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EDITORIAL

Current issues in endoscope reprocessing and infection control during gastrointestinal endoscopy

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Abstract

The purpose of this article is to review the evidence regarding transmission of infection during gastrointestinal endoscopy, factors important in endoscope reprocessing and infection control, areas to focus on to improve compliance, and recent developments and advances in the field.

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Key words: Endoscopy; Infection; Disinfection; Reprocessing; Infection control

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INTRODUCTION

Gastrointestinal (GI) endoscopy is an important tool for the identification and treatment of disorders of the gastrointestinal tract. A thorough understanding of infection control and its application to GI endoscopy is crucial to prevent lapses in reprocessing and the possibility of transmission of infection. Endoscopes reprocessed appropriately, in accordance with reprocessing and infection-control guidelines, pose virtually no risk of transmission of patient-borne or environmental microorganisms. In the absence of defective equipment, every reported case of nosocomial infection associated with a contaminated GI endoscope has been linked to a specific breech or violation of at least one of several requisite reprocessing steps[1].

TRANSMISSION OF INFECTION DURING GASTROINTESTINAL ENDOSCOPY

In a recent review of the published medical literature and the US FDA database, only 35 cases of transmission of infection during GI endoscopy have been reported in the last decade (again, all of which have been associated with breaches in reprocessing protocols)[1] It has been estimated that 17 million lower GI procedures (colonoscopy and flexible sigmoidoscopy) are performed annually in the U.S[2], and a similar number of upper GI procedures are performed[3,4]. If this procedure rate was constant during the past decade, these 35 cases occurred during an estimated 340 million procedures, yielding an infection rate that approaches 1 in ten million procedures. It is very likely that this simple calculation underestimates the actual incidence of transmission of infection, (unreported or unrecognized infections), however it does put the documented risk into perspective. Even if reported infections represented only 1% of the actual infection rate ("tip of the iceberg"), the transmission rate would be extremely low. We review the published literature with regard to documented cases of transmission of infection. Although there are few published data regarding some novel pathogens (SARS, Avian Influenza), their physical properties and anticipated susceptibility to current disinfection practices are discussed.

Viruses

Hepatitis C virus (HCV): There have been 8 cases of HCV transmission that have attributed to gastrointestinal endoscopy[5-10]. A serious attempt at investigation (other than temporal association) and genotyping was performed in only three cases, in which transmission was firmly established by nucleotide sequencing[7,8]. While both reports implicated inadequate disinfection of the colonoscope, they each also raised the possibility of contamination of syringes or multi-dose vials as the source of transmission. There have been several epidemiologic studies that have suggested an association between gastrointestinal endoscopy and HCV infection from several countries[11-18]. The relevance of these observations may be limited. All of the studies relied on self-reports of exposure risks, which are unreliable for many of the socially stigmatized behaviors associated with hepatitis C virus (HCV) transmission, particularly IV substance abuse[19]. A major concern for studies utilizing cross-sectional methodology is the inability to verify when infection occurred relative to

the procedure (i.e., the studies do not establish causality). It is not known whether currently accepted reprocessing protocols were being used during the periods under study, or even the degree to which endoscope reprocessing complied with these protocols. Finally, compliance with general infection control practices was not assessed, and the improper use (or reuse) of syringes and multiple-dose vials for sedation is increasingly recognized as an important risk factor for pathogen transmission[20-23]. In a particularly notable example in 2001 it was extensively reported in the lay press that eight individuals having undergone endoscopy at a New York City endoscopy center had become infected with hepatitis C. Although initial reports suggested that it was due to the endoscopic equipment, a subsequent investigation by the New York City Department of Health concluded that the cause was in fact not the endoscopy, but rather improper handling of contaminated needles, syringes, and or multi-dose vials[24]. Although transmission of infection resulted from a contact with the medical system, it did not reflect on the adequacy of endoscope reprocessing. Unless this aspect is controlled for in epidemiologic studies, the resulting association might reflect more on the need for better general infection control measures, rather than focusing on changes in endoscope reprocessing.

In fact, there are numerous studies demonstrating that HCV can be completely removed/eradicated from endoscopes during reprocessing[25-29]. It could be argued that these results are somewhat artificial, and do not represent the state of endoscope reprocessing out in the community, i.e. endoscope reprocessing may have been more rigorous in the setting of the study. However, a landmark study comprising 8260 patients undergoing endoscopy who were tested for HCV seropositivity before and 6 mo after the procedure found no cases of seroconversion[30]. This large study is the best evidence that appropriate endoscope reprocessing as performed in the community effectively prevents the transmission of hepatitis C virus.

Human immunodeficiency virus (HIV): While HIV may arguably be the most concerning pathogen for transmission of infection, it is actually a fragile virus that is highly susceptible to chemical disinfection. Mechanical cleaning alone can often completely remove the virus from contaminated endoscopes, and complete chemical disinfection is easily accomplished with glutaraldehyde[26,31-34]. There are no reported cases of endoscopic transmission of HIV in the world literature.

