Community Acquired Pneumonia: Update for 2016

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Epidemiology of CAP

- CAP is the leading infectious cause of mortality in patients > 65 in the US
- Risk factors: Age > 65, DM, COPD, CAD, chronic liver disease, chronic kidney disease, aspiration
- Smokers are at higher risk of bacteremic pneumococcal infection
- Substance abuse (ETOH, IVDA) associated with late presentation
CAP vs HCAP

- CAP: An acute infection of the pulmonary parenchyma acquired in the community
- HCAP: Health care associated pneumonia
  - Hospitalization within 90 days
  - Long term care facility residence
  - Long term dialysis, outpatient wound care or home infusion, or IV antibiotics within 30 days
- Higher risk for MRSA and resistant gram negative pathogens (Pseudomonas)

CAP Diagnosis

- Acute onset of signs of lower respiratory tract infection:
  - Dyspnea, cough, fever, new focal chest signs
    - None of these has a sensitivity > 45%
  - New lung infiltrates on CXR needed for definite diagnosis
  - Differential diagnosis: URI, CHF, alternative sites of infection
Causative Agents

- *Strep pneumoniae*
- *H. influenzae*
- Atypicals: *Mycoplasma, Chlamydia, Legionella*
- Respiratory viruses: influenza, rhinovirus, coronaviruses
- Viral and bacterial coinfection increasingly recognized

Less Common Causes

- Chlamydia psittaci, Cryptococcus neoformans (bird exposure)
- Histoplasma capsulatum (bat exposure)
- Coccidioidomycosis (Southwestern US)
- Tuberculosis (immigration from an endemic area)
Appropriate Testing

• Outpatients:
  – Chest radiograph recommended for all patients with suspected pneumonia
  – Oximetry
  – Testing to evaluate alternative diagnoses
  – Consider sputum culture and PCR testing for respiratory viral pathogens

• Inpatients:
  – Chest radiograph
  – Sputum culture & 2 blood cultures
  – Urine antigens for *Strep pneumo* & *Legionella*
  – PCR testing for respiratory viral pathogens
  – CBC, chemistry panel
  – Procalcitonin
CAP Pathogen Detection

• Not generally recommended for outpatients
  – Etiology determined in < 50% with sputum & blood cultures, urine antigens for \textit{Strep. pneumo} & \textit{Legionella pneumophila}
    • \textit{S. pneumo} urine Ag. 82% sens. 97% specific
    • \textit{Legionella} urine Ag. only detects serogroup 1 (which accounts for 80% of cases).

CAP Pathogen Detection

• Recommended for inpatients
  – sputum & blood cultures \textbf{BEFORE} antibiotics, urine antigens for \textit{Strep. pneumo} & \textit{Legionella}
  – \textit{Significant increase in diagnostic yield with addition of molecular diagnostics}
  – \textit{Can now identify a pathogen in as many as 80% of patients}.
**Sputum & Blood Cultures**
- *S. Pneumo* & *Legionella Urine Ag*
- Nasopharyngeal Swab for PCR:
  - *S. pneumoniae*
  - *S. aureus*
  - *Mycoplasma pneumoniae*
  - *Chlamydia pneumoniae*
  - *Bordatella pertussis*
  - 5 types of influenza
  - 4 types of parainfluenza
  - adenovirus
  - Rhinovirus/enterovirus
  - Human metapneumovirus
  - RSV
  - 4 types of coronavirus

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**Procalcitonin**

- Procalcitonin: peptide precursor of calcitonin, normally undetectable, increases in response to bacterial infection
  - Half life of 25-30hrs
  - Has been proposed as a tool to determine the presence of bacterial pneumonia and reduce antibiotic use:

<table>
<thead>
<tr>
<th>Procalcitonin level</th>
<th>Antibiotic Recommendation</th>
</tr>
</thead>
<tbody>
<tr>
<td>&lt; 0.1 µ/L</td>
<td>Discouraged</td>
</tr>
<tr>
<td>&gt; 0.25 µ/L</td>
<td>Recommended</td>
</tr>
<tr>
<td>&gt; 0.5 µ/L</td>
<td>Strongly Recommended</td>
</tr>
</tbody>
</table>

Procalcitonin

- Using procalcitonin to decide whether to treat with antibiotics has been shown to decrease median antibiotic duration from 8 days to 4 days without increase in treatment failure or mortality.


