COMMUNITY ACQUIRED PNEUMONIA: DIAGNOSIS AND TREATMENT DURING THE COVID-19 ERA

Tuesday, January 26, 2021
1:00 p.m. – 2:00 p.m. ET

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Professor, Department of Medicine
University of Texas San Antonio
Chief, Pulmonary Section
The South Texas Veterans Health Care System

Norman Moore, PhD - Moderator/Speaker
Director of Infectious Disease and Scientific Affairs
Abbott Rapid Diagnostics

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This provides does not provide continuing medical education (CME) credits.
Program Objectives

• Describe the relationship between COVID-19 and pneumonia and the associated public health risks

• Examine experiences and best practices for evaluating and managing COVID-19 patients with pneumonia

• Explain the guidance and practical clinical value of urinary antigen testing (UAT), including mortality reduction and antibiotic stewardship

• Discuss UAT performance characteristics and potential value related to laboratory workflow in times of strained respiratory testing resource
COMMUNITY ACQUIRED PNEUMONIA: DIAGNOSIS AND TREATMENT DURING THE COVID-19 ERA

Antonio Anzueto
University of Texas Health Science Center
San Antonio, USA
Dr. Anzueto

Personal financial interests in commercial entities that are relevant to my presentation:
• Being compensated by ABBOTT to give this presentation

Non-commercial, non-governmental interests relevant to my presentation:
• Member of the ATS/ERS Task force on COPD and COPD Exacerbations,
• Member of the ATS/IDSA CAP Guidelines committee
• GOLD Past Member of the Executive and current member Scientific Committee
CASE STUDY
Case Study

55-year-old male presented to ED complaining 2-3 days of left chest pain, cough and chills.

**Medications:** Metoprolol and ASA 650 mg/day
Case Study

Physical Examination:
- Fever 101.7°F, HR 87/bpm, RR 32/min, BP 70/40
- Bilateral Crackles and dullness at bases

Other Information:
- WBC 14.6 x 10³/mL
- Oxygen Saturation at rest 85%
Case Study

What questions do we need to ask?
Case Study

What questions do we need to ask?

• Any Travel history?
• Any use of electronic cigarette or Vaping?
• Sick contacts?
Chest Radiograph
Respiratory Viral PCR
NEGATIVE

Need to order COVID Test
PUI
CAP and Risk Factors
Top 10 Global Causes of Death, 2019

1. Ischaemic heart disease
2. Stroke
3. Chronic obstructive pulmonary disease
4. Lower respiratory infections
5. Neonatal conditions
6. Trachea, bronchus, lung cancers
7. Alzheimer’s disease and other dementias
8. Diarrhoeal diseases
9. Diabetes mellitus
10. Kidney diseases

World Health Organization Global Health Estimates. The top 10 causes of death. 2019
Defining CAP, HCAP, HAP, and VAP

CAP (Community Acquired Pneumonia)
• Signs and symptoms of pneumonia with radiographic confirmation

HCAP (Healthcare-Associated Pneumonia)
• Prior hospitalization (within 90 days)
• Resided in nursing home or long-term care facility
• Received recent IV antibiotics (within 30 days)
• Etiological agent is often not isolated or is identified late in course of treatment

• Broad-spectrum antibiotics are prescribed early and empirically to reduce mortality

• Inappropriate antibiotic use can cause antimicrobial resistance and C. difficile infections

• Pathogen identification allows for targeted treatment


# Table 4  Bundles for lifestyle interventions to reduce the risk of CAP in adults

<table>
<thead>
<tr>
<th>Risk factor</th>
<th>Evidence</th>
<th>Recommendation</th>
</tr>
</thead>
<tbody>
<tr>
<td>Smoking</td>
<td>Risk of CAP increased in current and former smokers (9 studies)(^1)(^9)-(^2)(^3) 38 42 46 47</td>
<td>Smoking cessation</td>
</tr>
<tr>
<td>Alcohol consumption</td>
<td>Risk of CAP increased with high consumption or history of alcohol abuse (4 studies(^1)^(^9)-(^2)(^3) 38 47</td>
<td>Reduce alcohol consumption</td>
</tr>
<tr>
<td>Nutritional status</td>
<td>Being underweight was generally associated with an increased risk of CAP (4 studies(^3) 38 44 47)</td>
<td>Dietary advice to ensure good nutritional status</td>
</tr>
<tr>
<td>Contact with children</td>
<td>Regular contact with children increased the risk of CAP (3 studies(^1)^(^3) 38 44)</td>
<td>Avoid contacts with children with lower respiratory tract infections</td>
</tr>
<tr>
<td>Dental hygiene</td>
<td>Risk of CAP decreased in individuals with a recent (within past year) dental visit (2 studies(^3) 38)</td>
<td>Ensure regular dental visits</td>
</tr>
<tr>
<td>Vaccination against influenza and Streptococcus pneumoniae</td>
<td>Current guidelines(^8)(^8) 89</td>
<td>Ensure compliance with guidelines</td>
</tr>
</tbody>
</table>

