Community-Acquired, Health Care Associated, and Hospital Acquired Pneumonia
Management of the Hospitalized Patient
Update 2008

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University of Michigan
Overview

Community Acquired Pneumonia (CAP)
- Pneumonia developing outside the hospital
- But not HCAP

Healthcare Associated Pneumonia (HCAP)
- Pneumonia developing outside the hospital
- But the patient has been “touched” by the healthcare system

Hospital Acquired Pneumonia (HAP)
- Pneumonia that develops ≥ 48 hrs after admission
- Ventilator Associated Pneumonia (VAP) is a subset of HAP
CAP: Overview

COMMON
• 5-6 million cases / year
• 1 million hospitalizations / year

MORBIDITY / MORTALITY
• 64 million days of restricted activity
• High 30 day mortality: 10-35%
• Leading cause of infectious death

COSTLY
• Costs: $12-20 Billion / Year
• Inpatients: Mean $10k / episode
Community-Acquired Pneumonia

Care of the Hospitalized Patient

- Admission Decision
- Etiologic Testing
- Antibiotic Therapy
- Discharge Decision
- Prevention
Community-Acquired Pneumonia

Care of the Hospitalized Patient

• Admission Decision (Predicting ICU Care)
• Etiologic Testing
• Antibiotic Therapy
• Discharge Decision
• Prevention
SMART-COP
A tool for predicting which patients with community-acquired pneumonia (CAP) are likely to require intensive respiratory or vasopressor support (IRVS).

CAP confirmed on CXR

S  Systolic BP <90 mmHg  □ (2 points)
M  Multilobar CXR involvement  □ (1 point)
A  Albumin <3.5 g/dL*  □ (1 point)
R  Respiratory rate – age-adjusted cut-offs  □ (1 point)

<table>
<thead>
<tr>
<th>Age</th>
<th>≤50 yo</th>
<th>&gt;50 yo</th>
</tr>
</thead>
<tbody>
<tr>
<td>RR</td>
<td>≥25 br/min</td>
<td>≥30 br/min</td>
</tr>
</tbody>
</table>

T  Tachycardia ≥125 bpm  □ (1 point)
C  Confusion (new onset)  □ (1 point)
O  Oxygen low – age-adjusted cut-offs  □ (2 points)

<table>
<thead>
<tr>
<th>Age</th>
<th>≤50 yo</th>
<th>&gt;50 yo</th>
</tr>
</thead>
<tbody>
<tr>
<td>PaO₂*</td>
<td>&lt;70 mmHg</td>
<td>&lt;60 mmHg</td>
</tr>
<tr>
<td>or: O₂ Saturation</td>
<td>&lt;93%</td>
<td>&lt;90%</td>
</tr>
<tr>
<td>or (if on O₂): PaO₂/FiO₂*</td>
<td>&lt;333</td>
<td>&lt;250</td>
</tr>
</tbody>
</table>

P  Arterial pH <7.35*  □ (2 points)

Total Score □ points
## SMART-COP

### Interpretation:

<table>
<thead>
<tr>
<th>Points</th>
<th>Interpretation</th>
</tr>
</thead>
<tbody>
<tr>
<td>0 – 2</td>
<td>Low risk of needing IRVS</td>
</tr>
<tr>
<td>3 – 4</td>
<td>Moderate risk (1 in 8) of needing IRVS</td>
</tr>
<tr>
<td>5 – 6</td>
<td>High risk (1 in 3) of needing IRVS</td>
</tr>
<tr>
<td>≥7</td>
<td>Very high risk (2 in 3) of needing IRVS</td>
</tr>
</tbody>
</table>

*For primary care physicians, results for albumin, arterial pH, and PaO2 can be overlooked and the following interpretation be used:*

<table>
<thead>
<tr>
<th>Points</th>
<th>Interpretation</th>
</tr>
</thead>
<tbody>
<tr>
<td>0</td>
<td>Very low risk of needing IRVS</td>
</tr>
<tr>
<td>1</td>
<td>Low risk (1 in 20) of needing IRVS</td>
</tr>
<tr>
<td>2</td>
<td>Moderate risk (1 in 10) of needing IRVS</td>
</tr>
<tr>
<td>3</td>
<td>High risk (1 in 6) of needing IRVS</td>
</tr>
<tr>
<td>≥4</td>
<td>High risk (1 in 3) of needing IRVS</td>
</tr>
</tbody>
</table>
Admission Decision

Predicting the Need for ICU Level Care

SMART COP: Sens=92%, Spec=62%

AUC
SMART COP 0.87
PSI IV&V 0.69
CURB-65 0.67

CID 2008
Community-Acquired Pneumonia

Care of the Hospitalized Patient

- Admission Decision
- Etiologic Testing
- Antibiotic Therapy
- Discharge Decision
- Prevention
Etiologies / Diagnosis

MRSA Pneumonia: The New Nightmare

• CDC surveillance of 2003-2004 influenza season
• 17 cases identified
• 15/17 (88%) were MRSA; 85% PVL gene+
• Median age 21, 75% with no MRSA risk factors
• 82% with +sputum, 50% +bld culture
• 80% in ICU, 30% fatal
• 100% erythromycin resistant, 50% fluoro resistant
ARS #1

• How many patients with CA-MRSA pneumonia have you (or your group) treated in the past year?
  – 1) 0
  – 2) <5
  – 3) 5-10
  – 4) >10
CA-MRSA

- IDSA Emerging Infections Network Survey 2007
- 500 physicians across U.S.
- 30% treated 560 cases of *S. Aureus* CAP

