Pneumonia Update 2012

Management of the Hospitalized Patient

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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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<tbody>
<tr>
<td>IHI/CDC-Project Faculty</td>
<td>NONE</td>
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<td>SHM-CAUTI Project</td>
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<table>
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<tr>
<th>Research and Grant Support</th>
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<td>CDC Foundation</td>
<td>NONE</td>
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<td>NIH-CTSA</td>
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<td>Blue Cross Blue Shield, MI</td>
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</tr>
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</table>
A 72 y.o. man with a history of COPD and CHF (EF 25%) is admitted with worsening shortness of breath, mild wheezing and low grade temps after “catching a bug” from his 5 y.o. grandson. His vitals are stable. T=38, O2 sat =89% RA. CXR shows cardiomegaly, mild venous congestion and LLL infiltrate vs. atelectasis (“suggest clinical correlation”). He is started on levofloxacin, nebulized albuterol treatments, and IV Lasix. On hospital day 3 you hand him off to your partner. The patient feels back at his baseline and is ready for discharge. What does your partner do with the antibiotics?

1) Stops everything
2) Treats for 2 more days (5 total)
3) Treats for 4 more days (7 total)
4) Treats for 7 more days (10 total)
Overview

- Antibiotic Overuse
- Performance Measures
- Antibiotic Treatment
- Aspiration Pneumonia
- Adjunctive Treatment
less is more.

[more or less]
Estimated burden of healthcare-associated CDI

- Hospital-acquired, hospital-onset: 165,000 cases, $1.3 billion in excess costs, and 9,000 deaths annually

- Hospital-acquired, post-discharge (up to 4 weeks): 50,000 cases, $0.3 billion in excess costs, and 3,000 deaths annually

- Nursing home-onset: 263,000 cases, $2.2 billion in excess costs, and 16,500 deaths annually


<table>
<thead>
<tr>
<th>Characteristic</th>
<th>Adjusted Hazard Ratio (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Daily Doses</td>
<td></td>
</tr>
<tr>
<td>3-8</td>
<td>1.2 (0.7-2.1)</td>
</tr>
<tr>
<td>8-21</td>
<td>2.8 (1.7-4.6)</td>
</tr>
<tr>
<td>&gt;21</td>
<td>5.3 (3.1-9.0)</td>
</tr>
<tr>
<td>Antibiotic Days</td>
<td></td>
</tr>
<tr>
<td>4-7</td>
<td>1.4 (0.8-2.4)</td>
</tr>
<tr>
<td>8-18</td>
<td>3.0 (1.9-5.0)</td>
</tr>
<tr>
<td>&gt;18</td>
<td>7.8 (4.6-13.4)</td>
</tr>
<tr>
<td>Number of Antibiotics</td>
<td></td>
</tr>
<tr>
<td>2-3</td>
<td>2.5 (1.6-4.0)</td>
</tr>
<tr>
<td>3-4</td>
<td>3.3 (2.2-5.2)</td>
</tr>
<tr>
<td>5 or more</td>
<td>9.6 (6.1-15.1)</td>
</tr>
</tbody>
</table>

Stevens V, et al. CID, 2011
Antibiotic Misuse, Resistance, and Outcomes

• Use of antibiotics for a given patient
  – Increases risk of colonization by resistant bacteria
  – Increases risk of infection by resistant bacteria
  – Higher rates of adverse events (non- *C. diff*)
  – Resistant bacteria associated with worse outcomes

• Overuse at the hospital level
  – Increases prevalence of resistant bacteria

• “Improved” Use
  – Reduces resistance
  – Can improve outcomes
  – Can reduce costs
Current Challenges

Antibiotic Use in U.S. Hospitals

• 63% of hospitalized patients in academic medical centers in 2006 received antibiotics

• 10% increase over 4 years prior


• Up to 50% of use is felt to be inappropriate

  Dellit TH, Clin Infect Dis. 2007
An Outbreak of Severe Clostridium difficile–Associated Disease Possibly Related to Inappropriate Antimicrobial Therapy for Community-Acquired Pneumonia

Philip M. Polgreen
Joseph E. Cavanaugh
Stacy Coffman, MF
Daniel J. Diekema,

We report a severe outcome to a chart review of bacterial pneumonia patients not having had prior pneumonia care plan.

