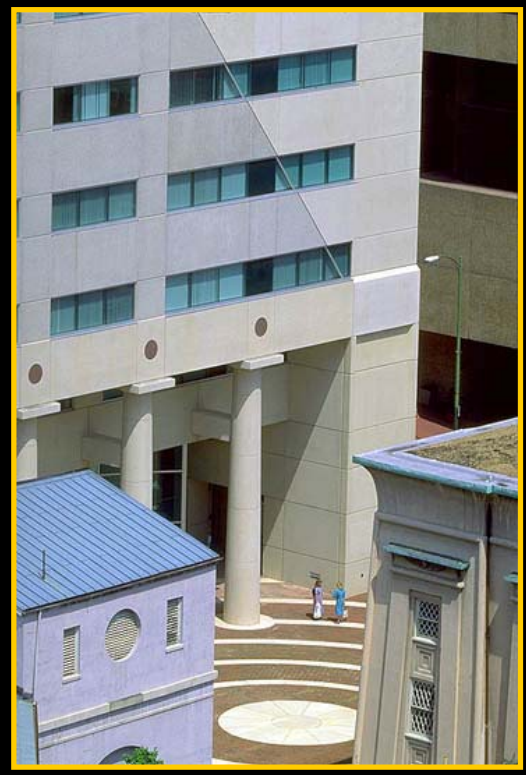
Infectious Diseases Outbreaks: CA-MRSA, *A.baumanii* and *C.difficile*

SEACM

Virginia Spring Meeting

April 21, 2006



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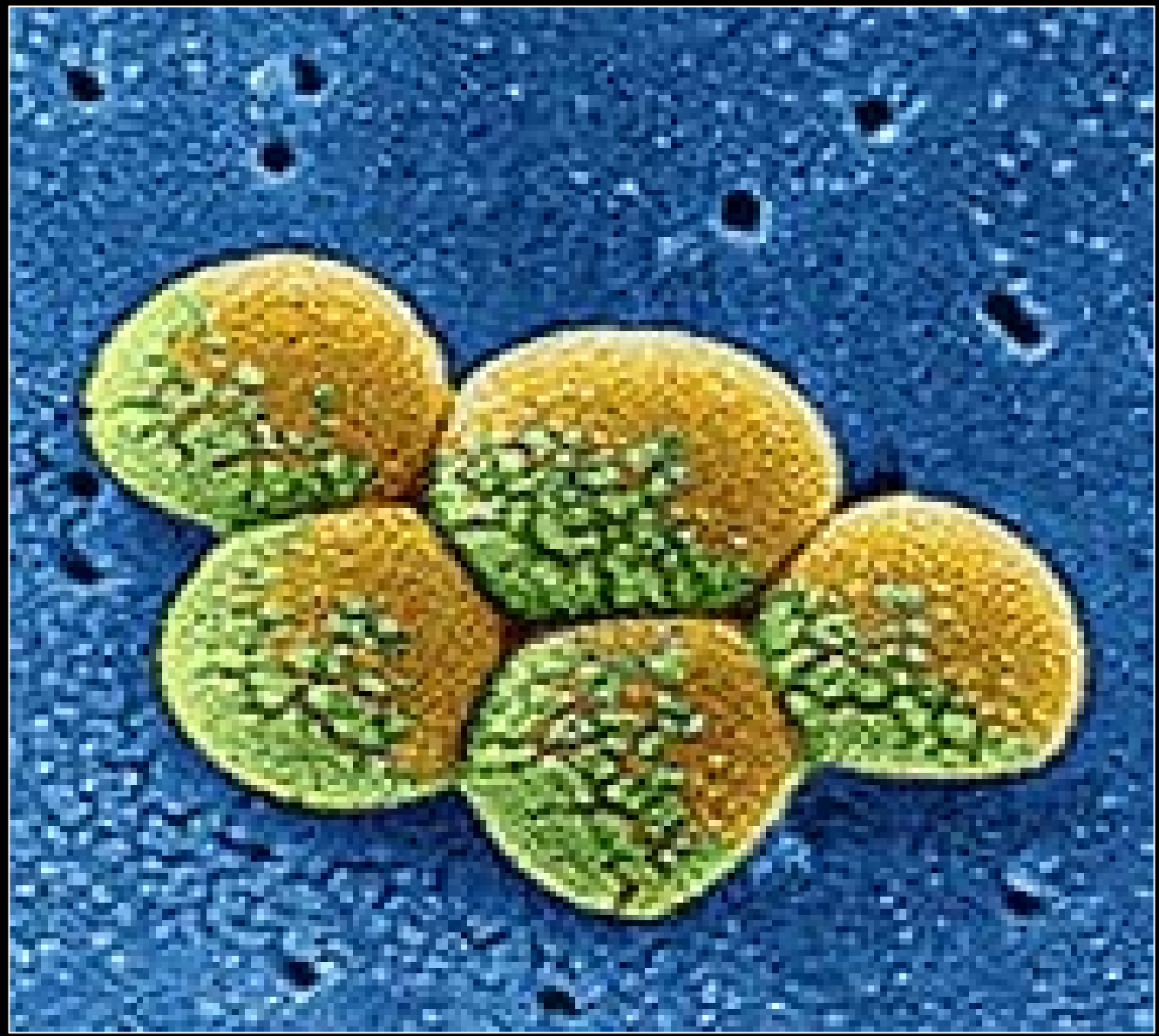
Outline

- Community acquired MRSA
  - Epidemiology
  - Important Clinical Syndromes
  - Outbreaks and risk factors
- *A.baumanii*
  - Epidemiology
  - Important nosocomial outbreaks and risk factors
- *C.difficile*
  - Epidemiology, emergence of a new, more virulent strain
  - Outbreaks
  - Risk factors
- Importance of infection control to limit cross transmission

Community Acquired MRSA



Staphylococcus aureus Facts

- • Up to 30% of healthy people carry *S. aureus* in their anterior nares and other hairy or moist body areas.
- • *S. aureus* causes approximately 12% of all hospital-acquired infections in the United States.
- Pooled data from all ICUs in the National Nosocomial Infections Surveillance (NNIS) System reveal that *S. aureus* causes :
  - 13% of bloodstream infections
  - 18 % of nosocomial pneumonias
  - 2% of urinary tract infections.

Staphylococcus aureus Facts

- Half of all *S. aureus* strains in U.S. healthcare facilities are resistant to methicillin.
- Historically, methicillin-susceptible *S. aureus* (MSSA) strains were mostly acquired in the community, whereas methicillin–resistant strains (MRSA) were typically acquired in healthcare facilities.
- There have been increasing reports of MRSA acquired in the community setting.

Community Acquired MRSA

- Definition:
  - MRSA clinical isolate from a patient without established risk factors for MRSA infection.
  - Risk factors include:
    - Within the last year:
      - History of hospitalization, surgery, or residence in a long term care facility
    - Presence of indwelling catheter or percutaneous device
    - Prior history of MRSA infection or colonization

Adapted from Fridkin et al. New England Journal of Medicine, April 7, 2005

Community Acquired MRSA

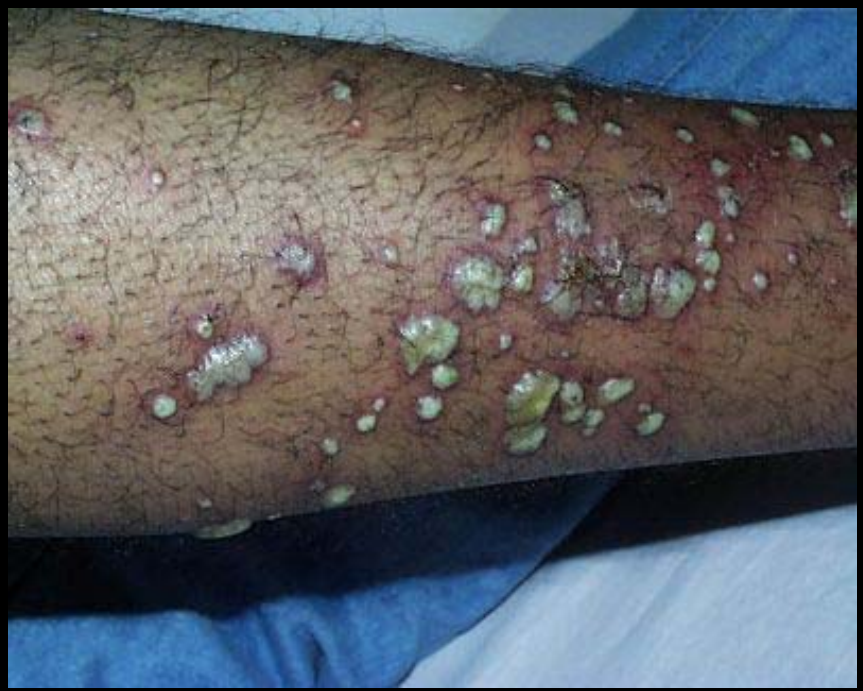
	Comment
Epidemiology	**CA-MRSA infections were first recognized in the 1980s** **Persons with CA-MRSA infections are typically younger and healthier than persons with healthcare-associated MRSA.** **CA-MRSA bacteria are usually susceptible to more types of antibiotics than are healthcare-associated strains of MRSA** • Typically susceptible to Bactrim, Clindamycin, Doxycycline

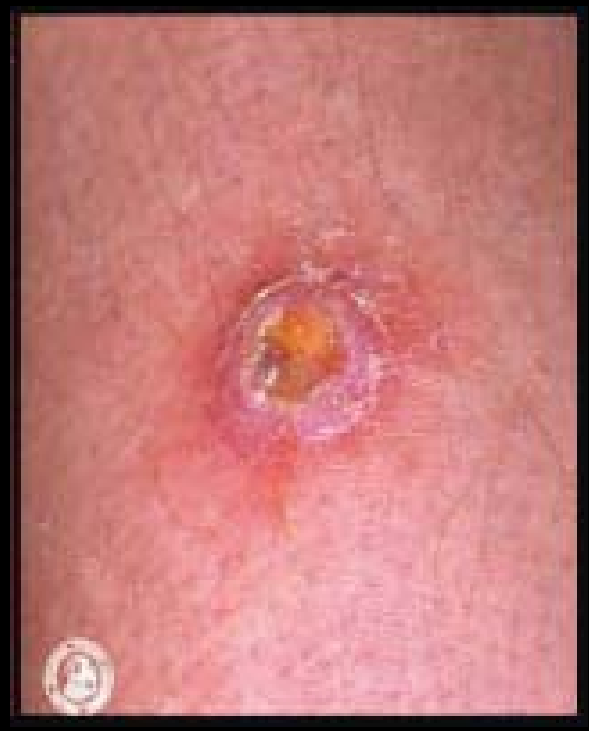
Community Acquired MRSA

- PVL positive Community acquired MRSA
  - Panton-Valentine-Leukocidine (PVL) gene
    - Cytotoxin produced by <5% of *S.aureus* strains
    - Lina et al* screened for PVL in 172 *S.aureus* strains
      - 93% of strains associated with furunculosis
      - 85% of strains associated with severe, necrotizing pneumonia

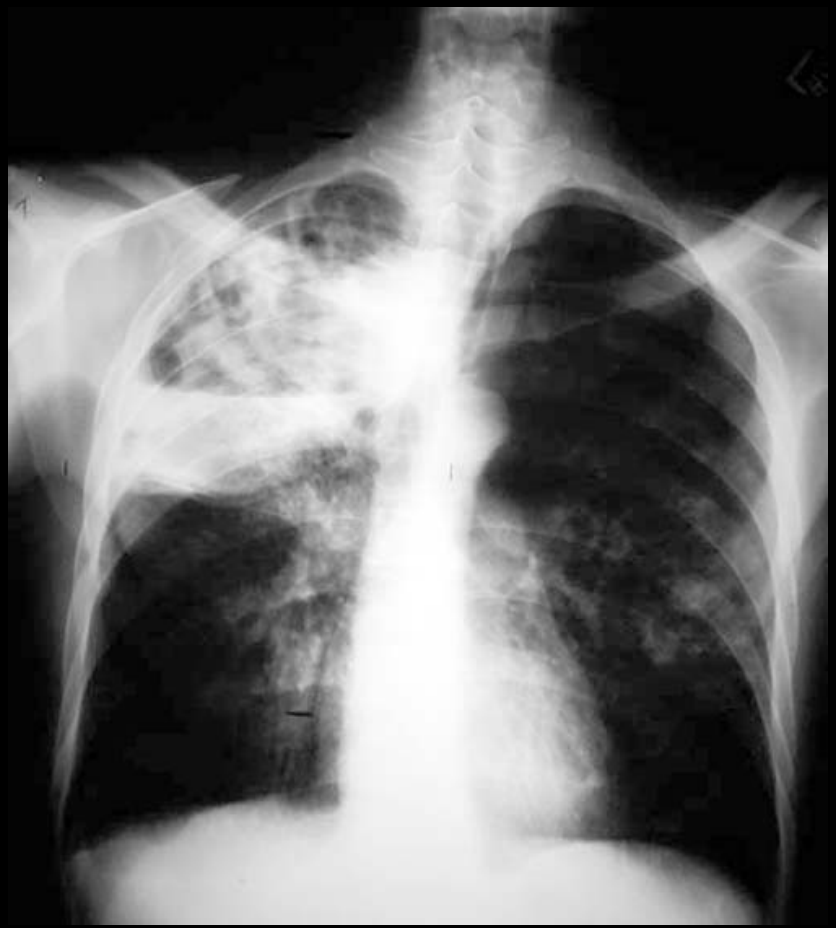
Lina et al. Arch Pediatr. 2001 Sep;8 Suppl 4:769s-775s.

