What's new in reprocessing endoscopes: Are we going to ensure *"the needs of the patient come first"* by shifting from disinfection to sterilization?

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Key Words:
Patient safety
high-level disinfection
Instrument reprocessing
Infection

Millions of gastrointestinal endoscopes are performed each year in the United States. Gastrointestinal endoscopes become highly contaminated during use (ie, internal channels contain 7-10-$\log_{10}$ enteric microorganisms). Currently, endoscopes (eg, bronchoscopes and gastrointestinal endoscopes) are classified as semicritical items because they contact intact mucous membranes and most commonly undergo cleaning followed by high-level disinfection, which may result in as little as a 6-$\log_{10}$ reduction of microorganisms. Therefore, and not surprisingly, in recent years there have been multiple reports that have documented that endoscopes, especially duodenoscopes, frequently remain contaminated with bacterial pathogens after proper cleaning and disinfection. Multiple outbreaks of multidrug-resistant organisms from contaminated duodenoscopes have resulted in substantial death and morbidity. Because duodenoscopes commonly contact nonintact mucous membranes and sterile tissue, such endoscopes should be considered critical items. We propose that to ensure patient safety, we follow the Spaulding scheme and move from high-level disinfection to sterilization of reusable endoscopes or use an alternative diagnostic/therapeutic method (eg, disposable sterile endoscopes).

For more than a century, the founders of Mayo Clinic instilled "*the needs of the patient come first*" into the culture of the institution. The profound allegiance of Mayo Clinic to its patient-centered culture connects all staff to the purpose of their work and promotes an environment that is committed to excellence and continuous improvement.[1] The purpose of this article is to consider this primary value, in the context of the contemporary challenge of endoscope reprocessing, and how to provide the best care to the 18 million patients who receive an endoscopic procedure each year in the United States through improved cleaning and a shift from disinfection to sterilization.[2-5]

During the past few years, there have been >25 outbreaks of multidrug-resistant organisms (MDROs) (such as carbapenem-resistant *Enterobacteriaceae* [CRE]) in major hospitals in the United States and in the world that have killed dozens of patients and caused morbidity in hundreds more.[6,7] These outbreaks have been linked primarily to contaminated duodenoscopes that are used to diagnose and treat disease of the liver, bile ducts, and pancreas.[6,7] Gastrointestinal (GI) endoscopes (eg, colonoscopes, gastroscopes, and duodenoscopes) and bronchoscopes have been associated with >130 outbreaks causing more death and illness.[6,8] Although GI endoscopes and bronchoscopes have contact with intact mucous membranes, but frequently have contact with nonintact mucous membranes and sterile tissue (via a biopsy or entrance into normally sterile areas such as bile ducts, lung, etc), there is a risk of patient-to-patient transmission of potential pathogens with a subsequent risk of infection.[6,8-10]

The key concern raised by these outbreaks is whether current reprocessing guidelines for endoscopes are adequate to ensure a patient-safe endoscope (ie, 1 devoid of potential pathogens) or if endoscopes, with their long, narrow channels, right-angle turns, difficult-to-clean and disinfect components, heavy microbial contamination, and presence of biofilm, make it impossible to achieve

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Conflicts of interest: W.A.R. is a consultant for Advanced Sterilization Products. D.J.W. is a consultant for Germitec.

https://doi.org/10.1016/j.ajic.2019.01.017

high-level disinfection (HLD). To examine this concern and to offer recommendations, understanding the current knowledge on endoscope reprocessing is necessary.

