Editorial

Low-Temperature Sterilization Technologies: Do We Need to Redefine "Sterilization"?

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The provocative article by Alfa and colleagues in this issue of *Infection Control and Hospital Epidemiology*[1] should lead to a reevaluation of our current concept of sterilization. This editorial will address several important issues relevant to evaluating the new low-temperature sterilization processes. These include the factors contributing to the development of alternative technologies to the current standard of ethylene oxide with a chlorofluorocarbon (CFC) carrier; characteristics of an ideal sterilization process for use in health care; review of current low-temperature sterilization technologies using the criteria for an ideal sterilant; recommendations for testing protocols when assessing the microbiocidal efficacy of sterilants (eg, spore load, inoculated vehicle, presence of proteinaceous material); and the need to develop a standard measure of cleaning efficacy.

Ethylene oxide (EtO) has been used widely as a low-temperature sterilant since the 1950s. It has been the most prevalent process for sterilizing temperature- and moisture-sensitive medical devices and supplies in healthcare institutions in the United States. Current EtO sterilizers combine EtO with a CFC stabilizing agent, most commonly in a ratio of 12% EtO mixed with 88% CFC (referred to as 12/88 EtO). For several reasons, hospitals are exploring the use of new low-temperature sterilization technologies. First, CFCs are to be phased out in December 1995 under provisions of the Clean Air Act.[2] 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 (eg, California, New York, Michigan) require the use of EtO abatement technology to reduce the amount of EtO being released into ambient air by 90% to 99.9%. Third, the Occupational Safety and Health Administration regulates the acceptable vapor levels of EtO due to concerns that EtO exposure represents an occupational hazard. These constraints have led to recent development of alternative technologies for low-temperature sterilization in the healthcare setting.

Alternative technologies to EtO with CFC include 100% EtO, EtO with a different stabilizing gas such as carbon dioxide or hydrochlorofluorocarbons, vaporized hydrogen peroxide, gas plasmas, ozone, and chlorine dioxide. These new technologies should be compared against the characteristics of an ideal low-temperature (<60°C) sterilant (Table 1).[3] While it is apparent that all technologies will have limitations (Table 2), understanding the limitations imposed by restrictive device designs (eg, long, narrow lumens) is critical for proper application of new sterilization technology.[4] 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.

The article by Alfa and colleagues provides important data in assessing the efficacy of several low-

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TABLE 1
CHARACTERISTICS OF AN IDEAL LOW-TEMPERATURE STERILANT

High efficacy—the agent should be virucidal, bacteriocidal, tuberculocidal, fungicidal, and sporicidal.
Rapid activity—ability to achieve sterilization quickly.
Strong penetrability—ability to penetrate common medical device packaging materials and penetrate into the interior of device lumens.
Material compatibility—produce negligible changes in either the appearance or function of processed items and packaging materials, even after repeated cycling.
Nontoxic—present no health risk to the operator or to the patient and pose no hazard to the environment.
Organic material resistance—withstand 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.

Adapted from Schneider PM. *Tappi Journal* 1994;77:115-119.[3]

temperature sterilization technologies to include 100% EtO from two manufacturers (AMSCO, Apex, NC; 3M, Minneapolis, MN), vaporized hydrogen peroxide (VHP), and gas plasma systems (AbTox, Mundelein, IL; Sterrad, Advanced Sterilization Products, Irvine, CA) from two manufacturers. The AbTox system uses two alternating gases: a mixture of 1 mg/L peracetic acid vapor and 4 mg/L hydrogen peroxide vapor, and a mixture of oxygen, hydrogen, and argon gas. The Sterrad system uses hydrogen peroxide as a substrate gas. Each of these latter two systems create a plasma by exposing a precursor gas or vapor to an electromagnetic field, such as microwave or radio frequency energy. This results in a variety of charged and uncharged excited chemical species with excellent biocidal properties. Important features of the article by Alfa and colleagues include testing multiple new low-temperature sterilization processes, the use of multiple test organisms, inclusion of positive and negative controls with each experimental run, development of a standardized method for assessing penetration into a narrow lumen vehicle, and challenge with a serum and salt load.

In brief, Alfa and coworkers found the following. All sterilants were able to eliminate all bacteria on inoculated penicylinders in the absence of serum or salt. However, it should be noted that the final bacterial load (ie, four to five logs) associated with these experiments did not fulfill the Food and Drug Administration (FDA) criteria of a six-log reduction to define a sterilization process.[5] When penicylinders were inoculated in the presence of serum and salt, which presents a more stringent challenge of the sterilization process, all sterilants, including 12/88 EtO, demonstrated a number of sterilization failures. Sterilization efficacy (percentage of all penicylinders rendered sterile) was as follows: 12/88 EtO, 97%; 100% EtO-AMSCO, 78%; 100% EtO-3M, 49%; AbTox, 32%; Sterrad, 37%; and VHP, 35%. Alfa and coworkers reported that, compared with the 12/88 EtO, all other sterilization processes demonstrated significantly reduced efficacy. Sterilization efficacy was decreased markedly when a serum and salt load was combined with a narrow lumen vehicle as the test challenge: 12/88 EtO, 44%; 100% EtO-AMSCO, 33%; 100% EtO-3M, 29%; AbTox, 6%; and Sterrad, 35%.