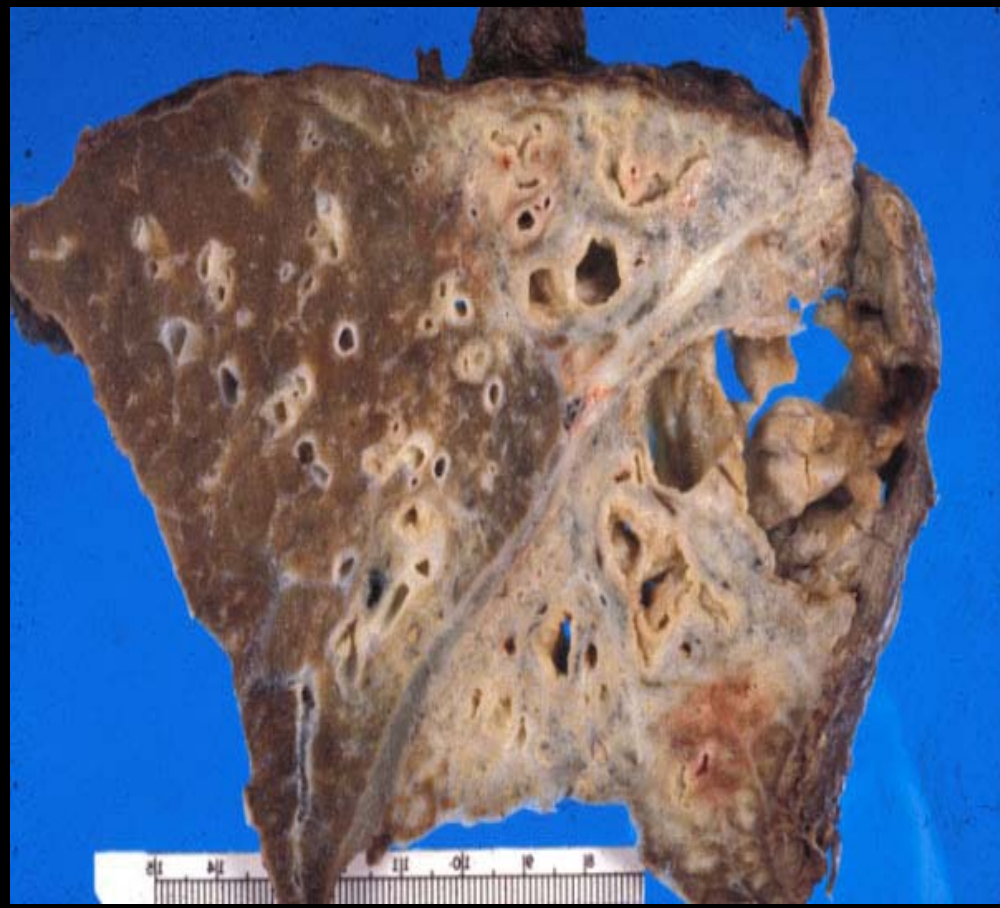
MRSA-Skin and Soft Tissue Infections





MRSA-Necrotizing Pneumonia



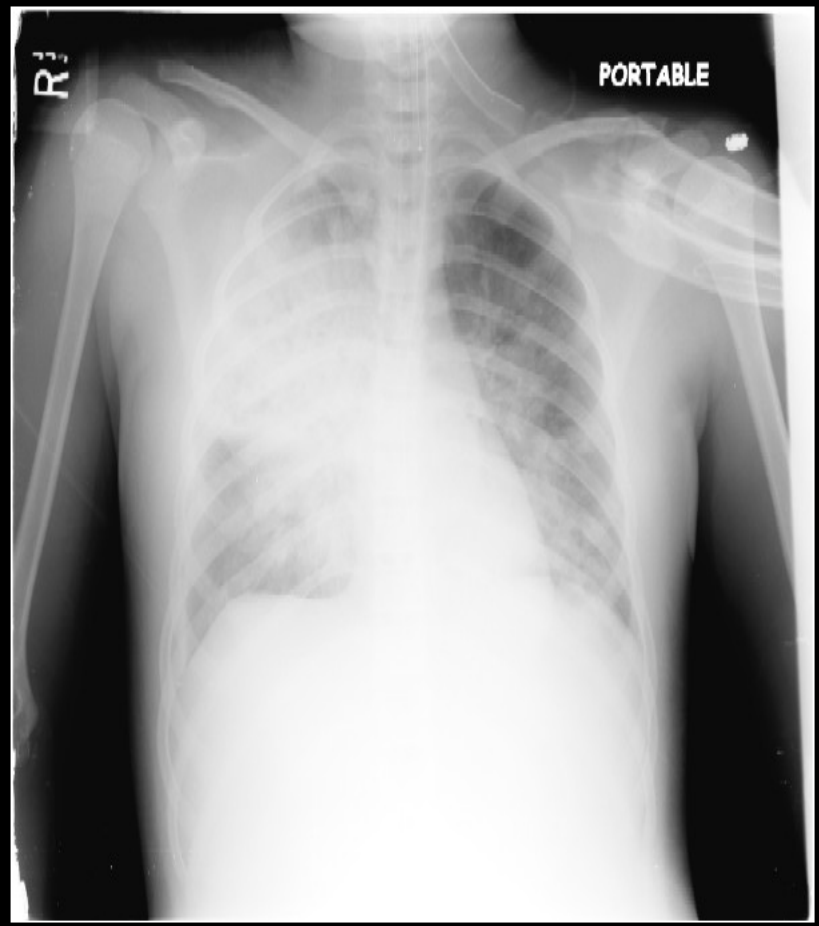


CA-MRSA at VCUMC

- 11 year old girl admitted with 4 day history of fever, chills, blood tinged sputum, generalized weakness and sore throat.
- Progressive respiratory distress leading to endotracheal intubation.
- Admitted to the ICU with sepsis and toxic shock.

CA-MRSA at VCUMC

- Influenza A antigen positive on respiratory secretions.
- Endotracheal sputum culture positive for MRSA
- Blood culture positive for MRSA
- Both MRSA isolates susceptible to Vancomycin, Clindamycin, Erythromycin, Gentamicin and Bactrim



Methicillin-Resistant *Staphylococcus aureus* Disease in Three Communities

- Methods:
  - **MRSA** infections evaluated in patients identified from population-based surveillance in Baltimore and Atlanta and from hospital-laboratory–based sentinel surveillance of 12 hospitals in Minnesota.
  - Patients were interviewed, medical records were reviewed.
  - Infections were classified as **community-acquired MRSA** disease if no established risk factors were identified.

Fridkin et al. New England Journal of Medicine, April 7, 2005

Methicillin-Resistant *Staphylococcus aureus* Disease in Three Communities

- From 2001 through 2002:
  - 1647 cases of **community-acquired MRSA** infection were reported
    - Represents 8-20 percent of all **MRSA** isolates.
  - The annual disease incidence varied according to site and population
    - 25.7 cases per 100,000 population in Atlanta
    - 18.0 per 100,000 in Baltimore
    - Age less than two years old vs. age > two years of age (relative risk, 1.51; 95 percent confidence interval, 1.19 to 1.92
    - Blacks vs whites in Atlanta (age-adjusted relative risk, 2.74; 95 percent confidence interval, 2.44 to 3.07).

Fridkin et al. New England Journal of Medicine, April 7, 2005

Methicillin-Resistant *Staphylococcus aureus* Disease in Three Communities

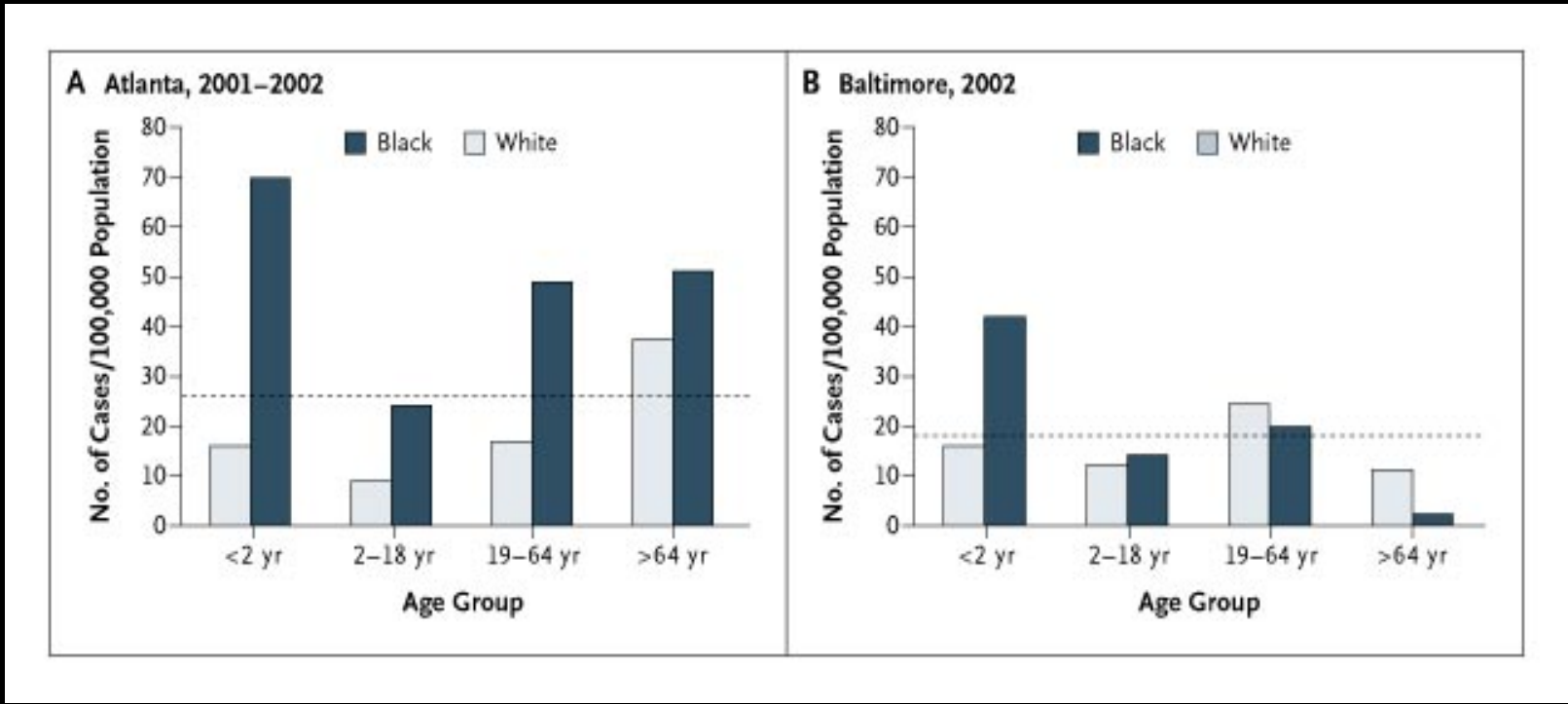


Figure 1. Incidence of Community-Associated MRSA Disease in Atlanta and Baltimore, According to Race and Age Group.

Fridkin et al. New England Journal of Medicine, April 7, 2005

Methicillin-Resistant *Staphylococcus aureus* Disease in Three Communities

Infections associated with CA-MRSA				
Variable	Atlanta N=1267	Baltimore N=115	Minnesota N=265	P value
Bacteremia	32 (2)	7 (6)	6 (2)	0.66
Meningitis	1 (<1)	1 (1)	0	0.84
Osteomyelitis	11 (1)	6 (5)	7 (3)	<0.01
Bursitis	12 (1)	0	7 (3)	0.04
Arthritis	13 (1)	0	2 (1)	0.52

Fridkin et al. New England Journal of Medicine, April 7, 2005

Methicillin-Resistant *Staphylococcus aureus* Disease in Three Communities

Infections associated with CA-MRSA				
Variable	Atlanta N=1267	Baltimore N=115	Minnesota N=265	P value
Skin & Soft Tissue	973 (77)	95 (83)	198 (75)	<0.01
Wound	136 (11)	8 (7)	13 (5)	0.97
Pneumonia	23 (2)	4 (3)	4 (2)	0.01
Urinary Tract	57 (4)	4 (3)	3 (1)	<0.01
Sinus	60 (5)	0	1 (<1)	0.08

Fridkin et al. New England Journal of Medicine, April 7, 2005

Methicillin-Resistant *Staphylococcus aureus* Disease in Three Communities

Potential Risk Factor	No. of Patients (%)
Any visit to a physician's office in the past year	357 (62)
Receipt of any antimicrobial agent in the past year	224 (39)
Chronic non-infectious skin disease	190 (33)
Crowded household (>1person/bedroom)	121 (51)
Healthcare related employment in past 5 years	69 (12)

Fridkin et al. New England Journal of Medicine, April 7, 2005

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

- **Objective:**
  - To determine the proportion of infections caused by community-acquired MRSA
  - To determine the clinical characteristics associated with community-acquired MRSA
  - To determine the molecular epidemiology of community-acquired MRSA among persons with community-onset *S. aureus* skin and soft-tissue infection

King et al. Annals of Internal Medicine. March 7, 2006

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

- **Design:** Active, prospective laboratory surveillance to identify *S. aureus* recovered from skin and soft-tissue sources.
- **Setting:** 1000-bed urban hospital and its affiliated outpatient clinics in Atlanta, Georgia

King et al. Annals of Internal Medicine. March 7, 2006

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

S.aureus infections	389 episodes
MRSA infections	279/389 (72%)
Community onset MRSA infections of all *S.aureus* infection	244/389 (63%)
Community onset MRSA of all MRSA infections	244/279 (87%)
MRSA isolates undergoing PFGE	175
PFGE consistent with CA-MRSA	159/175 (91%)
MRSA USA 300 Clone	157/159 (99%)
Community-acquired MRSA USA 300 genotype usually demonstrates resistance to ß-lactams and erythromycin and retains susceptibility to clindamycin, trimethoprim–sulfamethoxazole, and fluoroquinolones	

