Control of Epidemiologically Important, resistant gram-positive bacteria

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Learning Objectives:

- Overview
  - *S. aureus*
  - *Enterococcus*
- Epidemiology of MRSA/VRE
- Hospital interventions for MRSA/VRE
- MRSA in non-acute care
- Conclusions
Multidrug-resistant organisms (MDROs)

ESKAPE Bugs

Enterococcus faecium
Staphylococcus aureus
Klebsiella pneumoniae
Acinetobacter baumannii
Pseudomonas aeruginosa
Enterobacter spp.

“...extraordinarily important...they cause the lion’s share of nosocomial infections but also because they represent paradigms of pathogenesis, transmission and resistance.”

Rice, JID 2004

Staphylococcus aureus resistance

• Methicillin-resistant Staphylococcus aureus (MRSA) resistant to beta-lactams antibiotics
  – methicillin, oxacillin, pencillin, and amoxicillin

• Traditionally MRSA associated with resistance to other antibiotics
  – “community-associated” MRSA more susceptible (bactrim, clindamycin, doxycycline)

Gorwitz et al. JID. 2008
MRSA antibiotics

<table>
<thead>
<tr>
<th>Antibiotics</th>
</tr>
</thead>
<tbody>
<tr>
<td>Vancomycin</td>
</tr>
<tr>
<td>Daptomycin (not lungs)</td>
</tr>
<tr>
<td>Linezolid (oral)</td>
</tr>
<tr>
<td>Tigecycline</td>
</tr>
<tr>
<td>Ceftaroline</td>
</tr>
<tr>
<td>Clindamycin/ doxycycline/ bactrim (oral)</td>
</tr>
</tbody>
</table>

Treatment of *S. aureus*

Methicillin-susceptible *S. aureus* (MSSA)

- Nafcillin/cefazolin better than vancomycin

- For MRSA some feel daptomycin > vancomycin
  but data minimal

Taper antibiotics to treat specific organism!

Mohr & Murray CID 2007
Treating Staph bacteremia

• *S. lugdunensis* — CoNS, manage like *S. aureus*
• *S. aureus* — Generally treat 4-6 weeks
  – Short course (14 days) if
    • catheter removed
    • patient non-diabetic & non-immunocompromised, no hardware
    • negative U/S & TEE
    • fever and BSI resolved within 72 hours of initiation of ABX
    • no signs/symptoms of metastatic infection

Fowler et al. AIM 2003

VRE

An isolate of *Enterococcus* that is resistant to vancomycin

• Endemic in most US hospitals
• Asymptomatic carriage (GI tract)
• Illness ranges from very minor to life-threatening
• Vancomycin resistance is more commonly seen in isolates of *E. faecium* than *E. faecalis*.
  – *E. faecium* - 80% vancomycin resistant
  – *E. faecalis* - 6.9% vancomycin resistant

Hidron ICHE 2008
Antibiotic exposure as a risk factor for resistance

• MRSA and VRE are resistant through acquisition of genes
  Acquisition of genes is very rare!
  Clones with resistant genes transfer between people
  • Antibiotics kill off normal flora
    – Easier to acquire MRSA/VRE
    – Easier to spread MRSA/VRE

Antibiotics do not cause bacteria that are present to develop into MRSA or VRE!

Treatment of Enterococcus

• Amoxicillin/ampicillin (most *E. faecalis*, BEST!)
  If resistant then

• Vancomycin
  if resistant then

• Daptomycin/linezolid/tigecycline (VRE)

• Aminoglycosides for synergy (endocarditis)
Epidemiology

MRSA
• Community and healthcare acquired
• Nose>skin>GI tract (swab nose)

VRE
• Healthcare acquired only
• GI Tract (swab perirectal area)

Infections in the hospital
• ~60% of patients receive antibiotics
• 4% hospitalized patients have healthcare associated infections
  • 1% CLABSI/CAUTI/VAP
  • 1% Surgical Site Infections
  • 1% pneumonia (non-VAP)
  • <1% GI
• Most common organisms:
  • 12% C. difficile
  • 11% S. aureus (~6% MRSA)
  • 10% Klebsiella
  • 9% E. coli
  • 9% Enterococcus (~3% VRE)

Braykov et al. IDWeek 2012; Magill et al NEJM 2014
Multidrug-Resistant HAIs in 2007

16% of all HAIs are multidrug-resistant
1. Methicillin-resistant *Staphylococcus aureus* (8%)
2. Vancomycin-resistant *Enterococcus* (4%)
3. Carbapenem-resistant *P. aeruginosa* (2%)
4. ESBL *K. pneumoniae* (1%)
5. ESBL *E. coli* (0.5%)
6. Carbapenem-resistant *A. baumannii, K. pneumoniae, K. oxytoca*, and *E. coli* (0.5%)

