Legionella Infections

Chapter 164 | Part 5: Infectious Diseases

KEY CLINICAL POINTS

1. Legionella species cause two primary diseases: Legionnaires' disease (severe pneumonia) and Pontiac fever (mild, self-limited illness).
2. L. pneumophila serotype 1 is responsible for >80% of Legionnaires' disease cases.
3. Diarrhea, hyponatremia, and confusion are strong predictors of Legionella pneumonia compared to other atypical pneumonias.
4. Urinary antigen testing detects only L. pneumophila serotype 1 (sensitivity ~70%, specificity high).
5. Culture on BCYE agar is the gold standard but requires 3-5 days for growth; essential for outbreak investigation.
6. First-line treatment for Legionnaires' includes macrolides (azithromycin, clarithromycin) or fluoroquinolones (levofloxacin, moxifloxacin, ciprofloxacin).
7. Pontiac fever does not require antibiotics and resolves spontaneously.
8. Outbreaks are linked to water sources such as cooling towers, fountains, and spa systems.
9. Risk factors include age >40 years, male sex, smoking, and immunocompromise.
10. Case-fatality rate is ~10% for Legionnaires' disease; 30-50% in immunocompromised patients or those with severe lung disease.

1. DEFINITION & OVERVIEW

Legionella species cause two distinct clinical syndromes:

- **Legionnaires' disease**: Severe pneumonia with systemic symptoms (fever, confusion, diarrhea)
- **Pontiac fever**: Mild, self-limited influenza-like illness without pneumonia
- **Extrapulmonary disease**: Rare presentations including endocarditis and septic arthritis

Definition (Harrison's 22e): *Legionella species are responsible for >50% of all waterborne outbreaks and >10% of disease related to drinking water in the United States.*

1.1 Disease Classification

- **Legionnaires' disease**: Severe pneumonia with systemic symptoms
- **Pontiac fever**: Self-limited influenza-like illness without pneumonia
- **Extrapulmonary manifestations**:
  - Skin/soft tissue infections (cellulitis-like)
  - Endocarditis (prosthetic valve)
  - Myocarditis/pericarditis
  - Septic arthritis/sinusitis

2. EPIDEMIOLOGY

- **Incidence**: 50,000-70,000 cases of Legionnaires' disease annually in the US
- **Trends**: Significant increase noted since 2014 (Figure 164-1)
- **Dominant Strain**: L. pneumophila serotype 1 accounts for >80% of human cases
- **Seasonality**: Increased incidence during summer/fall due to higher temperature and humidity

Table 164-1 highlights the variety of common-source outbreaks (2012-2022) involving sites like hotels, hospitals, and communities. Sources include potable water, fountains, spa systems, cooling towers, and hot-tub displays.

2.1 Risk Factors

- **Age**: >40 years (highest risk for complications)
- **Sex**: Male sex (3x higher risk than females)
- **Smoking**: Dose-dependent risk; impairs airway defenses
- **Chronic Disease**: COPD, emphysema, renal/hepatic/cardic disease
- **Immunocompromise**:
  - Cancer patients
  - Solid organ transplant recipients
  - Glucocorticoid use (prednisone)
  - TNF inhibitor therapy
- **Genetics**: Polymorphisms in innate immune genes

3. ETIOLOGY & PATHOPHYSIOLOGY

- **Microbiology**: Aerobic gram-negative bacteria; found in aquatic environments and soil
- **Life Cycle**:
  - Replicative phase (nutrient-rich/protozoa)
  - Noninfective transmissive phase (resource scarcity)
- **Transmission**: Inhalation or aspiration of aerosolized particles (<10 μm diameter)
- **Pathogenesis**:
  - Phagocytosis by alveolar macrophages
  - Evasion of lysosomal degradation
  - Intracellular replication in human cells
  - Immune response involving interferon γ and neutrophil recruitment

