 359].

Chemical Disinfectants

Alcohol

Overview

In the healthcare setting, "alcohol" refers to two water-soluble chemical compounds whose germicidal characteristics are generally underrated: ethyl alcohol and isopropyl alcohol [360]. 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 in the range of 60-90% solutions in water (volume/volume) [361, 362].

Mode of Action

The most feasible explanation for the antimicrobial action of alcohol is denaturation of proteins. This 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 [362, 363]. Protein denaturation also is consistent with the observations by Sykes [364] that alcohol destroys the dehydrogenases of *E. coli* and Dagley and associates [365] that ethyl alcohol increases the lag phase of *Enterobacter aerogenes* and this could be reversed by the addition of certain amino acids. The latter authors concluded that the bacteriostatic action was due to the 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 is seldom used in healthcare [366]. The bactericidal activity of various concentrations of ethyl alcohol (ethanol) was examined by Morton [361] against a variety of microorganisms in exposure periods ranging from 10 seconds to 1 hour. *P. aeruginosa* was killed in 10 seconds by all concentrations of ethanol from 30 to 100% (v/v) while *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 *S. aureus* and *Streptococcus pyogenes* were slightly more resistant, being killed in 10 seconds by ethyl alcohol concentrations from 60 to 95%. Coulthard and Sykes [367] found isopropyl alcohol (isopropanol) slightly more bactericidal than ethyl alcohol for *E. coli* and *S. aureus.*

Ethyl alcohol, at concentrations of 60-80%, is a potent virucidal agent inactivating all of the lipophilic viruses (e.g., herpes, vaccinia, influenza virus) and many hydrophilic viruses (e.g., adeno-, entero-, rhino-, and rotaviruses but not Hepatitis A virus [47]). Isopropyl alcohol is not active against the nonlipid enteroviruses but is fully active against the lipid viruses [49]. Studies also have demonstrated the ability of ethyl and isopropyl alcohol to inactivate the Hepatitis B virus [164, 165] and the herpes virus [368], and ethyl alcohol to inactivate HIV [167], rotavirus, echovirus, and astrovirus [369].

In testing the effect of ethyl alcohol against *M. tuberculosis*, Smith noted that 95% ethanol killed the tubercle bacilli in sputum or water suspension within 15 seconds [370]. 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 were 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 (10^6 *M. tuberculosis* per loop) and determined that 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 for the purpose of producing long survival times. Thus, these figures should not be extrapolated to the exposure times that are needed when these germicides are being used on medical or surgical material [360].

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 to <1 minute for the tissue phase [371, 372].

Isopropyl alcohol (20%) has been shown to be effective in killing the cysts of *Acanthamoeba_culbertsoni* [373] as have chlorhexidine, hydrogen peroxide, and thiomersal [374].

Uses

Alcohols are not recommended for sterilizing medical and surgical materials principally because of their lack of sporicidal action and their inability to penetrate protein-rich materials. Fatal post-operative wound infections with *Clostridium* have occurred when alcohols were used to sterilize surgical instruments contaminated with bacterial spores [375]. Alcohols have been used effectively to disinfect oral and rectal thermometers [376, 377] and fiberoptic endoscopes [378, 379]. 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 is occasionally used to disinfect external surfaces of equipment (e.g., stethoscopes, ventilators, manual ventilation bags [380]), CPR manikins [381], ultrasound instruments [382], or medication preparation areas. Two studies demonstrated the effectiveness of 70% isopropyl alcohol to disinfect reusable transducer heads in a controlled environment [383, 384]. In contrast, Beck-Sague and Jarvis described three bloodstream infection outbreaks when alcohol was used to disinfect transducer heads in an intensive care setting [385].

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 [360], and damage tonometer tips (deterioration of the glue) after the equivalent of one working year of routine use [386]. Lingel and Coffey also found that tonometer biprisms soaked in alcohol for 4 days developed rough front surfaces that could potentially cause corneal damage. This appeared to be caused by a weakening of the cementing substances used to fabricate the biprisms [387]. Corneal opacification has been reported when tonometer tips were swabbed with alcohol immediately before intraocular pressure measurements were taken [388]. Alcohols are flammable and consequently must be stored in a cool, well-ventilated area. They also evaporate rapidly and this makes extended exposure time difficult to achieve unless the items are immersed.

Chlorine and Chlorine Compounds

Overview

Hypochlorites are the most widely used of the chlorine disinfectants and are available in a liquid (e.g., sodium hypochlorite) or solid (e.g., calcium hypochlorite) form. The most prevalent chlorine products in the United States are aqueous solutions of 4 to 6% sodium hypochlorite, which usually are 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 [389], remove dried or fixed organisms and biofilms from surfaces [351], and the low incidence of serious toxicity [390-392]. Sodium hypochlorite at the concentration used in domestic bleach (4-6%) may produce ocular irritation or oropharygeal, esophageal, and gastric burns [251, 393-397]. 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 [398-400], and relative stability [401]. The microbicidal activity of chlorine largely is attributed to undissociated hypochlorous acid (HOCl). The dissociation of hypochlorous acid to the less microbicidal form (hypochlorite ion OCl^-) is dependent on pH. The disinfecting efficacy of chlorine decreases with an increase in pH that parallels the conversion of undissociated hypochlorous acid to hypochlorite ion [402, 403]. A potential hazard is the production of the carcinogen bis-chloromethyl ether when hypochlorite solutions come into contact with formaldehyde [404] and the production of the animal carcinogen trihalomethane when hot water is hyperchlorinated [405]. The EPA has decided after reviewing all environmental fate and ecological data that the currently registered uses of hypochlorites will not result in unreasonable adverse effects to the environment [406].

Alternative compounds that release chlorine and also are used in the hospital setting include demand-release chlorine dioxide, sodium dichloroisocyanurate, and chloramines-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 the microbicidal activity of solutions prepared from sodium dichloroisocyanurate tablets may be greater than that of sodium hypochlorite solutions containing the same total available chlorine for two reasons. First, with sodium dichloroisocyanurate only 50% of the total available chlorine present is free (HOCl and OCl^-) while the remainder is combined (mono- 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 while sodium hypochlorite solutions are alkaline and the more microbicidal type of chlorine (HOCl) is believed to predominate [407-410]. Disinfectants based on chlorine dioxide 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 10^6 of *S. aureus* in 1 minute and of *B. subtilis* spores in 2.5 minutes in the presence of 3 g/l bovine albumin. The potential for damaging equipment (e.g., endoscopes) requires consideration as long-term use can result in damage to the outer plastic coat of the insertion tube [411].

Mode of Action

The exact mechanism by which free chlorine destroys microorganisms has not been elucidated. Inactivation by chlorine may result from a number of factors: oxidation of sulfhydral 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 [270, 403]. The actual microbicidal mechanism of chlorine may involve a combination of these factors or the effect of chlorine on critical sites [270].

Microbicidal Activity

Low concentrations of free chlorine have a biocidal effect on mycoplasma (25 ppm) and vegetative bacteria (<5 ppm) in seconds in the absence of an organic load [321, 403]. Higher concentrations (1000 ppm) of chlorine are required to kill *M. tuberculosis* using the Association of Official Analytical Chemists

(AOAC) tuberculocidal test [50]. A concentration of 100 ppm will kill ≥99.9% of *Bacillus subtilis* spores within 5 minutes [412, 413] and destroy mycotic agents in <1 hour [403]. Klein and Deforest [49] reported that 25 viruses were inactivated in 10 minutes with 200 ppm available chlorine. Several studies have demonstrated the effectiveness of diluted sodium hypochlorite and other disinfectants to inactivate HIV [172]. Chlorine (500 ppm) showed inhibition of *Candida* after 30 sec of exposure [414]. Experiments using the AOAC Use-Dilution Method have shown that 100 ppm of free chlorine will kill 10^6-10^7 *S. aureus*, *Salmonella choleraesuis*, and *P. aeruginosa* in <10 minutes [401]. Since household bleach contains about 6.0% sodium hypochlorite, or 60,000 ppm available chlorine, a 1:1000 dilution provides about 60 ppm available chlorine and a 1:10 dilution of household bleach provides about 6000 ppm.

Some data are available for chlorine dioxide that support manufacturers' bactericidal, fungicidal, sporicidal, tuberculocidal, and virucidal label claims [415-418]. A chlorine dioxide generator has been shown effective for decontamination of flexible endoscopes [411]. Chlorine dioxide contains sodium chlorite and lactic acid in a formulation that is based on the formation of chlorous acid and subsequent release of chlorine dioxide. In 1986 a chlorine dioxide product was voluntarily removed from the market when its use was found to cause cellulose-based dialyzer membranes to leak, which allowed bacteria to migrate from the dialysis fluid side of the dialyzer to the blood side [419].

Sodium dichloroisocyanurate at 2500 ppm available chlorine has been found to be effective against bacteria in the presence of up to 20% plasma compared to 10% plasma for sodium hypochlorite at 2500 ppm [420].

Uses

Hypochlorites are widely used in healthcare facilities in a variety of settings [389]. Inorganic chlorine solution is used for disinfecting tonometer heads [125] and for spot disinfection of counter tops and floors. A 1:10 to 1:100 dilution of 6% sodium hypochlorite (i.e., household bleach)[15, 421, 422] or an EPA-registered tuberculocidal disinfectant [10] 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 6% sodium hypochlorite or an EPA-registered tuberculocidal disinfectant. Since hypochlorites and other germicides are substantially inactivated in the presence of blood [227, 420, 423, 424], 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. If there is a possibility of a sharps injury, there should be an initial decontamination [45, 251], followed by cleaning and terminal disinfection (1:10 final concentration)[227]. Extreme care should always be employed to prevent percutaneous injury. At least 500 ppm available chlorine for 10 minutes is recommended for decontamination of cardiopulmonary resuscitation training manikins [425]. Full-strength bleach is recommended for the disinfection of needles and syringes. 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 [426]. Clinicians should not alter their use of chlorine on environmental surfaces based on testing methodologies that do not simulate actual disinfection practices [427, 428]. Other uses in healthcare include as an irrigating agent in endodontic treatment [429] and for disinfecting manikins, laundry, dental appliances, hydrotherapy tanks, regulated medical waste before disposal, and the water distribution system in hemodialysis centers and hemodialysis machines [389, 430].

Chlorine has long been favored as the preferred disinfectant in water treatment. Hyperchlorination of a *Legionella*-contaminated hospital water system resulted in a dramatic decrease (30% to 1.5%) in the isolation of *L. pneumophila* from water outlets and a cessation of healthcare-associated Legionnaires' disease in the affected unit [405, 431]. Chloramine T [432] and hypochlorites [430] have been shown effective in disinfecting hydrotherapy equipment.

Hypochlorite solutions in tapwater at pH ≥8.0 are stable for a period of 1 month when stored at room temperature (23°C) in closed, opaque plastic containers [401]. The free available chlorine levels of solutions in opened or closed polyethylene containers are maximally reduced to 40-50% of the original

concentration in 1 month. Thus, if a user wished to have a solution containing 500 ppm of available chlorine at day 30, a solution containing 1000 ppm of chlorine should be prepared at time 0. There is no decomposition of sodium hypochlorite solution after 30 days when stored in a closed brown bottle.

The use of powders, composed of a mixture of a chlorine-releasing agent with highly absorbent resin, for disinfecting body fluid spills 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 as 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 chlorine fumes can be generated when they are applied to urine [389, 433].

Formaldehyde

Overview

Formaldehyde is used as a disinfectant and sterilant both in the liquid and gaseous states. The liquid form will be considered briefly in this section and a review of the gaseous form may be found elsewhere [434]. 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 [49, 62, 435-437]. 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 to a concentration of 0.75 ppm [438, 439]. For this reason, employees should have limited direct contact with formaldehyde and these considerations limit its role in sterilization and disinfection processes.

Mode of Action

Formaldehyde inactivates microorganisms by alkylating the amino and sulfhydral groups of proteins and ring nitrogen atoms of purine bases [288].

Microbicidal Activity

A wide range of microorganisms is destroyed by varying concentrations of aqueous formaldehyde solutions. Klein and Deforest demonstrated inactivation of poliovirus in 10 minutes required an 8% concentration of formalin but all other viruses tested were inactivated with 2% formalin [49]. Four percent formaldehyde is a tuberculocidal agent, inactivating 10^4 *M. tuberculosis* in 2 minutes [62], and 2.5% formaldehyde inactivates about 10^7 *Salmonella typhi* in 10 minutes in the presence of organic matter [436]. Rubbo and co-workers demonstrated that the sporicidal action of formaldehyde is slower than that of glutaraldehyde when they performed comparative tests with 4% aqueous formaldehyde and 2% glutaraldehyde against the spores of *Bacillus anthracis* [62]. The formaldehyde solution required a contact time of 2 hours to achieve an inactivation factor of 10^4 while glutaraldehyde required only 15 minutes.

Uses

Although formaldehyde-alcohol is a chemical sterilant and formaldehyde is a high-level disinfectant, the hospital uses of formaldehyde are limited by its irritating fumes and the pungent odor that is apparent at very low levels (<1 ppm). For these reasons and others such as carcinogenicity, this germicide is excluded from Table 1. When it is employed there is generally limited direct employee exposure; however, excessive exposures to formaldehyde have been documented for employees of renal transplant units [438, 440] and students in a gross anatomy laboratory [441]. Formaldehyde is used in the healthcare setting to prepare viral vaccines (e.g., poliovirus, influenza), as an embalming agent, to preserve anatomical specimens, and, in the past, for sterilizing surgical instruments, especially when mixed with ethanol. A 1997 survey conducted found that formaldehyde was used for reprocessing hemodialyzers by 34% of the hemodialysis centers in the United States, a 60% decrease from 1983 [442, 443]. If used at room

temperature, a concentration of 4% with a minimum exposure time of 24 hours is required to disinfect disposable hemodialyzers that are reused on the same patient [444]. Aqueous formaldehyde solutions (1-2%) also have been used to disinfect the internal fluid pathways of dialysis machines [445]. In order to minimize a potential health hazard to dialysis patients, the dialysis equipment must be thoroughly rinsed and tested for residual formaldehyde before use.

Paraformaldehyde, a solid polymer of formaldehyde, may be vaporized by heat for the gaseous decontamination of laminar flow biological safety cabinets when maintenance work or filter changes require access to the sealed portion of the cabinet.

Glutaraldehyde

Overview

Glutaraldehyde is a saturated dialdehyde that has gained wide acceptance as a high-level disinfectant and chemical sterilant [80]. Aqueous solutions of glutaraldehyde are acidic and generally in this state are not sporicidal. Only when the solution is "activated" (made alkaline) by use of alkalinating agents to pH 7.5 to 8.5 does the solution become sporicidal. Once "activated" these solutions have a shelf-life of 14 days because of the polymerization of the glutaraldehyde molecules at alkaline pH levels. This polymerization blocks the active sites (aldehyde groups) of the glutaraldehyde molecules that are responsible for its biocidal activity.

Novel glutaraldehyde formulations (e.g., glutaraldehyde-phenol-sodium phenate, potentiated acid glutaraldehyde, stabilized alkaline glutaraldehyde, glutaraldehyde-phenylphenol-amylphenol) produced in the past 30 years have overcome the problem of rapid loss of activity (e.g., use-life 28 to 30 days) while generally maintaining excellent microbicidal activity [446-450]. However, it should be recognized that antimicrobial activity is dependent not only on age but also on use conditions such as dilution and organic stress. Manufacturers' literature for these preparations suggests that the neutral or alkaline glutaraldehydes possess superior microbicidal and anti-corrosion properties when compared to acid glutaraldehydes, and a few published reports substantiate these claims[413, 451, 452]. There also are two studies that found no difference in the microbicidal activity of alkaline and acid glutaraldehydes [50, 453]. The use of glutaraldehyde-based solutions in hospitals is widespread because of their advantages that include: excellent biocidal properties; activity in the presence of organic matter (20% bovine serum); and noncorrosive action to endoscopic equipment, thermometers, rubber, or plastic equipment. The advantages, disadvantages, and characteristics of glutaraldehyde are listed in Tables 7 and 8.

Mode of Action

The biocidal activity of glutaraldehyde is a consequence of its alkylation of sulfhydral, hydroxyl, carboxy, and amino groups of microorganisms, which alters ribonucleic acid (RNA), deoxyribonucleic acid (DNA), and protein synthesis. For an extensive review of the mechanism of action of glutaraldehydes, the reader is referred to Scott and Gorman [454, 455].

Microbicidal Activity

The *in vitro* inactivation of microorganisms by glutaraldehydes has been extensively investigated and reviewed [454, 455]. Several investigators showed that ≥2% aqueous solutions of glutaraldehyde, buffered to pH 7.5 to 8.5 with sodium bicarbonate, were effective in killing vegetative bacteria in <2 minutes; *M. tuberculosis*, fungi, and viruses in <10 minutes; and spores of *Bacillus* and *Clostridium* species in 3 hours [413, 454-459]. Spores of *Clostridium difficile* are more rapidly killed by 2% glutaraldehyde than are spores of other species of *Clostridium* and *Bacillus* [59, 194, 195]. There have been reports of microorganisms with significant resistance to glutaraldehyde, including some mycobacteria (*Mycobacterium chelonae*, *M. avium-intracellulare, M. xenopi*)[460-462], *Methylobacterium mesophilicum* [463], *Trichosporon*, fungal ascospores (e.g., *Microascus cinereus*, *Cheatomium globosum*), and *Cryptosporidium* [229, 464]. *M. chelonae* persisted in a 0.2% glutaraldehyde solution that contained porcine prosthetic heart valves [465].

Collins and Montalbine reported that 2% alkaline glutaraldehyde solution inactivated 10^5 *M. tuberculosis* cells present on the surface of penicylinders within 5 minutes at 18°C [451]. However, subsequent studies conducted by Rubbo and coworkers [62] questioned the mycobactericidal prowess of glutaraldehydes. Rubbo and associates showed that 2% alkaline glutaraldehyde has slow action (20 to >30 minutes) against *M. tuberculosis* and compares unfavorably with alcohols, formaldehydes, iodine, and phenol [62]. Collins demonstrated that suspensions of *Mycobacterium avium, M. intracellulare,* and *M. gordonae* were more resistant to inactivation by a 2% alkaline glutaraldehyde (estimated time to sterility-60 minutes) than were virulent *M. tuberculosis* (estimated time to sterility-25 minutes)[466]. Collins also showed that the rate of kill was directly proportional to the temperature and that sterility of a standardized suspension of *M. tuberculosis* could not be achieved within 10 minutes [64]. A recently FDA-cleared chemical sterilant containing 2.5% glutaraldehyde uses increased temperature (35°C) to reduce the time required to achieve high-level disinfection (5 minutes)[79], but its use is limited to automatic endoscope reprocessors equipped with a heater. In another study employing membrane filters for measurement of mycobactericidal activity of 2% alkaline glutaraldehyde, Collins demonstrated that complete inactivation was achieved within 20 minutes at 20°C when the test inoculum was 10^6 *M. tuberculosis* per membrane [61]. Several investigators [50, 53, 54, 60, 61, 64, 466, 467] have demonstrated that glutaraldehyde solutions inactivate 2.4 to >5.0 $\log_{10}$ of *M. tuberculosis* in 10 minutes (including multidrug-resistant *M. tuberculosis*) and 4.0 to 6.4 $\log_{10}$ of *M. tuberculosis* in 20 minutes. On the basis of these data, 20 minutes at room temperature is the minimum exposure time needed to reliably kill organisms resistant to disinfectants, such as *M. tuberculosis*, with a ≥2% glutaraldehyde [10]. This exposure time and temperature have been validated [65, 468].

Dilution of glutaraldehyde during use commonly occurs and studies show a glutaraldehyde concentration decline after just 3 days of use in an automatic endoscope washer [469, 470]. This occurs because instruments are not thoroughly dried and water is carried in with the instrument, which increases the solution's volume and dilutes its effective concentration [471]. This emphasizes the need to ensure that semicritical equipment is disinfected with an acceptable concentration of glutaraldehyde. Data suggest that 1.0% to 1.5% glutaraldehyde is the minimum effective concentration when used as a high-level disinfectant [53, 451, 452, 470]. Chemical test strips or liquid chemical monitors [471, 472] are available for determining whether an effective concentration of glutaraldehyde is present despite repeated use and dilution. The frequency of testing should be based on how frequently the solutions are used (e.g., used daily, test daily; used weekly, test before use; used 30 times per day, test each tenth use) but the strips should not be used to extend the use life beyond the expiration date. Data suggest the chemicals in the test strip deteriorate with time [473] and a manufacturer's expiration date should be placed on the bottles. The bottle of test strips should be dated when opened and used for the period of time indicated on the bottle (e.g., 120 days). The results of test strip monitoring should be documented. The glutaraldehyde test kits have been preliminarily evaluated for accuracy and range [473] but the reliability remains to be established [474]. The concentration should be considered unacceptable or unsafe when a dilution to 1.0 to 1.5% glutaraldehyde or lower has occurred and the indicator has not changed color.

The performance of the test strips can be assessed by preparing a glutaraldehyde solution above and below the minimum effective concentration of the high-level disinfectant. For example, if the minimum effective concentration of glutaraldehyde is 1.5%, a glutaraldehyde solution of 1.25% and 1.75% concentration in water could be made. Test strips dipped in the 1.25% solution should exhibit no color change or an incomplete color change to yellow. Test strips dipped in the 1.75% solution should exhibit a uniform color change to yellow.

A 2.0% glutaraldehyde-7.05% phenol-1.20% sodium phenate product that contained 0.125% glutaraldehyde-0.44% phenol-0.075% sodium phenate when diluted 1:16 was not recommended as a high-level disinfectant because of its lack of bactericidal activity in the presence of organic matter and its lack of tuberculocidal, fungicidal, virucidal, and sporicidal activity [48, 50-59, 475]. In December 1991, the EPA issued an order to stop the sale of all batches of this product based on efficacy data that showed that this product is not effective against spores and possibly other microorganisms or inanimate objects as

claimed on the label [476]. A new diluted glutaraldehyde containing 0.95% glutaraldehyde with 1.64% phenol/phenate has been cleared by the FDA as a high-level disinfectant. The antimicrobial efficacy of this product should be independently validated.

A 10% glutaraldehyde-0.5% phenylphenol-0.1% amylphenol that contained 0.5% glutaraldehyde with 0.025% ortho-phenylphenol and 0.005% paratertiary amylphenol when diluted 1:20 was not recommended because of its lack of sporicidal activity at this dilution [58]. This latter product was registered by the EPA as a chemical sterilant at a 1:5 dilution, and since high-level disinfectants are chemical sterilants that are used at shorter exposure times [12, 288, 476], this product could have been used as a high-level disinfectant at a 1:5 dilution [58]. A 1:20 dilution of glutaraldehyde-phenylphenol-amylphenol was unable to inactivate spores of *C. difficile* at 10, 20, and 60 minutes exposure, whereas 2% glutaraldehydes were effective at all three contact times [59]. In November 1992 the manufacturer removed this product from the marketplace due to inconsistent test data and prohibitive costs involved in being regulated by both the EPA and FDA. The glutaraldehyde sterilants cleared by the FDA as of December 2000 contain 2.4 to 3.4% glutaraldehyde and are used undiluted [79].

Uses

Glutaraldehyde is used most commonly as a high-level disinfectant for medical equipment such as endoscopes [45, 80, 379], spirometry tubing, dialyzers [477], transducers, anesthesia and respiratory therapy equipment [478], hemodialysis proportioning and dialysate delivery systems [443, 479], and reused laparoscopic disposable plastic trocars [480]. Glutaraldehyde is noncorrosive to metal and does not damage lensed instruments, rubber or plastics. Glutaraldehyde should not be used for cleaning noncritical surfaces as it is too toxic and expensive.

Colitis believed due to glutaraldehyde exposure from residual endoscope solution contaminating the channels has been reported and is preventable by careful endoscope rinsing [251, 481-491]. Similarly, keratopathy and corneal decompensation were caused by ophthalmic instruments that were inadequately rinsed after soaking in 2% glutaraldehyde [492, 493].

Healthcare workers can become exposed to elevated levels of glutaraldehyde vapor when equipment is processed in poorly ventilated rooms, when spills occur, when activating or change-over of glutaraldehyde solutions [494], or when there are open immersion baths. Acute or chronic exposure may result in skin irritation or dermatitis, mucous membrane irritation (eye, nose, mouth), or pulmonary symptoms [251, 495-499]. Epistaxis, allergic contact dermatitis, asthma, and rhinitis also have been reported in healthcare workers exposed to glutaraldehyde [496, 500-506].

Glutaraldehyde exposure should be monitored to ensure a safe work environment. Testing can be done by four techniques: a silica gel tube/gas chromatography with a flame ionization detector, dinitrophenylhydrazine (DNPH)-impregnated filter cassette/high-performance liquid chromatography (HPLC) with an ultraviolet (UV) detector, a passive badge/HPLC, or a hand-held glutaraldehyde air monitor [507]. The silica gel tube and the DNPH-impregnated cassette are suitable for monitoring the 0.05 ppm ceiling limit. The passive badge, with a 0.02 ppm limit of detection, is considered marginal at the ACGIH ceiling level. The ceiling level is thought to be too close to the glutaraldehyde meter's 0.03 ppm limit of detection to provide confidence in the readings [507]. ACGIH does not require a specific monitoring schedule for glutaraldehyde; however, a monitoring schedule is needed to ensure that the level is less than the ceiling limit. For example, monitoring should be done initially to determine glutaraldehyde levels, after there are procedural or equipment changes, and in response to worker complaints [508]. If the glutaraldehyde level is higher than the ACGIH ceiling limit of 0.05 ppm, corrective action should be taken and monitoring repeated [508].

Engineering and work practice controls that may be used to combat these problems include ducted exhaust hoods, air systems that provide 7 to 15 air exchanges per hour, ductless fume hoods with absorbents for the glutaraldehyde vapor, tight-fitting lids on immersion baths, personal protection (e.g.,

gloves, goggles) to minimize skin or mucous membrane contact, and automated endoscope processors [72, 509]. Some workers have been fitted with a half-face respirator with organic vapor filter [500] or offered a type "C" supplied air respirator with a full facepiece operated in a positive pressure mode [510]. Even though enforcement of the ceiling limit was suspended in 1993 by the U.S. Court of Appeals [511], it is prudent to limit employee exposure to 0.05 ppm since at this level glutaraldehyde is irritating to the eyes, throat, and nose [251, 499, 511, 512]. If glutaraldehyde disposal via the sanitary sewer system is restricted, sodium bisulfate can be used to neutralize the glutaraldehyde and make it safe for disposal.

