Community Acquired Pneumonia (CAP)
Update for 2001/2002

John C. Rotschafer, Pharm. D., FCCP
Professor
College of Pharmacy
University of Minnesota
Pneumonia

- Many different types
  - Community acquired (CAP)
  - Hospital acquired (HAP)
    - Ventilator (VAP)
  - Aspiration
- Diagnosis
  - Sputum gram stain & culture
    - <10 epithelial cells & > 25 PMN’s per field
    - Appropriate cultures of blood and CSF
  - Chest x-ray infiltrate
  - Fever, elevated WBC, SOB & pleuritic chest pain
URTI & LRTI

Introduction

- **CAP**
  - Annual incidence ~ 4 million cases
  - Mortality 14%
  - Direct & indirect cost $23 billion / year

- **ABS**
  - Annual incidence ~ 30 million cases
  - Direct & indirect cost $2 billion / year

- **AECB**
  - Annual incidence ~ 20 million cases
Community Acquired Pneumonia - CAP

- Hospital cases represent the tip of the iceberg
  - Diagnosis in office setting confounded
    - +Gram Stain
    - +Culture (positive ~50% of the time) & antibiotic sensitivity
    - +X-ray
  - Differential Diagnosis
    - Bronchitis vs Pneumonia +Bacteremia
    - Viral vs Bacterial
      - Estimated ~50% of antibiotic Rx’s unnecessary
  - How should patients be treated?
    - Oral vs Parenteral
  - In what setting should patients be treated?
American Thoracic Society
- First published 1993
- Revision published Am J Respir Crit Care Med 163:1730-1754, 2001

Infectious Diseases Society of America
- First published April 1998
- Revision published CID 31:347-382, 2000

Center for Disease Control
- Arch Intern Med 160:1399-1408, 2000
- Promote macrolides, doxycycline, or beta-lactams
- Fluoroquinolones suggested if: 1) Failed previous Tx, 2) Allergy to alternative antibiotics, & 3) PCN MIC > 4mg/L
Scoring system incorporates

- Patient age
- Location
- Coexisting Illness
- Physical Findings
- Laboratory Findings
- Radiographic Findings

Difficult to use in clinical setting

- Point values vary for different parameters
- May not have all of the required data
- Cumbersome addition
# CAP Patient Scoring System


<table>
<thead>
<tr>
<th>Class</th>
<th>Score</th>
<th>All Patient Mortality</th>
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<tbody>
<tr>
<td>I</td>
<td>N/A</td>
<td>0.1%</td>
</tr>
<tr>
<td>II</td>
<td>≤ 70</td>
<td>0.6%</td>
</tr>
<tr>
<td>III</td>
<td>71-90</td>
<td>0.9%</td>
</tr>
<tr>
<td>IV</td>
<td>91-130</td>
<td>9.3%</td>
</tr>
<tr>
<td>V</td>
<td>&gt; 130</td>
<td>27%</td>
</tr>
</tbody>
</table>

Class I, II, & III mortality < 1%

Can likely be treated as outpatients with oral antibiotic
ATS CAP 2001 Classification Scheme

- **Group I** (1993 - outpatient <60 yrs no co-morbidity)
  - Outpatient CAP
  - No CHF or COPD
  - No risk factors for other resistant pathogens

- **Group II** (1993 – outpatient with co-morbidity&/or >60yrs)
  - Outpatient CAP
  - History of CHF & /or COPD
  - Risk factors for resistant pathogens may or may not be present

Am J Respir Crit Care Med 163:1730-1754, 2001
ATS CAP 2001 Classification Scheme

- **Group III** (1993 – hospitalized with CAP)
  - Inpatient but does not require ICU setting
    - No CHF or COPD and/or resistant bacteria risk factors
    - CHF and/or COPD plus possible risk factors for resistance and may be nursing home patient

- **Group IV** (1993 – hospitalized with severe CAP)
  - ICU patient
    - No risk for *P. aeruginosa*
    - At risk for *P. aeruginosa*

*Am J Respir Crit Care Med 163:1730-1754, 2001*
CAP Pathogens

- **Typical**
  - *S. pneumoniae*
  - *H. influenzae*
  - *M. catarrhalis*

- **Atypical**
  - *C. pneumoniae*
  - *L. pneumophila*
  - *Mycosplasma*
ATS Pathogen Risk Factors

Am J Respir Crit Care Med 163:1730-1754, 2001

❖ **PCN-NS/R *S. pneumoniae***
  - > 65 years
  - Multiple co-morbidities
  - Alcoholism
  - Exposure to children in day care
  - Immunosuppressed
  - Use of beta-lactam within last 90 days

