Prevention of Health-care Associated Infections (HAI)

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our target -
the nosocomial pathogen

Some Impressions of my University Town Greifswald

The Market Place

Monastery ruins

Drawbridge from the 19th century

My Experience

Prevention of infection begins in ones mind and

the knowledge of the problem is the beginning of quality assurance

Proposed Workshops

Workshop 1: Basic informations on epidemiology of HAI

1. **Sources of infections and spread of nosocomial pathogens**
2. **Persistence of pathogens on hospital surfaces**

Workshop 2: Role of hands in infection control

Workshop 3: Role of surface disinfection in infection control

Workshop 4: Prevention of HAI by antisepsis

1. **Antisepsis of skin,**
2. **Antisepsis of mucous membranes**
3. **Antisepsis of wounds**

Workshop 5: Prevention of MRE and outbreak management

1. **MRSA**
2. **VRE**
3. **MRGN**
4. **Outbreak management**

Workshop 1: Basic Informations on Epidemiology of HAI

Universitätsmedizin GREIFSWALD

Definition of Heath-care Associated Infections (HAI)

Any infection acquired 48 h after being admitted to a healthcare setting

Exceptions:

- **Infection must not be in its incubation period**
- **Residuals of an infection acquired during a previous admission**

HAI Prevalence 2011 in Germany

Most common

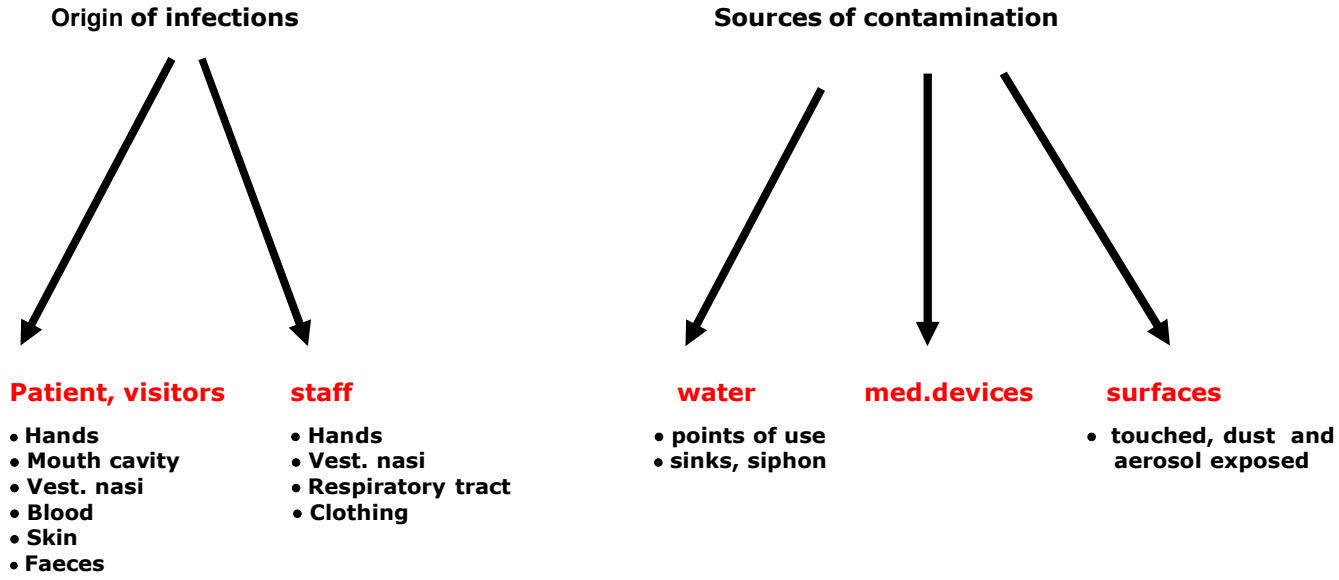
- **Surgical site infections** **25%**
- **Urinary tract infections** **22%**
- **Lower respiratory tract** **22%**
- **Bloodstream infections** **6%**

Most common pathogens

- ***E. coli*** **18.4 %**
- ***S. aureus*** **13.3 %**
- **Enterococci** **12.8 %**

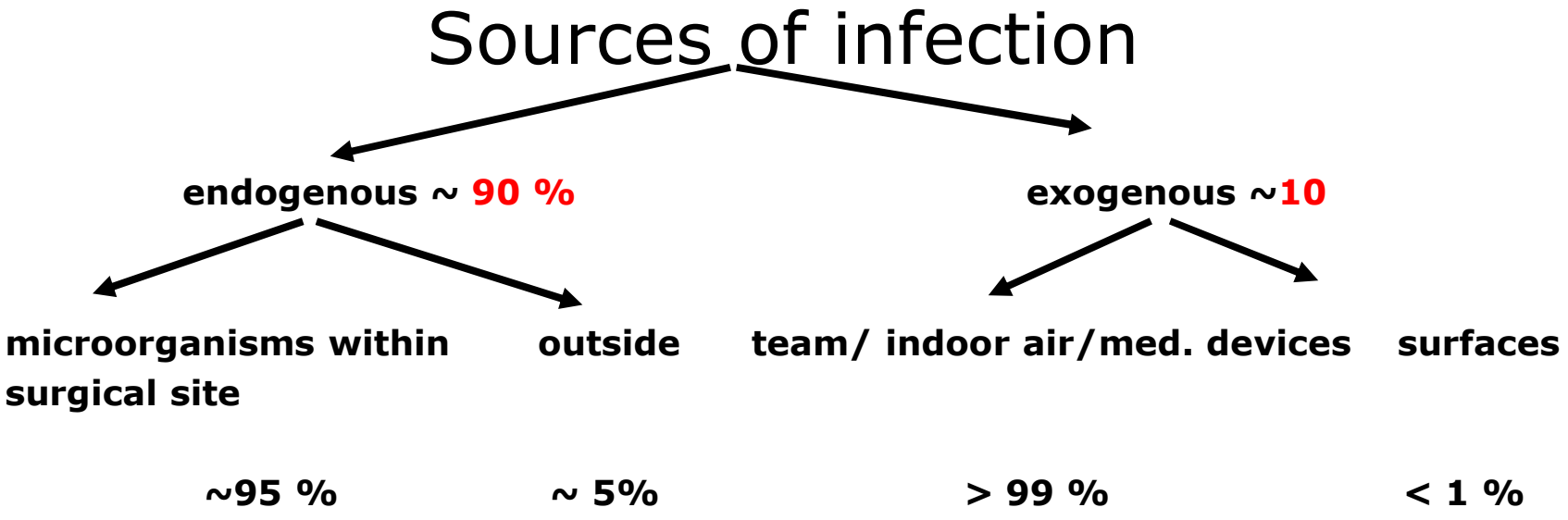
German data of the 1st European prevalence study of the ECDC. Epid Bull 2012; 26: 239-240

Main Sources of Nosocomial Infections in Health-care Facilities



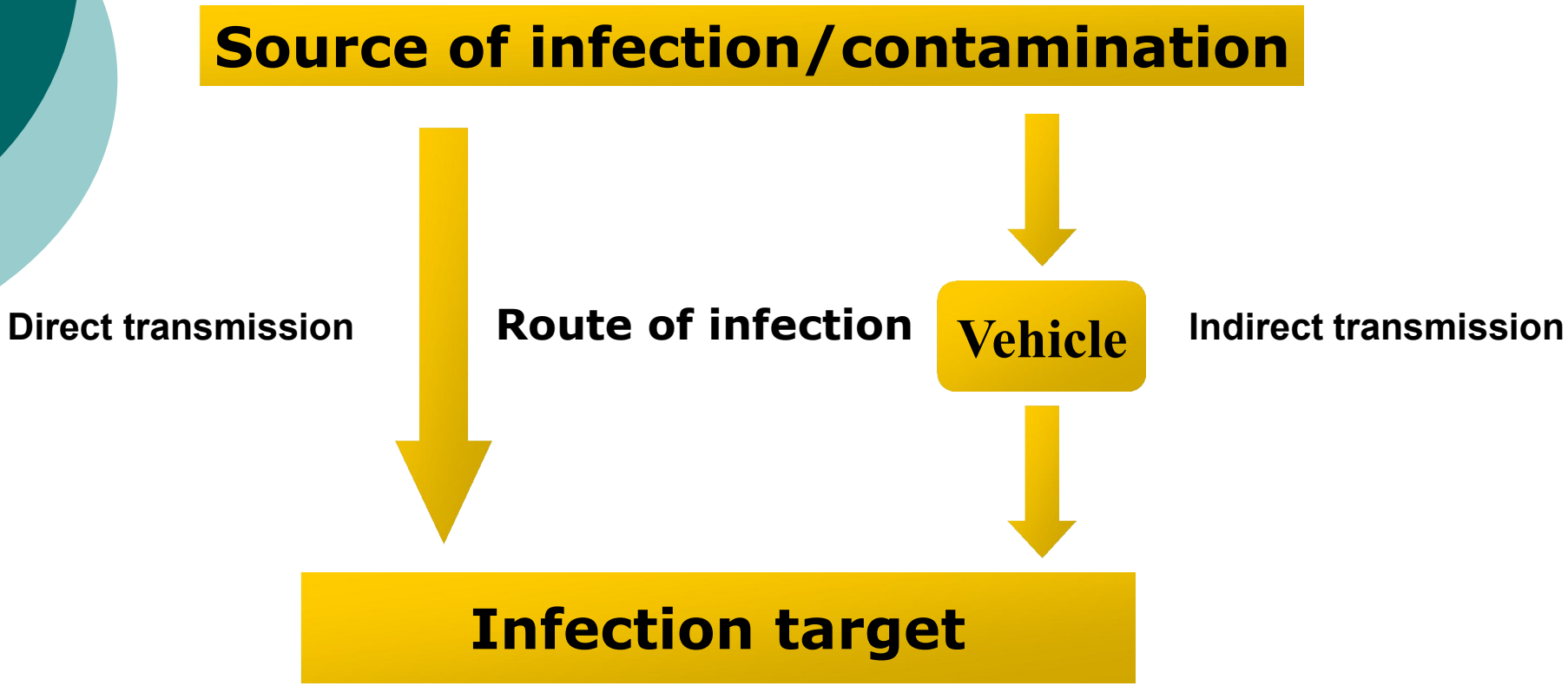
- In health-care settings, bacteria, bacterial spores, viruses and yeasts are mainly transmitted from infected and/or colonized patients, but also from staff, and in particularly to areas adjacent to patients and frequently touched surfaces by hands ("high-touch surfaces")
- Microbial flora of the respiratory tract and vestibulum nasi (MRSA) is correlated with a higher risk of contamination of surrounding surfaces through direct or indirect contact with hands
  - Intestinal infections caused i.e. by *Clostridium difficile* and noroviruses, or enteral colonization with nosocomial pathogens such as VRE, MRGN, MRSA are also associated with a risk of widespread environmental contamination

Main Sources for SSI



Patients and staff are the major sources of microorganisms

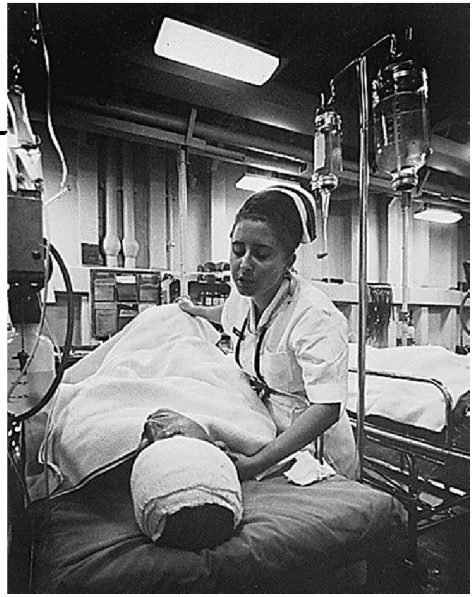
Transmission of HAI



Source

- Patient
- Healthcare worker
- Environment / equipment
- Visitor
- Animals (??)

important



less important

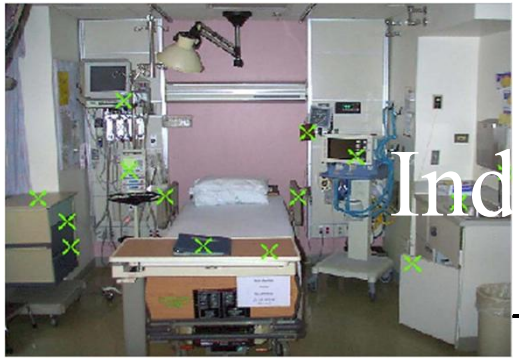
Direct Transmission

- **Infection in course of direct contact**
- **Transmission via droplets (aerogenous)**
- **Resident or transient flora of hands**

Hands Play a Special Role in Transmission

Indirect Transmission by Hands

Hayden M, ICAAC, 2001, Chicago, IL.



Indirect Transmission

In this study, hands of 131 HCWs were cultured before and gloved hands after routine care

After touching the patient and environment, 75% of ungloved HCWs hands and 9% of gloved HCWs hands were VRE+

After touching only the environment, 21% of ungloved and 0 gloved HCWs hands were contaminated.

The inanimate environment plays a role in facilitating transmission of organisms and gloves can prevent hand contamination

Hayden M, Infect Control Hosp Epidemiol. 2008;29:149-54.

Risk Factors of HAI

Patients side

- **Surgical intervention/ Implants**
- **Immunosuppression**
- **Metabolic diseases**
- **Neonates (especially VLBN)**
- **Elderly**
- **Long term hospitalization**
- **Immobility**

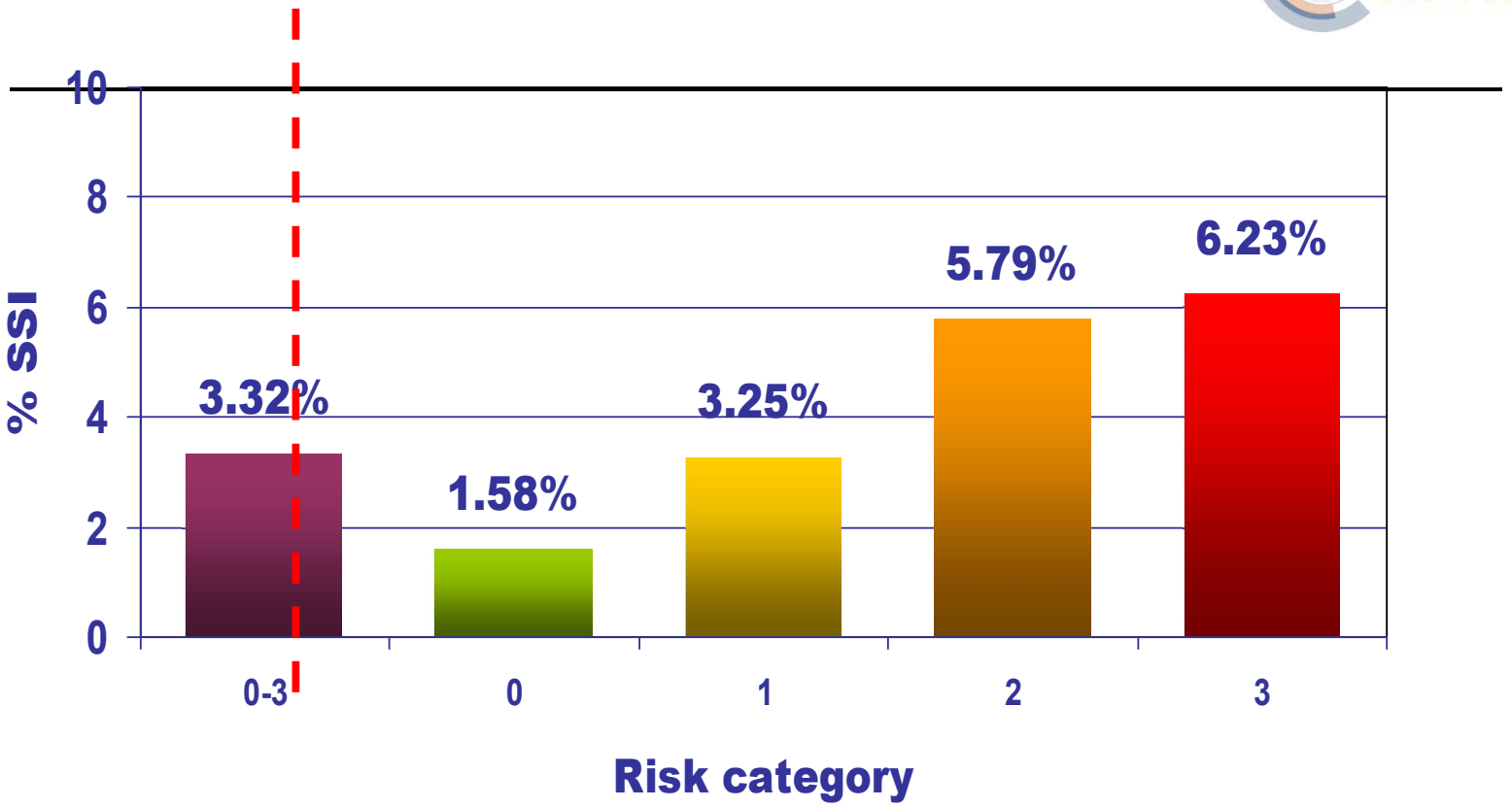
Change of pathogens

- **Resistance**
- **Virulence**
- **Contagiousness**

Additional Risk Factors for SSI

- **High NNIS Score**
- **Prolonged preoperative length of stay + higher age**
- **Diabetes mellitus: continous blood glucose control** with avoidance of levels > 200 mg/dl resp. > 11,1 mmol/l
- **Adipositas:** reduction to consider at adipositas grade II (BMI 35-40) and III (BMI > 40) at elective intervention, especially if success is influenced of BW (HEP, repair of grain hernia)
- **Malnutrition: Malnutrition is for elective surgery preoperatively compensate. In principle, patients should be fed until the day of surgery and as soon as possible postoperatively starting enterally**
- **Smoking:** Waiver strongly suggest. Avoidance of 6-8 weeks before elective surgery significantly reduce SSI. **Recommend smoking at least 30 d before surgery setting**. Given the vasoconstrictive effect, it makes sense, even immediately after the operation cease smoking
- **Anemia:** Anemia compensate preoperatively proven
- **Infection/colonisation:** with MRO, Infection another localisation, nasal colonisation with S. aureus/MRSA
- **Vitamin C deficiency**
- **Alkohol abuse**
- **Tumors**
- **Granulocytopenia < 1.500/µl**

Influence of NNIS Score in Reconstruction of Lower Extremity Arteries



NNIS risk category: one point each for

- **Duration longer than 75% of pooled interventions [longer than 168 minutes]**
- **Wound contamination class (contaminated or septic wound)**
- **ASA score ≥ 3**

Data: German National Reference Centre for Surveillance of Nosocomial Infection; 2005-2009 www.nrz-hygiene.de

Pitfalls of Pathogens

- Partially low infectious dosis
- Persistence on inanimate surfaces and hands → disinfection
- Biofilm formation → prevention and disinfection
- Development of antibiotic resistance → disinfection, antisepsis
- Invisible colonization from patients and staff → antisepsis

Infectious Doses for Selected Pathogens

Infectious dose	Organisms
(1)-10 - 100 viable particles	Norovirus, Rotavirus, EHEC, ETEC, *C. difficile*, Enterococci incl. VRE
≥ 1 viable particle in water	Oocysts of cryptosporidia
> 10^5 viable particles	*Salmonella enteritidis*

The level of microbial bio-burden on surface in healthcare settings is low compared to the numbers on patients' skin or in faeces. However, even at low particle numbers there is a risk of transmission.

