Finding Pneumo 2: In Search of *Legionella*

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Professor of Medicine,
University of Pittsburgh

Sponsored by:
Top Doctors Claim ‘Climate of Fear’ Created by Govt.

LEGIONNAIRES DISEASE – THE GREAT HOAX

How to Love And Be Loved
Legionella pneumophila

gram-negative rod
aerobic
non-spore-forming
grows on buffered charcoal yeast extract media
does not grow on blood agar
abundance of branched-chain fatty acids
confirmation of identity by gas liquid chromatography
direct immunofluorescence DNA hybridization
'Legionnaire' Cases Reach 16 in Vermont

Link Legion Fever & New Germ

New Legionnaires' Cases Probed

HEADLINES flare about the disease — but doctors say government officials fed scare stories to the press.
 Legionnaires’ Disease: New Clinical Perspective from a Prospective Pneumonia Study

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In an attempt to ascertain the incidence of Legionnaires’ disease at our hospital, a prospective case-control pneumonia study was conducted for 11 months. Specialized diagnostic tests for Legionella pneumophila, including serologic study, direct immunofluorescent examination, and selective culture, were made routinely available in our hospital. To our surprise, L. pneumophila was the most common cause of pneumonia (22.5 percent) attributable to a single pathogen, followed by Streptococcus pneumoniae (10.6 percent). In 68.8 percent of the cases, Legionnaires’ pneumonia was hospital-acquired. In contrast to other investigators, we found that abdominal pain, diarrhea, neurologic signs, abnormal liver function results, hypophosphatemia, and hematuria did not occur significantly more frequently in pneumonia caused by L. pneumophila than in that caused by other microorganisms. However, hyponatremia within five days of onset of pneumonia occurred significantly more frequently in Legionnaires’ disease (p < 0.0001). Since the clinical presentation is nonspecific, specialized laboratory tests are necessary to make the diagnosis. As a result of our experience, we suggest an approach using serologic tests as a screening device.
Factors not significantly different in LD when compared to other pneumonias

“Viral-like” prodrome
Cigarette smoking
Compromised host
High fever
Abdominal pain
Diarrhea
Neurologic signs
Serum phosphate
Abnormal liver function test
Hematuria
Clinical Clues for Consideration of Legionnaires’ Disease

Hyponatremia (Serum Na \leq 130 \text{ meg/L})

- Lack of clinical response to penicillin, cephalosporin, and/or aminoglycoside therapy

- Gram stain of TTA specimen shows abundant neutrophils without bacteria
Clinical Manifestations Distinctive for Legionnaires’ Disease

**Epidemiologic**
- Receipt of prior antibiotics

**Symptoms**
- Diarrhea
- Neurologic, especially confusion

**Signs**
- Fever 39°C

**Laboratory**
- Hyponatremia
- Hepatic dysfunction
- Hematuria
Cluster of cases of pneumonia within a community
- no point source identified
- contaminated reservoir of water with presumed aerosol transmission

Cluster of cases of nosocomial pneumonia
- outbreak associated with aerosol transmission from contaminated reservoir
- ongoing endemic disease

Sporadic cases
LEGIONNAIRES’ DISEASE
(LEGIONELLA pneumophila)

There’s an Accurate & Easy Urine Test for It

100% SPECIFICITY
97.7% SENSITIVITY
Step 1: Obtain Sample
Step 2: Insert Swab
Step 3: Add Reagent
Step 4: View Result
### Laboratory Diagnosis of Legionella

<table>
<thead>
<tr>
<th>Test</th>
<th>Sensitivity</th>
<th>Specificity</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Culture</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Sputum*</td>
<td>80%</td>
<td>100%</td>
</tr>
<tr>
<td>Transtracheal aspirate</td>
<td>90%</td>
<td>100%</td>
</tr>
<tr>
<td>Blood</td>
<td>20%</td>
<td>100%</td>
</tr>
<tr>
<td><strong>Serology +</strong></td>
<td>40%-60%</td>
<td>96%-99%</td>
</tr>
<tr>
<td>Direct fluorescent antibody</td>
<td>50%-70%</td>
<td>96%-99%</td>
</tr>
<tr>
<td>Urinary antigen†</td>
<td>80%</td>
<td>100%</td>
</tr>
<tr>
<td>DNA probe</td>
<td>60%</td>
<td>95%-99%</td>
</tr>
</tbody>
</table>

* Use of three media: BCYE; BCYE plus polymyxin, anisomycin, and cefamandole; BCYE plus Polymyxin, anisomycin, vancomycin, and dyes. Acid wash is used for overgrowth of microflora.

† IgG and IgM antibody testing in both acute and convalescent sera.

