



Legionnaires' Disease

Beta-lactams do not touch it · and a negative urine antigen excludes nothing

Ceftriaxone alone is no therapy
the atypical agent IS the cover

△ THE THREE THAT CARRY THE PAGE

△ A BETA-LACTAM IS NOT TREATING THIS

Legionella replicates INSIDE alveolar macrophages, and beta-lactams do not reach that compartment. **Ceftriaxone, pip-tazo, cefepime, meropenem and aminoglycosides are all inactive in practice.** Empiric inpatient CAP is ceftriaxone **plus** azithromycin, and the **second drug is the only one covering this** -so when azithromycin is held for a borderline QTc, or the team "narrows" to ceftriaxone on day 2, **the cover disappears silently.** △ **Apparent beta-lactam failure in CAP is itself a clue:** add a fluoroquinolone or macrolide, do not escalate the beta-lactam.

△ A NEGATIVE URINE ANTIGEN EXCLUDES NOTHING

It detects *L. pneumophila* SEROGROUP 1 ONLY, which is **50-80%** of cases, at a sensitivity of **70-80%** (specificity > 99%). **Used as the only test it misses on the order of 20-50% of cases.** Every other serogroup and species is invisible to it. **This is the commonest error on this diagnosis:** "Legionella negative" goes in the chart, the azithromycin is stopped, and the patient is left on a beta-lactam alone. **If suspicion persists, send a lower respiratory PCR or culture.**

REPORT IT, AND SEND A CULTURE ANYWAY

Legionnaires' disease AND Pontiac fever are notifiable, usually within 1-7 days, and it is the step teams skip. **Reporting triggers the environmental investigation that shuts down the water source**, and one case is often how a cluster is first found. **Send a culture even when the antigen has already made the diagnosis** -the isolate is what lets public health match the strain to a building. △ **Onset ≥ 48 h after admission: tell infection prevention today**, because other inpatients are still showering in that water.

WHO TO TEST, AND WITH WHAT *send the urine antigen AND a lower respiratory specimen, together -they fail in opposite directions*

Test	What it is for, and where it fails
△ Who to test	Testing every CAP is low yield. Test in SEVERE CAP, especially ICU · failure to improve on a beta-lactam · exposure (hotel, cruise, hot tub, outbreak) · onset ≥ 48 h after admission · immunocompromised
Urine antigen order it now	Positive as early as 1 day after onset , so it is the test that changes management today. △ Stays positive for WEEKS and is NOT blunted by antibiotics - unlike blood cultures, you lose nothing by treating first. The catch: a positive can reflect infection from weeks or months ago. Serogroup 1 only
△ Culture BCYE agar	Needs buffered charcoal yeast extract (BCYE) agar with L-cysteine. It will not grow on routine media , so the lab must be TOLD you suspect it or the plate is never set up and the culture reports "no growth". The only test yielding an isolate , which is what makes source-tracing possible
PCR	Sensitivity exceeds culture , specificity > 99%, results in hours. Detects the species and serogroups the urine antigen cannot , so this is what rescues the serogroup-1 blind spot. Availability varies by institution -know yours before 2am
Serology	Needs a 4-fold rise over weeks. Retrospective and epidemiological only -a single acute titer is uninterpretable and the convalescent sample returns long after discharge. Do not order it to make a treatment decision
Gram stain · imaging	Abundant neutrophils with NO visible organisms is the classic pattern, because Legionella stains poorly. Useful nudge, never a diagnosis. No radiographic pattern is specific , and △ worsening films in the first days of correct treatment are EXPECTED -follow fever, oxygen and mentation, or you will abandon a working antibiotic. Resolution takes weeks to months