First, endoscopes have been considered semicritical devices because they have contact with intact mucous membranes and require at least HLD. It is noteworthy that in the Spaulding scheme,[11] which identifies how an object should be disinfected or sterilized, it states that mucous membranes should be intact and that sterilization of semicritical items is desirable. HLD is supposed to achieve complete elimination of all microorganisms, except for small numbers of bacterial spores. However, the data demonstrated that 30% or more reprocessed endoscopes are contaminated with substantial numbers of potential pathogens.[12] Additionally, the data demonstrated that when screening and/or surveillance colonoscopy was performed on 1,580,318 patients, a biopsy intervention, which resulted in the penetration of a mucous membrane, occurred in 59.2% of cases. Therefore, in approximately 60% of screening colonoscopies, there is a high likelihood of contact with sterile tissue (ie, underlying tissue and blood).[9] Based on the Spaulding classification scheme, the colonoscope that has contact with nonintact mucous membranes would be a "critical" item requiring sterilization.[11] The duodenoscope, cystoscope, and bronchoscope would also be considered "critical," as they indirectly contact normally sterile tissue such as bile ducts, the bladder, and the lung, respectively.[11] Because flexible GI endoscopic and bronchoscopic instruments are heat labile, only HLD with chemical agents or low-temperature sterilization technologies (LTSTs) are possible.[13,14] Until recently, there were no LTSTs cleared for GI endoscopes using the Food and Drug Administration (FDA) guidance document.[15] However, currently there are 2 FDA-cleared LTSTs (Anderson Products, Haw River, NC and TSO3, Quebec, Canada).

Second, endoscopes have been associated with far more outbreaks of infections (>130 outbreaks) than any other reusable medical or surgical device in health care.[6-8] In the past, these outbreaks have been commonly traced to deficient practices such as inadequate cleaning, inappropriate disinfection, and damaged endoscopes or flaws in the design of the endoscope or automated endoscope reprocessor (AER).[8] However, in the past few years there have been at least 9 outbreaks of duodenoscope-related infections of MDROs without reprocessing breaches.[16-24] The Centers for Disease Control and Prevention and/or other investigators monitored endoscope-reprocessing procedures used in these outbreaks and concluded that the institutions were compliant with the manufacturer's instructions for use and professional organizational recommendations.[16-24]

Rubin et al[7] identified 32 outbreaks involving duodenoscopes with almost 400 patients between January 2000 and December 2017. There were 9 published outbreaks in which there were no identified breaches in endoscope reprocessing (Table 1).[16-24] In the patients who had undergone endoscopic retrograde cholangiopancreatography (ERCP) procedures, a clonal strain of the MDRO (eg, CRE) was identified, and there was a molecular link between a positive scope and the patient isolate. The number of patients infected in the outbreaks varied from 2-39 persons, and in several outbreaks there was propagated spread to patients who had not undergone endoscopy. At least on 1 occasion when the manufacturer evaluated the contaminated scope, the scope had 1 or more critical defects requiring a repair that had not been detected by the facility.[16] Transmission was attributed to design flaws, which prevented effective cleaning and allowed persistent contamination at the elevator region.[6,25] CRE and other MDROs are susceptible to disinfectants, and it is lack of exposure on the microbial contaminants that impeded effective inactivation.[26-28] Based on these and other studies,[6,7] it is likely that MDROs are acting as an "indicator" or "red-flag" organisms for ineffective reprocessing of the complex design of duodenoscopes, which are an infectious risk to patients. In addition to outbreaks, reprocessing failures (especially of endoscopes) have led to patient notifications and bloodborne pathogen testing in tens of thousands of patients.[29] To mitigate this risk, most endoscopy centers have implemented enhanced duodenoscope-reprocessing techniques (eg, 63% of 249 surveyed endoscopy centers repeated HLD).[30] Unfortunately, a randomly assigned trial of single versus double HLD of duodenoscopes and linear echoendoscopes showed that double HLD did not reduce culture positivity rates, compared with single HLD, and the elevator mechanism was colonized more frequently than the channel samples.[31] This finding suggests that there may be internal bacterial contamination of the duodenoscope in areas (eg, elevator mechanism) that are not adequately exposed to brushes, detergents, and/or disinfectants and therefore not addressed through a second HLD.[25]

Third, evidence-based endoscope-reprocessing guidelines have been prepared by professional organizations (eg, Society of Gastroenterology Nurses and American Society of Gastrointestinal Endoscopists)[32-34] and the Centers for Disease Control and Prevention.[14] Unfortunately, there are also data that demonstrate that all of the steps associated with manual endoscope reprocessing are rarely performed (1.4% compliance rate) and some essential steps (eg, brushing all endoscope channels and components) are commonly not performed.[35] Endoscope reprocessing was improved with the use of AERs because most steps were automated and standardized.[35]