A pulmonologist and an infectious disease physician independently reviewed each case of CDAD to determine whether they thought the antimicrobial treatment was appropriate. The reviewers evaluated the chief complaint, vital signs, results of chest radiograph, oxygen saturation level, peripheral leukocyte count, and results of sputum Gram stain and

The Use of Antimicrobial Agents after Diagnosis of Viral Respiratory Tract Infections in Hospitalized Adults: Antibiotics or Anxiolytics?

Kevin T. Shiley, MD; Ebbing Lautenbach, MD, MPH, MSCE; Ingi Lee, MD, MSCE

OBJECTIVE. Because extensive antibiotic use by inpatients has been associated with the development of multidrug-resistant organisms, we aimed to determine which variables were associated with the use of antibiotics after viral respiratory tract infection diagnosis among adult patients admitted to the hospital with respiratory symptoms.

METHODS. A retrospective cohort study was conducted at 2 affiliated urban hospitals in Pennsylvania. We identified all adult patients admitted to the hospital during the period from November 1, 2005, through August 1, 2007, with a viral assay positive for influenza A or
PNEUMONIA
Reducing Unnecessary Treatment

A Role for Procalcitonin (PCT)?

• Released in response to bacterial infection
  – IL-1, IL-6, TNF
  – NOT with viral, IBD, SLE, Gout, Stills’
  – Not affected by NSAIDs, steroids
• Rises within 3-4 hours after invasion
  – Earlier than CRP, ESR
• Degree and rate of rise associated with severity
• Rate of decline associated with resolution
• Numerous studies of its effect on antibiotic use

CID 2011
AJM 2011
Procalcitonin: The Algorithm

Moderate and high acuity patients
(CAP patients in ED, hospital ward or ICU setting)

**Diagnosis**
- **<0.1 μg/L**
  - Bacterial infection highly unlikely
  - → consider alternative diagnosis
- **<0.25 μg/L**
  - Bacterial infection unlikely
  - → consider alternative diagnosis
- **≥0.25 μg/L**
  - Bacterial infection likely
- **>0.5 μg/L**
  - Bacterial infection / sepsis highly likely

**Prognosis**
- **<0.1 μg/L**
  - Low risk for mortality despite high clinical risk score
- **<0.25 μg/L**
  - Low risk for sepsis related complication
- **≥0.25 μg/L**
  - High risk for bacteremic infection
- **>0.5 μg/L**
  - High risk for bacteremic infection and adverse outcome
  - → monitor PCT for treatment response

**Therapy**
- **<0.1 μg/L**
  - Consider AB treatment if high clinical suspicion of infection ("overruling")
  - → monitor PCT for early stopping AB treatment
- **<0.25 μg/L**
  - Consider AB treatment if high clinical suspicion of infection ("overruling")
  - → monitor PCT for early stopping AB treatment
- **≥0.25 μg/L**
  - Start AB
    - → monitor PCT for stopping AB treatment if decrease >80-90% or PCT <0.25 μg/L (ward) or <0.5 μg/L (ICU)
- **>0.5 μg/L**
  - Start AB
    - → monitor PCT for stopping AB treatment if decrease >80-90% or PCT <0.25 μg/L (ward) or <0.5 μg/L (ICU)
# Procalcitonin and Antibiotic Use

<table>
<thead>
<tr>
<th>RCT/Year</th>
<th>Patients with Respiratory Infection</th>
<th>Setting</th>
<th>Antibiotic Use</th>
<th>Clinical Outcomes</th>
</tr>
</thead>
<tbody>
<tr>
<td>Christ-Crain, 2004</td>
<td>243</td>
<td>ED</td>
<td></td>
<td>?</td>
</tr>
<tr>
<td>Christ-Crain, 2006</td>
<td>302</td>
<td>ED/Inpt.</td>
<td></td>
<td></td>
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<tr>
<td>Stolz, 2007</td>
<td>208</td>
<td>ED/Inpt.</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Briel, 2008</td>
<td>458</td>
<td>Multicenter</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Nobre, 2008</td>
<td>53</td>
<td>ICU</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Kristoffeger, 2009</td>
<td>210</td>
<td>ED/Inpt</td>
<td></td>
<td>?</td>
</tr>
<tr>
<td>Schuetz, 2009</td>
<td>1359</td>
<td>Multicenter</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Stolz, 2009</td>
<td>101</td>
<td>Multicenter, ICU</td>
<td></td>
<td></td>
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<tr>
<td>Long, 2009</td>
<td>127</td>
<td>ED</td>
<td></td>
<td>?</td>
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<td>Burkhardt, 2010</td>
<td>550</td>
<td>ICU</td>
<td></td>
<td></td>
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<td>Bouadma, 2010</td>
<td>397</td>
<td>ED</td>
<td></td>
<td></td>
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<tr>
<td>Long, 2011</td>
<td>156</td>
<td>ED</td>
<td></td>
<td>?</td>
</tr>
</tbody>
</table>
Procalcitonin and Antibiotic Use