CAP, community-acquired pneumonia.
### Differential Dx of COVID-19 and Pneumonia

#### SN-CAP, SARS-CoV-2 negative-community acquired pneumonia


#### Table 1: Clinical Characteristics of COVID-19 and SN-CAP

<table>
<thead>
<tr>
<th></th>
<th>COVID-19</th>
<th>SN-CAP</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Age, mean (SD), y</strong></td>
<td>61.5(13.3%)</td>
<td>61.8(16.1)</td>
<td>0.921</td>
</tr>
<tr>
<td><strong>Female</strong></td>
<td>166 (54.61%)</td>
<td>56 (40.66%)</td>
<td>&lt;0.01</td>
</tr>
<tr>
<td><strong>Male</strong></td>
<td>138 (45.39%)</td>
<td>82 (59.42%)</td>
<td></td>
</tr>
</tbody>
</table>

#### Signs and symptoms at admission, patient no

<table>
<thead>
<tr>
<th></th>
<th>COVID-19</th>
<th>SN-CAP</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Fever</td>
<td>172 (56.58%)</td>
<td>42 (30.43%)</td>
<td>&lt;0.01</td>
</tr>
<tr>
<td>Cough</td>
<td>134 (44.08%)</td>
<td>73 (53.82%)</td>
<td>0.06</td>
</tr>
<tr>
<td>Dyspnea</td>
<td>29 (9.54%)</td>
<td>3 (2.17%)</td>
<td>&lt;0.01</td>
</tr>
<tr>
<td>Fatigue</td>
<td>32 (10.53%)</td>
<td>5 (3.62%)</td>
<td>0.02</td>
</tr>
<tr>
<td>Chest distress</td>
<td>24 (7.89%)</td>
<td>3 (2.17%)</td>
<td>0.02</td>
</tr>
<tr>
<td>Expectoration</td>
<td>10 (3.29%)</td>
<td>53 (38.41%)</td>
<td>&lt;0.01</td>
</tr>
<tr>
<td>Sore throat</td>
<td>5 (1.64%)</td>
<td>5 (3.62%)</td>
<td>0.2</td>
</tr>
<tr>
<td>Diarrhea</td>
<td>5 (1.64%)</td>
<td>1 (0.72%)</td>
<td>0.4</td>
</tr>
<tr>
<td>Asymptomatic</td>
<td>39 (12.83%)</td>
<td>6 (4.35%)</td>
<td>&lt;0.01</td>
</tr>
</tbody>
</table>

#### Chronic medical illness, patient no

<table>
<thead>
<tr>
<th></th>
<th>COVID-19</th>
<th>SN-CAP</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Hypertension</td>
<td>83 (27.3%)</td>
<td>34 (24.64%)</td>
<td>0.56</td>
</tr>
<tr>
<td>CAD</td>
<td>21 (6.91%)</td>
<td>8 (5.8%)</td>
<td>0.66</td>
</tr>
<tr>
<td>Diabetes</td>
<td>40 (13.16%)</td>
<td>25 (18.12%)</td>
<td>0.17</td>
</tr>
<tr>
<td>COPD</td>
<td>7 (2.3%)</td>
<td>27 (19.57%)</td>
<td>&lt;0.01</td>
</tr>
<tr>
<td>Renal failure</td>
<td>27 (8.88%)</td>
<td>18 (13.04%)</td>
<td>0.18</td>
</tr>
<tr>
<td>Malignancy</td>
<td>3 (0.99%)</td>
<td>15 (10.87%)</td>
<td>&lt;0.01</td>
</tr>
</tbody>
</table>

