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EMPYEMA OF THE THORAX

INTRODUCTION

Definitions

Incidence

Bacteriology

DIAGNOSIS

Clinical Presentation

Diagnostic Procedures

THERAPY

Antimicrobials

Drainage

Results

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EMPYEMA OF THE THORAX

Empyema of the thorax continues to be a frequent problem on medical wards. However, it is clear that the treatment of patients with empyema is often hesitant and lacks an organized approach. Such results in an unacceptably high mortality and in extremely prolonged morbidity. For example, at one University Hospital the median hospital stay is 35 days for survivors of community acquired empyema and 58 days for hospital acquired empyema (1). Hospitalization for as long as eight months continues to be reported for some patients. These considerations have led to this review.

The literature on empyema is confusing and contradictory, and the clinical courses or results of treatment may not be comparable between different series of patients. Indeed, it has not been possible for physicians to agree on a specific definition of empyema. The most frequent definitions are indicated in Table 1.

Table 1

Most Frequent Definitions of Empyema

1. Purulent fluid in the pleural space
2. Purulent fluid in the pleural space with a positive culture for a (bacterial) pathogen
3. Infected pleural exudate
4. Parapneumonic effusion $\neq$ empyema

Purulent fluid or frank pus in the pleural space is the definition used by most authors (2-5). This definition does not require that a pathogen be identified by gram stain or subsequent culture of the pleural fluid. The definition obviously leads to a subjective interpretation of which fluids constitute frank pus. Only one author has further defined pus (6), and his definition was subsequently used by an additional author (7). It was said that "the pus may be thick or watery. It must have a specific gravity more than 1.018, a white blood cell count of more than 500 cells/mm^3 and a total protein content of more than 2.5 gm %. A positive bacterial culture is not required". This definition is clearly unacceptable, since transudates or exudates of multiple causes have been reported to have the same values (8-10). In only one study has the white blood cell count of pleural fluid been correlated with the gross appearance of the fluid (11). Fluid was reported as clear with up to 3,000 cells/mm^3, turbid with 3,280 to 39,600 cells/mm^3, and pus with 40,900 to 100,000 cells/mm^3 (12). These observations correlate only modestly with another author who defines empyema as pus with greater than 15,000 white blood cells/mm^3 (13).

A second definition requires that there is purulent fluid in the pleural space with a positive culture for a pathogen (14, 15). In addition to the problem of defining purulent fluid, this definition excludes from consideration patients with negative cultures. In some reported series, up to 80 percent of patients are considered to have empyema with negative pleural cultures (16). This definition is simplified by others to "an infected pleural exudate" with the deletion of the necessity for a purulent appearance (17). The problem of correlating such series with those without bacteriologic confirmation remains.

More recently the term parapneumonic effusion has been used by two groups of investigators (12, 18-21). A parapneumonic effusion is defined as a pleural effusion in association with an acute febrile illness in which pulmonary infiltrates and purulent sputum are present. This definition includes those pleural effusions secondary to pneumonia whether the pleural fluid is serous or frankly purulent. The purpose in this nomenclature is to emphasize that pleural effusions in association with pneumonia do not necessarily indicate that the pleural space is frankly infected and hence do not connote an illness more serious than the primary pneumonia. Thus, all empyemas in association with pneumonia are parapneumonic effusions, but not all parapneumonic effusions are empyemas. The importance of the differentiation relates to the ability to treat a simple parapneumonic effusion with antimicrobial therapy alone, whereas the treatment of empyema requires drainage of the pleural space in addition to antimicrobial therapy. The ability to prospectively predict the necessity for pleural drainage is the subject of investigations by these groups, and their studies will subsequently be enumerated. However, it should be emphasized that not all pleural effusions in association with pneumonia should be categorized as empyema.

Infections in the pleural space have frequently been divided into acute or chronic empyemas, especially in the old surgical literature (22- 25). Attempts to differentiate between the two on a purely chronologic basis are not satisfactory because of the poor correlation between the duration of the disease and the lesion that is present. An acute empyema is one in which the pleura is lined by infected fibrin and other purulent material, whereas in chronic empyema the material has largely changed to fibrous tissue. The former may respond to antimicrobials and simple drainage maneuvers, but the latter usually requires a thoracotomy with extensive debridement. Reasonable management of empyema in the acute stage should result in few cases of chronic empyema.

A more useful categorization of empyema emphasizes the primary event which led to the infected pleural space.

Table 2

Event Preceding Empyema
231 Cases - All Ages

	Number	Percent
Pulmonary Infection	184	55
Post-Thoracotomy	75	22
Esophageal Perforation	12	4
Iatrogenic	13	4
Trauma	13	4
Intra-Abdominal	8	2
Unknown/Other	31	9

Snider and Soleh; Emerson, et al; Weese, et al;
Sherman, et al; Davis and Johnson

The combined data of several groups allow the definition of the primary event preceding empyema in 231 patients (2, 6 - 7 , 26). These series include children as well as adults. In neonates, empyema virtually always follows pneumonia. Nevertheless, there is sufficient confirmation from other series to indicate that these data are approximately correct for adult patients.

By far the most frequent event leading to an infected pleural space is an antecedent pneumonia. Since the pneumonia usually dominates the clinical symptomatology at presentation, the characteristic features of pneumonias associated with empyema will be reviewed subsequently. In recent series an increasing number of patients with empyema have had lung resection, typically for bronchogenic carcinoma. Esophageal perforation, iatrogenically induced empyema and trauma each constitute a small fraction of the patients. Esophageal perforation leads to a syndrome sufficiently different from empyema with pneumonia that this problem will not be reviewed. Iatrogenic empyema is caused by the introduction of bacteria into a previously sterile fluid during a thoracentesis. Staphylococci and gram negative bacilli are the most frequent offending organisms in this circumstance. A hemothorax that subsequently becomes infected may be caused by either penetrating or non-penetrating trauma. Empyema is occasionally secondary to an intra-abdominal abscess, most commonly due to a mixed flora of anaerobic and aerobic bacteria. The antecedent event preceding empyema is not diagnosed in a significant fraction of patients.

The treatment of patients with post-thoracotomy or traumatic empyema may require extensive surgical procedures (27 - 30), and the therapy of these patients is usually directed by our thoracic surgical colleagues. These types of empyemas will not be addressed in this review.

