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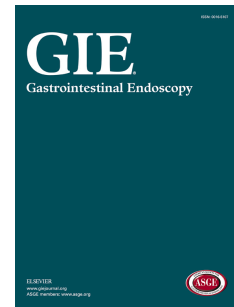
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**A randomized trial of single versus double high-level disinfection
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Abstract

Background and Aims: In a pilot study (8) we demonstrated that current guidelines for duodenoscope and linear echoendoscope (DLE) reprocessing using a single cycle of high-level disinfection (HLD) in an automated reprocessor may be inadequate. In August 2015, the FDA offered double-HLD as a possible response to address this concern. As a result, Providence Health & Services adopted double-HLD as standard procedure for DLE, but no rigorous clinical studies supported this practice. We undertook a quality improvement (QI) study to compare single-HLD versus double-HLD at 4 of our 34 hospitals.

Methods: HLD of DLE was randomized, separately in each facility, to either single-HLD or double-HLD on weekdays, with standard double-HLD on weekends or holidays. There was 99.7% compliance with the randomization scheme. Daily qualitative surveillance cultures of dried, post-HLD DLE were collected for 6 months (1 swab sample from elevator mechanism and 1 combined brush sample from suction and working channels for each encounter), and each sample was incubated for 48 hours. Positivity rates of any microbial growth and growth of high-concern pathogens (potentially pathogenic enteric flora) were compared between the two study arms.

Results: Altogether, 5850 surveillance culture specimens were obtained during 2925 encounters from the 45 DLEs in clinical use in the participating hospitals. Of these, 3052 (52.2%) were from endoscopes cleaned by double HLD. Double-HLD demonstrated no benefit over single-HLD as similar positivity rates were observed (all p -values > 0.05). The elevator mechanism was more frequently colonized than the biopsy channel (5.2% vs 2.9%, $p < 0.001$). Among the 224 encounters with positive growth, 140 (62.5%) recovered microbes from only the elevator mechanism specimens, 73 (32.6%) recovered microbes from only the channel specimens, and 11 (4.9%) recovered microbes from both types of specimens. Double-HLD failed to improve

contamination rates for either sample site at any of the 4 endoscopy facilities, although there were significant overall differences in contamination rates among the facilities ($p < 0.001$), as observed in our previous study. Only 8 high-concern pathogens were recovered from 5 DLE scopes, all from the elevator mechanism. Persistent growth was observed on two duodenoscopes. One grew *Enterococcus spp* (not vancomycin-resistant enterococci) on 3 occasions, *Escherichia coli* was present on 2 of these occasions, one of which was a multi-drug resistant organism (MDRO). The other grew different enteric flora on 2 specimens.

Conclusions: Our prospectively randomized study, involving 4 separate endoscopy facilities and standard automated endoscope reprocessing, showed that double-HLD did not reduce culture positivity rates compared with single-HLD in facilities with an already low positive culture rate. Alternative risk mitigation strategies will be assessed in an ongoing effort to reduce endoscope contamination.

Introduction

Duodenoscopes and linear echoendoscopes (DLE) are involved in more than 650,000 endoscopic retrograde cholangiopancreatography (ERCP) procedures annually in the United States, potentially exposing at least 4500 patients to infection each year, assuming a 0.7% defect rate (1). These endoscopes have been linked to several recent outbreaks of serious iatrogenic infections (2-4). Epidemiological investigation attributed most of the recently published ERCP-associated outbreaks to the complex design of DLE rather than reprocessing deficiencies or device defects (5-7). In a pilot study (8), we demonstrated that current guidelines for DLE reprocessing using a single cycle of high-level disinfection (single-HLD) in an automated reprocessor may be inadequate to prevent DLE contamination. Our study showed a residual 0.6-

0.9% enteric microbial recovery rate, similar to the 2% culture positivity in another recent study (9).

No single solution has been identified to rectify this problem. Current DLE materials may be damaged by heat-based and some chemical-based sterilization methods. Gas sterilization, using ethylene oxide, is time-consuming, not widely available, and requires substantial capital investment. Moreover, like high-level disinfection, sterilization may be ineffective if mechanical debridement of organic material and biofilm on the instrument is incomplete (10).

In August 2015, the Food and Drug Administration (FDA) suggested use of a double cycle of high-level disinfection (double-HLD) as a possible recourse to address this concern (11), seconded in subsequent editorials (12, 13). As a result, Providence Health and Services (PHS) adopted double-HLD as standard procedure for DLE processing, although no rigorous clinical data supported this practice. We, therefore, undertook a prospective quality improvement (QI) initiative study beginning in February 2016, with input from the Centers for Disease Control (CDC) and United States Food and Drug Administration (FDA), in order to compare the effectiveness of single-HLD versus double-HLD in eliminating residual enteric pathogen growth on DLE at 4 of our endoscopy facilities.