#### Laboratory result abnormalities, patient no

<table>
<thead>
<tr>
<th></th>
<th>COVID-19</th>
<th>SN-CAP</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>WBC count, &lt;3.7 x 109/L</td>
<td>42 (13.82%)</td>
<td>4 (2.9%)</td>
<td>&lt;0.01</td>
</tr>
<tr>
<td>Lymphocyte count, &lt;0.8 x 109/L</td>
<td>97 (41.91%)</td>
<td>68 (49.28%)</td>
<td>&lt;0.01</td>
</tr>
<tr>
<td>Lymphocyte ratio &lt;20%</td>
<td>134 (44.08%)</td>
<td>93 (57.39%)</td>
<td>&lt;0.01</td>
</tr>
<tr>
<td>Neutrophil count, x100/L</td>
<td>51 (16.79%)</td>
<td>37 (26.81%)</td>
<td>0.01</td>
</tr>
<tr>
<td>Platelet &lt;85 x 109/L</td>
<td>15 (4.93%)</td>
<td>7 (5.07%)</td>
<td>0.95</td>
</tr>
<tr>
<td>CRP &gt;10 mg/L</td>
<td>127 (41.78%)</td>
<td>98 (71.01%)</td>
<td>&lt;0.01</td>
</tr>
<tr>
<td>Albumin &lt;35 g/L</td>
<td>139 (45.72%)</td>
<td>95 (68.84%)</td>
<td>&lt;0.01</td>
</tr>
<tr>
<td>ALT/AST abnormal</td>
<td>99 (32.57%)</td>
<td>42 (30.43%)</td>
<td>0.66</td>
</tr>
<tr>
<td>Creatinine &gt;73 μmol/L</td>
<td>60 (19.74%)</td>
<td>28 (20.29%)</td>
<td>0.89</td>
</tr>
<tr>
<td>BUN, &gt;8 mmol/L</td>
<td>87 (28.62%)</td>
<td>30 (21.74%)</td>
<td>0.13</td>
</tr>
<tr>
<td>LDH &gt;250 U/L</td>
<td>42 (13.82%)</td>
<td>60 (43.48%)</td>
<td>&lt;0.01</td>
</tr>
<tr>
<td>Creatine kinase &gt;195 U/L</td>
<td>21 (6.91%)</td>
<td>6 (4.35%)</td>
<td>0.3</td>
</tr>
<tr>
<td>Troponin-I &gt;0.4 μg/L</td>
<td>49 (16.12%)</td>
<td>25 (18.12%)</td>
<td>0.6</td>
</tr>
<tr>
<td>Patients tested for procalcitonin, no.</td>
<td>31</td>
<td>117</td>
<td></td>
</tr>
<tr>
<td>Procalcitonin &gt;0.5 pg/mL</td>
<td>13 (41.94%)</td>
<td>55 (47.01%)</td>
<td>0.61</td>
</tr>
</tbody>
</table>

*P-value indicates differences between COVID-19 and SN-CAP; P < 0.05 was considered statistically significant.*
Poll Question #1

The following tests are performed to detect pathogens for community acquired pneumonia (CAP) in my facility (select all that apply):

a. Blood culture
b. Sputum culture
c. Sputum gram stain
d. Urinary antigen testing (UAT)
e. Molecular pneumonia panel
f. ELISA
g. Other
h. We send out all pneumonia testing
i. Don’t know or n/a
Pathogens:

*S. pneumoniae* and *Legionella*
**S. pneumoniae**

- Leading cause of CAP¹
- Leading cause of pneumonia mortality¹
- May cause secondary bacteremia²,³
- Difficult to diagnose using traditional culture methods⁴-⁶
  - Long turnaround time
  - Difficult to obtain high-quality sputum sample
  - Blood cultures have low sensitivity
  - Empiric antibiotics impact yield

## Etiology of CAP

<table>
<thead>
<tr>
<th>AMBULATORY PATIENTS</th>
<th>HOSPITALIZED (NON-ICU)</th>
<th>SEVERE (ICU)</th>
</tr>
</thead>
<tbody>
<tr>
<td><em>S. pneumoniae</em></td>
<td><em>S. pneumoniae</em></td>
<td><em>S. pneumoniae</em></td>
</tr>
<tr>
<td><em>M. pneumoniae</em></td>
<td><em>M. pneumoniae</em></td>
<td><em>H. influenzae</em></td>
</tr>
<tr>
<td><em>H. influenzae</em></td>
<td><em>C. pneumoniae</em></td>
<td><em>Legionella spp.</em></td>
</tr>
<tr>
<td><em>C. pneumoniae</em></td>
<td><em>H. influenzae</em></td>
<td><em>Gram-negative bacilli</em></td>
</tr>
<tr>
<td>Respiratory viruses*</td>
<td><em>Legionella spp.</em></td>
<td><em>S. aureus</em></td>
</tr>
<tr>
<td></td>
<td>Aspiration</td>
<td><em>Viral: H1N1</em></td>
</tr>
<tr>
<td></td>
<td>Respiratory viruses*</td>
<td></td>
</tr>
</tbody>
</table>

ICU = Intensive care unit

*Influenza A and B, adenovirus, respiratory syncytial virus, and parainfluenza

---

Etiology of Community-Acquired Pneumonia

Invasive Pneumococcal Disease
Cardiac lesion

Mortality of Hospital Admitted Patients with Invasive Pneumococcal Disease

1952−62
13% Mortality
n = 1130

1966−95
12% Mortality
n = 4432

1995−97
12% Mortality
n = 5837

Although the management of critically ill patients has improved by far and there are no resistance problems with regard to S. pneumoniae, mortality of IPD remains tremendous.

S. pneumoniae Serotypes and Risk of Cardiac Events

MACE, major adverse cardiac events
<table>
<thead>
<tr>
<th>AMBULATORY PATIENTS</th>
<th>HOSPITALIZED (NON-ICU)</th>
<th>SEVERE (ICU)</th>
</tr>
</thead>
<tbody>
<tr>
<td><em>S. pneumoniae</em></td>
<td><em>S. pneumoniae</em></td>
<td><em>S. pneumoniae</em></td>
</tr>
<tr>
<td><em>M. pneumoniae</em></td>
<td><em>M. pneumoniae</em></td>
<td><em>H. influenzae</em></td>
</tr>
<tr>
<td><em>H. influenzae</em></td>
<td><em>C. pneumoniae</em></td>
<td><em>Legionella spp.</em></td>
</tr>
<tr>
<td><em>C. pneumoniae</em></td>
<td><em>Respiratory viruses</em></td>
<td><em>Gram-negative bacilli</em></td>
</tr>
<tr>
<td>Respiratory viruses*</td>
<td></td>
<td><em>S. aureus</em></td>
</tr>
</tbody>
</table>