> 2000 Patients with Pneumonia

CID 2012
Cochrane 2012
Procalcitonin and Outcomes

14 Trials, 4221 Patients with Respiratory Infections

OR=0.94 (0.71-1.23)

5.7% 6.3%

19% 22%

OR=0.82 (0.71-0.97)

CID 2012
Cochrane 2012
Procalcitonin in Real Life

- Over 1700 LRTI pts; 14 centers (1 US hospital!)
- 54% with CAP as final dx
- 81% compliance; 19% used “clinical judgment”

**PCT Followed* vs. PCT Ignored**

<table>
<thead>
<tr>
<th>Antibiotic Days</th>
<th>PCT Followed</th>
<th>PCT Ignored</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>5.9</td>
<td>7.4 (p&lt;0.001)</td>
</tr>
</tbody>
</table>

(* Includes pts with valid reasons for overruling such as: ICU, severe resp / hemodynamic instability, severe immunosuppres, high PSI or CURB class)

Arch Intern Med., 2012
## Table 3. Safety of Initial Withholding of Antibiotic Therapy in Patients With Low PCT Values

<table>
<thead>
<tr>
<th>Variable</th>
<th>Adjusted OR (95% CI)(^a)</th>
<th>P Value</th>
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</thead>
<tbody>
<tr>
<td>In-hospital complications(^b)</td>
<td>0.627 (0.299 to 1.314)</td>
<td>.22</td>
</tr>
<tr>
<td>In-hospital mortality</td>
<td>1.048 (0.243 to 4.513)</td>
<td>.95</td>
</tr>
<tr>
<td>ICU admission</td>
<td>1.248 (0.368 to 4.232)</td>
<td>.72</td>
</tr>
<tr>
<td>Mechanical ventilation</td>
<td>1.701 (0.372 to 7.786)</td>
<td>.49</td>
</tr>
<tr>
<td>Empyema</td>
<td>0.812 (0.040 to 16.457)</td>
<td>.89</td>
</tr>
<tr>
<td>30-d Mortality</td>
<td>1.044 (0.330 to 3.301)</td>
<td>.94</td>
</tr>
<tr>
<td>Recurrences</td>
<td>0.655 (0.246 to 1.748)</td>
<td>.40</td>
</tr>
<tr>
<td>Rehospitalization</td>
<td>0.045 (&lt;0.001 to &gt;0.999)</td>
<td>.98</td>
</tr>
<tr>
<td>Any 30-d complication(^c)</td>
<td>0.830 (0.444 to 1.550)</td>
<td>.56</td>
</tr>
<tr>
<td>Antibiotic adverse effects(^d)</td>
<td>0.232 (0.059 to 0.908)</td>
<td>.04</td>
</tr>
</tbody>
</table>
Procalcitonin Use in the U.S.

U.S. Compliance < 40%!

Arch Intern Med., 2012
Procalcitonin: Caution!?

• Wide confidence intervals for mortality
• Compliance low in critically ill
  – PCT for “escalation” led to worse outcomes
• False negatives
  – Empyema, parapneumonic effusions
• False positives
  – Shock
  – Cardiac surgery
• Rapid bedside testing not available

Jensen, Crit Care Med, 2011
Hospitalist-centric CAP Stewardship

- Single, large academic center

- Outstanding performance on core measures, but suspicion for improvement opportunities

- Intervention
  - Survey of practice patterns
  - Educational sessions on rx recs and duration of rx
  - Prospective pharmacist review with direct feedback