METHODS

Setting

This assessment was conducted within 4 facilities with endoscopy labs, conducting a range of less than one procedure per day to more than 40 procedures per week. Forty-five linear EUS and ERCP endoscopes were in service during the study period, all manufactured by Olympus except 3 Pentax ERCP scopes (used in 1 facility). Because no human subjects were involved in this quality improvement project, no IRB approval was required by PHS.

All facilities used minimum specifications consistent with American Society for Gastrointestinal Endoscopy (ASGE) guidelines (14) and manufacturers' reprocessing recommendations for leak testing, cleaning, disinfection, drying, and storage. At the end of an endoscopic procedure, each facility conducted a bedside clean with an enzymatic cleaner while still inside the endoscopy suite, followed by a thorough manual clean in a designated decontamination area, before placing each DLE in an AER (automated endoscope reprocessor) for HLD. The manual cleaning consisted of wiping all external surfaces, brushing all internal channels and components, and flushing all internal channels.

Three of 4 facilities used an automatic endoscope flushing device. For the HLD step, each facility used a randomly generated list that assigned single HLD or double HLD on a daily basis for regular work days (on weekends or holidays, endoscopes were cleaned using double HLD). Endoscopes randomly assigned to double HLD (see randomization below) were left inside the AER for a second HLD cycle before being removed and stored for drying. Endoscopes were dried per manufacturer instructions for use (IFU) and stored in a hanging position in closed cabinets overnight in accordance with the 2016 Multisociety Guidelines (14). None of the sites used storage cabinets with continuous aeration with filtered medical air, but all cabinets exhibited positive air pressure with regard to the external environment. Three different AERs brands were used at the 4 study sites (Medivators, Custom Ultrasonics, and Steris Reliance). All necessary quality control parameters were reviewed before each cycle.

Sampling

Collection:

Between February 8 and August 19, 2016, daily cultures (Monday through Friday) from each DLE were collected at each facility. Culturing occurred each morning on stored DLEs that had previously undergone HLD and complete drying overnight.

All facilities followed the same sample collection protocol (see Appendix 1). HLD status (double or single) was unknown to the sampler at the time of sample collection. One sample was collected using a sterile swab to swab the auxiliary port (if available) and the elevator mechanism of the scope. A second sample was collected using a sterilized, reusable channel cleaning brush for sampling the inside of the suction channel and working channel. Swab tips were cut off and dropped into a vial containing 9 mL of tryptic soy broth plus Tween 80 neutralizer. Reusable, sterilized brush tips were vigorously agitated in a second vial containing 9 mL of tryptic soy broth plus Tween 80 neutralizer.

Laboratory Testing:

Detailed instructions for processing the collected samples were provided to each facility's laboratory (see Appendix 2). Processes were additionally reviewed via virtual meeting. Broth cultures were incubated at 35° to 37°C in ambient air and read at 24 and 48 hours. Positive cultures were worked up to genus or species level using routine microbiology methods. High-concern pathogens were defined as potentially pathogenic enteric flora and included *Escherichia (E) coli*, *Enterococcus faecalis*, *Enterococcus faecium*, *Enterococcus spp*, *Enterobacter cloacae*, and *Aeromonas spp*. Coagulase-negative *Staphylococci*, *Bacillus spp*, coryneform Gram-positive bacilli, and other Gram-negative glucose-non-fermenters were considered environmental colonizers.

Reporting and follow-up:

Culture results were documented in a shared electronic record. Endoscopy and infection prevention at each site were alerted immediately to the growth of any high-concern pathogens. If positive for microbial growth, the DLE was re-processed, re-cultured and quarantined before it was returned to use. DLEs positive after first re-culture were sent out for investigation and repair.

Sample size and randomization

Sample size calculation was based on high-concern pathogen positivity rate observed in our surveillance pilot study, which was 0.6% (specimen based) for the 4 participating sites (8). Because our goal was to determine whether adding one more HLD step could prevent virtually ALL growth of high-concern pathogens. We powered our study to detect a reduction from 0.6% to 0.001% (virtually no growth). The sample size required was 5200 specimens (2600 specimens per study arm) to achieve 80% power at the 0.05 significant level.

Four separate randomization lists, one for each participating site, were generated using a block randomization generator in the R software, with block sizes randomly assigned among 2, 6, and 8. The randomization assigned one of the two cleaning methods to each work day (ie, not to each scope up for cleaning) to accommodate the busy work flow in the Endoscopy lab. At the planning phase of the study, there were 35 DLEs in use at the 4 sites, resulting in an estimated study period of 82 work days if all scopes were used and cultured each day. However, we prepared the list to cover a total of 170 days in the case the average usage rate could be as low as 50%. The randomization in each list was assigned to the consecutive work days from the start of the study. For each month, a calendar with the cleaning assignment for each workday in that

month was sent to each site. The exact number of specimens collected for each arm were tracked monthly then weekly once they were within 200 samples from the target sample size. The study was stopped when at least 2600 specimens had been collected in both arms.