ICU = Intensive care unit

*Influenza A and B, adenovirus, respiratory syncytial virus, and parainfluenza

ICU, intensive care unit

Antimicrobial Resistance - Status

**Urgent Threats**
These germs are public health threats that require urgent and aggressive action

- Carbapenem-resistant *Acinetobacter*
- *Candida auris*
- *Clostridioides difficile*
- Carbapenem-resistant Enterobacteriaceae
- Drug-resistant *Neisseria gonorrhoeae*

**Concerning Threats**
These germs are public health threats that require careful monitoring and prevention action

- Erythromycin-resistant group A *Streptococcus*
- Clindamycin-resistant group B *Streptococcus*

**Serious Threats**
These germs are public health threats that require prompt and sustained action:

- Drug-resistant *Campylobacter*
- Drug-resistant *Candida*
- ESBL-producing Enterobacteriaceae
- Vancomycin-resistant *Enterococci*
- Multidrug-resistant *Pseudomonas aeruginosa*
- Drug-resistant nontyphoidal *Salmonella*
- Drug-resistant *Salmonella* serotype Typhi
- Drug-resistant *Shigella*
- Methicillin-resistant *Staphylococcus aureus*
- Drug-resistant *Streptococcus pneumoniae*
- Drug-resistant Tuberculosis

**Watch List**

- Azole-resistant *Aspergillus fumigatus*
- Drug-resistant *Mycoplasma genitalium*
- Drug-resistant *Bordetella pertussis*

Legionella

- Leading cause of waterborne disease outbreaks\(^1\)
- The deadliest pneumonia – up to 25% fatality rate\(^2\)
- Disease incidence continues to rise, and likely underdiagnosed\(^3\) – impact of shut-downs/reopenings?
- Outbreaks can lead to costly legal action with lasting negative impact on facility reputations\(^4\)
- Initial symptom presentation similar to COVID\(^5\)
- Risk factors\(^6\):
  - Age ≥ 50 years
  - Smoking
  - Underlying illness
  - Recent travel
  - Exposure to water sources

Etiology of Community-Acquired Pneumonia

Legionnaire’s Disease: Likely Underdiagnosed

Legionnaires’ disease is on the rise in the United States
2000-2018

9x rate of increase since 2000

Diagnosis and Treatment of Adults with CAP
Official Clinical Practice Guidelines from ATS/IDSA
## Diagnosis and Treatment of Adults with Community-acquired Pneumonia

An Official Clinical Practice Guideline of the American Thoracic Society and Infectious Diseases Society of America


The official clinical practice guideline was approved by the American Thoracic Society May 2019 and the Infectious Diseases Society of America August 2019.

### Background

This document provides evidence-based clinical practice guidelines on the management of adult patients with community-acquired pneumonia. Although some recommendations remain unchanged from the 2017 guideline, the availability of multiple new therapeutic trials and epidemiological investigations led to revised recommendations for empiric treatment strategies and additional management decisions.

### Methods

A multidisciplinary panel conducted pragmatic systematic reviews of the relevant research and applied Guiding of Recommendations, Assessment, Development, and Evaluation methodology for clinical recommendations.

### Results

The panel addressed 16 specific areas for recommendations spanning questions of diagnostic testing, determination of site of care, selection of initial empiric antibiotic therapy, and subsequent management decisions. Although some recommendations remain unchanged from the 2017 guideline, the availability of multiple new therapeutic trials and epidemiological investigations led to revised recommendations for empiric treatment strategies and additional management decisions.

### Conclusions

The panel formulated and provided the rationale for recommendations on selected diagnostic and treatment strategies for adult patients with community-acquired pneumonia.

### Keywords

Community-acquired pneumonia, pneumococcal patient management

### Contents

<table>
<thead>
<tr>
<th>Overview</th>
<th>Methods</th>
<th>Treatment</th>
<th>Other therapies</th>
<th>Diagnosis</th>
<th>Duration Therapy</th>
<th>Follow up</th>
</tr>
</thead>
</table>

### Diagnosis

**16 Questions**

<table>
<thead>
<tr>
<th>Question 1</th>
<th>Question 2</th>
</tr>
</thead>
<tbody>
<tr>
<td>In Adults with CAP, should Gram stain and culture of Lower Respiratory Secretions be obtained at the Time of Diagnosis?</td>
<td>In Adults with CAP, should Blood Cultures be Obtained at the Time of Diagnosis?</td>
</tr>
</tbody>
</table>

---

Evaluating Recommendations

Quality

QC

Interpretation

Strong

Weak

Conditional


Recommendations for Specific Management Questions:
Initial Diagnostic Evaluation

Question 1
In adults with CAP, should Gram stain and culture of lower respiratory secretions be obtained at the time of diagnosis?

