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HICSIG / ACIPC session

GESA Infection Control in Endoscopy
Consensus Statement on
Carbapenemase-Producing Enterobacteriaceae
(CPE)

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Committee

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- GESA CEO: Fiona Bailey (non-voting member)
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- GESA/GENCA set the highest standards in endoscope reprocessing.
- Statement is part 1 of a 2 part process:
 1. Infection Control in Endoscopy on CPE consensus statement
 2. Revision of the comprehensive Infection Control in Endoscopy guidelines



2nd publication on topic 1st under this title
 Published November 1987
 29 pages
 106 references
 Alistair Cowen

Published October 2010 (update 2011)
 63 pages
 303 References
 Andrew Taylor, Di Jones, Richard Everts,
 Alistair Cowen, Beth Wardle
 Mike Whitby, David Fielding, Maryann
 Todman, Lynn Rapley

Reprocessing Steps for Flexible Endoscopes

1. Precleaning
2. Leak testing
3. Manual cleaning
4. Rinse after cleaning
5. Visual inspection
6. High level disinfection
7. Rinse after high level disinfection (Alcohol flush)
8. Drying

Carbapenemase-Producing Enterobacteriaceae (CPE)

- Confer broad resistance to most β -lactam antibiotics including “last-line” carbapenems
- Prevalence of infection has increased over the past decade
- “Urgent public health threat” (CDC 2013)
 - 9000 health-care associated infections each year in USA
- Serious infections: Intra-abdominal infection, pneumonia, UTI, device related infections (approx. 600 deaths/year. CDC 2013)
- Asymptomatic colonisation
- Mortality: 18-48% (Akova M et al. Clin Microbiol Infect 2012)
- Limited treatment options

CPE - scale of problem

Requisite events	Probabilities/Rates
1. Index patient colonized with CPE	1.4 cases per 100,000 inpatient days
2. CPE colonized patient undergoes ERCP	500,000 ERCP /year in US
3. Duodenoscope becomes colonized with CPE despite disinfection	1.9% of duodenoscopes colonized with pathogenic bacteria despite disinfection
4. Patient has ERCP via contaminated duodenoscope and acquires CPE	14.4% transmission rate
5. Colonized patient becomes actively infected with CPE	53.3% of CRE transmitted cases

ACSQHC Recommendations for the control of CPE: A guide for acute care health facilities 2017

- Recommendations

- 1.1.2 The health facility should have in place systems for effective patient screening; including a system to screen and identify patients at risk for CPE carriage on admission to the health facility (see Section 2)
- 1.1.5 The health facility should have in place an alert system for colonised or infected patients to ensure that transmission-based precautions are used for subsequent admissions.
- 1.1.6 The health facility should educate staff on how to respond to cases of CPE. This would include information on the nature of CPE, standard and transmission-based precautions (contact precautions), use of personal protective equipment, cleaning and disinfection, and available resources, such as single rooms or dedicated patient equipment.
- 1.3.2 Routine environmental cleaning should include cleaning of the patient environment on a daily basis; this includes frequently touched surfaces and patient care equipment. Frequently touched surfaces in high-risk units should be cleaned at least twice daily. A cleaning schedule and regular cleaning audits should be implemented.
- 1.4.1 Health facilities should implement policies and procedures for reprocessing of all endoscopes and bronchoscopes. **Particular attention should be given to duodenoscopes used for ERCP procedures, which have been linked to CPE outbreaks internationally.**
- 1.4.2 Health facilities should implement quality control measures to ensure that reprocessing is undertaken in line with in the *Australian guidelines for the prevention and control of infection in healthcare* (Section B1.5). This may take the form of regular microbiological testing of endoscopes, evaluation or biological marker testing, such as adenosine triphosphate (ATP) testing.

