

Update on Clinical Management of Legionnaires' Disease

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6/12/2011

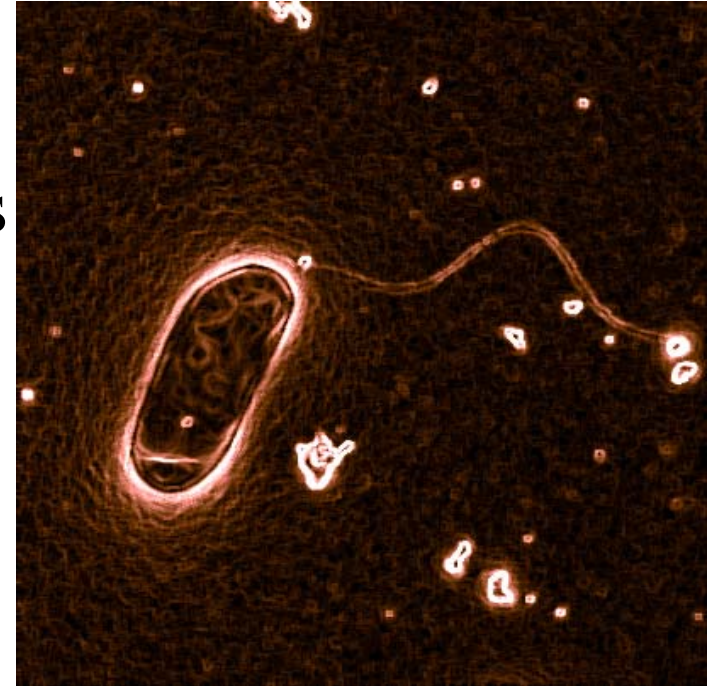
Background

- July 21st, 1976: First Discovered at the American Legion Convention.
- *Legionella pneumophila*: the Legions; “lung-loving” as it infects alveolar macrophages.



Basic information

- Family Legionellaceae
- Genus Legionella
 - At least 50 species with 70 serogroups
 - 1/2 of the species are implicated in human disease
- Gram-negative rod that is slender and pleomorphic
- Facultative intracellular parasite



•0.3 – 0.9 μm in width and
2 – 3 μm in length.

- Inhalation or aspiration of warm , contaminated water
- *L. pneumophila* cause most of the infections (about 85%).
 - Serogroup 1 is the most commonly isolated one

