CURRENT PULMONOLOGY

DANIEL H. SIMMONS

VOLUME 7

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YEAR BOOK MEDICAL PUBLISHERS, INC.
Chicago • London

International Standard Serial Number: 0163–7800
International Standard Book Number: 0–8151–7744–5

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Preface

As with earlier volumes of *Current Pulmonology,* the goal of Volume 7 is not only to provide internists and pulmonologists with information about problems currently of special interest, but to provide it from both basic and clinical viewpoints. In fact, we feel this characteristic of *Current Pulmonology* makes it unique and justifies its publication when so many other reviews are available. We hope this dual approach will provide more insight into clinical respiratory disease than is possible from purely basic or clinical discussions.

Although a mix of the basic and the clinical, some of the chapters do stress one or the other, but overall neither is emphasized. The contents of this volume bear this out. Only two of the chapters (''Tuberculosis'' and ''Fiberoptic Bronchoscopy'') stress the clinical. Only two (''Antimicrobial Defense of the Lung: Importance of Secretory Immunoglobulin A and Opsonic Immunoglobulin G Antibodies'' and ''The Function and Failure of the Ventilatory Muscles'') stress the basic, although both are clearly relevant to clinical usage. The six others—dealing with pneumonia, chronic obstructive disease, the respiratory distress syndrome, pulmonary fibrosis, dyspnea, and altitude sickness—each combine the basic and clinical within themselves.

Once again this volume maintains continuity with those before it and those to follow by annual updates of some broad topics (such as tuberculosis), more in-depth discussion of special aspects of broad topics (such as smoking and chronic obstructive disease), introducing new areas to be expanded on later (such as dyspnea) and by covering subjects (such as altitude sickness) that may not be included again for some time.

Finally, my thanks. While many people worked on this publication, inevitably those who contributed the most merit the most thanks: the authors. Using the

talent and the environment enabling them to become noted experts, they accepted the responsibility of organizing their knowledge for the benefit of the medical community with little reward other than knowing they have met this responsibility.

DANIEL H. SIMMONS, M.D., PH.D.

Contents

CHAPTER 1

Community-Acquired and Hospital-Acquired Pneumonia in Adults

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PNEUMONIA REMAINS a major clinical problem. Despite the availability of numerous antimicrobial agents, both community-acquired and hospital-acquired pneumonia occur with notable frequency and mortality rates remain alarmingly high. In fact, coincident with the introduction and expansion of antimicrobial therapy has been a shift in pneumonia etiologies toward more resistant and difficult-to-treat etiologies.[1, 2] Furthermore, it is clear that our understanding of the etiologic spectrum for pneumonia is incomplete and is likely to remain so.[2] This chapter reviews several aspects of the two most common pneumonia syndromes that occur in adults—community-acquired and hospital-acquired pneumonia. In many ways, the approach to these conditions is quite different. However, as more elderly and medically compromised patients are managed successfully in community settings, these two pneumonia syndromes are gradually beginning to resemble one another.[1, 3, 4]

0163-7800/86/0007-0001-0022-$04.00

COMMUNITY-ACQUIRED PNEUMONIA

The availability of antimicrobial agents has produced a remarkable improvement in the prognosis for community-acquired pneumonia. For example, survival among patients with untreated bacteremic pneumococcal pneumonia at Boston City Hospital, between 1929 and 1935, was recorded as 17%.[5] Therapy with antisera improved this survival rate to 53%. In a more recent clinical series, Austrian and Gold[6] recorded an 85% survival rate for a similar group of patients receiving penicillin treatment for bacteremic pneumococcal pneumonia. The impact of antimicrobial therapy on mortality associated with nonpneumococcal bacterial pneumonia is less well documented. It is clear, however, that appropriate specific therapy for nonpneumococcal bacterial pneumonias will result in lower mortality.[7] Finally, while so-called "atypical pneumonia" is infrequently life-threatening, the correct approach to management will often result in decreased morbidity,[8] and, in some cases, mortality.[9] Despite these encouraging observations, there continues to be a small but persistent mortality rate associated with community-acquired pneumonia, generally ranging from 10% to 25%.[4, 6, 10–14] These mortality data are recorded for patients hospitalized due to pneumonia. Undoubtedly, the mortality rate for the large number of patients with pneumonia treated in the ambulatory setting is much lower.