Hydrogen Peroxide

Overview

The literature contains several accounts of the properties, germicidal effectiveness, and potential uses for stabilized hydrogen peroxide in the hospital setting. Published reports ascribe good germicidal activity to hydrogen peroxide have been published and attest to its bactericidal, virucidal, sporicidal, and fungicidal properties [513, 514]. The advantages, disadvantages, and characteristics of hydrogen peroxide are listed in Tables 7 and 8.

Mode of Action

Hydrogen peroxide works by the production of destructive hydroxyl free radicals that can attack membrane lipids, DNA, and other essential cell components. Catalase, produced by aerobic and facultative anaerobes that possess cytochrome systems, may protect cells from metabolically produced hydrogen peroxide by degrading hydrogen peroxide to water and oxygen. This defense is overwhelmed by the concentrations used for disinfection [513, 514].

Microbicidal Activity

Hydrogen peroxide is active against a wide range of microorganisms, including bacteria, yeasts, fungi, viruses, and spores [58, 514]. Schaeffer and associates demonstrated the bactericidal effectiveness and stability of hydrogen peroxide in urine against a variety of healthcare-associated pathogens. They showed that organisms with high cellular catalase activity (e.g., *S. aureus*, *Serratia marcescens*, and *Proteus mirabilis*) required 30 to 60 minutes of exposure to 0.6% hydrogen peroxide for a 10^8 reduction in cell counts, whereas, organisms with lower catalase activity (e.g., *E. coli*, S*treptococcus* sp., and *Pseudomonas* sp.) required only 15 minutes exposure [515]. Wardle and Renninger investigated 3, 10, and 15% hydrogen peroxide for reducing spacecraft bacterial populations and got a complete kill of 10^6 sporeformers (i.e., *Bacillus* spp) with a 10% concentration and a 60 minutes exposure time. A 3% concentration for 150 minutes killed 10^6 sporeformers in 6 of 7 exposure trials [516]**.** Sagripanti and co-workers found that a 10% hydrogen peroxide solution resulted in a 10^3 decrease in *B. subtilis* spores and a 10^5 or greater decrease when tested against 13 other pathogens in 30 minutes at 20°C [517, 518]. A 3.0% hydrogen peroxide solution was ineffective against VRE after 3 and 10 minutes exposure times [519] but caused only a 2-$\log_{10}$ reduction in the number of *Acanthamoeba* cysts in approximately 2 hours [520].

Synergistic sporicidal effects were observed when spores were exposed to a combination of hydrogen peroxide (5.9% to 23.6%) and peracetic acid [521]. The antiviral activity of hydrogen peroxide against rhinovirus was demonstrated in studies by Mentel and Schmidt [522]. The time required for inactivating three serotypes of rhinovirus using a 3% hydrogen peroxide solution was 6 to 8 minutes; this time increased with decreasing concentrations (18-20 minutes at 1.5%, 50-60 minutes at 0.75%).

Under normal conditions hydrogen peroxide is extremely stable when properly stored (e.g., in dark containers). The rate loss in small containers is less than 2% per year [523].

Uses

Commercially available 3% hydrogen peroxide is a stable and effective disinfectant when used on inanimate surfaces. It has been used in concentrations from 3 to 6% for the disinfection of soft contact

lenses (3% for 2-3 hrs)[513, 524, 525], tonometer biprisms [387], ventilators [526], fabrics [304] and endoscopes [348]. Hydrogen peroxide was effective in spot-disinfecting fabrics in patients' rooms [304]. Corneal damage from a hydrogen peroxide-soaked tonometer tip that was not properly rinsed has been reported [527]. Hydrogen peroxide also has been instilled into urinary drainage bags in an attempt to eliminate the bag as a source of bladder bacteriuria and environmental contamination [528]. While the instillation of hydrogen peroxide into the bag reduced microbial contamination of the bag, this procedure did not reduce the incidence of catheter-associated bacteriuria [528].

Concentrations of hydrogen peroxide from 6 to 25% have promise as chemical sterilants. The product currently marketed as a sterilant is a premixed, ready-to-use chemical that contains 7.5% hydrogen peroxide and 0.85% phosphoric acid (to maintain a low pH)[45]. The mycobactericidal activity of 7.5% hydrogen peroxide has been corroborated by Sattar, who showed the inactivation of $>10^5$ multidrug resistant *M. tuberculosis* after a 10-minute exposure [529]. Thirty minutes were required for >99.9% inactivation of polio and hepatitis A viruses [530]. Mbithi and coworkers showed that 3 and 6% hydrogen peroxide were unable to inactivate the hepatitis A virus in 1 minute using a carrier test [47]. The effectiveness of 7.5% hydrogen peroxide at 10 minutes was compared to 2% alkaline glutaraldehyde at 20 minutes in manual disinfection of endoscopes; no significant difference in germicidal activity was observed [531]. There also were no complaints received from the nursing or medical staff in terms of odor or toxicity. In one study, 6% hydrogen peroxide (unused product was 7.5%) was more effective in the high-level disinfection of flexible endoscopes than was the 2% glutaraldehyde solution [348]. A new, rapid-acting 13.4% hydrogen peroxide formulation (that is not yet FDA-cleared) has demonstrated sporicidal, mycobactericidal, fungicidal, and virucidal efficacy. Manufacturer's data demonstrate that this solution sterilizes in 30 minutes and provides high-level disinfection in 5 minutes [532]. This product has not been used long enough to evaluate material compatibility to endoscopes and other semicritical devices, and further assessment by instrument manufacturers should be done.

A chemical irritation resembling pseudomembranous colitis, which was caused by either 3% hydrogen peroxide or a 2% glutaraldehyde, has been infrequently reported [482]. An epidemic of pseudomembrane-like enteritis and colitis in seven patients in a gastrointestinal endoscopy unit also has been associated with use of 3% hydrogen peroxide [533].

As with other chemical sterilants, dilution of the hydrogen peroxide must be monitored by regularly testing the minimum effective concentration (i.e., 7.5 to 6.0%). Compatibility testing by Olympus America of the 7.5% hydrogen peroxide found both cosmetic changes (e.g., discoloration of black anodized metal finishes)[45] and functional changes with the tested endoscopes (Olympus, November 1999, written communication).

Iodophors

Overview

Iodine solutions or tinctures have long been used by health professionals, primarily as antiseptics on skin or tissue. Iodophors, on the other hand, have been used both as antiseptics and disinfectants. An iodophor is a combination of iodine and a solubilizing agent or carrier; the resulting complex provides a sustained-release reservoir of iodine and releases small amounts of free iodine in aqueous solution. The best known and most widely used iodophor is povidone-iodine, a compound of polyvinylpyrrolidone with iodine. This product and other iodophors retain the germicidal efficacy of iodine but unlike iodine are generally nonstaining and are relatively free of toxicity and irritancy [534, 535].

Several reports that documented intrinsic microbial contamination of antiseptic formulations of povidone-iodine and poloxamer-iodine [536-538] caused a reappraisal of the chemistry and use of iodophors [539]. 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 [537]. Therefore, iodophors must be diluted according to the manufacturers' directions to achieve antimicrobial activity.

Mode of Action

Iodine is able to penetrate the cell wall of microorganisms quickly and it is thought that the lethal effects result from a disruption of protein and nucleic acid structure and synthesis.

Microbicidal Activity

Published reports on the *in vitro* antimicrobial efficacy of iodophors demonstrate that iodophors are bactericidal, mycobactericidal, and virucidal but may require prolonged contact times to kill certain fungi and bacterial spores [7, 48-50, 540-544]. Berkelman and associates found that three brands of povidone-iodine solution demonstrated more rapid kill (seconds to minutes) of *S. aureus* and *Mycobacterium chelonae* at a 1:100 dilution than did the stock solution [540]. Klein and Deforest demonstrated the virucidal activity of 75-150 ppm available iodine against seven viruses [49]. Other investigators have questioned the efficacy of iodophors against poliovirus in the presence of organic matter [542] and rotavirus SA-11 in distilled or tapwater [543]. Manufacturers' data demonstrate that commercial iodophors are not sporicidal but they are tuberculocidal, fungicidal, virucidal, and bactericidal at their recommended use-dilution.

Uses

Besides their use as an antiseptic, iodophors have been used for the disinfection of blood culture bottles and medical equipment such as hydrotherapy tanks, thermometers, and endoscopes. Antiseptic iodophors are not suitable for use as hard-surface disinfectants because of concentration differences. Iodophors formulated as antiseptics contain less free iodine than those formulated as disinfectants [288]. Iodine or iodine-based antiseptics should not be used on silicone catheter as the silicone tubing may be adversely affected [545].

Ortho-phthalaldehyde

Overview

Ortho-phthalaldehyde (OPA) is a chemical sterilant that received FDA clearance in October 1999. It contains 0.55% 1,2-benzenedicarboxaldehyde or OPA. OPA solution is a clear, pale- blue liquid with a pH of 7.5. The advantages, disadvantages, and characteristics of OPA are listed in Tables 7 and 8.

Mode of Action

Preliminary studies on the mode of action of OPA suggest that both OPA and glutaraldehyde interact with amino acids, proteins, and microorganisms. However, OPA is a less potent cross-linking agent. This is compensated for by the lipophilic aromatic nature of OPA that is likely to assist its uptake through the outer layers of mycobacteria and gram-negative bacteria [546, 547].

Microbicidal Activity

Studies have demonstrated excellent microbicidal activity in *in vitro* studies [45, 74, 229, 306, 548-557]. For example, Gregory and coworkers demonstrated that OPA has superior mycobactericidal activity (5-$\log_{10}$ reduction in 5 minutes) compared to glutaraldehyde. The mean times required to produce a 6-$\log_{10}$ reduction for *M. bovis* using 0.21% OPA was 6 minutes compared to 32 minutes using 1.5% glutaraldehyde [549]. OPA showed good activity against the mycobacteria tested, including the glutaraldehyde-resistant strains, but 0.5% OPA was not sporicidal with 270 minutes of exposure. Increasing the pH from its unadjusted level (about 6.5) to pH 8 improved the sporicidal activity of OPA [550]. Chan-Myers and Roberts showed that the level of biocidal activity was directly related to the temperature. A greater than 5-$\log_{10}$ reduction was observed in 3 hours at 35°C as compared to 24 hours at 20°C. Also, with an exposure time at or below 5 minutes, a decrease in biocidal activity was observed

with increasing serum concentration. However, there was no difference in efficacy when the exposure time was 10 minutes or longer [553]. Walsh and colleagues also found OPA effective (>5-$\log_{10}$ reduction) against a wide range of microorganisms, including glutaraldehyde-resistant mycobacteria and *Bacillus subtilis* spores [550].

Uses

OPA has several potential advantages compared to glutaraldehyde. It has excellent stability over a wide pH range (pH 3-9), is not a known irritant to the eyes and nasal passages, does not require exposure monitoring, has a barely perceptible odor, and requires no activation. OPA, like glutaraldehyde, has excellent material compatibility. A potential disadvantage of OPA is that it stains proteins gray (including unprotected skin) and thus must be handled with caution [45]. However, skin staining would indicate improper handling that requires additional training and/or personal protective equipment (PPE) (gloves, eye and mouth protection, fluid-resistant gowns). PPE should be worn when handling contaminated instruments, equipment, and chemicals [306]. In addition, equipment must be thoroughly rinsed to prevent discoloration of a patient's skin or mucous membrane.

Since OPA was only recently cleared for use as a high-level disinfectant, only limited clinical studies are available. In a clinical-use study, exposure of 100 endoscopes for 5 minutes to OPA resulted in a >5-$\log_{10}$ reduction in bacterial load. Further, OPA was effective over a 14-day usage cycle [74]. Manufacturer's data show that OPA will last longer in an automatic endoscope reprocessor before reaching its minimum effective concentration (MEC) limit (MEC after 82 cycles) compared to glutaraldehyde (MEC after 40 cycles) [306]. Disposal must be done in accordance with local and state regulations. If OPA disposal via the sanitary sewer system is restricted, glycine (25 grams/gallon) can be used to neutralize the OPA and make it safe for disposal.

The high-level disinfectant label claims for OPA solution at 20°C vary worldwide, e.g., 5 minutes in Europe, Asia, and Latin America; 10 minutes in Canada and Australia; and 12 minutes in the United States. These label claims are different worldwide because of differences in the antimicrobial efficacy tests. For example, the clearance of OPA by the FDA was based on a "simulated use" test requirement for a 6-$\log_{10}$ reduction of resistant bacteria suspended in organic matter and dried onto an endoscope. Since the FDA-required "simulated use" test does not include cleaning, an essential component of disinfection of reusable devices (e.g., endoscopes), it is likely that the time required for high-level disinfection of a medical device by OPA would be <12 minutes. Tuberculocidal efficacy tests using a quantitative suspension test support a 5-minute exposure time at room temperature for OPA. Canadian regulatory authorities require a 6-$\log_{10}$ reduction in mycobacteria (this requires approximately 6 minutes) and allow only 5-minute exposure time intervals, thus the exposure time was set at 10 minutes [306].

Peracetic Acid

Overview

Peracetic, or peroxyacetic, acid is characterized by a very rapid action against all microorganisms. A special advantage of peracetic acid is it has no harmful decomposition products (i.e., acetic acid, water, oxygen, hydrogen peroxide) and leaves no residue. It remains effective in the presence of organic matter and is sporicidal even at low temperatures. Peracetic acid can corrode copper, brass, bronze, plain steel, and galvanized iron but these effects can be reduced by additives and pH modifications. It is considered unstable, particularly when diluted; for example, a 1% solution loses half its strength through hydrolysis in 6 days, whereas 40% peracetic acid loses 1 to 2% of its active ingredients per month [514]. The advantages, disadvantages, and characteristics of peracetic acid are listed in Tables 7 and 8.

Mode of Action

Little is known about the mechanism of action of peracetic acid but it is thought to function as do other oxidizing agents, i.e., it denatures proteins, disrupts the cell wall permeability, and oxidizes sulfhydral and

sulfur bonds in proteins, enzymes, and other metabolites [514].

Microbicidal Activity

Peracetic acid will inactivate gram-positive and gram-negative bacteria, fungi, and yeasts in ≤5 minutes at <100 ppm. In the presence of organic matter, 200-500 ppm is required. For viruses the dosage range is wide (12-2250 ppm), with poliovirus inactivated in yeast extract in 15 minutes with 1500 to 2250 ppm. One study showed that 3.5% peracetic acid was ineffective against the hepatitis A virus after 1 minute exposure using a carrier test [47]. With bacterial spores, 500 to 10,000 ppm (0.05 to 1%) inactivates spores in 15 seconds to 30 minutes when in a spore suspension test [514, 517, 558, 559].

Uses

An automated machine using peracetic acid to chemically sterilize medical, surgical, and dental instruments (e.g., endoscopes, arthroscopes) is used in the United States [560, 561]. The sterilant, 35% peracetic acid, is diluted to 0.2% with filtered water at a temperature of 50°C. Simulated-use trials have demonstrated excellent microbicidal activity [468, 562-564] and three clinical trials have demonstrated both excellent microbial killing and no clinical failures leading to infection [27, 563, 565]. The high efficacy of the system was demonstrated by Alfa and coworkers, who compared the efficacies of the system with that of ethylene oxide. Only the peracetic acid system was able to completely kill 6 $\log_{10}$ of *M. chelonae, Enterococcus faecalis,* and *B. subtilis* spores with both an organic and inorganic challenge [566]. An investigation by Fuselier and Mason [27] compared the costs, performance, and maintenance of urologic endoscopic equipment processed by high-level disinfection (with glutaraldehyde) with those of the peracetic acid system and reported no clinical differences between the two systems. However, the use of this system led to increased costs when compared to high-level disinfection, including costs for processing ($6.11 vs. $0.45 per cycle), purchasing and training ($24,845 vs. $16), installation ($5,800 vs. $0), and endoscope repairs ($6,037 vs. $445)[27]. Further, three clusters of infection using the peracetic acid automated endoscope reprocessor were linked to inadequately processed bronchoscopes when inappropriate channel connectors were used with the system [567]. These clusters highlight the importance of model-specific reprocessing protocols, training, proper connector systems, and quality control procedures to ensure compliance with manufacturer's recommendations and professional organization guidelines. An alternative high-level disinfectant available in the United Kingdom contains 0.35% peracetic acid. Although this product is rapidly effective against a broad range of microorganisms [352, 568, 569], it tarnishes the metal of endoscopes and is unstable, resulting in only a 24-hour use life [569].

Peracetic Acid and Hydrogen Peroxide

Overview

Two chemical sterilants are available that contain peracetic acid plus hydrogen peroxide (0.08 peracetic acid plus 1.0% hydrogen peroxide [no longer marketed], 0.23% peracetic acid plus 7.35% hydrogen peroxide). The advantages, disadvantages, and characteristics of peracetic acid and hydrogen peroxide are listed in Tables 7 and 8.

Microbicidal Activity

The bactericidal properties of peracetic acid and hydrogen peroxide have been demonstrated [570]. Manufacturer's data demonstrated that, using the AOAC method, this product inactivated all microorganisms with the exception of bacterial spores within 20 minutes. The 0.08% peracetic acid plus 1.0% hydrogen peroxide product was effective in inactivating a glutaraldehyde-resistant mycobacteria [571].

Uses

The combination of peracetic acid and hydrogen peroxide has been used for disinfecting hemodialyzers [572]. The percentage of dialysis centers using a peracetic acid-hydrogen peroxide-based disinfectant for reprocessing dialyzers increased from 5% in 1983 to 56% in 1997 [443]. Olympus America does not

endorse the use of 0.08% peracetic acid plus 1.0% hydrogen peroxide on any Olympus endoscope due to cosmetic and functional damage and will not assume liability for chemical damage as a result of the use of this product (Olympus America, April 1998, written communication). The manufacturer has removed this product from the marketplace. A new chemical sterilant with 0.23% peracetic acid and 7.35% hydrogen peroxide has been cleared by the FDA and the characteristics, advantages, and disadvantages are shown in Tables 7 and 8.

Phenolics

Overview

Phenol has occupied a prominent place in the field of hospital disinfection since its initial use as a germicide by Lister in his pioneering work on antiseptic surgery. In the past 30 years, however, work has been concentrated upon the numerous phenol derivatives or phenolics and their antimicrobial properties. Phenol derivatives originate when a functional group (e.g., alkyl, phenyl, benzyl, halogen) replaces one of the hydrogen atoms on the aromatic ring. Two phenol derivatives commonly found as constituents of hospital disinfectants are ortho-phenylphenol and ortho-benzyl-para-chlorophenol. The antimicrobial properties of these compounds and many other phenol derivatives are much improved over those of the parent chemical. Phenolics are assimilated by porous materials and the residual disinfectant may cause tissue irritation. In 1970, Kahn reported that depigmentation of the skin is caused by phenolic germicidal detergents containing para-tertiary butylphenol and para-tertiary amylphenol [573].

Mode of Action

Phenol, in high concentrations, acts as a gross protoplasmic poison, penetrating and disrupting the cell wall and precipitating the cell proteins. Low concentrations of phenol and higher molecular-weight phenol derivatives cause bacterial death by the inactivation of essential enzyme systems and leakage of essential metabolites from the cell wall [574].

Microbicidal Activity

Published reports on the antimicrobial efficacy of commonly used phenolic detergents showed that phenolics were bactericidal, fungicidal, virucidal, and tuberculocidal [7, 48, 50, 167, 172, 320, 437, 574-580]. One study demonstrated little or no virucidal effect of a phenolic against coxsackie B4, echovirus 11, and poliovirus 1 [578]. Similarly, Klein and Deforest made the observation that 12% ortho-phenylphenol failed to inactivate any of the three hydrophilic viruses after a 10-minute exposure time, although 5% phenol was lethal for these viruses [49]. A 0.5% dilution of a phenolic (2.8% ortho-phenylphenol and 2.7% ortho-benzyl-para-chlorophenol) inactivated HIV [167] and a 2% solution of a phenolic (15% ortho-phenylphenol and 6.3% para-tertiary-amylphenol) inactivated all but one of 11 fungi tested [48].

Manufacturers' data using the standardized AOAC methods demonstrate that commercial phenolic detergents are not sporicidal but are tuberculocidal, fungicidal, virucidal, and bactericidal at their recommended use-dilution. Generally, these efficacy claims against microorganisms have not been verified by independent laboratories or the EPA. Attempts to substantiate the bactericidal label claims of phenolic detergents using the AOAC Use-Dilution Method have failed on occasion [320, 579]. However, these same studies have shown extreme variability of test results among laboratories testing identical products.

Uses

This class of compounds is used for decontamination of the hospital environment, including laboratory surfaces, and noncritical medical items. Phenolics are not recommended for semicritical items because of the lack of published efficacy data for many of the available formulations and because the residual disinfectant on porous materials may cause tissue irritation even when thoroughly rinsed.

The use of phenolics in nurseries has been questioned because of the occurrence of hyperbilirubinemia in infants placed in bassinets where phenolic detergents were used [581]. In addition, Doan and co-workers

demonstrated bilirubin level increases in phenolic-exposed infants compared to nonphenolic-exposed infants when the phenolic was prepared according to the manufacturers' recommended dilution [582]. If phenolics are used to clean nursery floors, they must be diluted according to the recommendation on the product label. Phenolics should not be used to clean in-use infant bassinets and incubators. If phenolics are used to terminally clean infant bassinets and incubators, the surfaces should be rinsed thoroughly with water and dried before the infant bassinets and incubators are reused [10].

Quaternary Ammonium Compounds

Overview

The quaternary ammonium compounds are widely used as disinfectants but should not be used as antiseptics. The elimination of such solutions as antiseptics on skin and tissue was recommended by the Centers for Disease Control and Prevention [8] because of several outbreaks of infections associated with in-use contamination [583-590]. There also have been a few reports of healthcare-associated infections associated with contaminated quaternary ammonium compounds used to disinfect patient-care supplies or equipment such as cystoscopes or cardiac catheters [591, 592]. The quaternaries are good cleaning agents but high water hardness [593] and materials such as cotton and gauze pads may make them less microbicidal because of insoluble precipitates or these materials absorb the active ingredients, respectively. As with several other disinfectants (e.g., phenolics, iodophors) gram-negative bacteria have been found to survive or grow in them [311].

Chemically, the quaternaries are organically substituted ammonium compounds in which the nitrogen atom has a valence of 5, four of the substituent radicals (R1-R4) are alkyl or heterocyclic radicals of a given size or chain length, and the fifth (X^-) is a halide, sulfate, or similar radical [594]. Each compound exhibits its own antimicrobial characteristics, hence the search for one compound with outstanding antimicrobial properties. Some of the chemical names of quaternary ammonium compounds used in hospitals are alkyl dimethyl benzyl ammonium chloride, alkyl didecyl dimethyl ammonium chloride, and dialkyl dimethyl ammonium chloride. The newer quaternary ammonium compounds (i.e., fourth generation), referred to as twin-chain or dialkyl quaternaries (e.g. didecyl dimethyl ammonium bromide and dioctyl dimethyl ammonium bromide), purportedly remain active in hard water and are tolerant of anionic residues [595].

Mode of Action

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 [595]. Evidence in support of these and other possibilities is provided by Sykes [594] and Petrocci [596].

Microbicidal Activity

Results from manufacturers' data sheets and from published scientific literature indicate that the quaternaries sold as hospital disinfectants are generally fungicidal, bactericidal, and virucidal against lipophilic (enveloped) viruses; they are not sporicidal and generally not tuberculocidal or virucidal against hydrophilic (nonenveloped) viruses [7, 47, 48, 50, 54, 55, 172, 248, 414, 596-599]. Best et al. and Rutala et al. demonstrated the poor mycobactericidal activities of quaternary ammonium compounds [50, 54]. Attempts to reproduce the manufacturers' bactericidal and tuberculocidal claims using the AOAC tests with a limited number of quaternary ammonium compounds have failed on occasion [50, 320, 579]. Studies have shown, however, extreme variability of test results among laboratories testing identical products [579 320, 579].

Uses

The quaternaries are commonly used in ordinary environmental sanitation of noncritical surfaces such as floors, furniture, and walls.

Miscellaneous Inactivating Agents

Other Germicides

Several compounds have antimicrobial activity but for various reasons have not been incorporated into our armamentarium of hospital disinfectants. These include mercurials, ether, acetone, chloroform, sodium hydroxide, beta-propiolactone, chlorhexidine gluconate, cetrimide-chlorhexidine, glycols (triethylene and propylene), and the Tego disinfectants. A detailed examination of these agents is presented in two authoritative references [9, 317].

A peroxygen-containing formulation had marked bactericidal action when used as a 1% weight/volume solution and virucidal activity at 3% [57] but did not have mycobactericidal activity at concentrations of 2.3% and 4% and exposure times ranging between 30 and 120 minutes [600]. It also required 20 hours to kill *B. subtilis* spores [601]. A powder-based or peroxygen compound for disinfecting contaminated spill was strongly and rapidly bactericidal [602].

Metals such as silver, iron, and copper could be used for the disinfection of water, reusable medical devices, or incorporated into medical devices (e.g., intravascular catheters) [603-608]. While additional work is needed, they appear to be effective against a wide variety of microorganisms.

Superoxidized Water

Recent reports have examined the microbicidal activity of a new disinfectant, superoxidized water. The concept of electrolyzing saline to create a disinfectant or antiseptics is appealing as the basic materials of saline and electricity are cheap and the end product (i.e., water) is not damaging to the environment. The main products of this water are hypochlorous acid at a concentration of about 144 mg/l and chlorine. The disinfectant is generated 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. While superoxidized water is intended to be generated fresh at the point of use, when tested under clean conditions the disinfectant is effective within 5 minutes when 48 hours old [609]. Unfortunately, the equipment required to produce the product may be expensive as parameters such as pH, current, and redox potential must be closely monitored. The solution has been shown to be nontoxic to biological tissues. Although the solution is claimed by the manufacturer in the United Kingdom to be noncorrosive and nondamaging to endoscopes and processing equipment, one flexible endoscope manufacturer has voided the warranty on the endoscopes if superoxidized water is used to disinfect them [610].