❖ ***P. aeruginosa***
  - Use of broad spectrum antibiotic for > 1 week in last month
  - Structural lung disease
  - Steroid use
  - Malnutrition

❖ **Gram Negatives**
  - Nursing home resident
  - Cardiopulmonary disease
  - Multiple co-morbidities
  - History of recent antibiotic therapy
Definition of PCN-R *S. pneumoniae*

- **Sensitive**
  - PCN MIC $\leq 0.06$ mg/L
- **Non-susceptible**
  - PCN MIC = 0.12 to 1.0 mg/L
- **Resistant**
  - PCN MIC $\geq 2.0$ mg/L
  - Mechanism of resistance is an alteration of penicillin binding proteins (PBP)
### TRUST Studies 1999-2001: Comparison of Antimicrobial Resistance of *S. pneumoniae*

<table>
<thead>
<tr>
<th></th>
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</thead>
<tbody>
<tr>
<td>% R</td>
<td>% R</td>
<td>% R</td>
<td>% R</td>
</tr>
<tr>
<td>Penicillin (MIC ≥ 2µg/mL)</td>
<td>14.7</td>
<td>16.0</td>
<td>16.9</td>
</tr>
<tr>
<td>Azithromycin</td>
<td>22.7</td>
<td>23.4</td>
<td>27.5</td>
</tr>
<tr>
<td>Ceftriaxone</td>
<td>3.4</td>
<td>3.8</td>
<td>3.0</td>
</tr>
<tr>
<td>Levofloxacain</td>
<td>0.6</td>
<td>0.5</td>
<td>0.8</td>
</tr>
<tr>
<td>No. of institutions</td>
<td>96</td>
<td>238</td>
<td>240</td>
</tr>
<tr>
<td>No. of isolates</td>
<td>4,296</td>
<td>9,499</td>
<td>6,362</td>
</tr>
</tbody>
</table>

S. pneumoniae
Penicillin Resistance
(Resistant, MIC $\geq 2$ µg/mL)

S. pneumoniae
Azithromycin Resistance
(Resistant, MIC $\geq 2$ µg/mL)

National Rate:
Penicillin=17% R

National Rates:
Azithromycin=28% R
Clarithromycin=28% R
Erythromycin=28% R

*6,362 isolates, 240 labs.
Lab report vs Clinical Outcome Disconnect

- In-vitro susceptibility does not seem to correlate with clinical outcome in LRTI
  - Clinical failures with conventional antibiotics & resistant pathogens are rare for RTI’s
  - Phenomena poorly studied
    - Cultures & susceptibility studies rarely done
  - Question as to the timeframe where PCN & multiply antibiotic resistant strains will become an issue
Macrolide Resistant *S. pneumoniae*

- **Three Types**
  - **Ribosomal resistance (erm ~30% of strains)**
    - Alters the binding of macrolide to the 50S ribosome
    - Conveys resistance to all macrolides
  - **Efflux pump (mef ~70% of strains)**
    - Macrolide pumped out of bacteria
    - Resistance is macrolide dependent
  - **23S r RNA or ribosomal protein mutations**, only 20 strains reported *(AAC 44:3395-3401, 2000)*

- **Testing is problematic**
  - **Erythromycin used as class disk**
  - **Quick check erythromycin vs clindamycin susceptibility**
    - Many labs do not report clindamycin result
Fluoroquinolone Resistant Respiratory Pathogens

- **S. pneumoniae**
    - 0% FQ-R in 1993 to 1.7% in 1997/1998
  - **Hong Kong** (Ho, P.L. AAC 43:1310-1313, 1999)
    - PCN-R (MIC>0.06) 69.1%
    - Cipro-R (MIC>2) 12.1% Clonal Problem
    - Levo-R (MIC>2) 5.5%
    - Trova-R (MIC>1) 2.2%

- **H. influenzae & M. catarrhalis**
  - (Biedenbach, D.J. Diagn Micro & Infect Dis 36:255-259, 2000)
    - 4 FQ-R *H. influenzae* (Sentry Data 1997-1999)
    - 1 FQ-R *M. catarrhalis*
Outpatient Empiric Selection

- Macrolide
- Fluoroquinolone (expanded spectrum)
- Doxycyline
ATS Guidelines
Am J Respir Crit Care Med 163:1730-1754, 2001