Avdic, CID 2012
Hospitalist-centric CAP Stewardship

<table>
<thead>
<tr>
<th></th>
<th>Pre</th>
<th>Post</th>
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<tbody>
<tr>
<td>n</td>
<td>56</td>
<td>63</td>
</tr>
<tr>
<td>LOS</td>
<td>4 days</td>
<td>5 days</td>
</tr>
<tr>
<td>Rx duration</td>
<td>10 days</td>
<td>7 days</td>
</tr>
<tr>
<td>Excess days</td>
<td>241</td>
<td>93</td>
</tr>
<tr>
<td>Median excess</td>
<td>4 days</td>
<td>1 day</td>
</tr>
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</table>

(Narrowing of treatment increased by 48% and there was no difference in 30 day readmissions)

Avdic, CID 2012
Hospitalist-centric CAP Stewardship

• Treatment duration algorithm:
  – 5 days  (for most patients)
  – 7 days  (mild-mod immune compromise, structural lung dz)
  – 10 days (severe immune compromise, poor initial response)

• Consistent with literature / guidelines
  – Levofloxicin 750 x 5d = Levofloxicin 500 x 10d  (Clin Ther 2005)
  – Amoxicillin x 3d = Amoxicillin x 8d  (BMJ 2006)
  – ATS / IDSA Guidelines = no less than 5 days

Avdic, CID 2012
Guideline Based Duration

Stopping Antibiotics

- Rx > 7 days no better than Rx ≤ 7 days
- Pts should be afebrile for 48-72 hours
- Have no more than 1 CAP-associated instability*
- Usually this is after 5 days of therapy
- If it wasn’t CAP, stop when another dx is made

*HR<100
SBP>90
RR<24
Temp <37.8
O2 Sat >90
Mental status at baseline
Taking orals

CAP Process Measures

- CMS Hospital Compare
  - Abx within 6 hours (retired Jan. 2012)
  - Blood cx prior to abx
  - Appropriate initial abx
  - Smoking cessation
  - Pneumovax
  - Flu vaccination
  - 30 d mortality*
  - 30 d readmissions*

* Reported as better, worse, or no different from average
CAP Process Measures

• Joint Commission / Value Based Purchasing (VBP)
  – Blood cultures
    - performed in the ED prior to antibiotics
    - performed within 24 hours of arrival for patients in ICU within 24 hours of arrival
  – Initial antibiotics consistent with guidelines

• Value Based Purchasing
  – Started Oct 1, 2012
  – Hospital DRG payment reductions of 1% (2% by 2017)
  – 50% of hospitals get a net $ increase, 50% decrease
A 64 y.o. woman presents to the ED with cough, SOB, and fever to 38.4 C. BP is normal, pulse is 87, RR is 17. O2 sat is 93% on RA. CBC shows mild anemia but normal WBC. CXR shows LLL infiltrate. She is given IV ceftriaxone and oral azithromycin and is admitted and called up to the medical team. After hearing the story the admitting hospitalist asks the ED to draw blood cultures. This pt:

1) “fails” the blood culture measure and didn’t need cx
2) “fails” the blood culture measure but needed cx
3) “passes” the measure and didn’t need cx
4) “passes” the measure and needed cx
Blood Cultures and CAP

- Blood stream infection (BSI); Mortality 14-37%
- In ICUs, BSI excess mortality of 35%
- Only 4-7% of cultures are positive (many false +)
- False positive cultures:
  - 50% increase in charges
  - 65% increase in LOS
- Pre-test probability in CAP= 0.07 (7%)
- Fever or leukocytosis alone not predictive
- Shaking chills + LR 4.7

Coburn, JAMA, 2012
Blood Cultures and CAP

> 2 SIRS criteria
- 36 > T > 38
- HR > 90 / min
- RR > 22 or PCO2 <32
- 4k>WBC>12k or 10% bands

Shapiro Criteria
• 1 major or 2 minor
  • Major
    – Suspect endocarditis
    – T ≥ 39.4
    – Indwelling catheter
  • Minor
    – 39.4 > T > 38.3
    – Chills
    – Emesis
    – SBP < 90 mmHg
    – WBC > 18k
    – Cr > 2