Table 3

Incidence and Mortality of Empyema
at Boston City Hospital

Year	No. Cases / 1000 Adm.	No. Deaths / 100 Hosp. Deaths	Mortality Rate (%)	Percent Cases Hosp.-Acquired
1935	3.18	1.75	38.4	14.4
1951	0.84	0.67	54.5	39.4
1961	1.52	1.25	52.0	58.0
1972	1.85	2.16	59.0	61.5

Finland and Barnes: J. Infect. Dis. 137:274, 1978

The incidence of empyema is indicated by the report of Finland and Barnes from Boston City Hospital. Their definition of empyema includes the identification of a bacterial pathogen in purulent pleural fluid causing an underestimation of the true incidence (14). In the pre-antimicrobial era there were three cases of empyema per 1,000 hospital admissions which resulted in 1.75 deaths per 100 hospital deaths. The mortality rate for patients with empyema was about 38 percent. In that era, almost all empyema followed community acquired pneumonia with only 14 percent of the cases hospital acquired. *Str. pneumoniae* accounted for about half of these cases, and hemolytic streptococci were the second most common cause. After the introduction of penicillin the total number of cases decreased dramatically, and a greater fraction of the cases were hospital acquired. Recently, however, there has been an increasing incidence, and the number of deaths per 100 hospital deaths has exceeded the pre-antimicrobial era. The very high mortality rate of approximately 60 percent in this series was related to the large number of cases which were hospital acquired and thus due to organisms resistant to antimicrobials, most commonly gram negative bacilli or *Staphylococcus aureus*.

These data substantiate the continued importance of empyema both in the number of patients affected and in mortality. It should be indicated, however, that the mortality rate and the fraction of hospital acquired cases are higher than in other recent series and likely reflect some bias in selection.

Table 4

Bacterial Etiology of Empyema
837 Cases - All Ages

	Number	Percent
Staphylococcus aureus	155	19
Gram Negative Bacilli	114	14
Str. pneumoniae	70	8
Hemolytic Streptococci	51	6
Mixed Aerobes	53	6
Anaerobes	47	6
Other	48	6
"Sterile"	299	36

Finland and Barnes; Sullivan, et al; Morin, et al; Geha; Cohn and Blaisdell; Bryant, et al

Several combined series report the bacterial etiology of empyema in 837 cases (3, 4, 14, 31 - 33). These data are included because they are representative of the empyema literature. However, the information is probably spurious for the following reasons. The definition of empyema, the acceptance of patients without positive bacteriology, and the inclusion of post-thoracotomy cases varies from series to series. Several series also include children, and for the past several years virtually all empyema in childhood is caused by *Staphylococcus aureus* (34-36). The fraction of cases with gram negative bacilli depends in part on the number of cases of hospital acquired and of post-thoracotomy empyema. The number of cases due to anaerobic bacteria is exceptionally small. These series are all retrospective analyses, and it is highly unlikely that adequate anaerobic technique was used for culturing the pleural fluid. The large fraction of cases which were recorded as "sterile" supports this hypothesis.

Despite the limitations indicated, credence can be given to certain of these data owing to confirmation from every recent article on empyema. *Str. pneumoniae* and hemolytic streptococci, the most common causes of empyema in the pre-antimicrobial era, are now infrequent causes of empyema.

Information concerning bacteriology from a much smaller series of patients is more likely to be correct for empyema as it occurs on medical wards.

Table 5

Bacterial Etiology of Empyema
Adult Medical Cases Only

	Total Cases	Anaerobes Only	Anaerobes Plus Aerobes	Aerobes Only
Prospective Cases	35	13 (37%)	12 (34%)	10 (29%)
Retrospective Cases	48	16 (33%)	22 (46%)	10 (21%)
Total	83	29 (35%)	34 (41%)	20 (24%)

Bartlett, et al: Lancet 1:338, 1974

Bartlett and colleagues have reported the bacteriological findings of 83 patients with empyema admitted to adult medical wards (37). Children and patients with complications of thoracic surgery were excluded. Their definition of empyema was infected pleural exudate. In the prospective series it is said that patients were not selected, but the retrospective cases may have had a selection factor. The specimens could be sent by the primary care physician either to a clinical laboratory or to an anaerobic research laboratory.

A major question concerning the applicability of these data to all medical patients relates to the recognized interest of Bartlett and Finegold in infections caused by anaerobic bacteria allowing the possibility for unintentional bias in submission of specimens to them. Their data are partially supported by two small, recent series in which the number of anaerobic bacteria recovered were fewer but of a generally similar frequency (38, 39). These findings are also supported by a retrospective study by Sullivan and colleagues (31). They found an incidence of anaerobic empyemas of 19 percent and mixed anaerobes and aerobes of 9 percent among 226 culture positive empyemas. However, since only 47 percent of all patients with empyema were culture positive, the investigators inferred that anaerobic organisms likely caused a larger fraction of the empyema cases they reported.

Recognizing the limitations of each of the studies indicated, it is reasonable to conclude that anaerobic bacteria or a mixture of anaerobic and aerobic bacteria cause a large fraction of the cases of empyema observed on medical wards. Such is especially likely to be true for community acquired empyema. It is likely that gram negative bacilli cause a larger number of cases which are hospital acquired.

Table 6

Aerobic Bacterial Etiology of 83 Cases of Empyema
Adult Medical Cases Only

	Number Isolates	Pure Isolates
Staphylococcus aureus	17	6
Gram Negative Bacilli	30	3
Str. pneumoniae	5	2
Hemolytic Streptococci	9	0

Bartlett, et al: Lancet 1:338, 1974

Among Bartlett's patients whose empyema was due to aerobic bacteria, the culture results support the findings of other physicians. That is, *Staphylococcus aureus* and gram negative bacilli comprise the most frequent aerobes found in empyema fluid. It is common for multiple gram negative bacilli species to be recovered from a hospital acquired empyema.

Since the relative frequency of specific bacteria as a cause of empyema is imprecisely known, it is useful to determine the frequency with which empyema occurs with pneumonias of a specific bacterial etiology.

Table 7

Frequency of Empyema in Bacterial Pneumonia

Organisms	References	No. Pts.	Empyema No.	Empyema Percent
S. aureus Infants	Huxtable, et al	25	22	88
Adults	Musher and McKenzie; Schwarzmann, et al	41	4	10
Gram Negative Bacilli	Tillotson and Lerner; Lampe	75	24	32
Str. pneumoniae	Austrian	529	18	3
Hemolytic Streptococci	Burmeister and Overholt; Basiliere, et al	100	59	59
Anaerobic Bacteria	Bartlett and Finegold	143	47	33

In small children most pneumonia is caused by *Staphylococcus aureus*, and up to 90 percent develop empyema (40, 41). The incidence of empyema is much lower, however, in adults who develop staphylococcal pneumonia (42, 43), and 10 percent is a reasonable estimate. Different species of gram negative bacilli vary in their propensity to cause empyema (44-46). However, as a group about a third of patients with pneumonia due to these organisms develop empyema. Only about 3 percent of patients with pneumococcal pneumonia develop empyema (47), but the incidence among persons with pneumonia due to hemolytic streptococci is approximately 60 percent (48, 49). Anaerobic bacterial pneumonia is similar to gram negative bacillary pneumonia in causing empyema in about one-third of patients (17).