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

- Factors independently associated with community-acquired MRSA infection:
  - Black race (prevalence ratio, 1.53 [95% CI, 1.16 to 2.02])
  - Female sex (prevalence ratio, 1.16 [CI, 1.02 to 1.32]),

King et al. Annals of Internal Medicine. March 7, 2006

CA-MRSA In Athletes

CA-MRSA In Athletes

Reference	Study	Comment
Kazakova et al. NEJM 352;5,468-75. 2005	A Clone of Methicillin-Resistant *Staphylococcus aureus* among Professional Football Players	5 of 58 players on the St. Louis Rams with skin/soft tissue abscesses, all PVL positive
Cohen, P. Southern Medical Journal; 98,6 2005	Cutaneous Community acquired MRSA Infections in Participants of Athletic Activities	7 student athletes with abscesses with or without cellulitis
Lindenmayer et al. Archive of Internal Med 1998;158-895-899	Methicillin-resistant Staphylococcus aureus in High School Wrestling Team and Surrounding Community	6 cutaneous infection/boils transmitted by close contact among members of a wrestling team
Begier et al. Clinical Infectious Diseases 2004:39; 1446-1452	A High Morbidity Outbreak of MRSA Among Players on a College Football Team, Facilitated By Cosmetic Shaving and Turf Burns	

CA-MRSA In Athletes

- Risk factors:
  - Physical contact
  - Skin damage, turf burns, improper wound care
  - Sharing of equipment, clothing, skin products, razors, towels
  - Body Shaving- especially groin and genitals
  - Shared whirlpool baths

MMWR
Weekly

October 17, 2003 / 52(41);992-996

Methicillin-Resistant *Staphylococcus aureus* Infections in Correctional Facilities --- Georgia, California, and Texas, 2001--2003

- 12,700 MRSA infections
  - Nearly all cases were skin and soft tissue infections
  - Many cases misclassified as spider-bites

MMWR
Weekly

October 17, 2003 / 52(41);992-996

- Four important risk factors identified:
  - Poor access to soaps and inadequate laundry practices
  - Poor access to medical care (co-payments) and poor wound care supplies
  - Frequent medical staff turnover was a detriment to infection control practice
  - Frequent misdiagnosis of furuncular lesions as spider bites

Community-associated methicillin-resistant *Staphylococcus aureus* in hospital nursery and maternity units.

- Outbreak of 7 cases of skin and soft tissue infections due to a strain of CA-MRSA.
  - All patients were admitted to the labor and delivery, nursery, or maternity units during a 3-week period.
  - Genetic fingerprinting showed that the outbreak strain was closely related to the USA 400 strain that includes the midwestern strain MW2

Emerg Infect Dis. 2005 Jun;11(6):808-13.

Community-associated methicillin-resistant *Staphylococcus aureus* in hospital nursery and maternity units

Table 1. Clinical information for patients with methicillin-resistant *Staphylococcus aureus* infection during the outbreak period

Patient	Age at onset	Sex	Strain	Infection type	Initial therapy	Definitive therapy
P1, newborn	8 d	F	USA 400	Preseptal cellulitis	Nafcillin, cefotaxime	Topical gentamicin
P2, newborn	13 d	F	USA 400	Omphalitis, otitis externa	Ampicillin, cefotaxime	Topical mupirocin
P3, mother	33 y	F	USA 400	Breast abscess	Cefazolin	Surgical drainage, vancomycin, topical mupirocin
P4, newborn	2 d	M	USA 400	Omphalitis, pustulosis	Nafcillin Gentamicin	Gentamicin, topical mupirocin
P5, newborn	4 d	M	USA 400	Pustulosis	Cephalexin	Topical bacitracin
P6, newborn	2 d	M	USA 400	Pustulosis	None	Local wound care
P7, newborn	1 d	F	USA 400	Pustulosis, mastitis	Topical mupirocin	Vancomycin
P8, mother	24 y	F	Unique	Peripheral IV catheter site	Cefazolin	Trimethoprim-sulfamethoxazole, catheter removal

Emerg Infect Dis. 2005 Jun;11(6):808-13.

Epidemic of *Staphylococcus aureus* nosocomial infections resistant to methicillin in a maternity ward

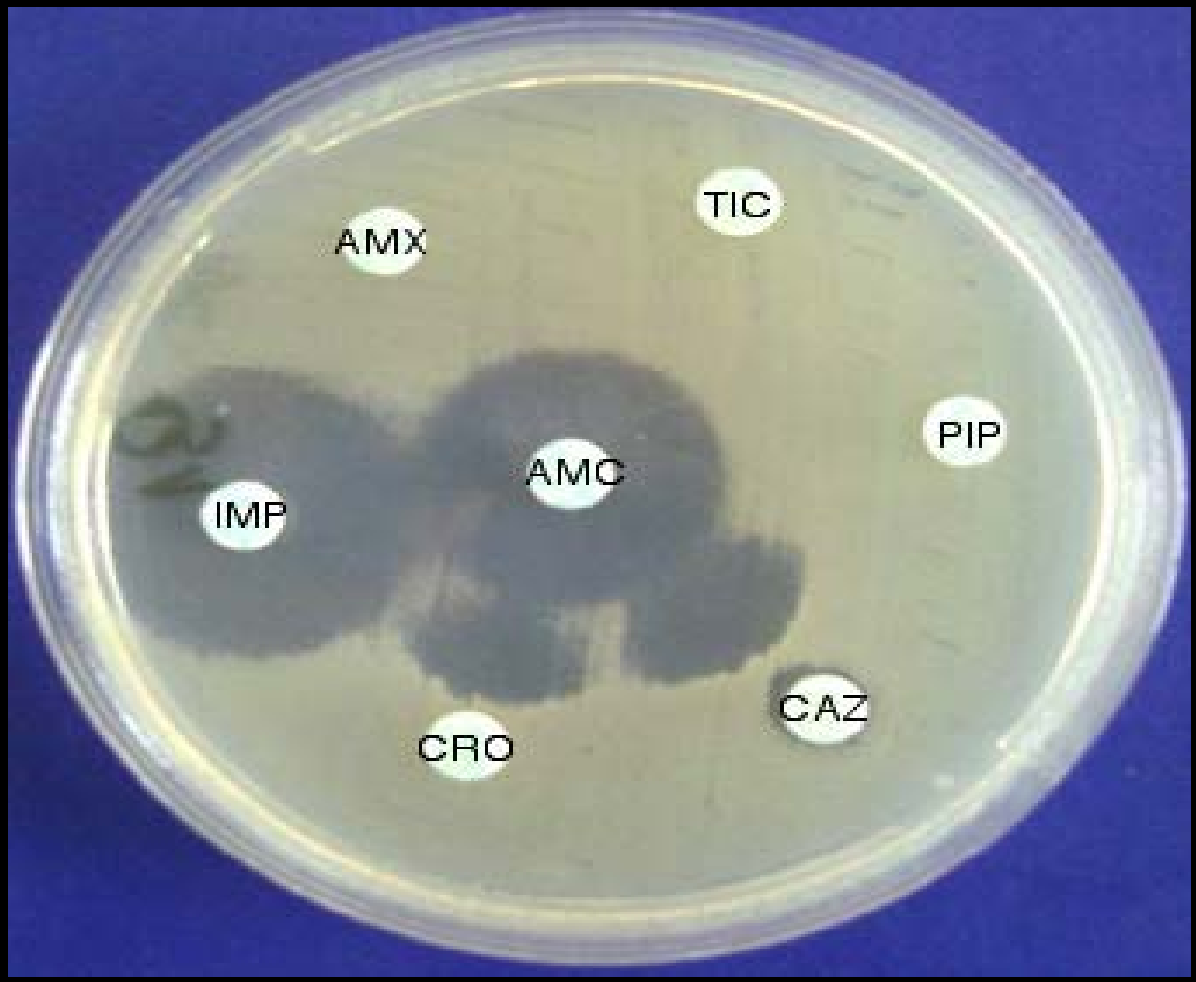
- Seventeen cases were recorded over a nine-week period (two cases per week).
  - All were skin and soft tissue infections
- Pulsed field gradient gel electrophoresis confirmed the clonal character of the strain.
- No definite risk factors were determined by a case-control study.
- Environmental factors were considered key in the persistence of this MRSA outbreak.

Pathol Biol (Paris). 2001 Feb;49(1):16-22.

Community Acquired MRSA

- CA-MRSA is an emerging pathogen
- Risk factors for CA-MRSA include:
  - Crowding, chronic skin conditions,skin to skin contact, poor hygiene
- The majority of CA-MRSA infections are skin and soft tissue infections, necrotizing pneumonia has also been reported
- A major difference between CA-MRSA and HA-MRSA is their resistance patterns

Acinetobacter baumanii



Epidemiology & Prevention of *Acinetobacter* Infections

- Microbiology
- Infections:
  - Scope of the problem
  - Impact
  - Outbreaks
- Reservoirs of *Acinetobacter* in the hospital
  - Colonization
    - HCWs, patients, environment
  - Cross transmission
- Limiting cross transmission of *Acinetobacter*
  - Infection control

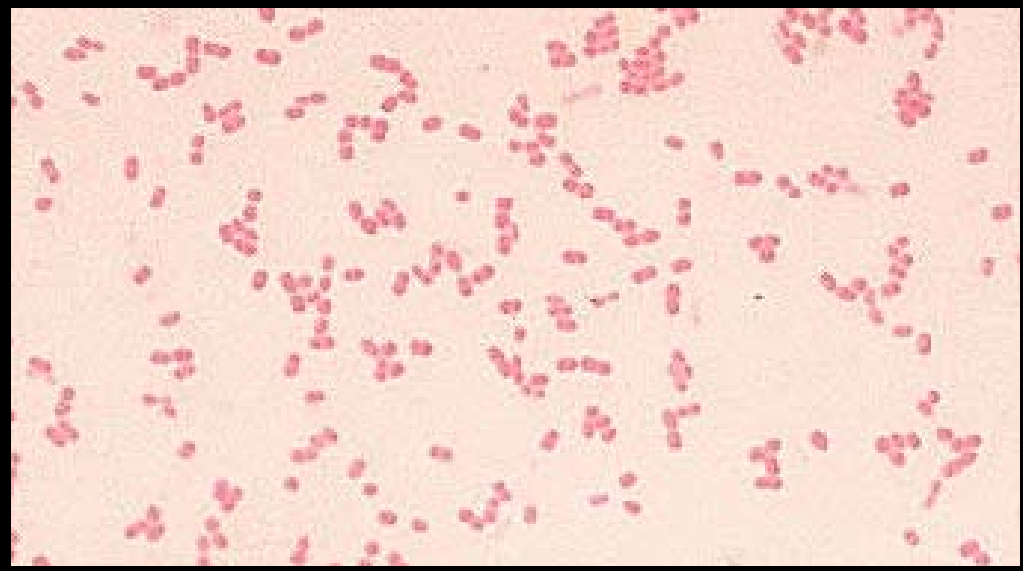
Acinetobacter

- Akinetos, Greek adjective, unable to move
- Bakterion, Greek noun, rod
- Nonmotile rod

Brisou and Prévot, 1954

Microbiology

- Oxidase negative
- Nitrate negative
- Catalase positive
- Nonfermentative
- Nonmotile
- Strictly aerobic
- Gram negative coccobacillus
  - Sometimes difficult to decolorize
- Frequently arranged in pairs



Bergogne-Bérézin E, Towner KJ. Clin Microbiol Rev 1996;9:148-165.

Microbiology

- Ubiquitous:
  - Widely distributed in nature (soil, water, food, sewage) & the hospital environment
- Survive on moist & dry surfaces
- 32 species
  - >2/3 of *Acinetobacter* infections are due to *A. baumanii*
- Highly antibiotic resistant
  - Numerous mechanisms of resistance to β-lactams described in *A. baumanii*
  - 15 aminoglycoside-modifying enzymes described
  - Quinolone resistance due to mutations in DNA gyrase

Hospital acquired *Acinetobacter* infections

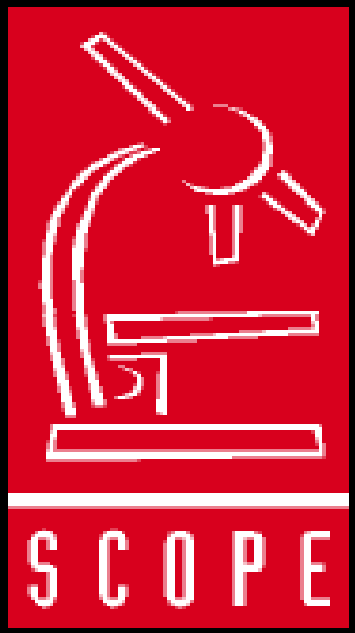
Major infections due to *Acinetobacter*

- Ventilator-associated pneumonia
- Urinary tract
- Bloodstream infection infection
- Secondary meningitis
- Skin/wound infections
- Endocarditis
- CAPD-associated peritonitis
- Ventriculitis

Acinetobacter Ventilator-Associated Pneumonia

- *Acinetobacter* accounts for 5-25% of all cases of VAP
- Risk factors:
  - Advanced age
  - Chronic lung disease
  - Immunosuppression
  - Surgery
  - Use of antimicrobial agents
  - Invasive devices
  - Prolonged ICU stay

Nosocomial Bloodstream Infections



49 US centers

1995-2002

N= 24,179

Rank	Pathogen	BSI/10,000 admissions	Percent
1	Coagulase-negative Staph	15.8	31%
2	*S. aureus*	10.3	17%
3	Enterococci	4.8	12%
4	*Candida* spp	4.6	8%
5	*E. coli*	2.8	6%
6	*Klebsiella*	2.4	5%
7	*Ps. aeruginosa*	2.1	4%
7	*Enterobacter*	1.9	4%
8	*Serratia*	1.7	2%
9	*Acinetobacter baumanii*	0.6	1%