Places that have been linked to
disease transmission

Cooling Towers



Showers



Storage Tanks



Spa pools

Others

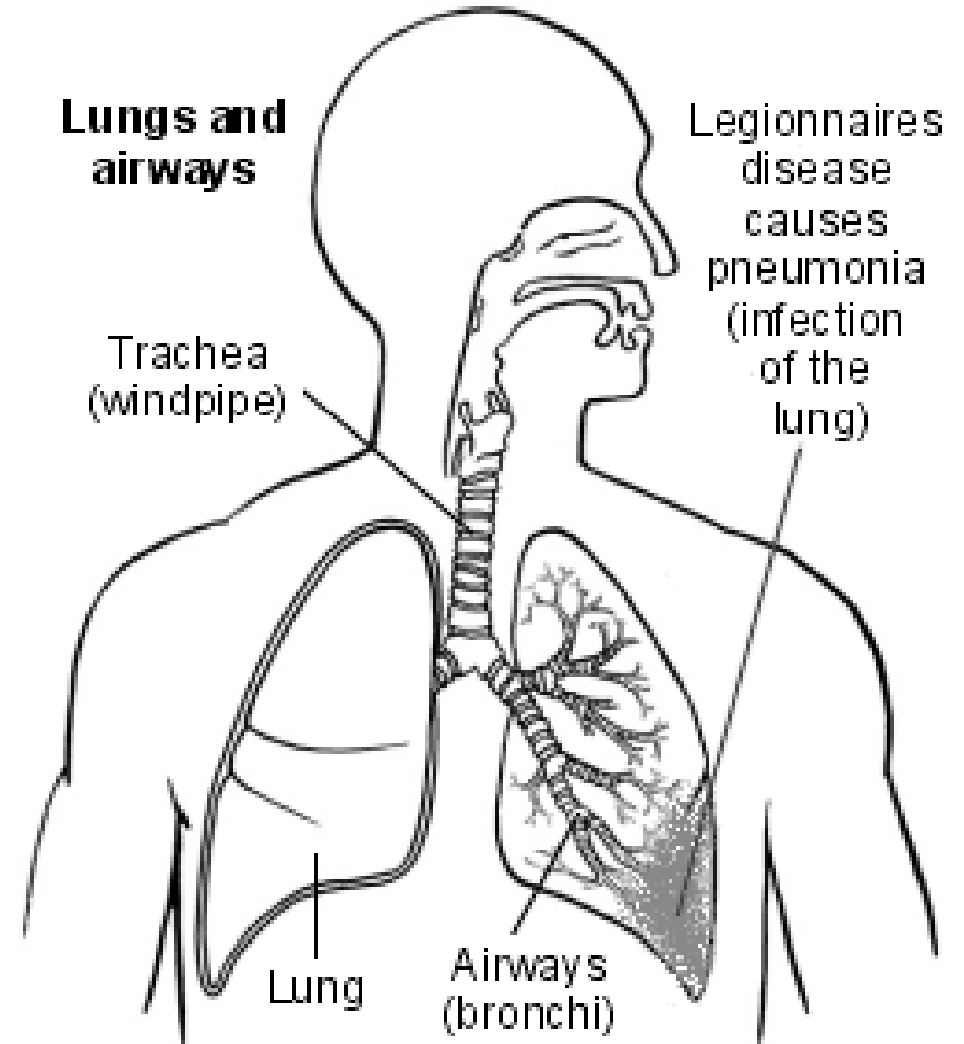
- Whirlpool baths
- Mist machines
- Humidifiers
- Respiratory therapy equipment

Epidemiology

- Most epidemics occur in late summer and autumn where it proliferates in water reservoirs during these warm months
- Elderly persons, greater than 50, alcoholic, heavy smokers and the immunocompromised (decreased cellular immunity) are at a higher risk of becoming infected
- Person to person transmission have not been found

Clinical Diseases

- Two forms of Symptomatic infections :
 - Pontiac fever
 - Influenza-like illness
 - Legionnaires' Disease
 - Severe form of pneumonia



Pontiac Fever

- Named after an epidemic in Pontiac, Michigan in 1968
- Epidemic
- Self-limiting disease with symptoms of fever, chill, muscle pain, general body weakness and malaise, headache,
- Incubation period 1-2 days
- No evidence of pneumonia
- Symptoms develop over a 12 hour period and then stick around for 2 to 5 days, then spontaneously disappears without antibiotic treatment.
- There have been no deaths reported
- Hypersensitivity reaction maybe the cause of pathology

Legionnaires' disease

- Pneumonia. May have multi-organ involvement involving the GI tract, CNS, liver, and kidneys.
- Epidemic/sporadic
- Community/nosocomial acquired
- Incubates for 2 to 10 days followed by symptoms of fever, chills, dry nonproductive cough, headache
- Pulmonary function deteriorates in patients with no treatment
- More severe; causes morbidity and death unless treated properly
 - Mortality rate is 15-20%

Clinical Features of Legionnaire's Disease

Epidemiologic Reviews, 1991; 13:329 and Chest, 1994; 105:1817

- Headache
- Fever (maybe absent)
- Myalgia
- Cough, often no sputum
- Dyspnea => respiratory failure
- Pleuritic chest pain
- Extrapulmonary manifestations
 - Watery Diarrhea / abdominal symptoms
 - Delirium / CNS

Other features that may be present

- Relative bradycardia
- Hypotension
- Microscopic hematuria, proteinuria
- Acute renal failure
- Hyponatremia
- Hypophosphatemia
- Deranged liver function test
- Increased CPK