Hepatitis B virus (HBV): There have been 5 cases of HBV transmission attributed to GI endoscopy[6,35-38]. In the two cases reported by Morris and Birnie, reprocessing practices now known to be insufficient were used (failure to disinfect between patients, and when performed at the end of the day an inadequate disinfectant was used; failure to brush all channels in the second report)[35,37]. The case mentioned in the introduction of the report as the impetus for the study by Seefeld in 1981 gives no details about the reprocessing practices and thus it is difficult to ascertain whether these were adequately performed. Reprocessing practices common at that time (now known to be suboptimal) included failure to disinfect between patients, being performed only at the end of the day, the use of inadequate disinfectants, or inadequate exposure times[39,40]. Fully immersible endoscopes were not introduced until 1983 (leaving a substantial part of the endoscope unexposed to the disinfectant) and the nature of the report suggests that the use of an aldehyde disinfectant was a new practice. In two later cases reported by Davis and Federman[6,38]. the association with endoscopy may be spurious. In each case, no investigation was performed to substantiate the association or evaluate other possible etiologies of transmission; in each case HBV infection was simply attributed to a prior colonoscopy due to the absence of self-reported risk factors. There are a number of prospective studies in which patients were followed for serologic evidence of HBV transmission following endoscopy. In six studies, a total of 223 patients in whom endoscopy was performed with an instrument known to have been used on a patient with HBV were followed for 6 mo; there were no seroconversions[41-46]. Three other studies conducted in patient populations with relatively high rates of HBV infection followed a total of 600 seronegative patients for up to one year after endoscopy and found no episodes of seroconversion attributable to endoscopy[47-49]. What makes these findings even more remarkable is that the reprocessing in all of the studies was, by current standards, suboptimal (endoscope "disinfection" performed with detergents rather than disinfectants, use of low-level disinfectants, or in one study exposure to glutaraldehyde for less than two minutes) implying that current reprocessing standards may provide an additional safety margin.

SARS-associated coronavirus (SARS-CoV): Severe acute respiratory syndrome is a recently identified, potentially fatal atypical pneumonia clinically characterized by fever, cough, myalagias, and shortness of breath. It was first recognized in 2003 in the Guangdong Province of China, but has since affected more than 8000 people in 25 countries across 5 continents. The etiologic agent has been identified as the SARS-associate coronavirus (SARS-CoV), a virus not previously endemic to humans. The mechanism of transmission is predominantly infectious respiratory droplets, although aerosolization and fomites may also be contributory[50]. SARS CoV has been identified in respiratory secretions and feces, and can be found in intestinal epithelial cells of affected individuals, suggesting that GI endoscopes can be exposed to potentially infectious material[51,52]. It is not known whether the virus can be transmitted *via* the oral route. One recent study evaluated a variety of hand and surface disinfectants (low-level disinfectants), as well as a glutaraldehyde-based medical instrument disinfectant. The study found that SARS-CoV was readily inactivated by all the disinfectants[53]. Thus it appears likely that current reprocessing protocols and high-level disinfectants are adequate to prevent transmission of the virus as a result of endoscopy itself; there are no published reports of transmission of SARS *via* contaminated GI endoscopes. However, the endoscopy suite itself may serve as a vector of transmission (including the health care workers in it), and the most important factors in preventing nosocomial transmission are respiratory precautions (face masks) and appropriate hand hygiene[54].

Avian influenza A virus (H5N1): The H5N1 virus is a specific subtype of the avian influenza A virus that has recently received significant media attention. This virus infects the respiratory and gastrointestinal tracts of poultry, is highly contagious, spreads rapidly, and has been identified as the cause of several recent outbreaks of avian influenza in a number of countries. Of greatest concern to public health, this avian influenza virus can mutate quickly and cross the species barrier. Once thought to be exclusive to birds, the H5N1 virus was first reported to infect humans in Hong Kong in 1997[55]. Since then, more cases of human infection with this highly pathogenic strain have been reported in Asia. These cases resulted from direct or close contact with infected poultry, infected respiratory tract secretions and feces, and/or contaminated environmental surfaces. Person-to-person transmission of the H5N1 influenza virus has also been reported but to date this mode of transmission appears to be very limited. The recent surge of the H5N1 (avian influenza) virus has raised questions about whether current endoscope disinfection protocols are sufficient in the healthcare setting to prevent its transmission. Although there are few data specific to GI endoscopy, there are several reasons to suggest that current reprocessing guidelines are sufficient. Because the natural reservoir hosts of the virus are waterfowl, the risk of nosocomial patient-to-patient transmission during any type of surgical/endoscopic procedure is (currently) negligible. Geographically, there have been no reported cases in North America. More importantly, the H5N1 virus is lipid-enveloped, and like other viruses in this class (e.g. other influenza viruses, SARS virus, HIV), they are the easiest to inactivate by physical or chemical decontamination methods compared to all other types of pathogenic microorganisms. An EPA-registered cleaner/disinfectant labeled to achieve low-level (or intermediate-level) disinfection is sufficient to remove and destroy virtually all enveloped viruses including the H5N1 virus. Therefore, current recommended reprocessing practices for GI endoscopes and other types of flexible endoscopes-specifically, cleaning, followed by at least high-level disinfection and drying–provide a sufficient margin of safety to prevent GI endoscopes from transmitting the H5N1 virus from patient-to-patient. Additionally, cleaning followed by either low-level disinfection (which lacks a tuberculocidal claim) or intermediate-level disinfection (which includes a tuberculocidal claim, but not a sporicidal claim) of environmental surfaces (e.g., bedside tables, bed stands, table tops) are similarly sufficient to destroy the H5N1 virus and prevent its nosocomial spread. Review of the cleaner/disinfectant's label is necessary to ensure proper dilution and adequate contact time to effect its outcome. Frequent hand washing is also necessary to prevent transmission of the H5N1 virus.