Wisplinghoff H, Edmond MB et al. Clin Infect Dis. 2004 Aug 1;39(3):309-17

SCOPE

Acinetobacter Nosocomial BSI

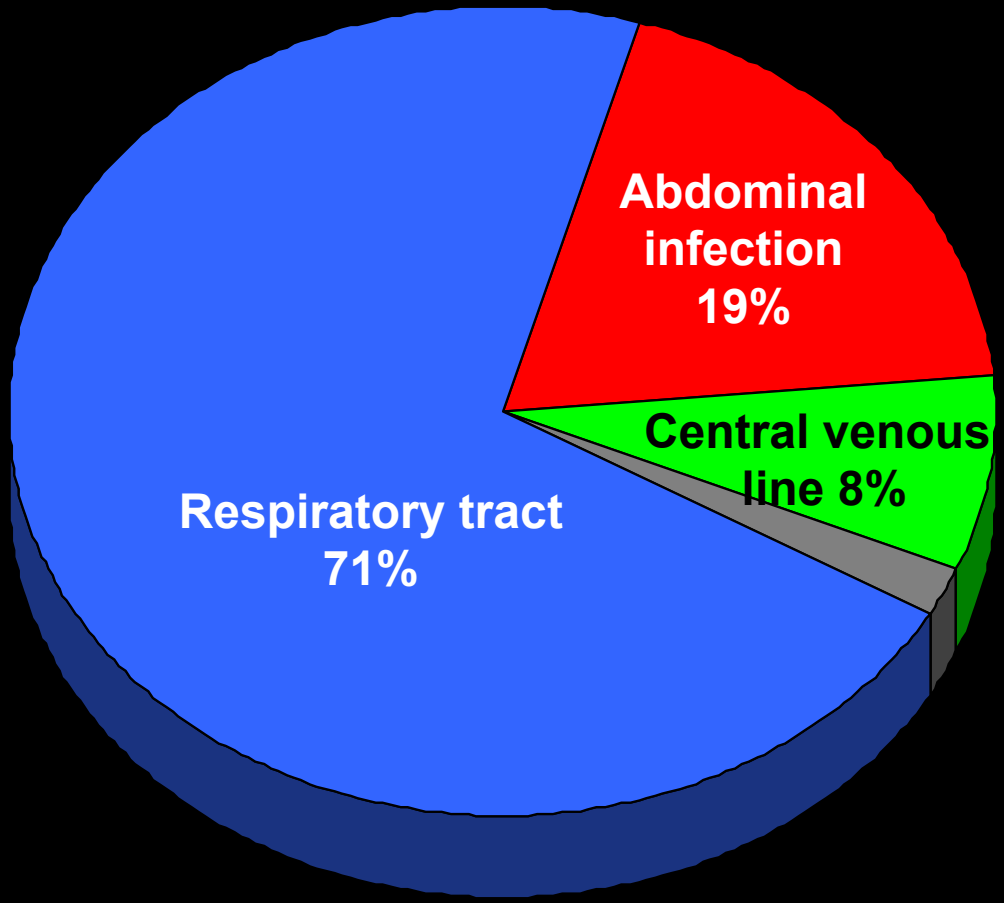
- Incidence = 0.6/10,000 admissions
- Accounts for 1.3% of all nosocomial BSI
- Accounts for 1.6% of all nosocomial BSI in the ICU setting
- Crude mortality:
  - Overall 34%
  - ICU 43%

Despite the low incidence, the mortality is high

Wisplinghoff H, Edmond MB et al. Clin Infect Dis. 2004 Aug 1;39(3):309-17

Source of *A. baumanii* Nosocomial Bloodstream Infection

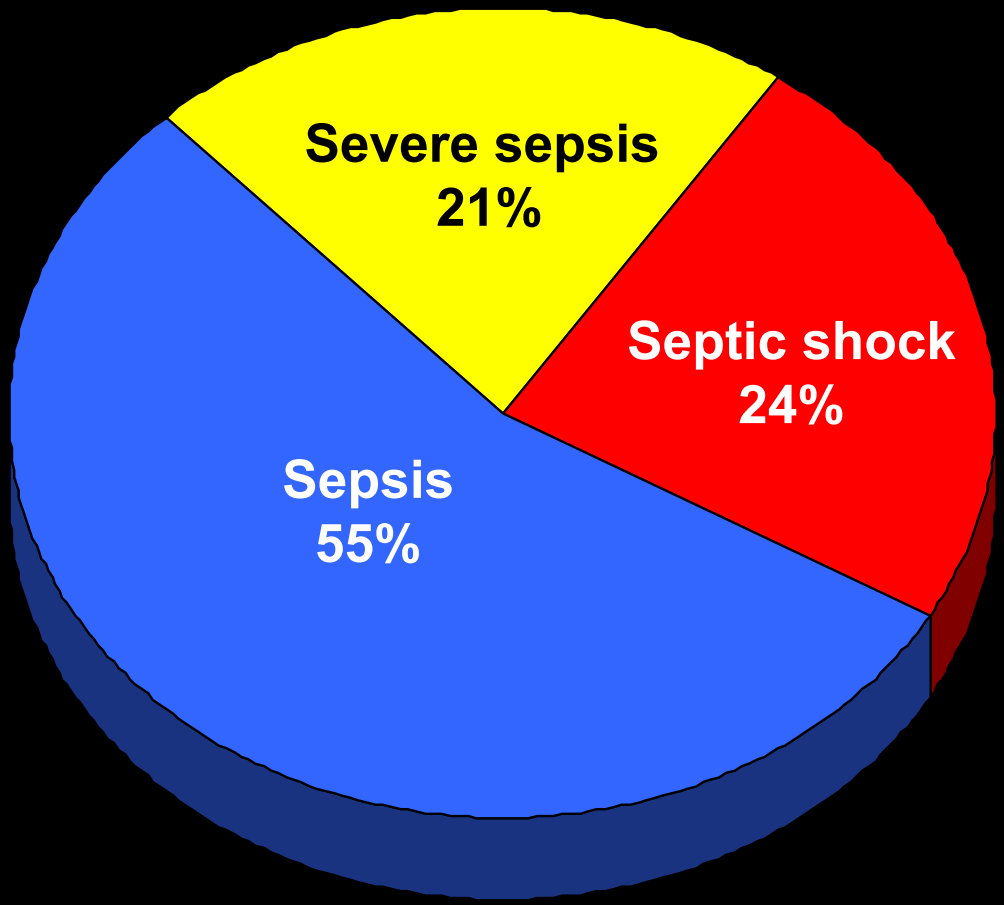
The respiratory tract is an important reservoir for *Acinetobacter* bloodstream infections



N=37

Garcia-Garmendia J-L et al. Clin Infect Dis 2001;33:939-946.

Inflammatory Response to *A. baumanii* Nosocomial Bloodstream Infection



N=42

Garcia-Garmendia J-L et al. Clin Infect Dis 2001;33:939-946.

Independent Predictors of *A. baumanii* Nosocomial Bloodstream Infection

Risk factors	*A. baumaniil* (n=42)	Other gram negative (n=35)	Odds Ratio (CI_{95})
Immunosuppression	24%	3%	3.0 (1.3-7.1)
Unscheduled admission	86%	51%	3.3 (1.3-8.5)
Respiratory failure at admission	60%	14%	2.9 (1.4-5.8)
Previous antibiotic therapy	64%	13%	2.3 (1.1-5.0)
Previous sepsis in ICU	79%	17%	4.4 (1.8-10.3)
Invasive procedure index* (mean value)	3.7	2.5	1.8 (1.4-2.4)

No. of invasive procedure-days/number of days in ICU prior to BSI

Garcia-Garmendia J-L et al. Clin Infect Dis 2001;33:939-946.

Impact of *Acinetobacter* Infection in the ICU

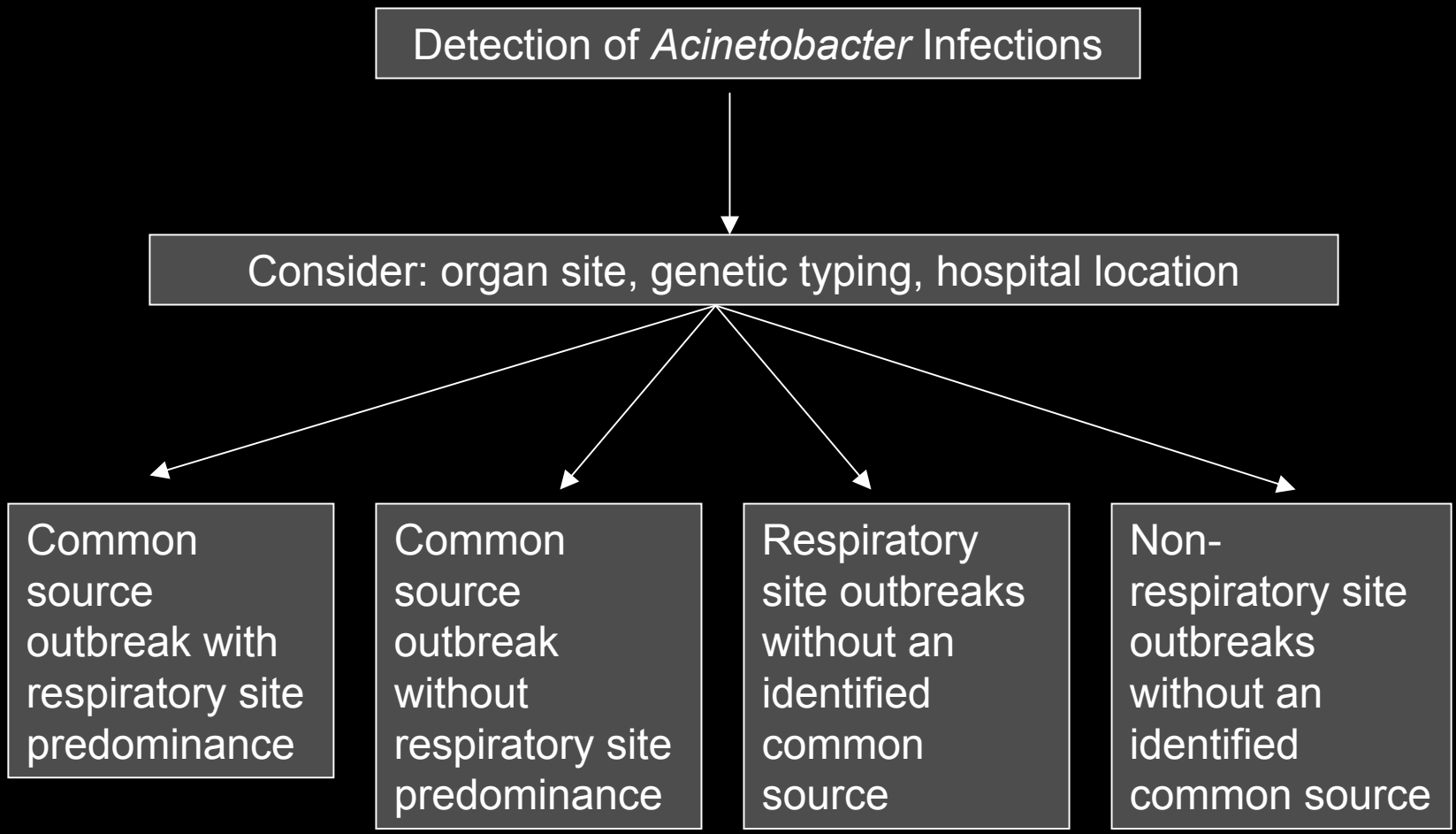
Impact of *Acinetobacter* Bloodstream Infection in the ICU

Outcome	Group	Bloodstream infection
Mortality	Cases	42%
	Controls	34%
Attributable mortality		8%
Risk ratio for death		1.0 (CI_{95} 0.7-1.4)
Length of ICU stay (median)	Cases	25 days
	Controls	20 days
Excess ICU LOS		5 days

- **Historical cohort study of 45 patients with *Acinetobacter* bloodstream infection matched 1:2 to patients without infection**
- **Controls were matched to cases on: APACHE II (± 2 points), principal diagnosis at ICU admission, LOS at least as long as case until bacteremia**

Blot S. Intensive Care Med 2003;29:471-475.

Acinetobacter outbreaks



Villegas M, Hartstein A. *Infect Control Hosp Epidemiol*. 2003;24:284-295

Acinetobacter outbreaks 1977-2000

Extensive Literature review and summary of 51 *Acinetobacter* outbreaks

Characteristic	Number of reports	Comment
Publication year: **1977-1990** **1991-2000**	 **24** **27**	**The majority of the reports occurred over the last 9 years**
ICU setting	**38**	**75 percent of reports were exclusively or predominantly ICU related outbreaks or clusters**
Patient age category: **Adult** **Pediatric**	 **45** **6**	**88 percent of all outbreaks were in an adult population**

Villegas M, Hartstein A. *Infect Control Hosp Epidemiol*. 2003;24:284-295

Acinetobacter outbreaks 1977-2000

Studies with a focus on antimicrobial resistance	
Antimicrobial class	Number of studies reporting new or increasing resistance
Aminoglycosides	6
Multiple classes	14
Carbapenems	3

Villegas M, Hartstein A. *Infect Control Hosp Epidemiol*. 2003;24:284-295

Acinetobacter outbreaks 1977-2000

13 Studies with a common source outbreak with a respiratory cluster:

- **Clonal transmission confirmed by PFGE or PCR-based typing**

Setting:	Common Source:
Adult ICU	Ventilator spirometers
Adult,neonatal and pediatric ICU	Reusable ventilator circuits
Adult mixed ICU	In line temperature monitor probes
Surgical and medical ICU	Ventilator temperature probes
Adult ICU	'Y' piece of ventilator
Neonatal ICU	Suction catheter and bottle
Adult mixed ICU	Peak flow meter

Villegas M, Hartstein A. *Infect Control Hosp Epidemiol*. 2003;24:284-295

Acinetobacter outbreaks 1977-2000

12 Studies with a common source outbreak without a respiratory cluster:

- Clonal transmission confirmed by PFGE or PCR-based typing

Setting:	Common Source:
Medical Wards	Bedside humidifiers
Medical ICU	Warming bath water
Cardiac Catheterization Lab	Hospital prepared distilled water
Dialysis center	Heparinized saline solution
Burn unit	Patient mattresses
Hospital wide	Feather pillows
Pediatric oncology war	Water taps in staff room with mesh aerators

Villegas M, Hartstein A. *Infect Control Hosp Epidemiol*. 2003;24:284-295

Acinetobacter outbreaks 1977-2000

•16 Studies with a predominant respiratory site outbreak without an identifiable common source •8 Studies with a predominant non-respiratory site outbreak without an identifiable common source	
Settings	Medical ICU Surgical ICU Shock-Trauma ICU Medical Wards Nursery Mixed Medical/Surgical ICU Burn and Plastic Surgery Wards

Villegas M, Hartstein A. *Infect Control Hosp Epidemiol*. 2003;24:284-295

Reservoirs of *Acinetobacter:*
Where do these organisms reside?