Hidron et. al. ICHE. 2008

Healthcare-Associated MRSA

- National estimates:
  - 94,000 invasive MRSA infections per year
    - 86% among people with exposures to hospitals or health care settings
- Impact of acquiring MRSA in the hospital:
  - 33% develop MRSA disease within one year
  - 9% die with MRSA
- The risk of invasive disease extends beyond one year

Kleven et al. *JAMA*. 2007
Huang et al. *Clin Infect Dis* 2003
Datta et al. *Clin Infect Dis* 2008
S. aureus transmissions

- One ICU
- 37 apparent acquisitions of S. aureus
- Only 19% matching whole genome sequence
- What about other “acquisitions”?
  - Visitors
  - Healthcare-workers
  - Fomites
  - Undetected previous S. aureus carriage

Price et al. CID 2014; David & Daum CID 2014

MRSA infections

- In the community, most MRSA infections are skin infections.

- More severe or potentially life-threatening MRSA infections occur most frequently among patients in healthcare settings.

- Illness ranges from very minor to life-threatening

Gorwitz et al. JID. 2008
Healthcare-Associated MRSA

- Greater length of stay and $ than methicillin-susceptible infections
- Colonization with MRSA associated with higher risk of subsequent MRSA infection
  - Infections with same colonizing organism
- Outbreak investigations suggest patient-to-patient transmission in hospital units

Cosgrove et al. ICHE 2005
Albrich et al. Lancet Infect Dis 2008
Kallen et al. JAMA 2010

Community-Associated MRSA

- “Community-associated” strains are genetically distinct from typical healthcare-associated strains (“USA 300”)
- 2000-2010 MRSA emerged as a community pathogen
- Initially associated with reservations/prisons/sports teams
- In recent years, “CA-MRSA” has become predominant MRSA in many healthcare systems
Comparison of Healthcare-and Community-Associated MRSA

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>HA-MRSA</th>
<th>CA-MRSA</th>
</tr>
</thead>
<tbody>
<tr>
<td>Classic risk factors</td>
<td>Health care exposure, antibiotic therapy, underlying illness, increasing age</td>
<td>Crowding, contact, compromised skin, shared personal care items, environmental</td>
</tr>
</tbody>
</table>

CA vs. HA becoming less important - treat syndromes - antibiotics by antibiogram/susceptibility

<table>
<thead>
<tr>
<th>Common PFGE types</th>
<th>USA100, USA200</th>
<th>USA300, USA400</th>
</tr>
</thead>
<tbody>
<tr>
<td>Panton-Valentin leukocidin (PVL)</td>
<td>Rare</td>
<td>Common</td>
</tr>
</tbody>
</table>

How we identify organisms in the hospital?

**Surveillance**

**Passive**
- Antibiograms
- Clinical Cultures
- Infections

**Active**
- Screening
- Asymptomatic Colonization

**Why do we do it?**
- Prevent the spread of pathogens
- Prevent infection
- Monitor epidemiologic trends
- Detect newly emerging pathogens
- Measure effectiveness of interventions
Clinical Cultures

Asymptomatic Colonization

MRSA colonization vs. infection

- Persons may be colonized or infected with MRSA
  - **Colonization**: organism is present in or on the body but is not causing illness
  - **Infection**: organism is present and is causing signs and symptoms of illness
  - **Clinical cultures**: some mix of above

Community:
- 1/3 people are colonized in the nose with *S. aureus*
- less than 2% are colonized with MRSA
Health Care–Associated Invasive MRSA Infections, 2005-2008

<table>
<thead>
<tr>
<th>Epidemiological Category and Year</th>
<th>Population (Denominator)</th>
<th>Case Count</th>
<th>Pooled Mean Incidence Per 10000 Person-Years (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Hospital-onset</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>2006</td>
<td>14,755,694</td>
<td>1500</td>
<td>1.02 (0.97-1.07)</td>
</tr>
<tr>
<td>2006</td>
<td>14,964,451</td>
<td>1054</td>
<td>0.91 (0.86-0.96)</td>
</tr>
<tr>
<td>2007</td>
<td>15,155,918</td>
<td>1289</td>
<td>0.85 (0.81-0.90)</td>
</tr>
<tr>
<td>2008</td>
<td>15,315,152</td>
<td>1130</td>
<td>0.74 (0.70-0.78)</td>
</tr>
<tr>
<td>Health-care–associated community-onset</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>2006</td>
<td>14,755,694</td>
<td>9217</td>
<td>2.18 (2.11-2.26)</td>
</tr>
<tr>
<td>2006</td>
<td>14,964,451</td>
<td>3125</td>
<td>2.09 (2.02-2.16)</td>
</tr>
<tr>
<td>2007</td>
<td>15,155,918</td>
<td>3074</td>
<td>2.03 (1.96-2.10)</td>
</tr>
<tr>
<td>2008</td>
<td>15,315,152</td>
<td>2819</td>
<td>1.84 (1.77-1.91)</td>
</tr>
</tbody>
</table>