Bacterial infections

***Salmonella*:** Since 1974, there have been 48 cases of endoscopic transmission of various *Salmonella* species[56-64]. Each of these cases has been associated with at least one breach in currently accepted reprocessing guidelines, usually a failure to mechanically clean the internal instrument channel, although the use of an inappropriate disinfectant, or an inadequate disinfection time were also common. It is interesting to note that there have been no reported cases of salmonella transmission since the publication in 1988 of standardized cleaning and disinfection recommendations from the American Society of Gastroenterology (ASGE), the Society for Gastrointestinal Nurses and Associates (SGNA), and the British Society of Gastroenterology (BSG)[65,66].

***Pseudomonas aeruginosa*:** *Pseudomonas aeruginosa*, a Gram-negative bacillus that is an opportunistic pathogen found widely in the environment, is of particular concern in the endoscopy setting due to its predilection for a moist environment (e.g., endoscope water/irrigation systems, wet internal channels after reprocessing, or even the hospital water supply itself). Unlike *salmonella*, which does not appear to be a persistent infection control problem, *Pseudomonas aeruginosa* continues to pose a challenge to endoscope reprocessing, and is the most commonly reported organism responsible for transmission of infection during endoscopy. There have been 216 reported cases of *Pseudomonas aeruginosa* transmission[67-83]. While early reports of pseudomonas infection resulting from endoscopy were most commonly related to inadequate cleaning or the use of inadequate disinfectants, later reports tend to implicate three major areas: (1) the automated endoscope reprocessor (AER) or the water supply to the endoscope that become colonized with the organism, (2) failure to disinfect the elevator channel of duodenoscopes, and most importantly, (3) failure to completely dry any or all channels of the endoscope with a 70% alcohol solution and forced air.

***H pylori*:** There have been 12 reported cases of *H pylori* infection that have been attributed to endoscopic transmission[84-88]. In each case, suboptimal cleaning and disinfection were implicated (most commonly an inappropriate liquid chemical germicide, or LCG). Several studies have addressed whether current reprocessing protocols are sufficient to eradicate the organism. Three studies reported the presence of the organism after cleaning and disinfection (2 using culture methods and the third using PCR amplification)[89-91]; however in two of the studies an inadequate exposure time to the LCG was used, and in the third the reprocessing protocol was not described at all. In a study using both manual and automated disinfection, well-described conventional reprocessing protocols consistent with currently accepted guidelines resulted in 100% eradication of the organism as determined by PCR analysis[92]. Of interest, there have been numerous studies suggesting a higher incidence of *H pylori* in healthcare workers, and in most studies particularly endoscopy-related staff, than in age-matched controls[93-104]. Four studies, however, found no such association[105-108], although it has been suggested that failure to find an association may be due to inadequate study power or residual confounding from other exposure risks. The possibility of transmission of pathogens from patients to health care workers underscores the need for good general infection control practices, including the use of appropriate personal protective equipment (PPE), such as gloves, gowns, masks and protective eyewear.

Miscellaneous Organisms: One study raised the

possibility of 2 cases of endoscopic transmission of *Tropheryma whipplei*, the organism responsible for Whipple' s disease, although this conclusion is tenuous at best. The sole rationale for this association was that each patient had undergone an endoscopy for upper gastrointestinal tract symptoms approximately 3 years preceding the final diagnosis[109]. Given the rarity and novelty of the disease, it would not be difficult to determine if any other cases had been reported at the institution, and whether or not they had undergone endoscopy prior to either index case, thus providing at least a temporal association. The authors themselves make the point that the organism has a very slow growth rate, and a more plausible explanation is that the initial procedure was performed for symptom investigation in patients that already harbored the organism in an early stage of the disease that was simply undetected. There are also methodologic problems that undermine the conclusions of the article about the *in-vitro* resistance of the organism to high-level disinfection[110]. Two studies have reported transmission of various *Enterobacteriacea* strains during biliary endoscopy (ERCP), including *E coli, Klebsiella, Enterobacter,* and *Serratia marcescens*[82,111]. In both studies, flaws in the cleaning and disinfection process were noted.

