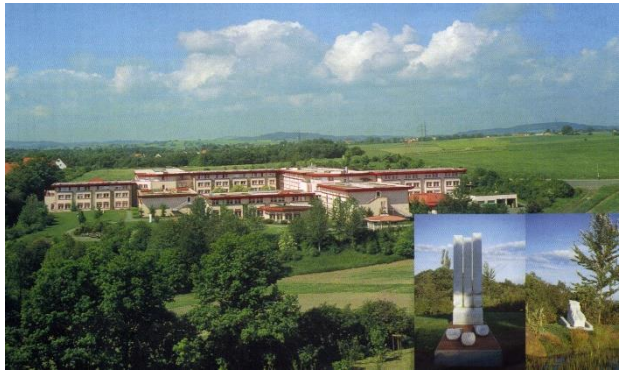
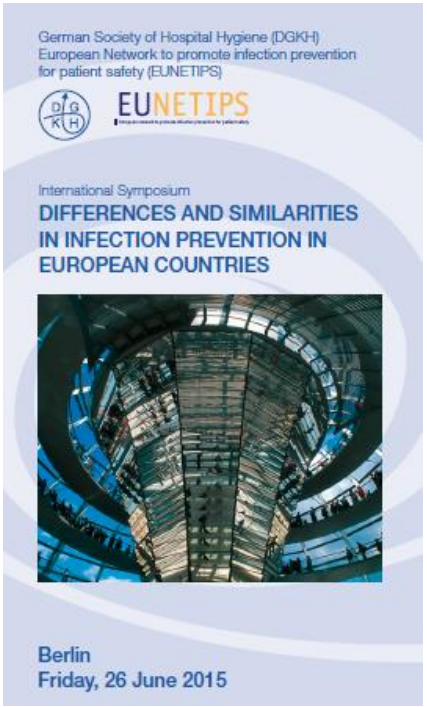
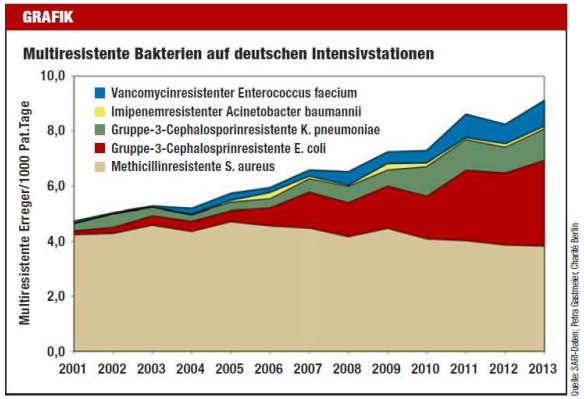
Lessons learnt from outbreaks of multi-resistant bacteria – consequences for prevention

Martin und Daniel Exner







“ The greatest obstacle to knowledge is not ignorance, it is the illusion of knowledge.”

Daniel Boorstein, Historian -

Topics

- Significance of multiresistant pathogens
- General Requirements for an outbreak management
- Priciples in hospital outbreak management
- Ecology and Transmission pathways
- Some examples
- Conclusion

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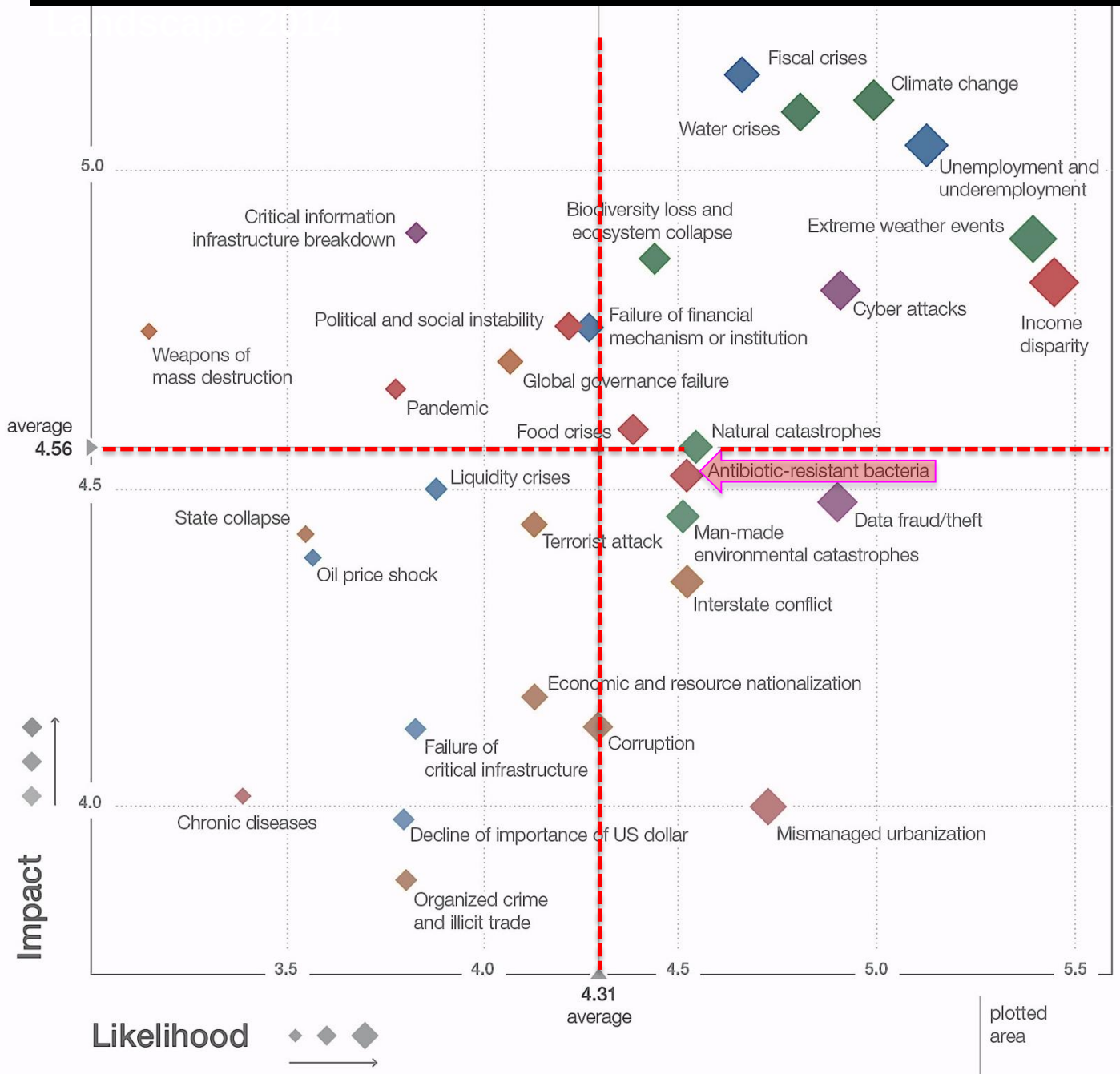
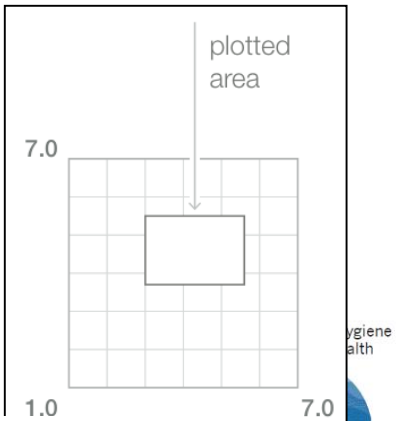
Global Risks 2014 report Figure 1.1.: The Global Risk



THE GLOBAL RISKS:

- **Economic**
- **Enviromental**
- **Geopolitical**
- **Societal**
- **Technological**



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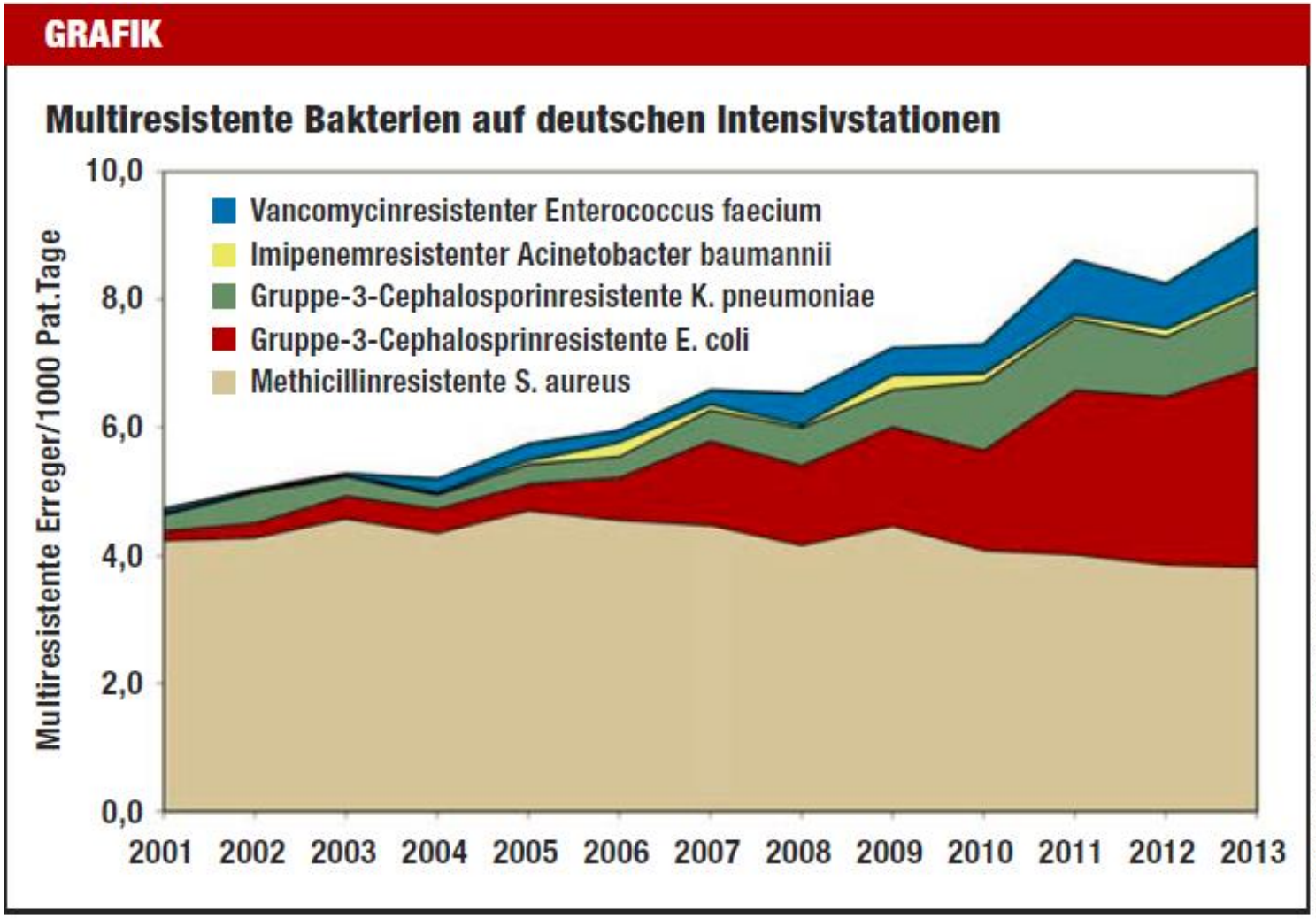
Multiresistent pathogens Development in Germany 2001 – 2013



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Outbreak as a chance ?

- *Outbreak analysis is like a big experiment (R. Koch)*
- Never waste a good crisis *(B. Obama)*

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Operational Disease outbreak managment operational Guideline Public health England 2014

Communicable Disease Outbreak Management

Operational guidance

Definition of a trigger event

An event or situation which threatens or causes damage to the health of our patients and/ or health care workers for whom we are responsible and that requires urgent action from outbreak management team at whatever level

Aim of a comprehensive outbreak management

To ensure that an effective and coordinated approach is taken to outbreak management, from initial detection to formal closure and review of lessons identified. It promotes a consistent approach across all levels of OMT (Outbreak management team) and includes a set of standards for outbreak response.

