Community Acquired Pneumonia: Measures to Improve Management and Healthcare Quality: Antibiotic management, blood culture collection and smoking cessation

Gonzalo Bearman MD, MPH
Assistant Professor of Internal Medicine
Divisions of Quality Health Care & Infectious Diseases
Associate Hospital Epidemiologist
VCU Health System
Outline

• VHQC Pneumonia collaborative: overview
  – CAP: scope of the problem
  – Baseline indicator rates

• Key process measures
  – Scientific evidence and rationale:
    • Timing and choice of antibiotics
      – ICU vs Non-ICU populations
    • Blood culture collection
    • Smoking cessation for the hospitalized patient

• Barriers to implementation

• Conclusion
VHQC Pneumonia Collaborative

• Mission:
  – Improve the quality of healthcare for patients admitted to the hospital for the treatment of community acquired pneumonia.
VHQO Pneumonia Collaborative

• Scope of the current clinical problem: Community-Acquired Pneumonia
  Epidemiology:
  • Sixth leading cause of death
    – number one cause of death from infectious disease
  • Up to 5.6 million cases per year
    – >10 million physician visits
    – 1.1 million hospitalizations
  • Average rate of mortality for hospitalized patients 12%
Pneumonia Project Performance Measures

- Increase timely antibiotic administration
- Increase initial antibiotic therapy consistent with current guidelines (IDSA / ATS)
- Decrease smoking by providing cessation advice/counseling
- Increase arterial oxygenation assessment in the first 24 h
- Increase blood culture collection in the first 24 hours
- Increase blood culture collection prior to first antibiotic dose
- Increase screening for influenza & pneumococcal immunization status & vaccinate prior to discharge, if indicated
- Increase state wide immunization rates for influenza & pneumococcal vaccines
# Virginia Baseline Indicator Rates: 2001

<table>
<thead>
<tr>
<th>Performance Measure</th>
<th>RATE</th>
</tr>
</thead>
<tbody>
<tr>
<td>Antibiotics within 4 hours</td>
<td>59.9%</td>
</tr>
<tr>
<td>Appropriate antibiotic</td>
<td>65.0%</td>
</tr>
<tr>
<td>Blood culture within 24 hours</td>
<td>69.3%</td>
</tr>
<tr>
<td>Blood culture prior to antibiotics</td>
<td>83.9%</td>
</tr>
<tr>
<td>Influenza vaccination</td>
<td>12.6%</td>
</tr>
<tr>
<td>Pneumococcal vaccination</td>
<td>17.5%</td>
</tr>
<tr>
<td>Smoking cessation counseling</td>
<td>N/A</td>
</tr>
</tbody>
</table>
VHQC Pneumonia
Collaborative

Performance measures, rationale and supporting data
### Table 1. Categories for ranking recommendations in the therapeutic guidelines.

<table>
<thead>
<tr>
<th>Category</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>Strength of recommendation</td>
<td></td>
</tr>
<tr>
<td>A</td>
<td>Good evidence to support a recommendation for use</td>
</tr>
<tr>
<td>B</td>
<td>Moderate evidence to support a recommendation for use</td>
</tr>
<tr>
<td>C</td>
<td>Poor evidence to support a recommendation</td>
</tr>
<tr>
<td>D</td>
<td>Moderate evidence to support a recommendation against use</td>
</tr>
<tr>
<td>E</td>
<td>Good evidence to support a recommendation against use</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Quality of evidence</th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>I</td>
<td>Evidence from at least 1 randomized, controlled trial</td>
</tr>
<tr>
<td>II</td>
<td>Evidence from at least 1 well-designed clinical trial without randomization</td>
</tr>
<tr>
<td>III</td>
<td>Evidence from opinions of respected authorities, based on clinical experience, descriptive studies, or reports of expert committees</td>
</tr>
</tbody>
</table>
Timing and Choice of Antibiotics

Antibiotic Timing at 4 hours cutoff: IDSA B-III recommendation.