Kallen et al. JAMA 2010

Central-line associated BSI 2001-2009

- CDC NHSN data
- ICU patients nationwide
- 43,000 CLABSI to 18,000
- 58% reduction
- Reductions in *S. aureus* more marked than GNR, *Candida* and *Enterococcus*

MMWR 2011
Interventions to prevent MRSA & VRE in healthcare settings

Horizontal vs. vertical interventions

• Horizontal interventions affect multiple organisms/HAs
• Vertical interventions target one organism

Wenzel & Edmond 2010
Edmond & Wenzel NEJM 2013
Transmission of bacteria (colonization)

General horizontal measures

- Hand hygiene
- Antimicrobial stewardship
- Standard Precautions
- General HAI prevention
- Environmental cleaning
The most basic intervention

http://www.cdc.gov/mmwr/PDF/rr/rr5116.pdf
Antimicrobial stewardship

• 50% of hospital antimicrobial use unnecessary
• Antimicrobial stewardship programs can decrease unnecessary use
• Probably decrease *C. difficile* and adverse drug events
• Possibly decrease resistance

Contact Precautions

• VRE, MRSA
  (multiple antibiotic resistant gram negative rods, *Clostridium difficile*)
  – most common form of isolation
• private room
  – cohort same organisms
• gloves & gowns for any contact with patient or environment
• Once MDRO-positive, we assume the patient remains positive and continue Contact Precautions
  – Remove MRSA after 3 negative cxs
How to prevent MRSA/VRE device infections

• Do not use device
• Remove device as soon as possible
• Insert device in proper fashion (checklist)
• Perform routine care of device
• Use antibiotic/antiseptic compounds on devices (biopatch/antibiotic impregnated materials)

Environmental Cleaning

Patient A → Terminal Cleaning → Patient B
Transmission of MRSA/VRE to next room occupant

- Risk of VRE or MRSA increases if prior occupant had MRSA or VRE

Table 3. Predictors of Methicillin-Resistant Staphylococcus aureus (MRSA) and Vancomycin-Resistant Enterococci (VRE) Acquisition

<table>
<thead>
<tr>
<th>Model</th>
<th>Odds Ratio (95% CI)</th>
<th>P Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>MRSA</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Prior occupant MRSA positive</td>
<td>1.4 (1.0-1.8)</td>
<td>.04</td>
</tr>
<tr>
<td>Age, in decades</td>
<td>1.1 (1.0-1.2)</td>
<td>.02</td>
</tr>
<tr>
<td>Pre-ICU LOS†</td>
<td>1.2 (1.1-1.4)</td>
<td>&lt;.001</td>
</tr>
<tr>
<td>Leukemia</td>
<td>0.4 (0.2-0.9)</td>
<td>.02</td>
</tr>
<tr>
<td>VRE</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Prior occupant VRE positive</td>
<td>1.4 (1.0-1.9)</td>
<td>.02</td>
</tr>
<tr>
<td>Age, in decades</td>
<td>1.2 (1.1-1.3)</td>
<td>&lt;.001</td>
</tr>
<tr>
<td>Pre-ICU LOS†</td>
<td>1.4 (1.3-1.6)</td>
<td>&lt;.001</td>
</tr>
<tr>
<td>Diabetes mellitus</td>
<td>1.3 (1.0-1.7)</td>
<td>.03</td>
</tr>
</tbody>
</table>

Huang et al. AIM 2006
Drees et al. CID 2008
Effects of enhanced cleaning

<table>
<thead>
<tr>
<th></th>
<th>Before cleaning</th>
<th>After cleaning</th>
</tr>
</thead>
<tbody>
<tr>
<td>Acquisition of MRSA</td>
<td>3.0%</td>
<td>1.5%</td>
</tr>
<tr>
<td>Acquisition of VRE</td>
<td>3.0%</td>
<td>2.2%</td>
</tr>
<tr>
<td>Previous MRSA room</td>
<td>3.9%</td>
<td>1.5%</td>
</tr>
<tr>
<td>Previous VRE room</td>
<td>4.5%</td>
<td>3.5%</td>
</tr>
</tbody>
</table>