Persistence on Inanimate Surfaces

Bacterium	Range of survival
Acinetobacter spp.	3 days up to 1 year
Enterococcus spp. incl. *VRE*	5 days up to 30 months
E. coli	1.5 hours up to 16 months
Klebsiella spp.	2 hours up to > 30 months
Pseudomonas aeruginosa	6 hours up to 16 months
Serratia marcescens	3 days up to 2 months
MSSA, MRSA	7 days up to 1 year
Streptococcus pneumoniae	1 day up to 30 month

Kramer A, Assadian O. Survival of microorganisms on inanimate surfaces. In: Use of Biocidal Surfaces in Clinical Settings for the Reduction of Healthcare Acquired Infections. Springer: New York, 2014

Survival of Clinically Relevant Viruses on Dry Inanimate Surfaces

Organisms	Range of survival (environment)
Adeno	< 6 h up to 3 months (type dependent), ≤ 301 days (in water)
SARS Corona	< 5 min up to 24 hours (on paper)5 to 28 days (at room temp.)28 days (at 4 °C)
Coxsackie	7 to 10days, up to > 2 weeks
Hepatitis A	2 hours up to 60 days
HIV	Up to 7 days, 7 days (in peritoneal dialysis effluent), 48 hours (on peritoneal dialysis exchange and tubing), 4 to 8 weeks (on glass cover slides)
Influenza	1 to 28 days (strain dependent),1 to 3 days (on banknotes), up to 8 days (admixed in mucous)
Noro, FCV, MNV	8 hours up to 7 days, MNV > 40 d (in diapers and gauze)

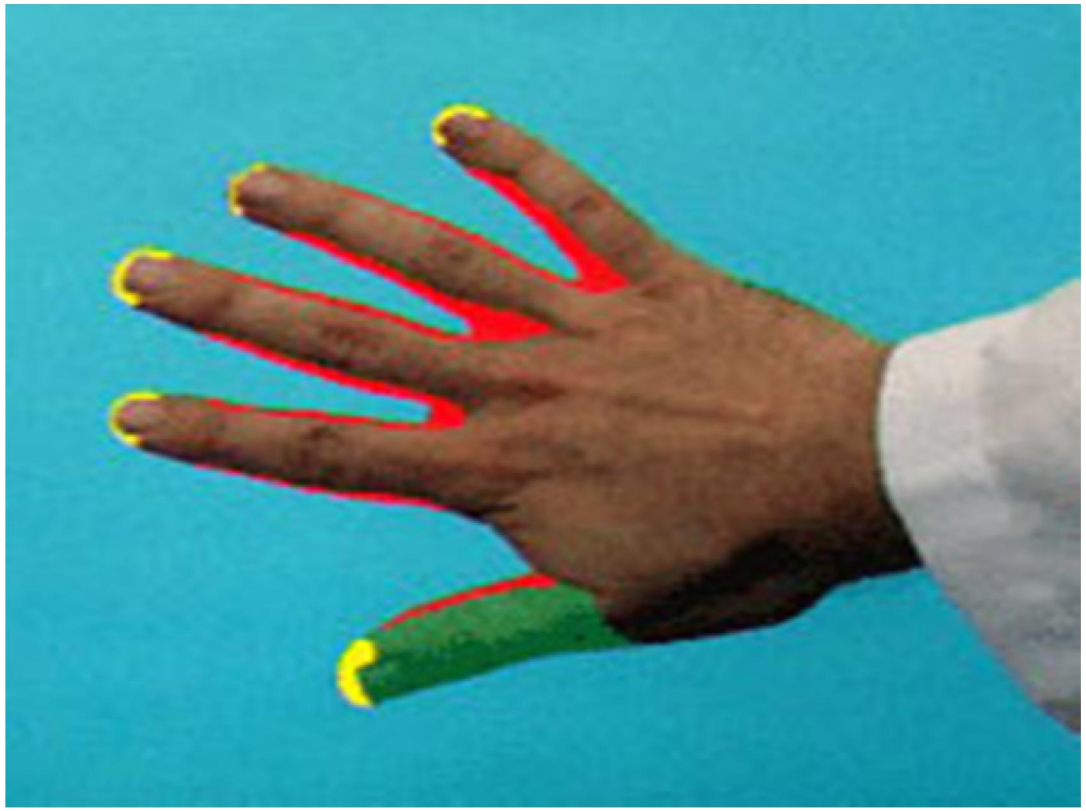
Survival of Clinically Relevant Viruses on Dry Inanimate Surfaces

Organisms	Range of survival (environment)
Papilloma	≤ 7 days
Parvo	> 1 year
Polio type 2	1 day up to 8 weeks
Rhino	2 hours up to 7 days
Rota	30 min, 6 up to 60 days
Vaccinia	3 weeks up to > 20 weeks

Survival of Clinically Relevant Fungi on Dry Inanimate Surfaces

Organisms	Range of survival (environment)
Aspergillus spp.	**> 30 days**
Candida albicans	**1 up to 120 days, 24 weeks (in soil-water mixture)**
***Cryptococcus* spp.**	**24 weeks (in soil-water mixture)**
Fusarium spp.	**> 30 days**
***Mucor* spp.**	**> 30 days**
Torulopsis glabrata	**102 up to 150 days**

Workshop 2: Role of Hands in Infection Control



Importance of Hand Disinfection

Hand hygiene is generally considered to be the most important measure to prevent the spread of HAI

2002 HICPAC/SHEA/APIC/IDSA guidelines and the World Alliance for Patient Safety recommend hand hygiene in health-care settings as fundamental method for infection control

Boyce JM, Pittet D. Guideline for hand hygiene in health-care settings. Recommendations of the healthcare infection control practices advisory committee and the ICPAC/SHEA/APIC/IDSA hand hygiene task force. *MMWR* 2002; 51: 1-45.

Kampf, Kramer. Epidemiologic background of hand hygiene and evaluation of the most important agents for scrubs and rubs. Clin Microbiol Rev 2004, 17(4) 863-93.

Milestones for Evidence of Hand Hygiene

- Semmelweis. Pest: Hartleben`s, 1861 → Mortality at the 1st Obstetric Dep Vienna General Hospital → 1.3 vs. 8.2%
- Khan. Interruption of shigellosis by hand rub. Trans R Soc Trop Med Hyg 1982; 76: 164-8 → 10.1 vs. 32.4%
- Maki. The use of antiseptics for handwashing by medical personnel. J Chemother 1989; 1: 3-11 → 50% decrease of HAI
- Webster et al. Elimination of MRSA from a neonatal ICU after hand washing with triclosan. J Paed 1994; 30: 59-64 → sign. decrease of HAI
- Pittet et al. Effectiveness of a hospital-wide programme to improve compliance with hand hygiene. Lancet 2000; 356: 1307-12 → 59 % decrease of HAI
- Kampf, Kramer. Epidemiologic background of hand hygiene and evaluation of the most important agents for scrubs and rubs. Clin Microbiol Rev 2004, 17(4) 863-93 review

Efficacy of Hand Hygiene Preparations in Killing Bacteria

Limitations of Hand Wash

- **Insufficient efficacy**
- **Not effective for interruption of HAI with one exception: C. difficile (and other bacterial spores)**
- **usual aim:**
  - to clean the hands at start of the work
  - when visible dirty and
  - after toilet use (defecation)
- **Hand wash as rarely as possible! because of lower dermal tolerance than alcohols**
  - drying (defattaning)
  - disturbance (attack) of skin barrier: increase of TEW
  - next steps are → irritation → deterioration dermatitis
- **necessity of sinks and contamination of nearby surfaces during hand wash**

Limitations of Scrubs

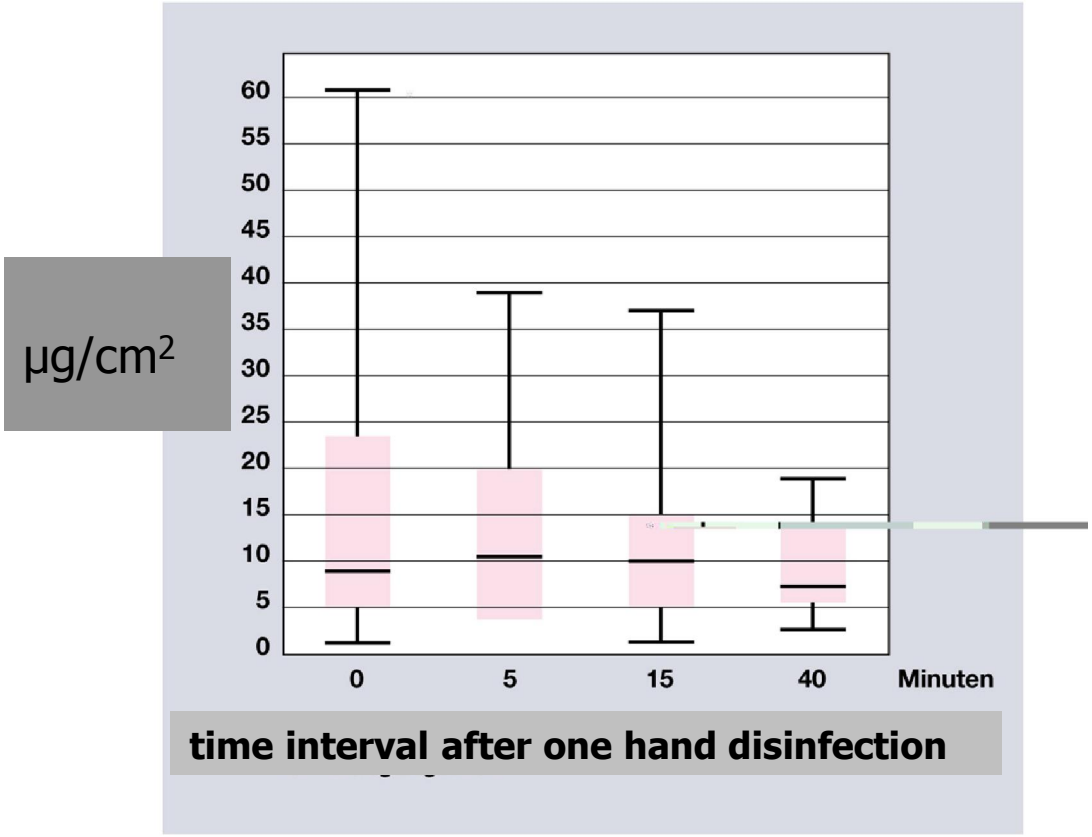
Lower efficacy + longer duration of the procedure of scrubs tested by EN 1500

Active agent	exposure (s)	conc. (%)	lg reduction
Propan-1-ol/ Propan-2-ol	15	30/45	4.2
	20		4.3
	30		4.9
Propan-1-ol	20	70	4.3
Ethanol	30	75	4.8
Chlorhexidin based detergent	60	4	3.1
Triclosan based detergent	60	0.1	2.8

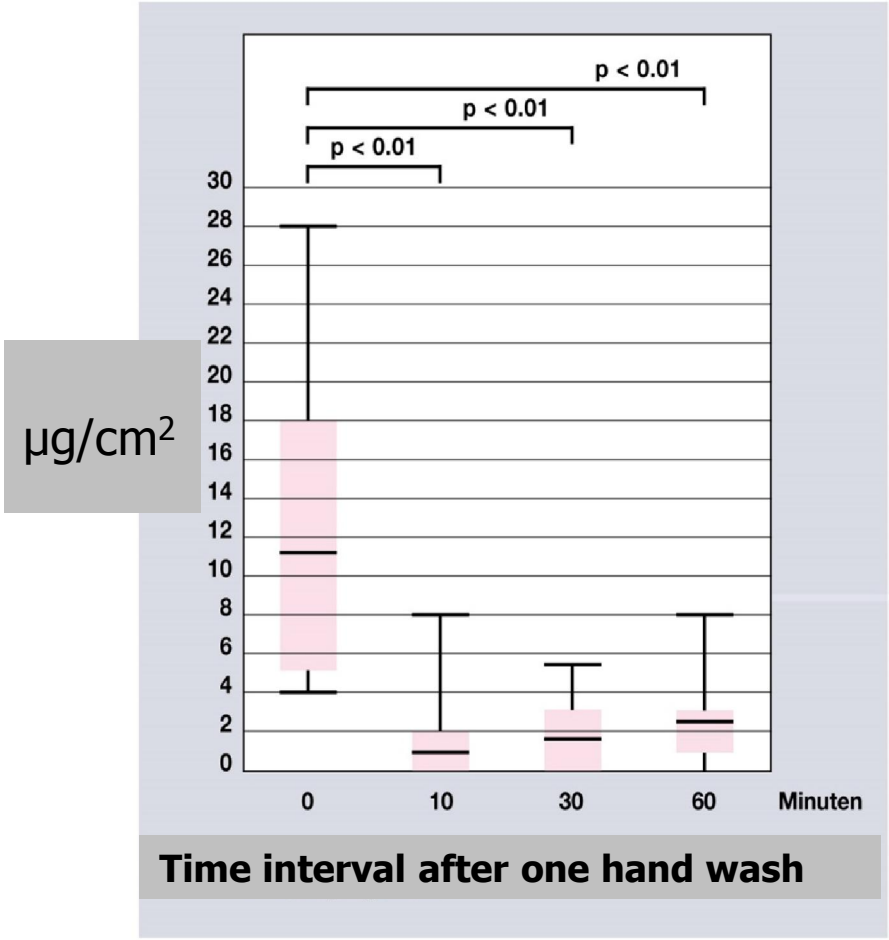
Minimal Required Concentrations of Alcohols in Hand Rubs

- **Ethanol ≥ 75 % v/v or lower if synergistic combinations**
- **Propan-1-ol ≥ 55% v/v**
- **Propan-2-ol ≥ 60% v/v**

Alcohols no Affect Content of Sebum (µg/cm^2) after one Single Hand Rub for 1 Minute



Soap Decrease Sebum Content (µg/cm²) after one Single Hand Wash of 30 s longer than 1 Hour



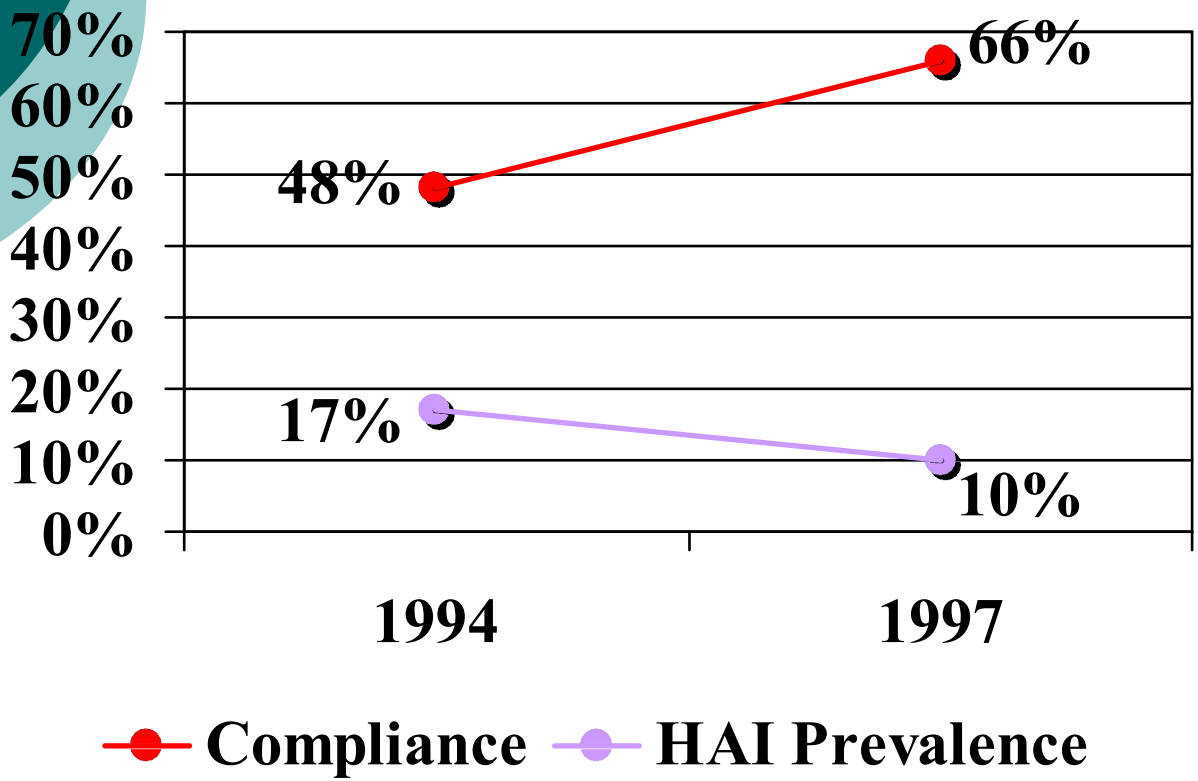
Clinical and Epidemiological Evidence for Better Skin Tolerance of Rubs

Scrubs compared with rubs (clinical controlled studies in US, Germany, Finland, Great Britain) induced

- ↑ **roughness**
- ↑ **scaling**
- ↑ **TEWL**
- ↑ **dryness**
- ↑ **skin damages**

Kramer. Toxicological assessment of hand rubs. In: Kampf G (ed) Hand Hygiene, Springer, New York: Berlin, 2003, 105-174

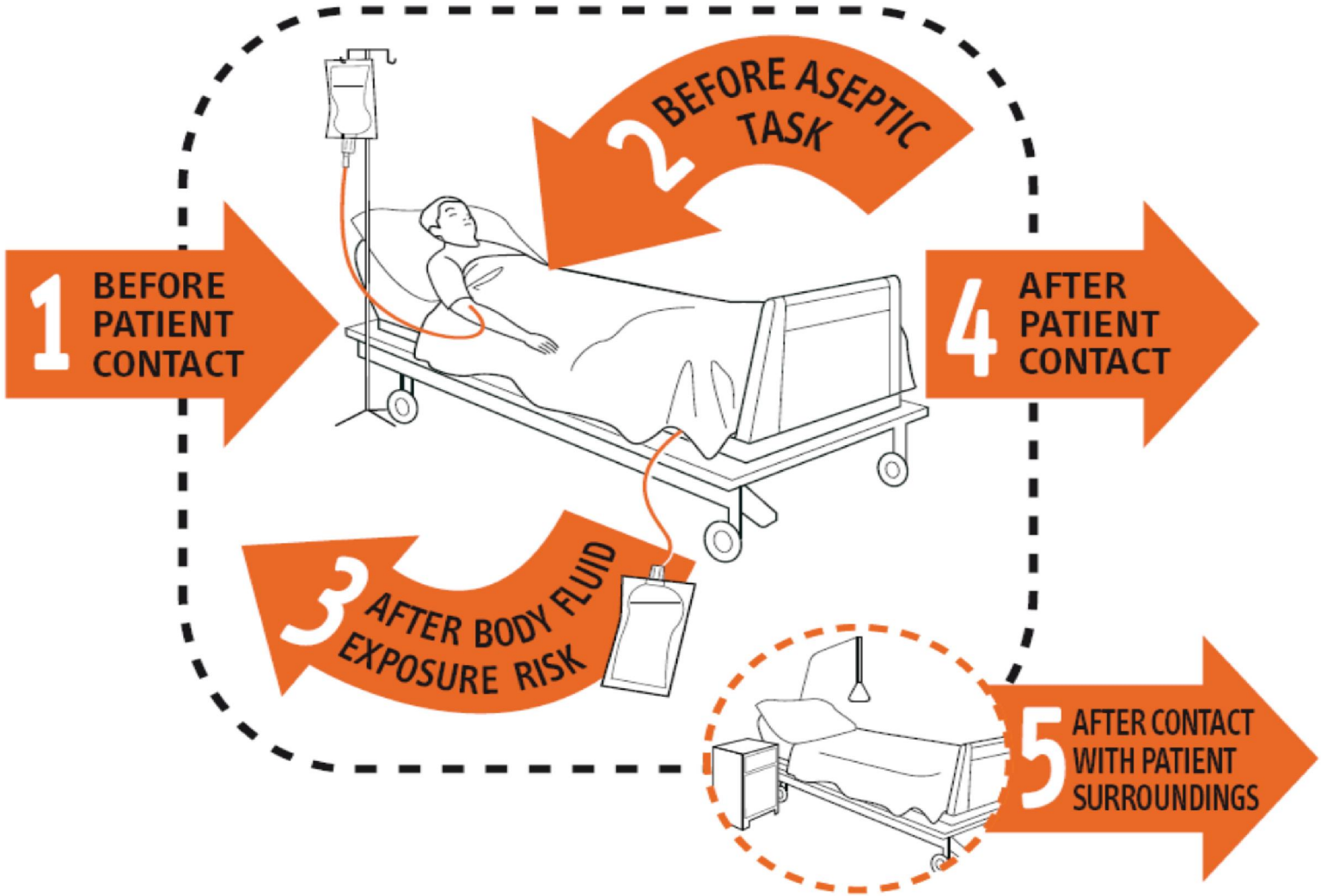
Examples for Epidemiological Evidence of Hand Disinfection



parallel to increase of compliance from 48 to 66% the rate of HAI significantly decreased from 16.9 to 9.9%

Pittet et al. Effectiveness of a hospital-wide programme to improve compliance with hand hygiene. Lancet 2000; 356: 1307-12

Your 5 moments for HAND HYGIENE



Prevention of HAI
in Very Low Birth Weight (VLBW) Neonates

Handwashing with detergent (0.5% triclosan) vs. **hand hygiene program** using **antimicrobial soap** (4% chlorhexidine gluconate) + alcohol-based **hand rub:**

- **HAI after 72 hours of life 18.8% vs. 6.3%**
- **rate of central venous catheter colonization 16.6% vs. 5.8%**

Capretti et al. Impact of a standardized hand hygiene program on the incidence of nosocomial infection in very low birth weight infants. Am J Infect Control 2008;36(6):430-5

Reducing Spread of Multi-resistant Bacteria

Introduction of alcohol/chlorhexidine based rub

- **use increased from 5.7 to 28.6 L/1000 bed-days**
- **46 months post intervention reduction of**
  - **total MRSA isolates 40%** ($p < 0.001$)
  - **patient-episodes of MRSA bacteraemia 57%** ($p = 0.01$)
  - **clinical isolates of ESBL-producing E. coli and Klebsiella spp. 90%** ($p < 0.001$).

