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

SEACM
Virginia Spring Meeting
April 21, 2006

Gonzalo Bearman MD, MPH
Assistant Professor of Medicine,
Epidemiology and Community Health
Associate Hospital Epidemiologist
Virginia Commonwealth University
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

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

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

<table>
<thead>
<tr>
<th>Infections associated with CA-MRSA</th>
<th>Variable</th>
<th>Atlanta N=1267</th>
<th>Baltimore N=115</th>
<th>Minnesota N=265</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Bacteremia</td>
<td>32 (2)</td>
<td>7 (6)</td>
<td>6 (2)</td>
<td></td>
<td>0.66</td>
</tr>
<tr>
<td>Meningitis</td>
<td>1 (&lt;1)</td>
<td>1 (1)</td>
<td>0</td>
<td></td>
<td>0.84</td>
</tr>
<tr>
<td>Osteomyelitis</td>
<td>11 (1)</td>
<td>6 (5)</td>
<td>7 (3)</td>
<td></td>
<td>&lt;0.01</td>
</tr>
<tr>
<td>Bursitis</td>
<td>12 (1)</td>
<td>0</td>
<td>7 (3)</td>
<td></td>
<td>0.04</td>
</tr>
<tr>
<td>Arthritis</td>
<td>13 (1)</td>
<td>0</td>
<td>2 (1)</td>
<td></td>
<td>0.52</td>
</tr>
</tbody>
</table>

Fridkin et al. New England Journal of Medicine, April 7, 2005
Methicillin-Resistant *Staphylococcus aureus* Disease in Three Communities

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

Fridkin et al. New England Journal of Medicine, April 7, 2005
## Methicillin-Resistant *Staphylococcus aureus* Disease in Three Communities

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

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

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

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

<table>
<thead>
<tr>
<th></th>
<th>Count</th>
<th>Percentage</th>
</tr>
</thead>
<tbody>
<tr>
<td><em>S. aureus</em> infections</td>
<td>389</td>
<td></td>
</tr>
<tr>
<td>MRSA infections</td>
<td>279/389 (72%)</td>
<td></td>
</tr>
<tr>
<td>Community onset MRSA infections of all <em>S. aureus</em> infection</td>
<td>244/389 (63%)</td>
<td></td>
</tr>
<tr>
<td>Community onset MRSA of all MRSA infections</td>
<td>244/279 (87%)</td>
<td></td>
</tr>
<tr>
<td>MRSA isolates undergoing PFGE</td>
<td>175</td>
<td></td>
</tr>
<tr>
<td>PFGE consistent with CA-MRSA</td>
<td>159/175 (91%)</td>
<td></td>
</tr>
<tr>
<td>MRSA USA 300 Clone</td>
<td>157/159 (99%)</td>
<td></td>
</tr>
</tbody>
</table>

Community-acquired MRSA USA 300 genotype usually demonstrates resistance to β-lactams and erythromycin and retains susceptibility to clindamycin, trimethoprim–sulfamethoxazole, and fluoroquinolones.
Emergence of Community-Acquired Methicillin-Resistant \textit{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]),

CA-MRSA In Athletes
## CA-MRSA In Athletes

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

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

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

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.

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

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
- 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

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

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

Source of *A. baumanii* Nosocomial Bloodstream Infection

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

- Respiratory tract: 71%
- Abdominal infection: 19%
- Central venous line: 8%

N=37

Inflammatory Response to *A. baumanii* Nosocomial Bloodstream Infection

- **Sepsis**: 55%
- **Severe sepsis**: 21%
- **Septic shock**: 24%

N=42

### Independent Predictors of *A. baumanii* Nosocomial Bloodstream Infection

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

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

Impact of *Acinetobacter* Infection in the ICU
# Impact of *Acinetobacter* Bloodstream Infection in the ICU

<table>
<thead>
<tr>
<th>Outcome</th>
<th>Group</th>
<th>Bloodstream infection</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mortality</td>
<td>Cases</td>
<td>42%</td>
</tr>
<tr>
<td></td>
<td>Controls</td>
<td>34%</td>
</tr>
<tr>
<td>Attributable mortality</td>
<td></td>
<td>8%</td>
</tr>
<tr>
<td>Risk ratio for death</td>
<td></td>
<td>1.0 (CI\textsubscript{95} 0.7-1.4)</td>
</tr>
<tr>
<td>Length of ICU stay (median)</td>
<td>Cases</td>
<td>25 days</td>
</tr>
<tr>
<td></td>
<td>Controls</td>
<td>20 days</td>
</tr>
<tr>
<td>Excess ICU LOS</td>
<td></td>
<td>5 days</td>
</tr>
</tbody>
</table>

