Healthcare-Associated Pneumonia
Evidence-Based Treatment
2012

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Disclosure of Financial Relationships
Scott A. Flanders, MD

Has disclosed relationships with entities producing, marketing, re-selling, or distributing health care goods or services consumed by, or used on, patients.

<table>
<thead>
<tr>
<th>Consultant</th>
<th>Advisory Boards</th>
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<tr>
<td>IHI/CDC-Project Faculty</td>
<td>NONE</td>
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<th>Research and Grant Support</th>
<th>Speakers Bureau</th>
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<td>CDC Foundation</td>
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<td>NIH-CTSA</td>
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<td>Blue Cross Blue Shield, MI</td>
<td>Board Member</td>
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<td>NONE</td>
</tr>
</tbody>
</table>
Healthcare Associated Infections

• Three hospital study of 500 pts. with bacteremia
  – Community-acquired (CA)
  – Healthcare-associated (HA)
  – Nosocomial (N)

• Intravascular devices common
  – CA: 0%
  – HA: 40% (only 15% of patients had pneumonia as source)
  – N: 50%

• MRSA
  – CA: 2%
  – HA: 20%
  – N: 20%

Friedman, Ann Intern Med. 2002
Healthcare Associated Pneumonia
IDSA / ATS Guidelines: Am J Resp Crit Care 2005

• **Home Therapy**
  – IV
  – Wound Care
  – Nursing care through health agency

• **Hospital or Dialysis Clinic in past 30 days for**
  – Dialysis / Any IV therapy

• **Hospitalized ≥ 2 days in past 90? days**

• **Nursing Home or Long-Term Care Facility**

  *At Risk for Multidrug-Resistant Organisms (MDRs)*
# HCAP Criteria by Study


## Table 1  Health Care-Associated Pneumonia Inclusion Criteria, By Publication

<table>
<thead>
<tr>
<th>Health Care-Associated Pneumonia Risk Factor</th>
<th>Publication</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>1</td>
</tr>
<tr>
<td>Hospital admission in past 30 days</td>
<td>X</td>
</tr>
<tr>
<td>Hospital admission in past 90 days</td>
<td>X</td>
</tr>
<tr>
<td>Hospital admission or pneumonia treatment in 90 days</td>
<td>X</td>
</tr>
<tr>
<td>Hospital admission/surgery in past 180 days</td>
<td>X</td>
</tr>
<tr>
<td>Hospital admission in past 12 months</td>
<td>X</td>
</tr>
<tr>
<td>Admission from nursing home/extended care facility</td>
<td>X</td>
</tr>
<tr>
<td>Transfer from other health facility</td>
<td>X</td>
</tr>
<tr>
<td>Home infusion/intravenous therapy</td>
<td>X</td>
</tr>
<tr>
<td>Chronic dialysis</td>
<td>X</td>
</tr>
<tr>
<td>Home wound care</td>
<td>X</td>
</tr>
<tr>
<td>Family member with MDR pathogen</td>
<td>X</td>
</tr>
<tr>
<td>Attended hospital or HD clinic past 30 days</td>
<td>X</td>
</tr>
<tr>
<td>Regular clinic visits (HD, PD, and infusions)</td>
<td>X</td>
</tr>
<tr>
<td>Intravenous chemotherapy in past 30 days</td>
<td>X</td>
</tr>
<tr>
<td>Immunocompromised state</td>
<td>X</td>
</tr>
</tbody>
</table>

* For publication 2
† For publication 3
‡ For publication 4
§ For publication 5
Healthcare Associated Pneumonia

• Multiple Studies of CULTURE POSITIVE patients
  – (Kollef 05, Micek 07, Carratala 07, Venditti 09, etc.)