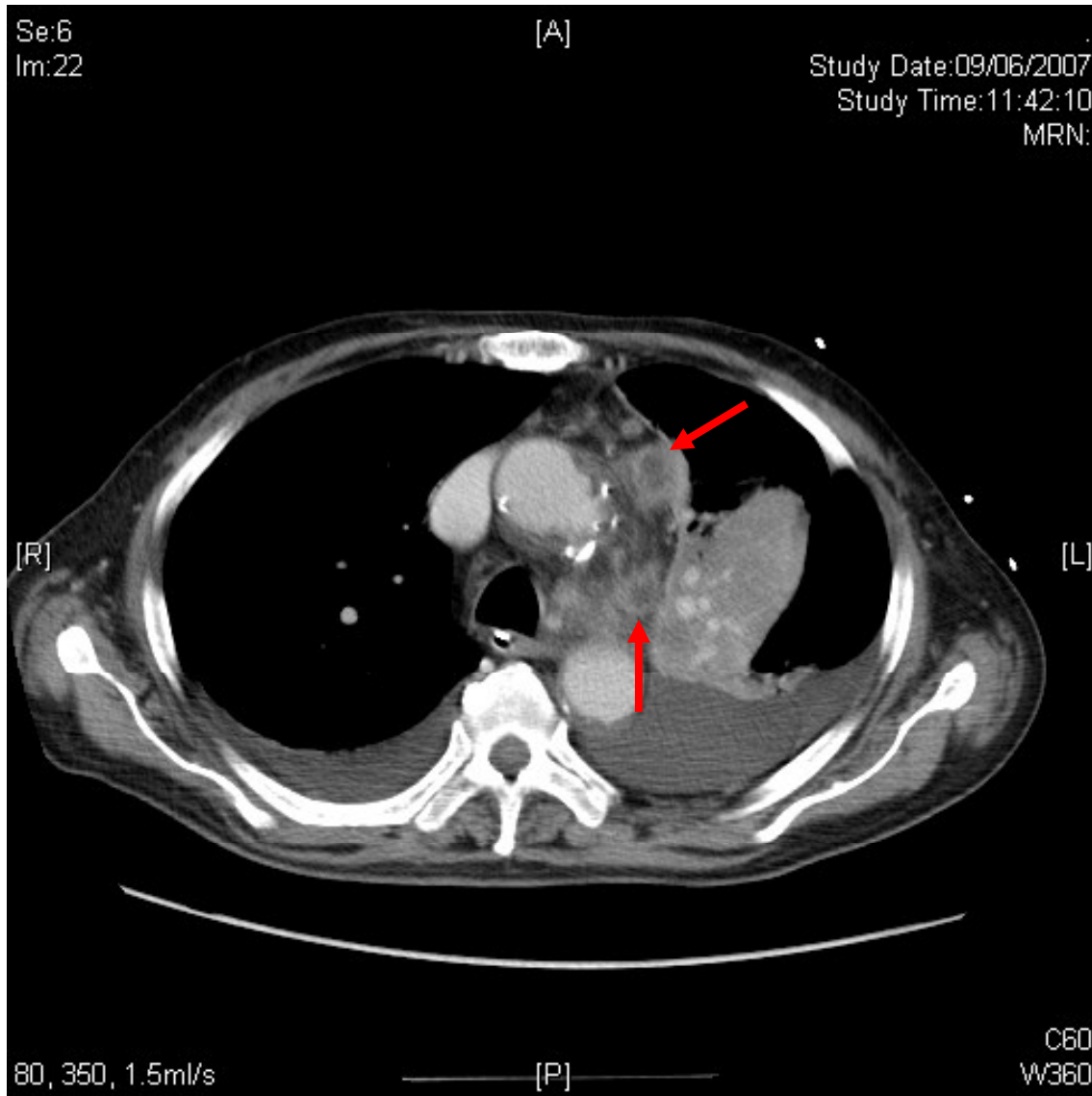
Chest radiograph findings

- Patterns: lobar consolidation, patchy or interstitial infiltrate
- Pleural effusion (1/3)
- Lower lobe usually
- Cavity and abscess formation are rare
- Improvement on CXR can lag behind the clinical improvement for 5-7 days. The abnormalities on CXR can take up to 4 months to resolve completely.

Chest X Ray of a patient with Legionnaires' Disease



CT Thorax of a patient with Legionnaires' Disease



- Left upper lobe and left lower lobe collapse consolidation.
- Multiple enlarged and necrotic mediastinal lymph nodes mainly at prevascular, aortopulmonary window and left hilum. (**mimic TB**)
- Bilateral pleural effusions of watery homogeneous density, L>R.