Johnson et al. Efficacy of an alcohol/chlorhexidine hand hygiene program in a hospital with high rates of noso-comial methicillin-resistant Staphylococcus aureus (MRSA) infection. Med J Aust 2005 21;183(10):509-14

Outbreak Management Using Hand Disinfection

- **A. baumannii**: After proved compliance with **hand hygiene**, strict patient isolation and meticulous environmental disinfection **stop of outbreak**
- **hand** hygiene and adequate environmental disinfection were essential to **prevent recurrent outbreaks** in the burn unit

Simor et al. An outbreak due to multiresistant Acinetobacter baumannii in a burn unit: risk factors for acquisition and management. Infect Control Hosp Epidemiol 2002;23(5):261-7.

Outbreak Interruption by Virucidal Hand Disinfection

At the beginning of a norovirus outbreak in our neonatal ICU we used a hand disinfectant which was recommend as highly effective on enveloped viruses (mixture of propan-1-ol and propan-2-ol).

As we could not stop the outbreak herewith we changed to Manorapid Synergy and within 2 days the outbreak was finnished.

For floor disinfection Perform™ 1% was used which is an active oxygen based highly effective disinfectant containing 45 g Pentakaliumbis(peroxymonosulfate)bis(sulfate) and has been tested as being effective against non-enveloped viruses.

Armbrust, Kramer, Olbertz et al. Norovirus infections in preterm infants: wide variety of clinical courses. BMC Res Notes 2009; 2: 96

Outbreak Management of Noroviruses by Hand Disinfection

- **Formulation of the used virucidal broad spectrum hand disinfectant: ethanol (55%) + 10% propan-1-ol + 5.9% propan-1.2-diol + 0.7% phosphoric acid (manorapid synergy)**

Kramer et al. Virucidal activity of a new hand disinfectant with reduced ethanol content: comparison with other alcohol-based formulations. J Hosp Inf 2006;62:98-106

Efficacy of Hygienic Hand Rub in Public Institution

Aim: to interrupt infections, especially acute infectious respiratory and gastrointestinal diseases

while no specific protection such as immunisation exists, but high economial impact (23.1% of disablement by resp. and gastroontestinal infections in Germany

Hübner, Hübner, Wodny, Kampf, Kramer. Effectiveness of alcohol-based hand disinfectants in a public administration: impact on health and work performance related to acute respiratory symptoms and diarrhoea. BMC Infect Dis 2010, 10: 250

Characteristics of the Prospective Controlled Study

- **Employees were recruited from administration of the university and municipality**
- **applied formula: 2-propanol (45 %), 1-propanol (30 %) + mecetronium etilsulfate (0.2 %)**
  $\rightarrow$ active against bacteria, fungi and enveloped viruses
- **the hand rub was only used at work - the intervention group were instructed how to use the hand rub and advised to use it al least five times daily, especially after toilet use, blowing nose, before eating and after contact with ill colleges, customers, and archive material without supervision**

Survey of Participants

Monthly were sent by E-mail to both groups a questionnaire to record

- **illness symptoms: common cold, sinusitis, sore throat, fever, cough, bronchitis, pneumonia, influenza, diarrhoea +**
- **absenteeism**

Test persons reported illness and absenteeism days per month for each symptom. Appearance of at least one day ill was counted as an illness episode for the current month.

Number of Single Episodes of Illness

Symptom	Control		Intervention		OR
	healthy	ill	healthy	ill	
Common cold	599	89	526	59	0,70*
Sinusitis	640	5	575	10	2.23
Sore throat	576	68	529	56	0.88
Fever	625	20	571	14	0.77
Coughing	579	66	538	47	0.77*
Bronchitis	640	5	576	9	2.00
Pneumonia	644	1	585	0	1.00
Influenza	642	3	582	3	1.1
Diarrhoea	607	38	576	9	0.25*

*statistically significant ($\chi 2$- Test, $p < 0.05$)

Number of Single Episodes of Absence

Symptom	Control		Intervention		OR
	healthy	ill	healthy	ill	
Common cold	625	20	571	14	0.77
Sinusitis	643	2	577	8	4.46*
Sore throat	632	13	570	15	1.28
Fever	634	11	576	9	0.9
Coughing	627	18	571	14	0.85
Bronchitis	643	2	576	9	5.02*
Pneumonia	644	1	585	0	1.0
Influenza	642	3	582	3	1.1
Diarrhoea	637	8	582	1	0.14*

*statistically significant ($\chi 2$- Test, $p < 0.05$)

Percentage of Days Ill

Symptom	Control	Intervention	p-values
Common cold	2.78	2.07	0.008*
Sinusitis	0.12	0.34	0.312
Sore throat	1.53	1.34	0.424
Fever	0.31	0.25	0.037*
Coughing	2.00	1.85	0.024*
Bronchitis	0.2	0.39	0.235
Pneumonia	0,08	0.00	0.283
Influenza	0.12	0.13	1.000
Diarrhoea	0.92	0.11	0.074

*statistically significant ($\chi 2$- Test, $p < 0.05$)

Compliance of Hygienic Hand Rub

The compliance of hand disinfection in health care system is in average at 50 %

(compliance range: 16-94 %)

Concluding, only about half of the situations where an hand disinfection is necessary, the implementation is carried out.

- Dubbert PM et al., Inf Cont Hosp Epidemiol 1990; 11: 191-3: **81% - 94%**
- Raju NK et al., Am J Med Sci 1991; 302: 355-8: **28% - 63%**
- Tibbals J. Med J Aus 1996; 164: 395-8: **33% - 64**
- Larson EL et al., Am J Infect Cont 1997; 25: 3-10: **59% - 69%**
- Gould D et al., J Clin Nurs 1997; 6: 55-67: **13% - 14%**
- Cognard B et al., Inf Cont Hosp Epidemiol 1998; 19: 510-3: **4% - 8%**
- Khatib M et al., Chest 1999; 116: 172-5: **29% - 78%**
- Pittet D et al., Lancet 2000; 356: 1307-12: **48% - 66%**
- Muto et al., Am J Infect Control 2000; 28: 273-6: **60% - 62%**

Reasons for Inadequate Compliance

Improving compliance is imperative at any time!

Compliance is influenced by education + poster + pictograms = "safety culture" of the hospital, important factors are

- **human deficiencies (lack of discipline, indifference, anonymity of misconduct)**
- **no time for hand hygiene → 15 -30 seconds**
- **lack of consumption analysis**
- **actual or perceived skin intolerance of the used products**
- **unclear instructions**
- **lack by control of conduct, i.e. electronic handwashing counters, and model of a superior dispenser**
- **insufficient equipment and localization of hand disinfectant dispenser**
- **lack of information in the field of infection-data collection**
- **personnel shortage**
- **observational control of the discipline of HCWs by patients**

Possibilities to Improve the Compliance

The focus of improving the compliance is to increase the consciousness and responsibility to the importance of hand disinfection of employees to protect patients against HAI

Therefore, by WHO, national campaigns with the initiative "Clean care is safer care" was initiated.

The campaign focused changes in behavior by education and training programs (at least annually) with additionally control measures, formulation of SOPs in connection with training of them, measurement of disinfectant consumption, impact evaluation of the HAI rate, ensuring an easily accessible wall dispensers, and model role by superiors.

FIRST GLOBAL PATIENT SAFETY CHALLENGE

To reduce

health care-associated infections

Hand hygiene as the cornerstone

Possibilities to Improve the Compliance

- **Inspections of hand disinfection are required for didactic reasons.**
- **Microbiological assays can be carried out at specific epidemiological questions, but are not suitable for routine examinations of the effectiveness of hand disinfection.**
- **Assessment of the compliance of HCWs by patients via questionnaire**
- **Training videos + online campaign**
- **Education of patients to self-protection**

Questions (selection) about Realisation of Disinfection of Hands and Patient´s Contact Surfaces

Question Do personnel…..	please mark with a cross			
Hand disinfection when entering and leaving from the patient room?	al-ways	fre-quently	rarely	never
Hand disinfection during visit between each patient contact?	yes		no	
Hand disinfection between dirty and clean phase of changing wound dressing?	yes		no	
Skin antisepsis before injection?	yes		no	
Disinfection of blood pressure seal between each patient?	yes		no	
Disinfection of contact part of stethoscops	yes		no	
Disinfection of door handles?	yes		no	

Significantly improve of compliance of the HCWs, especially at physicians

Technical Options to Improve Compliance

- **Sufficient numbers of disinfection dispensers, that mean bedside and at the entrance as well as the exit of the patient room, ward round- or bandage-trolley, in the sanitary unit and sluice gates.**
  - **The installation of disinfectant dispensers for the staff members requires an analysis about the individual dispenser consumption over a longer period.**
  - **Private disinfection bottles (carry along in white coat) support the compliance if no dispenser can be installed.**
- **WHO-recommendation on ICU: One dispenser for each bed and for peripheral stations with 2 beds -preferably no more than 2 m towards next dispenser (campaign "clean hands")**
- **Especially in sluice gates an installation could be useful, which gives access only after the disinfection. Additionally, visitors have to make a hand disinfection without control by the personnel.**
- **Type of disinfection dispenser (automatic dispenser showed an increased compliance)**
- **Electronically data capture of hand disinfection**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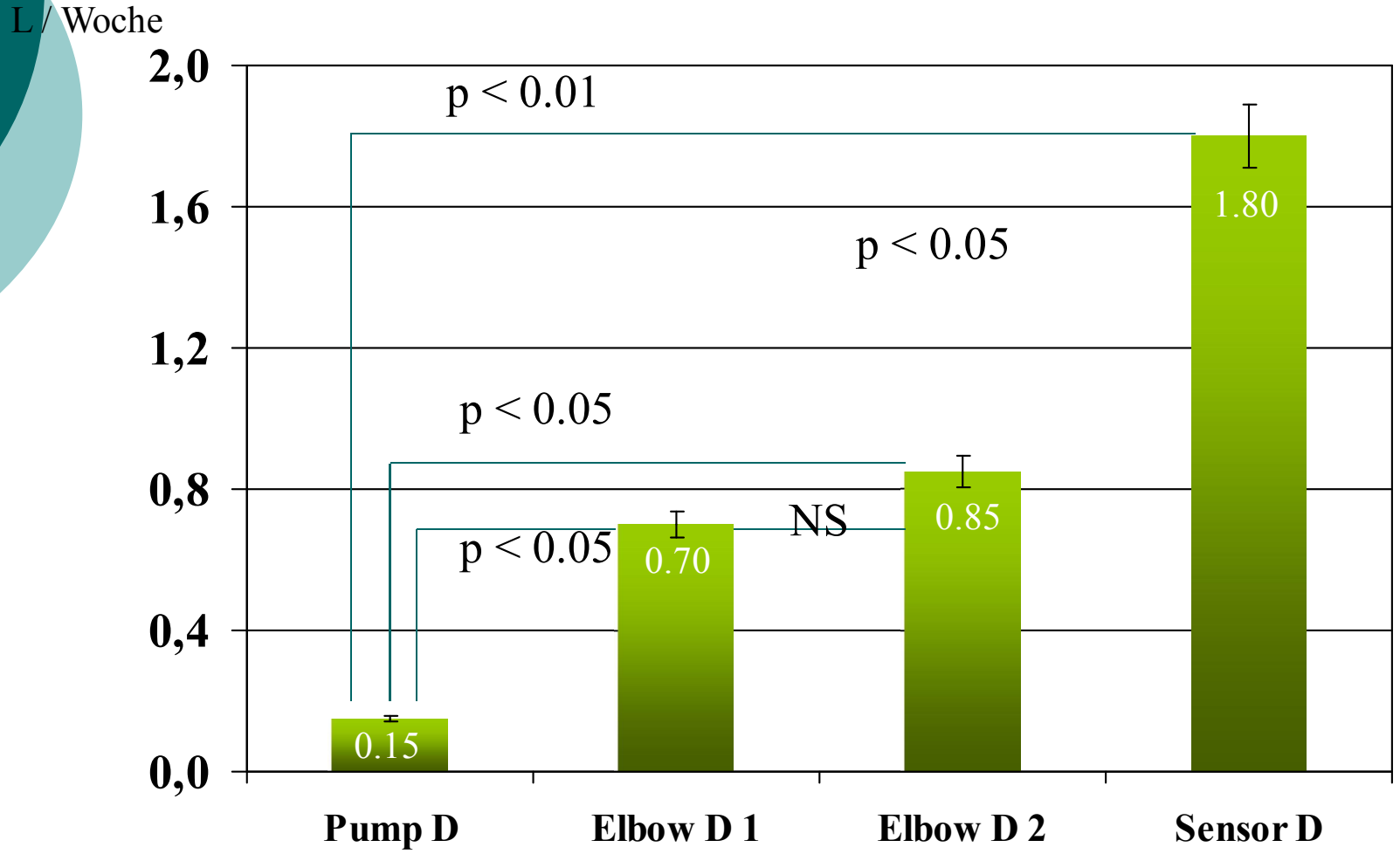
dispenser available
useable?
X

Influence of the Dispenser Type on Consumption of Hand Rub

3 months observational study

- **înstallation of different dispenser models**
- **no pre-study teaching or demonstration of usage**

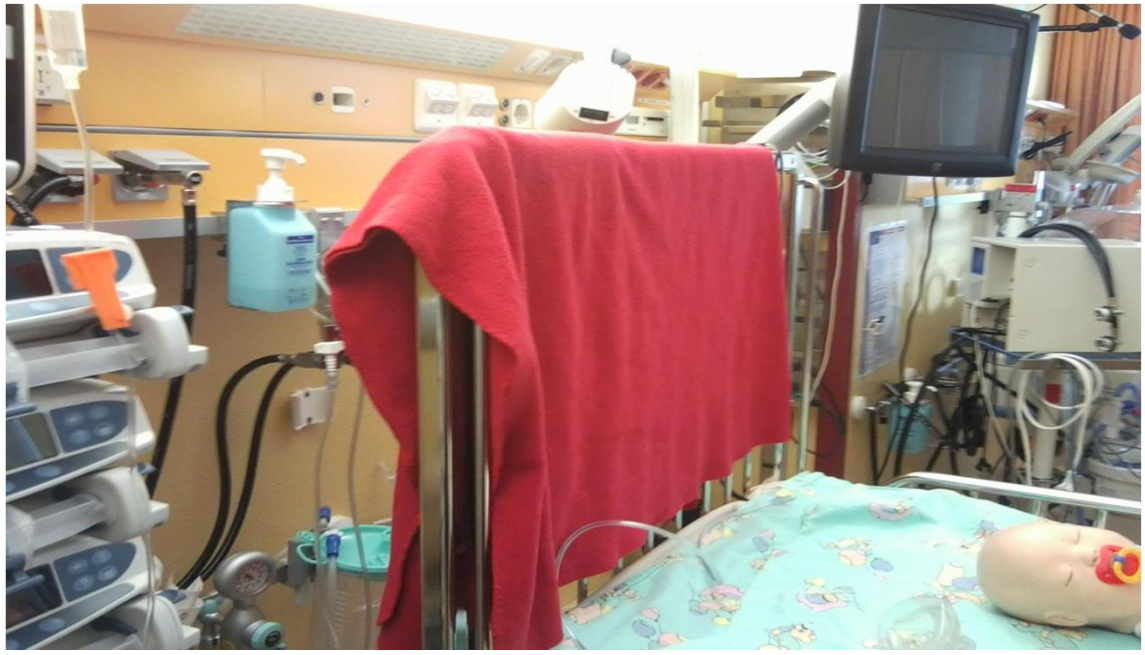
Highest Consumption with Sensor Steered Dispenser



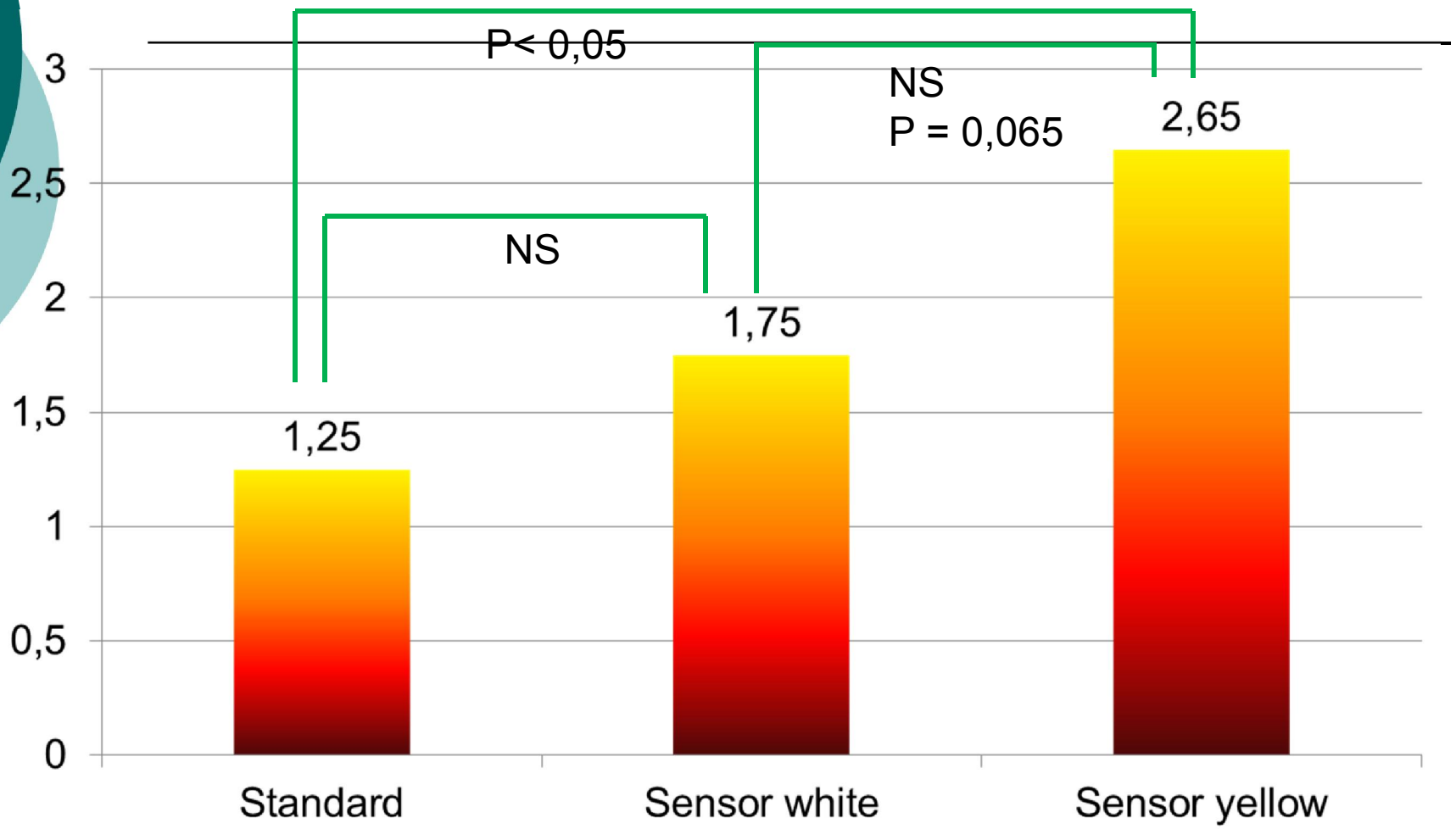
Assadian, Kramer et al. in prep.