When a patient presents to a physician with empyema associated with pneumonia, it is usually the pulmonary infection that dominates the findings. Thus, clinical features of the pneumonias caused by these organisms will be reviewed to place the empyema in proper prospective.

Table 8

Aerogenous *Staphylococcus aureus* Pneumonia in Adults

Antecedent debility or influenza
Symptoms similar to any bacterial pneumonia
Segmental or lobar consolidation
Cavitation common, pneumothorax possible
Staphylococci in sputum by gram stain
Empyema at the time of presentation

Miller, et al; Schwarzmann, et al; Musher and McKenzie; Louria, et al

Staphylococcus aureus causes approximately 10 percent of the pneumonias in adults which are severe enough to lead to hospitalization (42, 50-52). Staphylococcal pneumonia causes two distinctive clinical syndromes, one of which is referred to as aerogenous pneumonia. This type of disease rarely occurs in previously normal persons. It affects persons who have some antecedent debility or persons who are recovering from influenza (42, 43, 53) 54). The onset of pneumonia is similar to that of most bacterial pneumonias; an abrupt onset of chills, fever, pleuritic chest pain, cough with purulent sputum, and perhaps dyspnea. Chest radiographs may show diffuse alveolar infiltrates, frequently with segmental or lobar consolidation. Cavitation is common; the cavities are usually small and may be multiple. Pneumothorax in association with empyema occurs more frequently than with other pneumonias, although not as frequently in adults as in children. The sputum gram stain

commonly suggests the correct diagnosis (42). When empyema occurs it is usually present at the time of presentation and may be of massive proportion. However, large pleural effusions are more common in pediatric than adult patients.

Table 9

Hematogenous *Staphylococcus aureus* Pneumonia in Adults

Antecedent drug abuse or instrumentation

Symptoms include chills and fever; pulmonary symptoms variable

Discrete pulmonary nodules

Cavitation common, pneumothorax possible

May be no sputum for examination

Empyema at the time of presentation

Louria, et al; Ramsey, et al; Jaffe and Koschmann; Musher and McKenzie

The other type of pneumonia due to *Staphylococcus aureus* is referred to as hematogenous pneumonia and follows septicemia caused by antecedent illicit drug abuse or iatrogenic instrumentation (43, 55-57). The onset of infection in these patients is frequently subacute but includes chills and fever. The pulmonary symptoms are variable. They may include cough, which is often only minimally productive, pleuritic pain, and dyspnea. Although the pneumonia is due to septic embolization and is frequently from an acute bacterial endocarditis of the tricuspid valve, the heart examination may be normal. The chest examination may also be normal. The chest radiograph may reveal only accentuated interstitial markings, but more commonly there are randomly distributed, relatively discrete pulmonary nodules. Cavitation of the nodules is common, frequently producing a thin walled cystic appearance. These patients may also develop pneumothorax. There is often no sputum available for examination. When empyema occurs, it is usually present at the time of presentation and usually small in amount.

Table 10

Gram Negative Bacillary Pneumonia

Antecedent debility, especially alcoholism

Symptoms similar to any bacterial pneumonia

Broncho or lobar consolidation; nodular infiltrates

Cavitation common

Sputum gram stain frequently negative for GNB

Empyema at presentation or during treatment

Lampe; Tillotson and Lerner; Edmondson and Sanford; Reid, et al; Dorff, et al

Gram negative bacilli cause about 20 percent of community acquired pneumonias resulting in hospitalization and an even larger fraction of hospital acquired pneumonias (42, 50-52). These infections virtually always occur in chronically ill, debilitated persons (44-46, 52, 58-60). The most frequent form of debility is alcoholism. The symptoms are similar to any bacterial pneumonia and include an abrupt onset of rigors, pleuritic pain, purulent sputum and the physical findings of consolidation. On chest radiography most patients have bronchopneumonia or lobar consolidation. Patients with pneumonia due to *Pseudomonas aeruginosa* may have an infiltrate consisting of small, ill defined nodular densities. Cavitation is common with all species of gram negative bacilli and may be present at the time of the initial visit. The cavities with *Klebsiella pneumoniae* tend to be quite large, while those caused by other gram negative bacilli tend to be small. The initial sputum gram stain is often negative for gram negative bacilli (61, 62). When empyema occurs in conjunction with a gram negative bacillary pneumonia, it is usually present early in the course except with pneumonias caused by *Escherichia coli*. In either event, the effusions may be quite large. Although many gram negative bacilli cause bilateral pneumonia, the empyema is usually unilateral.

Table 11

Streptococcus pneumoniae Pneumonia

Occurs in any age group with or without debility

Symptoms similar to any bacterial pneumonia

Segmental or lobar consolidation

Cavitation rare

Sputum gram stain suggestive in two-thirds

Small, sterile effusions frequent at any time

Empyema occurs only with delayed treatment

Austrian and Gold; Jay, et al; Taryle, et al

Str. pneumoniae remains the most common cause of bacterial pneumonia, accounting for two-thirds of patients hospitalized with community acquired pneumonia (42, 50-52). Pneumococcal pneumonia occurs in any age group in normal or debilitated persons (47, 63). The symptoms do not distinquish it from other bacterial pneumonias: abrupt onset of chills, fever, pleuritic chest pain, cough productive of purulent sputum and perhaps dyspnea. Most commonly pneumococcal pneumonia causes a segmental or lobar consolidation. Cavitation is extremely rare. The sputum gram stain is suggestive in approximately two-thirds of patients. It recently has been reported that a high fraction of patients with pneumococcal pneumonia have small, sterile effusions at some time during the course of their illness (15). It should be emphasized, however, that such effusions are small and commonly require lateral decubitus radiographs to be visualized. Empyema occurs only with delayed or ineffectual treatment, in which case it may be present at the time the patient is first examined.

Table 12

Hemolytic Streptococcal Pneumonia

Epidemics in closed populations, especially military recruits

Symptoms similar to any bacterial pneumonia

Patchy bronchopneumonia

Sputum gram stain suggestive

Empyema present on admission

Burmeister and Overholt; Basiliere, et al

Pneumonia due to hemolytic streptococci is rare, accounting for no more than one percent of community acquired pneumonias requiring hospitalization (42, 50-52). It typically occurs as epidemics in closed populations of young persons living in close proximity, especially among military recruits (48, 49). The symptoms are similar to any other bacterial pneumonia with an abrupt onset of chills, fever, pleuritic chest pain, and cough with purulent or bloody sputum; dyspnea is more likely than with other bacterial pneumonias. The radiographic appearance is that of a patchy bronchopneumonia. The sputum gram stain is frequently suggestive of the appropriate diagnosis. Empyema is common with this pneumonia and occurs early in the course. The volume of the empyema fluid is frequently large.