Environmental Contamination with *Acinetobacter*

- Bed rails
- Bedside tables
- Ventilators
- Infusion pumps
- Mattresses
- Pillows
- Air humidifers
- Patient monitors
- X-ray view boxes
- Curtain rails
- Curtains
- Equipment carts
- Sinks
- Ventilator circuits
- Floor mops

Factors Promoting Transmission of of *Acinetobacter* in the ICU

- Long survival time on inanimate surfaces
  - In vitro survival time 329 days
    (Wagenvoort JHT, Joosten EJAJ. J Hosp Infect 2002;52:226-229)
  - 11 days survival on Formica, 12 days on stainless steel
    (Webster C et al. Infect Control Hosp Epidemiol 2000;21:246)
  - Up to 4 months on dry surfaces
    (Wendt C et al. J Clin Microbiol 1997;35:1394-1397)
- Extensive environmental contamination
- Highly antibiotic resistant
- High proportion of colonized patients
- Frequent contamination of the hands of healthcare workers

Acinetobacter Transmission in the Hospital Setting

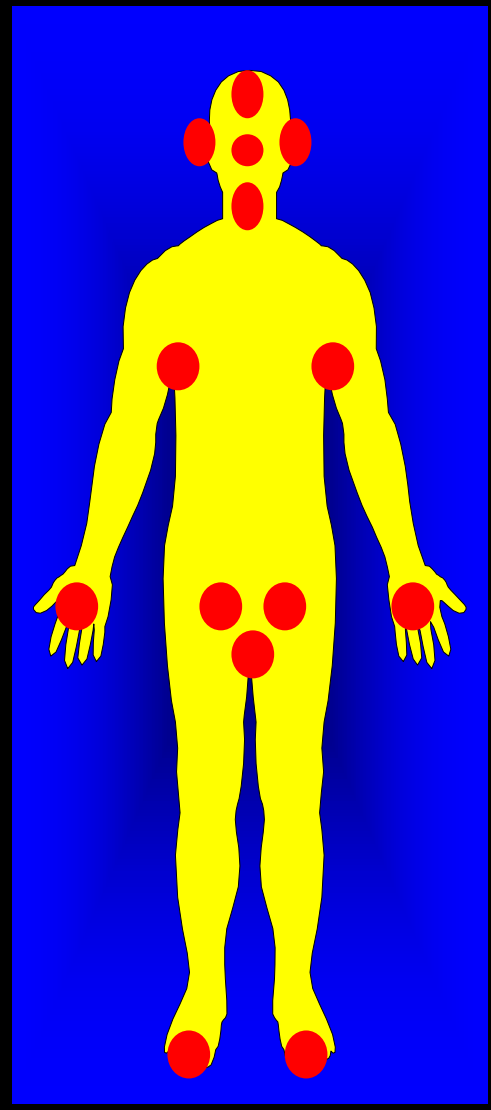
- Direct or indirect contact
  - Contaminated hands of healthcare workers
- Airborne transmission via aerosol production (e.g., hydrotherapy) may occur

Simor AE et al. Infect Control Hosp Epidemiol 2002;23:261-267.

Acinetobacter spp Skin Colonization

Body site	Hospitalized patients (n=40)	Healthy controls (n=40)
Forehead	33%	13%
Ear	35%	7%
Nose	33%	8%
Throat	15%	0%
Axilla	33%	3%
Hand	33%	20%
Groin	38%	13%
Perineum	20%	3%
Toe web	40%	8%
Any site	75%	42.5%

A. baumanii isolated from 2 patients & 1 control only



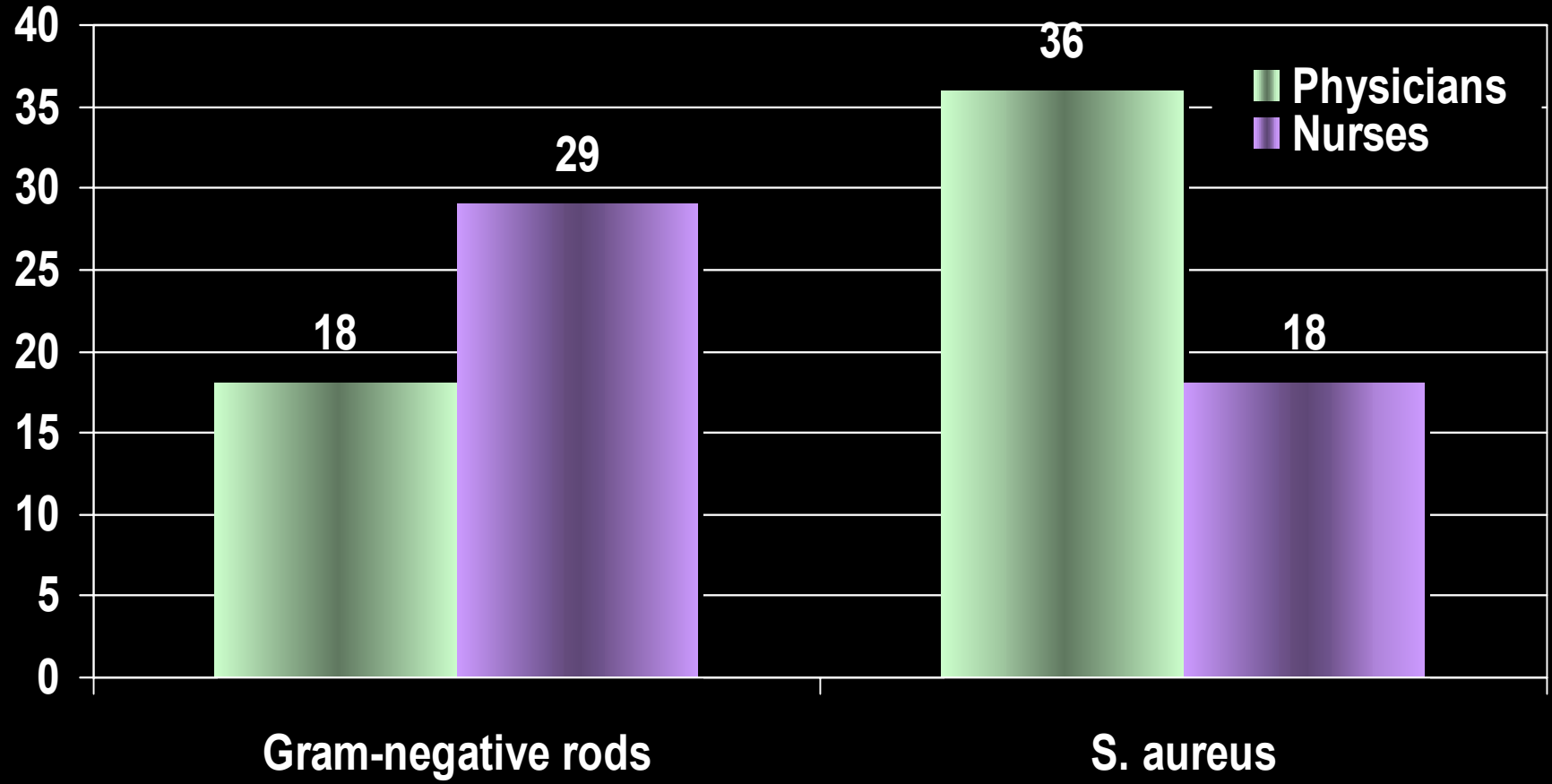
Seifert H et al. J Clin Microbiol 1997; 35:2819-2825.

Acinetobacter Transmission in the Hospital Setting
Colonization of Healthcare Workers

- Outbreak of multidrug resistant *A. baumanii* in a Dutch ICU involving 66 patients with an epidemic strain
- Nursing staff were cultured (nares & axilla, same swab)
  - 15 nurses found to harbor epidemic strain
  - All were culture negative when re-cultured (nose, throat, axilla, perineum)

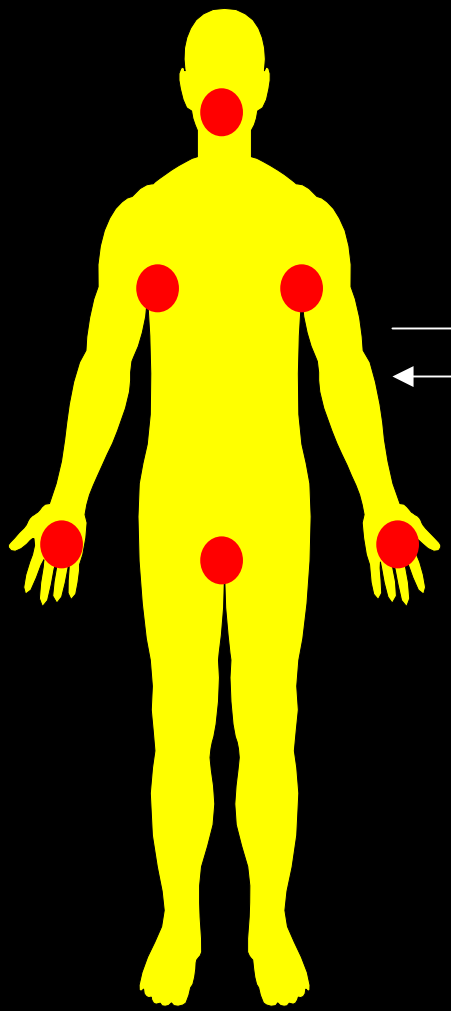
Wagenvoort JHT et al. Eur J Clin Microbiol Infect Dis 2002;21:326-327.

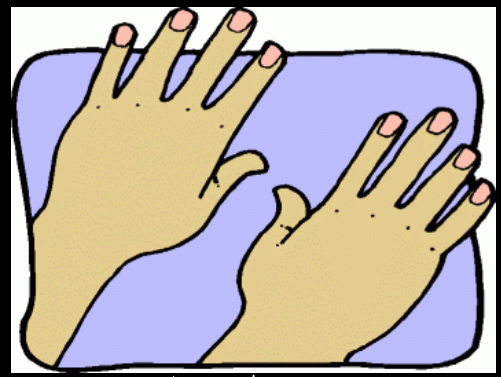
Hand Contamination in HCWs



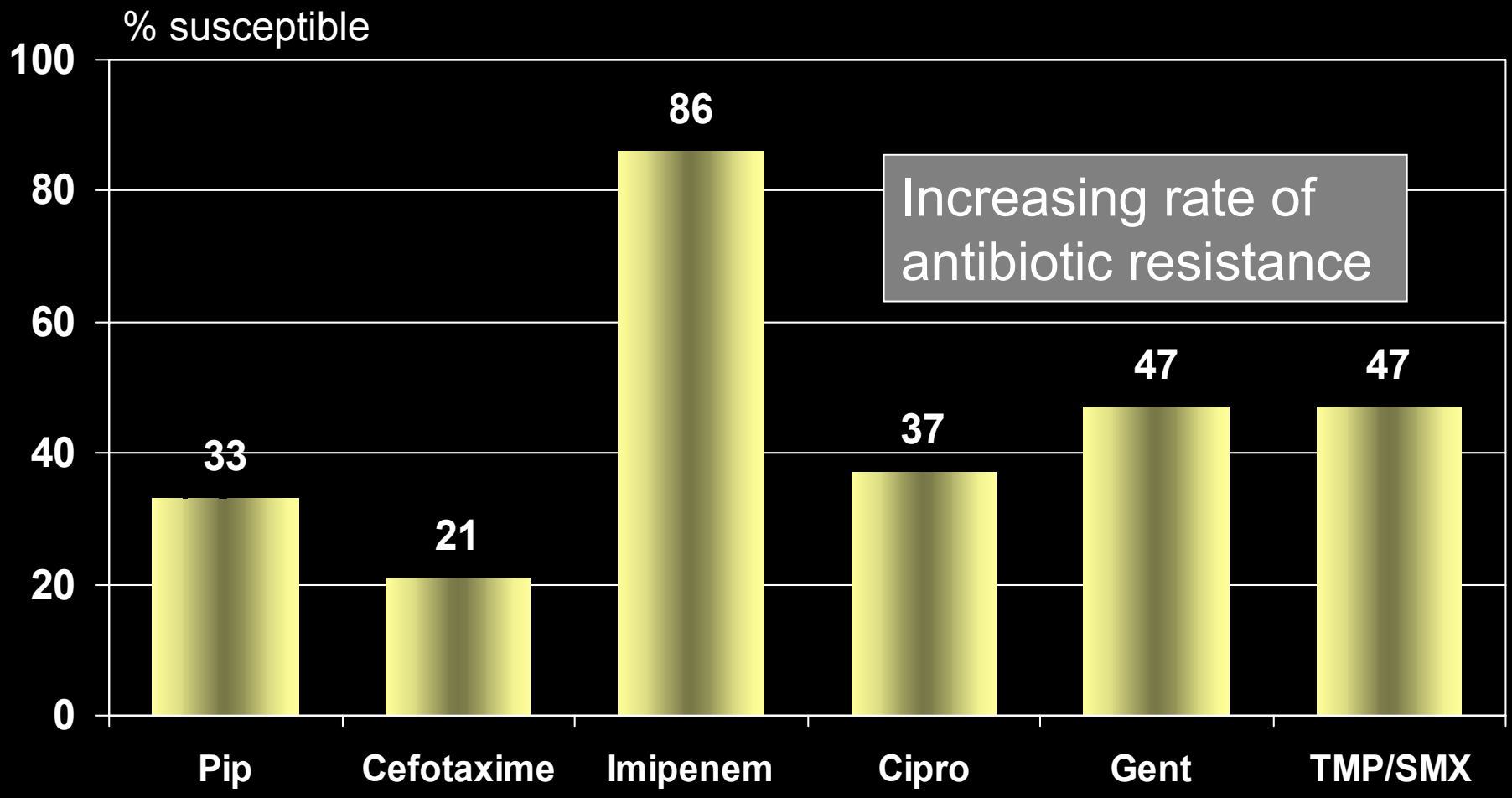
Bauer TM et al. J Hosp Infect 1990;15:301-309.