TREATMENT

Point	Regimen, and what to know
First-line	Levofloxacin 750 mg IV/PO daily (500 mg is an accepted alternative with a longer course) · moxifloxacin 400 mg daily (not renally dosed, handy in AKI, but poor urinary levels) · azithromycin 500 mg IV/PO daily. Start IV in severe disease -a vomited dose is no dose. Levofloxacin's oral bioavailability is excellent, so IV to PO needs no dose change. Doxycycline 100 mg BID only for mild outpatient disease
△ Fluoroquinolone or macrolide? the evidence disagrees	Kato (J Infect Chemother 2021; 5 RCTs + 12 retrospective) found mortality OR 0.59, 95% CI 0.35-0.98 favoring fluoroquinolones with shorter stay - but in the levofloxacin subgroup only length of stay improved, mortality did not differ. Jasper (Clin Infect Dis 2021; 21 studies, 3,525 patients) found 6.9% vs 7.4%, OR 0.94, 95% CI 0.71-1.25 -no difference. Either is first-line; choose on QT, interactions and pregnancy. △ What is NOT optional is starting one early -delay in starting an active agent, not the class you picked, is what tracks with worse outcomes
Duration	5-10 days if immunocompetent and responding (azithromycin at the short end , since its long intracellular half-life keeps drug at the site after the last dose). 7-10 days in severe disease. △ 14-21 days if IMMUNOCOMPROMISED -relapse after a short course is the specific failure mode, because clearing an intracellular pathogen needs the cell-mediated immunity they lack. ≥ 21 days with cavitation, abscess, empyema or extrapulmonary disease
Complications · steroids	△ Rhabdomyolysis and AKI -send a CK if the creatinine is rising, or you miss a treatable driver. Hyponatremia from SIADH. Less often myocarditis, encephalitis, pancreatitis, DIC. △ Steroids have NO Legionella-specific indication -treat by severe-CAP criteria only, noting chronic steroids are themselves a major risk factor

△ THE CLASSIC CLUES · AND WHERE IT COMES FROM

△ EVERY CLASSIC FEATURE IS SOFT

Hyponatremia (SIADH, the most reproducible clue), **diarrhea** (a quarter to half of cases), **transaminitis** (~2× normal), **hypophosphatemia**, **confusion out of proportion to hypoxemia**, high fever with rigors. Each is commoner than in pneumococcal CAP, but none is specific enough to rule in, and absence rules nothing out. **Use the cluster to trigger testing, never to replace it.** △ **Relative bradycardia (Faget sign) is OVEREMPHASIZED** -expect HR to rise ~10 bpm per 1°F, so **102°F → 110, 103 → 120, 104 → 130, 105 → 140, 106 → 150;** under that is relative bradycardia, **but only if age ≥ 13, temp 102-106°F, pulse and temp taken together, sinus rhythm, no beta-blocker, pacemaker or heart block.** Ignore those and you are describing a rate-controlled patient.

THE EXPOSURE HISTORY, WITH DATES

Aerosolized fresh water: building plumbing and showers, **cooling towers** (the classic community outbreak, clustered around one building), **hot tubs and decorative fountains**, and **hospital water systems.** Infection follows aerosol inhalation or aspiration of colonized water. △ *L. longbeachae* comes from **POTTING SOIL and compost, not water** (major in Australia and New Zealand) and is **invisible to the urine antigen** -gardening plus a negative antigen is exactly when you need PCR or culture. **Incubation 2-14 days, usually 5-6**, so **record dates, not just places:** that window is what public health uses to identify the building. **Person-to-person spread essentially does not occur** -standard precautions only.

LEGIONNAIRES' DISEASE vs PONTIAC FEVER · AND WHO GETS SICK

Point	Detail
Pontiac fever	Self-limited influenza-like illness with NO pneumonia , incubation hours to ~3 days rather than 2-14, resolving in days. Supportive care only -antibiotics have no established role. △ Still notifiable , because it flags the same water source and often the same outbreak
Highest-risk hosts	Age over 50, male, smoker, chronic lung disease , malignancy, diabetes, alcohol use disorder · △ immunosuppression above all -TNF-alpha inhibitors, glucocorticoids, transplant , because containing an intracellular pathogen depends on the cell-mediated immunity these drugs blunt.

References: CDC clinical guidance on Legionella infections (diagnosis, preferred paired testing, reporting) · IDSA/ATS 2019 community-acquired pneumonia guideline ·

Jasper AS et al, Clin Infect Dis 2021;72:1979 · Kato H et al, J Infect Chemother 2021;27:424 · Fraser DW et al, N Engl J Med 1977;297:1189.

Educational aid; verify against current CDC guidance, local formulary and patient factors.

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