Fourth, recent microbial surveillance of GI endoscopes demonstrates GI endoscope contamination rates (>100 colony forming units [CFU]/endoscope) of 30% or greater, and high contamination rates were associated with endoscopes older than 2 years and not stored in storage cabinets.[12] Recently, investigators found all endoscopes (n = 20) had visible irregularities as well as fluid discoloration (95%)

Table 1
Recent duodenoscope-related outbreaks of CRE and other MDROs without reprocessing breaches

MDRO	Resistance gene	No. of patients (infected)	Propagated outbreak	Positive scope(s)	Molecular link	Reference
Klebsiella pneumoniae	*mcr-1*	2	No	No	Yes-WGS	Shenoy et al, 2018[21]
K pneumoniae	$bla_{\text{oxa-232}}$	15 (8)	No	No	Yes-PCR	Kim et al, 2016[19]
Escherichia coli (AmpC)	$bla_{\text{CMY-2}}$	35	No	Yes (2)	Yes-PCR, PFGE	Wendorf et al, 2015[16]
K pneumoniae	$bla_{\text{oxa-48}}$	12	Yes	No	Yes-PCR, PFGE	Kola et al, 2015[23]
K pneumoniae	bla_{KPC}	34?	No	Yes (3)	Yes-PCR, PFGE, MLST, WGS	Marsh et al, 2015[22]
E coli	bla_{NDM}	39	Yes	Yes (1)	Yes-PCR, PFGE	Epstein et al, 2014[17]
Pseudomonas aeruginosa	$bla_{\text{VIM-2}}$	22	Yes	Yes (1)	Yes-PCR*, PFGE, repetitive-sequence-based PCR typing	Verfaillie et al, 2015[24]
E coli	$bla_{\text{NDM-1}}$	3 (3)	No	No	Unknown	Smith et al, 2015[20]
K pneumoniae	$bla_{\text{KPC-2}}$, $bla_{\text{SHV-12}}$	13	Yes	Yes (2)	Yes-PCR, PFGE, MLST	Carbonne et al, 2010[18]

CRE, carbapenem-resistant *Enterobacteriaceae*; *MDRO*, multidrug-resistant organism; *MLST*, multilocus sequence typing; *PCR*, polymerase chain reaction; *PFGE*, pulsed-field gel electrophoresis; *WGS*, whole-genome sequencing.
*PCR for resistance gene.

and debris in the channels.[36] Microorganisms can reside in scratches, grooves, and irregular surfaces and are likely to be protected from disinfectant exposure.[37,38] Further, residual microorganisms can lead to biofilm formation, which further degrades the effectiveness of disinfection.

Fifth, endemic transmission of infections associated with GI endoscopes may go unrecognized owing to inadequate or complete lack of surveillance of outpatient procedures, the long lag time between colonization and infection, and a low frequency of infection. Therefore, it is likely that we are seeing only a very small subset of the colonizations and/or infections from these endoscopes, as transfer of some normal enteric microflora (eg, *Escherichia coli, Enterococcus*) may not be pathogenic, or immediately pathogenic, and may therefore go unnoticed. In the outbreaks studied by Epstein et al[17] and Wendorf et al,[18] it was the presence of an unusual pathogen (eg, New Delhi metallo-β-lactamase-producing *E coli*) that resulted in an investigation and recognition that duodenoscopes were the source of the outbreak. Additionally, the risk for some procedures might be lower than other procedures in which normally sterile areas are contaminated (eg, colonoscopy vs ERCP). Furthermore, the risk is likely increased owing to the increasing use of these procedures (eg, ERCPs and bronchoscopies) in patients with advanced age, cancers, organ transplantation, severe underlying disease, and other host defense abnormalities or immunocompromising diseases or medications.

