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Knowledge that will change your world

Can Endoscopes be rendered bacteria-free through High Level Disinfection?

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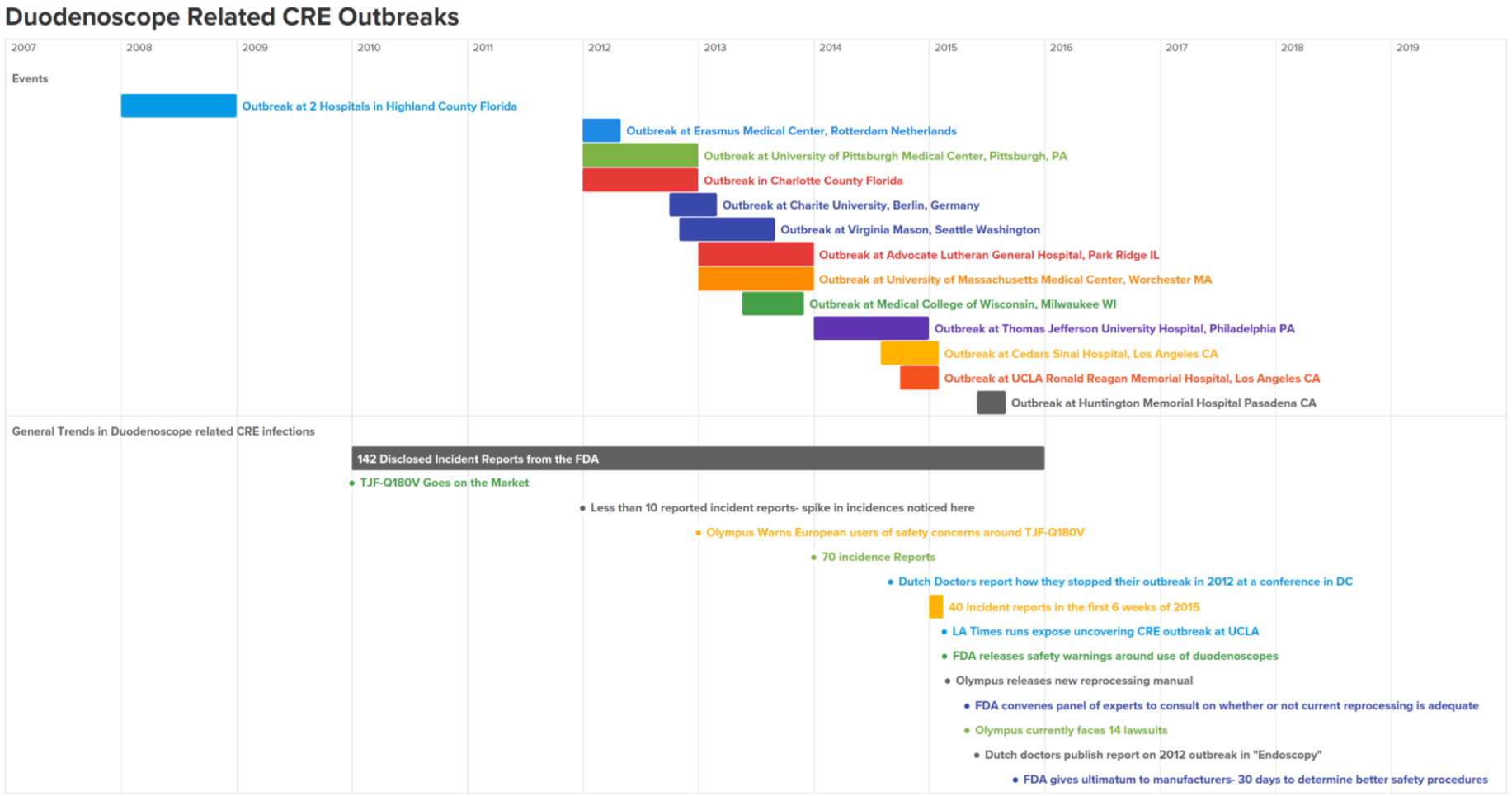
2018 Patient Safety & Quality Congress

No Conflicts of Interest to Disclose

Learning Objectives

- Know the enhanced reprocessing methods recommended by the FDA
- Learn the limitations of the recommended enhanced reprocessing methods
- Learn about reported outbreaks of Multidrug-Resistant Gram Negative Bacilli associated with duodenoscopes

