RUDOLF SCHÜLKE STIFTUNG

Agenda for the Symposium of the Rudolf Schülke Foundation

"Worldwide Significance of Gram-Negative Antibiotic Resistant Rods: Epidemiology, Prevention and Control Strategies"

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Introduction and objective of the symposium

Prof Martin Exner, MD

Institute of Hygiene and Public Health, University of Bonn,

Chairman of the Rudolf Schülke Foundation (Germany)

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

Daniel Boorstein, Historian -

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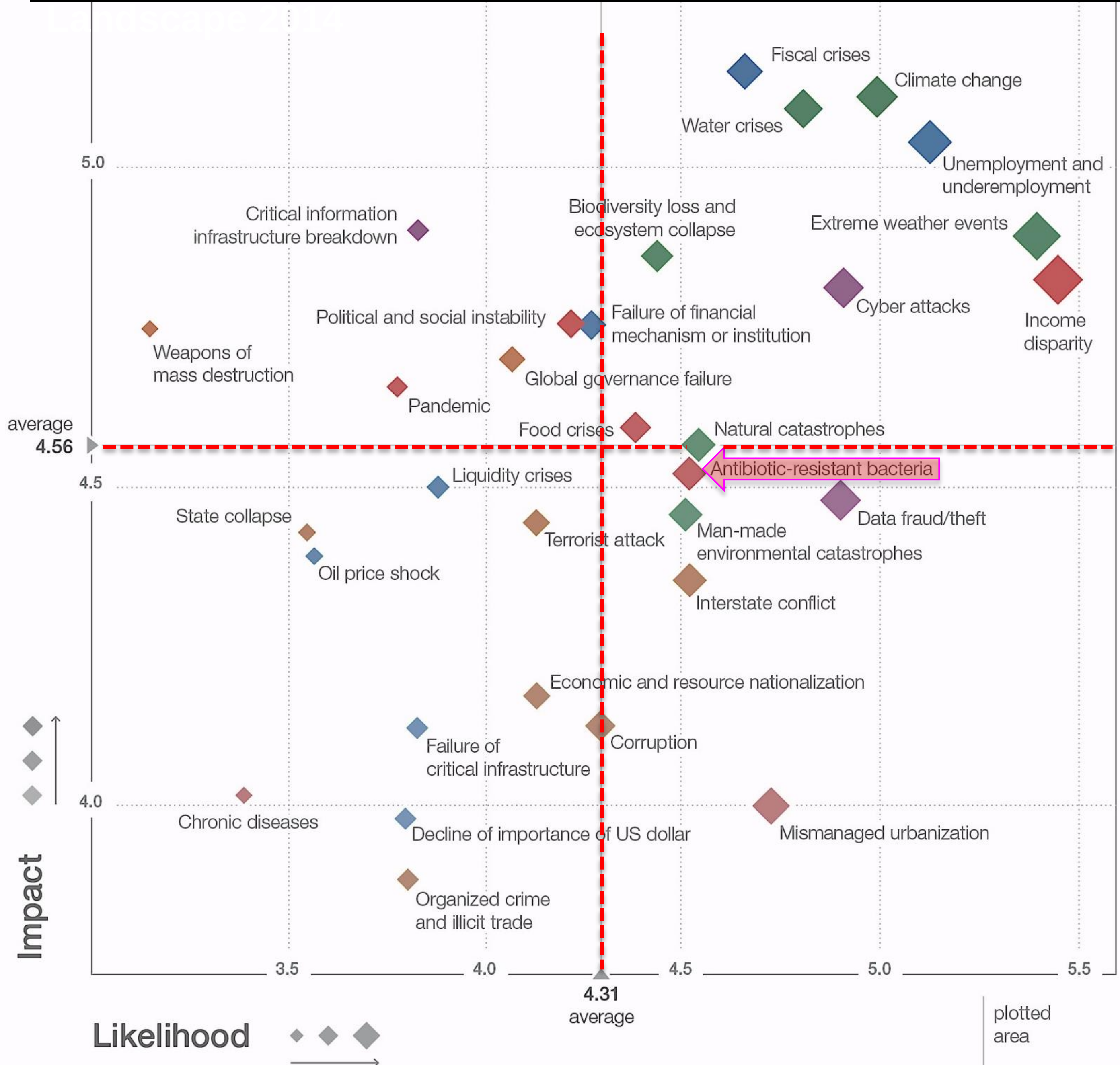
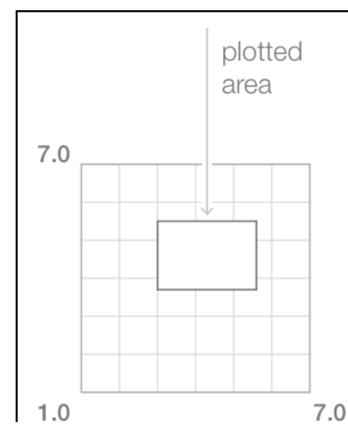
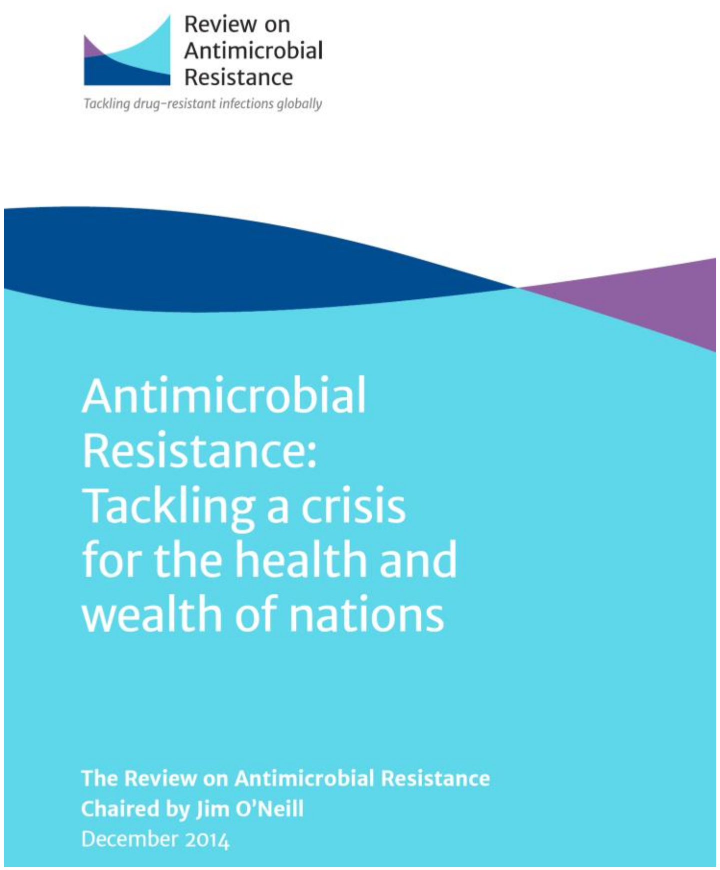
Global Risks 2014 report Figure 1.1.: The Global Risk Landscape 2014



THE GLOBAL RISKS:

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




Review on Antimicrobial Resistance
Tackling drug-resistant infections globally

Antimicrobial Resistance: Tackling a crisis for the health and wealth of nations

The Review on Antimicrobial Resistance
Chaired by Jim O'Neill
December 2014


KPMG
cutting through complexity

The global economic impact of anti-microbial resistance

KPMG LLP

11 December 2014

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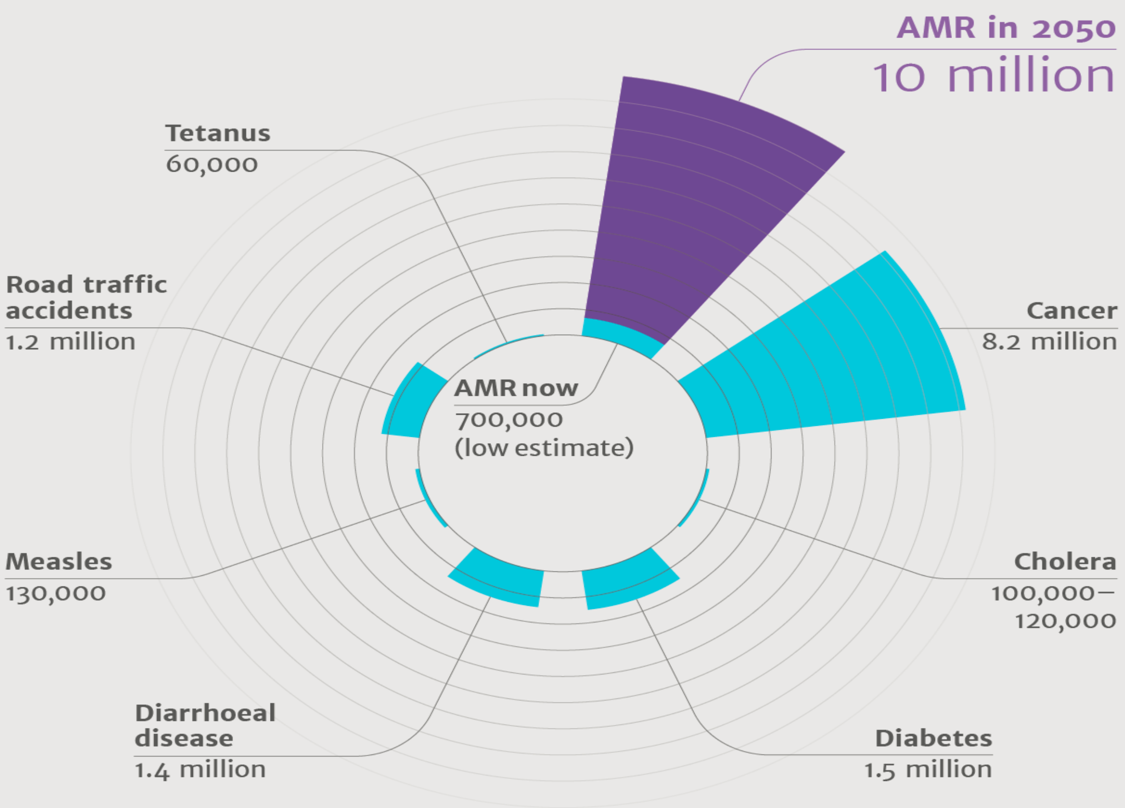
Deaths attributable to AMR every year compared to other major causes of death



Sources

Diabetes	www.who.int/mediacentre/factsheets/fs312/en/
Cancer	www.who.int/mediacentre/factsheets/fs297/en/
Cholera	www.who.int/mediacentre/factsheets/fs107/en/
Diarrhoeal disease	www.sciencedirect.com/science/article/pii/S0140673612617280
Measles	www.sciencedirect.com/science/article/pii/S0140673612617280
Road traffic accidents	www.who.int/mediacentre/factsheets/fs358/en/
Tetanus	www.sciencedirect.com/science/article/pii/S0140673612617280

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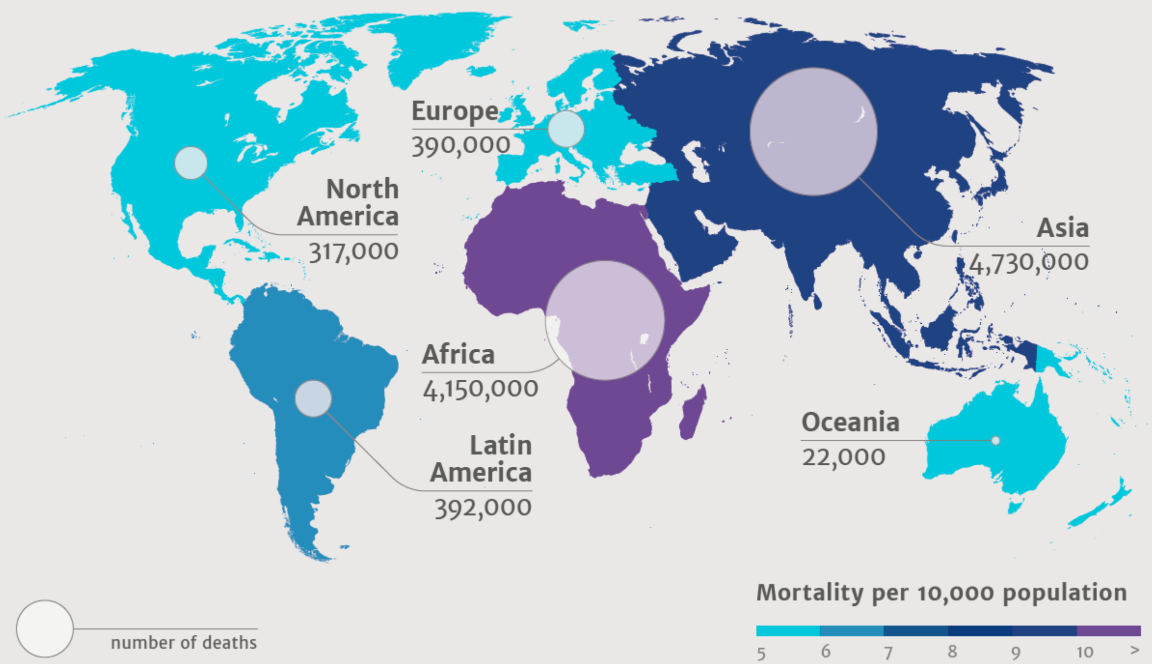
Deaths attributable to AMR every year
by 2050



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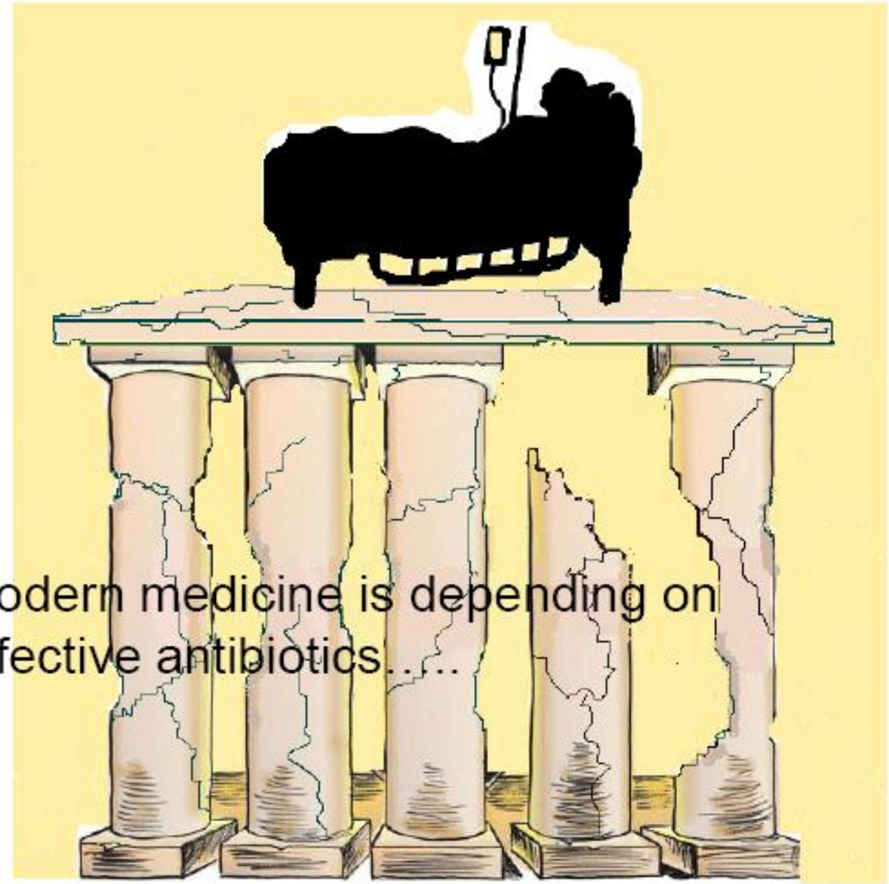

Modern medicine is depending on effective antibiotics…..

Strama

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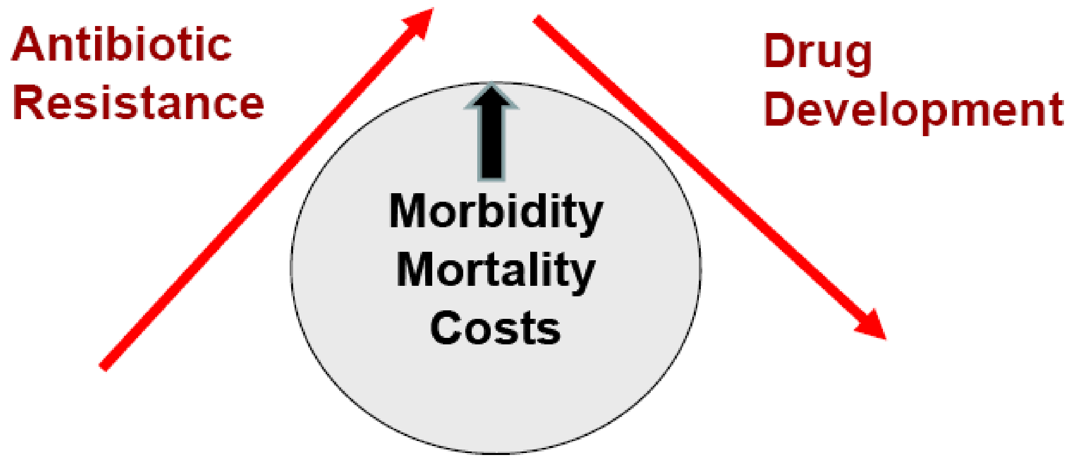
The Current Paradox:



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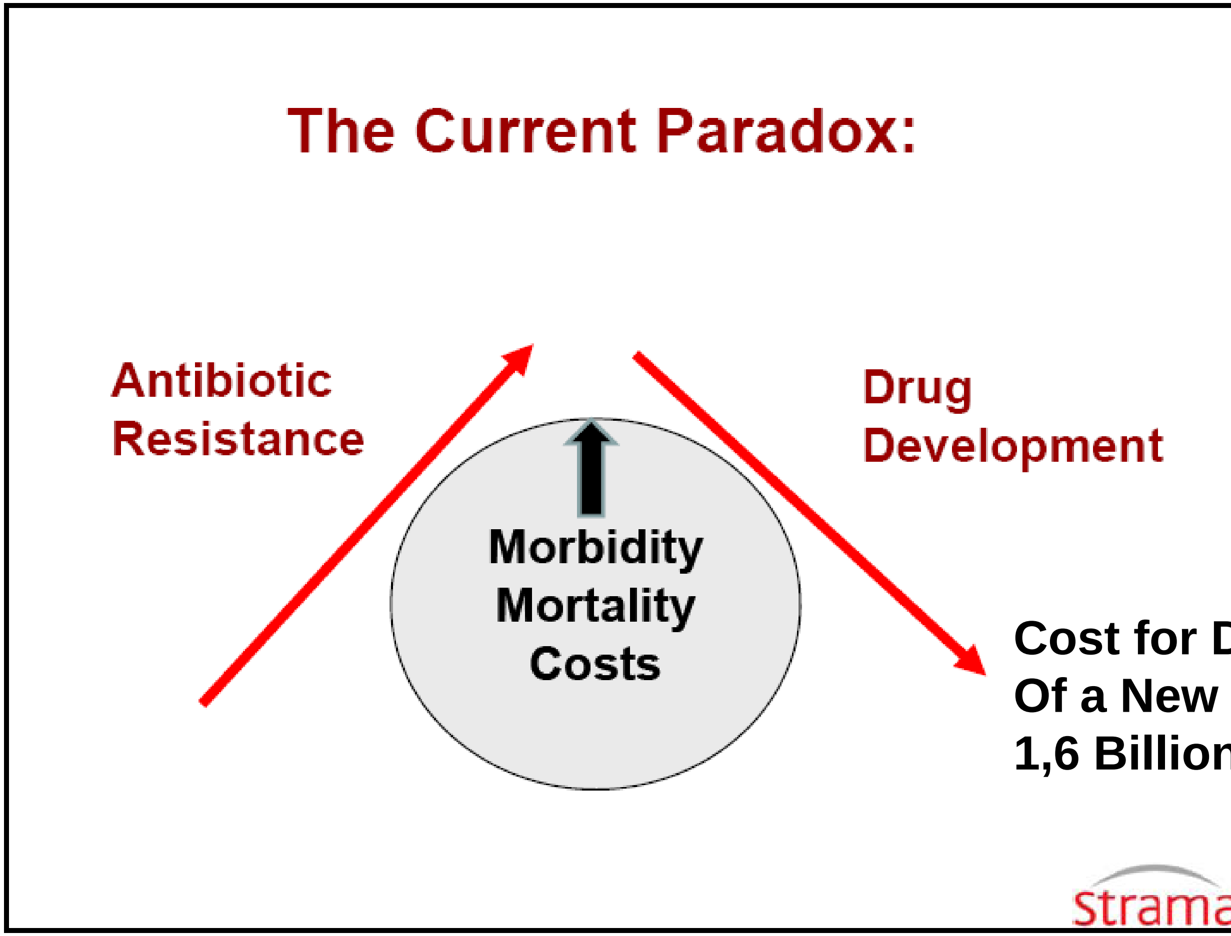