Transmissible spongiform encephalopathy (TSE)

Creutzfeldt-Jakob disease (CJD) and variant CJD (vCJD) are degenerative neurological disorders known as transmissible spongiform encephalopathies (TSEs). These disorders are associated with aberrant proteins referred to as prions. The incubation period from acquisition to overt clinical disease is thought to range from months to years (in some cases decades). Prions present a unique challenge to endoscope reprocessing because of their extraordinary resistance to traditional disinfection and sterilization processes. Because endoscopic procedures such as percutaneous endoscopic gastrostomies (PEGs) are commonly performed on patients with dementia that may harbor occult TSEs, concern had been expressed that endoscopy may serve as a vector for transmission of these agents.

Creutzfeldt-Jakob disease (CJD): CJD is the most common form of TSE, and approximately 90% of CJD is sporadic[112,113]. Iatrogenic transmission has been reported after use of contaminated neurosurgical equipment, or after inadvertent inoculation with infectious materials (dura matter grafts, pituitary hormones). From animal studies, transmission is most efficient with intracerebral or intracranial inoculation; peripheral (extracranial inoculation) requires substantially larger doses. Unfortunately, there is general agreement that currently available liquid chemical germicides used for high level disinfection of gastrointestinal endoscopes are unable to eliminate prion infectivity. Although one study claimed to show that peracetic acid could inactivate prion protein[114].the controls (without peracetic acid) also demonstrated the absence of detectable protein after two cycles. Other studies have demonstrated that peracetic acid is unable to reliably inactivate prions[115-118]. While oral transmission has been reported in primates, it requires ingestion of large quantities of highly infectious material[119]. Although prions have recently been found in the spleen, skeletal muscle, and olfactory epithelium of individuals with sporadic CJD[120,121], fortunately, they are not found in bodily secretions or gut mucosa[122,123]. Because gastrointestinal endoscopes do not contact prion-containing tissue or secretions, and even trace contamination would be reduced or eliminated with simple mechanical cleaning, thus rendering any potential inoculum far below the threshold for oral acquisition, infection control experts have stated that currently accepted cleaning and disinfection protocols should be adequate for reprocessing endoscopes[113,124,125]. The adequacy of current guidelines for endoscope reprocessing with regard to CJD are supported by the fact that there have been no reported cases in the world literature of transmission of CJD or other TSEs by endoscopy.

Variant Creutzfeldt-Jakob disease (vCJD): Variant Creutzfeldt-Jakob disease (vCJD) is a more recently described TSE that is believed to be caused by the consumption of contaminated beef products containing the bovine spongiform encephalopathy (BSE) agent[126]. The disease may also require a person to have a susceptible genotype. To date approximately 155 cases of vCJD have been reported in the world. The one reported case in the United States was found in a 22 year-old patient that had contracted the disease in the UK and developed symptoms after moving to the US[127]. Unlike CJD, the prions associated with vCJD can be detected in the lymphoid tissue of affected individuals (although at much lower concentrations than the CNS), notably the tonsil, the appendix, and possibly the ileum and rectum (with obvious relevance to GI endoscopy)[126,128-131]. However, this tissue was approximately 50% less infective than CNS tissue when homogenated and injected intracerebrally in mice[132]. The infectivity of intact tissue that might be encountered at endoscopy and subsequent transmissibility is unknown, but would presumably be much lower. Given the virtual absence of this disease in the US, rigorous adherence to current guidelines for the cleaning and disinfection of endoscopes would seem to be the best protection for the public. There is no evidence that changes to current endoscopic practices or endoscope reprocessing guidelines are warranted, but these should be responsive to new information as it evolves. The fact that the risk of transmission of prions associated with CJD or vCJD is negligible should not be seen as advocating complacency. In the absence of an endoscope-compatible germicide that can completely and reliably inactivate prion infectivity, there is a window of vulnerability (albeit a small one) and further work is needed. Conversely, we should not rush to adopt a new technology without considering the overall risk to the patient. As an example, the adoption of single-use surgical equipment for tonsillectomy in the UK (to prevent the theoretical risk of prion transmission) actually led to a substantial increase in the rate of postoperative hemorrhage, and subsequently the recommendation was abandoned by health authorities in the UK[133-135].