Timeline of Duodenoscope-related CRE Outbreaks



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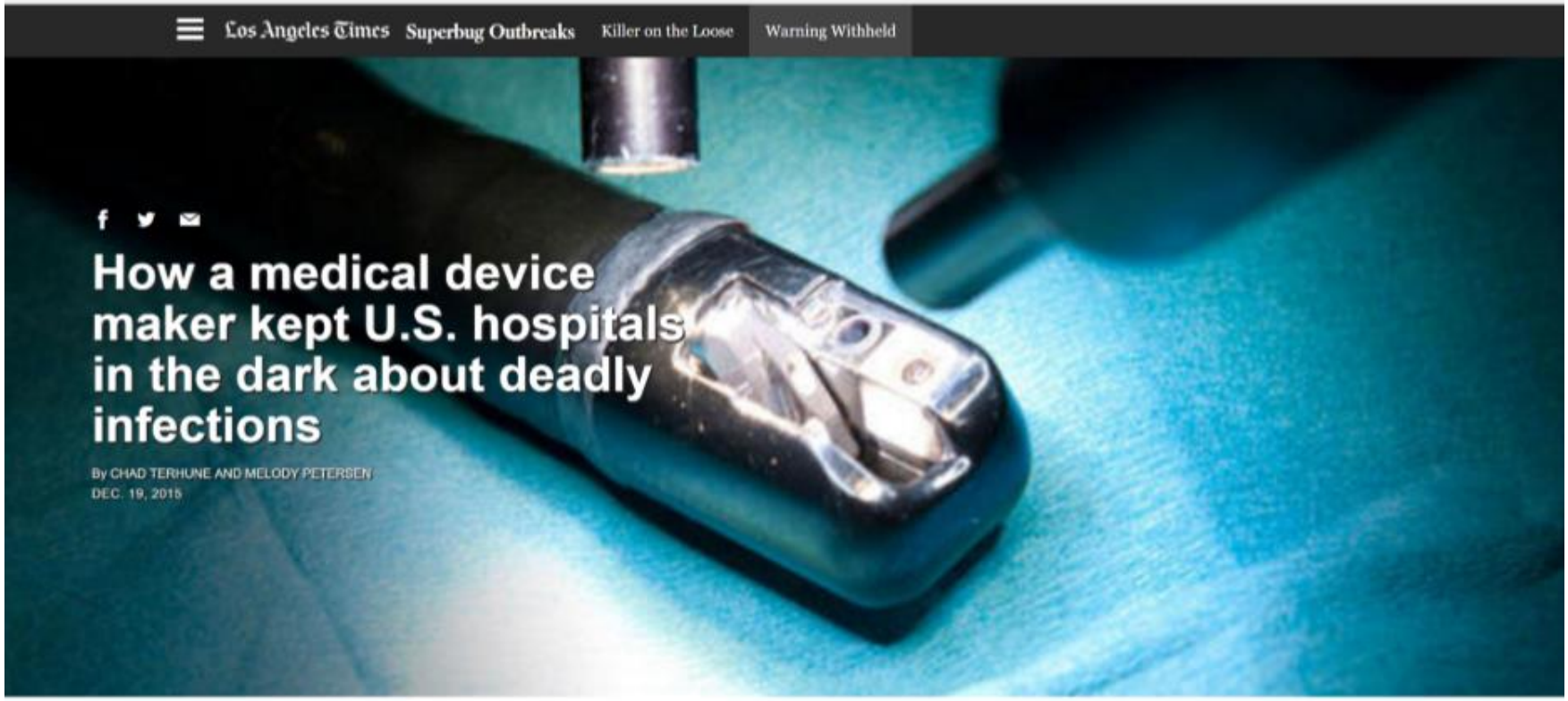


How a medical device maker kept U.S. hospitals in the dark about deadly infections

By CHAD TERHUNE AND MELODY PETERSEN
DEC. 19, 2015

The hunt for a deadly superbug that sickened 22 patients at a Dutch hospital began just before noon on a spring day in 2012.

Inside a lab in the tiny hamlet of Zoeterwoude, a technician carefully peeled back the tip of a state-of-the art medical scope. Watching him intently was a small group of hospital officials and executives from Olympus Corp., the maker of the device.

Timeline

Recent events involving scope-related outbreaks of antibiotic-resistant superbug infections

2010

Supplemental Measures for Endoscope Reprocessing Recommended by the FDA (August 2015)

1. Ethylene oxide sterilization
2. Use of a liquid chemical sterilant processing system
3. Microbiological culturing
4. Repeat high-level disinfection process

https://www.fda.gov/MedicalDevices/Safety/AlertsandNotices/ucm454766.htm

FDA Activities since August 2015

- February 26, 2018--the FDA, CDC, and the American Society for Microbiology (ASM) released voluntary standardized protocols for duodenoscope surveillance sampling and culturing.
- March 9, 2018--the FDA issued Warning Letters to all three manufacturers who make duodenoscopes sold in the U.S. for failure to provide sufficient data to address the postmarket surveillance studies requirements under Section 522 of the Federal Food, Drug, and Cosmetic Act (the Act).

How were the FDA Recommendations Implemented?

Characteristics of Survey Responders (n= 249) November 2016		
Procedure volume (ERCPs/year)	n	Percentage
<50	29	11.6
51-100	55	22.1
101-250	75	30.1
251-500	36	14.5
>500	52	20.9
Practice setting		
University hospital	38	15.3
University affiliated	49	19.7
Hospital – not university affiliated	168	67.5
Freestanding ambulatory center	1	0.4
Other	1	0.4

Thaker et al. *Gastrointestinal Endoscopy* 2018; 4: 2340

Practices among US Healthcare Institutions

Duodenoscope manufacturer*	n	Percentage
Olympus	225	90.4
Pentax	21	8.4
Fujifilm	6	2.4

Thaker et al. *Gastrointestinal Endoscopy* 2018; 4: 2340

Supplemental Reprocessing Method

	n	Percentage
Repeat high-level disinfection	157	63.1
Surveillance microbiological culturing	133	53.4
Liquid chemical sterilization	86	34.5
Ethylene oxide (EtO) sterilization	30	12.0
None of the above	26	10.4

Thaker et al. *Gastrointestinal Endoscopy* 2018; 4: 2340

Additional Measures

	n	Percentage
Patient MDRO screening	38	15.3
ATP Bioluminescence testing	84	33.7
Drying technique		
Ventilated cabinet	152	61.0
Hang overnight	134	53.8
Forced-air drying	119	47.8
None (used immediately)	22	8.8
Other	11	4.4
Unknown	8	3.2

Thaker et al. *Gastrointestinal Endoscopy* 2018; 4: 2340

Supplemental Processing Method by Number of ERCPs Performed

ERCP/year, n (%)	Number of centers (n = 249)	Repeat HLD (n = 157)	Surveillance microbiological culturing (n = 133)	Liquid chemical sterilization (n = 86)	EtO sterilization (n = 30)	None (n = 26)
0-50	29	23 (79)	10 (34)	14 (48)	2 (7)	5 (17)
51-100	55	32 (58)	28 (51)	15 (27)	3 (5)	9 (16)
101-250	75	45 (60)	36 (48)	25 (33)	6 (8)	7 (9)
251-500	36	26 (72)	23 (64)	11 (31)	5 (14)	2 (6)

