Risk of Flexible Endoscopes, Including Gastroscopes and Echoendoscopes, Transmitting "Superbugs" Infections

An Important Update

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ABSTRACT

"Superbug" infections linked to newer models of duodenoscopes featuring a sealed channel design were first recognized in 2012. This article provides a review of the published medical literature and of the FDA's medical-device database to evaluate the potential for other types of flexible endoscopes to transmit multidrug-resistant bacteria, including carbapenem-resistant *Enterobacteriaceae*, or CRE. Several cases document the contamination of bronchoscopes, cystoscopes, curvilinear-array echoendoscopes, flexible laryngoscopes, gastroscopes and ureteroscopes with concerning bacteria, and in some cases these devices were linked to superbug infections or outbreaks. Public notices focusing on the potential for these other types of flexible endoscopes, too, to transmit superbugs are few, however, suggesting that these devices may pose an under-recognized risk of multidrug-resistant bacterial infections. Recommendations for preventing these devices from infecting patients with potentially untreatable bacteria are provided, including that users consider applying at least one enhanced practice, previously recommended by the FDA to mitigate the risk of duodenoscopes transmitting superbugs, to these other types of flexible endoscopes, as deemed appropriate, feasible and warranted, particularly to curvilinear-array echoendoscopes, which like duodenoscopes feature a forceps elevator mechanism. Efforts to increase public awareness about the potential for these devices to infect patients with superbugs is recommended.

INTRODUCTION and BACKGROUND

Almost six years ago, a hospital in the Netherlands linked an outbreak of VIM-2-producing *Pseudomonas aeruginosa* to gastrointestinal (GI) endoscopy.[1] Twenty-two (22) patients tested positive for this superbug after undergoing endoscopic retrograde cholangiopancreatography, or ERCP, performed in 2012 using a duodenoscope model that features a sealed channel design. The investigation reportedly was the first to link this model to an infection cluster of a carbapenem-resistant superbug.[1] While one of this duodenoscope model's channels, known as the elevator-wire channel, is intended to be closed to prevent contamination, this channel in some older duodenoscope models is open requiring cleaning and disinfection – or, reprocessing – after each procedure. No significant gaps between the hospital's reprocessing practices and the duodenoscope manufacturer's instructions were identified; however, investigators recovered VIM-2-producing *P. aeruginosa* clonally related to the outbreak's strain under the duodenoscope's forceps elevator mechanism.[1] Removal of this duodenoscope model from clinical use terminated this hospital's outbreak.

The next year, a hospital near Chicago (IL) similarly linked ERCP to an outbreak of NDM-1-producing *E. coli*, which is a type of carbapenem-resistant *Enterobacteriaceae,* or CRE.[2-4] Like the outbreak in the Netherlands,[1] bacteria closely related to the outbreak's superbug were recovered from a reprocessed duodenoscope.[2,3] No additional infections of CRE were identified once the hospital began sterilizing duodenoscopes using ethylene oxide (EO) gas.[2] The investigation of this CRE outbreak in 2013 was notable for a number of reasons. First, it

confirmed that carbapenem-resistant superbugs could be transmitted during GI endoscopy, specifically ERCP[1-10]. Second, for the first time in the U.S., an outbreak of CRE had been publicly linked to a duodenoscope model[1] with an elevator-wire channel designed to be sealed or closed.[2,3] Third, the duodenoscope reportedly remained contaminated with CRE despite the hospital apparently having correctly reprocessed the device in accordance with the manufacturer's instructions,[2,6] a finding other studies have similarly reported.[1,6,7] As the FDA has previously warned, duodenoscopes may transmit multidrug-resistant bacteria "despite confirmation that the users were following proper manufacturer cleaning and disinfection or sterilization instructions."[8] Publicizing this risk, the FDA advised in February 2015 that duodenoscopes may impede effective reprocessing.[7] The FDA further advised that meticulous cleaning of duodenoscopes "should reduce the risk of transmitting infection, but may not entirely eliminate it."[7]

