Staphylococcal Empyema in Children *

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Following the introduction of the clinical use of penicillin in 1942, even severe staphylococcal infections usually responded rapidly to antibiotic therapy. After a few years of rather widespread and, at times, indiscriminate use of this drug, resistant strains began to appear. In recent years, staphylococcal infections have again become a frequent and distressing problem. In infants and children, empyema caused by this organism likewise has shown both an increase in incidence and a lack of response to penicillin and other antibiotics.

When dealing with staphylococcal empyema, treatment should be directed into three main channels: 1) control of the infecting organism; 2) obliteration of the empyema space; and 3) general supportive measures. With the emergence of an increasing number of strains resistant to the commonly used antibiotics, it seemed worthwhile to review our recent cases of empyema with particular emphasis on the bacteriological aspects.

Materials and Methods

The subjects of this study comprised 23 children with primary coagulase positive staphylococcal pneumonia with empyema. More than two-thirds of these cases were infants under two years of age. Routine cultures were taken from the pleural exudate on all patients by thoracentesis immediately following the x-ray diagnosis of empyema. Subsequent cultures were done at varying periods of time until fluid could no longer be obtained from the pleural cavity. The pus was filmed and cultured both aerobically and anaerobically. Sensitivity studies were performed using commercially obtainable antibiotic discs.

Bacteriology

At this hospital there appears to be a definite increase in the number of cases of staphylococcal empyema seen in the past few years (Table 1). It is also obvious that empyema of all etiologic types has tripled during the two periods studied, and that the relative incidence of staphylococcal empyema, which in 1953 to 1956 amounted to only half of the total number, reached 75 per cent in 1957 to 1959.

The initial sensitivity of the offending organism to antibiotics is of great importance to the outcome and management of these cases. Table 2 represents data on the resistance and sensitivity of the initial pleural cultures to the three drugs used most commonly at this institution. In the earlier years, very few patients were admitted with resistant strains. In the latter years, however we have had an increasing incidence of organisms resistant to penicillin. Of considerable importance is the fact that to date no case of staphylococcal empyema was associated with initial resistance to erythromycin.

Table 3 represents data on the antibiotic sensitivity of the bacteria during treatment. It should be noted that the number of cases studied with each antibiotic does not represent the total 23 cases investigated during this time period. This is accounted for in two ways: 1) in several instances only

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one specimen of pleural fluid was obtainable and then the pleural space became dry and the patient cured; and 2) not all patients were treated with the antibiotics under consideration. Consequently, the data in Table 3 represents only those cases in which multiple cultures were obtained and for which a given specific antibiotic was used.

Between 1953 and 1959, approximately 25 per cent of all patients admitted were initially infected with penicillin resistant staphylococci. Fifty per cent of the infections were due to strains initially sensitive to penicillin which became resistant sometime during treatment. Twenty-five per cent remained sensitive throughout the entire period of therapy. Only 14 per cent of the patients on admission had bacterial strains resistant to chloramphenicol. Approximately 43 per cent became resistant during therapy on this drug, another 43 per cent remained sensitive throughout treatment. All staphylococcal strains were sensitive to erythromycin on admission. Over 75 per cent of them retained this sensitivity throughout the course on this drug with only 25 per cent becoming resistant.

Factors which might predispose to the emergence of resistant strains of *Staphylococcus aureus* to the various antibiotics have been studied. The most important of these was the relationship of dosage to the emergence of resistance. In this rather small group of cases, there appeared to be no relationship between the dosage of penicillin used and the period of time elapsed for resistance to develop. Dosages of penicillin varied between 3,000 and 300,000 units per kilogram of body weight for 24 hours. Chloramphenicol and erythromycin were given in the standard approved dosages so that no correlation could be made in this respect. Of interest was the observation that, after initiation of antibiotic therapy, resistant strains emerged at between one and 24 days without showing any consistent pattern.

The following conclusions may be drawn. The patients admitted to this hospital in the past few years with staphylococcal empyema have shown an increase in penicillin resistant strains on cultures taken prior to institution of treatment. Also, in half of the patients treated with penicillin, the pathogen became resistant to this antibiotic sometime during therapy. There appeared to be no relationship between the amount of penicillin used and the emergence of resistance; likewise, there was no specific time interval necessary for the development of penicillin resistant organisms. There has been no apparent increase in the number of strains resistant to chloramphenicol; however, half of all cases on this drug showed resistance to this antibiotic sometime during therapy. To date, no strain was initially resistant to erythromycin and only 25 per cent of the patients on this antibiotic developed resistant organisms before the pleural space was sterilized.