Thaker et al. *Gastrointestinal Endoscopy* 2018; 4: 2340

Limitations of Supplemental Reprocessing Methods

Limitations of Ethylene Oxide Sterilization

- Inadequate when performed in the presence of organic debris after suboptimal manual cleaning
- Highly flammable and carcinogenic
- Damages endoscopes
- Not accessible to all healthcare facilities

Kim 2016 *Curr Gastroenterol Rep;* 18:54
Alfa 1998 *Am J Infect Control;* 26: 469
Naryzhny 2016 *Gastrointest Endosc*; 84:289

Liquid Chemical Sterilization

- Bathing endoscope in peracetic acid solution
- Requires prior appropriate cleaning and high-level disinfection
- Technically difficult--exact concentration, exposure time, and temperature to be effective
- The final step of flushing with purified water can recontaminate the endoscope

Rubin and Murthy 2016 *Curr Opin Infect Dis*; 29:407-414
Rutala & Weber 2016 Am J Infect Control; 44: e47-e51
Naryzhny 2016 *Gastrointest Endosc*; 84:289

Microbiological Culturing

- Sampling and culturing the instrument channel and distal end of the duodenoscope
- Culture results available within 48-72 hours; if positive cultures for high risk organism then reprocess then reculture
- **Sensitivity of culturing the channel is unknown**
- Optimal frequency of culturing has not been established

Rubin and Murthy 2016 *Curr Opin Infect Dis*; 29:407-414
Rutala & Weber 2016 Am J Infect Control; 44: e47-e51
Naryzhny 2016 *Gastrointest Endosc*; 84:289

Microbiological Culturing

- Culturing after a preset number of ERCP procedures
  - What to disclose to patients if positive
  - How to treat patients who were potentially exposed
- Very complicated task
  - Needs two people to accomplish
- Most diagnostic laboratory will not process environmental cultures
  - Reference laboratories would add significant expense
  - Adds additional lag time

Rubin and Murthy 2016 *Curr Opin Infect Dis*; 29:407-414
Rutala & Weber 2016 Am J Infect Control; 44: e47-e51
Naryzhny 2016 *Gastrointest Endosc*; 84:289

Microbiological Culturing (Failure)

- Some outbreaks have occurred in which the bacteria have not been cultured from the implicated endoscope
- A negative culture does not ensure sterility

Kim 2017 *Gastrointest Endosp*; Epub
Kola 2015 *Antimicrob Resist Infect Control*; 4:8

Repeat High Level Disinfection (HLD)

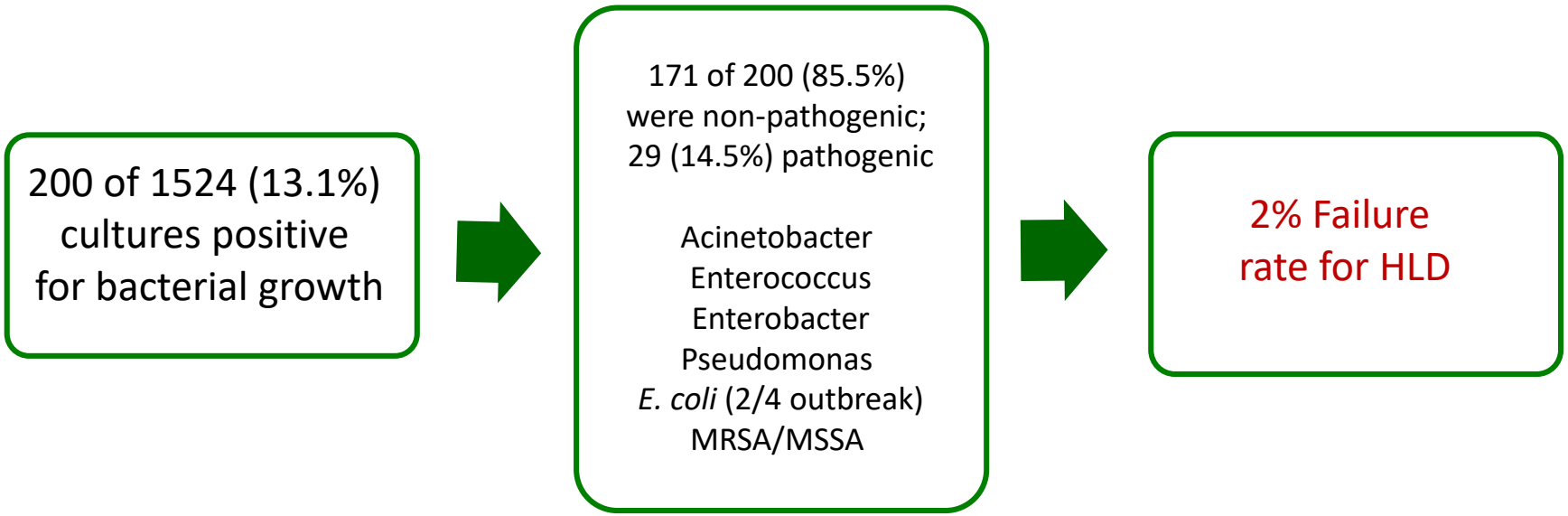
- Only works in theory
- Even with the new "enhanced" HLD processes, no data is available that even strict adherence leads to a bacteria-free duodenoscopes
- 10^{10} bacteria ➡ 10^{5} bacteria ➡ 0 bacteria?
- May not work because several outbreaks have occurred despite multiple cycles of reprocessing

Rubin and Murthy 2016 *Curr Opin Infect Dis*; 29:407-414
Rutala and Weber 2015 Infect Control Hosp Epidemiol 36; 643-8
Rutala & Weber 2016 Am J Infect Control; 44: e47-e51
Naryzhny 2016 *Gastrointest Endosc*; 84:289

Repeat High Level Disinfection

(Virginia Mason Quarantine Process)