DUODENOSCOPES and SUPERBUGS

Duodenoscopes are used during ERCP to examine and diagnose diseases of the liver, bile ducts, and pancreas. An adjustable forceps elevator mechanism is located at the duodenoscope's distal tip. A thin wire enclosed in the duodenoscope's elevator-wire channel connects this cantilevered mechanism, or lever, to a manually-controlled knob on the endoscope's control body. This knob is used to angulate this lever and, in turn, to control and "thread" an accessory, such as a guide wire or catheter, into the pancreatic and biliary ducts during ERCP.[4] Also for background, the antibiotic resistance of many types of superbugs, including both VIM-2-producing *P. aeruginosa* and NDM-1-producing *E. coli* (among other strains), is conferred through genes that encode the organism's production of carbapenemases.[4] These enzymes degrade carbapenems, which are otherwise powerful, "last resort" antibiotics used to treat serious multidrug-resistant gram-negative infections. Other CRE strains that have been recovered from contaminated duodenoscopes linked to infections include carbapenemase-producing *Klebsiella pneumoniae*[5] and AmpC–producing *E. coli*.[9] Infections caused by CRE and related superbugs[2] may be associated with a mortality rate of as high as 50%.[6]

AIMS, OBJECTIVES, METHODOLOGY and SCOPE

The potential for duodenoscopes to transmit CRE and related superbugs during ERCP is now well-documented.[1-10] Whether other types of flexible endoscopes might pose a similar risk of superbug infections is less clearly defined. Therefore, the published medical literature was reviewed, as well as recent regulatory reports submitted to the FDA's medical device (or, "MAUDE") database, to evaluate the potential for bronchoscopes, cystoscopes, echoendoscopes, flexible laryngoscopes, gastroscopes and ureteroscopes, like duodenoscopes,

[1] This duodenoscope was manufactured by a different company than the model linked the previous year to the outbreak in the Netherlands.[1]

[2] This article defines "related superbugs" as gram-negative bacteria that are resistant to carbapenems but are not of the *Enterobacteriaceae* family and therefore are not CRE *per se*. VIM-2-producing *P. aeruginosa* is an example.

to remain contaminated and possibly expose patients to multidrug-resistant bacteria, including CRE and related superbugs. Another objective of this article is to provide guidance to improve safety and enhance the reprocessing of these other types of flexible endoscopes. While other superbugs are discussed, this article focuses primarily on CRE. Moreover, this article's discussion is limited only to flexible (not rigid) endoscopes and to curvilinear-array[3] (not radial) echoendoscopes used during GI endoscopy.

FINDINGS and RESULTS

This review found that bronchoscopes, cystoscopes, (curvilinear-array) echoendoscopes, flexible laryngoscopes, gastroscopes and ureteroscopes, like duodenoscopes, may become contaminated and expose patients to multidrug-resistant bacteria including CRE and related superbugs. In some cases, transmission of superbugs reportedly occurred even when the device was correctly reprocessed (in accordance with the manufacturer's instructions), as has been similarly reported with duodenoscopes.[2,6,7,8] Publications focusing on the potential for these other types of flexible endoscopes to infect patients with potentially untreatable bacteria – and how to mitigate this risk – are few, however. The paucity of such publications suggests that the risk of these devices transmitting CRE and related superbugs appears to be under-recognized and warrants greater awareness. A number of risk factors for disease transmission associated with these other types of flexible endoscopes were identified and include the device's design and wear and/or damage to the device's internal channels.[11]

This article also provides guidance to reduce the potential for these other types of flexible endoscopes to infect patients with superbugs. Some of this advice is based on, or "borrowed from," recommendations published by the FDA: In August 2015 the FDA issued a safety communication suggesting that hospitals (performing ERCP), in addition to meticulously following manufacturer reprocessing instructions, consider adopting one or more of four "supplemental measures" to mitigate the risk of duodenoscopes transmitting multidrug-resistant bacteria.[10] Broadening the scope of this safety communication, this article herein suggests that users consider, too, applying at least one of these measures, when deemed appropriate, feasible and warranted, to these other types of flexible endoscopes, particularly to echoendoscopes featuring a forceps elevator mechanism. The moving parts of this mechanism featured in the designs of duodenoscopes contain microscopic crevices that, according to the FDA, may remain contaminated with superbugs if not thoroughly cleaned and disinfected.[10]

