EDITORIAL

Duodenoscope reprocessing: risk and options coming into view

In recent months, medical reports and intense media interest have highlighted the problem of patient-to-patient transmission of carbapenem-resistant Enterobacteriaciae (CRE) and other multidrug-resistant organisms (MDRO) by contaminated duodenoscopes during ERCP. Details of a non-CRE MDRO outbreak were recently published by the staff of the King County Health Department and the Virginia Mason Medical Center (VMMC) in Seattle, Washington.[1] In this issue of *Gastrointestinal Endoscopy*, Ross and colleagues of VMMC outline their institutional response to the outbreak and the results of their practice of universal duodenoscope culture and quarantine over the past year.[2] Their experience provides valuable data regarding the success of duodenoscope reprocessing while also generating further questions about how we should all respond in our local settings.

EVOLVING AWARENESS OF MDRO AND CRE INFECTIONS IN ENDOSCOPY

Before the recent episodes of CRE transmission, virtually all clusters of infection related to endoscopy were attributed to gaps in administering medications or the multiple steps of endoscope reprocessing.[3] Transmission of *Pseudomonas aeruginosa* through ERCP in the 1980s and 1990s was largely eradicated with the adoption of alcohol flushing and complete forced air drying of channel lumens after high-level disinfection (HLD)—practices that are integral to longstanding guidelines for reprocessing.[4,5]

The first known transmission of CRE at ERCP in the United States was attributed to insufficient cleaning practices.[6] At least 8 subsequent reports describe outbreaks of CRE despite apparently appropriate and optimal reprocessing techniques at major academic medical centers[7-10] and suburban hospitals.[11] Although these early reports were widely communicated within the gastroenterology community, they gained little public traction because they were buried in an avalanche of reporting and hysteria about the Ebola epidemic. Similar outbreaks have been reported from Europe.[12,13]

In early 2014, the Centers for Disease Control and Infection Prevention (CDC) initiated discussions with gastroenterology and nursing specialty societies, the U.S. Food and Drug Administration (FDA), other content experts, and their national consulting community of epidemiologists (Hospital Infection Control Professional Advisory Committee, or HICPAC). Concurrently, the FDA undertook discovery and regulatory conversations with industry, leading to several guidance documents[14] in addition to updated reprocessing instructions for use from Olympus America.[15] Most recently, on May 14 to 15, 2015, the FDA convened an advisory panel to review the entire problem of infection transmission from duodenoscopes. The concluding nonbinding opinions of the panel strongly reiterated the importance of ensuring the availability of duodenoscopes for clinical care, whereas the majority thought that current reprocessing practices, even when appropriately performed, appear insufficient for ensuring the safety of existing endoscope designs.

> Of greatest concern is VMMC's ongoing 2% rate of culture positivity for enteric pathogens, despite aggressive oversight and optimal performance of standard reprocessing. This is low enough to suggest weekly or monthly surveillance cultures may not detect serious lapses, yet high enough to confirm ongoing risks for transmission using business-as-usual.

CURRENT UNDERSTANDING AND CHALLENGES

Our current understanding of the reported experience to date and the likely contributing factors is outlined in Table 1. The experience of Ross and colleagues in Seattle, where 2 strains of multidrug-resistant *Escherichia coli* were ultimately found in 32 patients subsequent to endoscopy over 10 months,[1,2] demonstrates the sophistication and diligence required by collaborating teams from multiple departments (Epidemiology, Infectious Diseases, Microbiology, and Gastroenterology) to identify and eliminate the infectious source. This mirrors the experience from other centers,[11] where tracing the source of transmitted MDROs is challenging because of multiple preexisting comorbidities and delayed or unrelated clinical

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TABLE 1. Current understandings