Definition of an outbreak or a trigger event

- an incident in which two or more people experiencing a similar illness are linked in time or place
- a greater than expected rate of infection compared with the usual background rate for the place and time where the outbreak has occurred
- a single case in time of hospital stay for certain rare diseases such as, Aspergillosis, legionnaires disease, pertussis, EHEC/HUS, conjunctivitis epidemica, scabies, diphtheria, botulism, viral haemorrhagic fever
- a single case of colonization/ infection of 4 fold resistant pathogen (enterobacteriaceae, Gram-negative non-fermenting bacteria like P.aeruginosa, Acinetobacter)
- a suspected, anticipated or actual event involving microbial or chemical contamination of food or water

Management arrangements for outbreaks

- The protection of the public's health, of our patients/HCW´s takes priority over all other considerations.
- The primary objective in outbreak management is to protect public health, patients/ HCW´s by identifying the source and implementing control measures to prevent further spread or recurrence of the infection.
- Secondary objectives include refining outbreak management, training, adding to the evidence base about sources and transmission of infectious agents and lessons learnt for improving communicable disease control

Members of the OMT- Core team

- Hospital hygienist (infection control practioner)
- Hygiene appointee practioner
- Hospital hygiene nurse – infection control nurse
- Commissioner of the hospital management
- Nursing service ,
- Microbiologist
- Delegate of the public health departement (public health officer) with clear appointment and communication lines
- Communications officer

Standards for managing outbreaks

Outbreak recognition	Initial investigation to clarify the nature of the outbreak begun within 24 hours
	Immediate risk assessment undertaken and recorded following receipt of initial information
Outbreak declaration	Decision made and recorded at the end of the initial investigation regarding outbreak declaration and convening of outbreak control team
Outbreak Control Team	OCT held as soon as possible and within three working days of decision to convene
	All agencies/disciplines involved in investigation and control represented at OCT meeting
	Roles and responsibilities of OCT members agreed and recorded
	Lead organisation with accountability for outbreak management agreed and recorded

Standards for managing outbreaks

Outbreak investigation and control	Control measures documented with clear timescales for implementation and responsibility
	Case definition agreed and recorded
	Descriptive epidemiology undertaken and reviewed at OCT. To include: number of cases in line with case definition; epidemic curve; description of key characteristics including gender, geographic spread, pertinent risk factors; severity; hypothesis generated.
	Review risk assessment in light of evidence gathered
	Analytical study considered and rationale for decision recorded
	Investigation protocol prepared if an analytical study is undertaken
Communications	Communications strategy agreed at first OCT meeting and reviewed throughout the investigation.
	Absolute clarity about the outbreak lead at all times with appropriate handover consistent with handover standards
End of outbreak	Final outbreak report completed within 12 weeks of the formal closure of the outbreak
	Report recommendations and lessons learnt reviewed within 12 months after formal closure of the outbreak

The ideal Outbreak management

- Extremly in time recognition of an outbreak
- Rapid recognition and prevention of further cases and control of the risk situation – security of patients and hcw
- Immediate analysis of epidemiology, reservoirs of infection, transmission pathways by microbiological and environmental culture and molecular typing methods
- Generating a hypothesis
- Critical and falsified analysis of reservoirs, transmission pathways and control strategies
- Good risk – and crisis communication (if necessary)
- Implementation of sustainable prevention strategies
- Analysis of its efficacy over a longer time
- Report recommendations and lessons learnt
- Proposal for risk regulation, legal regulation or technical rules

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Significance of a plausible and falsified hypothesis in a comprehensive outbreak management

Without

a plausible Hypothesis

No sustainable and complete control and prevention of future outbreaks

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Knowledge of the ecological characteristics of the identified outbreak pathogen is decisive for a successful outbreak management

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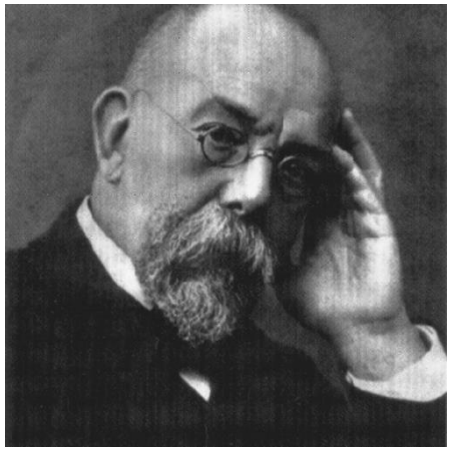
Cholera outbreak in Hamburg 1892 - example of an ideal type of sustainable outbreak management



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Robert Koch und Ausbruchmanagement der Hamburger Choleraepidemie 1892

R. Koch in Hamburg 24.8.1892 These: Trinkwasser als Vehikle

Am 16.8.1892 2 Choleraer-krankungen- Beginn der Cholera-Epidemie

Ortsbe-Sichtigung durch R.Koch 25.8.1892

1000 Mann Einschl. Militärarbeiten An Fertigstellung Wasserfiltration 17.9.1892

Abkoch gebot für Trinkwasser 26.8.1892

R.Koch: Wasserfiltration und Cholera
Zeitschrift für Hygiene und Infektionskrankheiten
26.5.1893
R.Koch: Die Cholera in Deutschland
Während des Winters 1892/93
Zeitschrift für Hygiene und Infektionskrankheiten
24.7.1893
Grundsätze für die Reinigung von Oberflächenwässern durch Sandfiltration
Durch Cholerakommission über Reichskanzler an Bundesregierungen
10.2.1894

(Quelle: MS, 1892, S. 29 f)

Abb. 9 Cholerafälle in Hamburg, August bis Oktober 1892

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German Guideline Outbreakmanagement of nosocomial infections 2002

Bundesgesundheitsbl - Gesundheitsforsch - Gesundheitsschutz
2002 · 45:180–186 © Springer-Verlag 2002

Empfehlungen

Ausbruchmanagement und strukturiertes Vorgehen bei gehäuftem Auftreten nosokomialer Infektionen

Empfehlung der Kommission für Krankenhaushygiene und Infektionsprävention beim Robert Koch-Institut

Phases of a holistic outbreak management

- **Proactive Phase**
- Reactive Phase

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Proactive Phase

- Definition of trigger events
- Clear structure and implementation of the outbreakmanagment

I) Infektionen, die bereits bei vereinzeltem Auftreten Anlass für eine hygienische Analyse darstellen können

Während eines Krankenhausaufenthaltes auftretende:

- Legionellose,
- Aspergillus spp.-bedingte Organmykose,
- Pertussis,
- Infektion mit Streptococcus pyogenes (Gruppe A),
- Konjunctivitis epidemica,
- Scabies.

II) Infektionen, bei denen bei einem Auftreten bei zwei oder mehr Patienten ein epidemischer Zusammenhang gegeben sein kann

Infektionen mit Erregern mit speziellen Resistenzen (bei identischem Resistenzmuster) (z. B. die nach § 23 Abs. 1 IfSG erfassten Erreger mit speziellen Resistenzen und Multiresistenzen [2])

- Methicillin-resistente Staphylococcus aureus (MRSA),
- Vancomycin-resistente Enterokokken (VRE),
- S. pneumoniae,
- E. coli,
- Klebsiella spp.,
- Enterobacter cloacae,
- Citrobacter spp.,
- Serratia marcescens,
- Pseudomonas aeruginosa,
- Stenotrophomonas maltophilia,
- Burkholderia cepacia,
- Acinetobacter baumannii,
- Candida spp. (invasive Candidainfektion).

Infektionen mit ungewöhnlichem Erreger

Sepsis mit einheitlichem Erreger (Einheitlichkeit auf Speciesebene und gegebenenfalls im Resistenzmuster)

Infektionen durch blutübertragene Erreger (z. B. HBV, HCV. Aufgrund der langen Inkubationszeit auch bei Auftreten nach Entlassung, wenn ein Zusammenhang der Fälle aufgrund eines vorausgegangenen Aufenthaltes in der gleichen Einrichtung anzunehmen ist)

Erreger der Gastroenteritis (z. B. Clostridium difficile, Rotaviren)

Proactive Phase

- Definition of responsibilities and communication line
- Implementation of the outbreak management Team

Proactive Phase

- Definition of communication and information lines together with the public health departement

- Communication with the media in the acute phase of an outbreak

ECDC - Effective risk communication

- **Do more good than harm (beneficence, nonmalificence).**
- **Ensure an equitable distribution of risk (equity).**
- **Fair process of decision making (fairness, natural justice).**
- **Seek optimal use of limited risk management resources (utility).**
- **Promise no more risk management than can be delivered (honesty).**
- **Impose no more risk than you would tolerate yourself (the Golden Rule).**
- **Be cautious in the face of uncertainty ('better safe than sorry').**
- **Foster informed risk decision making for all stakeholders (autonomy).**
- **Risk management processes must be flexible and evolutionary to be open to new knowledge and understanding (evolution, evaluation, iterative process).**
- **The complete elimination of risk is not possible (life is not risk free).**

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Impact of media and so- called experts

- Tendency of scandalization
- Only bad news are good news
- Some so-called experts use also outbreaks to blame and scandalize to win awarness
- Those experts must demand themselve:
- - do I have detailed information
- - do I want to change in a sustainable way things which go wrong
- - do I want to profile myself
- - which consequences will have my words for the medical faciltity
- For a structured outbreak management so called experts may be a substantial risk

Publication of the Gießener Klebsiella oxytoca outbreak, Lancet 2000

Disinfectant contaminated with *Klebsiella oxytoca* as a source of sepsis in babies

Irwin Reiss, Arndt Borkhardt, Roswitha Füssle, Andreas Sziegoleit, Ludwig Gortner

We report an outbreak of sepsis from contaminated disinfectant in a neonatal and paediatric intensive-care unit. 28 infants were infected with *Klebsiella oxytoca* and basic measures to control the outbreak failed. The resistance of *K oxytoca* against the disinfectant was probably mediated by capsule formation, visible as mucoid colonies.

Formaldehyde-based disinfectants are commonly used to prevent nosocomial infections. Usually, they are considered to be effective against a wide range of bacteria including gram-negative species.

Specifically, *Klebsiella* spp infections in neonatal and paediatric intensive-care units have been reported and are frequently associated with serious systemic infections or death.[1-3] Babies colonised with *Klebsiella* spp are a source of infection as well as distilled water containers, resuscitation apparatus, hand-washing scrubbers, and bottles of 1% chloroxylenol soap.[4]

We report an outbreak of nosocomial sepsis in 28 infants with *Klebsiella oxytoca* in a 12-bed neonatal and paediatric intensive-care unit from October, 1996, to March, 1999. 16 of 27 patients were preterm infants with a gestational age of less than 37 weeks (median postnatal age 8 days; range 2–34), two were term infants with meconium-aspiration syndrome (6 days) and congenital malformation (7 days), and eight infants (median 4 months; range 2 weeks to 7 months) and one 13-year-old child had congenital heart malformation. 22 (82%) of the patients were initially diagnosed by typical clinical signs of sepsis with thrombocytopenia, and increased C-reactive protein; 11 of them in addition had signs of septic shock with catecholamine-dependent hypotension and respiratory failure. One preterm infant (27 weeks gestation), died 6 h after the onset of septic shock. Secondary to disseminated intravascular coagulation, two preterm infants developed severe intracerebral haemorrhage— one of them died from this complication, the other survived with severe disability. All other patients survived.

All strains of *K oxytoca* isolated from blood cultures since October, 1996 showed identical fermentation characteristics and were sensitive to aminoglycosides, quinolones, third-generation cephalosporins, and carbapenems. They exhibited various degrees of sensitivities towards broad-spectrum penicillins in combination with β-lactamase inhibitors, second-generation cephalosporins, and cotrimoxazole.

Basic measures to control the outbreak failed. Beside faecal samples taken from all babies to exclude translocation of the pathogen from the gastrointestinal tract, carriage by medical staff was investigated by oropharyngeal and anal smears. Identical samples were taken from babies weekly and cultured. In addition, air conditioning and water devices were investigated, as well as water reservoirs and sinks; all samples were free from *K oxytoca*. Eventually, *K oxytoca* was isolated at a concentration of about 20 cfu/100 mL from a sample of a 0·25% disinfectant solution (8·0 g/dL formaldehyde, 8·0 g/dL glyoxal, 4·5 g/dL glutaral) used for disinfection of surfaces, laminar air systems, and infusion pumps. The disinfectant solution was prepared daily and stored in plastic buckets. Bacterial isolates from each plastic bucket with disinfectant showed an identical enzyme and antibiotic pattern to those isolated from blood cultures. The identity of Klebsiella strains isolated from blood cultures and disinfectant solution was proven by plasmid analysis and sequencing of the 16 S rRNA gene. All isolates contained two plasmids of 250 kbp and two of 60 kbp. Thus, molecular characterisation showed the identity of *K oxytoca* isolated from blood cultures and disinfectant solution. Bacteriological investigations of the disinfectant showed that *K oxytoca* grew slowly in 0·25% solution of the disinfectant at room temperature with generation times of about 20 h, whereas *Staphylococcus aureus* and *Pseudomonas aeruginosa* were killed within 2 h. The resistance of *K oxytoca* against the disinfectant is probably mediated by capsule formation, visible as mucoid colonies. 0·5% of the disinfectant reliably killed the same strain within a few minutes. 3 months before the first neonatal sepsis by *K oxytoca* was noted in October, 1996, the disinfectant concentration was lowered from the recommended concentration of 0·5% to 0·25% by the local infectious-disease-control institution because of complaints of non-specific irritation by several staff members.

After detection of the disinfectant solution as the source of nosocomial infections the concentration was immediately increased to 0·5% and plastic pails were replaced by autoclavable metal pails. No further Klebsiella sepsis has occurred since then.

