Superbugs: Why bother?

Marc Bonten, University Medical Center Utrecht, The Netherlands

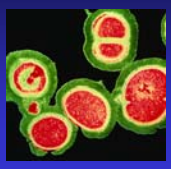
The most important superbugs

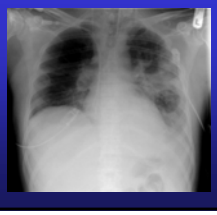
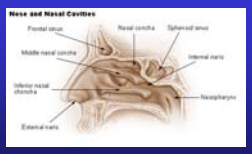
Methicillin-Resistant Staphylococcus aureus (MRSA)

Vancomycin-Resistant Enterococci (VRE)

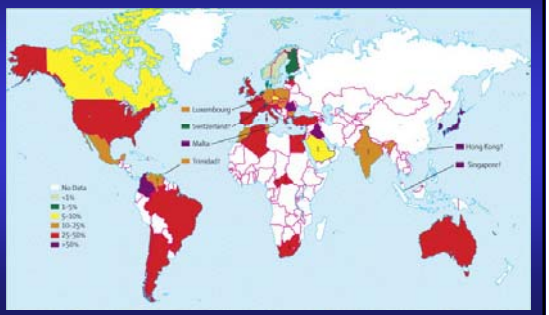
Clostridium difficile type 027

Methicillin-resistant Staphylococcus aureus



Global prevalence of MRSA (% of S. aureus bacteremia)

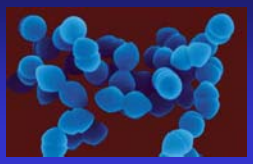


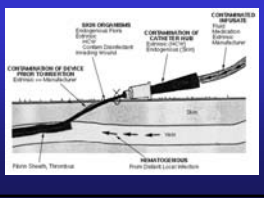
Clostridium difficile 027




C. difficile colitis

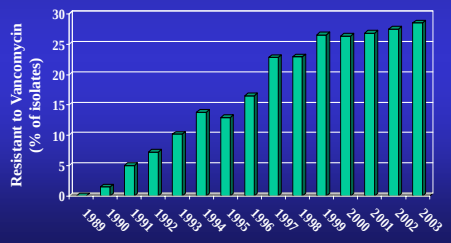
Vancomycin-resistant enterococci



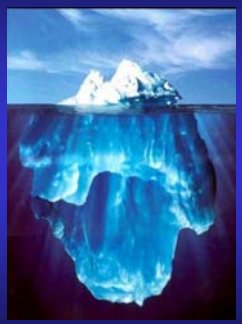
VRE in US hospitals

1986: First VRE in UK and France



NNIS October 2004; Am J Infect Control 2004

The ice-berg phenomena



Documented infection

Non-documented carriage

Antibiotics active at time of introduction

	S. aureus	Enterococcus	C diff
Penicillin	+	+	X
Oxacillin	+	+	X
Cephalosporins	+	X	X
Ciprofloxacin	+	+	+
Metronidazole	X	X	+
Vancomycin	+	+	+
Linezolid	+	+	X
Daptomycin	+	+	X

Antibiotics active in 2007

	MRSA	VRE	C diff 027
Penicillin	X	X	X
Oxacillin	X	X	X
Cephalosporins	X	X	X
Ciprofloxacin	X	X	X
Metronidazole	X	X	+
Vancomycin	+	X	+
Linezolid	+	+	X
Daptomycin	+	+	X

What promotes the spread of superbugs?

