MEDICAL GRAND ROUNDS

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SPECIFIC BACTERIAL ETIOLOGIES

A CLINICAL APPROACH TO PATIENTS WITH COMMUNITY ACQUIRED PNEUMONIA

Pneumonia remains a common and serious medical problem in the United States with an attack rate of 10 to 14 per 1000 persons per year (1). Overall, it is still the fifth most common cause of death (2) with an annual mortality in excess of 30,000 attributed to *Streptococcus pneumonia*, the most common cause of serious community acquired pneumonia (3). A recently released pneumococcal polysaccharide vaccine causes antibody formation against the 14 pneumococcal capsular types that are responsible for 80 percent of pneumococcal pneumonia in adults. The vaccine has been demonstrated to be approximately 80 percent protective against pneumonia caused by these organisms (4-7). The widespread use of this vaccine may reduce the incidence and seriousness of pneumococcal pneumonia and may thus alter the clinical approach to community acquired pneumonia. However, at present, not all issues are resolved concerning the vaccine (8), and its use will not likely change the management of individual patients with pneumonia in the near future.

It should be made clear that this discussion pertains only to patients who initially present to a physician because of the signs and symptoms of pneumonia; that is, community acquired infection. The bacterial causes and clinical findings of pneumonia acquired by patients hospitalized for other serious illnesses, i.e. nosocomial pneumonia, are sufficiently different from community acquired pneumonia to require a different approach to diagnosis and management (9, 10). Additionally, this discussion does not apply to persons who are immune deficient owning to steroids and cytotoxic agents. They may develop pneumonia from organisms which do not cause disease in a more general population (11), and their clinical findings may also differ from those who are not so compromised (12).

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Although pneumonia is potentially a life threatening illness, a biased view of community acquired pneumonia may be obtained from mortality statistics and from reports of series of hospitalized patients. Persons with pneumonia judged to be sufficiently ill to require admission to a general hospital are pre-selected to represent only the most serious cases. Many such series note that only a fraction, usually less than half, of all patients presenting to their clinics or emergency room with pneumonia are hospitalized and therefore available for study. Additionally, many studies are performed in municipal hospitals which serve the medically indigent, and chronically ill or alcoholic patients are over represented relative to the general population. Perhaps the best data on pneumonia as it occurs in the general population is that reported by the School of Public Health at the University of Washington (13-15). This group for many years has been studying the causes and clinical characteristics of pneumonia as it occurs in the members of The Group Health Cooperative of Puget Sound.

This prepaid medical care group has 150,000 members representing 12 percent of the Seattle urban and surburban population with an age distribution similar to that of the U. S. population. All socioeconomic groups are well represented except the "unemployed, the destitute, and the very rich". In this average population it is found that only 15 to 20 percent of patients with radiographically proven community acquired pneumonia are sufficiently ill to require hospitalization. Like other investigators who attempt to determine the infectious etiology of pneumonia (16-18), this group finds that despite relatively extensive laboratory testing the infectious agent cannot be identified in a large fraction of patients. Of all patients with community acquired pneumonia, viral or mycoplasmal infections are implicated in about 50 percent of childhood and 35 percent of adult disease (14). Pneumococcal pneumonia in childhood is uncommon but it represents about 15 to 20 percent of adult pneumonias (15). When hospitalization is not required for pneumococcal pneumonia, the degree of illness tends to be mild and is clinically similar to nonbacterial pneumonia. Gram negative bacillary pneumonia is rare among the general population.

The data of the Seattle group indicate that patients presenting to the physician with mild pneumonia do not require hospitalization or extensive laboratory investigation. A chest radiograph demonstrating the absence of dense lobar consolidation and a complete blood count revealing a normal or mildly elevated white blood count should suffice. Since the most likely potentially treatable infectious agents, *Mycoplasma pneumonia* and *Streptococcus pneumoniae*, both respond to tetracycline and erythromycin (13, 19, 20), these antimicrobial agents are the most reasonable therapy for outpatients with pneumonia. The occurrence of strains of pneumococcus resistant to tetracycline suggests erythromycin is the better choice (21).

Features Suggesting Need for Hospitalization

Certain features in the clinical presentation of a patient with pneumonia suggest a more serious infection exists which requires hospitalization and a more thorough evaluation. Although no single feature is specific for serious bacterial pneumonia, Table 1 indicates helpful parameters.

TABLE 1

CLINICAL FEATURES SUGGESTING SERIOUS BACTERIAL PNEUMONIA

Clinical toxicity	Purulent sputum
Abrupt onset	Advancing age
True rigors	Lobar consolidation
Pleuritic pain	Associated diseases

A crisp delineation of the parameters that indicate clinical toxicity is not possible but certainly include marked tachycardia, tachypnea, hypotension, changes in skin coloration, perspiration, and mental changes such as anxiety, confusion, or stupor. The degree of temperature elevation is of little help in separating viral, mycoplasmal and bacterial pneumonias (22, 23). Although difficult to enunciate, the clinical judgement to recognize the severely ill patient is perhaps the most important criterion for hospitalization.

Patients with viral or mycoplasmal pneumonia tend to have an indistinct onset of severe cough that merges with antecedent symptoms such as milder cough, malaise, fatigue, and weakness, and especially in the case of viral infections, coryza and pharyngitis (22-25). Although a significant fraction of patients with a serious bacterial pneumonia may also have a similar antecedent prodrome, the onset of pulmonary infection is usually abrupt and unambiguous (26-28). The onset of bacterial pneumonia is frequently marked by the almost simultaneous occurrence of a true shaking chill and pleuritic chest pain (26-28). Although chilly sensations are common in patients with viral or mycoplasmal pneumonia (22), true rigors are not common. Similarly, many patients with viral or mycoplasmal pneumonias complain of vague substernal or parasternal discomfort, but pleuritic pain is not common (22, 23, 25, 29). Purulent sputum is common in bacterial pneumonias, but a nonproductive cough or the production of small amounts of mucoid sputum is more characteristic of viral or mycoplasmal disease. Bacterial pneumonia is more prevalent in middle aged and older persons while viral and mycoplasmal infections tend to be diseases of younger persons (14, 18, 23, 24), so that relaxation of admission policies irrespective of other criteria should occur in patients over 40 years. The finding on physical examination of pulmonary consolidation should also make one suspect a bacterial etiology, for, although it occurs with viral or mycoplasmal disease (22), consolidation is typical of bacterial pneumonia (26-28). Chronic medical conditions, especially alcoholism, chronic obstructive lung disease, cardiac disease and diabetes mellitus (30-32) and diseases associated with a depressed sensorium (33), should strongly suggest a bacterial etiology.