<table>
<thead>
<tr>
<th>% of pts</th>
<th>Vent Support</th>
<th>Mortality</th>
<th>Assoc Influenza</th>
<th>MRSA</th>
<th>+ Sputum Cx</th>
<th>+ Blood Cx</th>
<th>Vanco Rx</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>49%</td>
<td>13%</td>
<td>26%</td>
<td>72%</td>
<td>77%</td>
<td>43%</td>
<td>73%</td>
</tr>
</tbody>
</table>

CID; 2007
CA-MRSA

• Risk factors
  – Past skin infection (abscess)
  – IVDU
  – Influenza (concurrent with flu; resp sx 2-6 d prior to ED)

• Presentation:
  – Severe, necrotizing infection
  – Hemoptysis, Leukopenia
  – High fever / cavitary infiltrate

• Treatment:
  – Vancomycin or Linezolid (NOT Daptomycin)
  – Vanco troughs 15-20 mcg / mL

Ann Emerg Med 2007
## Etiologies / Diagnosis

**Who has gram negative rods or pseudomonas?**
(560 non-immunosuppressed pts with CAP)

<table>
<thead>
<tr>
<th>Gram negative predictors</th>
<th>OR (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Aspiration</td>
<td>2.3 (1.02-5.2)</td>
</tr>
<tr>
<td>Prior admit*</td>
<td>3.5 (1.7-7.1)</td>
</tr>
<tr>
<td>Prior antibiotics**</td>
<td>1.9 (1.01-3.7)</td>
</tr>
<tr>
<td>Pulmonary comorbidity</td>
<td>2.8 (1.5-5.5)</td>
</tr>
</tbody>
</table>

1 of the above factors  \hspace{1cm} 4.2 (1.4-16.7)
2 of the above factors  \hspace{1cm} 9.1 (2.8-37.2)
3 of the above factors  \hspace{1cm} 39.3 (9.3-188.3)

**Pseudomonas predictors**

| Pulmonary comorbidity    | 5.8 (2.2-15.3) |
| Prior admit              | 3.8 (1.8-8.3) |

(*48 hrs in last month, **any in past month)
Etiologies / Diagnosis

Who has pseudomonas?
(530 ICU pts from 33 hospitals with CAP)

Pseudomonas predictors | OR
--- | ---
COPD | 18
Malignancy | 11
Prior Antibiotics | 6
Rapid CXR spread | 4

CID 2005

- 75% of pts with pseudomonas had inappropriate rx
- Severe COPD warrants Pseudomonal rx in ICU or Ward

Restrepo, et al. CHEST 2008
Community-Acquired Pneumonia

Care of the Hospitalized Patient

- Admission Decision
- Etiologic Testing
- Antibiotic Therapy
- Discharge Decision
- Prevention
# Antibiotic Therapy

## Antibiotic Regimens and Outcomes

<table>
<thead>
<tr>
<th>Study</th>
<th>Patients</th>
<th>Design</th>
<th>[RX] vs. BL Mono</th>
</tr>
</thead>
<tbody>
<tr>
<td>Gleason 00’</td>
<td>13,000</td>
<td>Retrospec</td>
<td>BL+macro: HR= .74 fluoro: HR=.64</td>
</tr>
<tr>
<td>Dudas 00’</td>
<td>3000</td>
<td>Retrospec</td>
<td>BL+macro: lower 30d mortality and LOS</td>
</tr>
<tr>
<td>Houck 01’</td>
<td>10,000</td>
<td>Retrospec</td>
<td>BL+macro: lower 30d mortality</td>
</tr>
<tr>
<td>Brown 03’</td>
<td>45,000</td>
<td>Retrospec</td>
<td>BL+macro: lower 30 d mortality</td>
</tr>
<tr>
<td>Flanders 03’</td>
<td>340</td>
<td>Retrospec</td>
<td>BL+doxy: lower 30 d mortality</td>
</tr>
<tr>
<td>Morten 04’/06’</td>
<td>420/700</td>
<td>Retrospec</td>
<td>Guideline concordant rx: lower 48h mortality</td>
</tr>
</tbody>
</table>
Antibiotic Therapy
Is it the Atypical Coverage that is Important?

• Shefet D, et al. Cochrane 2005 (Updated 2008)
  – Meta-analysis of 24 RCTs; atypical coverage vs. not
  – Hospitalized patients; 11/24 “Severe Pneumonia”
  – 18/24 identified trial were pharma sponsored
  – Atypical drugs: 19 fluoro; 4 macrolide; 1 both

Atypical Coverage vs. Non-Atypical

<table>
<thead>
<tr>
<th>Outcome</th>
<th>RR (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mortality</td>
<td>1.1 (0.8-1.5)</td>
</tr>
<tr>
<td>Clinical failure</td>
<td>.92 (0.8-1.1)</td>
</tr>
<tr>
<td>Clinical Failure Subset</td>
<td></td>
</tr>
<tr>
<td>Atypical orgs</td>
<td>0.5 (0.2-1.1)</td>
</tr>
<tr>
<td>Legionella</td>
<td>0.2 (0.1-0.6)   (only 43 cases)</td>
</tr>
</tbody>
</table>
Antibiotic Therapy

The Guidelines: Inpatient

- IDSA / ATS 2007
  - β-lactam + macrolide (or doxycycline)
  - Respiratory fluoroquinolone
  - ICU: β-lactam + macrolide, or β-lactam + fluoroquinolone
  - Anti-pseudomonal (many options) or CA-MRSA Rx (Vanco or Linezolid) if risk factors: independent of ICU status
Antibiotic Therapy

