Why California's Superbug Outbreak Isn't As Scary As It Seems

UCLA superbug: Outbreak 'not a threat to public health,' officials say

2 dead, nearly 180 possibly infected after 'superbug' outbreak at UCLA hospital

FDA faces more scrutiny in Congress over response to superbug outbreaks
<table>
<thead>
<tr>
<th>Country</th>
<th>Outbreaks</th>
</tr>
</thead>
<tbody>
<tr>
<td>France</td>
<td>1997(B), 2008, 2009, 2012 (G), 2013 (G)</td>
</tr>
<tr>
<td>Germany</td>
<td>2012, 2013</td>
</tr>
<tr>
<td>Italy</td>
<td>2006(G &amp; ERCP), 2011, 2012 (G &amp; B)</td>
</tr>
</tbody>
</table>
Outbreaks

Publications in peer reviewed journals generate most publicity

**But** – Under reporting

- failure to diagnose
- failure to report
<table>
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</thead>
<tbody>
<tr>
<td>Peer Rev Journals</td>
<td>1(B)</td>
<td>1</td>
<td>1</td>
<td></td>
<td></td>
<td>1</td>
<td>2</td>
<td></td>
</tr>
<tr>
<td>FDA Maude</td>
<td>4</td>
<td>3</td>
<td>8</td>
<td>15</td>
<td>60</td>
<td></td>
<td></td>
<td>4.5/wk</td>
</tr>
</tbody>
</table>
Outbreak publications

Confirm a problem exists

Are not a measure of extent
Epidemiology

Insight into cause

Timing of first outbreak
  New endoscope design

Transmission
  Reprocessing
  AER, endoscope
## Timing

<table>
<thead>
<tr>
<th>Country</th>
<th>First reported culture</th>
<th>First outbreak post endoscopy</th>
</tr>
</thead>
<tbody>
<tr>
<td>USA</td>
<td>1996</td>
<td>1997 Pseudomonas/bronchoscopy</td>
</tr>
<tr>
<td></td>
<td></td>
<td>2004 Pseudomonas/ERCP</td>
</tr>
<tr>
<td></td>
<td></td>
<td>2008 K pneumoniae/ERCP</td>
</tr>
<tr>
<td>France</td>
<td>2005</td>
<td>2009 K pneumoniae/ERCP</td>
</tr>
<tr>
<td>Italy</td>
<td>2008</td>
<td>2008 K pneumoniae/gastroscopy and bronchoscopy</td>
</tr>
</tbody>
</table>
Transmission

Often no breaches of reprocessing protocols identified

Single species transmitted on multiple occasions despite reprocessing

Outbreaks usually traced back to a single endoscope
Transmission

Duodenoscopes, bronchoscopes, gastroscopes and cystoscopes

All manufacturers and models

Patients colonised initially – small number of bacteria transmitted

Subsequent clinical infections 3-6 months later, high mortality
Biofilm is the problem

Reversible attachment

Irreversible attachment

Growth and differentiation

Dissemination

Bacterial cells

Biofilm

Surface of implant
Properties

- Antibiotic block
- Diffusion barrier
- Host immune cell
- EPS charge
- pH variation
- Alcohol
- Acid
- Gene exchange
- Release of nutrients into biofilm
- Substrate
- Multispecies cells
- Persister cells
- O2 variation
- Dead cells
- Inflammation
- Surface inactivation
- Quorum sensing
Biofilm is the problem

Biofilm in channel/on tip

CPE is incorporated into a multispecies biofilm

Biofilm acts as a reservoir of CPE and protects bacteria from cleaning and disinfection
Authorities slow to react

CDC Morbidity & Mortality Report after first outbreak of carbapenemase producing *Pseudomonas aeruginosa*

Incidence of outbreaks underestimated - unrecognised or unreported. Endoscopes small lumens vulnerable to damage and subsequent biofilm formation compromising cleaning and disinfection.

**Recommends**
- Follow guidelines and manuals
- Manufacturers develop better reprocessing protocols
- Training
- Quality control – surveillance cultures, routine maintenance
Timeline

1996  First +ve culture CRE USA
1997  First endoscopy outbreak – bronchoscopy
1998  CDC MMW Report and recommendations

2012  ASGE/Olympus aware multiple outbreaks Europe/USA

2014  Sept  Epstein publication, widespread publicity, letter to GESA

2015  Feb   four outbreaks each week reported to FDA
       May   FDA meeting

Recommends
- Follow guidelines and manuals
- Manufacturers develop better reprocessing protocols
- Training
- Quality control – surveillance cultures, routine maintenance
Sitting on our hands

Healthcare professionals have trouble accepting ideas that do not accord with their belief system.