Delphi Methodology

- Statements formulated and distributed to committee members (3 pairs of two)
- Extensive literature review
- Statements voted-on anonymously on 2 occasions:
 - 1st electronically (Survey Monkey)
 - 2nd at the face-to-face meeting ([www. Mentimeter.com](http://www.Mentimeter.com))

Statement Grading and Recommendation

Level/grade	Description
Evidence level	
I-A	Evidence from meta-analysis of RCTs
I-B	Evidence from at least 1 RCT
II-A	Evidence from at least 1 controlled study without randomization
II-B	Evidence from at least 1 other type of quasi-experimental study
III	Evidence from nonexperimental descriptive studies, such as comparative studies, correlation studies, and case-control studies
IV	Evidence from expert committee reports or opinions or clinical experience of respected authorities, or both
Recommendation grade	
A	Directly based on category I evidence
B	Directly based on category II evidence or extrapolated recommendation from category I evidence
C	Directly based on category III evidence or extrapolated recommendation from category I or II evidence
D	Directly based on category IV evidence or extrapolated recommendation from category I, II, or III evidence
Voting on recommendation	
A	Accept completely
B	Accept with some reservation
C	Accept with major reservation
D	Reject with reservation
E	Reject completely

Adapted from Shekelle et al.²

Statements

- Many of the recommendations in the statements reflect procedures and policies already widely practised in endoscopy units around Australia
- Aim: To further raise the standard of endoscopic reprocessing in Australia to reduce the risk of CPE transmission.

The statements are:

- Evidence based
- Considered (Multi-disciplinary assessment)
- Decisive
- Preventative

Statement 1:

Endoscopic procedures should only be performed in centres where adequate facilities for safe cleaning and reprocessing are available for appropriately trained staff to reprocess endoscopes

- Accept completely x 6
- Evidence level: IV
- Recommended Grade: D

Statement 1 Comments

- Global statement:
 - Focussed on the facility irrespective of size or case numbers
 - Essential starting point in ensuring the highest reprocessing standards
 - Current reprocessing techniques are not optimal
- Necessitates adherence to:
 - The statements in this document
 - ICEndoscopy guidelines document
 - Australasian Facility Healthcare standards checklist for infection control
(www.healthfacilityguidelines.com.au/full-guidelines)
- Expert opinion, inferred from extensive literature base

Statement 2

The most important component of decontamination is timely and meticulous cleaning prior to disinfection

- Accept completely x 6
- Evidence level: IIb
- Recommendation grade: B

Statement 2 Comments

1. Clean it, clean it, clean it!!”
2. “If it’s not clean it can’t be high level disinfected/sterilised”
3. Every step of the reprocessing procedure must be completed accurately and consistent with manufacturers’ instructions

NB: Increased attention to the drying phase, but cleaning remains the most important component

Instruments with Complex Tips: Difficulties with Cleaning

- Duodenoscopes:
 - First known transmission of CPE at ERCP in the USA was attributed to insufficient cleaning practices
 - At least 8 subsequent reported outbreaks despite apparently appropriate and optimal reprocessing technique (Petersen BT GIE 2017)
 - Similar reports from Europe
- Linear echoendoscopes:
 - 4.2% primary cultures: positive for pathogenic gram-negative bacilli (Chapman CG et al. GIE 2017)

Statement 2: “Timely”

- After immediate bed-side flushing, cleaning of the instrument should commence within 15 minutes
 - When manual cleaning is undertaken, AFER HLD should commence within 45 minutes.
- French guidelines:
 - Manual clean within 10 minutes and AFER within 45 minutes
(Saviuc P et al. Infect Control Hosp. Epidemiol 2015)
- Outbreak of KPC-K pneumoniae
 - Delayed ‘pre-wash’ cleaning of endoscope
 - Inadequate drying
(Naas et al. J Antimicrob Chemother 2010)

Statement 3

The use of a TGA-approved automated flexible endoscope reprocessor (AFER) is mandated for reprocessing in accordance with manufacturers' instructions.

- Accept Completely x 6
- Evidence level: IIb
- Recommendation grade: B

Statement 3 Comments

- AFER's are widely used in endoscopic units throughout Australia
- Statement 3 refers to automated HLD, not automated cleaning
- "There is no standardisation without mechanisation"
- Increasing automation increases compliance with reprocessing protocols

AFER vs manual Reprocessing

- AFER cleaning versus manual cleaning:
 - Multisite observational study
 - AFER vs Manual cleaning: 75.4% versus 1.4% compliance
(Ofstead CL et al. Gastroenterol Nurse 2010)
- Automated versus manual cleaning and Biofilm growth (China):
 - 92.3% of hospitals that grew biofilm used manual cleaning
 - If no biofilm 50% used manual cleaning (p 0.001).
 - Formulation of biofilm may be related to reuse of detergent, manual cleaning and incomplete drying
(Ren-Pei W et al. Am J Infect. Control 2014)
- AFER with automated cleaning:
 - 98.8% of surfaces and 99.7% of lumens met or surpassed the cleaning endpoints set for protein, haemoglobin and bioburden residuals
(Alfa et al. BMC Infectious Diseases 2010)

Statement 4

Quality control is fundamental to the delivery of efficient and safe endoscopic procedures, and incorporates proof of process with adequate staff training (including continuing education, professional development and assessment), documentation and microbiological surveillance cultures.

