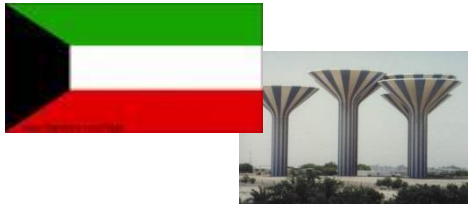

7th GCC Conference on Infection Prevention and Control
Kuwait, 1st to 3rd December 2013

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

Prof. Dr. Peter Heeg

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SPAIN
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Ionian Sea
GREECE
Athens
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BALEARIC ISLANDS
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Mediterranean Sea

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

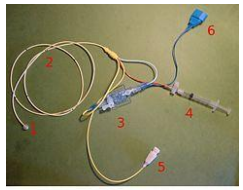
- Pharmaceuticals, food

- 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

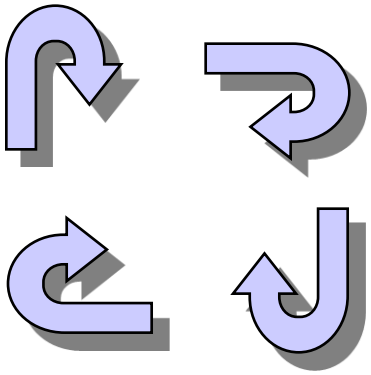
- semicritical devices: disinfection
  - manual (wiping, spray, immersion), mechanical (washer disinfector)
  - washer disinfector: thermal (80 – 95°C), chemical, chemothermal (40 – 60°C + chemical disinfectant)



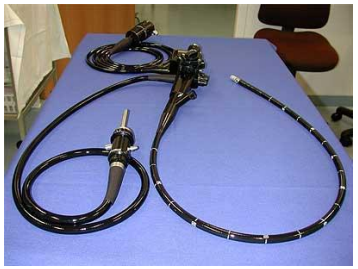
- critical devices: sterility
  - cleaning and disinfection (manual or mechanical)
  - sterilization: thermal, chemical sterilant + low temperature

Device-associated infections: factors affecting patient‘s safety

microorganism/pathogen

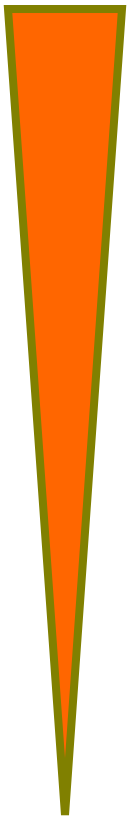


medical device
(type/design, mode of application



processing technology

Sensitivity of pathogens against chemical disinfectants



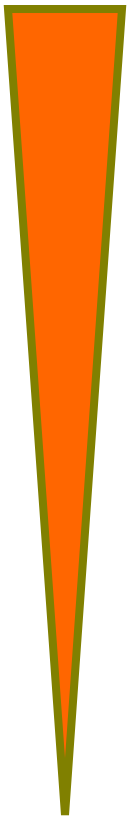
1. Low to moderate resistance
   lipophilic (coated) viruses
   vegetative bacteria
   yeasts and moulds

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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MRSA
VRE
MRGN

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   bacterial endospores
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C. diff.-spores

* not inactivated by chemical disinfectants

Resistance of bacteria against disinfectants

?

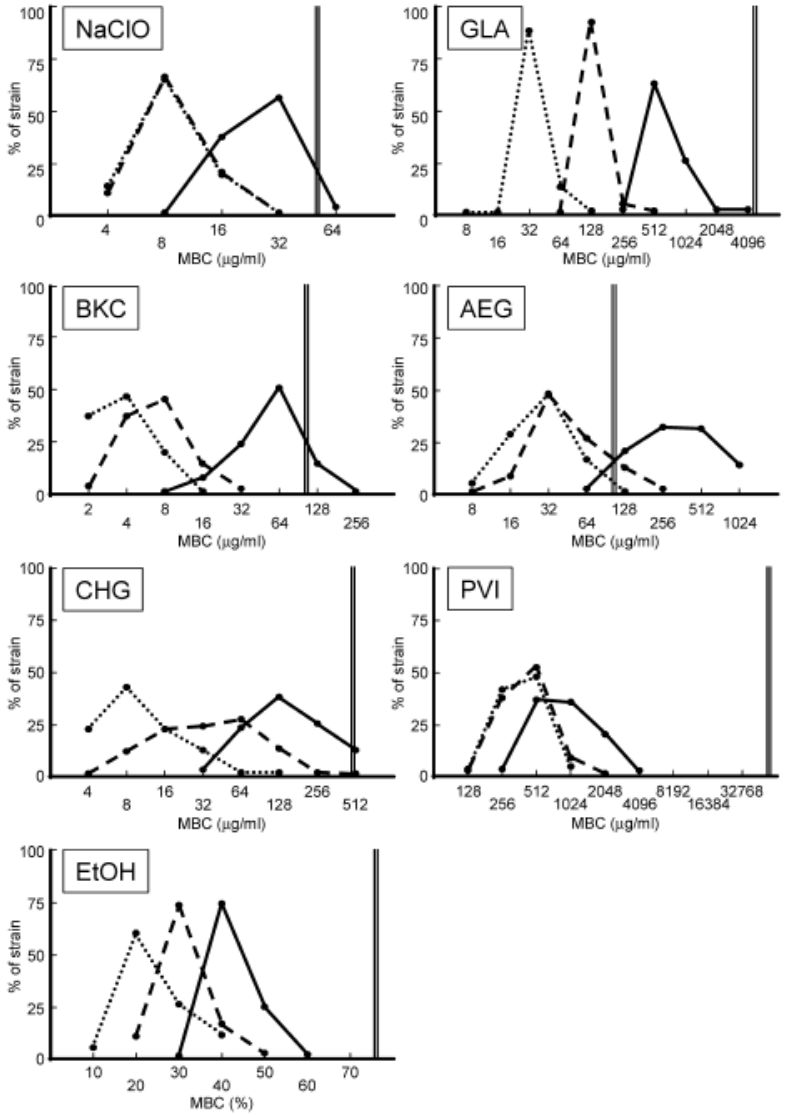


Fig. 2. MBCs of Biocides for 42 MRSA Isolates in Each Exposure Time

NaClO, Sodium hypochlorite; GLA, glutaraldehyde; BKC, benzalkonium chloride; AEG, alkyldiaminoethylglycine hydrochloride; CHG, chlorhexidine digluconate; PVI, povidone iodine; EtOH, ethanol. The solid, broken, and dotted lines indicate MBCs for 42 MRSA isolates at 5, 30, and 180 min, respectively. The double lines indicate minimum user concentration.