The antimicrobial activity of this new sterilant has been tested against bacteria, mycobacteria, viruses, fungi, and spores [609, 611, 612]. Data have shown that freshly generated superoxidized water is rapidly effective (<2 minutes) in achieving a 5-$\log_{10}$ reduction of pathogenic microorganisms (i.e., *M. tuberculosis*, *M. chelonae*, poliovirus, HIV, MRSA, *E. coli, Candida albicans*, *Enterococcus faecalis, Pseudomonas aeruginosa*) in the absence of organic loading. However, the biocidal activity of this disinfectant was substantially reduced in the presence of organic material (5% horse serum)[609]. No bacteria or viruses were detected on artificially contaminated endoscopes after 5 minutes exposure to superoxidized water [613]. Additional studies are needed to determine if this solution may be used as an alternative to other disinfectants or antiseptics for handwashing, skin antisepsis, room cleaning, or equipment disinfection (e.g., endoscopes)[306, 611, 614].

Metals as Microbicides

Comprehensive reviews of antisepsis [615], disinfection [616], and anti-infective chemotherapy [617] barely

mention the antimicrobial activity of heavy metals [607, 608]. Nevertheless, it has been known since antiquity that some heavy metals possess anti-infective activity. Disinfection and sterilization most commonly are achieved by physical means (e.g., heat) or use of no heavy metal-containing disinfectants or chemical sterilants. Heavy metals such as silver have been used for prophylaxis of conjunctivitis of the newborn, topical therapy for burn wounds, and bonding to indwelling catheters, and the use of heavy metals as antiseptics or disinfectants is also being reexplored.

A new silver-containing germicide with antimicrobial persistence has been developed for use on environmental surfaces and skin. This germicidal coating combines an immobilized polymeric biocide with an insoluble silver salt. The coating is proposed to transfer the active biocide (i.e., silver) on demand directly to the microorganisms without elution of silver ions into solution. Microorganisms contacting the coating accumulate silver until the toxicity threshold is exceeded; dead microorganisms eventually lyse and detach from the surface. The duration of efficacy of the coating is determined by the amount of silver present and on the number of microorganisms contacting the treated surface. Preliminary studies show that treated surfaces result in excellent elimination of antibiotic-resistant bacteria (e.g., VRE) inoculated directly on various surfaces at challenge levels of 100 CFU/ $inch^2$ for at least 13 days [618]. Antimicrobial activity is retained even when the surface is subjected to repeated dry wiping or wiping with a quaternary ammonium compound. Data from the manufacturer demonstrate inactivation of bacteria, yeast, fungi, and viruses upon application of the product at challenge levels of up to 10^6 CFU/ml. Sustained antimicrobial activity has been shown for the tested microorganisms (i.e., bacteria, yeast, and fungi)[619]. Inactivation times for microorganisms vary as a function of the ratio of surface area of the coated surface (substrate) to the volume of the microbial suspension in contact with the surface.

If novel surface treatments such as this prove to be effective in reducing microbial contamination, are cost-effective, and have long-term residual activity, they may be useful in limiting transmission of healthcare-associated pathogens. The antimicrobial activity of this coating makes it potentially suitable for a wide range of applications, including surface disinfection, and hand antisepsis [306, 620, 621].

Clinical uses of other heavy metals include the use of copper-8-quinolinolate as a fungicide against *Aspergillus*, ionization for *Legionella* disinfection [622-624], the use of organic mercurials as an antiseptic (e.g., mercurochrome) and preservative/disinfectant (e.g., thimerosal) in pharmaceuticals and cosmetics, and the use of miscellaneous metals such as melarsoprol, an arsenoxide, to treat African trypanosomiasis, and sodium stibogluconate, an antimonial compound, to treat leishmaniasis [608].

Ultraviolet Radiation

UV has a wavelength range between 328 and 210 nm (3280 and 2100 A). Its maximum bactericidal effect occurs at 240-280 nm. Mercury vapor lamps emit more than 90% of their radiation at 253.7 nm, which is near the maximum microbicidal activity [625]. Inactivation of microorganisms is due to destruction of nucleic acid via induction of thymine dimers. UV has been employed in the disinfection of drinking water, air [625], titanium implants [626], and contact lenses [627]. Studies have shown that bacteria and viruses are more easily killed by UV light than are bacterial spores [625]. UV has several potential applications but unfortunately its germicidal effectiveness and use is influenced by the following factors: organic matter; wavelength; type of suspension; temperature; type of microorganism; and UV intensity, which is affected by distance and dirty tubes [628]. The application of UV in the hospital (i.e., operating rooms, isolation rooms, and biological safety cabinets) is limited to the destruction of airborne organisms or inactivation of microorganisms located on surfaces. The effect of UV radiation on postoperative wound infections has been investigated by means of a double-blind, randomized study in five university medical centers. After following 14,854 patients over a 2-year period, the investigators reported the overall wound infection rate to be unaffected by UV although there was a significant reduction (3.8 to 2.9%) in postoperative infection in the "refined clean" surgical procedures [629]. There are no data that support the use of UV lamps in isolation rooms, and this practice has caused at least one epidemic of UV-induced skin erythema and

keratoconjunctivitis in hospital patients and visitors [630].

Pasteurization

This is not a sterilization process; its purpose is to destroy all pathogenic microorganisms with the exception of bacterial spores. The time-temperature relation for hot-water pasteurization is generally >70°C (158°F) for 30 minutes. The water temperature should be monitored as part of a quality assurance program [631]. Pasteurization of respiratory therapy [632, 633] and anesthesia equipment [634] is a recognized alternative to chemical disinfection. The efficacy of this process has been tested using an inoculum that the authors believed might simulate contamination by an infected patient. Using a large inoculum (10^7) of *P. aeruginosa* or *A. calcoaceticus* in sets of respiratory tubing before processing, Gurevich and associates demonstrated that machine-assisted chemical processing was more efficient than machine-assisted pasteurization with a disinfection failure rate of 6% and 83%, respectively [632]. Other investigators found hot water disinfection to be effective (inactivation factor >5 $\log_{10}$) for the disinfection of reusable anesthesia or respiratory therapy equipment [633, 634].

Flushing- and Washer-Disinfectors

Flushing- and washer-disinfectors are automated and closed equipment that clean and disinfect objects from bedpans and washbowls to surgical instruments and anesthesia tubes. Items such as bedpans and urinals can be cleaned and disinfected in flushing-disinfectors. They have a short cycle of a few minutes. They clean by flushing with warm water, possibly with a detergent, and then disinfect by flushing the items with hot water at approximately 90°C, or with steam. Since this machine empties, cleans, and disinfects, manual cleaning is eliminated, fewer disposable items are needed, and less chemical germicides are used. A microbiological evaluation of one unit demonstrated that suspensions of *Enterococcus faecalis* or poliovirus were completely inactivated [635]. Other studies have shown that strains of *Enterococcus faecium* are able to survive the British Standard for heat disinfection of bedpans (80°C for 1 minute). The significance of this finding with reference to the potential for enterococci to survive and disseminate in the hospital environment is debatable [636-638]. These machines are available and used in many European countries.

Surgical instruments and anesthesia equipment, which are more difficult to clean, are run in washer-disinfectors with a longer cycle of some 20-30 minutes with the use of a detergent. These machines also disinfect by hot water at approximately 90°C [639].

Evaluation and Neutralization of Germicides

Any discussion of germicidal efficacy would be incomplete without a few comments regarding the evaluation of germicides to assure that they meet manufacturers' label claims. Chemical germicides formulated as disinfectants or chemical sterilants in the United States were registered and regulated in interstate commerce by the Disinfectants Branch, Office of Pesticides Program, EPA. The authority for this activity was mandated by the Federal Insecticide, Fungicide and Rodenticide Act (FIFRA) of 1947. Until recently, the EPA required manufacturers of chemical germicides formulated as sanitizers, disinfectants, or chemical sterilants to test formulations by using accepted methods for microbicidal activity, stability, and toxicity to animals and humans. In June 1993, the FDA and EPA issued a "Memorandum of Understanding" that divided responsibility for review and surveillance of chemical germicides between the two agencies. Under the agreement, the FDA regulates chemical sterilants used on critical and semicritical devices and the EPA regulates disinfectants used on noncritical surfaces [640]. In 1997, Congress passed the Food Quality Protection Act (FQPA). This act amended FIFRA in regard to several products regulated by both EPA and FDA. One provision of FQPA is that regulation of liquid chemical sterilants was removed from the jurisdiction of EPA and now rests solely with the FDA [641]. The

FDA and EPA have considered the impact of FQPA and will publish notices or guidance documents to inform industry about its recommendations on product submissions and labeling.

The methods that EPA has used for registration are standardized by the AOAC; however, a survey of scientific literature indicates numerous deficiencies associated with these tests [47, 53, 60, 329, 578, 579, 642-647] that cause them to be neither accurate nor reproducible [320, 579]. It is the responsibility of both the EPA and FDA to support the development and validation of methods for assessing disinfection claims [648, 649]. Sattar and co-workers have developed a two-tier quantitative carrier test that can be used to assess sporicidal, mycobactericidal, bactericidal, fungicidal, virucidal, and protozoacidal activity of chemical germicides [557]. The EPA is accepting label claims against hepatitis B virus using the duck hepatitis B model to quantify disinfectant activity [90, 650]. EPA also may do the same for hepatitis C virus using the bovine viral diarrhea virus as a surrogate. Antiseptics are considered to be antimicrobial drugs used on living tissue and thus are regulated by the FDA under the Food, Drug and Cosmetic Act.

For nearly 30 years, the EPA also performed intramural pre- and post-registration efficacy testing of some chemical disinfectants, but in 1982 this was stopped, reportedly for budgetary reasons. Thus, manufacturers presently do not need verification of microbiological activity claims by the EPA or an independent testing laboratory when registering a disinfectant or chemical sterilant [651]. This occurred at a time when the frequency of contaminated germicides and infections secondary to their use had increased [311]. Investigations which demonstrated that interlaboratory reproducibility of test results was poor and manufacturers' label claims were not verifiable [320, 579] and symposia sponsored by the American Society for Microbiology [647] heightened awareness of these problems and reconfirmed the need to improve the AOAC methods and reinstate a microbiological activity verification program. A General Accounting Office report entitled "Disinfectants: EPA Lacks Assurance They Work" [652] seemed to provide the necessary impetus for EPA to initiate some corrective measures, which include cooperative agreements to improve the AOAC methods and independent verification testing for all products labeled as sporicidal. These measures will eventually improve the aforementioned problems if interest and funds are sustained. A list of products registered with the EPA and labeled for use as sterilants, tuberculocides, or against HIV and/or HBV is available through the National Antimicrobial Information Network [406]. Organizations (e.g., Organization for Economic Cooperation and Development) are working to achieve harmonization of germicide testing and registration requirements.

One of the difficulties associated with the evaluation of the bactericidal activity of disinfectants is to prevent bacteriostasis due to disinfectant residues that are carried over into the subculture media. Likewise, small amounts of disinfectants on environmental surfaces may make it difficult to get an accurate bacterial count when performing microbiologic sampling of the hospital environment as part of an epidemiologic or research investigation. One of the ways these problems may be overcome is by employing neutralizers that inactivate residual disinfectants [653, 654]. Two commonly used neutralizing media for chemical disinfectants are Letheen Media and D/E Neutralizing Media. The former contains lecithin to neutralize quaternaries and polysorbate 80 (Tween 1980) to neutralize phenolics, hexachlorophene, formalin, and, with lecithin, ethanol. The D/E Neutralizing media will neutralize a broad spectrum of antiseptic and disinfectant chemicals, including quaternary ammonium compounds, phenols, iodine and chlorine compounds, mercurials, formaldehyde, and glutaraldehyde [655]. A review of neutralizers used in germicide testing can be found in references [653].

STERILIZATION

Most medical and surgical devices used in healthcare facilities are made of materials that are heat stable and thus are sterilized by heat, primarily steam sterilization. However, since 1950, there has been an increase in medical devices and instruments made of materials (e.g., plastics) that require low-temperature sterilization. Ethylene oxide gas has been used since the 1950s for heat- and moisture-sensitive medical devices. Within the past 10 years, a number of new, low-temperature sterilization

systems (e.g., hydrogen peroxide gas plasma, peracetic acid immersion) have been developed and are being used to sterilize medical devices. This section reviews sterilization technologies used in healthcare and makes recommendations for optimum performance in the processing of medical devices [1, 11, 295, 656-660].

Sterilization removes or destroys all microorganisms on the surface of an article or in a fluid to prevent disease transmission associated with the use of that item. While the use of inadequately sterilized critical items represents a high risk of transmitting pathogens, documented transmission of pathogens associated with an inadequately sterilized critical item is exceedingly rare [661, 662]. This is likely due to the wide margin of safety associated with the sterilization processes used in healthcare facilities. The concept of what constitutes "sterile" is measured as a probability of sterility for each item to be sterilized. This probability is commonly referred to as the sterility assurance level (SAL) of the product and is defined as the $\log_{10}$ number of the probability of a survivor on a single item. For example, if the probability of a spore surviving were one in one million, the SAL would be 10^{-6} [663, 664]. A SAL of 10^{-6} is the most often used level for sterile devices and drugs in the United States. In short, a SAL is an estimate of lethality of the entire sterilization process and is a conservative calculation [663].

Medical devices that have contact with sterile body tissues or fluids are considered critical items. These items should be sterile when used because any microbial contamination could result in disease transmission. Such items include surgical instruments, biopsy forceps, and implanted medical devices. If these items are heat resistant, the recommended sterilization process is steam sterilization, because it has the largest margin of safety. However, reprocessing heat- and moisture-sensitive items requires use of a low-temperature sterilization technology (e.g., ethylene oxide, hydrogen peroxide gas plasma, peracetic acid)[665]. A summary of the advantages and disadvantages for commonly used sterilization technologies is presented in Table 9.

Steam Sterilization

Overview

Of all the methods available for sterilization, moist heat in the form of saturated steam under pressure is the most widely used and the most dependable. Steam sterilization is nontoxic, inexpensive [666], rapidly microbicidal, sporicidal, and rapidly heats and penetrates fabrics (Table 9)[667]. Like all sterilization processes, steam sterilization has some deleterious effects on some materials, including corrosion and combustion of lubricants associated with dental handpieces [149]; reduction in ability to transmit light associated with laryngoscopes [668]; and increased hardening time (5.6 fold) with plaster-cast [669].

The basic principle of steam sterilization, as accomplished in an autoclave, is to expose each item to direct steam contact at the required temperature and pressure for the specified time. Thus, there are four parameters of steam sterilization: steam, pressure, temperature, and time. The ideal steam for sterilization is 100% “dry” saturated steam, with no water in the form of a fine mist. Pressure serves as a means to obtain the high temperatures necessary to quickly kill microorganisms. Specific temperatures must be obtained to ensure the microbicidal activity. The two common steam-sterilizing temperatures are 121°C (250°F) and 132°C (270°F). These temperatures (and other high temperatures [670]) must be maintained for a minimal time to kill microorganisms. Recognized exposure periods for sterilization of wrapped hospital supplies are 30 minutes at 121°C in a gravity displacement sterilizer or 4 minutes at 132°C in a prevacuum sterilizer (Table 10). At constant temperatures, sterilization times vary depending on the type of item (e.g., metal versus rubber, plastic, items with lumens), whether the item is wrapped or unwrapped, and the sterilizer type.

The two basic types of steam sterilizers (autoclaves) are the gravity displacement autoclave and the high-speed prevacuum sterilizer. In the former, steam is admitted at the top of the sterilizing chamber and, because the steam is lighter than air, forces air out the bottom of the chamber through the drain vent. The gravity displacement autoclaves are primarily used to process laboratory media, water,

pharmaceutical products, regulated medical waste, and nonporous articles whose surfaces have direct steam contact. For gravity displacement sterilizers the penetration time is prolonged because of incomplete air elimination. This point is illustrated with the decontamination of 10 lbs of microbiological waste, which requires at least 45 minutes at 121°C because the entrapped air remaining in a load of waste greatly retards steam permeation and heating efficiency [671, 672]. The high-speed prevacuum sterilizers are similar to the gravity displacement sterilizers except they are fitted with a vacuum pump to ensure air removal from the sterilizing chamber and load before the steam is admitted. The advantage of using a vacuum pump is that there is nearly instantaneous steam penetration even into porous loads. The Bowie-Dick test using 100% cotton surgical towels (huck towels) is used daily in the first cycle of all vacuum-type steam sterilizers to evaluate the efficacy of air removal. Air that is not removed from the chamber will interfere with steam contact. Smaller disposable test packs have been devised to replace the stack of folded surgical towels for testing the efficacy of the vacuum system in a prevacuum sterilizer [673].

Another design in steam sterilization is a steam-flush pressure pulsing process, which removes air rapidly by repeatedly alternating a steam flush and a pressure pulse above atmospheric pressure. Air is rapidly removed from the load as with the prevacuum sterilizer, but air leaks do not affect this process because the steam in the sterilizing chamber is always above atmospheric pressure. Typical sterilization temperatures and times are 132°C to 135°C with 3 to 4 minutes exposure time for porous loads and instruments [667, 674].

Like other sterilization systems, the steam cycle is monitored by mechanical, chemical, and biological monitors. Steam sterilizers usually are monitored using a printout (or graphically) by measuring temperature, the time at the temperature, and pressure. Typically, chemical indicators are incorporated into the pack to monitor the temperature. The effectiveness of steam sterilization is monitored with a biological indicator containing spores of *B. stearothermophilus.* Positive spore test results are a relatively rare event [675] and can be attributed to operator error, inadequate steam delivery [676], or equipment malfunction.

Portable steam sterilizers are used in outpatient, dental, and rural clinics [677]. These sterilizers are designed for small instruments, such as hypodermic syringes and needles and dental instruments. The ability of the sterilizer to reach physical parameters necessary to achieve sterilization can be monitored by mechanical, chemical, and biological indicators.

Microbicidal Activity

The oldest and most recognized agent for inactivation of microorganisms is heat. D-values (time to reduce the surviving population by 90% or 1 $\log_{10}$) allow a direct comparison of the heat resistance of microorganisms. Because a D-value can be determined at various temperatures, a subscript is used to designate the exposure temperature (i.e., D_{121C}). D_{121C}-values for *Bacillus stearothermophilus* used to monitor the steam sterilization process range from 1 to 2 minutes. Heat-resistant nonspore-forming bacteria, yeasts, and fungi have such low D_{121C} values that they cannot be experimentally measured [678].

Mode of Action

Moist heat destroys microorganisms by the irreversible coagulation and denaturation of enzymes and structural proteins. In support of this fact, it has been found that the presence of water significantly affects the coagulation temperature of proteins and the temperature at which microorganisms are destroyed.

Uses

Steam sterilization should be used whenever possible on all critical and semicritical items that are heat and moisture resistant (e.g., steam sterilizable respiratory therapy and anesthesia equipment), even when not essential to prevent pathogen transmission. Steam sterilizers also are used in healthcare facilities to decontaminate microbiological waste and sharps [671, 672, 679] but additional exposure time is

required in the gravity displacement sterilizer for these items.

Flash Sterilization

Overview

"Flash" steam sterilization was originally defined as sterilization of an unwrapped object at 132°C for 3 minutes at 27-28 lbs. of pressure in a gravity displacement sterilizer [680]. Although the wrapped method of sterilization is preferred for the reasons listed below, correctly performed flash sterilization is an effective process for the sterilization of critical medical devices [681, 682].

Flash sterilization is a modification of conventional steam sterilization (either gravity or prevacuum) in which the flashed item is placed in an open tray or is placed in a specially designed, covered, rigid container to allow for rapid penetration of steam. Historically, it is not recommended as a routine sterilization method because of the lack of timely biological indicators to monitor performance, absence of protective packaging following sterilization, possibility for contamination of processed items during transportation to the operating rooms, and the sterilization cycle parameters (i.e., time, temperature, pressure) are minimal. To address some of these concerns, many hospitals have done the following: placed equipment for flash sterilization in close proximity to operating rooms to facilitate aseptic delivery to the point of use (usually the sterile field in an ongoing surgical procedure); extended the exposure time to ensure lethality comparable to sterilized unwrapped items (e.g., 4 minutes at 270°C)[683, 684]; used new biological indicators that provide results in 1 hour for flash-sterilized items [683, 684]; and used protective packaging that permits steam penetration [1, 657, 660, 682, 685]. Further, some rigid, reusable sterilization container systems have been designed and validated by the container manufacturer for use with flash cycles. When sterile items are open to air, they will eventually become contaminated. Thus, the longer a sterile item is exposed to air, the greater the number of microorganisms that will settle on it. Sterilization cycle parameters for flash sterilization are shown in Table 11.

A few adverse events have been associated with flash sterilization. When evaluating an increased incidence of neurosurgical infections, the investigators noted that surgical instruments were flash sterilized between cases and 2 of 3 craniotomy infections involved plate implants that were flash sterilized [686]. A report of two patients who received burns during surgery from instruments that had been flash sterilized reinforced the need to develop policies and educate staff to prevent the use of instruments hot enough to cause clinical burns [687].

Uses

Flash sterilization is considered acceptable for processing cleaned patient-care items that cannot be packaged, sterilized, and stored before use. It also is used when there is insufficient time to sterilize an item by the preferred package method. Flash sterilization should not be used for reasons of convenience, as an alternative to purchasing additional instrument sets, or to save time [1]. Because of the potential for serious infections, flash sterilization is not recommended for implantable devices (i.e., devices placed into a surgically or naturally formed cavity of the human body if it is intended to remain there for a period of 30 days or more); however, flash sterilization may be unavoidable for some devices (e.g., orthopedic screw, plates). If flash sterilization of an implantable device is unavoidable, recordkeeping is essential for epidemiological tracking (e.g., of surgical site infection) and for an assessment of the reliability of the sterilization process (e.g., evaluation of biological monitoring records and sterilization maintenance records noting preventive maintenance and repairs with dates). This requires documentation of a biological result for the item sterilized that can be traced directly to the patient who received the item.

Low-Temperature Sterilization Technologies

Ethylene oxide (ETO) has been widely used as a low-temperature sterilant since the 1950s. It has been

the most commonly used process for sterilizing temperature- and moisture-sensitive medical devices and supplies in healthcare institutions in the United States. Until recently, ethylene oxide sterilizers combined ETO with a chloroflourocarbon (CFC) stabilizing agent, most commonly in a ratio of 12% ETO mixed with 88% CFC (referred to as 12/88 ETO).

For several reasons, healthcare personnel have been exploring the use of new low-temperature sterilization technologies [665, 688]. First, CFCs were phased out in December 1995 under provisions of the Clean Air Act [689]. CFCs were classified as a Class I substance under the Clean Air Act because of scientific evidence linking them to destruction of the earth's ozone layer. Second, some states (e.g., California, New York, Michigan) require the use of ETO abatement technology to reduce the amount of ETO being released into ambient air by 90-99.9%. Third, OSHA regulates the acceptable vapor levels of ETO (i.e., 1 ppm averaged over 8 hours) due to concerns that ETO exposure represents an occupational hazard [251]. These constraints have led to the recent development of alternative technologies for low-temperature sterilization in the healthcare setting.

Alternative technologies to ETO with chlorofluorocarbon that are currently available and cleared by the FDA for medical equipment include 100% ETO; ETO with a different stabilizing gas, such as carbon dioxide or hydrochlorofluorocarbons (HCFC); immersion in peracetic acid; and hydrogen peroxide gas plasma. Technologies under development for use in healthcare facilities, but not cleared by the FDA, include vaporized hydrogen peroxide, ozone vapor, vapor phase peracetic acid, gaseous chlorine dioxide, liquid performic acid, ionizing radiation, or pulsed light [306, 690].

These new technologies should be compared against the characteristics of an ideal low-temperature (<60°C) sterilant (Table 12)[688]. While it is apparent that all technologies will have limitations (Table 9), understanding the limitations imposed by restrictive device designs (e.g., long, narrow lumens) is critical for proper application of new sterilization technology [691]. For example, the development of increasingly small and complex endoscopes presents a difficult challenge for current sterilization processes. This occurs because microorganisms must be in direct contact with the sterilant for inactivation to occur. Several peer-reviewed scientific publications have data demonstrating concerns about the efficacy of several of the low-temperature sterilization processes (i.e., gas plasma, vaporized hydrogen peroxide, ETO, peracetic acid), particularly when the test organisms are challenged in the presence of serum and salt and a narrow lumen vehicle [354, 665, 692-694]. Factors shown to affect the efficacy of sterilization are shown in Table 13.

Ethylene Oxide "Gas" Sterilization

Overview

ETO is a colorless gas that is flammable and explosive. Four essential elements - gas concentration, temperature, humidity (water molecules carry ETO to reactive sites), and exposure time - influence the effectiveness of ETO sterilization [695, 696]. The operational ranges for each of these four parameters is 450 to 1200 mg/l, 37 to 63°C, 40 to 80%, and 1 to 6 hours, respectively [658]. Within certain limitations, an increase in gas concentration and temperature may shorten the time necessary for achieving sterilization.

The main disadvantages associated with ETO are the lengthy cycle time, the cost, and its potential hazards to patients and staff; the main advantage is that it can sterilize heat- or moisture-sensitive medical equipment without deleterious results (Table 9). Acute exposure to ETO may result in irritation (e.g., to skin, eyes, gastrointestinal or respiratory tracts) and central nervous system depression [697-700]. Chronic inhalation has been linked to the formation of cataracts, cognitive impairment, neurologic dysfunction, and disabling polyneuropathies [698, 699, 701-704]. Occupational exposure in hospitals has been linked to hematologic changes [705] and an increased risk of spontaneous abortions and various cancers [251, 706-708]. ETO should be considered a potential teratogen, mutagen, and carcinogen [251].

The basic ETO sterilization cycle consists of five stages (i.e., preconditioning and humidification, gas

introduction, exposure, evacuation, and air washes) and takes approximately 2 1/2 hrs excluding aeration time. Mechanical aeration for 8 to 12 hours at 50 to 60°C allows desorption of the toxic ETO residual contained in exposed absorbent materials. Most modern ETO sterilizers combine sterilization and aeration in the same chamber as a continuous process. These ETO models minimize potential ETO exposure during door opening and load transfer to the aerator. Ambient room aeration also will achieve desorption of the toxic ETO but requires 7 days at 20°C. There are no federal regulations for ETO sterilizer emission; however, many states have promulgated emission-control regulations [658].

The use of ETO evolved when few alternatives existed for sterilizing heat- and moisture-sensitive medical devices; however, favorable properties (Table 9) account for its continued widespread use [709]. Two ETO gas mixtures are available to replace ETO-chlorofluorocarbon (CFC) mixtures for large capacity, tank-supplied sterilizers. The ETO-carbon dioxide (CO_2) mixture consists of 8.5% ETO and 91.5% CO_2. This mixture is less expensive than ETO-hydrochlorofluorocarbons (HCFC), but a disadvantage is the need for pressure vessels rated for steam sterilization, because higher pressures (28-psi gauge) are required. The other mixture, which is a drop-in CFC replacement, is ETO mixed with HCFC. HCFCs are approximately 50-fold less damaging to the earth's ozone layer than are CFCs. The EPA will begin regulation of HCFC in the year 2015 and will terminate production in the year 2030. Two companies provide ETO-HCFC mixtures as drop-in replacement for CFC-12; one mixture consists of 8.6% ETO and 91.4% HCFC, and the other mixture is composed of 10% ETO and 90% HCFC [709].