- Hospital intervention 10 ICUs
- Education
- Evaluation with fluorescent dots

Datta et al. AIM 2011

Specific trials for MRSA & VRE in healthcare settings

(Cluster Randomized trials)
Veterans Affairs Initiative to Prevent Methicillin-Resistant Staphylococcus aureus Infections

Improved hand hygiene
Positive deviance
MRSA Active Detection and isolation
Institutional culture change
Administrative pressure to reduce HAI rates

MRSA Transmission decreased 17%
Jain et al. NEJM 2011

Intervention to Reduce Transmission of Resistant Bacteria in Intensive Care

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>Baseline Period</th>
<th>Intervention Period</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Intervention ICUs</td>
<td>control ICUs</td>
</tr>
<tr>
<td>Colonization or infection during previous year — %</td>
<td>median (range)</td>
<td>median (range)</td>
</tr>
<tr>
<td>18 ICUs</td>
<td>Active detection and Isolation</td>
<td>Presumptive universal glove</td>
</tr>
</tbody>
</table>
Mandatory MRSA screening

Daily Bathing with Chlorhexidine

- Use of chlorhexidine, rather than regular soap and water, for daily patient bathing has been associated with a reduced incidence of:
- CLABSI
- VRE contamination of patients' skin, HCW hands, and the environment
- Acquisition of MRSA and VRE

Kassakian SZ, ICHE 2011
Climo MW. Crit Care Med 2009
Vernon MO. Arch Intern Med 2006
Bleasdale SC. Arch Intern Med 2007
Trial of Chlorhexidine Gluconate (CHG) Bathing

- Once a day bathing with 2% CHG
- All patients in 9 units
- Crossover-cluster trial
- Reduced bacteremia 28%
  - CoNS
  - Candida
- Decreased MRSA/VRE 23%
  - Mostly VRE

Climo et al NEJM 2013

REDUCE-MRSA Trial

- Active surveillance + isolation
- Active surveillance + targeted decolonization
- Decolonization for all (mupirocin + chlorhexidine)
- Cluster trial 74 ICUs
- Reduced MRSA clinical cultures
- Reduced bacteremias
  - Mostly CoNS

Huang et al NEJM 2013
Universal Gown and Glove in ICUs

Historically:
• Used in outbreaks
• In Children, isolation decreased HAIs

BUGG Study 20 ICUs
   – Jan – Oct 2012
   – 10 hospitals to intervention

40% decrease in MRSA, no impact on VRE, no increase
Adverse events
Isolation.

Klein et al 1989, Harris et al JAMA 2013

Non-acute care prevention of MRSA
MRSA in LTCF

• Admission Prevalence higher than acute care
  – 20-30% vs. 2-15% of admissions

• Acquisition Rate lower than acute care
  – 0.4-1.8 vs. 3.0-25 per 1000 patient days

• Infection Risk lower than acute care
  – 0.2 vs. 0.6 per 1000 patient days

  Bradley, Ann Intern Med, 1991; Furuno, ICHE, 2011;
  Trick, Am J Geriat, 2004; Huang, JID, 2007;

Residents in long term care cannot be “isolated” like patients in acute care

<table>
<thead>
<tr>
<th>Acute care</th>
<th>Long-term care</th>
</tr>
</thead>
<tbody>
<tr>
<td>• Single room</td>
<td>• Few single rooms; difficult to move patients</td>
</tr>
<tr>
<td>• Contact Precautions</td>
<td>• Residents are encouraged to interact with one</td>
</tr>
<tr>
<td>– Gloves for walking into room</td>
<td>another, eat in common areas and share other</td>
</tr>
<tr>
<td>– Gowns for touching patient</td>
<td>activities</td>
</tr>
<tr>
<td>or environment</td>
<td></td>
</tr>
</tbody>
</table>
Use of Contact Precautions in Long Term Care

– the individual patient’s clinical situation
– prevalence or incidence of MDRO in the facility

Consider CP for:

• Ill residents
  – those totally dependent upon healthcare personnel for healthcare and activities of daily living
• Residents whose infected secretions or drainage cannot be contained
  – ventilator dependent

HICPAC MDRO Guidelines

Other non-acute care settings

(clinics, surgical centers, hemodialysis etc.)

• Poorly defined precautions
• Standard Precautions key
  – Hand hygiene
  – Gowns/gloves/goggles for possible exposure
• Other precautions based on risk of transmission/infection
Summary

• MRSA & VRE most common MDROs but appear to be decreasing in US hospitals
• Prevention better defined than for other organisms
  – Hand hygiene
  – HAI prevention bundles
  – Antibiotic stewardship
  – Contact Precautions
  – Environmental cleaning
• Active detection and isolation *not clearly* important
• Chlorhexidine bathing in ICUs appears helpful

Prevention of MRSA/VRE outside the hospital uncertain