Empiric Antibiotic Choice of Therapy: IDSA A-I recommendation.
Timing of antibiotics

• Bratzler et al; *Archives of Internal Medicine* 2004. In press
  – Retrospective study 13,771 patient from a random Medicare registry sample
  • CAP; Age >65; 7/1998-3/1999
  • Outcome Measures
    – Antibiotic administration within 4 hours
    – Mortality (severity-adjusted)
    – Readmission within 30 days
    – Length of stay (LOS)
## First Dose Timing and Outcomes

<table>
<thead>
<tr>
<th>Timing of First Dose</th>
<th>Group 1 Mortality %</th>
<th>Group 2 Mortality %</th>
<th>Adjusted Odds Ratio (95% CI)</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>≤ 1 hour vs &gt; 1 hour</td>
<td>12.9</td>
<td>12.0</td>
<td>0.99 (.81-1.21)</td>
<td>0.906</td>
</tr>
<tr>
<td>≤ 2 hours vs &gt; 2 hours</td>
<td>12.5</td>
<td>11.9</td>
<td>0.94 (.83-1.06)</td>
<td>0.322</td>
</tr>
<tr>
<td>≤ 3 hours vs &gt; 3 hours</td>
<td>11.7</td>
<td>12.3</td>
<td>0.88 (.79-.99)</td>
<td>0.030</td>
</tr>
<tr>
<td>≤ 4 hours vs &gt; 4 hours</td>
<td>11.6</td>
<td>12.7</td>
<td>0.85 (.76-.95)</td>
<td>0.005</td>
</tr>
<tr>
<td>≤ 5 hours vs &gt; 5 hours</td>
<td>11.6</td>
<td>13.0</td>
<td>0.86 (.76-.97)</td>
<td>0.017</td>
</tr>
<tr>
<td>≤ 6 hours vs &gt; 6 hours</td>
<td>11.6</td>
<td>13.5</td>
<td>0.84 (.73-.95)</td>
<td>0.008</td>
</tr>
<tr>
<td>≤ 7 hours vs &gt; 7 hours</td>
<td>11.7</td>
<td>13.5</td>
<td>0.87 (.76-1.01)</td>
<td>0.060</td>
</tr>
<tr>
<td>≤ 8 hours vs &gt; 8 hours</td>
<td>11.7</td>
<td>13.8</td>
<td>0.85 (.73-.99)</td>
<td>0.040</td>
</tr>
<tr>
<td>≤ 9 hours vs &gt; 9 hours</td>
<td>11.8</td>
<td>13.8</td>
<td>0.86 (.73-1.02)</td>
<td>0.075</td>
</tr>
<tr>
<td>≤ 10 hours vs &gt; 10 hours</td>
<td>11.9</td>
<td>13.4</td>
<td>0.91 (.76-1.09)</td>
<td>0.327</td>
</tr>
</tbody>
</table>

**Retrospective analysis: early antibiotic treatment associated with decreased odds of mortality**

Using multivariate logistic regression [the model included the timing of antibiotic first dose, PSI score, ICU admission, US census region, race/ethnicity, other processes of care (oxygenation assessment, performance of blood cultures, and antibiotic selection)]. Patients who were on antibiotics prior to admission are excluded from this analysis. (Houck PM, Bratzler DW, et al. *Arch Intern Med*. In Press)
# Association between Antibiotic First Dose Timing and Outcomes

<table>
<thead>
<tr>
<th>Outcome</th>
<th>Within 4 hours %</th>
<th>After 4 hours %</th>
<th>Adjusted Odds Ratio aOR (95% CI)</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>30-day mortality</td>
<td>11.6</td>
<td>12.7</td>
<td>0.85 (.76-.95)</td>
<td>0.005</td>
</tr>
<tr>
<td>In-hospital mortality</td>
<td>6.8</td>
<td>7.4</td>
<td>0.85 (.74-.98)</td>
<td>0.029</td>
</tr>
<tr>
<td>Length of stay &gt; 5 days</td>
<td>42.1</td>
<td>45.1</td>
<td>0.90 (.83-.96)</td>
<td>0.003</td>
</tr>
<tr>
<td>30-day readmission</td>
<td>13.1</td>
<td>13.9</td>
<td>0.95 (.85-1.06)</td>
<td>0.344</td>
</tr>
</tbody>
</table>

Using multivariate logistic regression [the model included the timing of antibiotic first dose, PSI score, ICU admission, US census region, race/ethnicity, other processes of care (oxygenation assessment, performance of blood cultures, and antibiotic selection)].