Statistical Analysis

Because two specimens were collected/cultured at each culturing encounter, both specimen-based and encounter-based culture positivity rates were reported. Positivity rates were compared between the two HLD methods, and then among the facilities, using Chi-squared test or Fisher exact test as appropriate. For the positivity rate of any microbial growth, mixed-effect logistic regression with random intercept for each scope was performed to control for the correlation within repeated measures from the same scope (not implemented for high-concern pathogen growth due to the extremely small number of events observed, which would result in unreliable estimates in the regression modeling). Further, these comparisons were repeated within stratified subgroups to control for potential confounding effect among the factors examined (ie, HLD methods, study site, and culture sample site). Positivity rates between the 2 sampling sites (elevator mechanism vs channel samples) were compared using the McNemar test due to the matched-pair nature. The analyses were performed using R 3.1.0 statistical program (R Foundation for Statistical Computing, Vienna, Austria).

Results

Altogether, 5850 surveillance culture specimens were obtained from 2925 encounters for the 45 DLEs in clinical use (including 7 on loan) at the 4 participating facilities. Of these, 235 specimens (4.0%) or 224 encounters (7.7%) showed microbial contamination after manual cleaning, AER, and drying procedures. High-concern pathogens was detected in only 8 (0.1%) of

specimens and 8 (0.3%) of encounters from 5 different endoscopes. The mean/median number of days between reprocessing and culturing was 1.7/1.

There was 99.7% compliance with the randomization scheme (7, out of 2573, non-compliant cleaning incidences, 4 being assigned to double-HLD but reprocessed with single-HLD, and 3 vice versa). Other than 2 loaner scopes with only a single HLD cycle performed on each one, the others all encountered both single- and double-HLD cycles. The average proportion of double-HLD cycles for individual scopes was 50%, with the median (IQR) proportion being 50% (45.8%-54%). Overall, culture specimens collected after double-HLD cycles accounted for 3052 (52.2%) of specimens obtained. The total number of culture encounters performed on each scope varied widely, with a median (IQR) of 59 (38-102) and mean of 65 encounters. The encounter-based positivity rate for any microbial growth for each scope was shown in Figure 1. Wider variations in the positivity rates were seen among scopes with fewer encounters (with the 2 extreme outliers being the 2 loaner scopes with only 1 and 2 culture encounters). The encounter number did not exert any clear influence over the positivity rates, as confirmed by the logistic regression with random intercept for each scope ($p=0.09$).

All 8 high-concern pathogens cultures were isolated from the elevator mechanism of 5 different endoscopes in 2 separate facilities, as shown in Table 1. Persistent growth was observed on two duodenoscopes: one grew *Enterococcus faecalis* (not vancomycin-resistant enterococci) on 3 occasions, with *E coli* also showing up on 2 of the 3 occasions, one of which carried an extended spectrum β -lactamase (ESBL+). The other duodenoscope grew different enteric flora on two specimens. Both scopes were returned to the manufacturers for overhaul and replacement of damaged parts.

Double-HLD demonstrated no benefit over single-HLD; no significant differences were observed between single-HLD and double-HLD for specimens or encounters (Table 2, all p -values >0.05), even after stratified by either facility, or sample type (elevator mechanism vs channel samples). No differences were noted between cultures collected the next day versus a few days (due to weekend or holiday interruption) after cleaning (data not shown). The study was underpowered with regard to high-concern pathogens growth because we assumed that the single-HLD arm would have a specimen-based positivity rate similar to our pilot study (0.6%). Instead, we saw a significantly lower positivity rate of 0.1% (Table 3).

As shown in Table 4, the elevator mechanism was more frequently colonized than the channel samples, both for any growth (5.2% vs 2.9%, $p<0.001$) and for high-concern pathogens (0.3% vs 0%, $p=0.01$). In fact, the 8 high-concern pathogens cultures were, again, all recovered from elevator mechanism samples. When stratified by reprocessing method, for the outcome of any growth, the elevator mechanism remained more likely to be colonized among the double-HLD sample (5.8% vs 2.6%), while trending higher though not significant among single-HLD samples (4.5% vs 3.2%). Among the 224 encounters with positive growth, only 11 (4.9%) recovered microbes (all environmental) from both swab and brush samples. In all other encounters we found growth in only one of the two specimens (140 (62.5%) from elevator mechanism samples only and 73 (32.6%) from channel samples only), an indication that there are possibly different underlying mechanisms responsible for contamination between the two sample sites. Although we did not control for potentially differential recovery rates of swab versus brush methods, swab samples in this study had a similar positivity rate to swab samples used in our pilot study (8). As in our pilot study, the elevator mechanism site has a higher culture positivity than the working channel in these specialty scopes. Therefore, it seems prudent to say

that an effective and reliable scope culture protocol must include some method of elevator channel sampling. However, there is not enough evidence at this time to suggest elimination of the channel brush/flush from the protocol, because our data also pointed out very little overlap in the positivity rate by the 2 sampling approaches (only 4.9%).