Coburn, JAMA, 2012
Processes of Care and Outcomes

- Multicenter, 32 ED, RCT in 2 states, 2076 pts
- 4 process measures recommended

<table>
<thead>
<tr>
<th>Measure</th>
<th>Performance</th>
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<tbody>
<tr>
<td>O2 assess</td>
<td>98%</td>
</tr>
<tr>
<td>Cx before abx</td>
<td>63%</td>
</tr>
<tr>
<td>Abx in 4hrs</td>
<td>79%</td>
</tr>
<tr>
<td>Abx selection</td>
<td>63%</td>
</tr>
</tbody>
</table>

- 34% received all 4 processes

## Processes of Care and Outcomes

<table>
<thead>
<tr>
<th># Processes</th>
<th>Mortality OR</th>
</tr>
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<tbody>
<tr>
<td>0-2</td>
<td>Reference</td>
</tr>
<tr>
<td>3</td>
<td>0.9 (0.5-1.3) NS</td>
</tr>
<tr>
<td>4</td>
<td>0.7 (0.4-1.1) NS</td>
</tr>
</tbody>
</table>

- No association with readmission rates
- No change when only patients ≥ 65 yrs. included
- "Results cast doubt on sole use of process measures to reflect high quality CAP care"

Antibiotic Therapy

The Guidelines: Inpatient

• IDSA / ATS 2007
  – β-lactam + macrolide (or doxycycline)
    (β-lactam : Ceftriaxone, Cefotaxime, Amp / Sul, Ertapenem)
  – Or, 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

The Guidelines: Inpatient

- IDSA / ATS 2007 Pseudomonal Risk: Non-ICU
  - Bronchiectasis
  - Structural lung disease (COPD / ILD) AND documented history of repeated antibiotics or long term chronic steroids in past 3 months
  - MD documentation of psuedomonal risk: “will cover for psudomonas”
MRSA and CAP

- 12 Urban Academic Emergency Departments
- 630 pts with ED and Hospital d/c dx CAP
- 14 pts (2.4%) with MRSA (but 5% of ICU cases)
- Sputum: 90% +; Blood Cx: 40% +
- 30% with no risk factors; 1 factor = 5% risk of MRSA

<table>
<thead>
<tr>
<th>Risk Factor</th>
<th>RR</th>
<th>Risk Factor</th>
<th>RR</th>
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<tbody>
<tr>
<td>cirrhosis</td>
<td>8.1</td>
<td>h/o MRSA</td>
<td>7.6</td>
</tr>
<tr>
<td>prior LTAC</td>
<td>5</td>
<td>wound contact</td>
<td>5.1</td>
</tr>
<tr>
<td>cavity</td>
<td>5.6</td>
<td>multilobar</td>
<td>4.5</td>
</tr>
<tr>
<td>intubation</td>
<td>6.9</td>
<td>pressors</td>
<td>8.8</td>
</tr>
<tr>
<td>death in ED!</td>
<td>23</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Moran G., CID 2012
An 83 yo woman with PMHX of HTN, CAD, is brought to the ED by her daughter with 2-3 days of altered mental status, fever, and cough. She lives in an assisted living facility and has not been recently hospitalized. PEX: 38.5, O2 sat: 88% RA, RR: 16, BP: 115 / 75, Pulse: 90. She is confused, edentulous, with bronchial breath sounds over the right lower lung fields. CXR read as “RLL infiltrate consistent with aspiration pneumonia”. She is admitted. You prescribe:

1) Ceftriaxone + Macrolide
2) Vancomycin + Pip / Tazo
3) Ceftriaxone + Clindamycin
4) Ceftriaxone + Clindamycin + Macrolide
5) Pip / Tazo + Macrolide
Aspiration Pneumonia

• All pneumonia is essentially aspiration pneumonia
  – > 50% of healthy adults aspirate during sleep
  – Pneumonia if reduced host defenses / high bacterial load
  – 5-15% of CAP cases diagnosed as “aspiration pneumonia”

Silent Aspiration

  Elderly with CAP  70%
  Elderly w/o  CAP  10%

• Risk for pneumonia:
  – Colonization (HAP / HCAP risk factors)
  – Poor oral hygiene

Marik, Curr Op Pulm Med. 2011
Aspiration Pneumonia: Anaerobes

  - 95 elderly NH patient with “severe aspiration”
  - Quantitative bronchial sampling
  - 67 pathogens isolated
    - 50% GNRs
    - 15% staph
    - 15% anaerobes (over half also had GNR); low virulence orgs
  - Poor functional status associated with anaerobes
  - 85% of patients with an anaerobe isolated improved on regimens without anaerobic coverage
Aspiration Pneumonia: Anaerobes

When to cover anaerobes

- Periodontal disease
- Putrid sputum
- Necrotizing / cavitary lesions
- Large effusions (empyema?)
- Elderly with poor functional status?
- Recurrent aspirators? Alcoholics?
Aspiration Pneum(onitis vs. onia)

Time to Symptom Resolution

Pneumonitis?

