Multidrug Resistant Outbreaks After Endoscopy

Rapidly increasing numbers of outbreaks of multidrug resistant bacteria, including carbapenem resistant enterobacterial (CRE) have been reported in the United States and Europe as these bacteria become more common in hospitals and the community. GESA/GENCA have established a working party of the Infection Control Committee to review the problem and make recommendations.

The Working Party has reviewed the literature, consulted with experts in microbiology, biofilms, detergents, surface cleaning, manufacturers, and other stakeholders including government committees and the professional societies. Members made a site visit to a manufacturer’s facility, the results of surveillance cultures of endoscopies in Australia were reviewed and the outcomes presented to the FDA Meeting in May 2015.

Initial recommendations were sent to all GESA and GENCA members in September 2015 and circulated widely to other stakeholders for comment.

Research into multidrug resistant outbreaks is a rapidly evolving field. These recommendations will be updated in 2019 or earlier as relevant new information is published.

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SUMMARY OF RECOMMENDED CHANGES

GUIDELINE CHANGES RELATED TO CRE

1. Be aware of the CRE status of your hospital. Have a unit Standing Committee with regular access to a microbiologist and/or Infectious Diseases specialist.

2. Ensure that known CRE positive patients are notified to the unit BEFORE arriving at the unit.

3. CRE infected patients or those at high risk who are yet to be cultured should be examined last on the list and managed in isolation from other patients with use of a separate toilet.

4. Decontaminate procedure room after the endoscopy procedure as per specific protocols for terminal cleaning of contaminated areas.

5. Sinks, taps and plumbing should comply with the standards in the Australasian Health Facility Guidelines to minimise the risks of spray from drains in sinks or overflow of waste water from blocked pipes.

6. The emergence of CRE is another compelling reason to meticulously follow standard infection control procedures including hand hygiene and the use of gloves and impervious gowns for each procedure. Endoscopy units should provide regular education and assessment of compliance with hand hygiene and environmental decontamination.

CHANGES TO LIMIT BIOFOILM FORMATION AND GROWTH

REPROCESSING AND STORAGE (Note duodenoscopes are considered separately)

1. Precleaning must be carried out IMMEDIATELY after use.

2. Manual cleaning must be carried out PROMPTLY (promptly in these Guidelines means less than 30 minutes) after pre-cleaning.

3. Reprocessing in AFERs which have FDA & TGA approved mechanical cleaning must be undertaken promptly after pre-cleaning.

4. After manual cleaning of the endoscope, machine or manual disinfection must be undertaken promptly.

5. After disinfection by any means the endoscope must have prompt drying and storage in an approved drying cabinet. (see Drying Cabinets)

Endoscopes must remain in approved drying cabinets until next patient-use.
GUIDELINE CHANGES FOR DUODENOSCOPES

Endoscopy units performing ERCP should:-

1. Consider if they are performing ERCP procedures with sufficient frequency to continue offering this clinical service.

2. Have dedicated staff reprocessing duodenoscopes who are aware of, and have undertaken specific training in, the particular problems of cleaning, disinfecting and obtaining tip samples for bacteriological surveillance.

3. Perform MONTHLY bacteriological surveillance tip cultures (i.e. as part of the existing monthly culture of all channels).

4. Have appropriate risk notification of possible MDRO transmission in their Informed Consent information.

5. Send duodenoscopes for regular yearly maintenance.

6. Have instrument channels and “O-rings” replaced yearly

Endoscope drying

IT IS CRITICAL THAT FOLLOWING MANUAL OR AFER REPROCESSING ALL ENDOSCOPES ARE PROMPTLY TRANSFERRED TO AN APPROVED ENDOSCOPE DRYING CABINET AND FORCED AIR DRYING COMMENCED. THIS SHOULD CONTINUE UNTIL THE ENDOSCOPE IS USED AGAIN OR STORAGE PERIOD HAS ELAPSED. THIS ALSO APPLIES TO ENDOSCOPES REPROCESSED IN AFERs WITH A DRYING CYCLE REGARDLESS OF MANUFACTURER’S CLAIMS.

Endoscope and AFER maintenance

1. Endoscopes with positive surveillance bacterial cultures with organisms of concern detected should be sent for service (unless there is an alternative explanation eg staff error).

2. Endoscopes should have preventative maintenance examination at least yearly.

3. Regular replacement of channels during preventative maintenance should be considered

INFECTION CONTROL IN ENDOSCOPY GUIDELINES HAVE BEEN MODIFIED SIGNIFICANTLY. IMMEDIATE IMPLEMENTATION IS ADVISED.

These changes are interim measures that may be further altered as and when current and projected research results become available.
Background:

The changes to the infection control guidelines have arisen based on the rapid and dramatic increase in outbreaks of endoscopy associated infections (FDA, 2015). There is a need for an urgent response to address this risk. The FDA MDR reports show the number of infections after ERCP increased from 8 in 2012, 15 in 2013, 64 in 2014 to 30 in the first six weeks of 2015. (Fig 1)

FDA Report May 2015 Executive Summary

Figure 1. Number of MDR reports 1, 2, 3 received for duodenoscopes associated with patient infection, patient exposure or device contamination

1. Each MDR may report events associated with one or more patients
2. 2015 year only includes data received as of February 17, 2015. That is these reports are for just the first six weeks of 2015
3. Reports received prior to 2010 (n=4) not shown in this figure.

Many of the outbreaks have occurred in the United States but there are reports from various parts of Europe and elsewhere. A total of 5% or less of outbreaks in the USA have been reported in peer reviewed literature (Dirlam Langlay et al, 2013). The paucity of reports from less developed countries is likely to be due to failure of detection and reporting rather than a true absence.

Many of the outbreaks have been associated with ERCP; however bronchoscopy, gastroscopy, EUS and cystoscopy have all been reported as sources of outbreaks.

It is critical to appreciate that most of the recent outbreaks have occurred with CARBAPENEM-RESISTANT ENTEROBACTERIAEAE (CRE) being the responsible organism (see section on CRE). Transmission of CRE often results in colonisation that is asymptomatic for many months before causing clinical infection. Invasive clinical infections
due to CRE have a 40 – 50% mortality rate. The hospital and community incidence of CRE is rapidly increasing across the world and is particularly common in Greece, India, China and many South East Asian countries.

The committee is aware the significant capital costs of the recommended guideline changes may challenge the viability of small or occasional services. However some changes, drying cabinets and routine maintenance, are probably cost effective; the overall cost of delivering endoscopic services may not increase and may even decrease. They will also call into question the appropriateness of undertaking Endoscopic Ultrasound and ERCP in units that do not have dedicated reprocessing staff who are fully trained in the particular problems and risks of reprocessing and sampling ultrasound endoscopes and duodenoscopes. While recognizing the inconvenience and cost pressures, the committee believes that there is no other option in the face of rapidly rising numbers of outbreaks of a clinical disease associated with a high mortality and an unknown rate of asymptomatic transmission.