Despite all 4 facilities following the same 2-specimen culture protocol for all encounters, a facility effect upon positivity rates remained, as previously seen in our pilot study (Table 5). Adjusted for reprocessing method, Facility A and Facility B, the two largest facilities by volume, displayed lower positivity rates for any growth ($p<0.001$), but not high-concern pathogens growth ($p=0.49$). We do not have individual endoscope usage data in order to explore whether this is a factor as well. These differences in positivity rates were noted for both single-HLD ($p<0.001$) and double-HLD reprocessing ($p=0.003$), as well as when stratified by sample site ($p<0.001$ for both elevator mechanism and channel samples).

Discussion

No clearly efficacious, cost-effective method currently exists to ensure high level disinfection or sterilization of scopes or linear echoendoscopes, prompting federal agencies and specialty societies to proffer a variety of steps to reduce the risk of transmission of infection by centers that perform ERCP (15). Investigators of one recent outbreak adopted repeated washing and HLD for their culture positive endoscopes, noting a further 1-log reduction of persistent infection (from 29 to 2 persistently positive cultures) (9). Another group also recently showed a similar 1-log reduction in culture positivity (from 22 to 2 persistently positive cultures) after repeated HLD (16). We explored a routinely enhanced approach to reprocessing in a non-outbreak setting, prospectively comparing standard single-HLD to double-HLD after automatic

reprocessing of DLE in a randomized, prospective fashion for each of 4 facilities over a 6.5-month period.

After processing nearly 6000 surveillance culture specimens in 45 DLEs in clinical use, about half of which were from scopes cleaned by double-HLD, we found no added benefit of a routine second HLD processing step. We did not see the same decline as Ross and colleagues, but our surveillance cultures were not performed in an outbreak setting. Moreover, our study protocol differed from the “culture and hold” followed by a separate repeated HLD processing as done in the study by Chapman. However, we recovered only 8 high-concern pathogens from 5 DLE scopes, all from the elevator mechanism, with only 1 scope repeatedly positive for *E coli* and enterococci over a 15-day period. Non-critical abrasions were identified on this scope by the third-party repair company when it was sent for overhaul. A second scope also tested positive on 2 separate occasions during the review period, but with different organisms. In accordance with Alfa et al’s findings (25), biofilm build-up within the scope may be responsible for these repeat positive results. We concur with Almario et al that neither a “culture and hold” nor an ethylene oxide sterilization step would seem to be warranted in a non-outbreak setting in our facilities at this time, given our low prevalence of CRE and other MDRO (17).

We perceive several limitations to the present study, including a significantly lower positivity rate for both any microbial growth and for high-concern pathogens growth. We planned the sample size for this study based on our pilot study on the high-concern pathogens growth outcome (8). However, significantly lower culture positivity rates were observed in this QI study than in our pilot study, not only for the high-concern pathogens growth (0.1% vs 0.6%, $p<0.001$) but also for any microbial growth (4.0% vs 5.0%, $p=0.02$). Our study thus remains underpowered to detect potential small differences in efficacy of double-HLD versus single-

HLD for high-concern pathogens growth. Our culture methods may have been insensitive compared with other published methods (18) or “Duodenoscope Sampling and Culturing Overview and Protocols,” currently in preparation by FDA along with other key stakeholders (24). Even with a very rigorous culture protocol, culture of buildup biofilm may be problematic and not represent the actual bioburden present within the scope (25). Finally, we may have seen a positive carry-over effect on performance of the multiple-step scope reprocessing after our previous pilot study, given the small margin of error (19).

Pineau and De Phillipe have suggested that assaying total organic carbon may serve as a marker for assessing endoscope reprocessing (20), based on previous work by Alfa et al (21) and the AAMI (22,23). Further validation of such an approach seems warranted.

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Table 1. Details of 8 cultures positive for high-concern pathogens, cultured from 5 different scopes.

