Legionnaire's Disease Since Philadelphia

Lessons Learned and Continued Progress

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KEYWORDS

• Atypical pneumonias • Legionnaire's disease • Legionella
• Community-acquired pneumonia

KEY POINTS

- After the Philadelphia outbreak, Legionnaire's disease was recognized as a newly described cause of severe community-acquired pneumonia (CAP).
- Legionnaire's disease has characteristic extrapulmonary findings, which, when considered together, are the basis for a presumptive clinical diagnosis.
- The widespread use of *Legionella* culture, sputum DFA, serology, urinary antigen testing, and polymerase chain reaction (PCR) have allowed earlier diagnosis of Legionnaire's disease.
- Excluding common source outbreaks (eg, from water towers), CAP caused by Legionnaire's disease is manifested as sporadic cases. In contrast, nosocomial Legionnaire's disease, which clinically has the same features as community-acquired Legionnaire's disease, occurs in clusters or outbreaks from common *Legionella* species-contaminated water sources.
- Improved diagnostic tests have permitted accurate diagnosis, which allows Legionnaire's disease mimics to be differentiated from *Legionella* species CAP. Bacterial coinfections with Legionnaire's disease are uncommon, but when present, are most often associated with bacteremia pneumococcal pneumonia.

THE PHILADELPHIA OUTBREAK AND EARLY CASES

There are many clinical lessons that came from the Philadelphia outbreak and early cases.[1] When it was finally determined that the new atypical pneumonia in Philadelphia was due to Legionnaire's disease, 2 clinical varieties were described. The usual clinical manifestation of Legionnaire's disease was that of an atypical pneumonia (ie, a

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pneumonia with extrapulmonary manifestations). In some cases, there was an acute febrile illness without pneumonia, which was termed Pontiac fever. There has been little progress in the understanding of why *Legionella* uncommonly presents as Pontiac fever, while most cases of *Legionella* manifest as Legionnaire's disease.[2] When it was finally established that Legionnaire's disease was caused by to a gram-negative intracellular pathogen in alveolar microphages, tests were developed to diagnose Legionnaire's disease by a variety of methods. First sputum culture on selective media was developed, followed by DFA and serologic methods.[2]

The initial clinical descriptions of Legionnaire's disease remain among the best classic descriptions in the history of newly described infectious diseases.[3–5] Virtually all of the characteristic clinical findings of Legionnaire's disease were so well described in the early cases, (eg, high fever with relative bradycardia, mental confusion, watery diarrhea, abdominal pain, relative lymphopenia, hypophosphatemia, hyponatremia, and renal insuffiency).[6–10] Although Legionnaire's disease was recognized as a new atypical pneumonia, it had distinctive extrapulmonary clinical features. Many investigators tried to find individual clinical findings that would be diagnostic of Legionnaire's disease to no avail. Rather, it is the pattern of extrapulmonary organ involvement that is characteristic in Legionnaire's disease, not isolated findings (eg, degree of fever, pulmonary symptoms, and hyponatremia). Key Legionnaire's disease clinical findings, considered together as a diagnostic pattern, are the basis of presumptive clinical syndromic diagnosis.[11–13] Also, still underappreciated is that all Legionnaire's disease characteristic findings do not have the same diagnostic weight or diagnostic significance.[14,15] It is important to realize the diagnostic importance relative diagnostic weights of Legionnaire's disease clinical findings (eg, in CAP patients, hyponatremia is common and consistent with the diagnosis of *Legionella* disease, but otherwise unexplained hypophosphatermia, when present, has much more diagnostic weight as a prediction of Legionnaire's disease).[15] Similarly, in a hospitalized adult with zoonotic atypical pneumonias that can be reasonably excluded by negative history, CAP, a fever greater than 102°F, and an otherwise unexplained pulse deficit (ie, relative bradycardia), limit diagnostic possibilities to Legionnaire's disease. This key finding also eliminates the other causes of typical bacterial pneumonias and other non-zoonotic atypical pneumonias, *Mycoplasma pneumoniae, Chlamydophila pneumonia*.[15,16]

HOST FACTORS

Initially, it was thought that Legionnaire's disease was primarily to be a disease of the elderly and compromised hosts. It is now appreciated that Legionnaire's disease is a common cause of severe pneumonias in normal hosts.[12] With the widespread use of immunosuppresive medications, there is increased awareness that Legionnaire's disease is not uncommon in these patients.[17] It is now known that impaired cell meditated immunity (CMI) is the host defense defect that predisposes to Legionnaire's disease.[18] Given the increasing use of immunosuppressive therapies, more Legionnaire's disease is to be expected in the future.

MICROBIOLOGY AND EPIDEMIOLOGY

Legionella species are fresh water microorganisms with the ability to survive in biofilms, which has important implications for outbreak investigations and disinfection of water systems containing *Legionella* species like other microbes, are profoundly affected by temperature. Optimal growth of *Legionella* species is between 20°C and 40°C, and *Legionella* species growth is inhibited by temperatures of 40° to 70°C.

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