Recommendation
In the setting of severe CAP, especially if they are intubated
Or, are being empirically treated for MRSA or *P. aeruginosa*

Interpretation
Strong

Quality
Very low quality of evidence

Or, were previously infected with MRSA or *P. aeruginosa*, especially those with prior respiratory tract infection

Or, were hospitalized and received parenteral antibiotics, whether during the hospitalization event or not, in the last 90 days

Interpretation
Conditional

Quality
Very low quality of evidence

Recommendations for Specific Management Questions:
Initial Diagnostic Evaluation

Question 2
In adults with CAP, should blood cultures be obtained at the time of diagnosis?

Recommendations
Obtain pretreatment blood cultures in the setting of severe CAP

Or, if being empirically treated for MRSA or P. aeruginosa

Interpretation
Strong

Or, were previously infected with MRSA or P. aeruginosa, especially those with prior respiratory tract infection

Or, were hospitalized and received parenteral antibiotics, whether during the hospitalization event or not, in the last 90 days

Interpretation
Conditional

Sputum Gram Stain for Bacterial Pathogen Diagnosis in Community-acquired Pneumonia: A Systematic Review and Bayesian Meta-analysis of Diagnostic Accuracy and Yield

Hiroaki Ogawa,1 Georgios D. Kitsios,2 Mitsunaga Iwata,1 and Teruhiko Terasawa,1,∗

Poll Question #2

The following UAT are performed in-house:

a. S. pneumoniae
b. L. pneumophila
c. Both
d. Neither
e. n/a
Recommendations for Specific Management Questions:
Initial Diagnostic Evaluation

Question 3
In adults with CAP, should *Legionella* and pneumococcal
urinary antigen testing be performed at the time of
diagnosis?

Recommendation

*Legionella* and *S. pneumoniae* antigen testing

- **In adults with severe CAP**
  - *(Legionella)* also collect lower respiratory tract secretions
    for culture or NAAT

- Where indicated by epidemiological factors *(Legionella)*
  - i.e., known outbreaks or recent travel

Interpretation
Conditional
Quality
Low quality of evidence

UAT Guideline Recommendation Based On Observed Mortality Reduction in Large Observational Studies

57% lower odds of in-hospital mortality and 66% lower odds of 30-day mortality compared to patients not tested

(Adjusted for baseline demographic/clinical differences)

<table>
<thead>
<tr>
<th>Table 5 Multivariable regression analyses for in-hospital and 30-day mortality, length of hospital stay and duration of antibiotic therapy</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
</tr>
<tr>
<td>In-hospital mortality</td>
</tr>
<tr>
<td>N = 561</td>
</tr>
<tr>
<td>OR</td>
</tr>
<tr>
<td>-----------------</td>
</tr>
<tr>
<td>Socio-demographic characteristics and other potential confounders</td>
</tr>
<tr>
<td>Age in years (continuous)</td>
</tr>
<tr>
<td>Male gender (vs. female gender)</td>
</tr>
<tr>
<td>Admission from nursing home (vs. from own home)</td>
</tr>
<tr>
<td>Five or more comorbidities (vs. less than five)</td>
</tr>
<tr>
<td>ATS criteria for CAP severity (continuous)</td>
</tr>
<tr>
<td>Admission in 2012 (vs. admission in 2015)</td>
</tr>
<tr>
<td>Stay in a respiratory ward (vs. stay in a non-respiratory ward)</td>
</tr>
<tr>
<td>Mechanical ventilation</td>
</tr>
<tr>
<td>Adherence to diagnostic procedures</td>
</tr>
<tr>
<td>Blood culture</td>
</tr>
<tr>
<td>Urinary Antigen tests</td>
</tr>
</tbody>
</table>

UAT Guideline Recommendation Based On Observed Mortality Reduction in Large Observational Studies
Uematsu, et al. 2014

Table 3  Crude mortality and the association of microbiological tests with 30-day mortality, stratified by disease severity

<table>
<thead>
<tr>
<th>Severity class</th>
<th>Death(^a/)total (%)</th>
<th>OR (95% CI)</th>
<th>P</th>
<th>OR (95% CI)</th>
<th>P</th>
<th>OR (95% CI)</th>
<th>P</th>
<th>OR (95% CI)</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>Very severe</td>
<td>2075/7935 (26.1)</td>
<td>0.93 (0.82–1.05)</td>
<td>0.24</td>
<td>1.22 (1.05–1.41)</td>
<td>0.009</td>
<td>1.11 (0.98–1.26)</td>
<td>0.11</td>
<td>1.00 (0.50–2.00)</td>
<td>0.99</td>
</tr>
<tr>
<td>Severe</td>
<td>977/8224 (11.9)</td>
<td>0.81 (0.70–0.93)</td>
<td>0.004</td>
<td>0.71 (0.60–0.85)</td>
<td>&lt;0.001</td>
<td>0.79 (0.68–0.93)</td>
<td>0.003</td>
<td>1.67 (0.79–3.53)</td>
<td>0.18</td>
</tr>
<tr>
<td>Moderate</td>
<td>1214/36186 (3.4)</td>
<td>0.75 (0.64–0.87)</td>
<td>&lt;0.001</td>
<td>0.75 (0.63–0.89)</td>
<td>0.001</td>
<td>0.80 (0.69–0.94)</td>
<td>0.005</td>
<td>0.39 (0.16–0.99)</td>
<td>0.047</td>
</tr>
<tr>
<td>Mild</td>
<td>41/12213 (0.3)</td>
<td>Reference</td>
<td>Reference</td>
<td>Reference</td>
<td>Reference</td>
<td>Reference</td>
<td>Reference</td>
<td>Reference</td>
<td></td>
</tr>
</tbody>
</table>