In order to understand the recommended changes and underlying principles of the changes it is necessary to examine two areas in some detail:

1. CRE
2. Biofilms

**CRE & NOSOCOMIAL INFECTION**

The most common bacteria in recent reports of outbreaks following ERCP are Carbapenem-Resistant Enterobacteriaceae (CRE). The Family Enterobacteriaceae includes the following genera; Escherichia, Shigella, Salmonella, Klebsiella, Enterobacter, Serratia, Citrobacter, Proteus, Providencia and Morganella. The carbapenem group of antibiotics (imipenem, meropenem, doripenem, and ertapenem) offer broad antibiotic cover and are effective treatment for severe infections. Carbapenem resistant Enterobacteriaceae (CRE) develop antibiotic resistance by acquiring the genes encoding carbapenemase enzymes or less commonly other mechanisms (e.g. Porin loss). Within the Enterobacteriaceae family carbapenemases are most commonly found in *Klebsiella pneumoniae* and *Escherichia coli*, although they have also been reported in other genera of gram negative bacteria such as *Pseudomonas spp.* and *Acinetobacter spp.*

The genes encoding for carbapenemase are found on mobile genetic elements (plasmids) together with genes that code for resistance to other classes of antibiotics (aminoglycosides, fluoroquinolones and cephalosporins) making CRE multi-drug resistant. There are a number of different types of carbapenemase found in CRE: Table 1 shows the five most important.
### Table 1  Characteristics of most important carbapenemases

<table>
<thead>
<tr>
<th>Enzyme</th>
<th>Geographic Distribution</th>
</tr>
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<tbody>
<tr>
<td><strong>KPC</strong></td>
<td>First reported from the USA in 1996. Now prevalent in hospitals on the United States Eastern seaboard, Israel, Greece, China and Latin America.</td>
</tr>
<tr>
<td><em>Klebsiella pneumoniae</em> carbapenemase</td>
<td></td>
</tr>
<tr>
<td><strong>NDM</strong></td>
<td>Widespread in <em>Enterobacteriaceae</em> from Indian sub-continent hospitals and also appear to be spreading in the community. Detected in hospital outbreaks in USA</td>
</tr>
<tr>
<td>New Delhi based metallo-β-lactamase</td>
<td></td>
</tr>
<tr>
<td><strong>VIM</strong></td>
<td>Scattered globally with increased prevalence in Greece.</td>
</tr>
<tr>
<td>Verona integrin-encoded metallo-β-lactamase</td>
<td></td>
</tr>
<tr>
<td><strong>OXA</strong></td>
<td>Europe (in particular Turkey), Israel and northern African countries</td>
</tr>
<tr>
<td>Oxacillinases</td>
<td></td>
</tr>
<tr>
<td><strong>IMP</strong></td>
<td>Scattered worldwide, no clear associations. Endemic in Australia.</td>
</tr>
<tr>
<td>Imipenemase</td>
<td></td>
</tr>
</tbody>
</table>

(W.A Guidelines)

*Klebsiella pneumoniae* is the most commonly reported bacteria in outbreaks following ERCP. Tzovelekis et al (2014) have recently published an excellent review on Klebsiella and other CRE.

*Klebsiella pneumoniae* is a common colonizer of the gastrointestinal tract, skin and nasopharynx in humans and other mammals, and is also found in various environmental niches (soil and water). In the past it was considered an important causative agent of community acquired pneumonia, however this has become rare recently. In the early 1970’s both the epidemiology and spectrum of infections caused by *K. pneumoniae* changed dramatically when this bacterium was established in the hospital environment and became a leading cause of nosocomial infections. *K. pneumoniae* is a notorious “collector” of multi drug resistant plasmids. The acquired drug resistance enables *K. pneumoniae* to persist and spread rapidly in hospitals. During the 1970s to 1980s plasmids encoding resistance to the new cephalosporins were acquired by many Enterobacteriaceae. The bacteria produced lactamases, the most resistant had extended spectrum beta lactamases (ESBLs). Later again resistance to fluoroquinolones developed. This left carbapenem as the first choice drug for treatments caused by *K. pneumoniae*.
However 15 years ago there was a rapid dissemination of *K. pneumoniae* strains producing carbapenemase encoded by transmissible plasmids. These CRE caused serious infections in debilitated and immunocompromised patients with a mortality rate ranging from 24 to 70% depending on the patient population.

Gram negative bacteria prefer moist and damp sites. However recent reports suggest both *E.coli* and *Klebsiella spp.* may survive more than a year on dry surfaces (Kramer et al, 2006). The health care environment is an important reservoir for these gram negative bacteria. Studies have found *E.coli* and *Klebsiella spp.* on bedside tables, chairs, floors and from bathroom sites including sinks, shower fittings and toilet seats. These environmental coliforms were indistinguishable from those colonising patients whose environment was sampled (Lemmen et al, 2004).

Traditional sites for *Klebsiella spp.* and *E.coli* in hospitals have been those constantly or intermittently exposed to water. This includes hand wash basins, sinks, sluices, showers, baths and toilets. Bacterial biofilm builds up in the plumbing components, including taps, water filters and sink traps underneath water outlets. Biofilm forming *Klebsiella pneumoniae* have been shown to be more likely to produce extended spectrum beta lactamases (Yang et al, 2008).

**Antibiotic resistance, virulence and transmission**

Drug resistant bacteria have a selective advantage in transmission to and colonization of patients treated with broad spectrum antibiotics. It had been thought that the genetic and phenotypic changes that confer resistance come at a cost and result in reductions in intrinsic virulence and transmission. However a recent study (Roux et al, 2015) has found the opposite: antibiotic resistance is associated with increased virulence.

Roux et al (2015) performed a comprehensive analysis of the genetic basis of *P. aeruginosa* virulence in an animal model and found that genes that bestowed antibiotic resistance provided a positive *in vivo* fitness advantage. These findings were confirmed in two other bacterial species.

In the absence of selective pressure from antibiotics drug resistant bacteria may still out-compete less resistant but also less fit strains for environmental persistence, host infectivity and transmission. The increased virulence in antibiotic strains in animal models suggests that the difficulty in treating clinical infection is due to both the problem in selecting appropriate antibiotics plus increased virulence. This study raises the possibility that bacteria that are both drug resistant and more pathogenic may be establishing themselves as the predominant organism able to infect at-risk humans. Investigations of outbreaks after endoscopy have confirmed CRE colonises exposed patients and that colonisation persists. In Illinois NDM producing *E.coli* colonised 23 of 58 patients undergoing ERCP with a contaminated duodenoscope and these patients remained colonised six or more months after exposure (Epstein 2014).
Environmental survival

CRE has been found in hospital waste water in Brazil and China (Munoz-Price et al, 2013). In two English hospitals colonisation of the waste water system resulted in an outbreak of multidrug resistant (VIM producing) *Pseudomonas aeruginosa* (Breathnach et al, 2012). A total of 85 infections occurred between 2005 and 2011; there were 34 deaths, a 40% mortality rate. The outbreak was controlled with enhanced cleaning and decontamination and replacement/refurbishment of taps, sinks and toilets emphasising the importance of hospital design and engineering in preventing infections. Outbreaks of CRE have been described in intensive care units in Australia (Peleg et al, 2005; Kotsanas et al, 2013). One outbreak was traced to a sink that had the tap placed directly above the drain causing spray from the drain to contaminate the sink. Attempts to disinfect the drain were unsuccessful and the outbreak only resolved when the sinks and plumbing were replaced with new fittings complying with Australasian Health Facilities Guidelines standards (Kotsanas et al, 2013).

