Update in Community-Acquired Pneumonia

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Roadmap

• Background
• Etiology
• Diagnosis
• Treatment
• Prevention

Specific Goals:

• Describe the most common causes of community-acquired pneumonia in the outpatient setting
• Order appropriate diagnostic tests for CAP
• Initiate appropriate antibiotics in the treatment of community-acquired pneumonia (CAP)
• State the optimal duration of therapy in CAP
• State the benefits and need for preventative measures for CAP
Caveats

- Will not talk about healthcare-associated pneumonia (HCAP)
- Will not discuss admission decision (complex)
- Syllabus (sharpeb@medicine.ucsf.edu)

CAP: Background

- 5 million cases/year in the U.S.
- 80% of CAP is treated outpatient
- Sixth leading cause of death
- Inpatient mortality 10-35%
- Outpatient mortality < 1%

Higher mortality among Caucasians
Some evidence that quality of care for African-Americans with CAP is worse

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

* Yet, only 4% of all visits for cough are pneumonia

Clinical Presentation: Geriatrics

- Less “classic” presentations
  - 10% have NONE of the classic signs or symptoms
- Up to 40% will not have fever
- Up to 45% will have altered mental status

Riquelme R, et al. Am J Respir Crit Care Med
1997;156:1008.

“Typical” vs. “Atypical”

- Classic teaching is not supported by the literature
- Some general trends
  - S. pneumoniae in older pts, co-morbidities
  - Viruses more common in older patients
  - Mycoplasma in patients < 50 years old

“Typical” vs. “Atypical”

- Classic teaching is not supported by the literature
- Some general trends
  - But - no history, exam, laboratory, or radiographic features predict organism
    - “Walking pneumonia”
    - “Classic lobar pneumonia”

Microbiology of CAP

- Prospective study of 2320 patients with CAP admitted to 5 hospitals
- All extensive diagnostic evaluation
  - Blood cultures, sputum cultures
  - Urine antigen for S. pneumoniae & Legionella
  - Nasopharyngeal PCR for viruses, Chlamydia, Mycoplasma
  - Some serologic testing

Jain S, et al. NEJM.
Microbiology of CAP

1) Rhinovirus
2) Influenza
3) Streptococcus pneumoniae

Jain S, et al. NEJM. 2015

Microbiology of CAP

- Pathogen detected in less than 40% of patients
  - Real-world ~ 15%
- Many possible explanations
  - Mainly viruses?
  - Inadequate diagnostic testing

Jain S, et al. NEJM. 2015

Etiology of CAP

Outpatients (mild)
- Resp. viruses
- S pneumoniae
- M pneumoniae
- C pneumoniae
- H influenzae

Non-ICU inpatients
- Resp. viruses
- S pneumoniae
- M pneumoniae
- C pneumoniae
- H influenzae
- Legionella spp

ICU inpatient
- S pneumoniae
- Legionella
- H influenzae
- GNRs
- S aureus
- Resp. viruses (?)


Take Home Points

1)
2)
3)
4)
5)
Diagnosis of CAP

1) Select clinical features (e.g. cough, fever, sputum, pleuritic chest pain)
   AND
2) Infiltrate by CXR or other imaging

Chest Radiograph – Gold Standard

- All expert guidelines state should have positive CXR to make diagnosis
  - History, exam, etc. not good enough
- In outpt setting, should see an infiltrate.
  - Order CXR if you are concerned about CAP
  - If CXR negative, likely should not treat for CAP
- In the inpatient setting, the CXR can be negative

Chest Radiograph – Gold Standard?

- Should order CXR in all patients with suspected pneumonia.
- In the hospital, a positive CXR is not necessary to treat as CAP (but consider other diagnoses).

Blood Cultures

- Specific organism vs. contaminants, cost
- Reality:
  - No evidence of a benefit
  - Rarely positive = _____
  - Contaminant rate = _____
  - More likely to be positive if sicker
    - ICU, septic shock, etc.
**Blood Cultures in CAP**

- In general, do not get blood cultures for outpatient CAP
- For inpatient CAP, blood cultures are **optional**
- Consider if risk factors:
  - ICU, severe sepsis, cavitary infiltrates, pleural effusion


**Sputum for CAP**

- Complicated and controversial
- Simple, inexpensive, specific for pneumococcus
- Problems include:
  - Up to 30% could not produce adequate sputum
  - Good quality available in only 14%
  - Most don’t narrow antibiotics

**Sputum Cultures in CAP**

- In general, sputum cultures are **not** indicated in outpatient CAP
- For inpatient CAP, sputum is indicated:
  - High-quality specimen, right to the lab
  - ICU, cavitary infiltrates, underlying lung disease


**The future in CAP - biomarkers**

- Procalcitonin: precursor of calcitonin
  - No hormonal activity
  - Inflammatory marker
  - Increased in sepsis, bacterial infection
Meta-analysis/systematic review

- Four studies, ~3500 patients with respiratory tract infections
- Less antibiotic exposure**
  - A 22% decrease in prescriptions
  - Average 2.3 days less abx overall
- No difference in mortality/clinical outcomes


Take Home Points

1) Cover typical and atypical bacteria
2)
3)
4)
5)

Roadmap

- Background
- Etiology
- Diagnosis
- **Treatment**
- Prevention

Treatment Principle #1

Outpatients (mild)

- Resp. viruses
- *S pneumoniae*
- *M pneumoniae*
- *C pneumoniae*
- *H influenzae*

Must cover all these organisms*

- Come back on Friday for a review of new data on atypical coverage
Treatment Principle #2

Outpatients (mild)

- Resp. viruses
- S. pneumoniae
- M. pneumoniae
- C. pneumoniae
- H. influenzae

"Wimpy" pneumococcus

Drug-resistant S. pneumoniae (DRSP)

Penicillin, erythromycin, macrolides, etc.