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Early (within 4 hours) administration of antibiotics associated with decreased mortality and shorter LOS.
Appropriateness of antibiotic

• Appropriate selection of initial antibiotic therapy
  – *Streptococcus pneumoniae* causes two-thirds of all cases of bacteremic pneumonia
  – Need to cover potentially resistant strains of *S. pneumoniae* and atypical organisms for patients admitted to ICU
## Initial Antibiotic Selection

<table>
<thead>
<tr>
<th>Non-ICU</th>
<th>ICU</th>
<th>Pseudomonal Risk*</th>
</tr>
</thead>
<tbody>
<tr>
<td>β-lactam (IV or IM) + macrolide (IV or Oral)</td>
<td>β-lactam (IV) + macrolide (IV)</td>
<td>*In addition to the antibiotics listed under ICU, if the patient had a secondary ICD-9 code of bronchiectasis, or a positive response to the bronchiectasis question, or malnutrition [as reflected by a serum albumin below 3], these antibiotics would also be considered acceptable:</td>
</tr>
<tr>
<td>or β-lactam (IV or IM) + doxycycline (IV or Oral)</td>
<td>or β-lactam (IV) + quinolone (IV)</td>
<td>Antipseudomonal β-lactam (IV) + Antipseudomonal quinolone (IV)</td>
</tr>
<tr>
<td>or Quinolone monotherapy (IV or Oral)</td>
<td>If documented β-lactam allergy: Quinolone (IV) + Clindamycin (IV)</td>
<td>Or Antipseudomonal β-lactam (IV) + Aminoglycoside (IV) + either a [Macrolide (IV) or Antipneumococcal quinolone (IV)]</td>
</tr>
<tr>
<td></td>
<td>or Quinolone (IV) + Vancomycin (IV)</td>
<td>If documented β-lactam allergy: Aztreonam (IV) + Aminoglycoside (IV) + Antipneumococcal quinolone (IV)</td>
</tr>
</tbody>
</table>

*Adapted from IDSA: *Update of Practice Guidelines for the Management of Community Acquired Pneumonia in Adults. CID 2003;37:1405-1432*
# Initial Antibiotic Selection

## 30-day mortality - Community-dwelling Patients (14,150 patients)

<table>
<thead>
<tr>
<th>Initial Antibiotics</th>
<th>30-day mortality</th>
<th>Adjusted Odds</th>
<th>P Value</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>N/D (%)</td>
<td>Reference</td>
<td>Ref</td>
</tr>
<tr>
<td>3rd generation cephalosporin*</td>
<td>277/3072 (9.0)</td>
<td>Reference</td>
<td>Ref</td>
</tr>
<tr>
<td>Macrolide monotherapy‡</td>
<td>19/431 (4.4)</td>
<td>0.63 (.39-1.04)</td>
<td>0.069</td>
</tr>
<tr>
<td>2nd generation cephalosporin</td>
<td>73/844 (8.6)</td>
<td>1.13 (.85-1.51)</td>
<td>0.406</td>
</tr>
<tr>
<td><strong>Quinolone monotherapy‡</strong></td>
<td>121/1716 (7.1)</td>
<td><strong>0.78 (.62-.98)</strong></td>
<td><strong>0.037</strong></td>
</tr>
<tr>
<td>At least 1 aminoglycoside</td>
<td>80/445 (18.0)</td>
<td>1.51 (1.11-2.04)</td>
<td>0.008</td>
</tr>
<tr>
<td><strong>Cephalosporin + macrolide‡</strong></td>
<td>231/3618 (6.4)</td>
<td><strong>0.74 (.61-.89)</strong></td>
<td><strong>0.002</strong></td>
</tr>
<tr>
<td>Cephalosporin + quinolone‡</td>
<td>63/723 (8.7)</td>
<td>0.90 (.67-1.22)</td>
<td>0.506</td>
</tr>
<tr>
<td>β-lactam/β-lactamase inhibitor + macrolide‡</td>
<td>17/158 (10.8)</td>
<td>1.12 (.65-1.94)</td>
<td>0.689</td>
</tr>
</tbody>
</table>

*monotherapy with cefotaxime or ceftriaxone.

†Results adjusted for age, gender, neoplastic disease, cardiovascular disease, altered mental status, respiratory rate > 30/min, systolic BP < 90 mmHg, temperature < 35°C or ≥ 40°C, pulse ≥ 125/min, blood pH < 7.35, BUN > 10.7 mmol/L, sodium < 130 mEq/L, hematocrit < 30%, pO2 < 60 mmHg, pleural effusion, admission to ICU in the first 24 hours after arrival, antibiotics administered within the first 4 hours after arrival, and US census region.