Facility	Culture Date	Scope ID	HLD Method	High-Concern Pathogen(s) Detected
A	2/26/2016	1	Single HLD	<i>Enterococcus</i> spp
A	4/8/2016	2	Double HLD	<i>Enterococcus</i> spp
A	4/29/2016	2	Single HLD	<i>Enterobacter cloacae</i>
A	5/6/2016	3	Double HLD	<i>Aeromonas</i> spp
A	8/8/2016	4	Double HLD	<i>E. coli</i> (ESBL+), <i>Enterococcus</i> spp
B	7/15/2016	5	Single HLD	<i>E. coli</i> (ESBL-) and <i>Enterococcus faecalis</i>
B	7/29/2016	5	Single HLD	<i>E. coli</i> (ESBL+) and <i>Enterococcus faecalis</i>
B	8/1/2016	5	Single HLD	<i>Enterococcus faecium</i>

Table 2. Summary of culture positivity rates in the two study arms

	Double HLD	Single HLD	P value*
All cultures			
<i>Specimen-based</i>			
No. of Specimens	3052	2798	
Any Growth	127 (4.2%)	108 (3.9%)	0.60 (0.64)
Growth of High-Concern Pathogens	3 (0.1%)	5 (0.2%)	0.49 (0.43)
<i>Encounter-based</i>			
No. of Encounters	1526	1399	
Any Growth	122 (8.0%)	102 (7.3%)	0.52 (0.54)
Growth of High-Concern Pathogens	3 (0.2%)	5 (0.4%)	0.49 (0.43)
Stratified by Facility (reported only the encounter-based rates)			
<i>Site A</i>			
No. of Encounters	647	654	
Any Growth	37 (5.7%)	31 (4.7%)	0.50 (0.42)
Growth of High-Concern Pathogens	3 (0.5%)	2 (0.3%)	0.69 (0.65)
<i>Site B</i>			

No. of Encounters	409	394	
Any Growth	35 (8.6%)	22 (5.6%)	0.13 (0.10)
Growth of High-Concern Pathogens	0	3 (0.8%)	0.12 (-)
<i>Site C</i>			
No. of Encounters	344	252	
Any Growth	31 (9.0%)	35 (13.9%)	0.08 (0.06)
Growth of High-Concern Pathogens	0	0	-
<i>Site D</i>			
No. of Encounters	126	99	
Any Growth	19 (15.1%)	14 (14.1%)	0.99 (0.87)
Growth of High-Concern Pathogens	0	0	-
Stratified by Sample Type/Method			
<i>Brush Sample</i>			
No. of Encounters	1526	1399	
Any Growth	39 (2.6%)	45 (3.2%)	0.34 (0.13)
Growth of High-Concern Pathogens	0	0	
<i>Swab Sample</i>			
No. of Encounters	1526	1399	
Any Growth	88 (5.8%)	63 (4.5%)	0.14 (0.10)
Growth of High-Concern Pathogens	3 (0.2%)	5 (0.4%)	0.49 (0.43)

**P* values within the parentheses were based on mixed-effect logistic regression analysis (with random intercept for each scope), the others were based on Chi-squared test or Fisher exact test as appropriate.

Table 3. Comparing the culture positivity rates to the Pilot study

	Single	Double	Overall	Pilot Study	<i>P</i> value*	<i>P</i> value [#]
<i>Specimen-based</i>						
No. of specimens	2798	3052	5850	4032		

Any Growth	108 (3.9%)	127 (4.2%)	235 (4.0%)	201 (5.0%)	0.03	0.02
Growth of High-Concern Pathogens	5 (0.2%)	3 (0.1%)	8 (0.1%)	23 (0.6%)	0.01	<0.001
<i>Encounter-based</i>						
No. of encounters	1399	1526	2925	2238		
Any Growth	102 (7.3%)	122 (8.0%)	224 (7.7%)	189 (8.4%)	0.24	0.32
Growth of High-Concern Pathogens	5 (0.4%)	3 (0.2%)	8 (0.3%)	21 (0.9%)	0.04	0.002

* Comparing Single to the Pilot Study; # Comparing Overall to the Pilot Study. Comparisons were performed using either Chi-squared test or Fisher exact test as appropriate.

Table 4. Comparing the positivity rates between the 2 sample types/methods

	Brush (Other Channels)	Swab (Elevator Mechanism)	P value
All cultures			
No. of Specimens	2925	2925	
Any Growth	84 (2.9%)	151 (5.2%)	<0.001
Growth of High-Concern Pathogens	0	8 (0.3%)	0.008
Stratified by Reprocessing Method			
<i>Double HLD</i>			
No. of Specimens	1526	1526	
Any Growth	39 (2.6%)	88 (5.8%)	0.001
Growth of High-Concern Pathogens	0	3 (0.2%)	0.25
<i>Single HLD</i>			
No. of Specimens	1399	1399	
Any Growth	45 (3.2%)	63 (4.5%)	0.10
Growth of High-Concern Pathogens	0	5 (0.4%)	0.06

Table 5. Comparing the positivity rates among the 4 facilities.