Bojer reported a persistent outbreak of ESBL *K. pneumoniae* in a Danish hospital, possibly related to flexible endoscopes (Bojer et al, 2010). They investigated the factors that increased the resistance to environmental stresses that could explain the persistence of the bacteria in the nosocomial environment. They found the strain exhibited a markedly higher thermal tolerance compared to other strains of *K. pneumoniae*. This resistance was encoded by a single gene clpK and was found in 30% of a collection of nosocomial *K. pneumoniae* isolates. A subsequent study (Bojer et al, 2011) confirmed thermal resistance of the bacteria in both the planktonic cultures and in biofilm stage cells. The development of thermal tolerance is a possible mechanism for persistence of *K pneumoniae* in the healthcare environment and may contribute to resistance to disinfection by thermo-chemical treatments.

The CRE that have been causing outbreaks in intensive care and haematology units in debilitated patients have now caused outbreaks following endoscopic procedures, particularly ERCP. Endoscopes have become another risk factor for the spread of CRE. Most endoscopes have become contaminated after exposure to infected patients however the possibility that endoscopes may also be contaminated by bacteria from the hospital environments must also be considered.

GUIDELINE CHANGES RELATED TO CRE

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4. Decontaminate procedure room after the endoscopy procedure as per specific protocols for terminal cleaning of contaminated areas.
5 Sinks, taps and plumbing should comply with the standards in The Australasian Health Facility Guidelines (2016) to minimise the risks of spray from drains in sinks or overflow of waste water from blocked pipes.

6 The emergence of CRE is another compelling reason to meticulously follow standard infection control procedures including hand hygiene and the use of gloves and impervious gowns for each procedure. Endoscopy units should provide regular education, and assessment of compliance with hand hygiene and environmental decontamination.

CRE Outbreaks following endoscopy – European experience

France

Nosocomial outbreaks of infection due to drug resistant *K. pneumoniae* have been reported since 1984. Despite colonizing the gastrointestinal tract *K. pneumoniae* was an unusual cause of outbreaks of infection post endoscopy until recently. Branger reports one of the first endoscopy related outbreaks of drug resistant *K. pneumoniae* (Branger et al, 1997). During investigation of five outbreaks in France between 1991 and 1998 one outbreak was found where 13 patients were infected with ESBL *K. pneumoniae* after bronchoscopy. Cultures from the bronchoscope were positive. The outbreak resolved when the bronchoscope was repaired.

Two other publications from France describe four outbreaks of multi-drug resistant infection following ERCP between 2008 and 2010. Between December 2008 and August 2009 in Clermont-Ferrard there were 16 infections with ESBL *K. pneumoniae* following ERCP with an Olympus TJF 145 duodenoscope (fixed distal tip, open elevator wire channel) (Aumeran et al, 2010). A breach of cleaning and disinfection guidelines was identified; the duodenoscopes were not dried before storage. Other multi-drug resistant bacteria were isolated from duodenoscope cultures: *Pseudomonas aeruginosa* and *Morganella morganas*, and from blood cultures post ERCP. The outbreak resolved when endoscopes were dried before storage. The report mentions two other outbreaks were reported to French authorities but gives no further details.

The first clinical isolate of KPC producing *K. pneumoniae* in France was found in 2005 in blood cultures of a patient previously treated in a hospital in New York (Munoz-Price et al, 2013). In September 2009 the first outbreak of KPC producing *K. pneumoniae* infection after ERCP was detected in Paris (Carbone et al, 2010). The investigation found a failure to adequately dry the duodenoscopes after disinfection. The outbreak resolved when the duodenoscopes were dried after each disinfection cycle.

The Netherlands

There have been three reports of multi-drug resistant infections following ERCP in The Netherlands since 2008.

Buss, in a report of an investigation in Groningen of positive surveillance cultures from duodenoscopes and therapeutic gastroscopes between September 2002 and January 2005, incidentally mentioned an outbreak of multi-resistant *E.coli* after endoscopy without giving
any further details (Buss et al, 2008). Positive surveillance cultures were found in 7.9 to 31% of samples taken routinely from all endoscopes. The highest contamination rates were seen in two duodenoscopes. Defects were found in four endoscopes, two had channels replaced and two could not be repaired and were withdrawn from service. Scanning electron microscopy of the interior surfaces of one duodenoscope dismantled for repair found a biofilm on the inside and the outside of the biopsy channel and on the surface of the elevator wire.

In Groningen another three patients were infected with multi-drug resistant *Pseudomonas aeruginosa* after ERCP in 2008 (Kovaleva et al, 2009). The duodenoscope responsible was sterilized in ethylene oxide. Repeat cultures were negative initially but two different strains of *Pseudomonas* were cultured four months later from the same endoscope. The duodenoscope was disassembled and structures resembling biofilm were found in the channels. The channels were replaced.

At Erasmus University Medical Centre in Rotterdam, between January and April 2012 VIM-2 producing *Pseudomonas aeruginosa* was transmitted from a single duodenoscope to 22 patients (Verfaillie et al, 2015). Standard cultures from the culprit duodenoscope were negative but cultures from under the elevator and from beneath the distal tip cap were positive. An investigation of the design of the endoscope by a biomedical engineer from the Delft University of Technology found the fixed distal tip hampered cleaning and disinfection and that the O-ring might not seal the forceps axis sufficiently. The outbreak ended when the two TJF-Q180V duodenoscopes were withdrawn from service. Details of the investigations and the structural defects found were presented to the FDA meeting in May and are detailed later in this report.

**Germany**

In Berlin between December 2012 and January 2013 OXA-48 producing *K pneumoniae* was transmitted to six patients by a single duodenoscope (Kola et al, 2015). Cultures from the culprit endoscope were negative, the outbreak ended when defects in the external layers and the tip of the duodenoscope were repaired. Contact tracing found a further six patients were infected by patient to patient transmission.

A review of the literature documented two unpublished outbreaks of OXA-48 *K. pneumoniae* in Germany in 2013 (Gastmeier et al, 2014). One occurred after ERCP, probably due to a defect in the duodenoscope, the other occurred after bronchoscopy.

**Gastroscopy/Cystoscopy**

CRE outbreaks have also occurred following gastroscopy. Naas et al (2010) reported an outbreak of nine cases of KPC-2 producing *K. pneumoniae* following gastroscopy. Two breaches of cleaning and disinfection guidelines were identified: pre-cleaning was delayed for 24 hours allowing debris to dry before cleaning; the gastroscopes were not completely dried after disinfection. New local guidelines for reprocessing were established.

