The Incidence of Legionella pneumophila as the Cause of Acute Ambulatory Lower Respiratory Tract Infection

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Seventy-nine ambulatory patients with acute lower respiratory tract infection were evaluated for Legionella pneumophila by acute and convalescent antibody titers. None of the patients met the traditional criteria for the diagnosis of acute infection caused by Legionella pneumophila. Currently accepted criteria for diagnosing legionellosis by serologic means may or may not be applicable to mild respiratory tract infections.

Acute lower respiratory tract infections are a frequent cause of office visits to the family physician. Reports regarding the content of family practice have identified acute bronchitis as the fifth or sixth leading cause of office visits to family physicians.[1,2] Excellent treatment efficacy studies of acute bronchitis have been conducted in the last three years. Williamson[3] showed no improvement in patients' clinical course with doxycycline treatment. Franks and Gleiner,[4] Brickfield et al,[5] and Dunlay et al[6] showed improvement in the patient's clinical course with trimethoprim-sulfamethoxazole and erythromycin, respectively. These studies point toward a treatable cause or causes for nonpneumonia, acute lower respiratory tract infections without having defined the infecting agents. There are, unfortunately, no North American studies addressing the etiologic patterns or responses to treatment in ambulatory patients with pneumonia.

Legionella pneumophila has been widely known as the cause of acute respiratory tract infections since its identification following the Philadelphia outbreak in 1976. It was subsequently identified as the cause of localized outbreaks of acute pneumonia in a number of different settings,[7–9] as the cause of a modest percentage of community-acquired pneumonias,[10–12] and as a cause of often severe nosocomial infections.[13–15] There has not been any evaluation of Legionella pneumophila in moderately ill ambulatory patients with acute lower respiratory tract infections who did not require hospitalization. This study was designed to investigate whether infection caused by Legionella pneumophila was associated with lower respiratory tract infection in ambulatory patients.

METHODS

The study was the initial project conducted utilizing the new Affiliated Central Ohio Research Network (ACORN) of the Department of Family Medicine of The Ohio State University. The network recruited one academic Family Practice Center (at The Ohio State University Hospital) and ten individual practitioners to participate in this project.

Because of the difficulty of obtaining proper cultures of or direct fluorescent antibodies to Legionella pneumophila on ambulatory patients, acute and convalescent antibody titers were used to indicate recent infections caused by Legionella pneumophila. This method is accepted as having the highest rates of sensitivity in detecting acute infections caused by Legionella organisms.[16,17] Since antibiotic treatment does not affect the development of convalescent antibody levels in patients with acute legionellosis, any treatment by the physician would not alter the accuracy of the diagnostic methods.

Patients with acute lower respiratory tract infections who did not require hospitalization were enrolled. While previous studies had concentrated on acute bronchitis, acute lower respiratory tract infections were chosen for this study to include patients with pneumonia in addition

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to those with acute bronchitis. Patients with acute upper respiratory tract infections were excluded to avoid enrolling patients whose cough was secondary to upper respiratory congestion rather than infection of the bronchi or the lung parenchyma. The patients were classified as having an acute lower respiratory tract infection upon the judgment of their physician. Exclusion criteria included presence of chronic obstructive pulmonary disease or any other significant chronic respiratory disease, and the presence of symptoms of upper respiratory tract infections. The illness must have been of less than two weeks' duration with the presence of cough, sputum, or shortness of breath that would indicate acute bronchitis or mild pneumonia. Recognizing that these diagnoses (especially bronchitis) are clinical diagnoses and that the study was designed to gather data about the incidence of this infection in patients treated in routine ambulatory family medicine patterns, the individual physicians were allowed to practice in their own style and decide which of their patients had an acute lower respiratory tract infection.

At the time of enrollment, the study was explained to the patient and written consent was obtained. A comprehensive examination of the upper and lower respiratory tracts was performed, and any additional laboratory tests and treatment were left to the judgment of the physician. Demographic and symptom data about each patient were obtained. Physical findings of rales, rhonchi, wheezes, dullness to percussion, temperature, and sputum were noted. A 20-mL sample of blood was drawn, spun, frozen, and then transported to The Ohio State University Hospitals laboratory. After 30 days the patient was recalled, and a convalescent sample of 20 mL was again obtained, spun, frozen, and transported to The Ohio State University Hospitals laboratory. The antibodies to Legionella pneumophila were identified by indirect fluorescent antibody testing, a widely used and accurate method of determination of Legionella pneumophila antibodies.[18]

RESULTS

Initially 113 patients were enrolled in the study; 79 completed the study by having acute and convalescent titers determined. Two patients, both elderly, died; one death was possibly related to the respiratory tract infection, and one death was unrelated. Thirty-three other patients declined repeated requests to return at 30 days for the convalescent titer determination.