Influence of Dispenser Colour on Consumption of Hand Tub

- Neonatal ICU - observational study
- Sequential installation of white and yellow dispenser models
- No pre-study teaching or demonstration of usage



Influence of Dispenser Colour on Consumption of Hand Rub



Resulting of Dispenser Heterogenicity

Recommendations for requirements and design of soap- and disinfectant dispensers in healthcare facilities

O. Assadian, A. Kramer, B. Christiansen, M. Exner, H. Martiny, A. Sorger, M. Suchomel. Hyg Med 2011; 36 (10): 407-8

Summary of the Recommendation

- Usage without contact of hands (elbow or sensor)
- Only cartridge usage, no refillable "top-up"
- Able to use products of different manufacturers
- Designed such that no contamination of pump may occur
- Used products and level of content must be identifiable
- Dispenser must withstand surface disinfection. Manufacturer must state appropriate method!
- Dispenser must withstand machine based cleaning and disinfection at A0-value of 60 (e.g. 80°C/ 1 min)
- Dispenser must maintain concentration of alcohol constant over 3 months (- 5% tolerance)

Skin Protection and Skin Care

Large deficites in practice by nurses as well as surgeons

- **evaluation of 205 questionnaires in 4 ICUs**
- **49% perform skin care at least 1–2 times per day**
- **9% never apply skin care to their hands**
- **almost 30% of healthcare workers use a combination of protection and care products**
- **at the beginning of daily work, 28% of respondents perform skin care or protection**

Große-Schütte K, Assadian O, Hübner NO, Löffler H, Kramer A. Practices of skin care among nurses in medical and surgical intensive care units: results of a self-administered questionnaire. GMS Krankenhaushyg Interdiszip 2011;6(1):Doc08

Practice of Skin Protection and Skin Care at German Surgeons

- **Questionare at the professional organisation of the German surgeons 2010**
- **For evaluation 1433 data sets were valid**

Harnoss JC, Brune L, Goerdt A, Heidecke CD, Kramer A. Importance of skin care ans skin protection to support the surgical hand disinfection - Condition risk or contradiction? Passion Chir 2014; 4(01): 2-6

Results of Inquiry

- 40% does not known the distinction between skin protection and skin care
- 5.2% carry out skin protection at the beginning of the work
- 13.7% start with skin care
- 77.8% nothing of both at start
- 3.3% no answering

Results of Inquiry

- 49% no skin problems
- 37.% dry and rough skin
- 13.7% breaking of nails
- 12.4% pruritus
- 10.1% reddening
- 4.4% contact dermatitis
- 5% other skin problems
- 5 % no answer

Consequences of the Reply

- **Education +**
- **Introduction of skin safety plan**
  - at the beginning of work skin protection
  - in between skin care if want
  - after longer interruption of work (lunch) again skin protection

Skin Protection Cream Does Not Reduce the Efficacy of Hand Disinfection

Hand wash	protection cream before hand disinfection		lg reduction	
	5 min	1 h	mean*	s
+	+	-	**3,3**	**0,59**
+	-	+	**3,3**	**0,73**
+	-	-	**3,2**	**0,75**
-	+	-	**3,5**	**0,64**
-	-	+	**3,35**	**0,59**
-	-	-	**2,97**	**0,46**

Große-Schütte K, Assadian O, Hübner NO, Löffler H, Kramer A. Practices of skin care among nurses in medical and surgical intensive care units: Results of a self-administered questionnaire. GMS Krankenhaushyg interdis 2011;6(1):Doc08

Influence of Skin Protection (SP) and Skin Care (SC) on efficacy of Surgical Hand Rub and on Skin Moisture

Day	Group A	Group B
1-8	in the morning + at midday SP, in the evening SC	no SP, no SC
9= 1st measurement	in the morning SC, after 1 hour hand rub	no SC, after 1 hour handrub
10-17	no SP, no SC	in the morning + at midday SP, in the evening SC
18 2nd measurement	no SC, after 1 hour hand rub	in the morning SC, after 1 hour hand rub

Harnoss JC, Brune L, Ansorg , Heidecke CD, Assadian O, Kramer A. Practice of skin protection and skin care among German surgeons and influence on the efficacy of surgical hand disinfection and surgical glove perforation. BMC Inf Dis 2014, 14:315

Results

Parameter	Without SP and SC	With SP and SC	Significance
Skin moisture	**34.5 ± 11.8**	**43.2 ± 11.8**	**0.0006**
Log_{10} reduction			
immediate	**2.8 ± 1.49**	**1.98 ± 1.83**	**0.137**
sustained (after 3 h)	**1.57 ± 2.4**	**1.84 ± 1.41**	**0.681**

The moist condition of hands was improved from "very dry" to "dry" or even "well hydrated".

Prospective Study at Surgeons

Method

Collection of the initial state of the skin through daily measurement for 2 weeks, thereafter introduction of the skin safety plan:

- **to beginning of the work skin protection**
- **again skin protection after the lunch break**
- **skin care at the end of the work**

Daily in the morning before the first application measuring of the skin parameters for the duration of 10 d

Care product characteristics: without conservation, without perfume, no content of urea, refattening with natural fatty acids

Results

- **sign. increase of TEWL of the skin**
- **sign. increase of water content in the skin**
- **sign. increase of lipid content in the skin**
- **sign. increase of AOP on the skin surface**

Workshop 3: Role of surface disinfection

With comments of 3 examples for efficacy of surface disinfection

Role of Surface Contamination

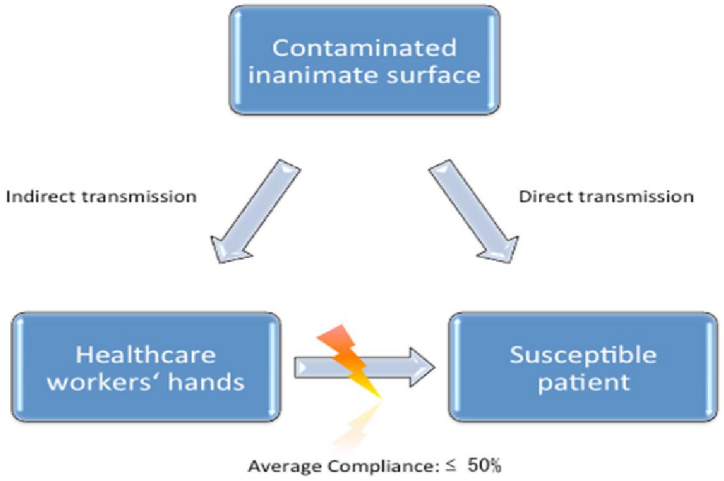
- **Origin of single infectious episodes**
- **Origin of HAI outbreaks**
  - **VRE**
  - ***C. difficile***
  - **MRSA**
  - **Noro**

The importance of surface contamination is demonstrated by reduction in the rate of HAI when effective measures of environmental disinfection are implemented (Hayden et al. 2006, Boyce et al.2008, Dancer et al 2012).

A recent observational study showed a significant reduction in *C. difficile* infection rates following the introduction of sporocidal wipes in an environmental cleaning regimen in an acute London trust (Carter and Barry 2011).

Consequences

Interruption of cross infections by effective disinfection which is thoroughly carried out



Example 1: Change of the Room Class of a Cardiac Procedure Room after Disinfection

- **Room ventilation by turbulent mixed airflow**
- **Before intervention room class C was present, after intervention room class B**
- **The intervention includes**

  - disinfection of all surfaces including all furniture and equipment after the last operation and again in the next morning before the first operation

  - draping of furniture and all equipment that could not be removed from the room with sterile surgical drapes

  → thereafter the State Office of Drug Surveillance and Testing of the Ministry of Health and Social Welfare, Mecklenburg-Pomerania, granted the manufacturing authorization to produce sterile bone marrow extract by iliac crest puncture

Below H, Ryll S, Empen K, Dornquast T, Felix S, Rosenau H, Kramer S, Kramer A. Impact of surface disinfection and sterile draping of furniture on room air quality in a cardiac procedure room with a ventilation and air-conditioning system (extrusion airflow, cleanroom class 1b (DIN 1946-4)) GMS Krankenhaushyg Interdiszip 2010; 5(2):Doc10 (20100921)

The Draped Cardiac Procedure Room

Example 2: Excessive Water Damage in an Aseptic Working Area of our Blood Donation Service Centre

- **Two weeks after repair of a shower drain, an unnoticed leak resulted in large-scale water penetration into the blood product fractionation room. Both 120m^2 of floor and 10m^2 of wall were heavily soaked.**
- **Such a situation usually required the immediate interruption of manufacturing, and start of maintenance work. However, as this service provides blood products for an university hospital, it was necessary to ensure the maintenance of good manufacturing practices and product safety by implementation of a bundle of preventive measures.**
- **For forced drying, the floor covering was completely removed, the drywalls were opened, and damp insulating material was removed. For 11 weeks, room air dryers were installed.**
- **Simultaneously, a moisture and microbiological monitoring and disinfection regime were implemented.**

Disinfection Regime

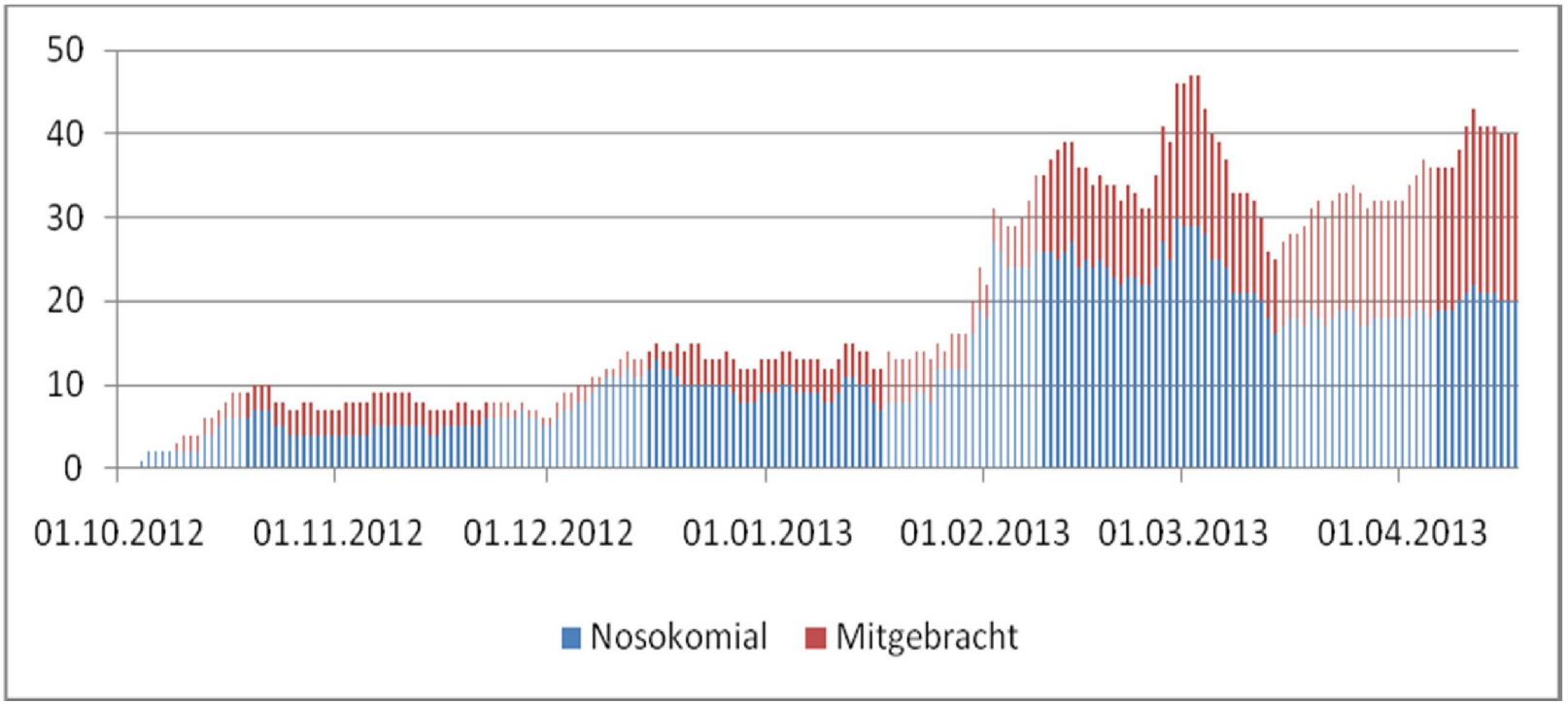
- **The floors were disinfected twice daily by wiping them off with Oxygenon S 1 % (Antiseptica GmbH Pulheim). During the operation of the dryers on weekends, the floor was disinfected only once daily.**
- **One hour after switching off the dryers, the floor and working surfaces were disinfected with a bactericidal, fungicidal, and sporicidal oxygen-releasing peroxide (Oxygenon S 1 %). The disinfection measures were repeated daily after the end of the manufacturing process and until the end of forced drying.**
- **Immediately prior to blood handling in the room, the contact surfaces between the blood bag and the press were disinfected with Oxygenon S 2% by the staff of the blood donation service.**
- **During the manufacturing process, disinfection was repeated every hour at a lower concentration of 0.25%.**
- **On day 3, surface disinfection of produced blood bags was also introduced.**

Result

- **Because of the accelerated disinfection regime, the indoor air bacterial and fungal contamination was reduced below normal values; neither on working surfaces nor on manufacturing devices was critical microbial contamination detected at any time**

Kramer A, Assadian O, Ryll S,Selleng K, Below H. Immediate infection control measures and preventive monitoring after excessive water damage in an aseptic working area of a blood donation service centre. *Indoor Built Environment* 2013 DOI: 10.1177/1420326X13508144

Example 3: Interruption of a VRE Outbreak



Successful Intervention by

Prolongation of terminal disinfection from 1 hour to 2.5 hour, because contamination was shown after to short terminal disinfection, i.e. on

- **Perfusor**
- **Ultrasonic and EKG equipment**
- **Computer tomograph**
- **OR lamp**
- **Infusomat**
- **Device toolbar**
- **Operating elements**
- **Bedside table**
- **Surfaces of wardrobe, doorway, window, dispensers**

+ introduction of 1 foreman for 10 cleaning staff
+microbiological control of the quality of terminal disinfection
+in the meantime, till all measures were effective implemented, room fumigation by hydrogen peroxide

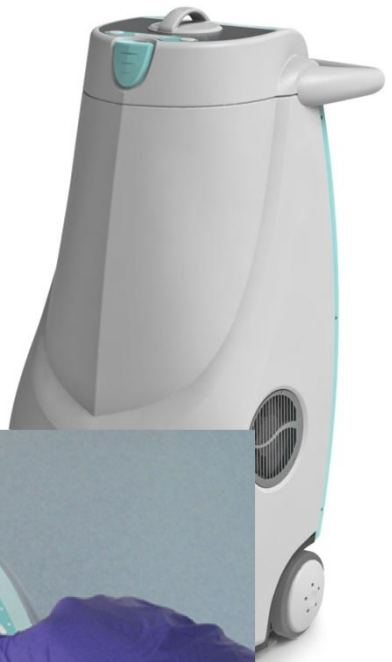
Conclusion

In order to realize the aim of 100% terminal disinfection of relevant surfaces

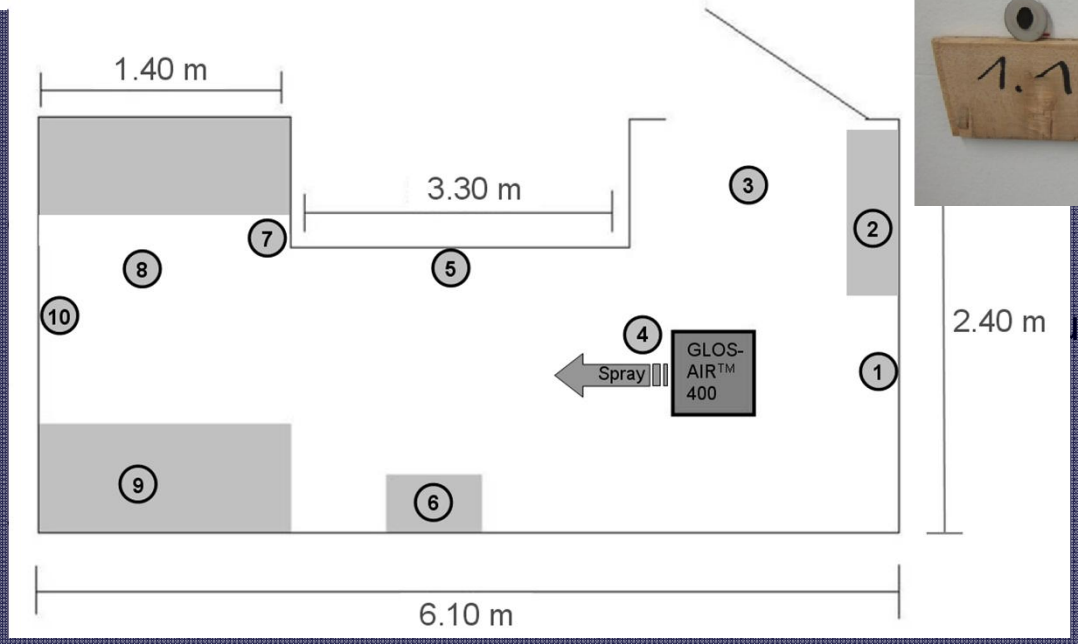
- **Choose of well tolerable active agents without unpleasant odor; i.e. alcohols, oxidants, formic acid**
- **comfortable usage; i.e. wipe dispensing systems**
- **Education, training and supervision**

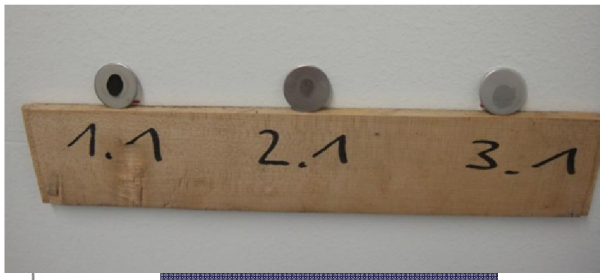
Room Fumigation by Hydrogen Peroxide with GLOSAIR TM 400

- mist technology / automatic room fumigation
- rooms between 10 m³ - 200 m³
- hydrogen peroxide along with silver cations
- GLOSAIR™ Solution



Laboratory Testing – Test principle





ut off ventilation

RF calculation,

(1) Wall behind GLOSAIR™ 400, 1.30 m above the floor
(2) Right side behind GLOSAIR™ 400, 2.00 m above the floor, on top of fuse box
(3) Floor next to GLOSAIR™ 400, 1.00 m away
(4) Floor directly in front of GLOSAIR™ 400
(5) Wall to the right of and about 2.00 m away from GLOSAIR™ 400, 1.70 m above the floor
(6) On top of a cardboard box (0.40 m) to the left of and about 2.50 m away from GLOSAIR™ 400
(7) Floor around the corner in front of locker, about 4.00 m away from GLOSAIR™ 400
(8) Ceiling, contaminated side of the carrier facing down, 2.50 m above the floor, about 4.20 m away from GLOSAIR™ 400
(9) Left side in front of GLOSAIR™ 400, 2.00 m above the floor, on top of locker, about 4.20 m away from GLOSAIR™ 400
(10) Wall opposite of GLOSAIR™ 400, 1.70 m above the floor, about 5.00 m away from GLOSAIR™ 400

Laboratory Testing – Results

	Efficacy depending on bioburden			Efficacy depending on buffer system	
				NaCl-Tryptone (EN 13697 / DGHM standard)	Butterfield's Phosphate Buffer
fungal load / carrier	6.51 log	5.48 log	4.28 log	6.41 log	6.40 log
Log reduction (RF)	0.38	1.27	≥ 4.28	< 0.90	≤ 0.98

Tab. 1 Efficacy obtained with **GLOSAIR™ 400 Area Decontamination System** for different bioburden concentration (mean of 3 carriers at Pos. 1, 5 and 7 in each case) and buffer systems (mean of 10 positions with 1 carrier each) under EN 13697 / DGHM clean conditions in 2 h for reference strain *A. brasiliensis*.