An outbreak of multidrug resistant *Pseudomonas aeruginosa* was reported in Reims, France (Bajolet et al, 2013). A total of four patients developed clinical infections after gastroscopy during a five month period in 2011. The outbreak resolved after the endoscope was withdrawn from service, breaches of reprocessing guidelines including inadequate drying were corrected and a new endoscope storage cabinet was purchased.
In Italy KPC producing *K. pneumoniae* was isolated for the first time in 2008 from a patient in Florence. Orsi performed a case control study in Umberto 1 Hospital in Rome between July 2008 and December 2009 comparing 38 patients with a porin variant entapenum resistant *K. pneumoniae* with 62 patients with antibiotic sensitive *K. pneumoniae* infections (Orsi et al., 2011). Endoscopy was identified as a risk factor with an odds ratio of 5.6 as well as recent use of broad spectrum antibiotics. A KPC producing *K. pneumoniae* displaced the porin variant *K. pneumoniae* in the hospital and the study was extended from July 2008 to June 2011. Endoscopy was again identified as a risk factor, OR 6.7 as well as recent treatment with a carbapenem OR 7.7 (Orsi et al., 2012).

A CRE outbreak has also been described after cystoscopy (Koo et al., 2012). There were nine cases of MDM *K. pneumoniae* infection; investigations identified a breach of the cleaning and disinfection protocols.

**Summary**

The first report of an outbreak of multidrug resistant *K. pneumoniae* was in France in 1994 following bronchoscopy. Further reports from France, Holland, Germany and Italy of outbreaks have often occurred after ERCP but also gastroscopy, bronchoscopy and cystoscopy. Reports of outbreaks after endoscopy followed closely on the reports of the first clinical isolates of CRE in Italy (12 months) and France (4 years).

Outbreaks have been identified by epidemiological studies that find a single type of CRE is usually transmitted from one endoscope over many months. Patients are colonised initially and some may develop clinical infections with CRE several months later. The epidemiology of a single type of CRE transmitted on multiple occasions from one endoscope is best explained by a reservoir of bacteria in a biofilm fixed to the endoscope. The biofilm intermittently releases bacteria that multiply in the endoscope channel and are subsequently transmitted to the next patient.

Outbreaks of CRE found in duodenoscopes and breaches of cleaning and disinfection protocols. Breaches of cleaning and disinfection protocols particularly a failure to adequately dry the endoscope, enabled biofilms to grow and release bacteria into the channel. Occult endoscope defects are often contaminated by biofilm. The defects reduce the ability of standard techniques to remove the biofilm and debris. Two studies that dismantled endoscopes and examined surfaces with scanning electron microscopy found debris and biofilm on difficult to access areas (Verfaille et al., 2015; Buss et al., 2008).

**CRE Outbreaks - USA Experience**

**Peer Reviewed Reports**

The details of some outbreaks in the USA have been published in the peer reviewed literature. However only a small proportion of cases are detected and only a small proportion of those detected are published (Rutala & Weber, 2015). Dirlam Langlay et al examined peer reviewed and non-peer reviewed literature such as newspapers and press releases in North America.
2005 to 2012 (Dirlam Langlay et al, 2013). Numerous lapses in reprocessing were identified including several associated with infection, injury or death. Only one episode was reported in the peer reviewed literature. Lack of reporting in peer reviewed journals contributes to the perception that lapses are rare and inconsequential.

Humphries also considered the incidence of infection post endoscopy was underestimated due to under reporting and lack of detailed surveillance (Humphries et al, 2015). Current estimates of risk of infection post endoscopy are far too low. Case reports are an indication of the existence of the problem but not the extent.


Multidrug resistant *Pseudomonas aeruginosa* (imipenem resistant) was transmitted to 18 patients at bronchoscopy in New York in 1998 (Sorin et al, 2001). Three patients were colonised and developed clinical infections; one died nine days after the procedure. The outbreak resolved when incorrect connecters on the Steris AER were replaced.

An outbreak of multidrug resistant *Pseudomonas aeruginosa* after ERCP occurred at the Cleveland Clinic in July 2002 (Fraser et al, 2004). *Pseudomonas* was transmitted to five patients, three developed clinical infections all recovered. Cultures from the culprit endoscope were negative; the outbreak resolved when the endoscope was withdrawn from service.

In Tampa, Florida, between June 2008 and January 2009, carbapenem resistant *Klebsiella pneumoniae* was transmitted to nine patients from a single duodenoscope. (Sanderson et al, 2010; Alrabaa et al, 2013). Cleaning procedures were inadequate, culture from debris under the elevator was positive for carbapenemase producing *E coli, Pseudomonas and Serratia species* but not for *K pneumoniae*. There were five clinical infections with one death and two patients developed renal failure requiring dialysis after treatment with colistin.

An outbreak of NDM–producing *E coli* at a teaching hospital in Illinois attracted widespread media attention (Epstein et al, 2014; CDC, 2014). NDM producing *E coli* was transmitted to 27 patients from three duodenoscopes between January 2013 and December 2013 (endoscope A 23 cases, endoscope B one case, endoscope C three cases). NDM producing *E coli* and KPC producing *Klebsiella pneumoniae* were recovered from the tip of one endoscope two months after it was withdrawn from service, but not from endoscope B or C. The facility changed from high level disinfection reprocessing to ethylene oxide gas sterilisation.

In Milwaukee, Wisconsin, over six months from May 2013 NDM producing *E coli* was transmitted to four patients from a single duodenoscope, three developed clinical infections (Smith et al, 2015). Cultures from the duodenoscope were negative. The facility sterilised all duodenoscopes with ethylene oxide and placed them back into routine clinical use. Ethylene oxide sterilisation is now used only when an endoscope is used on a patient known to be infected or colonised with CRE.
In Seattle, Washington, between November 2012 and August 2013, 32 patients were identified who had one of two clonal strains of a multidrug resistant *E. coli* transmitted from duodenoscopes (Ross et al, 2015). Four of eight duodenoscopes in use at that time were culture positive. Three of the four duodenoscopes had occult defects requiring repair. The facility introduced a culture and quarantine management for duodenoscopes. Cultures were performed after reprocessing, if these were negative after 48 hours the duodenoscope was released for use. Twenty new duodenoscopes were purchased in January 2014 so that the quarantine process could be initiated.

**FDA Response**

The FDA noted an increasing number of multi drug resistant outbreaks following ERCP some time ago and began investigations in September 2013, reviewing the MAUDE data base. MAUDE – (Manufacturer and User Facility Device Experience) is the data base of suspected device associated death, serious injuries and malfunctions. The FDA found a rapidly increasing number of reports of infections following ERCP beginning in 2012. Infection control physicians and hospitals epidemiologists from nine hospitals reporting outbreaks were interviewed. Six hospitals used Olympus duodenoscopes (TJF-160 and/or TJFQ-180v), two used Pentax ED-3490TK scopes and one FUJI ED 530X5 scopes. The proportion of the number of outbreaks for each manufacturer is roughly equal to their market share (Olympus supplies about 85% of duodenoscopes in the USA).

Several hospitals reported concerns about the difficulty cleaning the tip of the endoscope and elevator channel. Duodenoscope manufacturers were consulted and determined that in most cases reprocessing that had been done followed their recommendations. In some cases the CDC and/or State regulators were involved and also confirmed reprocessing procedures followed manufacturers guidelines.

In September 2014 the FDA requested information from duodenoscope manufacturers and reviewed their validation protocols analysing data from their cleaning and disinfection studies. The FDA repeatedly interacted with manufacturers to identify design features that may be contributing to infection. In January 2015 after reviewing manufacturer’s validation study protocols and analysing the data the FDA recommended additional more rigorous testing with more robust reprocessing protocols to enhance safety margins.