Table 13

Anaerobic Bacterial Empyema

Aspiration, bronchogenic carcinoma, subphrenic abscess

Symptoms present days to weeks, weight loss

Localized infiltrates, especially basilar segments

Cavitation common

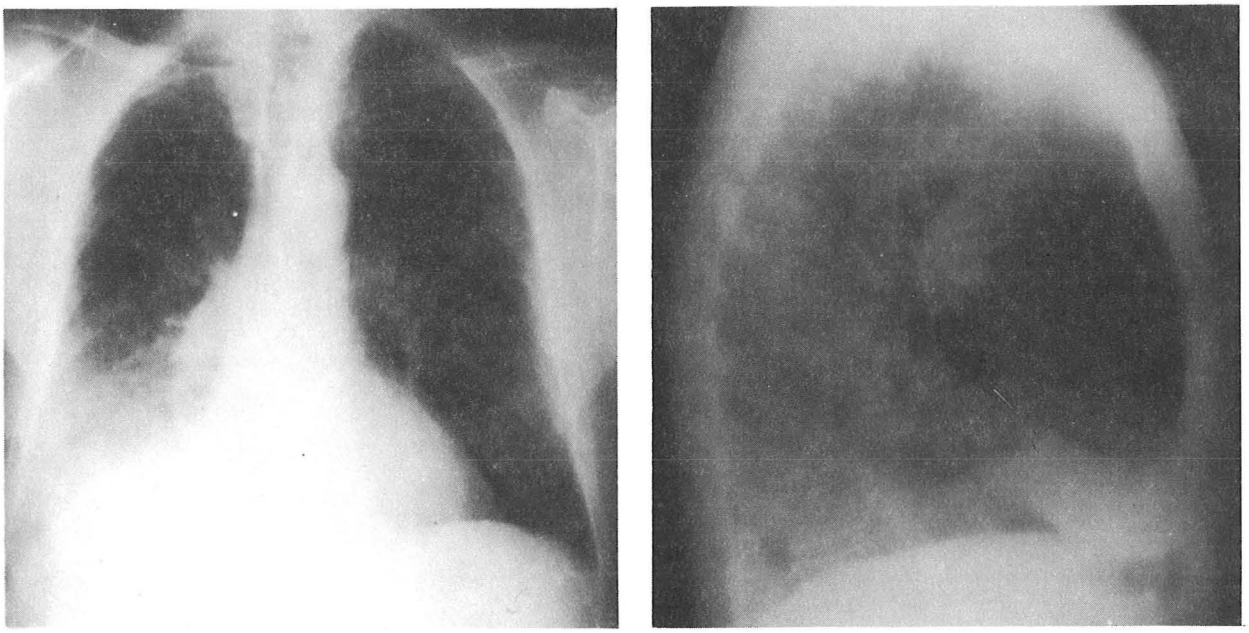
Loculated empyema on admission

Tillotson and Lerner; Sullivan, et al; Bartlett and Finegold

It is not possible to give a precise frequency of anaerobic bacterial pneumonia relative to aerobic bacterial pneumonia. Most patients have a history of depressed consciousness, frequently due to alcoholism, which has predisposed to the aspiration of oropharyngeal contents (17, 31, 64). Other patients develop pneumonia distal to a partially obstructed airway caused by bronchogenic carcinoma. Empyema in association with a subphrenic abscess also is caused by anaerobes. These patients are usually chronically ill. Although an episode of acute pleural pain may be the event that causes the patient to seek medical aid, symptoms have usually been present for days to weeks, and excessive weight loss is common. Anaerobic bacterial pneumonia leads to localized infiltrates, which in the absence of empyema are most commonly in the posterior segments of the upper lobes. However, when empyema is associated with a pneumonia the basilar segments are more commonly involved (27). Cavitation is usually present, and the cavities may be small to moderate in size. Since the low grade symptoms allow the patient to seek medical aid late in the course of infection, the empyema is frequently loculated on admission to the hospital.

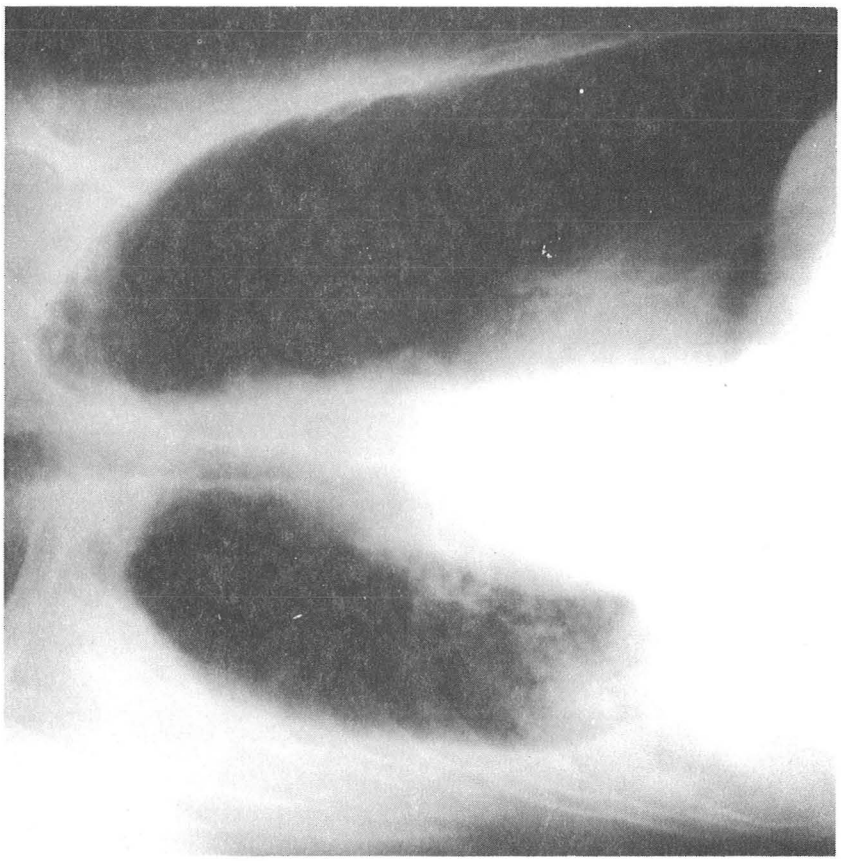
It is possible, therefore, to suspect the most likely bacterial etiology of pneumonia based on the clinical and epidemiologic features determined from the initial workup. It is also possible to predict the likelihood of empyema. This information is used to decide the extent of diagnostic procedures to detect potential empyema. It is important to do so at the onset of treatment, since antimicrobial therapy alone will not cure patients with this complication. Unfortunately, the presence of pleural fluid is not always obvious from standard postero-anterior and lateral chest radiographs.