Field Test

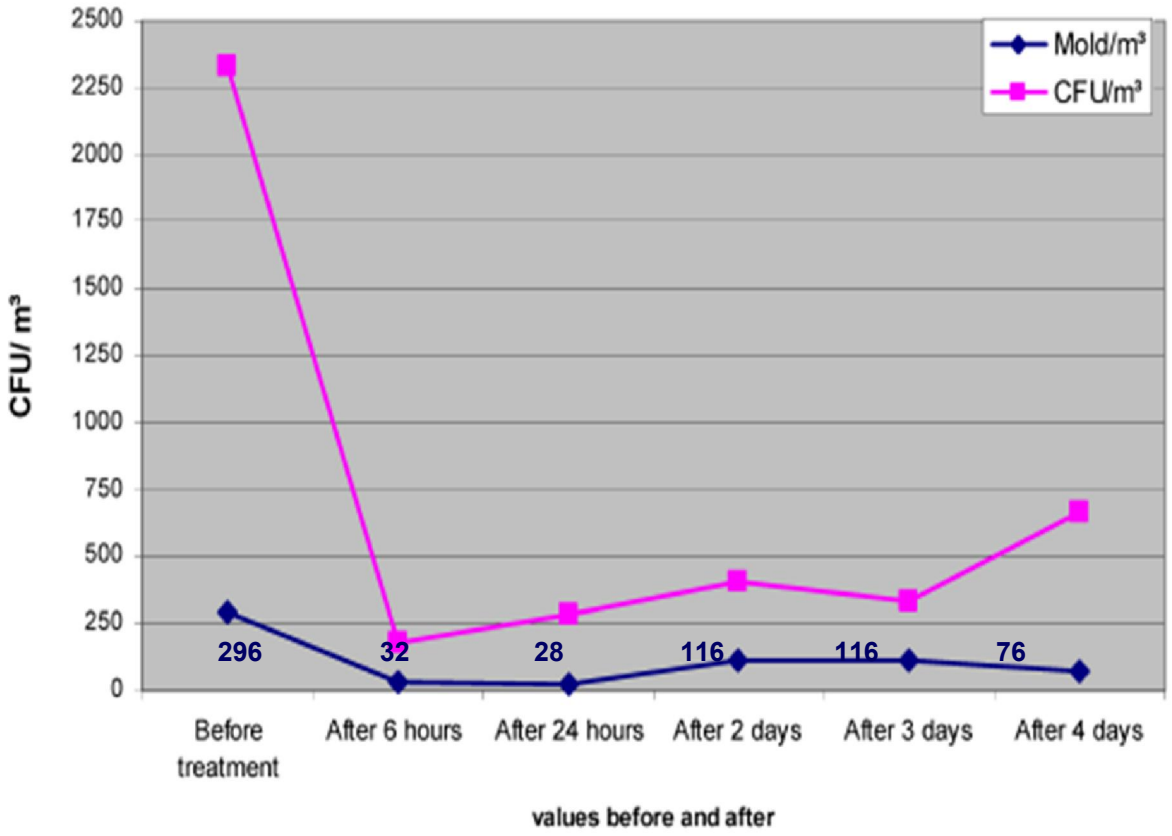
Room 1

Wall at window soaked for some years, mold infested
health problems; construction substance exposed due to structural renovation,
drying not completed, not cleaned for nebulization,
not used / entered.

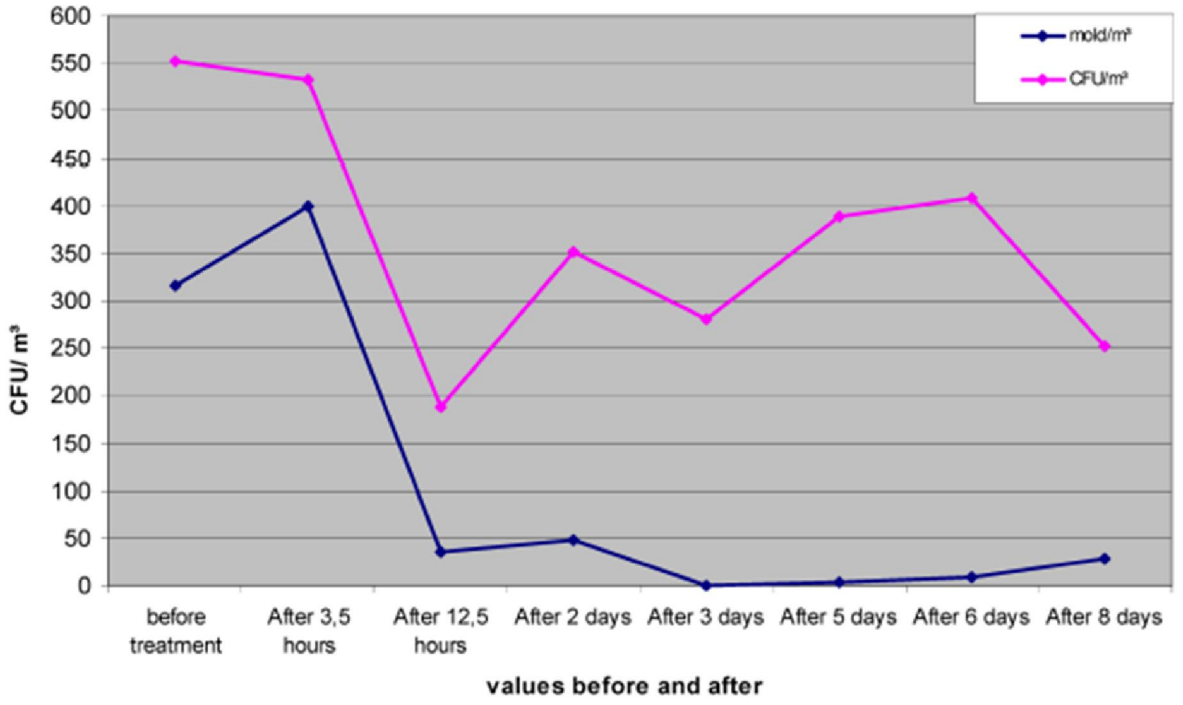
Room 2

Water damage, renovation without prior drying, air with
increased mold content, in use (entered and vented at
the users' discretion before and after fumigation)

Field Test 1 – Results; mold infestation, Room 1



Field Test 1 – Results; mold infestation, Room 2



Workshop 4: Prevention of HAI by Antisepsis

Aim: Killing, inactivating and/ or removal of microorganisms and viruses on the body surface for prophylaxis or treatment of infection or colonization with local anti-infectives

Concept of Antisepsis

Term

Antisepsis includes all measures on the body surface based on prophylactical or therapeutical indications

Targets

a) resident + transient flora

- **to prevent spreading in normally non-colonized areas or**
- **to prevent increase or metastasis in cases of impaired defense**

b) critical colonization (i.e. by MRSA, chronic wounds)

- **decolonization**

c) infection

- **therapy**

Reasons for the Renaissance of Antisepsis are the Following Advantages Compared to Antimicrobial Chemotherapeutics

1. **Reaches or exceeds efficacy of antibiotics at local application**
2. **Microbicidal instead microbistatic mode of action**
3. **Depending on antiseptic agent no risk of development of resistance**
4. **Lower or at least equal cytotoxicity**
5. **Missing or lower risk of systemic side effects due to reaching local tissue levels without absorption**
6. **Missing or lower allergenic potential**

Important Prophylactical Indications for Clinical Use of Antiseptics

Intact Skin

- Localized application
  - Prevention of infections before injection and puncture
  - Prevention of CABSI (catheter assoc. blood stream infections)
  - Prevention of SSI
- Whole body wash
  - MRSA decolonization
  - Prevention of spreading of MDRO

Wound antiseptics

- Infected wounds
- Wounds with infection risk

Mucous membranes

- Prior to urinary catheterization
- Eye: Prevention of endophthalmitis
- Mouth rinse: prevention of ventilator-associated pneumonia

Requirements for Antiseptics

- **Antiseptic effective**

Quant. suspension test without bioburden: RF ≥ 5 lg, for yeasts 4 lg
Quant. suspension test with bioburden: ≥ 3 lg
Pitten FA, Werner HP, Kramer A. A standardized test to assess the impact of different organic challenges on the antimicrobial activity of antiseptics. J Hosp Inf 2003; 55: 108-5

Carrier test: with bioburden RF ≥ 3 lg
Kramer A, Assadian O, Below H, Willy C. Wound antiseptics today - an overview. In: Willy C (ed) Antiseptics in Surgery – update 2013. Lindqvist, Berlin 2013; 85-111.

- **No development of antimicrobial resistance**
- **Biocompatible**
- **No sensibilisation potency**
- **No systemic risks**

Kramer A, Assadian O, Below H, Willy C. Wound antiseptics today - an overview. In: Willy C (ed) Antiseptics in Surgery – update 2013. Lindqvist, Berlin 2013; 85-111.

Skin Antisepsis

- **Before injection or punction**
  - **alcohols: 15 s – spray or swab**
- **Before preoperative skin antisepsis and in care of CVC:**
  - **alcohols with remanent additives, i.e. chlorhexidin - 30 s mechanically application under pressure by swab and dressing forceps, thereafter 1 min moisten**

Reichel et al. Antimicrob Agents Chemother 2009, 53(11) 4778-82
Dettenkofer et al. Infection 2002; 30: 282–5.

- **For antiseptic body wash**
  - **detergents/ liquid soaps with remanent additives, i.e. chlorhexidin**

PVP-iodine is significant lower effective than alcohols + thyrotoxic critical

Antiseptic Body Wash

- **By daily whole body wash with chlorhexidine based detergent decrease of CABSI from 5,3 auf 0,7 pro 1,000 Kathetertage**

  Popovich, et al. Effectiveness of routine patient cleansing with chlorhexidine gluconate for infection prevention in the medical intensive care unit. ICHE 2009; 30(10): 959-63.

- **Prevention at endemic occurence of *A. baumanii,* MRSA and VRE in ICU**

  Borer A, Gilad J, Porat N, et al. Impact of 4% chlorhexidine whole-body washing on multidrug-resistant Acinetobacter baumannii skin colonisation among patients in a medical intensive care unit. J Hosp Infect 2007; 67(2): 149-55.

  Derde LP, et al. Chlorhexidine body washing to control antimicrobial-resistant bacteria in intensive care units: a systematic review. Intensive Care Med 2012, 38(6): 931-9

- **No influence on SSI**

  Webster J, Osborne S. Preoperative bathing or showering with skin antiseptics to prevent surgical site infection. Cochrane Database Syst Rev 2007; (2) pCD004985.

Antiseptic Body Wash for Decolonization of MRSA

Efficacy of the decolonization bundle with octenidine:

- **Antiseptic body wash incl. hair (detergent + octenidine) 1x/d**
- **Antiseptic ointment in the vestibulum nasi (octenidine based 3x/day)**
- **Antiseptic mouth rinsing 2x/day)**
- **in case of colonization of wounds (octenidine based 3x/day)**

Eradication after 1st cycle (7 day) 68%, after 2nd cycle 93.5% (n = 107)

Hübner NO, Wander K, Ryll S, Lindstedt G, Kramer A. ***Antibiotic-free decolonization of MRSA-positive staff.*** *GMS Krankenhaushyg Interdiszip 2009; 4(2):Doc04. (20091216)*

Efficacy of analogous decolonization bundle with chlorhexidine (RCT, n=114) → no difference to placebo *Wendt C, et al.* ***Value of whole-body washing with chlorhexidine for the eradication of methicillin-resistant Staphylococcus aureus: a randomized, placebo-controlled, double-blind clinical trial.*** *ICHE 2007 ; 28(9) : 1036-43.*

Octenidine is sign. more effective than chlorhexidine

Koburger T, Müller G, Kramer A. ***Standardized comparison of antiseptic efficacy of triclosan, PVP-iodine, octenidine dihydrochloride, polyhexanide and chlorhexidine digluconate.*** *JAC 2010, 65(8):1712-9.*

Antiseptic Body Wash

- **By antiseptic soap (undecylenamidopropyl-trimoniummethosulfat + phenoxyethanol) + nasal Turixin decolonisation after 1st cycle 71 %, after 2nd cycle 91 %, after 3rd cycle 94 %**

  Kampf G, Kramer A. Eradication of methicillin-resistant Staphylococcus aureus with an antiseptic soap and nasal mupirocin among colonized patients--an open uncontrolled clinical trial. Ann Clin Microbiol Antimicrob 2004; 3: 1-6

- **Nasal mupirocin, mouth rinsing + body wash with chlorhexidine, vaginal chlorhexidin and oral vancomycin or cotrimoxazol for intestinal and urogenital decolonisation in prospective kohort study decolonisation in 87 %**

  Buehlmann M, Frei R, Fenner L, et al. Highly effective regimen for decolonization of methicillin-resistant Staphylococcus aureus carriers. Infect Control Hosp Epidemiol 2008; 29(6): 510-6.

SSI Reduction by Preoperative Decolonisation of *S. aureus* resp. MRSA in Vestibulum Nasi with Mupirocin + Chlorhexidin Body Wash

MRSA

- **Reduction of all SSI**

  Pofahl WE, et al. Importance of methicillin-resistant Staphylococcus aureus eradication in carriers to prevent postoperative methicillin-resistant Staphylococcus aureus surgical site infection. Am Surg 2011; 77(1): 27-31.

- **Reduction of SSI after knee- and hip- implantation**

  Goyal N, et al. Methicillin-resistant Staphylococcus aureus screening in total joint arthroplasty: a worthwhile endeavor. J Knee Surg 2012; 25(1): 37-43.

S. aureus

- **Reduction of Hip-implantation**

  Rao N, et al. Preoperative screening/decolonization for Staphylococcus aureus to prevent orthopedic surgical site infection: prospective cohort study with 2-year follow-up. Arthroplasty 2011, 26(8): 1501-7

- **sign. reduction in hemodialysis-catheter-ass. infektions, heart sugery and orthopedics**

  Hebert C, Robicsek A. Decolonization therapy in infection control. Curr Opin Infect Dis 2010; 23(4): 340-5.

Antiseptic Mouth Rinsing - Prevention of Ventilator-associated Pneumonia at Ventilation > 48 Hours

5 Metaanalysis: Antiseptic mouth rinsing with chlorhexidine

→ significant decrease of ventilator-associated pneumonia

Labeau SO, Van de Vyver K, Brusselaers N, Vogelaers D, Blot SI. ***Prevention of ventilator-associated pneumonia with oral antiseptics: a systematic review and metaanalysis.*** *Lancet Infect Dis 2011; 11: 845-54.*

Tantipong H, Morkchareonpong C, Jaiyindee S, Thamlikitkul V. ***Randomized controlled trial and meta-analysis of oral decontamination with 2% chlorhexidine solution for the prevention of ventilator-associated pneumonia.*** *ICHE 2008; 29:131-6.*

Chan EY, Ruest A, Meade MO, Cook DJ. ***Oral decontamination for prevention of pneumonia in mechanically ventilated adults: systematic review and meta-analysis.*** *BMJ 2007; 334:889*

Chlebicki MP, Safdar N. ***Topical chlorhexidine for prevention of ventilator associated pneumonia: a meta-analysis.*** *Crit Care Med 2007; 35:595-602.*

Kola A, Gastmeier P. ***Efficacy of oral chlorhexidine in preventing lower respiratory tract infections. Meta-analysis of randomized controlled trials.*** *J Hosp Infect 2007; 66:207-16.*

PVP iodine → also significantly effective

Mori H, Hirasawa H, Oda S, Shiga H, Matsuda K, Nakamura M. ***Oral care reduces incidence of ventilator-associated pneumonia in ICU populations.*** *Intensive Care Med 2006; 32:230-236*

wiping the mouth with atiseptic swab soaked (3x/d)

Antisepsis of Mouth Cavity

- **Prevention of mucositis at leukopenic patientS (stem cell transplantation): Aminfluorid + tin fluorid**

Pitten FA, Kiefer T, Buth C, Doelken G, Kramer A. Do cancer patients with chemotherapy-induced leukopenia benefit from an antiseptic chlorhexidine-based oral rinse? A double-blind, block-randomized, controlled study. J Hosp Infect 2003; 53(4): 283-91.

Eye Antisepsis

Indikations

- **Preoperative: PVP-I 1.25% or polihexanide 0.04 %**

Speaker MG, Menikoff JA. Prophylaxis of endophthalmitis with topical povidone-iodine. Ophthalmol 1991, 98(12): 1769-75

Hansmann F, Kramer A, Ohgke H, Strobel H, Geerling G (2004) Polyhexamethylbiguanid (PHMB) as preoperative antiseptic for cataract surgery . Ophthalmol 101: 377-83.

Hansmann F; Kramer A; Ohgke H; Strobel H; Muller M; Geerling G (2005) Lavasept as an alternative to PVP-iodine as a preoperative antiseptic in ophthalmic surgery. Randomized, controlled, prospective double-blind trial. Ophthalmol 2005, 102(11):1043-6, 1048-50.

Hansmann F, Below H, Kramer A, Müller G, Geerling G. Prospective study to determine the penetration of iodide into the anterior chamber following preoperative application of topical 1.25% povidone-iodine. Graefes Arch Clin Exp Ophthalmol 2007, 245(6) 789-93

- **Ophthalmia neonatorum – Risk assessment + epidemiologisch: PVP-I 1.25**

Below, Behrens-Baumann, Bernhardt, Völzke, Kramer, Rudolph. Systemic iodine absorption after preoperative antisepsis using povidone-iodine in cataract surgery-an open controlled study. Dermatol 2006, 212 Suppl 1: 41-6

Richter, Below, Kadow, Kramer, Müller, Fusch. Effect of topical 1.25% PVP-iodine eyedrops used for prophylaxis of ophthalmia neonatorum in healthy term newborns on renal iodine excretion and TSH level. J Pediat 2006, 148(3) 401-3

Genital Antisepsis

Indications:

- **before catheterisation of bladder**
- **before transurethral interventions**
- **before transvaginal interventions**

Agent of choice:

- **Octenidine**
- **Chlorhexidine**

At transurethral urinary catheter or in the puncture site of suprapubic catheter reaches daily cleaning of the meatus and of the genital with non-medical soap solution and water to reduce the contamination and colonization

Additional Requirements for Wound Antiseptics

- **Biocompatibility index > 1**
- **No inhibition of wound healing, ideally promotion of wound healing**

Kramer A, Assadian O, Below H, Willy C. Wound antiseptics today - an overview. In: Willy C (ed) Antiseptics in Surgery – update 2013. Lindqvist, Berlin 2013; 85-111.

Surgical Aphorism

Apply nothing into a wound
what you cannot apply into your eye!

This conclusion should be a rule for

- **polihexanid (introduction 2004 0.04 % for presurgical eye antisepsis in Germany)**
- **octenidine < 0,05 % (animal study)**
- **PVP-iodine 1 % (but use conc. on wounds 10 %)**
- **chlorhexidine <0,006 %**

impossible for

- **silver sulfadiazine**

Hansmann F, Kramer A, Ohgke H, Strobel H, Geerling G (2004) Polyhexamethylbiguanid (PHMB) as preoperative antiseptic for cataract surgery . Ophthalmol 101: 377-83.

Hansmann F; Kramer A; Ohgke H; Strobel H; Muller M; Geerling G (2005) Lavasept as an alternative to PVP-iodine as a preoperative antiseptic in ophthalmic surgery. Randomized, controlled, prospective double-blind trial. Ophthalmol 2005, 102(11):1043-6, 1048-50.

Indications of Prophylactic Wound Antisepsis

Antisepsis is recommended at ≥ 3 points of the wounds at risk score

Expert´s Consensus of Germany, UK, Austria, Italy

Dissemond J, Assadian O, Gerber V, Kingsley A, Kramer A, Leaper DJ, Mosti G, Piatkowski de Grzymala A, Riepe G, Risse A, Romanelli M, Strohal R, Traber J, Vasel-Biergans A, Wild T, Eberlein T. ***Classification of wounds at risk and their antimicrobial treatment with polihexanide: a practice-oriented expert recommendation.*** *Skin Pharmacol Physiol 2011; 24(5) 245-55.*

Wounds at Risk Score

Risk factor	Risk class
• Immunosuppressive disease or immunosuppression • Solid tumour • Haematological disease • Postoperative wound healing disorder and healing by secondary intention • Heavily contaminated wounds (e.g. perineal or genital wounds) • Patient age > 80 years or < 1 year • Wounds persisting for > 1 year • Wound surface > 10 cm^2 • Chronic wounds of all etiologies with a depth >1.5 cm • Inpatient stay > 3 weeks	1 point per risk
• Severe acquired immune deficiency (e.g. AIDS) • Stab or gun shot wounds with a depth of 1.5–3.5 cm	2 points per risk

Wounds at Risk Score

Risk factor	Risk class
• Accidental contamination with risk of infection • Extensive dirty/contaminated wounds • Burn wounds with an involvement of > 15% body surface area • Wounds that communicate with organs or functional structures (e.g. joints) or contain foreign material • Severe congenital immune deficiency (e.g. gammaglobulinaemia) • Penetrating bite wounds • Stab and gun shot wounds with a depth > 3.5 cm	3 points per risk

Biocompatibility Index (BI)

Quotient from IC_{50} and RF >lg 3 within 30 min, testet in FBS

Agent	BI [30 min]	
	L929/*E. coli*	L929/ *S. aureus*
Octenidine + phenoxyethanol	1.7	2.1
Polihexanide + macrogolum	1.5	1.4
Chlorhexidine digluconate	0.8	1.0
PVP-I (related to I_2)	0.7	0.7
Triclosan	0.2	0.5
Ag protein (related to Ag)	0.2	0.1
Ag(I)-sulfadiazine,$AgNO_3$	not calculable	not calculable

Müller G, Kramer A. Biocompatibility index of antiseptic agents by parallel assessment of antimicrobial activity and cellular cytotoxicity. J Antimicr Chemother 2008; 61(5) 1281-7.

