catheters and sheath introducers exceeded $10^3$ CFUs on 14% (3 of 21) and 21% (6 of 28), respectively[907].

**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[426, 469]. However, other studies have suggested that these concerns may not be clinically relevant. One study 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[426]. These tests were conducted by inoculating Alfa soil (tissue-culture media and 10% fetal bovine serum) [469] containing $10^6$ *G. 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 10). Based on these experimental data, cleaning procedures would eliminate the detrimental effect of high salt content on a low-temperature sterilization process.

These articles [426, 469, 721] 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[472]. Sterilization of instruments and medical devices is compromised if the process is not preceded by meticulous cleaning.

The cleaning of any narrow-lumen medical device used in patient care presents a major challenge to reprocessing areas. While attention has been focused on flexible endoscopes, cleaning issues related to other narrow-lumen medical devices such as sphinctertomes have been investigated[913]. This study compared manual cleaning with that of automated cleaning with a narrow-lumen cleaner and found that only retro-flushing with the narrow lumen cleaner provided adequate cleaning of the three channels. If reprocessing was delayed for more than 24 hours, retro-flush cleaning was no longer effective and ETO sterilization failure was detected when devices were held for 7 days [913]. In another study involving simulated-use cleaning of laparoscopic devices, Alfa found that minimally the use of retro-flushing should be used during cleaning of non-ported laparoscopic devices[914].

**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, medical devices). There are no FDA-cleared ionizing radiation sterilization processes for use in healthcare facilities. Because of high sterilization costs, this method is an unfavorable alternative to ETO and plasma 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 [915] and delamination and cracking in polyethylene knee bearings[916]. Several reviews [917, 918] 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 the slow rate of heat penetration and microbial killing makes this a time-consuming method. In addition, the high temperatures

are not suitable for most materials[919]. 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. atrophaeus* spores should be used to monitor the sterilization process for dry heat because they are more resistant to dry heat than are *G. 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[920].

***Liquid Chemicals.*** Several FDA-cleared liquid chemical sterilants include indications for sterilization of medical devices (Tables 4 and 5)[69]. The indicated contact times range from 3 hours to 12 hours. However, except for a few of the products, the contact time is based only on the conditions to pass the AOAC Sporicidal Test as a sterilant and not on simulated use testing with devices. These solutions are commonly used as high-level disinfectants when a shorter processing time is required. Generally, chemical liquid sterilants cannot be monitored using a biological indicator to verify sterility[899, 900].

The survival kinetics for thermal sterilization methods, such as steam and dry heat, have been studied and characterized extensively, whereas the kinetics for sterilization with liquid sterilants are less well understood[921]. The information that is available in the literature suggests that sterilization processes based on liquid chemical sterilants, in general, may not convey the same sterility assurance level as sterilization achieved using thermal or physical methods[823]. The data indicate that the survival curves for liquid chemical sterilants may not exhibit log-linear kinetics and the shape of the survivor curve may vary depending of the formulation, chemical nature and stability of the liquid chemical sterilant. In addition, the design of the AOAC Sporicidal Test does not provide quantification of the microbial challenge. Therefore, sterilization with a liquid chemical sterilant may not convey the same sterility assurance as other sterilization methods.

One of the differences between thermal and liquid chemical processes for sterilization of devices is the accessibility of microorganisms to the sterilant. Heat can penetrate barriers, such as biofilm, tissue, and blood, to attain organism kill, whereas liquids cannot adequately penetrate these barriers. In addition, the viscosity of some liquid chemical sterilants impedes their access to organisms in the narrow lumens and mated surfaces of devices[922]. Another limitation to sterilization of devices with liquid chemical germicides is the post-processing environment of the device. Devices cannot be wrapped or adequately contained during processing in a liquid chemical sterilant to maintain sterility following processing and during storage. Furthermore, devices may require rinsing following exposure to the liquid chemical sterilant with water that typically is not sterile. Therefore, due to the inherent limitations of using liquid chemical sterilants, their use should be restricted to reprocessing critical devices that are heat-sensitive and incompatible with other sterilization methods.

Several published studies compare the sporicidal effect of liquid chemical germicides against spores of *Bacillus* and *Clostridium*[78, 659, 660, 715].

***Performic Acid.*** Performic acid is a fast-acting sporicide that was incorporated into an automated endoscope reprocessing system[400]. Systems using performic acid are not currently FDA cleared.

***Filtration.*** Although filtration is not a lethality-based process and is not an FDA-cleared sterilization method, 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[923]. 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[924].

***Microwave.*** Microwaves are used in medicine for disinfection of soft contact lenses, dental instruments, dentures, milk, and urinary catheters for intermittent self-catheterization[925-931]. However, microwaves must only be used with products that are compatible (e.g., do not melt) [931]. 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[932-934]. 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 *G. stearothermophilus* spores within 60 seconds to 5 minutes depending on the challenge organism[933, 935-937]. Another study confirmed these results but also found that higher power microwaves in the presence of water may be needed for sterilization[932]. Complete destruction of *Mycobacterium bovis* was obtained with 4 minutes of microwave exposure (600W, 2450 MHz)[937]. 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.[926]. Of concern is that home-type microwave ovens may not have even distribution of microwave energy over the entire dry device (there may be hot and cold spots on solid medical devices); hence there may be areas that are not sterilized or disinfected. 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 [931]. Microwaves used for sterilization of medical devices have not been FDA cleared.