• Findings:
  
  **HCAP**
  - More MRSA, Pseudomonas
  - Higher mortality
  - More inappropriate RX

  **CAP**
  - More S. Pneumo
  - Lower Mortality
  - More appropriate RX
HCAP: How Common is it?

<table>
<thead>
<tr>
<th>Study</th>
<th>HCAP</th>
<th>CAP</th>
</tr>
</thead>
<tbody>
<tr>
<td>Kollef '05</td>
<td>30.8%</td>
<td>69.2%</td>
</tr>
<tr>
<td>Micek '07 &amp; Shorr '08</td>
<td>67.4%</td>
<td>32.6%</td>
</tr>
<tr>
<td>Carratala '07</td>
<td>17.3%</td>
<td>82.7%</td>
</tr>
<tr>
<td>Venditti '09</td>
<td>28.8%</td>
<td>71.2%</td>
</tr>
<tr>
<td>Shindo '09</td>
<td>38.0%</td>
<td>62.0%</td>
</tr>
<tr>
<td>Average</td>
<td>36.5%</td>
<td>63.9%</td>
</tr>
</tbody>
</table>

% HCAP of Community-Dwelling Adults Hospitalized for Pneumonia
Q3, a, b, c
Antimicrobial Therapy

Treatment for Patients at Risk for MDR Organisms

• Anti-pseudomonal beta-lactam
  +
• Aminoglycoside or Fluoroquinolone
  +
• Vancomycin or Linezolid

IDSA/ATS 2005
Kollef CID 2008
Treating HCAP by the Guidelines

- Survey of 1300 faculty
- Hospitalists, Pulm/Crit Care, ED
- 9 clinical case questions
- Also asked:
  - “Are you familiar with the HCAP guidelines?”
  - “Do you agree with the HCAP guidelines?”

Seymann, et al. CID, 2009
## Predicting MDR Infections

- Retrospective review
- 640 culture + pneumonia pts

### MDR Variables OR

<table>
<thead>
<tr>
<th>Variable</th>
<th>OR</th>
</tr>
</thead>
<tbody>
<tr>
<td>Recent Hosp</td>
<td>4.2</td>
</tr>
<tr>
<td>NH or LTC</td>
<td>2.8</td>
</tr>
<tr>
<td>Dialysis</td>
<td>2.1</td>
</tr>
<tr>
<td>ICU</td>
<td>1.6</td>
</tr>
</tbody>
</table>

### MRSA Risk

<table>
<thead>
<tr>
<th>Variable</th>
<th>OR</th>
</tr>
</thead>
<tbody>
<tr>
<td>Recent Hosp</td>
<td>2.4</td>
</tr>
<tr>
<td>NH</td>
<td>1.9</td>
</tr>
<tr>
<td>ICU</td>
<td>1.7</td>
</tr>
</tbody>
</table>

(Points: *4pts-recent hosp, 3pts-NH, 2pts-HD, 1pt-ICU, 10pts max*

(Of all patients with HCAP criteria only 50% had MDR organisms)

Arch Intern Med, 2008
Validating the Score

977 Culture Positive Patients

- 1/3 had a score of 0
- Risk of resistance < 15%
Predicting MDR Infections

- 6 VA Medical Centers
- 1300 HCAP patients; 30% culture +; 10% with MDR bug

<table>
<thead>
<tr>
<th>MRSA</th>
<th>OR</th>
<th>Pseudomonas*</th>
<th>OR</th>
</tr>
</thead>
<tbody>
<tr>
<td>MRSA + (&lt;90 days prior)</td>
<td>7.7</td>
<td>Prior Ceph (&lt;365 d)</td>
<td>3.8</td>
</tr>
<tr>
<td>NH &lt;6 mo. prior</td>
<td>2.8</td>
<td>Prior Pseud + cx</td>
<td>3.3</td>
</tr>
<tr>
<td>Prior Abx</td>
<td>2.1-2.4</td>
<td>Steroid use (&gt;10/d)</td>
<td>3.0</td>
</tr>
<tr>
<td>Diabetes</td>
<td>2.2</td>
<td>Prior Hosp</td>
<td>2.5</td>
</tr>
</tbody>
</table>