DISCUSSION

This article focuses on the potential for bronchoscopes, cystoscopes, curvilinear-array echoendoscopes, flexible laryngoscopes, gastroscopes and ureteroscopes to transmit

[3] Echoendoscopes use either a radial array or curvilinear-array design to provide ultrasound images of the GI tract and its wall layers during endoscope ultrasound, or EUS.

multidrug-resistant bacteria, including CRE. These devices are used to perform many different types of procedures in several different healthcare settings. Briefly, bronchoscopes are routinely used to examine (and monitor), diagnose and treat diseases of the airways and lungs. Curvilinear-array echoendoscopes are used to perform endoscopic ultrasound, or "EUS," in both the upper and lower GI tracts. Cystoscopes and ureteroscopes are primarily used to examine, diagnose and treat diseases of the lower and upper urinary tract, respectively. Flexible laryngoscopes are used to examine, diagnose and treat diseases of the larynx, nasal lumens and cavity, nasal pharynx and the upper airway anatomy; these devices may also be used for airway management and during endotracheal intubation. The author of this article herein previously evaluated the risk of infections associated with flexible laryngoscopes, and provided a formal set of step-by-step instructions for reprocessing these devices.[12]

Four supplemental measures

The FDA's safety communication published in August 2015 suggests that users might consider performing at least one of the following four supplemental measures to further mitigate the risk of duodenoscopes transmitting multidrug-resistant bacteria: (1) the microbiological culturing and sampling of the reprocessed duodenoscope; (2) the use of EO gas to sterilize the duodenoscope; (3) the use a liquid chemical sterilant processing system; and/or (4) cleaning and high-level disinfecting the duodenoscope *twice*.[10] The FDA clarified in this communication that these four measures are adjunctive processes to be performed in addition to (not to replace) the duodenoscope manufacturer's reprocessing instructions.[10] The FDA's communication further notes that, if not thoroughly reprocessed, the duodenoscope's elevator mechanism may remain contaminated with residual bacteria.[10] This communication did not clarify whether any of these four measures could, or possibly should, be applied to other types of flexible endoscopes to reduce the risk of infection. In response, this article herein suggests that users consider adopting and applying one or more of these four adjunctive measures (which would be performed *in addition to* the device manufacturer's reprocessing instructions) – as deemed appropriate, feasible and warranted – to enhance safety and reduce the potential for bronchoscopes, cystoscopes, flexible laryngoscopes, gastroscopes, ureteroscopes and particularly (curvilinear) echoendoscopes to transmit superbugs.[13-15]

Bronchoscopes

Zweigner et al. (2014) reported that three patients were infected (or colonized) with CRE following bronchoscopy performed at a German hospital in 2013.[11] A bronchoscope was found to be contaminated with bacteria closely related to the outbreak's superbug. As others have similarly reported about CRE outbreaks linked to duodenoscopes,[1-3,6,7,10] Zweigner et al. (2014) reported that the implicated bronchoscope was properly reprocessed in accordance with the manufacturer's instructions and published guidelines.[11] No additional infections of the outbreak's CRE were identified once the implicated bronchoscope was repaired by its manufacturer, who identified "defects" in the device's internal channel during this servicing.

These authors emphasize the importance of thorough reprocessing and proper maintenance of the bronchoscope to prevent disease transmissions. This report may document the first outbreak of CRE (in Europe) linked to a contaminated bronchoscope.