ETO toxicity has been established in a variety of animals. In a variety of *in vitro* and animal studies, ETO has been demonstrated to be mutagenic and carcinogenic. Acute exposure may result in irritation (e.g., to skin, eyes, gastrointestinal or respiratory tracts) and central nervous system depression. Chronic inhalation may result in peripheral neuropathies. Occupational exposure in healthcare facilities has been linked to an increased risk of spontaneous abortions and various cancers [251]. Injuries (e.g., tissue burns) to patients have been associated with ETO residues in implants used in surgical procedures [710]. Residual ETO in capillary flow dialysis membranes has been shown to be neurotoxic *in vitro* [711]. OSHA has established a permissible exposure limit (PEL) of 1 ppm airborne ETO in the workplace, expressed as a time-weighted average (TWA) for an 8-hour work shift in a 40-hour work week. The "action level" for ETO is 0.5 ppm, expressed as an 8-hour TWA, and the excursion limit is 5 ppm, expressed as a 15-minute TWA [658]. Several personnel monitoring methods (e.g., charcoal tubes and passive sampling devices) are in use [658].

Mode of Action

The microbicidal activity of ETO is considered to be the result of alkylation of protein, DNA, and RNA. Alkylation, or the replacement of a hydrogen atom with an alkyl group, within cells prevents normal cellular metabolism and replication [712].

Microbicidal Activity

The excellent microbicidal activity of ETO has been demonstrated in several studies [354, 694, 713, 714] and summarized in published reports [712]. ETO inactivates all microorganisms although the bacterial spores (especially *B. subtilis*) are more resistant than other microorganisms. For this reason *B. subtilis* is the recommended biological indicator.

Like all sterilization processes, the effectiveness of ETO sterilization can be altered by lumen length, lumen diameter, inorganic salts, and organic materials [354, 692, 694, 714]. For example, although ETO is not used commonly for reprocessing endoscopes [17], several studies have shown failure of ETO in inactivating contaminating spores in endoscope channels [692] or lumen test units [354, 693] and residual ETO levels averaging 66.2 ppm even after the standard degassing time [348]. Failure of ETO also has been observed when dental handpieces were contaminated with *Streptococcus mutans* and exposed to ETO [715].

Uses

ETO is used in healthcare facilities to sterilize critical items (and sometimes semicritical items) that are moisture or heat sensitive and cannot be sterilized by steam sterilization.

Hydrogen Peroxide Gas Plasma

Overview

New sterilization technology based on plasma was patented in 1987 and marketed in the United States in 1993. Gas plasmas have been referred to as the fourth state of matter (i.e., liquids, solids, gases, and gas plasmas). Gas plasmas are generated in an enclosed chamber under deep vacuum using radio frequency or microwave energy to excite the gas molecules and produce charged particles, many of which are in the form of free radicals. A free radical is an atom with an unpaired electron and is a highly reactive species. The free radicals produced within a plasma field are capable of interacting with essential cell components (e.g., enzymes, nucleic acids) and thereby disrupt the metabolism of microorganisms. The type of seed gas used and the depth of the vacuum are two important variables that can determine the effectiveness of this process.

In the late 1980s the first hydrogen peroxide gas plasma system for sterilization of medical and surgical devices was field-tested. In this process, the sterilization chamber is evacuated and hydrogen peroxide solution is injected from a cassette and is vaporized in the sterilization chamber to a concentration of 6 mg/l. The hydrogen peroxide vapor diffuses through the chamber (50 minutes), exposes all surfaces of the load to the sterilant, and initiates the inactivation of microorganisms. An electrical field created by a radio frequency is applied to the chamber to create a gas plasma. Microbicidal free radicals (e.g., hydroxyl and hydroperoxyl) are generated in the plasma. The excess gas is removed and in the final stage (i.e., vent) of the process the sterilization chamber is returned to atmospheric pressure by introduction of high-efficiency filtered air. The by-products of the cycle (e.g., water vapor, oxygen) are nontoxic and eliminate the need for aeration. Thus, the sterilized materials can be handled safely, either for immediate use or storage. The process operates in the range of 37-44°C and has a cycle time of 75 minutes. If any moisture is present on the objects the vacuum will not be achieved and the cycle aborts [694, 716-718].

A newer version of the unit improves sterilizer efficacy by using two cycles with a hydrogen peroxide diffusion stage (>6 mg/l) and a plasma stage per sterilization cycle. This revision, which is achieved by a software modification, reduces total processing time from 73 to 52 minutes. The manufacturer believes that the enhanced activity obtained with this system is due in part to the pressure changes that occur during the injection and diffusion phases of the process and to the fact that the process consists of two equal and consecutive half cycles, each with a separate injection of hydrogen peroxide [694, 719, 720]. This system has received FDA 510K clearance with limited application for sterilization of medical devices (Table 9). The biological indicator used with this system is *Bacillus subtilis* spores [688].

Penetration of hydrogen peroxide vapor into long or narrow lumens has been addressed by the use of a diffusion enhancer. This is a small, breakable glass ampoule of concentrated hydrogen peroxide (50%) with an elastic connector that is inserted into the device lumen and crushed immediately before sterilization [355, 720]. The diffusion enhancer has been shown to sterilize bronchoscopes contaminated with *Mycobacteria tuberculosis* [721]. It is now under regulatory review in the United States.

Another gas plasma system, which differs from the above in several important ways, including the use of peracetic acid-acetic acid-hydrogen peroxide vapor, was removed from the marketplace because of reports of corneal destruction to patients when ophthalmic surgery instruments had been processed in the sterilizer [722, 723]. In this investigation, exposure of potentially wet ophthalmologic surgical instruments with small bores and brass components to the plasma gas led to degradation of the brass to copper and zinc [723, 724]. The experimenters showed that when rabbit eyes were exposed to the rinsates of the gas

plasma-sterilized instruments, corneal decompensation was documented. This toxicity is highly unlikely with the hydrogen peroxide gas plasma process since a toxic, soluble form of copper would not form (LA Feldman, written communication, April 1998).

Mode of Action

This process inactivates microorganisms primarily by the combined use of hydrogen peroxide gas and the generation of free radicals (hydroxyl and hydroproxyl free radicals) during the plasma phase of the cycle.

Microbicidal Activity

This process has the ability to inactivate a broad range of microorganisms, including resistant bacterial spores. Studies have been conducted against vegetative bacteria (including mycobacteria), yeasts, fungi, viruses, and bacterial spores [354, 694, 716, 718, 725-727]. Like all sterilization processes, the effectiveness can be altered by lumen length, lumen diameter, inorganic salts, and organic materials [354, 692, 694, 725, 726].

Uses

Materials and devices that cannot tolerate high temperatures and humidity, such as some plastics, electrical devices, and corrosion-susceptible metal alloys, can be sterilized by hydrogen peroxide gas plasma. This method has been compatible with most (>95%) medical devices and materials tested [719, 728, 729].

Peracetic Acid Sterilization

Overview

Peracetic acid is a highly biocidal oxidizer that maintains its efficacy in the presence of organic soil. Peracetic acid removes surface contaminants (primarily protein) on endoscopic tubing [561, 730]. An automated machine using peracetic acid to sterilize medical, surgical, and dental instruments chemically (e.g., endoscopes, arthroscopes) was introduced in 1988. This microprocessor-controlled, low-temperature sterilization method is commonly used in the United States [80]. The sterilant, 35% peracetic acid, and an anticorrosive agent are supplied in a single-dose container. The container is punctured at the time of use when the lid of the sterilizer is closed. The concentrated peracetic acid is diluted to 0.2% with filtered water (0.22 μm) at a temperature of approximately 50°C. The diluted peracetic acid is circulated within the chamber of the machine and pumped through the channels of the endoscope for 12 minutes, decontaminating exterior surfaces, lumens, and accessories. Interchangeable trays are available to permit the processing of up to three rigid endoscopes or one flexible endoscope. Connectors are available for most types of flexible endoscopes for the irrigation of all channels by forced flow. Rigid endoscopes are placed within a lidded container, and the sterilant fills the lumens by diffusion (see below for the importance of channel connectors). The peracetic acid is discarded via the sewer and the instrument rinsed four times with filtered water. Clean filtered air is passed through the chamber of the machine and endoscope channels to remove excess water [563]. As with any sterilization process, the system can only sterilize surfaces that can be contacted by the sterilant. For example, bronchoscopy-related infections occurred when bronchoscopes were processed using the wrong connector [116, 567]. Investigation of these incidents revealed that bronchoscopes were inadequately reprocessed when inappropriate channel connectors were used and when there were inconsistencies between the reprocessing instructions provided by the manufacturer of the bronchoscope and the manufacturer of the automatic endoscope reprocessor [116]. The importance of channel connectors to achieve sterilization was also shown for rigid lumen devices [694, 731].

The manufacturers suggest the use of biological monitors both at the time of installation and routinely to ensure effectiveness of the process. *B. subtilis* spore strips were recommended for monitoring by the manufacturer. The manufacturer's clip must be used to hold the strip in the designated spot in the machine as a broader clamp will not allow the sterilant to reach the spores trapped under it [732]. One

investigator reported a 3% failure rate when the appropriate clips were used to hold the spore strip within the machine [562]. The use of biological monitors designed to monitor either steam sterilization or ETO for a liquid chemical sterilizer has been questioned for several reasons including spore wash-off from the filter paper strips which may cause less valid monitoring [733-736]. A chemical monitoring strip, which is a conductivity reading of the in-use solution and is not a direct indicator of peracetic acid, is routinely used in each cycle as an additional process control [562].

Mode of Action

Only limited information is available regarding the mechanism of action of peracetic acid, but it is thought to function as other oxidizing agents, i.e., it denatures proteins, disrupts cell wall permeability, and oxidizes sulfhydral and sulfur bonds in proteins, enzymes, and other metabolites [514, 568].

Microbicidal Activity

Peracetic acid will inactivate gram-positive and gram-negative bacteria, fungi, and yeasts in <5 minutes at <100 ppm. In the presence of organic matter, 200-500 ppm is required. For viruses, the dosage range is wide (12-2250 ppm), with poliovirus inactivated in yeast extract in 15 minutes with 1500 to 2250 ppm. Bacterial spores in suspension are inactivated in 15 seconds to 30 minutes with 500 to 10,000 ppm (0.05 to 1%)[514].

Simulated-use trials have demonstrated excellent microbicidal activity [562, 563, 737], and three clinical trials have demonstrated both excellent microbial killing and no clinical failures leading to infection [27, 565, 738]. Alfa and co-workers, who compared the peracetic acid system with ETO, demonstrated the high efficacy of the system. Only the peracetic acid system was able to completely kill 6-$\log_{10}$ of *Mycobacterium chelonae*, *Enterococcus faecalis*, and *B. subtilis* spores with both an organic and inorganic challenge [566]. Like other sterilization processes, the efficacy of the process can be diminished by soil challenges [739] and test conditions [694].

Uses

This automated machine is used to chemically sterilize medical (e.g., flexible endoscopes), surgical (e.g., rigid endoscopes), and dental instruments in the United States. Lumened endoscopes must be connected to an appropriate channel connector to ensure that the sterilant has direct contact with the contaminated lumen [694, 731, 740].

Microbicidal Activity of Low-Temperature Sterilization Technologies

Sterilization processes used in the United States must be cleared by the FDA, and they require that sterilizer microbicidal performance be tested under simulated-use conditions [741]. The FDA requires that the test article be inoculated with 10^6 colony-forming units of the most resistant test organism and prepared with organic and inorganic test loads. The inocula must be placed in various locations of the test articles, including those least favorable to penetration and contact with the sterilant (e.g., lumens). Cleaning before sterilization is not allowed in the demonstration of sterilization efficacy. Several studies have evaluated the relative microbicidal efficacy of these low-temperature sterilization technologies (Table 14). These studies have either tested the activity of a sterilization process against specific microorganisms [727, 742, 743], evaluated the microbicidal activity of a singular technology [563, 692, 714, 717, 718, 725, 726, 730, 738, 744] or evaluated the comparative effectiveness of several sterilization technologies [229, 327, 354, 566, 693, 694, 719, 727, 742, 743, 745, 746]. Several test methodologies use stainless steel or porcelain carriers that are inoculated with a test organism. Commonly used test organisms include vegetative bacteria, mycobacteria, and spores of *Bacillus* species. The available data demonstrate that low-temperature sterilization technologies are able to provide a 6-$\log_{10}$ reduction of microbes when inoculated onto carriers in the absence of salt and serum. However, tests can be constructed such that all of the available sterilization technologies are unable to reliably achieve complete inactivation of a microbial load [326, 327, 354, 693, 694]. For example, almost all of the sterilization processes will fail to reliably inactivate the

microbial load in the presence of salt and serum [354, 693].

The effect of salts and serums on the sterilization process were studied initially in the 1950s and 1960s [325, 747]. These studies showed that a high concentration of crystalline-type materials and a low protein content provided greater protection to spores than did serum with a high protein content [327]. A study by Doyle and Ernst demonstrated resistance of spores by crystalline material applied not only to low-temperature sterilization technology but also to steam and dry heat [326]. These studies showed that occlusion of *Bacillus subtilis* spores in calcium carbonate crystals dramatically increased the time required for inactivation as follows: 10 seconds to 150 minutes for steam (121°C), 3.5 hours to 50 hours for dry heat (121°C), 30 seconds to >2 weeks for ETO (54°C). More recently, investigators have corroborated and extended these findings [354, 355, 692, 745, 746]. While soils containing both organic and inorganic materials impair microbial killing, soils that contain a high inorganic salt-to-protein ratio favor crystal formation and impair sterilization by occlusion of organisms [326, 327, 716].

Alfa and colleagues demonstrated a 6-$\log_{10}$ reduction of the microbial inoculum of porcelain penicylinders using a variety of vegetative and spore-forming organisms (Table 14)[354]. However, if the bacterial inoculum was in tissue-culture medium supplemented with 10% serum, only the ETO 12/88 and ETO-HCFC sterilization mixtures could sterilize 95% to 97% of the penicylinder carriers. The other plasma and ETO sterilizers demonstrated significantly reduced activity (Table 14). For all sterilizers evaluated using penicylinder carriers (i.e., ETO 12/88, 100% ETO, hydrogen peroxide gas plasma), there was a 3- to 6-$\log_{10}$ reduction of inoculated bacteria even in the presence of serum and salt. For each sterilizer evaluated, the ability to inactivate microorganisms in the presence of salt and serum was reduced even further when the inoculum was placed in a narrow-lumen test object (3 mm diameter by 125 cm long). Although there was a 2- to 4-$\log_{10}$ reduction in microbial kill, less than 50% of the lumen test objects were sterile when processed using any of the sterilization methods evaluated except the peracetic acid immersion system (Table 14)[693]. Complete killing (or removal) of 6-$\log_{10}$ of *Enterococcus faecalis, Mycobacterium chelonei*, and *Bacillus subtilis* spores in the presence of salt and serum and lumen test objects was observed only for the peracetic acid immersion system.

With respect to the results by Alfa and coworkers [354], Jacobs showed that the use of the tissue culture media created a technique induced sterilization failure [327]. Jacobs et al. showed that microorganisms mixed with tissue culture media, used as a surrogate body fluid, formed physical crystals that protected the microorganisms used as a challenge. If the carriers were exposed for 60 sec to nonflowing water, the salts dissolved and the protective effect disappeared. Since any device would be exposed to water for a short period of time during the washing procedure, these protective effects would have little clinical relevance [327].

Narrow lumens provide a challenge to some low-temperature sterilization processes. For example, Rutala and colleagues showed that, as lumen size decreased, increased failures occurred with some low-temperature sterilization technologies. However, some low-temperature processes such as ETO-HCFC and the hydrogen peroxide gas plasma process remained effective even when challenged by a lumen as small as 1 mm in the absence of salt and serum [694].

The importance of allowing the sterilant to come into contact with the inoculated carrier is demonstrated by comparing the results of two investigators who studied the peracetic acid immersion system. Alfa and coworkers demonstrated excellent activity of the peracetic acid immersion system against three test organisms using a narrow-lumen device. In these experiments, the lumen test object was connected to channel irrigators, which ensured that the sterilant had direct contact with the contaminated carriers [566]. This effectiveness was achieved through a combination of organism wash-off and peracetic acid sterilant killing the test organisms [566]. The data reported by Rutala et al. demonstrated failure of the peracetic acid immersion system to eliminate *Bacillus stearothermophilus* spores from a carrier placed in a lumen test object. In these experiments, the lumen test unit was not connected to channel irrigators. The authors attributed the failure of the peracetic acid immersion system to eliminate the high levels of spores from

the center of the test unit to the inability of the peracetic acid to diffuse into the center of 40-cm long, 3-mm diameter tubes. This may be caused by an air lock or air bubbles formed in the lumen, impeding the flow of the sterilant through the long and narrow lumen and limiting complete access to the *Bacillus* spores [694, 731]. Recent experiments using a channel connector specifically designed for 1-, 2-, and 3-mm lumen test units with the peracetic acid immersion system were completely effective in eliminating an inoculum of 10^6 *Bacillus stearothermophilus* spores [72]. The restricted diffusion environment that exists in the test conditions would not exist with flexible scopes processed in the peracetic acid immersion system, because the scopes are connected to channel irrigators to ensure that the sterilant has direct contact with contaminated surfaces. Alfa and associates attributed the efficacy of the peracetic acid immersion system to the ability of the liquid chemical process to dissolve salts and remove protein and bacteria due to the flushing action of the fluid [566].

Bioburden of Surgical Devices

In general, used medical devices are contaminated with a relatively low bioburden of organisms [119, 748, 749]. Nystrom evaluated medical instruments used in general surgical, gynecological, orthopedic, and ear-nose-throat operations and found that 62% of the instruments were contaminated with $<10^1$ organisms after use, 82% with $<10^2$, and 91% with $<10^3$. After being washed in an instrument washer, more than 98% of the instruments had $<10^1$ organisms, and none $>10^2$ organisms [748]. Other investigators have published similar findings [119, 749]. For example, Rutala and colleagues found that, after a standard cleaning procedure, 72% of 50 surgical instruments contained $<10^1$ organisms, 86% $<10^2$, and only 6% had $>3 \times 10^2$ [749]. In a study by Chan-Myers and associates of rigid-lumen medical devices, the bioburden on both the inner and outer surface of the lumen ranged from 10^1 to 10^4 organisms per device. After cleaning, 83% of the devices had a bioburden $\leq 10^2$ organisms [749]. In all of these studies, the contaminating microflora consisted mainly of vegetative bacteria, usually of low pathogenicity (e.g., coagulase-negative *Staphylococcus*) [119, 748, 749].

Penna and coworkers evaluated the microbial load on used critical medical devices such as spinal anesthesia needles and angiographic catheters and sheaths. Mesophilic microorganisms were detected at levels of 10^1 to 10^2 in only two of five needles. The bioburden on used angiographic catheters and sheath introducers exceeded 10^3 CFUs on 14% (3 of 21) and 21% (6 of 28), respectively [744].

Effect of Cleaning on Sterilization Efficacy

The effect of salt and serum on the efficacy of low-temperature sterilization technologies has raised concern regarding the margin of safety of these technologies. Experiments have shown that salts have the greatest impact on protecting microorganisms from killing [327, 354]. However, experiments by Jacobs and colleagues suggest that these concerns may not be clinically relevant. Jacobs et al. evaluated the relative rate of removal of inorganic salts, organic soil, and microorganisms from medical devices to better understand the dynamics of the cleaning process [327]. These tests were conducted by inoculating Alfa soil (tissue-culture media and 10% fetal bovine serum)[354] containing 10^6 *B. stearothermophilus* spores onto the surface of a stainless-steel scalpel blade. After drying for 30 minutes at 35°C followed by 30 minutes at room temperature, the samples were placed in water at room temperature. The blades were removed at specified times, and the concentration of total protein and chloride ion was measured. The results showed that soaking in deionized water for 60 seconds resulted in a >95% release rate of chloride ion from NaCl solution in 20 seconds, Alfa soil in 30 seconds, and fetal bovine serum in 120 seconds. Thus, contact with water for short periods, even in the presence of protein, rapidly leads to dissolution of salt crystals and complete inactivation of spores by a low-temperature sterilization process (Table 13). Based on these experimental data, cleaning procedures would eliminate the detrimental

effect of high salt content on a low-temperature sterilization process.

These articles [327, 354, 693] assessing low-temperature sterilization technology reinforce the importance of meticulous cleaning before sterilization. These data support the critical need for healthcare facilities to develop rigid protocols for cleaning contaminated objects before sterilization [357]. Sterilization of instruments and medical devices is compromised if the process is not preceded by cleaning.

Other Sterilization Methods

Ionizing Radiation

Sterilization by ionizing radiation, primarily by cobalt 60 gamma rays or electron accelerators, is a low-temperature sterilization method that has been used for a number of medical products (e.g., tissue for transplantation, pharmaceuticals). Because of high sterilization costs, this method is an unfavorable alternative to ETO sterilization in healthcare facilities but is suitable for large-scale sterilization. Some deleterious effects on patient-care equipment associated with gamma radiation include induced oxidation in polyethylene [750] and delamination and cracking in polyethylene knee bearings [751]. Several reviews [752, 753] dealing with the sources, effects, and application of ionizing radiation may be referred to for more detail.

Dry-Heat Sterilizers

This method should be used only for materials that might be damaged by moist heat or that are impenetrable to moist heat (e.g., powders, petroleum products, sharp instruments). The advantages for dry heat include the following: it is nontoxic and does not harm the environment; a dry heat cabinet is easy to install and has relatively low operating costs; it penetrates materials; and it is noncorrosive for metal and sharp instruments. The disadvantages for dry heat are that the slow rate of heat penetration and microbial killing makes this a time-consuming method and the high temperatures are not suitable for most materials [754]. The most common time-temperature relationships for sterilization with hot air sterilizers are 170°C (340°F) for 60 minutes, 160°C (320°F) for 120 minutes, and 150°C (300°F) for 150 minutes. B. subtilis spores should be used to monitor the sterilization process for dry heat because they are more resistant to dry heat than are B. stearothermophilus spores. The primary lethal process is considered to be oxidation of cell constituents.

There are two types of dry-heat sterilizers: the static-air type and the forced-air type. The static-air type is referred to as the oven-type sterilizer as heating coils in the bottom of the unit cause the hot air to rise inside the chamber via gravity convection. This type of dry-heat sterilizer is much slower in heating, requires longer time to reach sterilizing temperature, and is less uniform in temperature control throughout the chamber than is the forced-air type. The forced-air or mechanical convection sterilizer is equipped with a motor-driven blower that circulates heated air throughout the chamber at a high velocity, permitting a more rapid transfer of energy from the air to the instruments [188, 755].

Liquid Chemicals

Several FDA-registered chemical sterilants are capable of producing sterile medical and surgical materials after immersion periods for 3 to 12 hours(Tables 7, 8)[45]. Sterilization with chemical sterilants is an alternative for those materials that cannot be sterilized by heat. These solutions are most commonly used as high-level disinfectants when a shorter processing time is required. While chemical sterilants may achieve sterilization of medical/surgical devices after a prolonged exposure time, the processed item would have to be rinsed with sterile water in a sterile environment and delivered to the use area in an aseptic manner to maintain sterility. This would be difficult unless the chemical sterilant was used in an automatic reprocessing system. Generally, chemical sterilants cannot be monitored using a biological indicator to verify sterility [734, 735].

Several published studies compare the sporicidal effect of liquid chemical germicides against spores of

Bacillus and *Clostridium* [58, 517, 518, 559].

Performic Acid

A new automated endoscope reprocessing system has been submitted to FDA for clearance. This process is designed to provide rapid, automated, point-of-use chemical sterilization of flexible endoscopes. The system consists of a computer-controlled endoscope reprocessing machine and a new, proprietary liquid sterilant using performic acid. The sterilant is produced, as needed by the machine, by automatic mixing of the two component solutions of hydrogen peroxide and formic acid. This sterilant is fast-acting against spore-forming bacteria (e.g., 10 minute exposure to 1800 ppm performic acid kills *B. subtilis* spores). The major features of the system are an automatic cleaning process; capability to process two flexible scopes asynchronously; automated channel blockage and leak detection; filtered-water rinsing and scope drying after sterilization; hard-copy documentation of key process parameters; user-friendly machine interface/control; and total cycle time less than 30 minutes [306].

Filtration

This technology is used to remove bacteria from thermolabile pharmaceutical fluids that cannot be purified by any other means. In order to remove bacteria, the membrane pore size (e.g., 0.22 μm) must be smaller than the bacteria and uniform throughout [756]. Some investigators have appropriately questioned whether the removal of microorganisms by filtration really is a sterilization method because of slight bacterial passage through filters, viral passage through filters, and transference of the sterile filtrate into the final container under aseptic conditions entail a risk of contamination [757].

Microwave

Microwaves are used in medicine for disinfection of soft contact lenses, dental instruments, dentures, milk, and urinary catheters for intermittent self catheterization [758-763]. Microwaves are radio-frequency waves, which are usually used at a frequency of 2450 MHz. The microwaves produce friction of water molecules in an alternating electrical field. The intermolecular friction derived from the vibrations generates heat and some authors believe that the effect of microwaves depends on the heat produced while others postulate a nonthermal lethal effect [764, 765]. The initial reports showed microwaves to be an effective microbicide. The microwaves produced by a "home-type" microwave oven (2.45 GHz) completely inactivate bacterial cultures, mycobacteria, viruses, and *B. stearothermophilus* spores within 60 seconds to 5 minutes depending on the challenge organism [765-768]. Najdovski et al. confirmed these results but also found that higher power microwaves in the presence of water may be needed for sterilization [764]. Other investigators showed the complete destruction of *Mycobacterium bovis* was obtained with 4 minutes of microwave exposure (600W, 2450 MHz). The effectiveness of microwave ovens for different sterilization and disinfection purposes should be tested and demonstrated as test conditions affect the results (e.g., presence of water, microwave power). Sterilization of metal instruments can be accomplished but requires certain precautions [759]. The use of microwave ovens to disinfect intermittent-use catheters also has been suggested. Researchers found that test bacteria (e.g., *E.coli*, *Klebsiella pneumoniae*, *Candida albicans*) were eliminated from red rubber catheters within 5 minutes [769].