Cost for Development Of a New Antibiotic: 1,6 Billion EU

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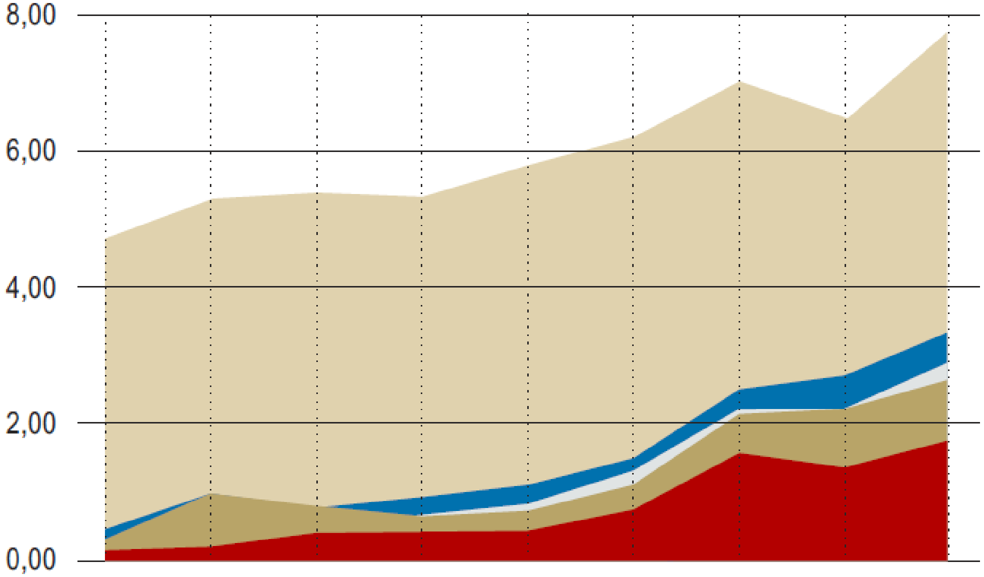
GRAFIK

Anzahl MRE pro 1 000 Patiententage



	2001	2002	2003	2004	2005	2006	2007	2008	2009
	4,24	4,29	4,57	4,37	4,67	4,67	4,51	3,73	4,39
	0,07	0,04	0,04	0,20	0,26	0,14	0,25	0,48	0,44
	0,03	0,01	0,02	0,04	0,07	0,25	0,11	0,05	0,25
	0,25	0,69	0,34	0,27	0,31	0,40	0,61	0,82	0,83
	0,16	0,26	0,45	0,43	0,48	0,75	1,54	1,39	1,81

MRSA VRE Imi R Aci G3C R Kleb G3C R Eco

Darstellung von Inzidenzdichten von 55 Intensivstationen, die am SARI-Projekt teilnehmen. Patienten mit multiresistenten Erregern (MRE) pro 1 000 Patiententage (2). SARI, Surveillance der Antibiotika-Anwendung und der bakteriellen Resistenzen auf Intensivstationen; MRSA, Methicillin-resistenter S. aureus; VRE, Vancomycin-resistenter Enterococcus faecium; Imi R Aci, Imipenem-resistenter Acinetobacter baumanii; G3C R Kleb, Gruppe-3-Cephalosporin-resistente Klebsiella pneumoniae; G3C R Eco, Gruppe-3-Cephalosporin-resistente Escherichia coli

David Garner,Consultant Microbiologist
Surrey, UK

- I have recently had the pleasure of interviewing for new Consultant colleagues and I thought it would be good to ask them “what infection keeps you awake at night?”
- Their answers where all the same:

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carbapenemases.

The “Big Five” Carbapenemases

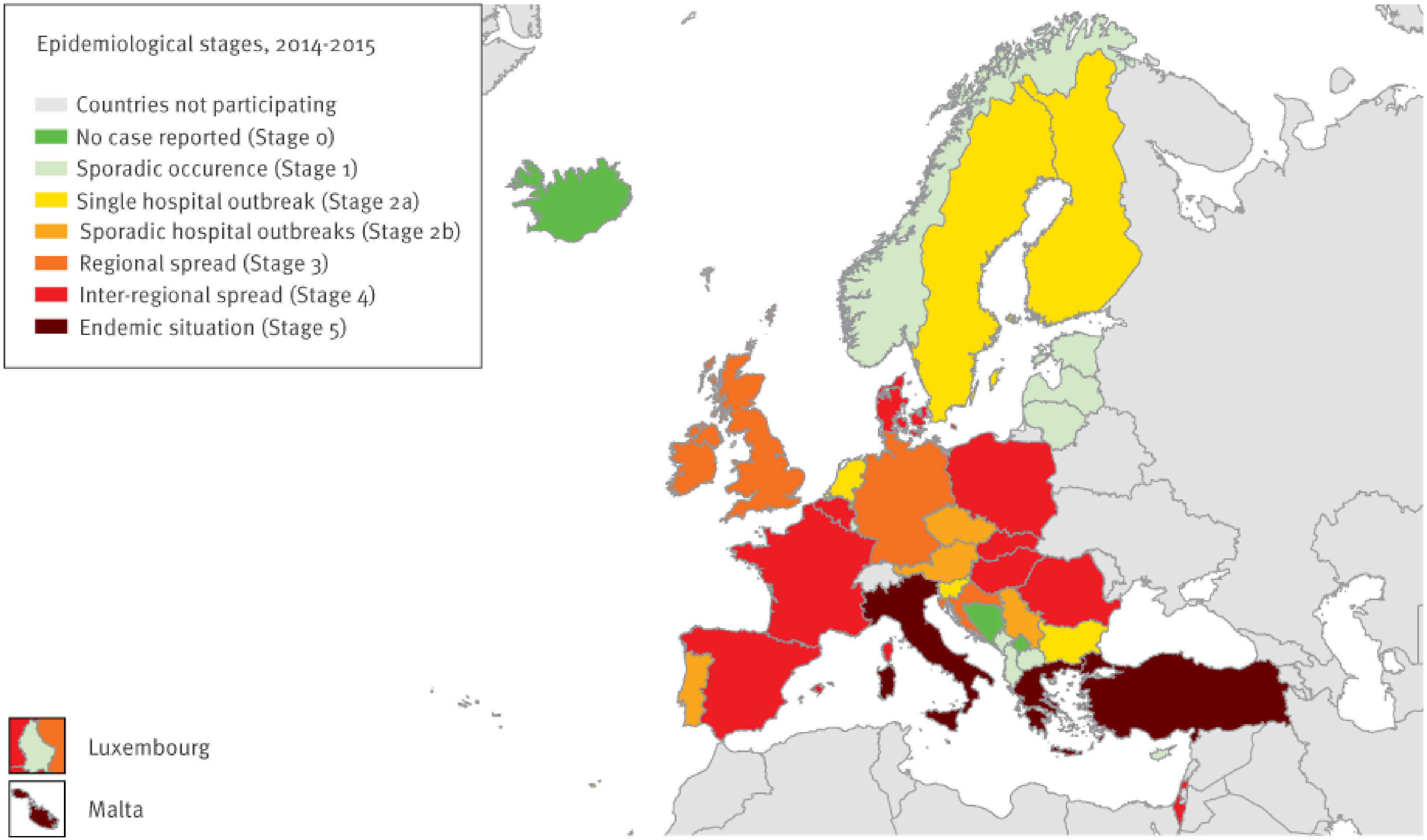
- **KPC** (Klebsiella pneumoniae carbapenemase)
- **IMP** (Imipenemase metallo-beta-lactamase)
- **NDM** (New Delhi metallo-beta-lactamase)
- **VIM** (Verona integron-encoded metallo-beta-lactamase)
- **OXA** (Oxacillin carbapenemases)

Carbpenemase Enzymes and Details

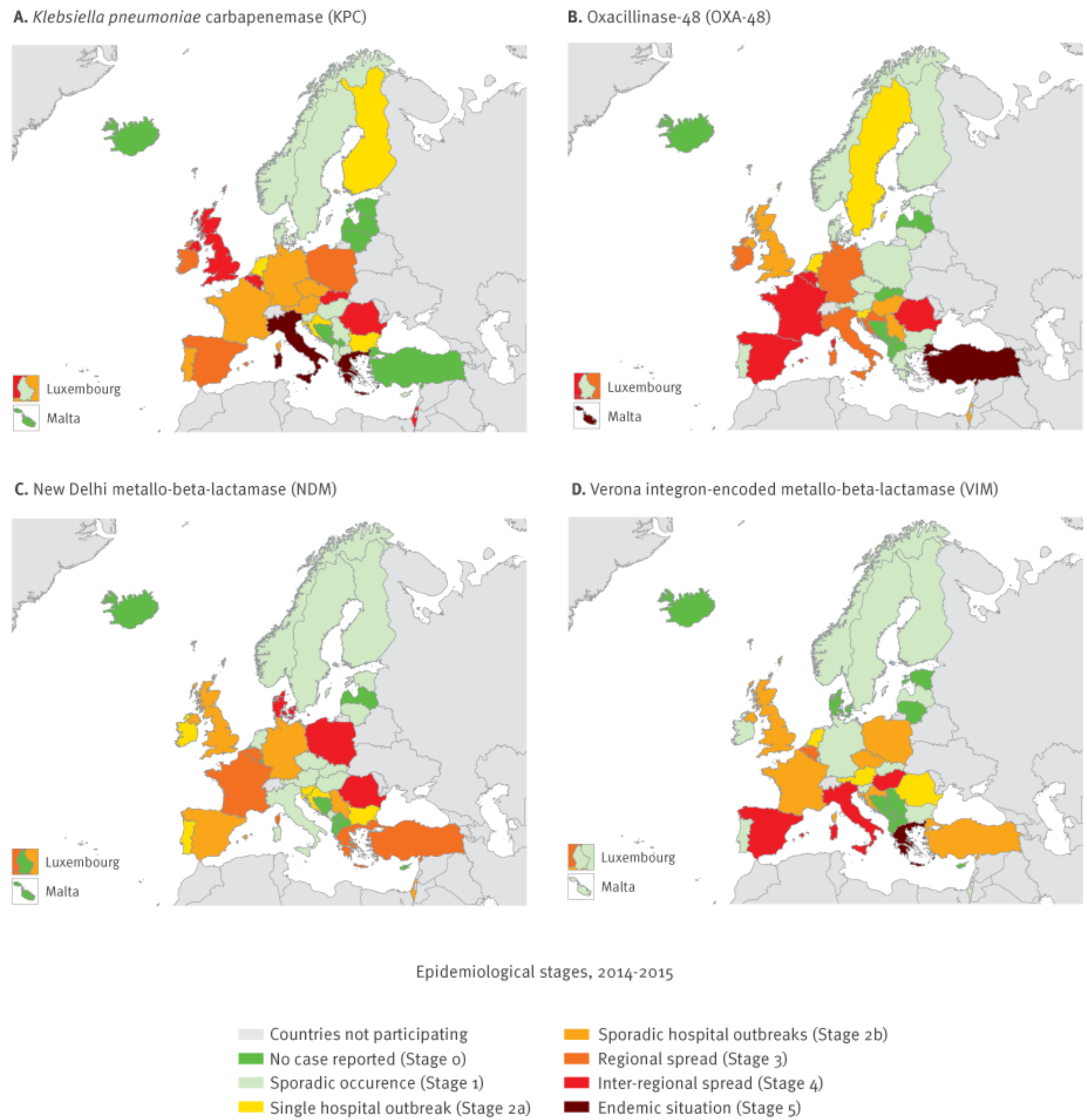
Enzymes	Details
KPC	• First detected in 1996 in the USA • Initially found in a single clone of *K. pneumoniae* but now found in many different bacteria • Endemic in the USA, Greece, Italy, Israel and China
IMP, VIM, NDM	• All 3 can occur in multiple different bacteria • Require activation by a metal ion (zinc) therefore often known as metallo-beta-lactamases • IMP-1 first detected in 1991 in Japan • VIM-1 first detected in 1999 in Verona, Italy • NDM first detected in 2008 in Sweden but the patient had previously been hospitalised in New Delhi • NDM is estimated to be carried by 80% of the 1.4 billion population of the Indian Subcontinent
OXA	• Very diverse group of enzymes first detected in 2003 in Turkey • The main type in Enterobacteriaceae is OXA 48 associated with a specific plasmid which can transfer between bacterial species

David Garner,Consultant Microbiologist
Surrey, UK

Occurrence of carbapenemase-producing *Enterobacteriaceae* based on self-assessment by national experts, 38 European countries, May 2015



Geographic distribution of carbapenemase-producing Enterobacteriaceae by resistance mechanism, based on self-assessment by national experts, 38 European countries, May 2015



Lancet Inf. Dis. 18. Nov. 2015

Emergence of plasmid-mediated colistin resistance mechanism MCR-1 in animals and human beings in China: a microbiological and molecular biological study

Yi-Yun Liu, Yang Wang*, Timothy R Walsh, Ling-Xian Yi, Rong Zhang, James Spencer, Yohei Doi, Guobao Tian, Baolei Dong, Xianhui Huang, Lin-Feng Yu, Danxia Gu, Hongwei Ren, Xiaojie Chen, Luchao Lv, Dandan He, Hongwei Zhou, Zisen Liang, Jian-Hua Liu, Jianzhong Shen*

Summary

Background Until now, polymyxin resistance has involved chromosomal mutations but has never been reported via horizontal gene transfer. During a routine surveillance project on antimicrobial resistance in commensal *Escherichia coli* from food animals in China, a major increase of colistin resistance was observed. When an *E coli* strain, SHP45, possessing colistin resistance that could be transferred to another strain, was isolated from a pig, we conducted further analysis of possible plasmid-mediated polymyxin resistance. Herein, we report the emergence of the first plasmid-mediated polymyxin resistance mechanism, MCR-1, in Enterobacteriaceae.

Lancet Infect Dis 2015

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November 18, 2015
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See Online/Articles
http://dx.doi.org/10.1016/S1473-3099(15)00463-6

Bundesgesundheitsbl 2012 · 55:1311–1354
DOI 10.1007/s00103-012-1549-5

Hygienemaßnahmen bei Infektionen oder Besiedlung mit multiresistenten gramnegativen Stäbchen

Empfehlung der Kommission für Krankenhaushygiene und Infektionsprävention (KRINKO) beim Robert Koch-Institut (RKI)

1 Einleitung, Definitionen und Hintergrund

Nachdem die letzten Jahrzehnte durch eine zunehmende Ausbreitung grampositiver nosokomialer Infektionserreger gekennzeichnet waren, zeichnet sich in den letzten Jahren eine Zunahme der Resistenzen bei gramnegativen Stäbchen-Bakterien ab. Diese Zunahme ist nicht nur durch die Verbreitung einzelner Resistenzgene in einzelnen Spezies gekennzeichnet, sondern auch durch das Auftreten und die rasche Verbreitung immer neuer Resistenzgene, die zwischen verschiedenen gramnegativen Spezies ausgetauscht werden können.

Die zum Teil einschneidenden klinischen Konsequenzen mit fehlenden Therapieoptionen und hoher Mortalität der Infektionen haben dazu geführt, dass empirisch verschiedene Maßnahmen der Kontrolle eingeführt wurden. Es wurden international und national Vorschläge zum Umgang mit Patienten, die mit multiresistenten gramnegativen Stäbchen besiedelt oder infiziert sind, vorgelegt [1-5]. Diese Vorschläge unterscheiden sich sowohl hinsichtlich der verwendeten Definitionen für Multiresistenz, als auch hinsichtlich der empfohlenen Maßnahmen. Dies ist sicher zum Teil der noch geringen wissenschaftlichen Evidenz für Ursachen und Konsequenzen der Verbreitung und der Wirksamkeit verschiedener Maßnahmen geschuldet.

Andererseits erfordert die derzeitige Epidemiologie ein abgestimmtes Vorgehen, welches transparent sowohl für die behandelnden Ärzte, als auch für die betroffenen Patienten ist. Daher wurde auf Basis der vorliegenden Literatur eine Empfehlung zum Umgang mit Patienten mit Infektion oder Besiedelung mit multiresistenten gramnegativen Stäbchen erstellt. Die zum Teil noch unzulängliche Datenlage macht eine Anpassung einzelner empfohlener Maßnahmen an neue Erkenntnisse in kürzeren Abständen wahrscheinlich. Hier sei auf entsprechende Publikationen der KRINKO verwiesen.

1.1 Zielgruppe dieser Empfehlung

Diese Empfehlung richtet sich primär an die Träger und Mitarbeiter von Krankenhäusern. Auch in anderen medizinischen Einrichtungen, in denen invasive Therapien z. B. Beatmungen in der neurologischen Rehabilitation durchgeführt werden, kann sie hilfreich sein. Andere Einrichtungen, die den Lebensbereich der Patienten darstellen (Alten- und Pflegeheime), werden in dieser Empfehlung derzeit nicht berücksichtigt. Hier ist eine eigene individuelle Risikoabwägung empfehlenswert, wie sie in den Empfehlungen zur Infektionsprävention in Heimen [6] dargestellt wird. Aufgrund der Eigenschaften der gramnegativen Stäbchen sollten die Maßnahmen in Heimen jedoch nicht über die Maßnahmen, die für MRSA-positive Bewohner festgelegt sind, hinausgehen.

1.2 Bezug zu vorausgegangenen Empfehlungen der KRINKO

Die Empfehlungen stellen speziell Maßnahmen zur Prävention der Übertragung von multiresistenten gramnegativen Stäbchen zusammen. Hierbei wird ausdrücklich die endemische Situation oder das Auftreten von einzelnen Fällen behandelt. Für Maßnahmen, die bei Ausbrüchen zu ergreifen sind, sei auf die Empfehlungen zum Ausbruchsmanagement und strukturierten Vorgehen bei gehäuftem Auftreten nosokomialer Infektionen [7] verwiesen. Diese Maßnahmen sind selbstverständlich auch erforderlich, wenn die Häufung Mikroorganismen mit anderen Resistenzmustern als den hier behandelten betrifft.

Grundlegende Maßnahmen zur Infektionsprävention sind den entsprechenden weiteren Empfehlungen der KRINKO zu entnehmen. Hier sei ins-

2012

ESCMID PUBLICATIONS 10.1111/1469-0691.12427

ESCMID guidelines for the management of the infection control measures to reduce transmission of multidrug-resistant Gram-negative bacteria in hospitalized patients

E. Tacconelli[1], M. A. Cataldo[2], S. J. Dancer[3], G. De Angelis[4], M. Falcone[5], U. Frank[6], G. Kahlmeter[7], A. Pan[8,9], N. Petrosillo[2], J. Rodríguez-Baño[10,11,12], N. Singh[13], M. Venditti[5], D. S. Yokoe[14] and B. Cookson[15]

1) Division of Infectious Diseases, Department of Internal Medicine I, Tübingen University Hospital, Tübingen, Germany, 2) Clinical Department, National Institute for Infectious Diseases "L. Spallanzani", Rome, Italy, 3) Department of Microbiology, Hairmyres Hospital, East Kilbride, UK, 4) Infectious Diseases, Universitá Cattolica Sacro Cuore, 5) Department of Public Health and Infectious Diseases, Policlinico Umberto I, "Sapienza" University, Rome, Italy, 6) Division of Infection Control and Hospital Epidemiology, Department of Infectious Diseases, Heidelberg University Hospital, Heidelberg, Germany, 7) Department of Clinical Microbiology, Central Hospital, Växjö, Sweden, 8) Infectious and Tropical Diseases, Istituti Ospitalieri di Cremona, Cremona, 9) Infectious Risk Area, Health and Social Regional Agency of Emilia-Romagna, Bologna, 10) Unidad Clínica de Enfermedades Infecciosas y Microbiología, Hospital Universitario Virgen Macarena, Seville, 11) Departmento de Medicina, Universidad de Sevilla, Sevilla, Spain, 12) Spanish Network for Research in Infectious Diseases, Instituto de Salud Carlos III, Madrid, Spain, 13) Department of Pediatrics, Epidemiology and Global Health, Children's National Medical Center, The George Washington University, Washington, DC, USA, 14) Infectious Diseases Division, Department of Medicine, Brigham and Women's Hospital and Harvard Medical School, Boston, MA, USA and 15) Medical Microbiology, Honorary Professor in Medical Microbiology, Division of Infection and Immunity, University College London, London, UK

Abstract

Healthcare-associated infections due to multidrug-resistant Gram-negative bacteria (MDR-GNB) are a leading cause of morbidity and mortality worldwide. These evidence-based guidelines have been produced after a systematic review of published studies on infection prevention and control interventions aimed at reducing the transmission of MDR-GNB. The recommendations are stratified by type of infection prevention and control intervention and species of MDR-GNB and are presented in the form of 'basic' practices, recommended for all acute care facilities, and 'additional special approaches' to be considered when there is still clinical and/or epidemiological and/or molecular evidence of ongoing transmission, despite the application of the basic measures. The level of evidence for and strength of each recommendation, were defined according to the GRADE approach.