- Insufficient hand hygiene
- Contamination of inanimate surfaces
  - Everything surrounding a patient
- Antibiotics
  - Suppress other bacteria, but not the resistant ones

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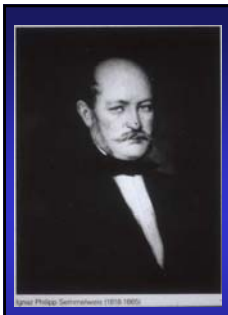
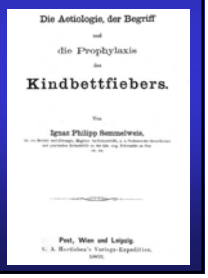


Ignaz Philipp Semmelweis, born in Budapest 1815

The principles of hospital infection control

- 1847: hand-hygiene with chloride reduced death from puerperal fever
- 1848: fired
- 1850-56: worked in Budapest
- 1861: first publication


Die Aetiologie, der Begriff
und
die Prophylaxis
des
Kindbettfiebers.
Von
Ignaz Philipp Semmelweis.
Pest, Wien und Leipzig.

Water and soap

1-2 minutes

Alcohol-based hand gel

10-20 seconds

Theoretical framework for pathogen acquisition and spread

What fueles cross-transmission?

- Insufficient hand hygiene
- High contact rates
- Contacts with different patients

What fueles cross-transmission?

- Insufficient hand hygiene
  - Workload of health care workers
  - Unavailibility of alcohol rub dispensers / sinks
  - Neglecting existing protocols!
- High contact rates
  - Workload of health care workers
  - Staffing levels
- Contacts with different patients
  - Staffing levels

Chicago — Who's to blame?

Chicago — Who's to blame?

Transmission depends on:

Number of nurses/docters

Contact rate

Level of hand hygiene

Level of cohorting

= likelihood that the next patient contact is with the same patient

Number of potentially contaminated contacts for nurses and physicians

S. Nijssen et al. Arch Intern Med 2003

Potential number of contaminated contacts per hour

CR x N_{hcw} x (1 – q) x (1 – p)

- CR = contact rate
- q = cohort level
- p = compliance level

Nurses (as a group)

2.6 x 9.6 (1 – 0.77) x (1 – 0.59) = **2.4 per hour**

Physicians (as a group)

1.2 x 6 x (1 – 0.08) x (1 – 0.43) = **3.8 per hour**

Physicians' Relative Risk for transmission = 3.8/2.4 = 1.6 (+60%)

What promotes the spread of superbugs?

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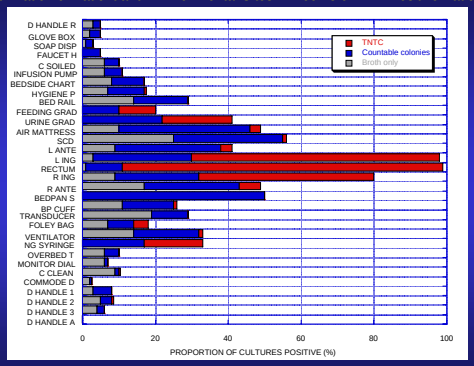
Colonization of Patient and Environmental Sites in Rooms of VRE-Positive Patients



Blom D et al, 40th ICAAC, 2000, Abst. No. 1963, p. 432.

What promotes the spread of superbugs?

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Why bother?

- If total burden of infections increases
  - More patients develop infections
- If patient outcome after infections decreases
  - More patients die from infections, or length of stay after infection increases
- Horror scenario: Total burden increases and outcome decreases

The case Clostrdium difficile 027 in Quebec

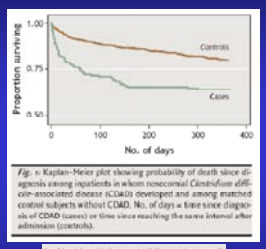
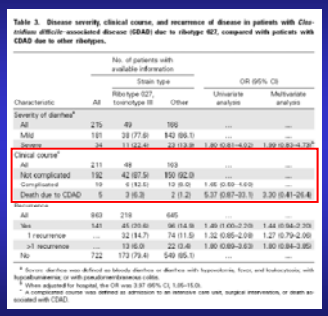


Fig. 1. Kaplan–Meier plot showing probability of death since diagnosis among inpatients in whom nosocomial *Clostridium difficile*–associated disease (CDAD) developed and among matched control subjects without CDAD. No. of days = time since diagnosis of CDAD (cases) or time since reaching the same interval after admission (controls).