Several important conclusions flow from the data of Alfa and coworkers. First, the combination of salt and serum provided protection not only for spores but also for vegetative bacteria. Even 12/88 EtO did not demonstrate sterilization consistently. The exact mechanism by which salt and serum protect against microbial inactivation is understood incompletely, but most likely represents impedance of vapor penetration in a microenvironment. A separate set of experiments using salt or serum alone would be interesting to determine the relative contributions of each factor to the reduction in microbial killing. Second, the combination of salt and serum with a narrow lumen provided extraordinary protection for multiple organisms with all technologies, including the standard 12/88 EtO. The inclusion of a series of test runs using the narrow lumen vehicle without the addition of salt and serum would have been useful to assess the protection afforded by a narrow lumen. Additionally, tests using the narrow lumen vehicle combining cleaning and sterilization would have been helpful in assessing the combined efficacy of these processes. Third, the efficacy of microbial elimination varied not only by sterilization process but also by the test organism. As expected, spore-producing bacteria consistently were difficult to eliminate. Surprisingly, enterococci proved extremely difficult to eradicate in the presence of serum and salt, even when not also challenged by the use of a narrow lumen. The finding is of considerable concern, as enterococci routinely would contaminate medical devices used in the gastrointestinal tract, they represent an important nosocomial pathogen, and enterococci recently have developed clinically

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TABLE 2
SUMMARY OF ADVANTAGES AND DISADVANTAGES FOR LOW-TEMPERATURE STERILIZATION TECHNOLOGIES EVALUATED BY ALFA AND COLLEAGUES

Sterilization Method	Advantages	Disadvantages
Hydrogen peroxide plasma sterilization (Sterrad)	• Safe for the environment and healthcare worker • Leaves no toxic residuals • Cycle time is 75 min, and no aeration necessary • Ideal for heat- and moisture-sensitive items, since process temperature <50°C • Simple to operate, install (208 V outlet), and monitor	• Cellulose (paper), linens, and liquids cannot be processed • Sterilization chamber is small, approximately 3.5 ft^3 • Endoscopes or medical devices with lumens longer than >12 in or a diameter of <¼ in (6 mm) cannot be processed at this time in the United States • Requires synthetic packaging (polypropylene wraps, polyolefin pouches) and special container tray
Plasma sterilization (AbTox)	• Safe for the environment and healthcare workers • Cycle time depends on load and varies from 4 to 6 hrs, and no aeration necessary • Ideal for heat- and moisture-sensitive items • No corrosive effects and no harmful residues	• Sterilization chamber is small, 5.5 ft^3 • No liquids or products harmed by vacuum can be processed • Effectiveness not verified in peer-reviewed literature • Limited to stainless steel surgical instruments (excludes lumen devices and hinged instruments) at this time
Vapor phase hydrogen peroxide	• Rapid cycle time (30 to 45 min) • No corrosive effects • Low temperature • Environmentally friendly byproducts (H_2O, O_2) • Simple to operate, install (electrical outlet), and monitor	• Cellulose cannot be processed • Nylon becomes brittle • Penetration capabilities less than EtO • Material incompatibility with anodized aluminum surfaces and some epoxies
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 some 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 cabinets
12% EtO/88% CFC	• Very effective at killing microorganisms • Penetrates medical packaging and many plastics • Compatible with most medical materials • Cycle easy to control and monitor	• Some states (California, New York, Michigan) require EtO emission reduction of 90% to 99.9% • CFC (inert gas that eliminates explosion hazard) banned after 1995 • Potential hazards to staff and patients • Lengthy cycle-aeration time • EtO is toxic, a probable carcinogen, and flammable

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important resistance to a variety of antimicrobial agents including penicillin, ampicillin, aminoglycosides, and vancomycin. Fourth, a comparison of the initial inoculum used in these experiments with the post-processing cultures reveals that when salt and serum are combined with a narrow lumen, either a small reduction or no reduction in bacterial levels may occur with the more resistant microbes. For example, under these conditions, the AbTox process did not achieve even a one-log reduction in bacterial counts of *M chelonei, B stearothermophilus, B subtilis, B circulans,* and *E faecalis.*