ENDOSCOPE CLEANING AND DISINFECTION

The US Multi-Society guidelines and the WGO-OMGE/OMED guidelines provide comprehensive recommendations for reprocessing gastrointestinal endoscopes[136,137]. Briefly, endoscope-reprocessing is a three-stage process that includes: (1) pre-processing, or cleaning the endoscope and its detachable components using a detergent solution and brushes; (2) processing, or high-level disinfection of the endoscope using an LCG (in the US, cleared by the Food and Drug Administration [FDA]) followed by thorough water rinsing to remove residual LCG from the instrument; and (3) post-processing, which includes proper handling and storage of the endoscope. This third and final step also includes drying the endoscope and its internal channels after terminal water rinsing[138]. Review of these guidelines is beyond the scope of the present article, but the importance of endoscope drying and water quality will be discussed below.

In addition to patient-to-patient transmission of pathogens during endoscopy, environment-to-patient transmission of gram-negative bacteria during GI endoscopy has been reported, primarily during endoscopic retrograde cholangiopancreatography (ERCP)[76,79,81,82]. Due in part to the anatomy, physiology, and sterile nature of the biliary tract, the design of the side-viewing duodenoscope (elevator channel), and the nature and characteristics of the procedure, ERCP is probably more vulnerable to bacterial infection than other GI endoscopic procedures. Several of these reports highlight, first, an association between wet or improperly dried GI endoscopes and true and pseudo-outbreaks of waterborne microorganisms, and, second, the abrupt termination of these outbreaks following the implementation of endoscope drying. Moreover, some of these reports identified the rinse water used during endoscope reprocessing as the source of the microorganisms responsible for these outbreaks[76,79,81,82]. Despite the thoroughness and success of cleaning and high-level disinfection, failure to dry the endoscope can render the reprocessing procedure invalid and clinical use of the endoscope an infection risk. The contribution of post-processing in general and drying in particular to the prevention of disease transmission *via* a GI endoscope cannot be overstated.

Endoscope drying and storage

Although the importance of cleaning and high-level disinfection of GI endoscopes after each procedure is well recognized, the contribution of post-processing-particularly endoscope drying and storage-to the prevention of disease transmission and nosocomial infection is sometimes overlooked. Surveys indicate that not all GI endoscopy units dry the endoscope after water rinsing and prior to reuse or storage[139,140]. Rinse water that is not removed during drying and remains in the endoscope's narrow internal channels between patient procedures or more importantly during storage can provide the ideal environment for waterborne microorganisms to colonize and multiply. Indeed, cases of nosocomial infection due to the transmission of microorganisms that have colonized and proliferated in the moist internal channels of inadequately dried and improperly stored endoscopes to the patients undergoing GI endoscopy have been reported, resulting in patient injury and death[70,71,76,79,82].

Allen[76] reported that bile cultures from ten patients who had undergone ERCP were contaminated with *Pseudomonas aeruginosa*. Inadequate drying after reprocessing of the ERCP endoscope using an AER was identified as the cause of this outbreak. *P. aeruginosa* was found to have survived and proliferated in the moist internal channels of an ERCP endoscope that transmitted this bacterium to patients during ERCP. Contamination ended and this outbreak was terminated only after modifying the facility' s reprocessing procedure to include after cleaning and high-level disinfection a manual drying step achieved by suctioning alcohol through the ERCP endoscope's channels followed by air drying. Classen *et al.* reported the identification of seven cases of *P. aeruginosa* bacteremia within 5 d following ERCP[79]. In addition to each infected patient having undergone the first or only scheduled ERCP of the day, the mean duration between reprocessing the ERCP endoscope and its clinical use was significantly longer for infected patients than for matched controls, suggesting that improper storage of the endoscope played a role in this outbreak. Each patient was found to be infected with the same serotype of *P. aeruginosa* as microbiologically sampled from, among other surfaces, the tap water basin used to rinse the ERCP endoscopes with water after disinfection. This report's authors suggest that inadequate drying of the endoscope's channels prior to storage was, at least in part, responsible for this outbreak. *P. aeruginosa* remaining in the endoscope's moist internal channels after reprocessing and water rinsing likely colonized and multiplied to high numbers during overnight storage, posing an increased risk of nosocomial infection to the first scheduled patient of the day. Among other control measures including more frequent changing of, and addition of chlorine into, the tap water bath, no additional infections were identified once the endoscope's channels were flushed with 70% alcohol followed by forced air.

Provided the endoscope is properly reprocessed and dried prior to storage, reprocessing the endoscope immediately before its first use of the day does not appear to be necessary[141]. There are few data that provide insight into the number of days a specific type of GI endoscope may remain in storage without posing an infection risk and requiring reprocessing before its reuse. Two studies, however, suggest that properly reprocessed and dried endoscopes may remain in storage for five to seven days without requiring reprocessing before reuse[142,143]. The type of endoscope, its frequency of reuse, and the effectiveness of the reprocessing and drying protocols may all be factors that influence and affect the number of days a GI endoscope can remain safely in storage without posing a risk of bacterial colonization and nosocomial infection. Research to determine storage intervals is encouraged.