- Accept completely x 6
- Evidence level: IIb
- Recommendation grade: B

Statement 4 Comments

- Key to the performance of optimal endoscope reprocessing is monitoring and documentation of:
 - Each step of the reprocessing procedure (aided by automation)
 - Staff education, reassessment of competency
 - Microbiological cultures
- CDC pilot infection control audit: 67 centres: 28% not compliant with uniform endoscope reprocessing
(Schaefer MK et al JAMA 2010)
- “All centers using duodenoscopes should “closely evaluate whether they have the expertise, training and resources to implement one or more of several options,” including microbiologic culturing.
(FDA 2015)

Microbiological Cultures

- Retrospective series, France, teaching hospital
- 2006-2014: 846 samples:
 - Compliance 86%
 - 118 samples (14%) cultured indicator organisms
- Microbiological surveillance is indispensable to monitoring reprocessing, reinforces good practice and detects endoscopes requiring maintenance
(Saviuc P et al. Infect Control Hosp Epidemiol 2015)

Statement 5

Patient-to-patient transmission of CPE by endoscopic instruments can result in serious illness, and its prevention must be a priority of every endoscopic unit.

- Accept completely x 6
- Evidence level: III
- Recommendation grade: D

Role of Endoscopy in CPE Outbreak

- Dec 2012-Jan 2013: CP *K pneumoniae*
- University hospital in Berlin
- Patient 1 (gut flora) transmitted to patients 2-5 in ward A.
- Patient 3 ERCP-contaminated duodenoscope-contaminated patient 6
- Patient 6-patient 7 and 8 on ward B
- Duodenoscope transmitted to patients 9-12
- ? Reprocessing issue

(Kola et al. Anti-microbial resistance and infection control 2015)

Statement 5(a)

Informed consent for patients undergoing endoscopic procedures with duodenoscopes or linear echoendoscopes must include disclosure of the risk of CPE colonisation or infection.

- Accept completely x 6
- Evidence level: IV
- Recommendation grade: D
- “Healthcare providers should inform patients of the benefits and risks associated with ERCP procedures” (FDA Safety communication 2015)
- An example consent statement can be provided upon request

Statement 5 Comments

- Endoscopic procedures have been reported to be the mode of transmission of CPE
 - Gastrosopes, duodenoscopes, echoendoscopes
- CPE may colonise exposed patients and/or result in clinical infections
- Infections with CPE are associated with a **mortality rate** of up to **48%** in reported series.

Statement 6

Reported endoscopic transmission of CPE has been predominantly related to instruments with complex tips (e.g. duodenoscopes and linear echoendoscopes), but all endoscopic instruments may transmit CPE.

- Accept completely x 5, Accept with some reservation x 1
- Evidence level: III
- Recommendation grade C

Transmission without known reprocessing failures

- Gastroscope: 6/10 patients colonised, 2 clinical infections
(Naas T, et al. J Antimicrob Chemother 2010)
- Bacteria detected in 9/15 (60%) of patient-ready endoscopic instruments
 - Gastroscopes n=2, colonoscopies n=3, bronchoscopes n=4
(Ofstead CL et al. [Tool Kit] Am J Infect Control 2016)
- Ertapenam-resistant K pneumoniae
 - Endoscopy an independent risk factor to acquisition of ER-Kp
(Orsi GB et al. J Hosp Infect 2011)
- Viable microbes recovered from 64% of scopes after HLD
(Ofstead CL et al. Am J Infect Control 2015)

Statement 7

Instrument reprocessing and environmental management protocols need to be augmented in an effort to reduce the risk of CPE.

