THE PNEUMOCOCCUS IN INFECTIONS OTHER THAN PNEUMONIA

Importance of Increased Recognition Because of the Efficacy of Chemotherapy

H. S. VanORDSTRAND, M.D.

Many of us think of and search for the pneumococcus in pneumonic disease only, even though it has been known for many years that this specific organism can cause or complicate infection in parts of the body other than the lungs. Since Fränkel recognized the pneumococcus in 1886, this organism usually has been considered as the cause of severe disease processes. When thinking of the pneumococcus in apneumonic conditions, most of us associate it with such serious diseases as peritonitis and meningitis. On the contrary, in recent years it has been shown that many people are carriers of this organism, which is harbored as part of the bacterial flora, particularly in the upper respiratory tract and at certain seasons of the year, with no pathogenic effects. The advent of chemotherapy has renewed interest in the search for the pneumococcus in all its habitats. In pneumococcic infections other than pneumonia, chemotherapy has been of equal value in reducing mortality. As these infections are ordinarily more benign than pneumonia, however, the reduction in morbidity has been of even greater importance.

At the Cleveland Clinic in the past twenty-four months, one or more types of pneumococci have been bacteriologically demonstrated from 51 patients who were suffering from diseases other than pneumonia. The variety of sources of pneumococci and of conditions from which these patients were suffering, as well as their response to chemotherapy, when employed, has been enlightening. It is the purpose of this presentation to review the varying habitats and pathogenicity of the pneumococcus as seen in this group of patients, as well as to illustrate the importance of chemotherapy in reducing morbidity.

The most common form of the pneumococcus is the so-called lance-shape, which usually occurs in pairs (diplococci), each pair being surrounded by a single capsule. However, it is often difficult to recognize, as it may be found in chains of single cocci which are not lance-shaped, especially in an avirulent form. The capsule may likewise be absent or non-demonstrable at times. Fortunately, it stains readily with all the usual aqueous aniline dyes. As everyone is constantly on the lookout for this organism, it may be suspected even in abnormal forms, and its presence proved through Neufeld's staining and typing. When secretions to be examined are very scant, they may first be implanted on Löffler's medium which, in the presence of pneumococci, will allow rapid growth

and secondary typing within a few hours. The pneumococcus, although difficult to grow on some media, is both aerobic and anaerobic. Neufeld, in 1910, first recognized the presence of varying types; newer ones were recognized in succeeding years, the last being Type XXXIII. Only Type III can be classified on smear alone, chiefly because of its large capsule. It has long been known as Streptococcus mucosus.

The source of material in 51 patients suffering from diseases other than pneumonia was as follows:

Sputum	18
Ear	9
Bronchoscopic aspiration	7
Throat	5
Paranasal sinus	4
Pleural fluid	3
Peritoneum	1
Joint	1
Culture of post-thyroidectomy wound infection	1
Culture of primary brain abscess	1
Culture of extradural abscess of spinal cord	1
Total	51

All of these patients had one or more examinations of the chest, including roentgenograms. In no patient was pneumonia demonstrable.

The following seasonal relationship was noted:

January	3
February	4
March	6
April	5
May	6
June	6
July	0
August	1
September	3
October	3
November	7
December	7
Total	51

This agrees in some measure with the seasonal incidence of the pneumococcus and pneumococcic pneumonia as found in public health surveys.

The pneumococci were type-specific as follows (58 type-specific pneumococci were found in 51 patients; 2 patients had 3 types each, and one had 4).

Type I	2	Type XVII	2
Type II	1	Type XVIII	2
Type III	19	Type XIX	1
Type IV	1	Type XX	2
Type V	0	Type XXI	2
Type VI	1	Type XXII	4
Type VII	4	Type XXIII	0
Type VIII	5	Type XXIV	2
Type IX	0	Type XXV	0
Type X	0	Type XXVI	0
Type XI	2	Type XXVII	0
Type XII	0	Type XXVIII	0
Type XIII	2	Type XXIX	1
Type XIV	1	Type XXX	0
Type XV	1	Type XXXI	1
Type XVI	0	Type XXXII	0
		Type XXXIII	3

The Type III pneumococcus was found to be the most frequent, the other types being fairly well distributed.