1 Hable KA, Matsen JM, Wheeler DJ, et al. Klebsiella type 33 septicaemia in an infant intensive care unit. *J Pediatr* 1972; **80:** 920–24.
2 Kayyali MZ, Nicolson DP, Smith IM. A Klebsiella outbreak in a pediatric nursery: emergency action and preventive surveillance. *Clin Pediatr* 1972; **11:** 422–26.
3 Hill HR, Hunt CE, Matson JM. Nosocomial colonization with Klebsiella, type 26, in a neonatal intensive care unit associated with an outbreak of sepsis, meningitis and necrotizing enterocolitis. *J Pediatr* 1974; **85:** 415–19.
4 Outbreak of extended spectrum β lactamase producing *Klebsiella pneumoniae* in a neonatal unit. *Arch Dis Child Fetal Neonatal Ed* 1999; **80:** F64–68.

Department of Pediatrics, Institute of Medical Microbiology, Justus-Liebig-University Giessen, D-35392 Germany (I Reiss MD, A Borkhardt MD, R Füssle MD, Prof A Sziegoleit MD, Prof L Gortner MD)
Correspondence to: Dr Irwin Reiss
(e-mail: irwin.reiss@pediat.med.uni-giessen.de)

Myocardial blood-flow response during mental stress in patients with coronary artery disease

James A Arrighi, Matthew Burg, Ira S Cohen, Alexander H Kao, Steven Pfau, Teresa Caulin-Glaser, Barry L Zaret, Robert Soufer

Positron emission tomography was used to quantify changes in myocardial blood flow during mental stress in patients with and without coronary artery disease. Blunted augmentation of myocardial blood flow during mental stress was observed in regions without significant epicardial stenosis.

Mentally stressful tasks in patients with coronary artery disease (CAD) can produce acute cardiac effects that are consistent with ischaemia, including reductions in left ventricular function and relative myocardial perfusion.[1,2] Traditional assessment of CAD severity by angiography or exercise stress testing may not adequately assess the propensity for mental stress ischaemia, and may specifically underestimate the contribution of abnormal coronary vascular reactivity in its pathogenesis. Previous studies in which invasive techniques limited to one vascular territory were used have shown vasoconstriction of stenosed coronary arteries[3] and blunted augmentation of blood flow remote from such stenotic arteries,[4] but the relative contribution of epicardial stenosis versus abnormal vascular reactivity during mental stress is unknown.

We assessed myocardial blood-flow response during mental stress and dipyridamole vasodilator stress by dynamic positron emission tomography (PET) with N-13 ammonia and compared this with coronary anatomy by quantitative coronary angiography in ten patients with CAD and in five control

- After publication of the outbreak without information of the details to the parents of the children in advance the public prosecutor started the inquiry with the consequence of conviction
- A dilemma between obligation of transparency and empathy to the patient and their families and the need to communicate the lessons learnt: Klebsiella can icrease their tolerance against disinfectants

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Phases of an outbreak management

- Proactive Phase
- **Reactive Phase**

10 steps of the reactive Phase

- Step 1: recognition of a trigger event
- Step 2: Assessment of the present situation
- Step 3: description and confirmation
- Step 4: in site inspection / Delta analysis
- Step 5: intervention to prevent further cases
- Step 6: Infection source tracking
- Step 7: evaluation /weighting of the results

10 Steps of the reactive Phase

- Step 7: determination of specific intervention procedure in a dynamic way
- Step 8: official declaration of the end of the outbreak
- Step 9: final Evaluation, Deficit analysis and definition of future prevention strategies –
- Step 10: final consensus report (and publication) with lessons learnt and consequences for sustainable risk regulation

Reactive Phase

- Epidemiologic Characterising
- Time Line
- In Site inspection, survey and auditing of procedures
- Hygienic- microbiological investigation
- Typing (PFGE, Whole genome sequencing etc.)

Questions concerning the efficacy of the outbreak management

- In time recognition of the infection source tracking by hygienic, microbiological, epidemiological and typing methods ?
- Causual identification of infection source and transmission pathways ?
- Are there any open questions concerning reservoirs and transmission
- extraoridnary expenditure and cost in context with the outbreak
- Which basic prevention and control strategies must to be changed or modified
- Publication and information of the infection control community
- Consequences for risk regulation

Topics

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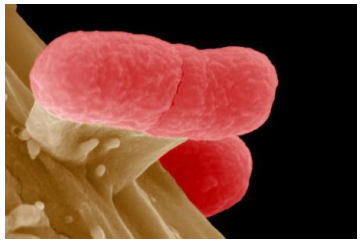
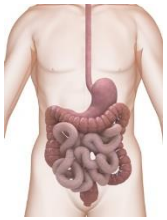
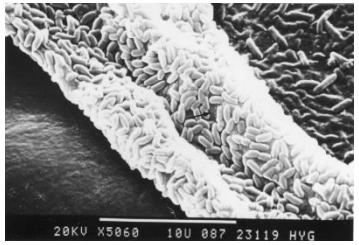
Hygienecascade gram- negative bacteria



Reservoir



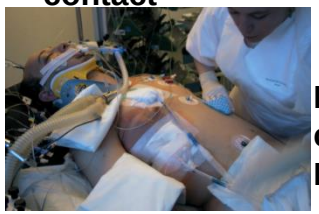


Release

By
direct and indirect contact

High Persistence in Wet areas and Biofilm

Transmission



Direct transmission: contact Water, solutions, Infusions etc.

Infection

Indirect transmission: Hands

disease

No Clearance like MRSA possible

Martin Exner

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German Classification of Antibiotic resistance of gram-negative bacteria

Tab. 2 Klassifizierung multiresistenter gramnegativer Stäbchen auf Basis ihrer phänotypischen Resistenzeigenschaften (R=resistent oder intermediär empfindlich, S = sensibel)

Antibiotikagruppe	Leitsubstanz	Enterobakterien		*Pseudomonas aeruginosa*		*Acinetobacter baumannii*	
		3MRGN[1]	4MRGN[2]	3MRGN[1]	4MRGN[2]	3MRGN[1]	4MRGN[2]
Acylureidopenicilline	Piperacillin	R	R	Nur eine der 4 Antibiotikagruppen wirksam (sensibel)	R	R	R
3./4. Generations-Cephalosporine	Cefotaxim und/oder Ceftazidim	R	R		R	R	R
Carbapeneme	Imipenem und/oder Meropenem	S	R		R	S	R
Fluorchinolone	Ciprofloxacin	R	R		R	R	R

[1] 3MRGN (**M**ulti**r**esistente **g**ram**n**egative Stäbchen mit Resistenz gegen **3** der 4 Antibiotikagruppen)
[2] 4MRGN (**M**ulti**r**esistente **g**ram**n**egative Stäbchen mit Resistenz gegen **4** der 4 Antibiotikagruppen)

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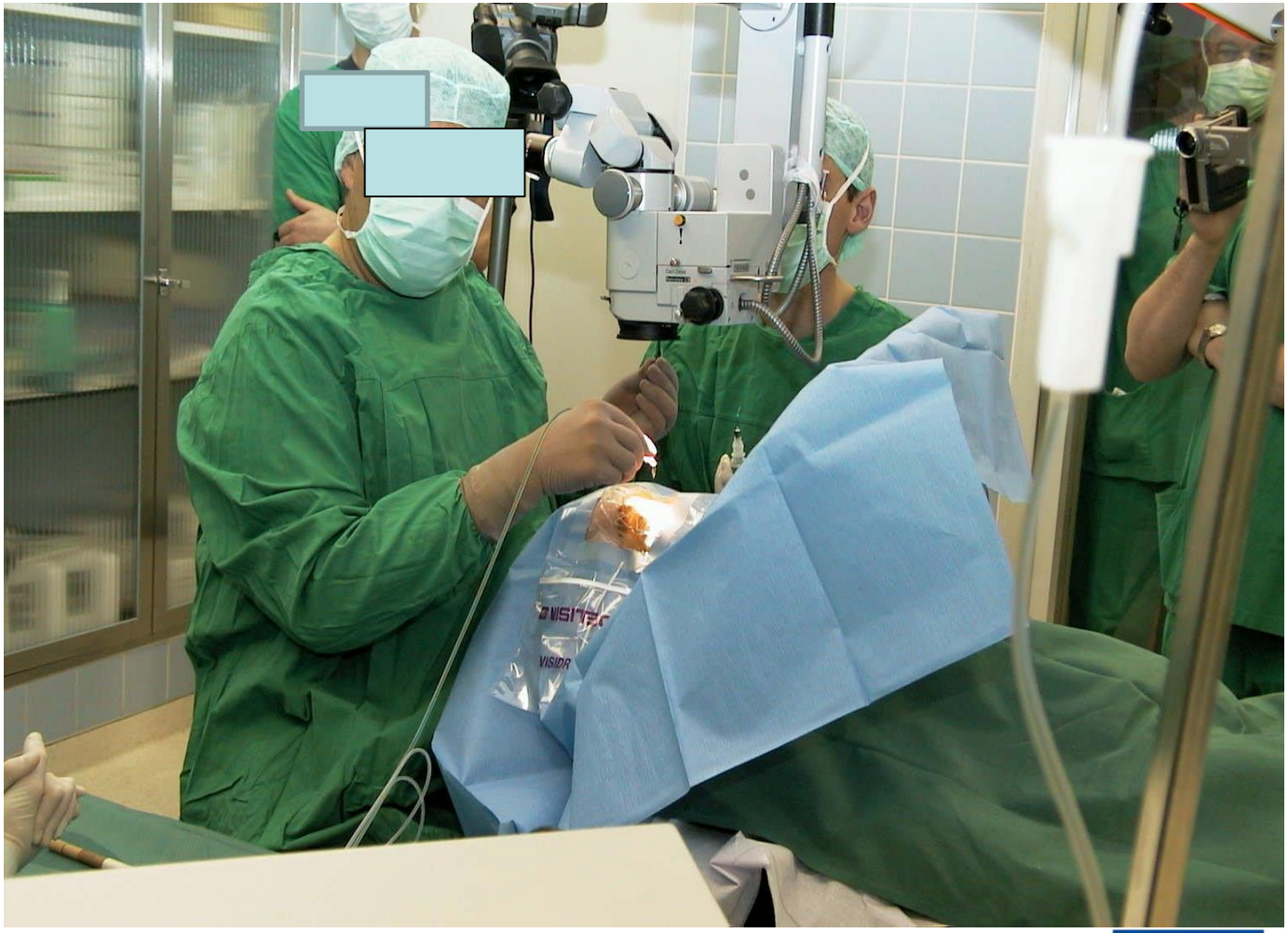
Outbreak of 6 P. aeruginosa Endophtalmitidis after Cataract- Surgery and site survey by police



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Lessons learnt

- You have to train your co-worker in advance in managing machines
- Techical rules for construction of devices

Legionella Outbreak in a new ReHa Hospital with 11 Legionellosis (4 letal)

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Faulty construction of the airconditioning system

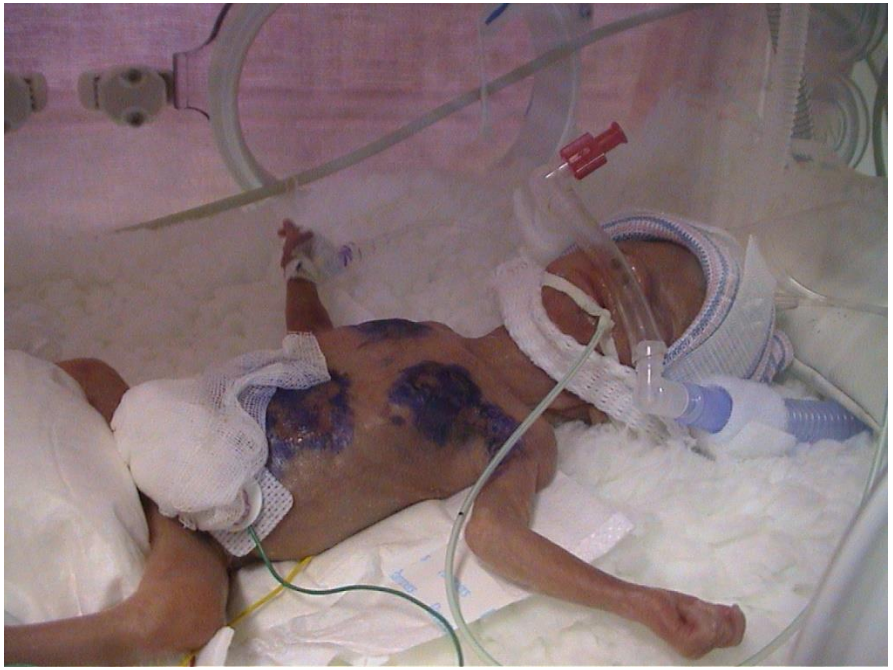
Abb. 1. Dachzentrale der Raumluft-technischen Anlage. 1 = Ansaugung, 2 = Strangentlüftung, 3 = Abluft (Gebläse).