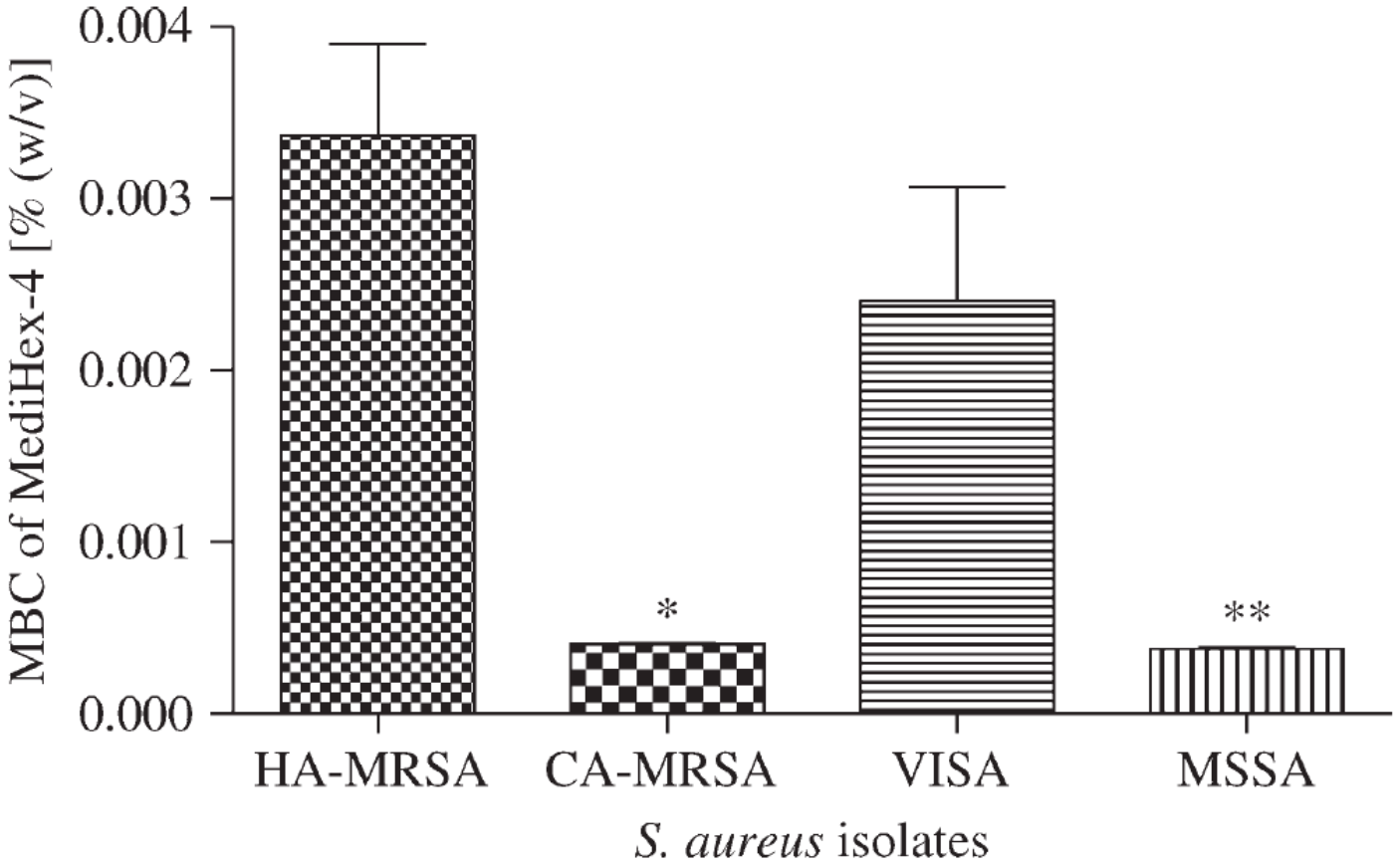
Susceptibility of MRSA-isolates aginst seven biocides (MBC)

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

solid line: 5 min exposure time
double 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)

Culture number	Original MIC (μg/mL CHX) before multiple exposure to CHX (5μg/mL)	MIC (μg/ml CHX) after five subcultures in CHX (5μg/ml)
1*	8–10	>70‡
2	28†	>70‡
3	>40†	>70‡
4	>50†	>70‡
5	70†	>70‡

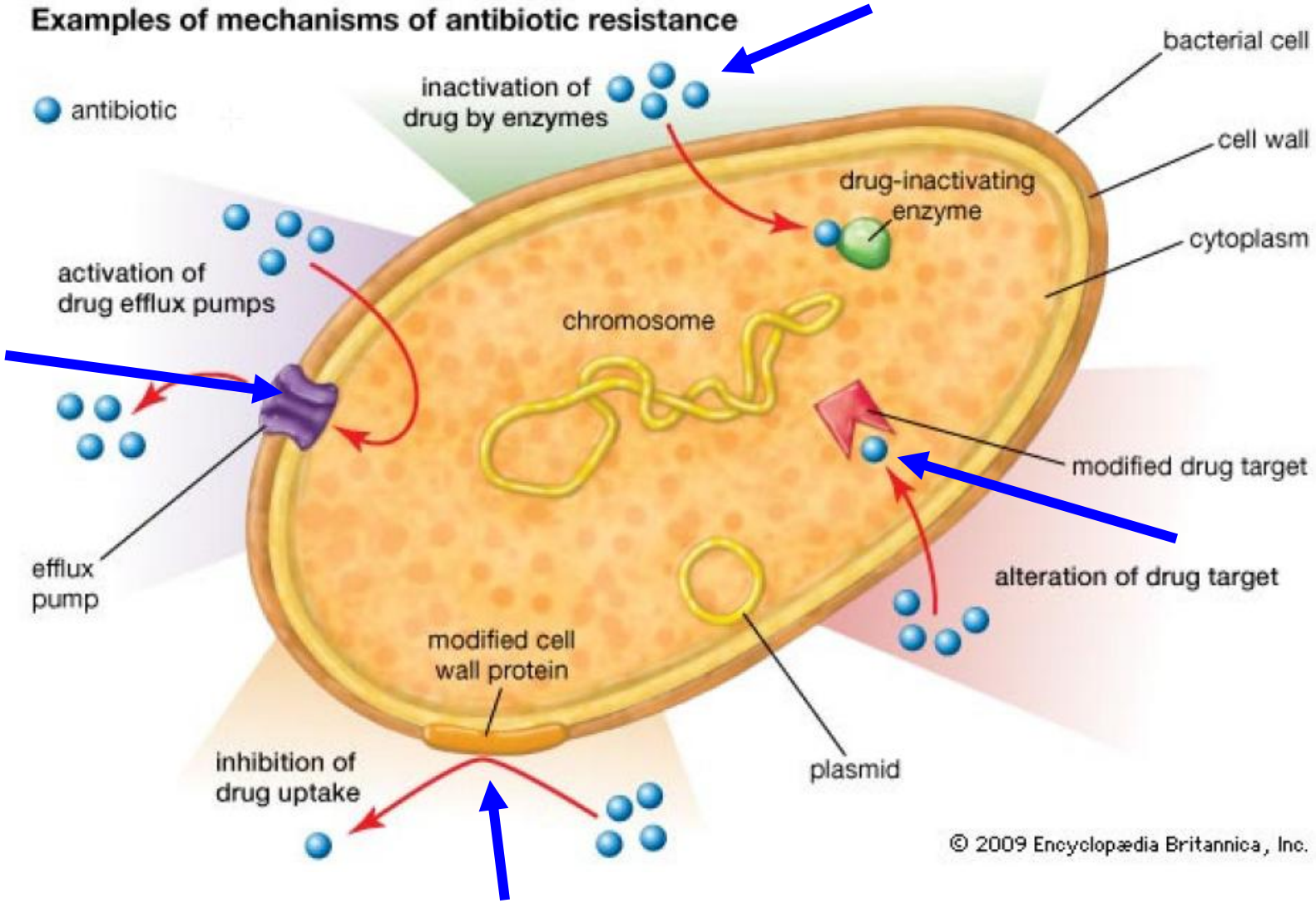
*Standard parent strain;

† 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.