Opportunities for cross transmission are multiple





Acinetobacter Susceptibility, US, 2002-2003



TSN Database. http://www.geis.ha.osd.mil/GEIS/SurveillanceActivities/AntimicrobialResistance/AcinetobacterGraphs.htm

Antibiotic Resistance

Community vs. Hospital Acquisition

- Comparison of *A. baumanii* isolates obtained from the hands of homemakers to isolates obtained from 2 US hospitals
  - 23/222 (10.4%) homemakers had *A.baumanii* isolated from hands

Antimicrobial resistance	Hospital (n=101)	Community (n=23)	Odds Ratio (CI_{95})
3rd generation cephalosporins	88%	9%	78 (15-553)
Carbapenems	64%	4%	39 (5-811)
Aminoglycosides	43%	4%	16 (2-337)
Multidrug resistant*	37%	0%	Not calculable

*3rd gen. cephalosporins + carbapenem + aminoglycoside

Zeana C. Infect Control Hosp Epidemiol 2003;24:275-279.

Limiting the cross transmission of *Acinetobacter*

Preventing *Acinetobacter* Transmission in the ICU

General Measures

- Hand hygiene
  - Use of alcohol-based hand sanitizers
- Contact precautions
  - Gowns/gloves
  - Dedicate non-critical devices to patient room
- Environmental decontamination
- Prudent use of antibiotics
- Avoidance of transfer of patients to Burn Unit from other ICUs

Preventing *Acinetobacter* Transmission in the ICU

Outbreak Interventions

- Hand cultures
- Surveillance cultures
- Environmental cultures following terminal disinfection to document cleaning efficacy
- Cohorting
- Ask laboratory to save all isolates for molecular typing
- Healthcare worker education
- If transmission continues despite above interventions, closure of unit to new admissions

In Vitro Activity of Alcohol Hand Rubs

- Each agent diluted 1/10 & tested against a strain of *A. baumanii* resistant to 3rd generation cephalosporins

Alcohol(s)	**Other agents**	**Log ↓**
60% isopropyl, 0.05% phenoxyethyl		-0.02
46% ethyl, 27% isopropyl, 1% benzyl		-0.05
70% ethyl	0.3% triclosan	0.3
30% I-propanol, 45% isopropyl	0.2% mecetronium	3.2
60% isopropyl	0.5% chlorhexidine	>5.0
70% isopropyl	0.5% chlorhexidine, 0.45% H_2O_2	>5.0
89% isopropyl/ethyl	0.1% chlorhexidine	>5.0
40% I-propanol, 30% isopropyl	0.1% octenidine	>5.0
55% isopropyl	0.5% triclosan	>5.0

Rochon-Edouard S et al. Am J Infect Control 2004;32:200-204.

Chlorhexidine Resistance in *Acinetobacter*

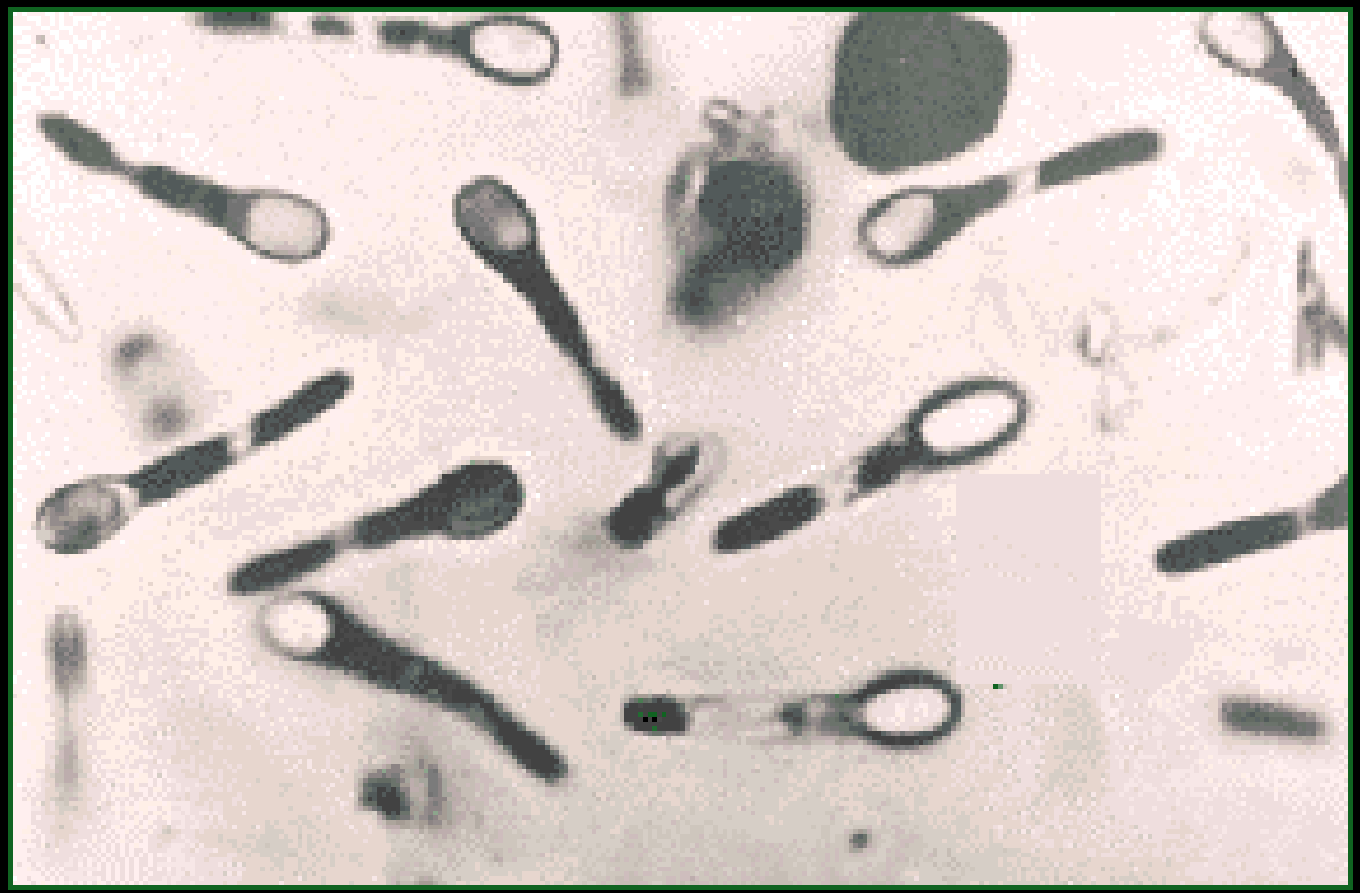
- Biocide resistance in gram-negative organisms is mainly intrinsic & chromosomal (plasmid mediated in gram-positive organism)
- 10 strains of *A. baumanii* tested for chlorhexidine susceptibility
  - Median MIC 32 mg/L
  - Median MBC 32 mg/mL
  - Chlorhexidine resistance increased with increased antibiotic resistance

Kõljalg S et al. J Hosp Infect 2002;51:106-113.

Summary

- Although commonly found on the skin of healthy humans, *Acinetobacter* plays the role of an opportunistic pathogen in the critically ill patient
- High level of antibiotic resistance makes it well suited as a pathogen in areas with high use of antibiotics (e.g., ICU setting)
- Control requires good hand hygiene, barrier precautions & environmental decontamination
  - Alcohol-based products containing chlorhexidine should be considered the hand hygiene agents of choice

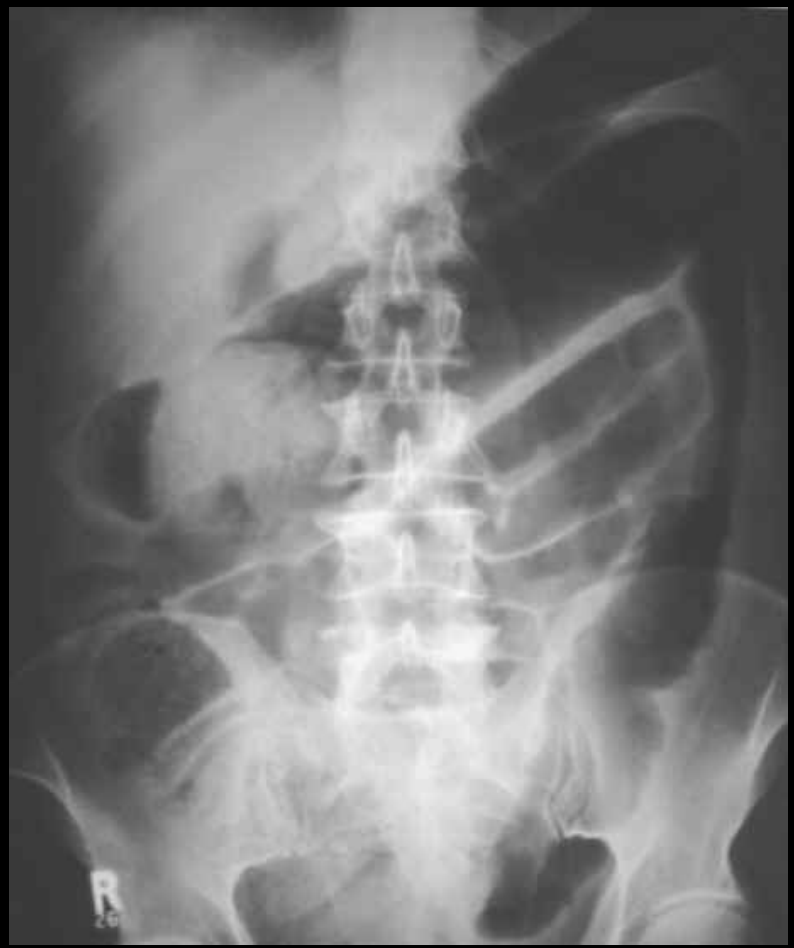
Clostridium difficile

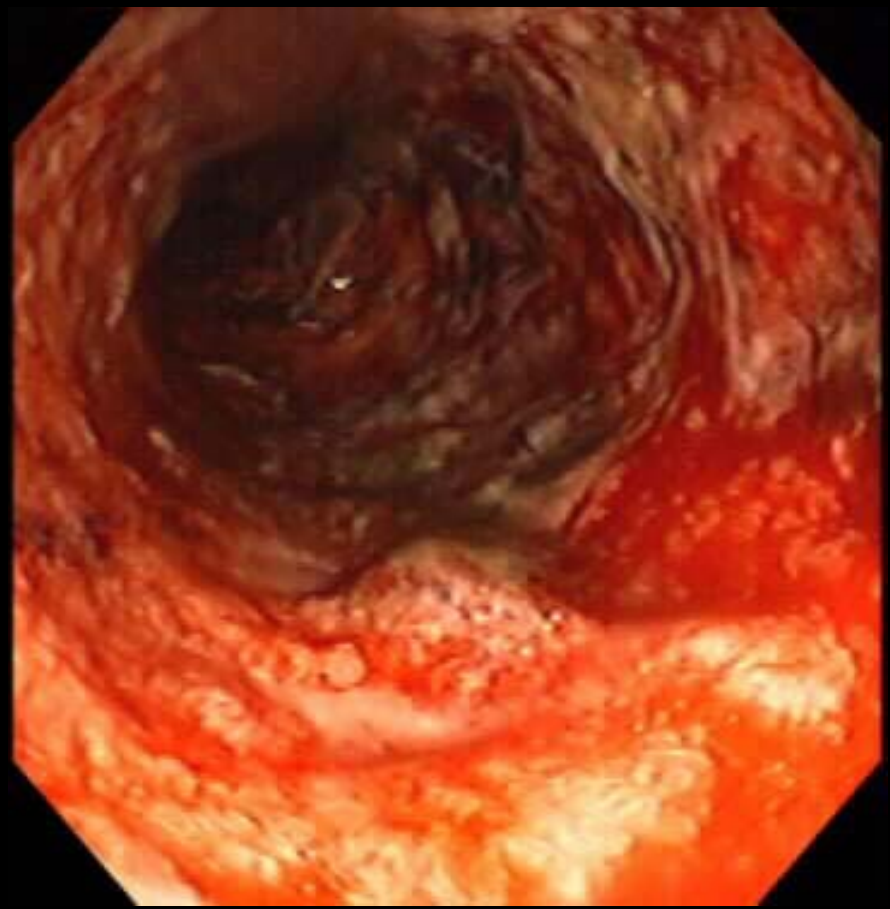


Clostridium difficile

- *Clostridium difficile* is a gram-positive, anaerobic, spore-forming bacillus that is responsible for the development of antibiotic-associated diarrhea and colitis
- *C difficile* colitis results from a disturbance of the normal bacterial flora of the colon, colonization with *C difficile*, and release of toxins that cause mucosal inflammation and damage