TABLE 2

LABORATORY FEATURES SUGGESTING SERIOUS BACTERIAL PNEUMONIA

WBC greater than 15,000 or less than 5,000 mm^3
Dense or multilobed consolidation
Pleural effusion
Abscess

The white blood cell count or the chest radiograph indicated as the only studies necessary for most patients with pneumonia may suggest a more complicated pneumonia than had been previously suspected. White cell counts greater than 15,000 mm^3 (13, 22, 23, 29) or less than 5,000 mm^3 (34) are not common in viral or mycoplasmal pneumonias, and such values dictate a careful reappraisal of the patient. It should be stressed that the chest radiograph is almost never diagnostic of the infectious agent responsible for pneumonia (35). Nevertheless, dense lobar or multilobed consolidation should cause the diagnosis of bacterial pneumonia to be strongly considered. Further, although small pleural effusions demonstrable on lateral decubitus films have been reported to be present in 20 percent of viral or mycoplasmal pneuminias (36), larger effusions indicate a complicated pneumonia that requires hospital admission and more extensive evaluation. Abscess formation has been reported in only three patients with mycoplasmal pneumonia (37, 38) and virtually always constitutes an indication for hospital admission.

DIAGNOSTIC PROCEEDURES

When it is determined that a patient with pneumonia is sufficiently ill to require hospitalization, what diagnostic proceedures are available and what is the reliability of these proceedures? Throughout the subsequent analysis I shall emphasize our disappointing lack of precision in establishing a definitive etiologic diagnosis. This lack of precision leads to some skepticism concerning the relative frequency of various types of bacterial pneumonia and even the frequency with which bacterial pneumonias occur in relation to pneumonia due to viruses or mycoplasma. Perhaps more importantly, however, our lack of diagnostic precision may lead to considerable uncertainty on the part of the physician faced with a patient with pneumonia in regard to the most correct antimicrobial therapy.

Frequency of Multiple Pathogens

To what source of culture material may we turn as a "gold standard" for comparison of other materials? The most satisfactory "gold standards" available are cultures of blood, pleural fluid, or material obtained from the pneumonic lung by percutaneous lung puncture. This immediately biases our results. Blood cultures are positive only in a fraction of patients with pneumonia and that fraction varies depending on the causative organism. Empyemas occur in a small fraction of patients, and that fraction likewise varies with the causative organism. The results of lung puncture have been infrequently reported in recent years. Since these are the best standards we have, however, I would first like to establish by reports of cultures of these sources the frequency of pneumonia in adults proven to be caused by multiple organisms.

TABLE 3

PNEUMONIA IN ADULTS "PROVEN" TO BE CAUSED BY MULTIPLE ORGANISMS*

	Number of Cases		
	Total	Multiple	Percent
Bullowa (1937)	~1288	46	3.6
Austrian and Gold (1964)	592	4	0.7
Mufson, et al (1974)	325	2	0.6
Tempest, et al (1974)	40	1	2.5
Davidson, et al (1976)	17	2	11.8

* "Proven by blood, lung puncture, or pleural cultures.

Although quite old, I have included the work of Bullowa (39), because his is by far the largest series of lung punctures. His methods of culture should have been sufficient to recover most pathogens. Bullowa performed in excess of 2500 lung punctures; approximately 1288 of these yielded a pathogen, and of these 46 yielded more than one pathogen. Thus, he demonstrated multiple organisms in 3.6 percent of his cases in which lung puncture was positive. The large series by Austrian and Gold (40) and by Mufson, et al (41) were concerned with patients with bacteremic pneumococcal pneumonia or pneumococcal pneumonia with extrapulmonary foci. Lung puncture was not performed in these patients. Thus, the incidence of pneumonia due to multiple organisms of 0.6 to 0.7 percent may be an underestimate of the true incidence. However, these series give additional credence to the general order of magnitude of pneumonias due to multiple organisms. The last two series (42, 43) have been reported much more recently. Although the total number of patients with positive percutaneous lung aspirates was small, the incidence of cultures of lung aspirates containing more than one pathogen is of the same order of magnitude as the other series. Despite the limitations that I have indicated, these data support the concept that most community acquired pneumonia due to aerobic bacteria is caused by a single pathogen. The incidence of pneumonia due to more than one pathogen is probably less than 5 percent. Whether aerobic bacterial pneumonias acquired by debilitated patients already in the hospital are more commonly due to multiple pathogens cannot be determined by available studies utilizing these rigorous standards.

TABLE 4

CAUSE OF PNEUMONIA IN ADULTS DUE TO
MULTIPLE AEROBIC ORGANISMS

Organisms	No. Cases	Percent
Pneumococcus and		
Pneumococcus	15	27
β streptococcus	20	36
Gram negative bacillus	12	22
Other	7	13
Gram negative bacillus		
β streptococcus	1	2
Total	55	100

Bullowa; Austrian and Gold; Mufson, et al;
Tempest, et al; Davidson, et al.

In almost all of the patients reported in these series at least one of the two bacteria obtained from lung puncture, blood or pleural fluid was a pneumococcus. Even if the patients of Austrian and Gold and Mufson, et al, are excluded, since they reported only on patients with bacteremic pneumococcal pneumonia, the results are not significantly different. In approximately one-quarter of the cases the second organism identified was a separate stain of pneumococcus. In almost 40 percent of the cases the second organism was a beta streptococcus. Virtually all of these cases were in the series reported by Bullowa in the 1930's. In approximately 20 percent of the cases the second organism was a gram negative bacillus. *Staphylococcus aureus* accounts for most of the "other" strains of bacteria.