- 8 duodenoscopes returned to manufacturer (4/8 positive for outbreak strain *E. coli*)
- 4/8 returned duodenoscopes required critical repairs despite the lack of functional defects
- 3/4 duodenoscopes that required critical repairs had cultured positive for outbreak strain
- 20 new duodesnoscopes purchased



- 2 duodenoscopes were culture positive despite two HLD cycles and returned to manufacturer
- 1 duodenoscope taken out of service because it was positive even after multiple HLD cycles

Ross et al 2015 *Gastrointest Endosc*; 82: 477-83

The Providence Experience

- Daily qualitative surveillance of dried, post-HLD duodenoscope and linear echoendoscope was conducted for a minimum of 30 days at 21 hospitals in the Providence-area.
- Culture was positive from 201 of 4032 specimens (5%) or 189 of 2238 encounters (8.4%); 23 specimens (0.6%) or 21 encounters (0.9%) for a high-concern pathogen.
- Custom Ultrasonics AER seemed to perform better than Medivators AER (0/1079 vs 21/2735 specimens or 0/547 vs 20/1582 encounters positive for high concern pathogen).
- Two endoscopes grew intestinal flora on several occasions despite multiple HLD.

Brandabbur et al. *Gastrointest Endosc* 2016; 84: 392-9

How effective are the Supplemental Measures Recommended by the FDA Special Panel?

- DISINFECTS trial (Duodenoscope Infection Surveillance IN Functioning automated Endoscope reprocessors in Conjunction with eThylene oxide Sterilization)
- Randomized Controlled Trial (18 duodenoscopes)
  - Single High Level Disinfection (sHLD; 5 scopes)
  - Double High Level Disinfection (dHLD; 5 scopes)
  - High Level Disinfection by Ethylene Oxide (HLD/ETO; 8 scopes)

Snyder et al. *Gastro* 2017; 153: 1018-25.

	Growth, Elevator Mechanism or Working Channel (%)			
	(N)	≥1 MDRO	> 0 CFU[a]	≥10 CFU[b]
sHLD	174	0	28 (16.1)	4 (2.3)
dHLD	169	0	27 (16.0)	7 (4.1)
HLD/ETO	173	0	39 (22.5)	9 (4.2)
Total	516	0	94 (18.3)	20 (3.9)

[a]p = .21
[b]p= .36 by Fisher's exact test

Snyder et al. *Gastro* 2017; 153: 1018-25.

Monitoring Adherence to IFUs with ATP Bioluminescence Meters

- Validated in a study to ensure that all disinfected endoscopes had <200 relative light units (RLU)
- The average detected RLUs for the suction-biopsy channel and the air-water channel were 27.7 RLUs and 154 RLUs respectively
- <200 RLUs is equivalent to <4 log10 CFU/cm2 which can be equivalent to 10^6 CFU per endoscope

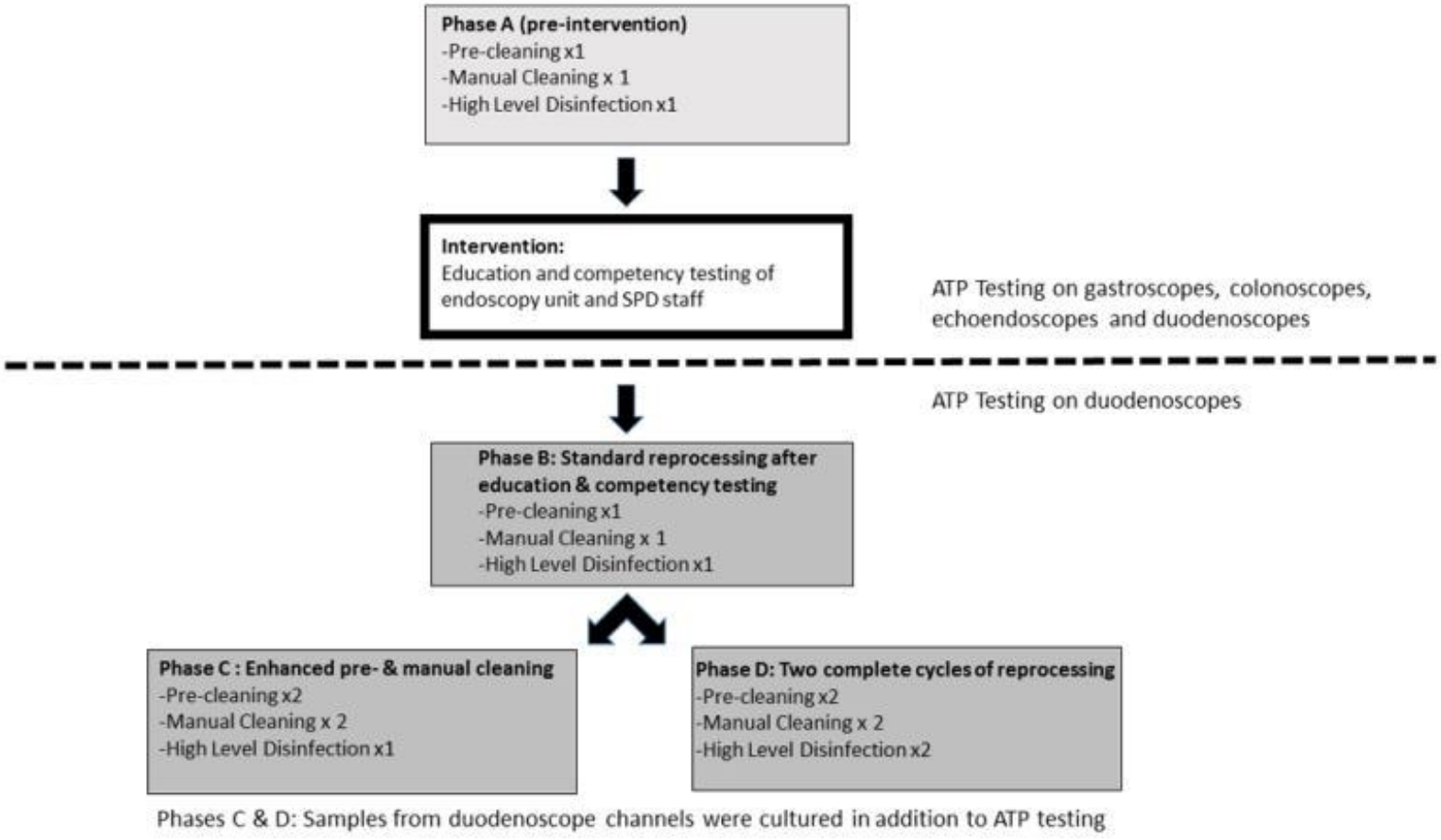
Alfa 2013 *Am J Infect Control*; 41:245-8
Rutala & Weber 2016 *Am J Infect Control*; 44: e47-e51