Regarding carbapenem-resistant Enterobacteriaciae and ERCP outbreaks
• 4 sites published in medical literature
• 5 more sites publicly disclosed
• 1 cluster before 2010, most exposures 2012-2014
• ~ 60 clinical infections and 20+ deaths
• >1000 patients notified for screening; estimated >100 silent carriage
• Some transmissions confirmed by endoscope culture, others negative
• Occurrence with all three endoscope manufacturers and multiple designs
• Attributed to persistent contamination at elevator region, cable channels, or both
Regarding carbapenem-resistant Enterobacteriaciae
• Increasingly prevalent in the United States
• Transmitted despite apparent optimal high-level disinfection
• Not inherently more resistant to high-level disinfection agents and process
• Patients with multiple comorbidities or immunosuppression at greatest risk of infection and death
• Silent carriage develops in many patients, with risk of future infection or transmission
• Clinical infections often removed in time (months) and organ location from exposure
• Mortality of clinical infection is significant (up to 50%)

presentations weeks to months later with diverse non-pancreatobiliary infections. Other patients who are identified only by surveillance sampling may be at risk of resulting serious disease for months or years to come.

Ross's group found that 2 of 8 duodenoscopes, including both 160 and 180 series Olympus instruments, harbored the clonal strain of *E. coli* despite repeated optimal manual washing and automated HLD. Similar optimal reprocessing practices have been confirmed by manufacturers, health departments, CDC review, or a combination in all but 1 of the 9 outbreak sites in the United States. Some have raised concerns about the sealed elevator cable design of the Olympus 180 series duodenoscopes.[16] Indeed, this design has been further incriminated as a result of Olympus's interpretation that a formal 510k submission to the FDA was unnecessary, followed by delayed FDA clarification that such clearance is required and expected. The FDA further clarified, however, that they do not consider this the central issue in the recent outbreaks and that 180 series duodenoscopes should not be removed from service on this basis[17] because instruments from all manufacturers and multiple model series have been involved in outbreaks. The 510k submission is now under review. The more common association of infections with the 180 series instrument likely relates primarily to its dominant position in the marketplace. One similar transmission has been attributed to a linear echoendoscope, which also uses an elevator mechanism.[18] Improved designs that facilitate cleaning and reprocessing of the elevator region will certainly be required features of future instruments. Duodenoscopes with removable tips, as are currently available in Europe, should be efficiently validated for function and cleaning efficacy, then submitted for early FDA review and clearance in the United States.

The VMMC group submitted all 8 normally operational duodenoscopes to the manufacturer for evaluation of function and integrity. Three required "critical" repairs (leaks, cracked or chipped lens covers, channel damage), including 1 of 2 with MDRO contamination. When coupled with a recent description of hairline fractures and gross soil in inaccessible areas,[16] this prompts concern about the durability of endoscopes and the efficacy of high-level disinfection after prolonged use. The question of endoscope durability was posed in the 2011 Multisociety Reprocessing guideline, but no other post-market surveillance data are available. Scheduled detailed endoscope "checkups" may be warranted.

Endoscope cultures have identified contaminated instruments in most outbreaks. Presumably, instruments that persistently yield positive cultures harbor biofilms that cannot be eradicated with standard reprocessing. Most outbreak sites, and some other major centers, have opted to use ethylene oxide (ETO) treatment of all duodenoscopes subsequent to HLD after each procedure. In all reported instances, ETO has eradicated persistent culture positivity. This is an inadequate long-term solution, however, because ETO cannot sterilize residual gross soil, some centers and manufacturers have concerns about materials durability, and ETO is costly, inefficient, and associated with potential toxicity to personnel. Indeed, most centers and some cities and states do not have ETO facilities available.

Ross et al describe the VMMC experience with a culture and 48-hour quarantine approach to ensuring clearance of enteric organisms by high-level disinfection. Over a 1-year interval involving 1524 reprocessing cycles, 2% of duodenoscope cultures returned positive for enteric pathogens, prompting repeated washing, HLD, culture, and quarantine before reuse. This regimen, which successfully halted their outbreak of MDRO transmission, required tripling the number of duodenoscopes in their practice and the adoption of rigorous and expensive sampling and culture practices. This approach to ensuring clean instruments for each procedure does not appear financially or technically practical for most settings.

Endoscope sampling and culture techniques are challenging and perhaps not uniformly reassuring, inasmuch as several centers have been unable to confirm endoscope contamination despite convincing epidemiologic evidence for the duodenoscope as a source of transmission. The CDC has publicized their advised method for obtaining endoscope cultures, but they acknowledge that the technique, designed for investigation of outbreaks, is not validated for ensuring sterility.[19] After thorough review, the recent FDA panel concluded that the current form of the