**Short Course Therapy**

- Blinded, multicenter, RCT
- 3 days vs. 8 days
- All centers in the Netherlands
- Adults, PSI ≤ 110; (no PSI Class V, 15% were class IV)
- Exclude: ICU, NH, Abx > 24 hr, aspiration, large effusion, or “suspicion” of Staph or Atypicals.
- All pts received IV ampicillin
- Pts randomized at 72 hrs if
  - Clinical improvement (decreased cough, etc.)
  - Temp < 38 C
  - Tolerating orals

BMJ 2006
Antibiotic Therapy

**Short Course Therapy**

- 186 patients; 38 no improvement, 3 resistant bug
- 121 randomized; bacteremic patients included

<table>
<thead>
<tr>
<th></th>
<th>Amox 750 tid x 5d</th>
<th>Placebo x 5d</th>
</tr>
</thead>
<tbody>
<tr>
<td>Patients</td>
<td>64</td>
<td>57</td>
</tr>
<tr>
<td>Cure (d 10)</td>
<td>93%</td>
<td>93%</td>
</tr>
<tr>
<td>Cure (d 28)</td>
<td>88%</td>
<td>90%</td>
</tr>
<tr>
<td>Adverse Event</td>
<td>21%</td>
<td>11%</td>
</tr>
</tbody>
</table>

No difference in symptom or CXR scores between groups

BMJ 2006
Antibiotic Therapy

Short Course Therapy

Am J Med, 2007; Meta-Analysis: 15 RCTs

< 7 days vs. > 7 days

Clinical Failure

OR = 0.89 (0.78-1.02)
Antibiotic Therapy

Short Course Therapy

Am J Med, 2007; Meta-Analysis: 15 RCTs

\( \leq 7 \) days vs. \( > 7 \) days

- **Mortality**
  - OR = 0.81 (0.45-1.43)

- **Adverse Events**
  - OR = 0.86 (0.71-1.04)
Antibiotic Therapy

Stopping Antibiotics

- Pts should be afebrile for 48-72 hours
- Have no more than 1 CAP-associated instability*
- Usually this is after 5 days of therapy

*HR<100
SBP>90
RR<24
Temp <37.8
O2 Sat >90
Mental status at baseline
Taking orals
Antibiotic Timing and Outcomes
13,700 Medicare Patients: 30 d mortality

**Odds also lower for inpatient mortality, and LOS > 5d. No effect if antibiotics are given prior to admission**

Antibiotic Timing and Outcomes

Delayed Timing and Atypical Presentation

- 450 pts with + CXR and CAP symptoms
- Mean age 60; 50% > 4 hours

<table>
<thead>
<tr>
<th>Delay</th>
<th>Early Abx (&lt;2hr)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Altered Mental Status</td>
<td>Shock</td>
</tr>
<tr>
<td>No Hypoxia</td>
<td>T &gt; 101</td>
</tr>
<tr>
<td>No Fever</td>
<td>Hypoxia</td>
</tr>
</tbody>
</table>

**Mortality**

<table>
<thead>
<tr>
<th>Mortality</th>
<th>Odds Ratio</th>
</tr>
</thead>
<tbody>
<tr>
<td>Altered Mental Status</td>
<td>3.5</td>
</tr>
<tr>
<td>No fever</td>
<td>2.5</td>
</tr>
<tr>
<td>Abx &gt; 4 hrs</td>
<td>1.8 (not significant)</td>
</tr>
</tbody>
</table>

CHEST 2006
# Antibiotic Timing and Outcomes

## Antibiotic Overuse: Gaming the System?

<table>
<thead>
<tr>
<th></th>
<th>2003</th>
<th>2005</th>
</tr>
</thead>
<tbody>
<tr>
<td>ED CAP dx</td>
<td>200</td>
<td>320</td>
</tr>
<tr>
<td>Abx in 4 hrs</td>
<td>54%</td>
<td>66%</td>
</tr>
<tr>
<td>Abx / pt</td>
<td>1.4</td>
<td>1.7</td>
</tr>
<tr>
<td>CXR is nl</td>
<td>20%</td>
<td>30%</td>
</tr>
<tr>
<td>Final CAP dx</td>
<td>76%</td>
<td>59%</td>
</tr>
</tbody>
</table>

- Many misdiagnoses were cardiac / non-CAP-pulmonary dz
- Substantial antibiotic overuse

CHEST 2007
Arch Int Med 2008
Antibiotic Timing and Outcomes

So now what?

• Change the measure
  – A 6 hr data point has been added. Based on?
  – IDSA / ATS 2007: Recommend: “Give in ED”

• Lessons re Performance Indicators
  – Caution when evidence is questionable
  – Create “bands of performance”
  – End-users (ie hospitalists / ED docs) need a voice
  – Performance indicators need constant reassessment

Wachter, Ann Intern Med 2008
Community-Acquired Pneumonia

Care of the Hospitalized Patient

- Admission Decision
- Etiologic Testing
- Antibiotic Therapy
- Discharge Decision
- Prevention
# Discharge Decision

*N*=686 PORT Database

<table>
<thead>
<tr>
<th>Stability Criteria</th>
<th>Median Time (days)</th>
</tr>
</thead>
<tbody>
<tr>
<td>HR ≤ 100</td>
<td>2</td>
</tr>
<tr>
<td>SBP ≥ 90</td>
<td>2</td>
</tr>
<tr>
<td>RR ≤ 24</td>
<td>3</td>
</tr>
<tr>
<td>O2 sat ≥ 90%</td>
<td>3</td>
</tr>
<tr>
<td>Temp ≤ 37.8</td>
<td>3</td>
</tr>
<tr>
<td>Able to eat</td>
<td>2</td>
</tr>
<tr>
<td>Mental Status</td>
<td>3</td>
</tr>
<tr>
<td>Overall Stability</td>
<td>3 (3-7)</td>
</tr>
</tbody>
</table>

