Community-Acquired Pneumonia

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Community Acquired Pneumonia (CAP): definition

- At least 2 new symptoms
  - Fever or hypothermia
  - Cough
  - Rigors and/or diaphoresis
  - Chest pain
  - Sputum production or color change
  - Dyspnea
- New infiltrate on chest x-ray and/or abnormal chest exam
- No hospitalization or other nursing facility prior to symptom onset
CAP: Symptom Frequency

- Cough 90%
- Dyspnea 66%
- Sputum 66%
- Pleuritic chest pain 50%

But, only 4% of all visits for cough turn out to be pneumonia…


Epidemiology: Acute Lower Respiratory Tract Infections

- In U.S., influenza and pneumonia listed as 8th most common cause of death by the Centers for Disease Control and Prevention
  - Most common cause of death from infectious disease
- Among those 85 and older, at least 1 in 20 hospitalized each year

Epidemiology: Acute Lower Respiratory Tract Infections

- Inpatient mortality averages 14% (2-30%)
- Outpatient mortality < 1%
  - About 80% of CAP treated in outpatient setting
- More common in winter months
Health Disparities

- Some data regarding disparities with socioeconomic status and race/ethnicity
- Study of 4870 adults with community acquired bacteremic pneumonia in 9 states 2003 – 2004
- Annual incidence 24.2 episodes per 100,000 Black adults vs. 10.1 episodes per 100,000 White adults
- Black residents in most impoverished areas with 4.4 times the incidence of White residents in least impoverished areas

Burton et al. AJPH 2010;100(10):1904-11

Host Defenses

- Mechanical factors
  - Nasal hair
  - Turbinates
  - Mucociliary apparatus
  - Cough
  - Airway branching

- Antimicrobial factors
  - IgA (and IgG, IgM)
  - Complement
  - Alveolar lining fluid
  - Cytokines (TNF, IL-1, IL-8, others)
  - Macrophages
  - PMNs
  - Lymphocytes

Diagnosis

- Chest radiograph – needed in all cases?
  - Avoid over-treatment with antibiotics
  - Differentiate from other conditions
  - Specific etiology, e.g. tuberculosis
  - Co-existing conditions, such as lung mass or pleural effusion
  - Evaluate severity, e.g. multilobar

- Unfortunately, chest physical exam not sensitive or specific and significant variation between observers
Microbiological Investigation

- Sputum Gram stain and culture
  - Controversial
  - 30-40% patients cannot produce adequate sample
  - Most helpful if single organism in large numbers
  - Probably unnecessary in outpatients
  - Culture (if adequate specimen < 10 squamous cells/LPF; > 25 PMNs/LPF): antibiotic sensitivities
  - Limited utility after antibiotics

Microbiological Investigation - Inpatients

- Blood cultures x 2 before antibiotics
  - Blood cultures positive in 5 – 14% of hospitalized patients
  - Severe disease most important predictor

- Consider evaluation for *Legionella*
  - Urinary antigen test for *L. pneumophila* serogroup 1 (70%)
  - Culture with selective media

- Pneumococcal urinary antigen test
  - Simple, takes apx. 15 minutes
  - In adults, sensitivity 50-80%, specificity ~90% but specificity poor in children, possibly due to carriage

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<table>
<thead>
<tr>
<th>Table 5. Clinical indications for more extensive diagnostic testing.</th>
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<tbody>
<tr>
<td><strong>Indications</strong></td>
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<tr>
<td>-----------------</td>
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<tr>
<td>Intensive care unit admission</td>
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<tr>
<td>Failure of outpatient antibiotic therapy</td>
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<tr>
<td>Surgery (recent)</td>
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<tr>
<td>Chronic obstructive lung disease</td>
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<tr>
<td>Pulmonary fibrosis</td>
</tr>
<tr>
<td>Recent travel (within past 2 weeks)</td>
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<tr>
<td>Positive urinary (UAT) result</td>
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<tr>
<td>Pneumococcal (UAT) result</td>
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<tr>
<td>Notes:</td>
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</tbody>
</table>

*NOTE: NA not applicable, UAT urinary antigen test
* Strictly defined as isolated pansinusitis or endobronchial bronchus suis lesion
* Requires sputum culture analysis
* See Table 3 for details
* In adults, sensitivity 50-80%, specificity ~90% but specificity poor in children, possibly due to carriage