Keywords: *Acinetobacter*, *Burkholderia*, Enterobacteriaceae, extended-spectrum β-lactamase, guideline, infection control, multidrug-resistant Gram-negative, outbreak, *Pseudomonas*, *Stenotrophomonas*

Clin Microbiol Infect 2014; **20 (Suppl. 1)**: 1–55

2014

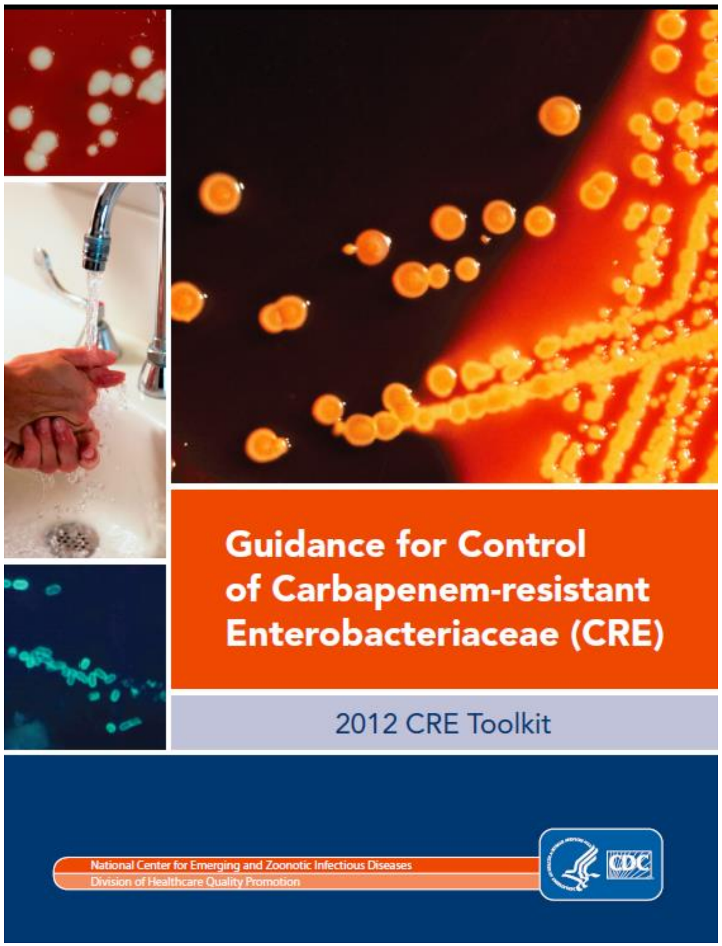
German Classification of Antibiotic resistance of gram-negative bacteria

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

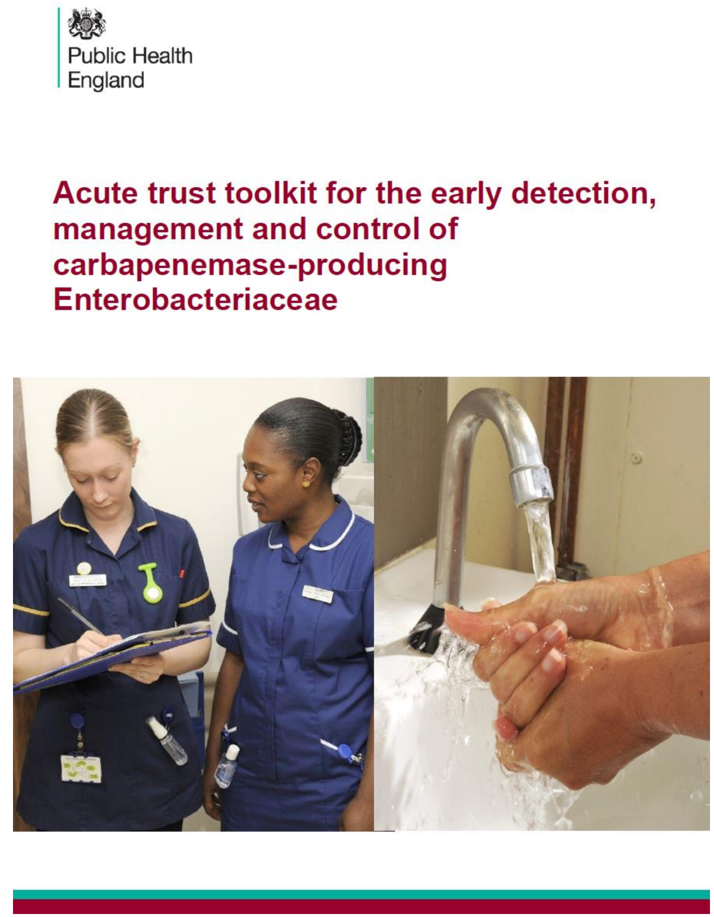
Antibiotikagruppe	Leitsubstanz	Enterobakterien		*Pseudomonas aeruginosa*		*Acinetobacter baumannii*	
		3MRGN[1]	4MRGN[2]	3MRGN[1]	4MRGN[2]	3MRGN[1]	4MRGN[2]
Acylureidopenicilline	Piperacillin	R	R	Nur eine der 4 Antibiotikagruppen wirksam (sensibel)	R	R	R
3./4. Generations-Cephalosporine	Cefotaxim und/oder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



Under revision



2014

CDC

Summary Of Prevention Strategies For Acute And Long-Term Care Facilities

Core Measures for All Acute and Long-term Care Facilities

1. Hand hygiene
   - Promote hand hygiene
   - Monitor hand hygiene adherence and provide feedback
   - Ensure access to hand hygiene stations
2. Contact Precautions

   Acute care
   - Place CRE colonized or infected patients on Contact Precautions (CP)
     - Preemptive CP might be used for patients transferred from high-risk settings
   - Educate healthcare personnel about CP
   - Monitor CP adherence and provide feedback
   - No recommendation can be made for discontinuation of CP
   - Develop lab protocols for notifying clinicians and IP about potential CRE

   Long-term care
   - Place CRE colonized or infected residents that are high-risk for transmission on CP (as described in text); for patients at lower risk for transmission use Standard Precautions for most situations
3. Patient and staff cohorting
   - When available cohort CRE colonized or infected patients and the staff that care for them even if patients are housed in single rooms
   - If the number of single patient rooms is limited, reserve these rooms for patients with highest risk for transmission (e.g., incontinence)
4. Minimize use of invasive devices
5. Promote antimicrobial stewardship
6. Screening
   - Screen patient with epidemiologic links to unrecognized CRE colonized or infected patients and/or conduct point prevalence surveys of units containing unrecognized CRE patients

Supplemental Measures for Healthcare Facilities with CRE Transmission

1. Conduct active surveillance testing
   - Screen high-risk patients at admission or at admission and periodically during their facility stay for CRE. Preemptive CP can be used while results of admission surveillance testing are pending
   - Consider screening patients transferred from facilities known to have CRE at admission
2. Chlorhexidine bathing
   - Bathe patients with 2% chlorhexidine

Public health England (PHE)

Section A – intended for use by frontline staff in acute healthcare settings

A.1 Acute trust – patient admission flow chart for infection prevention and control (IP&C) of carbapenemase-producing Enterobacteriaceae

A.2 Early recognition of individuals who may be colonised / have an infection

A.3 Early isolation of suspected and laboratory-confirmed cases

A.4 Early detection – screening of suspected cases and contacts

A.5 Effective treatment – antibiotics and a view on decolonisation

A.6 Early instigation of effective infection prevention and control (IP&C) measures

A.7 Cleaning and decontamination

A.8 Early communication including on discharge of patients or on medical transfer

ECDC EVIDENCE BRIEF

November 2015

Update on the spread of carbapenemase-producing *Enterobacteriaceae* in Europe

Summary of the May 2015 expert assessment

November 2015

Measures to prevent and control outbreaks of carbapenemase-producing *Enterobacteriaceae* in hospitals and other healthcare settings

The following measures were identified in an ECDC systematic review and an ECDC risk assessment [5,6]. There is only evidence that these measures are effective when they are applied together as a bundle of measures.

Active surveillance

- Identify patients at high risk for CPE, including those transferred across borders.
- Rectal screening for CPE on admission for high-risk patients
- Consider pre-emptive isolation of patients at high risk for CPE (see below).
- Additional active surveillance by rectal screening for CPE during outbreaks
- Fast diagnostic turnaround time and timely communication of the results of rectal screening by the laboratory to the ward and the infection control team
- Case notification/flagging and contact tracing.

Isolation and contact precautions

- Patient isolation and contact precautions (gloves and gowns) for all CPE-positive patients
- Cohort nursing by separate dedicated staff and equipment for all CPE-positive patients
- Consider geographic cohorting of all CPE-positive patients.
- Monitoring of compliance with the above measures.

Hygiene precautions

- Enforced hand hygiene
- Environmental cleaning.

Education of staff

- Education about the above measures

Prudent use of antibiotics

- Prudent use of antibiotics, including restriction of certain antibiotics/antibiotic groups such as carbapenems.

More information, including on national guidelines, can be found online [7].

German Antibiotic Resistance Strategy 2020

- ZIEL 1: One-Health-Ansatz national und international stärken
- ZIEL 2: Resistenz-Entwicklungen frühzeitig erkennen
- ZIEL 3: Therapie-Optionen erhalten und verbessern
- ZIEL 4: Infektionsketten frühzeitig unterbrechen und Infektionen vermeiden
- ZIEL 5: Bewusstsein fördern und Kompetenzen stärken
- ZIEL 6: Forschung und Entwicklung unterstützen

Management of the infection control measures to reduce transmission of multidrug-resistant Gram-negative bacteria in hospitalized patients

Mechanisms of Transmission

- A review of the literature on mechanisms of transmission of MDR-GNB was problematic for three main reasons:
- (i) the low number of studies;
- (ii) the low availability of high-quality studies; and
- (iii) the high heterogeneity of definitions, settings and pathogens.

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Clin Microbiol Infect 2014; **20 (Suppl. 1)**: 1–55

Critics of reservoir and transmission hypothesis

- Patient-to-patient transmission was frequently thought to be the most important route of transmission based on the hypothesis that colonized or infected patients are the only reservoir for the microorganism.
- However, intermediate vectors for spread between patients, including contaminated hands of healthcare workers (HCWs), environment, and visitors should also be taken into consideration for the prevention and control of healthcare-associated MDR-GNB transmission.

Strategies to control Gram-positive bacteria cannot control Gram-negative Bacteria

Without integration of the full spectrum of classical hygiene strategies it will not possible to win the war against gram-negative Bacteria

Introduction and objective of the symposium

- Focus on Gram-negative nosocomial bacteria
- Strategies are not the same as for Gram- positive bacteria
- Patient is not the only reservoir
- Ecology of bacteria oriented strategies
- Wet environment as a niche for persistance and transmission
- Prevention and control strategies must take into account these reservoirs and changend if we want to bring under control Gram- negative AB resistant bacteria

Agenda for the Symposium of the Rudolf Schülke Foundation

"Worldwide Significance of Gram-Negative Antibiotic Resistant Rods:

Epidemiology, Prevention and Control Strategies"

26 und 27 November 2015 Madison Hotel / Hamburg

Chair: Prof (em.) Hans-Günter Sonntag, Heidelberg

<u>Thursday, 26 November 2015, 11:00 – 16:40, Room Elbe</u>

11:00 – 11:20

1. **Introduction and objective of the symposium**
   Prof Martin Exner, MD / Institute of Hygiene and Public Health, University of Bonn, Chairman of the Rudolf Schülke Foundation (Germany)

11:25 – 11:45

2. **The role of drug-resistant Gram-negative pathogens for public health - situation in Germany**
   Prof Martin Mielke, MD / Robert Koch Institute, Berlin (Germany)

11:50 – 12:10

3. **Drug resistant gram negative pathogens in the US**
   Prof Elaine Larson, RN, PhD, FAAN, CIC / Columbia University, New York (United States)

12:15 – 12:35

4. **The relevance of Gram-negative pathogens for public health – situation in India**
   Sanjay Bhattacharya, MD, DNB, DipRCPath, FRCPath, CCT / Tata Medical Center, Kolkata (India)

12:40– 13:00

5. **Ecology of Gram-negative pathogens in the environment – where are their habitats?**
   Prof Martin Exner, MD / Institute of Hygiene and Public Health, University of Bonn, Chairman of the Rudolf Schülke Foundation (Germany)

13:05 – 13:45

Lunch

13:45 – 14:05

6. **Infectiological consequences of antibiotic-resistant Gram-negative pathogens**
   Birgit Ross, MD / Hospital Hygiene, Essen University Hospital (Germany)

14:10 – 15:25

Discussion Part 1

15:25 – 15:40

Coffee break

15:40 – 16:40

Discussion Part 2

17:30

Start of the evening event

RUDOLF SCHÜLKE STIFTUNG

Friday, 27 November 2015, 09:00 – 15:00, Room Elbe

9:00 – 9:15

1. **Introduction**
   Prof em Hans-Günter Sonntag, MD PhD / Institute of Hygiene, University of Heidelberg (Germany)

9:20 – 9:40

2. **One-health concept and risk management in agriculture**
   Ricarda Schmithausen, MD / Institute of Medical Microbiology, Immunology and Parasitology (IMMIP), University of Bonn (Germany)

9:45 – 10:05

3. **Efficacy of biocides against Gram-negative pathogens**
   Peter Goroncy-Bermes, PhD / Schülke & Mayr GmbH, Norderstedt (Germany)

10:10 – 10:30

4. **Restrictions in the use of biocides for disinfection procedures**
   Peter Oltmanns, PhD / Schülke & Mayr GmbH, Norderstedt (Germany)

10:30 – 10:50

Coffee break

10:55 – 13:00

Discussion Part 3

13:05 – 13:40

Lunch

13:40 – 14:50

Discussion Part 4

RUDOLF SCHÜLKE STIFTUNG

Ecology of Gram-negative pathogens in the environment – where are their habitats?

M. Exner

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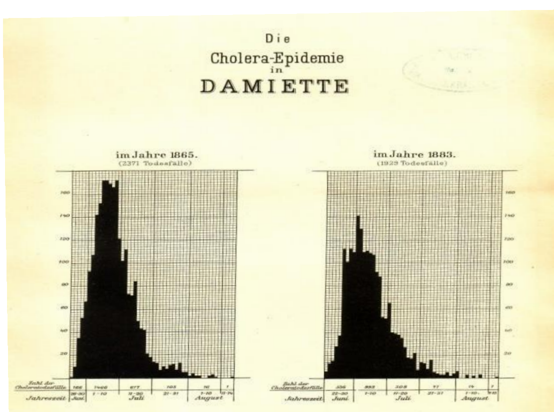
Topics

- Historical aspect (successful strategies in the past)
- Ecological aspects of Gram- negative bacteria
- Examples of reservoir from outbreak investigations
- Additional strategies
- The international perspective
- Conclusion

Cholera in der Kunst

National Institute of Health, USA,
Künstler: Unbekannt



Klinisches Bild der Cholera

Massive wässrige Diarrhö, schwerste Dehydratation Innerhalb von wenigen Stunden nach Infektion, ängstlicher Blick, rastlos, Augen eingesunken, Waschfrauenhände