Further, this review identified a regulatory report, submitted to the FDA in December 2014 by a bronchoscope manufacturer, discussing an apparent outbreak of CRE. According to this report,[4] fourteen (14) patients had tested positive for CRE following bronchoscopy. This regulatory report also states that an implicated bronchoscope, which had been repaired using "third-party vendor" components, repeatedly tested positive for bacterial cultures after reprocessing. The manufacturer stated in this report that "the device is not validated when it is serviced/repaired by a third-party vendor," and that the use of third-party components to service or repair a damaged bronchoscope "may compromise the device and could result in harboring bacteria if the inside of the device becomes damaged." The bronchoscope's biopsy channel was "boroscoped"[5] (*sic*) and reported to be scraped in several areas, and the channel wall possibly to be contaminated with debris. This regulatory report may be the first to document an outbreak of CRE in the U.S. linked to a bronchoscope. (Other reports have previously linked contaminated bronchoscopes in the U.S. to infections of multidrug-resistant bacteria, such as imipenem-resistant *P. aeruginosa*, but not to CRE.[16])

Nine months after this regulatory report was submitted (and six weeks after the agency issued its safety communication discussing the four supplemental measures intended to further mitigate the risk of duodenoscopes infecting patients with superbugs), the FDA published a safety alert on September 17, 2015, that focused on the risk of bronchoscopes transmitting infections.[17] Comparing risks, this federal alert reported that "the risk of infection transmission presented by reprocessed bronchoscopes appears to be lower than the risk of infection transmission presented by reprocessed duodenoscopes," while aptly acknowledging that inadequately reprocessed bronchoscopes can transmit infections. This federal alert did not directly warn hospitals that bronchoscopy might now be an emerging risk factor for CRE and other superbug transmissions. Nevertheless, this alert provided three important recommendations (among others) to prevent bronchoscopes from transmitting diseases: (1) reprocess the bronchoscope in strict accordance with the manufacturer's instructions; (2) do not use a bronchoscope that fails a leak test, or that is visibly worn or damaged; and (3) follow the manufacturer's recommendations for preventive maintenance and repair of the bronchoscope.(17)

Cystoscopes and ureteroscopes

Koo et al. (2012) discussed an outbreak of NDM-1-producing *K. pneumoniae* in the urology department of a hospital in the United Kingdom, in 2010.[18] Twelve patients were infected (or

[4] FDA. MAUDE database report number: 2951238-2014-00662.

[5] "Boroscoped" in this context is defined as visually inspecting the internal channel using a smaller, narrower flexible probe.

colonized) with this CRE strain, and three were diagnosed with urosepsis requiring intravenous antibiotic treatment. The infections were linked to a contaminated video camera head. This may be the first report of CRE infections in the United Kingdom linked to contaminated urological instrumentation. These authors report that endoscopic urology "confers the potential for direct exposure and transmission" of NDM-1-producing superbugs.[18] Similarly, Chang et al. (2013) reported that the urine cultures of 15 patients tested positive for ertapenem-resistant *Enterobacter cloacae* following ureteroscopy performed in 2010 at a regional teaching hospital in Asia.[19] An investigation traced the bacteria to a ureteroscope, which was cultured and found to be contaminated with a closely related strain of the bacteria. Cultures of this instrument remained positive for the bacteria until, as has been reported with duodenoscopes,[2] it was sterilized using EO gas (in addition to disinfection).[19]

Further, this review did not identify any safety alerts that specifically discussed the risk of contaminated urological equipment transmitting CRE and related superbugs. The FDA's MAUDE database, however, includes reports of infections, clusters and outbreaks of *E. coli* and other potentially concerning bacteria following cystoscopy, suggesting that endoscopic urology could be more of a risk factor for CRE transmissions than currently recognized. One recently filed regulatory report describes as many as 17 infections (prostatitis) among patients who underwent cystoscopy in 2017.[6] Surveillance culturing of the cystoscope (more specifically, a cysto-nephro videoscope) yielded negative results; however, the medical facility reportedly considered the possibility that the endoscope may have remained contaminated with bacteria because of the significant number of patients diagnosed with prostatitis following the procedure. This regulatory report does not clarify the type of bacteria responsible for the infections or its antibiotic resistance profile. (If resistant to carbapenems, the bacteria could be CRE.) The report concludes that some identified reprocessing lapses could have contributed to the infections. The risk of bacterial infections linked to cystoscopy, including those caused by multidrug-resistant *P. aeruginosa*, is well-documented.[20,21]