Lessons learnt

- Until this outbreak no limit values for legionella in water in Germany – when is it possible to re-open a hospital after a legionella outbreak
- Need to generate guidance values for acceptable legionella concentrations in watertoday 100 legionella / 100ml
- Air conditioning technical rules to avoid intake of legionella aerosols and air filtration also in rehabiltiation clinics

Biofilm and humidifier

Endemic high rate of Gram negative infection rate in neonates



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Results of in site inspection and microbiological sampling

Abb. 8 Aufnahme eines Inkubators mit offenem Befeuchtersystem. In der ausgezogenen Plastikwanne mit Aufschrift „Isolette Infant Incubator“ wird sterile Wasser zur Befeuchtung eingefüllt

Abb. 10 Aufnahme der inneren Anschlussstelle für die Plastikwanne

Abb. 11 Aufnahme des normalerweise weißen Abstrichtupfers, mit welchem ein Abstrich aus dem Inneren des Anschlussteiles (siehe auch Abb. 10) genommen wurde. Der Abstrichtupfer ist voll mit schmierigem Belag (Biofilm)

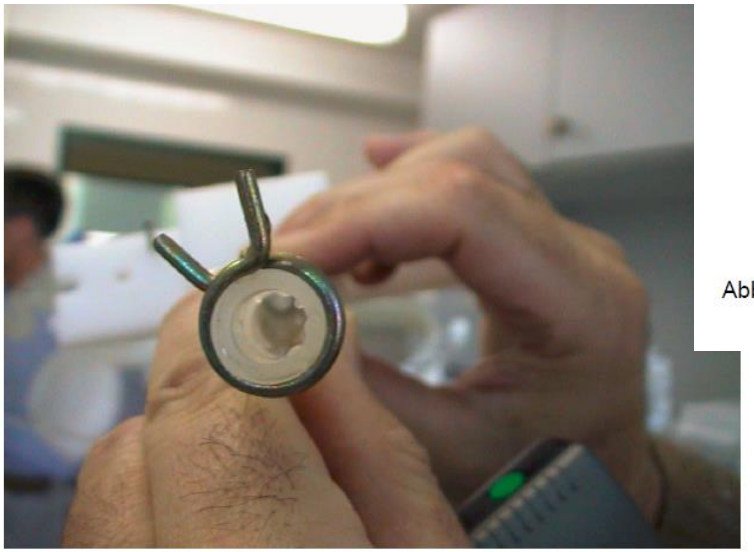

Abb. 12 Aufnahme des Schlauchstückes im Inneren des Inkubators, der von der inneren Anschlussstelle (siehe auch Abb. 10) zur Wanne mit Heißaggregat und Ventilator führt

Abb. 13 Aufnahme des normalerweise weißen Abstrichtupfers aus dem Schlauchstück (siehe auch Abb. 12) mit schmierigem Belag (Biofilm)

Abb. 14 Aufnahme der Wanne mit Heizaggregat und Ventilator, wohin das Schlauchstück (siehe auch Abb. 12) führt

Lessons learnt

- Where ever you have wet areas there is the risk of build up of biofilm
- Devices must be constructed in a way that you can clean and disinfect all these areas
- In high risk areas you must use only sterile water
- Devices which don´t fulfill these requirements must be changed

Sinks as a reservoir

Severe Serratia liquefaciens Sepsis follwing Infusion by a naturopathic practitioner

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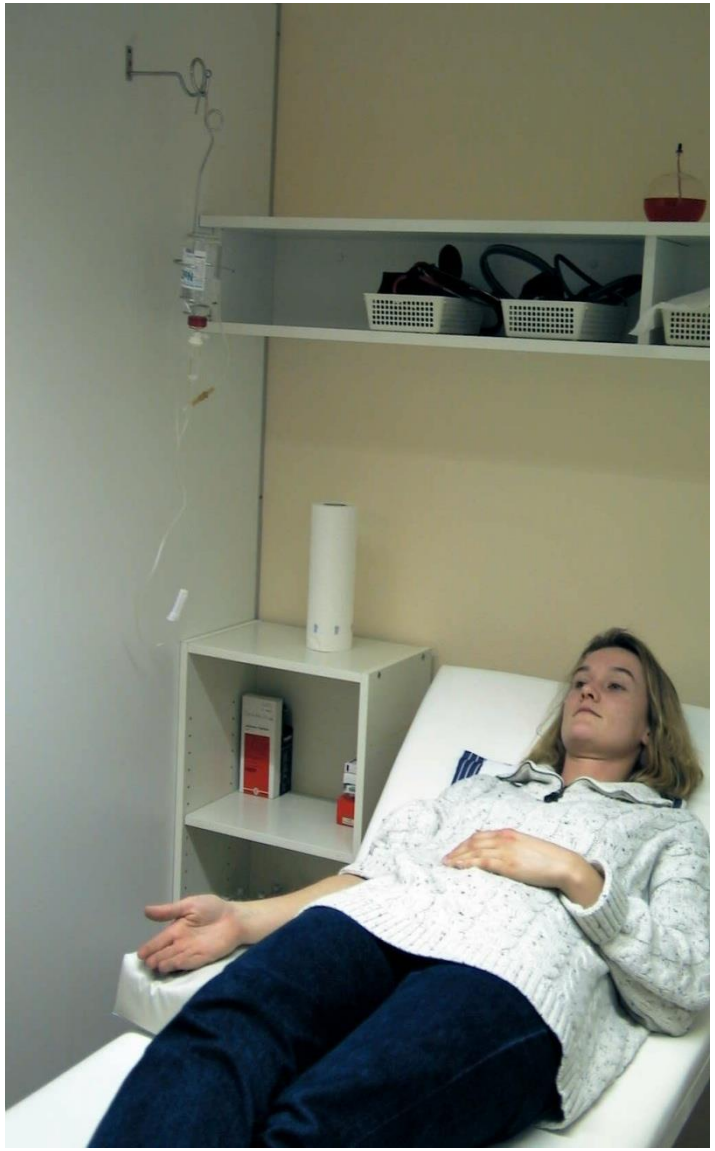
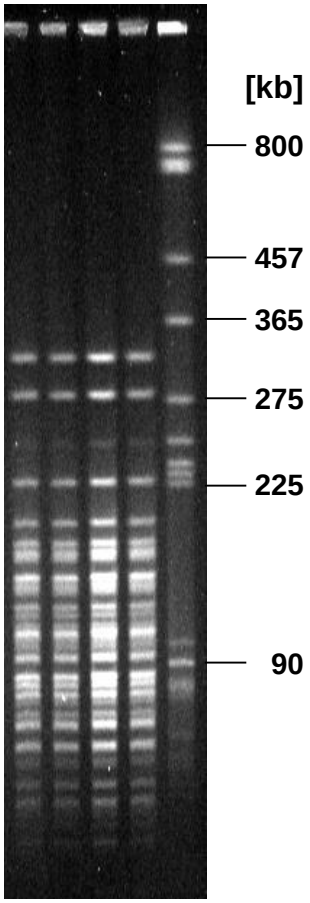


PFGE - Vergleich von vier Serratia liquefaciens - Stämmen



Spur	Orig.-Nr.	RKI-Nr.
1	360	00-00527
2	368	00-00528
3	550	00-00529
4	551	00-00530
S	Standard S. Typhimurium LT2	

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Publication of this case report

JOURNAL OF CLINICAL MICROBIOLOGY, Aug. 2003, p. 3986–3988 Vol. 41, No. 8
0095-1137/03/$08.00+0 DOI: 10.1128/JCM.41.8.3986–3988.2003

Severe *Serratia liquefaciens* Sepsis following Vitamin C Infusion Treatment by a Naturopathic Practitioner

S. Engelhart,[1]* F. Saborowski,[2] M. Krakau,[2] G. Scherholz-Schlösser,[3] I. Heyer,[3] and M. Exner[1]

Institute of Hygiene and Public Health, University of Bonn,[1] and Gesundheitsamt der Bundesstadt,[3] Bonn, and Medizinische Klinik, Krankenhaus Holweide, Köln,[2] Germany

Received 21 October 2002/Returned for modification 24 February 2003/Accepted 25 April 2003

A 66-year-old female patient developed severe *Serratia liquefaciens* sepsis following vitamin C infusion treatment by a naturopathic practitioner. The clinical course of the infection was characterized by several complications, and the direct costs of the hospital stay amounted to about 40,000 Euro. Genotypically identical *S. liquefaciens* was isolated from the residue of the infusate given to the patient, as well as from the washbasin overflow and from two other infusion bottles. A careful inspection of the dispensing facilities and review of procedures used to prepare the infusate revealed several indications of poor hygiene. However, the source of contamination could not be fully clarified. This case report raises questions about the local facilities and personal qualifications required for naturopathic practitioners to conduct invasive procedures and demonstrates that lapses in hygiene can lead to severe morbidity and high cost.

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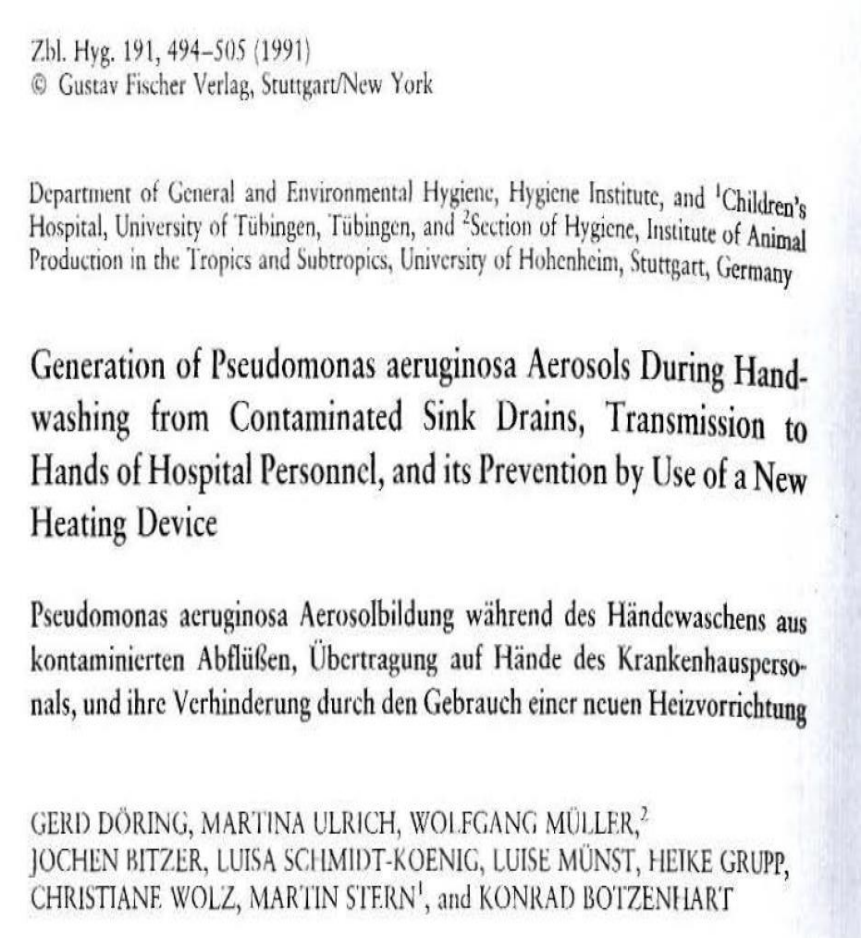
Lessons learnt

- Sinks as reservoir
- Construction requirements for sinks
- Avoidance of overflow
- Handling of high risk devices near the sink can be devastating

Sink drains as Reservoir for P. aeruginosa



Zbl. Hyg. 191, 494–505 (1991)

Department of General and Environmental Hygiene, Hygiene Institute, and [1]Children's Hospital, University of Tübingen, Tübingen, and [2]Section of Hygiene, Institute of Animal Production in the Tropics and Subtropics, University of Hohenheim, Stuttgart, Germany

Generation of Pseudomonas aeruginosa Aerosols During Handwashing from Contaminated Sink Drains, Transmission to Hands of Hospital Personnel, and its Prevention by Use of a New Heating Device

Pseudomonas aeruginosa Aerosolbildung während des Händewaschens aus kontaminierten Abflüßen, Übertragung auf Hände des Krankenhauspersonals, und ihre Verhinderung durch den Gebrauch einer neuen Heizvorrichtung

GERD DÖRING, MARTINA ULRICH, WOLFGANG MÜLLER,[2]
JOCHEN BITZER, LUISA SCHMIDT-KOENIG, LUISE MÜNST, HEIKE GRUPP,
CHRISTIANE WOLZ, MARTIN STERN[1], and KONRAD BOTZENHART

- 81%of all sinks were contaminated with P. aeruginosa.
- Before entering the ward all hands of HCW´s were free of *P.* aeruginosa
- In the afternoon 42,5% of all HCW´s hands were colonized with different genotypes of P.aeruginosaon their hands .
- *P. aeruginosa Genotypes on hands were identical to those in sinks*.
- Opening of the water taps produce an aerosol from the sink drain which contaminated the hands by handwashing

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Sink drains as reservoir for Klebsiella oxytoca on a neonatal ward > 10^8 CFU/ ml

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Environmental sampling from sink drain

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Results from the sinks

- In the sink in the cleaning room samples were taken before and after flushing with water.
- Before flushing *Klebsiella oxytoca* together with *Raoutella terrigena* and Enterobacter cloacae could be found in high concentrations of $1,6x10^{6}$ CFU/ml.
- After flushing *Klebsiella oxytoca* could not be isolated.
- In the sink of the health care workers room *Klebsiella oxytoca* together with *Pseudomonas. aeruginosa* could be isolated in concentrations of up to $3,0x10^{5}$ CFU /ml.