- **Group I**
  - Clarithromycin or Azithromycin or Doxycycline

- **Group II**
  - **Oral**
    - Cefpodoxime, Cefuroxime, HD Amoxicillin, or Augmentin plus macrolide or doxycycline
    - Antipneumococcal fluoroquinolone
  - **Parenteral**
    - Ceftriaxone followed by oral cefpodoxime
IDSA CAP Guidelines

- **General Medical Ward**
  - Cefotaxime or Ceftriaxone plus Macrolide
  - Fluoroquinolone alone

- **Performance Indicators**
  - Blood cultures prior to antibiotic therapy
  - Antibiotics within 8 hours of hospitalization
Empiric Selection for Intensive Care

- Cefotaxime or
- Ceftriaxone or
- Ampicillin/sulbactam or
- Piperacillin/tazobactam

PLUS

- Fluoroquinolone or Macrolide
ATS Treatment Guidelines
Am J Respir Crit Care Med 163:1730-1754, 2001

❖ Group III

- **Subgroup A (No risk factors)**
  - IV Azithromycin alone
  - Doxycycline plus beta-lactam
  - Antipneumococcal fluoroquinolone

- **Subgroup B (CHF &/or COPD &/or antibiotic risk)**
  - Cefotaxime, Ceftriaxone, Unasyn, or high dose Ampicillin plus IV or PO Macrolide or Doxycycline
  - Antipneumococcal fluoroquinolone
ATS Treatment Guidelines
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- **Group IV**
  - **Subgroup A (No *P.aeruginosa* risk)**
    - Cefotaxime or Ceftriaxone plus Azithromycin or Fluoroquinolone
  - **Subgroup B (*P.aeruginosa* risk)**
    - Cefepime, imipenem, meropenem, or Zosyn plus Ciprofloxacin or Aminoglycoside
      - PLUS
    - Azithromycin or nonpseudomonal fluoroquinolone
Factors Contributing to Increased Morbidity &/or Mortality

- **Symptoms**
  - HR $\geq 125$/min, BP $< 90$ or/ $< 60$ mm Hg, RR $\geq 30$/min, pH $< 7.35$
  - Hyper($\geq 40^\circ$C) or hypo($< 35^\circ$C) thermic

- **Factors**
  - Advanced age and state of consciousness
  - CHF
  - COPD / Bronchiectasis
  - Cancer
  - Diabetes
  - Chronic renal and/or hepatic disease
  - Alcoholism
  - Cerebral vascular disease
  - Malnutrition
  - Hospitalized within last year
  - Splenectomy
Parenteral to Oral Conversion for CAP Patients

- **Four Criteria for IV to PO Conversion**
  - Improvement in cough and dyspnea
  - Afebrile on two occasions spaced by eight hours
  - WBC returning toward normal
  - Functional GI tract with evidence patient able to take fluids, food, and/or medications

  *Am J Respir Crit Care Med 163:1730-1754, 2001*
# Antibiotic Overview

<table>
<thead>
<tr>
<th>Pathogen</th>
<th>BL</th>
<th>MAC</th>
<th>FQ</th>
<th>DOX</th>
</tr>
</thead>
<tbody>
<tr>
<td>S. pneumoniae</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>+</td>
</tr>
<tr>
<td>PCN-R</td>
<td>±</td>
<td>±</td>
<td>+</td>
<td>±</td>
</tr>
<tr>
<td>H. influenzae</td>
<td>±</td>
<td>±</td>
<td>+</td>
<td>+</td>
</tr>
<tr>
<td>M. catarrhalis</td>
<td>±</td>
<td>+</td>
<td>+</td>
<td>+</td>
</tr>
<tr>
<td>Atypicals</td>
<td>0</td>
<td>+</td>
<td>+</td>
<td>+</td>
</tr>
</tbody>
</table>

- Antibiotic choice highly dependent on specific agent selected
- For *S. pneumoniae* with PCN MIC >2 mg/L, vancomycin or FQ probably best choice depending on circumstances
Looking Down the Road

- Presently, there is a lack of clinical failures with conventional therapy
- Should NCCLS redefine PCN-R *S. pneumoniae* ???
  - 35% resistance going to ~ 12-14% in U.S.A.
- Unknown time frame for level of PCN-R to go from ≤ 2 mg/L to ≥ 4 mg/L
- Increasing rate of vaccination for *S. pneumoniae*
  - Pneumovax & Heptavalent vaccine
- Increasing rate of FQ-R *S. pneumoniae* & others
- Safety concerns with new fluoroquinolones