Glass Bead "Sterilizer"

Glass bead "sterilization" uses small glass beads (1.2-1.5 mm diameter) and high temperature (217-232°C) for brief exposure times (e.g., 45 seconds) to inactivate microorganisms. These devices have been used for several years in the dental profession [770-772]. The FDA believes there is a risk of infection with this device because of its potential failure to sterilize dental instruments and has required that commercial distribution of these devices cease unless the manufacturer files a premarket approval application with the FDA.

Vaporized Hydrogen Peroxide (VHP)

Hydrogen peroxide solutions have been used as chemical sterilants for many years. However, VHP was not developed for the sterilization of medical equipment until the mid-1980s. One method for delivering

VHP to the reaction site uses a deep vacuum to pull liquid hydrogen peroxide (30% concentration) from a disposable cartridge through a heated vaporizer and then, following vaporization, into the sterilization chamber. A second approach to VHP delivery is the flow-through approach in which the VHP is carried into the sterilization chamber by a carrier gas such as air using either a slight negative pressure (vacuum) or slight positive pressure. Applications of this technology include a dental sterilizer, an endoscope sterilizer (VHP 100), and a portable VHP generator (VHP 1000) for decontamination of large and small-enclosed areas. One VHP system (VHP 1000) is commercially available and a VHP endoscope sterilizer (VHP 100) is under review [690]. VHP offers several appealing features that include rapid cycle time (30-45 minutes); low temperature; environmentally safe by-products (H_2O, oxygen [O_2]); good material compatibility; and ease of operation, installation and monitoring. VHP's limitations are cellulose cannot be processed; nylon becomes brittle; and the penetration capabilities are less than those of ETO.

Ozone

Ozone has been used for years as a drinking water disinfectant. Ozone is produced when O_2 is energized and split into two monatomic (O_1) molecules. The monatomic oxygen molecules then collide with O_2 molecules to form ozone, which is O_3. Thus, ozone consists of O_2 with a loosely bonded third oxygen atom that is readily available to attach to, and oxidize, other molecules. This additional oxygen atom makes ozone a powerful oxidant that destroys microorganisms but is highly unstable (i.e., half-life of 22 minutes at room temperature).

The first model of ozone sterilizer to be submitted to the FDA operates on standard 110V electricity and a medical-grade oxygen. No special venting or drains are required. The system has a total cycle time of 3 hours. In operation, the sterilizer is fed a supply of oxygen, which is filtered and supplied to the ozone generator. The resulting oxygen/ozone mixture then is humidified and introduced into the sterilization chamber. Following the exposure, any remaining ozone is run through a destruction device and is catalytically converted back into oxygen, which is filtered and vented to the room. The system uses a modular container/chamber system in which a rigid aluminum sterilization container serves as the primary sterilization chamber. The rigid container is placed inside a stationary master chamber and connected to feed gas lines via quick-connect fittings. After the sterilization cycle is complete, the sterilization container can be disconnected and sterile instruments can be transported and stored inside the container. The system requires no degassing of instruments before use or handling. Material degradation is the major concern with using ozone as a sterilant. The reactive nature of ozone gas will cause permanent damage to natural fibers and some plastics (e.g., latex, rubber, polypropylene). This system is awaiting FDA 510K clearance before marketing [690].

A gaseous ozone generator was investigated for decontamination of rooms used to house patients colonized with MRSA. The results demonstrated that the device tested would be inadequate for the decontamination of a hospital room [773].

Formaldehyde Steam

Low-temperature steam with formaldehyde is used as a low-temperature sterilization method in many countries, particularly in Scandinavia, Germany, and the United Kingdom. The process involves the use of formalin, which is vaporized into a formaldehyde gas that is admitted then into the chamber. A formaldehyde concentration of 8-16 mg/l is generated at an operating temperature of 70-75°C. The sterilization cycle consists of a series of stages that include an initial vacuum to remove air from the chamber and load, followed by steam admission to the chamber with the vacuum pump running to purge the chamber of air and to heat the load, followed by a series of pulses of formaldehyde gas, followed by steam. Formaldehyde is removed from the sterilizer and load by repeated alternate evacuations and flushing with steam and air. This system has some advantages, e.g., the cycle time for formaldehyde gas is faster than that for ETO and the cost per cycle is relatively low. However, ETO is more penetrating and operates at lower temperatures than do steam/formaldehyde.

Formaldehyde vapor cabinets also may be used in healthcare facilities to sterilize heat-labile medical equipment [774]. Commonly, there is no circulation of formaldehyde and no temperature and humidity

controls. The release of gas from paraformaldehyde tablets (placed on the lower tray) is slow and produces a low partial pressure of gas. The microbicidal quality of this procedure is unknown [775].

Reliable sterilization using formaldehyde is achieved when performed with a high concentration of gas, at a temperature between 60° and 80°C and with a relative humidity of 75 to 100%.

Studies indicate that formaldehyde is a mutagen and a potential human carcinogen, and OSHA regulates formaldehyde. The permissible exposure limit for formaldehyde in work areas is 0.75 ppm measured as a 8-hour TWA. The OSHA standard includes a 2 ppm short-term exposure limit (STEL) (i.e., maximum exposure allowed during a 15-minute period). As with the ETO standard, the formaldehyde standard requires that the employer conduct initial monitoring to identify employees who are exposed to formaldehyde at or above the action level or STEL. If this exposure level is maintained, employers may discontinue exposure monitoring until there is a change that could affect exposure levels or an employee reports formaldehyde-related signs and symptoms [225].

Gaseous chlorine dioxide

A gaseous chlorine dioxide system for sterilization of healthcare products was developed in the late 1980s [690, 776, 777]. Chlorine dioxide has low toxicity in humans and is not mutagenic or carcinogenic. As the chlorine dioxide concentration increases, the time required to achieve sterilization becomes progressively shorter. For example, only 30 minutes were required at 40 mg/l to sterilize the 10^6 *B. subtilis* spores at 30° to 32°C [778].

Vaporized Peracetic Acid

The sporicidal activity of peracetic acid vapor at 20, 40, 60, and 80% relative humidity and 25°C was determined on *Bacillus subtilis* var. *niger* spores on paper and glass surfaces. Appreciable activity occurred within 10 minutes of exposure to 1 mg of peracetic acid per liter at 40% or higher relative humidity [779].

Sterilizing Practices

Overview

The delivery of sterile products for use in patient care depends not only on the effectiveness of the sterilization process but also on the unit design, decontamination, disassembling and packaging of the device, loading the sterilizer, monitoring, and other aspects of device reprocessing. Hospital personnel should perform most cleaning, disinfecting, and sterilizing of patient-care supplies in a central processing department in order to more easily control quality. The aim of central processing is the orderly processing of medical and surgical instruments to protect patients from infections while minimizing risks to staff and preserving the value of the items being reprocessed [780]. Some healthcare facility personnel are able to promote the same level of efficiency and safety in the preparation of supplies in other areas like the operating room and anesthesia and respiratory therapy.

Ensuring consistency of sterilization practices requires a comprehensive program that ensures operator competence and proper methods of cleaning and wrapping instruments, loading the sterilizer, operating the sterilizer, and monitoring of the entire process. Furthermore, care must be consistent from an infection prevention standpoint in all patient-care settings, such as hospital and outpatient facilities.

Sterilization Cycle Validation

A sterilization process must be validated before it is put into routine use. Validation is the demonstration that a specified process, operated within defined tolerances, will consistently produce a product complying with a predetermined specification [781, 782]. The key factors that need to be demonstrated in validation of a sterilization process are that the devices are indeed sterile and that the sterilizer performs as intended without presenting a hazard to the patient or the user. Medical device manufacturers have

numerous standards and guidelines to assist in the development of their sterilization programs (e.g., Association for Advancement of Medical Instrumentation [AAMI])[656, 657]. Validation of these processes is frequently accomplished through the development of customized sterilization cycles for a particular product or product family.

Physical Facilities

The central processing area(s) ideally should be divided into at least three areas: decontamination, packaging, and sterilization and storage. Minimally, physical barriers should separate the decontamination area from the other sections to contain contamination on used items, but ideally physical barriers should separate all three sections. In the decontamination area reusable supplies (and possibly disposable items that are reused) are received, sorted, and decontaminated. If physical separation of decontamination and clean/sterile areas is not achievable, spatial separation may be satisfactory by good work-flow patterns, appropriate ventilation controls, and work practices [656]. The recommended airflow pattern should contain contaminates within the decontamination area and minimize the flow of contaminates to the clean areas. The American Institute of Architects [783] recommends negative pressure and no fewer than six air exchanges per hour in the decontamination area and 10 air changes per hour in the sterilizer equipment room. The packaging area is for inspecting, assembling, and packaging clean, but not sterile, material. The sterile storage area should be a limited access area with a controlled temperature (68-73°F) and relative humidity (30-60%). The floors and walls should be constructed of materials capable of withstanding chemical agents used for cleaning or disinfecting. Ceilings and wall surfaces should be constructed of non-shedding materials. Physical arrangements of processing areas are presented schematically in two references [656, 755].

Cleaning

As repeatedly mentioned, items must be cleaned using water with detergents or enzymatic cleaners [351, 352] before processing. Cleaning reduces the bioburden and removes foreign material (i.e., organic residue and inorganic salts) that interferes with the sterilization process by acting as a barrier to the sterilization agent [119, 327, 350, 748, 749]. Precleaning in patient-care areas may be needed on items that are heavily soiled with feces, sputum, blood, or other material. Items sent to central processing without removing gross soil may be difficult to clean because of dried secretions and excretions. Cleaning and decontamination should be done as soon as possible after items have been used.

Several types of mechanical cleaning machines (e.g., utensil washer-sanitizer, ultrasonic cleaner, washer-sterilizer, dishwasher, washer-disinfector) may facilitate cleaning and decontamination of most items. This equipment often is automated and may increase productivity, improve cleaning effectiveness, and decrease worker exposure to blood and body fluids. Delicate and intricate objects and heat- or moisture-sensitive articles may require careful cleaning by hand. All used items sent to the central processing area should be considered contaminated (unless decontaminated in the area of origin), handled with gloves (forceps or tongs are sometimes needed to avoid exposure to sharps), and decontaminated by one of the aforementioned methods to render them safer to handle. Items composed of more than one removable part should be disassembled. Care should be taken to ensure that all parts are kept together, so that reassembly can be accomplished efficiently [656].

Investigators have described the degree of cleanliness by visual and microscopic examination. One study found 91% of the instruments to be clean visually but, when examined microscopically, 84% of the instruments had residual debris. Sites that contained residual debris included junctions between insulating sheaths and activating mechanisms of laparoscopic instruments and articulations and grooves of forceps. More research is needed to understand the clinical significance of these findings [784].

Personnel working in the decontamination area should wear household-cleaning-type rubber or plastic gloves when handling or cleaning contaminated instruments and devices. Face masks, eye protection, and gowns/aprons should be worn when splashing may occur (e.g., when manually cleaning contaminated devices). Contaminated instruments are a source of microorganisms that could inoculate personnel through nonintact skin on the hands or through contact with the mucous membranes of eyes,

nose, or mouth [224, 656]. Reusable sharps that have been in contact with blood present a special hazard. Employees must not reach with their gloved hands into trays or containers that hold these sharps to retrieve them [224].

Packaging

Once items are cleaned, dried, and inspected, those requiring sterilization must be wrapped or placed in rigid containers and should be arranged in instrument trays/baskets according to the guidelines provided by the AAMI [656-658]. These guidelines state that hinged instruments should be opened; items with removable parts should be disassembled unless the device manufacturer or researchers provide specific instructions or test data to the contrary [120]; complex instruments should be prepared and sterilized according to device manufacturer's instructions and test data; devices with concave surfaces should be positioned to facilitate drainage of water; heavy items should be positioned not to damage delicate items; and the weight of the instrument set should be based on the design and density of the instruments and the distribution of metal mass [656].

There are several choices in methods to maintain sterility of surgical instruments, including rigid containers, peel pouches of plastic and/or paper, and sterilization wraps (woven and nonwoven). While hospitals may use many of these packaging options, the most commonly used is sterilization wraps. The packaging material must allow penetration of the sterilant, provide protection against contact contamination during handling, provide an effective barrier to microbial penetration, and maintain the sterility of the processed item after sterilization. An ideal sterilization wrap would successfully address barrier effectiveness, penetrability (i.e., allows sterilant to penetrate), aeration (e.g., allows ETO to dissipate), ease of use, drapeability, flexibility, puncture resistance, tear strength, toxicity, odor, waste disposal, linting, cost, and transparency [785]. Unacceptable packaging must not be used for ETO (e.g., foil, polyvinylchloride, and polyvinylidene chlorine [Saran wrap])[658] or hydrogen peroxide gas plasma (e.g., linens and paper cannot be used to wrap medical items).

In central processing, double wrapping can be done sequentially or nonsequentially (i.e., simultaneous wrapping). The sequential wrap uses two sheets of the standard sterilization wrap, one wrapped after the other. This procedure creates a package within a package. The nonsequential process uses two sheets wrapped at the same time so that the wrapping needs to be performed only once. This latter method provides multiple layers of protection of surgical instruments from contamination and saves time since wrapping is done only once. Multiple layers are still common practice due to the rigors of handling within the facility even though the barrier efficacy of a single sheet of wrap has improved over the years [785]. Written and illustrated procedures for preparation of items to be packaged should be readily available and used by personnel when packaging procedures are performed [346].

Loading

All items to be sterilized should be arranged so all surfaces will be directly exposed to the sterilizing agent. Thus, loading procedures must allow for free circulation of steam (or another sterilant) around each item. Historically, it was recommended that muslin fabric packs should not exceed the maximal dimensions, weight, and density of 12 x 12 x 20 inches, 12 lbs, and 7.2 lbs per cubic foot, respectively. Due to the variety of textiles on the market, the textile manufacturer should be consulted for sterilization recommendations.

There are several important basic principles for loading a sterilizer: allow for proper steam circulation; nonperforated containers should be placed on their edge; nonporous containers must be positioned so air can get out and steam can get in; small items should be loosely placed in wire baskets; and peel packs should be placed on edge [346, 656].

Storage

Studies in the early 1970s suggested that wrapped surgical trays remained sterile for varying periods depending on the type of material used to wrap the trays. Safe storage times for sterile packs vary with the porosity of the wrapper and storage conditions (e.g., open versus closed cabinets). Heat-sealed,

plastic peel-down pouches and wrapped packs sealed in 3-mil (3/1000 inch) polyethylene overwrap have been reported to be sterile for as long as 9 months after sterilization. The 3-mil polyethylene is applied after sterilization to extend the shelf life for infrequently used items [786]. Supplies wrapped in double-thickness muslin comprising four layers, or equivalent, remain sterile for at least 30 days. Any item that has been sterilized should not be used after the expiration date has been exceeded or if the sterilized package is wet, torn, or punctured.

Although some hospitals continue to date every sterilized product and use the time-related shelf-life practice, many hospitals have switched to an event-related shelf-life practice. This latter practice recognizes that the product should remain sterile until some event causes the item to become contaminated (e.g., tear in packaging, packaging becomes wet)[787]. Event-related factors that contribute to the contamination of a product include bioburden (i.e., the amount of contamination in the environment), air movement, traffic, location, humidity, insects, vermin, flooding, storage area space, open/closed shelving, temperature, and the properties of the wrap material [785, 788]. There are data that support the event-related shelf-life practice [789, 790]. Butt and coworkers examined the effect of time on the sterile integrity of paper envelopes, peel pouches, and nylon sleeves. The most important finding was the absence of a trend toward an increased rate of contamination over time for any pack when placed in covered storage [790]. Thus, contamination of a sterile item is event-related and the probability of contamination increases with increased handling [791].

Sterile supplies should be stored far enough from the floor (8 to 10 inches), the ceiling (5 inches unless near a sprinkler head), and the outside walls (2 inches) to allow for adequate air circulation, ease of cleaning, and compliance with local fire codes (e.g., supplies must be at least 18 inches from sprinkler heads). Medical and surgical supplies should not be stored under sinks or in other locations where they can become wet. Sterile items that become wet are considered contaminated because moisture brings with it microorganisms from the air and surfaces. Closed or covered cabinets are ideal but open shelving may be used for storage. Any package that has fallen or been dropped on the floor must be inspected for damage to the packaging or contents. If the package is heat-sealed in impervious plastic and the seal is still intact, the package should be considered not contaminated. If undamaged, items packaged in plastic need not be reprocessed.

Monitoring (Mechanical, Chemical, Biological Indicators)

The sterilization procedure should be monitored routinely by using a combination of mechanical, chemical, and biological indicators to evaluate the sterilizing conditions and indirectly the microbiologic status of the processed items. The mechanical monitors for steam sterilization include the daily assessment of cycle time and temperature by examining the temperature record chart (or computer printout) and an assessment of pressure via the pressure gauge. The mechanical monitors for ETO include time, temperature, and pressure recorders that provide data via computer printouts, gauges, and/or displays [658]. Unfortunately, two essential elements for ETO sterilization (i.e., the gas concentration and humidity) cannot be monitored in healthcare ETO sterilizers.

Chemical indicators are convenient, are inexpensive, and indicate that the item has been exposed to the sterilization process. In one study, chemical indicators were more likely than biological indicators to indicate sterilization at marginal sterilization times (e.g., 2 minutes)[684]. Chemical indicators could be used in conjunction with biological indicators, but based on current studies should not replace them because they indicate sterilization at marginal sterilization time and because only a biological indicator consisting of resistant spores can measure the microbial killing power of the sterilization process [684]. Chemical indicators are affixed on the outside of each pack to show that the package has been processed through a sterilization cycle, but these indicators do not prove sterilization has been achieved. Preferably, a chemical indicator also should be placed on the inside of each pack to verify steam penetration. Chemical indicators usually are either heat-or chemical-sensitive inks that change color when one or more germicidal-related parameter (e.g., temperature) is present. If the internal and/or external indicator suggests inadequate processing, the item should not be used [659]. An air-removal test (Bowie-Dick Test) must be performed daily in an empty prevacuum steam sterilizer to ensure air removal.

Biological indicators are recognized by most authorities as being closest to the ideal monitors of the sterilization process [792] because they measure the sterilization process directly by using the most resistant microorganisms (i.e., *Bacillus* spores), and not by merely testing the physical and chemical conditions necessary for sterilization. Since the *Bacillus* spores used in biological indicators are more resistant and present in greater numbers than are the common microbial contaminants found on patient-care equipment, the demonstration that the biological indicator has been inactivated strongly implies that other potential pathogens in the load have been killed [681].

An ideal biological monitor of the sterilization process should be easy to use, be inexpensive, not be subject to exogenous contamination, provide positive results as soon as possible after the cycle so that corrective action may be accomplished, and provide positive results only when the sterilization parameters (e.g., time and temperature) are inadequate to kill microbial contaminates. However, the biological indicator should not be so resistant as to cause needless recall and reprocessing [684].

Biological indicators are the only process indicators that directly monitor the lethality of a given sterilization process. Spores to monitor a sterilization process have demonstrated resistance to the sterilizing agent and are more resistant than the bioburden found on medical devices [119, 748, 749]. *B. subtilis* spores (10^6) are used to monitor ETO, hydrogen peroxide gas plasma, and dry heat, and *B. stearothermophilus* spores (10^5) are used to monitor steam sterilization and liquid peracetic acid sterilizers. *B. stearothermophilus* is incubated at 55°C, and *B. subtilis* is incubated at 35-37°C. Steam and low temperature sterilizers (e.g., ETO) should be monitored at least weekly with the appropriate commercial preparation of spores. If a sterilizer is used frequently (e.g., several loads per day), daily use of biological indicators allows earlier discovery of equipment malfunctions or procedural errors and thus minimizes the extent of patient surveillance and product recall needed in the event of a positive biological indicator [656]. Each load should be monitored if it contains implantable objects. If feasible, implantable items should not be used until the results of spore tests are known to be negative.

Originally, spore-strip biological indicators required up to 7 days of incubation to detect viable spores from marginal cycles (i.e., when few spores remained viable). A next generation of biological indicator was self-contained in plastic vials containing a spore-coated paper strip and a growth media in a crushable glass ampoule. This indicator had a maximum incubation of 48 hours but significant failures could be detected in $\leq$24 hours. A rapid-readout biological indicator that detects the presence of enzymes of *B. stearothermophilus* by reading a fluorescent product produced by the enzymatic breakdown of a nonfluorescent substrate has been marketed for the past 10 years. Studies demonstrate that the sensitivity of rapid-readout tests for steam sterilization (1 hour for flash sterilization, 3 hrs for 121°C gravity and 132°C vacuum sterilizers) parallels that of the conventional sterilization-specific biological indicators [683, 684, 793, 794]. The rapid-readout biological indicator is a dual indicator system as it also detects acid metabolites produced during growth of the *B. stearothermophilus* spores. This system is different from the rapid indicator system that uses only a chemical (i.e., enzyme) to monitor the sterilization cycle. The manufacturer of the latter system claims this product is equivalent to biological indicators but independent comparative data using suboptimal sterilization cycles (e.g., reduced time or temperature) have not been published [795].

A new rapid-readout ETO biological indicator has been designed for rapid and reliable monitoring of ETO sterilization processes. The indicator is available outside the United States, but has not yet been cleared by the FDA for use in the United States [306]. The rapid-readout ETO biological indicator detects the presence of *B. subtilis* by detecting the activity of an enzyme present within the *B. subtilis* organism, beta-glucosidase. The fluorescence indicates the presence of an active spore-associated enzyme and a sterilization process failure. This indicator also detects acid metabolites produced during growth of the *B. subtilis* spore. Per manufacturer's data, the enzyme always was detected whenever viable spores were present. This was expected because the enzyme is relatively ETO resistant and is inactivated at a slightly longer exposure time than the spore. The rapid-readout ETO biological indicator can be used to monitor 100% ETO, EO-CFC, and ETO-HCFC mixture sterilization cycles. It has not been tested in ETO-

CO_2 mixture sterilization cycles.

Perkins et al. found that the standard biological indicator used for monitoring full-cycle steam sterilizers may not be adequate for monitoring flash sterilizers [796]. Biological indicators specifically designed for monitoring flash sterilization are now available, and studies comparing them have been published [683, 684, 797].

Since sterilization failure can occur (about 1% for steam)[798], a procedure to follow in the event of positive spore tests has been provided by CDC and the Association of periOperating Room Nurses (AORN). The 1981 CDC recommendation is that "objects, other than implantable objects, do not need to be recalled because of a single positive spore test unless the steam sterilizer or the sterilization procedure is defective." The rationale for this recommendation is that single positive spore tests in sterilizers occur sporadically. They may occur for reasons such as slight variation in the resistance of the spores [799], improper use of the sterilizer, and laboratory contamination during culture (uncommon with self-contained spore tests). If the mechanical (e.g., time, temperature, pressure in the steam sterilizer) and chemical (internal and/or external) indicators suggest that the sterilizer is functioning properly, a single positive spore test probably does not indicate sterilizer malfunction but the spore test should be repeated immediately [799]. If the spore tests remain positive, use of the sterilizer should be discontinued until it is serviced [12]. Similarly, AORN states that a single positive spore test does not necessarily indicate a sterilizer failure. If the test is positive, the sterilizer should immediately be rechallenged for proper use and function. Items, other than implantable ones, do not necessarily need to be recalled unless a sterilizer malfunction is found. If a sterilizer malfunction is discovered, the items must be considered nonsterile, and the items from the suspect load(s) should be recalled, insofar as possible, and reprocessed [800]. A suggested protocol for management of positive biological indicators is shown in Table 15 [676]. This approach or a more conservative approach of considering any unexplainable positive spore test as a sterilizer malfunction that requires retrieval and reprocessing of all items are the only defensible positions that can be assumed unless there is strong evidence for the biological indicator being defective [799] or the growth medium contained a *Bacillus* contaminant [801]. This more conservative approach should be used for sterilization methods other than steam (e.g., ETO, hydrogen peroxide gas plasma).

If patient-care items were used before retrieval, the infection control professional should assess the risk of infection in collaboration with central processing, surgical services, and risk management staff. The factors that should be considered include the chemical indicator result (e.g., nonreactive chemical indicator may indicate temperature not achieved); the results of other biological indicators that followed the positive biological indicator (e.g., positive on Tuesday, negative on Wednesday); the parameters of the sterilizer associated with the positive biological indicator (e.g., reduced time at correct temperature); the time-temperature chart (or printout); and the microbial load associated with decontaminated surgical instruments (e.g., 85% of decontaminated surgical instruments have less than 100 CFU). The margin of safety in steam sterilization is sufficiently large that there is minimal infection risk associated with items in a load that show spore growth, especially if the item was properly cleaned and the temperature was achieved (e.g., as shown by acceptable chemical indicator or temperature chart). There are no published studies that document disease transmission via a nonretrieved surgical instrument from a sterilizer with a positive biological indicator.

False-positive biological indicators may occur from improper testing or faulty indicators. The latter may occur from improper storage, processing, product contamination, material failure, or variation in resistance of spores. Gram stain and subculture of a positive biological indicator may determine if a contaminant has created a false-positive result [676, 802]. However, in one incident, the broth used as growth medium contained a contaminant, *B. coagulans,* which resulted in broth turbidity at 55°C [801]. Testing of paired biological indicators from different manufacturers can assist in assessing a product defect [676].

The size and composition of the biological indicator test pack should be standardized to create a

significant challenge to air removal and sterilant penetration and to obtain interpretable results. There is a standard 16-towel pack recommended by AAMI for steam sterilization [803] consisting of 16 all-cotton unwrapped huck towels (average size of 9.4 in x 8.9 in x 6.1 in, average weight of 3.3 lbs, and density of 11.3 lbs/cu ft). One or more biological indicators are placed between the seventh and eight towels in the approximate geometric center of the pack. This test pack has not gained universal use as a standard pack that simulates the actual in-use conditions of steam sterilizers. Commercially available disposable test packs that have been shown to be equivalent to the AAMI test pack also may be used. The test pack should be placed flat in an otherwise empty sterilizer chamber, in the area least favorable to sterilization. This area is normally in the front, bottom section of the sterilizer, near the drain [656]. A control biological indicator from the lot used for testing should be left unexposed to the sterilant, and then incubated to verify the presterilization viability of the test spores and proper incubation. There also is a routine test pack for ETO where a biological indicator is placed in a plastic syringe with plunger, then placed in the folds of a clean surgical towel, and wrapped. The test pack is placed in the center of the sterilizer load [658]. Sterilization records (mechanical, chemical, and biological) should be retained for a time period in compliance with standards (e.g., Joint Commission for the Accreditation of Healthcare Facilities requests 3 years) and state and federal regulations.