To be accepted a theory must fit into a person’s mental framework.

The absence of a simple framework is referred to as hypocognition – Mariotto 2010.
Hypocognition

Tahitians – sorrow and guilt

Inuit – ice

Personal experience
1986
2007
Old paradigm

Infection Control in Endoscopy 2010

HLD

Quality control – negative cultures = no bacteria

Outbreaks are due to breaches of reprocessing protocols
New paradigm

Need a new framework to orient discussion and formulation of a response

Dr Cowen’s Advice

1) The Australian guideline “Infection Control in Endoscopy” was designed to prevent endoscopic transmission of infection by PLANKTONIC BACTERIA.

2) The guideline was NOT designed to prevent disease transmission by biofilm associated bacteria.

3) I repeat the guideline will not now, or in the future, prevent biofilm associated endoscopic transmission of infection without major modification.

FDA – Current reprocessing protocols do not provide reasonable assurances of safety and effectiveness
Biofilm is the new paradigm

Live bacteria in biofilm on most endoscopes

Current reprocessing does not remove biofilm

Endoscopes have been transmitting small numbers of enteric bacteria for many years without any recognised clinical consequences

Emergence of CPE has exposed reprocessing defects

Outbreaks are due to biofilm on endoscopes
Biofilms – the evidence

Role of biofilm in Reprocessing Medical Devices  Roberts 2013

Kirschke 2003 - Poor endoscope design facilitates biofilm formation

   bacteria in biofilm on most endoscopes
   biofilm found in surface defects
### Biofilm on endoscopes

Scanning electron microscopy - patient ready endoscopes

<table>
<thead>
<tr>
<th></th>
<th>Pajkos 2004</th>
<th>Ren-Pei 2014</th>
</tr>
</thead>
<tbody>
<tr>
<td>Biopsy channels</td>
<td>5/13</td>
<td>36/66</td>
</tr>
<tr>
<td>Air/water channels</td>
<td>12/12</td>
<td>10/13</td>
</tr>
</tbody>
</table>

Recent outbreaks - Buss 2008, Verfaillie 2015
Positive cultures

Bisset & Vickery 2006

Patient ready endoscopes

Gastroscopes n=1376 1.8%
Colonoscopes n=987 1.9%

Coliform DNA on 40% suggesting biofilm
Biofilms – the evidence

Reprocessing Medical Devices  Roberts 2013

Kirschke 2003 - Poor endoscope design facilitates biofilm formation

- bacteria in biofilm on most endoscopes
- biofilm found in surface defects
- cultures positive in 2% patient ready endoscopes
- biofilm reduces effectiveness of disinfectants, need 10-100 fold increase in concentration

Alfa 2009 – Build up biofilm compromises HLD of endoscopes

Alfa 1990, Kovaleva 2010 – Drying reduces growth of biofilm and release of bacteria

Pineau 2008 – Benefits of drying cabinets
Biofilm – the evidence

Not a new idea, identified 15 years ago

Biofilm on endoscopes is similar to that on other medical devices

Good data on incidence, research models confirm biofilm is resistant to current reprocessing protocols

Epidemiology of recent outbreaks consistent with transmission of bacteria from biofilms persisting on endoscopes despite appropriate reprocessing
No outbreaks so far

Old paradigm

HLD = no bacteria

New tip, new manuals

No worries
No outbreaks so far

Old paradigm

HLD = no bacteria

New tip, new manuals

No worries

New paradigm

Biofilm is not removed by current reprocessing

All endoscopes are transmitting bacteria
Australia

2014 case reports CPE in travellers

Outbreak St Vs Melbourne 2012-2014

2015 Victoria 34 new cases
CARAlert

Australian Commission on Safety and Quality in Healthcare

Critical Antimicrobial Resistance Alert

Surveillance established March 2017

Recent report - data 17 March – 31 December 2017
Figure 8: Carbapenemase types as a proportion of all carbapenemases, number (A) and percentage (B) reported by state and territory, March-December 2016

A. Number by state and territory

<table>
<thead>
<tr>
<th>State or territory</th>
<th>Number</th>
</tr>
</thead>
<tbody>
<tr>
<td>NSW (108)</td>
<td></td>
</tr>
<tr>
<td>VIC (88)</td>
<td></td>
</tr>
<tr>
<td>QLD (88)</td>
<td></td>
</tr>
<tr>
<td>WA (21)</td>
<td></td>
</tr>
<tr>
<td>SA (9)</td>
<td></td>
</tr>
<tr>
<td>TAS (2)</td>
<td></td>
</tr>
<tr>
<td>ACT (11)</td>
<td></td>
</tr>
<tr>
<td>NT (0)</td>
<td></td>
</tr>
<tr>
<td>Unknown (1)</td>
<td></td>
</tr>
<tr>
<td>Total (326)</td>
<td></td>
</tr>
</tbody>
</table>

B. Percentage by state and territory

State or territory

- IMP
- NDM
- OXA-48-like
- KPC
- NDM, OXA-48-like
- VIM
- KPC, NDM
- SME

Total (326)
Risk management not guideline revision

CPE has dramatically increased the morbidity and mortality of transmitting bacteria at endoscopy.