TABLE 5

PNEUMONIA IN INFANTS "PROVEN" TO BE CAUSED
BY MULTIPLE ORGANISMS*

	Number of Cases		
	Total	Multiple	Percent
Mimica, et al (1971)	228	10	4.4

* "Proven" by lung puncture cultures.

In the contemporary literature the use of lung puncture to diagnose the bacterial etiology of pneumonia has been reported more frequently in infants than in adults. The most recent large series of which I am aware is that by Mimica and associates in 1971 (44). Among 505 lung aspirate specimens from infants under two years of age with pneumonia, these investigators obtained 228 positive cultures. Ten of these 228 positive cultures yielded more than one pathogen for an incidence of 4.4 percent. These data suggest that pneumonia in infants caused by multiple organisms is no more frequent than pneumonia caused by multiple organisms in adults. Since these investigators were working in Chile, and since many of their infants were malnourished, the organisms that they recovered may not be representative of the cause of pneumonia in well nourished infants in the United States, so I shall not indicate their results in that regard.

I have attempted to demonstrate that for community acquired pneumonia due to aerobic bacteria the incidence of pneumonia due to multiple pathogens is of a low order of magnitude, perhaps in the range of 5 percent. Diagnostic techniques which frequently yield more than one pathogen in patients with pneumonia, therefore, may be misleading. With this background, I shall review the diagnostic techniques available to the clinician.

Gram Stain of Sputum

TABLE 6

CORRELATION BETWEEN POSITIVE SPUTUM CULTURES AND GRAM STAIN

Culture	Number	Gram Stain Positive	(%)	Gram Stain Negative	(%)
S. pneumoniae	86	55	(64)	31	(36)
H. influenzae	60	18	(30)	42	(70)
Gram neg. bacilli	81	21	(26)	60	(74)

Lepow, et al; Merrill, et al; Dipoala

A gram stain of expectorated sputum is the only diagnostic technique available to the physician at the outset of therapy. Older literature indicated that this is a very reliable tool in the diagnosis of pneumococcal pneumonia (45, 46). In more recent studies the gram stained sputum was examined by experienced bacteriologists or bacteriology technicians without knowledge of the subsequent cultural results, and these data are presented in Table 6 (16, 47, 48). When pneumococci were successfully cultured from the sputum, such could be correctly predicted by gram stain in 64 percent of the specimens. Two of these studies (17, 47) note,

however, that pneumococci were very frequently reported by gram stain in sputum from which no pneumococci could be cultured. Such was especially true when the gram stain was examined by house officers rather than by more experienced observers. The precision with which *Hemophilus influenzae* and other gram negative bacilli can be identified in gram stained sputum is even less impressive.

One must conclude that the gram stain of sputum of patients with pneumonia, like many other laboratory aids in clinical medicine, may be helpful but should not be considered diagnostic. Conversely, the absence of organisms suspected on other clinical grounds certainly does not exclude them as a cause of the pneumonia.

TABLE 7

PROCEDURES SUGGESTED TO IMPROVE RELIABILITY
OF BACTERIOLOGY OF EXPECTORATED SPUTUM

Repeated washing
Quantitative culture techniques
Scoring quality of sputum

The use of expectorated sputum cultures for the diagnosis of pneumonia due to aerobic bacteria is controversial (49-53), although it is agreed that such is inappropriate for anaerobic bacterial cultures (54). Expectorated sputum is known to be contaminated by oropharyngeal flora. Since the oropharynx of some normal persons is colonized by pneumococci (15, 49, 55) and of some debilitated persons by gram negative bacilli (9, 10), expectorated sputum may yield a pathogen that is not the cause of the patient's pneumonia. Additionally, upper airway secretions may dilute lower respiratory secretions and make the recovery of fastidious organisms such as pneumococci more difficult (49). The procedures listed in Table 7 have been suggested to improve the reliability of the bacteriology of expectorated sputum. These include repeated washing, the use of quantitative culture techniques (56-59), and the histological scoring of the quality of sputum (60-63).

TABLE 8

NUMBER OF SALINE WASHINGS NECESSARY TO CLEAR
Serratia marcescens FROM THE SPUTUM

	No. Pts.	No. Washings
Anterior oral area	4	1-3
Posterior oral area	4	1-3
Pharynx	6	5-9

Laurenzi, Potter and Kass: New Engl. J. Med. 265:1273, 1961.

The value of repeated washing of the sputum has been examined by Laurenzi, Potter, and Kass (64) and their data are indicated in Table 8. These investigators swabbed broth cultures of *Serratia marcescens* into the anterior or posterior oral area or the pharynx of patients producing purulent sputum. Immediately after the oral or pharyngeal areas had been inoculated with this marker organism, the patients coughed and expectorated into a sterile saline solution. After each washing, the supernates were decanted from the sputum, and cultures were taken from multiple areas of the remaining mucopurulent mass. They found that as many as nine washes of the sputum were necessary to remove pharyngeal contamination. Such a procedure is clearly impractical for a clinical bacteriology laboratory.

TABLE 9

CRITERIA FOR 'CLINICALLY SIGNIFICANT' RESPIRATORY INFECTION

Radiographic appearance of new or progressive pulmonary infiltrate

Fever

Leukocytosis

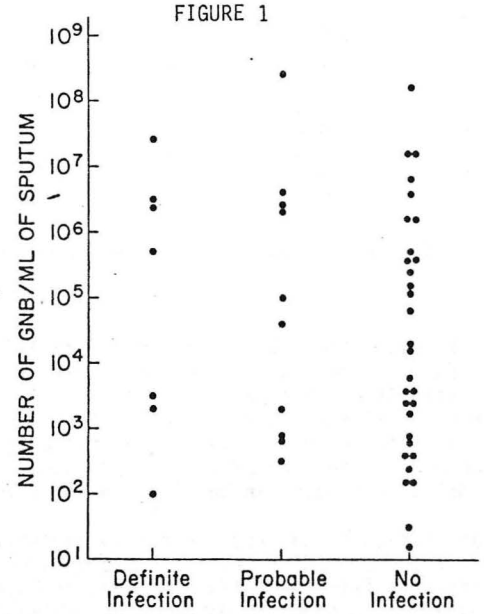
Purulent tracheobronchial secretions

Johanson, et al: Ann. Intern. Med. 77:701, 1972.