Figure 1



The PA and lateral film of a patient with pneumococcal pneumonia of the right lower lobe in Figure 1 illustrates this problem. Because the water density of the pneumonia outlines the long fissure, one can determine from the lateral view that there has been volume loss in the affected lobe. However, the parenchymal water density is sufficiently dense and extensive that it is not possible to appreciate the water density of a pleural effusion.

Figure 2



The right lateral decubitus radiograph in Figure 2 is of the same patient and clearly demonstrates that pleural fluid is present. Lateral decubitus films should be obtained at the time of admission when the radiographic infiltrate obliterates the lateral costo-phrenic sulcus in patients who have clinical features suggesting a bacterial pathogen that causes empyema. Decubitus films are also obtained in patients who have physical or radiographic signs suggestive of a pleural effusion. Small amounts of freely moving fluid can be demonstrated in most patients even if the majority of the empyema is loculated. Unfortunately, however, such is not invariably the case. If any features of the illness suggests a loculated empyema, or if a patient does not respond to appropriate antimicrobial therapy, additional studies should be undertaken.

Table 14

Diagnostic Accuracy of Ultrasonic and Radiographic Techniques in 80 Patients with Pleural Effusion

Results of Examination	Ultrasound		Radiology	
	No.	%	No.	%
Fluid detected	74	93	66	83
False negative	1	1	4	4
Indeterminate	5	6	10	13

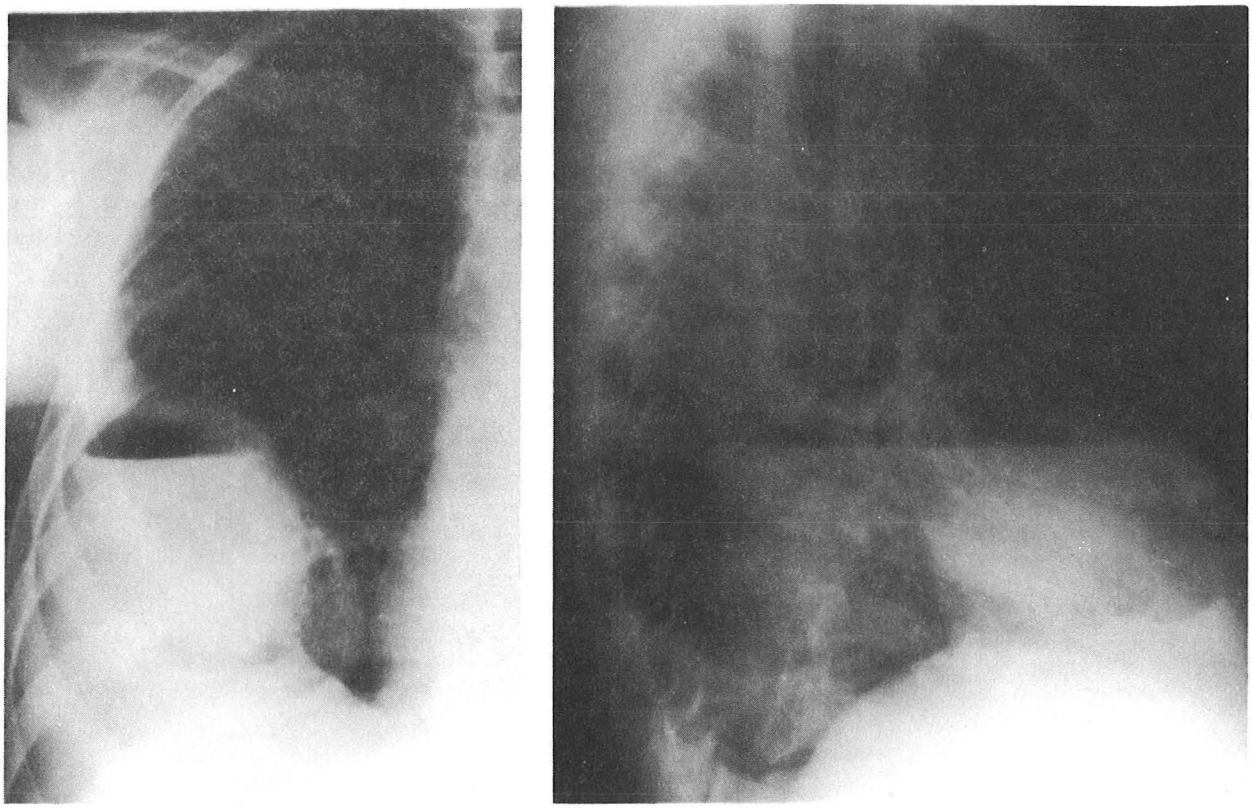
Gryminski, et al: Chest 70:33, 1976

The diagnosis of loculated pleural fluid may be facilitated by ultrasonic techniques (65-69). The results of Gryminski and colleagues presented in Table 14 illustrate the value of ultrasonic examination. These investigators examined 80 patients who were shown to have a pleural effusion by subsequent thoracentesis. The radiographic examination included postero-anterior, lateral, and lateral decubitus views on all patients and fluoroscopy in some patients. Ultrasound correctly detected fluid in 93 percent of their patients and yielded a false negative report in only one. The results were indeterminant in six percent of patients. The radiographic examination was less likely to detect fluid and yielded a higher number of false negative results. Ultrasonic examinations were especially impressive relative to radiologic examination when the volume of fluid was small. If 50 or fewer milliliters of fluid could be obtained by thoracentesis, ultrasound detected the fluid 84 percent of the time with five percent false negative studies, while radiology could detect such fluid only 61 percent of the time with 16 percent false negatives. The ultrasonic technique gave 100 percent positive results when the amount of pleural fluid exceeded 100 ml while the radiographic method gave 100 percent positive results only when the amount of pleural fluid exceeded 500 ml. No false negative results were obtained using the ultrasonic method if the amount of aspirated fluid was more than 50 ml. With the radiographic method, false negative results were not eliminated until the amount of fluid exceeded 250 ml. Additionally, ultrasound may be useful to the clinician in determining

where to perform a thoracentesis in a patient with a loculated empyema. The ultrasonographer can indicate the best location on the chest wall to attempt thoracentesis and can indicate the depth at which the fluid can be expected. In some instances, pockets of fluid containing no more than 10 ml have been aspirated utilizing this technique (69).