Limit of Detection of ATP Bioluminescence Meters

	Charm	Hygiena	3M	Kikkoman
Least detected CFU count	6.17E+05	2.40E+02	8.98E+02	5.60E+04
Correlation of RLU readings to plate counting (both in logarithmic scales)	0.9955	0.97737	0.9746	0.95634

Omidbakhsh N et al. *PLoS ONE* 9(6): e99951

Utility of Adenosine triphosphate bioluminescence for bacteriologic surveillance and reprocessing



Sethi et al. *Gastrointest Endosc* 2017; 85: 1180-7

ATP Values from Suction-Biopsy Channels by Endoscope

Endoscope	Pre-Cleaning	Manual Cleaning	High-Level Disinfection	*P*-value
Gastroscopes	1879.0 (883.0–3665.0)	32.5 (22.0–42.0)	12.5 (9.0–15.0)	PC→MC <0.01 MC→HLD <0.01
Colonoscopes	5446.5 (4023.0–7165.0)	31.0 (18.0–43.0)	10.0 (6.0–13.0)	PC→MC <0.01 MC→HLD 0.01
Radial Echoendoscopes	2289.5 (2041.0–3216.0)	23.0 (14.0–30.0)	10.0 (6.0–17.0)	PC→MC <0.01 MC→HLD 0.05
Linear Echoendoscopes	30483.5 (2666.0–46754.0)	88.5 (67.0–125.0)	23.5 (19.0–33.0)	PC→MC <0.01 MC→HLD <0.01
Duodenoscopes	4276.5 (1650.0–5285.0)	87.5 (53.0–101.0)	23.5 (11.0–37.0)	PC→MC <0.01 MC→HLD 0.01

Sethi et al. *Gastrointest Endosc* 2017; 85: 1180-7

ATP Values from Suction-Biopsy Channels by Presence of Elevator Channel

Cleaning Stage	Elevator Channel Absent	Elevator Channel Present	*P*-value
Pre-Cleaning	3497.0 (1954.0–5253.0)	5078.5 (2014.0–30483.5)	0.12
Manual Cleaning	28.0 (20.0—39.0)	88.5 (58.5–106.0)	<0.01
High-Level Disinfection	11.0 (7.5—14.5)	23.5 (17.5–33.0)	<0.01

Sethi et al. *Gastrointest Endosc* 2017; 85: 1180-7

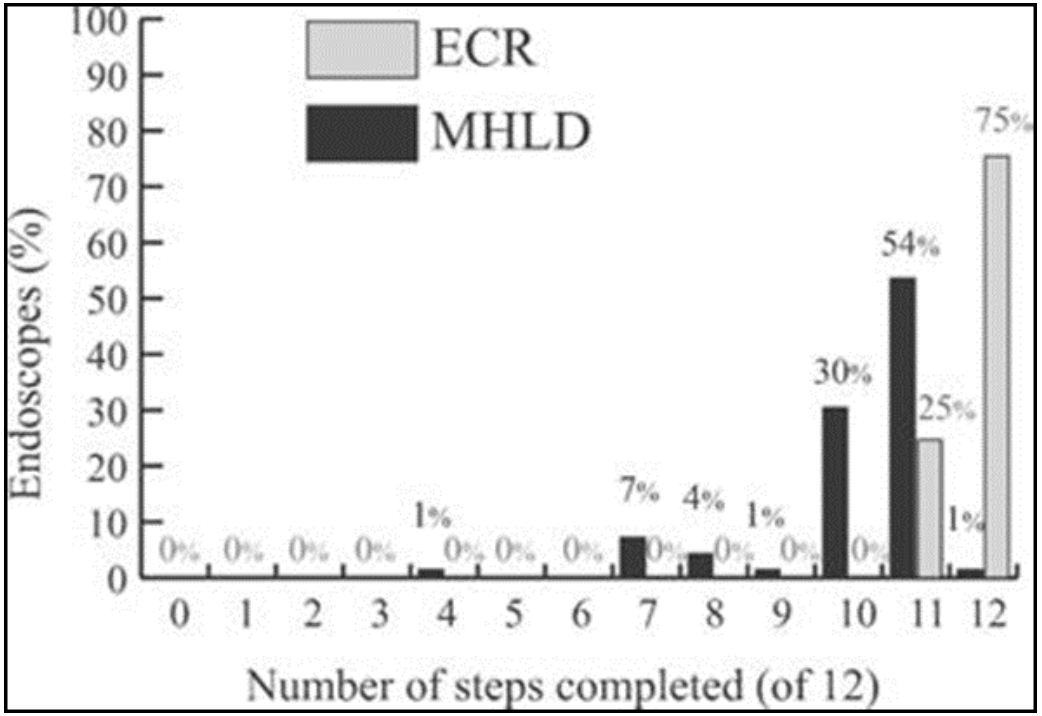
ATP Values from Elevator Channels

Endoscope	Pre-Cleaning	Manual Cleaning	High-Level Disinfection	*P* value
Duodenoscopes	23218.0 (18247.0-34965.0)	531.0 (337.0—675.0)	177.0 (92.0—254.0)	PC→MC <0.01 MC→HLD <0.01
Linear Echoendoscopes	30946.5 (27435.0–38034.0)	562.5 (465.0–693.0)	190.5 (121.0–297.0)	PC→MC <0.01 MC→HLD <0.01

Sethi et al. *Gastrointest Endosc* 2017; 85: 1180-7

Issues with the Manual Steps of Reprocessing

Manual precleaning is tedious and difficult



Personnel completion of endoscope reprocessing steps (p = .000).