Long term outbreaks with Antibiotic resistant Pathogens – why is it possible ?

RESEARCH ARTICLES

Epidemiological investigation of *Pseudomonas aeruginosa* isolates from a six-year-long hospital outbreak using high-throughput whole genome sequencing

L A Snyder[1,2], N J Loman[1], L A Faraj[3], K Levi[4], G Weinstock[5], T C Boswell[4], M J Pallen (m.pallen@warwick.ac.uk)[6], D A Ala'Aldeen[3]
1. Institute of Microbiology and Infection, School of Biosciences, University of Birmingham, Birmingham, United Kingdom
2. Kingston University, Kingston upon Thames, Surrey, United Kingdom (current affiliation)
3. Molecular Bacteriology and Immunology Group, School of Life Sciences, University of Nottingham, Nottingham, United Kingdom
4. Nottingham University Hospitals NHS Trust, Nottingham, United Kingdom
5. Department of Genetics, Washington University School of Medicine, St. Louis, Missouri, United States
6. Division of Microbiology and Infection, Warwick Medical School, University of Warwick, Coventry, United Kingdom

Citation style for this article:
Snyder LA, Loman NJ, Faraj LA, Levi K, Weinstock G, Boswell TC, Pallen MJ, Ala'Aldeen DA. Epidemiological investigation of Pseudomonas aeruginosa isolates from a six-year-long hospital outbreak using high-throughput whole genome sequencing. Euro Surveill. 2013;18(42):pii=20611. Available online: http://www.eurosurveillance.org/ViewArticle.aspx?ArticleId=20611

Article submitted on 18 December 2012 / published on 17 October 2013

American Journal of Infection Control 43 (2015) 635-9

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American Journal of Infection Control

journal homepage: www.ajicjournal.org

Major article

Detection and termination of an extended low-frequency hospital outbreak of GIM-1–producing *Pseudomonas aeruginosa* ST111 in Germany

Andreas F. Wendel MD[a], Susanne Kolbe-Busch MD[a], Sofija Ressina[a], Roland Schulze-Röbbecke MD[a], Detlef Kindgen-Milles MD[b], Christel Lorenz MD[b], Klaus Pfeffer MD[a], Colin R. MacKenzie MBBCh[a,*]

[a] *Institute of Medical Microbiology and Hospital Hygiene, University Hospital, Heinrich-Heine-University, Düsseldorf, Germany*
[b] *Department of Anaesthesiology, University Hospital, Heinrich-Heine-University, Düsseldorf, Germany*

Key Words:
Outbreak
Multidrug resistance
Metallo-β-lactamase
Pseudomonas aeruginosa
German imipenemase-1
Environmental sampling

Background: Metallo-β-lactamase German imipenemase-1 (GIM-1)–mediated carbapenem resistance is emerging in Germany but has not spread beyond a very localized region. The aim of this study was to describe the first outbreak of an extensively drug-resistant GIM-1–carrying *Pseudomonas aeruginosa* strain affecting 29 patients in a tertiary care hospital from 2002-2013.
Methods: The outbreak was studied retrospectively and prospectively by a combination of molecular methods (carbapenemase polymerase chain reaction [PCR]), genotyping (DiversiLab, pulsed field gel electrophoresis and multi-locus sequence typing, bioMérieux, Marcy l'Etoile, France), descriptive epidemiology, and extensive environmental investigations using swabs with liquid transport medium, bla_{GIM-1} PCR, directly from the medium and culture.
Results: Of the 29 affected patients, 24 had been admitted to a surgical intensive care unit at some point, where environmental sampling revealed a high burden of bla_{GIM-1} in the wastewater system. The outbreak strain was found in several sinks and on a reusable hair washbasin. Initially, general infection control measures were applied; thereafter, specific measures were implemented, including the restriction of washbasin use. Continued surveillance over a period of 2 years has revealed no further case of GIM-1–carrying *Pseudomonas aeruginosa*.
Conclusion: This long-term outbreak highlights the potential of molecular methods in surveillance for multidrug-resistant pathogens and in environmental sampling and the successful containment by application of specific control measures targeting biofilms within sink drains as potential environmental reservoirs for *P aeruginosa*.

Lessons learnt

- Sink drains are an ideal ecological niche for gram-negative bacteria in which they can persist over years
- There is a need for disinfection and reconstruction of sinks drains
- There is an urgent need for research on the construction requirements for sink and sink drains
- When there is a cluster of gramnegative pathogens don´t forget to take into account sink drains

Sewage system

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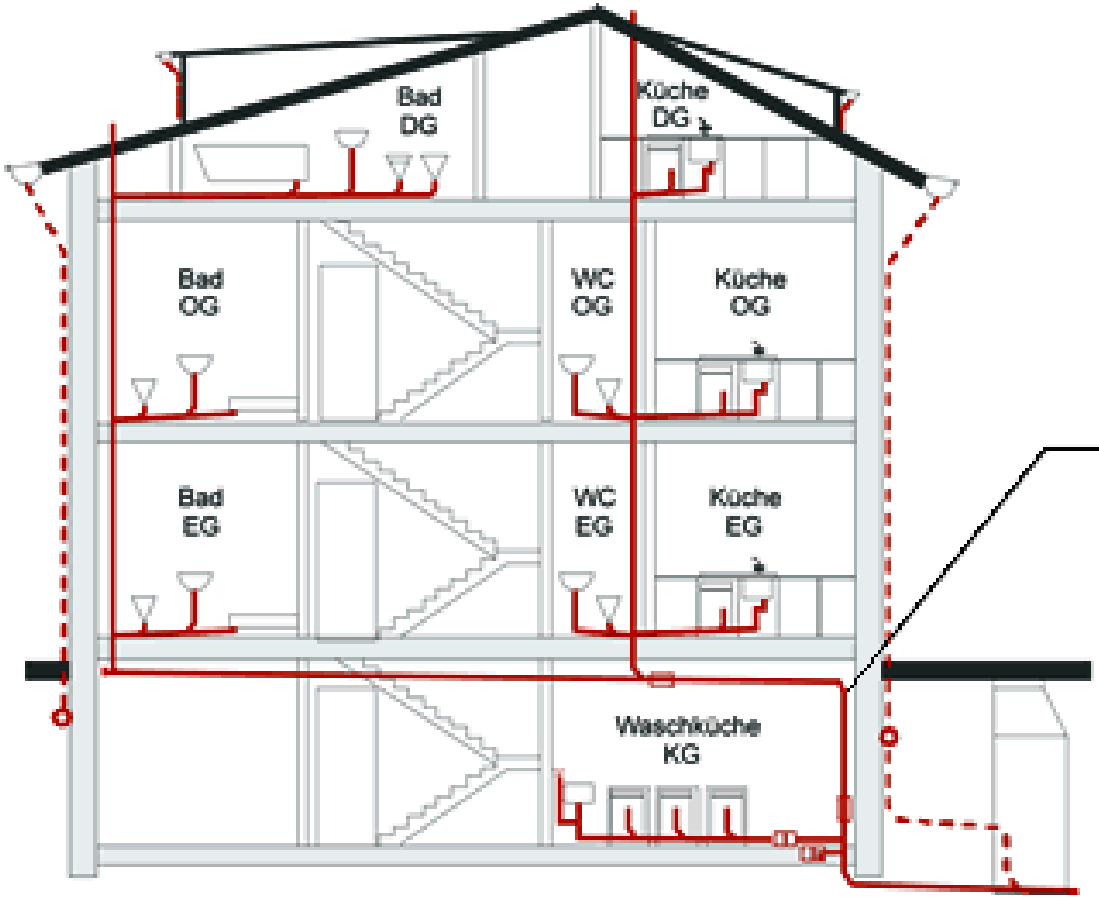

Sammelleitungen unter der Kellerdecke statt Grundleitungen unter der Boden-platte

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Acinetobacter and Sewage drainage system

Management of a multidrug-resistant *Acinetobacter baumannii* outbreak in an intensive care unit using novel environmental disinfection: A 38-month report

Carlo La Forgia, MD,[a,b] John Franke, PhD,[c] Donna M. Hacek, MT (ASCP),[d] Richard B. Thomson Jr, PhD,[d,e] Ari Robicsek, MD,[a,f] and Lance R. Peterson, MD[a,d,e,f]
Chicago and Evanston, Illinois

Background: Between June 1, 2004, and March 14, 2005, 16 patients in the surgical/medical intensive care unit (ICU) were infected and another 2 were colonized with multidrug-resistant (MDR) *Acinetobacter baumannii*. We describe the systematic investigation initiated to discover an environmental reservoir and a novel measure taken to terminate the outbreak.
Methods: Cultures were taken from moist areas in the ICU, including sink traps, sink and counter surfaces, drains, and faucets. Strains were characterized using restriction endonuclease analysis. A weekly full drainpipe chase cleansing protocol with sodium hypochlorite (bleach) solution for all 24 ICU and waiting room area sinks connected by common plumbing was initiated in March 2005.
Results: Eleven of 16 infected patients (69%) had a clonal MDR strain, 1 patient (6%) was infected with an unrelated strain, and in 4 patients (25%) strains were not available for typing. The reservoir for the *A baumannii* clone was detected in a sink trap within one of the ICU patient rooms that likely represented contamination of the entire horizontal drainage system. The bleaching protocol initiated in March 2005 successfully decontaminated the reservoir and eliminated the MDR *A baumannii* infections.
Conclusion: A systematic search for an environmental reservoir followed by decontamination significantly reduced ($P < .01$) the incidence of MDR *A baumannii* infection.
Key Words: *Acinetobacter baumannii*; environmental disinfection; healthcare-associated infection; multidrug resistance.

(Am J Infect Control 2009;■:1-5.)

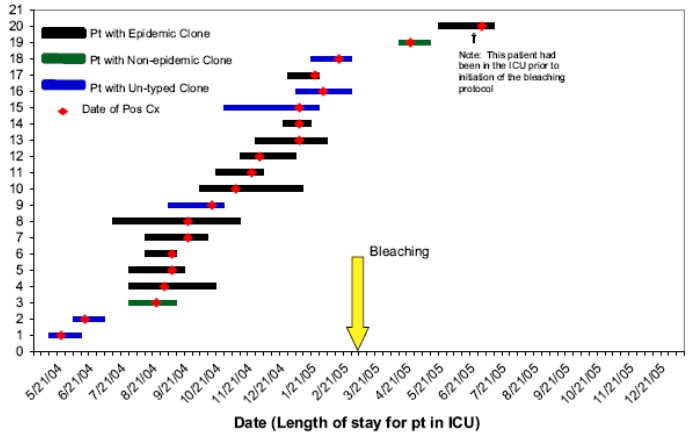

Fig 1. Timeline of the *A baumannii* outbreak in the ICU during the period when the epidemic clone was present.

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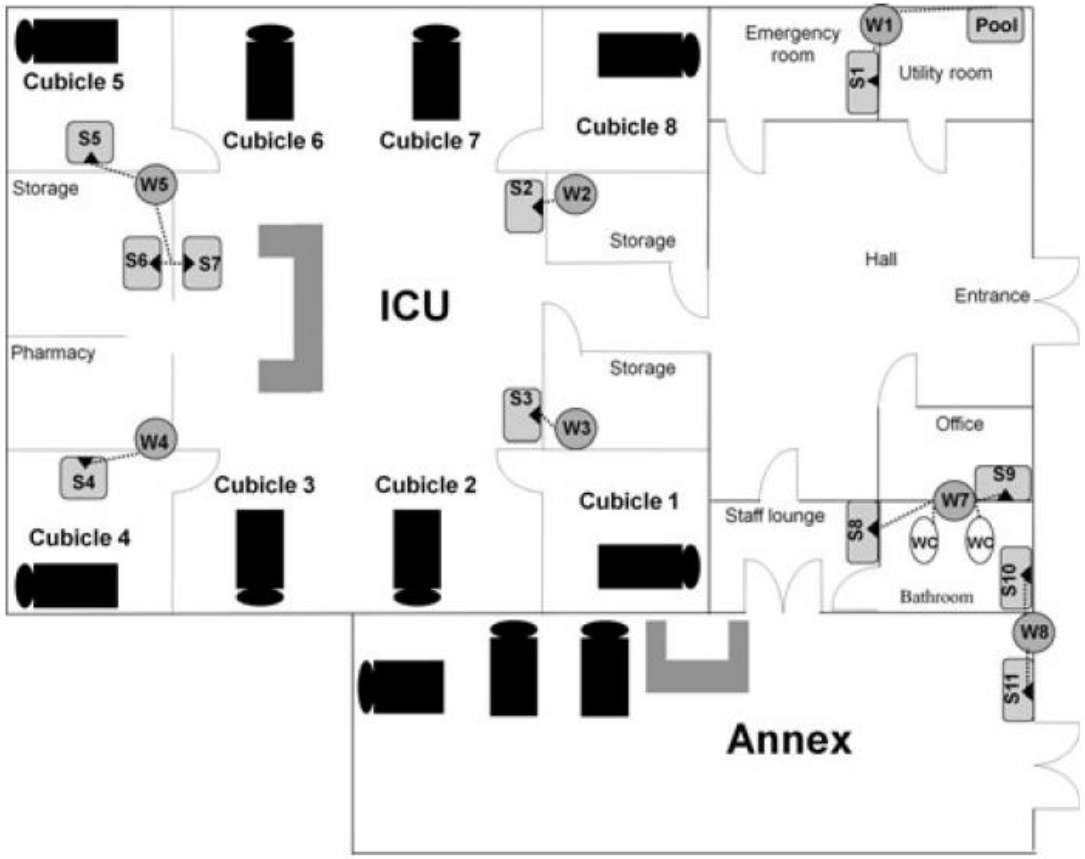

FIG. 1. Plan of the ICU. Grey square: sink. Grey circle: wastepipe. Discontinous line: drainpipe. S: sink. W: wastepipe.