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 → (mostly) one target**
  - **one step mutation my cause AR (e.g. PbP2b and MRSA)**
  - **co-induction of DR rare**
- **Disinfectants → several targets**
  - **multiple step mutation essential**
  - **co-induction of AR possible**

Co-selection of resistance against antibiotics and a biocide

J Antimicrob Chemother 2012
doi:10.1093/jac/dks108
Advance Access publication 27 March 2012

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

Jennie Fischer[1], Irene Rodríguez[1], Silvia Schmoger[1], Anika Friese[2], Uwe Roesler[2], Reiner Helmuth[1] and Beatriz Guerra[1]*

[1]Federal Institute for Risk Assessment, BfR, Department for Biological Safety, Max-Dohm Strasse 8–10, D-10589 Berlin, Germany; [2]Free 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

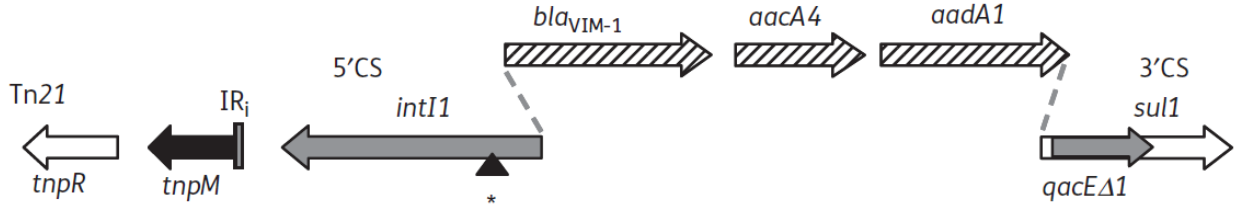
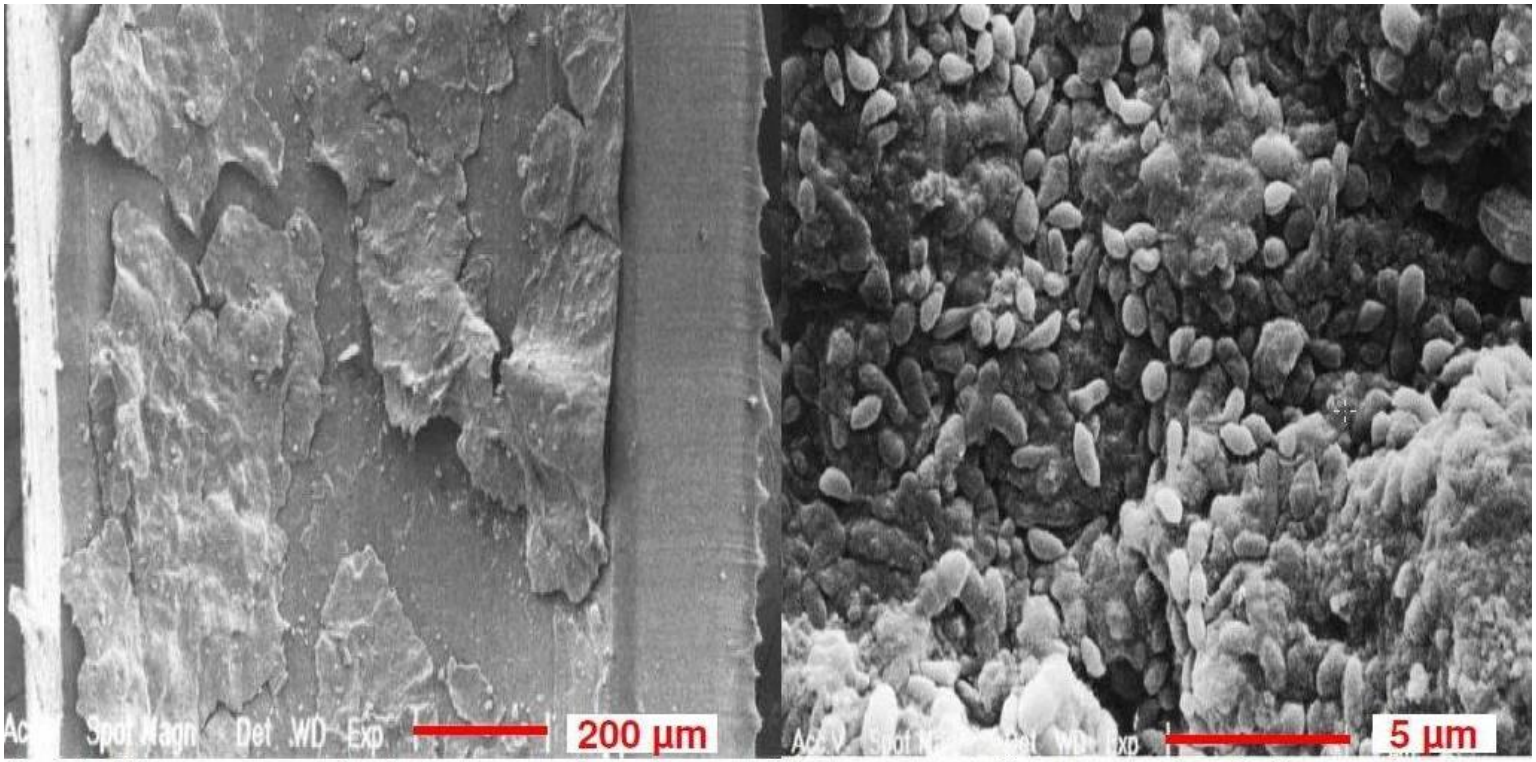


Figure 1. Schematic representation of a 5385 bp pRH-R178 region that contains part of the bla_{VIM-1} In110 integron and its genetic environment (HE663536). **intI1* sequence identical to the one shown in accession no. AM180753 (In71 integron). The triangle indicates a mutation inside the P1 promoter (−35 T**T**GACA; −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.