In Europe, biological monitors are not used routinely to monitor the sterilization process. Instead, the method of assuring sterility by monitoring the physical conditions of the sterilization process is termed "parametric release." It has been defined as the release of sterile product based on process compliance to physical specifications. At present in Europe, parametric release is accepted for steam, dry heat, and ionizing radiation processes, as the physical conditions are understood and can be monitored directly [804]. For example, with steam sterilizers the load could be monitored with probes that would yield data on temperature, time, and humidity at representative locations in the chamber.

Periodic infection control rounds to areas using sterilizers to standardize the sterilizer's use may identify correctable variances in operator competence; documentation of sterilization records, including chemical and biological indicator test results; sterilizer maintenance and wrapping; and load numbering of packs. These rounds also may identify improvement activities to ensure that operators are adhering to established standards [805].

REUSE OF MEDICAL DEVICES

The reuse of single-use medical devices began in the late 1970s. Before this time most devices were considered reusable. Reuse of single-use devices increased as a cost-saving measure. Approximately 20 to 30% of U.S. hospitals report that they reuse at least one type of single-use device. Reuse of single-use devices involves regulatory, ethical, medical, legal and economic issues and has been extremely controversial for more than two decades [806]. The U.S. public has expressed increasing concern regarding the risk of infection and injury when reusing medical devices intended and labeled for single use. Although some investigators have demonstrated it is safe to reuse disposable medical devices such as cardiac electrode catheters [807-809], additional studies are needed to define the risks and document the benefits.

In August 2000, the FDA released a guidance document on single-use devices reprocessed by third parties or hospitals [810]. In this guidance document, the FDA states that hospitals or third- party reprocessors will be considered "manufacturers" and regulated in the same manner. A reused single-use device will have to comply with the same regulatory requirements of the device when it was originally manufactured. This document presents FDA's intent to enforce premarket submission requirements within 6 months (February 2001) for class III devices (e.g., cardiovascular intra-aortic balloon pump, transluminal coronary angioplasty catheter); 12 months (August 2001) for class II devices (e.g., blood pressure cuff, bronchoscope biopsy forceps); and 18 months (February 2002) for class I devices (e.g., disposable medical scissors, ophthalmic knife). The FDA uses two types of premarket requirements for

nonexempt class I and II devices, a 510(k) submission that may have to show that the device is as safe and effective as the same device when new, and a premarket approval application. The 510(k) submission must provide scientific evidence that the device is safe and effective for its intended use. The FDA allowed hospitals a year to comply with the nonpremarket requirements (registration and listing, reporting adverse events associated with medical devices, quality system regulations, and proper labeling). The options for hospitals are to stop reprocessing single-use devices, comply with the rule, or outsource to a third-party reprocessor. The FDA guidance document does not apply to permanently implantable pacemakers, hemodialyzers, opened but unused single-use devices, or healthcare settings other than acute-care hospitals.

CONCLUSION

When properly used, disinfection and sterilization can ensure the safe use of invasive and non-invasive medical devices. However, current disinfection and sterilization guidelines must be strictly adhered to.

RECOMMENDATIONS FOR DISINFECTION AND STERILIZATION IN HEALTHCARE FACILITIES

A. Rationale

The Guideline for Disinfection and Sterilization in Healthcare Facilities, 2002, provides recommendations with the ultimate goal of reducing rates of healthcare-associated infections through the appropriate use of disinfectants and sterilization processes. Each recommendation is categorized on the basis of existing scientific data, theoretical rationale, and applicability. The CDC system for categorizing recommendations is as follows.

B. Rankings

Category IA. Strongly recommended for implementation and strongly supported by well-designed experimental, clinical, or epidemiologic studies.

Category IB. Strongly recommended for implementation and supported by some experimental, clinical, or epidemiologic studies and a strong theoretical rationale.

Category IC. Required by state or federal regulations. Because of state differences, readers should not assume that the absence of an *IC* recommendation implies absence of state regulations.

Category II. Suggested for implementation and supported by suggestive clinical or epidemiologic studies or a theoretical rationale.

No recommendation. Unresolved issue. Practices for which insufficient evidence or no consensus regarding efficacy exists.

C. Recommendations

1. Cleaning of Patient-Care Equipment

a. Hospitals should perform most cleaning, disinfection, and sterilization of patient-care equipment in a central processing department in order to more easily control quality. *Category II*.
b. Meticulous cleaning of patient-care items with water and detergent, or water and enzymatic cleaners must precede high-level disinfection or sterilization procedures. *Category IA* [5, 63, 76-78, 90, 119, 327, 748, 749].
c. Cleaning should remove all visible organic residue (e.g., residue of blood and tissue) and inorganic salts. *Category IA* [325-327, 354, 745, 747].
d. Cleaning should be done as soon as practical after use as soiled materials become dried onto the instruments. Dried or baked materials on the instrument make the removal process more difficult and the disinfection or sterilization process less effective or ineffective. *Category IA* [54, 55, 351, 599, 811, 812].
e. Cleaning can be done manually, using friction, or mechanically (e.g., with ultrasonic cleaners, washer-decontaminators, washer-sterilizers). *Category IB* [327, 348, 356, 813].
f. If an automatic cleaner/disinfector is used, ensure the unit is used in accordance with the manufacturer's recommendations. *Category IB* [72, 96, 116, 567].
g. Ensure that detergents or enzymatic detergents are compatible with metals and other materials used in medical instruments. *Category II* [350].
h. Equipment that no longer functions as intended should be discarded or repaired. *Category II* [723].

2. Indications for Sterilization, High-Level Disinfection, and Low-Level Disinfection

a. Critical medical and surgical devices and instruments that enter normally sterile tissue or the vascular system or through which a sterile body fluid flows (e.g., blood) must be sterile before each patient use. *Category IA* [119, 375, 661, 662, 744, 748, 749, 814].
b. Semicritical patient-care equipment that touches mucous membranes (e.g., gastrointestinal endoscopes, endotracheal tubes, anesthesia breathing circuits, and respiratory therapy equipment) or nonintact skin should receive, as a minimum, high-level disinfection. *Category IA* [5, 10, 71-73, 75, 81, 85, 86, 93, 100, 101, 108, 113-115, 356, 815].
c. Noncritical patient-care surfaces (e.g., bedrails, over-the-bed table) and equipment (e.g., blood pressure cuff) that touch intact skin should receive low-level disinfection. *Category IB* [10, 39-42, 44, 289, 291, 294, 308, 816].

3. Selection and Use of Disinfectants for Noncritical Patient-Care Items

a. Process noncritical patient-care equipment using a disinfectant and concentration of germicide as listed in Table 1. *Category IB* [10, 39-42, 44, 289, 291, 294, 308, 816].
b. Disinfect noncritical medical equipment (e.g., blood pressure cuff, stethoscope) with a disinfectant or disinfectant/detergent at the proper use dilution and a contact time of at least 30 seconds. *Category IB* [10, 39-42, 47, 54, 55, 234, 289, 291, 294, 414, 816].
c. The frequency for disinfecting noncritical patient-care surfaces should comply with hospital policies and should minimally be done when visibly soiled and on a regular basis (e.g., after each patient use, daily, or weekly). *Category IB* [291, 293, 817].
d. Disinfect noncritical patient-care equipment if used on a patient on Contact Precautions before use by another patient or use dedicated, disposable equipment. *Category IB* [40, 300, 818].

4. Disinfecting Environmental Surfaces in Healthcare Facilities

a. Clean housekeeping surfaces (e.g., floors, wall, tabletops) on a regular basis, as spills occur, and when visibly soiled. *Category IB* [291, 293, 294, 817, 819].
b. The frequency for environmental surface disinfection should comply with hospital policies and should minimally be done when visibly soiled and on a regular basis (e.g., daily, three times per week). *Category IB* [291, 293, 817].
c. Follow manufacturers' instructions for proper use of disinfecting products, especially the recommended use-dilution. *Category IB*. [285, 311].
d. Clean walls, blinds, and window curtains in patient-care areas when visibly contaminated or soiled. *Category II.*
e. Prepare disinfecting solutions as needed and replace with fresh solution frequently (e.g., floor mopping solution every three patient rooms or changed no longer than 60-minute intervals) according to the facility's policy. *Category IB* [44].
f. Decontaminate mop heads and cleaning cloths regularly to prevent contamination (e.g., launder at least daily and heat dry). *Category IB* [44, 309, 310].
g. Use a one-step process and an Environmental Protection Agency (EPA)-registered hospital grade disinfectant/detergent designed for housekeeping purposes. *Category IB* [40-42, 292, 294].
h. Do not use high-level disinfectants/liquid chemical sterilants for disinfection of non-critical surfaces. *Category II* [45, 251].
i. Wet-dust horizontal surfaces regularly (e.g., daily, three times per week) using clean cloths moistened with an EPA-registered hospital disinfectant. Prepare the disinfectant as recommended by the manufacturer. *Category IB* [44, 291, 293, 309, 310, 817].
j. The contact time for low-level disinfection of noncritical items is at least 30 seconds. *Category II* [41, 42, 47, 54, 55, 234].
k. Phenolics should not be used to clean infant bassinets and incubators during the stay of an infant. If phenolics are used to terminally clean infant bassinets and incubators, the surfaces should be rinsed thoroughly with water and dried before the infant bassinets and incubators are reused. *Category IB* [10, 581, 582].
l. Promptly clean and decontaminate spills of blood or other potentially infectious materials. *Category IC* [224].
m. Occupational Safety and Health Administration (OSHA) requires that blood spills be disinfected using an EPA-registered tuberculocidal agent or a solution of 6.00% sodium hypochlorite (household bleach) diluted between 1:10 and 1:100 with water. An EPA-registered disinfectant that is labeled effective against Human Immunodeficiency Virus (HIV) and Hepatitis B Virus (HBV) would be considered an appropriate disinfectant provided the surfaces have not been contaminated with agent(s) or volumes of or concentrations of agent(s) for which higher level disinfection is recommended. *Category IC* [224, 226].
n. For site decontamination of spills of blood or other potentially infectious materials (OPIM), use protective gloves and other personal protective equipment (PPE) appropriate for this task. If sodium hypochlorite solutions are selected use a 1:100 dilution (500 ppm available chlorine) to decontaminate nonporous surfaces after cleaning a small spill of either blood or OPIM. If a spill involves large amounts (e.g., >10 ml) of blood or OPIM, use a 1:10 dilution for the first application of germicide before cleaning. *Category IB* [226, 227].
o. In units with high endemic *Clostridium difficile* infection rates or in an outbreak setting, the use of dilute solutions of 6.0% sodium hypochlorite (1:10 dilution of bleach) can be used for routine environmental disinfection. *Category II* [191, 192].
p. If chlorine solution is not prepared fresh daily, chlorine may be stored for up to 30 days in a capped plastic bottle with a 50% reduction in chlorine concentration over 30 days (e.g., 1000 ppm chlorine at day 0 decreases to 500 ppm chlorine by day 30). *Category IB* [401, 820].

5. Disinfectant Fogging

a. Do not perform disinfectant fogging for routine purposes in patient-care areas. *Category II* [169].

6. Management of Equipment and Surfaces in Dentistry

a. Dental instruments that penetrate soft tissue or bone (e.g., forceps, scalpels, bone chisels, scalers, and burs) are classified as critical and should be sterilized before each reuse or discarded. Dental instruments that are not intended to penetrate oral soft tissue or bone (e.g., amalgam condensers, air-water syringes) but may come into contact with oral tissues are classified as semicritical and should be sterilized after each use. Noncritical surfaces, such as uncovered operatory surfaces (e.g., countertops, chair switches), should be disinfected between patients with an intermediate- or low-level disinfectant. *Category IB* [145-147].

b. Barrier protective coverings may be used for noncritical surfaces that are touched frequently with gloved hands during the delivery of patient care, likely to become contaminated with blood or body substances, or difficult to clean. The coverings should be changed when visibly soiled, when damaged, and on a routine basis (e.g., between patients). *Category II* [146].

7. High-Level Disinfection of Endoscopes

a. Meticulous cleaning of the endoscope with an enzymatic detergent recommended by the endoscope manufacturer should be performed immediately after use. Cleaning is essential before the use of currently available automatic endoscope reprocessors. *Category IA* [63, 75-78, 85, 90, 92, 348, 351, 352, 356, 821].

b. Disconnect and disassemble accessories as far as possible and completely immerse accessories in the enzymatic detergent. *Category 1B* [351, 352].

c. All of the channels should be flushed and brushed, if accessible, to remove all organic (e.g., blood, tissue) and other residue. Clean the external surfaces and accessories of the devices by using a soft cloth, sponge, or brushes. *Category IA* [5, 10, 36, 81, 85, 106, 109, 567, 659, 694, 731, 740].

d. Enzymatic detergents (or detergents) should be discarded after each use, as these products are not microbicidal and may allow microbial growth. *Category IB* [36, 85, 352].

e. Endoscopes (e.g., arthroscopes, cystoscope, laparoscopes) that pass through normally sterile tissues must be subjected to a sterilization procedure before each use; if this is not feasible, they should receive at least high-level disinfection. Disinfection should be followed by a sterile water rinse. *Category IB* [10, 12, 26-28, 30, 33, 36, 85, 422].

f. Reusable accessories (e.g., biopsy forceps or other cutting instruments) that break the mucosal barrier should be cleaned (e.g., ultrasonic clean biopsy forceps) and then sterilized between each patient. *Category IA* [5, 10, 12, 36, 71, 81, 85, 100, 106, 109, 114, 239, 659].

g. Endoscopes and accessories that come in contact with mucous membranes are classified as semicritical items and should receive at least high-level disinfection after each patient use. *Category IA* [5, 10, 12, 36, 71, 81, 85, 93, 100, 106, 109, 113-115, 239, 659].

h. An FDA-cleared sterilant or high-level disinfectant should be used for sterilization or high-level disinfection (Table 1). *Category IA* [5, 10, 12, 36, 71, 72, 79, 81, 85, 659].

i. Formulations containing glutaraldehyde, ortho-phthalaldehyde, hydrogen peroxide, chlorine, peracetic acid, and both hydrogen peroxide and peracetic acid can achieve high-level disinfection if the objects are properly cleaned (see Table 1 for recommended concentrations). *Category IB* [5, 10, 12, 36, 71, 72, 79, 81, 85, 659].

j. The exact time for disinfecting semicritical patient-care equipment varies for the Food and Drug Administration (FDA)-cleared high-level disinfectants (Table 7). The longer the

exposure of an item to a disinfectant, the more likely it is that all contaminating microorganisms will be inactivated. Extending exposure times beyond the minimum effective time (see below and text) should not be done because with extended exposure to a high-level disinfectant it is more likely to damage delicate and intricate instruments such as endoscopes. *Category IB* [10, 45, 50, 53, 58, 63].

k. The FDA-cleared label claim for high-level disinfection should be used unless scientific studies demonstrate an alternative exposure time is effective for disinfecting semicritical items. For example, if >2% glutaraldehyde is used, scientific data show that all immersible internal and external surfaces should be in contact with this high-level disinfectant for not less than 20 minutes at 20°C. *Category IA* [10, 50, 53, 54, 60, 61, 63, 64, 68, 75, 76, 83, 91, 176, 177, 183, 184, 466-468].

l. When using other FDA-cleared high-level disinfectants, use manufactures' recommended exposure times. These products may have a reduced exposure time (e.g., 0.55% ortho-phthalaldehyde for 12 minutes at 20°C, 7.35% hydrogen peroxide plus 0.23% peracetic acid for 15 minutes at 20°C) compared to glutaraldehyde at room temperature because of their rapid inactivation of mycobacteria or reduced exposure time due to increased mycobactericidal activity at elevated temperature (2.5% glutaraldehyde at 5 minutes at 35°C). *Category IB* [63, 74, 547, 549, 556].

m. The disinfectant or chemical sterilant selected should have no or minimal deleterious effects on the objects (e.g., chlorine may corrode metals; see text for more information). Avoid the use of high-level disinfectants on an endoscope if the endoscope manufacturer warns against use because of functional damage (with or without cosmetic damage). *Category IB* [45].

n. Completely immerse the instrument in the high-level disinfectant and ensure all channels are perfused. Nonimmersible endoscopes should be phased out immediately. *Category IB* [81, 85, 694, 717, 731].

o. After high-level disinfection, endoscopes (including channels) must be rinsed with sterile water, filtered water, or tap water, followed by a rinse with 70 to 90% ethyl or isopropyl alcohol. *Category IA* [10, 28, 30-33, 36, 37, 81, 85, 97, 108, 822].

p. The instrument and its channels should be thoroughly forced-air dried. A final drying step that includes flushing all channels with alcohol followed by purging the channels with air greatly reduces the possibility of recontamination of the endoscope by waterborne microorganisms. *Category IB* [37].

q. Endoscopes should be hung in a vertical position to facilitate drying. *Category II* [10, 36, 81, 85, 106, 109, 659].

r. Endoscopes should be stored in a manner that will protect them from contamination. *Category II* [10, 36, 81, 85, 106, 109, 659].

s. The water bottle, used to provide intraprocedural flush solution, and its connecting tube should be sterilized or receive high-level disinfection at least daily. Sterile water should be used to fill the water bottle. *Category IB* [28, 30-33, 85, 822].

t. A log should be maintained indicating for each procedure, the patient's name and medical record number (if available), the procedure, the endoscopist, and the serial number or other identifier of the endoscope used. *Category IB* [36, 81, 85, 106, 109, 659].

u. Facilities where endoscopes are used and disinfected should be designed to provide a safe environment for healthcare workers and patients. Air-exchange equipment (e.g., ventilation system, exhaust hoods) should be used to minimize the exposure of all persons to potentially toxic vapors (e.g., glutaraldehyde). The vapor concentration of the chemical sterilant used should not exceed allowable limits (e.g., those of American Conference of Governmental Industrial Hygienists, OSHA). *Category IB, IC* [251, 253, 511, 512].

v. Routine testing of the liquid sterilants/high-level disinfectants should be performed to ensure minimal effective concentration of the active ingredient. Check the solution each day of use (or more frequently) and document the results. If the chemical indicator indicates that the concentration is less than the minimum effective concentration, discard the solution. *Category IA* [36, 53, 81, 85, 106, 109, 469, 470, 659].

w. Personnel assigned to reprocess endoscopes must receive device-specific reprocessing instructions to ensure proper cleaning and high-level disinfection or sterilization. Competency testing of personnel reprocessing endoscopes should be done on a regular basis (e.g., commencement of employment, annually). *Category IA* [5, 36, 71, 72, 81, 85, 106, 109, 116, 659].

x. All personnel using chemicals must be educated about the biological, chemical, and environmental hazards present while performing procedures that use disinfectants. *Category IC* [823].

y. Personal protective equipment (e.g., gloves, eyewear, respiratory protection devices) should be readily available and should be used, as appropriate, to protect workers from exposure to chemicals or microorganisms (e.g., HBV). *Category IC* [224, 823].

z. The selection and use of disinfectants in the healthcare field is dynamic, and products may become available that were not in existence when this guideline was written. As newer disinfectants become available, persons or committees responsible for selecting disinfectants should be guided by products cleared by the FDA and information in the scientific literature. *Category II* [10, 79].

aa. If an automatic endoscope reprocessor (AER) is used, place the endoscope in the reprocessor and attach all channel connectors according to the AER manufacturer's instructions to ensure exposure of all internal surfaces with the high-level disinfectant/chemical sterilant. *Category IB* [71, 72, 116, 567, 740].

bb. If an AER is used, ensure that the endoscope can be effectively reprocessed in the automatic endoscope reprocessor (e.g., elevator wire channel of duodenoscopes not effectively disinfected by most AERs). *Category IB* [71, 72, 116, 567].

cc. Since design flaws have compromised the effectiveness of AERs, the infection control staff routinely should review the FDA advisories and the scientific literature for reports of AER deficiencies that may lead to infection. *Category II* [72, 96, 97, 116, 567].

dd. Healthcare facility personnel should develop protocols to ensure that users can readily identify whether an endoscope is contaminated or is ready for patient use. *Category II*.

8. Processing Patient-Care Equipment Contaminated with Bloodborne Pathogens (HBV, Hepatitis C Virus, HIV), Antibiotic-Resistant Bacteria (Vancomycin Resistant Enterococci, Methicillin Resistant Staphylococcus aureus, Multidrug Resistant Tuberculosis), or Emerging Pathogens (Crytosporidium, Helicobacter pylori, E. coli O157:H7, C. difficile, Mycobacterium tuberculosis, or Viruses (Human Papilloma, Norwalk)

a. Standard sterilization and disinfection procedures for patient-care equipment (as recommended in this guideline) are adequate to sterilize or disinfect instruments or devices contaminated with blood or other body fluids from persons infected with bloodborne pathogens and emerging pathogens, with the exception of prions (see below). No changes in procedures for cleaning, disinfecting, or sterilizing need to be made. *Category IA* [15, 50, 59-61, 77, 91, 92, 161, 164-177, 183-186, 194, 195, 229-231, 234, 238, 240, 241, 244, 245, 277-279, 529].

9. Processing Creutzfeldt Jakob Disease (CJD)-Contaminated Patient-Care Equipment and Environmental Surfaces

a. The following recommendations should be used with high-risk tissues (defined as brain [including dura mater], spinal cord, and eyes) from high-risk patients (e.g., those with known or suspected CJD) and with critical/semicritical items. *Category IB* [10, 198, 201-205, 207-209, 211-213, 220, 824, 825 6, 200, 214-219, 221-223, 826].

1. Those devices (e.g., surgical instruments) constructed so that cleaning procedures result in effective tissue removal can be cleaned and then sterilized by autoclaving either at 134°C for ≥18 minutes in a prevacuum sterilizer or at 121°C-132°C for 1 hour in a gravity displacement sterilizer. *Category IB* [10, 198, 201-205, 207-209, 211-213, 220, 824, 825 6, 200, 214-219, 221-223, 826].

2. Those devices that are impossible or difficult to clean could be discarded. Alternatively, the

contaminated items could be placed in a container filled with a liquid (e.g., saline, water, or phenolic solution) to retard adherence of material to the medical device, followed by initial decontamination by autoclaving at 134°C for 18 minutes in a prevacuum sterilizer (liquids must be removed before sterilization), or 121°C to 132°C for 1 hour in a gravity displacement sterilizer, or soaking in 1N NaOH for 1 hour. Finally, terminal cleaning, wrapping, and sterilization by conventional means would be used. *Category IB* [10, 198, 201-205, 207-209, 211-213, 220, 824, 825 6, 200, 214-219, 221-223, 826].

3. To minimize drying of tissues and body fluids on the object, keep instruments moist until cleaned and decontaminated. *Category IB* [10, 198, 201-205, 207-209, 211-213, 220, 824, 825 6, 200, 214-219, 221-223, 826].
4. Flash sterilization should not be used for reprocessing. *Category IB* [10, 198, 201-205, 207-209, 211-213, 220, 824, 825 6, 200, 214-219, 221-223, 826].
5. Items that permit only low-temperature sterilization (e.g., ETO, hydrogen peroxide gas plasma) should be discarded. *Category IB* [10, 198, 201-205, 207-209, 211-213, 220, 824, 825 6, 200, 214-219, 221-223, 826].
6. Contaminated items that have not been processed according to these recommendations (e.g., medical devices used for brain biopsy before diagnosis) should be recalled and appropriately reprocessed. *Category II.*
7. To minimize patient exposure to neurosurgical instruments later determined to have been used on a CJD patient, hospital personnel should consider using the sterilization guidelines above for neurosurgical instruments used on patients undergoing brain biopsy when a specific lesion has not been demonstrated (via computerized tomography or magnetic resonance imaging). Alternatively, neurosurgical instruments used in such patients could be disposable. *Category IB* [10, 198, 201-205, 207-209, 211-213, 220, 824, 825 6, 200, 214-219, 221-223, 826].
8. Environmental surfaces (noncritical) contaminated with high-risk tissues (e.g., laboratory surface in contact with brain tissue of a CJD-infected person) should be cleaned with a detergent and then spot decontaminated with a 1:10 dilution of sodium hypochlorite (i.e., bleach). In order to minimize environmental contamination, disposable cover sheets could be used on work surfaces. *Category IB* [10, 198, 201-205, 207-209, 211-213, 220, 824, 825 6, 200, 214-219, 221-223, 826].
9. Noncritical equipment contaminated with high-risk tissue should be cleaned and then disinfected with a 1:10 dilution of sodium hypochlorite or 1N NaOH, depending on material compatibility. All contaminated surfaces must be exposed to the disinfectant. *Category IB* [10, 198, 201-205, 207-209, 211-213, 220, 824, 825 6, 200, 214-219, 221-223, 826].
10. Equipment that requires special prion reprocessing should be tagged after use. Clinicians and reprocessing technicians should be thoroughly trained on how to properly tag the equipment and on the special prion reprocessing protocols. *Category IB* [10, 198, 201-205, 207-209, 211-213, 220, 824, 825 6, 200, 214-219, 221-223, 826].

b. The following recommendations should be used with low-risk tissues (defined as cerebrospinal fluid, kidney, liver, spleen, lung, and lymph nodes) from high-risk patients and critical/semicritical medical device. *Category IB* [10, 198, 201-205, 207-209, 211-213, 220, 824, 825 6, 200, 214-219, 221-223, 826].

1. These devices can be cleaned and disinfected or sterilized using conventional protocols of heat or chemical sterilants or high-level disinfection. *Category IB* [10, 198, 201-205, 207-209, 211-213, 220, 824, 825 6, 200, 214-219, 221-223, 826].
2. Environmental surfaces contaminated with low-risk tissues require only standard disinfection (use disinfectants recommended by OSHA for disinfecting blood-contaminated surfaces). *Category IB* [10, 198, 201-205, 207-209, 211-213, 220, 824, 825 6, 200, 214-219, 221-223, 826].

c. The following recommendation should be used with no-risk tissue (defined as peripheral nerve, intestine, bone marrow, blood, leukocytes, serum, thyroid gland, adrenal gland, heart, skeletal muscle, adipose tissue, gingiva, prostate, testis, placenta, tears, nasal mucus, saliva, sputum, urine, feces, semen, vaginal secretions, milk) from high-risk patients and critical/semicritical medical devices. *Category IB* [10, 198, 201-205, 207-209, 211-213, 220, 824, 825 6, 200, 214-219, 221-223, 826].