My colleagues and I have investigated the value of quantitative culture techniques (10). We defined a clinically significant respiratory

infection by the criteria indicated in Table 9. A "definite infection" was defined by the radiographic appearance of new or progressive pulmonary infiltrates, fever, leukocytosis, and purulent tracheobronchial secretions. "Probable infections" were considered to be present if the patient had fever and leukocytosis and either radiographic infiltrates or purulent tracheobronchial secretions.

FIGURE 1



Patients in an intensive care unit who did not have pneumonia at the outset were studied prospectively with twice weekly quantitative sputum cultures. Among 22 patients who developed definite or probable infection, 17 specimens contained potentially pathogenic gram negative bacilli. The number of gram negative bacilli per mililiter of sputum in these patients is plotted on the vertical axis and compared to the number of gram negative bacilli from 31 patients who had no clinical signs of infection. It is clear that the groups are not significantly different and that the quantitative sputum cultures were of no value in distinguishing colonization from infection. Further, in individual patients, the number of bacilli per milliliter of sputum was not a useful measure of response to treatment. In some patients gram negative bacilli promptly disappeared after the initiation of antimicrobial therapy; more commonly they decreased slightly in number or remained unchanged, despite a clinically favorable response to treatment. These results are similar to those of Kalinske and associates (65) and Hahn and Beaty (66) who found that quantitative cultures of expectorated sputum were difficult to interpret and did not correlate well with cultures of material aspirated percutaneously from the trachea.

TABLE 10

RELATIONSHIP BETWEEN CELLULAR CONTENT AND BACTERIAL ISOLATES IN EXPECTORATED SPUTUM

Group	Specimens	Number cells/field Epithelial	PMN	'Pathogens" Isolated (Mean)
1	54	>25	>10	0.57
2	42	>25	10-25	0.59
3	119	>25	>25	1.04
4	68	10-25	>25	1.05
5	99	>10	>25	1.05
TTA	47			1.29

Van Scoy: Mayo Clin. Proc. 52:39, 1977.

Thirdly, it has been suggested that greater precision may be obtained from sputum cultures if one estimates the source of the specimen by its cellular content. A large number of squamous epithelial cells indicate considerable contamination with saliva while a large number of polymorphonuclear leukocytes suggest material from the site of the infection (60). This technique has been assessed by Murray and Washington (61) whose data were reanalyzed by Van Scoy (63) and are reported in Table 10.

These investigators examined specimens of sputum grossly and microscopically. The macroscopic detection of blood, mucus, or saliva in sputum was not found to correlate with bacterial isolates. When using low power magnification sputum which microscopically revealed more than 25 leukocytes per low-power field (groups 3 through 5) yielded similar numbers of potential pathogens and was comparable to transtracheal aspirates. These findings are interpreted by Van Scoy to indicate that sputum with greater than 25 leukocytes per low power field is satsifactory for cultural purposes while less purulent material is not. This conclusion is somewhat at varience with that of Geckler, et al, (62) who reported that the best correlation of sputum with transtracheal aspirate, 79 percent, was obtained in specimens which contained fewer than 25 epithelial cells per low power field irrespective of the leukocyte count. Taken together, however, these studies indicate that a sputum specimen with a small number of epithelial cells and a large number of leukocytes appraoches the reliability of a transtracheal aspirate.

Murray and Washington (61) state that it is less work for a busy bacteriology lab to screen sputum specimens microscopically and culture only adequate specimens than to culture all specimens received. I am not in a position to evaluate the operation of such a laboratory. It is

apparent, however, that the value of a sputum examination to a clinician depends on his or her insuring that real sputum and not just upper airways secretions is obtained for gram stain and culture.

TABLE 11

CORRELATION BETWEEN LUNG ASPIRATE AND UPPER RESPIRATORY TRACT CULTURES IN INFANTS

Source of Specimens	Number Specimens	Lung Organisms Found in Upper Respiratory Tract	
		Number	Percent
Pharynx	228	25	10.8
Anterior nasal	228	30	13.1
Transtracheal aspirate	10	2	20.0
Per laryngeal tracheal aspirate	10	2	20.0

Mimica, et al: Amer. J. Dis. Child. 122:278, 1971

Owing to the lack of availability of expectorated sputum in infants, it is frequently the custom to obtain cultures from sites in the upper airway. The efficacy of this practice was investigated by Mimica and associates (44) in their study of pneumonia in which the bacterial etiology had been proven, insofar as possible, by lung puncture. Of the 228 patients with a pathogen recovered from lung tissue, only 25 or 10.8 percent had the same pathogen recoverable from the pharynx. A similarly small number had the same pathogen in the nose and lung. Transtracheal aspiration percutaneously is a difficult procedure in small children and was performed in this study only 10 times. Similarly, perlaryngeal tracheal aspiration through the mouth is difficult and was done only 10 times. By either route, the bacteria causing the pneumonia which had been established by lung puncture was recovered from the trachea only 20 percent of the time. These results certainly do not support upper airway culture sites as reasonable sources for diagnosing the cause of aerobic bacterial pneumonia in infants.

Transtracheal Aspiration

Transtracheal aspiration was introduced in 1959 (67) with the intent of bypassing the upper airways and thus obviating part of the problems inherent in expectorated sputum. The studies by Murray and Washington (61) and Mimica (44) report data relevant to this technique which suggest

that the bacteria recovered may not be the cause of the pneumonia. Other studies, however, have been specifically designed to determine the reliability of transtracheal aspirates (65, 66, 68-70).