Additional diagnostic problems arise in patients who have a radiographically dense lesion contiguous to the chest wall which contains air-fluid levels (70).

Figure 3

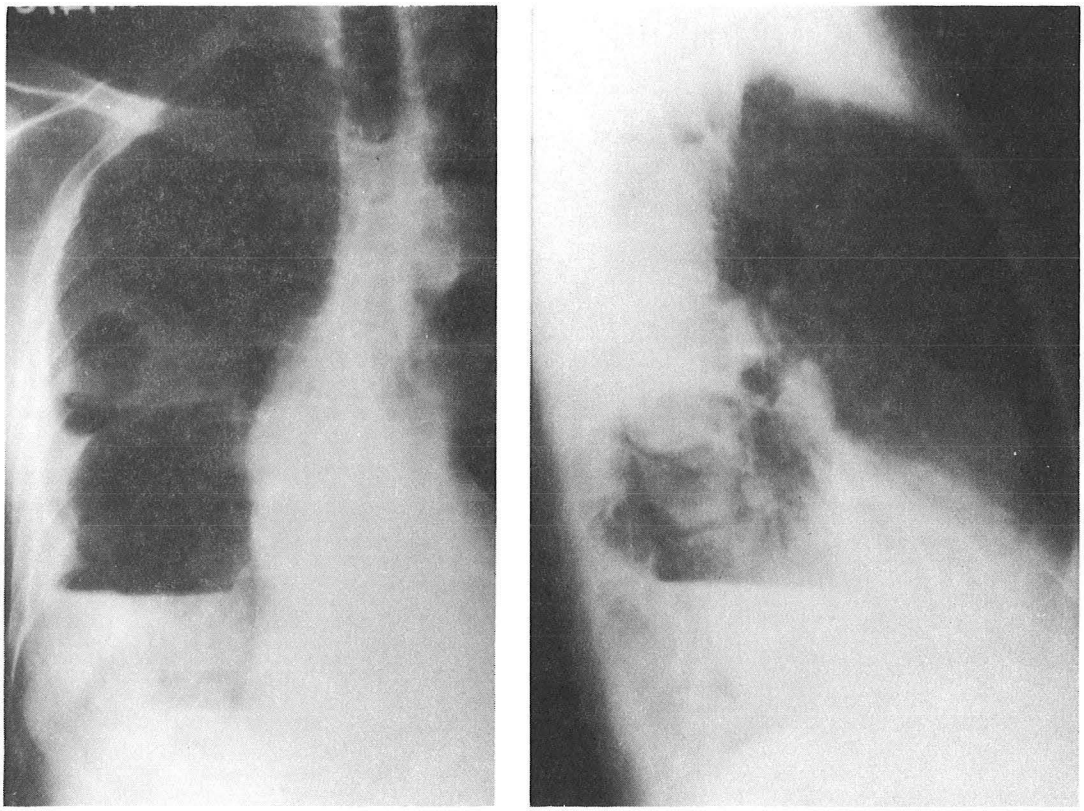


The differentiation of empyema from an intrapulmonary abscess is of considerable importance. In both instances, therapy consists of antimicrobials and drainage. For empyema drainage is usually established with chest tube thoracostomy, while for lung abscess drainage is by a bronchial route. The mistaken insertion of a chest tube into an intraparenchymal abscess may lead to empyema, a pneumothorax, a bronchopleural fistula, or hemorrhage.

The presence of an air-fluid level does not insure that the lesion is in the lung parenchyma. Gas in the pleural space may result from a pyopneumothorax, especially in the case of staphylococcal infections (41), a bronchopleural fistula, or occasionally from an empyema due to gas forming organisms (71-74). If a previous thoracentesis has been performed air may have been introduced into the pleural space.

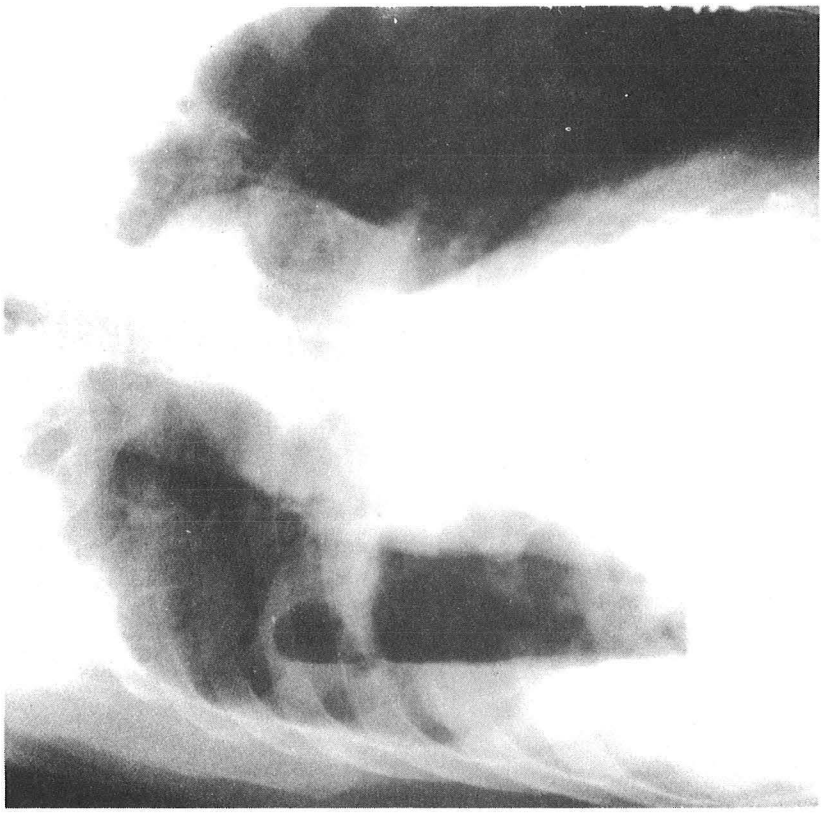
Standard or specialized chest radiographic techniques may be suggestive of the correct localization of the air pocket (75, 76), but such studies are certainly not always conclusive. In the lateral roentenogram demonstrated in Figure 3 the air-fluid level is observed to extend from near the anterior to near the posterior chest wall. The fluid level thus crosses the appropriate location of the long fissure. Since intraparenchymal abscess cavities are usually contained within a single lobe, the film suggests that the fluid and air are in the pleural space. Even this degree of confidence cannot be realized in all patients, however.