Halm E, et al. JAMA 1998;279
Discharge Decision

- RCT at 7 Pittsburgh Hospitals; guidelines to reduce LOS
- 577 patients discharged
- 70 (12%) readmitted by 30 days

<table>
<thead>
<tr>
<th>Reason for Readmission</th>
<th>n(%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Pneumonia related</td>
<td>14 (20)</td>
</tr>
<tr>
<td><strong>Comorbidity</strong></td>
<td>52 (74)</td>
</tr>
<tr>
<td>Cardiac</td>
<td>14</td>
</tr>
<tr>
<td>Pulmonary</td>
<td>6</td>
</tr>
<tr>
<td>Neuro</td>
<td>6</td>
</tr>
</tbody>
</table>

(No GED degree, unemployed, CAD, COPD all predicted readmits)
Community-Acquired Pneumonia

Care of the Hospitalized Patient

• Admission Decision
• Etiologic Testing
• Antibiotic Therapy
• Discharge Decision
• Prevention
Prevention

**Pneumococcal Vaccine**
- Is the vaccine efficacious in our hospitalized patients (age>65, medical comorbidities)?

**Influenza Vaccine**
- Does it prevent CAP?
ARS #2

- In hospitalized patients meeting CDC indications for vaccination, the 23-valent pneumococcal vaccine:
  - 1) Prevents pneumonia
  - 2) Prevents bacteremia
  - 3) Reduces mortality
  - 4) All of the above
Prevention

Pneumococcal Vaccine

Cochrane Systematic Review: 2008

• All RCT’s Reviewed
  – No effect on pneumonia
  – No effect on mortality

• Case-Control Studies
  – 53% efficacy for invasive disease
  – OR=0.62 (0.42-0.92) for death or ICU if hospitalized with CAP

NNT=20,000 Bacteremia
NNT=50,000 Death

ACP J-Club 2004
Moberley, Cochrane 2008

Arch Intern Med 2007
Prevention

**Influenza Vaccine:**

- Retrospective cohort study; 3 managed care organizations
- 2 flu seasons; 285,000 patients

<table>
<thead>
<tr>
<th>Flu Vaccine 99-00’</th>
<th>Odds Ratio (95% CI)</th>
<th>NNT</th>
</tr>
</thead>
<tbody>
<tr>
<td>Hospitalization</td>
<td></td>
<td></td>
</tr>
<tr>
<td>CAP or Flu</td>
<td>0.71 (0.62-0.80)</td>
<td>431</td>
</tr>
<tr>
<td>Cardiovascular dz</td>
<td>0.81 (0.73-0.89)</td>
<td>376</td>
</tr>
<tr>
<td>Cerebrovascular dz</td>
<td>0.77 (0.66-0.89)</td>
<td>621</td>
</tr>
<tr>
<td>Death</td>
<td>0.50 (0.46-0.55)</td>
<td>118</td>
</tr>
</tbody>
</table>

- Effects similar in all subgroups (by risk, and age group up to ≥ 85 yrs)

NEJM 2003
**Prevention**

**Influenza Vaccine: 2008**

- Nested case-control study; 3500 pts > 65 yrs old
- 1200 vaccinated cases; 2300 controls

<table>
<thead>
<tr>
<th></th>
<th>Pre-Influenza</th>
<th>OR for CAP</th>
</tr>
</thead>
<tbody>
<tr>
<td>Vaccinated</td>
<td>0.60 (0.38-0.95)</td>
<td></td>
</tr>
<tr>
<td>Adjusted / Controlled</td>
<td>1.01 (0.58-1.76)</td>
<td></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th></th>
<th>Post-Influenza</th>
<th>OR for CAP</th>
</tr>
</thead>
<tbody>
<tr>
<td>Adjusted / Controlled</td>
<td>1.04 (0.88-1.22)</td>
<td></td>
</tr>
</tbody>
</table>

Lancet 2008
Community-Acquired Pneumonia

No Progress Since 1988?

• National Hospital Discharge Survey; >65 y.o.

• Hospitalization rates (per 1000) for pneumonia
  – 20% increase from 1988-2002 for 65-84 y.o.
  – No change in “all-cause” hospitalizations

• Pts with comorbid disease; 77% (vs 66% in 88’)

• Risk of death in hospital
  – 50% greater for CAP than 10 next most common dx
  – AND no change from 1988-2002

JAMA 2006
Community-Acquired Pneumonia

Steroids, Statins, Cytokines, and other Ideas

• No major impact on outcomes for pneumonia
  – Diagnostic testing
  – Specific antibiotic regimens?
  – Timing of antibiotics?
  – Pneumococcal vaccination
  – Flu vaccine?

• Time to start thinking outside of the BOX
Antibiotic Therapy + Steroids?

- 46 patients from 6 hospitals with “severe CAP”: ICU
- Hydrocortisone 200mg x 1, then 10mg / hr x 7 d
- Trial stopped after 48 pts due to pre-specified criteria

<table>
<thead>
<tr>
<th>Day 8</th>
<th>Placebo</th>
<th>Steroids</th>
</tr>
</thead>
<tbody>
<tr>
<td>On vent</td>
<td>65%</td>
<td>26%</td>
</tr>
<tr>
<td>P/F improve</td>
<td>35%</td>
<td>85%</td>
</tr>
<tr>
<td>Delayed shock</td>
<td>43%</td>
<td>0%</td>
</tr>
<tr>
<td>Mortality</td>
<td>10%</td>
<td>0%</td>
</tr>
<tr>
<td>Hospital Mortality</td>
<td>30%</td>
<td>0%</td>
</tr>
<tr>
<td>60d Mortality</td>
<td>35%</td>
<td>0%</td>
</tr>
<tr>
<td>Median LOS</td>
<td>21</td>
<td>13</td>
</tr>
</tbody>
</table>