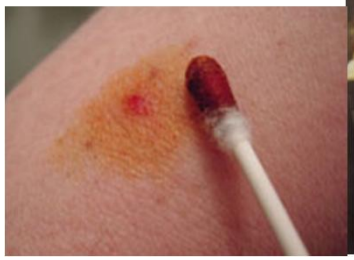
Comparison of Selected Antiseptic Agents on the Basis of the Requirements

Agent	Biocom-patibility index	Wound healing	Antisepsis on cartilage	Develop-ment of resistance	Sensiti-zation	Syste-mic risks
Polihe-xanide	> 1	Promo-tion	≤ 0.005%	No	No	No ab-sorption
Octeni-dine	> 1	No inhibition	No	No	No	No risk, absorpt. < 6%
PVP iodine	< 1	Inhibition	Yes	No	High	Thyro-toxic
NaOCl	< 1	No inhibition	?	No	No	No risk
Silver	<< 1	Inhibition	No	Yes	No	Hepato-, Nephro-toxic
Chlor-hexidine	< 1	Inhibition	No	Yes	Yes	No absorp-tion

Conclusion: **Only polihexanide fulfills all requirements and has replaced chlorhexidine and partly PVP-iodine for wound antisepsis**

Iodine and Silver in Wound Care

- **Iodine well known antiseptic Over a century**
- **Effectiveness and safety under discussion**
- **Its use is still defendable**
  - **Easy available and to use**
  - **Not expensive**



J Hosp Infect. 2010 Nov;76(3):191-9. **Benefit and harm of iodine in wound care: a systematic review.**
Vermeulen H, Westerbos SJ, Ubbink DT.

Cons & Pros

- **Discouraging reports**
  - **Cytotoxicity**
  - **Thyrotoxicity**
  - **Allergic reactions**
  - **Poor penetration**

- **Positive reports**
  - **Well tolerated**
  - **Not cytotoxic**
  - **Effective**
  - **Cost effectiveness**

Systematic Review - Inclusion Criteria

- All RCTs on Iodine in any kind of wounds
- Any concentration or product
- At least one primary endpoint reported
  - Wound infection
    - Bacterial load, number of infections
  - Wound healing
    - Number healed, reduction wound surface, surgical closure, SSG loss or take
- Secondary
  - Adverse events
    - Including: pain, skin rash, thyroid function disturbance, and allergic reactions
  - Cost
  - Hospital stay

Results

- **1976 till 2007: 27 RCTs, 27-2142 patients, totalling 4531, Median 1.5 months (12 days–14 months), Overall trial quality: limited**
  - **12 chronic wounds**
  - **3 pressure sores**
  - **7 acute wounds**
  - **3 burn wounds**
  - **2 skin grafts**

Kinds of iodine

Povidone-Iodine	**13 trials**
Cadexomer	**9 trials**
Repithel	**4 trials**
Other	**1 trial**

Controls

No antiseptics	**14 trials**
Other antiseptics	**6 trials**
Best treatment	**5 trials**
Antibiotics	**2 trials**

Significant Outcomes

	Chronic 12 trials	Pressure 3 trials	Acute 7 trials	Burns 3 trials	SSG 2 trials
Infection	NR	+	000 (3) - -	NR	0
Healing	000000000 (9) ++++ (4) -	0000 (4) + -	0000 (4) -	0 ++	++
Adverse events	000000000 (9) +++++ (5) - - - - (4)	0 -	00	00	00
Cost (overall)	+ -	NR	NR	NR	NR
Hospital stay	NR	NR	-	NR	NR

+: significantly more, 0: no difference, -: significantly less, NR: not reported

Vote Count

	Chronic 12 trials	Pressure 3 trials	Acute 7 trials	Burns 3 trials	SSG 2 trials
Infection	NR	+	0 + - - - -	NR	+
Healing	0 +++++++++ ++++ (13) - - - - (4)	0 +++ - -	0 +++ - -	+++	++++
Adverse events	0 ++++++++(8) - - - - - - - - - - - - (12)	+ -	+++ - - -	+ -	00
Costs (overall)	+ -	NR	NR	NR	NR
Hospital stay	NR	NR	-	NR	NR

+: significantly more, 0: no difference, -: significantly less, NR: not reported

Conclusion

The use of iodine is still defendable

Topical silver

- **Insufficient high–level evidence exists to recommend silver–containing dressings or topical agents to enhance wound healing to treat or prevent wound infection.**

Topical **silver** for **treating** infected wounds.
Vermeulen H, van Hattem JM, Storm-Versloot MN, Ubbink DT.
Cochrane Database Syst Rev. 2007 Jan 24;(1):CD005486.

Topical **silver** for **preventing** wound infection.
Storm-Versloot MN, Vos CG, Ubbink DT, **Vermeulen H**.
Cochrane Database Syst Rev. 2010 Mar 17;(3):CD006478.

Results of Silver Releasing Treatment

- 347 titles of possible relevance
- 3 RCTs met the inclusion criteria
- 847 participants
- poor methodological quality

Kinds

- silver-containing foam vs hydrocellular foam
- silver-containing alginate vs alginate
- silver-containing foam dressing vs best local practice

Results

- **No increase in complete ulcer healing**
- **No differences in the use of antibiotics, pain, patient satisfaction, length of hospital stay, and costs**
- **less leakage and odour**

Insufficient high–level evidence to recommend silver–containing dressings or topical agents to enhance wound healing of infected wounds.

Results of SR Prevention

- **367 titles of possible relevance**
- **19 RCTs met the inclusion criteria**
- **1681 participants**
- **poor methodological quality**

Kinds

- **burns (15), venous leg ulcers (2), finger tip injuries (1), soft tissue wounds (1), any chronic wound (1)**
- **16 studied 1% silver sulfadiazine cream (SSD)**
- **7 silver-containing dressings**

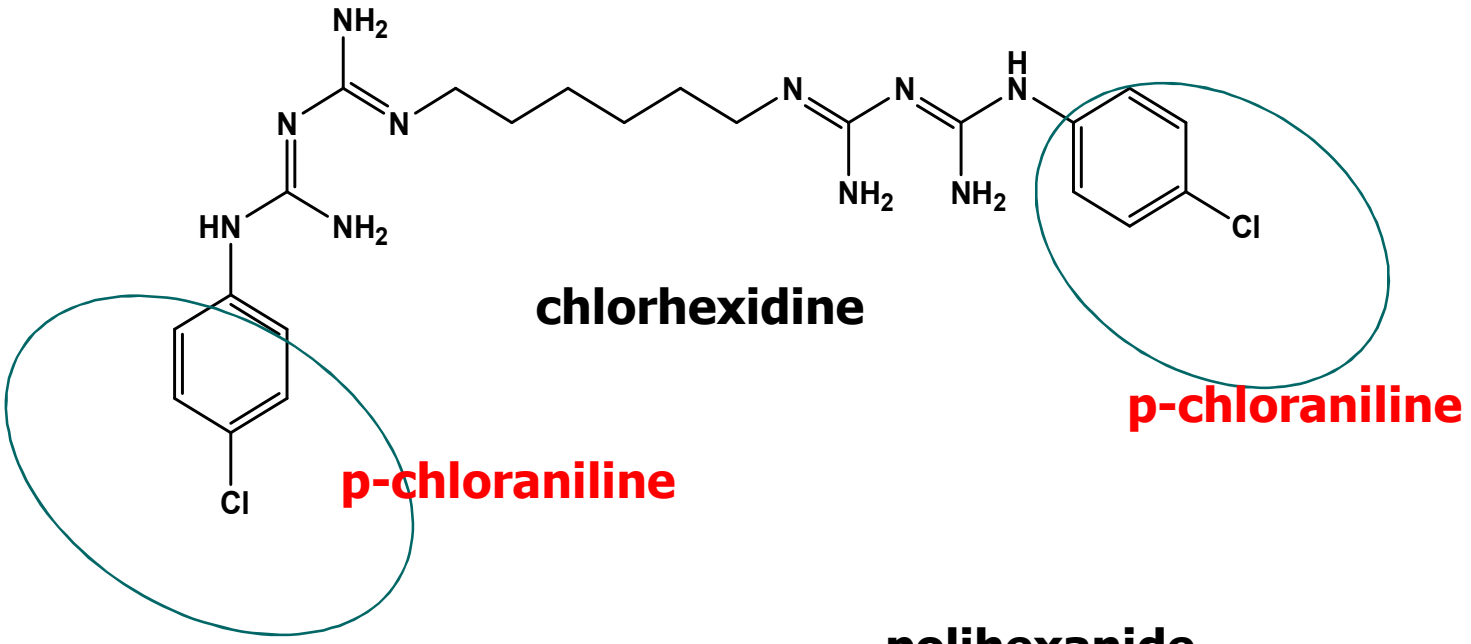
Results SR Prevention

	In favour of silver	No difference	In favour of non-silver	Totals
Primary Outcomes				
Infection Rate	3	19	1	23
Healing rate	0	8	4	12
Secondary Outcomes				
Pain	1	6	2	9
Length of Stay	1	2	0	3
Costs	0	1	2	3

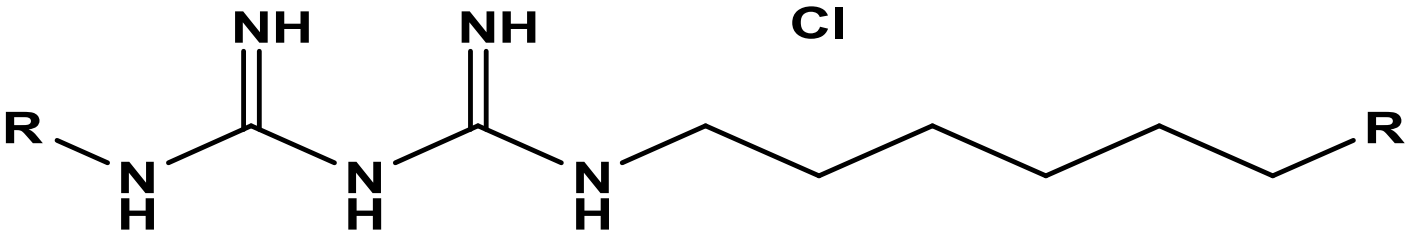
Conclusion

- **Silver may reduce leakage and odour, but may also delay wound healing.**
- **Hence, insufficient high−level evidence exists to recommend silver−containing dressings or topical agents to enhance wound healing to treat or prevent wound infection.**

Polihexanide: Structural Comparison with Chlorhexidine



polihexanide



Characteristic of Polihexanide

Characteristics	Use restrictions/disadvantages
○ **BI > 1** ○ **remanence and postantiseptic effect** ○ **no protein or blood failure** ○ **no absorption** ○ **compatible for cartilage** (≤ 0.005%) ○ **no allergic or toxic risks** ○ **stimulation of wound healing**	○ **entry of effect after 5-20 min or longer**

Mode of Action

Selective action against microorganisms

- strong interaction with negatively charged bilayers composed of phosphatidylglycerol (PG) alone or of PG and phosphatidylcholine (PC), whereas neutral PC bilayers of human cells were not affected → consequences
- increased permeability of the cell wall with inhibition of metabolism
- finally coagulation of cell contents

consequences of selective action

low toxicity for human cells

Hübner NO, Kramer A. Review on the efficacy, safety and clinical applications of polihexanide, a modern wound antiseptic. Skin Pharmacol Physiol 2010; 23 (Suppl): 17-27.

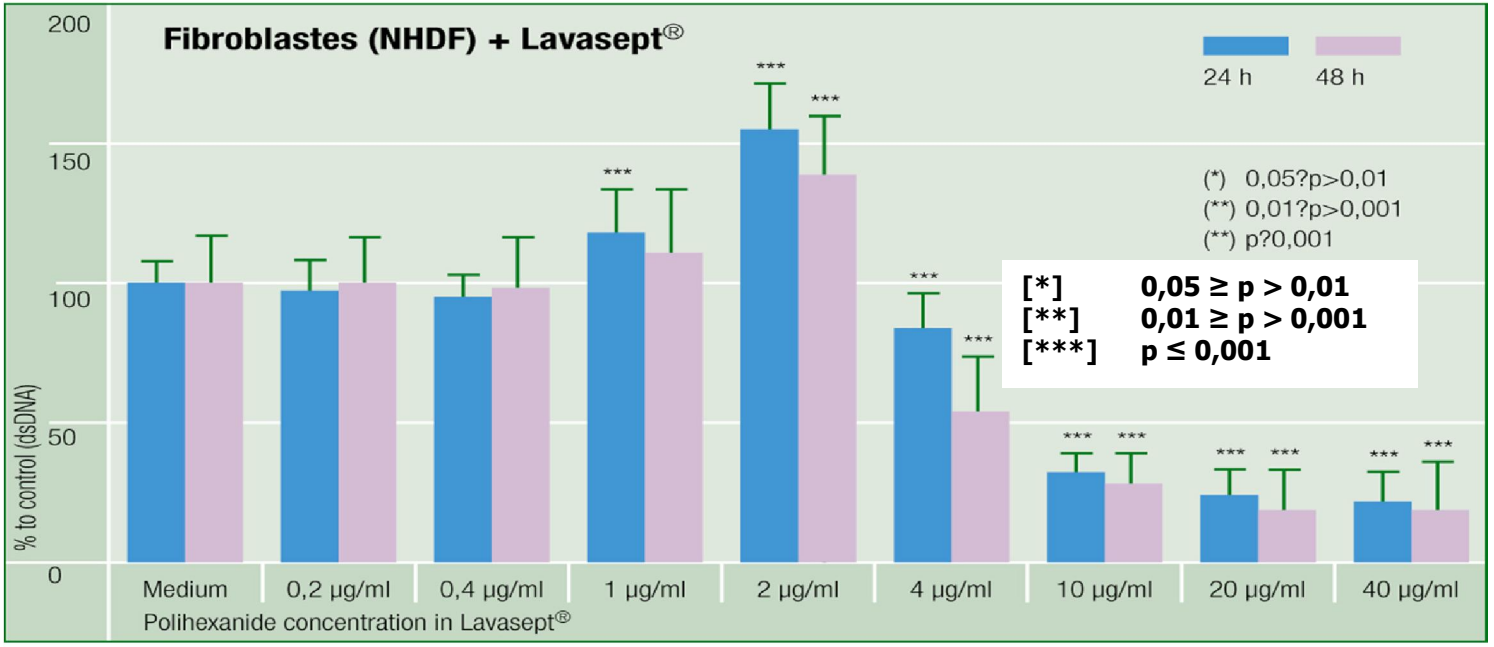
Stimulation of Wound Healing by Polihexanide

Not only well tolerable for wounds, but in opposite stimulation of wound healing which is demonstrated for an antiseptic agent only in case of polihexanide and also of 10 % ethanol

- **in vitro**
- **in animals**
- **in humans**

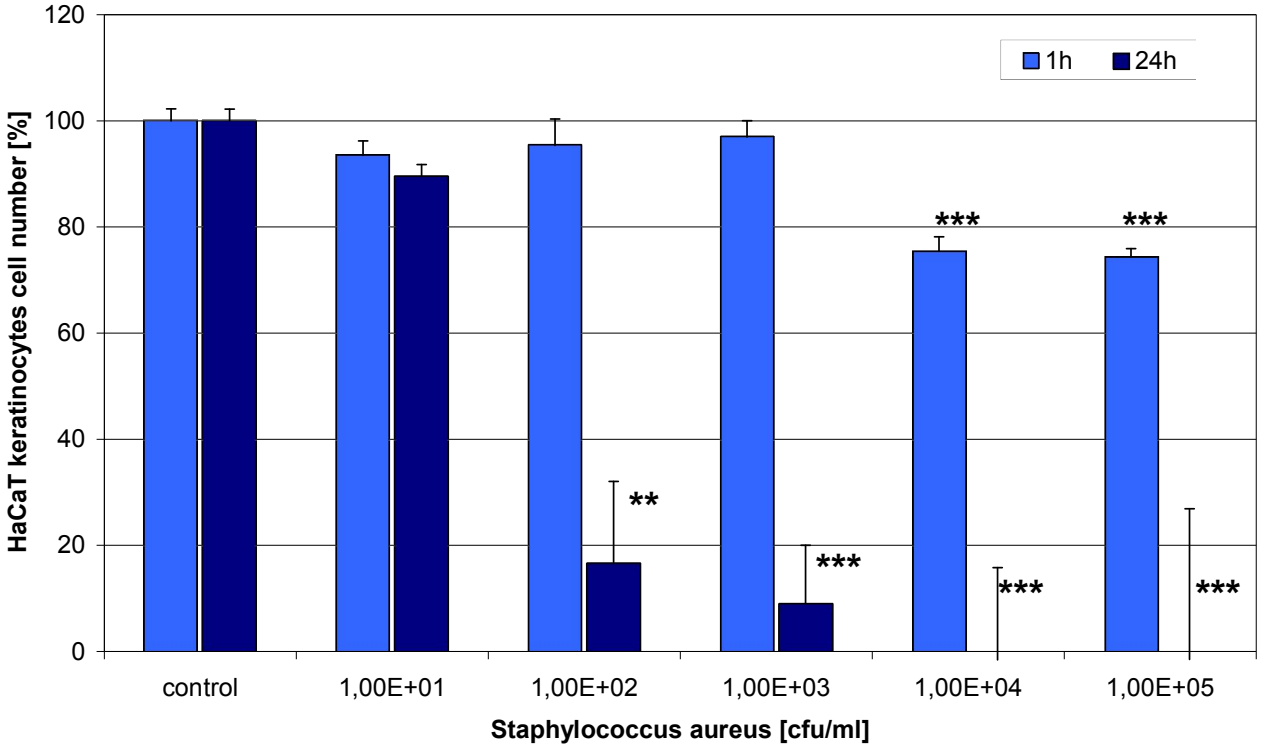
Stimulation of Cell Metabolism of Fibroblast

[3H]thymidine incorporation into cellular DNA increase of cell proliferation by polihexanide at 1-3 µg/ml



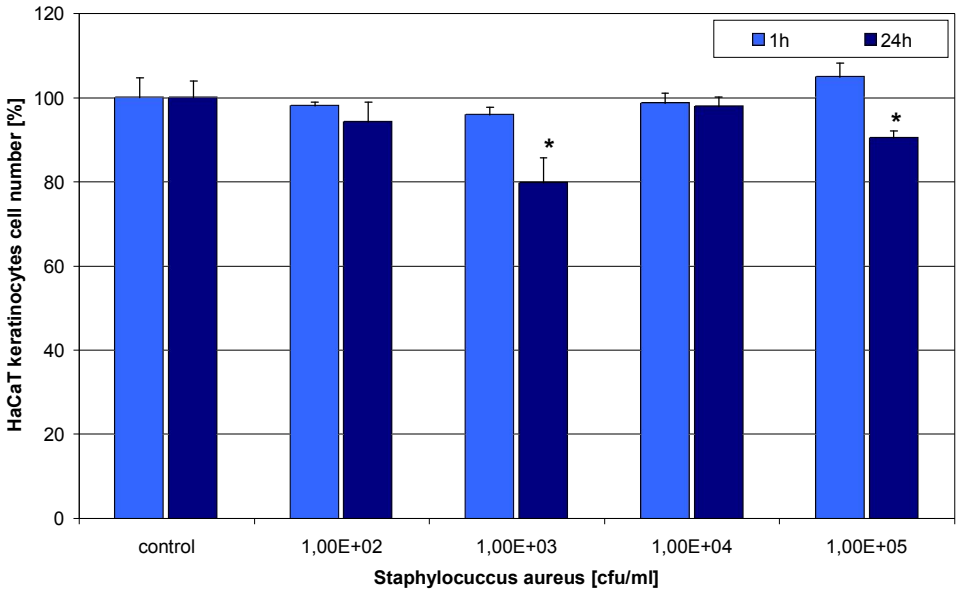
Wiegand C, Abel M, Kramer A, Müller G, Ruth P, Hipler UC. GMS Krankenhaushyg Interdiszip 2007; 2(2):Doc43 (2007,1228)

Inhibition of HaCaT Keratinocytes by S. aureus



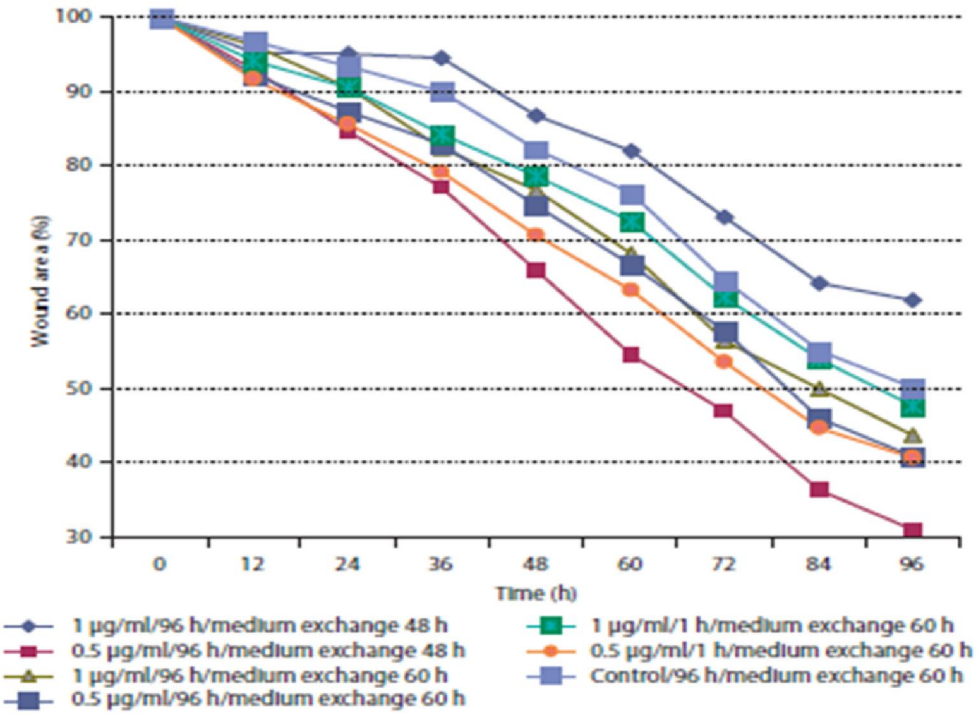
Wiegand C, Abel M, Ruth P, et al. HaCaT keratinocytes in co-culture with Staphylococcus aureus can be protected from bacterial damage by polihexanide. Wound Repair Regen 2009; 17(5): 730-8