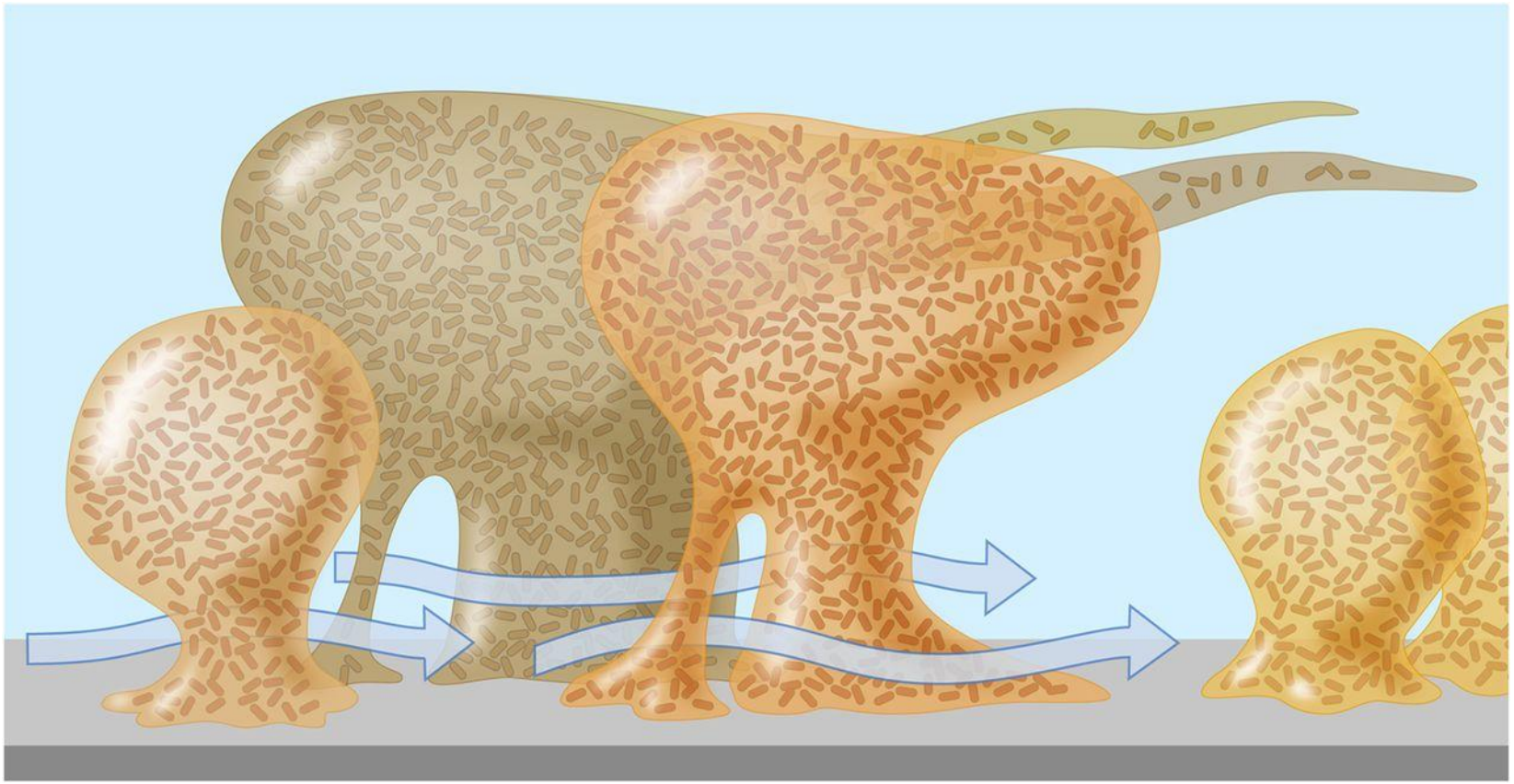
Factors influencing the results of processing

- 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.

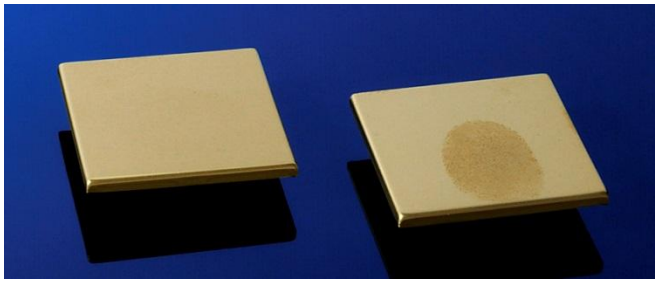


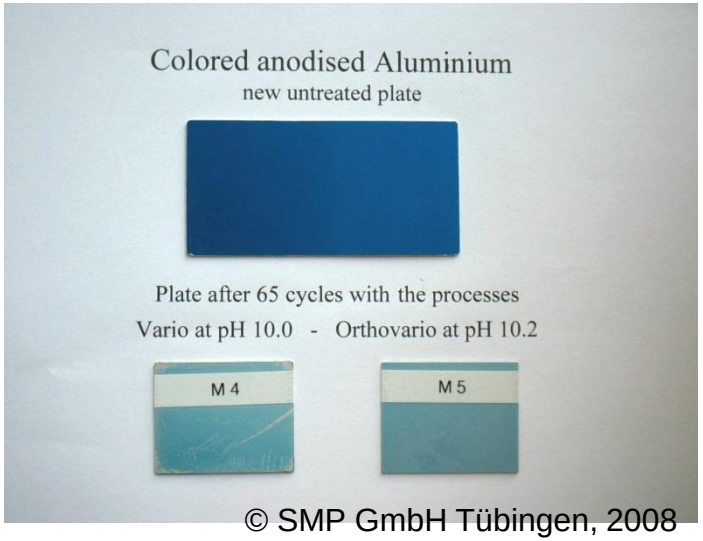
Kovaleva J et al. Clin. Microbiol. Rev. 2013;26:231-254