Robert Koch and the Cholera Expedition 1883/84 to Egypt and India

28 Die Mitglieder der Cholera-Expedition 1883
von links: Gaffky, Treskow (stehend), Koch, Fischer

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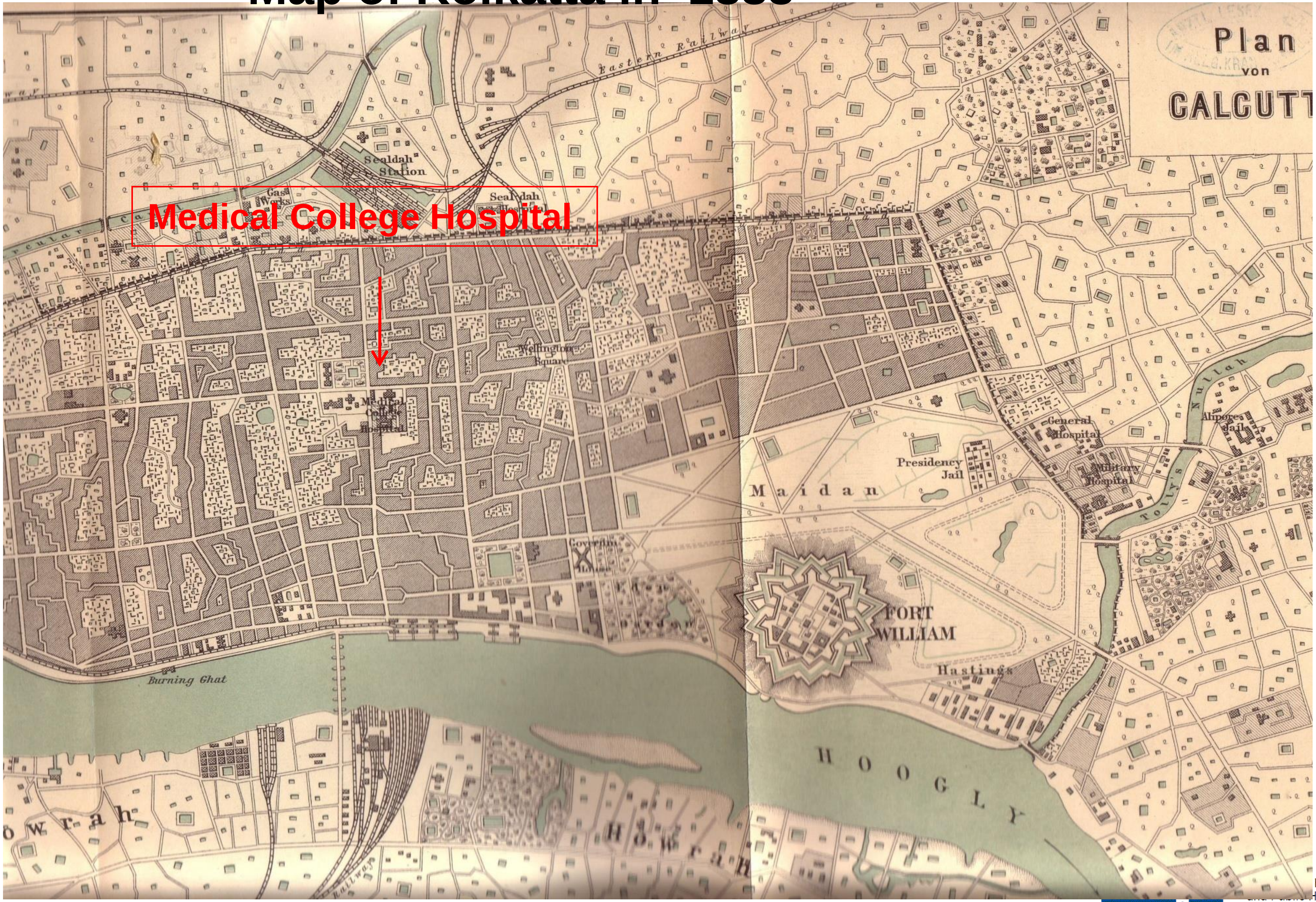
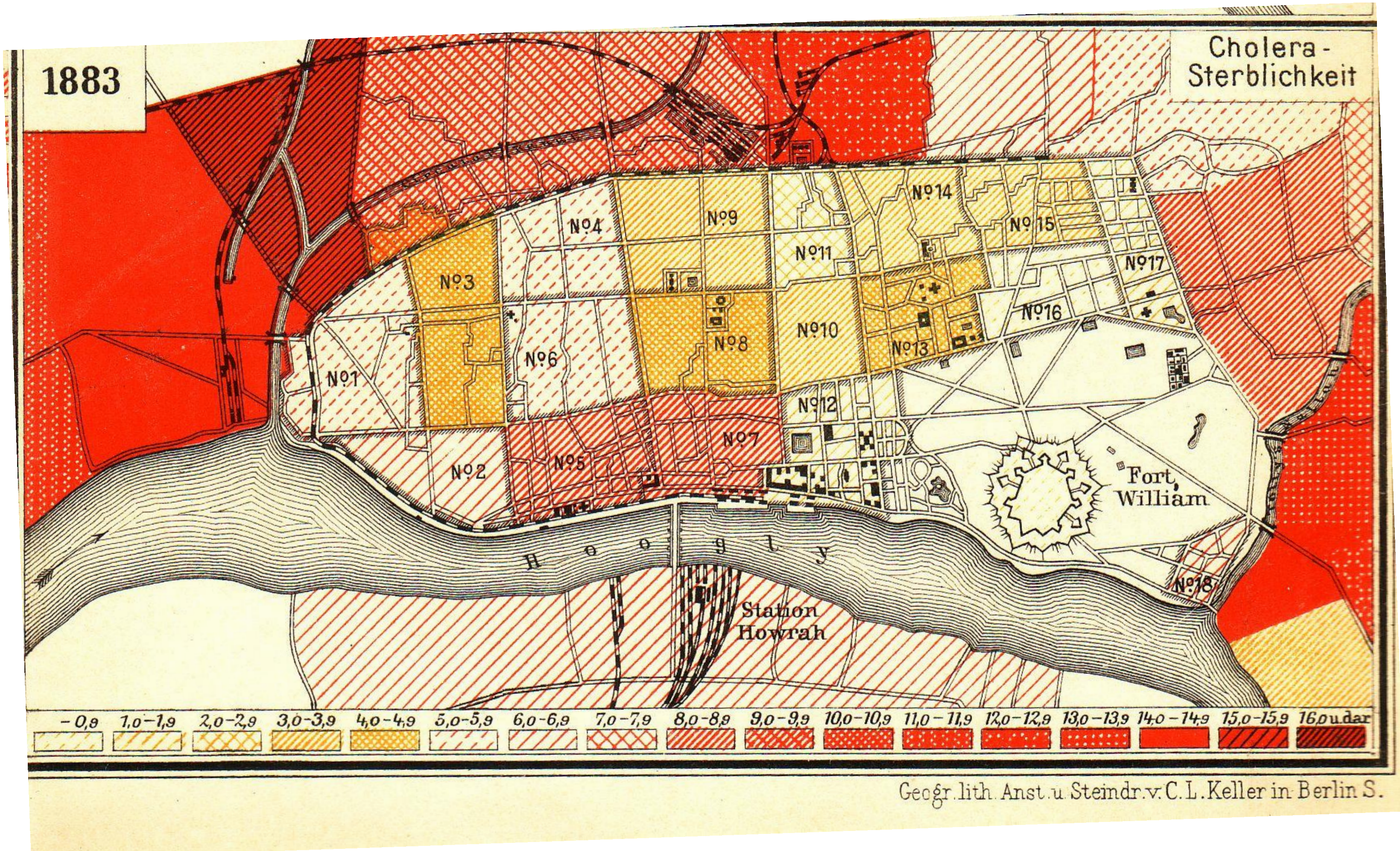
Map of Kolkatta in 1883



Geographische Verteilung der Cholera- Sterblichkeit in Kalkutta



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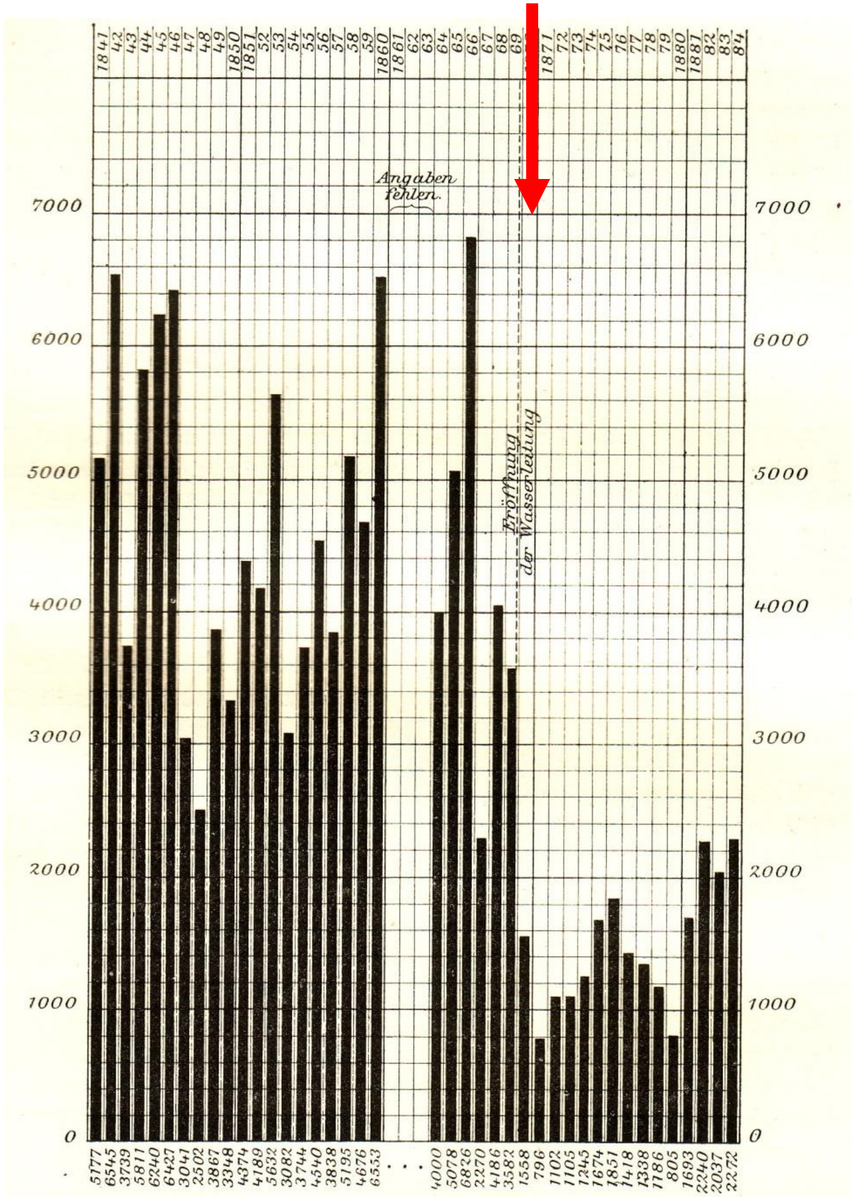
Cholera Mortality in Kolkata in the years before and after implementation of public water supply



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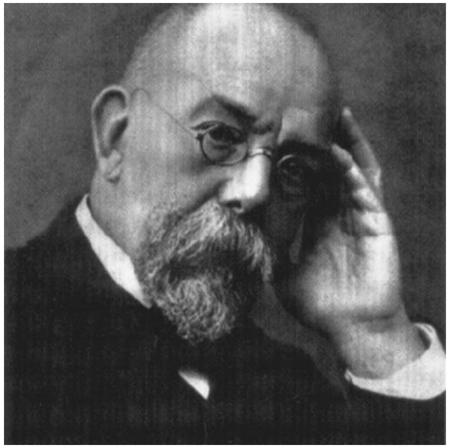
Cholera outbreak in Hamburg 1892
- example of an ideal type of sustainable outbreak management



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Robert Koch und Ausbruchmanagement der Hamburger Choleraepidemie 1892

R. Koch
in Hamburg
24.8.1892
These:
Trinkwasser
als Vehikle

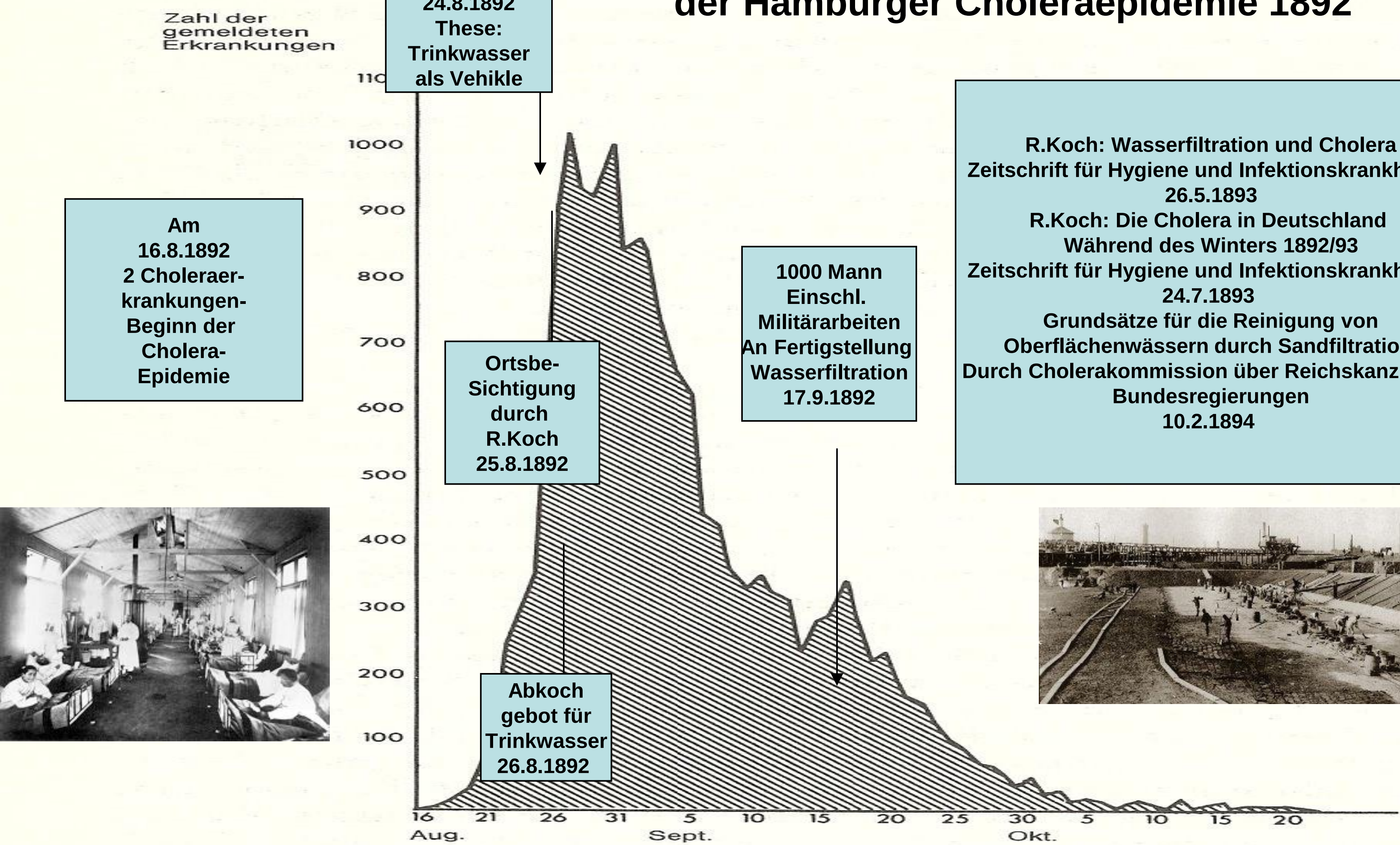
Am
16.8.1892
2 Choleraer-
krankungen-
Beginn der
Cholera-
Epidemie

Ortsbe-
Sichtigung
durch
R.Koch
25.8.1892

Abkoch
gebot für
Trinkwasser
26.8.1892

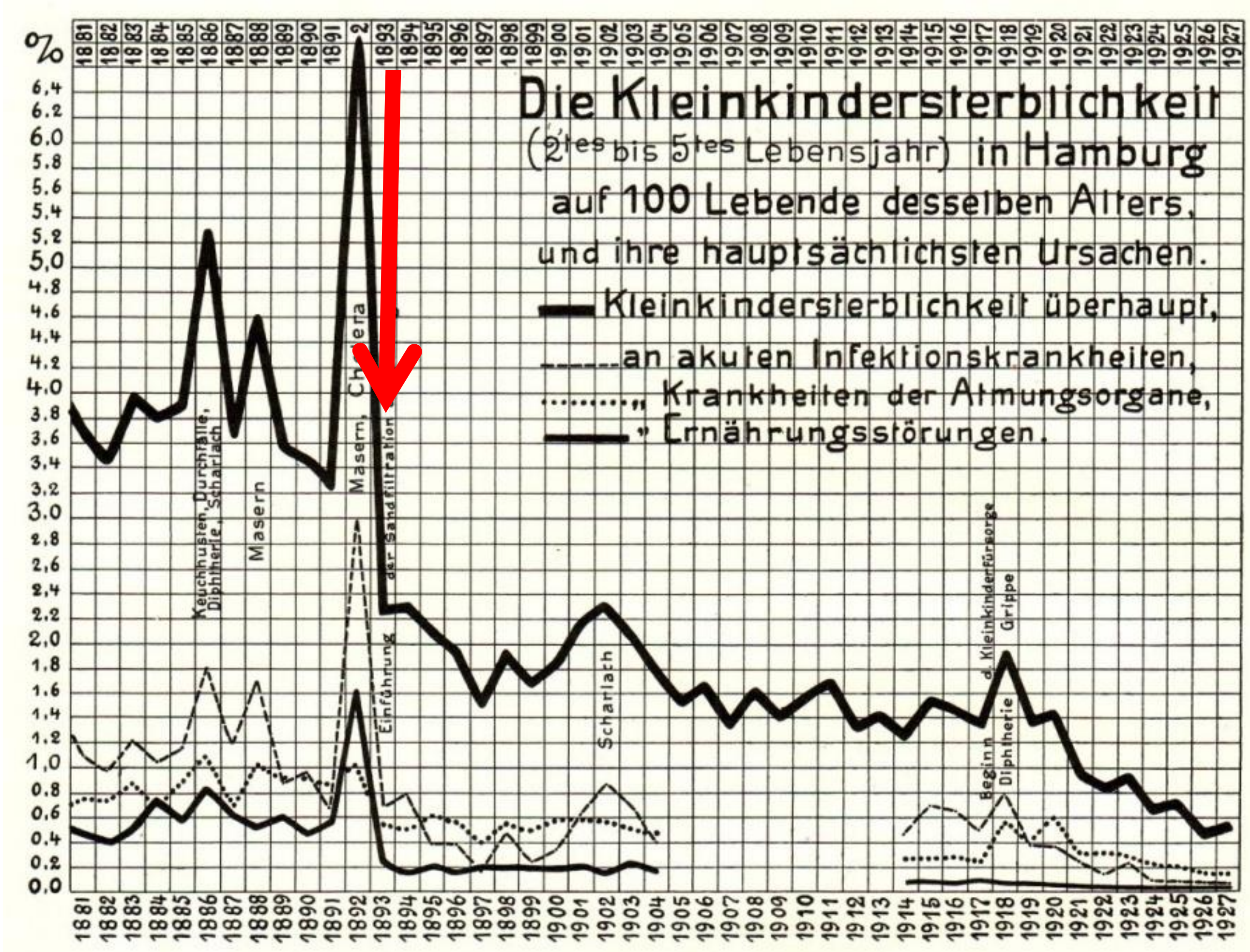
1000 Mann
Einschl.
Militärarbeiten
An Fertigstellung
Wasserfiltration
17.9.1892

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



Red arrow: Introduction of filtrated Water and Under 5 mortality

Under 5 Mortality rate per 100 live birth´s in Hamburg from 1881- 1927. Before 1892 the under 5 mortality rate was 4 % with an sharp increase in1892, the year of the cholera epidemic in Hamburg. After Koch´s proposal to install water filtration there was a sharp and immediate decrease of child under 5 mortality rate to 2 % in 1893. The general lesson which still holds is that passive health protection is often the best way to improve population health

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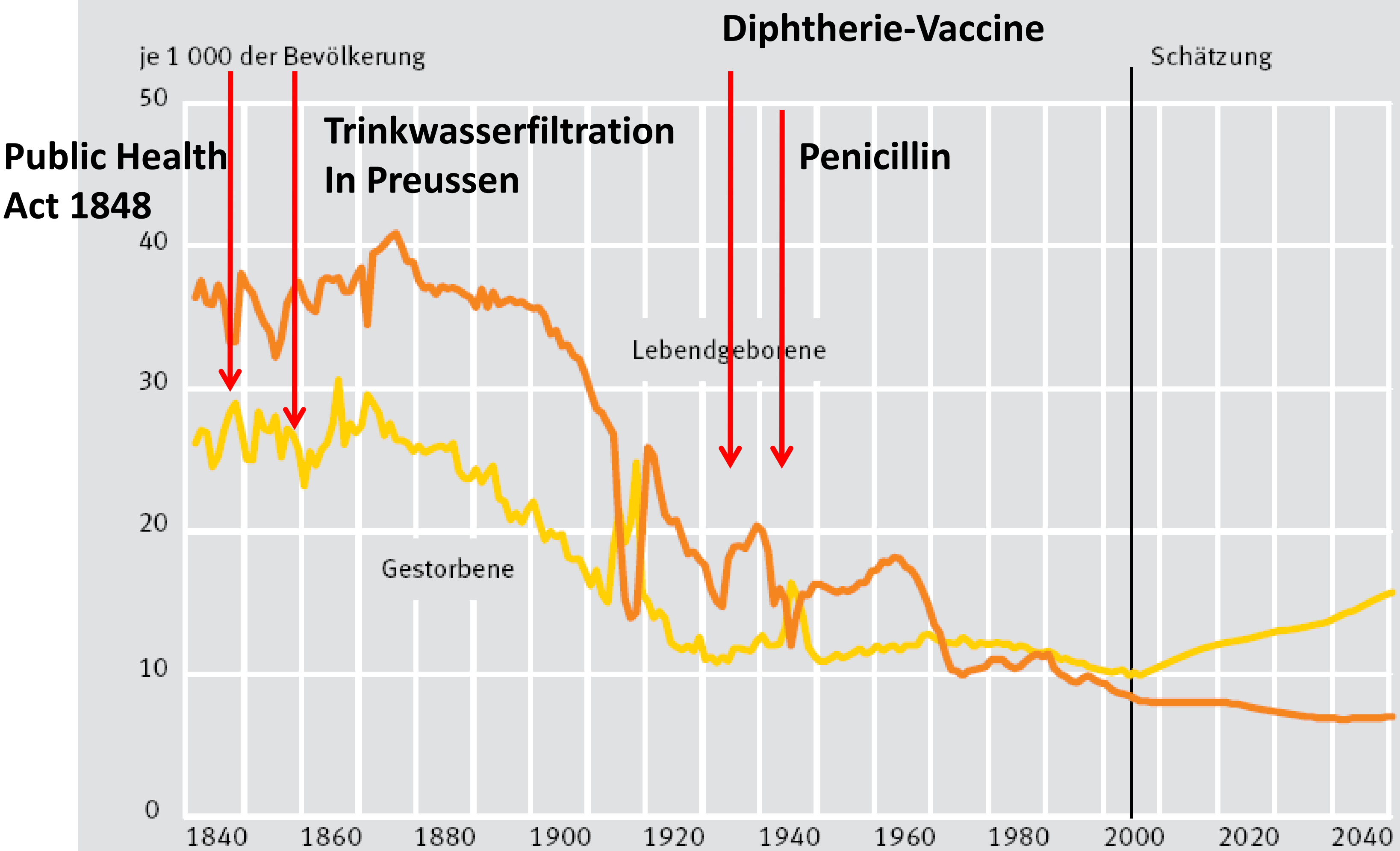
Kochnische im Laubenganghaus Heidhörn
Architekt: Paul A. R. Frank

Lebendgeborene und Gestorbene
je 1 000 der Bevölkerung,
1841 bis 2050



Datenquelle: Statistisches Bundesamt, grafische Darstellung: BiB

The Value of Hygiene and Public Health in the perception of the medical community 2007

BMJ readers choose sanitation as greatest medical advance since 1840

Annabel Ferriman BMJ

More than 11 300 readers of the *BMJ* chose the introduction of clean water and sewage disposal—“the sanitary revolution”—as the most important medical milestone since 1840, when the *BMJ* was first published. Readers were given 10 days to vote on a shortlist of 15 milestones, and sanitation topped the poll, followed closely by the discovery of antibiotics and the development of anaesthesia.