Severity Assessment & Site of Care

- CURB-65
  - 5 items to classify into 6 categories
  - Does not account for comorbidities
- Pneumonia Severity Index (PSI)
  - 20 items used to classify into 5 risk categories
  - Comorbidities and age highly weighted
**CURB 65**

<table>
<thead>
<tr>
<th>Clinical Factor</th>
<th>Points</th>
</tr>
</thead>
<tbody>
<tr>
<td>C Confusion</td>
<td>1</td>
</tr>
<tr>
<td>U BUN ≥ 20 mg/dL</td>
<td>1</td>
</tr>
<tr>
<td>R Respiratory rate ≥ 30 breaths/min</td>
<td>1</td>
</tr>
<tr>
<td>B Systolic BP &lt; 90mmHg or Diastolic BP ≤ 60mmHg</td>
<td>1</td>
</tr>
<tr>
<td>65 Age ≥ 65</td>
<td>1</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Total Score</th>
<th>Mortality</th>
<th>Site of Care</th>
</tr>
</thead>
<tbody>
<tr>
<td>0</td>
<td>0.6%</td>
<td>Outpatient</td>
</tr>
<tr>
<td>1</td>
<td>2.7%</td>
<td>Outpatient</td>
</tr>
<tr>
<td>2</td>
<td>6.8%</td>
<td>Inpatient vs. close outpt follow up</td>
</tr>
<tr>
<td>3</td>
<td>14.0%</td>
<td>Inpatient</td>
</tr>
<tr>
<td>4 or 5</td>
<td>27.8%</td>
<td>ICU</td>
</tr>
</tbody>
</table>

**Antibiotic Choice**

<table>
<thead>
<tr>
<th>American (IDSA/ATS)*</th>
<th>British (NICE/BTS)**</th>
</tr>
</thead>
<tbody>
<tr>
<td>Preferred</td>
<td>Alternative</td>
</tr>
<tr>
<td>Preferred</td>
<td>Alternative</td>
</tr>
<tr>
<td>Outpatient without comorbidities; low severity</td>
<td>Macrolide</td>
</tr>
<tr>
<td>Outpatient with comorbidities or high rate bacterial resistance</td>
<td>β-lactam+ macrolide</td>
</tr>
<tr>
<td>Inpatient not in ICU; moderate severity</td>
<td>β-lactam+ plus macrolide</td>
</tr>
<tr>
<td>Inpatient in ICU; high severity</td>
<td>β-lactam+ plus macrolide</td>
</tr>
</tbody>
</table>

Antibiotic Choice

- Macrolides:
  - azithromycin, clarithromycin, erythromycin
- Respiratory fluoroquinolones:
  - levofloxacin, moxifloxacin, gemifloxacin
- Preferred β-lactams:
  - ceftriaxone, cefotaxime, ampicillin

Antibiotic Choice

non-ICU hospitalized patients

- β-lactam monotherapy has recently been shown to be non inferior to β-lactam + macrolide or fluoroquinolone therapy
- Debate remains regarding the efficacy of β-lactam monotherapy in hospitalized patients


ICU patients

- β-lactam + macrolide or fluoroquinolone
- If Pseudomonas is suspected:
  - Anti-pseudomonal β-lactam:
    - Piperacillin-tazobactam, cefepime, imipenem, or meropenem
    +
    - Levofloxacin or ciprofloxacin
- If CA-MRSA is a consideration:
  - add vancomycin or linezolid

Duration of Therapy

- Two meta-analyses with no difference in outcomes with $\leq 7$ days vs. $> 7$ days of treatment.
- 5 days of treatment is adequate for mild severity with improvement after 3 days
- Discontinue antibiotics when procalcitonin level $< 80$-$90\%$ from peak or $< 0.25 \mu g/mL$

Longer Treatment Course

- Certain pathogens: MRSA, Legionella, Pseudomonas may benefit from longer duration of treatment
- Extrapulmonary complications:
  - Empyema
  - Endocarditis (particularly with MRSA)
  - Meningitis (*Strep pneumo*)
Transition to Oral Therapy

- Transition to oral therapy when:
  - Able to tolerate PO
  - Not confused
  - Temp < 38.3\(^\circ\)
  - Hemodynamically stable (HR < 100, SBP > 90mmHg)
  - Respiratory rate < 25
  - Oxygen saturation > 90% on room air or low flow supplemental oxygen

Steroids for CAP

Reduction in Length of Hospitalization

<table>
<thead>
<tr>
<th>Study, Year (Reference)</th>
<th>Participants</th>
<th>Mean Difference (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Low risk of bias</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Baeh et al. 2015 (12)</td>
<td>795</td>
<td>-1.06 (-1.13 to -0.99)</td>
</tr>
<tr>
<td>Arregui et al. 2015 (42)</td>
<td>204</td>
<td>-1.27 (-2.35 to -0.19)</td>
</tr>
<tr>
<td>Steroids et al. 2016 (43)</td>
<td>199</td>
<td>-0.88 (-4.05 to 2.28)</td>
</tr>
<tr>
<td>Random effects: $I^2$ = 5%</td>
<td></td>
<td>-1.28 (-5.79 to -1.21)</td>
</tr>
<tr>
<td>High risk of bias</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Confortin et al. 2006 (54)</td>
<td>46</td>
<td>-7.00 (-16.62 to 2.62)</td>
</tr>
<tr>
<td>El-Chami et al. 2008 (60)</td>
<td>54</td>
<td>-8.76 (-16.20 to -1.32)</td>
</tr>
<tr>
<td>Fernández-Gimeno et al. 2011 (60b)</td>
<td>45</td>
<td>-3.33 (-4.59 to -1.39)</td>
</tr>
<tr>
<td>Hönigl et al. 2007 (44)</td>
<td>37</td>
<td>-2.40 (-5.14 to 0.34)</td>
</tr>
<tr>
<td>Niazi et al. 2013 (49)</td>
<td>80</td>
<td>-7.31 (-13.68 to -0.94)</td>
</tr>
<tr>
<td>Torres et al. 2010 (73)</td>
<td>120</td>
<td>-2.04 (-5.29 to 1.21)</td>
</tr>
<tr>
<td>Random effects: $I^2$ = 58%</td>
<td></td>
<td>-2.41 (-5.75 to 1.17)</td>
</tr>
<tr>
<td>Total</td>
<td></td>
<td>-2.96 (-5.28 to -0.73)</td>
</tr>
</tbody>
</table>