Last, the margin of safety associated with reprocessing endoscopes is nonexistent or <0 (ie, risk is >0). Endoscopes are heavily contaminated with microbes because they enter the GI tract with its very high microbial load (eg, microbial load in the colon is $10^{9\text{-}12}$ [9-12-$\log_{10}$]/mL). Studies have shown that the internal channel of GI endoscopes may contain 7-10-$\log_{10}$ enteric microorganisms.[39-43] Investigations have demonstrated that the cleaning step in endoscope reprocessing results in a 2-6-$\log_{10}$ reduction of microbes and the HLD step results in another 4-6-$\log_{10}$ reduction of mycobacteria for a total 6-12-$\log_{10}$ reduction of microbes (ie, sum of reduction from cleaning and HLD).[39-43] Therefore, the margin of safety associated with cleaning and HLD of GI endoscopes is nonexistent or <0 (level of contamination after reprocessing can be 10,000 microbes; the calculation considers maximal contamination [10-$\log_{10}$] and minimal cleaning/HLD [6-$\log_{10}$]).[3-5] This nonexistent margin of safety associated with endoscope reprocessing compares to the 17-$\log_{10}$ margin of safety associated with cleaning and sterilization of surgical instruments.[3-5]

If the margin of safety for endoscope reprocessing is so small that perfect compliance with >100 pages of the manufacturer's instructions for use is required, then the endoscope design is too complex, the microbial load is too high, and the process is too unforgiving to be practical in the real world. Therefore, what must be done to ensure "*the needs of the patient come first*" and these commonly used devices are reliably devoid of microbial contamination? There are 3 essential components. First, endoscopy is an important diagnostic and therapeutic modality and should continue to be used while clinicians strictly enforce evidence-based practices, which rely on objective scientific data and are essentially insulated from human bias.[14,32-34] These practices include proper equipment maintenance (eg, minimally annually), routine audits (and follow-up of deficiencies), adequate drying of endoscope channels via drying cabinets (scope dry within 3 hours), consistent and standardized reprocessing among medical facilities, and the need for thorough training of reprocessing staff, with at least initial and yearly competency testing (including training on new instruments and new reprocessing steps such as a new brush [MAJ-1888] for Olympus duodenoscopes (Olympus Corp., Center Valley, PA) or positioning the elevator lever at 45° when a duodenoscope is placed in an AER).[44] Moisture remaining in the channels after inadequate drying may contribute to the development of a biofilm.[36] In addition, we must understand what facilitates the formation of biofilms (eg, incomplete drying)[45] and the role of biofilms as a source of pathogens.[46] Tolerance of bacteria in biofilms to high-level disinfectants (eg, peracetic acid) has been demonstrated[47] and might contribute to disinfection failure of endoscope reprocessing if biofilms build-up in the endoscope channels.[48] Inspection of endoscope channels after reprocessing using a borescope has been used by some endoscopy centers to audit reprocessing performance and to identify moisture, debris, discoloration, scratches, and biofilm.[49]

Second, real-time monitoring methods need to be developed and validated to assess the effectiveness of cleaning and be predictive of microbial contamination. Cleaning must consistently and reliably remove and/or reduce the organic and inorganic materials so as not to interfere with the effectiveness of HLD or sterilization.[50] Current cleaning assessment tools (eg, visual, adenosine triphosphate [ATP]) are primitive and not predictive of microbial contamination[51] or infection risks. Detection of ATP, a molecule found in and around living cells, has been used to assess the cleanliness of surfaces and devices. A validation study of ATP used to audit cleaning of flexible endoscope channels used a benchmark for clean of <200 relative light units, which equated to <4-$\log_{10}$ CFU/cm^2 (or 10^4 CFUs/cm^2)[52] or about 10^6 CFU per endoscope as the surface area of an endoscope channel exceeds 100 cm^2. Thus, an endoscope assessed as clean by ATP could still have a substantial microbial load (eg, 10^6) and ATP correlates poorly with terminal culture results.[53] Other cleaning verification measures that have been used include protein, total organic carbon, carbohydrate, hemoglobin, bilirubin, and detecting enzymes specific to gram-negative bacteria.[40,54] Preferably, cleaning verification tests would directly monitor or be predictive of microbial contamination. Some health care facilities have implemented a systematic microbiologic sampling program to monitor the efficacy of endoscope reprocessing.[55] Cleaning should consistently reduce the microbial load by at least 6-8-$\log_{10}$. This should be accomplished by the use of AERs, new cleaning methods (eg, pull-through cleaners;[56] NanoCleaning Technology, NovaFlux Technologies, Princeton, NJ) and new chemistries. Ideally, new cleaning and/or antimicrobial chemistries will have biofilm-inhibiting or destruction properties. Improved automated cleaning and drying may prevent the development of intractable biofilm that cannot be eradicated by standard reprocessing practices. Automated cleaning technologies that clean the inside and outside on endoscopes beyond the Association for the Advancement of Medical Instrumentation standards and more effectively than certified technicians must be developed and used.