Staphylococcal empyema is obviously not a localized disease. Infection often starts in the nose and/or throat and extends to the tracheobronchial tree and lungs; the pleural space then becomes infected secondarily. Following this, or possibly at the same time, a bacteremia may develop, causing secondary foci of infection, such

<table>
<thead>
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<th>Bacteria</th>
<th>1953–1956</th>
<th>1957–1959</th>
<th>Totals</th>
</tr>
</thead>
<tbody>
<tr>
<td><em>Staphylococcus</em></td>
<td>5 (55%)</td>
<td>18 (72%)</td>
<td>23</td>
</tr>
<tr>
<td>Other bacteria</td>
<td>4 (45%)</td>
<td>7 (28%)</td>
<td>11</td>
</tr>
<tr>
<td>Totals</td>
<td>9</td>
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<td>34</td>
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<thead>
<tr>
<th></th>
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</thead>
<tbody>
<tr>
<td>Penicillin</td>
<td>0</td>
<td>5</td>
<td>4</td>
</tr>
<tr>
<td>Chloramphenicol</td>
<td>2</td>
<td>3</td>
<td>1</td>
</tr>
<tr>
<td>Erythromycin</td>
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<td>0</td>
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as in the bone or skin. Nose and throat cultures taken on all of our patients consistently showed a profuse growth of coagulase positive *Staphylococcus aureus*. In 13 of the total patients studied, blood cultures were obtained. In this group, even with many of the patients on antibiotic therapy, three of the 13 had a positive blood culture of staphylococcus. Two other children had evidence of bacteremia manifested by distal metastatic abscesses; one had multiple cutaneous lesions following the onset of the empyema and the other osteomyelitis of the femur. These two patients with distant infections occurring after the onset of the staphylococcal empyema clearly represent evidence of bacteremia. It is obvious that many patients with empyema have generalized disease with sepsis, a fact which should be kept in mind when instituting treatment.

The popularity in the use of each of these drugs often has a geographical distribution and, consequently, therapy should be directed to initially using the ones least commonly prescribed and most likely to be effective against staphylococcus.

**Treatment**

Based on earlier clinical experience with cases of staphylococcal empyema and bacteriological studies, the following antibiotic program has been devised to control the infecting organism. Intravenous penicillin should be given in large doses along with one of the newer antibiotics specific for gram positive cocci, such as erythromycin, vancomycin, ristocetin or kanamycin.* The latter three drugs should be seriously considered in severely ill infants under six months of age and in patients treated unsuccessfully with penicillin. Also, any child under one year old should be treated with one of the broad spectrum antibiotics, such as chloramphenicol, to prevent an overgrowth of gram negative bacilli. Consequently, on admission, patients were started immediately on 4 to 10 million units of intravenous penicillin in conjunction with chloramphenicol and erythromycin. These drugs were continued until sensitivity studies were obtained and then altered accordingly. Penicillin was used until the acute infection appeared to be controlled. Erythromycin was continued until the child had been afebrile and chest x-rays showed complete obliteration of the empyema space for at least five days.

One of the most important aspects in the treatment of staphylococcal empyema is obliteration of the empyema space. Thoracentesis with evacuation of all fluid was performed as soon as possible on all children with roentgen evidence of pleural effusion. X-rays were then taken daily thereafter and, if evidence of fluid reaccumulation occurred, intercostal tube drainage was instituted under local anesthesia. The usual site for insertion of these tubes, if there was no loculation, was in the seventh interspace in the mid to posterior axillary line. If there was evidence of pyopneumothorax with bronchopleural fis-

*Recently, a synthetic penicillin, which is resistant to penicillinase produced by penicillin G resistant strains of staphylococci, has been added to the armamentarium, under the name of Staphcillin, and probably is the drug of choice now in the treatment of serious staphylococcal infections due to penicillin G resistant staphylococci, including empyema.
tula, two tubes were initially inserted, one anteriorly in the second or third interspace, the other in the mid or posterior axillary line in the sixth or seventh interspace. Intercostal tubes were inserted by making a small incision through the skin, subcutaneous tissue and muscle and then introducing the tube through the interspace on the end of a fine hemostat. This permitted the use of a larger caliber tube than can be introduced with a trochar. These tubes were then attached to underwater seal drainage; no suction, however, was used for the first 24 to 48 hours. If, after that period of time, there was still evidence of continued accumulation of air within the pleural space, approximately 10 to 15 cm. of water suction was applied. The tubes were then left in place for at least three to four days after there was evidence of complete re-expansion of the lung. This was done, since we have had the experience of recurrence of the pneumothorax space following too early removal.

The general care of the patient consisted of the administration of oxygen with high humidity content, either in an isolette or tent. All cases were placed on strict isolation technic. Aspirin was given rectally to keep the temperature below 38.8° C. rectally, as a safeguard in the prevention of febrile convulsions. Intravenous solutions were given either by needle or cut-down, both to administer the large dose of penicillin and to supply the child with water, calories and electrolytes. This was particularly necessary in the infants, since they often have an accompanying ileus which subjected them to the dangers of vomiting and possible aspiration if they were fed. Whole blood was most important, since our cases showed a consistent decrease in hemoglobin levels between 2.5 and 4.5 Gm.%. Consequently, blood transfusions were used generously and given in small, repeated amounts daily, using 20 cc./kg. of body weight so that the hemoglobin level was maintained around 13.5 Gm.%.

