Multiresistant pathogens and medical device processing: How safe are our patients?

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Transmission of healthcare associated infections

- Hands
- Contaminated medical devices
- Contaminated items, which are close to the patient (nursing utensils, blood pressure cuff, stethoscope, mobile phones, keyboards, doorhandles, sanitary equipment)
- Beds, furniture, floors
- Pharmaceuticals, food
- Air
Different requirements for different classes of devices

- Uncritical devices: cleaning
  - Cleaning manual, mechanical
  - Detergent: alkaline, neutral, acidic, enzymatic
  - Certain devices require disinfection: bedpans, urine bottles

- Semicritical devices: disinfection
  - Manual (wiping, spray, immersion), mechanical (washer disinfecter)
  - Washer disinfecter: thermal (80 – 95°C), chemical, chemothermal (40 – 60°C + chemical disinfectant)

- Critical devices: sterility
  - Cleaning and disinfection (manual or mechanical)
  - Sterilization: thermal, chemical sterilant + low temperature
Device-associated infections: factors affecting patient’s safety

- microorganism/pathogen
- medical device (type/design, mode of application)
- processing technology
Sensitivity of pathogens against chemical disinfectants

1. Low to moderate resistance
   lipophilic (coated) viruses
   vegetative bacteria
   yeasts and moulds

2. Moderate to high resistance
   hydrophilic (uncoated) viruses, Hepatitis B-virus

3. High to very high resistance*
   bacterial endospores
   prions

* not inactivated by chemical disinfectants
Sensitivity of pathogens against chemical biocides

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   - lipophilic (coated) viruses
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2. Moderate to high resistance
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   - bacterial endospores
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* not inactivated by chemical disinfectants

- MRSA
- VRE
- MRGN
- C. diff.-spores
Resistance of bacteria against disinfectants
Susceptibility of MRSA-isolates against seven biocides (MBC)

NaClO: sodium hypochlorite
GLA: glutaraldehyde
BKG: benzalkonium chloride
AEG: alkyl-diaminoethylglycin
CHG: chlorhexidine
PVI: povidone iodine
EtOH: ethylenoxide

green line: 5 min exposure time
black line: user concentration

Narui K et al. Biol Pharm Bull 2007; 30:585-587
Biocide tolerance of MRSA strains expressing genes for QAC efflux pumps

Smith K et al. J Antimicrob Chemother 2008;61:78-84
MIC of *P. aeruginosa* cultures following repeated exposure to CHX (5 μg/mL)

<table>
<thead>
<tr>
<th>Culture number</th>
<th>Original MIC (μg/mL CHX) before multiple exposure to CHX (5μg/mL)</th>
<th>MIC (μg/ml CHX) after five subcultures in CHX (5μg/ml)</th>
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</thead>
<tbody>
<tr>
<td>1*</td>
<td>8–10</td>
<td>&gt;70‡</td>
</tr>
<tr>
<td>2</td>
<td>28†</td>
<td>&gt;70‡</td>
</tr>
<tr>
<td>3</td>
<td>&gt;40†</td>
<td>&gt;70‡</td>
</tr>
<tr>
<td>4</td>
<td>&gt;50†</td>
<td>&gt;70‡</td>
</tr>
<tr>
<td>5</td>
<td>70†</td>
<td>&gt;70‡</td>
</tr>
</tbody>
</table>

*Standard parent strain;
† Cultures from step-wise training method, trained to higher MIC than standard parent strain;
‡ These cultures were found to be stable after 15 subcultures in CHX-free nutrient broth.