Ofstead 2010 *Gastroenterol nurs*; 33:304

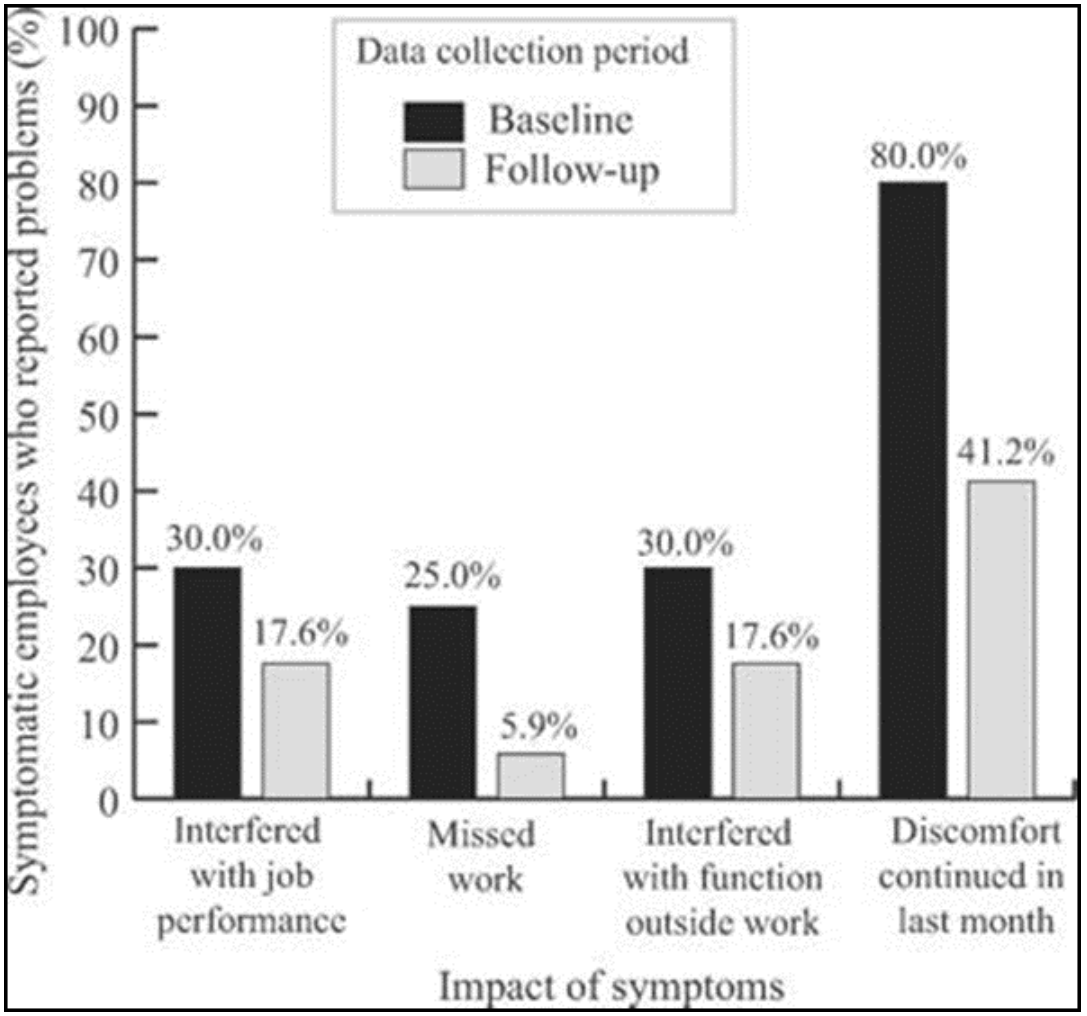
Adherence to all the steps for manual reprocessing

Observed Activity	Steps Completed (%) (n = 69)
Leak test performed in clear water	77
Disassemble endoscope completely	100
Brush all endoscope channels and components	43
Immerse endoscope completely in detergent	99
Immerse components completely in detergent	99
Flush endoscope with detergent	99
Rinse endoscope with water	96
Purge endoscope with air	84
Load and complete automated cycle for high-level disinfection	100
Flush endoscope with alcohol	86
Use forced air to dry endoscope	45
Wipe down external surfaces before hanging to dry	90

Documented Completion of Steps During Manual Cleaning With High-Level Disinfection Reprocessing

Ofstead 2010 *Gastroenterol nurs*; 33:304

Manual cleaning leads to injuries and dissatisfaction



Impact of occupational health problems attributed to reprocessing endoscopes (p = .000).

Ofstead 2010 *Gastroenterol nurs*; 33:304

Are we fighting a lost cause?

Can endoscopes really be disinfected adequately?