*Beware: *There are “issues” with this study*

Am J Respir Crit Care 2006
<table>
<thead>
<tr>
<th>Study</th>
<th>Patients</th>
<th>Design</th>
<th>Outcome</th>
</tr>
</thead>
<tbody>
<tr>
<td>Schlienger 07’</td>
<td>134,262</td>
<td>Retrospec</td>
<td>Mortality: OR= 0.47*</td>
</tr>
<tr>
<td>V. de Garde 06’</td>
<td>142,175</td>
<td>Retrospec</td>
<td>CAP: OR=0.49*</td>
</tr>
<tr>
<td>Majumdar 06’</td>
<td>3415</td>
<td>Prospec</td>
<td>Death / ICU: OR=NS</td>
</tr>
<tr>
<td>Mortensen 05’</td>
<td>787</td>
<td>Retrospec</td>
<td>Mortality: OR=0.36*</td>
</tr>
<tr>
<td>Fernandez 06’</td>
<td>438</td>
<td>Retrospec</td>
<td>ICU infection: OR=NS</td>
</tr>
<tr>
<td>Frost 07’</td>
<td>76,232</td>
<td>Retrospec</td>
<td>CAP Mortality: OR=0.60*</td>
</tr>
<tr>
<td>(Influenza Pts)</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

* p<0.05

Pneumonia Disease Mechanisms

Balancing Inflammation

More Inflammation
Bacterial Clearance

LTB4
TNF
IL-1
TREM-1

Balancing Inflammation

PGE2
STAT3
PGI2

Less Inflammation
Bacterial Clearance
**Avoid Overuse of PPIs?**

- Denmark; Large Pop.-Based Database
- 7642 cases of CAP, 34,000 controls

<table>
<thead>
<tr>
<th>Pt Population</th>
<th>Risk for CAP: OR(95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Current PPI</td>
<td>1.5 (1.3-1.7)</td>
</tr>
<tr>
<td>Current H2RA</td>
<td>1.1 (0.8-1.3)</td>
</tr>
<tr>
<td>Recent start (&lt;1wk)</td>
<td>5.0 (2.1-11.7)</td>
</tr>
</tbody>
</table>

- UK Study; 80,000 cases, 800,000 controls
- Recent PPI start (2d, OR=6.5; 7d OR=3.8)
- Current use; OR=1.02 (NS)
### Prevention

#### Beware: Antipsychotics in the Elderly

- Denmark; Large Pop.-Based Database
- 22,944 elderly on antipsychotics
- 543 CAP cases; 2163 controls

<table>
<thead>
<tr>
<th>Antipsychotic Use</th>
<th>Risk for CAP: OR (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>&lt;8 days</td>
<td>4.3 (2.9-7.2)</td>
</tr>
<tr>
<td>8-14 days</td>
<td>2.3 (1.2-4.6)</td>
</tr>
<tr>
<td>15-30 days</td>
<td>1.8 (1.0-3.1)</td>
</tr>
<tr>
<td>&gt;30 days / past users</td>
<td>NS</td>
</tr>
</tbody>
</table>

*Risk > with atypical antipsychotics*
Overview

Community Acquired Pneumonia (CAP)
• Pneumonia developing outside the hospital
• But not HCAP

Healthcare Associated Pneumonia (HCAP)
• Pneumonia developing outside the hospital
• But the patient has been “touched” by the healthcare system

Hospital Acquired Pneumonia (HAP)
• Pneumonia that develops ≥ 48 hrs after admission
• Ventilator Associated Pneumonia (VAP) is a subset of HAP
Healthcare Associated Infections

• **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**
Risk Factors for MDR Infections

- Antimicrobial rx in past 90 days
- Current hospitalization > 5 days
- High rates of resistance in community or ward
- Risk factors for HCAP
  - Home Therapy
  - Hospital or Dialysis Clinic in past 30 days
  - Hospitalized ≥ 2 days in past 90? days
  - Nursing Home or Long-Term Care Facility
- Family member with multidrug resistant pathogen
- Immunosuppressive disease or therapy

MDR = Multidrug-resistant
MDR Pathogens

- *Pseudomonas aeruginosa*
- Drug resistant gram negatives
  - ESBL producing Klebsiella
  - Enterobacter
  - Serratia
- *Acinetobacter spp.*
- MRSA

MDR = Multidrug-resistant
Etiologies
(HEALTH CARE ASSOCIATED PNEUMONIA)

- Evaluation of HCAP at 60 U.S. Hospitals; 02-03’ database
- Evaluated culture + patients only
- HCAP = NH, ECF, SNF, dialysis, hospital contact in 30 d

<table>
<thead>
<tr>
<th></th>
<th>CAP</th>
<th>HCAP</th>
<th>HAP</th>
<th>VAP</th>
</tr>
</thead>
<tbody>
<tr>
<td>Patients</td>
<td>2200(50%)</td>
<td>990(20%)</td>
<td>835(20%)</td>
<td>500(10%)</td>
</tr>
<tr>
<td>Mortality%</td>
<td>10</td>
<td>20</td>
<td>20</td>
<td>30</td>
</tr>
<tr>
<td>Organisms%</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td><em>Staph</em></td>
<td>25</td>
<td>45</td>
<td>45</td>
<td>45</td>
</tr>
<tr>
<td><em>MRSA</em></td>
<td>35</td>
<td>57</td>
<td>49</td>
<td>34</td>
</tr>
<tr>
<td><em>Pseud</em></td>
<td>15</td>
<td>25</td>
<td>20</td>
<td>20</td>
</tr>
<tr>
<td>LOS (mean d)</td>
<td>7.5</td>
<td>9</td>
<td>15</td>
<td>23</td>
</tr>
</tbody>
</table>