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- The elimination of the horizontal drainage system finally eradicated the outbreak.
- In conclusion, damp environmental reservoirs (mainly sink drains, traps and the horizontal drainage system) could explain why standard cross-transmission control measures failed to control the outbreak; such reservoirs should be considered even when environmental cultures of surfaces are negative.

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Epidemiologisches Bulletin

16. Juni 2014 / Nr. 24

AKTUELLE DATEN UND INFORMATIONEN ZU INFEKTIONSKRANKHEITEN UND PUBLIC HEALTH

Häufung von KPC-2 produzierenden Stämmen verschiedener *Enterobacteriaceae*-Spezies in Hessen

Diese Woche 24/2014

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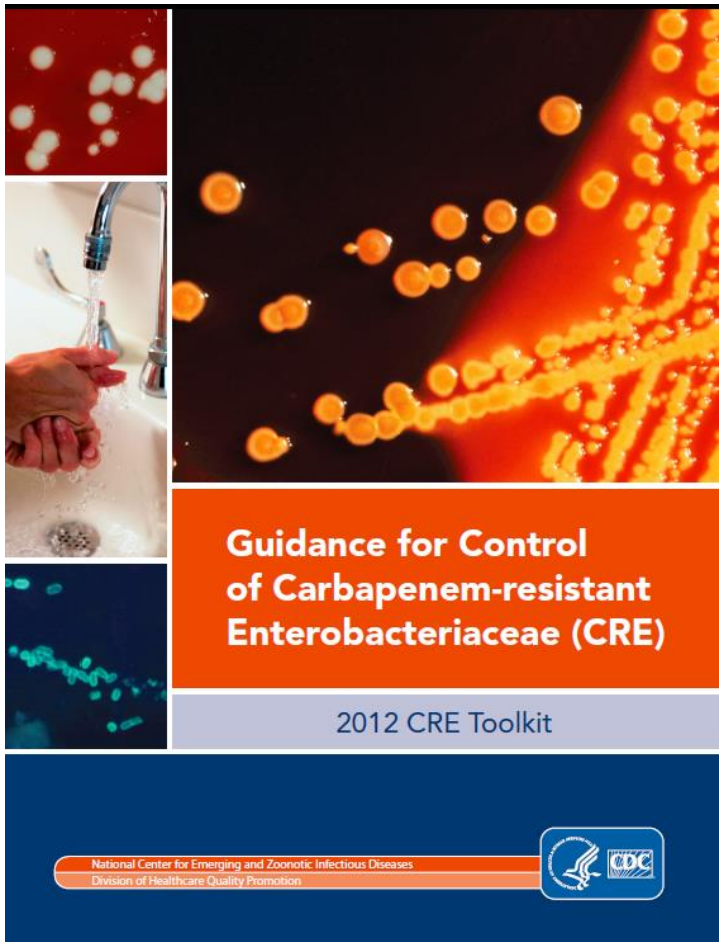
Spezies	Nordosthessen			Mittelhessen			Rhein-Main			Südhessen		
	2012	2013	2014	2012	2013	2014	2012	2013	2014	2012	2013	2014
Citrobacter freundii												12
Enterobacter aerogenes												2
Escherichia coli											1	3
Klebsiella oxytoca										1		3
Klebsiella pneumoniae	3							4	1		1	4
Raoultella ornithinolytica												1

Tab. 1: Meldungen KPC produzierender *Enterobacteriaceae*; n = 36 (n = 26 KPC-2, darunter n = 19 im Jahr 2014 gemeldet), nach Region und Jahr, Hessen, 2012–2014 (Stand: 5.6.2014)



CRE are epidemiologically important for several reasons:

- CRE have been associated with high mortality rates (up to 40 to 50% in some studies).
- In addition to β-lactam/ carbapenem resistance, CRE often carry genes that confer high levels of resistance to many other antimicrobials, often leaving very limited therapeutic options. "Pan-resistant" KPC-producing strains have been reported.
- CRE have spread throughout many parts of the United States and have the potential to spread more widely.

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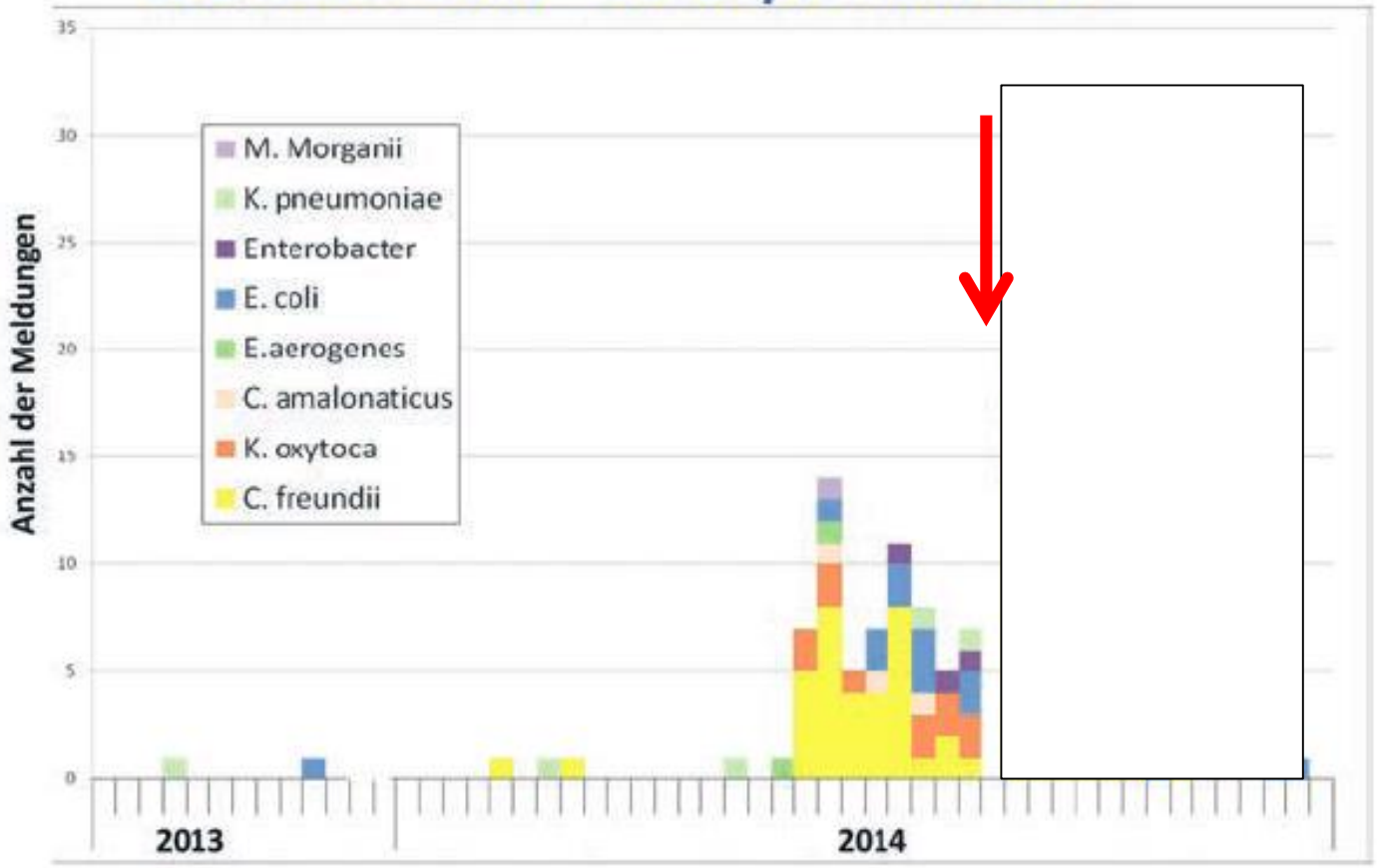
KPC 2-Meldungen aus Ausbruchsklinik
1. Oktober 2013 – 30. September 2014



Sink drainage and toilets of patient rooms

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Multiplex real-time PCR with HRM

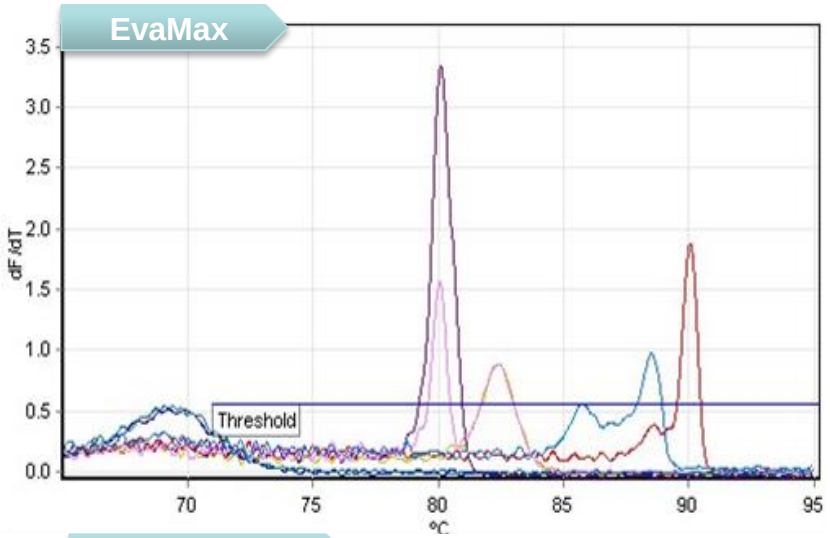
Temperatur (˚C) EvaMax	Target genes	Temperatur° C Monteiro *et al.*
78 and 79 (double peak)	OXA-24/-72	/
80	OXA-48	81.6
81	OXA-23	/
82	NDM	84
86	GES	88.4
88	VIM	90.3
90	KPC-2	91.6

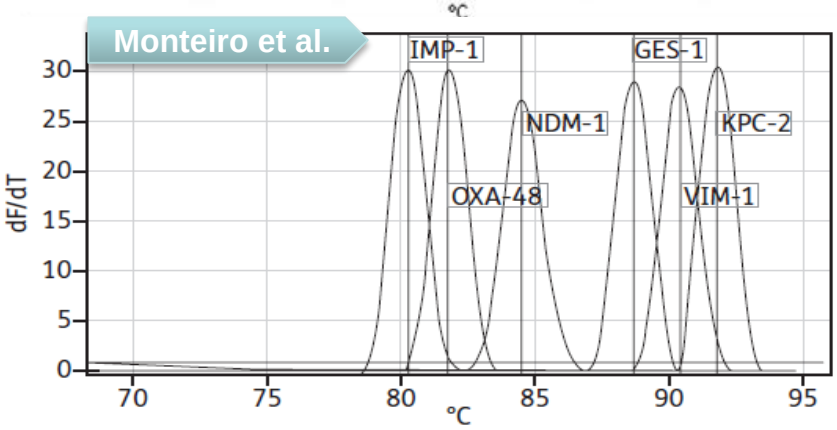
Average temperature deviation:

- **Monteiro et al.: +/- 1.98 °C**
- **EvaMax: +/- 1 °C**

Total volumen	*25,0 µL*
Master Mix	*12,5 µL*
Primer	*0,2 µM*
-IMP	*1,2 µM*
DNA-Template	*1,0 µL*

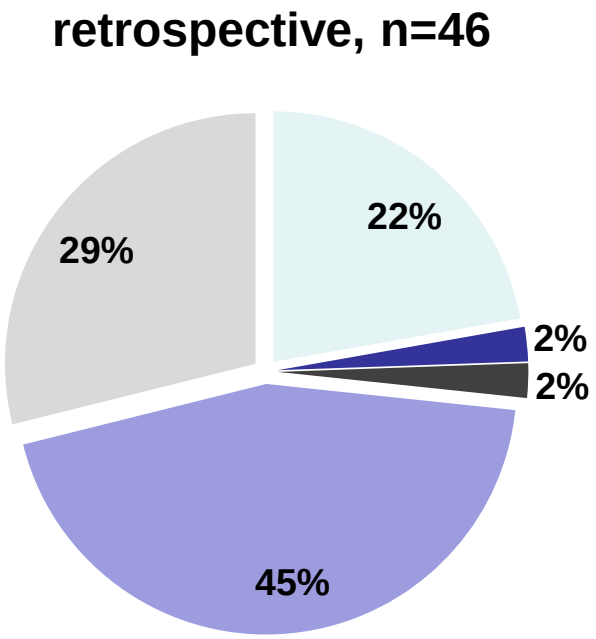
HRM Master Mix (Hot-Start-Taq *Plus* DNA Polymerase):
Type-it HRM PCR buffer, EvaGreen dye, Q-Solution dNTP mix with Rnase-free Water