Cumulative no. performed

| 0 | Reference | 0.97 (0.85–1.12) | 0.69 | Reference | 1.03 (0.87–1.21) | 0.74 | Reference | 0.81 (0.70–0.93) | 0.003 | Reference | 1.03 (0.50–2.11) | 0.93 |
| 1 | 0.74 (0.63–0.86) | <0.001 | 0.78 (0.64–0.94) | 0.010 | 0.78 (0.66–0.92) | 0.004 | 0.50 (0.17–1.47) | 0.21 |
| 2 | 0.51 (0.40–0.64) | <0.001 | 0.70 (0.54–0.91) | 0.008 | 0.83 (0.66–1.04) | 0.11 | 1.08 (0.36–3.26) | 0.89 |

\(^a\)In-hospital deaths within 30 days of admission.

25% reduced odds of 30-day mortality
Testing Warranted in Endemic Populations

- Identifies cases that would otherwise remain undetected
- Facilitates targeted antibiotic therapy
- Provides surveillance for potential outbreaks

“Routine Legionella testing affords confidence that cases were not missed...and infection prevention protocols remained effective.”


<table>
<thead>
<tr>
<th>A</th>
<th>SP</th>
<th>IDSA/ATS indications for SP UAT</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Positive</td>
<td>Negative</td>
</tr>
<tr>
<td>SP UAT positive</td>
<td>49 (4.1%)</td>
<td>32 (4.2%)</td>
</tr>
<tr>
<td>SP UAT negative</td>
<td>1135 (95.9%)</td>
<td>725 (95.8%)</td>
</tr>
<tr>
<td></td>
<td>1184</td>
<td>757</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>B</th>
<th>LP</th>
<th>IDSA/ATS indications for LP UAT</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Positive</td>
<td>Negative</td>
</tr>
<tr>
<td>LP UAT positive</td>
<td>20 (1.6%)</td>
<td>12 (1.8%)</td>
</tr>
<tr>
<td>LP UAT negative</td>
<td>1238 (98.4%)</td>
<td>671 (98.2%)</td>
</tr>
<tr>
<td></td>
<td>1258</td>
<td>683</td>
</tr>
</tbody>
</table>
Multivariable Models for Predicting Positive *Streptococcus pneumoniae* and *Legionella pneumophila* Urinary Antigen Tests

<table>
<thead>
<tr>
<th></th>
<th>Multivariable OR (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Streptococcus pneumoniae (n = 81)</strong></td>
<td></td>
</tr>
<tr>
<td>Male sex</td>
<td>0.69 (0.43–1.09)</td>
</tr>
<tr>
<td>Age ≥65</td>
<td>1.04 (0.61–1.77)</td>
</tr>
<tr>
<td>Failure of outpatient antibiotics</td>
<td>0.67 (0.36–1.26)</td>
</tr>
<tr>
<td>Fever (&gt;38°C)</td>
<td>1.50 (0.93–2.42)</td>
</tr>
<tr>
<td>Hyponatremia</td>
<td>1.81 (0.96–3.41)</td>
</tr>
<tr>
<td>ICU admission</td>
<td>1.29 (0.75–2.24)</td>
</tr>
<tr>
<td>Pneumonia Severity Index risk class ≥IV</td>
<td>1.46 (0.84–2.55)</td>
</tr>
<tr>
<td>Empiric broad spectrum antibiotics</td>
<td>1.16 (0.70–1.94)</td>
</tr>
<tr>
<td><strong>Legionella pneumophila (n = 32)</strong></td>
<td></td>
</tr>
<tr>
<td>Recent travel</td>
<td>2.18 (0.99–4.76)</td>
</tr>
<tr>
<td>Fever (&gt;38°C)</td>
<td>3.21 (1.56–6.60)</td>
</tr>
<tr>
<td>Hyponatremia</td>
<td>7.44 (3.5–15.67)</td>
</tr>
<tr>
<td>Diarrhea</td>
<td>2.88 (1.39–5.95)</td>
</tr>
</tbody>
</table>

Pneumococcal Urinary Antigen Testing in United States Hospitals: A Missed Opportunity for Antimicrobial Stewardship

39.6% hospitals did not order any UAT

16.2% UAT in pneumonia population (n=159,894)

Rate of De-escalation Following UAT Positivity Tended To Increase With Increasing Hospital Use

Hospital UAT use was strongly correlated with de-escalation following a positive test.
What are the clinical scenarios where UAT can be useful?