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*Thomas et al. J Hosp Inf 46: 297-303*
Mechanisms of resistance against disinfectants
Resistance against disinfectants

- **Triclosan**  
  (multidrug efflux pump)

- quaternary ammonium compounds (BZK)  
  (efflux pumps, downregulation of porins)

- **chlorhexidin**  
  (inactivation of porins, efflux pumps)

- aldehydes, oxygen-releasing compounds (rare)  
  (enzymes e. g. formaldehyde-dehydrogenase, antioxidants, endonuclease for DNA repair)
Antibiotic resistance (AR) vs. disinfectant resistance (DR)

- **Antibiotics** $\rightarrow$ (mostly) one target
  - one step mutation my cause AR (e.g. PbP2b and MRSA)
  - co-induction of DR rare

- **Disinfectants** $\rightarrow$ several targets
  - multiple step mutation essential
  - co-induction of AR possible
Co-selection of resistance against antibiotics and a biocide

**Escherichia coli** producing VIM-1 carbapenemase isolated on a pig farm

Jennie Fischer¹, Irene Rodríguez¹, Silvia Schmoger¹, Anika Friese², Uwe Roesler², Reiner Helmuth¹ and Beatriz Guerra¹*

¹Federal Institute for Risk Assessment, BfR, Department for Biological Safety, Max-Dohm Strasse 8–10, D-10589 Berlin, Germany; ²Free University Berlin, FU, Institute of Animal Hygiene and Environmental Health, Philippstr. 13, D-10115 Berlin, Germany

resistance against: penicillins, cephalosporins, streptomycin/spectinomycin, sulfonamides, carbapenems, quaternary ammonium compounds

**Figure 1.** Schematic representation of a 5385 bp pRH-R178 region that contains part of the bla<sub>VIM-1</sub> In110 integron and its genetic environment (HE663536). *intI1* sequence identical to the one shown in accession no. AM180753 (In71 integron). The triangle indicates a mutation inside the P1 promoter (−35 TTGACA; −10 TAAGCT) with respect to the sequence with accession no. GQ422826 (position 6421, G→T), corresponding to Pc hybrid 2. The white arrows indicate partial sequences. The striped arrows indicate resistance gene cassettes contained in the variable region of the integron.
Factors influencing the results of processing

- organic load, microbial load, biofilm

Is biofilm accumulation on endoscope tubing a contributor to the failure of cleaning and decontamination? Pajkos, Vickery, Cossart; J Hosp Infect (2004)
A mature biofilm in a flowing environment comprises a complex mushroom-shaped architecture, long streamers, and water channels which permit the bulk fluid to penetrate deep within the biofilm, carrying oxygen and nutrients.

Factors influencing the results of processing

- adhesiveness of instrument surface (smooth, rough, porous, wear and tear)

- limited material compatibility (temperature, pH)
Factors influencing the results of processing

- accessibility of the surfaces of the device: hollow instruments, narrow lumens and spaces
Factors influencing the results of processing

- effectivity of cleaning (washer disinfecter performance, water quality, water pressure and temperature)

The Sinner Circle

- Temperature (T)
- Mechanics (M)
- Time (t)
- Chemicals (Ch)
Factors influencing the results of processing

- standardization and monitoring of the process (“human factor”)
You can clean without sterilizing, but you cannot sterilize without cleaning

The microbiological condition of any reusable medical device is the result of cleaning and disinfection/sterilization

Example: Validation of reprocessing of flexible endoscopes according to EN ISO/TS 15883-5: reduction of test bacteria from contaminated PTFE-tubes (L 2 m, Ø 2 mm):

\[
9 \text{ log} = 3 \text{ log by mechanical cleaning} + 6 \text{ log by disinfection}
\]
Evaluation of disinfection and sterilization of reusable angioscopes with the duck hepatitis B model

X. Chaufour, MD; K. Vickery, PhD; Sydney, Australia; J Vasc Surg 1999; 30: 277-282.

Control N = 38

Proper cleaning
Submerging in clean tap water, brushing and flushing. Submerging in enzymatic detergent and flushing with detergent mix. Brushing and soaking in detergent mix (10 min) before flushing and rinsing with tap water  N = 88