TABLE 12

RECOVERY OF AEROBIC BACTERIA BY TRANSTRACHEAL ASPIRATION IN PATIENTS WITH PNEUMONIA

Study	No. Species Isolated		
	0	1	>1
Kalinske, et al (1967)	7	22	19
Schreiner, et al (1972)	23	16	5
Ries, et al (1974)	12	36	16
Totals (%)	42 (27)	74 (47)	40 (26)

The series by Kalinske (65), Schreiner (69), and Ries (70) and their co-workers allow the tabulation of the number of species recovered by transtracheal aspiration in patients who were thought to have aerobic bacterial pneumonia on admission to the hospital and who had not received antimicrobials. In most instances the organisms were potential pathogens. I have not included the large series by Bartlett (71), since many of his patients had nosocomial pneumonia.

In about a quarter of the patients no bacteria were isolated. In approximately half of the aspirates a single specie was isolated, and it is reasonable to believe that it was the causative organism. However, in approximately a quarter of the patients more than one organism was recovered. From the data previously presented it is highly unlikely that this large fraction of patients had pneumonia due to multiple aerobic bacteria. It thus appears that transtracheal aspirates are not absolutely reliable in assessing the cause of aerobic bacterial pneumonia.

TABLE 13

RECOVERY OF AEROBIC BACTERIA BY TRANSTRACHEAL ASPIRATION IN PATIENTS WITHOUT PNEUMONIA

Study	No. Species Isolated		
	0	1	>1
Pecora (1963)	34	4	4
Kalinske, et al (1967)	24	11	4
Ries, et al (1974)	21	0	7
Berman, et al (1975)	5	5	5
Totals (%)	84 (68)	20 (16)	20 (16)

This impression is supported by the data in Table 13 which indicate the recovery of aerobic bacteria by transtracheal aspiration in patients who did not have pneumonia at the time of the study. The types of patients studied include those with bronchogenic carcinoma, tuberculosis, pleural disease, hemoptysis of unknown etiology, fungal disease, sarcoidosis, pulmonary edema, and pulmonary disease of unknown etiology. It is not clear from the available information how many of these patients had chronic bronchitis except in the study of Berman, et al (72), who investigated normal subjects.

Although two-thirds of these patients yielded no bacteria on transtracheal aspiration, it is disturbing that approximately 15 percent had one specie and 15 percent had more than one specie recovered. From these reports it is not possible to determine what species were recovered in each instance, but it is clear that a significant fraction of the organisms were potential pathogens. These results support the conclusion that transtracheal aspirates may give false positive results a significant fraction of the time.

TABLE 14

COMPARISON OF TRANSTRACHEAL ASPIRATE WITH BLOOD OR LUNG PUNCTURE CULTURES

Study	Transtracheal Aspirate Culture			
	Sterile	Same Single Pathogen	Other Species Pathogen	'Nonpathogen'
Tempest, et al (1974)	0	7	6	3
Davidson, et al (1976)	0	8	6	2
Bartlett (1977)	0	16	7	?
Total	0	31	19	5?

A comparison of transtracheal aspiration with blood or lung puncture cultures, our most reliable methods of diagnosing aerobic bacterial pneumonias, has been reported in only 55 patients (42, 43, 71). Two studies are from the Pneumococcal Research Project, Indian Hospital Service. The observations were made on patients presenting to the hospital with pneumonia who had not received antimicrobial drugs prior to the study. It is not clear whether Bartlett's patients meet these criteria. Among the patients with a lung puncture or blood positive for a pathogenic organism, none had a sterile transtracheal aspirate and 31 had the same single pathogen recovered by both techniques. However, 19 of the patients had additional pathogens recovered from the transtracheal aspirate that were not recovered from the lung puncture, and at least 5 patients had non-pathogens in addition to the pathogen recovered from both sources. Although cultural results in these latter 5 patients would have been satisfactory, gram stain of the tracheal aspirate may have been misleading. Despite the limited number of observations, these studies support the conclusion that cultures of transtracheally obtained material, although more reliable than expectorated sputum (50), may nevertheless give a false positive result.

Feasibility of Lung Puncture

TABLE 15

INCIDENCE OF SIGNIFICANT COMPLICATIONS
DUE TO LUNG PUNCTURE IN CHILDREN

Study	Number Punctures	Pneumothorax No Tube	Tube
Schuster, et al (1968)	10	0	0
Klein (1969)	32	3	0
Hughes, et al (1969)	18	1	0
Mimica, et al (1971)	543	7	2
Total (Percent)	603	11 (1.8)	2 (0.3)

If upper airway secretions in infants, and expectorated sputum or transtracheal aspiration in adults may yield a significant number of false negative or false positive results when compared to lung puncture, it is reasonable to consider the advisability of lung puncture in patients with confusing clinical pictures. Several series of this procedure in children yield sufficient numbers to assess the potential risk (44, 73-75). These data are indicated in Table 15. None of these authors reported a death related to lung puncture. Hemoptysis was rare, and the formation of empyema did not occur. The only complications related to pneumothorax, and it is clear that this was unusual. In

most series lung puncture was performed by a limited number of persons as an investigational technique, but the 32 procedures reported by Klein were performed by pediatric house officers at Boston City Hospital each of whom did only a small number. These data support the use of lung puncture for the diagnosis of complicated pneumonias in infants.

TABLE 16

INCIDENCE OF SIGNIFICANT COMPLICATIONS

DUE TO LUNG PUNCTURE IN ADULTS

Study	Number Punctures	Pneumothorax No Tube	Tube
Gherman and Simon (1965)	18	3	1
Bandt, et al (1972)	22	0	1
Davidson, et al (1976)	25	5	0
Total (Percent)	65	8 (12.3)	2 (3.1)

The data are more ambiguous in adults. Bullowa (39) reported one death from air embolism in approximately 2500 lung punctures. He also had 2 cases of persistent hemiplegia from air embolism and 4 cases of embolism without sequale. As in children hemoptysis is insignificant in adults and empyema apparently does not occur. The most frequent cause of increased morbidity is pneumothorax. Bullowa and other older series do not clearly tabulate the incidence of this complication. The more recent series (43, 76, 77) include a small number of patients, and each is in a research setting with a limited number of physicians performing the procedure. Additionally, patients with bullous emphysema are excluded from study, and most of the patients are middle-aged or younger. Despite these limitations, the pneumothorax rate is apparently greater than in infants. If lung puncture was more widely adopted as a routine clinical procedure the complication and probably mortality rate would almost surely increase. Additionally, only about 50 percent of lung aspirates yield the pathogen that is presumably causing the pneumonia. These considerations, in conjunction with the probability that most community acquired pneumonia will respond to standard antimicrobial regimens, lead me to believe that lung puncture is rarely indicated in persons who are not immunodeficient.