‡These antibiotic combinations include patients receiving either oral or parenteral macrolides or quinolones.

Organisms Causing CAP in Hospitalized Patients Requiring ICU Admission

- Overall up to 10% of admitted patients with CAP are brought to the ICU
  - 30% caused by *Streptococcus pneumoniae*
  - 50-60% have an unknown etiology
  - Other reported organisms
    - *Legionella*
    - *H.influenza*
    - *S.aureus*
    - *P.aeruginosa* (underlying bronchiectasis)
    - Enterobacteriaceae (underlying bronchiectasis)

Recommended Definition Severe CAP and Need for ICU Admission [1]

- Combination of 2 minor or 1 major criteria (retrospective analysis- sensitivity of 78% and Specificity of 94%) [2]
  - Minor:
    - RR>30/minute
    - PaO2/FiO2 ratio <250
    - Bilateral or multilobar pneumonia
    - Systolic BP<90 mmHg and diastolic BP<60 mmHg
  - Major
    - Need for mechanical ventilation
    - Increase in the size of infiltrates by 50% within 48hr
    - Septic shock or the need for pressors
    - Acute renal failure

# Initial Antibiotic Choice for CAP in an ICU Cohort

<table>
<thead>
<tr>
<th>Variable</th>
<th>Relative OR</th>
<th>95%CI</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Underlying Diseases</td>
<td>3.09</td>
<td>1.63-5.887</td>
<td>0.0007</td>
</tr>
<tr>
<td>Shock</td>
<td>2.85</td>
<td>1.23-6.61</td>
<td>0.016</td>
</tr>
<tr>
<td>Bacteremia</td>
<td>2.63</td>
<td>1.18-5.87</td>
<td>0.019</td>
</tr>
<tr>
<td>Ineffective initial therapy</td>
<td>4.71</td>
<td>2.85-8.58</td>
<td>0.0001</td>
</tr>
<tr>
<td>Non-pneumonia related complications</td>
<td>10.7</td>
<td>5.00-20.00</td>
<td>0.0001</td>
</tr>
</tbody>
</table>

Retrospective clinical study with multivariate Analysis of 299 patients admitted to an ICU

Summary: Current Practice Guidelines

• Antibiotic timing and antibiotic choice represent practice guidelines based on best available current evidence
  – These are retrospective, observational trials and expert (committee) opinion.
    • In some studies the measure of effect, although, statistically significant may be small
  – These guidelines are not based on extensive prospective, randomized controlled trials
    • Antibiotic timing
Blood Culture Collection

IDSA B-III recommendation
National CAP Guidelines

• 2 sets of blood cultures should be drawn before initiation of antibiotic therapy
  – Infectious Diseases Society of America, 2000
  – American Thoracic Society, 2001
Blood Culture Collection:
Process Indicators

- **Increase the collection of blood cultures prior to first antibiotic dose**
  - Blood cultures before antibiotics gives highest yield of identifying a pathogen

- **Increase the collection of blood cultures during the first 24 hours**
  - Better late than never!
Rationale for Obtaining Blood Cultures in Patients with Pneumonia

• Studies have shown that 2-14% of patients with pneumonia have positive blood cultures—low yield diagnostic test

• A positive blood culture provides definitive evidence of the cause of pneumonia in most cases; provides greater certainty than sputum cultures or serology
Rationale for Obtaining Blood Cultures in Patients with Pneumonia

• Pneumonia patients with bacteremia have 3-fold increase in mortality

• Establishing a microbiologic diagnosis allows streamlining of antibiotic therapy, which decreases potential for antibiotic resistance

• Collection of blood cultures associated with decreased mortality
Pathogens Retrieved by Blood Culture

- Prospective study
- 19 Canadian hospitals
- 760 patients
  - 43 with (+) blood cultures

S. pneumoniae 68%
Staph. aureus 11%
Enterobacteriaceae 16%
Other 5%

Performance of Microbiologic Studies in Pneumonia Patients

Multicenter (5 hospitals), prospective, observational study, 1991-94; n=2,287

<table>
<thead>
<tr>
<th>Test</th>
<th>%</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sputum gram stain within 48 hrs of admission</td>
<td>52</td>
</tr>
<tr>
<td>Sputum culture within 48 hrs of admission</td>
<td>58</td>
</tr>
<tr>
<td>Blood culture obtained before antibiotics</td>
<td>71</td>
</tr>
</tbody>
</table>