1. These devices can be cleaned and disinfected or sterilized using conventional protocols of heat or chemical sterilization or high-level disinfection. *Category IB* [10, 198, 201-205, 207-209, 211-213, 220, 824, 825 6, 200, 214-219, 221-223, 826].
2. Endoscopes (except neurosurgical endoscopes) would be contaminated only with no-risk materials and hence standard cleaning and high-level disinfection protocols would be adequate for reprocessing. *Category IB* [10, 198, 201-205, 207-209, 211-213, 220, 824, 825 6, 200, 214-219, 221-223, 826].

3. Environmental surfaces contaminated with no-risk tissues or fluids require only standard disinfection (use disinfectants recommended by OSHA for decontaminating blood-contaminated surfaces [e.g., 1:10 to 1:100 dilution of 6.0% sodium hypochlorite]). *Category IB* [10, 198, 201-205, 207-209, 211-213, 220, 824, 825 6, 200, 214-219, 221-223, 826].

10. Disinfection Strategies for Other Semicritical Devices

a. These devices (e.g., rectal probes, vaginal probes, cryosurgical probes) should be cleaned then high-level disinfected with a product that is not toxic to staff, patients, probes, and retrieved germ cells (if applicable). The high-level disinfectant should be used for the FDA-cleared exposure time until such time as the effectiveness of alternative procedures against microbes at the anatomic site is scientifically demonstrated. *Category IB* [5, 71, 72].
b. When available, a probe cover or condom should be used to reduce the level of microbial contamination. *Category II* [133-137].
c. The use of probe covers and condoms does not change the category of disinfection or the disinfectant recommendations, since sheaths and condoms may fail. *Category IB* [133-137].

11. Disinfection in Ambulatory Care and Home Care

a. The same classification scheme described above should be followed (i.e., critical devices require sterilization, semicritical devices require high-level disinfection, and noncritical equipment requires low-level disinfection) in the ambulatory care (outpatient medical/surgical facilities) setting since there is a similar infection risk as in the hospital setting (see Table 1). *Category IB* [5, 10, 71, 72, 256].
b. Reusable objects that touch mucous membranes (e.g., tracheostomy tubes) can be cleaned and disinfected by immersion in a 1:50 dilution of 6.0% sodium hypochlorite (household bleach) (3 minutes), 70% isopropyl alcohol (5 minutes), or 3% hydrogen peroxide (30 minutes) since the home environment should be safer as person-to-person transmission should be less likely. *Category II* [256, 257].
c. Noncritical items (e.g., crutches, blood pressure cuffs) in the home setting can be cleaned with a detergent. *Category II* [256].

12. Microbial Contamination of Disinfectants

a. Control measures that should be instituted to reduce the occurrence of contaminated disinfectants include prepare the disinfectant correctly to achieve the manufacturer's recommended use-dilution, and prevent common sources of extrinsic contamination of germicides (e.g., contaminated containers, general contamination of the hospital area where the germicide are prepared and/or used). *Category IB* [311, 313, 827].

13. Flash Sterilization

a. Implanted surgical devices should not be flash sterilized unless unavoidable. *Category IB* [686, 687].
b. When flash sterilization is used, certain parameters should be met: the item must be decontaminated before placement in the sterilizing container; exogenous contamination must be prevented during transport from the sterilizer to the patient; and sterilizer function must be monitored by mechanical, chemical, and biological monitors. *Category IB* [657, 683, 684].
c. Packaging materials and containers should not be used in flash sterilization cycles unless the sterilizer and the packaging material/container are designed for this use. *Category IB* [657, 828].
d. Flash sterilization may be used for patient-care items that will be used immediately (e.g., to reprocess an inadvertently dropped instrument). *Category IB* [1, 657, 682].
e. Flash sterilization may be used for processing patient-care items that cannot be packaged, sterilized, and stored before use. *Category IB* [657].

f. Do not use flash sterilization for reasons of convenience, as an alternative to purchasing additional instrument sets, or to save time. *Category II* [1].

14. Methods of Sterilization

a. Steam is the preferred method for sterilizing critical medical and surgical instruments not damaged by heat, steam, pressure, or moisture. *Category IA* [229, 326, 327, 667, 678, 829, 830].
b. Steam- or heat-sterilized items should be cooled before they are handled or used in the operative setting. *Category IB* [687].
c. Sterilization times, temperatures, and other operating parameters (e.g., gas concentration, humidity) should follow the written recommendations of the manufacturers of the instruments, the sterilizer and the container or wrap used, and guidelines published by government agencies and professional organizations. *Category IB* [656-658, 665, 667, 678, 829-831].
d. Use low-temperature sterilization technologies (e.g., ethylene oxide, hydrogen peroxide gas plasma) for reprocessing critical patient-care equipment that is heat- or moisture-sensitive. *Category IA* [354, 665, 693, 694, 713, 714, 717, 725, 726, 830].
e. Surgical and medical items sterilized in ETO sterilizer should be completely aerated (e.g., polyvinylchloride tubing requires 12 hours at 50°C, 8 hours at 60°C) before use in patient care. *Category IB* [658].
f. Sterilization using peracetic acid immersion may be used for medical and surgical items that can be immersed. *Category IB* [27, 561-563, 565, 738].
g. Critical items sterilized by the peracetic acid immersion process should be used immediately. *Category II* [1, 665].
h. Dry-heat sterilization (e.g., 340°F for 60 minutes) can be used to sterilize items (e.g., powders, oils) that can sustain high temperatures. *Category IB* [667].
i. Other sterilization technologies may be used for sterilization of critical medical items when cleared by the FDA and ideally, the microbicidal effectiveness of the technology has been published in the scientific literature. *Category IB* [741]
j. The sterilizer cycle parameters (e.g., time, temperature, concentration) should comply with the sterilizer manufacturer's instructions. *Category IB* [116, 567, 656-658].
k. Narrow-lumen devices provide a challenge to all low-temperature sterilization technologies. The sterilant must have direct contact with contaminated surfaces (e.g., scopes processed in peracetic acid must be connected to channel irrigators) to be effective. *Category IB* [567, 694, 731, 832].

15. Packaging

a. Packaging materials should be compatible with the sterilization process. *Category IA* [656-658, 785].
b. Packaging should provide a barrier to microorganisms and moisture and should be sufficiently strong to resist punctures and tears. *Category IA* [346, 656-658, 785].

16. Monitoring of Sterilizers

a. Use mechanical, chemical, and biological monitors to ensure the effectiveness of the sterilization process. *Category IA* [656-659, 792].
b. Each load should be monitored with mechanical (e.g., time, temperature, pressure) and chemical (internal and/or external) indicators. *Category II* [656-659, 683, 684, 792-794, 796].
c. If the mechanical (e.g., time, temperature, pressure) or chemical (internal and/or external) indicators suggest inadequate processing, the items should not be used. *Category IB* [656-658].
d. Biological indicators should be used to monitor the effectiveness of sterilizers at least weekly with a commercial preparation of spores intended specifically for the type of sterilizer (e.g., *Bacillus stearothermophilus* for steam). *Category IB* [12, 656, 658, 659, 683, 684, 793, 794].

e. Objects, other than implantable objects, do not need to be recalled because of a single positive spore test unless the sterilizer or the sterilization procedure is defective as determined by maintenance personnel or inappropriate cycle settings. *Category IB* [12].
f. If additional spore tests remain positive, the items must be considered nonsterile and the items from the suspect load(s) should be recalled and reprocessed. *Category IB* [12].
g. Biological indicators should be used for every load containing implantable items. *Category IB.* [656-658].

17. Load Configuration.

a. Items should be placed loosely into the basket, shelf, or cart so as not to impede contact between the sterilant and the microorganism. *Category IB* [346, 656].

18. Storage of Sterile Items

a. The sterile storage area should be a well-ventilated area that provides protection against dust, moisture, insects, and temperature and humidity extremes. *Category IB* [788].
b. Sterile items should be stored so that the packaging is not compromised (e.g., punctured, bent). *Category IB.* [787, 788, 833].
c. Sterilized items should be labeled with a load number that indicates the sterilizer used, the cycle or load number, the date of sterilization, and, if applicable, the expiration date. *Category IB* [656-658].
d. If expiration dates are used, the shelf life of a packaged sterile item depends on the quality of the wrapper, the storage conditions, the conditions during transport, the amount of handling, and other events (moisture) that compromise the integrity of the package. *Category IB* [787, 791, 833, 834].
e. Packages should be evaluated before use for loss of integrity (e.g., torn, wet, punctured). The pack may be used unless the integrity of the packaging is compromised. *Category IB* [787].
f. If the integrity of the packaging is compromised (e.g., torn, wet, punctured), the pack should be reprocessed before use. *Category II.*
g. Alternatively, the pack may be labeled at the time of sterilization with an expiration date. Once this date is exceeded the pack should be reprocessed. *Category II* [787].

19. Quality Control

a. Provide comprehensive and intensive training for all staff assigned to reprocess semicritical and critical medical/surgical instruments to ensure that they understand the importance of reprocessing instruments. To achieve and maintain competency, each member of the staff that reprocesses semicritical and/or critical instruments should be trained as follows: a) hands-on training based on the institutional policy for reprocessing critical and semicritical devices; b) all work should be supervised until competency is documented for each reprocessing task; c) competency testing should be conducted at commencement of employment and regularly thereafter (e.g., annually); and d) review the written reprocessing instructions regularly to ensure they are compliant with the scientific literature and the manufacturers' instructions. *Category IB* [5, 71, 72, 81, 86, 93, 116, 567].
b. Compare the reprocessing instructions provided by the instrument manufacturer and the sterilizer manufacturer and resolve any conflicting recommendations by communication with both manufacturers (e.g., the appropriate use endoscope connectors, the capping/noncapping of specific lumens). *Category IB* [116, 567].
c. The infection control staff should conduct infection control rounds periodically (e.g., annually) in high-risk reprocessing areas (e.g., Gastroenterology Clinic, Central Processing) to ensure that the reprocessing instructions are current and accurate and that they are correctly

implemented. Deviations from policy should be documented and stakeholders should identify what corrective actions will be implemented. *Category IB* [5, 71, 72, 93].

d. A quality control program for sterilized items should include a sterilizer maintenance contract with records of service; process monitoring; air-removal testing for prevacuum steam sterilizers; visual inspection of packaging materials; and traceability of load contents. *Category IB* [656-658].
e. Information recorded from every sterilization cycle should include, but not be limited to type of sterilizer and cycle used; load identification number; load contents; exposure parameters (e.g., time and temperature); operator's name; and results of mechanical, chemical, and biological monitoring. *Category IB* [656-658].
f. Sterilization records (mechanical, chemical, and biological) should be retained for a time period in compliance with standards (e.g., 3 years), statue of limitations, and state and federal regulations. *Category IB, IC* [835].
g. Items to be sterilized should be prepared and packaged so sterility can be achieved and maintained to the point of use. The Association for the Advancement of Medical Instrumentation and/or the manufacturers of surgical instruments, sterilizers, and container systems provide guidelines for the density of wrapped packages. *Category IB* [656-658].
h. Policies and procedures for sterilization should be reviewed periodically. *Category IB.* [835].
i. Preventive maintenance should be performed on sterilizers by qualified personnel and guided by the manufacturer's instruction. *Category IB*. [656-658].

20. Reuse of Single-Use Medical Devices

a. Hospitals should comply with the FDA enforcement document for single-use devices reprocessed by hospitals. The FDA considers the hospital that reuses a single-use device as the manufacturer of the device and regulates the hospital the same as the original equipment manufacturer. *Category IC.* [810].

21. Occupational Health and Exposure

a. Each worker should be informed of the possible health effects of their exposure to infectious agents (e.g., HBV, HCV, HIV) and/or chemicals (e.g., ETO, formaldehyde). The information should comply with OSHA requirements and identify the areas and tasks in which there is potential exposure. *Category IC* [224, 823].
b. Appropriate personal protective equipment must be worn to preclude exposure to infectious agents via the skin or mucous membranes of the eyes, ears, or mouth. *Category IC* [224].
c. A program for monitoring occupational exposure to regulated chemicals (e.g., formaldehyde, ethylene oxide) should be established and should comply with state and federal regulations. *Category IC* [823, 836, 837].
d. Healthcare workers with weeping dermatitis should not have direct contact with patient- care equipment. *Category IB* [838, 839].

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GLOSSARY

Action level: concentration of a regulated gas (e.g., ETO) within the employee breathing zone, above which OSHA requirements apply.

Activation of a sterilant: some chemical sterilants come in two containers: one is a small vial with the activator solution. The sterilant is activated when the contents of the two containers are mixed. Keeping the two chemicals separate until ready to use, extends the shelf life of the chemicals.

Aeration: method by which ETO is removed from ETO-sterilized items by the use of warm air circulation in an enclosed cabinet specifically designed for this purpose.

Antimicrobial agent: any agent that kills or suppresses the growth of microorganisms.

Antiseptic: a substance that prevents or arrests the growth or action of microorganisms, either by inhibiting their activity or by destroying them. The term is used especially for preparations applied topically to living tissue.

Asepsis: prevention of contact with microorganisms.

Autoclave: device that sterilizes instruments or other objects by using steam under pressure. The length of time required for sterilization depends on temperature and pressure.

Bacterial count: method of estimating the number of bacteria per unit sample. The term also refers to the estimated number of bacteria per unit sample, usually expressed as number of colony-forming units (CFUs).

Bactericide: an agent that kills bacteria.

Bioburden: number and types of viable microorganisms with which an item is contaminated; also known as *bioload* or *microbial load.*

Biological indicator: sterilization process monitoring device consisting of a standardized, viable population of microorganisms (usually bacterial spores) known to be resistant to the process of sterilization being monitored. Biological indicators are intended to demonstrate whether or not the conditions were adequate to achieve sterilization. A negative biological indicator does not prove that all items in the load are sterile or that they were all exposed to adequate sterilization conditions.

Bleach: Household bleach (6.00%-6.15% sodium hypochlorite) is normally diluted in water at 1:10 or 1:100. Approximate dilutions are 1.5 cups of bleach in a gallon of water for a 1:10 dilution (6,000 ppm) and 0.25 cup of bleach in a gallon of water for a 1:100 dilution (600 ppm).

Bowie-Dick test: a diagnostic test of a sterilizer's ability to remove air from the chamber of a prevacuum steam sterilizer. The air-removal or Bowie-Dick test is not a test for sterilization.

Ceiling limit: concentration of an airborne chemical contaminant that should not be exceeded during any part of the workday.

Centigrade (or Celsius): a temperature scale. Equivalents mentioned in the guideline are as follows: $20^oC = 68^oF$; $25^oC = 77^oF$; $121^oC = 250^oF$; $132^oC = 270^oF$; $134^oC = 273^oF$. For other temperatures the formula is: $F^o = (C^o \times 9/5) + 32$ *or* $C^o = (F^o - 32) \times 5/9$.

Central processing or central service department: the department within a healthcare facility that processes, issues, and controls professional supplies and equipment, both sterile and nonsterile, for some or all patient-care areas of the facility.

Challenge test pack: a pack used in installation, qualification, and ongoing quality assurance testing of hospital sterilizers.

Chemical indicator: sterilization process monitoring device designed to respond with a characteristic chemical or physical change to one or more of the physical conditions within the sterilizing chamber. Chemical indicators are intended to detect potential sterilization failures that could result from incorrect packaging, incorrect loading of the sterilizer, or malfunctions of the sterilizer. The "pass" response of a chemical indicator does not prove that the item accompanied by the indicator is sterile.

Contact time: the time a disinfectant is in direct contact with the surface or item to be disinfected. For surface disinfection, this time period is framed by the application to the surface until complete drying has occurred.

Contaminated: state of having been actually or potentially in contact with microorganisms. As used in healthcare, the term generally refers to the presence of microorganisms that could be capable of producing disease or infection.

Control, positive: biological indicator, from the same lot as a test biological indicator, which is left unexposed to the sterilization cycle and then incubated to verify the viability of the test biological indicator.

Cleaning: the removal, usually with detergent and water or enzymatic detergent and water, of adherent visible soil, blood, protein substances, and other debris from the surfaces, crevices, serrations, joints, and lumens of instruments, devices, and equipment by a manual or mechanical process that prepares the items for safe handling and/or further decontamination.

Culture: growth of microorganisms in or on a nutrient medium; to grow microorganisms in or on such a medium.

Culture medium: substance or preparation used to grow and cultivate microorganisms.

Cup: eight fluid ounces.

Decontamination: according to the Occupational Safety and Health Administration (OSHA), "the use of physical or chemical means to remove, inactivate, or destroy bloodborne pathogens on a surface or item to the point where they are no longer capable of transmitting infectious particles and the surface or item is rendered safe for handling, use, or disposal" [29 CFR 1910.1030]. The term is generally used in health-care facilities with reference to all pathogenic organisms, not just those transmitted by blood.

Decontamination area: the area of a healthcare facility designated for collection, retention, and cleaning of soiled and/or contaminated items.

Detergent: a cleaning agent that makes no antimicrobial claims on the label. Ther are composed of a hydrophilic component and a lipohilic component and can be divided into four types: anionic, cationic, amphoteric, and non-ionic detergents.

Disinfectant: an agent that frees from infection, usually a chemical agent but sometimes a physical one, that destroys disease causing pathogens or other harmful microorganisms but may not kill bacterial spores. It refers to substances applied to inanimate objects. The EPA groups disinfectants on whether the product label claims "limited," "general," or "hospital" disinfection.

Disinfection: the destruction of pathogenic and other kinds of microorganisms by thermal or chemical means. Disinfection is less lethal than sterilization because it destroys most recognized pathogenic microorganisms, but not necessarily all microbial forms, such as bacterial spores.

Endoscope: an instrument that allows the examination and treatment of the interior of the body canals and hollow organs.

EPA Registration number (or EPA Reg. No.): a hyphenated, two- or three-part number assigned by the EPA to identify each germicidal product registered within the United States. The first number is the company identification number, the second is the specific product number, and the third (when present) is the company identification number for a supplemental registrant.

Exposure time: period of time during a sterilization process in which items are exposed to the sterilant at the specified sterilization parameters. In a steam sterilization process, exposure time is the period during which items are exposed to saturated steam at the specified temperature.

Flash sterilization: process designed for the steam sterilization of patient-care items for immediate use.

Fungicide: an agent that destroys fungi (including yeasts) and/or fungal spores pathogenic to humans or other animals in the inanimate environment.

General disinfectant: an EPA-registered disinfectant that is labeled for use against both gram-negative and gram-positive bacteria. Efficacy is demonstrated against both *Salmonella choleraesuis* and *Staphylococcus aureus*. Also referred to as a "broad-spectrum disinfectant."

Germicide: an agent that destroys microorganisms, especially pathogenic organisms.

High-level disinfectant: an agent capable of killing bacterial spores when used in sufficient concentration under suitable conditions. It is therefore expected to kill all other microorganisms.

Hospital disinfectant: a disinfectant that is registered for use in hospitals, clinics, dental offices, or any other medical-related facility. Efficacy is demonstrated against *Salmonella choleraesuis*, *Staphylococcus aureus*, and *Pseudomonas aeruginosa.* EPA has registered about 1200 hospital disinfectants**.**

Huck towel: an all-cotton surgical towel with a honey-comb-effect weave; both warp and fill yarns are tightly twisted.

Implantable device: according to the FDA, "device that is placed into a surgically or naturally formed cavity of the human body if it is intended to remain there for a period of 30 days or more" [21 CFR 812.3(d)].

Inanimate surface: a nonliving surface (e.g., floors, walls, furniture).

Incubator: apparatus for maintaining a constant and suitable temperature for the growth and cultivation of microorganisms.

Infectious microorganisms: microorganisms capable of producing disease in appropriate hosts.

Inorganic and organic load: the naturally occurring or artificially placed inorganic (e.g., metal salts) or organic (e.g., proteins) contaminants on a medical device before exposure to a microbicidal process.

Intermediate-level disinfectant: an agent that destroys all vegetative bacteria, including tubercle bacilli, lipid and some nonlipid viruses, and fungus spores, but not bacterial spores.

Limited disinfectant: a disinfectant that is registered for use against a specific major group of organisms (gram-negative or gram-positive bacteria). Efficacy has been demonstrated in laboratory tests against either *Salmonella choleraesuis* or *Staphylococcus aureus* bacteria.

Lipid virus: a virus consists of a core of nucleic acid surrounded by a coat of protein and, in the case of a lipid virus, is surrounded by an envelope of lipoprotein. This type of virus (e.g., HIV) is generally easily inactivated by many types of disinfectants. Also referred to as enveloped or lipophilic viruses.

Low-level disinfectant: an agent that destroys all vegetative bacteria (except tubercle bacilli), lipid viruses, some nonlipid viruses, and some fungus, but not bacterial spores.

Mechanical indicator: automated devices that monitor the sterilization process (e.g., graphs, gauges, printouts).

Microbicide: any substance, or mixture of substances, that effectively kills microorganisms.

Microorganisms: animals or plants of microscopic size. As used in healthcare, the term generally refers to bacteria, fungi, viruses, and bacterial spores.

Minimum effective concentration (MEC): the minimum concentration of a liquid chemical germicide needed to achieve the claimed microbicidal activity as determined by dose-response testing.

Muslin: loosely woven (by convention, 140 threads per square inch), 100% cotton cloth.

Mycobacteria: bacteria with a thick, waxy coat that makes them more resistant to chemical germicides than other types of vegetative bacteria.

Nonlipid viruses: a virus consists of a core of nucleic acid is surrounded by a coat of protein. Nonlipid viruses are generally viewed as more resistant to inactivation than lipid viruses. Nonlipid viruses are also referred to as nonenveloped or hydrophilic viruses.

One-step disinfection process: refers to the simultaneous cleaning and disinfection of a noncritical surface or item.

Pasteurization: a process developed by Louis Pasteur of heating milk, wine, or other liquids to 60°C to 100°C (or the equivalent) for approximately 30 minutes to kill or markedly reduce the number of pathogenic and spoilage organisms other than bacterial spores.

Parametric release: declaring a product is sterile, based on physical and/or chemical process data rather than on the basis of sample testing or biological indicator results.

Permissible exposure limit (PEL): time-weighted average maximum concentration of an air contaminant to which a worker can be exposed, according to OSHA standards.

Personal protective equipment (PPE): specialized clothing or equipment worn by an employee for protection against a hazard. General work clothes (e.g., uniforms, pants, shirts) not intended to function as protection against a hazard are not considered to be PPE.

Parts per million or ppm: concentrations of trace contaminant gases in the air (or chemicals in a liquid) are commonly measured in parts per million by volume; 1 volume of contaminated gas per 1,000,000 volumes of contaminated air or 1 cent in $10,000 both equal 1 ppm.

QUAT: the abbreviated form of the term quaternary ammonium compound, a surface-active, water-soluble disinfecting substance that has four carbon atoms linked to a nitrogen atom through covalent bonds.

Sanitizer: an agent that reduces the number of bacterial contaminants to safe levels as judged by public health requirements. It commonly is used with substances that are applied to inanimate objects. According to the protocol for the official sanitizer test, a sanitizer is a chemical that kills 99.999% of the specific test bacteria in 30 seconds under the conditions of the test.

Shelf life: the length of time an undiluted or the use dilution of a product can remain active and effective.

Spaulding classification: a strategy for reprocessing contaminated medical devices. The system classifies medical devices as critical, semicritical, or noncritical based upon the risk from contamination on a device to patient safety. The system also established three levels of germicidal activity (sterilization, high-level disinfection, and low-level disinfection) for strategies with the three classes of medical devices (critical, semicritical, and noncritical).

Spore: a relatively water-poor round or elliptical resting cell consisting of condensed cytoplasm and nucleus surrounded by an impervious cell wall or coat. Spores are relatively resistant to disinfectant and sterilant activity and drying conditions (specifically in the genera *Bacillus* and *Clostridium*).

Spore strip: a paper strip impregnated with a known population of microorganisms that meets the definition of biological indicators.

Steam sterilization: sterilization process that uses saturated steam under pressure, for a specified exposure time and at a specified temperature, as the sterilizing agent.

Sterile/sterility: state of being free from all living microorganisms. In practice, usually described as a probability function, e.g., as the probability of a microorganism surviving sterilization as being one in a million.

Sterility assurance level (SAL): probability of a viable microorganism being present on a product unit after sterilization. An SAL is normally expressed as 10^{-6}. An SAL of 10^{-6} means that there is less than or equal to one chance in a million that a single viable microorganism is present on a sterilized item. It generally is accepted that a sterility assurance level of 10^{-6} is appropriate for items intended to come into contact with compromised tissue (i.e., tissue that has lost the integrity of the natural body barriers). The sterilizer manufacturer is responsible for ensuring that the sterilizer is capable of achieving the desired SAL. The user is responsible for monitoring the performance of the sterilizer to ensure that it is operating in conformance to the manufacturer's recommendations.

Sterilization: validated process used to render a product free of all forms of viable microorganisms. In a sterilization process, the presence of microorganisms on any individual item can be expressed in terms of probability. While this probability can be reduced to a very low number, it can never be reduced to zero.

Sterilization area: area of a healthcare facility designed to house sterilization equipment, usually steam or ethylene oxide sterilizers, or both.

Sterilizer: apparatus used to sterilize medical devices, equipment, or supplies by direct exposure to the sterilizing agent.

Sterilizer, gravity-displacement type: type of steam sterilizer in which incoming steam displaces residual air through a port or drain in or near the bottom (usually) of the sterilizer chamber. Typical operating temperatures are 121°C to 123°C (250°F to 254°F) and 132°C to 135°C (270°F to 275°F).

Sterilizer, prevacuum type: type of steam sterilizer that depends upon one or more pressure and vacuum excursions at the beginning of the cycle to remove air. This method of operation results in shorter cycle times for wrapped items because of the rapid removal of air from the chamber and the load by the vacuum system and because of the usually higher operating temperature (132°C to 135°C [270°F to 275°F]; 141°C to 144°C [285°F to 291°F]). This type of sterilizer generally provides for shorter exposure time and accelerated drying of fabric loads by pulling a further vacuum at the end of the sterilizing cycle.

Sterilizer, steam-flush pressure-pulse type: type of sterilizer in which a repeated sequence consisting of a steam flush and a pressure pulse removes air from the sterilizing chamber and processed materials using steam at above atmospheric pressure (no vacuum is required). Like a prevacuum sterilizer, a steam-flush pressure-pulse sterilizer rapidly removes air from the sterilizing chamber and wrapped items; however, the system is not susceptible to air leaks because air removal is achieved with the sterilizing chamber pressure at above atmospheric pressure. Typical operating temperatures are 121°C to 123°C (250°F to 254°F), 132°C to 135°C (270°F to 275°F), and 141°C to 144°C (285°F to 291°F).