- 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

Acinetobacter outbreaks

Detection of *Acinetobacter* Infections

Consider: organ site, genetic typing, hospital location

- Common source outbreak with respiratory site predominance
- Common source outbreak without respiratory site predominance
- Respiratory site outbreaks without an identified common source
- Non-respiratory site outbreaks without an identified common source

# Acinetobacter outbreaks 1977-2000

Extensive Literature review and summary of 51 *Acinetobacter* outbreaks

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

### Acinetobacter outbreaks 1977-2000

Studies with a focus on antimicrobial resistance

<table>
<thead>
<tr>
<th>Antimicrobial class</th>
<th>Number of studies reporting new or increasing resistance</th>
</tr>
</thead>
<tbody>
<tr>
<td>Aminoglycosides</td>
<td>6</td>
</tr>
<tr>
<td>Multiple classes</td>
<td>14</td>
</tr>
<tr>
<td>Carbapenems</td>
<td>3</td>
</tr>
</tbody>
</table>

Acinetobacter outbreaks 1977-2000

13 Studies with a common source outbreak with a respiratory cluster:
• Clonal transmission confirmed by PFGE or PCR-based typing

<table>
<thead>
<tr>
<th>Setting:</th>
<th>Common Source:</th>
</tr>
</thead>
<tbody>
<tr>
<td>Adult ICU</td>
<td>Ventilator spirometers</td>
</tr>
<tr>
<td>Adult, neonatal and pediatric</td>
<td>Reusable ventilator circuits</td>
</tr>
<tr>
<td>ICU</td>
<td>In line temperature monitor probes</td>
</tr>
<tr>
<td>Adult mixed ICU</td>
<td>Ventilator temperature probes</td>
</tr>
<tr>
<td>Surgical and medical ICU</td>
<td>‘Y’ piece of ventilator</td>
</tr>
<tr>
<td>Adult ICU</td>
<td>Suction catheter and bottle</td>
</tr>
<tr>
<td>Neonatal ICU</td>
<td>Peak flow meter</td>
</tr>
<tr>
<td>Adult mixed ICU</td>
<td></td>
</tr>
</tbody>
</table>

**Acinetobacter outbreaks 1977-2000**

12 Studies with a common source outbreak **without** a respiratory cluster:
- Clonal transmission confirmed by PFGE or PCR-based typing

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

**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

<table>
<thead>
<tr>
<th>Settings</th>
<th>Medical ICU</th>
<th>Surgical ICU</th>
<th>Shock-Trauma ICU</th>
<th>Medical Wards</th>
<th>Nursery</th>
<th>Mixed Medical/Surgical ICU</th>
<th>Burn and Plastic Surgery Wards</th>
</tr>
</thead>
</table>

Reservoirs of *Acinetobacter*: Where do these organisms reside?
Environmental Contamination with *Acinetobacter*

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

## Acinetobacter spp Skin Colonization

<table>
<thead>
<tr>
<th>Body site</th>
<th>Hospitalized patients (n=40)</th>
<th>Healthy controls (n=40)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Forehead</td>
<td>33%</td>
<td>13%</td>
</tr>
<tr>
<td>Ear</td>
<td>35%</td>
<td>7%</td>
</tr>
<tr>
<td>Nose</td>
<td>33%</td>
<td>8%</td>
</tr>
<tr>
<td>Throat</td>
<td>15%</td>
<td>0%</td>
</tr>
<tr>
<td>Axilla</td>
<td>33%</td>
<td>3%</td>
</tr>
<tr>
<td>Hand</td>
<td>33%</td>
<td>20%</td>
</tr>
<tr>
<td>Groin</td>
<td>38%</td>
<td>13%</td>
</tr>
<tr>
<td>Perineum</td>
<td>20%</td>
<td>3%</td>
</tr>
<tr>
<td>Toe web</td>
<td>40%</td>
<td>8%</td>
</tr>
<tr>
<td>Any site</td>
<td>75%</td>
<td>42.5%</td>
</tr>
</tbody>
</table>

*A. baumanii* isolated from 2 patients & 1 control only

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)

Hand Contamination in HCWs

Opportunities for cross transmission are multiple
Acinetobacter Susceptibility, US, 2002-2003

% susceptible

Increasing rate of antibiotic resistance

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

<table>
<thead>
<tr>
<th>Antimicrobial resistance</th>
<th>Hospital (n=101)</th>
<th>Community (n=23)</th>
<th>Odds Ratio (CI$_{95}$)</th>
</tr>
</thead>
<tbody>
<tr>
<td>3rd generation cephalosporins</td>
<td>88%</td>
<td>9%</td>
<td>78 (15-553)</td>
</tr>
<tr>
<td>Carbapenems</td>
<td>64%</td>
<td>4%</td>
<td>39 (5-811)</td>
</tr>
<tr>
<td>Aminoglycosides</td>
<td>43%</td>
<td>4%</td>
<td>16 (2-337)</td>
</tr>
<tr>
<td>Multidrug resistant*</td>
<td>37%</td>
<td>0%</td>
<td>Not calculable</td>
</tr>
</tbody>
</table>