‡ Serogroup 1 only.
<table>
<thead>
<tr>
<th>Gold Standard</th>
<th>No. of patients</th>
<th>Urine Antigen Positive</th>
<th>Sensitivity</th>
</tr>
</thead>
<tbody>
<tr>
<td>Blood culture</td>
<td>59</td>
<td>51</td>
<td>86.4% (51/59)</td>
</tr>
<tr>
<td>Pleural fluid culture</td>
<td>5</td>
<td>5</td>
<td>100% (5/5)</td>
</tr>
</tbody>
</table>
Management of Nonsevere Pneumonia in Military Trainees Using the Urinary Antigen Test for *Streptococcus pneumoniae*: An Innovative Approach to Targeted Therapy

Igor A. Guchev, Victor L. Yu, Alexander Sinopalnikov, Oleg I. Klochov, Roman S. Kozlov, Lenoid S. Stratchounski

*Clin Infect Dis*, June 2005
# ANTIBIOTIC THERAPY FOR LEGIONELLOSIS

<table>
<thead>
<tr>
<th>NAME</th>
<th>DOSE</th>
<th>DURATION</th>
<th>ROUTE</th>
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<tbody>
<tr>
<td><strong>Macrolide</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Azithromycin</td>
<td>500 mg</td>
<td>q 24 hours</td>
<td>po, iv</td>
</tr>
<tr>
<td>Clarithromycin</td>
<td>500 mg</td>
<td>q 12 hours</td>
<td>po, iv</td>
</tr>
<tr>
<td>Roxithromycin</td>
<td>300 mg</td>
<td>q 12 hours</td>
<td>po</td>
</tr>
<tr>
<td>Erythromycin</td>
<td>1 g</td>
<td>q 6 hours</td>
<td>iv</td>
</tr>
<tr>
<td></td>
<td>500 mg</td>
<td>q 6 hours</td>
<td>po</td>
</tr>
<tr>
<td><strong>Quinolones</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Levofloxacin</td>
<td>500 mg*</td>
<td>q 24 hours</td>
<td>po, iv</td>
</tr>
<tr>
<td>Ciprofloxacin</td>
<td>400 mg</td>
<td>q 8 hours</td>
<td>iv</td>
</tr>
<tr>
<td></td>
<td>750 mg</td>
<td>q 12 hours</td>
<td>po</td>
</tr>
<tr>
<td>Ofloxacin</td>
<td>400 mg</td>
<td>q 12 hours</td>
<td>po, iv</td>
</tr>
</tbody>
</table>
MYTH ON LEGIONNAIRES’ DISEASE

Showers colonized by *Legionella* transmit the microorganism
Home Sweet Home:

Potable Water
Isolation of *Legionella pneumophila* Serogroup 1 from the Environment of patients with Legionnaires’ Disease Serogroup 1

<table>
<thead>
<tr>
<th>Patient</th>
<th>Source</th>
<th>Pos. for <em>L. pneumophila</em></th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>Faucet</td>
<td>+</td>
</tr>
<tr>
<td>2</td>
<td>Right shower</td>
<td>-</td>
</tr>
<tr>
<td></td>
<td>Left shower</td>
<td>-</td>
</tr>
<tr>
<td></td>
<td>Faucet</td>
<td>-</td>
</tr>
<tr>
<td>3</td>
<td>Right shower</td>
<td>+</td>
</tr>
<tr>
<td></td>
<td>Left shower</td>
<td>-</td>
</tr>
<tr>
<td></td>
<td>Faucet</td>
<td>-</td>
</tr>
<tr>
<td>4</td>
<td>Right shower</td>
<td>-</td>
</tr>
<tr>
<td></td>
<td>Left shower</td>
<td>+</td>
</tr>
<tr>
<td></td>
<td>Faucet</td>
<td>+</td>
</tr>
<tr>
<td>5</td>
<td>Faucet</td>
<td>+</td>
</tr>
<tr>
<td>6</td>
<td>Faucet</td>
<td>+</td>
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</table>
## ENVIRONMENTAL SURVEY RESULTS

<table>
<thead>
<tr>
<th>SOURCE</th>
<th>NO. TESTED</th>
<th>NO. POSITIVE SITES</th>
<th></th>
<th></th>
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<tr>
<td></td>
<td></td>
<td>LDB</td>
<td>PPA</td>
<td></td>
</tr>
<tr>
<td>SHOWERS</td>
<td>15</td>
<td>9</td>
<td>0</td>
<td></td>
</tr>
<tr>
<td>FAUCETS</td>
<td>35</td>
<td>24</td>
<td>1</td>
<td></td>
</tr>
<tr>
<td>HOT WATER TANKS</td>
<td>3</td>
<td>3</td>
<td>1</td>
<td></td>
</tr>
</tbody>
</table>
Risk Factors for Legionnaires’ Disease

- Cigarette smoking – most prevalent
- Chronic obstructive pulmonary disease
- Corticosteroid administration
- Transplant recipient – most intense
UBIQUITOUSNESS OF LEGIONELLA PNEUMOPHILA IN THE WATER SUPPLY OF A HOSPITAL WITH ENDEMIC LEGIONNAIRES’ DISEASE

Janet Stout, M.S.,
Victor L. Yu, M.D.,
R. M. Vickers, B.S.,
Jeffrey Zuravleff, M.S.,
Michele Best, B.A.,
Arnold Brown, M.D.,
Robert B. Yee, Ph.D.,
and Robert Wadowsky, M.S.
Mode of transmission of Legionella is aspiration, not aerosolization.
Myth:

Cooling towers are a major source of Legionnaires’ disease
Why is Diarrhea associated with Legionnaires’ disease?
## Community-Acquired Pneumonia

### Microbiology of CAP

**“Typical” pathogens 40% to 60%**

- *Streptococcus pneumoniae* 15-25%
- *Haemophilis influenza* 2-10%
- *Moraxella catarrhalis* 0-50%

**“Atypical” pathogens 10% to 30%**

- *Mycoplasma pneumoniae* 1-10%
- *Chlamydophila pneumoniae* 5-15%
- *Legionella pneumophila* 0-15%

**Other Pathogens – 5% to 25%**

- Viruses
  - Influenza 2-10%
  - *Pneumocystis jiroveci* 0-4%
- *Mycobacterium tuberculosis* 0-4%
- Fungi (Histoplasmosis capsulatum, Coccidioides immitis)
  - Cryptococcus spp. 0-4%

**Unknown etiology** 30-60%
### Prospective Studies of Severe Community-Acquired Pneumonia Admitted to Intensive Care Units

<table>
<thead>
<tr>
<th>Author</th>
<th>Study Years</th>
<th>Site</th>
<th>N</th>
<th>S. pneumoniae</th>
<th>Legionella</th>
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<tr>
<td>Torres et al</td>
<td>1984-1987</td>
<td>Barcelona, Spain</td>
<td>92</td>
<td>First</td>
<td>Second</td>
</tr>
<tr>
<td>Pachon et al</td>
<td>1985-1987</td>
<td>Seville, Spain</td>
<td>67</td>
<td>First</td>
<td>Second</td>
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<tr>
<td>Fang et al</td>
<td>1986-1987</td>
<td>Pittsburgh, PA</td>
<td>44</td>
<td>Second</td>
<td>First</td>
</tr>
<tr>
<td>Falco et al</td>
<td>1988-1989</td>
<td>Barcelona, Spain</td>
<td>104</td>
<td>First</td>
<td>Second</td>
</tr>
<tr>
<td>Sorensen et al</td>
<td>Linkoping,</td>
<td>Sweden</td>
<td>36</td>
<td>First</td>
<td>Second</td>
</tr>
<tr>
<td>Potgieter et al</td>
<td>1987-1989</td>
<td>Cape Town, S. Africa</td>
<td>95</td>
<td>First</td>
<td>Fifth</td>
</tr>
<tr>
<td>Rello et al</td>
<td>1988-1990</td>
<td>Barcelona, Spain</td>
<td>58</td>
<td>First</td>
<td>Second</td>
</tr>
<tr>
<td>Olaechea et al</td>
<td>1991-1992</td>
<td>Vizcaya, Spain</td>
<td>262</td>
<td>First</td>
<td>Second</td>
</tr>
</tbody>
</table>

Vergis E. *Eur J Clin Microbiol Infect Dis*; 18:847-851
Community-acquired Legionella pneumonia, new insights from the German CAPNETZ Study:

Legionnaires’ diagnosed in 3.8% of sporadic community-acquired pneumonia in ambulatory patients and 3.7% of hospitalized patients. 10% were diagnosed with PCR and culture but were negative by urinary antigen test. An unacceptably high rate of discordant therapy was found.

QUESTION

How to make Holy Water?
ANSWER

Boil the Hell out of it!
The solution for emerging antimicrobial resistance is to minimize broad spectrum antibiotic therapy and to use narrow spectrum/pathogen-directed therapy.
Figure 3. Algorithm Depiction of Patient Flow in ED

Patient with CAP in the ED – Consent form signed

Experimental

Control

Targeted Strategy
Gram stain and Sputum Culture
Urinary Antigen for Legionella
*Streptococcus pneumoniae*
Blood Culture, if admitted
FilmArray, Xpert

Targeted Strategy

*Streptococcus pneumoniae*
Gram stain, urinary antigen +
Penicillin compound

*Legionella*
Urinary Antigen +
Azithromycin

Influenza
Viral test +

No Test Positive
ATS-IDSA Guidelines

Antiviral agents
No antibacterial agent conditions

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3 Intravenous penicillin, oral amoxicillin, oral penicillin VK, oral amoxicillin-clavulanate, if penicillin allergy, first or second generation cephalosporins. If type IV allergy, levofloxacin.

2 Respiratory tract quinolone as an alternate therapy.

Oseltamivir, Zanamavir-if onset symptoms less than 72 hours

Symptoms > 72 hours. PSI Class I, II, all other diagnostic tests negative, Procalcitonin test negative (see Figure 5)
Figure 5. Algorithmic Depiction of POC Testing for Influenza and Impact on Therapy
VA lapses cited in fatal Legionnaires’ disease outbreak

21 cases of hospital-acquired Legionnaires’ disease with 5 deaths
Seek and Ye Shall Find
www.legionella.org