Effect of Polihexanide on HaCaT Keratinocytes in Co-culture with S. aureus



1 µg/ml Polihexanid

Stimulation in an in vitro Wound Model



Roth C, Beule AG, Kramer A, Hosemann W, Kohlmann T, Scharf C. Response Analysis of Stimulating Efficacy of Polihexanide in an in vitro Wound Model with Respiratory Ciliary Epithelial Cells. Skin Pharmacol Physiol 2010;23(suppl 1):35–40

Artificial Wounds on Piglets/ Polihexanide

- **Double blinded, rand., strat., contr. study with parallel groups**
  - **polihexanide 0.04 %**
  - **Octenidine 0.1 %**
  - **Ringer**
- **6 wounds on back with 10 cm distance⇒ removing of epidermis + partially of dermis**
  - **daily tape change with spray application (0.2 ml/spray)**
- **measurement**
  - **computerised-planimetry**
  - **wound stating (exsudation, pus, odour)**
  - **histology**

Kramer et al. Influence of the antiseptic agents polihexanide and octenidine on FL-cells and on healing of experimental superficial aseptic wounds in piglets. A double-blind, randomised, stratified, controlled, parallel-group study. Skin Pharmacol Physiol 2004; 17: 141-6

Wound Healing

Agent	%	Wound area (mm^2) on day after exp. wounding				Duration (d) to wound closure
		0	9	18	28	
Polihexanide	0.04	338	171	23**	0**	22.9*, **
Octenidine	0.1	357	243*, **	99*, **	45*	28.3*
Ringer (control)		353	163*	30*	34*	24.1*

* difference to polihexanide $p < 0.05$ ** difference to Ringer $p < 0.05$

Toxicity of Polihexanide

- **Oral LD50/rat 5000 mg/kg → non toxic**
- **0.02 % no inhibition of ciliary epithel of nasal mucosa, no ototoxic, no vestibular damage or effects**
- **No absorption**
- **NOEL in 2-years-feeding test 200 mg/kg/d**
- **No advice for mutagenicity, carcinogenicity as well as for teratogenicity and embryotoxicity**

Hübner NO, Kramer A. Review on the efficacy, safety and clinical applications of polihexanide (PHMB), a modern wound antiseptic. Skin pharmacol2010; 23 (Suppl: 17-27

One example - Prevention of SSI by Antiseptic Rinsing of Dirty Contaminated Wounds

Agriculture workers with dirty heavy accidental injuries of soft tissues

- **Design: retrospective open controlled monocentric randomized cohort study 1974 - 2004**
- Standardized documentation for each patient
  - cause of injury
  - interval between injury and surgical intervention
  - characterization of the wound
- exclusion criterion: no prior systemic or local application of antibiotics

- **After surgical treatment before wound closure rinsing for 3 min with**
  - **0.04 % polihexanide**
  - **10 % PVP-I**
  - **H_2O_2 4 %**
  - **Ringer solution (placebo)**

Roth B, Neuenschwander R, Brill F, Wurmitzer F, Assadian O, Wegner C, Kramer A. ***Effect of initial antiseptic wound irrigation of traumatic soft tissue wounds on postoperative wound infection rates – results of a retrospective, non-randomized, controlled, mono-center study.*** *Plos One submitt.*

SSI in Different Treatment Groups without Differentiation of Severity (A1 and A 2)

Antiseptic solution	SSI rate (%)	Number (n) of treated patients	p for the comparison of polihexanide with any other group
Polihexanide 0.04%	1.5	3264	
PVP-iodine 1%	4.8	2552	<0.0001
Ringer's solution	5.9	645	<0.0001
Hydrogen peroxide 4%	11.7	643	<0.0001

Efficacy of Antiseptic Rinsing of Traumatic Wounds Divided to A1 and A2 SSI

Type of wound	Significance comparison (p)		
	polihexanide/ PVP- iodine	polihexanide/ Ringer	polihexanide/hy-drogen peroxide
crush wound A1-SSI A2-SSI	 0.056 0.002	 0.631* <0.001	 0.003 <0.001
Cuts A1-SSI A2-SSI	 0.002 <0.001	 0.003 0.001	 <0.001 <0.001

Polihexanide for Burn Wounds II. Degree

- **On mesh grafts polihexanide stimulated re-epithelialisation; contrary PVP iodine and silver nitrate induced deep necroses and fibrin discharge**
- **after previously unsuccessful split mesh skin grafting following pre-treatment with PVP iodine and silver nitrate, a complete re-epithelialisation occurred within 2 months after pre- and follow-up treatment with polihexanide**

Concluding the results, second degree burn wounds treated with polihexanide epithelialised without any further debridement after an average of 10 days with a remarkable freedom from pain. No fibrin film was observed on the wound.

Daeschlein G, Assadian O, Bruck JC, Meinl C, Kramer A, Koch S (2007) Feasibility and clinical applicability of polihexanide for treatment of second-degree burn wounds. Skin Pharmacol Physiol 2007; 20:292-296.

Randomised Controlled Double Blinded Trial of Efficacy on Contaminated Soft Tissue Wounds

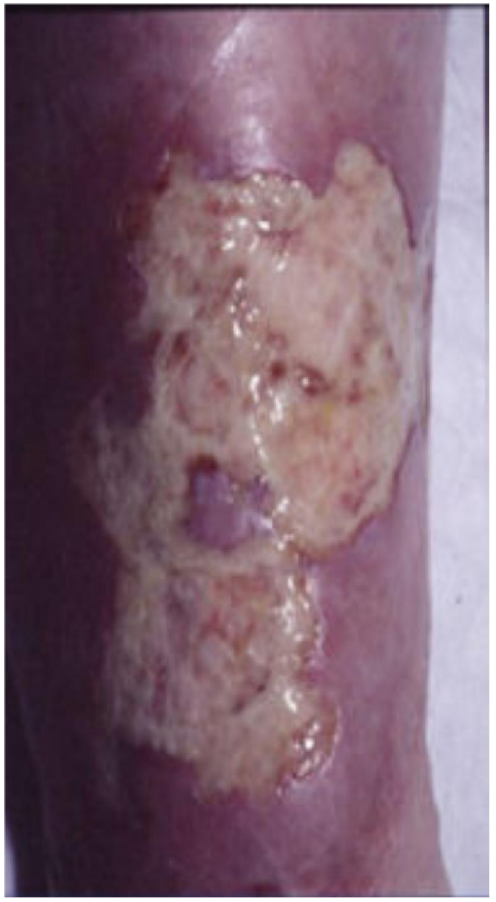
- **Postoperative trial**
  - **polihexanide 0.04 % (n=45) versus Ringer (n=35)**
  - **moist compression-dressing, 2x/d change after rinsing**
  - **clean contaminated soft tissue wounds after radical debridement type 2**
  - **wound smears 0., 2., 8., 15. d**
- **Results with polihexanide**
  - **fast reduction of grampositive wound bacteria (sign.)**
  - **better tissue tolerance (sign.)**

Schmit-Neuerburg et al. Efficacy of a novel antiseptic in the treatment of contaminated soft tissue wounds. Chirurg (2001) 61-71

Supportive Antiseptic Therapy of Venous Ulcus Cruris with Polihexanide

Patients

- **average therapy duration covered 4.2 years at the time of first consultation**
- **210 of 259 patients were treated by surgery**
- **All patients became local antisepsis with polihexanide (0.04%) soaked dressings, partially with previous débridement and following plastic surgery**



Supportive Antiseptic Therapy of Venous Ulcus Cruris with Polihexanide - Results

	negative bacteriol. cultures	number of species		
		1	2	3-4
before antisepsis	**2**	**35**	**155**	**38**
3 d after antisepsis	**72**	**53**	**105**	**0**
5 d after antisepsis	**139**	**22**	**69**	**0**

Roth B, Kramer A. GMS Krankenhaushyg Interdiszip 2009; 4(2):Doc16 (20091216)

Conclusion: Polihexanide

Agent of first choice

- **for infected chronic wounds and burns (0.02%)**
- **in dressings for stimulation of wound healing for chronic wounds**

Agent of choice for

- **SSI prevention of traumatic contaminated injuries (0,04 %)**
- **infected acute wounds (initially 0.04 %, thereafter 0.02 %)**

Properties of Octenidine Dihydrochloride

Characteristics	Use restrictions/disadvantage
○ BI > 1 ○ high effective within 30 s ○ remanence + postantiseptic effect ○ destruction of biofilms ○ no protein or blood failure ○ no absorption ○ no development of resistance ○ no allergic or toxic risks ○ stimulation of phagocytosis and PDGF	○ no bringing under pressure in sting injuries ○ incompatible for cartilage

Efficacy of Octenidine

Double-blinded, randomized controlled study on chronic wounds: sign. increased granulation compared with Ringer

Vanscheidt et al. Hyg Med 2005; 30(5):153-8

Octenisept-moistened gauze dressings were applied to the ulcers three times daily. S. aureus and P. mirabilis were eradicated in all ulcers. After three weeks of treatment, none of the ulcers developed an infection and there was an improvement in their clinical condition.

Sopata Met al. Effect of Octenisept antiseptic on bioburden of neoplastic ulcers in patients with advanced cancer. J Wound Care 2008, 17(1) 24-7

Number of antimicrobial formulations including chlorhexidine, silver nitrate, gentamicin, nitrofurazone, oxytetracycline and povidone-iodine, polymixine B and bacitracine have been used in TEN treatment [3,4]. But these formulations have controvertial issues in wound care, such as delaying epitheliazion [5]. Chlorhexidine is partly inhibited by the exsudate and other organic matters [6]. For indications such as wound antisepsis and treatment of mucosal infections, where a prolonged contact time for antiseptic treatment is feasible, octenidine was found mostly effective microbistatic and microbicidal concentration [7]. We use generally 0.07% of aqueous octenidine without delaying reepithelization in TEN management.

Coban YK et al. A useful combination in the treatment of toxic epidermal Necrolysis (TEN): Octenidine dihydrocholoride solution and Aquacel-Ag. Burns 2011, 37(3) 545-6

Efficacy of Octenidine

Prospective, randomized, non-blinded, clinical study; Flammazine vs. Octenidine-Gel before mesh-graft: less pain during dressing changes, tendency for better wound bed preparation

Radu CA et al. Optimizing Suprathel-therapy by the use of Octenidine-Gel. Burns 2011, 37(2) 294-8

Octenisept 1-2fold/d for 6 weeks, good and cost-effective alternative in the treatment of mild to moderate inflammatory acne lesions, allow reduced application of anti-acne antibiotics to prevent development of resistance

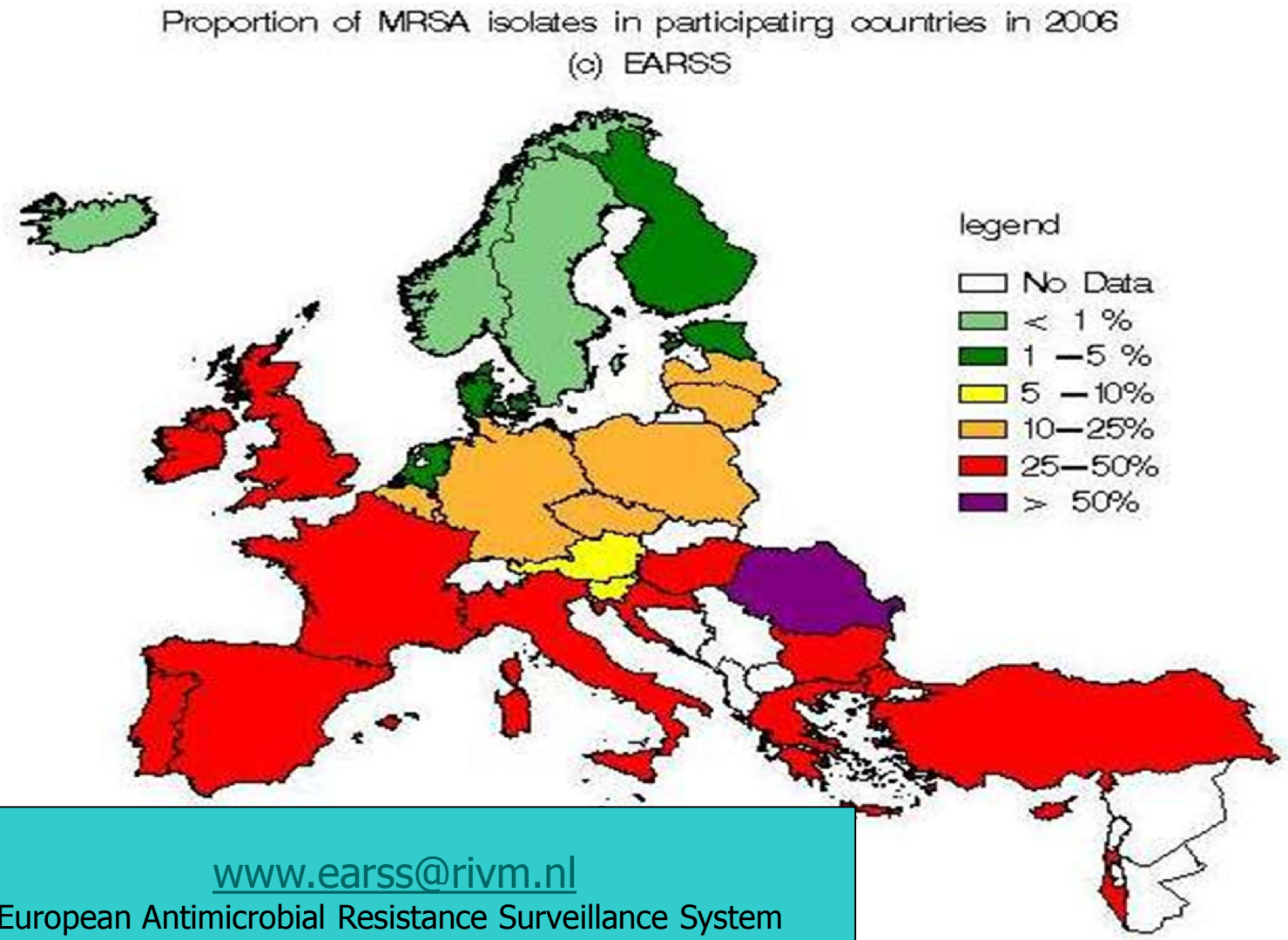
Mayr-Kanhauser S et al. Efficacy of octenidine dihydrochloride and 2-phenoxyethanol in the topical treatment of inflammatory acne. Acta Dermatoven Alp Panonica Adriat 2008, 17(3) 139-43

Conclusion

- **Polihexanide and octenidine are actually the antiseptic agents, which world-wide attained the greatest importance especially for wound antisepsis as well as for antisepsis of mucous membranes.**
- **In Europe, polihexanide has replaced chlorhexidine for wound antisepsis because it is more effective against pathogens but without the risk of development of antimicrobial resistance and the toxicological characteristics are more favorable.**
- **PVP-Iodine dispensable for chronic wounds, but agent of choice in combination with ethanol for sting and cut injuries as well as after accidental contamination with risk of HBV, HCV resp. HIV after spontaneous or induced bleeding**

Workshop 5: Prevention of MRE and Outbreak Management

MRSA Prevalence in Europe



www.earss@rivm.nl
European Antimicrobial Resistance Surveillance System

MRSA Pandemic → Change of Thinking in Hospital Hygiene

- **The success of Netherlands and Denmark** demonstrates the reduction of the selection and spread of MRSA **< 1 % is possible** by a nationwide strategy for prevention

→ **search and destroy of colonized and infected MRSA patients: preemptive isolation + rapid detection (PCR) + eradication**

→ **stringent antibiotics policy**

ca. 1 of 3 hospitalized patients receive antibiotics, in majority not necessary

→ **Multibarrier regime for infection control**
(Approach at the university of Greifswald)

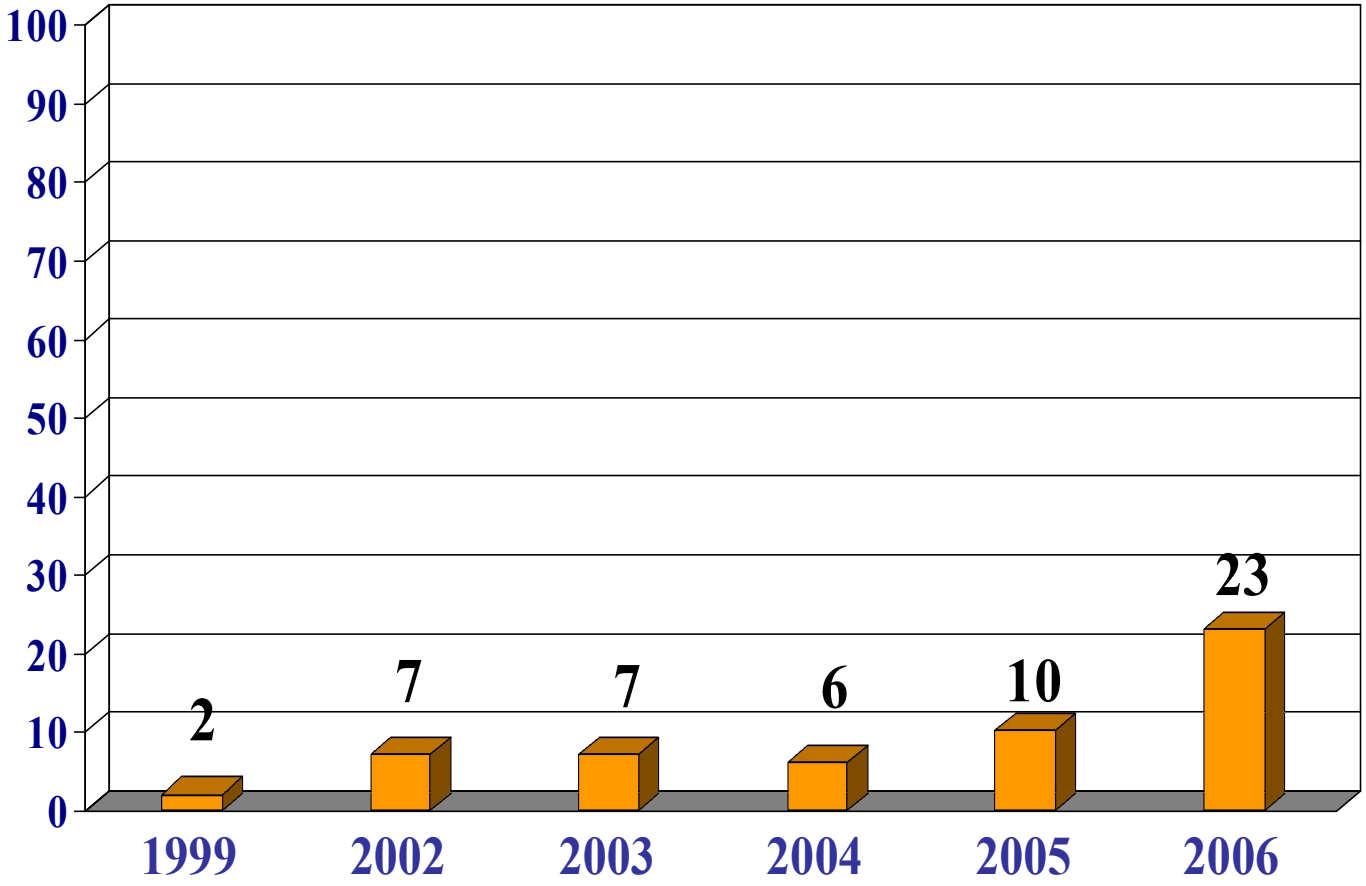
Medical Consequences of MRSA

Metaanalysis of 31 studies including 3.963 patients

- **Mortality of infections caused by MRSA: 30 %**
- **Mortality of infections caused by MSSA: 18 %**