The work of the 19th century lawyer Edwin Chadwick, who pioneered the introduction of piped water to people’s homes and sewers rinsed by water, attracted 15.8% of the votes, while antibiotics took 15%, and anaesthesia took 14%. The next two most popular were the introduction of vaccines, with 12%, and the discovery of the structure of DNA (9%).

A total of 11 341 people voted on the shortlist, which was chosen by a panel of experts from a list nominated by readers. Almost a third of the voters were doctors, while a fifth were members of the general public, and
one in seven were students
Another tenth were acade
researchers. Almost two fi
of the voters were from the
United Kingdom, and a fif
were from the United Stat
Johan Mackenbach, pro
of public health at Erasmu
Medical Center, Rotterdam
who championed the caus
sanitation, said, “I’m delig
that sanitation is recognise
by so many people as such
an important milestone. Th
general lesson which still
holds is that passive protection
against health hazards is
…
supplement is distributed with this week’s *BMJ*.

SCIENCE MUSEUM, LONDON

Demonstration model of sanitary fixtures (1895)

MEDICAL MILESTONES **SANITATION**

Pragmatism works

Johan P Mackenbach

Despite erroneous theories of disease causation and the lack of an evidence base, new sewage disposal and water supply systems in the 1800s revolutionised public health in Europe

Greatest medical advance since 1840 voted by 11341 readers of British Medical Journal

-15,8% of votes: sanitation (introduction of piped water to people´s homes and sewers rinsed by water)

-15,0% of votes:antibiotics

-14,0% of votes:anaesthesia

-12,0% of votes:vaccines

- 9,0% of votes:DNA discovery

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Topics

- Historical aspect (successful strategies in the past)
- Ecological aspects of Gram- negative bacteria
- Examples of reservoirs from outbreak investigations
- Additional strategies
- The international perspective
- Conclusion

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

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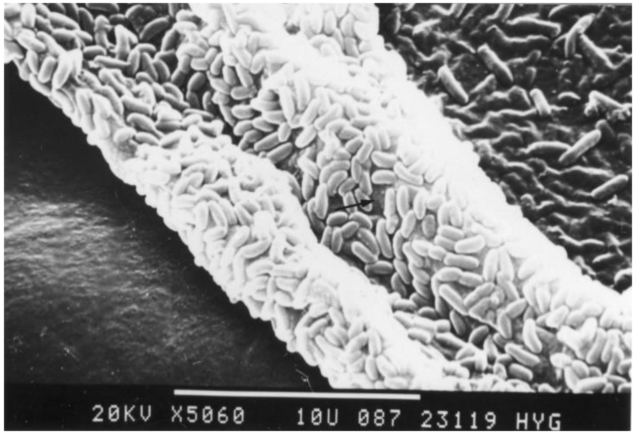
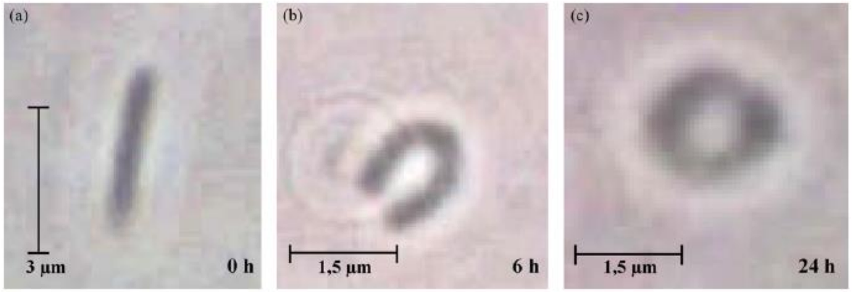
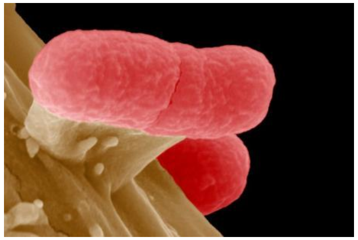
2 ecologic properties of Gram-negative pathogens with consequences

- Biofilm
- VBNC

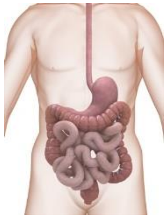


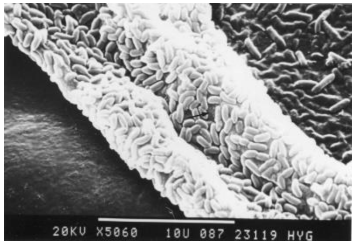


Hygienecascade gram- negative bacteria



Reservoir





High Persistence in
Wet areas and Biofilm

Release

By
direct and indirect
contact

Transmission

Direct transmission:
contact Water, solutions,
Infusions etc.

Infection

Indirect transmission:
Hands

disease

No Clearance like MRSA possible

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Martin Exner

Topics

- Historical aspect (successful strategies in the past)
- Ecological aspects of Gram- negative bacteria
- Examples of reservoirs from outbreak investigations
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- Conclusion

Biofilm and humidifier

Endemic high rate of Gram negative infection rate in neonates

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)

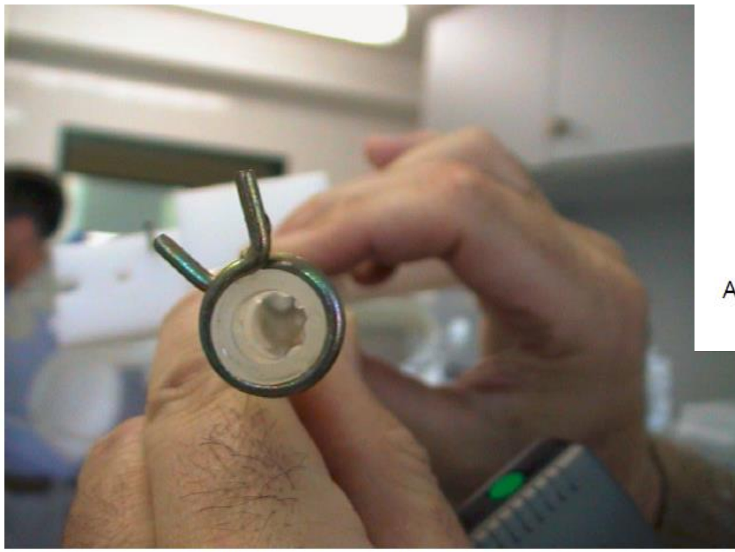

Abb. 12 Aufnahme des Schlauchstückes im Inneren des Inkubators, der von der inneren Anschlussstelle (siehe auch Abb. 10) zur Wanne mit Heißaggregat und Ventilator führt

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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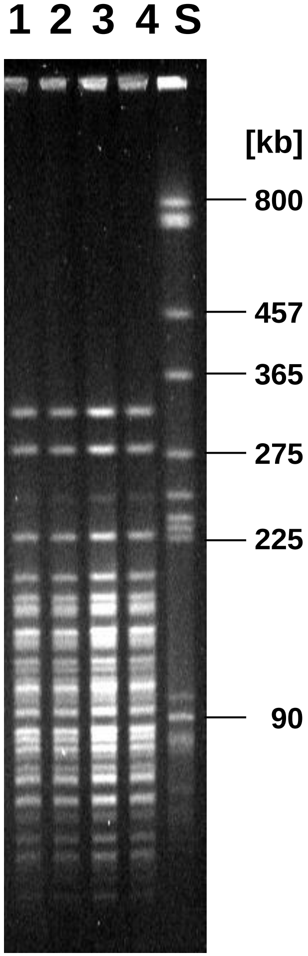
PFGE - Vergleich von vier Serratia liquefaciens - Stämmen



Euro Surveill. 2013;18(42):pii=20611

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

- Some patients acquired the multi-resistant *P. aeruginosa* without temporal overlap with other positive patients, suggesting an environmental source.
- Infection control investigations at the time suggested that the outbreak was associated with colonisation of hand washing basins.

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 Hand-washing 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 $1{,}6 \times 10^{6}$ 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 $3{,}0 \times 10^{5}$ 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
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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:
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American Journal of Infection Control 43 (2015) 635-9

ELSEVIER

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journal homepage: www.ajicjournal.org

AJIC American Journal of Infection Control

Major article

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

CrossMark

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, $bla_{\text{GIM-1}}$ 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 $bla_{\text{GIM-1}}$ 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

Toilets

Toilets as Reservoir for P. aeruginosa

Hyg Med 2014; 39 – Suppl. DGKH 2014

Toiletten als Reservoir für 4-fach resistente *P. aeruginosa*

S. Engelhart[1], D. Wolf[2], S. Abels[1], M. Exner[1]
[1] Institut für Hygiene und Öffentliche Gesundheit, Universitätsklinikum Bonn; [2] Medizinische Klinik III, Onkologie, Hämatologie und Rheumatologie, Universitätsklinikum Bonn

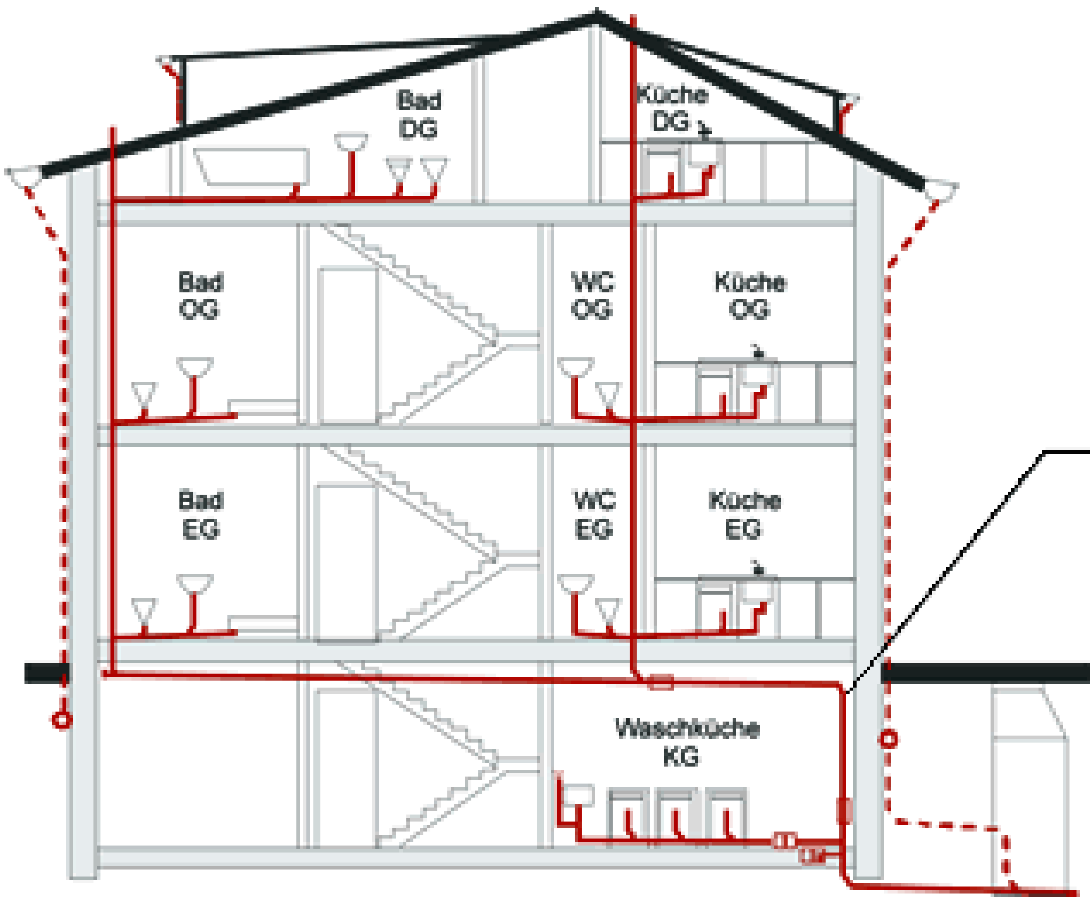
Einleitung: Hämato-onkologische Patienten weisen aufgrund der krankheits- und/oder therapiebedingten Immunsuppression und des hohen Selektionsdrucks durch häufigen Einsatz breit wirksamer Antibiotika vergleichsweise häufig Besiedelungen mit verschiedenen multiresistenten Erregern auf. Dies erfordert ein optimales Hygienemanagement und angemessene Screeninguntersuchungen zur Verhinderung von Transmissionen.

lungen, erhöhte HFK-Präsenz mit Anwendungsbeobachtungen, Quellensuche mittels Umgebungsuntersuchungen etc.) zu begegnen versucht wurde. Erst der Nachweis von Kontaminationen mit multiresistenten *P. aeruginosa* unter dem Spülrand mehrerer Toiletten und der komplette Austausch dieser Toilettenschüsseln durch spülrandlose Modelle führte zu einem raschen und nachhaltigen Absinken der Inzidenzdichte.

Schlussfolgerungen: Bei gehäuftem Nachweis von *P. aeruginosa*-ist insbesondere aufgrund der potenziellen Feuchtreservoirs das sanitäre Umfeld als mögliche Quelle zu untersuchen. Toiletten mit Spülrand können zu einer dauerhaften Besiedelungsquelle für *P. aeruginosa* werden. Der Ersatz durch spülrandlose Modelle führte im vorliegenden Fall zu einer Lösung des Problems.

The design of water taps, shower heads, water basins and sink trains must be considered and regulated.

Sewage system



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.)

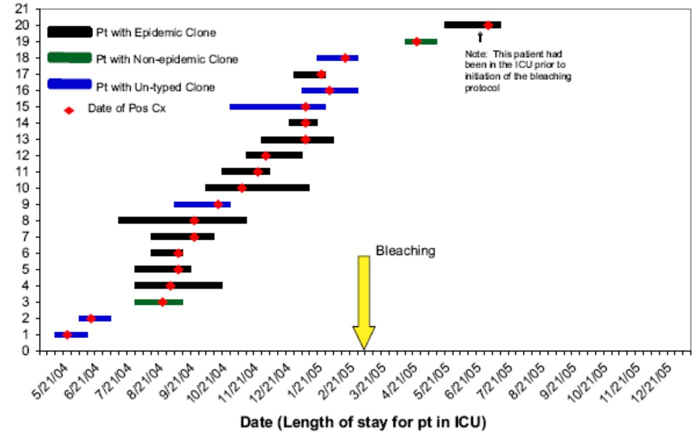

Fig 1. Timeline of the *A baumannii* outbreak in the ICU during the period when the epidemic clone was present.

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Wastewater drainage system as an occult reservoir in a protracted clonal outbreak due to metallo-β-lactamase-producing *Klebsiella oxytoca*

S. Vergara-López[1], M. C. Domínguez[2], M. C. Conejo[3], Á. Pascual[3,4] and J. Rodríguez-Baño[4,5]

1) *Internal Medicine Service, Hospital La Merced,* 2) *Laboratory of Microbiology, Hospital La Merced, Osuna, Seville,* 3) *Department of Microbiology, University of Seville,* 4) *Infectious Diseases and Clinical Microbiology Unit, University Hospital Virgen Macarena and* 5) *Department of Medicine, University of Seville, Seville, Spain*

Abstract

We describe the epidemiology of a protracted nosocomial clonal outbreak due to multidrug-resistant IMP-8 producing *Klebsiella oxytoca* (MDRKO) that was finally eradicated by removing an environmental reservoir. The outbreak occurred in the ICU of a Spanish hospital from March 2009 to November 2011 and evolved over four waves. Forty-two patients were affected. First basic (active surveillance, contact precautions and reinforcement of surface cleaning) and later additional control measures (nurse cohorting and establishment of a minimum patient/nurse ratio) were implemented. Screening of ICU staff was repeatedly negative. Initial environmental cultures, including dry surfaces, were also negative. The above measures temporarily controlled cross-transmission but failed to eradicate the epidemic MDRKO strain that reappeared two weeks after the last colonized patients in waves 2 and 3 had been discharged. Therefore, an occult environmental reservoir was suspected. Samples from the drainpipes and traps of a sink were positive; removal of the sink reduced the rate number but did not stop new cases that clustered in a cubicle whose horizontal drainage system was connected with the eliminated sink. 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.

Keywords: Carbapenemase, environmental reservoir, IMP-8, *Klebsiella oxytoca*, outbreak

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Editor: J.-M. Rolain

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Clin Microbiol Infect 2013; **19:** E490–E498

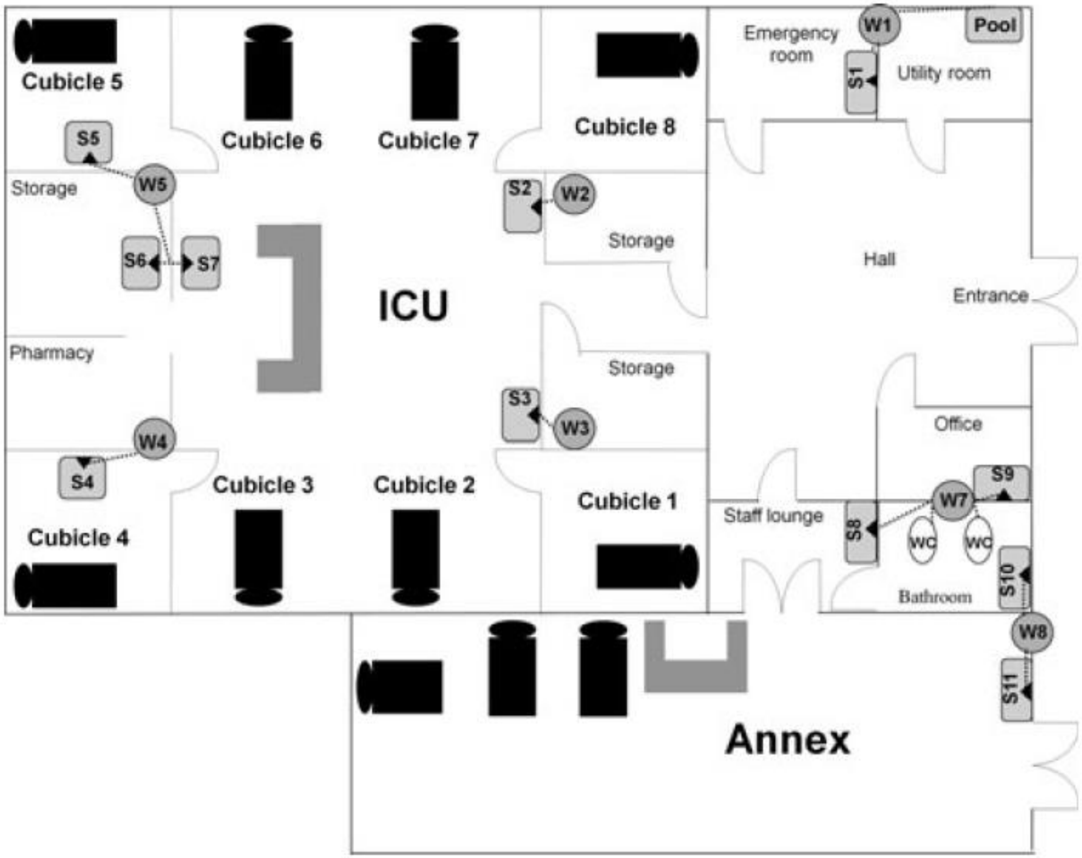

FIG. 1. Plan of the ICU. Grey square: sink. Grey circle: wastepipe. Discontinous line: drainpipe. S: sink. W: wastepipe.

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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.