IDSA/ATS Guidelines for CAP in Adults: CID 2007;44(Suppl 2)
**Microbiological Investigation - Inpatients**

- Other studies as clinically indicated, e.g. influenza
- Serologic studies, e.g. *M. pneumoniae*, *Chlamydia pneumoniae*, only for epidemiology
  - For *C. pneumoniae*, IgM is available, titer > 1:16 considered positive
- Bronchoscopy perhaps for fulminant course, unresponsive to conventional therapy, or for specific pathogens (e.g. *M. tuberculosis*, *Pneumocystis*)

**Etiology**

- Clinical syndrome and CXR not predictive
  - *Streptococcus pneumoniae* 20-60%
  - *Haemophilus influenzae* 3-10%
  - *Mycoplasma pneumoniae* up to 10%
  - *Chlamydia pneumoniae* up to 10%
  - *Legionella* up to 10%
  - Enteric Gram negative rods up to 10%
  - *Staphylococcus aureus* up to 10%
  - Viruses up to 10%
  - No etiologic agent 20-70%

**Typical vs. Atypical**

**Typical**
- Visible on Gram stain, grows in routine culture
- Susceptible to beta lactams
- *S. pneumoniae*, *H. influenzae*

**Atypical**
- Not visible on Gram stain, special culture techniques
- Not treated with beta lactams
- *M. pneumoniae*, *C. pneumoniae*, *Legionella*
S. pneumoniae

- 2/3 of CAP cases where etiology known
- 2/3 lethal pneumonia
- 2/3 bacteremic pneumonia
  - Apx. 20% of cases with pneumococcal pneumonia are bacteremic (variable)

- Risk factors include
  - Extremes of age
  - Alcoholism
  - COPD and/or smoking
  - Nursing home residence
  - Influenza
  - Injection drug use
  - Airway obstruction
  - HIV infection

S. pneumoniae – Drug Resistance

Clinical and Laboratory Standards Institute (CLSI) minimum inhibitory standards for penicillin in µg/mL

<table>
<thead>
<tr>
<th></th>
<th>Sensitive</th>
<th>Intermediate</th>
<th>Resistant</th>
</tr>
</thead>
<tbody>
<tr>
<td>Parenteral (penicillin G) Non-meningitis</td>
<td>≤ 2</td>
<td>= 4</td>
<td>&gt; 8</td>
</tr>
<tr>
<td>Parenteral (penicillin G) Meningitis</td>
<td>≤ 0.06</td>
<td>≥ 0.12</td>
<td></td>
</tr>
<tr>
<td>Oral (penicillin V)</td>
<td>≤ 0.06</td>
<td>0.12 - 1</td>
<td>&gt; 2</td>
</tr>
</tbody>
</table>

S. pneumoniae – Drug Resistance

- ~ 25-35% penicillin non-susceptible by old standard nationwide, but most ≤ 2 µg/mL
- Using the new breakpoints for patients without meningitis, 93% would be considered susceptible to IV penicillin
- Other beta-lactams are more active than penicillin, especially
  - Ceftriaxone, cefotaxime, cefepime, amoxicillin, amoxicillin-clavulanate
**S. pneumoniae – Drug Resistance**

- Other drug resistance more common with increasing penicillin resistance
  - Macrolides and doxycycline reliable for PCN susceptible pneumococcus, less for penicillin non-susceptible
- Trimethoprim-sulfamethoxazole not reliable
- Fluoroquinolones – most *S. pneumoniae* are susceptible
  - Clinical failures have been reported
- No resistance with vancomycin, linezolid

**Legionella**

- Geographic differences in rates
- Perhaps suggested by high fever, hyponatremia, markedly elevated LDH, CNS abnormalities, severe disease
- Severe disease: fluoroquinolone or azithromycin likely drug of choice; usual rx 14-21 days
- Risk factors: Age, Smoking, Immune compromise, cell mediated, Travel
  - Renal disease
  - Liver disease
  - Diabetes
  - Malignancy
**Haemophilus influenzae**

- Increased risk with smoking and COPD
- Beta-lactamase production ~30%
  - With beta-lactamase production, resistant to ampicillin and amoxicillin
- Active oral antibiotics include amoxicillin-clavulanate, fluoroquinolones, azithromycin, clarithromycin, doxycycline