The clinical diagnosis in this group of 51 patients varied as follows:

Acute infection of upper respiratory tract (common cold)	9
Otitis media	9
Acute 7	
Chronic 2	
Bronchiectasis	7
Chronic bronchitis, for which no cause except the pneumococcus could be found	5
Chronic suppurative sinusitis, paranasal	4
Incidental (cases of benign tumor of the mouth, rheumatic heart disease, and lung tumor)	3
Empyema (2 postoperative to pneumonectomy for primary carcinoma, and 1 associated with chronic lung abscess)	3
Asthma	3
Asthmatic bronchitis	2
Septic arthritis	1
Pulmonary aspergillosis	1
Peritonitis, secondary to perforated peptic ulcer	1
Primary brain abscess	1
Extradural abscess of the spinal cord	1
Post-thyroidectomy wound infection	1

TREATMENT

The diagnostic groups of patients are further discussed, particularly with reference to results of chemotherapy.

The 9 patients with acute infections of the upper respiratory tract described their colds as persistent, and of at least several weeks' duration, for which reason sputum or nasal or throat swab specimens were examined. Since the pneumococcus was present, all these patients were given chemotherapy, sulfapyridine being used in 3 cases and sulfathiazole in 6, with quite prompt subsidence of symptoms.

None of the 7 patients with acute otitis media was treated with chemotherapy. In each case the pneumococcus was found on establishment of drainage, the latter being the curative procedure. Sulfathiazole powder was used in one case of chronic otitis media, and was felt to be very helpful.

Chemotherapy was found to be particularly helpful in the 7 cases of bronchiectasis. In addition to a long-standing, copious, productive cough, 4 of the patients had had recurrent bouts of fever every two to six weeks. The attacks of fever promptly subsided following a course of sulfathiazole therapy and have not recurred to date. All 7 patients were found to have advanced bronchiectasis shown by lipiodol bronchograms, and were treated medically, 4 having lesions contraindicating surgery and the other 3 refusing surgical intervention. In 3 cases chemotherapy reverted the lesion to a dry stage with no other treatment. In summary, chemotherapy was of much symptomatic benefit in all the cases of bronchiectasis. One of the cases is reported as follows:

A 55 year old steel worker was seen at the clinic in November, 1940 because of a chronic, productive cough with recurrent bouts of fever of one-half to one year's duration. He stated that his symptoms followed lobar pneumonia. He expectorated from 6 to 8 ounces of purulent sputum daily, which was foul when associated with fever. Every two to four weeks the temperature was elevated 1 or 2 degrees for periods of two or three days.

Roentgen examination of the chest showed entirely normal findings except for an increase of the bronchial markings in the right base. Lipiodol bronchograms revealed a saccular type of bronchiectasis of the right lower lobe.

Bacteriologic study of purulent secretion aspirated through the bronchoscope showed the principal organism to be Type XXI pneumococcus. The other laboratory studies showed nothing of significance except for an elevation of the white blood cell count to 14,100.

The patient was advised to have a lobectomy, but this was refused. Sulfapyridine in doses of 4 grams daily was used, and he was instructed in postural drainage exercises. He did not carry out the latter, but when seen one week later, stated that his cough had entirely disappeared. He subsequently has followed no treatment of any kind, but has reported at intervals. When last seen on August 13, 1941, he had had no recurrence of cough and there had been complete freedom from the bouts of fever.

The 5 patients with chronic bronchitis had a chronic, slightly productive cough varying from 6 to 12 weeks in duration. Bronchoscopic examination performed in 3 cases revealed no abnormalities other than slight hyperemia of the tracheobronchial mucosa. The examination revealed no other possible cause for the symptoms, and chemotherapy promptly cured them in 4 of the 5 cases.

In the 2 cases of pneumococcic empyema complicating pneumonectomy for primary carcinoma, intensive chemotherapy was given orally and intravenously. Recovery occurred without the necessity of rib resection and drainage. In both cases the surgical incision was closed without tube drainage at the time of the operation. The patient with the chronic lung abscess of eight months' duration with empyema was

treated by incision and drainage along with chemotherapy one year ago. When seen on September 21, 1941, she was completely well, the lung being roentgenographically normal and the surgical drainage site entirely healed.