*recent infusions, dialysis, wound care NOT STRONG predictors

* < 5% of culture + cases

JHM, 2012
## Predicting MDR Infections

<table>
<thead>
<tr>
<th>Variable</th>
<th>Score</th>
</tr>
</thead>
<tbody>
<tr>
<td>Positive MRSA status prior to admission</td>
<td></td>
</tr>
<tr>
<td>≤90 days</td>
<td>+100</td>
</tr>
<tr>
<td>&gt;90 days but ≤365 days</td>
<td>+45</td>
</tr>
<tr>
<td>Nursing home residence or discharge ≤180 days prior to admission</td>
<td>+45</td>
</tr>
<tr>
<td>Infusion therapy ≤30 days prior to admission</td>
<td>+35</td>
</tr>
<tr>
<td>Cephalosporin exposure ≤365 days prior to admission</td>
<td>+30</td>
</tr>
<tr>
<td>Diabetes</td>
<td>+30</td>
</tr>
<tr>
<td>Direct ICU admission upon hospitalization</td>
<td>+25</td>
</tr>
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</table>

### B. Predicted Probability of CAP-Resistance*

<table>
<thead>
<tr>
<th>Total Score</th>
<th>% Chance of CAP-Resistance</th>
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</thead>
<tbody>
<tr>
<td>&lt;35</td>
<td>&lt;20</td>
</tr>
<tr>
<td>35–65</td>
<td>20–30</td>
</tr>
<tr>
<td>65–90</td>
<td>30–40</td>
</tr>
<tr>
<td>90–110</td>
<td>40–50</td>
</tr>
<tr>
<td>110–130</td>
<td>50–60</td>
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<tr>
<td>130–155</td>
<td>60–70</td>
</tr>
<tr>
<td>155–185</td>
<td>70–80</td>
</tr>
<tr>
<td>185–230</td>
<td>80–90</td>
</tr>
<tr>
<td>&gt;230</td>
<td>&gt;90</td>
</tr>
</tbody>
</table>

*JHM, 2011*
# Yet, Another Scoring System

<table>
<thead>
<tr>
<th>Variable</th>
<th>Score</th>
</tr>
</thead>
<tbody>
<tr>
<td>No risk factors for MDR pathogen (including comorbidities)</td>
<td>0</td>
</tr>
<tr>
<td>≥1 of the following: cerebrovascular disease, diabetes, COPD, antimicrobial therapy in preceding 90 days, immunosuppression, home wound care, home infusion therapy (including antibiotics)</td>
<td>0.5</td>
</tr>
<tr>
<td>Residence in a nursing home or extended-care facility</td>
<td>3</td>
</tr>
<tr>
<td>Hospitalization for ≥2 days in the preceding 90 days</td>
<td>4</td>
</tr>
<tr>
<td>Chronic renal failure</td>
<td>5</td>
</tr>
</tbody>
</table>

Abbreviations: COPD, chronic obstructive pulmonary disease; MDR, multidrug-resistant.
Identifying Low Risk Patients

935 Patients: < 20% Had Bacteria Isolated

<10% with resistant organisms
Q3,d
**Culture Negative HCAP**

900 HCAP Patients

<table>
<thead>
<tr>
<th></th>
<th>50% Culture +</th>
<th>50% Culture -</th>
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</thead>
<tbody>
<tr>
<td>Bugs*</td>
<td>30% MRSA / 25% Pseud</td>
<td></td>
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<tr>
<td>APACHE</td>
<td>20</td>
<td>12</td>
</tr>
<tr>
<td>Approp Rx</td>
<td>72%</td>
<td>15% (CAP rx)</td>
</tr>
<tr>
<td>LOS</td>
<td>12 days</td>
<td>7 days</td>
</tr>
<tr>
<td>RX</td>
<td>9 days</td>
<td>5 days</td>
</tr>
<tr>
<td>Mortality</td>
<td>25%</td>
<td>7%</td>
</tr>
</tbody>
</table>