Occurrence and Etiology

Since pneumonia is not reportable, the true incidence of community-acquired pneumonia is unknown. Also, while respiratory infection is a common illness among otherwise normal healthy individuals, pneumonia occurs in only a fraction of these cases. Dingle and associates[15] prospectively recorded respiratory illness among 292 people in 61 families from 1948 to 1950. A total of 4,428 respiratory infections occurred, but in only 29 patients was primary atypical pneumonia observed (0.7%), and only three cases of pneumococcal pneumonia (0.1%) occurred. These data have been used to provide an estimate that about 250,000 to 400,000 cases of pneumococcal pneumonia occur in the United States per year.

Precise determination of etiologic categories for community-acquired pneumonia is also impossible. The difficulty in obtaining a good quality sputum specimen for microscopic and bacteriologic examination,[16] or for that matter, the difficulty in obtaining any sputum in some patients; the lack of sensitivity of sputum smears,[17] or cultures;[18] the logistical difficulties obtaining acute and convalescent viral titers, mycoplasmal, and *Legionella sp.* serologic examinations, plus the nonavailability of cultures for these agents in many laboratories; and, finally, the inaccuracy of diagnosis of anaerobic pneumonia without invasive diagnostic techniques,[19] are all important reasons that the true incidence of specific etiologies cannot be determined.

Despite these adverse epidemiologic, microbiologic, and clinical conditions, a number of clinical studies have been designed to document specific etiologies for community-acquired pneumonia (Table 1). The rather high ratio of bacterial to viral etiologies in these series reflects the hospitalized status of the patient populations, and the incidence of underlying medical illnesses. Others estimate that more than half of all cases of community-acquired pneumonia are viral or mycoplasmal.[20]

For many years, community-acquired bacterial pneumonia and pneumococcal pneumonia have been considered synonymous. In 1966, a warning was served that nonpneumococcal bacterial etiologies were increasingly frequent etiologies of community-acquired pneumonia,[1] particularly for high-risk and elderly patients. This trend is illustrated in several recent series.[4, 10, 11, 13] Fortunately, there is some predictability regarding the likely etiologic agents in specific high-risk patient groups. For example, in alcoholics bacterial pneumonia is often caused by *Pneumococcus, Klebsiella, Hemophilus influenzae,* or *Staphylococcus*. In patients with recent viral influenza, the concerns are *Pneumococcus, Staphylococcus,* or *H. influenzae*. Likewise, the elderly and the patient with chronic lung disease, have a predictable group of bacterial etiologies. These are reviewed in the section on clinical management, since an understanding of which etiologies occur in which patient groups is crucial in selecting presumptive antibiotic therapy for a new case of pneumonia. Finally, it should be noted that in virtually every clinical series reporting community-acquired pneumonia, there is a sizable number of cases in which no specific etiology could be determined (see Table 1).

Clinical Approach

The clinician approaching a patient with community-acquired lower respiratory infection must consider two important questions. First, does the patient have bronchitis or pneumonia? Second, what is the etiologic agent causing the infection?

TABLE 1.—Reported Etiologies for Community-Acquired Pneumonia

		ETIOLOGIES* (%)		
SERIES, YR	BACTERIA	*Pneumococcus*†	*Mycoplasma* OR VIRUS	UNKNOWN
Mufson et al., 1967[14]	47	"Most"	20	33
Lepow et al., 1968[21]	47	"Most"	11	42
Fiala, 1969[22]	67	83	Uncertain	33
Fekety et al., 1971[23]	66	94	5	29
Sullivan et al., 1972[4]	57	62	?*	43
Dorff et al., 1973[10]	74	65	9	17

*Serologic evidence of viral infection in about 10% of "Bacteria" and "Unknown" categories.
†Percentage of total bacteria that are *Pneumococcus*.