ROBERT KOCH INSTITUT

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)

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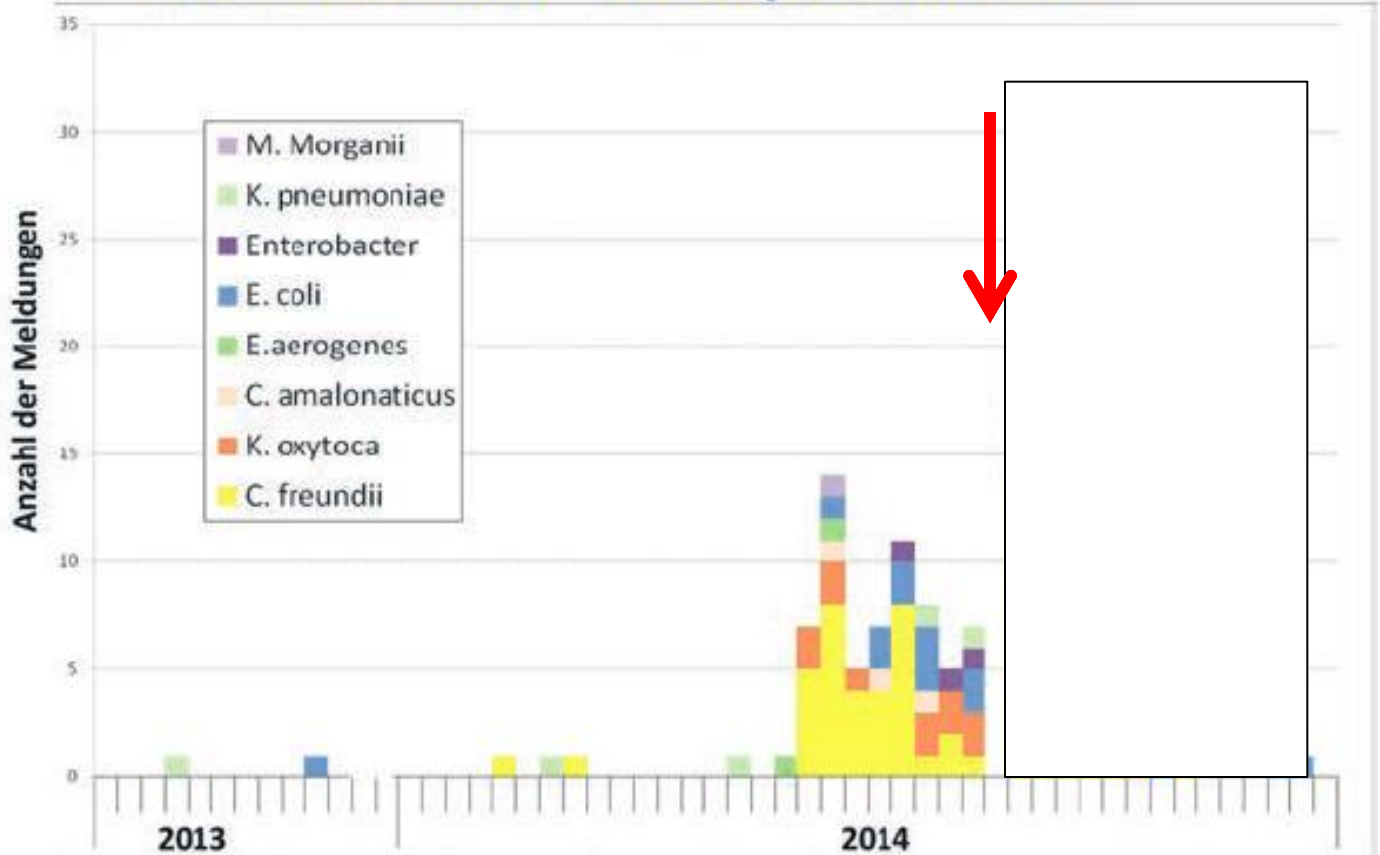
KPC 2-Meldungen aus Ausbruchsklinik
1. Oktober 2013 – 30. September 2014



Sink drainage and toilets of patient rooms

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Multiplex real-time PCR with HRM

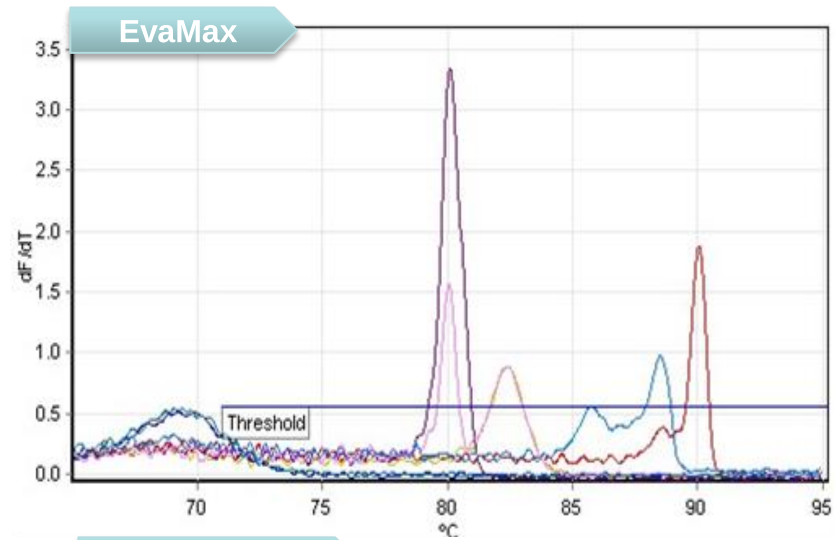
Temperatur (˚C) EvaMax	Target genes	Temperatur° C *Monteiro et al.*
78 and 79 (double peak)	OXA-24/-72	/
80	OXA-48	81.6
81	OXA-23	/
82	NDM	84
86	GES	88.4
88	VIM	90.3
90	KPC-2	91.6

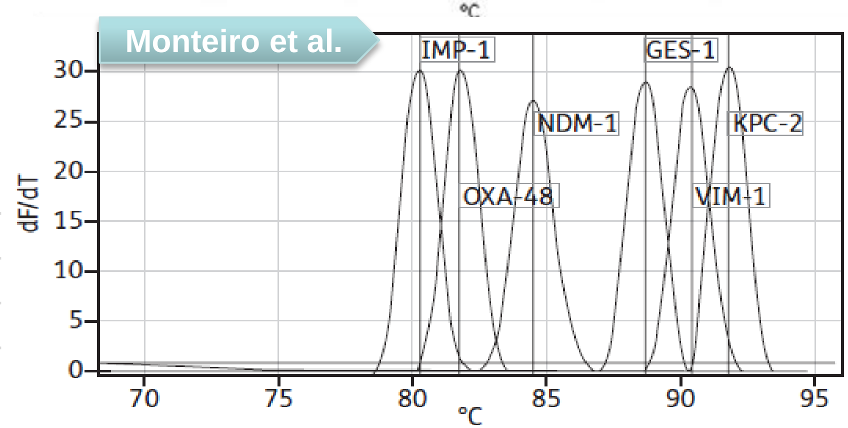
Average temperature deviation:

- **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

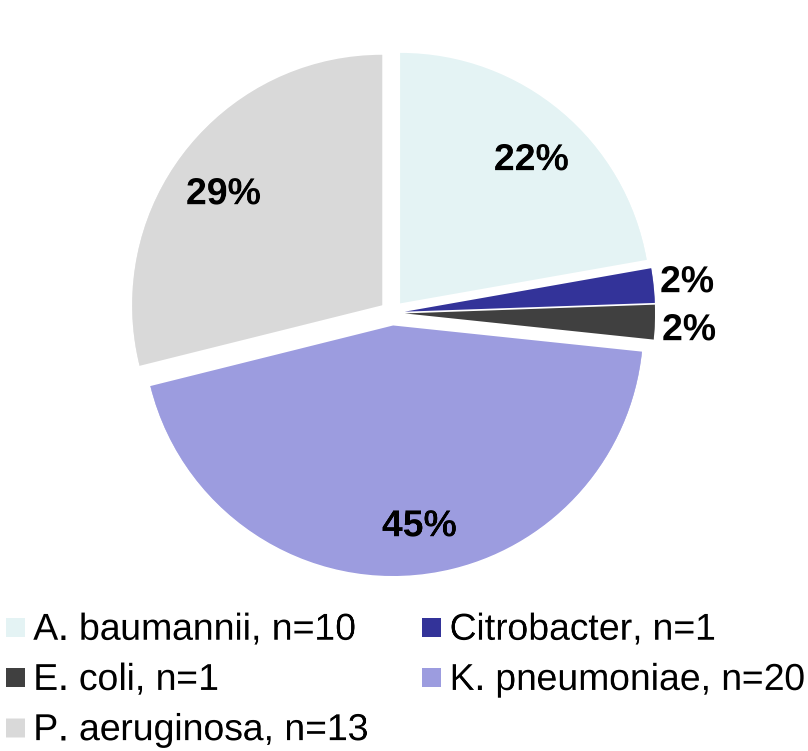




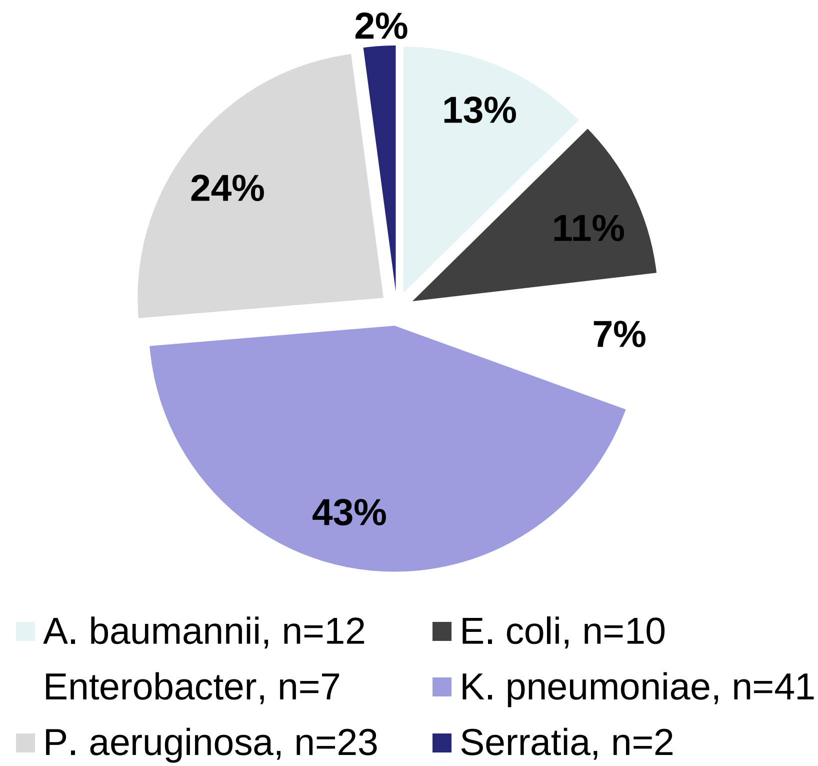
HR-RT-PCR VALIDATION

Validation: NRZ-Bochum

retrospective, n=46



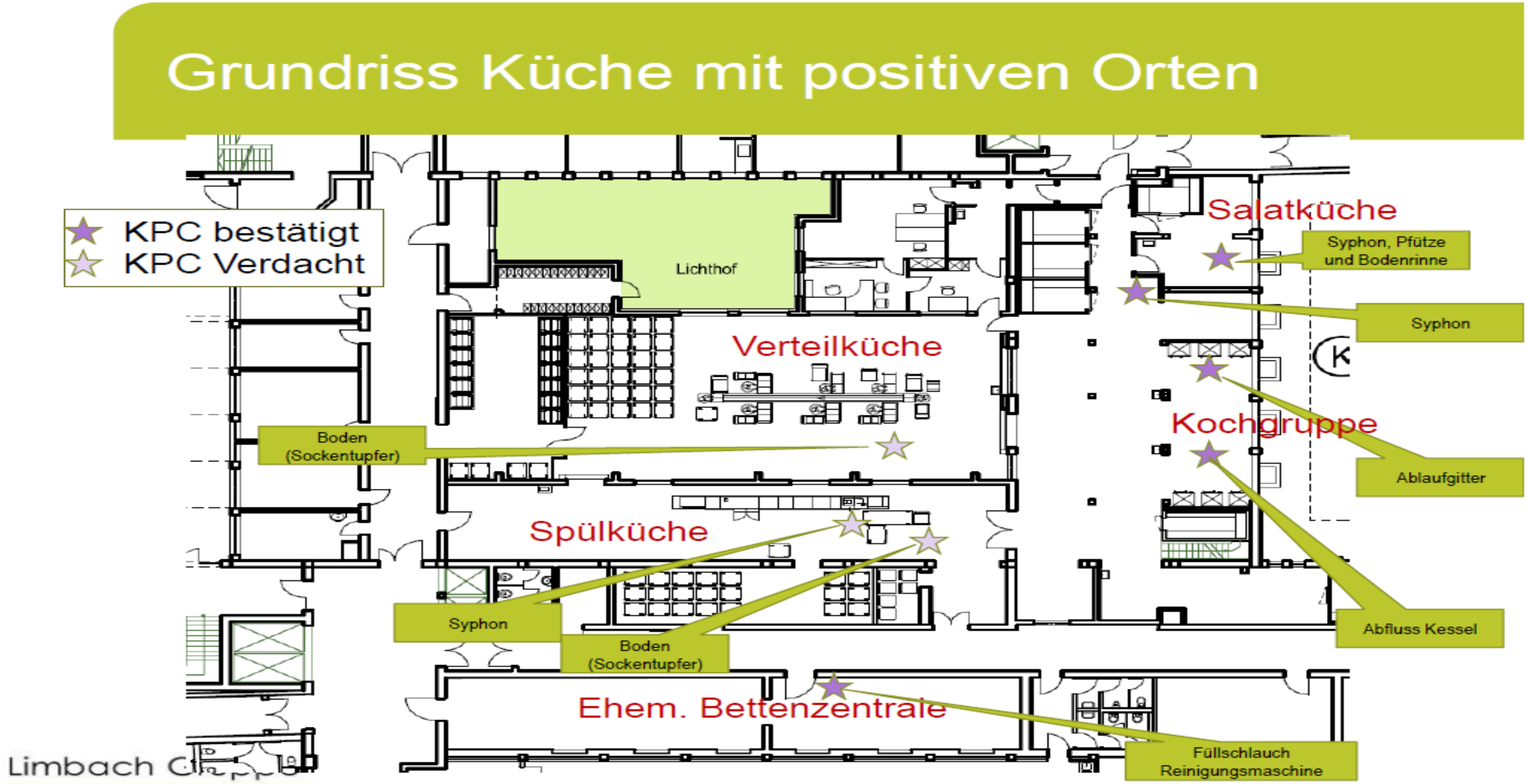
prospective, n=95



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

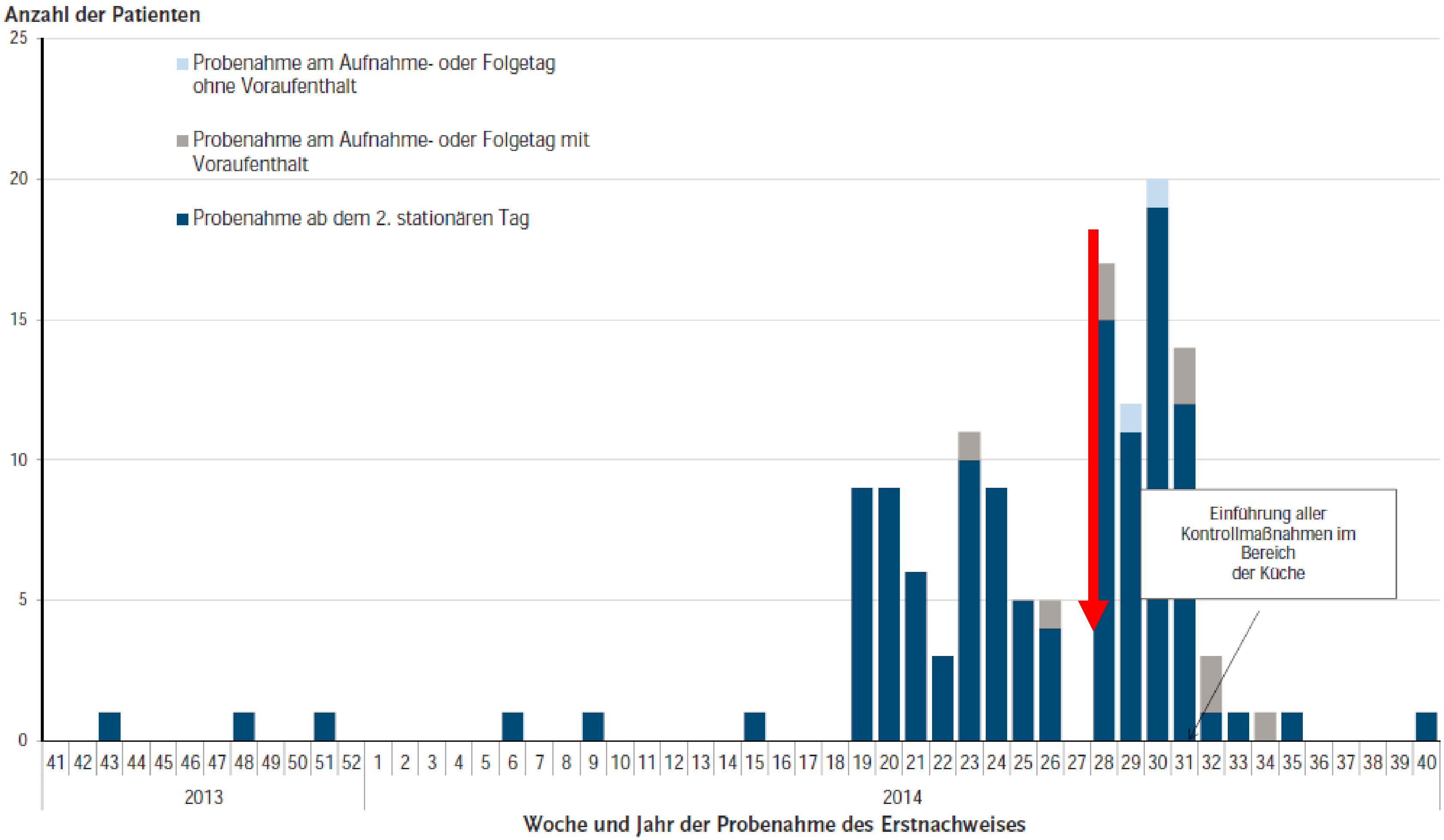

Abb. 1: Epidemische Kurve für 133 Patienten mit Kolonisation oder Infektion durch verschiedene Spezies Carbapenem-resistenter *Enterobacteriaceae*, nach Datum des Erstnachweises und Voraufenthalten, Südhessischer KPC-2-Ausbruch, 1. Oktober 2013 bis 30. September 2014.