The FDA participated in a CDC led effort to develop an interim protocol for surveillance cultures of duodenoscopes. This was discussed at a CDC meeting in July 2014 and interim guidelines were released on the 11th of March 2015.

The FDA issued frequent public communications in 2015 and on 26 March new processing instructions for the Olympus TJF-180-V were announced. These communications were widely reported in the American and international media.

The FDA convened its Gastroenterology-Urology Device Advisory Committee to meet on 14-15 May to address the effectiveness of reprocessing of duodenoscopes and to inform rigorous, practicable, reprocessing protocols that will enhance the safety margin of ERCP procedures. Experts and interested parties were invited to present at this meeting. The executive summary prepared for the meeting gives an overview of reprocessing of duodenoscopes and the findings of the FDA investigations.
FDA Meeting Overview

Most gastroenterologists do not appreciate the substantial morbidity and mortality associated with an outbreak of CRE. Clinical infections have a 40% mortality. Mrs Carla Warner the widow of a victim of CRE presented to the meeting giving her insight into the devastating impact of endoscopically transmitted CRE on her previously well 55 year old husband (FDA, 2015: p151). She implored those responsible for the delivery of safe and effective health care to take responsibility for solving the problem. The impact of CRE on the individual patient must be the starting point for those addressing the recent outbreaks.

Dr Ostroth introduced the topic. 500,000 ERCPs are performed in USA each year. There is little margin for error in reprocessing endoscopes. He noted that the endoscope manufacturers had declined invitations to attend the meeting.

Epidemiology

The rapidly increasing number of outbreaks in 2014 and 2015 is shown in Fig 1. This is an underestimate of the actual size of the problem. Outbreaks are difficult to detect and are only found if careful surveillance is performed (Ross, 2015: p169). A recent publication found most infections transmitted at endoscopy are not reported to the FDA or in peer reviewed literature.

CRE is an unusual organism so there is a detection bias in identifying recent outbreaks (Dr Ross. FDA, 2015: p169). Dr Rutala considered CRE to be a marker organism for transmission of infection. Transmission of low numbers of antibiotic sensitive bacteria will not be detected. Dr Rutala believes that most endemic transmission post endoscopy goes unrecognised. There is a long lag time between colonisation and infection and a low frequency of infection (FDA, 2015: p311). Dr M Alfa stated we have been transmitting enteric organisms for years and we just didn’t realise it, now we are able to track them because of multi drug resistance (FDA, 2015: p240). Reported outbreaks are the tips of the large icebergs of both outbreaks of CRE and transmitted antibiotic sensitive bacteria at endoscopy (Dr Ross. FDA, 2015: p169).

Dr A Kallen (FDA, 2015: p215) discussed the typical epidemiological pattern of transmission of a single species of CRE from one endoscope on multiple occasions despite reprocessing. In the Illinois outbreak one endoscope was reprocessed 100 times between the first and last transmission. Transmission occurred on 30-50% of occasions when the endoscope was used. One endoscope tested positive for the culprit organism two months after it was taken out of service. Dr Kallen considered these epidemiological findings highlighted the role of biofilm in transmission of infection

Identified Causes of Outbreaks

Investigations identified the causes of some outbreaks. Dr A Kallen (FDA, 2015: p201) reported four broad categories

1. Inadequate manual cleaning or inadequate drying.
2. Contaminated or improper use of AER
3. Occult endoscope defects
4. Inadequate disinfection
Dr Rutala considered the major problems are failure to clean and occult endoscope defects (FDA, 2015: p309). Dr Gardner-Bonner stated in summing up that the biggest problems that needed to be worked on were cleaning and drying.

Dr Voss presented the findings of an investigation of an outbreak of multi drug resistant *Pseudomonas* at Erasmus MC in the Netherlands and details of the findings from an examination by a biomedical engineer from the Technical University in Delft (FDA, 2015: p117). Dr Voss recommended that endoscope design should be changed to improve cleanability. This was a common theme with other speakers.

**Actions Recommended**

Instrument manufacturers have developed new reprocessing guidelines. While all agree that these should be used some were concerned the new guidelines were not the complete answer to the problem. Dr Michael Drues commented “….And please, let's be honest here, does anyone really believe that coming out with a 100 plus page cleaning procedure is a solution to any real problem here?” “does anybody really believe that coming out with a special brush is a real solution to the problem? These are, at best, band aids.” Dr Drues recommended that endoscope design must be changed to improve cleanability.

Dr S Haugen noted that reprocessing guidelines had been validated using planktonic bacteria. She suggested that reprocessing should be upgraded to remove and disinfect biofilm on endoscopes. The new guidelines should be validated using bacteria in biofilms rather than planktonic bacteria (FDA, 2015: p40).

Dr J Olsen (FDA, 2015: p74) and Dr G McDonald both advised that planktonic CRE was killed in under one minute by standard disinfectants. There is a wide safety margin. However a recent review found that bacteria in biofilms are 10 to 100 times more resistant to disinfectants than planktonic bacteria (Otter et al, 2015).

Ms Sharon Wicklin a leading guideline author from AORN recommended the use of drying cabinets with continuous airflow to completely dry endoscopes and to reduce the possibility of human error. She also recommended regular preventative maintenance of endoscopes (FDA, 2015: p135).

Dr Suzanne Schwartz in a summary notes some recurring themes to consider include the potential for biofilm build up, its impact, how to measure and how best to mitigate; the environment where reprocessing occurs and the role of human factors in reprocessing; the surveillance of duodenoscopes post-use and before being put back into clinical use; the longevity of these devices in the context of numbers of uses and reprocessing cycles; the premarket validation testing; and the emphasis on achieving effective rigorous cleaning of the scope as arguably one of the most demanding steps, where there is no margin for error.

On 24 August 2015 the FDA issued supplemental measures to enhance duodenoscope reprocessing as summarised below.

“Among the variety of infection mitigation strategies were discussed at the Advisory Committee meeting, several specific supplemental measures have been implemented in individual health care facilities. Combined with strict adherence to the duodenoscope
manufacturer’s reprocessing instructions, the following supplemental measures may further help reduce the risk of infection transmission associated with the use of duodenoscopes.

- **Microbiological Culturing**
- **Ethylene Oxide Sterilization**
- **Use of a Liquid Chemical Sterilant Processing System**
- **Repeat High-Level Disinfection**

These measures represent a double disinfection, once with high level disinfection followed by ethylene oxide, liquid chemical sterilant or a repeat high level disinfection.

The FDA recommends health care facilities performing ERCP evaluate whether they have the expertise, training and resources to implement one or more of these options.

We do not believe this advice addresses all the issues raised in Dr Schwartz’s summary. This may reflect the limitations to the FDAs authority. Dr Fisher noted that the FDA cannot mandate device redesign, cannot mandate microbiological surveillance and doesn’t regulate hospitals or hospital’s reprocessing procedures (FDA, 2015: p355).