## Aspiration Pneumonia

### Time to Clinical Stability

<table>
<thead>
<tr>
<th></th>
<th>&lt; 2 days</th>
<th>&gt; 2 days</th>
</tr>
</thead>
<tbody>
<tr>
<td>Patients</td>
<td>102</td>
<td>227</td>
</tr>
<tr>
<td>Nursing home</td>
<td>67%</td>
<td>64%</td>
</tr>
<tr>
<td>ICU transfer</td>
<td>0</td>
<td>23%*</td>
</tr>
<tr>
<td>LOS (d)</td>
<td>4</td>
<td>6.5*</td>
</tr>
<tr>
<td>30 d mortality</td>
<td>9%</td>
<td>37%*</td>
</tr>
<tr>
<td>β-lactam+macro</td>
<td>73%</td>
<td>70%</td>
</tr>
<tr>
<td>Added clinda</td>
<td>2%</td>
<td>6%</td>
</tr>
</tbody>
</table>

Authors propose stopping antibiotics in aspiration patients whose symptoms resolve in <48 hrs

* = significant difference

Aspiration Pneumonia

Treatment

• No risk factors for multidrug resistant organisms
  – TREAT AS CAP: Ceftriaxone + Macrolide

• Risk factors for multidrug resistant organisms
  – Vanco + Pip / Tazo (+/- Macrolide)
  – Vanco + Fluoroquinolone

• Risk factors for anaerobes
  – Add Clindamycin (but not to Pip / Tazo!)

• Duration no different than CAP
  – Consider earlier d/c in pts resolving in < 48 hrs

Marik, Curr Op Pulm Med. 2011
The First 5 Days

Ann Intern Med, 1964
Adjunctive Therapy

- Macrolides
- Steroids
- Statins
Macrolides and Statins: Immunomodulatory Properties

<table>
<thead>
<tr>
<th>Macrolides</th>
<th>Statins</th>
</tr>
</thead>
<tbody>
<tr>
<td>↓ IL-1, IL-6, IL-8, IL-10, GM-CSF and TNF-α&lt;sup&gt;22,23&lt;/sup&gt;</td>
<td>↓ IL-1, IL-6, and TNF-α&lt;sup&gt;48,49&lt;/sup&gt;</td>
</tr>
<tr>
<td>↓ Neutrophil chemoattractants, IL-8, ENA-78&lt;sup&gt;23&lt;/sup&gt;</td>
<td>↓ Monocyte chemoattractant, CCL5&lt;sup&gt;47,50,51&lt;/sup&gt;</td>
</tr>
<tr>
<td>↓ Endothelial adhesion molecules&lt;sup&gt;25&lt;/sup&gt;</td>
<td>↓ Endothelial adhesion molecules&lt;sup&gt;54&lt;/sup&gt;</td>
</tr>
<tr>
<td>↓ Leukocyte adhesion molecules&lt;sup&gt;26,27&lt;/sup&gt;</td>
<td>↓ Leukocyte adhesion molecules&lt;sup&gt;52,53,55&lt;/sup&gt;</td>
</tr>
<tr>
<td>↓ Oxidative burst, reactive oxygen species (ROS) production&lt;sup&gt;27,28&lt;/sup&gt;</td>
<td>↓ Oxidative burst, reactive oxygen species (ROS) production&lt;sup&gt;55,56&lt;/sup&gt;</td>
</tr>
<tr>
<td>↓ Generation of LT-B4&lt;sup&gt;24&lt;/sup&gt;</td>
<td>↓ Generation of cyclooxygenase 2&lt;sup&gt;57&lt;/sup&gt;</td>
</tr>
<tr>
<td>↓ Matrix metalloproteases and neutrophil elastase&lt;sup&gt;29,30&lt;/sup&gt;</td>
<td>↓ Constitutive NO synthase&lt;sup&gt;60,61&lt;/sup&gt;</td>
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<tr>
<td></td>
<td>↓ Matrix metalloproteases&lt;sup&gt;57,58&lt;/sup&gt;</td>
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<td>↓ Thromboxane&lt;sup&gt;59&lt;/sup&gt;</td>
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</tbody>
</table>