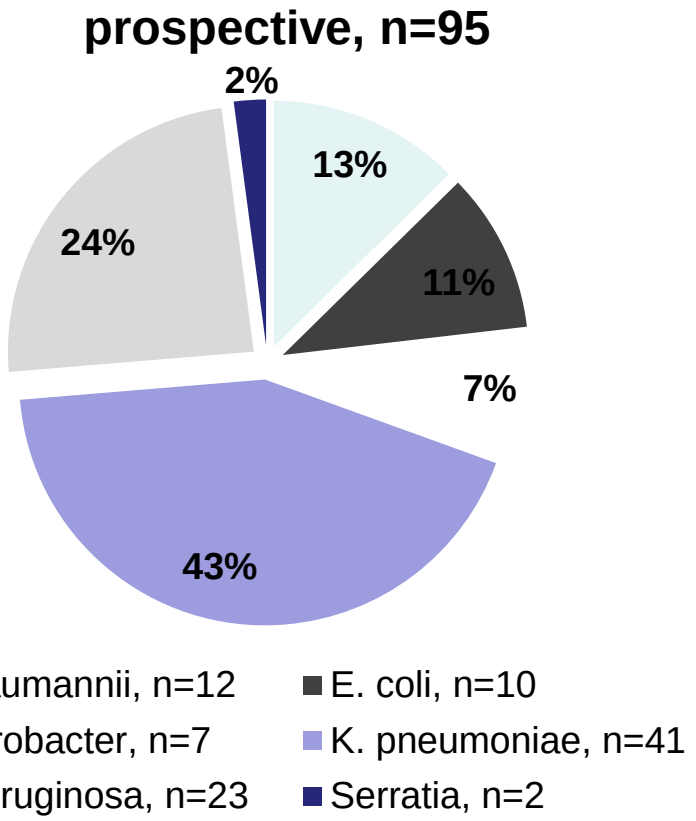




HR-RT-PCR VALIDATION

Validation: NRZ-Bochum

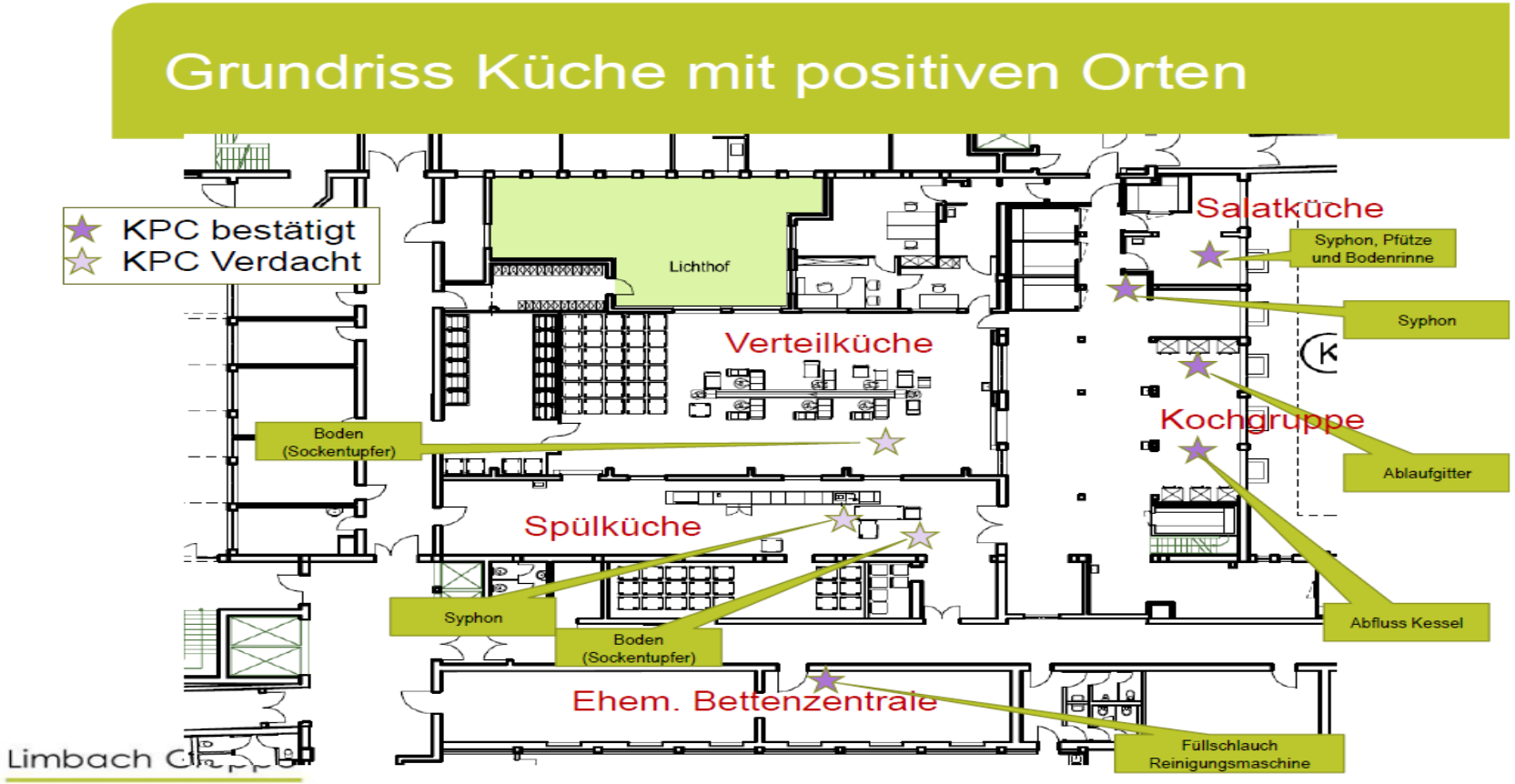




Discrepant results:

- **3 corrections through Bochum (EvaMax 2x false-negative and 1x false-positive)**
- **2 results were false-negative at NRZ-Bochum**

Drainage system in Kitchen and in food



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Cooking area, in which in drainage system KPC enterobacteriaceae could be isolated

KPC 2 Entero-bacteriaceae

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Outbreak –Plasmid in cold food prepared in hospital kitchen

C. freundii KPC2

K. oxytoca KPC2

Hypothesis for transmission of KPC 2 Enterobacteriaceae from patient wards to the Kitchen

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Central sewage system of the hospital with KPC carbapenemase

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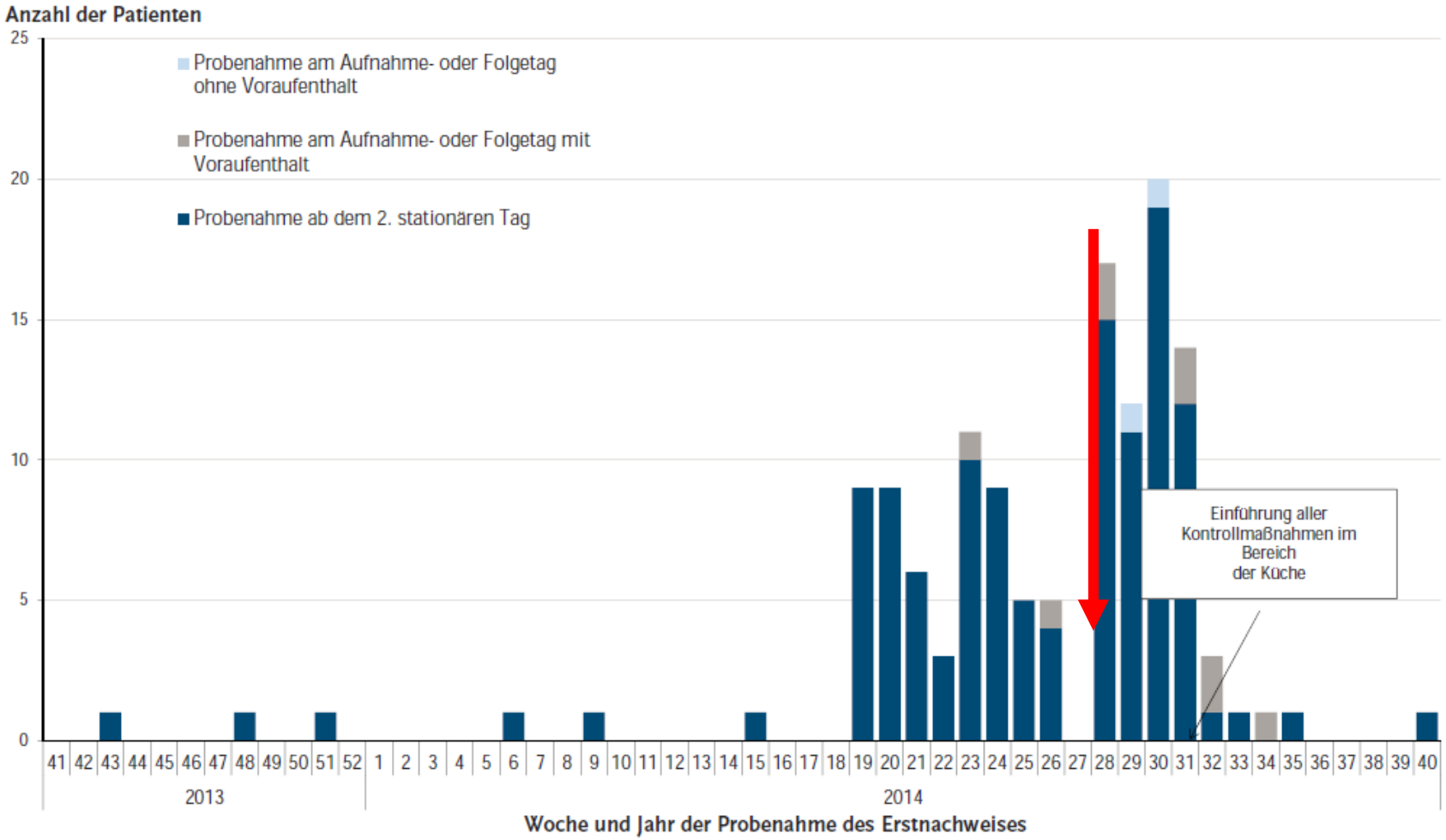

Abb. 1: Epidemische Kurve für 133 Patienten mit Kolonisation oder Infektion durch verschiedene Spezies Carbapenem-resistenter *Enterobacteriaceae*, nach Datum des Erstnachweises und Voraufenthalten, Südhessischer KPC-2-Ausbruch, 1. Oktober 2013 bis 30. September 2014.