We are concerned that the recommendation to consider ethylene oxide sterilization does not reflect the limitations of ethylene oxide in the presence of residual bioburden (Rutala & Weber, 2015). The addition of ethylene oxide to high level disinfection following the outbreak of NDM producing *E coli* after ERCP in Illinois (Epstein 2014) was not completely successful. In a follow up Naryzhny et al report that one of 84 surveillance cultures was positive for KPC producing *K pneumoniae* (Naryzhny et al, 2016). Both NDM producing *E. coli* and KPC producing *K. pneumoniae* were previously recovered from a duodenoscope removed from service during the outbreak.

The pivotal role of biofilms in transmission of infection after endoscopy mandates the measures needed to address the problem. We believe meticulous cleaning, attention to complete drying and elimination of occult endoscope defects will be of most benefit in the short term. Endoscope design and reprocessing technology must be addressed in the medium to long term.

**Biofilms and Endoscopes**

During procedures endoscopes are contaminated with biological debris and large numbers of planktonic bacteria. Reprocessing protocols are designed and validated to remove debris and planktonic bacteria. Smaller numbers of bacteria may be present on endoscopes attached to surfaces in biofilms.

Biofilms are matrix-enclosed microbial accretions that adhere to biological or non-biological surfaces and represent a significant and incompletely understood mode of growth for bacteria. Biofilm formation represents a protected mode of growth that allows cells to survive in hostile environments. Biofilms are not simply passive assemblages of cells that are stuck to surfaces but are structurally and dynamically complex biological systems (Hall-Stoodley et al, 2004). Biofilm microbiology is complex and not well represented by flask cultures (Russell, 2003). Parameters such as minimum inhibitory concentrations of disinfectants calculated with planktonic bacteria are not relevant for the same bacteria embedded in biofilms (Landini et al, 2010).
Cleaning biofilms from surfaces is difficult and bacteria in biofilms are resistant to disinfectants (Simoes et al, 2010). Otter et al (2015) recent comprehensive review of biocide susceptibility of planktonic versus surface attached bacteria and those in biofilm mode confirms that a species of bacteria in a biofilms is between 10 and 100 fold less susceptible to disinfectants than the same species in planktonic form. The parameters for endoscope disinfection protocols have been validated using tests of efficiency on planktonic bacteria not bacteria in biofilms. Standard endoscope reprocessing protocols do not kill all bacteria in experimental biofilms on endoscope channel surfaces (Neves et al, 2015).

New reprocessing protocols should be developed and validated with both planktonic and biofilm bacteria.

**The problem: planktonic bacteria, biofilms or both?**

The usual mode of transmission of contaminating bacteria from patient to endoscope and endoscope to patient is almost certainly free floating planktonic bacteria. However the epidemiology of outbreaks where a single species of bacteria is transmitted on multiple occasions from one endoscope over several months is best explained by a reservoir of CRE in a biofilm fixed to the endoscope, the bacteria protected from removal by cleaning and killing by disinfection (Kampf et al, 2014 Petersen, 2015). The biofilm intermittently releases planktonic bacteria that multiply in the channel and subsequently contaminate patients.

The fundamental problem is the formation and then persistence of biofilm on an endoscope and the subsequent release of planktonic bacteria from the biofilm. The best solution is to stop biofilms forming or if it does form remove it during reprocessing. This could be achieved by changing design to improve the cleanability of endoscopes and the development of new cleaning technology. These are long term solutions. In the medium term the parameters for cleaning and disinfecting in reprocessing protocols should be reassessed.

Both occult endoscope defects and failure to adequately dry endoscopes have been reported as causes of outbreaks of CRE (Petersen 2015; FDA, 2015). Occult endoscope defects facilitate the formation of biofilms and reduce the ability of standard reprocessing to remove the biofilm from a surface. Moisture on stored endoscopes promotes growth of biofilms and release of planktonic bacteria from the biofilm. These problems can be addressed immediately.

**Biofilms and culture**

Knowledge of the number of viable bacteria on an endoscope is important for quality control of reprocessing and investigation of outbreaks. Standard culture techniques measure free floating planktonic bacteria. Bacteria in experimental biofilms on channel surfaces treated with reprocessing are not reliably cultured with standard flush and brush methods. A variety of other analytical techniques are available to study bacteria in biofilms but these are difficult to apply to endoscopes and are mainly used in research (Pantanella et al, 2013).

Scanning electron microscopy (SEM) is more accurate than cultures in detecting biofilm on surfaces. SEM of channels removed from endoscopes found biofilm in all 12 air/water channels and in 5/13 suction biopsy channels (Pajkos et al, 2004). Biofilm was associated with surface defects, cracks, grooves and pits found in 12 of 13 biopsy/suction channels. The
authors concluded that the presence of soil and biofilm suggested that cleaning and disinfection processing of endoscopes was inadequate and that the presence of surface defects promotes accumulation of microorganisms and soil. Ren-Pei et al (2014) also found biofilm in both air/water and biopsy/suction channels in a more recent study.

Kovaleva used an in vitro model to access biofilms in channels and concluded “Biofilm formation in endoscope channels can result in failure of disinfection procedures and can create a viscous cycle of growth, disinfection, partial killing or inhibition and regrowth resulting in outbreaks of infection” (Kovaleva et al, 2010).

Cultures from patient ready endoscopes and routine surveillance from gastrosopes, colonoscopes and duodenoscopes are positive in about 2 to 4% of cases. The rate of positive cultures depends on several parameters including culture technique (the addition of a neutralizer increases sensitivity), the rate increases with the age of the endoscope and the timing of the culture in relation to the most recent cleaning and disinfection is also a factor (Aumeran et al, 2012; Bisset et al, 2006).

Follow up of endoscopes with documented positive cultures in surveillance research studies rarely finds clinical infections in routine diagnostic endoscopy and colonoscopy (Moses & Lee, 2003, FDA, 2015: D Jones p.142-5). Previous investigations however have found that clinical infection is more likely if therapeutic procedures are performed on the immune suppressed. This data suggests that for many years small numbers of bacteria have been transmitted by endoscopes. This transmission has been not been recognised and there have been no recognised clinical consequences.

The current recognised outbreaks of CRE may be related to the increasing prevalence of CRE rather than recent changes in endoscope design. CRE transmitted at endoscopy may colonise patients more frequently than antibiotic sensitive bacteria. It is also possible that the rate of colonisation is similar to sensitive bacteria but the clinical consequences differ.

Significance of Endoscope Cultures

Negative Cultures – Studies using experimental biofilm from endoscope channels have found viable bacteria in biofilms are not usually identified by standard culture techniques. Standard cultures of culprit endoscopes in CRE outbreaks are not always positive. A negative culture does not guarantee the endoscope is not contaminated with CRE or other pathogens. CURRENTLY THERE IS NO ENDOSCOPE SAMPLE COLLECTION TECHNIQUE OR CULTURE METHOD THAT CAN ALWAYS DETECT THE PRESENCE OF BACTERIA PROTECTED IN BIOFILM MATRIX AND IN A DORMANT STATE.