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)

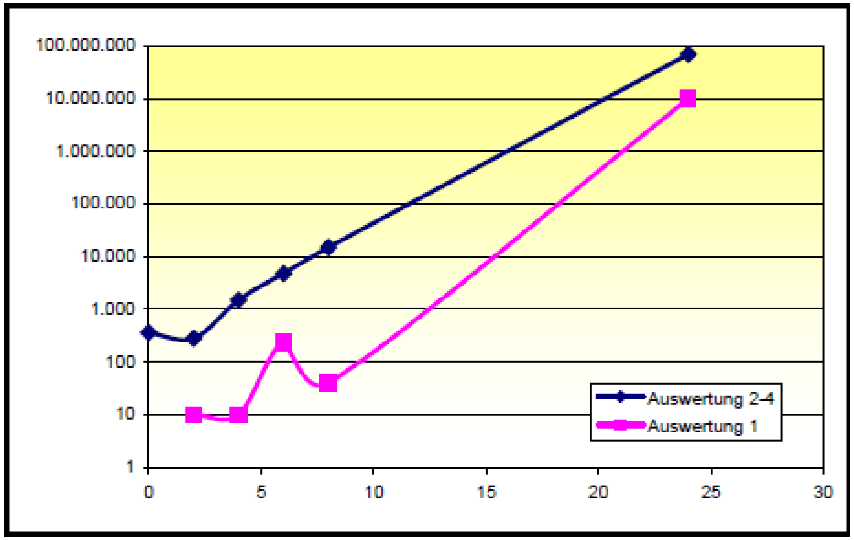
Inkubation bei Zimmertemperatur
Versuchsbeginn: 18.09.2014

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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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

Topics

- Historical aspect (successful strategies in the past)
- Ecological aspects of Gram- negative bacteria
- Examples of reservoir from outbreak investigations
- Additional strategies
- The international perspective
- Conclusion

Aditional strategies

- Disinfection strategies including wet areas especially for terminal cleaning
- Construction criteria (toilettes, sinks, Sink drainage)
- Microbial quality of drinking water, Coliforms, P. aeruginosa NTM)
- Sewage drainage and decontamination of hospital sewage
- Outbreak investigation

BMBF-Fördermaßnahme

NaWaM
Nachhaltiges Wassermanagement

RiSKWa

RiSKWa-Statuspapier

Bewertungskonzepte der Mikrobiologie mit den Schwerpunkten neue Krankheitserreger und Antibiotikaresistenzen

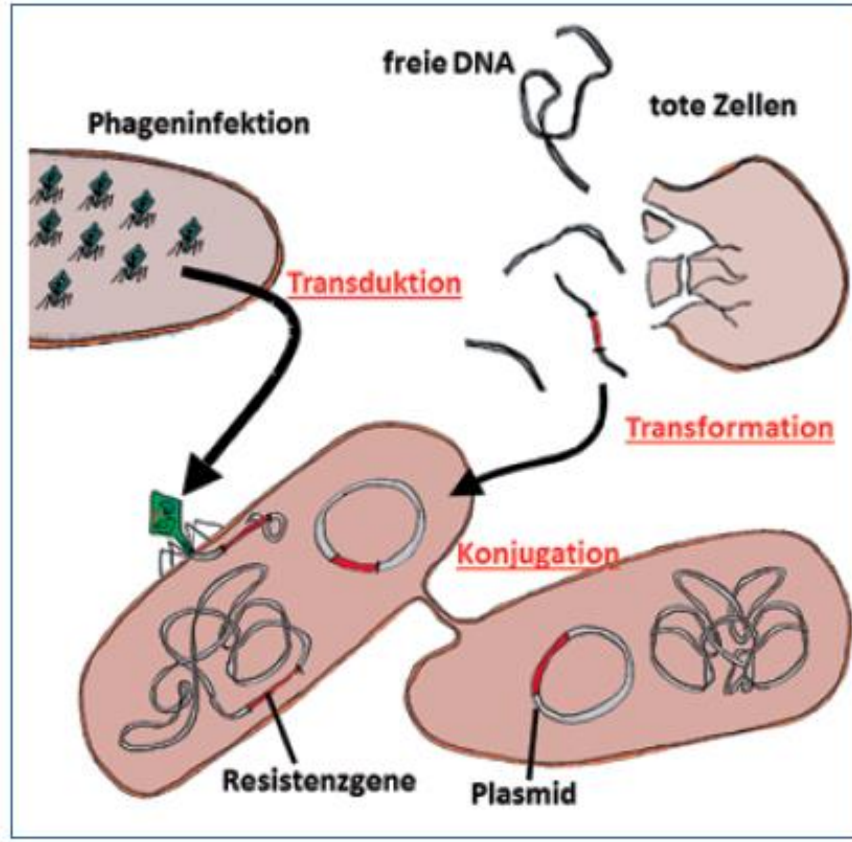
Ergebnisse des Querschnittsthemas „Bewertungskonzepte der Mikrobiologie“

Martin Exner und Thomas Schwartz

GEFÖRDERT VOM

Bundesministerium für Bildung und Forschung

FONA
Nachhaltiges Wassermanagement
BMBF



Distribution of antibiotic resistance in the environment

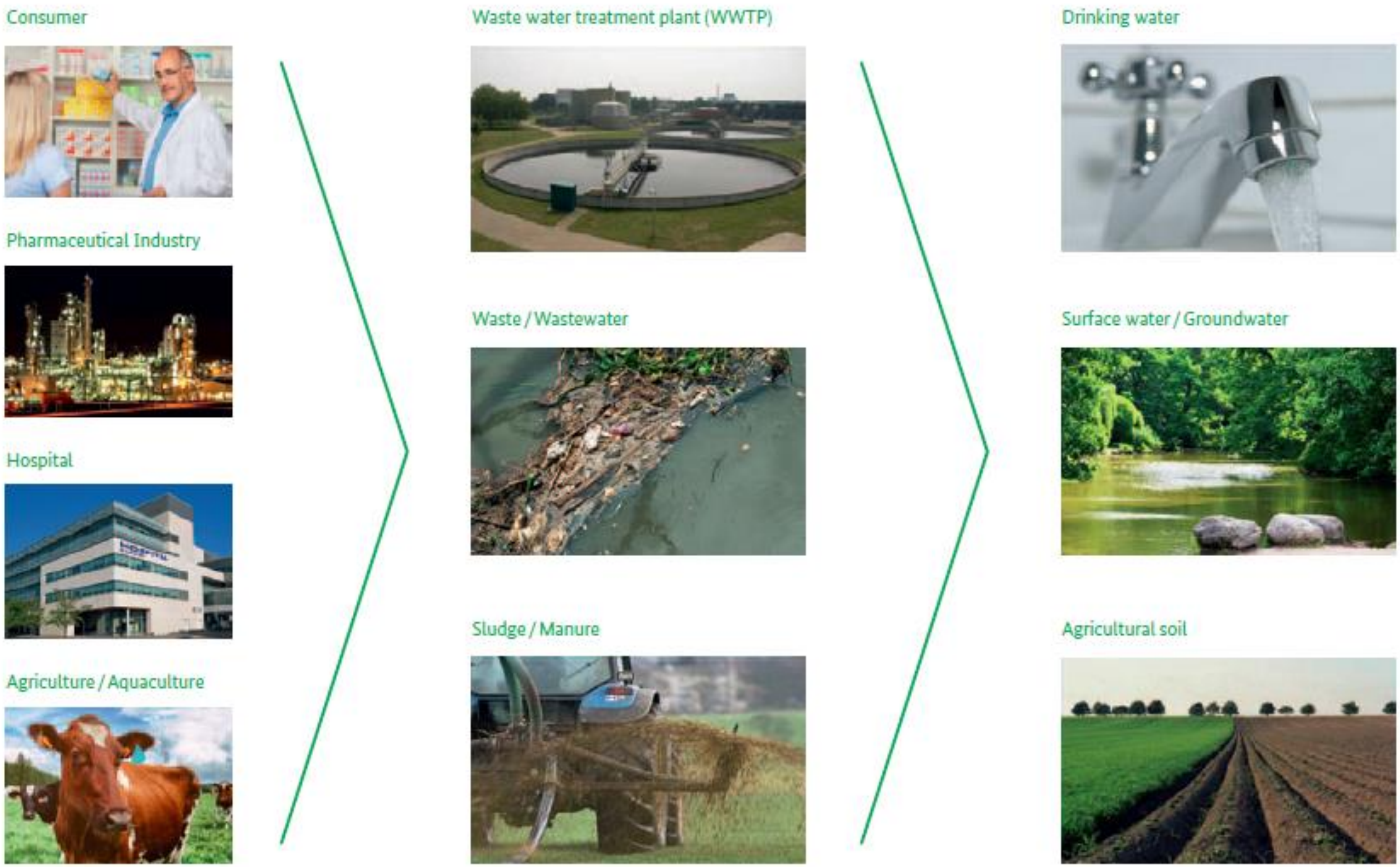
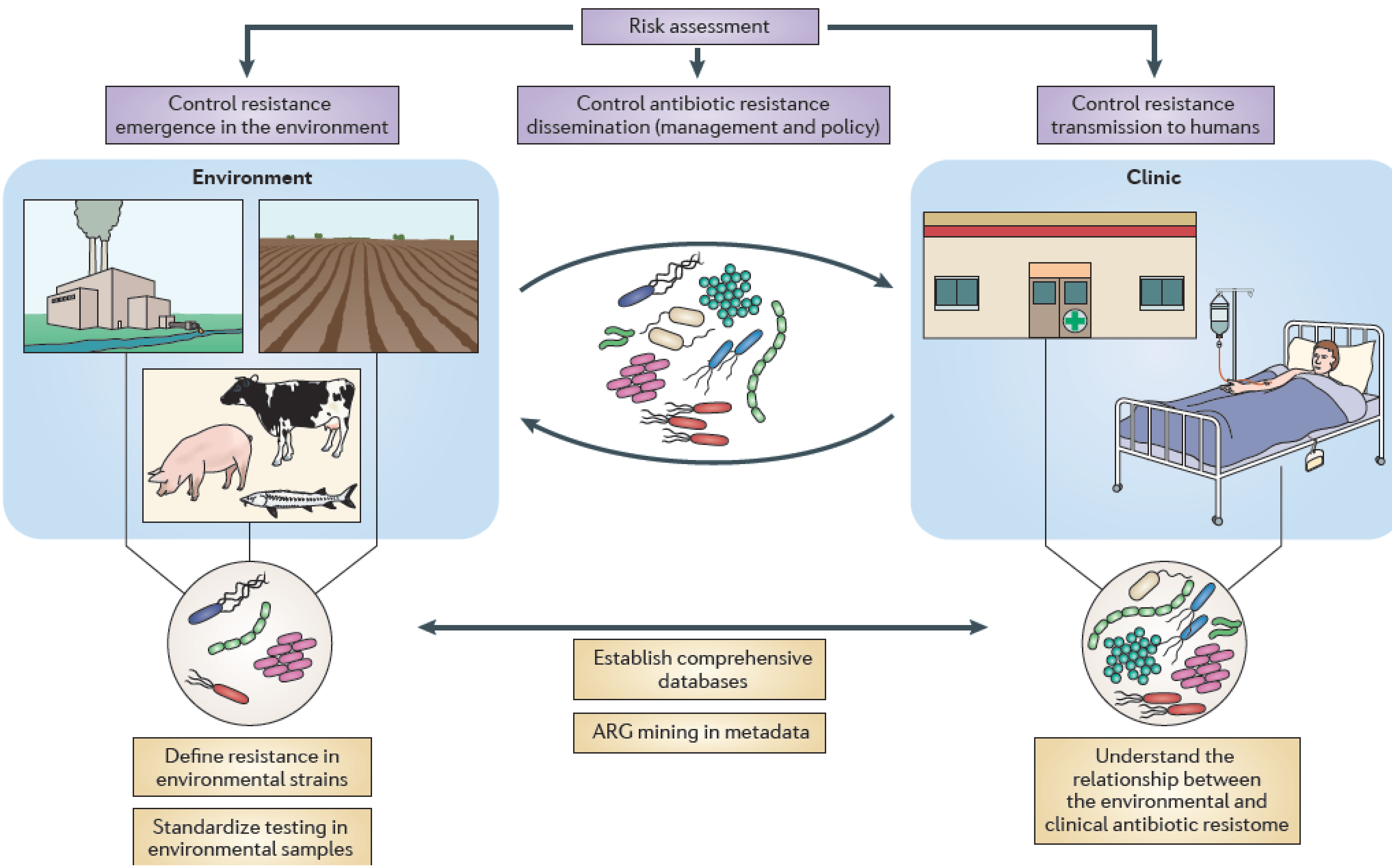
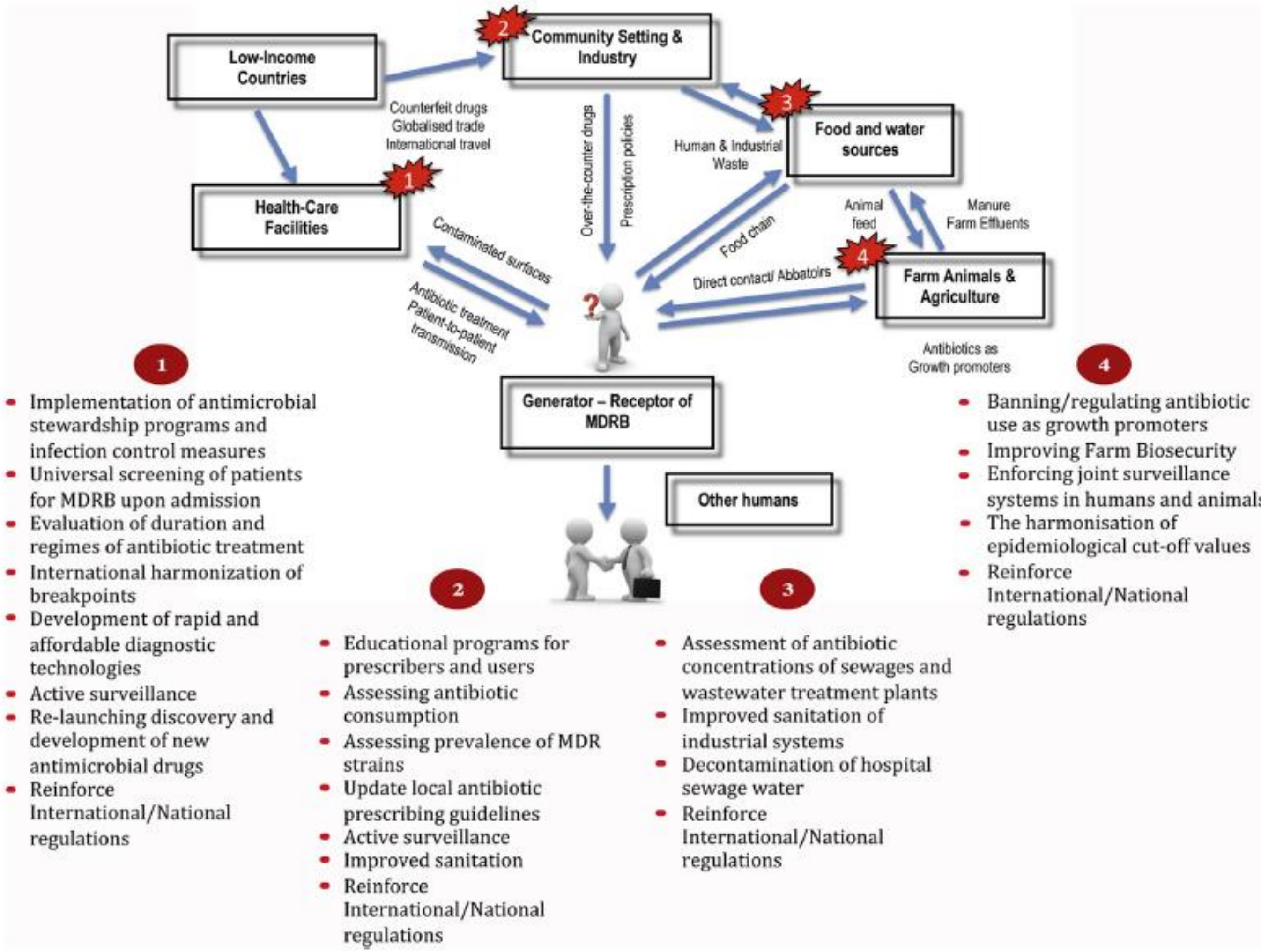


Figure 1: Main emission pathways of human and veterinary pharmaceuticals entering the environment.

Minimizing the spread of antibiotic resistance in the environment.



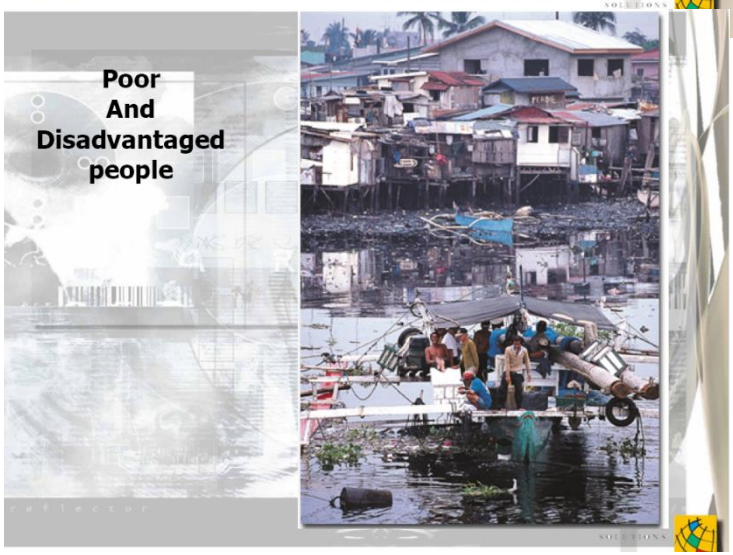
Intervention measures to tackle antibiotic resistance- New Microbe and New Infect 2015; 6: 22–29



Topics

- Historical aspect (successful strategies in the past)
- Ecological aspects of Gram- negative bacteria
- Examples of reservoir from outbreak investigations
- Additional strategies
- The international perspective
- Conclusion

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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Epidemiology of carbapenem resistant Enterobacteriaceae (CRE) during 2000-2012 in Asia - Yanling Xu et al. - J Thorac Dis 2015;7(3):376-385

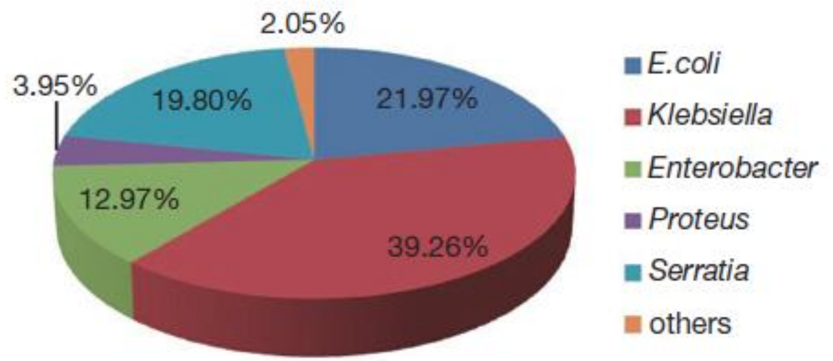

Figure 2 Pathogen distribution of CRE in Asia. CRE, carbapenem resistant *Enterobacteriaceae*.

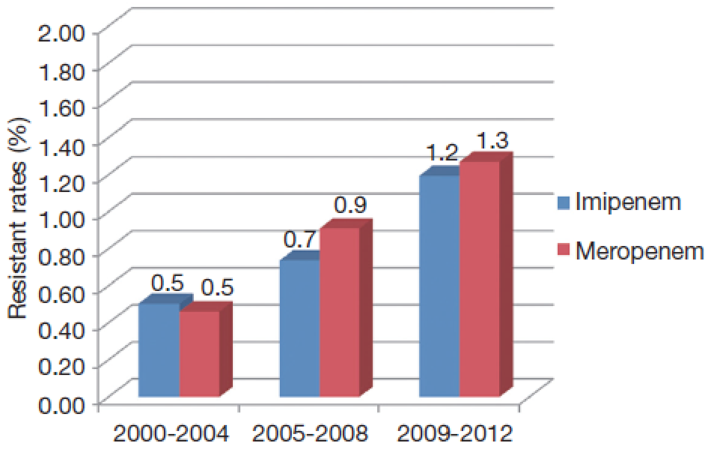

Figure 3 Resistance to impenem and meropenem in *Enterobacteriaceae* during 2000-2012.

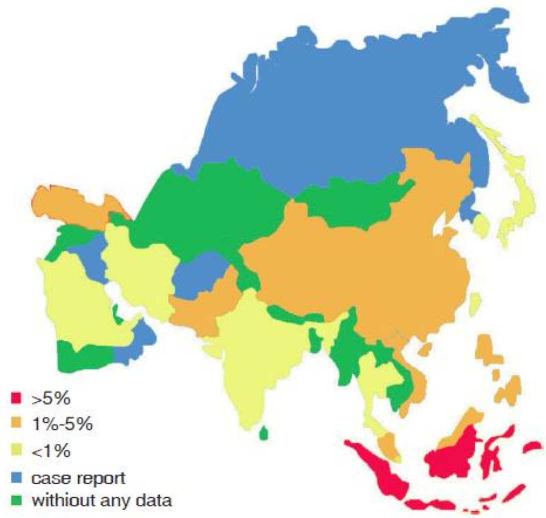

Figure 4 Prevalence of CRE in different Asian counties. CRE, carbapenem resistant *Enterobacteriaceae*.

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.