Extrapulmonary diseases

- Prosthetic valve endocarditis
- Sternal wound infections
- Sinusitis
- Myocarditis
- Pericarditis
- Peritonitis
- Dialysis shunt infections
- Abscesses
- Cellulitis

Laboratory Diagnosis

- Culture (sputum, BAL fluid, pleural fluid)
 - Require L-cysteine and iron salts
 - Use **BCYE** (buffered charcoal yeast extract agar)
 - Grown aerobically or grow using 3-5% CO₂ at 35° for 3 to 5 days
- Identification
 - Specific staining with fluorescein –labelled antibodies confirm the identity



Laboratory diagnosis

- Urinary antigen test
 - EIAs: Enzyme-linked immunoassays
 - Detect soluble lipopolysaccharide antigens
 - High sensitivity with serogroup 1: 60% to >90%. Other serogroups and species show a lower sensitivity
 - Specificity: ~95%
 - Urinary Ag becomes positive in 80% of patients on days 1-3 of clinical illness (**need to repeat test if highly suspected**)
 - Antigens persists in the urine of treated patients
 - 50% are positive after 1 month
 - 25% are positive after 2 months
 - Immunosuppressed patients are positive for up to a year

Workup for Community Acquired Pneumonia

Table 5. Clinical indications for more extensive diagnostic testing.

Indication	Blood culture	Sputum culture	<i>Legionella</i> UAT	Pneumococcal UAT	Other
Intensive care unit admission/ severe CAP	X	X	X	X	X ^a
Failure of outpatient antibiotic therapy		X	X	X	
Cavitary infiltrates	X	X			X ^b
Leukopenia	X			X	
Active alcohol abuse	X	X	X	X	
Chronic severe liver disease	X			X	
Severe obstructive/structural lung disease		X			
Asplenia (anatomic or functional)	X			X	
Recent travel (within past 2 weeks)			X		X ^c
Positive <i>Legionella</i> UAT result		X ^d	NA		
Positive pneumococcal UAT result	X	X		NA	
Pleural effusion	X	X	X	X	X ^e

NOTE. NA, not applicable; UAT, urinary antigen test.

^a Endotracheal aspirate if intubated, possibly bronchoscopy or nonbronchoscopic bronchoalveolar lavage.

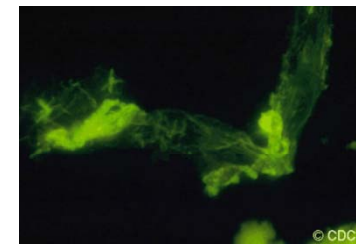
^b Fungal and tuberculosis cultures.

^c See table 8 for details.

^d Special media for *Legionella*.

^e Thoracentesis and pleural fluid cultures.

Lab diagnosis



- Direct fluorescent antibody staining of sputum
 - Sensitivity increased for samples from lower respiratory tract
- Paired Serology (for *L. pneumophila* serogroup 1 and non-serogroup 1)
 - Diagnosed with IFA (indirect fluorescent antibody) to test for a serologic response to infection
 - A 4-fold or greater increase of Ab level to 1: 128 or greater is considered diagnostic
 - In most cases a 4-fold ↑ in Ab titer is detected within 3-4 wks
 - **Up to 6 months may be required for seroconversion.**
 - Because high titers can persist, one positive test cannot be used to define acute disease
- PCR (sputum or NP swab) for *L pneumophila*:
 - New and fast
 - Highly specific and sensitive

Antibiotics

- Respiratory fluoroquinolone or macrolide (IV first for ill case)
 - Levofloxacin 750mg PO or IV once daily
 - Moxifloxacin 400mg PO or IV once daily
 - Azithromycin 500mg PO or IV once daily
- Total treatment duration: 7-10 days (may extend to 21 days for immunocompromised patient).
- For severe disease, consider adding rifampicin 300mg PO or IV bd
 - Efficacy of combination therapy not proven
- Doxycycline: Good activity in vitro, good activity in animal model. A better drug for Legionella than commonly thought

Thank you