Legionnaires' disease

Microorganism

- A bacterium, ***Legionella pneumophila*** , an intracellular Gram-negative bacillus. Sixteen serogroups have been identified, with **serogroup 1** accounting for over 85% of cases
- Other *Legionella* species such as *L. longbeachae, L. micdadei, L. anisa,* and *L. dumofii,* may cause infections, mainly in immunocompromised individuals.
- *Legionella* colonizes aquatic environments, including domestic hot water systems, cooling towers, and recreational water facilities (e.g., spas, jacuzzis). Optimal growth occurs between 25°C and 45°C, with reduced growth between 45°C and 60°C. The bacteria do not survive temperatures above **60°C**.
- Laboratory culture requires a specific medium: BCYE (buffered charcoal yeast extract)

Contamination

- Transmission occurs through the **inhalation of contaminated water aerosols**
- There is no **human-to-human transmission**

Contributing factors

• Age > 65 years • Smoking • Chronic respiratory diseases • Diabetes	• Hematologic malignancies or cancer • Corticosteroid therapy and other immunosuppressants • Other causes of immunosuppression

Incubation

- The incubation period is typically **2 to 10 days, but may extend up** to 21 days

Clinical manifestations

- Legionella can cause two types of infection: Legionnaires' disease and Pontiac fever. Both presentations are nonspecific.

Legionaires'disease	**Clinical features**	• Progressive onset pneumonia • Frequent extrapulmonary manifestations: - Neurological: confusion - Renal: acute kidney injury - Gastrointestinal: diarrhea… - Myalgia • Travel history, aerosol exposure, and failure of empiric β-lactam therapy may suggest legionellosis
	Imaging	• Multifocal alveolar consolidations, often bilateral, rarely cavitary, and may be accompanied by pleural effusion
	Biology	Nonspecific abnormalities may suggest legionellosis: • Hyponatremia • Elevated liver enzymes • Elevated creatine phosphokinase (CPK) • Elevated creatinine

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Diagnosis

- ***Diagnostic methods***

	Benefits	Boundaries
Urinary antigen test	• Rapid • Noninvasive • High sensitivity for serogroup 1 (> PCR) • Unaffected by antibiotic therapy	• Detects serogroup 1 only • Prolonged antigen excretion (up to 6 months)
PCR	• Detects *L. peumophila* serogroups and other *Legionella* species • High sensitivity • Unaffected by antibiotic therapy • Depending on the technique, simultaneous detection of other microorganisms is possible • Useful for outbreak investigation	• Requires invasive respiratory sampling • May take several hours, depending on the techniques
Culture	• Allows bacterial isolation for - Antibiotic susceptibility testing - Epidemiological analysis • Detects all Lp serogroups and all *Legionella* species	• Time-consuming • Low sensitivity
Serology	• Useful for epidemiological surveys and retrospective diagnosis	• Requires two samples taken 4 weeks apart

- ***Diagnostic Strategy***
  - **First-line tests: Urinary antigen test or PCR**
    →PCR may be preferred in severe cases (in intensive care) or immunocompromised patients.
  - If legionellosis is strongly suspected and the initial test is negative, the other method should be performed.
  - In cases of positive urinary antigen or PCR, the following should be **systematically** performed:
    o Culture of a respiratory sample
    o Submission of the sample and/or bacterial strain to the National reference Center (CNR)
- Legionnaires' disease is **notifiable.**

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Treatment

- ***Indications and duration***

Non-severe cases

Macrolide monotherapy

8 to 14 days [a]

Severe cases and immunocompromised patients

Fluoroquinolone monotherapy

21 days

OR

Combination of 2 antimicrobials from the following classes:
- Fluoroquinolones
- Macrolides
- Rifampicin

21 days [b]

[a] Except azithromycin: 5 days; [b] Except azithromycin: 10 days

- ***Molecules and dosages***

Classes	Molecules	Dosages	Per Os	IV
Macrolides and related compounds	**Azithromycin**	500 mg once daily	X	
	Clarithromycin	500 mg twice daily	X	
	Roxithromycin	150 mg twice daily	X	
	Josamycin	1 g twice daily	X	
	Spiramycin	3 million IU three times daily [a]	X	X
	Erythromycin [b]	1 g three times daily	X	
		1 g three to four times daily		X
Fluoroquinolones	**Levofloxacin**	500 mg once or twice daily	X	X [c]
	Ofloxacin	200 to 400 mg twice daily [d]	X	X [c]
	Ciprofloxacin	500 mg to 750 mg twice daily	X	
		400 mg two to three times daily		X [c]
Rifampicin		20 to 30 mg/kg/day in 2 doses	X	X

[a] Oral spiramycin can be administered in 2 doses per day
[b] Primarily, if other macrolides are unavailable, notably spiramycin for intravenous use
[c] Equivalent oral and IV bioavailability
[d] Oral or IV ofloxacin can be administered in 2 doses per day

Follow up

- Follow-up is based on clinical improvement in all cases
- In severe cases requiring intensive care, iterative PCR on respiratory samples may be considered

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