**Mycoplasma pneumoniae**

- Common cause respiratory infections in children/young adults
  - Pneumonia relatively uncommon
- Epidemics in close quarters
- May have sore throat, nausea, vomiting, hemolytic anemia, rash
- Treatment with doxycycline, macrolide, or fluoroquinolone

**Risk Stratification**

Cost differential in CAP: Colice et al, Chest 2004

- Inpatient: $10,227 / case
- Outpatient: $466 / case

Who can be safely managed as an outpatient???
Risk Stratification

- Outpatient vs. inpatient?
  - Pneumonia Patient Outcomes Research Team (PORT) study (Fine et al, NEJM 1997;336:243-250)
    - Prediction rule to identify low risk patients with CAP
    - Stratify into one of 5 classes
      - Class I: age < 50, none of 5 co-morbid conditions, apx. normal VS, normal mental status
      - Class II-V: assigned via a point system

- Mortality < 1% for classes I, II
- Low risk patients hospitalized more than necessary
- Caveats:
  - Does not take into account social factors

Pneumonia Severity Index Calculator

http://pda.ahrq.gov/clinic/psi/psicalc.asp

- Age and sex; resident of nursing home (yes/no)
- Comorbid diseases (yes/no): renal disease, liver disease, CHF, cerebrovascular disease, neoplasia
- Physical exam (yes/no): altered mental status, SBP < 90, temp < 35 or >=40, RR>=30, HR>=125
- Labs/studies (yes/no): pH<7.35, PO2<60 or Sat<90, Na<130, HCT<30, gluc>250, BUN>30, pleural eff
Hypothetical Patient #1

- 60 year-old man with diabetes presents with fever and dyspnea. Positive PORT items include HR=130, Na=129, glucose=300.
- Should this patient be hospitalized?

Pneumonia Severity Index Results

<table>
<thead>
<tr>
<th>Class</th>
<th>Score</th>
<th>Mortality</th>
</tr>
</thead>
<tbody>
<tr>
<td>Low</td>
<td>I</td>
<td>&lt; 51</td>
</tr>
<tr>
<td>Low</td>
<td>II</td>
<td>51 - 70</td>
</tr>
<tr>
<td>Low</td>
<td>III</td>
<td>71 - 90</td>
</tr>
<tr>
<td>Medium</td>
<td>IV</td>
<td>90 - 130</td>
</tr>
<tr>
<td>High</td>
<td>V</td>
<td>&gt; 130</td>
</tr>
</tbody>
</table>

Hospitalization is recommended for class IV and V. Class III should be based on clinical judgment.

Other Hypothetical Patients

- 55 year-old woman with no other risk factors?
  Class: I
  Score: 45
  Mortality: 0.1%

- 92 year-old man with no other risk factors?
  Class: IV
  Score: 92
  Mortality: 9.5%

- 20 year-old woman with SBP < 90 and a pleural effusion?
  Class: II
  Score: 40
  Mortality: 0.6%
Other Scoring Systems

- CURB-65 (British Thoracic Society)
  - Has only 5 variables, compared with 20 for Pneumonia Severity Index
- Severe Community Acquired Pneumonia (SCAP)
  - Has 8 variables
- SMART-COP
  - Used for predicting need for mechanical ventilation or vasopressors

Guidelines, guidelines, guidelines....

- Previously, at least 4 major sets:
  - American Thoracic Society (ATS)
  - Infectious Diseases Society of America (IDSA)
  - Canadian Infectious Diseases Society and Canadian Thoracic Society
  - British Thoracic Society

Infectious Diseases Society of America/American Thoracic Society Consensus Guidelines on the Management of Community-Acquired Pneumonia in Adults

Clinical Infectious Diseases; March 1, 2007
Supplement 2
Do guidelines improve outcomes?

- Maybe…results vary
- Studies generally not randomized
- Trend toward decreased length of hospital stay
- Possible decrease in mortality

*Editorial: Marrie, Clin Infect Dis, Dec. 2005*

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Is coverage of “atypical” organisms important?