Water quality

While proper mechanical cleaning (stage 1) and high-level disinfection (stage 2) are crucial to the prevention

of disease transmission during GI endoscopy, the success of an endoscope reprocessing procedure also depends on the adequacy of the drying step and the microbial quality of the water used to remove the residual liquid chemical germicide from the endoscope after disinfection. In general, three types of water are used to rinse endoscopes after chemical immersion: tap water, bacteria-free water, and "sterile" or "sterile filtered" water. Despite their label claim, however, all of these water types, including "sterile" water, have been linked to bacterial contamination and nosocomial infection following endoscopy[76,79,81,82,144-147]. Because the water used to rinse the endoscope after chemical immersion is not generally microbiologically monitored (i.e., periodically cultured), its microbial quality is almost always unknown[148]. The rinse water contacts the endoscope after high-level disinfection (or "liquid sterilization"), whether achieved manually or using an automated endoscope reprocessor (AER), and in many cases just prior to clinical use (if not exposed to a drying cycle). Thus any contamination of the rinse water will inevitably lead to contamination of the endoscope regardless of the potency, strength, or effectiveness of the preceding cleaning process or of the LCG, AER, or automated processing system. Drying the endoscope during post-processing (stage 3) is necessary, no matter the claimed microbial quality of the rinse water, to prevent potential re-contamination of the endoscope with waterborne microorganisms during terminal water rinsing[149].

The importance of microbiological monitoring of the rinse water used during the reprocessing of GI endoscopes is controversial. Whereas some countries encourage this practice[150,151], others (including the United States) do not, having concluded that the relationship between the presence of bacteria in the rinse water and nosocomial infection has not been adequately defined[148]. As discussed previously, contamination of endoscopes with waterborne, gram-negative bacteria has been linked to adverse patient outcomes. Unless the rinse water is monitored to evaluate its microbial quality and content, the potential exists for the rinse water to contain pathogenic microorganisms capable of re-contaminating the endoscope during terminal water rinsing, compromising the effectiveness of the reprocessing procedure, invalidating the disinfection (or "liquid sterilization") claim, and posing a risk of nosocomial infection. Periodic sampling of the rinse water used during endoscope reprocessing also provides independent verification that the bacterial filter, which is used to improve the microbial quality of the rinse water used by virtually all AERs, is working properly and producing "bacteria-free" or "sterile" water as labeled[148]. Bacterial filters have a limited life-span and have been reported to fail, allowing bacteria to pass, resulting in true and pseudo outbreaks[82,151-154]. It is for these and other reasons that some reports recommend microbiological monitoring of the rinse water, to preempt re-contamination of the endoscope[148,150,151]. The importance and necessity of this practice, and the recommendation that the rinse water be bacteria-free or sterile[151,155], is minimized, however, by thoroughly drying the endoscope after completion of every reprocessing cycle (i.e., between-patient procedures and before storage) to prevent the transmission of waterborne microorganisms that may reside in the rinse water[81]. Professional organizations and governmental agencies are encouraged to develop standards that establish permissible levels of waterborne bacteria (and endotoxins) for the rinse water, to ensure its microbial quality does not pose an infection risk during endoscopy.

GENERAL INFECTION CONTROL

When discussing infection control during gastrointestinal endoscopy, attention is almost invariably focused on the adequacy of the endoscope reprocessing for the prevention of patient-to-patient transmission of pathogens. Good general infection control practices are critical for the prevention of infection in any medical setting. There are now numerous examples of pathogen transmission from the improper use/reuse of syringes, multiple-dose drug vials, and IV equipment[21-23,156-159]. As mentioned previously, the widely publicized outbreak of HCV at an endoscopy clinic in New York that was initially attributed to improper endoscope reprocessing was subsequently found to be due to contaminated multiple-dose sedative medication vials[24].

As alluded to earlier in the discussion regarding the higher rate of *H pylori* infection in healthcare workers, patients may serve as a vector for transmission of infection to endoscopy staff. Although rare, there are case reports of transmission of HCV from a blood splash to the conjunctiva of health care workers[160-162]., and one case of bacterial conjunctivitis from a splash during colonoscopy[163]. One study reported that the overall splash rate to the eyes was 4.1%, and was not altered by the use of video endoscopy, highlighting the need for appropriate personal protective equipment[164]. Compliance with published infection control guidelines is necessary to minimize the potential for nosocomial transmission of infection, both to patients and health care workers.