Clinical Microbiology Reviews

Factors influencing the results of processing

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

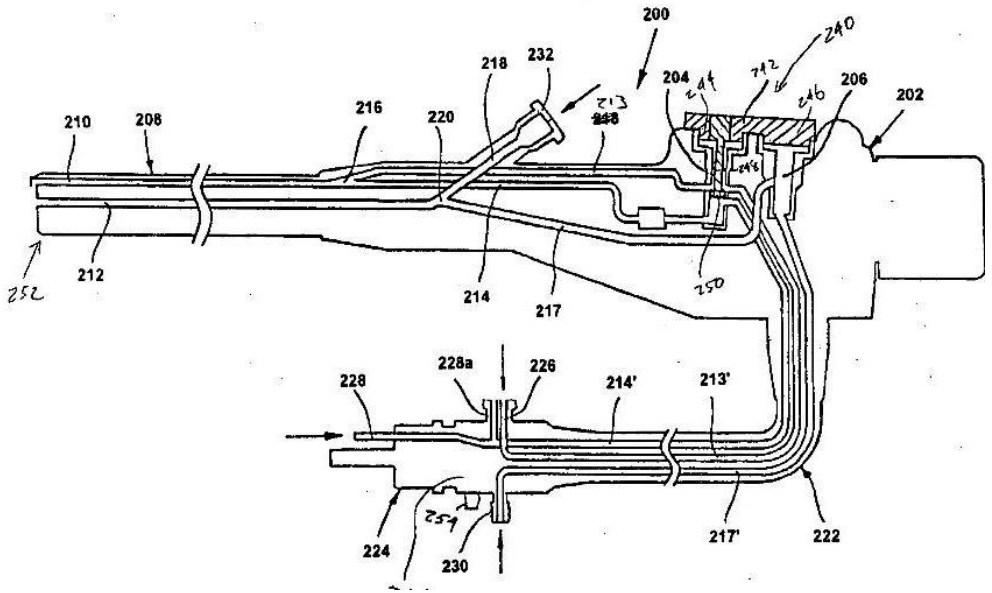


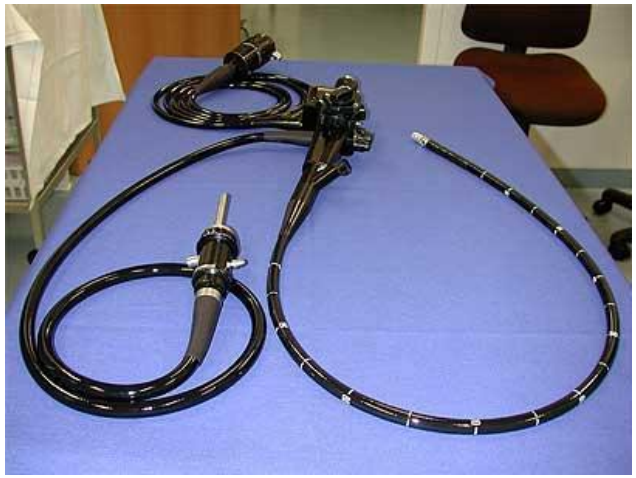


- limited material compatibility (temperature, pH)

Factors influencing the results of processing

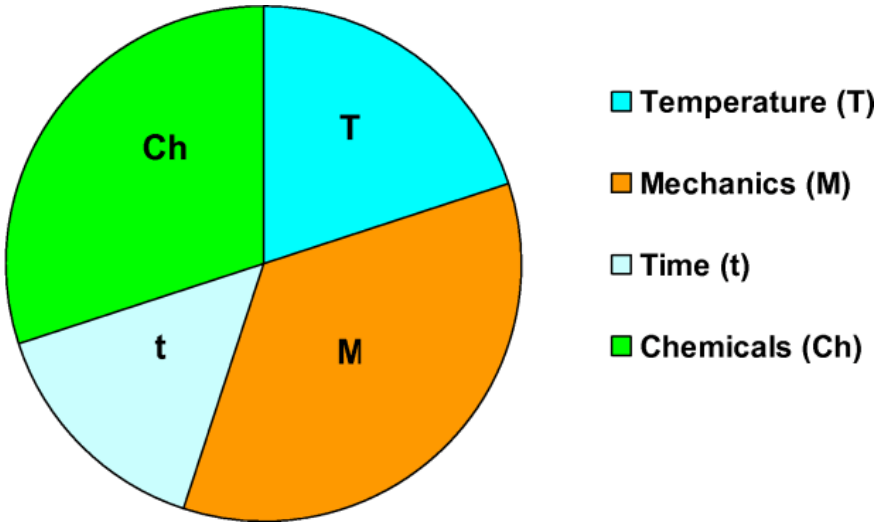
- accessibilty of the surfaces of the device: hollow instruments, narrow lumens and spaces