This article and another article[6] assessing low-temperature sterilization technology challenge our current concepts of both existing and new sterilization technologies, and methods for assessing their efficacy. Alfa and colleagues mention numerous times in their article the importance of meticulous cleaning prior to sterilization. Their data, using a small lumen vehicle in combination with salt and serum, supports the critical need for healthcare facilities to develop rigid protocols for cleaning contaminated objects prior to sterilization. Equally crucial is for manufacturers who are producing these new low-temperature sterilization techniques to develop a standardized method to validate the efficacy of cleaning. For example, some type of test solution could be passed over or through an instrument and indicate on a qualitative (or, preferably, quantitative) basis when proper cleaning had occurred. Such a solution or device presumably would detect a common chemical constituent (ie, protein, amino acid, blood component) present in human tissues and hollow viscera. In addition, manufacturers of instruments and medical devices, including endoscopes, should be required as a condition of FDA clearance to develop a validated protocol of cleaning and subsequent disinfection or sterilization. For example, they might be required to demonstrate that cleaning using their standardized protocol could remove three to four logs of a test organism inoculated into the most inaccessible part of the device in continuum with the lumen.

Currently, the "gold standard" for low-temperature sterilization in the United States is 12/88 EtO. As Alfa and associates have demonstrated, this method achieves complete sterilization using penicylinders inoculated with six logs of bacteria in the absence of serum or salt. However, due to natural die off, this level of killing does not equate to a six-log reduction in bacteria from the sterilization process. For example, *E faecalis* demonstrated almost a three-log reduction in bacteria just from overnight drying or retention within the penicylinder. Further, Alfa and associates have demonstrated that a salt and serum load in combination with a narrow lumen prevented 12/88 EtO from achieving more than a two- to three-log reduction for multiple organisms. How do we reconcile these findings with the current FDA requirements that a sterilizer's microbicidal performance must be tested under specified simulated use conditions, which include that the test articles must be inoculated with 10^6 CFU/unit of the most resistant test organism prepared with inorganic and organic test loads.[2] The inocula must be placed in various locations on the test articles, including those least favorable to penetration and contact with the sterilant (eg, lumens).[5] It is clear that neither current nor new sterilization technologies meet these standards. The current standards may be unnecessarily restrictive and too conservative. For this reason, the FDA should consider modifying their guidance documents to consider the combined effectiveness of cleaning and the subsequent sterilization process. Ideally, instrument or sterilization manufacturers should be able to demonstrate that cleaning followed by a sterilization process can inactivate a clinically relevant inoculum of highly resistant organisms in the presence of an organic load that is placed into the most inaccessible location of the device.

Unfortunately, it is not clear whether the above goal can be met by either current or new low-temperature sterilization technologies. Three essential research or regulatory questions need to be answered in the immediate future. First, what is the efficacy of cleaning followed by sterilization using clinically relevant test parameters? Second, what should be the relevant test parameters, including inoculating dose? The standard inoculating dose should be based on the level of contamination found after routine clinical use. Finally, who should be responsible for providing the scientific data to substantiate device claims? Clearly, the FDA needs to redefine the test parameters. Verification of efficacy could be the responsibility of the FDA, the instrument manufacturer (eg, endoscope manufacturer), or the sterilizer manufacturer.

Many healthcare facilities now are faced with choosing an alternative low-temperature sterilization process. They must make this decision in the face of potentially confusing product claims, evolving practice guidelines, and peer-reviewed scientific data demonstrating significant concerns about efficacy. We hope that this editorial will encourage independent investigators, federal regulatory agencies, and manufacturers to provide rigorous scientific data regarding the limitations and benefits of these new low-temperature sterilization processes. The new low-temperature sterilization technologies have the poten-

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tial for replacing EtO; however, sterilization manufacturers must refine their processes to enhance their microbiocidal efficacy. Equally important, device manufacturers must design their instruments to allow proper cleaning and effective sterilization.

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Smoke Tubes Not Reliable for Negative-Pressure Monitoring

by Gina Pugliese, RN, MS
Medical News Editor

It is recommended that TB isolation rooms be monitored regularly for the direction of airflow to assure that there is negative pressure in relation to the corridor. Researchers at the Montreal Chest Research Institute in Montreal, Quebec, Canada, developed a simple method to measure air-change rates and direction of airflow in patient-care areas. Pure carbon dioxide (CO_2) was released at 13.5 L/min for 5 minutes, then measured for 30 minutes within the room and outside in the hallway with a CO_2-reading instrument. Smoke tubes also were used to measure direction of airflow. If doors and windows were opened, there were significant changes in air-change rates and airflow direction. Smoke-tube measurements were inconsistent, agreed poorly with evidence of CO_2 movement from room to hall, and were affected strongly by room-to-hallway temperature differentials.

The authors concluded that smoke tubes, although inexpensive and simple, are unreliable and that CO_2 release and measurement provides more accurate measurement of air-change rates and airflow direction and the effect of door or window manipulation. The authors note that CO_2 is safe, nontoxic, and inexpensive, and the technique for measuring CO_2 is fairly simple. A direct-reading CO_2 detector is needed and costs approximately $1,500.

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