NEW TECHNOLOGIES

Cleaning, disinfection and sterilization processes and technologies are crucial to the prevention of disease transmission and nosocomial infection caused by both patient-borne and environmental microorganisms and other types of contagions. While current reprocessing products are effective and meet the requirements of infection-control and endoscope-reprocessing guidelines, the search for better-performing LCGs that are more effective in less time without damaging gastrointestinal endoscopes continues. The market's demand for new and more innovative products remains strong, primarily because the advantages that current reprocessing products offer are typically offset by disadvantages that limit their applications and usefulness. As an example, although 2% glutaraldehyde is cost-effective, can be used during manual reprocessing or with most automated endoscope reprocessors, and has a long track record of effectiveness and endoscope compatibility, its vapors may be irritating to endoscopy staff and requires a

relatively longer exposure time. Alternatively, ortho-phthalaldehyde (OPA) is tuberculocidal in 5 minutes, does not require activation, and has not been reported to cause endoscope damage. But these favorable characteristics are overshadowed to some extent by OPA's propensity for staining instrument surfaces and skin, significantly higher cost, and contraindication for reprocessing urological equipment, due to the identification of serious allergic reactions in some bladder cancer patients who underwent repeated cystoscopies. Development of an LCG that is compatible with flexible endoscopes and other delicate materials, rapidly tuberculocidal (and sporicidal), cost-effective, environmentally-friendly, not associated with allergic reactions for patients or healthcare workers, does not contain a high concentration of soapy surfactants or require heating to achieve high level disinfection, and can be used during both manual and automated reprocessing has proved challenging. While current products may satisfy several of these criteria, none satisfies all of them.

In the quest to improve the current standard of reprocessing for GI endoscopes and other types of flexible endoscopes, several new products have been developed and recently cleared by the US *Food and Drug Administration* (FDA) for marketing in the U.S. These new products and technologies range from enzymatic detergents that claim to facilitate the removal of different types of organic debris including fats from the surfaces of flexible endoscopes; to glutaraldehyde-based disinfecting solutions that are rapidly tuberculocidal at room temperature; to low-temperature sterilization processes that use a hydrogen peroxide based-plasma labeled to achieve sterilization of bronchoscopes and other instruments with narrow lumens or channels. Sheath-based technologies that cover the flexible endoscope's insertion tube to prevent its contact with the patient and contamination have been applied to GI endoscopes and other types of flexible endoscopes with measured results. Whether any of these reprocessing products or sheathed technologies improves the status quo and provides clear advantages over currently available technology will need to be established. Some of these new reprocessing technologies are discussed, below.

Cidex OPA concentrate (Advanced Sterilization Products, or ASP; FDA clearance No. K032959)

This liquid chemical concentrate was cleared by the FDA in April, 2005, and is manufactured by ASP. It contains 5.75% (w/v) *ortho*-phthaldehyde (OPA) and is a concentrated form of its predecessor, Cidex OPA (0.55% *ortho*-phthaldehyde), which was cleared by the FDA in October, 1999. This concentrate is mixed with tap water to achieve a diluted, single-use solution of 0.05% OPA, which is labeled to achieve high-level disinfection of flexible endoscopes and other types of reusable medical and dental devices in 5 min at an elevated temperature of 50℃. Cidex OPA Concentrate is contraindicated for manual reprocessing and is labeled exclusively for use in the EvoTech Integrated Endoscope Disinfection System, an automated endoscope reprocessor also recently cleared by the FDA and marketed by ASP.

Because this product will be marketed in tandem with the Evotech disinfecting system, the success of Cidex OPA Concentrate will depend on the success of the Evotech, and vice versa. Whether healthcare facilities will replace 2% glutaraldehyde or Cidex OPA-both of which are versatile and can be used manually or with any automated endoscope reprocessor-with Cidex OPA Concentrate and its accompanying reprocessor, is unclear. Because its active ingredient is *ortho*-phthaldehyde, which has not been reported to cause endoscope damage, Cidex OPA Concentrate is likely to be compatible with a wide range of delicate and heat-sensitive instruments and, therefore, is not likely to void the warranty provided with most endoscope models. As with any LCG, adequate room ventilation is required.

Of particular clinical importance, Cidex OPA Concentrate, like Cidex OPA, is likely to be contraindicated for reprocessing cystoscopes and other types of urological instrumentation to be used to treat patients who have a history of bladder cancer, due to reports of an association between these patients experiencing anaphylaxis-like reactions after having undergone repeated cystoscopies and contact with cystoscopes reprocessed using Cidex OPA (*ortho*-phthaldehyde). Whether contraindications for Cidex OPA Concentrate will include cystoscopes and possibly other types of flexible endoscopes is unclear. The labeling of Cidex OPA Concentrate does not include a sporicidal claim.