***Glass Bead "Sterilizer".*** Glass bead "sterilization" uses small glass beads (1.2-1.5 mm diameter) and high temperature (217 $^{o}$C -232$^{o}$C) for brief exposure times (e.g., 45 seconds) to inactivate microorganisms. These devices have been used for several years in the dental profession[938-940]. FDA believes there is a risk of infection with this device because of potential failure to sterilize dental instruments and their use should be discontinued until the device has received FDA clearance.

***Vaporized Hydrogen Peroxide* (VHP®).** Hydrogen peroxide solutions have been used as chemical sterilants for many years. However, the 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 (30-35% 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 vacuum systems for industrial sterilization of medical devices and atmospheric systems for decontaminating for large and small areas[853]. VHP offers several appealing features that include rapid cycle time (e.g., 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 has limitations including that cellulose cannot be processed; nylon becomes brittle; and VHP penetration capabilities are less than those of ETO. VHP has not been cleared by FDA for sterilization of medical devices in healthcare facilities.

The feasibility of utilizing vapor-phase hydrogen peroxide as a surface decontaminant and sterilizer was evaluated in a centrifuge decontamination application. In this study, vapor-phase hydrogen peroxide was shown to possess significant sporicidal activity [941]. In preliminary studies, hydrogen

peroxide vapor decontamination has been found to be a highly effective method of eradicating MRSA, *Serratia marcescens, Clostridium botulinum spores* and *Clostridium difficile* from rooms, furniture, surfaces and/or equipment; however, further investigation of this method to demonstrate both safety and effectiveness in reducing infection rates are required[942-945].

***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).

A new sterilization process, which uses ozone as the sterilant, was cleared by FDA in August 2003 for processing reusable medical devices. The sterilizer creates its own sterilant internally from USP grade oxygen, steam-quality water and electricity; the sterilant is converted back to oxygen and water vapor at the end of the cycle by a passing through a catalyst before being exhausted into the room. The duration of the sterilization cycle is about 4 h and 15 m, and it occurs at 30-35$^{o}$C. Microbial efficacy has been demonstrated by achieving a SAL of $10^{-6}$ with a variety of microorganisms to include the most resistant microorganism, *Geobacillus stearothermophilus*.

The ozone process is compatible with a wide range of commonly used materials including stainless steel, titanium, anodized aluminum, ceramic, glass, silica, PVC, Teflon, silicone, polypropylene, polyethylene and acrylic. In addition, rigid lumen devices of the following diameter and length can be processed: internal diameter (ID): > 2 mm, length ≤ 25 cm; ID > 3 mm, length ≤ 47 cm; and ID > 4 mm, length ≤ 60 cm.

The process should be safe for use by the operator because there is no handling of the sterilant, no toxic emissions, no residue to aerate, and low operating temperature means there is no danger of an accidental burn. The cycle is monitored using a self-contained biological indicator and a chemical indicator. The sterilization chamber is small, about 4 $ft^3$ (Written communication, S Dufresne, July 2004).

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[946].

***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 into the sterilization chamber. A formaldehyde concentration of 8-16 mg/l is generated at an operating temperature of 70-75$^{o}$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 sterilizers. Low-temperature steam formaldehyde sterilization has been found effective against vegetative bacteria, mycobacteria, *B. atrophaeus* and *G. stearothermophilus* spores and *Candida albicans*[947-949].

Formaldehyde vapor cabinets also may be used in healthcare facilities to sterilize heat-sensitive medical equipment[950]. 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[951].

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 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[269, 578]. The formaldehyde steam sterilization system has not been FDA cleared for use in healthcare facilities.

***Gaseous chlorine dioxide.*** A gaseous chlorine dioxide system for sterilization of healthcare products was developed in the late 1980s[853, 952, 953]. Chlorine dioxide is not mutagenic or carcinogenic in humans. 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. atrophaeus* spores at 30° to 32°C[954]. Currently, no gaseous chlorine dioxide system is FDA cleared.

***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 atrophaeus* 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[955]. No vaporized peracetic acid system is FDA cleared.

***Infrared radiation.*** An infrared radiation prototype sterilizer was investigated and found to destroy *B. atrophaeus* spores. Some of the possible advantages of infrared technology include short cycle time, low energy consumption, no cycle residuals, and no toxicologic or environmental effects. This may provide an alternative technology for sterilization of selected heat-resistant instruments but there are no FDA-cleared systems for use in healthcare facilities [956].

The other sterilization technologies mentioned above may be used for sterilization of critical medical items if cleared by the FDA and ideally, the microbicidal effectiveness of the technology has been published in the scientific literature. The selection and use of disinfectants, chemical sterilants and sterilization processes in the healthcare field is dynamic, and products may become available that are not in existence when this guideline was written. As newer disinfectants and sterilization processes become available, persons or committees responsible for selecting disinfectants and sterilization processes should be guided by products cleared by FDA and EPA as well as information in the scientific literature.

**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, sterilant quality and quantity, and the appropriateness of the cycle for the load contents, and other aspects of device reprocessing. Healthcare 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[957]. Healthcare facilities should promote the same level of efficiency and safety in the preparation of supplies in other areas (e.g., operating room, respiratory therapy) as is practiced in central processing.

Ensuring consistency of sterilization practices requires a comprehensive program that ensures operator competence and proper methods of cleaning and wrapping instruments, loading the sterilizer,