Risk Factors for DRSP

- Age > 65 years old
- Chronic disease
  - Heart, lung, renal, liver
- Diabetes mellitus
- Alcoholism
- Malignancy (active)
- Immunosuppression
- Antibiotics in the last 3 months

Treatment CAP

Outpatient, healthy, no DRSP risk factors

Doxycycline or macrolide

Macrolide = azithro, clarithro, erythro

Treatment CAP

Outpatient, DRSP risk factors

Oral fluoroquinolone
OR
Oral β-lactam + doxy or β-lactam + macrolide

- Oral fluoroquinolone: moxi, gemi, levofloxacin
- β-lactam: High-dose amoxicillin (1mg PO tid)
  Augmentin (875mg PO bid)
Take Home Points

1) Cover typical and atypical bacteria
2) Get the CXR, skip the cultures
3) 
4) 
5) 

Treatment CAP

<table>
<thead>
<tr>
<th>Inpatient, non-ICU</th>
<th>Fluoroquinolone OR β-lactam + macrolide</th>
</tr>
</thead>
<tbody>
<tr>
<td>Inpatient, ICU</td>
<td>IV β-lactam + macrolide + vancomycin OR</td>
</tr>
<tr>
<td></td>
<td>IV β-lactam + fluoroquinolone + vancomycin</td>
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</table>

Duration of therapy?

- Meta-analysis of 15 RCTs, 2796 patients with mild to moderate CAP
- Compared short-course (< 7 days) with longer courses.
- Looked at clinical failure, bacterial eradication, and mortality.

Duration of therapy?

- No difference in clinical failure
- No difference in bacterial eradication
- No difference in mortality
- In subgroup analysis, trend toward favorable efficacy with short-course.
Duration of therapy

- Minimum of 5 days
  - If afebrile for 48-72
- For most, 7 days total

Steroids in Pneumonia?

Take Home Points

1) Cover typical and atypical bacteria
2) Get the CXR, skip the cultures
3) Outpatient: Brad Pitt vs. Donald Rumsfeld
4)
5)

Follow-up CXR?

- Standard practice?
- Prior ATS guidelines said yes, recent guidelines do not address
- CXR resolution:
  - At 28 days, ~ 50% had not resolved
- Can consider in “high-risk” patients
  - Significant smoking history, etc.
  - Probably should wait > 3 months

Bruns AH. CID. 2007;45:983..
**Pneumovax**

- Updated meta-analysis of 18 RCTs (~64,000 pts) and 7 non-RCTs (~62,000 pts) trials,
- Only high-quality studies

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<th>Variable</th>
<th>Outcome</th>
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<tr>
<td>ICU admission</td>
<td>Decreased</td>
</tr>
<tr>
<td>Inpt complications</td>
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<tr>
<td>LOS</td>
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<td>Inpt mortality</td>
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**Relative Risk**

- All-cause pneumonia: 0.70 (0.45-1.12)
- All-cause mortality: 0.90 (0.74-1.09)

**No difference for elderly or chronic illness**


**Pneumovax - Efficacy**

- Four different trials looking at benefits of pneumovax in patients hospitalized with CAP.
- Compared vaccinated vs. non-vaccinated
- Looked at impact on ICU admission, inpatient mortality, inpatient complications, and LOS.

- Pneumococcal vaccine likely prevents invasive pneumococcal disease.
- Probably reduces death, ICU admission, complications, and LOS in patients hospitalized with CAP (“makes pneumonia less bad”)
**Influenza Vaccine - Efficacy**

- Adults aged < 65 years
  - Prevents influenza illness in ~ 70-90%

- Adults aged > 65 years
  - Prevents influenza illness in ~ 30-70%

**Hospitalization Risk Reduction**

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* All p values < 0.001

**Proton Pump Inhibitors**

  - Current use of PPI: CAP OR = 1.5
  - Recent start: CAP OR = 5.0

  - Recent PPI start: CAP OR = 3.8

- **Herzig, et al. JAMA. 2009.**
  - 52% of hosp pts got PPI, HAP OR = 1.3

  - Rates recurrent CAP after CAP admit
  - Starting PPI: OR 2.1% (7% abs risk)

**Anti-psychotics**

- **Knol W, et al. JAGS. 2009.**
  - Recent anti-psychotic start (1 wk); OR 4.3**

  - Population based study, 2000 patients.

**Current Use**

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2) Get the CXR, skip the cultures
3) Outpatient: Brad Pitt vs. Donald Rumsfeld
4) Treat for 7 days
5) Vaccines = good