Aldahol III high level disinfectant (Healthpoint, LTD; FDA clearance No: K041360)

This product was cleared by the FDA in May, 2005, and uses a novel mixture of two well known chemicals to achieve high-level disinfection of flexible endoscopes. Aldahol III (pH 7.6 after activation) contains a mixture of 3.4% glutaraldehyde and 26% isopropanol and, like most 2% glutaraldehyde formulations, can be reused for up to 14 d, depending on several factors including usage and how effectively the instrument is cleaned and dried prior to chemical immersion. This product achieves high-level disinfection in 10 min at 20℃ (room temperature), suggesting that the addition of alcohol (i.e., 26% isopropanol) to a solution of 3.4% glutaraldehyde enhances its tuberculocidal properties, reducing the time and temperature required to achieve high-level disinfection. Aldahol III is sporicidal in 10 h at 20℃, and its concentration of glutaraldehyde is monitored for effectiveness using chemical test strips, to ensure its concentration is above 2.1%, this product's minimum effective concentration.

Aldahol III contains isopropyl alcohol, which is ordinarily flammable and can, under certain conditions, pose a risk of injury to staff and to patients if not adequately removed from the endoscope during thorough water rinsing. Whether the chemistry of this product eliminates this risk is unclear. Prolonged immersion of the endoscope in solutions that contain isopropyl alcohol (as opposed to brief flushing of the endoscope' s internal channels with alcohol to facilitate drying) may damage the endoscope. Most published reprocessing guidelines contraindicate the use of LCG that contain high concentrations of surfactants. Before using this product to reprocess flexible endoscopes in an automated endoscope

reprocessor (AER), contact both respective manufacturers to ensure use of Aldahol III will not void the endoscope' s or AER's warranty. Also, the powdered contents of the activator added to each gallon of this solution may not immediately dissolve into solution as required prior to its use.

Acecide™ high level disinfectant and sterilant (Minntech; FDA clearance No: K041984)

This product, which is similar in chemical composition to some products that are used for dialyzer reprocessing (Actril, Renalin) and endoscope reprocessing (Peract 20), was cleared by the FDA in May, 2005. It contains a mixture of 8.3% hydrogen peroxide and 7.0% peracetic acid. These two chemical agents, referred to as Solution 1 and Solution 2, are packaged separately and for reasons of chemical instability are mixed by medical staff at the time of use. Acecide is labeled to achieve high-level disinfection of flexible endoscopes and other types of reusable medical and dental devices in 5 min at 25℃. Acecide is sporicidal in 5 h at 25℃ and can be reused for a maximum of 5 d, depending on several factors including usage (i.e., the number of endoscopes reprocessed using the solution) and how effectively the instrument is cleaned and dried prior to chemical immersion. This product's concentration of peracetic acid is monitored for effectiveness using chemical test strips, to ensure its concentration is above 1900 parts-per-million, which is Acecide's minimum effective concentration.

Acecide can be reused for a maximum of 5 d. As a result, its cost-per-cycle is likely to be more expensive than other LCGs (such as 2% glutaraldehyde) which may be reused for as many as 14 d. Acecide uses a mixture of hydrogen peroxide and peracetic acid which may be incompatible with delicate materials and result in endoscope damage. Contact the endoscope's manufacturer before using Acecide to ensure its use will not void the endoscope's warranty. Like other recently introduced LCGs that require an elevated immersion temperature to be effective, acecide may be contraindicated for manual reprocessing and require use of an automated endoscope reprocessor (AER)

STERRAD NX system (Advanced Sterilization Products, or ASP; FDA clearance No. K042116)

This sterilizing system was cleared by the FDA in April, 2005, and launched in the U.S. in May, 2005. It uses an electrical field in a low-temperature, negative-pressure chamber to convert a solution of hydrogen peroxide and water to a hydrogen peroxide plasma cloud that contains ultraviolet light and free radicals with sporicidal properties. Known as the Sterrad NX, this device is marketed as a safe and rapid-acting sterilizer designed to replace ethylene oxide (EtO) gas sterilizers, which pose a potential hazard to personnel and the environment and require as long as 24 h, with aeration, to complete a processing cycle. This device is labeled to sterilize a wide range of surgical instruments, including flexible endoscopes, although it is indicated only for those models of flexible endoscopes that feature a single working channel (no air, water, or accessory channels) with an inner diameter of at least 1 mm and a length not longer than 850 mm. Importantly, the Sterrad NX is contraindicated for reprocessing gastrointestinal endoscopes.

In summary, transmission of infection during gastrointestinal endoscopy is an extremely rare event, and in each case has been associated with a breach in currently accepted reprocessing guidelines or faulty equipment. When appropriate reprocessing guidelines are followed, endoscopes pose virtually no risk of transmission of infection. It is also important that general infection control measures, particularly during the administration of intravenous sedative agents, be meticulously adhered to in the endoscopy suite. Although novel pathogens may pose particular challenges to endoscope disinfection, current protocols appear to be sufficient to protect the patient from cross-infection. However, endoscope design improvements and new germicides to facilitate reprocessing and specifically address these challenges should be encouraged.

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