Figure 4



The patient whose radiograph is demonstrated in Figure 4 was expectorating putrid sputum and therefore clearly had an anaerobic lung infection. However, even the most skilled radiologist could not determine if a part of the disease was in the pleural space and thus required percutaneous drainage.

Figure 5



In this patient the lateral decubitus examination shown in Figure 5 did not clarify the issue. In such instances ultrasound may be helpful in distinquishing pleural from parenchymal lesions (77, 78), but the total number of patients reported is small, and mistakes in diagnosis have been noted (79). In a single patient a zenon ventilation study demonstrated a broncho-pleural fistula (80), and this technique deserves further evaluation. However, the most promising new technique is computed tomography.

Table 15

Value of CT Scans in Differentiating
Pleural and Parenchymal Disease

CT Results	No. Pts.	Percent
New definitive information	17	37
Clarified available information	20	44
No new information	9	20
Total Patients	46	

Pugatch, et al: J. Comput. Assist. Tomogr. 2:601, 1978

Pugatch and colleagues have used computed tomography in 46 patients in whom a distinction between pleural and parenchymal disease could not be clearly determined on standard posterior-anterior and lateral chest roentgenograms and physical examination (81). In 37 percent of their patients the scans made a contribution to further management which would not have been undertaken based on any other data. In an additional 44 percent of patients the scans clarified findings derived from other studies but did not reveal unexpected abnormalities. In 20 percent of patients the scans did not add to the information available from standard roentgenograms.

Through some combination of the diagnostic maneuvers enumerated most patients with pleural effusions complicating pneumonia may be identified. If the volume of fluid is estimated to be more than a few milliliters, if lateral decubitous films suggest that part of the fluid is loculated, or if the pneumonia is thought to be due to anaerobic bacteria or gram negative bacilli, a thoracentesis should be performed promptly. As large a gauge needle as possible, preferably a 14, should be utilized. since thick pus may be difficult to aspirate. In the case of loculated fluid thoracentesis should be performed in several locations. Osler's admonition to procede with diagnostic thoracentesis "seventy times in seven places" is a bit excessive, but it emphasizes the fact that benign, sterile effusions may be adjacent to walled-off pockets of infection. If foul smelling pus is obtained, the interpretation is not ambiguous. Less dramatic fluid may lead to greater uncertainty.

Table 16

Features Suggesting an Uncomplicated Parapneumonic Effusion

1. Clear or turbid freely moving fluid which may easily be aspirated
2. No bacteria demonstrable by gram stain
3. Pleural fluid pH greater than 7.30
4. Pleural fluid glucose greater than 60 mg %

Light, et al; Potts, Levin and Sahn; Potts, Taryle and Sahn; Light

An uncomplicated parapneumonic effusion is suggested by the findings indicated in Table 16 (12, 19-21). Clear or turbid fluid should be freely moving in the pleural space and easily aspirated through a large bore needle. No bacteria should be demonstrable by gram stain of the fluid. The pink staining background protein of the gram stain may obscure gram negative bacilli, and has led some physicians to prefer methylene blue. The pleural fluid pH should be greater than 7.30, and the pleural fluid glucose should be greater than 60 mg %. These latter features have only recently been described. Although several studies had reported pH and glucose values in pleural fluid caused by a variety of lesions (18, 82-87), the value of these measurements in predicting the subsequent course of a parapneumonic effusion was first suggested by Light and colleagues in 1973 (19). Their observation has been subsequently confirmed by the University of Colorado group (12, 21). A total of 57 patients with parapneumonic effusions have been reported by these two groups. At least 19 patients had complicated effusions requiring thoracostomy tube drainage and are best defined as patients with empyema. In each instance the pH of the pleural fluid was less than 7.30, and in 11 of 19 the pleural fluid glucose was less than 60 mg %. Conversely, among the 38 patients whose pleural fluid pH was greater than 7.30 and glucose greater than 60 mg % the parapneumonic effusion resolved spontaneously with antimicrobial treatment. In patients who did not have grossly purulent fluid the pH of the pleural fluid more correctly predicted loculation than the gross appearance. Similarly, the pH was a better predictor of loculation than the white blood cell count. At least three patients with WBC counts less than 1000 required subsequent thoracostomy tube drainage, while patients with counts as high as 38,000 cells/mm^3 cleared spontaneously.

The Denver group has subsequently pursued the mechanisms of pleural fluid acidosis both in patients and experimental models (88-91).

Table 17

Relationship Between Pleural Fluid Characteristics at Time of Thoracentesis

Variable	Correlation	P
Glucose vs pH	0.76	<0.001
Glucose vs lactate/pyruvate	-0.76	<0.001
Glucose vs Pco_2	-0.63	<0.001
pH vs lactate/pyruvate	-0.98	<0.001
pH vs Pco_2	-0.94	<0.001

Taryle, et al: J. Lab. Clin. Med. 93:1041, 1974

Pleural fluid acidosis and low glucose concentrations may be found not only in empyema but also in fluids due to rheumatoid and tuberculous pleurisy, and carcinomatous effusions. These investigators have studied such effusions as they exist *in vivo* and have determined the acid generation by the pleural fluid *in vitro*. The correlations are good between glucose, pH, and the generation of lactate and carbon dioxide as indicated in Table 17. Their data indicate that cells metabolize glucose with the generation of lactate and carbon dioxide. *In vivo* pH of fluid is determined by the acid production and by the character of the pleural lining which may prevent efflux of hydrogen ion and carbon dioxide. *In vitro* acid generation of empyema fluid indicates that activated leukocytes, and perhaps bacteria, generate the lactic acid and carbon dioxide. Carcinomatous effusions are only moderate acid generators *in vitro*, and the acid is generated by both cells in the pleural fluid and the infiltrated pleura. Rheumatoid pleural fluids generate minimal acid, and it is likely that glucose metabolism by the involved pleura is the origin of the hydrogen ion. Attempts have been made by this group of investigators (92) and others (93-95) to relate these findings to the coagulation and loculation of pleural fluid. The results of these investigations are not definitive at present.

Table 18

Features Suggesting Empyema

1. Loculated fluid or air-fluid levels in pleural space
2. Grossly purulent fluid or foul smell
3. Bacteria demonstrable by gram stain
4. Pleural fluid pH less than 7.30
5. Pleural fluid glucose less than 60 mg %
6. Fluid rapidly reaccumulates after thoracentesis

Light, et al; Potts, Levin and Sahn; Potts, Taryle and Sahn; Light

The features suggesting that a parapneumonic effusion is a true empyema are indicated in Table 18 (12, 19-21). If the fluid is loculated, contains air-fluid levels, is grossly purulent, or has a foul smell the fluid should be considered to be empyema. It is likely that bacteria present in sufficient concentration to be demonstrable by gram or methylene blue stain indicate empyema. The studies that have been reviewed strongly suggest that a pleural fluid pH less than 7.30 with a pleural fluid glucose less than 60 mg % predicts loculation, and the fluid should be considered to be an empyema. It is also reasonable to consider rapidly reaccumulating fluid to be an empyema.