Curvilinear-array echoendoscopes

Chapman et al. (2017) microbiologically sampled more than a dozen curvilinear echoendoscopes used by a hospital during a 12-month period beginning in early 2015.[13] During this prospective study, several cultures positive for certain "high-concern organisms," including *K. pneumoniae, E. coli,* and *P. aeruginosa,* were recovered from these tested endoscopes following standard reprocessing. No cases of patient-to-patient transmission were documented during their study, however. Notwithstanding federal alerts addressing the risk of duodenoscopes transmitting CRE infections, (curvilinear-array) echoendoscopes have "analogous complex designs" (e.g., a forceps elevator mechanism) and are also reportedly prone to "residual (bacterial) contamination."[14] The findings of Chapman et al. (2017) and others suggest, therefore, that the same mitigations published to enhance the reprocessing of

[6] FDA. MAUDE database. Report number: 8010047-2017-00866.

duodenoscopes and reduce their risk of transmitting superbugs be similarly considered for improving the safety of (curvilinear-array) echoendoscopes.[13,14]

Further, this review did not identify any safety alerts that specifically discussed the risk of contaminated curvilinear-array echoendoscopes transmitting CRE and related superbugs. Nevertheless, this review identified several regulatory reports describing contamination of these endoscopes with potentially concerning bacteria, which is consistent with Chapman et al.'s (2017) findings.[13] For instance, in June 2016, a regulatory report documents an ultrasound gastroscope (i.e., an echoendoscope) that remained contaminated with *K. pneumoniae* following repeated reprocessing. [7] The device's manufacturer concluded that improper maintenance of the device could have been a contributor to the contamination and failed reprocessing. This report does not disclose whether the echoendoscope exposed or infected any patients with the *K. pneumoniae* bacteria, or whether the bacteria were CRE.

Another regulatory report filed more recently, in May (2017), describes the forceps elevator mechanism of an ultrasound gastroscope remaining contaminated with *E. coli* following reprocessing.[8] This report does not disclose whether the bacteria were CRE, although it states that no patient infections were identified. However, the endoscope was found to be leaking and its biopsy channel torn. According to the report, improper maintenance of the endoscope may have contributed to the device testing positive for the bacteria. The report underscores the importance of "leak testing" the endoscope before manual cleaning, and not using the device if it fails the test. These cases suggest that echoendoscopes remaining contaminated with residual bacteria (that could be CRE) may pose an under-reported, emergent infection risk.[13,14]

Flexible laryngoscopes

Few published reports link contaminated flexible laryngoscopes to disease transmission.[12] Moreover, this review did not identify any safety alerts or federal notices that discuss the risk of contaminated flexible laryngoscopes transmitting CRE and related superbugs. However, this review did identify a regulatory report filed in August 2017 documenting a likely case of a flexible intubation endoscope, which is a type of flexible laryngoscope, transmitting *K. pneumoniae* from one patient to another.[9] According to this report, the endoscope remained contaminated despite reprocessing. The report does not clarify whether the bacteria were CRE or a related superbug. If the *Kl. pneumoniae* strain is resistant to carbapenems, this report might document the first case of possible patient-to-patient transmission of CRE during flexible laryngoscopy.

[7] FDA. MAUDE database. Report number: 2951238-2016-00498.

[8] FDA. MAUDE database. Report number: 2951238-2017-00299.

[9] FDA. Maude database. Report number: 9610877-2017-00406.

Gastroscopes

England et al. (2016) reported identifying five hospitalized patients in July 2015 who were (or had been) infected with CRE.[22] An investigation determined that recently undergoing an endoscopic procedure was a risk factor for the infection. A duodenoscope, three bronchoscopes and three gastroscopes were microbiologically sampled to determine the superbug's source. One of these tested gastroscopes – which had been used previously during the same month to perform esophagogastroduodenoscopy (or, EGD) on a patient known to be infected, not with CRE, but with unrelated multidrug-resistant *Kl. pneumoniae* – was found to be contaminated with a closely related *Kl. pneumoniae* strain, even though the gastroscope had been disinfected twelve (12) times since its use on this infected patient and prior to sampling. Identifying no reprocessing lapses, England et al. (2016) reported that contamination of this gastroscope had persisted despite the hospital having correctly reprocessed the device in accordance with the manufacturer's instructions,[22] as others have similarly reported with duodenoscopes and with the other types of flexible endoscopes that are the focus of this review article.[1-3,6-8,10,11,13]