<sup>a</sup> See text.
Macrolides and Outcomes

Meta-analysis; 23 studies with 138,000 patients

Macrolides vs. Nonmacrolides

Mortality: RR=0.78 (0.64-0.95)

Asadi, CID, 2012
Macrolides and Outcomes

Meta-analysis; 23 studies with 138,000 patients

Beta-lactam + macro vs. Fluoroquinolone
Mortality RR = 1.17 (0.91-1.50)

Macrolide vs. Nonmacrolide (RCTs only)
Mortality RR = 1.13 (0.65-1.98)
Macrolides and Pneumonia

- Most benefit shown in observational studies
- More benefit demonstrated in sicker patients
- If there is a clinical benefit, it is small
- There appears to be benefit in “following guidelines”
- There is enough equipoise for an RCT
Steroids for Pneumonia

• Chen Y, et. al. Cochrane Review, 2011
  – 6 RCTs with 437 patients
  – Only 2 studies of high quality
  – Accelerated time to clinical stability and resolution of sx
  – Reduced need for ventilation
  – No impact on LOS / Mortality
  – “Evidence not strong enough to make recommendations”

• Meijvis S, et. al. Lancet, 2011
  – RCT of 300 non-ICU pts; Dexamethasone 5 mg x 4d
  – Lower LOS by 1 day, more hyperglycemia
Statins and CAP Mortality

Mortality: OR=0.66 (0.55-0.79)

Statins and CAP Mortality

Healthy User Effect?

<table>
<thead>
<tr>
<th>Meta-Analytic Model</th>
<th>Odds Ratio (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Unadjusted</td>
<td>0.62 (0.54 – 0.71)</td>
</tr>
<tr>
<td>Adjustment for Smoking</td>
<td>0.63 (0.48 – 0.81)</td>
</tr>
<tr>
<td>Adjustment for Vaccination</td>
<td>0.74 (0.56 – 0.97)</td>
</tr>
<tr>
<td>Adjustment for Pneumonia Severity</td>
<td>0.75 (0.56 – 1.00)</td>
</tr>
<tr>
<td>Adjustment Using Propensity Score</td>
<td>0.75 (0.58 – 0.96)</td>
</tr>
<tr>
<td>Adjustment Using Uncommon Covariates</td>
<td>0.81 (0.69 – 0.96)</td>
</tr>
</tbody>
</table>

Pneumonia and Cardiac Events

- 90% of events in week 1; 50% within 24 hours
- OR 30 d mortality=1.6 (1.04-2.50)

Corrales-Medina, Circulation, 2012
Pneumonia and Cardiac Events

• **Musher CID, 2007**
  – 33 of 170 pts (19.4%) with pneumococcal pneumonia had a major cardiac event during admission

• **Ramirez CID 2008**
  – 500 pts; 6% with AMI; 15% of pts with severe CAP had AMI; AMI risk increased with “clinical failure”
Preventing Pneumonia: Stop the PPI

**PPI: OR=1.27 (1.11-1.46)**

**H2: OR=1.22 (1.09-1.36)**

Eom, CMAJ 2011
Preventing CAP

• Avoiding anti-psychotics
  – Current use OR=1.8-2.6 for CAP
  – Recent start OR=4.3

  JAGS 2008
  Ann Intern Med 2010

• Pneumococcal vaccination
  – No effect on mortality
  – No reduction in pneumonia (RR 1.2; 0.95-1.49)

  CMAJ 2010
Conclusions

- Antibiotic overuse is common
  - CAP treatment is a big driver
  - Shorter courses (5-7 days) are safe and effective
  - Procalcitonin helps reduce antibiotic use
- Performance measures
  - No escape (yet)
  - Use clinical rules to assist with blood cultures
  - Stick to antibiotic treatment guidelines
- Aspiration
  - Not all patients need anaerobic coverage
- Adjunctive Treatment
  - I favor macrolides (for now), and never stop statins
THANK YOU!

QUESTIONS?