3.1 Transmission Dynamics

- **Primary Routes**:
  - Domestic: Showerheads/sinks
  - Community: Cooling towers, fountains
  - Healthcare: Facility water systems
- **Attack Rates**:
  - Legionnaires' disease: ~5% among exposed individuals
  - Pontiac fever: ~90% among exposed individuals

4. CLINICAL FEATURES

Table 164-2 compares the clinical profiles of Legionnaires' disease and Pontiac fever:

- **Legionnaires' Disease**:
  - Incubation: 2–10 days
  - Symptoms: Fever, confusion, diarrhea, myalgias, shortness of breath, abdominal or chest pain, cough, sputum production
  - Severity: >90% hospitalization rate; 30-50% ICU admission; ~10% case-fatality
- **Pontiac Fever**:
  - Incubation: 24–72 h
  - Symptoms: Fever, headache, myalgias, nausea/vomiting, fatigue, vertigo
  - Severity: <1% hospitalization rate; extremely low ICU/fatality rates

4.1 Clinical Indicators

- **Key Predictors**: Presence of diarrhea, hyponatremia, and confusion strongly suggests Legionella over other atypical pneumonias
- **Radiographic Findings**:
  - CXR: Consolidation (often lower lobe, but can be upper lobe in immunocompromised hosts)
  - CT: Airspace disease with ground-glass opacities; may show nodules or cavitation in immunocompromised patients (Figures 3, 4, 5)

5. DIFFERENTIAL DIAGNOSIS

- **Primary Differentials**:
  - Mycoplasma pneumoniae
  - Chlamydia pneumoniae
  - Pneumocystis jirovecii (in immunocompromised hosts)
- **Diagnostic Challenges**:
  - Non-specific initial symptoms
  - Overlap with other atypical pneumonias
  - Limited rapid testing in primary care

5.1 CDC Reporting Criteria

- **Presumptive case**: Legionnaires' disease developing after ≥10 days of hospitalization
- **Possible case**: Legionnaires' disease with <10 days of hospitalization prior to symptom onset
- **Outbreak Investigation Required**:
  - Any presumptive case in a healthcare facility
  - Two or more possible cases within 12 months

6. INVESTIGATIONS & DIAGNOSIS

1. **Radiology**:
   - CXR: Identify consolidation/infiltrates (e.g., Figure 3, 4)

- CT: Assess extent of disease and identify complications like cavitation or nodules (Figure 5)

2. **Culture**:
   - Method: BCYE agar
   - Timing: 3-5 days for growth
   - Role: Gold standard; essential for serotyping and outbreak investigation3. **Urinary Antigen**:
   - Target: L. pneumophila serotype 1 only
   - Performance: Sensitivity ~70%, high specificity
4. **Molecular Testing**:
   - Method: PCR (e.g., on bronchoalveolar lavage fluid)
   - Role: Useful for non-serotype 1 strains and extrapulmonary disease

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7. MANAGEMENT & TREATMENT

1. **Pontiac Fever**:
   - Treatment: Supportive care only (no antibiotics required)
2. **Legionnaires' Disease**:
   - First-line options: Macrolides or Fluoroquinolones
   - **Macrolide Options** (Table 164-3):
     - Azithromycin: 500 mg PO once daily (day 1), followed by 250 mg PO once daily for ≥4 days
     - Clarithromycin: 400 mg PO daily
   - **Fluoroquinolone Options** (Table 164-3):
     - Levofloxacin: 750 mg PO once daily
     - Ciprofloxacin: 500 mg PO twice daily
     - Moxifloxacin: 400 mg PO once daily
3. **Duration**:
   - 5-10 days for stable patients
4. **Special Populations**:
   - Immunocompromised: May require longer treatment duration
   - Extrapulmonary disease: Same antimicrobial regimens as pneumonia

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8. PROGNOSIS & COMPLICATIONS