Counterimmunoelectrophoresis of Sputum

TABLE 17

COUNTERIMMUNOELECTROPHORESIS (CIE) OF SPUTUM FOR PNEUMOCOCCAL POLYSACCHARIDE IN PATIENTS WITH PNEUMOCOCCAL PNEUMONIA

Study	No. pts.	Pos. CIE	Percent
Verhoef and Jones (1974)	8	8	100
Spencer and Savage (1976)	92	91	99
Perlino and Shulman (1976)	19	18	95
Leach and Coonrod (1977)	39	29	74
Totals	158	146	92

Clinicians should also be aware of a newly developed test that may prove useful in determining the bacterial etiology of pneumonia. In 1973 Coonrod and Rytel (78, 79) reported that extremely small quantities of pneumococcal polysaccharide may be detected by counterimmunoelectrophoresis (CIE) of body fluids. Since that time pneumococcal polysaccharide has been identified in the serum, urine, and pleural fluid of many patients with pneumococcal pneumonia (80-87). It is not detected in these materials with sufficient frequency to be of significant clinical help, but the detection of pneumococcal polysaccharide in sputum offers great promise. The available data are presented in Table 17.

The 158 patients all had well documented pneumococcal pneumonia (80, 84, 85, 87). Of these, 92 percent were demonstrated to have pneumococcal polysaccharide in their sputum by CIE. Such was the case in many patients with blood cultures positive for pneumococci but from whom the organism was not recovered by sputum culture. These data are extremely encouraging, but the procedure probably should not be recommended for clinical use at present.

The incidence of false positivity of CIE has also been investigated and the results are presented in Table 18.

(18)

TABLE 18

COUNTERIMMUNOELECTROPHORESIS (CIE) OF SPUTUM FOR PNEUMOCOCCAL POLYSACCHARIDE IN PERSONS WITHOUT PNEUMOCOCCAL PNEUMONIA

Condition	No. Pts.	Pos. CIE	Percent
Saliva without pneumococci	82	0	0
Saliva with pneumococci	1	0	0
Nonpneumococcal pneumonia	13	0	0
Bronchitis with pneumococci	122	98	80

Verhoef and Jones; Spencer and Savage; Perlino and Shulman; Leach and Coonrod

Saliva from which no pneumococci can be cultured evidently is negative for pneumococcal polysaccharide (85), but an insufficient number of normal persons colonized with pneumococci have been reported to be sure that their respiratory secretions are negative. Only a small number of patients with pneumonia due to other aerobic bacteria have been shown to have no pneumococcal polysaccharide in their sputum (85, 87). False positive tests have been reported (81, 86, 87), but the true incidence and cause of spurious results is not known. It is clear that the antigen may be detected in the sputum of many patients with chronic bronchitis without pneumonia, and such may limit the usefulness of CIE in patients with chronic obstructive lung disease. Nevertheless, counterimmunoelectrophoresis of the sputum is the most innovative approach to the diagnosis of the bacterial etiology of pneumonia to have been suggested, and it may ultimately prove to be a reliable clinical tool, especially if techniques are developed to detect other common pathogens that cause pneumonia. Additionally, it should be noted that CIE requires only an hour to perform, and hence results are available rapidly enough to guide the initial antimicrobial therapy.

SPECIFIC BACTERIAL ETIOLOGIES

TABLE 19

BACTERIAL ETIOLOGIES OF COMMUNITY ACQUIRED PNEUMONIA IN HOSPITALIZED PATIENTS

Organism	Percent of Cases
Streptococcus pneumoniae	65
Gram negative bacilli	20
Staphylococcus aureus	10
Hemophilus influenzae	<10
Streptococcus pyogenes	1
Legionnaires' disease	
Anaerobic bacteria	

Schwartzmann, et al; Fekety, et al; Sullivan, et al; Dorff, et al.

Since I have shown that our diagnostic accuracy for pneumonia, even retrospectively, is poor, it is my opinion that the initial treatment of each patient must be based on the relative frequency of occurrence of specific pathogens, the clinical presentation of the patient, and an estimate of the severity of illness. An appraisal of the morphology of organisms in an area of gram stained sputum that has many leukocytes with few epithetial cells is supportive but not diagnostic, and transtracheal aspirate may only be recommended in severely ill patients who are unable to provide sputum by any other means. The most accurate determination of the relative frequency of various aerobic organisms in producing pneumonia from recent series (18, 31, 32, 88) is presented in Table 19.

Although recent series indicate an increasing incidence of gram negative bacillary pneumonia (89), pneumococcal pneumonia remains by far the most frequent community acquired bacterial pneumonia. It represents at least 65 percent of hospitalized cases in the adult age group both among persons who have been previously well and among persons with chronic disease. Because of this high rate of occurance most initial antimicrobial regimens should include drugs effective against the pneumococcus. Pneumonias caused by gram negative bacilli represent 20 percent of hospitalized cases, and those caused by staphylococci and *Hemophilus* are also sufficiently frequent to be considered in the correct clinical setting. The role of Legionnaires' disease (90-93), a disease which has

received excessive publicity because of the recent Philadelphia experience, has yet to be determined. Further, the frequency with which pneumonia due to anaerobic organisms occurs relative to aerobic bacteria is difficult to determine, but it must be strongly considered in any patient with a history of depressed consciousness.

Any of these pneumonias may cause an abrupt onset with true rigors, pleuritic chest pain, purulent sputum, and the radiographic appearance of consolidation. Any may produce marked clinicial toxicity and prove ultimately fatal. Thus, the features indicated at the outset of this presentation which suggest bacterial pneumonia do not help in differentiating among the specific bacterial pneumonias.

It is not the purpose of this discussion to review in detail the clinical characteristics, treatment and course of each of these pneumonias. However, I shall indicate some clinical features that may help in making decisions about antimicrobial therapy until the intial blood and sputum cultures are available and until the response to initial therapy is determined.