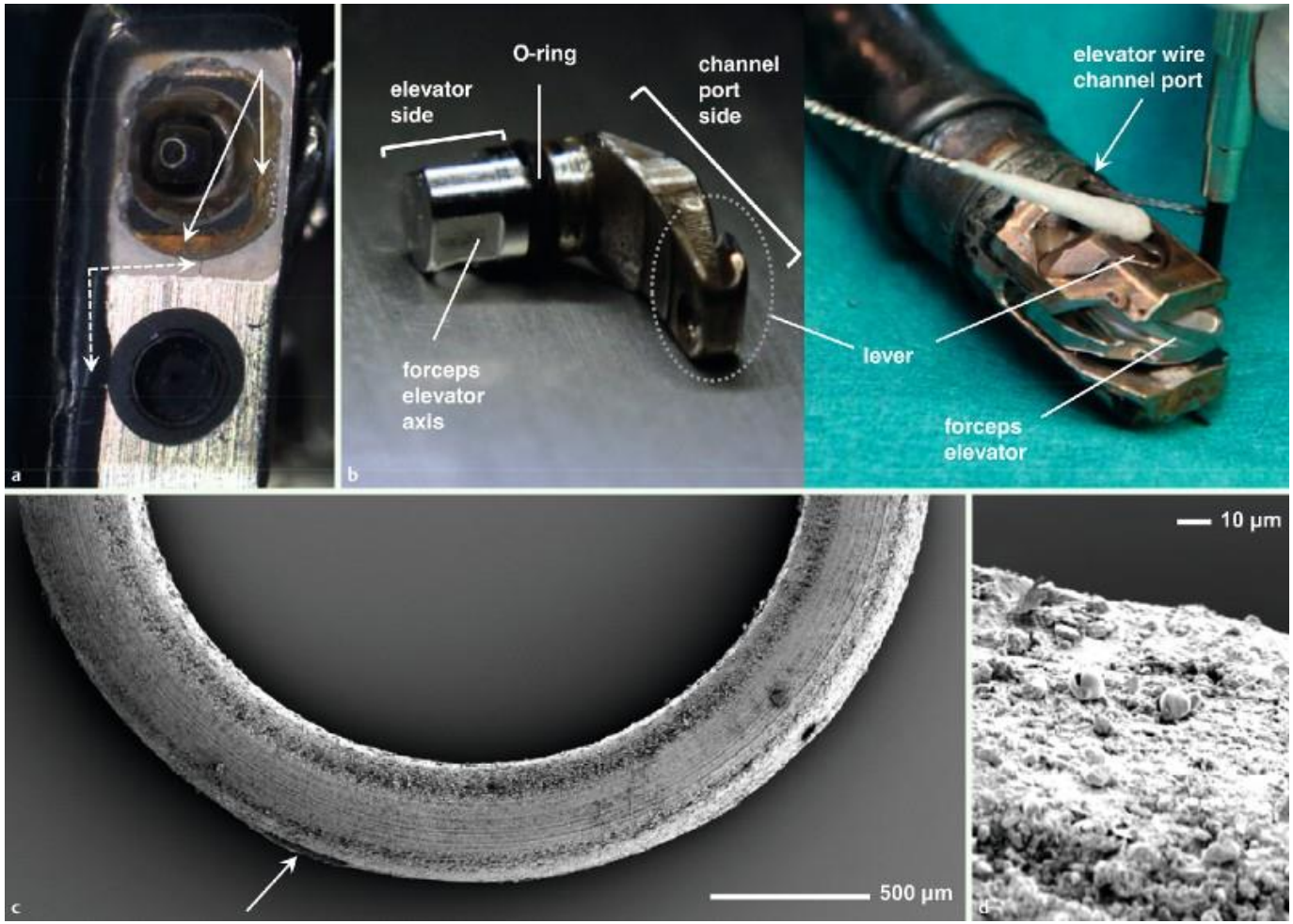
- Enzymatic cleaning according to IFU and brushing of the channels were ineffective at removing all proteinaceous residues from new endoscope channels after just a single contamination
- Rinsing immediately after contamination only led to a slight improvement in decontamination
- Standard high level disinfection was unable to completely remove protein residue (even in brand new channels)
- The residue increases with repeated use and disinfection

Herve and Keevil 2013 *J Hosp Infect*; 83:22-29
Herve and Keevil 2016 *Endoscopy*; 48:609-16