Unproper cleaning
Flushing of angioscope onc with 5 ml of sterile water  N = 105

Disinfection 2% Glutarald. 5 min 10min 20min EO

EO

Contamination N = 231

Disinfection 2% Glutarald. 5 min 10min 20min EO

N = 10  N = 10  N = 35  N = 35

Surgery in 1 day old ducklings
Evaluation of disinfection and sterilization of reusable angioscopes with the duck hepatitis B model

X. Chaufour, MD; K. Vickery, PhD; Sydney, Australia; J Vasc Surg 1999; 30: 277-282.

Transmission of DHB virus through invasive procedure

<table>
<thead>
<tr>
<th>Control</th>
<th>Flushed</th>
<th>Unproper cleaning</th>
<th>Proper cleaning</th>
</tr>
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<tbody>
<tr>
<td></td>
<td></td>
<td>Disinfection 2% Glutarald.</td>
<td>Disinfection 2% Glutarald.</td>
</tr>
<tr>
<td></td>
<td></td>
<td>5 min</td>
<td>10min</td>
</tr>
<tr>
<td>38</td>
<td>1</td>
<td>1</td>
<td>9</td>
</tr>
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<td></td>
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<td>14</td>
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<td></td>
<td></td>
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<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>9</td>
<td></td>
</tr>
<tr>
<td>100%</td>
<td>100%</td>
<td>100%</td>
<td>100%</td>
</tr>
</tbody>
</table>

Positive | Negative
0% | 10% | 20% | 30% | 40% | 50% | 60% | 70% | 80% | 90% | 100%

Transmission of DHB virus through invasive procedure
Sensitivity of pathogens against heat

- 60°C/30 min: viruses, bacteria, fungi
- 80°C/10 min: Hepatitis B-virus
- 90°C/1-5 min: bacterial endospores
- 121°C/15 min: C. diff. - spores
- 132°C/60 min: prions

MRSA, VRE, MRGN
Sensitivity of pathogens against heat

- 60°C/30 min
- 80°C/10 min
- 90°C/1-5 min
- 121°C/15 min
- 132°C/60 min

viruses, bacteria, fungi

no adaptive or genetic increase of heat resistance

MRSA
VRE
MRGN

C. diff.-spores

prions
Impact of microbial load (bioburden) on the kinetics of steam sterilization

Sterility acceptance level (SAL): $10^{-6}$
Impact of microbial load (bioburden) on the kinetics of steam sterilization

Sterility acceptance level (SAL): $10^{-6}$

lower bioburden $\rightarrow$ shorter inactivation time $\rightarrow$ higher safety in a standard (overkill) cycle
The grey zone:
Viable but not culturable (VBNC)
The grey zone:

Viable but not culturable (VBNC)

VBNC bacteria are cells demonstrating metabolic activity but are incapable of undergoing sustained cellular division required for growth in or on an artificial medium normally supporting growth of these cells.
Parameters to detect non-culturable microorganisms

- Enzymatic activity
  - Esterase
  - Redox activity
- Membrane permeability (live/dead, PMA)
- Membrane potential
- Protein production (rRNA, FISH)
- Cell elongation

All organisms with positive response of these parameters may recover

Courtesy Prof. Flemming, University of Essen
What do we need to warrant patient safety, facing MR pathogens?

Better sterilizers,
better washer disinfectors,
better chemical disinfectants?
What do we need primarily to warrant patient safety?

Better sterilizers, 
better washer disinfectors, 
better chemical products?

No!
What do we need to warrant patient safety? (1)

• Improved responsibility of caregivers: “Cleaning is something everybody can do??”

• Better information on the scientific basis and the significance of device processing (top - down!) including the role of MR pathogens

• Standardization and validation (if possible) of processing measures

• Application of chemical disinfectants under strict adherence to recommended concentrations and exposure times; avoidance of prolonged contact between disinfectant and bacteria under soiled conditions
What do we need to warrant patient safety? (2)

- Quality management including continuous monitoring of processes, education of staff, and update of documents

- Effective and reliable processing of medical instruments minimizes the risk of device-associated infection including the transmission of multiresistant bacteria
Thank you