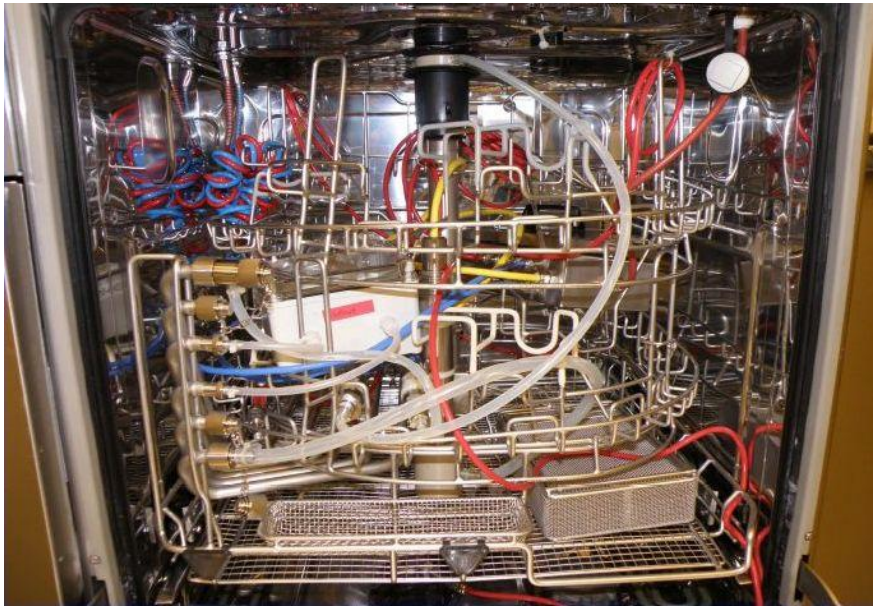


Factors influencing the results of processing

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



The Sinner Circle



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

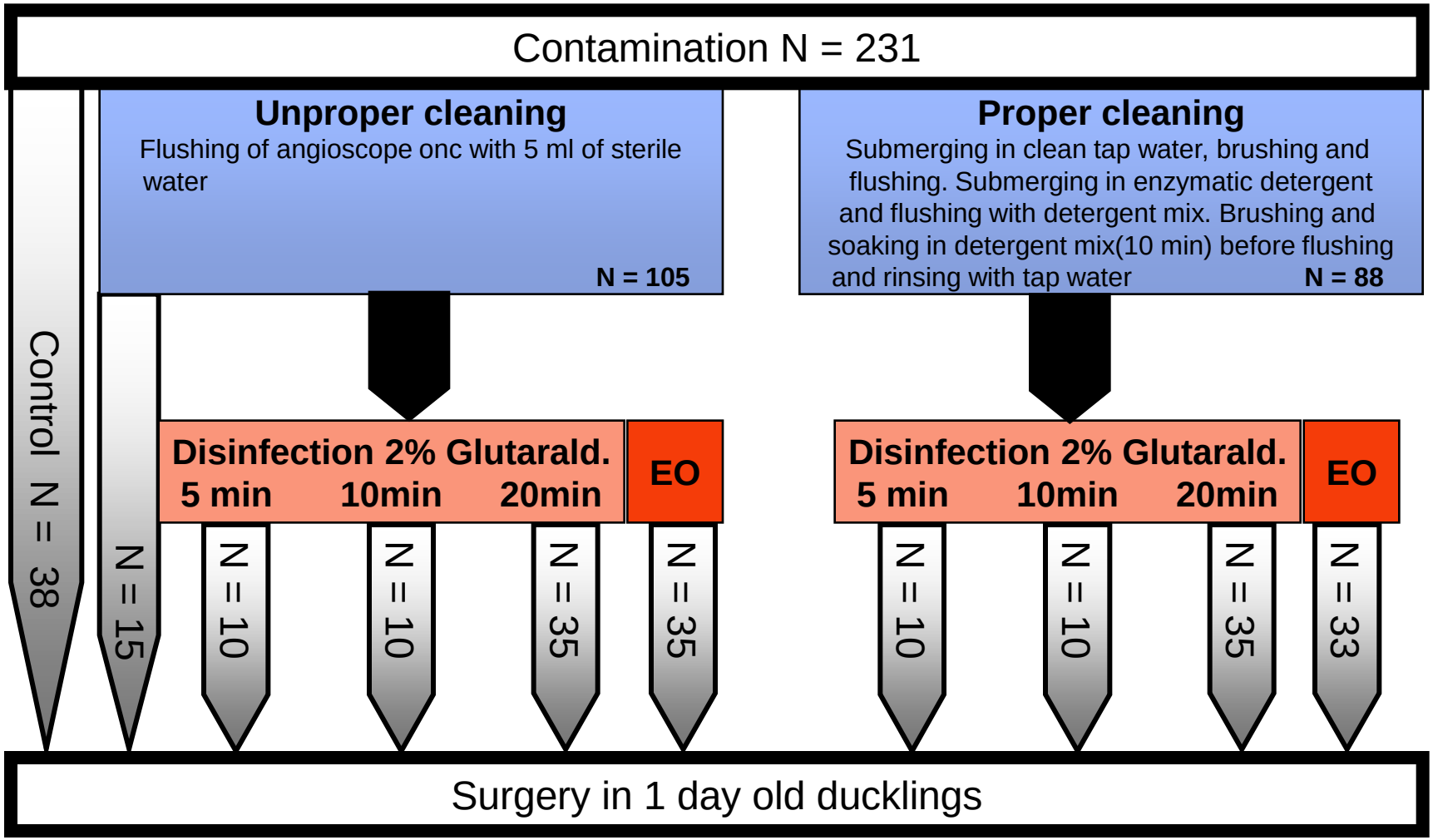
The microbiological condition of any reusable medical device is the result of cleaning **and** disinfection/sterilization

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 log = 3 log by mechanical cleaning
+ 6 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.



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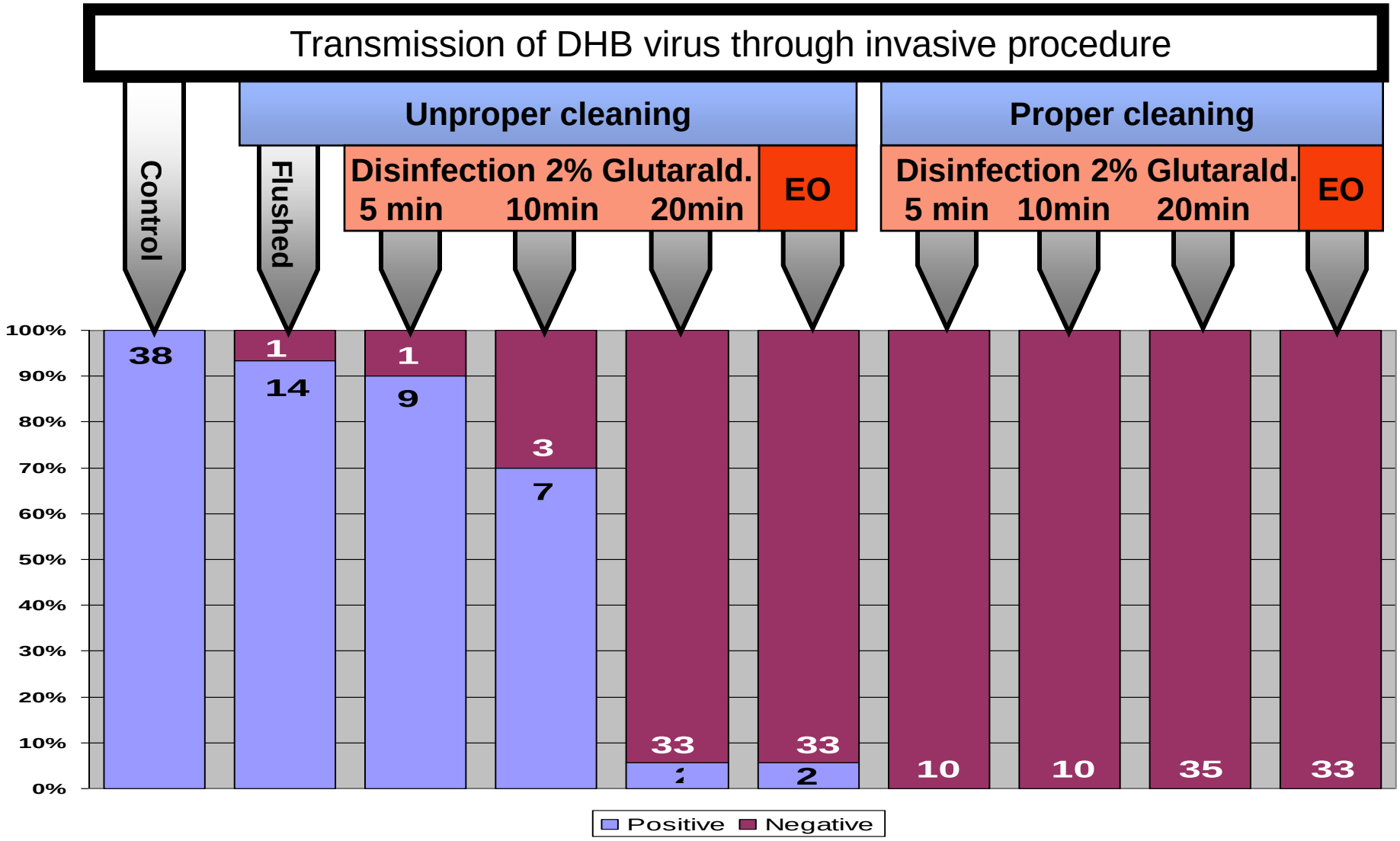
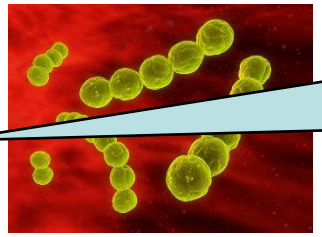