* Included Immunosuppressed Pts

Labelle, et. al., CHEST 2010
HCAP
Treatment and Outcomes

• Chalmers, et al. CID 2011
  – 1350 hospitalized pneumonia patients (20% HCAP)
  – HCAP patients sicker, older, less functional, aspirators, more likely to have “treatment restriction”
  – Higher mortality, BUT adjusted mortality (OR 0.97, 0.61-1.55)
  – NOT related to treatment failure with resistant bacteria

• Attridge, et. al. ERJ 2011
  – 150 VA hospitals
  – 15,000 pts with ≥ 1 HCAP risk factor
  – Only 8% received guideline concordant (GC) HCAP rx
  – GC-HCAP rx associated with HIGHER propensity matched mortality vs. CAP rx (OR 2.12, 1.82-2.48)
HCAP
Treatment and Outcomes

GST = MRSA drug + 1 anti-pseudomonal drug

- < 30% of 1300 HCAP pts received GST
- Only 4% of 1300 pts with guideline rec triple therapy
Nursing Home Acquired Pneumonia (NHAP)

Predictors of Drug Resistant Bacteria: ICU Pts

- **Antibiotic use > 48 hrs in past 6 months**
- **Poor functional status**
- Both positive: 90% MDRs, both negative: 0% MDRs

Treating NHAP Like CAP

- 150 cases of NHAP over 10 years
- 95% treated with CAP rx
- Mortality 8.7% (comparable to CAP)
- 60% S.Pneumo

References:

El Solh CID 2004
Polverino et. al. Thorax, 2010
EDITORIAL

Healthcare-associated pneumonia: meeting the yeti

S. Ewig* and A. Torres#

The concept of healthcare-associated pneumonia (HCAP) is based on three crucial notions: 1) a subgroup of patients with on-going contact with healthcare presents with community-acquired infections but nosocomial microbial patterns; 2) failure to cover multidrug-resistant (MDR) pathogens relating excess mortality to inadequate antimicrobial treatment may severely fail to recognise the true reasons behind.

Recent important data support this notion. First, in a Spanish study comparing HCAP and CAP patients with bacteraemic
HCAP Treatment Recommendations
Too Much Too Fast?

Criteria used to define health-care-associated pneumonia

- Residence in nursing home
- Home care (e.g., for wounds, intravenous infusions) through a health-care agency
- Previous admission to hospital
- Immunosuppression

- Community-acquired pneumonia
- Hospital-acquired pneumonia
- Pneumonia in immunosuppressed patients

Lancet 2010
HCAP Treatment Algorithm

HCAP is present: From a nursing home, recent hospitalization, hemodialysis, home infusion therapy

Assess severity of illness (need for mechanical ventilation, ICU admit) AND

Presence of risk factors for MDR pathogens (recent antibiotics, recent hospitalization, poor functional status, immune suppression)

Severe pneumonia

No

0–1 Risks
Treat for common CAP pathogens (consider oral rx) Quinolone or beta-lactam/macrolide

≥2 Risks
Consider hospital, Treat for MDR pathogens with HAP therapy

Yes

0 Risks
Treat for severe pneumonia in hospital. Beta-lactam PLUS macrolide or quinolone

≥1 Risk
Treat for MDR pathogens with HAP recommendations. Use 3 drugs

Cur Opinion Infect Dis 2009
HCAP Treatment Algorithm

ADD

- Prior MRSA / Pseudomonas
- Indwelling Devices (PICC, urinary catheter, feeding tube)
- Advanced Respiratory Disease (Severe COPD, bronchiectasis)

Cur Opinion Infect Dis 2009
Putting it All Together

• Strong Risk Factors for Resistant Organisms
  – Prior Hospitalization in past 90 days
  – LTAC / SNF if prior antibiotics, poor functional status
  – Critically Ill patients
  – Prior MRSA / Pseudomonas

• Weak or Unclear
  – Nursing home
  – Dialysis
  – Wound Care / Home Health

• Too heterogeneous
  – Immunosuppressed
Q5
University of Michigan Algorithm

ICU / Cardiopulmonary Instability
(Any HCAP Risk Factor)*

Vanco + Pip/Tazo + Tobra
+
Azithromycin if atypicals suspected

* Prior Hosp >2d in last 3mo., LTC, Dialysis, Home IV
University of Michigan Algorithm