Positive Cultures-

Non-biofilm associated bacteria are effectively removed and killed by standard cleaning and HLD. However, once bacteria form build-up biofilm after repeated rounds of reprocessing, they are not easily removed or killed by currently used methods. (Alfa & Howie, 2009; Kovaleva et al, 2010). Theoretically, if all steps in the endoscope reprocessing protocol are done properly, there should be no biofilm formation within flexible endoscopes. Detection of any level of Gram negative bacteria on culture of endoscope channels suggests that a build-up biofilm may have developed. The fundamental issue is the release of biofilm-associated
bacteria from a persisting build-up biofilm and not immediate transmission of bacteria from the previous patient. It is important to recognize that build-up biofilm is a process (i.e. due to repeated rounds of reprocessing) and that unless ALL steps in the process (i.e. cleaning, HLD, rinsing, drying) are done correctly EVERY TIME then there will be a gradual accumulation of material within the endoscope channels that will eventually protect Gram negative bacteria within the build-up biofilm from detergents and HLDs. A key factor in bacterial survival is moisture within channels during storage. As such ensuring dry storage of the channels is a critical consideration to prevent development of build-up biofilm.

**AFERs**

Biofilms can also form on surfaces in AFERs contaminating endoscopes during rinse cycles (Kampf et al, 2014). Strict adherence to water management protocols, particularly filter servicing and testing together with AFER bacteriological surveillance and strict adherence to machine servicing schedules are necessary to ensure endoscopes are not contaminated during AFER cycles.

**Surveillance Cultures**

Routine surveillance bacteriological sampling of the endoscopes and AFERs has been recommended in Australia since 1995 (Jones et al, 2008). Recent reviews of results have confirmed this is an important tool in detecting occult endoscope defects and unrecognised breaches of reprocessing protocols, problems likely to lead to outbreaks (Moses & Lee, 2003; FDA, 2015; Jones, p 142-5).

**Occult Endoscope Defects**

Occult endoscope defects are a well-recognised cause of outbreaks of infection. These defects include micro perforations with biofilm on the inside and outside of the channel (Buss et al, 2008), micro perforations, cracks/chips in the LG lens, C-cover insulation damage, leak in a biopsy port (Wendorf et al, 2015) leak across O-rings, failed seal around a lens (Verfaillie et al, 2015), defects in the cap and external layers (Kola et al, 2015) and non-specified channel defects (Buss et al, 2008: Kovaleva et al, 2009; Gastmeier et al, 2014).

Surveillance cultures will detect some but not all of these defects. Routine maintenance to detect occult problems and replace wearing parts has been proposed (Petersen, 2015; Rutala & Weber, 2015). At the FDA Meeting Dr Leggett stated “There must be some mandated maintenance schedule” (FDA, 2015: p414). Ms Van Wicklin also supported preventative maintenance (FDA 2015: p135).

During preventative maintenance many occult defects, lens chips/leaks and C-cover damage would be identified and repaired. Assessing the integrity of channels is technically more difficult. The surfaces of channels must be cleanable. Smooth surfaces are easiest to clean. Rough surfaces cannot be effectively cleaned by brushing or flushing and encourage the growth of biofilm (Pajkos et al, 2003). The surface of a biopsy channel will be progressively damaged by routine use: channels have a finite safe working life.

Channels are best replaced routinely during the maintenance inspection to maintain a smooth cleanable surface. One endoscope supply company has advised that their maintenance
contract includes annual channel replacement. This increased the reliability of the endoscopes and was more cost effective than repairing major defects occasionally.

Until there is good data on the safe working life of endoscope components we recommend annual preventative maintenance with replacement of channels and O-rings for duodenoscopes and linear echo endoscopes. All other endoscopes should have annual preventative maintenance and channel replacement every two years could be considered.

**Hands and the Environment**

Effective hand hygiene is the simplest and most important measure to prevent transmission of nosocomial infection. (Khan et al, 2012; Morgan et al, 2012). Endoscopy units have a high proportion of outpatients with a low risk of infection and are often left out of dedicated infection prevention and control programs. Most reprocessing guidelines do not specifically address hand hygiene. However healthcare workers hands could be vehicles for the spread of pathogens including transfer from patients to reprocessed endoscopes (Santos et al, 2013). Santos et al evaluated hand hygiene compliance before and after educational intervention in an endoscopy unit in Brazil. All healthcare workers had a good understanding of the importance of hand hygiene but initially compliance was poor. One month after educational intervention compliance had improved significantly and the improvement was maintained ten months later. Endoscopy units should provide regular education and assessment of compliance with hand hygiene.

**Biofilm: Implications for reprocessing.**

The epidemiology of outbreaks of CRE following endoscopy supports the role of biofilm as a reservoir of bacteria protected from reprocessing. A single species of bacteria is transmitted from one endoscope on multiple occasions over a long period of time despite multiple episodes of reprocessing. Investigations using scanning electron microscopy have found biofilm in the biopsy and air/water channels of many endoscopes.

If bacteria in biofilm are the problem this has important implications for the current reprocessing protocols. The cleaning protocols are not designed to remove biofilm. Repeated cycles of disinfection and drying may fix biofilm to surfaces and lead to build-up biofilm. Parameters for the use of disinfectants must be revised using bacteria in biofilms rather than planktonic bacteria.

Culture techniques currently used for surveillance and investigations of outbreaks have low sensitivity for detecting bacteria in biofilms. New techniques should be investigated.

As many endoscopes have bacteria in biofilms on channel surfaces the importance of complete drying after reprocessing has been underestimated in current guidelines. Keeping the endoscope, particularly all the channels, free of any moisture during storage must be a priority.

Biofilms form on occult endoscope defects and are difficult/impossible to remove. Introducing regular preventative maintenance of endoscopes as soon as possible will reduce
the incidence of occult defects. Duodenoscopes should have yearly channel and “O-ring” replacement. Lower risk endoscopes would require less frequent replacement of channels.

In the long term the solution to prevent endoscopy associated infection outbreaks due to biofilms involves fundamental changes in endoscope design and/or manufacture. The aim must be to have either an instrument capable of undergoing effective steam sterilization or the ability to recognize and totally remove channel biofilm. An alternative approach would to redesign endoscopes so they have a combination of disposable (all channels) and reusable components. New cleaning and disinfection technology should be investigated.

In the short term the aim is to use all available means to prevent biofilm formation and retard growth of any biofilm that does form.

CURRENT ENDOSCOPE REPROCESSING PROTOCOLS ARE NOT FAILURE PROOF AGAINST MICROBE TRANSMISSION.

GUIDELINE CHANGES TO LIMIT BIOFILM FORMATION AND GROWTH

REPROCESSING AND STORAGE (Note: duodenoscopes are considered separately)

1 Pre-cleaning must be carried out IMMEDIATELY after use.

2 Manual cleaning must be carried out PROMPTLY (promptly in these Guidelines means less than 30 minutes) after pre-cleaning.

3 Reprocessing in AFERs which have FDA & TGA approved mechanical cleaning must be undertaken promptly after pre-cleaning.