*3rd* gen. cephalosporins + carbapenem + aminoglycoside

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

<table>
<thead>
<tr>
<th>Alcohol(s)</th>
<th>Other agents</th>
<th>Log ↓</th>
</tr>
</thead>
<tbody>
<tr>
<td>60% isopropyl, 0.05% phenoxyethyl</td>
<td></td>
<td>-0.02</td>
</tr>
<tr>
<td>46% ethyl, 27% isopropyl, 1% benzyl</td>
<td></td>
<td>-0.05</td>
</tr>
<tr>
<td>70% ethyl</td>
<td>0.3% triclosan</td>
<td>0.3</td>
</tr>
<tr>
<td>30% I-propanol, 45% isopropyl</td>
<td>0.2% mecetronium</td>
<td>3.2</td>
</tr>
<tr>
<td>60% isopropyl</td>
<td>0.5% chlorhexidine</td>
<td>&gt;5.0</td>
</tr>
<tr>
<td>70% isopropyl</td>
<td>0.5% chlorhexidine, 0.45% H₂O₂</td>
<td>&gt;5.0</td>
</tr>
<tr>
<td>89% isopropyl/ethyl</td>
<td>0.1% chlorhexidine</td>
<td>&gt;5.0</td>
</tr>
<tr>
<td>40% I-propanol, 30% isopropyl</td>
<td>0.1% octenidine</td>
<td>&gt;5.0</td>
</tr>
<tr>
<td>55% isopropyl</td>
<td>0.5% triclosan</td>
<td>&gt;5.0</td>
</tr>
</tbody>
</table>

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

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
  - tcdA Toxin A
  - tcdB Toxin B
  - tcdC porin gene
    - Partial deletions of tcdC
      - The expression of tcdA and tcdB is downregulated by the tcdC 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**

<table>
<thead>
<tr>
<th>Results</th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>Total # of episodes</td>
<td>1719 Episodes of <em>C. difficile</em> diarrhea</td>
</tr>
<tr>
<td>Incidence</td>
<td>22.5 per 1000 hospital admissions</td>
</tr>
<tr>
<td>30 day attributable mortality</td>
<td>6.9 percent</td>
</tr>
</tbody>
</table>

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

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>Case Patients N=237</th>
<th>Control Patients N=237</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Number of antibiotics received</td>
<td>1.9 +/- 1.1</td>
<td>1.3 +/- 1.3</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Cephalosporins</td>
<td>115 (48.5)</td>
<td>65 (27.4)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Clindamycin</td>
<td>19 (8.0)</td>
<td>6 (2.5)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Quinolones</td>
<td>128 (54.0)</td>
<td>75 (31.6)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Enteral tube</td>
<td>44 (18.6)</td>
<td>28 (11.8)</td>
<td>0.04</td>
</tr>
</tbody>
</table>

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**

<table>
<thead>
<tr>
<th>Antibiotic</th>
<th>Odds Ratio</th>
<th>95% CI</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cephalosporins</td>
<td>3.8</td>
<td>2.2-6.6</td>
</tr>
<tr>
<td>Fluoroquinolones</td>
<td>3.9</td>
<td>2.3-6.6</td>
</tr>
<tr>
<td>Clindamycin</td>
<td>1.6</td>
<td>0.5-4.8</td>
</tr>
<tr>
<td>Penicillins -beta lactamase inhibitor</td>
<td>1.2</td>
<td>0.7-2.3</td>
</tr>
<tr>
<td>Carbapenems</td>
<td>1.4</td>
<td>0.3-6.3</td>
</tr>
</tbody>
</table>

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%; \( P < .05 \))
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

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


**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

Know your bugs!
- Viruses
- Bacteria
- Fungus
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
The inanimate environment is a reservoir of pathogens

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

Lemmen et al. Journal of Hospital Infection. 2004; 56:191-197
Walther et al. Biol Review, 2004
The inanimate environment is a reservoir of pathogens

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

Devine et al. Journal of Hospital Infection. 2001;43;72-75
Lemmen et al Journal of Hospital Infection. 2004; 56:191-197
The inanimate environment is a reservoir of pathogens.


The pathogens are ubiquitous.

- Contaminated surfaces increase cross-transmission -
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.

Visitors: Report to nurse before entry

- Handwashing after all patient / environmental contact and glove removal.
- Gloves required for all patient / environmental contact.
- Long sleeved gown required for all patient / environmental contact.
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