ICU / Cardiopulmonary Instability

- Levo instead of Tobra for renal insufficiency
- Vanco Trough: 10-15 mcg/ml
- Linezolid for Vanco intolerance or failure
- Treat for 7-8 days
  - (14 days for Pseudomonas, Stenotrophomonas, Acinetobacter or Burkholderia)
  - Longer rx may be appropriate: slow response, complicated
University of Michigan Algorithm

Mild to Moderate Severity
(With select HCAP risk factors)*

Vanco + Pip/Tazo
+

Azithromycin if atypicals suspected

* Prior Hosp >2d in last 3mo., LTC (poor functional status, prior antibiotics), Broad Spectrum Abx in past 90 d, h/o resistant pathogens, severe structural lung disease, frequent COPD exacerbations requiring steroids and/or abx
University of Michigan Algorithm

Mild to Moderate Severity
(With select “lower risk” HCAP risk factors)*

Ceftriaxone

+ Azithromycin

* Dialysis (no other risk factors), home infusion, wound care, nursing home / assisted living (absent other risk factors)
Q6
Linezolid vs. Vancomycin

- HAP / VAP RCT’s
  - Linezolid = Vancomycin
- Post-hoc Analysis of MRSA Cases
  - Linezolid > Vancomycin for mortality
  - Linezolid > Vancomycin for clinical cure
  - But post-hoc analyses are problematic
  - Vancomycin was not dose adjusted
- 2 meta-analyses found no overall differences

CHEST 2003, Crit Care Med 2004
CHEST 2011, Crit Care Med 2010
Linezolid vs. Vancomycin

CID 2012
Q7
De-escalation Trials in HCAP
De-escalation and VAP

• Numerous studies

• Discontinuation criteria
  – Negative BAL, mini-BAL, ETA
  – Clinical Criteria

• Clinical criteria
  – Non-infectious etiology identified (or)
  – Signs / symptoms resolving (WBC, Temp, CXR, Sputum, O2)

• Trial of 100 pts in MICU with VAP and negative BAL
  • Applied clinical criteria
  • NO patient received abx > 3 days
  • 5% relapse rate

Kollef, CHEST 2005
Niederman, Curr Opin Crit Care 2006
De-escalation: VAP and HAP

Reducing Treatment Duration

- Pittsburgh VA, non-blinded RCT
- 58% ventilated
- Used CPIS (temp, sputum, P/F ratio, CXR, trach aspirate)
- Scores >6-7 correlate well with invasive dx of NP
- Pts with scores > 6 were treated for NP
- Pts with scores ≤ 6 were randomized:
  - Standard rx of 10-21 days score > 6 treat as NP
  - Short course Cipro x 3 days score ≤ 6 d/c Cipro

## De-escalation: VAP and HAP

### Reducing Treatment Duration

<table>
<thead>
<tr>
<th></th>
<th>3 day therapy</th>
<th>Standard therapy</th>
<th>p-value</th>
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<tbody>
<tr>
<td>Patients</td>
<td>39</td>
<td>42</td>
<td></td>
</tr>
<tr>
<td>CPIS&gt;6 at 3d</td>
<td>21%</td>
<td>21%</td>
<td></td>
</tr>
<tr>
<td>Abx &gt; 3 d</td>
<td>28%</td>
<td>97%</td>
<td>0.0001</td>
</tr>
<tr>
<td>Abx duration (mean)</td>
<td>3 (d)</td>
<td>9.8 (d)</td>
<td>0.001</td>
</tr>
<tr>
<td>Abx cost</td>
<td>$6500</td>
<td>$16,000</td>
<td></td>
</tr>
<tr>
<td>14d mortality</td>
<td>8%</td>
<td>21%</td>
<td>NS</td>
</tr>
<tr>
<td>30d mortality</td>
<td>13%</td>
<td>31%</td>
<td>0.06 (NS)</td>
</tr>
<tr>
<td>ICU LOS</td>
<td>9.4 (d)</td>
<td>14.7 (d)</td>
<td>0.04</td>
</tr>
<tr>
<td>Superinfection</td>
<td>14%</td>
<td>38%</td>
<td>0.02</td>
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</table>