Clostridium difficile- Toxic Megacolon and Pseudomembranous Colitis





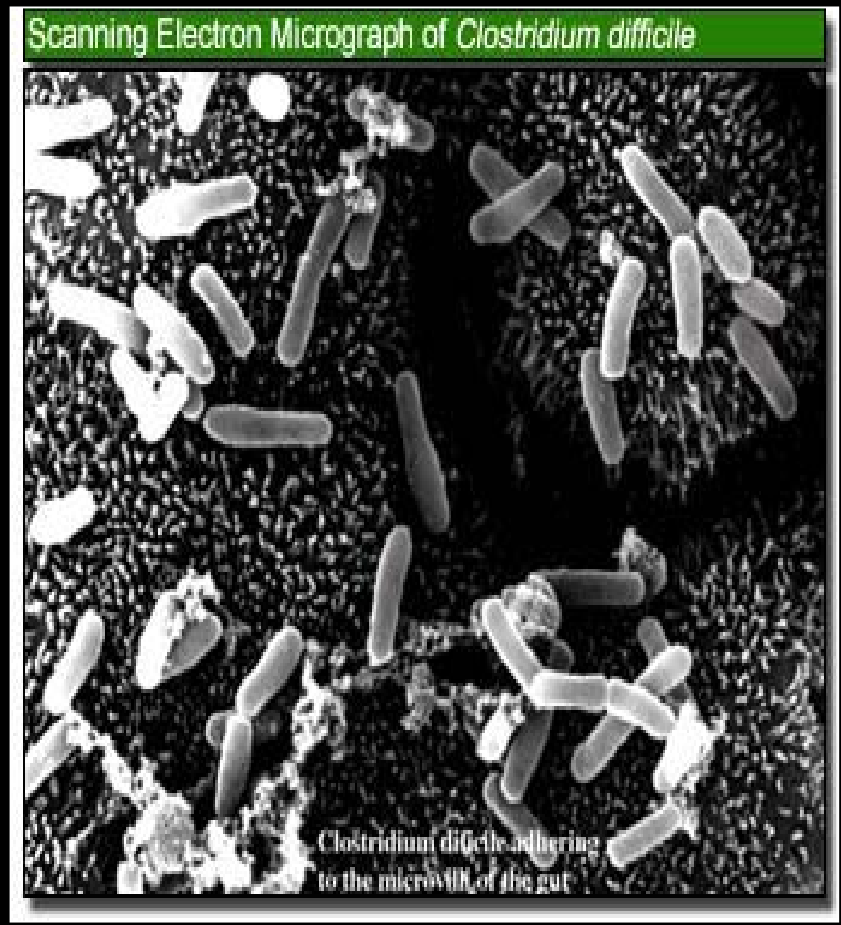
A Predominantly Clonal Multi-Institutional Outbreak of *Clostridium difficile*-Associated Diarrhea with High Morbidity and Mortality

- Prospective study in 12 Quebec Hospitals to determine the incidence of nosocomial *C.difficile*-associated diarrhea and its complications.
- Case-control study performed to determine risk factors
- All *C.difficile* isolates were PFGE typed with genetic analysis performed for key virulence factors.

Loo et al. New Eng. Journal of Medicine 353;23, 2442-2449

A Predominantly Clonal Multi-Institutional Outbreak of *Clostridium difficile*-Associated Diarrhea with High Morbidity and Mortality

- Analysis for chromosomal pathogenitcity
- Genes
  - *tcd*A Toxin A
  - *tcd*B Toxin B
  - *tcd*C porin gene
    - Partial deletions of *tcd*C
      - The expression of *tcd*A and *tcd*B is down regulated by the *tcd*C gene



Loo et al. New Eng. Journal of Medicine 353;23, 2442-2449

A Predominantly Clonal Multi-Institutional Outbreak of *Clostridium difficile*-Associated Diarrhea with High Morbidity and Mortality

Results	
Total # of episodes	1719 Episodes of *C.difficile* diarrhea
Incidence	22.5 per 1000 hospital admissions
30 day attributable mortality	6.9 percent

Loo et al. New Eng. Journal of Medicine 353;23, 2442-2449

A Predominantly Clonal Multi-Institutional Outbreak of *Clostridium difficile*-Associated Diarrhea with High Morbidity and Mortality

Case Control Study			
Characteristic	**Case Patients N=237**	**Control Patients N=237**	**P-value**
Number of antibiotics received	1.9 +/- 1.1	1.3 +/- 1.3	<0.001
Cephalosporins	115 (48.5)	65 (27.4)	<0.001
Clindamycin	19 (8.0)	6 (2.5)	<0.001
Quinolones	128 (54.0)	75 (31.6)	<0.001
Enteral tube	44 (18.6)	28 (11.8)	0.04

Loo et al. New Eng. Journal of Medicine 353;23, 2442-2449

A Predominantly Clonal Multi-Institutional Outbreak of *Clostridium difficile*-Associated Diarrhea with High Morbidity and Mortality

Multivariate analysis		
Antibiotic	**Odds Ratio**	**95% CI**
Cephalosporins	**3.8**	**2.2-6.6**
Fluoroquinolones	**3.9**	**2.3-6.6**
Clindamycin	**1.6**	**0.5-4.8**
Penicillins -beta lactamase inhibitor	**1.2**	**0.7-2.3**
Carbapenems	**1.4**	**0.3-6.3**

Loo et al. New Eng. Journal of Medicine 353;23, 2442-2449

A Predominantly Clonal Multi-Institutional Outbreak of *Clostridium difficile*-Associated Diarrhea with High Morbidity and Mortality

- Antibiotic susceptibility:
  - A predominant, fluoroquinolone resistant strain was found in 129/157 isolates (82.2%)
- Genetic typing
  - 82.2% of isolates with identical PFGE pattern
  - Binary toxin genes and partial deletion of tcdC gene were present in 132 isolates (84.1%)

Loo et al. New Eng. Journal of Medicine 353;23, 2442-2449

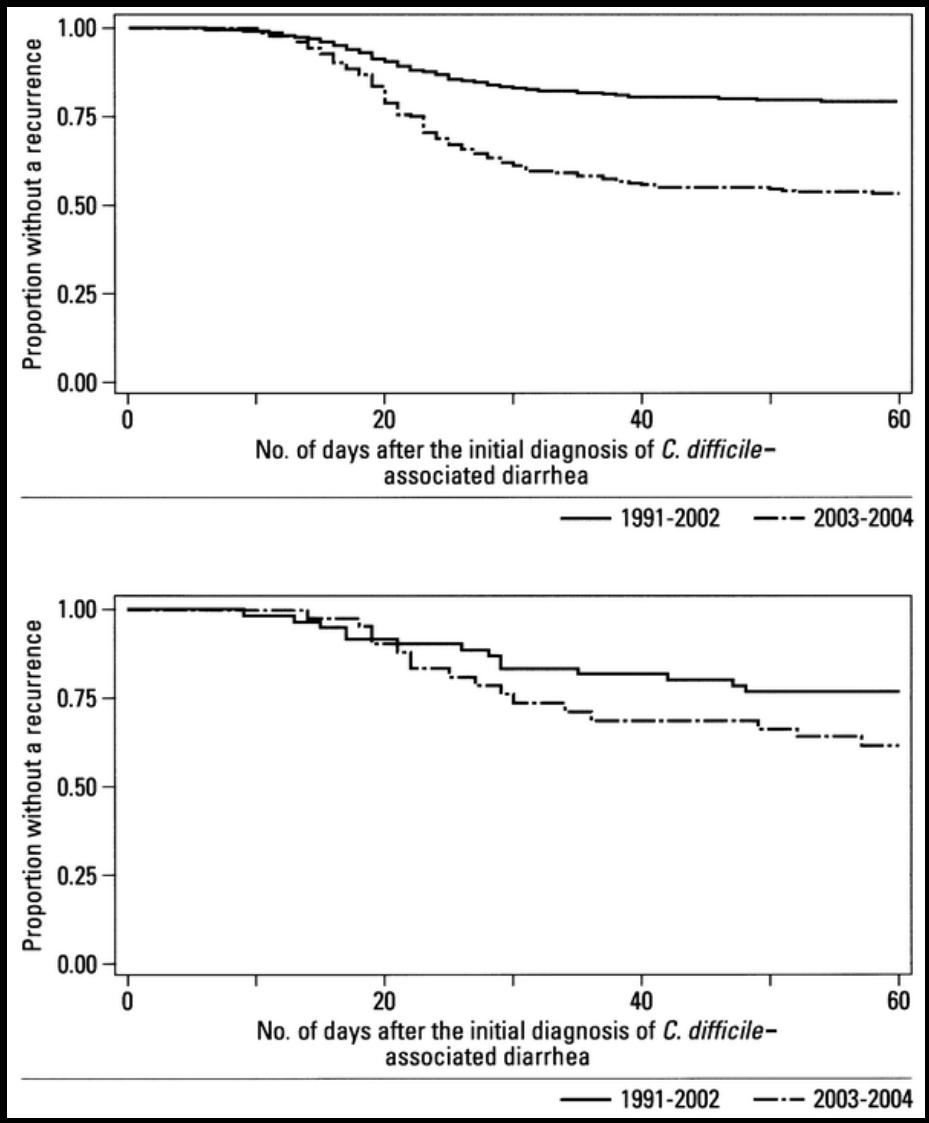
Relatively Poor Outcome after Treatment of *Clostridium difficile* Colitis with Metronidazole

Prospective, observational study of 207 patients who were treated with metronidazole for *C. difficile* colitis

- 103 patients (50%) were cured by the initial course of therapy and had no recurrence of disease.
- 22% continued to have symptoms of colitis for 10 days despite treatment
- 28% responded initially but had a recurrence within the ensuing 90 days.
- The mortality rate higher among patients who did not respond fully to an initial course of therapy, compared with those who did (33% vs. 21%; $P < .05$)

Clinical Infectious Diseases 2005;40:1586-1590

Increasing Risk of Relapse after Treatment of *Clostridium difficile* Colitis in Quebec, Canada



Kaplan-Meier plots of the 60-day probabilities of recurrence among patients with *Clostridium difficile* associated diarrhea treated with only **metronidazole**, comparing 1991-2002 to 2003-2004 *(top).*

Treatment with only **vancomycin** during 1991 2002 to 2003-2004 *(bottom)*

Clinical Infectious Diseases 2005;40:1591-1597

Clostridium difficile nosocomial outbreaks

Reference	Study
Muto et al. ICHE 2005;26:273-80	A large outbreak of *Clostridium difficile* associated disease with an unexpected proportion of deaths and colectomies at a teaching hospital following increased fluoroquinolone use.
Gaynes et al. CID. 2004;38:640-5	Outbreak of *Clostridium difficile* infection in a long-term care facility associated with gatifloxacin use
Johnson et al. NEJM 1999;341:1645-51	Epidemics of diarrhea caused by a clindamycin resistant strain of *Clostridium difficile* in four hospitals

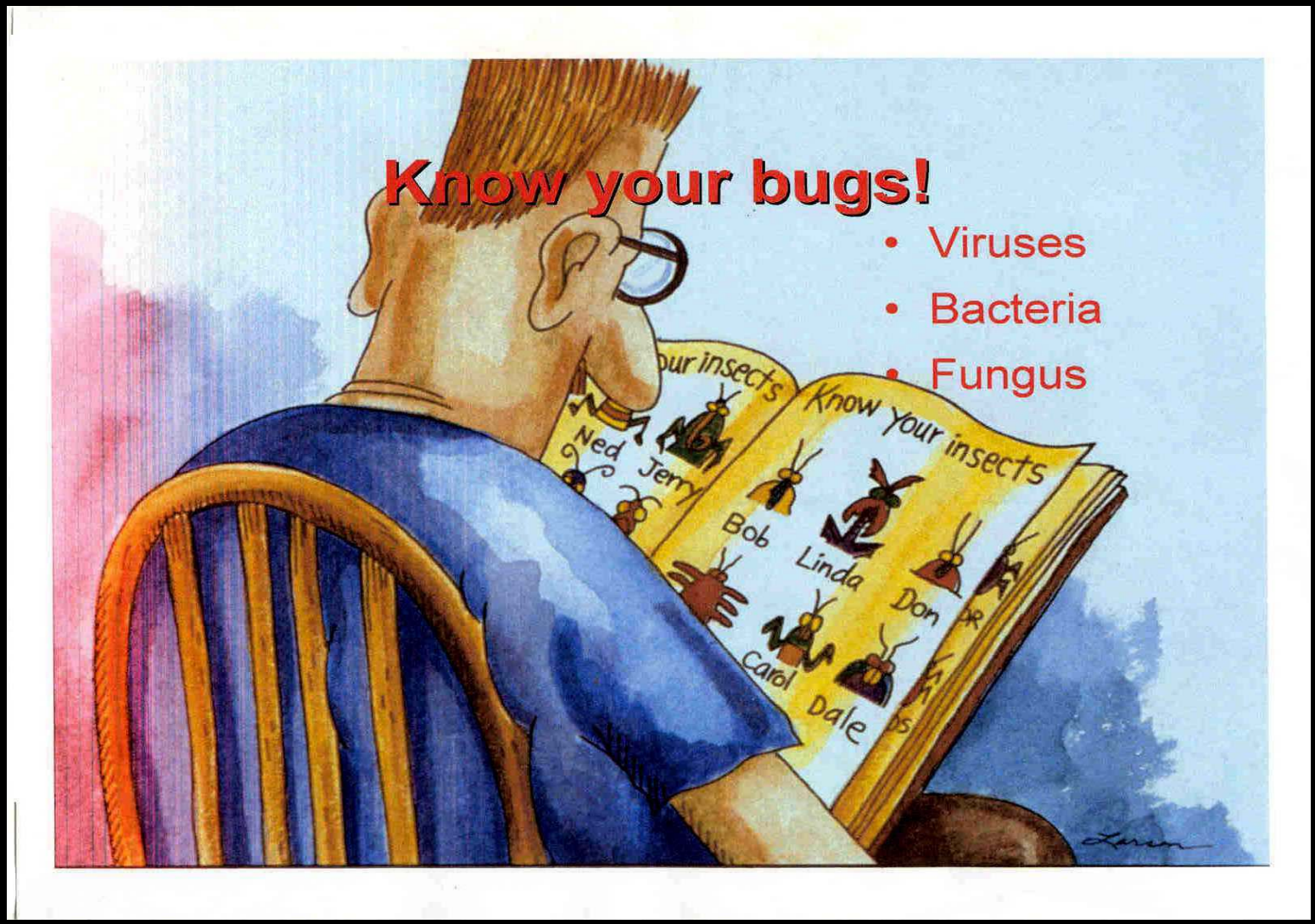
Clostridium difficile

- *Clostridium difficile* is becoming an increasingly important nosocomial pathogens
  - Outbreaks in acute and long term care facilities have been well described in the medical literature
- The associated morbidity & mortality is high
  - Diarrhea
  - Toxic megacolon
- Excessive antibiotic use, including fluoroquinolones and cephalosporins are associated risk factors