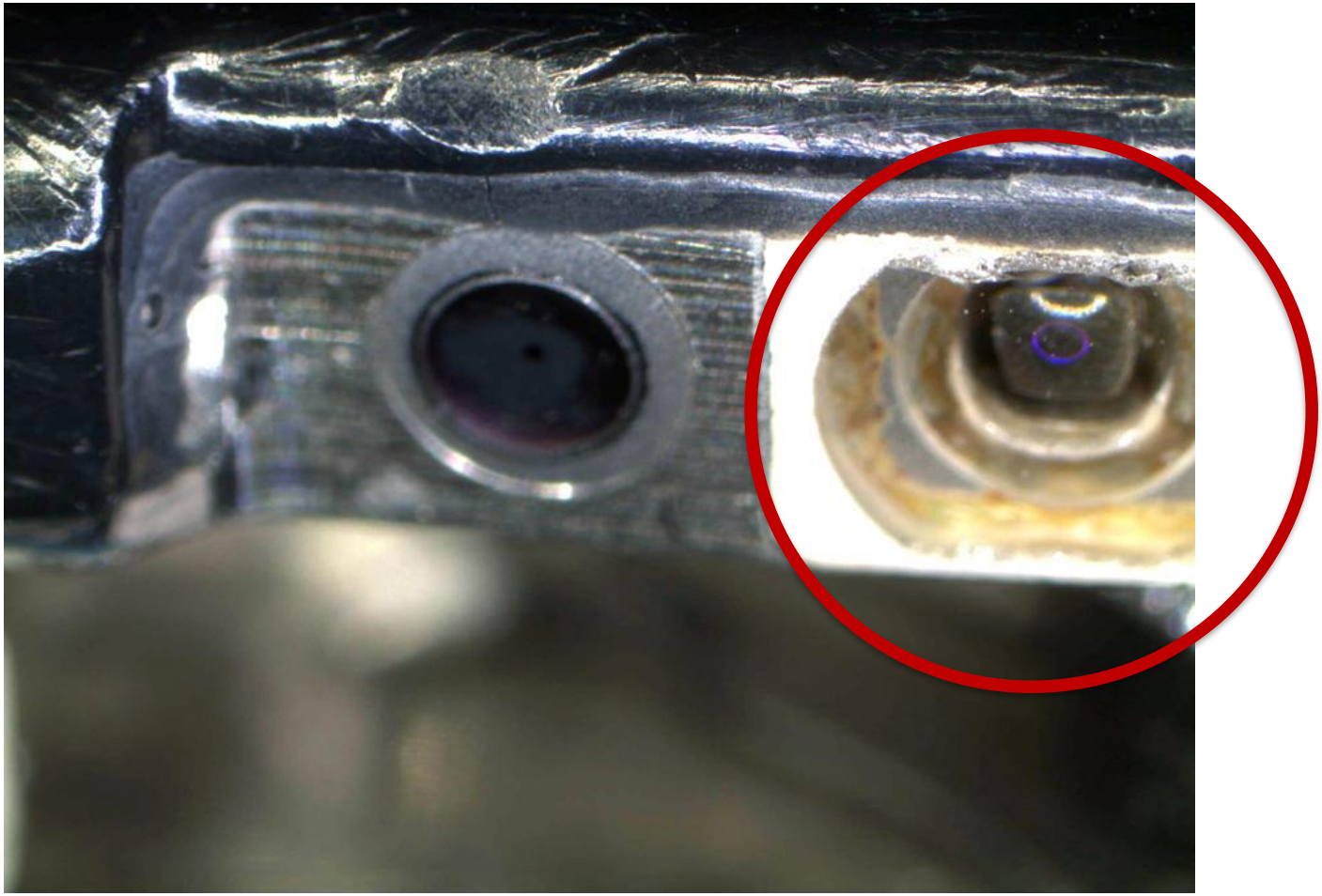
The Dutch Experience

- Highly-resistant Pseudomonas outbreak occurring after two new ERCP scopes were introduced
- The distal part of the endoscope has a fixed cover
  - Access by routine cleaning and brushing difficult
  - Less accessible to liquid chemical sterilant

Verfaillie 2015 *Endoscopy*; 47: 493



Verfaillie 2015 *Endoscopy*; 47: 493



LA Times 2015; Courtesy of Arjo Loeve / Delft University of Technology

BUSINESS

Bacteria survive cleaning efforts in damaged medical scopes, study finds

Damaged ends of colonoscopies show scratched, cloudy lenses and, right, dents and brown debris around channel outlets. (Courtesy of Ofstead & Associates Inc., American Journal of Infection Control)

By Chad Terhune

Ofstead et al 2017
Am J Infect Control; 45: e26-e33

LA Times, January 31, 2017


A
B
C
10/21/2015 14:49 2201996 ©2015 Ofstead & Associates, Inc.
10/27/2015 13:38 2201256 ©2015 Ofstead & Associates, Inc.
10/27/2015 14:13 2201261 ©2015 Ofstead & Associates, Inc.

Endoscope ID	Postcleaning		Post high-level disinfection	
	Protein (µg/mL)	Adenosine triphosphate* (RLU)	Cultures (CFU)	Species identification
AC-1	4	32	0	—
AC-2	11	24	0	—
AC-3	3	16	3	*Staphylococcus* spp; gram-positive rods
AC-4	5	27	1	*Corynebacterium* spp
AC-5	3	13	1	*Bacillus mycoides*
AC-6	3	17	15	*Staphylococcus* spp; *S epidermidis, S hominis*, *Bacillus atrophaeus*
PC-1	4	453	1	Gram-positive rod species
PC-2	6	19	0	—
PC-3	3	57	1	Gram-positive rod species
PC-4	4	11	0	—
PC-5	3	14	0	—
PC-6	4	16	1	*Micrococcus* spp
Gastro-1	5	1353	3	*Micrococcus* spp; *Staphylococcus* spp; gram-positive rod species
Gastro-2	3	1937	1	*Micrococcus* spp
Gastro-3	5	139	0	—
Gastro-4	6	54	2	*Bacillus subtilis*; gram-positive rod species
Gastro-5	3	3138	2	*Micrococcus* spp; *Staphylococcus* spp
Gastro-7†	3	775	1	*Methylobacterium extorquens*

Ofstead et al 2017 *Am J Infect Control*; 45: e26-e33

“We predict that we will continue to see outbreaks associated with ERCP endoscopes and GI endoscopes if we incorporate only the enhanced strategies described above.”

Rutala and Weber 2015 *Infect Control Hosp Epidemiol* 36; 643-8

BUSINESS

FDA to require proof that new devices can be cleaned reliably

FDA officials stand by their decision not to recall any of the devices, known as duodenoscopes, that are at the center of deadly superbug outbreaks at several U.S. hospitals. (Liz Martin /The Gazette)

By Chad Terhune and Melody Petersen · Contact Reporter

Alternative Disinfection/Sterilization Techniques

- Low temperature sterilization technologies
  - Hydrogen peroxide glass plasma
  - Vaporized hydrogen peroxide
- New sterilization technologies
  - Ozone plus hydrogen peroxide vapor
  - Nitrogen dioxide
  - Supercritical CO_2
  - Peracetic vapor
  - Gaseous chlorine dioxide
  - Steam sterilization (only for heat-resistant endoscopes)

Rutala & Weber 2016 *Am J Infect Control*; 44: e47-e51

Alternative Wish List

- Steam sterilizable GI endoscopes
- Disposable sterile GI endoscopes
- Improved GI endoscope design
- Non-endoscopic methods

Rutala and Weber 2015 *Infect Control Hosp Epidemiol* 36; 643-8

Conclusions

- Current culturing techniques are unreliable so any of the enhanced reprocessing measures cannot be reliably tested; negative test results may give a false sense of security.
- Strict oversight of endoscope reprocessing is essential.
- It is incumbent upon manufacturers to develop sterilization techniques that will ensure bacteria-free endoscopes.
  - Improved endoscopic design
  - Sterilizable endoscopes

Continue to see outbreaks associated with ERCP endoscopes and GI endoscopes if we incorporate only the enhanced strategies described above, we predict, we will.


BANG HEAD
HERE