All Cause Mortality

<table>
<thead>
<tr>
<th>Study, Year (Reference)</th>
<th>Participants</th>
<th>Risk Ratio (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Ellett et al. 2015 (56)</td>
<td>16/32</td>
<td>1.23 (0.69-2.23)</td>
</tr>
<tr>
<td>Confalonieri et al. 2005 (24)</td>
<td>0/23</td>
<td>0.60 (0.05-0.86)</td>
</tr>
<tr>
<td>El-Chami et al. 2006 (60)</td>
<td>1/17</td>
<td>1.00 (0.15-6.89)</td>
</tr>
<tr>
<td>Fernández-Gimeno et al. 2011 (60b)</td>
<td>1/22</td>
<td>0.96 (0.06-16.37)</td>
</tr>
<tr>
<td>Martí et al. 1999 (48)</td>
<td>1/14</td>
<td>0.94 (0.04-18.48)</td>
</tr>
<tr>
<td>MacNab et al. 1972 (45)</td>
<td>3/40</td>
<td>0.72 (0.20-2.51)</td>
</tr>
<tr>
<td>Mejías et al. 2011 (60)</td>
<td>9/155</td>
<td>0.88 (0.35-2.27)</td>
</tr>
<tr>
<td>Niazi et al. 2013 (49)</td>
<td>4/20</td>
<td>0.23 (0.07-0.71)</td>
</tr>
<tr>
<td>Sabry and Ouaou 2011 (47)</td>
<td>6/40</td>
<td>0.34 (0.05-2.16)</td>
</tr>
<tr>
<td>Snider et al. 2013 (42)</td>
<td>6/184</td>
<td>0.65 (0.36-1.15)</td>
</tr>
<tr>
<td>Torres et al. 2015 (17)</td>
<td>4/91</td>
<td>0.24 (0.04-1.70)</td>
</tr>
<tr>
<td>Wagner et al. 1956 (19)</td>
<td>1/52</td>
<td>1.17 (0.08-18.30)</td>
</tr>
<tr>
<td>Random effects: $I^2$ = 6%</td>
<td></td>
<td>0.67 (0.45-1.01)</td>
</tr>
</tbody>
</table>

Steroids for CAP

- Steroids appear to reduce length of hospital stay by approximately 1 day
- No change in mortality
- Only consistently demonstrated adverse effect is occurrence of hyperglycemia


Outcomes

- 7%-20% readmission rates within 30 days
  - Often related to comorbidities rather than treatment failure or pneumonia recurrence
- Very little data on effective interventions to reduce readmission rates
- In older patients may take as long as 12 weeks for CXR abnormalities to resolve

Prevention

• Influenza vaccination reduces rate of pneumonia from all causes

• Study of 286,000 patients > 65 found a 30% reduction in pneumonia with influenza vaccination & reduction in all cause mortality.


Prevention

• Pneumococcal vaccines:
  • Polysaccharide vaccine - 23 serotypes
    – Strong evidence for reduction in invasive pneumococcal disease
    – Less clear evidence for reduction of non-bacteremic pneumococcal infection, all cause pneumonia and mortality
  • Conjugate vaccine - 13 serotypes
    – Effective in prevention of pneumococcal pneumonia due to the covered serotypes (previously vaccinated patients excluded), but not all cause CAP
    – 38% of invasive pneumococcal disease in the US is caused by serotypes not covered by the conjugate vaccine

• CDC recommends both vaccines for patients ≥ 65 & for younger adults with COPD, tobacco use, immunosuppression, or DM

Pneumococcal Vaccination

Take Home Points

- CAP is the leading infectious cause of mortality among patients > 65
- Vaccinate against influenza and *Strep pneumoniae*
- Triage site of care based on clinical severity
- Timely use of guideline based antibiotics
- PCR diagnostics and procalcitonin can help with antibiotic stewardship
- The role of adjunctive steroids remains unclear
- Follow up after initiating antibiotics:
  - Early shift to oral therapy
  - Narrowing antibiotics based on micro results
  - Short duration of treatment (5 days) if clinical improvement at 3 days
References

- www.thoracic.org/statements/resources/mtpi/hsaats-cap.pdf