- **Case-fatality rate**:
  - Overall: ~10%
  - Immunocompromised/Severe Lung Disease: 30-50%
- **Clinical Complications**:
  - Acute respiratory failure
  - Septic shock
  - Multiorgan failure
- **Mortality Risk Factors**:
  - Age >65 years
  - Chronic lung disease

- Immunocompromise
- Delayed diagnosis/treatment

9. SPECIAL CONSIDERATIONS

- **Outbreak Management**:
  - Immediate investigation for presumptive healthcare-associated cases
  - Environmental sampling of water systems (cooling towers, showers)
  - Molecular typing to identify common-source outbreaks
  - Public health interventions: chlorination, temperature control, biofilm removal
- **Prevention Strategies**:
  - Regular maintenance of building water systems
  - Avoidance of stagnant water in unused plumbing
  - Use of point-of-use filters in high-risk facilities

10. KEY PEARLS & CLINICAL TRAPS

- **Diagnostic Clues**:
  - Presence of diarrhea and confusion are strong indicators for Legionella
  - Urinalysis is insufficient for non-serotype 1 strains
- **Clinical Traps**:
  - Delayed diagnosis due to non-specific symptoms
  - Over-reliance on urinary antigen without culture confirmation
  - Underestimating risk in immunocompromised patients

REFERENCE TABLES

TABLE 164-1

Examples of Legionella Common Source Outbreaks, Indicating the Wide Variety of Sources and Cases a SITE Hotel b...

SITE	YEAR	ORGANISMa	REPORTED SOURCE(S)	CASES
Hotelb	2012	L. pneumophila serotype 1	Potable water, fountain, spa	85 (29 suspect)
	2012	L. pneumophila	Potable water	
Communityd	2014	L. pneumophila serotype 1	Cooling tower	334 cases
	2014-15	L. pneumophila	Potable water, household, cooling towers	
Long-term care facilityf	2015	L. pneumophila	Potable water	74 cases
	2015	L. pneumophila	Hotel cooling towers	

SITE	YEAR	ORGANISMa	REPORTED SOURCE(S)	CASES
Hospitalh	2018	L. pneumophila serotype 1	Potable water, showers	13 cases
	2019	L. pneumophila	Fountain	
Communityj	2019	L. pnuemophilak	Hot-tub display	141 cases
	2022	L. pneumophila serotype 1	Cooling tower	

TABLE 164-2

Clinical and Epidemiologic Features of Legionella Pneumonia (Legionnaires' Disease) and Pontiac Fever FEATURE...

FEATURE	LEGIONELLA PNEUMONIA	PONTIAC FEVER
Incubation period	2–10 daysa	24–72 h
	Legionella infection	
Common symptoms	Abdominal or chest pain Anorexia Cough, sputum production Confusionb Diarrheab Fatigue Fever/chills Headache Myalgias Nausea/vomitingb Shortness of breath	Cough Diarrhea Fatigue Fever/chills Headache Myalgias Nausea/vomiting Vertigo
	Age >40 years Male Smoker Immunosuppressed host Neurologic disease Chronic lung disease Organ dysfunction/ chronic illness	
Attack rate among exposed individuals	~5%c	~90%
	>90%	
ICU admission rate	30–50%	Extremely low
	Antibiotics (macrolide or fluoroquinolone)	
Case-fatality rated	10%	Extremely low

TABLE 164-3

Legionella Treatment Options DISEASE Pontiac fever Legionella pneumonia

DISEASE	DISEASE SEVERITY	
	MILD	MODERATE/SEVEREa,b
Pontiac fever	None	N/A
	A) Fluoroquinolone: Levofloxacin, 750 mg PO once daily or Ciprofloxacin, 500 mg PO twice daily or Moxifloxacin, 400 mg PO once daily or B) Macrolide: Azithromycin, 500 mg PO once daily (day 1), followed by 250 mg PO once daily (for minimum of 4 days) or Clarithromycin, 400 mg PO daily	