  Cosgrove et al., Clin Inf Dis 2003; 36:53-59
- **Severe disease activity**
- **Prolonged stay in hospital, approx. 7 d**
- **Increased level of costs**

Development of Ratio of MRSA (%) Isolates (First Detection) in Inpatients in our University Hospital 1999 – 2006



2006 we Started these Main Priorities

- **Consequent standard precautions**
- **Screening of risk patients**
- **Stringent guidelines for antibiotics**
- **Consequent eradication of MRSA**
- **Implementation of guidelines for primary/home care**

Complete Screening in High-risk Wards

- **Surgical and medical ICUs**
- **Weaning Station**
- **Stroke Unit**
- **Dermatology**
- **Hematologic transplantation unit**

Other Wards: Screening of Patient with at least one Risk Factor

- Chronic care dependency
- Indwelling devices (e.g. blood stream or urinary catheters, PEG tubes)
- Dialysis
- Skin ulcers, chronic skin diseases, deep soft tissue infections
- Mechanical ventilation, tracheostomy
- Patients dialysed, treated surgically abroad or hospitalized abroad > 24 h with indwelling devices (except of Denmark, the Netherlands, Slovenia)
- Admittance of patients from other medical institutions with probably high MRSA ratio
- Inpatient care in the last 3 months (if there is no negative sampling)
- Patients from high-level ratio nations
- Re-admittance with MRSA in history (Cave-Box)
- Employees from pig farms

RKI: Screening of patient with at least 2 risk factors

+ regional Networking (primary care, admittance, relocation)

Personnel Screening

- **Personnel who cared for MRSA + patients, are screened for carrier state. If the personnel is positive, it would be restricted in patient contacts.**
- **Personnel before employment +**
- **Students/ trainees before clinical training**

Isolation Procedures

Before Entering

1. **Hand disinfection**
2. **Surgical cap**
3. **Mask**
4. **Gowns in patients room (shift work)**
5. **Gloves - disposed in isolation room**

At leaving

6. **Protective equipment disposed in isolation room**
7. **Hand disinfection**

Antiseptic Eradication

- **Whole body wash incl. hair 1/d 7d** (Octenisan)
- **Vestibulum nasi 3x/d 7 d** (Octenidine-ointment 0,05%, in 2. instance Mupirocin)
- **Mouth and oropharynx after every teeth cleansing 7 d** (Octenidol)

Antiseptic Decolonization of MRSA Carriers

- **Change or disinfection of bedding, clothes and personal cosmetics**

- **After every whole body decolonization procedure disinfection of patients contact surfaces**

⇓

prevention of re-infection

End of Isolation

- **After 3 negative swabs (nose, wound, tracheostoma, on 3 consecutive days**

Restrictions for MRSA pos. HCW in Non-risk Areas

Activity in patient care is possible under the following conditions

- **No runny nose / cough**
- **Immediate start of nasal antisepsis with wearing a surgical mouth nose protection**
- **Before and after each patient contact hand disinfection**
- **Used (nose) tissues are as infectious to dispose! Then again hand disinfection**

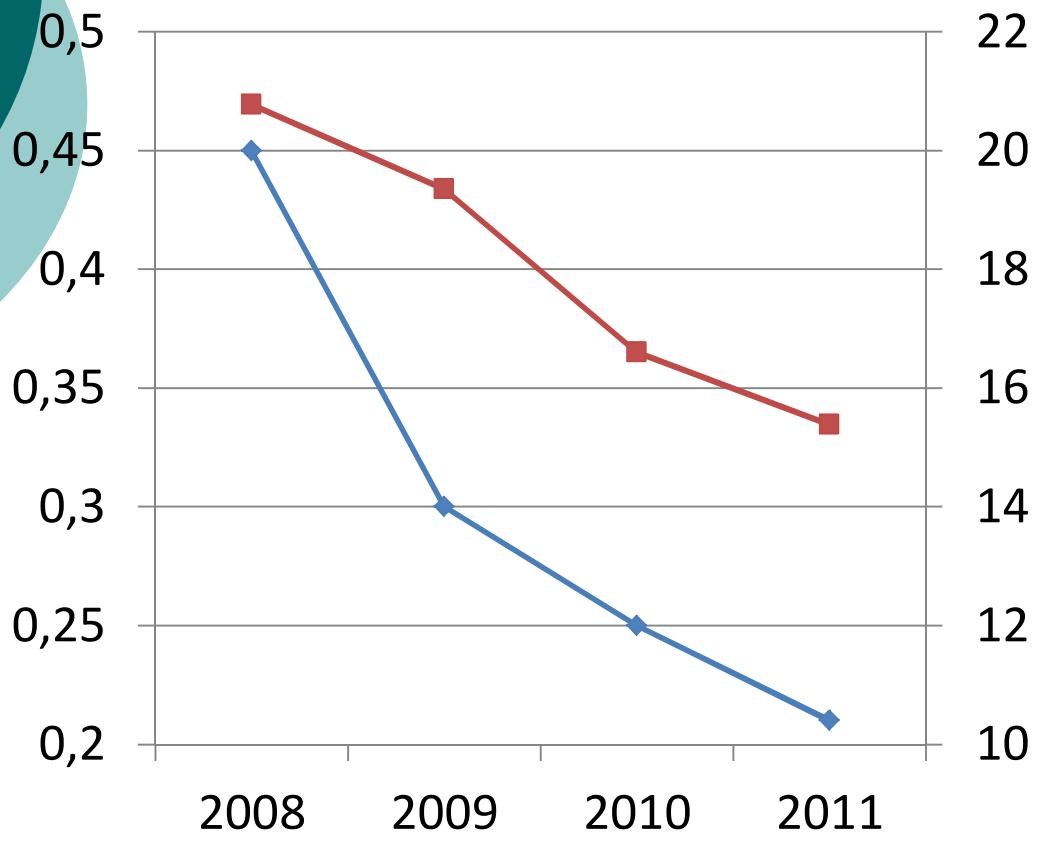
First Result

- **2007/2008: 3,5 % of screened patients are MRSA positive** (~7,5x of the expected value!)
  - apparently correct identification of risk groups
- **Increase of compliance**

- considerably less gradual erosio of the standards

- less closed beds

Decrease of Nosocomial MRSA Rates in our University Hospital



nosocomial incidence density nosok. = nosoc. MRSA/ 1000 patient

MRSA day associate nosoc. MRSA rate = nosoc. MRSA/ 1000 stationary MRSA patients

Cost Efficacy of Screening

- **Screening is cost efficient starting from a prevalence of 0,03% and 2,9 prevented MRSA-Infections/year**

Wernitz MH et al. Cost Analysis/effectiviness of a hospital-wide selective screening programme for MRSA carriers. Clin Microbiol Infect. 2005; 466-71

VRE

Resistance against glycopeptides

- **VanA: against vancomycin and teicoplanin**
- **VanB: only against vancomycin (teicoplanin sensible)**

Prevalence in Germany für VRE *E. faecium VanB*

- **2001: 1 %**
- **2004: 11%**
- **2007: 15 %**

- **High outbreak risk**

Risk Patients

- **Immunosuppressed patients**
  - **especially oncologic patients**
  - **Intensive care neonates**
- **Patients with previous glycopeptide therapy**
- **Patients from countries with high VRE prevalence**

Screening

- **Recommendation**
  - **After glycopeptid therapy**
  - **Contact patients**
  - **Positive history of VRE**
  - **Before organ transplantation**
  - **Patients from regions with higher VRE prevalence**
- **Smear places**
  - **Faeces (rectal swab)**
  - **Urin**

Precautions

- **Hand disinfection**
- **Isolation as in MRSA, but no mask**
- **After Patient discharge final disinfection inclusively siphon of sinks**
- **Decolonisation: Attempt with probiotics**

ESBL = Extended Spectrum Beta-Lactamasen

Penicilline

β-lactamase-sensitive (-instabil) penicillins (benzylpenicillin)

*β-lactamase-resistant (-stabil) penicillin*s (methicillin, flucloxacillin)

Broad-spectrum penicillins (amoxicillin, piperacillin)

Cephlosporins

Classic cephalosporins of 1st generation or basis cephalosporins without increased β-lactamase stability

Parenteral: Cefazolin

Oral: Cefadroxil, cefalexin

Cephalosporins of the 2nd generation with increased β-lactamase stability

Parenteral, oral: Cefuroxim

Cephalosporins of the 3rd generation *broad-spectrum cephalosporins* with high β-lactamase stability

Parenteral: **Ceftazidim, cefotaxim**

oral: Cefixim

ß-lactamase inhibitors (clavulansäure, sulbactam, **tazobactam in comb. with piperacillin)**

Other β-lactam antibiotics

*Carbapeneme (**imipenem, meropenem**)*

Monobactame

Fluorchinolone (**ciprofloxacin**)

Therapeutic Options of Enterobacteriaceae with Carbapenemases

- **Tigecyclin**
- **Colistin**
- **Fosfomycin**
- **evtl. Aztreonam**

Risk Factors of Colonization with ESBL Formers

- Long stay in hospitals (especially ICU)
- Therapy with antibiotics of 1st or 2nd generation
- Devices (z. B. catheters)
- Ulcera
- Elderly
- Male sex
- Necessity of high nursing care

Prevention

- **Basic hygiene = consequent Hand hygiene + gloves + close to the patient surface disinfection + protective clothing when handling with potentially infectious secrets or colonized regions**

- **In case of airborne communicable ESBL additional full-face protection**

Eradication of ESBL

So far, only few studies on eradication of ESBL E. coli without convincing success rates

- **Therapy with polymyxin E in combination with neomycin or erythromycin 4x/d, 17 of 37 patients (46 %) 2 negative controls under therapy; no follow-up**

  Troche, G., et al., Detection and treatment of antibiotic-resistant bacterial carriage in a surgical intensive care unit: a 6-year prospective survey. Infect Control Hosp Epidemiol, 2005; 26(2): 161-5.

- **It is assumed that in a subset of patients, the colonization loses after months spontaneously. In a study of ESBL epidemiology 6.8% of patients lost their colonization**

  Kola A, et al. Surveillance of extended-spectrum beta-lactamase-producing bacteria and routine use of contact isolation: experience from a three-year period. J Hosp Inf 2007; 66(1): 46-51.

E*nterobacter spp.*

- **SDD (parenteral cefotaxim, oral polymyxin E/ tobramycin); screening of children 2x weekly over 12 month: at 54% decolonization**
- **Decolonization with chlorhexidin 0,2 % mouth rinsing, paromomycin oral and parenteral antibiotics for detection in urine success rate 83 % (15/18 patients)**

  Buehlmann M, et al. Effectiveness of a new decolonisation regimen for eradication of extended-spectrum beta-lactamase-producing Enterobacteriaceae. J Hosp Inf 2011;77(2): 113-7.

Multi-resistant Gram-negative Germs (MRGN)

- **Occurence**
  - **Enterobacteriaceae**
    - **In gut of humans and animals**
    - **In environment (soil, water)**
  - **Nonfermenter**
    - **Soil and water bacteria ("wet pathogens")**
    - **in plants and animals**

Resistance Patterns of MRGN

	Enterobacteriaceae	
	3MRGN	4MRGN
Piperacillin/tazobactam	R	R
Cefotaxim and/or ceftazidim	R	R
Imipenem and/or meropenem (Carbapenemasen)	S	R
Ciprofloxacin	R	R

In case of detection of carbapenemases always 4 MRGN

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Resistance Patterns of MRGN

	Pseudomonas aeruginosa	
	3MRGN	**4MRGN**
Piperacillin/tazobactam	one group sensible	R
Cefotaxim and/or ceftazidim		R
Imipenem and/or meropenem		R
Ciprofloxacin		R

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Resistance Patterns of MRGN

	Acinetobacter spp.	
	3MRGN	**4MRGN**
Piperacillin/tazobactam	R	R
Cefotaxim and/or ceftazidim	R	R
Imipenem and/or meropenem	S	R
Ciprofloxacin	R	R

In case of detection of carbapenemases always 4 MRGN

Bundesgesundheitsbl 2012 · 55:1311–1354

MRGN

- **Transmission**
  - directly: from colonized/ infected body sites, secretions, excretions (i.e. feces, urin, tracheal secretions, wounds)
  - indirectly: by contaminated hands, surfaces, food, water inclusively siphons
  - as aerosol i.e. at bronchialer Besiedlung beim Absaugen

- **Risk patients**
  - Immunsuppressed
  - Hospitalization with frequent antibiotic therapies
  - (chronically ill patients with devices)
  - Patients from countries Ländern with high prevalence of MRGN

Screening

- **Screening** – no sufficient evidence, recommendation
  - Risk patients with contact to ESBL, 3 and 4 MRGN
  - Patients from Patients from countries Ländern with high prevalence
  - positive history for ESBL, 3 and 4 MRGN
  - Admission to ICU, transplant units in connection with minimal one risk factor, in urologic wards in case of chronic urinary tract infection
- **Localisation for smears**
  - Feces and urin for enterobacteria
  - Nose, throat for pseudomonas
  - Nose, throat, throat + larg area of skin for acinetobacter
- **Decolonization**
  - no evidence
    - Therapy of infection
    - Antiseptic whole body wash of patients in ICU
    - Antiseptic mounth rinsing

Precautions

Measure	Enterobacteriaceae		Nonfermenter	
	3 MRGN	4 MRGN	3 MRGN	4 MRGN
Isolation	**No**[1] Yes in risk wards no contact with risk patients	**Yes**	**preferably**[1] Yes in risk wards no contact with risk patients	**Yes**
Protective clothing	**Yes**	**Yes**	**Yes**	
Gloves	**Yes**	**Yes**	**Yes**	
Full-face protection	only in tracheal colonization		**Ja**	
Hair protection	**No**	**No**	**No**	

[1] **Compliance with basic hygiene and barrier nursing**

Ending of Isolation

No evidence

- Enterobacteria
  - **Reservoirs in the gut (possibly permanently)**
  - Nonfermenter
  - succesful therapy of Infection

- Strong basis hygiene **to discharge from the hospital**

- Education Compliance of patients for self-protection

Eradication of MRGN

- **In *Citrobacter* spp., *M. morganii, P. stuartii* and *P. mirabilis* up to now no succesful**

  → Measures for eradication of P. aeruginosa have been described only for cystic fibrosis patients and include local and systemic antibiotic therapies

- **Since skin is a common reservoir of *A. baumanii* , antiseptic wash was effective**

  - significant reduction of sepsis + ↓incidence of nosocomial *A. baumannii* isolates

  - during antiseptic wash 80 % of patients were negative (smear from perineum and axillae)

  Borer A, et al. Impact of 4% chlorhexidine whole-body washing on multidrug-resistant Acinetobacter baumannii skin colonisation among patients in a medical intensive care unit. J Hosp Inf 2007; 67(2):149-55.

Outbreak Investigation

1. Prepare for field work
2. Establish the existence of an outbreak
3. Verify the diagnosis
4. Define and identify cases
5. Describe/orient data in terms of time, place, and person
6. Develop hypotheses
7. Evaluate hypotheses
8. Refine hypotheses and carry out additional studies
9. Implement control and prevention measures
10. Communicate findings

Outbreak Investigation

Step 1: Prepare for Field Work

Before leaving for the field:

1) Research the disease
2) Gather the supplies and equipment
3) Make necessary administrative and personal arrangements

Outbreak Investigation

Step 1: Prepare for Field Work

Before leaving for the field:

4) Consult with all parties to determine your role in the investigation

5) Identify your local contacts once you arrive on the scene

Outbreak Investigation

Step 2: Establish the Existence of an Outbreak

An outbreak may exist if the observed number of cases exceeds the expected number.

Rule out:

- Changes in reporting
- Changes in case definition
- Increased public awareness
- Improved diagnostic testing

Outbreak Investigation

Step 2: Establish the Existence of an Outbreak

Factors influencing outbreak investigation:

- Severity of illness
- Potential for spread
- Political considerations
- Public relations
- Availability of resources

Outbreak Investigation

Step 3: Verify the Diagnosis

Twin Goals:

1) Ensure that the problem is correctly and properly diagnosed
2) For infectious diseases and toxic exposures, rule out laboratory error

Outbreak Investigation

Step 3: Verify the Diagnosis

1) Review clinical findings (symptoms, features of illness)
2) Review laboratory findings
3) Review laboratory techniques & procedures
4) Obtain specimens, isolates, materials for special laboratory tests

Outbreak Investigation

Step 3: Verify the Diagnosis

5) Interview cases
   - Observe signs, symptoms, behaviors directly
   - Ask about exposures
   - Ask about patient's perception of cause(s)
   - Ask about knowledge of other cases
   - Ask questions based on information from other interviews—looking for commonalities
6) Formulate ideas about cause, source, spread

Outbreak Investigation

Step 4: Define and Identify Cases

1) Develop a case definition
   - Clinical information about the disease
   - Characteristics of people who are affected
   - Location or place characteristics
   - Time characteristics
2) Case definition needs to be broad enough to capture most or all cases of disease

Outbreak Investigation

Step 4: Define and Identify Cases

3) Distinguish gradations of certainty
   - Confirmed: laboratory verification
   - Probable: typical clinical features without laboratory confirmation
   - Possible: fewer typical clinical features

Outbreak Investigation

Step 4: Define and Identify Cases

4) Start with “loose” case definition
5) Tighten case definition as investigation proceeds (consider dropping the “possible” cases)

Outbreak Investigation

Step 4: Define and Identify Cases

6) Identify and count cases
   - Use as many sources as possible
   - Determine whether to notify general public
   - Consider surveying entire population in a restricted setting (cruise ship, school)

Outbreak Investigation

Step 4: Define and Identify Cases

7) Obtain information from cases
   - Identifying and contact information (name, address, telephone)
   - Demographic information (age, race, sex, ethnicity, occupation)
   - Clinical informaton (signs, symptoms, date of onset, medical care sought and received)
   - Risk factor information

Outbreak Investigation

Step 5: Describe & Orient the Data

Descriptive epidemiology:

1) Identify data that are informative & reliable
2) Orient data by
   - Person (WHO—population affected)
   - Place (WHERE—geographic extent)
   - Time (WHEN—trends)

Outbreak Investigation

Step 5: Describe & Orient the Data

3) Characterizing by time
   - Construct an epidemic curve
   - Estimate probable times of exposure
   - Interpret the epidemic curve
     - Shape (defining time course)
     - Slope
     - Period of exposure
     - Mininum, maximum, median incubation period

Outbreak Investigation

Step 5: Describe & Orient the Data

4) Characterizing by place (geographic extent)
   - Construct an “spot map”
5) Characterizing by person
   - Personal characteristics (age, race, sex)
   - Exposures (occupation, risk factors)

Outbreak Investigation

Step 6: Develop Hypotheses

Generate testable hypotheses regarding:

1) Source of the agent
2) Mode of transmission
3) Exposures that caused the disease

Outbreak Investigation

Step 6: Develop Hypotheses

Generate hypotheses based on knowledge of the disease:

1) Reservoir
2) Mode(s) of transmission
3) Vehicles and vectors
4) Known risk factors

Outbreak Investigation

Step 7: Evaluate Hypotheses

Two approaches:

1) Compare hypotheses with established facts
2) Test hypotheses analytically
    - Cohort study
    - Case-control study

Outbreak Investigation

Step 7: Evaluate Hypotheses

Cohort Study:

1) Ask about exposures
2) Calculate attack rates
3) Pattern: high attack rate in *exposed* combined with low attack rate in *nonexposed*
4) Compute relative risk
5) Test for statistical significance

Outbreak Investigation

Step 7: Evaluate Hypotheses

Case-control Study:

1) Ask case-patients and controls about past exposures
2) Estimate odds for *cases* and *controls*
3) Compute odds ratio
4) Test for statistical significance

Outbreak Investigation

Step 8: Refine Hypotheses

Reasons:

1) Initial analytical study fails to confirm hypothesis
2) Need to perfect your hypothesis even if initial data are supportive
3) Supplement epidemiologic findings with laboratory and environmental evidence

Outbreak Investigation

Step 9: Implement Control and Prevention Measures

1) Implement control measures as soon as source of outbreak is known
2) Break the chain of infection
3) Target agent, source or reservoir
4) Interrupt transmission or exposure
5) Reduce susceptibility

Outbreak Investigation

Step 10: Communicate Findings

Types of communication:

1) Oral briefing for health authorities
2) Written report
    - Introduction
    - Background
    - Methods
    - Results
    - Discussion
    - Recommendations

The Knowledge of the Necessity of Prevention of HAI Must Grasp Everybody Like an Exploding Fire!

My Personally Conclusion

Hygiene is not everything
but without hygiene everything is nothing!