The profession is responsible for delivering safe endoscopy.

Don’t wait for 1st outbreak or GESA Council to make up their mind.

Each unit must act now to minimise the risks.
Risk management

Risk management is the implementation of practices that reduce patient risk and subsequently limit a facility’s exposure to liability.

Quality management is the process of actively assessing practices to determine the extent they achieve the desired outcomes – less infections, lower rates of positive surveillance culture.
What’s new?

After 30 years of world leading reprocessing guidelines Australia has now fallen behind
Response to outbreaks so far

New reprocessing guidelines

Olympus recalls duodenoscopes to adjust tips
Have changes worked?

No published evidence to support new reprocessing guidelines or duodenoscope tip modification

Surveillance cultures post changes not improved
## Cultures post new reprocessing

<table>
<thead>
<tr>
<th>Location</th>
<th>Sample Size</th>
<th>Positive Rate</th>
</tr>
</thead>
<tbody>
<tr>
<td>Rawers 71 Dutch hospitals 2015</td>
<td>156/1200</td>
<td>12%</td>
</tr>
<tr>
<td>Ross Seattle 2015</td>
<td>189/2238</td>
<td>8.4%</td>
</tr>
<tr>
<td>Brandabur Washington 2015</td>
<td>23/540</td>
<td>4.2%</td>
</tr>
</tbody>
</table>
FDA Supplemental Measures

4 August 2015

Adhere to manufacturers reprocessing instructions

Implement a comprehensive quality control program

Consider

  Surveillance cultures
  ETO, longer disinfection times
  Double disinfection or culture and quarantine
Seattle outbreak

Ross 2015

Micro lab identified outbreak of CPE after ERCP
Nov 2012- Aug 2013 32 patients 16 deaths

Response

Redesign reprocessing area
Routine endoscope maintenance 2 yrly
Culture and quarantine
Culture and quarantine

Purchased 20 new duodenoscopes (1500 procedures/yr)

Duodenoscopes cultured after overnight storage

Reprocessed after culture (details of drying sketchy)

Quarantined for 48 hours
Released for use if cultures negative
But

Biofilm is on most scopes
Biofilm is difficult to culture after reprocessing
Negative culture does not guarantee no bacteria
Biofilm will release bacteria if conditions are right, particularly if scope is stored damp

Transmission of bacteria dependant on drying and storage

Repeat +ve culture = critical defect scope/AER/reprocess
3 endoscopes occult defects detected
Double disinfection

HLD is good

Double HLD is better
Double disinfection

Brandabur 2017

Multi centre randomised trial
Duodenoscopes and linear EUS randomised to HLD or double HLD
Daily surveillance cultures (48 hrs incubation)
5850 cultures over 6 months from 4 hospitals

Positive cultures
HLD 3.9% = double HLD 4.2%
Elevator 5.2% > biopsy channel 2.9%

1 endoscope repeatedly positive cultures – occult defect
## Cultures post new reprocessing

<table>
<thead>
<tr>
<th>Location</th>
<th>Sample Size</th>
<th>Positive Rate</th>
<th>Quality Control</th>
</tr>
</thead>
<tbody>
<tr>
<td>Rawers 71 Dutch hospitals 2015</td>
<td>156/1200</td>
<td>1.3%</td>
<td>occult defect</td>
</tr>
<tr>
<td>Ross Seattle 2015</td>
<td>189/2238</td>
<td>8.4%</td>
<td>2 occult defects</td>
</tr>
<tr>
<td>Brandabur Washington 2015</td>
<td>23/540</td>
<td>4.2%</td>
<td>4/18 occult defect</td>
</tr>
</tbody>
</table>
Positive surveillance cultures

Saliou 2016

Brest France – 762 surveillance cultures 2008-2015

Prolonging incubation 48hr to 1 wk doubles +ve cultures

Duodenedoscopes = gastroscopes and colonoscopes

Older endoscopes (>4yr) 3 fold increase in +ve cultures

Drying cabinets (2014) 4 fold decrease in +ve cultures
Drying cabinets

Clinical Update – 20 integrated recommendations

Drying cabinets for gastroscopes and colonoscopes
part of one recommendation
approved by GENCA and AGEA
not approved by GESA Council

Cancellation of 60 orders for drying cabinets
One unit turned off the air in an already installed drying cabinet
Not enough evidence

25 pages, 63 references, are you kidding me?