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Room of the colonisied Patient with infusion food

Sondenkost
Fresubin

Nachweis
von KPC 2
Enterobacter
complex

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kinetic of KPC Enterobacteriaceae in Fresubin

Wachstumskinetik Isolate aus GPR Rüsselsheim in Fresubin (original fibre)

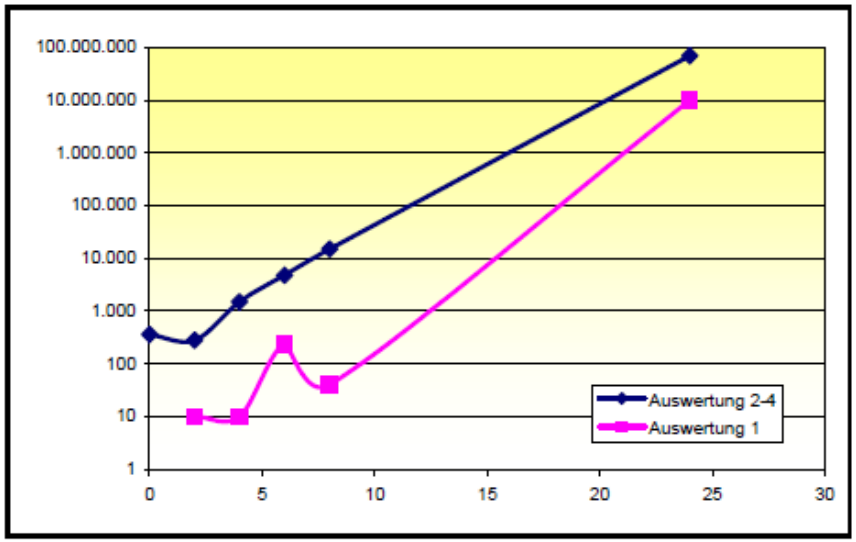
Inkubation bei Zimmertemperatur
Versuchsbeginn: 18.09.2014

Mischinokluat: E. coli = 1
C. freundii = 2
K. oxytoca = 3
E. aerogenes = 4

Mischkultur von KPC E.coli, C.freundii, K. oxytoca und E. aerogenes vermehrt sich in 23 Std. von niedrigen Konzentrationen auf Konz. von Bis zu 7,0E+07 KbE/ ml

Auswertung 2-4	Ausgangskonzentration		
Inkubation (h)	10e1 / ml		
0	3,6E+02		
2	2,8E+02		
4	1,5E+03		
6	4,8E+03		
8	1,5E+04		
24	7,0E+07		

Auswertung 1	Ausgangskonzentration		
Inkubation (h)	10e1 / ml		
0	0,0E+00		
2	1,0E+01		
4	1,0E+01		
6	2,3E+02		
8	4,0E+01		
24	1,0E+07		



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Epidemiologisches Bulletin

24. November 2014 / Nr. 47 AKTUELLE DATEN UND INFORMATIONEN ZU INFEKTIONSKRANKHEITEN UND PUBLIC HEALTH

Plasmid-vermittelter Multispezies-Ausbruch mit Carbapenem-resistenten *Enterobacteriaceae*

Diese Woche 47/2014

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Lessons learnt

- Notification of 4 fold resistant gram negative enterobactericeae can detect clusters
- Look for the casual species and take into account their ecological properties
- Citrobacter, Acinetobacter Klebsiella oxytoca have their reservoir also in the sinks, sink drainges and sewage system
- To bring under control hand hygiene, surveillance and isolation is important but not sufficient
- In site inspection and environmental sampling is a prerequisite for outbreak management
-

- Plasmids can exchange antibiotic resistance over species borders
- Avoid the blocking of sewage system with the risk of blockage of the sewage system with backwater in the sink
- Don´t use spirals in hospitals for cleaning of the sewage systems for different aereas like patient wards and kitchen
- Cleaning in kitchen with aerolisation can contaminate outlets of cooking pots – therefore we need cleaning procedure without production of aerosols
- Contaminated food is a very effective vehicle
- In a case of clusters of gram negative enterobacteria look also in the kitchen

The sewage system is the gastro-intinestinal tract of the hospital

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The international perspective

World wide pressure on antibiotic resistance with increase of world population to up 10 billion people under unsanitized conditions


Antibiotic use is totally uncontrolled in many parts of the world

High risk of introduction of antibiotic resistant pathogens from other countries with low sanitation standard.

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Antibiotic use is totally uncontrolled in many parts of the world

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The latest threat in the war on antimicrobial resistance

www.thelancet.com/infection Vol 10 September 2010

THE RISKS FROM MEDICAL TOURISM

Cosmetic surgery: Growing market

AS many as 50,000 Britons travel overseas for medical treatment each year – many of them unaware or unwilling to consider the health hazards.

India is one of the most popular destinations, along with Turkey, Hungary and other eastern European countries.

But research has revealed high rates of severe wound infections, HIV and hepatitis B and poor surgical technique.

'Sun and surgery' packages to India, including flights, operations, accommodation in a private hospital and recuperation time on the beach, have been sold by major tour operators.

Many private operations are significantly cheaper than in Britain.

The market is worth millions of pounds, with surveys suggesting dentistry is the most popular service followed by cosmetic surgery.

But there have also been scandals where Britons visiting India as 'transplant tourists' for black market kidneys from living donors died or suffered serious complications.

The British Association of Aesthetic Plastic Surgeons warns patients to investigate the credentials of clinics and surgeons, and says private cosmetic surgery in the UK often costs more because of better regulation here.

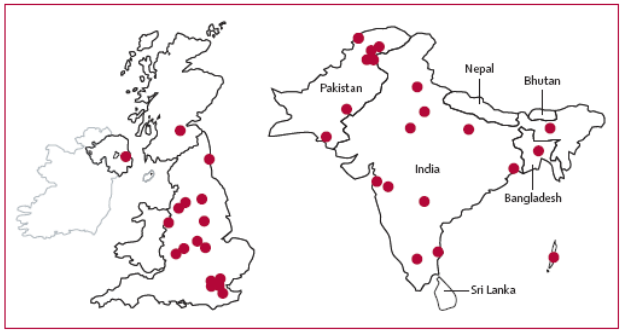
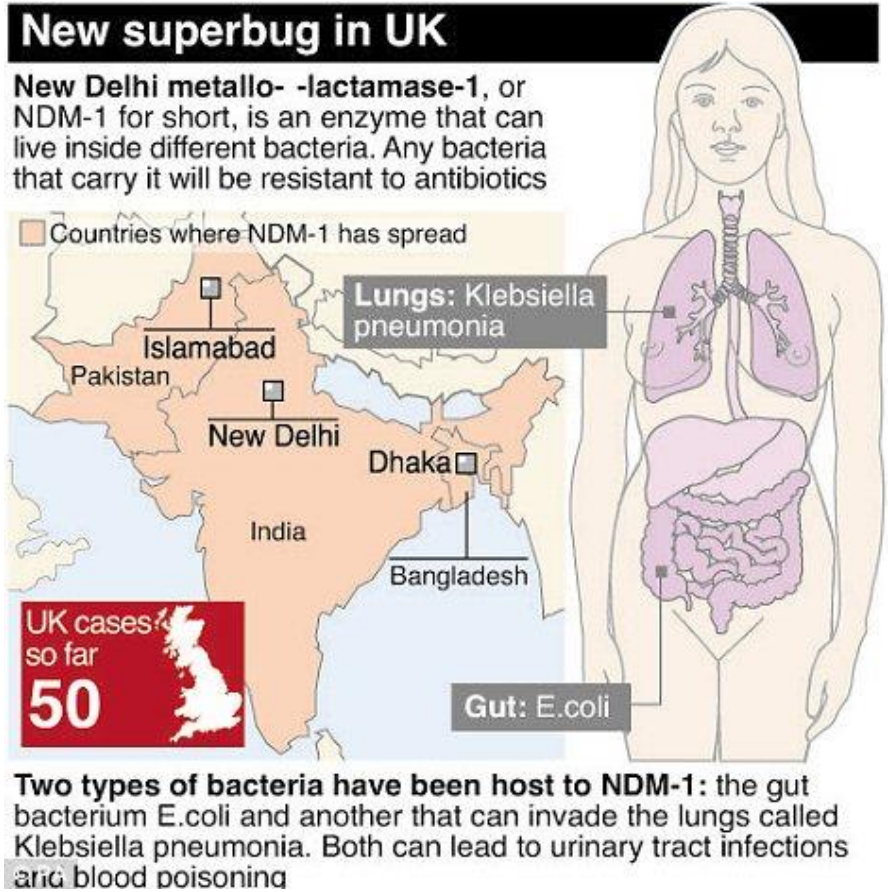


Figure 5: Distribution of NDM-1-producing Enterobacteriaceae strains in Bangladesh, Indian, Pakistan, and the UK

New superbug in UK

New Delhi metallo- -lactamase-1, or NDM-1 for short, is an enzyme that can live inside different bacteria. Any bacteria that carry it will be resistant to antibiotics



Two types of bacteria have been host to NDM-1: the gut bacterium E.coli and another that can invade the lungs called Klebsiella pneumonia. Both can lead to urinary tract infections and blood poisoning

Emergence of a new antibiotic resistance mechanism in India, Pakistan, and the UK: a molecular, biological, and epidemiological study

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The presence of NDM-1 β-lactamase-producing bacteria in environmental samples in New Delhi

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Dissemination of NDM-1 positive bacteria in the New Delhi environment and its implications for human health: an environmental point prevalence study

Timothy R Walsh, Janis Weeks, David M Livermore, Mark A Toleman

Summary

Background Not all patients infected with NDM-1-positive bacteria have a history of hospital admission in India, and extended-spectrum β-lactamases are known to be circulating in the Indian community. We therefore measured the prevalence of the NDM-1 gene in drinking water and seepage samples in New Delhi.

Methods Swabs absorbing about 100 µL of seepage water (ie, water pools in streets or rivulets) and 15 mL samples of public tap water were collected from sites within a 12 km radius of central New Delhi, with each site photographed and documented. Samples were transported to the UK and tested for the presence of the NDM-1 gene, bla_{NDM-1}, by PCR and DNA probing. As a control group, 100 µL sewage effluent samples were taken from the Cardiff Wastewater Treatment Works, Tremorfa, Wales. Bacteria from all samples were recovered and examined for bla_{NDM-1} by PCR and sequencing. We identified NDM-1-positive isolates, undertook susceptibility testing, and, where appropriate, typed the isolates. We undertook Inc typing on bla_{NDM-1}-positive plasmids. Transconjugants were created to assess plasmid transfer frequency and its relation to temperature.

Findings From Sept 26 to Oct 10, 2010, 171 seepage samples and 50 tap water samples from New Delhi and 70 sewage effluent samples from Cardiff Wastewater Treatment Works were collected. We detected bla_{NDM-1} in two of 50 drinking-water samples and 51 of 171 seepage samples from New Delhi; the gene was not found in any sample from Cardiff. Bacteria with bla_{NDM-1} were grown from 12 of 171 seepage samples and two of 50 water samples, and included 11 species in which NDM-1 has not previously been reported, including *Shigella boydii* and *Vibrio cholerae*. Carriage by enterobacteria, aeromonads, and *V cholera* was stable, generally transmissible, and associated with resistance patterns typical for NDM-1; carriage by non-fermenters was unstable in many cases and not associated with typical resistance. 20 strains of bacteria were found in the samples, 12 of which carried bla_{NDM-1} on plasmids, which ranged in size from 140 to 400 kb. Isolates of *Aeromonas caviae* and *V cholerae* carried bla_{NDM-1} on chromosomes. Conjugative transfer was more common at 30°C than at 25°C or 37°C.

Interpretation The presence of NDM-1 β-lactamase-producing bacteria in environmental samples in New Delhi has important implications for people living in the city who are reliant on public water and sanitation facilities. International surveillance of resistance, incorporating environmental sampling as well as examination of clinical isolates, needs to be established as a priority.

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Department of Infection, Immunity and Biochemistry, School of Medicine, Cardiff University, Heath Park, Cardiff, UK (Prof T R Walsh PhD, J Weeks BSc, M A Toleman PhD); University of Queensland Centre for Clinical Research, University of Queensland, Brisbane, Australia (Prof T R Walsh); and Health Protection Agency Microbiology Services, Colindale, London, UK (D M Livermore PhD)

Correspondence to:
Prof Timothy R Walsh, Centre for Clinical Research (UQCCR) I Level 8, Building 71/918 Royal Brisbane Hospital, Herston QLD 4006, Australia
t.r.walsh@uq.edu.au

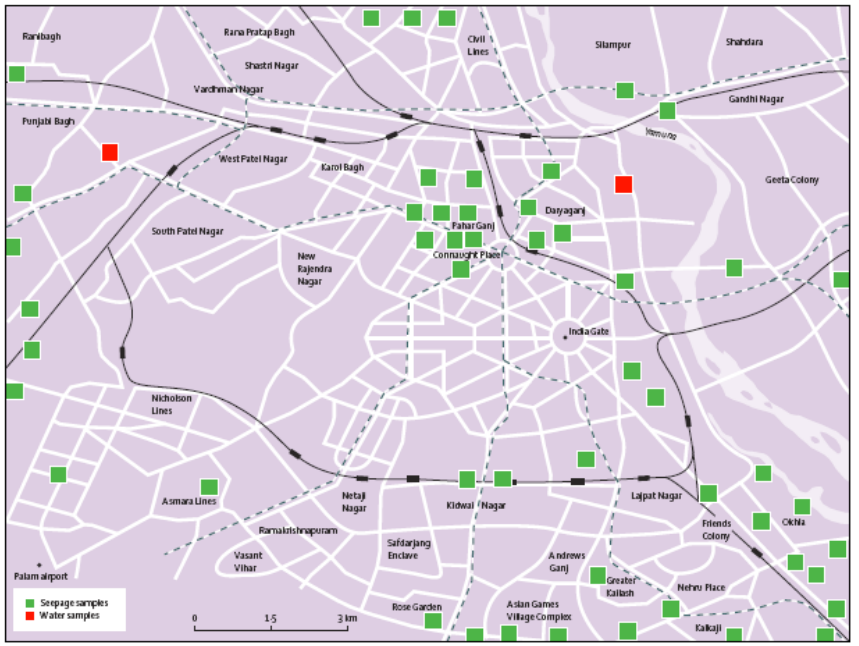

Figure 1: Map of NDM-1-positive samples from New Delhi centre and surrounding areas

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Conclusion

- Multiresistant bacteria and outbreak management must seen as a chance to have insight into reservoirs and transmission pathways when we try to use our scientific instruments and a systematic approach to bring under control these outbreaks and to learn for future to prevent infections in a sustainable way

Outbreak is a chance !

- *Outbreak analysis is like a big experiment (R. Koch)*
- Never waste a good crisis *(B. Obama)*

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Lessons learnt from outbreaks of multi-resistant bacteria – consequences for prevention

Thank you