TABLE 2.—EMPIRIC TREATMENT OF SUSPECTED BACTERIAL PNEUMONIA IN THE HIGH-RISK PATIENT

UNDERLYING CONDITION	USUAL PATHOGENS	PRESUMPTIVE THERAPY
Recent influenza	*Pneumococcus; Staphylococcus aureus; Hemophilus influenzae*	Cefamandole, 1–2 gm every 6 hr intravenously (IV)
Chronic bronchitis	*Pneumococcus; H. influenzae*	Ampicillin, 2 gm every 6 hr IV or cefamandole, 1–2 gm every 6 hr IV
Alcoholism	*Pneumococcus; Klebsiella; S. aureus; H. influenzae*	Cefamandole, 1–2 gm every 6 hr IV
Aspiration pneumonia	Mouth anaerobes	Penicillin G or clindamycin, 600 mg every 6 hr IV
Old age (residence in a nursing home)	*Pneumococcus; Klebsiella; S. aureus; H. influenzae*	Cefamandole, 1–2 gm every 6 hr IV

Physical examination and chest roentgenogram should resolve the first question. The second question will require a multifactorial analysis. A presumptive answer to this question must be determined on the day of presentation in order to guide management. That, of course, eliminates the use of such helpful items as sputum and blood cultures, as well as acute and convalescent serologic analyses for virus, *Mycoplasma,* or *Legionella sp.* Although microscopic examination of sputum may be useful in some cases, a surprisingly large number of patients produce either no sputum (dehydration, atypical pneumonia), or poor-quality sputum specimens. Analysis of several clinical features of the illness should be helpful in planning initial management strategy.

Setting in Which Pneumonia Was Acquired

Where, when, and in whom has pneumonia developed? About 95% of normal adults in whom pneumonia develops in the usual community setting will be infected with either virus, *Mycoplasma pneumoniae, Streptococcus pneumoniae,* or legionnaires' disease. In the altered host, however, a variety of additional nonpneumococcal bacterial etiologies might be considered (Table 2). Special attention to pneumonia developing in unusual settings should be given. College dormitories or military barracks are notorious for outbreaks of *M. pneumoniae* infection. Nursing homes are associated with increased rates of gram-negative pneumonia (particularly *Klebsiella*). Seasonal issues are also important. For example, the coincidence of influenza season and a reported outbreak in the community may lower the clinician's threshold for trying amantadine therapy early in a suspected case of viral pneumonia. Also, legionnaires' disease appears to be more frequent in late summer and early fall. Needless to say, exposure resulting from an unusual occupation or from travel must be considered (e.g., exposure to psittacine birds, travel in areas endemic for Q fever).

Microbiologic and Serologic Evaluation

The precise etiology of pneumonia may be determined using microbiologic and/or serologic tests. However, rapid and precise identification of an etiologic agent for pneumonia may be difficult. A number of reasons account for this difficulty, including contamination of sputum with noninfectious (''colonizing'') bacteria, and the inability to obtain an adequate lower respiratory tract specimen for proper evaluation (e.g., dehydration, atypical pneumonia). Furthermore, even if an acceptable sputum specimen is produced, the time required for cultural identification of the pathogen is generally too long to be of use in guiding initial therapy.

Gram-stained sputum smears remain the most accessible, rapid means for making a presumptive etiologic diagnosis for pneumonia. Unfortunately, this inexpensive, widely available test is among the least sensitive microbiologic methods for making a specific etiologic identification. Not only is the sensitivity of Gram stains only 40% to 60%,[17, 24, 25] an even greater problem exists in obtaining a specimen of adequate quality for microscopic examination. In one study using strict criteria for quality of the specimen (i.e., >25 leukocytes and <10 squamous cells per x100-power field), only 26% of 382 sputum samples submitted to the laboratory were of acceptable quality for microscopic or culture examination.[26] Several more specialized serologic tests have been employed for dealing with initial sputum or transtracheal aspirate specimens. The quellung reaction relies on the phenomenon of capsular swelling on contact with specific antiserum, and has been used primarily for diagnosing pneumococcal infections. This reaction increases the refractability of the pneumococci under the microscope, allowing for increased sensitivity in identification. In one study, the quellung reaction corresponded with sputum culture results in 89% of cases, while Gram stain findings corresponded in only 55%.[25] The Omniserum (Statens Seruminstitut, Copenhagen) used for this test contains antisera specific for all 83 known pneumococcal capsular polysaccharide antigens.