*As of 2005 CMS excludes HCAP from CAP GL Recs*

CHEST 2006
### Etiologies

**HEALTH CARE ASSOCIATED PNEUMONIA**

**Culture + CAP at an Academic Medical Center**

<table>
<thead>
<tr>
<th></th>
<th><strong>CAP</strong></th>
<th><strong>HCAP</strong></th>
</tr>
</thead>
<tbody>
<tr>
<td>Patients</td>
<td>208 (33%)</td>
<td>431 (67%)</td>
</tr>
<tr>
<td>S. Pneumo</td>
<td>41%</td>
<td>10%</td>
</tr>
<tr>
<td>MRSA</td>
<td>12%</td>
<td>30%</td>
</tr>
<tr>
<td>Psuedomonas</td>
<td>4%</td>
<td>25%</td>
</tr>
<tr>
<td>Other GNR</td>
<td>2%</td>
<td>10%</td>
</tr>
<tr>
<td>Inapprop. RX</td>
<td>13%</td>
<td>30%</td>
</tr>
<tr>
<td>Mortality</td>
<td>9%</td>
<td>25%</td>
</tr>
</tbody>
</table>

(HCAP: 70% hospitalized in past 90 days, 20% in past 180d)

*As of 2005 CMS excludes HCAP from CAP GL Recs*
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
ARS

When you have a patient with any one of the risk factors for HCAP do you:

- 1) Routinely treat broadly with guideline recommended antibiotics (2-3 drugs) for a full course
- 2) Routinely treat broadly with guideline recommended antibiotics (2-3 drugs) but narrow rx within 2-3 days
- 3) Usually treat more narrowly (like CAP)
- 4) What I do depends on my mood (and a little on the patient)
Nursing Home Acquired Pneumonia

Non-Severe Pneumonia

- Loeb, et al JAMA 2006
  - RCT 20 Nursing Homes; Pneumonia pathway vs. Usual care
  - 350 patients in each arm, mean age 85
  - Pathway: if po, HR <100, RR<30, SBP>90, sat > 90% then po Levo

<table>
<thead>
<tr>
<th></th>
<th>Pathway</th>
<th>Usual Care</th>
</tr>
</thead>
<tbody>
<tr>
<td>Admission</td>
<td>10%</td>
<td>20% (p=0.001)</td>
</tr>
<tr>
<td>Hosp days / pt</td>
<td>0.8</td>
<td>1.8 (p=0.004)</td>
</tr>
<tr>
<td>Mortality</td>
<td>3%</td>
<td>6% (p=0.23)</td>
</tr>
<tr>
<td>Costs / resident</td>
<td>$1200</td>
<td>$2200 (p &lt; 0.05)</td>
</tr>
</tbody>
</table>
Nursing Home Acquired Pneumonia (NHAP)

Predictors of Drug Resistant Bacteria

• 135 nursing home patients admitted to ICU
• *Antibiotic use > 48 hrs in past 6 months*
• *Poor functional status (ADL score > 12.5)*
• Both positive: 90% MDRs
• Both negative: 0% MDRs

ADL Score: 6 components, score each
1 point=independent, 2=partial, 3=independent

El Solh CID 2004
(HCAP) NHAP Empiric Treatment

Cover for MDRs if 2 of 3 criteria met

- Severe pneumonia (ICU)
- Antibiotic use > 48 hrs in past 6 months
- Poor functional status

Kollef CID 2008
Overview

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• Pneumonia developing outside the hospital
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Hospital Acquired Pneumonia (HAP)
• Pneumonia that develops ≥ 48 hrs after admission
• Ventilator Associated Pneumonia (VAP) is a subset of HAP
Hospital Acquired Pneumonia

• HAP is defined as pneumonia developing ≥ 48 hrs after admission, while VAP is pneumonia ≥ 48 hrs after MV

• 10 cases / 1000 admits; 20 fold higher with vents

• 30-70% mortality, attributable mortality ≈ 20-30%
  – If adequately treated, attributable mortality is < 10%

• Associated with prolonged hospitalization and increased costs
  – Avg increased LOS 7-11 days
  – Avg increase in hospital charges of $40,000.
Hospital Acquired Pneumonia

• THE EXTRAPOLATED DISEASE
• HAP is amazingly understudied
• 90% of HAP recommendations come from VAP data

WHY?

• Diagnosis is elusive
• Hard to get valid etiologic organisms (sputum issue)
• Therefore hard to do robust treatment studies
Hospital Acquired Pneumonia

Approach to Care

• Etiologies
• Diagnosis
• Treatment
• Prevention
## VAP Etiologies

Bronchoscopic dx in 24 studies of over 1650 cases

<table>
<thead>
<tr>
<th>Pathogen</th>
<th>Frequency (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td><em>Pseudomonas aeruginosa</em></td>
<td>25</td>
</tr>
<tr>
<td><em>Staph aureus</em></td>
<td>20</td>
</tr>
<tr>
<td>Enterobacteriaceae</td>
<td>15</td>
</tr>
<tr>
<td><em>Haemophilus spp.</em></td>
<td>10</td>
</tr>
<tr>
<td><em>Streptococcus spp.</em></td>
<td>8-12</td>
</tr>
<tr>
<td><em>Acinetobacter spp.</em></td>
<td>8</td>
</tr>
<tr>
<td>Anaerobes</td>
<td>&lt;1%</td>
</tr>
</tbody>
</table>

*Am J Respir Crit Care. 2002;165*
HAP Etiologies

Hospital-wide Surveillance at UNC 2000-2003

- Pathogens isolated: 92% of VAP cases
- Pathogens isolated: 77% of HAP cases
- Bacteriology / MDR orgs similar between groups