Table 19

Antimicrobial Therapy for Empyema

Staphylococcus aureus	Penicillinase-Resistant Penicillin eg Methicillin 2 gm q 4 h IV
Gram Negative Bacilli	Cephalosporin + Aminoglycoside eg Cephalothin 3 gm q 6 h IV Gentamicin 4.5 mg/kg/day IV
Streptococcus pneumoniae Hemolytic Streptococci Anaerobic Bacteria	Penicillin G eg 10-12 million units qd IV

Reasonable antimicrobial therapy for empyema is presented in Table 19 (96). A penicillinase-resistant penicillin such as methicillin is recommended for *Staphylococcus aureus*. For gram negative bacilli other than *Haemophilus influenzae* a cephalosporin such as cephalothin and an aminoglycoside such as gentamicin are recommended. *H. influenzae* is currently a rare cause of empyema which is best treated by ampicillin. For *Str. pneumoniae*, hemolytic streptococci, and anaerobic bacteria penicillin G remains the drug of choice (97). High dose therapy such as 10 to 12 million units intravenously daily is recommended not only on emperic grounds but also because of observations of inactivation of penicillin by empyema fluid (98, 99). When the empyema has been drained and the patient becomes afebrile, such high doses are probably no longer necessary.

Table 20

Drainage Procedures for Effusions Associated with Pulmonary Infections

1. Thoracentesis for parapneumonic effusions
2. Immediate thoracostomy tube for empyema
3. Open drainage if no response in 96 hours
4. Decortication if no response in 96 hours

It is clear that adequate drainage of the pleural space is at least as important in the cure of empyema as antimicrobial therapy. A multitude of surgical procedures have been devised for this purpose, and many series suggesting the most appropriate surgical management have been published (2-5, 7, 13, 16, 22-26, 32, 33, 100-107). For physicians unfamiliar with these procedures the concise review by Samson is recommended (29). It would serve no purpose to critically review each of these series and each of the operative approaches suggested. However, it is important to emphasize that most radical surgical procedures for empyema are obviated by prompt, adequate drainage of the pleural space. It is the responsibility of the primary care physician to insure such early drainage. A reasonable approach is indicated in Table 20.

Pleural fluid in association with pneumonia should be removed as completely as possible at the time of the initial thoracentesis. In the uncomplicated parapneumonic effusion, no further procedures are necessary. If the fluid rapidly reaccumulates, or if the initial thoracentesis suggests empyema, a thoracostomy tube of as large a diameter as possible should be inserted immediately. It is important for the tube to be positioned in the most dependent area of fluid accumulation, most commonly in the posterior costo-phrenic sulcus. In some patients more than one thoracostomy tube may be necessary. The tube should be attached to underwater seal drainage; it is not clear whether the application of subatmospheric pressure is helpful.

Adequate drainage results in the patient becoming afebrile (13) and the radiograph improving (3) promptly. A reasonable interval in which to expect improvement is 96 hours. A lack of such improvement should immediately lead to a more extensive procedure, usually described as open drainage. The term is somewhat of a misnomer, for it is not necessary for the pleural space to remain open to the atmosphere with this procedure (29). The thoracic surgeon resects a portion of a rib at the most dependent area of the empyema, manually debrides the pleural space, and inserts a large bore empyema tube. Alternately, the tube may be omitted and a pleural-cutaneous fistua maintained by a flap of skin, a procedure originally described by Eloesser (108).

If the open drainage procedure is successful, a radiographic and clinical response should be apparent promptly. Ninety-six hours is again a reasonable time in which to expect the patient to become afebrile (13). If such is not the case, more extensive pleural debridement by means of a major thoracotomy becomes necessary. The procedure most frequently undertaken is termed decortication, which means removal of the peel from the lung, although other procedures may be performed at the discretion of the surgeon. If this aggressive drainage regimen is followed, additional surgical procedures should rarely be necessary.

Table 21

Final Drainage Procedures for Empyema in 140 Patients with Pulmonary Infections

Procedure	Number	Percent
Thoracentesis	1	0.7
Thoracostomy Tube	84	60.0
Open drainage	50	35.7
Decortication	5	3.6

Bryant, et al; Cohn and Blaisdell; Vianna

Three series (3, 13, 33) comprised of 140 patients with empyema due to pulmonary infection allow an estimate of the most extensive drainage procedure necessary. These results are probably not optimal, since many of the patients reported did not have appropriate drainage performed in a timely manner. Nevertheless, about 60 percent of the patients could be managed by thoracostomy tube drainage. Of those failing to respond to that maneuver, almost all responded to open drainage with rib resection. Only a small fraction of patients required thoracotomy with decortication.

Pneumonia that leads to empyema tends to occur in debilitated persons, and such was the case for most of the patients reported in these series. Indeed several of the patients were comatose or hypotensive at the time of admission. Among all patients the mortality in these series was 12 percent. Bryant and colleagues (3) note that there was no mortality among their 16 patients who had no antecedent debility.

SUMMARY

In summary, pleural effusions are a common complication of pneumonia and should be searched for diligently, especially when the causative organisms are gram negative bacilli or anaerobic bacteria. If the volume of fluid is estimated to be more than a few milliliters or if lateral decubitus films suggest that part of the fluid is loculated, a thoracentesis with a large gauge needle should be undertaken promptly. If clear or turbid freely moving fluid which may be easily aspirated is obtained and reveals no bacteria and a pH greater than 7.30 and glucose greater than 60 mg %, the fluid may be regarded as an uncomplicated parapneumonic effusion and the patient treated with antimicrobial therapy alone. However, if the fluid is loculated, demonstrates air-fluid levels, is grossly purulent, has a foul smell, has bacteria demonstrable by gram stain, or a pleural fluid pH less than 7.30 and a glucose less than 60 mg %, it should be regarded as empyema. In patients with these findings a thoracostomy tube should be inserted immediately in a manner to insure dependent drainage. If the patient does not become afebrile and demonstrate a lessening of the fluid within approximately four days of tube drainage and antimicrobial therapy, an open drainage procedure should be performed. A few patients will not respond to this approach, and a thoracotomy with more extensive debridement will be necessary. This aggressive therapy should diminish the morbidity frequently reported for patients with empyema and should decrease the mortality to approximately the same as that of the underlying pneumonia.

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