Sensitivity of pathogens against heat

60°C/ 30 min
80°C/ 10 min

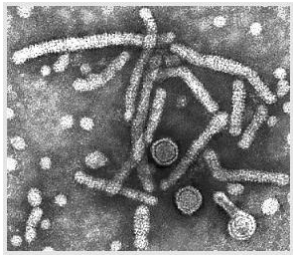
viruses, bacteria, fungi



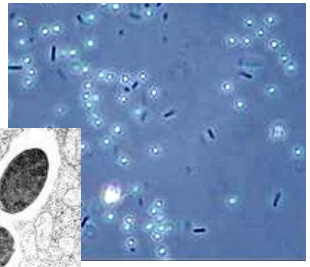
MRSA
VRE
MRGN

90°C/ 1-5 min

Hepatitis B-virus



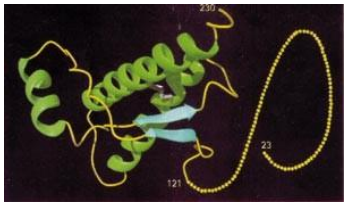
C. diff.-spores



bacterial endospores

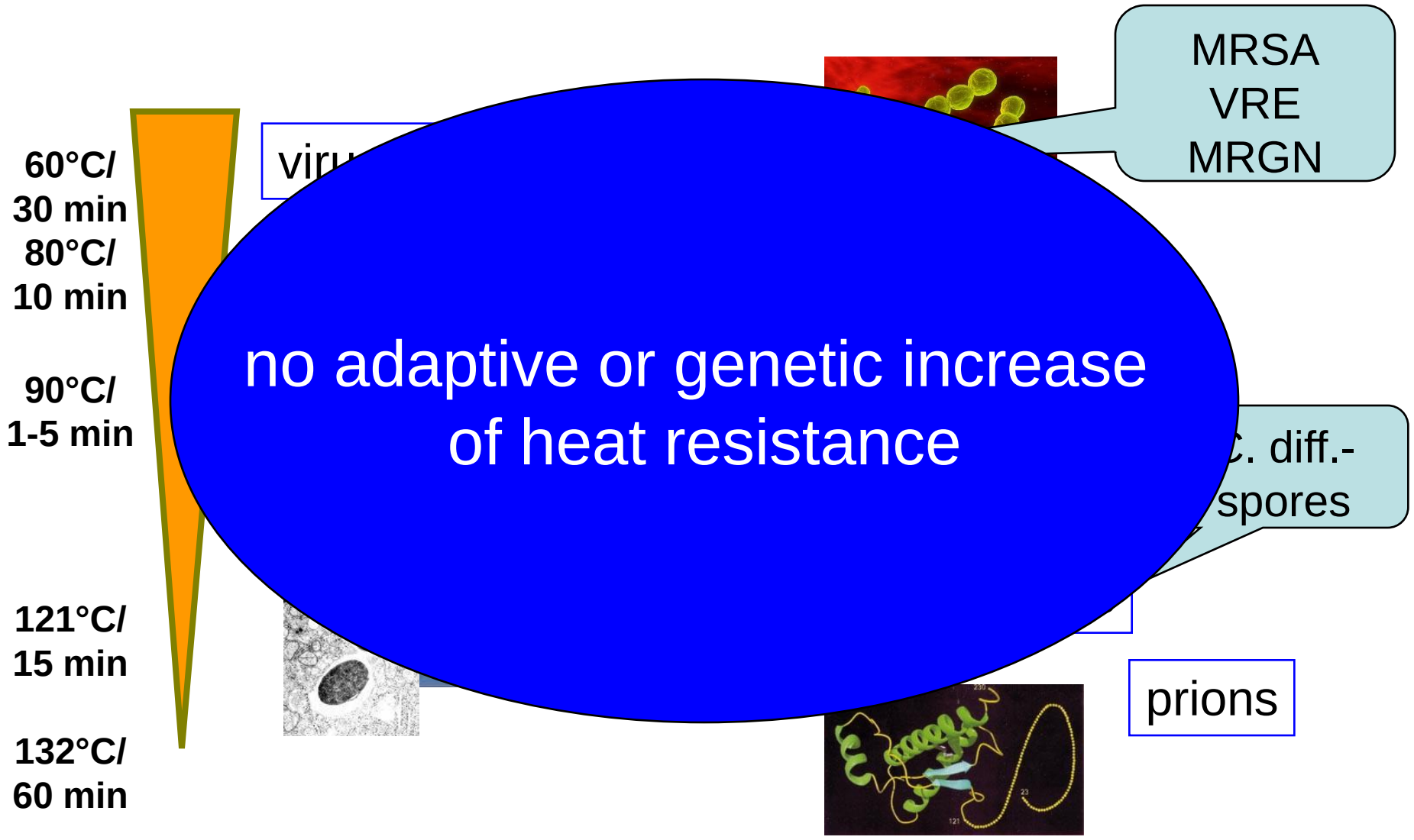
121°C/ 15 min

132°C/ 60 min

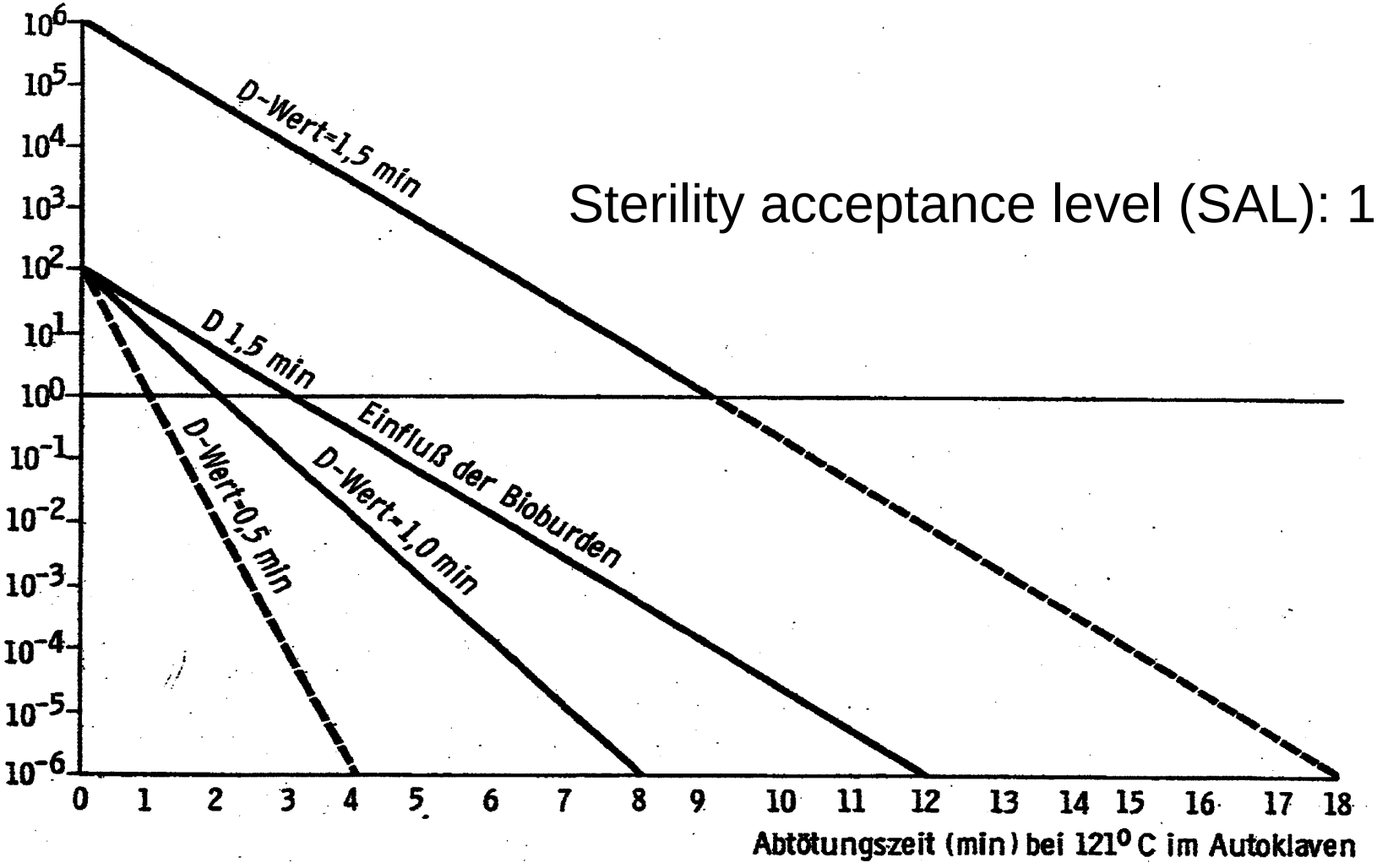


prions