- HAP: more MRSA, K. pneumoniae
- VAP: more P. aeruginosa, Acinetobacter
HAP: Etiologies

**Early: < 5-7 days**
- *S. pneumo*
- *H. flu*
- Anaerobes
- *S. aureus*(MSSA)
- EGNR

**Late: >5-7 days**
- EGNR
- *P. aeruginosa*
- Acinetobacter
- *S. aureus*(MRSA)
Risk Factors for MDR Infections

- Antimicrobial rx in past 90 days
- Current hospitalization > 5 days
- High rates of resistance in community or ward
- Risk factors for HCAP
  - Home Therapy
  - Hospital or Dialysis Clinic in past 30 days
  - Hospitalized ≥ 2 days in past 90? days
  - Nursing Home or Long-Term Care Facility
- Family member with multidrug resistant pathogen
- Immunosuppressive disease or therapy

MDR= Multidrug-resistant
HAP: Etiologies

Risk Factors

- **S. aureus**
  - Coma, DM, Renal Failure

- **P. aeruginosa**
  - Prolonged ICU, prior abx, steroids, structural lung dz

- **Legionella**
  - High dose steroids
HAP: Diagnosis

- The most controversial aspect of HAP
- NO GOLD STANDARD
- Many flawed studies evaluating diagnostic methods
- Multiple methods
  - Clinical: Infiltrate + fever or sputum or leukocytosis
  - CPIS: points for clinical factors
  - Endotracheal aspirate (ETA): no data on sputum analysis
  - Invasive: (BAL, PSB)
  - New Markers: procalcitonin, sTREM-1
HAP: CDC Diagnosis

• Radiologic signs:
  – 2 or more CXRs (1 if no pulm / cv dz) showing:
  – New or progressive and persistent infiltrate

• Clinical signs:
  – 1 of the following:
    – T > 38 and no other cause
    – WBC < 4 or >12
    – If age > 70, altered with no other cause
  – AND 2 of the following:
    – More sputum / Change in sputum
    – Cough, SOB, tachypnea
    – Rales or bronchial breath sounds
    – Worsening gas exchange

CDC 2004
HAP: Diagnosis

More Sensitive

+                +

CLINICAL

BRONCH (BAL / PSB)

+                +

More Specific
HAP: Diagnosis

**SPUTUM**

- Almost no data
- Clinical diagnosis alone is probably oversensitive
- Attempt to get a good sputum…..ETA may be better
- Perform ETA if possible and if negative, look elsewhere
  - If pt stable, safe to withhold abx if ETA cultures neg
- Prior Antibiotics
  - 25% of cultures negative after 12 hrs of new antibiotics
  - Diagnostic yield less affected by “ongoing therapy”
  - Do the diagnostic test before changing / adding antibiotics

Michaud S, et al. AJRCCM.2002
## HAP: Treatment

### Mortality: Early Inappropriate vs. Appropriate Therapy

<table>
<thead>
<tr>
<th>Study</th>
<th>n</th>
<th>Inadequate Rx</th>
<th>Adequate Rx</th>
</tr>
</thead>
<tbody>
<tr>
<td>Luna</td>
<td>49</td>
<td>92%</td>
<td>37.5%</td>
</tr>
<tr>
<td>Alvarez</td>
<td>490</td>
<td>25%</td>
<td>16%*</td>
</tr>
<tr>
<td>Rello</td>
<td>85</td>
<td>63%</td>
<td>41.5%</td>
</tr>
<tr>
<td>Kollef</td>
<td>130</td>
<td>61%</td>
<td>27%</td>
</tr>
<tr>
<td>Sanchez</td>
<td>38</td>
<td>43%</td>
<td>25%</td>
</tr>
<tr>
<td>Ruiz</td>
<td>46</td>
<td>50%</td>
<td>39%</td>
</tr>
<tr>
<td>Dupont</td>
<td>111</td>
<td>61%</td>
<td>47%</td>
</tr>
</tbody>
</table>

*attributable mortality

(multiple additional studies show early inappropriate antibiotic therapy to be an independent predictor of mortality)
HAP: Treatment
The challenge

Early, appropriate treatment reduces mortality

Reduce antibiotic overuse
HAP: Treatment
The solution

• Identify low risk patients who can receive narrow therapy (they are rare)

• Reduce length / quantity of antibiotic use
HAP Treatment

Reducing Treatment Duration

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

## HAP Treatment

### Reducing Treatment Duration

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

**Note:** ICU LOS: Intensive Care Unit Length of Stay.
HAP: Treatment

Reducing Treatment Duration

VAP: Randomized trial of 8 days vs. 15 days of rx

- 51 ICUs in France
- Required bronch dx with quant cultures and adequate empiric rx within 24 hrs
- Excluded early onset VAP (and a lot of others)
  - 400 enrolled out of 1200 eligible
- Repeat bronchs for any suspicion of recurrence

Chastre, et al. JAMA 2003
## HAP Treatment

### Reducing Treatment Duration

<table>
<thead>
<tr>
<th></th>
<th>8 days IV</th>
<th>15 days IV</th>
</tr>
</thead>
<tbody>
<tr>
<td>Patients</td>
<td>197</td>
<td>204</td>
</tr>
<tr>
<td><strong>28 day outcomes</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Mortality</td>
<td>19%</td>
<td>17%</td>
</tr>
<tr>
<td>-Resistant GNB</td>
<td>23%</td>
<td>30%</td>
</tr>
<tr>
<td>-MRSA</td>
<td>29%</td>
<td>24%</td>
</tr>
<tr>
<td>Abx Free Days</td>
<td>13</td>
<td>9*</td>
</tr>
<tr>
<td></td>
<td></td>
<td>+4 (3-6)</td>
</tr>
<tr>
<td>Recurrence</td>
<td>29%</td>
<td>26%</td>
</tr>
<tr>
<td>-Resistant GNB</td>
<td>41%</td>
<td>25%*</td>
</tr>
<tr>
<td>Recurrence with</td>
<td></td>
<td>+15% (4-27)</td>
</tr>
<tr>
<td>multi-resistant org</td>
<td>42%</td>
<td>62%*</td>
</tr>
<tr>
<td></td>
<td></td>
<td>p=0.04</td>
</tr>
</tbody>
</table>