Third, to provide a margin of safety we must transition from disinfection to sterilization. Because sterilization results in a 12-$\log_{10}$ reduction of spores (ie, 1 trillion spores) and HLD results in a 6-$\log_{10}$ reduction (ie, 1 million microorganisms, not spores), sterilization will provide a safety margin (approximately 6-$\log_{10}$). Improvements in cleaning, although essential, without transition to sterilization will not provide an essential margin of safety. This transition from disinfection to sterilization could be accomplished by a clarification of the Spaulding definition of critical items from "objects that enter sterile tissue or the vascular system or through which blood flows should be sterile" to "objects that directly or indirectly (ie, via a mucous membrane such as duodenoscope) enter normally sterile tissue or the vascular system or through which blood flows should be sterile." This clarification would minimally require instruments that enter a mucous membrane but indirectly contact normally sterile tissue be classified as critical (eg, cystoscope [bladder], bronchoscope [lung], and duodenoscope [duodenum, bile ducts]). Other GI scopes, such as colonoscopes, commonly disrupt mucous membranes and would be interpreted by the revised Spaulding scheme as also being "critical" and requiring sterilization.[3-5,11] Implementation of this recommendation requires sterilization technologies that achieve a sterility assurance level of 6-$\log_{10}$ using real-world testing methods (eg, spore

Table 2
Potential future sterilization methods for endoscopes and a proposed method for transitioning from disinfection to sterilization

Potential future sterilization methods or alternative methods
• Optimize current low-temperature sterilization methods or new LTST proving SAL 10^{-6} achieved.
• Disposable sterile GI endoscopes/bronchoscopes. A disposable endoscope costs from $170 (bronchoscope) to an estimated $225 (GI endoscope), whereas reprocessing HLD costs are $114-$281.[58]
• Steam sterilization for GI and other endoscopes.
• Use of nonendoscope methods to diagnosis or treat disease (eg, capsule endoscopy, stool or blood tests to detect GI cancer, and stool DNA test).
• Improved GI endoscope design (to reduce or eliminate reprocessing challenges; however, based on 50 years of experience, design changes are unlikely to resolve the endoscope-reprocessing problem [eg, the closed-channel duodenoscopes increased the infection risk]).
Proposed method for transitioning from disinfection to sterilization
• Professional and consensus standard organizations (eg, SHEA, APIC, SGNA, ASGE, and AAMI) should clarify the Spaulding classification scheme for critical items from "direct contact with sterile tissue" to "direct or indirect contact with sterile tissue."
• These organizations should incorporate this new clarification into the HLD and sterilization standards, guidelines, and guidance documents.
• These organizations should incorporate verbiage that this transition should happen as soon as new sterilization technology (or single-use endoscopes) is acceptable in terms of sterilization performance, scope performance (disposable), cost, throughput, and materials compatibility with the sterilization process.
• TJC, CMS, and other accrediting agencies should ensure implementation of these guidelines and consensus standards as soon as new sterilization technologies are available and acceptable (based on literature and hospital usage).
• Endoscope manufacturers must make their endoscopes compatible with LTST (eg, adhesives and lubricants [such as molybdenum disulfide]). The FDA must ensure endoscope manufacturers facilitate compatibility with LTST.
• The FDA must clear in a timely manner LTST or single-use/disposable endoscopes when data demonstrate they achieve an SAL 10^{-6}. Validation tests of LTST must be robust and reflect worst-case conditions (eg, high spore load, clinical fluids, organic matter, manual cleaning, and used endoscopes [not new endoscopes]), and the FDA should mandate clinical-use studies. Validation tests with a LTST using a few replicates (eg, 5 replicates), low inoculum (eg, 10^6), new scopes or surrogate models, and/or no organic soil do not represent real-world conditions. LTST that have not been cleared by the FDA to achieve an SAL of 10^{-6} using the FDA-guidance document (or preferably a more challenging method than the FDA-guidance document) are not likely to reliably result in sterilization of endoscopes.[59]
• To protect the public health and to prevent endoscope-related infections and outbreaks, the FDA should mandate a shift from HLD to sterilization, as they did in 1992 with dental handpieces.
• Manufacturers that submit critical devices to the FDA for clearance that directly/indirectly enter normally sterile tissue need to offer an FDA-cleared sterilization method.
• Professional organizations must facilitate this change via guidelines, research, education, and presentations at professional meetings.