	Site A	Site B	Site C	Site D	P value*
All cultures					
<i>Specimen-based</i>					
No. of Specimens	2602	1606	1192	450	
Any Growth	69 (2.7%)	60 (3.7%)	71 (6%)	35 (7.8%)	<0.001 (<0.001)
Growth of High-Concern Pathogens	5 (0.2%)	3 (0.2%)	0 (0%)	0 (0%)	0.49 (-)
<i>Encounter-based</i>					
No. of Encounters	1301	803	596	225	
Any Growth	68 (5.2%)	57 (7.1%)	66 (11.1%)	33 (14.7%)	<0.001 (<0.001)
Growth of High-Concern Pathogens	5 (0.4%)	3 (0.4%)	0	0	0.49 (-)
Stratified by Cleaning Method (reported only the encounter-based rate)					
<i>Double HLD</i>					
No. of Encounters	647	409	344	126	
Any Growth	37 (5.7%)	35 (8.6%)	31 (9.0%)	19 (15.1%)	0.003 (0.02)
Growth of High-Concern Pathogens	3 (0.5%)	0	0	0	0.49 (-)
<i>Single HLD</i>					
No. of Encounters	654	394	252	99	
Any Growth	31 (4.7%)	22 (5.6%)	35 (13.9%)	14 (14.1%)	0.001 (<0.001)
Growth of High-Concern Pathogens	2 (0.3%)	3 (0.8%)	0	0	0.59 (-)

*P values within the parentheses were based on mixed-effect logistic regression analysis (with random intercept for each scope), the others were based on Chi-squared test or Fisher exact test as appropriate.

Figure 1. Encounter based positivity rate for any microbial growth for each duodenoscope, plotted against the total number of culture encounters and color-coded for study sites.

References

1. Peterson BT, Koch J, Ginsberg GG. Infection using ERCP endoscopes. *Gastroenterology* 2016; 151:46-50
2. Epstein L, Hunter JC, Arwady MA, et al. New Delhi metallo-beta-lactamase-producing carbapenem-resistant *Escherichia coli* associated with exposure to duodenoscopes. *JAMA* 2014;312:1447-55.
3. Kovaleva J, Peters FT, van der Mei HC, et al. Transmission of infection by flexible gastrointestinal endoscopy and bronchoscopy. *Clin Microbiol Rev* 2013;26:231-54.
4. Wendorf KA, Kay M, Baliga C, et al. Endoscopic retrograde cholangiopancreatography-associated AmpC *Escherichia coli* outbreak. *Infect Control Hosp Epidemiol* 2015;36:634-42.
5. Division of Industry and Consumer Education (DICE), U.S. FDA. Design of endoscopic retrograde cholangiopancreatography (ERCP) duodenoscopes may impede effective cleaning: FDA safety communication. Available at: <https://wayback.archive-it.org/7993/20170723124406/https://www.fda.gov/downloads/AdvisoryCommittees/CommitteesMeetingMaterials/MedicalDevices/MedicalDevicesAdvisoryCommittee/Gastroenterology-UrologyDevicesPanel/UCM445596.pdf> .Accessed September 13, 2017.
6. Center for Devices and Radiological Health, U.S. FDA. Meeting of the Gastroenterology and Urology Devices Panel of the Medical Devices Advisory Committee: Effective reprocessing of endoscopes used in endoscopic retrograde cholangiopancreatography (ERCP) procedures, May 14-15, 2015. Available at: <https://wayback.archive-it.org/7993/20170723124406/https://www.fda.gov/downloads/AdvisoryCommittees/CommitteesMeetingMaterials/MedicalDevices/MedicalDevicesAdvisoryCommittee/Gastroenterology-UrologyDevicesPanel/UCM445596.pdf>

- [it.org/7993/20170113091323/http://www.fda.gov/downloads/AdvisoryCommittees/CommitteesMeetingMaterials/MedicalDevices/MedicalDevicesAdvisoryCommittee/Gastroenterology-UrologyDevicesPanel/UCM445592.pdf](http://www.fda.gov/downloads/AdvisoryCommittees/CommitteesMeetingMaterials/MedicalDevices/MedicalDevicesAdvisoryCommittee/Gastroenterology-UrologyDevicesPanel/UCM445592.pdf) .Accessed September 13, 2017.
7. Rutala WA, Weber DJ. ERCP scopes: what can we do to prevent infections? *Infect Control Hosp Epidemiol* 2015;36:643-8.
 8. Brandabur JJ, Leggett JE, Wang L, Bartles RL, Baxter L, Diaz GA, Grunkemeier GL, Hove S, Oethinger M. Surveillance of guideline practices for duodenoscope and linear echoendoscope reprocessing in a large healthcare system. *Gastrointest Endosc* 2016;84:392-9.
 9. Ross AS, Baliga C, Verma P, Duchin J, Gluck M. A quarantine process for the resolution of duodenoscope-associated transmission of multidrug-resistant *Escherichia coli*. *Gastrointest Endosc* 2015;82:477-83.
 10. Rutala WA, Weber DJ. Outbreaks of carbapenem-resistant Enterobacteriaceae infections associated with duodenoscopes: What can we do to prevent infections? *American Journal of Infection Control* 44 (2016) e47-e51.
 11. U.S. FDA, Supplemental Measures to Enhance Duodenoscope Reprocessing: FDA Safety Communication 2015. Available at: <https://wayback.archive-it.org/7993/20170111065959/http://www.fda.gov/MedicalDevices/Safety/AlertsandNotices/ucm454766.htm> .Accessed September 13, 2017.
 12. Petersen BT. Duodenoscope reprocessing: risk and options coming into view. *Gastrointest Endosc* 2015;82:484-7.
 13. Visrodia K, Petersen BT. Echoing concerns related to endoscope reprocessing. *Gastrointest Endosc* 2017;85:398-400.