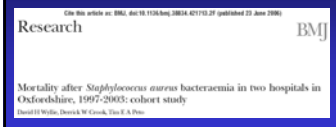
Two thousand deaths is the most plausible number based on the data available. — Dr. Jacques Pépin

Quebec's official numbers:
439 *C. difficile* deaths

The case Clostrdium difficile 027 in the Netherlands

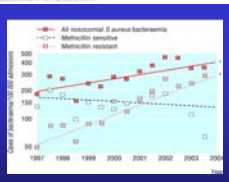


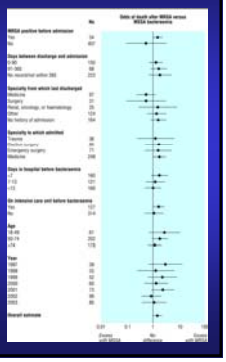
The case of MRSA in Oxford, UK


Research

BMJ

Mortality after *Staphylococcus aureus* bacteraemia in two hospitals in Oxfordshire, 1997-2003: cohort study





If the trend is your friend

Trends in nosocomial blood stream infections (NB) 1996-2005

Number per year: on average 495 ±38, no change in time

But, no. of admissions decreased with 18%

length of stay decreased from 7 days to 6 days

no of patientdays decreased with 31%

Incidence NB / 10,000 admission increased with 31%

Incidence NB / 100,000 patient days at risk increased with 58%

MRSA in Europe 2005

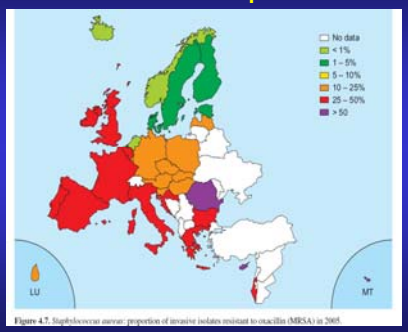


Figure 4.7. Staphylococcus aureus: proportion of invasive isolates resistant to oxacillin (MRSA) in 2005.

EARSS Annual Report 2006

The Search & Destroy policy

I Identified carriers are isolated
II High-risk patients are screened on admission and precautiously isolated
III Unexpected case of MRSA -> screening of contact patients
IV Evidence of MRSA-transmission -> ward closed
V Unexpected case of MRSA -> screening of health care workers
VI Decolonization of carriers

Justification of MRSA-control policy

1. MRSA infection is detrimental for a patient
2. MRSA-control policy is NOT detrimental for a patient
3. This policy is cost-effective
4. There are no (hardly) antibiotic alternatives for MRSA-infections
5. Policy guarantees future success

Medisch Contact: May 30, 2003: Nurse reports on her experience with Search & Destroy

- Man, summer 2002, motor accident in Scotland, multiple fractured right rechter femur + left radius, aorta-endoprothesis, university hospital A.
- After 2 surgical procedures, after 2 weeks, repatriated to the the Nederlands
- Non-university hospital -> MRSA-isolation
- 3 days waiting: no blood exams, no physical exam, no nursing care
- 40^0 C fever, 10/d green diarrhea, almost dehydrated
- Food placed in ante-room (2 crutches, 1 fixed to left arm)
- Day 3 lab: ESR 125, CRP 97, Hb 4.7
- End of day 4: no MRSA
- Left hospital against medical advice

Frequency and Duration of Contact Between Healthcare Workers and Patients

	Pts in Contact Isolation	Controls	P
Mean (range) room entries/h	3.9 (0-8)	7.9 (1-26)	0.06
Mean (range) contacts/h	2.1 (0-6)	4.2 (1-13)	0.03
Mean (range) duration of interaction (min)	4.5 (0.08-30)	2.8 (0.08-18)	0.6

Kirkland Kathryn B and Weinstein Jill M, Adverse effects of contact isolation, *Lancet* 1999; 352:1177-8.