Common complaint by those without scientific evidence

Every new recommendation since 1970 opposed
  disinfectants
  AERs
  Drying 1980s
  ISO 9001 - surveillance cultures, proof of process
  Drying cabinets - 2016
Different clinical practices

Nurses – Standards

Gastroenterologists - Guidelines
**Medical guidelines**  
address a narrow clinical question, bicap vs injection for ulcers  
evidence is graded, strongest recommendations are based on  
randomised trials  
clinician decides whether the GL is relevant for an individual

**Standards**  
set out specifications and procedures designed to ensure  
products, services and systems are safe, reliable and  
consistently perform the way they were intended  
based on science, technology and experience.  
Minimum accepted practice
## Standards for Endoscopy

### Reprocessing
- Infection Control in Endosc
- Detergents
- Disinfectants
- AERs
- Water quality
- Drying cabinets
- Not endoscopes

### Facilities
- Standards for endoscopic facilities
- AS 2211.1 Laser safety
- AS 2773.1 Ultrasonic cleaners
- AS 3009 Emergency power
- AS 3200.1 Electrical safety
- AS 3200.1 Radiation safety
Infection Control in Endoscopy

A Standard for endoscope reprocessing

Used with other relevant Standards to deliver safe and effective endoscopic services

Supporting evidence is science, technology and experience, very few randomised trials

Minimum accepted practice
Drying cabinets - the evidence

Biofilm is the problem, moisture is the enemy, drying is the answer

Drying cabinets

Automate the process, built in failsafe monitoring, documents process parameters, reduces human error

Cost effective – cheaper reprocessing

Clinically effective - Pineau’s study found a 4 fold reduction in +ve surveillance cultures
New guidelines

2016 Multisociety guideline update
ASGE, ACG, AGA, ASCRS, SGNA, APIC, SHEA, AASLD
Well referenced, conservative, minimal biofilm, many unresolved issues due to incomplete data

2016 SGNA
Extensive references incl Infection Control in Endoscopy, good sections on biofilm and drying

Nov 2016 AORN
See overview in AORN Journal Nov 2016
Important changes

Current reprocessing protocols do not provide reasonable assurance of safety and effectiveness. (FDA, Multisociety)

Doing nothing is not an option

Consider feasibility of adding one or more of culture and quarantine, double disinfection &/or ETO to current reprocessing protocol. (Multisociety 24)

Alcohol rinse and forced air to dry endoscope after every reprocessing cycle both between patient procedures and before storage. (Multisociety, SGNA, AORN)

Drying cabinets for all endoscopes

AORN recommends

Multisociety, SGNA - You choose
Important changes

Endoscope shelf life

SGNA – 7 days
Multisociety, AORN – You choose

Read the literature

“staff should routinely review and document their attention to FDA advisories, manufacturers alerts, and the scientific literature for reports of endoscope and AER deficiencies”

(Multisociety 19)
Risk management/You choose

Develop and implement

local reprocessing plan

guidelines for quality management

review facility design and build
Engage with other experts

AORN 2016

Multidisciplinary Team

Endoscopy nurses, endoscopists, infection control personnel, microbiologists, biomedical engineers, and facilities and engineering personnel

See AAMI Preventing Device Related HAIs Report 2016 for discussion of strategies and advantages of working as a team. Include senior management
Conclusions

CPE is spreading around Australia

Biofilm is the enemy

Minimize wet scope time

Eliminate endoscope defects

Plan for the inevitable
Inevitable

Outbreaks will occur

Outbreaks will occur soon

All outbreaks will be detected
Reading tonite

Multisociety guidelines update

SGNA guidelines

AORN guidelines

Biofilms and reprocessing medical devices Roberts 2013

CARAlert

AAMI Preventing Device Related HAIs
Preventing device related HAIs


Endoscopes are the device with highest risk of transmitting infection

Analysed systemic causes of HAIs

Human behaviour and social environment

Safety culture “Pointing out a problem is risky unless there is a culture of safety where the facility rewards such behaviour and there is no fear of punishment”
Preventing device related HAIs

Systemic causes of HAIs
  Human behaviour and social environment
  Facilities, governance, patient care

Poor facility design compromises reprocessing
Accountability for HAIs at all staffing levels from senior management down
Preventing device related HAIs

Systemic causes of HAIs
  Human behaviour and social environment
  Facilities, governance, patient care
  Device

Design should consider human factors and usability
Plan and budget for whole process - training, use, reprocessing, maintenance and storage