England et al. (2016) reported that their finding "demonstrates a need for more effective methods of cleaning and disinfection and an improvement in the (gastroscope) design that allows for better disinfection."[22] This conclusion suggests that gastroscopes, even though they are less complex and easier to reprocess than duodenoscopes, might pose a greater risk of both remaining contaminated after reprocessing and transmitting multidrug-resistant bacteria, including CRE, than currently recognized. According to these authors, this case is likely the first report of cross contamination of multidrug-resistant bacteria from a patient to a gastroscope, with "subsequent persistent contamination despite reprocessing using the manufacturer's instructions."[22] Three years earlier, Bajolet et al. (2013) reported an outbreak of multidrug-resistant *P. aeruginosa* in France that was linked to a contaminated gastroscope.[23] These authors concluded that certain identified endoscope reprocessing lapses and a minor defect in the gastroscope "may have contributed to the development and persistence of bacterial biofilm in this case." Whether the gastroscope's defect may have been primarily responsible for the persistent contamination and disease transmission, not ineffective reprocessing, is not clarified.

Additionally, Parr et al. (2016) reported a cluster of six patients in a hospital's surgical intensive care unit who tested positive for CRE in January 2016.[24] A preliminary review found that each of these patients was exposed to the same gastroscope. As part of its investigation to identify the source of this cluster's bacteria, the hospital microbiologically sampled the gastroscope, as well as examining the gastroscope's working channel using a borescope. No breaches in the gastroscope's reprocessing procedure were identified, and although no bacteria were recovered from the gastroscope, the borescope revealed several deep scratches and debris in the working channel. No additional CRE cases were identified after this damaged channel was replaced and the gastroscope returned to service. Parr et al. (2016) suspected that the gastroscope transmitted the cluster's CRE, noting that "non-recovery of organisms from a

suspected scope should not preclude a scope from suspicion." Similar to England et al.'s (2016) findings,[22] Parr et al. (2016) concluded that gastroscopes and other types of flexible endoscopes less complex in design than duodenoscopes may, too, "fail high level disinfection and cause infections."[24]

Further, this review did not identify any safety alerts that specifically discussed the risk of contaminated gastroscopes transmitting CRE and related superbugs. Nevertheless, this review identified several regulatory reports describing gastroscopes that tested positive for bacteria, including superbugs. One regulatory report filed in March 2016 describes four gastroscopes that tested positive for CRE.[10] The report states, however, that it appears these gastroscopes were not linked to any patient infections. The report provides few additional details, save to conclude that the hospital was using an inadequate concentration of the detergent solution to clean the gastroscope, and that this factor (combined with other observed deviations) "cannot be ruled out" as contributing to inadequate reprocessing of the gastroscopes. Another regulatory report filed more recently in December 2017 describes a gastroscope's suction channel that was microbiologically tested and found to be positive for *Kl. pneumoniae* (although the report does not disclose whether the strain was found to be CRE).[11] According to this report, no patient infections were identified, and the medical facility reprocessed the gastroscope using an automated endoscope reprocessor, or AER, in accordance with its instructions.

RECOMMENDATIONS

This review found that, not only duodenoscopes, but also bronchoscopes, cystoscopes, echoendoscopes, flexible laryngoscopes, gastroscopes and ureteroscopes can pose a risk of superbug transmissions. Factors that increase the risk of these devices infecting patients include, in addition to inadequate reprocessing, the flexible endoscope's complex physical design, poor maintenance or improper servicing. Based on this review's findings, recommendations are provided, below, to help users improve quality and safety, and mitigate the risk of one of these other types of flexible endoscopes remaining contaminated and transmitting multidrug-resistant bacteria, particularly CRE or a related superbug. These recommendations are not intended to be all-inclusive, however, and should be supplemented with the advice of other published reports, studies, guidelines, and federal alerts, including guidance provided in another review that this article's author published in 2014 focusing primarily on the prevention of superbug transmissions during ERCP.[4]