Safety of patients isolated for infection control.

Stelfox et al. JAMA 2003; 290: 1899-1905

	Isolated patients (n=150) vs control patients (n=300)
Measures	Test Statistic (95% CI)
Vital signs incompletely recorded	1.92 (1.61-2.30)
Days with no nursing narrative notes	1.77 (1.40-2.34)
Days with no physician narrative notes	2.91 (1.90-4.47)
Adverse events (any, rate /1000 days)	2.20 (1.47-3.30)
Nonpreventable events	0.99 (0.54-1.81)
Preventable events	6.96 (3.38-14.3)
Supportive care failure	8.27 (3.09-22.1)
Patient dissatisfaction, (in)+ formal complaints	23.5 (8.20-66.4)

3.
Policy is cost-effective

Costs associated with a strict policy to eradicate MRSA in a Dutch UMC: a 10-year survey.
Vriens et al. Eur J Clin Microbiol Infect Dis 2002; 21: 782-6

Reason costs were incurred	Explanation of costs	Costs (kEuro)
Cleaning	ICU and wards	207
HCW	Temporary suspension from work	149
Cultures	Patients and HCW	953
Drugs	Additional/special	72
Department costs	Additional material	213
Loss of hospitalization days		931
Fewer surgical procedures		249
Total		2.774

4.
No antibiotic alternatives

Linezolid
Quinipristin/dalfopristin
Daptomycine

5.

Control policy guarantees future success

All predictions are difficult, especially when they involve the future
Niels Bohr/Yogi Bear

Annals of Internal Medicine | ARTICLE

Emergence of Community-Acquired Methicillin-Resistant *Staphylococcus aureus* USA 300 Clone as the Predominant Cause of Skin and Soft-Tissue Infections

Conclusions: The community-acquired MRSA USA 300 clone was the predominant cause of community-onset *S. aureus* skin and soft-tissue infection. Empirical use of agents active against community-acquired MRSA is warranted for patients presenting with serious skin and soft-tissue infections.

Ann Intern Med. 2006;144:309-317.

THE NEW ENGLAND JOURNAL of MEDICINE

ORIGINAL ARTICLE

Methicillin-Resistant *S. aureus* Infections among Patients in the Emergency Department

Gregory J. Moran, M.D., Anusha Krishnadasan, Ph.D., Rachel J. Gorwitz, M.D., M.P.H., Gregory E. Fosheim, M.P.H., Linda K. McDougal, M.S., Roberta B. Carey, Ph.D., and David A. Talan, M.D., for the *EMERGEncy* ID Net Study Group*

CONCLUSIONS

MRSA is the most common identifiable cause of skin and soft-tissue infections among patients presenting to emergency departments in 11 U.S. cities. When antimicrobial therapy is indicated for the treatment of skin and soft-tissue infections, clinicians should consider obtaining cultures and modifying empirical therapy to provide MRSA coverage.

N ENGL J MED 355;7 WWW.NEJM.ORG AUGUST 17, 2006

Conclusions I (facts)

- There is emergence of multiple antibiotic-resistant bacteria in hospitals, worldwide.
- There is no evidence, that infections with these bacteria are associated with improved patient outcome.
- Failure of adherence to basic hygiene measures is generally considered to contribute to this emergence.
- Problems with multiple antibiotic-resistant bacteria are increasingly occurring in the community.

Conclusions II (but…)

- It is unknown if (or to what extent) the total burden of infections in hospitals increases.
- The possible (or probable) detrimental effect of these infections on patient outcome are not quantified.
- The contribution of different aspects of basic hygiene measures to control spread are not quantified.
- Staffing levels are seldomly (but increasingly) considered a parameter of infection control.
- The negative effects of infection control measures are not quantified.