- Accept completely x 6
- Evidence level: IIb
- Recommendation grade: C

Statement 7 Comments

- Reduce the transmission of all microorganisms (Including other MRO's)
- Existing protocols target planktonic organisms
- Our understanding of biofilm has evolved:
 - Develops on endoscope channels
 - May harbour microorganisms
 - It is very difficult to detect
 - It is very difficult to remove
 - Instrument drying important in preventing its formation

Biofilm

- “Build-up biofilm” model:
 - Mimics the cumulative effect of reprocessing protocols on flexible endoscopes
 - Associated with survival of a wide range of microorganisms
 - “Assurance of effective high-level disinfection may decrease if build-up biofilm develops within the flexible endoscope channels”
(Alfa et al. BMC Infect Dis 2009)
- Viable microorganisms in endoscope channel biofilm survive reprocessing (confocal microscopy)
(Neves et al GIE 2015)
- *E coli* and *P aeruginosa* biofilm model:
 - If biofilm accumulates within endoscope channels during repeated rounds of reprocessing, then neither the detergent nor high level disinfection will provide the expected level of bacterial removal
(Luciano C et al. Am J Infect Control 2016)

Statement 7(a)

All endoscopic instruments, except those in sterile packaging, should be stored in TGA-approved forced-air drying cabinets.

- Accept completely x 5, Accept with some reservation x 1
- Evidence level: IIb
- Recommendation grade: C

Drying

- Alfa M and Sitter DL. found that the concentration of bacteria and the ratio of gram-negative to gram-positive bacteria were significantly higher at 48 hours than at two hours in the group of duodenoscopes that were less thoroughly dried.
 - Nearly half of the duodenoscopes were contaminated at 48 hours.
 - None of the 19 duodenoscopes that received the extra 10 minutes of forced air drying showed any microbial growth at 48 hours.
 - Adequate drying prevented bacterial overgrowth.
(J Hosp Infect 1991)
- Single and dual species biofilm model:
 - An in-vitro biofilm model was applied to mimic biofilm formation inside endoscope channels
 - Routine cleaning procedures do not remove biofilm reliably from endoscope channels if the adequate drying procedure is not applied
(Kovaleva J et al. J Hosp Infect 2010)

Drying

- Correlation between the growth of bacterial biofilm in flexible endoscopes and endoscope reprocessing methods
 - 79 endoscope channels. 66 hospitals in China. Electron-microscopy
 - Biofilm detected: Biopsy/suction: 36/66 (54.6%), Air/water: 10/13 (76.9%)
 - Biofilm build up may relate to drying
(Ren-Pei W et al. AM J Infect Control 2014).

Timeline

- Forced-air drying cabinets should be operational by January 1, 2022
 - Units should commence planning now for drying cabinet installation
- Coincides with the compliance date for Australian Standard 4187
(Reprocessing of reusable medical devices in health service organisations)
 - Drying cabinets are already referred to in this document

Statement 7(b)

Endoscopes stored in TGA-approved forced air drying cabinets may be used for a period of up to 7 days without reprocessing, unless otherwise stated by the manufacturer.

- Accept completely x 6
- Evidence level: IIb
- Recommendation grade: C

Safe storage time for reprocessed flexible endoscopes: a systematic review

Table 5 : Proportion of contaminated endoscopes (defined as the presence of any pathogen and > 10 CFU in the 7 studies that sampled all channels) for length of time and type of storage

Schmelzer M et al. JBI Database of Systematic Reviews and Implementation reports 2015

Proportion of contaminated endoscopes (number of contaminated endoscopes/total endoscopes sampled)													
Study	Length of storage (days)												
	< 1	2	3	4	5	7	14	16	21	28	42	56	
Conventional storage													
Alfa et al., 2012 ¹⁷		20/141 ^b											
Brock et al., 2015 ⁴³	1/10 ^c					1/10 ^d	1/10 ^e		2/10 ^f				
Foxcroft et al., 2008 ²⁴	0/15		1/15 ^g			0/14							
Ingram et al. 2012 ⁴⁴	0/4		0/4		0/4	0/4	0/4		0/4	0/4	0/4	0/4	
Riley et al., 2002 ²⁸	0/5					0/5							
Specialized drying cabinet													
Foxcroft et al., 2008 ²⁴	0/32		0/32										
Grandval et al., 2013 ¹⁸			0/41										
Wardle, 2007 ²⁵	0/8		0/21	0/16	0/2	0/13		0/6					
Total number of samples													
Total number of samples (442)	74	141	113	16	6	46	14	6	14	4	4	4	4