1. **"Supplemental measures":** When deemed appropriate, feasible and warranted, consider enhancing the safety and reprocessing of bronchoscopes, cystoscopes, flexible laryngoscopes, gastroscopes, ureteroscopes and particularly echoendoscopes featuring

[10] FDA. MAUDE database report number: 2431293-2016-00013.
[11] FDA. MAUDE database report number: 8010047-2017-02079.

a forceps elevator mechanism by adopting and applying to these devices at least one of the four supplemental measures the FDA provided (in August 2015) to mitigate (but not necessarily eliminate) the risk of duodenoscopes transmitting multidrug-resistant bacteria during ERCP.[2,10,13,14]

a. These four supplemental measures, if adopted, are adjunctive processes intended to be performed in addition to – not to replace – reprocessing of the flexible endoscope according to its manufacturer's instructions (and published guidelines).

    i. These additional steps include the microbiological sampling and culturing (and quarantining) of the endoscope to evaluate its bacterial contamination after reprocessing and prior to reuse.[10,25]

        1. The FDA, Centers for Disease Control and Prevention (CDC) and the American Society for Microbiology (ASM) recently developed new protocols for duodenoscope surveillance sampling and culturing.[25]

        2. Remove the endoscope from use and contact its manufacturer if it is sampled and found to remain persistently contaminated with bacteria (despite reprocessing).

    ii. Another of these steps is the use of EO gas sterilization to eradicate persistent bacterial contamination of the endoscope.[2,10,13,15,19]

    iii. Cleaning and high-level disinfection of the duodenoscope twice before reuse, a third measure suggested by the FDA[10], may be the "most immediately feasible option available to the majority of endoscopy practices."[14]

b. Application of one or more of the FDA's four supplemental measures to these other types of flexible endoscopes will likely be influenced by a number of factors, including individual practices and a medical facility's equipment, resources, and capabilities.[14]

    i. More research is necessary to evaluate and compare the appropriateness and effectiveness of using these four supplemental measures to enhance the reprocessing of these other types of flexible endoscope.

2. **Endoscope cleaning:** Both clean and disinfect (or sterilize) the flexible endoscope in accordance with the its manufacturer's reprocessing instructions and with published guidelines.[26]

    a. Use detergents, disinfectants and other reprocessing products, equipment and accessories according to their respective labeling.

i. Manually clean the endoscope at "bedside" and in the reprocessing area using a properly formulated detergent validated for effectiveness and verified to be both compatible with the flexible endoscope and consistent with the endoscope manufacturer's reprocessing instructions.[26]

1. Enzymatic detergents are commonly used and have been recommended to clean flexible endoscopes.[27-31]

a. Enzymatic detergents contain enzymes capable of digesting organic material such as blood and mucous.[26,31]

b. Use each automated endoscope reprocessor, or AER, according to its instructions and labeling.

i. However, consider manually cleaning the flexible endoscope meticulously (according to the endoscope's reprocessing instructions), even if the AER has an automated wash cycle.[32]

1. This manual step is emphasized when cleaning the echoendoscope's (and duodenoscope's) forceps elevator mechanism.

3. **Leak testing:** Leak test the flexible endoscope prior to manual cleaning according to its manufacturer's instructions.[26]

a. Do not use a flexible endoscope that fails the leak test.[9,17] Contact the endoscope's manufacturer for further instructions.

b. As this review article highlights, testing the endoscope for leaks is an important measure to prevent the transmission of multidrug-resistant bacteria.

4. **Visual inspections:** Inspect the flexible endoscope prior to use to identify visible signs of damage.[17]

a. Do not use the endoscope if it is visibly worn or damaged, or if its safety is otherwise in doubt.[17] Contact the endoscope's manufacturer for further instructions

b. Consider visually examining the flexible endoscope's working channel, as deemed warranted and when feasible, using a borescope to optically evaluate whether the channel might be soiled or damaged.[24]

5. **Service, maintenance, repair:** Routinely service and maintain the flexible endoscope, and ensure it is repaired as required, in accordance with the manufacturer's instructions.[17]

a. As this review article highlights, proper maintenance and repair of the endoscope are important to facilitate effective reprocessing, and to prevent the transmission of multidrug-resistant bacteria.