Hospitalized patients with CAP

COVID + patients – required hospitalization due to acute respiratory failure

Hospitalized patient that you suspect a nosocomial pneumonia
Recommendations for Specific Management Questions: Initial Diagnostic Evaluation

Question 5
In adults with CAP, should serum procalcitonin plus clinical judgement versus clinical judgment alone be used to withhold initiation of antibiotic treatment?

Recommendation
Serum procalcitonin should not be used to withhold initiation of empiric antibiotic therapy in adults with CAP.

Interpretation
Strong

Quality
Moderate quality of evidence

Procalcitonin Differentiates between Bacterial and Viral Infections

- **bacterial infections** (proinflammatory cytokines - IL-1, IL-6 and TNF-a - and endotoxin)

- **in viral infections** (interferon gamma)

inflammation-mediated expression of the CALC I gene
<table>
<thead>
<tr>
<th>Authors</th>
<th>Study name</th>
<th>Research question</th>
<th>Setting</th>
<th>n=</th>
<th>Mortality Control vs PCT group</th>
<th>AB exposure Control vs PCT</th>
<th>Relative AB reduction</th>
</tr>
</thead>
<tbody>
<tr>
<td>Christ-Crain et al</td>
<td>ProRESP</td>
<td>Reduction of antibiotic prescription for LRTI in the ED?</td>
<td>ED, single center</td>
<td>243</td>
<td>4/119 (3.4%) vs 4/124 (3.2%)</td>
<td>10.7 vs 4.8*</td>
<td>55.1%</td>
</tr>
<tr>
<td>Christ-Crain et al</td>
<td>ProCAP</td>
<td>Reduction of antibiotic exposure in ED and hospital?</td>
<td>ED and hospital, single center</td>
<td>302</td>
<td>20/151 (13.2%) vs 18/151 (11.9%)</td>
<td>12.9 vs 5.7*</td>
<td>55.8%</td>
</tr>
<tr>
<td>Stolz et al</td>
<td>ProCOLD</td>
<td>Reduction of antibiotic exposure in ED, single center</td>
<td></td>
<td>208</td>
<td>9/106 (8.5%) vs 5/102 (4.9%)</td>
<td>7.0 vs 3.7*</td>
<td>47.1%</td>
</tr>
<tr>
<td>Briel et al</td>
<td>PARTI</td>
<td>Safety &amp; reduction of antibiotic exposure in upper and lower RTI?</td>
<td>Primary Care, multicenter</td>
<td>458</td>
<td>1/232 (0.4%) vs 0/226 (0%)</td>
<td>6.8 vs 1.5*</td>
<td>77.9%</td>
</tr>
<tr>
<td>Nobre et al</td>
<td>&quot;ProSEP&quot;</td>
<td>Reduction of antibiotic exposure in ICU, single center</td>
<td></td>
<td>79</td>
<td>8/39 (20.5%) vs 8/40 (20%)</td>
<td>9.5 vs 6**</td>
<td>36.8%</td>
</tr>
<tr>
<td>Schuetz et al</td>
<td>ProHOSP</td>
<td>Safety &amp; feasibility in LRTI in a multicenter setting?</td>
<td>ED and hospital, multicenter</td>
<td>1359</td>
<td>33/671 (4.9%) vs 34/688 (4.9%)</td>
<td>8.7 vs 5.7*</td>
<td>34.5%</td>
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<tr>
<td>Stolz et al</td>
<td>ProVAP</td>
<td>Reduction of antibiotic exposure in ICU, VAP in different ICUs?</td>
<td></td>
<td>101</td>
<td>12/50 (24%) vs 8/51 (15.7%)</td>
<td>9.5 vs 13***</td>
<td>26.9%</td>
</tr>
<tr>
<td>Kristoffersen et al</td>
<td>1-PCT</td>
<td>Reduction of antibiotic exposure for LRTI in Denmark?</td>
<td>ED and hospital, single center</td>
<td>210</td>
<td>1/107 (0.9%) vs 2/103 (1.9%)</td>
<td>6.8 vs 5.1*</td>
<td>25.0%</td>
</tr>
<tr>
<td>Hochreiter et al</td>
<td>ProSICU</td>
<td>Guiding antibiotic therapy with PCT in a surgical ICU?</td>
<td>Surgical ICU, single center</td>
<td>110</td>
<td>14/53 (26.4%) vs 15/57 (26.3%)</td>
<td>7.9 vs 5.9*</td>
<td>25.3%</td>
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<tr>
<td>Bouadma et al</td>
<td>ProRATA</td>
<td>Reduction of antibiotic exposure for sepsis in different french ICUs?</td>
<td>ICU, multicenter</td>
<td>621</td>
<td>64/314 (20.4%) vs 65/307 (21.2%)</td>
<td>11.6 vs 14.3***</td>
<td>18.9%</td>
</tr>
<tr>
<td>Burckhardt et al</td>
<td>&quot;PARTI Germany&quot;</td>
<td>Safety &amp; reduction of only initial PCT measurement in primary care?</td>
<td>Primary Care, multicenter</td>
<td>550</td>
<td>0/275 (0%) vs 0/275 (0%)</td>
<td>36.7% vs 21.5%***</td>
<td>42.0%</td>
</tr>
</tbody>
</table>