## Treatment Duration: VAP

**VAP: 51 ICUs; RCT of 8 days vs. 15 days of rx**

<table>
<thead>
<tr>
<th></th>
<th>8 days IV</th>
<th>15 days IV</th>
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</thead>
<tbody>
<tr>
<td><strong>Patients</strong></td>
<td>197</td>
<td>204</td>
</tr>
<tr>
<td><strong>28 day outcomes</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Mortality</strong></td>
<td>19%</td>
<td>17%</td>
</tr>
<tr>
<td><strong>Abx Free Days</strong></td>
<td>13</td>
<td>9*</td>
</tr>
<tr>
<td><strong>Recurrence</strong></td>
<td>29%</td>
<td>26%</td>
</tr>
<tr>
<td>- Resistant GNB</td>
<td>41%</td>
<td>25%*</td>
</tr>
<tr>
<td><strong>Recurrence with multi-resistant org</strong></td>
<td>42%</td>
<td>62%*</td>
</tr>
<tr>
<td></td>
<td>p=0.04</td>
<td></td>
</tr>
</tbody>
</table>

*Chastre, et al. JAMA 2003*
De-escalation: HCAP

- Single Center Retrospective Chart Review
- 102 cases of HCAP

<table>
<thead>
<tr>
<th></th>
<th>De-escalation</th>
<th>No De-escalation</th>
</tr>
</thead>
<tbody>
<tr>
<td>Patients</td>
<td>77</td>
<td>25</td>
</tr>
<tr>
<td>Culture+</td>
<td>28%</td>
<td>28%</td>
</tr>
<tr>
<td>LOS</td>
<td>7 days</td>
<td>13 days</td>
</tr>
<tr>
<td>Mortality</td>
<td>3%</td>
<td>28%</td>
</tr>
<tr>
<td>Antibiotic</td>
<td>62% Moxifloxacin</td>
<td></td>
</tr>
<tr>
<td>Time to de-esc</td>
<td>4 days</td>
<td></td>
</tr>
</tbody>
</table>

(culture neg. pts more likely to get moxi)

Infection 2010
De-escalation: HCAP

Oral Antibiotic Options

Respiratory Fluoroquinolone
(Levofloxacain, Moxifloxacain)

Oral 3rd generation cephalosporin

Something creative
Driving Appropriate Antibiotic Use

De-escalation

• Success rates in clinical studies: 70%
• Success rates in actual clinical practice: 10%

Masterton, Crit Care Clinics, 2011
IHI ANNOUNCES PILOT PROGRAM WITH CDC TO IMPROVE ANTIBIOTIC USE IN HOSPITALS

Aiming to Reduce Life-Threatening Antibiotic Resistance, Initiative Will Develop Practical Steps Guiding the Appropriate Use of Antibiotics

Cambridge, MA – November 14, 2011 – The Institute for Healthcare Improvement (IHI) today announced the launch of a pilot testing program designed to avoid overuse
Driving Appropriate Antibiotic Use

De-escalation

• De-escalate based on culture results
  – “Critical results” communicated by page
  – Communicate when cultures likely represent contamination / colonization
  – Emphasize the 48-72 hour reassessment
  – Tailor to susceptibility of pathogens
  – “If you didn’t find it, you may not need to cover it”
  • MRSA
Driving Appropriate Antibiotic Use

De-escalation

• Utilize multidisciplinary rounds / handoffs
  – Handoffs: ED-floor, ICU-floor, doctor-doctor
  – Communicate
    • Pending culture results
    • Indication for antibiotic
    • Anticipated duration of treatment / switch to oral
    • Guideline recommended stop date
  – Ask “Are we able to narrow the regimen or stop?”
THANK YOU!

QUESTIONS?