TABLE 20

PNEUMONIA CAUSED BY *Streptococcus Pneumoniae*

Virtually the only bacterial pneumonia in young, previously health adults who do not use illicit drugs.

Most common bacterial pneumonia in elderly or debilitated adults.

Unusual features include abscess formation or pleural fluid during early course.

Pneumococcal pneumonia is virtually the only type of bacterial pneumonia among young, civilian adults who have been previously healthy and who have no unusual social or epidemiologic history. Young adults in military populations may develop more unusual bacterial pneumonias (50, 62, 94). Pneumococci also account for most bacterial pneumonias among older persons and patients with chronic debilitating diseases including alcoholism (18, 31, 32, 88). Thus, I would argue that virtually all adult patients with serious pneumonia should have an initial antimicrobial regimen that is effective against the pneumococcus irrespective of the clinical and laboratory features of their disease at time of presentation. Since a variety of antimicrobials are effective in this regard (95-98), an agent effective against both pneumococci and other bacteria may usually be chosen if a different etiology is suspected. Features which should make one concerned about a different etiology include a history of illicit intravenous drug use (99-105), anticedent influenza (31, 106, 107), handling wild game (108), travel in Southeast

Asia (109), or most commonly a chronic debilitating disease. Abscess formation and a pleural effusion early in the course of pneumonia are also sufficiently uncommon with pneumococcal pneumonia to cause a suspicion of a different etiology.

It should also be noted that only standard doses of penicillin are necessary even in patients with pneumococcal pneumonia who are seriously ill (110). The response to antimicrobial therapy is frequently helpful in confirming the diagnosis, since most patients improve dramatically within hours of beginning the antimicrobial, but up to 30 percent of patients have been reported to remain febrile for longer than 4 days owing to a alcoholic hepatitis or other complicating factors (97, 98). Clearing of the radiographic infiltrate should not be used as an index of clinical response, since such may be protracted in some patients (111).

TABLE 21

PNEUMONIA CAUSED BY GRAM NEGATIVE BACILLI

Almost always in chronically ill persons. Especially: alcoholism, heart disease, diabetes, renal failure, chronic lung disease, malignant diseases, persons in chronic care facilities.

Pleural effusions and abscess formation early in illness.

Volume expansion of consolidated lobe.

Gram negative bacilli now cause approximately 20 percent of community acquired pneumonias requiring admission to general hospitals (32, 88). Whereas *Klebsiella pneumoniae* had been the only such organism reported in older series to cause pneumonia, other gram negative bacilli have been implicated with increasing frequency (28, 89, 112-116). For emphasis I shall repeat that gram negative bacillary pneumonia most commonly has an abrupt onset with true rigors, pleuritic pain, purulent sputum, and physical and radiographic evidence of consolidation (28, 112-118), and thus pneumonia due to these organisms cannot be differentiated from pneumococcal pneumonia on these clinical findings.

This type of pneumonia almost always occurs in chronically ill or debilitated persons. The most frequently associated conditions include alcoholism, heart disease with or without heart failure, diabetes mellitus, renal failure, chronic obstructive lung disease, malignant diseases, and debilitating diseases leading to residence in a chronic care facility. Some patients with gram negative bacillary pneumonia have pleural effusions and parenchymal lung abscesses at the time of the initial evaluation,

features that are uncommon in pneumococcal pneumonia. An occasional patient with klebsiella pneumonia may have an expansion of the volume of the consolidated lobe, a finding that is unusual in other bacterial pneumonias (119). Since effusions, abscesses, and volume expansion are not consistently present, however, their absence does not weigh heavily against the possibility that the pneumonia in a specific debilitated patient is due gram negative bacilli.

In many patients with gram negative bacillary pneumonia the organisms are identified by gram stain of expectorated sputum (28). However, such is not invariably the case (48). Thus, in my opinion, chronically ill persons who present with a life threatening pneumonia should be initially treated for gram negative bacillary pneumonia irrespective of whether such organisms are seen in the sputum. This course of action may result in administering nephrotoxic antimicrobials unnecessarily to many patients. However, it is also likely to improve survival among patients with gram negative bacillary pneumonia whose mortality is reported to be from 45 to 79 percent (28, 32, 88). Appropriate antimicrobial regimens include penicillin and gentamycin or a cephalosporin and gentamycin. Most pneumococcal pneumonia patients improve clinically within two to three days while patients with gram negative bacillary pneumonia have a more protracted illness. Thus, by the time sputum and blood cultures become available, one may correlate these data with the patient's clinical course, and inappropriate antimicrobials may be discontinued in the majority of instances.

TABLE 22

PNEUMONIA CAUSED BY *Staphylococcus aureus*

Rarely occurs *de novo*. Usually follows influenza or illicit intravenous drug abuse.

Following influenza: difuse 'patchy' alveolar infiltrates, abscess formation, pleural effusion.

Following drug abuse: subacute onset, multiple nodular lesions, abscess formation, pleural effusion.

Community acquired pneumonia due to *Staphylococcus aureus* may frequently be strongly suspected at the time of admission owing to epidemiologic and clinical features. It uncommonly occurs *de novo*, although it sometimes does so in chronically ill persons (31) and occasionally causes a septicemic pneumonia from a remote abscess. Most commonly, however, staphylococcal pneumonia follows influenza or illicit intravenous drug abuse.

In the form that occurs following influenza, there is frequently an asymptomatic interval of a few days as the patient recovers from the previous viral infection (31, 106, 107). The onset of the bacterial pneumonia is then marked by an abrupt onset of chills, fever, pleuritic chest pain, cough with purulent sputum, and perhaps dyspnea. Chest radiographs usually reveal diffuse, patchy alveolar infiltrates, and abscess formation and pleural effusions are common. The abscesses, when present, tend to be small. Pneumatocele formation is not frequent in adults. The sputum gram stain very commonly suggests the correct diagnosis (31).