Surfactant: an agent that reduces the surface tension of water or the tension at the interface between water and another liquid; a wetting agent found in many sterilants and disinfectants.

Table-top steam sterilizer: a compact steam sterilizer that has a chamber volume of not more than 2 cubic feet and that generates its own steam when distilled or deionized water is added by the user.

Time-weighted average (TWA): an average of all the concentrations of a chemical to which a worker has been exposed during a specific sampling time, reported as an average over the sampling time. The permissible exposure limit for ETO is 1 ppm as an 8-hour TWA. Exposures above the ppm limit are permitted if they are compensated for by equal or longer exposures below the limit during the 8-hour workday.

Tuberculocide: an agent that kills *Mycobacterium tuberculosis* (tubercle bacilli). EPA has registered about 200 tuberculocides. Such agents also are referred to as “mycobactericides.”

Use-life: the length of time a diluted product can remain active and effective. The stability of the chemical and the storage conditions (e.g., temperature and presence of air, light, organic matter, or metals) determine the use-life of antimicrobial products.

Vegetative bacteria: bacteria that are devoid of spores and usually can be readily inactivated by many types of germicides.

Virucide: an agent that kills viruses to make them noninfective.

Adapted from Association for the Advancement of Medical Instrumentation 656-658; Association of periOperating Room Nurses (AORN) 659, American Hospital Association 252, and Block 9, 840.

Table 1. Methods of sterilization and disinfection

	Sterilization		Disinfection		
	Critical items (will enter tissue or vascular system or blood will flow through them)		**High-level** (semicritical items; [except dental] will come in contact with mucous membrane or nonintact skin)	**Intermediate-level** (some semicritical items[1] and noncritical items)	**Low-level** (noncritical items; will come in contact with intact skin)
Object	**Procedure**	**Exposure time**	**Procedure** (exposure time 12-30 min at 20°C)[2,3]	**Procedure** (exposure time ≤10 min)	**Procedure** (exposure time ≤10 min)
Smooth, hard Surface[1,4]	A B C D E F G H	MR MR MR 10 h NA 6 h 12 m, 55°C 3-8 h	D E F H I[6] J	J[5] K M N	K L M N O
Rubber tubing and catheters[3,4]	A B C D E F G H	MR MR MR 10 h NA 6 h 12 m, 55°C 3-8 h	D E F H I[6] J		
Polyethylene tubing and catheters[3,4,7]	A B C D E F G H	MR MR MR 10 h NA 6 h 12 m, 55°C 3-8 h	D E F H I[6] J		
Lensed instruments[4]	B C D E F G H	MR MR 10 h NA 6 h 12 m, 55°C 3-8 h	D E F H		
Thermometers (oral and rectal)[8]				K[8]	
Hinged instruments[4]	A B C D E F G H		D E F H I[6] J		

Modified from 8, 10, 11, 616.

A, Heat sterilization, including steam or hot air (see manufacturer's recommendations, steam

sterilization processing time from 3-30 minutes, see Table 10)

B, Ethylene oxide gas (see manufacturer's recommendations, generally 1-6 hours processing time plus aeration time of 8-12 hours at 50-60°C)

C, Hydrogen peroxide gas plasma (see manufacturer's recommendations, processing time between 45-72 minutes; endoscopes or medical devices with lumens >40 cm or a diameter <3 mm cannot be processed at this time in the United States)

D, Glutaraldehyde-based formulations (≥2% glutaraldehyde, caution should be exercised with all glutaraldehyde formulations when further in-use dilution is anticipated); glutaraldehyde (0.95%) and 1.64% phenol/phenate

E, Ortho-phthalaldehyde 0.55%

F, Hydrogen peroxide 7.5% (will corrode copper, zinc, and brass)

G, Peracetic acid, concentration variable but ≤1% is sporicidal

H, Hydrogen peroxide (7.35%) and 0.23% peracetic acid; hydrogen peroxide 1% and peracetic acid 0.08% (will corrode metal instruments)

I, Wet pasteurization at 70°C for 30 minutes after detergent cleaning

J, Sodium hypochlorite (5.25% household bleach diluted 1:50 provides 1000 ppm available chlorine; will corrode metal instruments)

K, Ethyl or isopropyl alcohol (70-90%)

L, Sodium hypochlorite (5.25% household bleach diluted 1:500 provides 100 ppm available chlorine)

M, Phenolic germicidal detergent solution (follow product label for use-dilution)

N, Iodophor germicidal detergent solution (follow product label for use-dilution)

O, Quaternary ammonium germicidal detergent solution (follow product label for use-dilution)

MR, Manufacturer's recommendations.

NA, Not applicable

[1] See text for discussion of hydrotherapy.

[2] The longer the exposure to a disinfectant, the more likely it is that all microorganisms will be eliminated. Ten-minute exposure is not adequate to disinfect many objects, especially those that are difficult to clean because they have narrow channels or other areas that can harbor organic material and bacteria. Twenty-minute exposure at 20°C is the minimum time needed to reliably kill *M. tuberculosis* and nontuberculous mycobacteria with a 2% glutaraldehyde. With the exception of >2% glutaraldehydes, follow the FDA-cleared high-level disinfection claim. Some high-level disinfectants have a reduced exposure time (e.g., ortho-phthalaldehyde at 12 minutes at 20°C) because of their rapid activity against mycobacteria or reduced exposure time due to increased mycobactericidal activity at elevated temperature (2.5% glutaraldehyde at 5 minutes at 35°C).

[3] Tubing must be completely filled for disinfection; care must be taken to avoid entrapment of air bubbles during immersion.

[4] Material compatibility should be investigated when appropriate.

[5] Used in laboratory where cultures or concentrated preparations or microorganisms have spilled. This solution may corrode some surfaces.

[6] Pasteurization (washer-disinfector) of respiratory therapy or anesthesia equipment is a recognized alternative to high-level disinfection. Some data challenge the efficacy of some pasteurization units.

[7] Thermostability should be investigated when appropriate.

[8] Do not mix rectal and oral thermometers at any stage of handling or processing.

Table 2. Properties of an ideal disinfectant.

Broad spectrum: should have a wide antimicrobial spectrum

Fast acting: should produce a rapid kill

Not affected by environmental factors: should be active in the presence of organic matter (e.g., blood, sputum, feces) and compatible with soaps, detergents, and other chemicals encountered in use

Nontoxic: should not be irritating to the user or patient

Surface compatibility: should not corrode instruments and metallic surfaces and should not cause the deterioration of cloth, rubber, plastics, and other materials

Residual effect on treated surfaces: should leave an antimicrobial film on the treated surface

Easy to use with clear label directions

Odorless: should have a pleasant odor or no odor to facilitate its routine use

Economical: should not be prohibitively high in cost

Solubility: should be soluble in water

Stability: should be stable in concentrate and use-dilution

Cleaner: should have good cleaning properties

Environmentally friendly: should not damage the environment on disposal

Modified from 155.

Table 3. Comparative frequency of infectivity in organs/tissue/body fluids of humans with transmissible spongiform encephalopathies.

Infectious Risks[1]	Tissue
High	Brain (including dura mater), spinal cord, eyes
Low	Cerebrospinal fluid, liver, lymph node, kidney, lung, spleen
None	Peripheral nerve, intestine, bone marrow, whole blood, leukocytes, serum, thyroid gland, adrenal gland, heart, skeletal muscle, adipose tissue, gingiva, prostate, testis, placenta, tears, nasal mucus, saliva, sputum, urine, feces, semen, vaginal secretions, milk

Modified from 205.

[1]Infectious risks: high=transmission to inoculated animals ≥50%; low=transmission to inoculated animals ≥10-20% (except for lung tissue, for which transmission is 50%); none=transmission to inoculated animals 0% (several tissues in this category had few tested specimens).

Table 4. Efficacy of chemical disinfectants in inactivating prions.

Ineffective chemical disinfectants (≤3-$\log_{10}$ reduction in 1 hour)	Effective chemical disinfectants (>3-$\log_{10}$ reduction in 1 hour)
Alcohol 50%	Chlorine >1,000 ppm
Ammonia 1.0M	Guanidine thiocyanate
Chlorine dioxide 50 ppm	NaOH ≥1N
Formaldehyde 3.7%	Phenolic >0.9%
Glutaraldehyde 5%	
Hydrochloric acid 1.0 N	
Hydrogen peroxide 3%	
Iodine 2%	
Peracetic acid	
Phenol/phenolics 0.6%	
Potassium permanganate 0.1-0.8%	
Sodium deoxycholate 5%	
Sodium dodecyl sulfate 0.5-5%	
Tego 5%	
Triton X-100 1-5%	
Urea 4-8 M	

Modified from [205].

Table 5. Efficacy of sterilization processes in inactivating prions.

Ineffective sterilization processes ($\leq$3-$\log_{10}$ reduction in 1 hour)	Effective sterilization processes (>3-$\log_{10}$ reduction in 1 hour)
Autoclaving at conventional exposure conditions (121°C for 15 minutes)	Autoclaving at 134°C for 18 minutes (prevacuum sterilizer)
Steam sterilization at conventional exposure conditions (132°C for 15 minutes)	Autoclaving 121-132°C for 1 hr (gravity displacement sterilizer)
Ethylene oxide	0.09N or 0.9N NaOH for 2 hours plus 121°C for 1 hour (gravity displacement sterilizer)
Formaldehyde	
Dry heat	
Boiling	
Ultraviolet light	
Ionizing radiation	

Modified from [205].

Table 6. Epidemiologic evidence associated with the use of surface disinfectants or detergents on noncritical surfaces.

Justification for Use of Disinfectants for Noncritical Surfaces
Surfaces may contribute to transmission of epidemiologically important microbes (e.g., vancomycin-resistant Enterococci, methicillin-resistant *S. aureus*, viruses)
Disinfectants are needed for surfaces contaminated by blood and other potentially infective material
Detergents become contaminated and result in seeding the patient's environment with bacteria
Disinfectants are more effective than detergents in reducing microbial load on floors
Disinfection of noncritical equipment and surfaces is recommended for patients on isolation precautions by the Centers for Disease Control and Prevention.
Newer disinfectants have persistent antimicrobial activity
Advantage of using a single product for decontamination of noncritical surfaces, both floors and equipment
Justification for Using a Detergent on Floors
Noncritical surfaces contribute minimally to endemic healthcare-associated infections
No difference in healthcare-associated infection rates when floors are cleaned with detergent versus disinfectant
No disinfectant disposal issues
No occupational health exposure issues
Lower costs
Use of antiseptics/disinfectants selects for antibiotic-resistant bacteria (?)
More aesthetically pleasing floor

Modified from [291].

Figure 1. Decreasing order of resistance of microorganisms to disinfection and sterilization and the level of disinfection or sterilization.

Resistant		**Level**
↓	Prions (e.g., Creutzfeldt-Jakob Disease)	Prion reprocessing
	Bacterial spores (*Bacillus subtilis*)	Sterilization
	Coccidia (*Cryptosporidium*)	
	Mycobacteria (*M. tuberculosis, M. terrae*)	High Disinfection
	Nonlipid or small viruses (polio, coxsackie)	Intermediate Disinfection
	Fungi (e.g., *Aspergillus*, *Candida*)	
	Vegetative bacteria (*S. aureus*, *P. aeruginosa*)	Low Disinfection
	Lipid or medium-sized viruses (HIV, herpes, hepatitis B)	
Susceptible		

Modified from [6].

Table 7. Comparison of the characteristics of chemical sterilants used primarily as high-level disinfectants.

	HP (7.5%)	PA (0.2%)	Glut (≥2.0%)	OPA (0.55%)	HP/PA (7.35%/.23%)
HLD Claim	30 m @ 20°C	NA	20-90 m @ 20°-25°C	12 m @ 20°C	15m @ 20°C
Sterilization Claim	6 h @ 20°	30 m @ 50°C	10 h @ 20°-25°C	None	3 h @ 20°C
Activation	No	No	Yes (alkaline glut)	No	No
Reuse Life[1]	21d	Single use	14-30 d (acid glut-1yr)	14d	14d
Shelf Life Stability[2]	2 y	6 mo	2 y	2 y	2 y
Disposal Restrictions	None	None	Local[3]	Local[3]	None
Materials Compatibility	Good	Fair	Excellent	Excellent	No data
Monitor MEC[4]	Yes (6%)	No	Yes (1.5% or higher)	Yes (0.3% OPA)	No
Safety	Serious eye damage (safety glasses)	Serious eye and skin damage (conc soln)[5]	Respiratory	Eye irritant, stains skin	Eye damage
Processing	Manual or automated	Automated	Manual or automated	Manual or automated	Manual
Organic material resistance	Yes	Yes	Yes	Yes	Yes
OSHA exposure limit	1 ppm TWA	PA-none	0.05 ppm Ceiling	None	HP-1 ppm TWA
Sterilant Cost[6]	$24.99/gal	$4.95/container	$13.00/gal	$35.00/gal	$32.00/gal
Cost profile (per cycle)[7]	$0.40 (manual), $2.38 (automated)	$4.95 (automated)	$0.25 (manual), $1.49 (automated)	No data	

Modified from [45].
Abbreviations: HLD=high-level disinfectant; HP=hydrogen peroxide; PA=peracetic acid; glut=glutaraldehyde; PA/HP=peracetic acid and hydrogen peroxide; OPA =ortho-phthalaldehyde; m=minutes; h=hours; NA=not applicable; TWA=time-weighted average for a conventional 8-hour workday.
[1]number of days a product can be reused as determined by re-use protocol
[2]time a product can remain in storage (unused)
[3]no U.S. EPA regulations but some states and local authorities have additional restrictions
[4]MEC=minimum effective concentration is the lowest concentration of active ingredients at which the product is still effective
[5]Conc soln=concentrated solution
[6]figure includes only the cost of the processing solution (suggested list price to healthcare facilities in August 2001)
[7]per cycle cost profile assumes maximum use life (e.g., 21 days for hydrogen peroxide, 14 days for glutaraldehyde), 3 reprocessing cycles per day, 1-gallon basin for manual processing, and 6-gallon tank for automated processing

Table 8. Summary of advantages and disadvantages of chemical sterilants[1] used primarily as high-level disinfectants.

Sterilization Method	Advantages	Disadvantages
Peracetic Acid/Hydrogen Peroxide	• No activation required • Odor or irritation not significant	• Materials compatibility concerns (lead, brass, copper, zinc) both cosmetic and functional • Limited clinical use
Glutaraldehyde	• Numerous use studies published • Relatively inexpensive • Excellent materials compatibility	• Respiratory irritation from glutaraldehyde vapor • Pungent and irritating odor • Relatively slow mycobactericidal activity • Coagulates blood and fixes tissue to surfaces
Hydrogen Peroxide	• No activation required • May enhance removal of organic matter and organisms • No disposal issues • No odor or irritation issues • Compatible with metals, plastics, and elastomers (Olympus scopes) • Does not coagulate blood or fix tissues to surfaces • Inactivates *Cryptosporidium* • Use studies published	• Material compatibility concerns (brass, zinc, copper, and nickel/silver plating) both cosmetic and functional • Serious eye damage with contact
Ortho-phthalaldehyde	• Fast acting high-level disinfectant • No activation required • Odor not significant • Excellent materials compatibility claimed • Does not coagulate blood or fix tissues to surfaces claimed	• Stains skin, clothing, and environmental surfaces • Limited clinical use • More expensive than glutaraldehyde
Peracetic Acid	• Rapid sterilization cycle time (30-45 minutes) • Low temperature (50-55°C) liquid immersion sterilization • Environmental friendly by-products (acetic acid, O_2, H_20) • Fully automated • Standardized cycle • No adverse health effects to operators • Compatible with wide variety of materials and instruments • Does not coagulate blood or fix tissues to surfaces • Sterilant flows through scope facilitating salt, protein, and microbe removal • Rapidly sporicidal • Provides procedure standardization (constant dilution, perfusion of channel, temperatures, exposure)	• Potential material incompatibility (e.g., aluminum anodized coating becomes dull) • Used for immersible instruments only • Biological indicator may not be suitable for routine monitoring • One scope or a small number of instruments can be processed in a cycle • More expensive (endoscope repairs, operating costs, purchase costs) than high level disinfection • Serious eye and skin damage (concentrated solution) • Point-of-use system, no long-term sterile storage

Modified from [45].

[1]All products effective in presence of organic soil, relatively easy to use, and have a broad spectrum of antimicrobial activity (bacteria, fungi, viruses, bacterial spores, and mycobacteria). The above characteristics are documented in the literature; contact the manufacturer of the instrument and sterilant for additional information.

Table 9. Summary of advantages and disadvantages of commonly used sterilization technologies.

Sterilization Method	Advantages	Disadvantages
Steam	• Nontoxic to patient, staff, environment • Cycle easy to control and monitor • Rapidly microbicidal • Least affected by organic/inorganic soils among sterilization processes listed • Rapid cycle time • Penetrates medical packing, device lumens	• Deleterious for heat labile instruments • Microsurgical instruments damaged by repeated exposure • May leave instruments wet, • causing them to rust
Hydrogen Peroxide Gas Plasma	• Safe for the environment and health-care worker • Leaves no toxic residuals • Cycle time is 45-73 minutes and no aeration necessary • Used for heat- and moisture-sensitive items since process temperature <50°C • Simple to operate, install (208 V outlet), and monitor • Compatible with most medical devices • Only requires electrical outlet	• Cellulose (paper), linens and liquids cannot be processed • Sterilization chamber is small, about 3.5 to 7.3 ft^3 • Endoscopes or medical devices with lumens >40 cm or a diameter of < 3mm cannot be processed at this time in the United States • Requires synthetic packaging (polypropylene wraps, polyolefin pouches) and special container tray
100% Ethylene Oxide (ETO)	• Penetrates packaging materials, device lumens • Single-dose cartridge and negative-pressure chamber minimizes the potential for gas leak and ETO exposure • Simple to operate and monitor • Compatible with most medical materials	• Requires aeration time to remove ETO residue • Sterilization chamber is small, • 4 ft^3 to 8.8 ft^3 • ETO is toxic, a probable carcinogen, and flammable • ETO emission regulated by states but catalytic cell removes 99.9% of ETO and converts it to CO_2 and H_2O • ETO cartridges should be stored in flammable liquid storage cabinet • Lengthy cycle/aeration time
ETO Mixtures 12% ETO/88% CFC 8.6% ETO/91.4% HCFC 10% ETO/90% HCFC 8.5% ETO/91.5% CO_2	• Penetrates medical packaging and many plastics • Compatible with most medical materials • Cycle easy to control and monitor	• Some states (CA, NY, MI) require ETO emission reduction of 90-99.9% • CFC (inert gas that eliminates explosion hazard) banned in 1995 • Potential hazards to staff and patients • Lengthy cycle/aeration time • ETO is toxic, a probable carcinogen, and flammable
Peracetic Acid	• Rapid cycle time (30-45 minutes) • Low temperature (50-55°C liquid immersion sterilization • Environmental friendly by-products • Sterilant flows through endoscope which facilitates salt, protein and microbe removal	• Point-of-use system, no long-term sterile storage • Biological indicator may not be suitable for routine monitoring • Used for immersible instruments only • Some material incompatibility (e.g., aluminum anodized coating becomes dull) • One scope or a small number of instruments processed in a cycle

Modified from [665].
Abbreviations: CFC=chlorofluorocarbon, HCFC=hydrochlorofluorocarbon.

Table 10. Examples of steam sterilization parameters for wrapped or containerized items.

Type of sterilizer	Load configuration	Temperature	Time
Gravity displacement	Porous or nonporous	121°-123°C (250°-254°F)	15 to 30 minutes
		132°-135°C (270°-275°F)	10 to 25 minutes
Prevacuum	Porous or nonporous	132°-135°C (270°-275°F)	3 to 4 minutes
Steam-flush/pressure-pulse	Porous or nonporous	121°-123°C (250°-254°F)	20 minutes
		132°-135°C (270°-275°F)	3 to 4 minutes

Modified from [656].

Table 11. Examples of flash steam sterilization parameters.

Type of sterilizer	Load configuration	Temperature	Time
Gravity displacement	Nonporous items only (i.e., metal instruments, no lumens)	132°C (270°F)	3 minutes
	Nonporous and porous items (e.g., rubber, plastic, items with lumens) sterilized together	132°C (270°F)	10 minutes
Prevacuum	Nonporous items only (i.e., metal instruments, no lumens)	132°C (270°F)	3 minutes
	Nonporous and porous items (e.g., rubber, plastic, items with lumens) sterilized together	132°C (270°F)	4 minutes
Steam-flush pressure-pulse	Nonporous or mixed nonporous/porous items	132°-135°C (270°-275°F); Manufacturers' instruction	3 minutes

Modified from [657].

Table 12. Characteristics of an ideal low-temperature sterilization process.

High efficacy: the agent should be virucidal, bactericidal, tuberculocidal, fungicidal and sporicidal

Rapid activity: ability to quickly achieve sterilization

Strong penetrability: ability to penetrate common medical-device packaging materials and penetrate into the interior of device lumens

Material compatibility: produces negligible changes in neither the appearance nor function of processed items and packaging materials even after repeated cycling

Nontoxic: presents no toxic health risk to the operator or the patient and poses no hazard to the environment

Organic material resistance: withstands reasonable organic material challenge without loss of efficacy

Adaptability: suitable for large or small (point of use) installations

Monitoring capability: monitored easily and accurately with physical, chemical, and biological process monitors

Cost effectiveness: reasonable cost for installation and for routine operation

Modified from [688].

Table 13. Factors affecting the efficacy of sterilization.

Factors	Effect
Cleaning[1]	Failure to adequately clean instrument results in higher bioburden, protein load, and salt concentration. These will decrease sterilization efficacy.
Bioburden[1]	The natural bioburden of used surgical devices is 10^0 to 10^3 organisms, which is substantially below the 10^6 required for FDA clearance.
Pathogen type	Spore-forming organisms are most resistant to sterilization and are the test organisms required for FDA clearance. However, the contaminating microflora on used surgical instruments consists mainly of vegetative bacteria.
Protein[1]	Residual protein decreases efficacy of sterilization. However, cleaning appears to rapidly remove protein load.
Salt[1]	Residual salt decreases efficacy of sterilization more than does protein load. However, cleaning appears to rapidly remove salt load.
Biofilm accumulation[1]	Biofilm accumulation reduces efficacy of sterilization by impairing exposure.
Lumen length	Increasing lumen length impairs sterilant penetration. May require forced flow through lumen to achieve sterilization.
Lumen diameter	Decreasing lumen diameter impairs sterilant penetration. May require forced flow through lumen to achieve sterilization.
Restricted flow	Sterilant must come into contact with microorganisms. Device designs that prevent or inhibit this contact (e.g., sharp bends, blind lumens) will decrease sterilization efficacy.

Modified from [355, 665].

[1] Factor only relevant for reused surgical/medical devices

Table 14. Comparative evaluation of the microbicidal activity of low-temperature sterilization technology.

	Carriers Sterilized by Various Low-temperature sterilization Technologies						
Challenge	ETO 12/88	100% ETO	HCFC-ETO	HPGP 100	HPGP 100S	PA	Reference
No salt or serum1	100%	100%	96%	100%	ND	ND	693
10% serum and 0.65% salt2	97%	60%	95%	37%	ND	ND	693
Lumen (125 cm long x 3 mm wide) without serum or salt1	ND	96%	96%	ND	ND	ND	693
Lumen (125 cm long x 3 mm wide) with 10% serum and 0.65% salt2	44%	40%	49%	35%	ND	100%1	693
Lumen (40 cm long x 3 mm wide)3	ND	ND	100%	95%	100%	8%	694
Lumen (40 cm long x 2 mm wide)3	ND	ND	100%	93%	100%	ND	694
Lumen (40 cm long x 1 mm wide)3	ND	ND	100%	26%	100%	ND	694
Lumen (40 cm long x 3 mm wide)4	ND	ND	100%	100%	100%	ND	694

Modified from [665].

Abbreviations: ETO=ethylene oxide; HCFC=hydrochlorofluorocarbon; ND=no data; HPGP=hydrogen peroxide gas plasma; PA=peracetic acid.

[1]Test organisms included *Enterococcus faecalis*, *Mycobacterium chelonei*, and *Bacillus subtilis* spores.

[2]Test organisms included *E. faecalis*, *P. aeruginosa*, *E. coli*, *M. chelonei*, *B. subtilis* spores, *B. stearothermophilus* spores, and *B. circulans* spores.

[3]Test organism was *B. stearothermophilus* spores . The lumen test units had a removable 5 cm center piece (1.2 cm diameter) of stainless steel sealed to the narrower steel tubing by hard rubber septums.

[4]Test organism was *B. stearothermophilus* spores. The lumen test unit was a straight stainless steel tube.

Table 15. Suggested protocol for management of positive biological indicator in a steam sterilizer.

1. Take the sterilizer out of service. Notify area supervisor and infection control department.
2. Objects, other than implantable objects, do not need to be recalled because of a single positive spore test unless the sterilizer or the sterilization procedure is defective. As soon as possible, repeat biological indicator test in three consecutive sterilizer cycles. If additional spore tests remain positive, the items should be considered nonsterile, and supplies processed since the last acceptable (negative) biological indicator should be recalled. The items from the suspect load(s) should be recalled and reprocessed.
3. Check to ensure the sterilizer was used correctly (e.g., verify correct time and temperature setting). If not, repeat using appropriate settings and recall and reprocess all inadequately processed items.
4. Check with hospital maintenance for irregularities (e.g., electrical) or changes in the hospital steam supply (i.e., from standard ≥97% steam, <3% moisture). Any abnormalities should be reported to the person who performs sterilizer maintenance (e.g., medical engineering, sterilizer manufacturer).
5. Check to ensure the correct biological indicator was used and appropriately interpreted. If not, repeat using appropriate settings.

If steps 1 through 5 resolve the problem

6. If all three repeat biological indicators from three consecutive sterilizer cycles (step 2 above) are negative, put the sterilizer back in service.

If one or both biological indicators are positive, do one or more of the following until problem is resolved.

7. A. Request an inspection of the equipment by sterilizer maintenance personnel.
   B. Have hospital maintenance inspect the steam supply lines.
   C. Discuss the abnormalities with the sterilizer manufacturer.
   D. Repeat the biological indicator using a different manufacturer's indicator.

If step 7 does not resolve the problem

Close sterilizer down until the manufacturer can assure that it is operating properly. Retest at that time with biological indicators in three consecutive sterilizer cycles.

Modified from [676].

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