Sensitivity of pathogens against heat

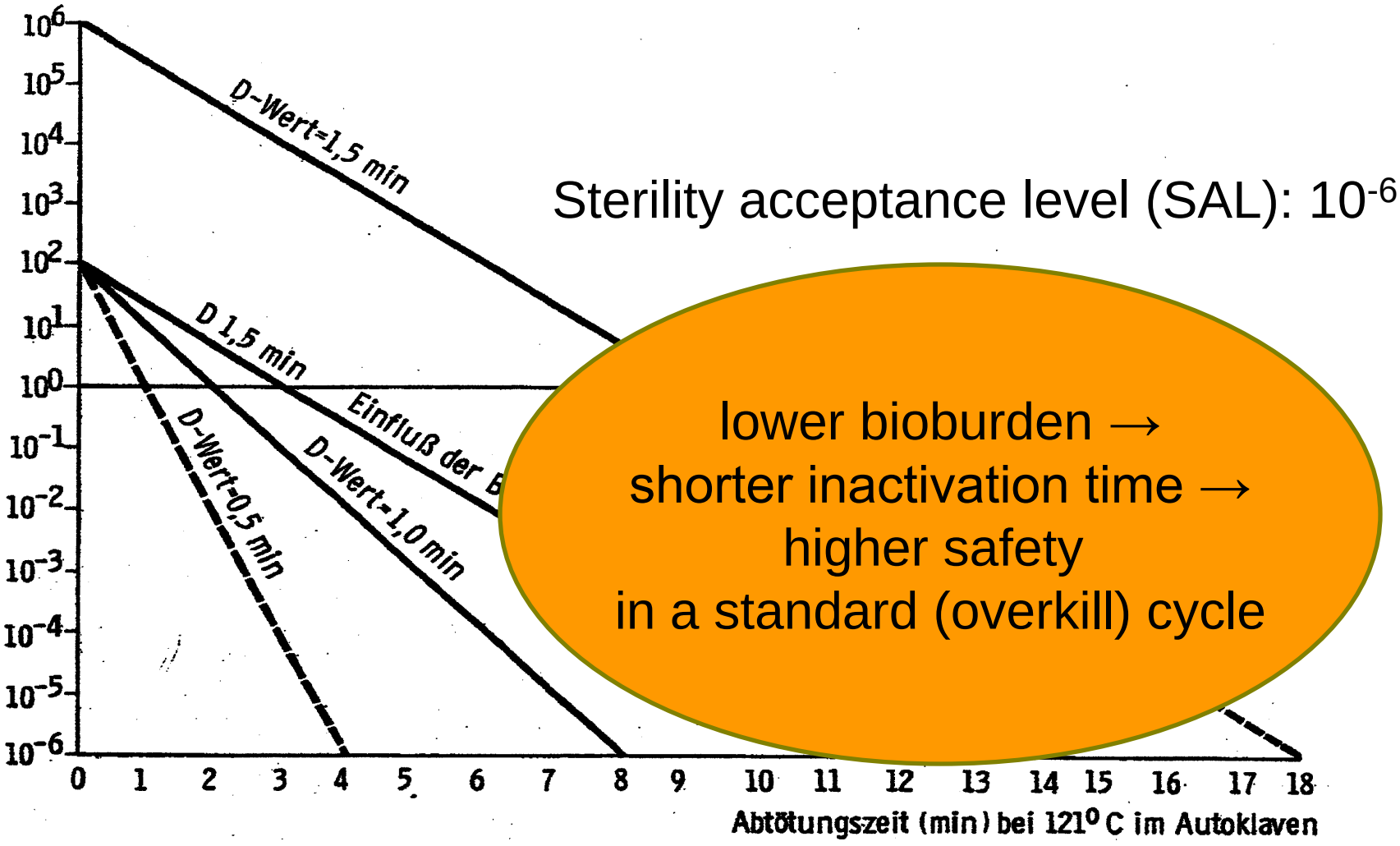


Impact of microbial load (bioburden) on the kinetics of steam sterilization



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 →
shorter inactivation time →
higher safety
in a standard (overkill) cycle

The grey zone:

Viable but not culturable (VBNC)

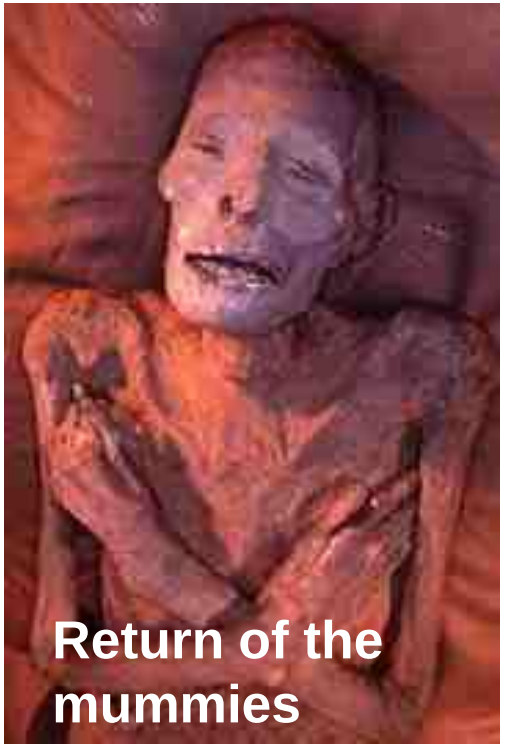
The grey zone:

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