- In Europe, amoxicillin commonly used as a single drug with data supporting a short course (3 days in responding patients)
  
  *el Moussaoui et al, BMJ;332:1355 - 62*

- One review shows no benefit of empirical atypical coverage on survival or clinical efficacy in hospitalized patients
  
  *Shefet et al, Arch Intern Med;165:1992-2000*

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Treatment

- Empirical therapy is usually required, at least initially

- Timing of antibiotics
  - Better outcomes if given within 8 hrs of admission; 4 hrs even better
  
  *(Houck et al, Arch Intern Med. 2004;164:637-44)*
  - Centers for Medicare & Medicaid Services (CMS): now, compromise measure of 6-hour standard of care
  - Very controversial: delays mostly with atypical presentations; antibiotic overuse
Empirical Treatment: IDSA/ATS Consensus Guidelines

Outpatient treatment

- Previously healthy, no antibiotics in 3 months
  - Macrolide (1st choice) or
  - Doxycycline
- Co-morbid conditions or antibiotics within 3 months (select a different class)
  - Respiratory fluoroquinolone: moxifloxacin, gemifloxacin, or levofloxacin (750 mg)
  - Beta-lactam (especially high dose amoxicillin) plus a macrolide (1st choice) or doxycycline

Empirical Treatment: IDSA/ATS Consensus Guidelines

Inpatient treatment, non-ICU

- Respiratory fluoroquinolone or
- Beta-lactam (cefotaxime, ceftriaxone, ampicillin; consider ertapenem) plus a macrolide (1st choice) or doxycycline

Empirical Treatment: IDSA/ATS Consensus Guidelines

Inpatient treatment, ICU

- Beta-lactam (cefotaxime, ceftriaxone, or ampicillin-sulbactam) plus
- Azithromycin or a respiratory fluoroquinolone

  ➢ For penicillin allergy: respiratory fluoroquinolone + aztreonam
Empirical Treatment: IDSA/ATS Consensus Guidelines

For suspected *Pseudomonas aeruginosa*:

- Antipneumococcal, antipseudomonal beta-lactam (piperacillin-tazobactam, cefepime, imipenem, or meropenem) plus either ciprofloxacin or levofloxacin (750 mg)  
  Or
- The above beta-lactam plus an aminoglycoside and either azithromycin or a respiratory fluoroquinolone
  - For penicillin allergy: substitute aztreonam for the beta-lactam

Suspect with structural lung disease (e.g. bronchiectasis), frequent steroid use, prior antibiotic therapy

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Empirical Treatment: IDSA/ATS Consensus Guidelines

Inpatient therapy, concern for community methicillin-resistant *Staphylococcus aureus* (MRSA):

- Add vancomycin or linezolid to regimen you would select otherwise

*Recommend as a routine measure for patients admitted to the ICU – Gram strain of respiratory specimen (sputum or tracheal aspirate) can be very helpful*
Length of Therapy

- 7 – 10 days has been standard for most patients but may not be necessary
  - Shorter course with azithromycin or high dose levofloxacin
  - Meta-analysis that patients with mild to moderate disease can be treated with 7 days or less

  *Li et al. Am J Med. 2007;120(9):783-90*

Switch to Oral Therapy

- Reduces costs, shortens length of stay, may reduce complications
- As soon as improving clinically, able to take POs, GI tract functioning
  - Usually within 3 days; no need to observe in hospital
- Narrow spectrum agent if organism identified (usually *S. pneumoniae*)
- Empirical therapy: macrolide, doxycycline, antipneumococcal fluoroquinolone, or combination therapy

Joint Commission and CMS Performance Measures
Prevention

There are steps patients and providers can take.

Influenza vaccine

Pneumococcal vaccine

- ~60% effective for pneumococcal bacteremia in immunocompetent adults

Few side effects

Can be given simultaneously

Give prior to hospital discharge

- Standing orders facilitate

Prevention

- Smoking, with or without COPD, is a significant risk factor

- Do gastric acid-suppressive drugs, especially proton pump inhibitors, increase risk for CAP?

  - Risk may only be associated with drugs that are recently started, not with long-term use; may not be causal

**Prevention**

- Elderly patients with dementia appear to have increased risk for all-cause mortality when treated with both atypical and typical antipsychotic medications
  - Much of this risk may be due to pneumonia
- Dutch case-control study showed a dose-dependent association of atypical and typical antipsychotic drugs with CAP in older patients
  - ??? Increased risk of aspiration through mouth dryness, impaired swallowing and/or sedation