Other tests less readily available, but in some reports more sensitive than sputum Gram stains, are counterimmunoelectrophoresis (CIE) and coagglutination (COAG). Counterimmunoelectrophoresis has been reported to be more sensitive than sputum cultures.[24, 26] In another report, CIE and sputum gram stains were equal in sensitivity for patients with pneumonia.[27] It has also been pointed out that CIE is much less useful once antibiotic therapy has been begun.[28] Coagglutination of sputum was equal to CIE in sensitivity in one report,[28] but was a considerably more sensitive test in a more recent study.[24] In the latter study, the combined sensitivity of COAG for proved (blood culture–positive cases) pneumococcal, *H. influenzae,* and *Klebsiella* pneumonias was 94%, as contrasted to 64% for CIE.[24] Both CIE and COAG were highly specific tests in that study.

The recent description of yet another fastidious etiologic agent for community-acquired pneumonia, *Legionella pneumophila,* has initiated development of several new rapid diagnostic methods specific for this organism. The direct immunofluorescent antibody (DFA) examination of respiratory secretions (sputum,

transtracheal aspirates, pleural fluid) is now widely available. This test requires a skilled microscopist, and of course, will only be positive if the antisera for the test corresponds to the serotype of the infecting strain of *Legionella*. While DFA appears to be highly specific, considerable controversy exists regarding the sensitivity of DFA.[29–31] In one report[29] sputum DFA examination was relatively sensitive (50%), while in another report,[31] the sensitivity was only 33% in transtracheal aspirates. Some have observed that DFA of sputum may be superior to DFA of transtracheal aspirates.[29] All agree that DFA testing is less sensitive than properly cultured respiratory specimens. Unfortunately, most cultures will not turn positive for *Legionella* until three to five days of incubation. Recent reports have described the detection of *Legionella* antigen in the urine of 70% to 80% of patients with proved Legionnaires' disease.[32, 33] Urinary antigen may be detected using a variety of methods. Unfortunately, these tests are not yet widely available. Furthermore, this serologic test is only useful for serogroup 1 of *L. pneumophila* (approximately 60% of cases).

Cultures of sputum and blood may or may not be diagnostically useful. Unfortunately, virtually all common etiologic agents causing community-acquired pneumonia are fastidious (pneumococci, *H. influenzae*) or require special culture procedures (*M. pneumoniae, Legionella sp.*, viral agents). The sensitivity of sputum cultures for pneumococci appears to be only about 50%.[18] Thus, if numerous pneumococci are seen on sputum smear but do not grow in culture, that does not exclude a diagnosis of pneumococcal pneumonia. Blood cultures may be helpful, as they are positive in up to one third of cases of bacterial pneumonia. They may be positive when sputum is not.[18]

Invasive Diagnostic Techniques

Several invasive diagnostic procedures have been evaluated in patients with community-acquired pneumonia.[34] These include transtracheal aspiration (TTA),[35, 36] fiberoptic bronchoscopy with a plugged telescoping catheter,[37] and transthoracic needle aspiration of lung tissue.[34] These procedures have usually been reserved for the more unusual pneumonias, since the potential for complications from the procedures is not small.[34, 38] The diagnostic results reported with these procedures have emphasized their usefulness in excluding contamination with upper airway bacteria. Thus, a more accurate assessment of the actual pathogen(s) in the lungs may be determined. By and large, most studies have emphasized the usefulness of invasive procedures in improving accuracy of culture, rather than speed of diagnosis. The precise role of invasive diagnostic methods in rapid diagnosis of community-acquired pneumonias remains unsettled at this time. One point is certain: if the patient cannot produce a sputum specimen for initial microscopic examination, these methods offer a means to obtain material for such an examination. Whether the benefit warrants the risk will be a clinical decision.