Chastre, et al. JAMA 2003
HAP Treatment

General Principals

• Identify “low-risk” patients
  – Early onset (< 5 days)
  – No prior broad spectrum antibiotics
  – No recent hospitalizations
  – No clear risk for specific pathogens (i.e. structural lung dz)

• Rx consistent with ATS / IDSA guidelines
  – 3rd generation cephalosporin or
  – Beta-lactam / lactamase inhibitor or
  – Fluoroquinolone (Levo, Moxi)
HAP Treatment

General Principals

• High risk patients
  – Late onset (> 5 days)
  – HCAP + MDR risk factors
  – Prior abx / hospitalization
  – At risk for MRSA, Acinetobacter, Pseudomonas

• RX*
  – **Know your local flora!**
  – Imipenem or beta-lactam / lactamase or cefepime +
    aminoglycoside# or fluoroquinolone (#7mg / kg / day)
  – + / - Vancomycin / Linezolid

*ATS/IDSA Guidelines. Am J Respir Crit Care. 2005
HAP: Management

Suspicion
(infiltrate+F/WBC/sputum)

Start Treatment, Secretion Sampling
(Sputum, ETA?)

48-72 hrs

Clinical Suspicion AND + culture or sepsis/shock

Clinical Suspicion OR + culture

Low Suspicion AND - cultures
HAP: Management

- Clinical Suspicion AND + culture or sepsis/shock: Treat x 7 days Or until resolution
- Clinical Suspicion OR + culture
- Low Suspicion AND - cultures: Stop RX

High Clinical Suspicion

- Treat x 7 days

Low Clinical Suspicion (CPIS <6)

- Stop RX
# HAP Prevention and Blood Products

## Transfusion Related Immunomodulation (TRIM)

<table>
<thead>
<tr>
<th>Study</th>
<th>Result</th>
</tr>
</thead>
<tbody>
<tr>
<td>Leal-Noval 2001</td>
<td>&gt; 4 U PRBC assoc with HAP</td>
</tr>
<tr>
<td>Shorr, 2004</td>
<td>VAP: PRBC, OR=1.9 (1.3-2.7)</td>
</tr>
<tr>
<td>Sarani, 2008</td>
<td>VAP: FFP: RR=1.97 (1.03-3.78) (not sig when PRBCs also given)</td>
</tr>
</tbody>
</table>
HAP Prevention and Blood Products

Transfusion Related Immunomodulation (TRIM)

- Causal or an association?
- Mediated by allogeneic WBCs?
- RCTs suggest no difference in infections of Allo vs. Auto?
- Most data comes from the surgical population
- Regardless;
  - Hgb targets=7-9 g/dL no worse and likely better that Hgb target=10

Crit Care Med 2006
NEJM 1999
CAP / HCAP / HAP

Key Points

• START
  – CAP: Risk stratifying for CA-MRSA, Pseudomonas and consider rx
  – CAP: Addressing comorbid illness at discharge
  – HCAP: Risk stratifying for MDR pathogens
  – HCAP: Treating those at risk with broad spectrum abx
  – HAP: Trying to get a respiratory isolate to guide rx
  – HAP: Considering narrow spectrum rx in low risk patients

• STOP
  – CAP: Routinely treating beyond 7 days
  – CAP: Trying to get antibiotics into everyone within 4 hours
  – HCAP: Treating all NHAP with broad spectrum abx
  – HAP: Broad spectrum therapy beyond 72 hrs if stable and no bad bugs
  – HAP: Routinely treating beyond 8 days
Key Points

• CONSIDER
  – CAP: SMART-COP to risk stratify for ICU admissions
  – CAP: Atypical coverage may not be adding much
  – CAP: Pneumococcal and Flu vaccine may not prevent much CAP
  – CAP: Avoiding / Stopping unnecessary PPIs, antipsychotics
  – HCAP: Outpt narrow spectrum rx for low risk patients (NHAP)
  – HAP: Avoiding blood products unless absolutely necessary
Appendix

Clinical Pulmonary Infection Score (CPIS)

- **Temperature**(°C)
  - 36.5-38.4 = 0 points
  - 38.5-38.9 = 1 point
  - ≥ 39 or ≤ 36.5 = 2 points

- **WBC**
  - ≥4000 and ≤11000 = 0
  - <4000 or >11000 = 1 point
  - ≥500 bands = +1 point

- **Tracheal Secretions**
  - Purulent = 1 point
  - Suctioned ≥14 times / 24 hrs = +1 point

- **Oxygenation** (PaO2/FiO2 ratio mmHg)
  - >240 or ARDS = 0 points
  - ≤ 240 and no ARDS = 2 points

- **CXR**
  - no infiltrate = 0 points
  - diffuse infiltrate = 1 point
  - local infiltrate = 2 points

- **Semiquant ETA** (1+, 2+, 3+)
  - no or <1+ bact = 0 points
  - >1+ pathologic bact = 1 point
  - bact seen on gram stain = +1 point

Scores >6 correlate well with BAL dx of NP.