Clostridium difficile

- Because of the increasingly poor response to therapy, additional approaches to prevention and/or treatment of *C. difficile* colitis are in order
- Newer therapies
  - nitazoxanide or tinidazole
  - probiotics, such as *Saccharomyces boulardii* and *Lactobacillus* species
- Stringent application of infection control measures
  - Contact isolation
  - Meticulous hand hygiene
  - Thorough terminal disinfection of patient rooms
    - Sporicidal Agents

The Importance of Infection Control in Limiting the Cross Transmission of Pathogens



The inanimate environment is a reservoir of pathogens

Recovery of MRSA, VRE, C.*diff*, CNS and GNR

Devine et al. *Journal of Hospital Infection.* 2001;43;72-75

Lemmen et al *Journal of Hospital Infection*. 2004; 56:191-197

Trick et al. *Arch Phy Med Rehabil* Vol 83, July 2002

Walther et al. *Biol Review,* 2004:849-869

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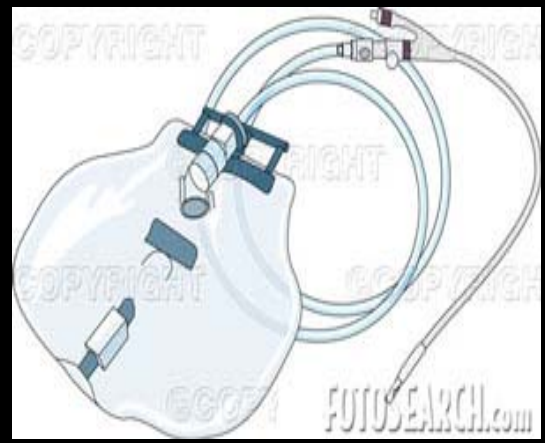

Lemmen et al *Journal of Hospital Infection*. 2004; 56:191-197

Trick et al. *Arch Phy Med Rehabil* Vol 83, July 2002

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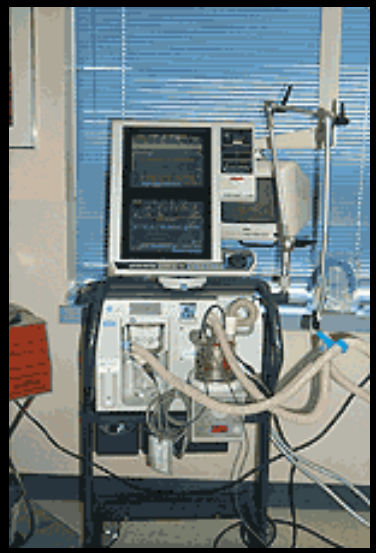

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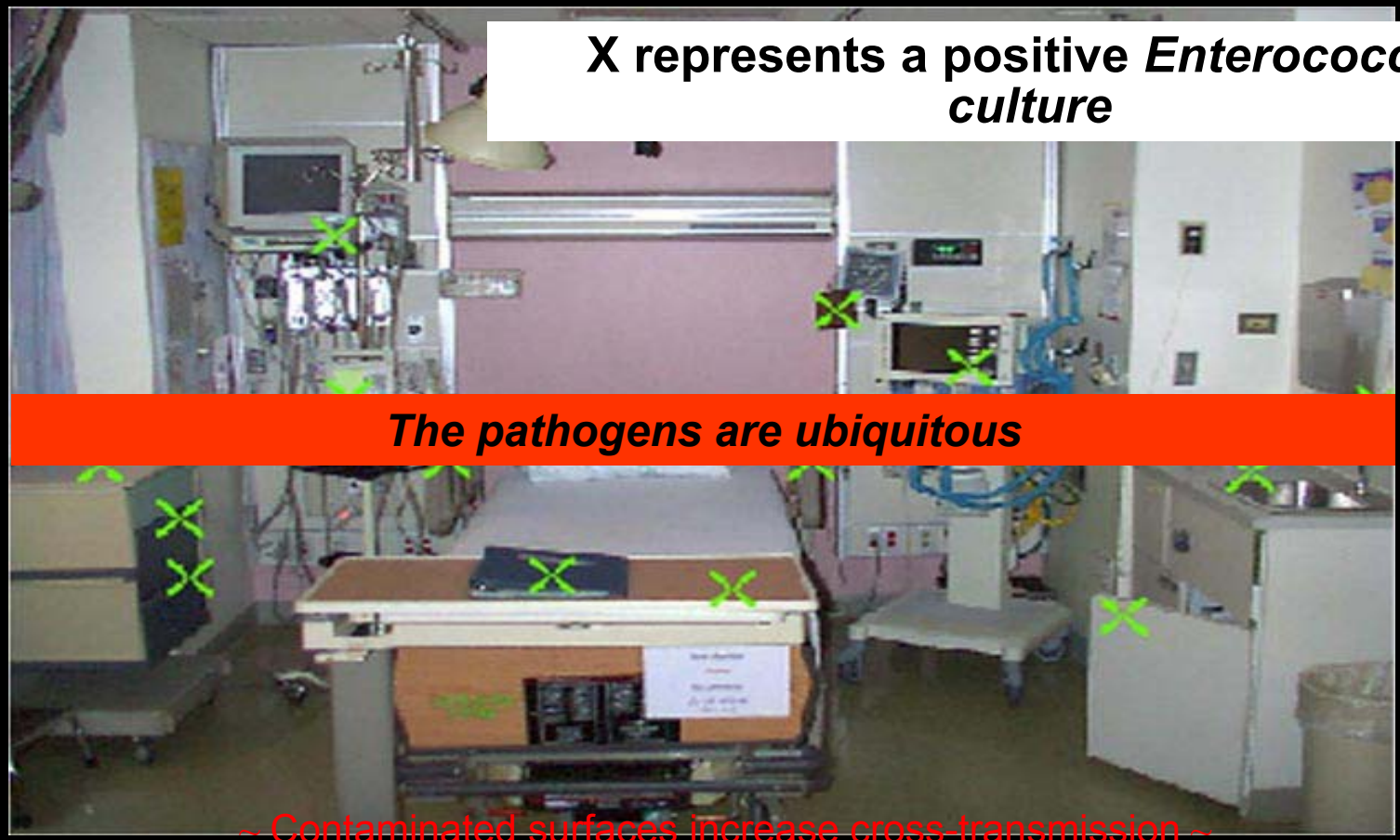
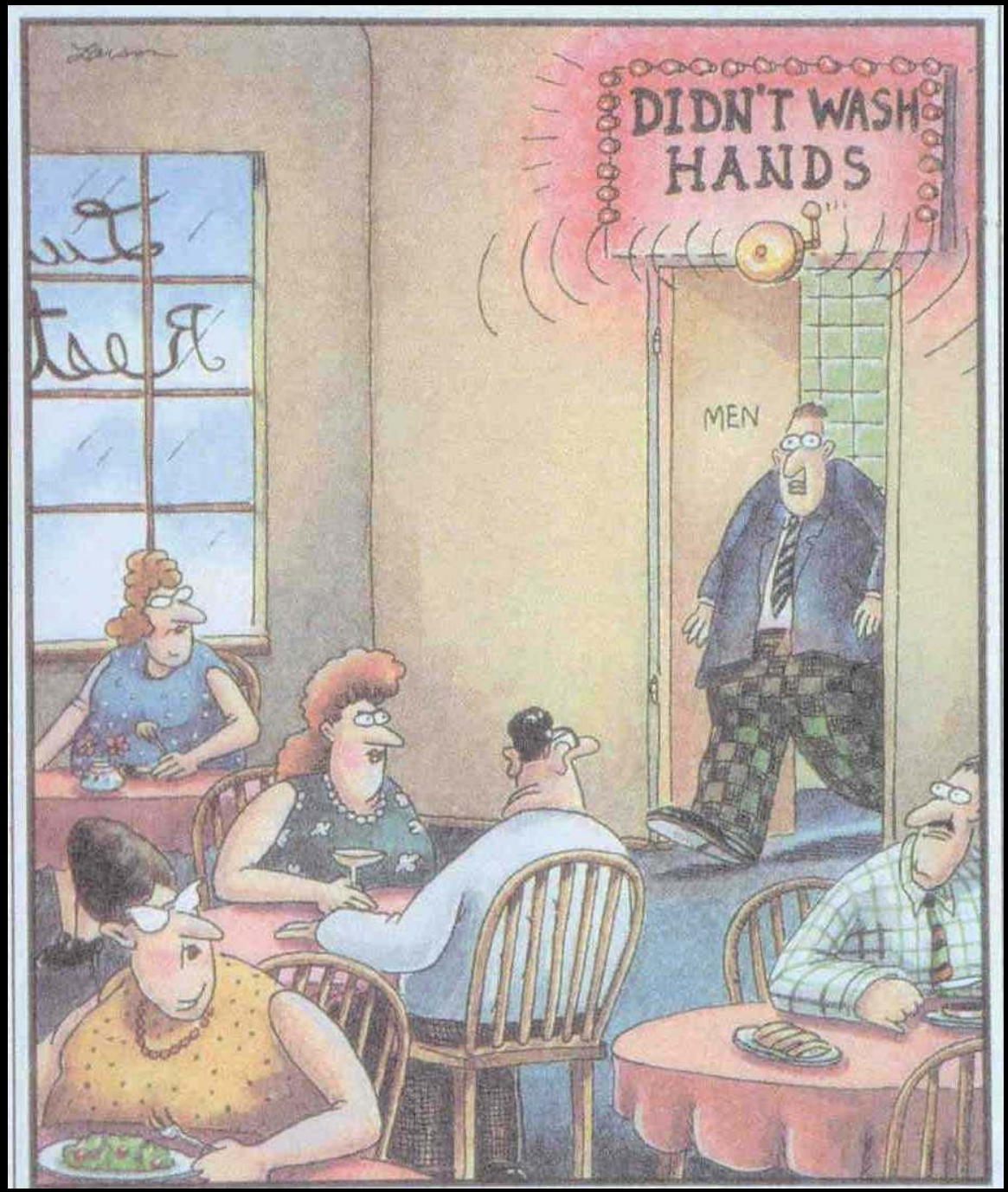


Abstract: The Risk of Hand and Glove Contamination after Contact with a VRE (+) Patient Environment. Hayden M, ICAAC, 2001, Chicago, IL.


DIDN'T WASH HANDS
MEN

Alcohol based hand hygiene

Quick

Easy to use

Very effective antisepsis due to bactericidal properties of alcohol

Hand Hygiene

- Single most important method to limit cross transmission of nosocomial pathogens
- Multiple opportunities exist for HCW hand contamination
  - Direct patient care
  - Inanimate environment
- Alcohol based hand sanitizers are ubiquitous
  - **USE THEM BEFORE AND AFTER PATIENT CARE ACTIVITIES**

Hand Hygiene

Clostridium difficile

•Hand washing with antiseptic impregnated soap is preferred method for hand hygiene.

•Alcohol based hand sanitizers do not consistently and adequately remove *Clostridium difficile* spores.

http://www.bumc.bu.edu/www/bumc/ehs/images/hands.jpg

Contact Precautions for drug resistant pathogens.

Gowns and gloves must be worn upon entry into the patient's room

Terminal Disinfection of Patient Rooms Harboring Drug Resistant Pathogens

- All touchable surfaces and all equipment in the room should be cleaned thoroughly at the time of patient discharge using a hospital approved disinfectant
- Goal:

Decontamination of inanimate environment

Conclusion

- Important emerging and resurgent pathogens include CA-MRSA, *A.baumanii* and *C.difficile*
- CA-MRSA
  - PVL gene virulence factor
  - Skin/soft tissue infections & necrotizing pneumonia
  - Outbreaks seen in communities, prisoners and athletic teams

Conclusion

- *A.baumanii*
  - Important nosocomial pathogen
  - Associated with multidrug resistance
  - Outbreaks are well documented in the ICU environment
- *C.difficile*
  - Increased incidence
  - New strain with increased toxin production
  - Significant morbidity and mortality
  - Excessive antibiotic use is an important risk factor

Conclusion

- Important infection control measures to limit cross transmission
  - Meticulous hand hygiene
  - Contact isolation precautions
  - Environmental decontamination
  - Judicious use of antibiotics

The End