14. Petersen BT, Cohen J, et al. (2017). Multisociety guideline on reprocessing flexible GI endoscopes: 2016 Update. *Gastrointestinal Endoscopy* 85 (2) 282-294.
15. Centers for Disease Control and Prevention (CDC). Interim Protocol for Healthcare Facilities Regarding Surveillance for Bacterial Contamination of Duodenoscopes after Reprocessing. Available at: <https://www.cdc.gov/hai/organisms/cre/cre-duodenoscope-surveillance-protocol.html> . Accessed September 13, 2017.
16. Chapman CG, Siddiqui UD, Manzano M, Konda VJ, Murillo C, Landon EM, Waxman I. Risk of infection transmission in curvilinear array echoendoscopes: results of a prospective reprocessing and culture registry *Gastrointest Endosc* 2017;85:390-7.
17. Almario CV, May FP, Shaheen NJ, Murthy R, Gupta K, Jamil LH, Lo SK, Spiegel BMR. Cost Utility of Competing Strategies to Prevent Endoscopic Transmission of Carbapenem-Resistant *Enterobacteriaceae*. *Am J Gastroenterol* 2015; 110:1666–1674.
18. Gazdik MA, Coombs J, Burke JP, Lopansria BK. Comparison of Two Culture Methods for Use in Assessing Microbial Contamination of Duodenoscopes. *J Clin Microbiol* 54:312–316.
19. Beekmann SE, Palmore TN, Polgreen PM, Bennett JE. Adequacy of Duodenoscope Reprocessing Methods as Reported by Infectious Disease Physicians. *Infect. Control Hosp. Epidemiol.* 2016;37:226–228.
20. Pineau L, De Philippe E. Evaluation of endoscope cleanliness after reprocessing: a clinical-use study. *Central Service* 2013;1:22-27.
21. Alfa MJ, Fatima I, Olson N. The adenosine triphosphate test is a rapid and reliable audit tool to assess manual cleaning adequacy of flexible endoscope channels. *American Journal of Infection Control* 2013;41:249-53.

22. Association for the Advancement of Medical Instrumentation. Safe handling and biological decontamination of medical devices in health care facilities and in nonclinical settings. AN SI/AA MI ST35: 2003.
23. Association for the Advancement of Medical Instrumentation. A compendium of processes, materials, test methods, and acceptance criteria for cleaning reusable medical devices. AAMI TIR 30: 2003.
24. Duodenoscope Sampling and Culturing Overview and Protocols,” currently in preparation by FDA along with other key stakeholders. Received via personal communication, Catherine Kashork.
25. Alfa, M.J., Ribeiro, M.M., da Costa Luciano, C., Franca, R., Olson, N., DeGagne, P. & Singh, H. 2017. A novel polytetrafluoroethylene-channel model, which simulates low levels of culturable bacteria in buildup biofilm after repeated endoscope reprocessing. *Gastrointestinal Endoscopy Journal* 86(3) 442-451.

Appendix 1: Specimen Collection Process**Supplies (per scope):**

1. One sterile channel cleaning brush (reusable – Olympus BW-20T or equivalent)
2. One dacron swab – Copan 172C or equivalent such as BD swabs- Lawson Number 224140, PH&S Contract PLB0220, Mfr BD, Vendor (Distributor) Cardinal
3. One sterile Scissor
4. One 500 mL sterile water
5. Two tryptic soy broth plus Tween 80 (TSB-T80) vials 5 mL
6. Lab requisition
7. Lab specimen bag with biohazard symbol

Note: The following process requires 2 people.