- a) Foxcroft et al. had one group in conventional storage and one group in the specialized drying cabinet.
- b) Limit of detection for cultures was 10 CFU/mL.
- c) All microorganisms were less than 10 CFU/mL of typical skin and environmental contaminants except for 1 CFU/ mL of *Aureobasidium pullulans* which was only present on the biopsy channel of a colonoscope on the first day.
- d) All micro-organisms were 1 CFU/mL or less of typical skin and environmental contaminants except for 1 CFU/mL of *Enterococcus* which was cultured from the biopsy channel of one colonoscope on Day 7.
- e) All micro-organisms were 1 CFU/mL or less of typical skin and environmental contaminants except for α -hemolytic streptococcus that was only cultured with the thio broth (detects <1 CFU) on the biopsy channel of a gastroscope on Day 14.
- f) All typical skin and environmental contaminants were 1 CFU/mL except for 49 CFU of *Micrococcus*. The only pathogen was 1 CFU/mL of *Candida parapsilosis* which was cultured from the biopsy channel of a duodenoscope on Day 21.
- g) One gastroscope had 1 CFU of *Streptococcus* and 1 CFU of *Propionibacterium*.

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- g) One gastroscope had 1 CFU of *Streptococcus* and 1 CFU of *Propionibacterium*.

Statement 8

When endoscopic procedures are performed on known CPE-positive patients, specific environmental and instrument reprocessing protocols should be utilised.

- Accept completely x 6
- Evidence level: III
- Recommendation grade: C

Specific Guidelines for Endoscopy Units:

A known CPE positive patient having an endoscopic procedure

- All staff should strictly adhere to contact precautions.
- CPE positive patients should have as little contact as possible with other patients in the endoscopy unit.
- Endoscopy rooms should be prepared to minimise potential aerosol surface contamination.
- Safe work practices associated with standard precautions must be applied to all patients and the environment (especially environmental cleaning and instrument reprocessing)

Statement 8(a)

Following an endoscopic procedure on a known CPE-positive patient, the instrument should undergo microbiological testing and be quarantined until a negative culture result is obtained at 48hours.

- Accept completely x 6
- Evidence Level: III
- Recommendation grade: C

Statement 8(a) Comments

- Duodenoscope cultures and 48 hour quarantine a component of effective Seattle CPE outbreak resolution.
(Ross et al. GIE 2015)
- 48 hours is a sufficient time interval for Enterobacteriaceae culture
- Will be an essential component of outbreak investigation
 - Transmission tracking

Statement 9

All cases of suspected CPE transmission related to endoscopic procedures should be investigated by an outbreak management team.

- Accept completely x 6
- Evidence level: IV
- Recommendation grade: D

Statement 9 Comments

- If transmission is identified, implement an outbreak management plan, establish effective communication between laboratory services and infection control team, consider targeted environmental screening, minimise patient movement into and out of the unit as directed by infection control team
(ACSQHC *Recommendations for the control of CPE. A guide for acute care health facilities.* 2017)

Summary

- Consensus statements:
 - Offer specific guidance in addition to the Infection Control in Endoscopy guidelines
 - Multi-society assessment
 - Considered and evidence based
 - Preventative
 - Specific to CPE
 - Future potential to extrapolate to other MRO's
 - Aim to ensure the highest possible standards in flexible endoscope reprocessing thereby optimising patient safety.

Conclusion

- All units should aim for compliance with the recommendations in these statements as soon as possible
- Except compliance date for forced air drying cabinets:
 - January, 2022
 - Units should commence processes as soon as possible to achieve compliance

Acknowledgements

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Consent Example

- “The endoscopic device used for your procedure has undergone high level disinfection in accordance with the highest international standards. Despite this, there is a very small risk of transmission of infectious microorganisms, including multi-antibiotic resistant bacteria (“Superbugs”) by this endoscopic device. Superbugs can result in life threatening infections. The exact risk of transmission is not known but is very low at approximately 1 in 1.8 million procedures.”