**Clinical Results**

There were three deaths among the 23 cases of staphylococcal empyema. One occurred approximately one week following apparent cure in a child with essential thrombocytopenic purpura. This patient had a massive subarachnoid hemorrhage on the day prior to discharge and expired. The other two deaths could be definitely attributed to failure of therapy. One case admitted acutely ill expired within 36 hours due to overwhelming pulmonary infection; the empyema space had been obliterated prior to death by the intercostal tubes. The other child died approximately two and one-half weeks after admission. This patient showed a good early response to treatment with antibiotics and intercostal tube drainage. Unfortunately, a re-exacerbation of the infection with pneumothorax occurred. Following this, massive involvement of the tracheobronchial tree and lungs occurred with *Staphylococcus aureus hemolyticus*, which was completely resistant to all chemotherapeutic agents then available. This child was on single antibiotics over short intervals rather than the multiple antibiotic regimen that is now used. We were impressed that the regimen of using multiple antibiotic therapy early during the initial period of therapy was essential in controlling these infections.

**Discussion**

The increasing incidence of staphylococcal pneumonia and empyema in the past few years at our hospital is not a unique experience. Koch, Carson and Donnell recently have reported that in their experience between 1944 and 1955, 0 to 3 cases occurred per year, and from 1956 to 1958, 20 to 27 cases per year. Similar observations have been recently published by Fisher and Swenson, Kiesewetter, Rusnock and Girdany and Sabiston, Hopkins, Cooke and Bennett.

The problems involved in therapy have
been compounded in recent years by the increasing incidence of strains resistant to the various antibiotics commonly used. Twenty-five per cent of our patients with empyema showed penicillin resistant staphylococci on admission. Sabiston and associates\(^8\) found that 83 per cent of their patients showed organisms initially resistant to penicillin, while Koch et al.\(^5\) reported a resistance rate of 91 per cent. By contrast, chloramphenicol exhibited a much higher sensitivity rate in our group of cases (86 per cent), similar to the findings of others.\(^2\), \(^5\), \(^8\) Likewise, erythromycin resistant strains were rarely encountered. Sabiston et al.\(^9\) reported only 15 per cent of the organisms in his series to be resistant; Hendren and Haggerty’s\(^2\) experience paralleled ours in that they had not yet encountered any organisms resistant to erythromycin. Moreover, even during therapy few strains emerged with resistance to this antibiotic.

That staphylococcal pneumonia and empyema are often associated with a generalized infection is well borne out by the fact that five of 23 patients had evidence of sepsis, manifested by either positive blood culture or clinical evidence of distal metastatic abscesses. This observation has been noted by others as well. Fisher and Swenson\(^1\) reported nine of ten patients with positive blood cultures; Hendren and Haggerty\(^2\) observed ten of 51 patients who manifested staphylococcus on blood culture, while Sabiston et al.\(^9\) reported seven of their 38 patients to be positive. Welch and Finland\(^9\) recently have pointed out in their monograph that there has been increasing difficulty in the antibiotic management of all staphylococcal infections. It was because of these observations that we believed the antibiotic treatment of staphylococcal empyema should be an intensive program with the initial use of multiple antibiotics. As a consequence, our management has evolved so that we use large doses of penicillin intravenously, believing that even though the organisms may be resistant \textit{in vitro} in the routine disc test, high doses may be of definite therapeutic value.\(^4\) Staphcillin appears to be of promise in penicillin-resistant infections. In combination with this drug, chloramphenicol plus either erythromycin, vancomycin, ristocetin or kanamycin may be given. We concur with Hendren\(^2\) that, along with antibiotic therapy, attention should be directed toward correcting the anemia that is practically always present.

The method of draining an empyema is still of some controversy. We agree with Magovern and Blades,\(^6\) however, that repeated thoracenteses are unsatisfactory. It is our opinion that, if fluid reaccumulates after the initial thoracentesis, intercostal tube drainage is mandatory. Likewise, in the presence of pyopneumothorax, immediate intercostal tube drainage is the only effective treatment.

Oliver, Smith and Clatworthy\(^7\) have stated in their study on staphylococcal empyema that late recognition and inadequate treatment of empyema appeared responsible for, or contributed to, the mortality. This has been our experience in the two deaths that we attributed to inadequate management. Therefore, it is our judgement that an early diagnosis is imperative and that an aggressive program of treatment be instituted, which is directed towards multiple antibiotic therapy, proper pleural drainage, and intensive supportive care. If these principles are diligently followed, the still appreciable fatality rate of staphylococcal empyema should be reduced.

**Conclusions**

1. Staphylococcal empyema is becoming more prevalent as a pediatric problem and more resistant to the previously accepted forms of therapy.

2. There is an increasing number of strains emerging which are resistant to penicillin.
3. No bacterial strains have been encountered on initial culture which are resistant to erythromycin.

4. Antibiotic therapy should be directed towards administering large doses of intravenous penicillin combined with other specific antibiotics and should be adapted according to the sensitivity of the offending strain.

5. Adequate drainage of the infected pleural space should be instituted early, so as to obliterate the dead space.

6. Supportive treatment with oxygen, blood transfusions and adequate fluid and electrolyte replacement during the acute stage constitutes an important aspect of treatment.

7. There is still an appreciable mortality in this disease, and all efforts should be directed toward early diagnosis with prompt and effective therapy.

Bibliography