Fine MJ. Arch Intern Med 1999;159:970.
Performance of Microbiologic Studies in Pneumonia Patients

Multicenter (3,555 hospitals), retrospective cohort study, 1994-95; n=14,069

<table>
<thead>
<tr>
<th>Test</th>
<th>%</th>
<th>Range by state</th>
</tr>
</thead>
<tbody>
<tr>
<td>Blood culture within 24 hrs of admission</td>
<td>69</td>
<td>46-83%</td>
</tr>
<tr>
<td>Blood culture obtained before antibiotics</td>
<td>57</td>
<td>32-74%</td>
</tr>
</tbody>
</table>

Blood culture collection within 24 hours of arrival was associated with a 10% lower odds of 30-day mortality

Meehan TP et al. JAMA 1997;278:2080-2084.
Performance of Microbiologic Studies in Pneumonia Patients

Multicenter (38 academic hospitals), retrospective study, 1997-98; n=1,062

<table>
<thead>
<tr>
<th>Test</th>
<th>%</th>
<th>Range</th>
</tr>
</thead>
<tbody>
<tr>
<td>Blood culture obtained before antibiotics</td>
<td>72</td>
<td>9-100%</td>
</tr>
<tr>
<td>Blood culture within 24 hrs of admission</td>
<td>82</td>
<td>54-100%</td>
</tr>
</tbody>
</table>

Blood Culture Collection within 24 hrs: Independent Predictors

Multivariate analysis: 14,069 patients ≥65 years old with pneumonia throughout the US

- **Patient factors**
  - Nursing home
  - Cerebrovascular disease
  - Abnormal mental status
  - Tachycardia
  - Hypotension (BP<90)
  - Fever (T>37.8°C)

- **Hospital Factors**
  - Limited teaching status
  - >100 beds
  - Nurse-bed ratio ≥0.75
  - ED admission
  - ER volume >10,000 visits/year
  - Northeast region

Smoking Cessation

IDSA B-II recommendation
Smoking Cessation Counseling

• Inpatient smoking cessation counseling is not typically part of routine clinical practice

• **However:**
  – The hospital is a unique venue for intervention, given the smoke free environment and the presence of patients who have experienced acute illness due to their smoking habits.
    • This may serve to increase patient motivation
Inpatient smoking cessation and all cause mortality among the elderly

• Cooperative Cardiovascular Project (1/94-7/95)
  – Retrospective analysis of 788 Medicare beneficiaries
    • Information on smoking cessation abstracted from charts
    • Smoking cessation counseling and association with 5-year mortality was assessed by Cox Proportional Hazards modeling.

Inpatient smoking cessation and all cause mortality among the elderly

Figure 1. Age-adjusted survival estimates of 788 smokers, aged ≥65 years, who were admitted and discharged alive with acute myocardial infarction, by smoking cessation counseling status: North Carolina Cooperative Cardiovascular Project. Log-rank test for equality of survival functions: $\chi^2 = 11.78$, $p < 0.001$.

Barriers to Implementation

• Physician and Staff Acceptance
  – Quality of the data
    • Most pneumonia outcomes studies are retrospective, observational
      – Lack of randomized controlled trials

• Education
  – Unfamiliarity with CAP treatment guidelines
  – Hospital wide education campaigns are logistically difficult
Barriers to Implementation

• Lack of automated systems
  – Automated decision, clinical support and electronic medical record (EMR):
    • Guide physicians on antibiotic management
    • Guide decisions/management based on admitting diagnosis
      – Blood cultures
      – Sputum gram stain
      – Vaccination prompts: pneumococcal and influenza vaccine
      – Smoking cessation prompts
  – Limitations of non-centralized EMR
    • Limitations in accurate patient history: prior vaccination?
    • Limitations in data extraction for quality control
Conclusion:

• Leading process indicators are timing and choice of antibiotics, obtainment of blood cultures, pneumococcal and influenza vaccination, and inpatient smoking cessation counseling.

• Achievement of process indicators will likely require: a collaborative and systems wide approach which includes:
  – Education
  – Acceptance from physicians and staff
    • Participation on multiple provider levels
      – Emergency department
      – Medical ward
      – Intensive care units
  – Assistance from automated hospital information systems: decision support
    • Standing orders
    • Antibiotic recommendations
    • Physician prompts such as vaccination and smoking cessation