    i. Perform scheduled "checkups" of the endoscope as recommended by the manufacturer.[15]

b. Abnormalities in the endoscope's working channel, or defects due to wear, can increase the risk of superbug infections despite users otherwise adhering to the manufacturer's reprocessing instructions.

b. According to some device manufacturers,[12] the flexible endoscope may not be validated for safety and performance if it is serviced or repaired by a third-party vendor (instead of the original equipment manufacturer). Contact the endoscope's manufacturer for additional information.

    i. Whether independent servicing companies can become authorized (e.g., by the original equipment manufacturer) to safely and effectively repair an endoscope using third-party components is unclear and warrants further investigation.

6. **Improved designs:** Improvements in the designs of flexible endoscopes and accessories, as well as more effective reprocessing methods and technologies, are recommended to mitigate the risk of superbug transmissions.[10,14,22]

    a. Reports indicate that flexible endoscopes less complex in physical design, and easier to reprocess, than duodenoscopes can transmit multidrug-resistant bacteria, including CRE.[11,17-24]

        i. It appears that these less-complex devices may pose more of a risk of superbug transmissions than currently recognized.

        ii. Some data suggest, too, that these other types of flexible endoscopes, like duodenoscopes, can be prone to remaining contaminated with superbugs despite being reprocessed according to the manufacturer's instructions.[11,13,22,24]

    b. Designing these other endoscope types with removable or single-use (disposable) components may reduce the risk of superbug infections.

        i. Some endoscope models may be used with disposable valves, instead of reusable air/water, suction and/or biopsy valves that require reprocessing.[33]

7. **Quality control, ATP test kits:** Implement an active and comprehensive quality assurance and surveillance program in these other flexible endoscopic settings to

[12] FDA. MAUDE database. Regulatory report no.: 2951238-2014-00662.

reduce the risk of contaminated flexible endoscopes infecting patients with multidrug-resistant bacteria.[21]

a. As provided in a recommendation above, consider microbiologically sampling the reprocessed endoscope to evaluate its safety and level of bacterial contamination after reprocessing and prior to reuse.[10]

b. Additionally, consider using a test to monitor the quality of cleaning.

    i. One such test uses adenosine triphosphate (ATP) as a marker to detect the presence of soils, such as residuals from patient secretions, on the surfaces of flexible endoscopes.[25,34]

        1. Residual ATP detected on a "cleaned" reusable medical device may indicate an ineffective cleaning process warranting prompt correction and improvements.[25]

c. As part of a complete safety and quality assurance program, detection and termination of a bacterial outbreak in these other flexible endoscopic settings will likely require collaboration between the departments of epidemiology, infectious diseases and microbiology.[15]

8. **Public awareness:** Efforts to increase public awareness about the potential for bronchoscopes, cystoscopes, flexible laryngoscopes, gastroscopes, ureteroscopes and echoendoscopes to expose patients to superbugs is recommended.

CONCLUSION

Not only duodenoscopes, but also bronchoscopes, cystoscopes, echoendoscopes, flexible laryngoscopes, gastroscopes and ureteroscopes can pose a risk of remaining contaminated after reprocessing and transmitting multidrug-resistant bacteria. Several factors including ineffective reprocessing may contribute to this risk, which appears to be under-recognized. Efforts to increase public awareness about the potential for these other types of flexible endoscopes to infect patients with CRE and related superbugs are justified. Recommendations for preventing these devices from transmitting multidrug-resistant bacteria – especially curvilinear echoendoscopes, which are complex in design and feature a forceps elevator mechanism – are provided and include consideration of applying to these other flexible endoscope types, when appropriate, feasible and warranted, one or more of the supplemental measures that the FDA previously published to mitigate the risk of duodenoscopes transmitting superbugs. The introduction of safe endoscope designs that facilitate more thorough cleaning and feature detachable or disposable components is encouraged. Users may consider periodic surveillance sampling and testing of these other flexible endoscope types to detect contamination. The development of new products and technologies validated for the enhanced reprocessing of flexible endoscopes is also recommended.

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