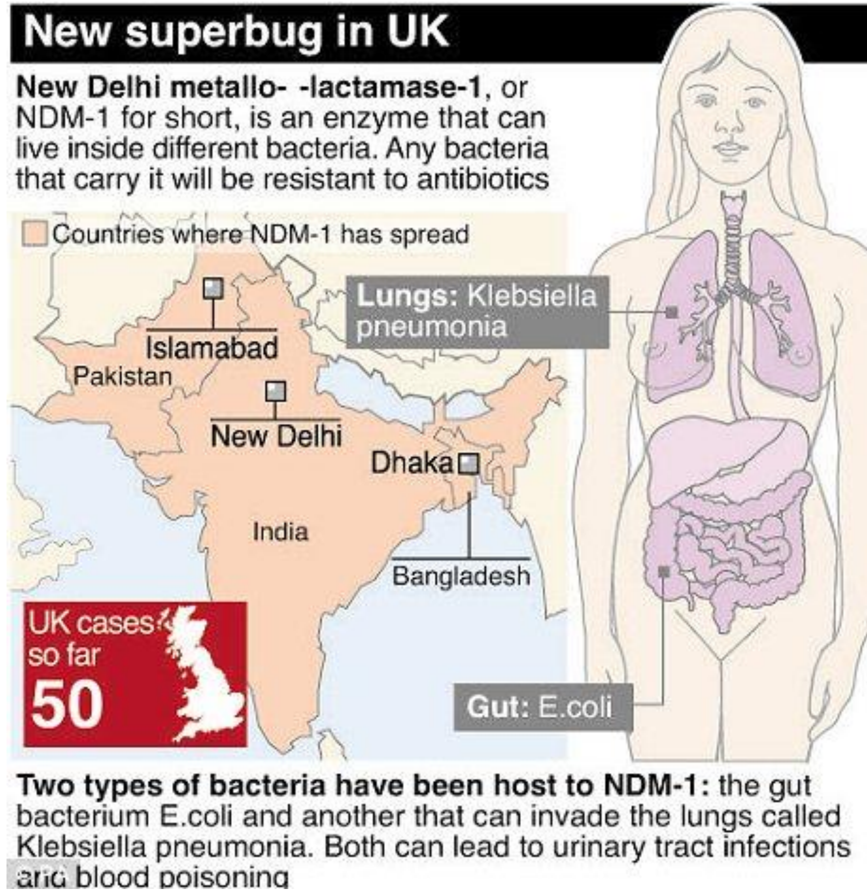

Figure 5: Distribution of NDM-1-producing Enterobacteriaceae strains in Bangladesh, Indian, Pakistan, and the UK

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

Karthikeyan K Kumarasamy, Mark A Toleman, Timothy R Walsh, Jay Bagaria, Fafhana Butt, Ravikumar Balakrishnan, Uma Chaudhary, Michel Doumith, Christian G Giske, Seema Irfan, Padma Krishnan, Anil V Kumar, Sunil Maharjan, Shazad Mushtaq, Tabassum Noorie, David L Paterson, Andrew Pearson, Claire Perry, Rachel Pike, Bhargavi Rao, Ujjwayini Ray, Jayanta B Sarma, Madhu Sharma, Elizabeth Sheridan, Mandayam A Thirunarayan, Jane Turton, Supriya Upadhyay, Marina Warner, William Welfare, David M Livermore, Neil Woodford

Hygiene Health

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

www.thelancet.com/infection **Vol 11 May 2011**

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.

Funding European Union.

Lancet Infect Dis 2011; 11: 355–62

Published Online April 7, 2011 DOI:10.1016/S1473-3099(11)70059-7

See Comment page 334

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

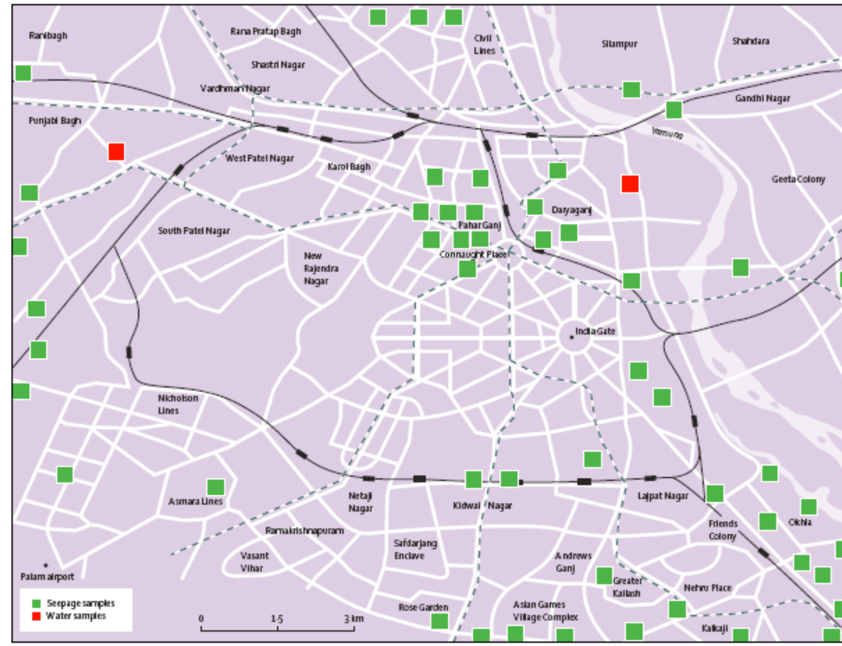

Figure 1: Map of NDM-1-positive samples from New Delhi centre and surrounding areas

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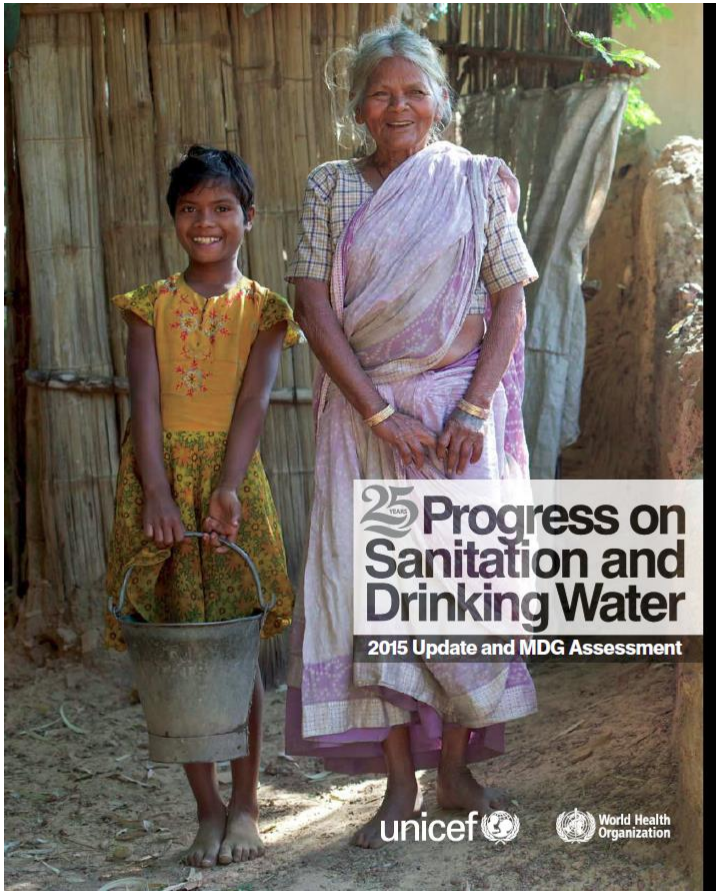


In 47 countries, areas or territories, less than half the population uses improved sanitation in 2015

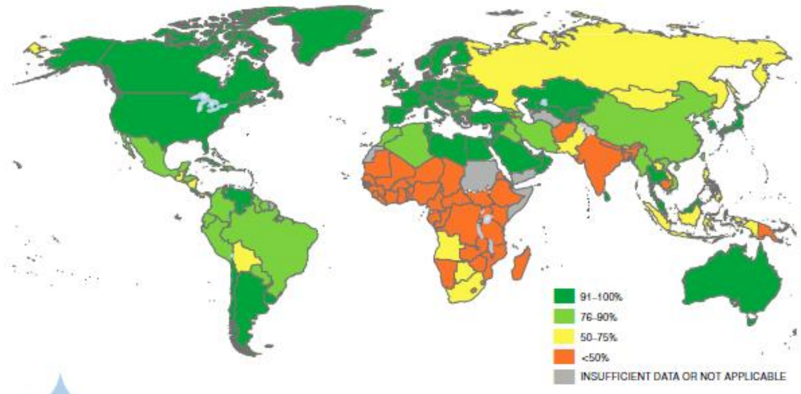


Fig.16 Proportion of the population using improved sanitation facilities in 2015

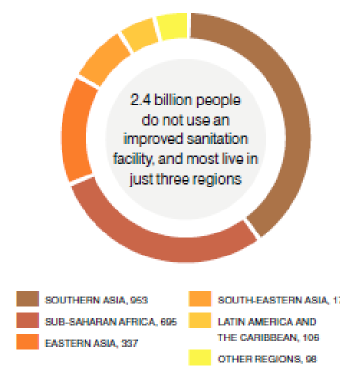
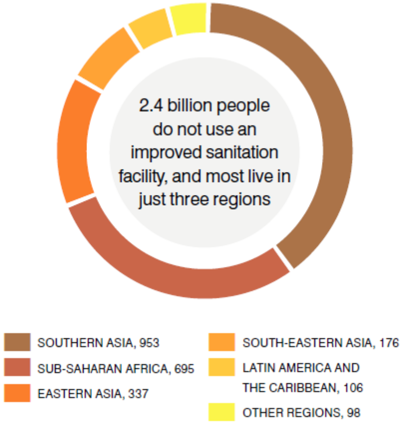
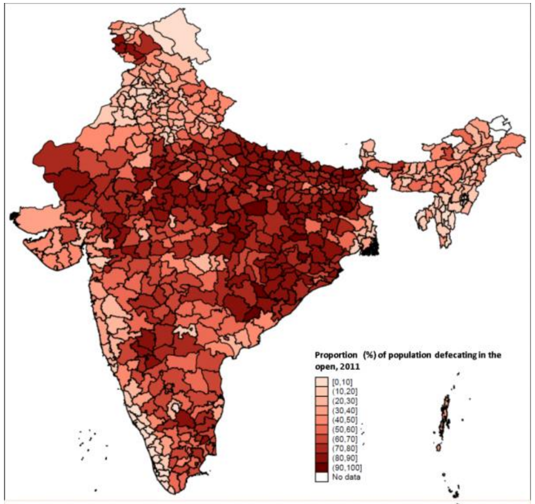


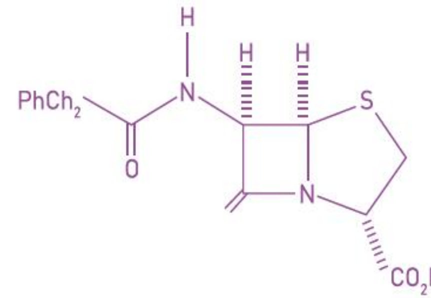
Fig.18 Population without improved sanitation in 2015, by region

Open defecation





Proportion of population defecating in the open, 2011



What you need to know

WHO's first global report on antimicrobial resistance, with a focus on antibiotic resistance, reveals that it is no longer a prediction for the future. Antibiotic resistance - when bacteria change and antibiotics fail - is happening **right now**, across the world

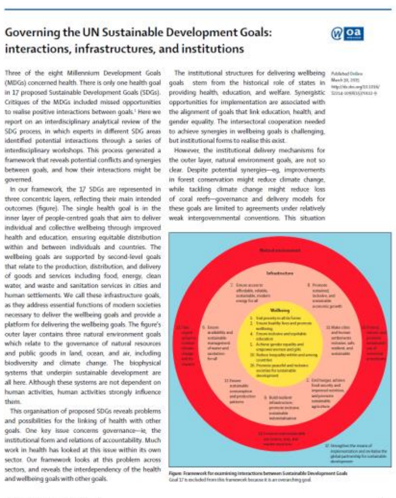
What does this mean?

Without urgent action we are heading for a post-antibiotic era, in which common infections and minor injuries can once again kill

How can infections be prevented in the first place to reduce the need for antibiotics?

- Better hygiene
- Access to clean water and sanitation
- Infection control in healthcare facilities
- Vaccination

Governing the UN sustainable development goals



Governing the UN Sustainable Development Goals: interactions, infrastructures, and institutions

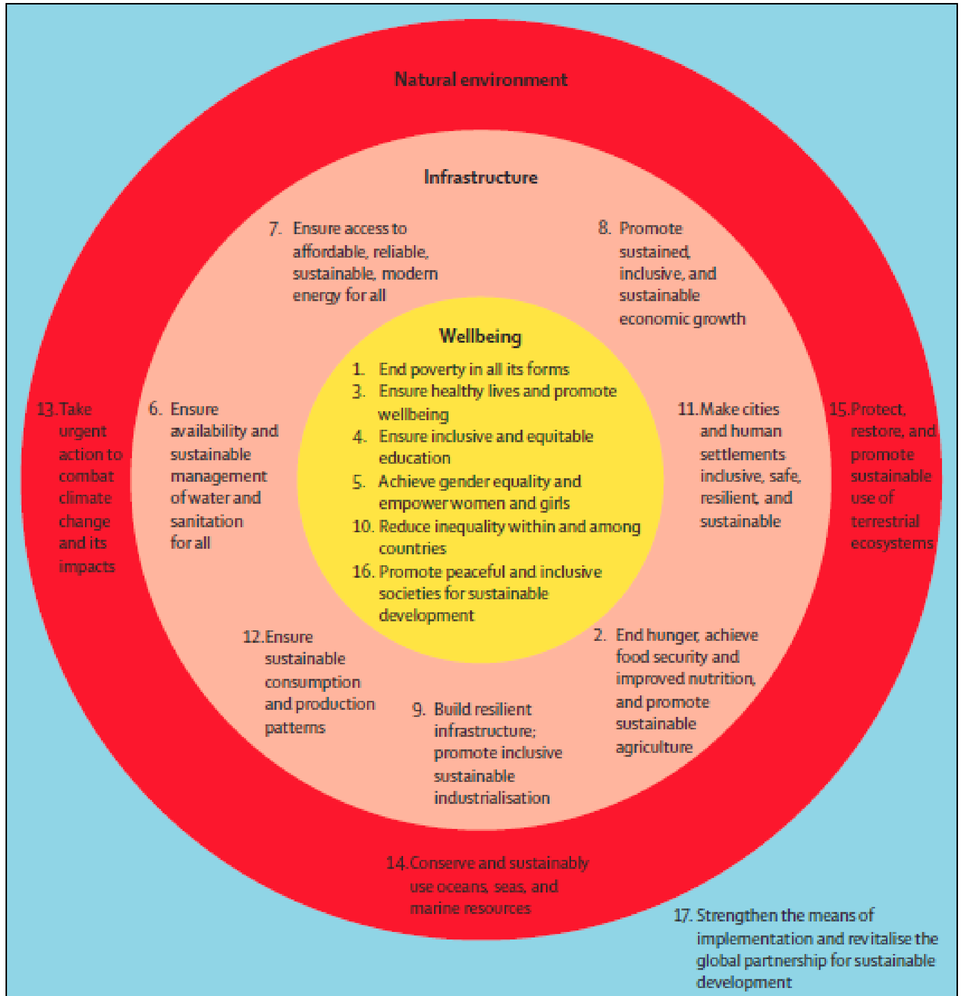


***Figure:* Framework for examining interactions between Sustainable Development Goals**
Goal 17 is excluded from this framework because it is an overarching goal.

TRANSFORMING OUR WORLD:
THE 2030 AGENDA FOR SUSTAINABLE DEVELOPMENT
Finalised text for adoption (1 August 2015)

Goal 6. Ensure availability and sustainable management of water and sanitation for all

6.1 By 2030, **achieve universal and equitable access to safe and affordable drinking water for all**

6.2 By 2030, **achieve access to adequate and equitable sanitation and hygiene for all and end open defecation,** paying special attention to the needs of women and girls and those in vulnerable situations

6.3 By 2030, **improve water quality by reducing pollution, eliminating dumping and minimizing release of hazardous chemicals and materials, halving the proportion of untreated wastewater and substantially increasing recycling and safe reuse globally**

Lancet Infectious diseases Sept. 2015

Editorial

Concerns raised over water quality at the Rio Olympics

A recent investigation by Associated Press on water quality at aquatic venues for the 2016 Olympic Games in Rio de Janeiro, Brazil, has raised concerns about the risk to the health of athletes who will compete next year. The article says that athletes "will be swimming and boating in waters so contaminated with human faeces that they risk becoming violently ill and unable to compete". In fact, it goes on to say that competitors have already fallen ill while training in Rio in preparation for the games. However, the quality of water in Brazil is not a new problem; the article points out that "extreme water pollution is common" since most sewage goes untreated. Hence, "raw waste runs through open-air ditches to streams and rivers that feed Olympic water sites".

The issues of sanitation and the risk to the health of athletes raised in this news story are indeed a concern. Nearly 1400 of the more than 10 000 athletes competing at the games will be directly exposed to the contaminants in this water as they engage in sailing, swimming, canoeing, rowing, etc. Athletes competing in aquatic events should be familiar with the risks of water-borne infections: only 5 years ago former British Olympic rower Andy Holmes died from Weil's syndrome caused by infection with leptospira caught from the freshwater of Lincolnshire, UK. However, despite the very real worries about the health of competitors, the story largely glosses over the broader and more important issue of how water quality affects the people of Brazil, and misses the opportunity to, even briefly, reflect on how poor sanitation is still an urgent worldwide problem.

That sanitation is still a pressing issue is particularly disappointing given that the challenge to reduce the proportion of the global population without safe drinking water or basic sanitation was laid out in the millennium development goals (MDGs). A recent joint WHO and UNICEF report, *Progress on sanitation and drinking water: 2015 update and MDG assessment*, outlines that there is still much to do. The report highlights that, although major advances have been made, 2·4 billion people live without sanitation facilities, meaning the MDG target has been missed by nearly 700 million people. The reasons behind this shortfall are given as inadequate investments in behaviour change campaigns, lack of affordable products for poor people, and social norms that accept or even encourage open defecation.

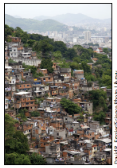
The WHO/UNICEF report puts access to adequate water, sanitation, and hygiene in clear terms: improvements are crucial for the prevention of 16 of the 17 neglected tropical diseases and care of those with these diseases. The report also makes it clear that the solutions go beyond specific interventions and infrastructure, since a major problem is open defecation, which the report states "is one of the clearest manifestations of extreme poverty".

To take efforts forward, plans for improvements in sanitation are laid out in the sustainable development goals (SDGs) to be set by the UN General Assembly in September. The sixth of these goals (SDG 6) will be to ensure availability and sustainable management of water and sanitation for all. This goal encompasses many ambitious targets to be met by 2030, including "access to adequate and equitable sanitation and hygiene for all, and end open defecation, paying special attention to the needs of women and girls and those in vulnerable situations".

Broader still is the importance adequate water, sanitation, and hygiene has on the prevention of childhood diarrhoeal diseases—the second leading cause of death in children younger than 5 years, killing more children each day than AIDS, malaria, and measles combined. Yet despite the enormous importance of these diseases, it seems easier to get press attention about potential digestive upset of Olympic athletes.

Issues of water quality and sanitation worldwide need to be voiced while they are the focus of public attention. The risks to athletes, although real and serious, are only transient when compared with the day-in day-out risk to the residents of poorer countries, particularly children. Among all SDGs, achievement of SDG 6 could have the greatest bearing on health worldwide. We should keep in mind that sanitation and hygiene are the greatest human achievements in terms of extending life expectancy, and we must seize every opportunity to raise awareness and make these benefits available to all.

■ *The Lancet Infectious Diseases*



David R. Frazier/Science Photo Library

For the **report on water quality at the Rio Olympics** see http://bigstory.ap.org/article/d92f6af5121f49d982601a657d745e95/ap-investigation-rios-olympic-water-rife-sewage-virus

For more on the **death of Andy Holmes** see Newsdesk *Lancet Infect Dis* 2010; **10:** 823

For the **proposed SDGs** see https://sustainabledevelopment.un.org/sdgsproposal.html

For more on **diarrhoeal diseases** see http://www.who.int/mediacentre/factsheets/fs330/en/

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Topics

- Historical aspect (successful strategies in the past)
- Ecological aspects of Gram- negative bacteria
- Examples of reservoir from outbreak investigations
- Additional strategies
- The international perspective
- Conclusion

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Ecology of Gram-negative pathogens in the environment – where are their habitats?

Thank you

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