Step 1: Preparation of Site and Materials

- Don surgical mask, goggles and isolation gown
- Place a sterile drape on working surface
- Label 2 vials (“brush” or “swab”) with scope model, scope serial number, date and time cultured, staff initials
- Place labeled vials on working surface, outside of sterile field
- Open sterile water and place immediately outside of sterile field
- Open sterile scissors, swabs, and brushes and drop onto sterile field (or open as being used)

Step 2: Swab of Auxiliary Port and Elevator

- Don sterile gloves
- Place scope on one far end of sterile field
- Dip swab in sterile water
- Swab auxiliary port (if available)
- Swab elevator on top, bottom, sides and the wire.
- Cut end of swab off with sterile scissors into tryptic soy broth vial labeled “swab”

Step 3: Brush of all other channels

- Dip sterile brush into sterile water
- Run brush down both suction channels
- Run brush down working channel
- Vigorously swish brush in tryptic vial labeled “brush”

Step 4: Clean-up

- Place scope back in tray
- Clean reusable channel cleaning brush and send for reprocessing per facility procedure
- Place both vials (“brush” and “swab”) in lab specimen bag with pre filled lab requisition
- Fold used portion of drape over
- Remove sterile gloves and perform hand hygiene
- Repeat steps No. 2-4 until all scopes are cultured

- Take all vials to microbiology lab

Step 5: Documentation

- Log micro results onto ERCP scope culturing log
- For positive results, follow facility-specific designated response protocol

ACCEPTED MANUSCRIPT

Appendix 2: Lab Processing Protocol

Specimen Processing –

The endoscopy department will send two samples to the designated laboratory for each accession. They will have an identifier for the scope that was tested and the sample location: “swab” (will contain a swab), “brush” (container will not have a brush in it).

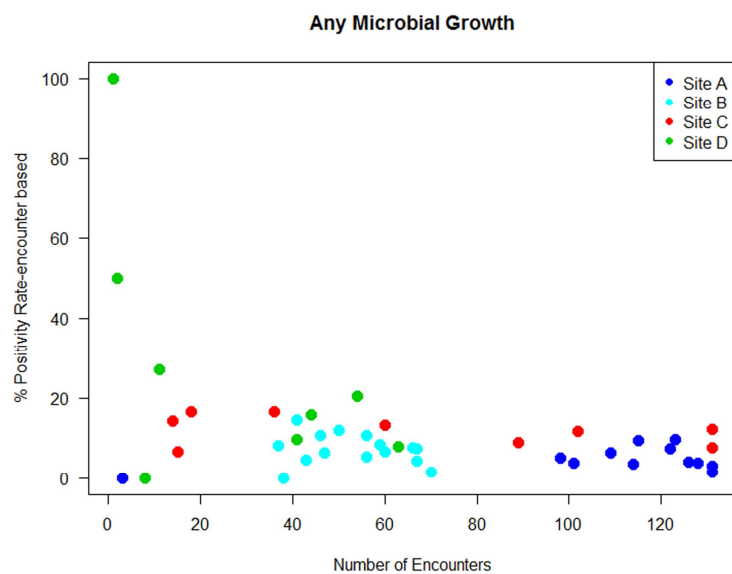
Microbiology Laboratory—

1. Accession the test.
2. Incubate tubes at 35-37°C.

Broth Culture Work-up—

1. Examine broths for turbidity.
 - If all broths are clear at 24 hours, re-incubate at 35-37°C for an additional day.
 - If broth is clear at 48 hours, report each sample as “no growth”. Include the collection method (“swab” or “brush”).
 2. If a broth is turbid, subculture the broth to Sheep Blood Agar and MacConkey Agar plates. Do not issue a preliminary result. Document which broth is turbid.
 - a. Examine the MacConkey agar for Gram-negative rods.
 - Perform ID and susceptibility according to microbiology standard operating procedures (SOP).
 - Rule out multidrug resistant organisms among high-concern organisms (MDRO).
 - b. Examine the Blood Agar for *Staph aureus* and *Enterococcus* species.
 - Perform ID and susceptibility testing according to microbiology standard operating procedures (SOP).
 - Rule out MRSA and/or VRE if present.
 - c. Freeze ALL potentially pathogenic isolates of high concern (see above).
 - d. Report using facility-specific verbiage:
 - Potentially pathogenic organisms are reported with susceptibility.
 - Organisms of low concern are collectively reported as “Environmental flora”
- For all results include the collection method (“swab” or “brush”, as noted above).

Immediately call any culture positive for a high-concern pathogen to Endoscopy and Infection Control (per your facility’s agreed-upon communication structure). Provide verbal result including: collection date, model/serial number of scope, organism, and susceptibility profile.



**A Randomized Trial of Single- versus Double High-Level Disinfection
of Duodenoscopes and Linear Echoendoscopes
Using Standard Automated Reprocessing**

Acronyms

AER - Automated Endoscope Reprocessor
ASGE - American Society of Gastrointestinal Endoscopy
CDC – Center for Disease Control
DLE - duodenoscope and linear echoendoscope
ERCP - endoscopic retrograde cholangiopancreatography
ESBL+ - extended spectrum beta-lactamase
FDA – Food & Drug Administration
HLD- high-level disinfection
MDRO – multi-drug resistant organism
PHS – Providence Health & Services
QI – Quality Improvement