AAMI, Association for the Advancement of Medical Instrumentation; *APIC*, Association for Professionals in Infection Control and Epidemiology; *ASGE*, American Society for Gastrointestinal Endoscopists; *CMS*, Centers for Medicare and Medicaid Services; *FDA*, Food and Drug Administration; *GI*, gastrointestinal; *HLD*, high-level disinfection; *LTST*, low-temperature sterilization technologies; *SAL*, sterility assurance level; *SGNA*, Society of Gastrointestinal Nurses and Associates; *SHEA*, Society of Healthcare Epidemiology of America; *TJC*, The Joint Commission.

load, clinical fluids, and used [not new] endoscopes) of complex medical instruments such as duodenoscopes.[15]

This shift to sterilization is likely to occur by 1 of 5 technologies: new or optimized LTSTs,[16,17,57] disposable sterile endoscopes (Ambu Inc., Columbia, MD), steam sterilization for GI endoscopes, use of nonendoscopic methods (eg, capsular endoscopy, stool or blood test to detect cancer), and possibly an improved design (Table 2). Manufacturers are meeting the demand for sterilization as there are now 2 sterilization technologies that are FDA-cleared for endoscopes,[16,17] 1 disposable sterile GI endoscope manufacturer, 1 disposable sterile bronchoscope manufacturer (Ambu Inc., Columbia, MD), and 1 manufacturer of an autoclavable flexible bronchoscope (Olympus Corp., Center Valley, PA).

A proposed method on how to facilitate this shift from disinfection to sterilization of endoscopes with the cooperation of standards and professional organizations, the FDA), and accrediting agencies is shown in Table 2. The FDA mandated a similar shift from disinfection to sterilization for dental handpieces in 1992. This mandate occurred although there were no documented cases of disease transmission associated with dental handpieces.

Unlike dental handpieces, the infection data are overwhelming and irrefutable, and the need is urgent. Based on the infection data and risks, the transition to sterilization of duodenoscopes was recommended by an FDA panel in May 2015. Now, professional organizations (eg, Society of Healthcare Epidemiology of America, Society of Gastroenterology Nurses and Associates, and American Society of Gastrointestinal Endoscopy) and a consensus standards organization (eg, Association for the Advancement of Medical Instrumentation) must clarify the term "critical," as stated earlier, which would facilitate the transition from disinfection to sterilization for endoscopes. Technologies to allow this change to occur are being developed[16,17] and FDA-cleared and should be used when acceptable in terms of sterilization performance, scope performance (for disposable scopes), cost, throughput, and compatibility of materials (eg, adhesives) to sterilization technology. Device and sterilization manufacturers, regulatory agencies, GI physicians, inpatient and outpatient endoscope-reprocessing centers as well as professional organizations must reach a general agreement regarding the need for sterilization and the willingness to replace existing disinfection technologies. This transition will occur when we put "*the needs of the patient first*" and offer every patient an endoscope that is sterile and, therefore, devoid of potential pathogens.

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