Total 4241 166/2117 (7.8%) vs 159/2124 (7.5%)

PCT-guidance treatment compared to standard-of-care after 180 days

Infection-associated adverse events
(PCT vs. SOC)

Day 7

Day 28

$P = 0.01$

Survival patients (%)

28-day survival in the intention-to-treat population

Hazard ratio, 0.51
(95% CI, 0.29–0.89)

$P = 0.02$

What are the clinical scenarios where PCT levels can be useful?

- Recognizing response to and shortening duration of antibiotic therapy
- Determining the need for antibiotics in patients with LRTI (i.e., AECOPD)
- Determining severity of infection (e.g. localized versus systemic)
- Differentiating between septic and other forms of shock
- Distinguishing viral from bacterial infection in febrile patients
CAP Test Methods:

*S. pneumoniae*  
*Legionella*
### LEGIONELLA

<table>
<thead>
<tr>
<th>METHODOLOGY</th>
<th>COMPONENT DETECTED</th>
<th>SAMPLE TYPE</th>
<th>SENSITIVITY</th>
<th>SPECIFICITY</th>
<th>TURNAROUND TIME</th>
</tr>
</thead>
<tbody>
<tr>
<td>Culture</td>
<td>organism</td>
<td>sputum</td>
<td>Gold Standard*</td>
<td>Gold Standard*</td>
<td>4 - 10 days</td>
</tr>
<tr>
<td>UAT(^1)</td>
<td>antigen</td>
<td>urine</td>
<td>95%</td>
<td>95%</td>
<td>15 minutes</td>
</tr>
<tr>
<td>DFA(^2)</td>
<td>organism</td>
<td>sputum</td>
<td>33% - 70%</td>
<td>&gt;95%</td>
<td>40 - 60 minutes</td>
</tr>
<tr>
<td>Serology/IFA(^2)</td>
<td>antibody</td>
<td>serum</td>
<td>40% - 60%</td>
<td>&gt;95%</td>
<td>60 - 90 minutes</td>
</tr>
</tbody>
</table>

### STREPTOCOCCUS PNEUMONIAE

<table>
<thead>
<tr>
<th>METHODOLOGY</th>
<th>COMPONENT DETECTED</th>
<th>SAMPLE TYPE</th>
<th>SENSITIVITY</th>
<th>SPECIFICITY</th>
<th>TURNAROUND TIME</th>
</tr>
</thead>
<tbody>
<tr>
<td>UAT(^3)</td>
<td>antigen</td>
<td>urine</td>
<td>86%**</td>
<td>94%**</td>
<td>15 minutes</td>
</tr>
<tr>
<td>Blood Culture</td>
<td>organism</td>
<td>blood</td>
<td>10% - 30%(^4)</td>
<td>N/A</td>
<td>24 - 48 hours</td>
</tr>
<tr>
<td>Sputum Culture</td>
<td>organism</td>
<td>sputum</td>
<td>29% - 94%(^5)</td>
<td>66%(^6) - 94%(^7)</td>
<td>24 - 48 hours</td>
</tr>
<tr>
<td>Sputum Gram Stain(^8)</td>
<td>organism</td>
<td>sputum</td>
<td>15% - 100%</td>
<td>11% - 100%</td>
<td>15 minutes</td>
</tr>
</tbody>
</table>

* Sensitivity and specificity data for methodologies listed were obtained through comparison to clinical diagnosis including culture.
** Sensitivity and specificity data are retrospective for urine only.

UAT for *S. pneumoniae* and *Legionella*

Guideline-concordant testing\(^1\)
Non-invasive, ease of urine sample collection\(^3\)
No instrument required
Easy to use\(^2,3\)
Rapid results\(^2,3\)
Low cost per test/Inexpensive\(^2,3\)
Guide for antibiotic de-escalation\(^2,3\)

UAT may provide cost-effective off-instrument testing option to avoid disrupting molecular workflows and higher technical demands

CAP Dx - Take Home Messages

✓ CAP is changing - clinical diagnosis is pivotal for patient’s management

✓ UAT helps identify two important CAP pathogens associated with high mortality
  ✓ *Legionella*, of increasing prevalence and poses new risks with building re-openings
  ✓ *S. pneumoniae, the leading cause of CAP*

✓ Procalcitonin is important diagnosis tool for the diagnosis and management of CAP

✓ During COVID 19, CAP diagnosis and management should be managed according to the ATS/IDSA CAP Guidelines
“Problems are not stop signs, they are guidelines”

- Robert H. Schuller