Staphylococcal pneumonia following drug abuse tends to have a subacute onset of fever and cough which is frequently minimally productive (99-105). By the time of presentation most patients are extremely toxic, and pleuritic pain and dyspnea are common. Although the pneumonia is due to septic embolization from tricuspid valvular endocarditis, the heart examination is commonly normal, and chest physical findings are minimal. Chest radiographs may reveal only accentuated interstitial markings, but randomly distributed ill defined nodular lesions are more frequent. Abscess formation and pleural effusions are common. If pulmonary abscesses have been present for a protracted interval, systemic arterial emboli with abscess formation is not rare, especially to the kidneys, spleen, and brain.

These distinctive clinical syndromes usually allow specific antimicrobial therapy from the outset. A penicillinase resistant synthetic penicillin, such as methicillin, is the drug of choice, although a cephalosporin is satisfactory in patients with penicillin hypersensitivity. It should be noted that even following influenza, pneumococcal pneumonia is more common than staphylococcal pneumonia (31, 120), and the dosage of methicillin should exceed 8 grams per day to be sufficient for pneumococci. Gram negative bacillary pneumonias are not common following influenza, but such may occur.

TABLE 23

PNEUMONIA CAUSED BY *Hemophilus influenzae*

Apparent increasing frequency among adults

May occur in previously healthy persons

Most severe form with bacteremia more common in persons with alcoholism or chronic obstructive lung disease

Pleural disease common

The frequency of pneumonia due to *Hemophilus influenzae* is apparently increasing in adults (212-126). The increased reporting of this pneumonia

correlates with improved culture techniques of sputum and blood (126), however, and many cases may have been previously missed. Almost all adult disease is due to encapsulated strains, almost always Type B, but unencapsulated, nontypable strains have been implicated.

This type of pneumonia may occur in young, previously health adults. It is apparently more common, however, in persons with chronic debilitating diseases. Community acquired cases are especially associated with alcoholism and chronic obstructive lung disease. Further, the most severe disease is usually associated with bacteremia, and such is clearly more commonly associated with underlying diseases and with older age groups. Pleural thickening or free pleural fluid on presentation occurs more commonly than with pneumococcal pneumonia, but is present in the minority of patients. Other radiographic features are not definitive. Most patients demonstrate bronchopneumonia, especially in the lower lobes, but many patients have lobar or segmental consolidation.

Except for patients presenting with pleural disease, there is nothing in the clinical presentation of patients with pneumonia due to *Hemophilus influenzae* to suggest this bacterial etiology. A gram stain of expectorated sputum revealing large numbers of small, pleomorphic, gram negative bacilli should strongly suggest the correct diagnosis. It should be emphasized, however, that poorly prepared specimens are frequently misinterpreted, especially by inexperienced observers (126). A transtracheal aspirate clearly facilitates the diagnosis, since most extraneous organisms are eliminated (125, 126). However, I doubt that *Hemophilus influenzae* pneumonia that is not suggested by a well stained sputum occurs with sufficient frequency to make this proceedure indicated on a routine basis.

Ampicillin remains the therapy of choice for patients with pneumonia due to this organism. Resistant strains have been reported in other diseases but not as a cause of adult pneumonia. In extremely ill patients it would be reasonable to use chloramphenacol to obviate this possibility.

TABLE 24

PNEUMONIA CAUSED BY ANAEROBIC BACTERIA

Clinical Finding	Frequency
Depressed consciousness	72%
Symptoms > 7 days	57%
Abscess formation or empyema	69%
Putrid discharge	41%

Bartlett and Finegold: Amer. Rev. Resp. Dis. 110:56, 1974.

Although the incidence of pleuropulmonary infections due to anaerobic organisms is not known, it is clear that a significant fraction of pneumonias admitted to a general hospital are caused by these organisms. A variety of studies (33, 127-135) indicate that the diagnosis may usually be made by the clinical presentation of the patient. The data in Table 24 are those of Bartlett and Finegold based on 143 patients (33).

Most patients have a history of an episode of depressed consciousness, most commonly from alcoholism. Anaerobic bacterial pneumonia is also frequently associated with bronchial obstruction due to bronchogenic carcinoma. In this series symptoms had been present in approximately 60 percent of patients for over a week. These authors included patients with hospital acquired pneumonia. An even greater fraction of community acquired disease has such a subacute or chronic onset. Abscess formation and empyema are common. The occurance of putrid sputum is virtually diagnostic if the patient does not have severe peridontal disease. This type of pneumonia tends to be localized to a single bronchopulmonary segment, most commonly the posterior segment of the right upper lobe or the superior segment of the right lower lobe followed by the corresponding segments of the left lung (33, 127). Anaerobic bacterial pneumonia is not common in the right middle lobe or the lingula.

It is clear that most patients with pneumonia due to anaerobic organisms may be diagnosed on clinical grounds. These patients usually respond to penicillin, even low dosage regimens (136), and those who do not do so respond to clindamycin (128-130, 129, 131, 134, 135). Moreover, those patients who have a more acute onset without the classic features indicated tend to respond to treatment with penicillin much like patients with pneumococcal pneumonia (33). Thus, in my opinion, a transtracheal aspirate is rarely indicated in this group of patients.

SUMMARY

In summary, community acquired pneumonia is usually a mild disease due to viruses, mycoplasma, or pneumococci and may be treated by the outpatient administration of erythromycin. More severely ill patients who have been previously well and who have no unusual epidemiological history most commonly have pneumococcal pneumonia, although pneumonia due to *Hemophilus influenzae* is apparently becoming more frequent in adults. Persons with chronic, debilitating conditions are most likely to have pneumococcal pneumonia, but they are at significant risk for having gram negative bacillary pneumonia. Pneumonia due to staphylococci or anaerobic organisms can most commonly be suspected from the history and clinical presentation.

A gram stain of expectorated sputum from an area with many leukocytes and no epithelial cells may suggest the causative organism but is not diagnostic. Sputum culture may be retrospectively helpful, but only if it is true sputum with minimal salivary contamination, and sputum is also not definitive. Transtracheal aspiration is rarely indicated.

Initial antimicrobial regimens are most reasonably constructed from the clinical presentation of the patient with laboratory aids of secondary importance.

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