4 After manual cleaning of the endoscope, machine or manual disinfection must be undertaken promptly.

5 After disinfection by any means the endoscope must have prompt drying and storage in an approved drying cabinet. (see Drying Cabinets)

6 Endoscopes must remain in approved drying cabinets until next patient-use.

It is critical to recognize that these recommendations apply to each and every time the endoscope is used. Months of effective biofilm growth control can be undone if an endoscope is used for an after hours emergency, pre-cleaned and then left for the day staff to reprocess. Biofilms require moisture and time to grow. The only way to prevent growth is to NEVER allow significant “wet time” opportunities.
ENDOSCOPE AND AFER MAINTENANCE

The reprocessing and storage recommendations should significantly reduce biofilm formation and growth. They cannot guarantee that no biofilm formation will occur. Borescopes and similar devices allow inspection of the inner lumen of the larger endoscope channels. Preventative maintenance channel inspection to detect biofilm would be useful. However there are a number of problems to be resolved before this can become routine.

Current recommendations are:

1. Endoscopes with positive surveillance bacterial cultures with organisms of concern detected should be sent for service (unless there is an alternative explanation e.g. staff error).

2. Endoscopes should have preventative maintenance examination at least yearly.

3. Regular replacement of channels during preventative maintenance should be considered

DUODENOSCOPES

Duodenoscopes have much more complicated reprocessing requirements. The majority of endoscopy associated infection outbreaks have been related to duodenoscopes. The major problem in duodenoscope design is the necessity for an elevator-wire channel to allow the duodenoscope lever to move up and down in order to position accessory devices that are inserted through the instrument channel to be positioned to facilitate entry and operation in the bile and pancreatic ducts. This involves a wire attached to a metal plate in the duodenoscope tip passing upward through a very fine channel to a wheel in the endoscope head. The inner diameter of the channel needs to be limited to prevent flexing of the wire within the elevator-wire channel. This results in very limited space for cleaning fluid to be injected down the channel. This causes problems for both manual and AFER reprocessing. In an attempt to solve this problem duodenoscopes were redesigned so the distal end of the elevator-wire channel was sealed and did not require reprocessing. As a result of this design change the only barrier between the contaminated outside of the instrument and the interior is an “O ring” on a stainless steel shaft which cannot be seen or easily replaced by users. Duodenoscopes marketed in USA have never had removable tip covers, possibly because of litigation fears if the tip detaches within the patient. The result of these changes is that it is extraordinarily difficult to visualize and effectively clean and disinfect all areas of the tip. It is unlikely that these problems can be solved without a redesign of the tip structure. In the meanwhile it is difficult to recommend reprocessing changes which will remove the risks of infection transmission. However, some of the endoscope manufacturers have revised their cleaning protocols with more specific instructions regarding cleaning of the elevator lever and lever cavity. This includes use of specific brushes to facilitate the cleaning process.

A number of factors not related to duodenoscope design also contribute to the increase of CRE transmission. Patients undergoing ERCP are frequently very ill, often with infection and/or immunosuppression from chemotherapy or radiotherapy and frequently they are on broad spectrum antibiotics.
GUIDELINE CHANGES FOR DUODENOSCOPES

Endoscopy units performing ERCP should:-

1. Consider if a site is performing ERCP procedures with sufficient frequency to continue offering this clinical service.

2. Have dedicated staff reprocessing duodenoscopes who are aware of, and have undertaken specific training in, the particular problems of cleaning, disinfecting and obtaining tip samples for bacteriological surveillance.

3. Perform MONTHLY bacteriological surveillance tip cultures (i.e. as part of the existing monthly culture of all channels).

4. Have appropriate risk notification of MDRO transmission in their Informed Consent information.

5. Send duodenoscopes for regular yearly maintenance.

6. Have instrument channels and “O-rings” replaced yearly.

DRYING CABINETS

The reprocessing step of drying has often been ignored or incompletely carried out and is prone to human error. Biofilms need moisture to grow. Alfa and Sitter in a pivotal paper demonstrated that if duodenoscopes were left damp after reprocessing there was rapid growth of *Pseudomonas* and *Acinetobacter* species (Alfa and Sitter, 1991). Drying for 10 minutes with forced air prevented this overgrowth in all duodenoscopes studied. Implementation of an alcohol flush followed by forced air drying ended outbreaks of Pseudomonas infections following ERCP in the 1980s (Petersen, 2015).

Muscarella reviewed published reports and clinical studies that demonstrate the significant contribution of endoscopic drying to the prevention of disease transmission (Muscarella, 2006). He considered endoscope drying is as important to the prevention of infection as cleaning and high level disinfection and recommended drying after every reprocessing cycle both between patients and before storage plus storage of endoscopes in a dry, well ventilated environment.

The importance of drying was raised at the FDA Meeting by Dr G McDonald (FDA, 2015: p96, Dr Gardner-Bonnear (FDA, 2015: p395), and Ms S Van Wicklin recommended the use of drying cabinets with continuous air flow (FDA, 2015: p135).

There is often confusion over the terms "storage cabinet" and "drying cabinet". The term storage cabinet simply means what it says - a place to store endoscopes. It does NOT necessarily imply any drying function. Nor does it necessarily imply functions that are designed to prevent proliferation of any remaining organisms in or on the endoscope, nor to prevent environmental pathogens contaminating the stored endoscope.
DRYING CABINET is used in these Guidelines for systems designed to use forced air to flush the channels to remove any remaining moisture from endoscopes after reprocessing. Forced air drying requires continuous forced air through endoscope channels and over the surface of the endoscope. The drying cabinet cycle can use a defined length of time for the channel flush after initial drying but the air pressure must remain continuously higher in the cabinet than externally to prevent contaminant ingress. The air used for drying must be free of biological, particulate and chemical significant contamination. Alarms and automatic system failure reports are necessary.

Drying cabinets are designed to maintain the microbiological quality of reprocessed endoscopes for a period validated by the manufacturer. These cabinets improve drying quality and storage conditions and increase endoscope shelf life (Grandval et al, 2013). The authors of a recent systematic review concluded that endoscopes can be stored for 7 days if they have been effectively reprocessed to remove all pathogens and almost all other microorganisms, and are stored in a way that keeps them completely dry and free from environmental and human contamination (Schmelzer et al, 2015). A longer endoscope shelf life reduces the need to reprocess prior to lists saving staff time, and reducing costs of reprocessing per procedure (Grandval et al 2013).

The committee recommends;
IT IS CRITICAL THAT FOLLOWING MANUAL OR AFER REPRESSING ALL ENDOSCOPES ARE PROMPTLY TRANSFERRED TO AN APPROVED ENDOSCOPE DRYING CABINET AND FORCED AIR DRYING COMMENCED. THIS SHOULD CONTINUE UNTIL THE ENDOSCOPE IS USED AGAIN OR STORAGE PERIOD HAS ELAPSED. THIS ALSO APPLIES TO ENDOSCOPES REPROCESSED IN AFERs WITH A DRYING CYCLE REGARDLESS OF MANUFACTURER’S CLAIMS.

In general endoscope drying cabinets should conform with European Standard EN 16442 Controlled Environment Storage Cabinet For Processed Thermolabile Endoscopes EUROPEAN COMMITTEE FOR STANDARDIZATION (CEN) CEN-CENELEC MANAGEMENT CENTRE AVENUE MARNIX 17 B-1000 BRUSSELS

The committee recommends:

1. These measures are introduced as a matter of urgency for duodenoscopes.

2. These measures be introduced as soon as possible for all other endoscopes but certainly within 18 months
REFERENCES:


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