The patients were well-distributed among the participating practices. The largest number enrolled at The Ohio State University Family Practice Center, with 51 enrolled and 31 completing the study. The other 63 patients who enrolled and 48 who completed the study were from the eight private practices that were active in the study. Patient demographic data, symptom patterns, and physical signs are summarized in Table 1.

TABLE 1. PATIENT DATA FROM PATIENTS COMPLETING THE STUDY (n = 79) AND PATIENTS NOT AVAILABLE FOR FOLLOW-UP (n = 35)

	Patients Completing Study No. (%)	Patients Not Available for Follow-up No. (%)
Average age (years)	45.6	48.5
Male	32 (41)	16 (46)
Female	47 (59)	19 (54)
Smoker	16 (20)	9 (26)
Alcohol use		
Moderate	2 (2.5)	2 (6)
Occasional	29 (37)	8 (23)
Cough	77 (97)	34 (97)
Dyspnea	41 (52)	24 (69)
Chest discomfort	46 (58)	26 (74)
Fever or chills	44 (56)	20 (57)
Anorexia	32 (41)	18 (51)
Arthralgia or myalgia	33 (42)	15 (43)
Headache	46 (58)	19 (54)
Gastrointestinal symptoms	19 (24)	14 (40)
Fatigue or malaise	66 (84)	28 (80)
Rales	28 (35)	12 (34)
Rhonchi	38 (48)	18 (51)
Wheezes	23 (29)	16 (46)
Sputum		
Purulent	46 (58)	20 (57)
Clear	12 (15)	6 (17)
Dullness to percussion	15 (19)	7 (20)
Elevated temperature	20 (25)	7 (20)
Chest roentgenogram		
Infiltrate	2 (2.5)	3 (8.5)
Normal	9 (11)	7 (20)
No result	7 (9)	7 (20)

Traditional antibody levels recommended by the Centers for Disease Control were used for the diagnosis of acute infection caused by Legionella pneumophila. These standards include demonstration of a fourfold rise in titer to a level of 1:128 or above between the acute and convalescent titers or a single titer at a level of 1:256 as diagnostic of acute infection. The utility of the fourfold rise in titer has been compromised because nearly all laboratories, including The Ohio State University laboratory, have come to consider levels of 1:32 or less as negative, and therefore do not test for antibody at dilutions of 1:32 or lower.

Test results for 70 patients were negative for antibodies to Legionella pneumophila at titers of 1:32 or less at both acute and convalescent blood testing. Nine patients demonstrated some level of elevated antibodies to Legionella pneumophila; serologic data from these nine are summarized in Table 2. None of these patients met the accepted criteria for definite or probable diagnosis of acute legionellosis (fourfold rise in titer to 1:28 or greater, or single titer of 1:256).

TABLE 2. LEGIONELLA PNEUMOPHILA ANTIBODIES TITERS IN ACUTE AMBULATORY LOWER RESPIRATORY TRACT INFECTIONS

Patient	Acute	Convalescent
1	1:64	1:128
2	1:128	1:128
3	1:128	1:64
4	Negative	1:64
5	Negative	1:64
6	Negative	1:64
7	Negative	1:64
8	Negative	1:64
9	1:64	Negative

DISCUSSION

Legionella pneumophila was not found to be a significant infective agent in lower respiratory tract infections in ambulatory patients. None of the patients met the traditional criteria for diagnosis of acute legionellosis. Two previously mentioned studies had shown improvement in the course of acute bronchitis when patients were treated with erythromycin.[5,6] The findings in this study do not indicate that Legionella pneumophila is part of this response to treatment.

Various serologically based studies of Legionella pneumophila have found that a considerable number of asymptomatic patients had titers of 1:128 or greater. Broome et al[7] found that 16 percent of asymptomatic patients in Vermont, in 1977, had these levels. Politi et al[8] found that 15 percent and 28 percent in two control groups had these levels or greater in Bloomington, Indiana, in 1978; and Snowman et al[19] found that between 16 to 20 percent of asymptomatic patients in Columbus, Ohio, in 1982 had levels of 1:128 or greater.

The reason for the presence of these levels of antibody in people with no history of clinical legionellosis remains unknown. The traditional diagnostic criteria to identify infections caused by Legionella pneumophila were developed on patients with pneumonia, frequently severe. The effective host defense against Legionella pneumophila is cellular immunity, not the humoral immunity measured by immunoglobulin G antibody.[20] The antibody created against Legionella pneumophila may, in fact, reduce the effectiveness of the cellular immune system defense rather than contribute to the defense itself.[21] This possibility would allow conjecture that patients with milder respiratory tract infections could manifest lower antibody levels from both a lower antigenic stimulus and a more effective cellular immune defense system than the patients studied in the previous investigations in which the patients had much more severe infections.

By accepted diagnostic criteria, there is no evidence of acute legionellosis in patients with lower respiratory tract infections treated in an ambulatory setting. The potential for underdiagnosis of legionellosis in this population exists, however, and further study with particular attention to evaluating all patient specimens at lower than traditional baseline antibody levels would be in order.

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