Of the 3 patients manifesting asthma, one was treated with combined allergy management and chemotherapy, and the other 2 with chemotherapy alone, with satisfying results. One of the latter cases is summarized as follows:

A 40 year old grocer was admitted to the hospital on January 28, 1940, complaining chiefly of periodic attacks of asthma over the previous 20-year period. According to the referring physician, he had been in status asthmaticus during the previous three weeks.

The general physical examination was negative except for the typical findings of asthma. Sibilant and sonorous inspiratory and prolonged expiratory rhonchi were heard in all lung fields. No moist râles were elicited.

Roentgen examination of the chest showed a bilateral minimal apical lesion of tuberculous type. Activity could not be determined from the roentgenographic appearance. The remainder of the lung fields was entirely clear. In addition, lipiodol bronchograms were made for complete exclusion of bronchiectasis.

Bronchial secretion obtained through the bronchoscope revealed that the predominant organism was Type III pneumococcus.

The patient was placed on sulfanilamide therapy. He left the hospital after only five days' stay. The examining physician maintained the sulfanilamide therapy in dosages of 90 grains daily for the succeeding three weeks at home. The patient was entirely freed of his asthma in two weeks, and when last heard from six months ago, had remained symptom-free. Progress roentgenograms at intervals of six months have shown the apical lesion to be stationary. The diagnosis of arrested minimal tuberculosis has no bearing on the asthma.

In the 2 patients clinically suffering from asthmatic bronchitis, the demonstration of the type-specific pneumococcus was particularly helpful. It was felt to be the cause of the symptoms, and was proved to be such by the response to chemotherapy. A case history of one of these patients follows.

A 62 year old grocer was seen at the clinic on April 11, 1941, for recurrent attacks of asthmatic bronchitis. He stated that he had always been in the best of health until a little over two years previously, at which time he developed a head cold which then progressed into bronchitis. He described the latter as paroxysmal coughing with white, thick, mucoid expectoration, shortness of breath, and wheezing. The shortness of breath and wheezing were entirely related to the paroxysms of coughing, would occur at any time day or night, and were not described as true bronchial asthma. An attack observed at the clinic was not thought to be bronchial asthma. According to the history, the initial episode lasted for six or seven weeks. Since then the patient had had a recurrence every three or four months with each episode slightly longer, so that he was having only three or four week intervals of freedom. In these intervals he was entirely free of all symptoms. The patient stated that his present period of asthmatic bronchitis had lasted one week.

The positive findings on the physical examination were entirely limited to the chest. They consisted of a moderate degree of emphysema, an increase in the anteroposterior chest diameter, with a hyperresonant percussion note in the lower half of both lung fields, with diffusely scattered fine, sibilant inspiratory rhonchi throughout both lungs. The temperature was normal.

Roentgen examination of the chest revealed diffuse, fine, nodular fibrosis of the silicotic type with no evidence of an exudative lesion.

The bronchoscopic examination showed the trachea in the midline, and the carina normal in shape and position, with the bifurcation angle normal. The entire tracheobronchial mucous membrane, however, was deeply injected with several patchy areas of granulation, the latter most prominent in the main stem bronchi. A considerable amount of mucopurulent secretions was aspirated from both main stem and bronchi, and the study of these secretions revealed the predominant organism to be diplococci. The Type III pneumococcus was recognized on smear alone, and typing not only confirmed this but revealed Types XIII, XVII, and XXII as well. The aspirated secretions were negative for tubercle bacilli, fusospirochetes and fungi on complete smear and culture studies. The patient was placed on a course of sulfathiazole therapy, 6 grams of the drug daily for four days and then 4 grams daily for the succeeding ten days. Within one week's time he was entirely symptom-free, and when seen again for recheck examination four months later had remained so. A recheck roentgen examination of the chest at the last visit showed no change in the fine, diffuse nodular fibrosis and no evidence of any exudative lesion.

The patient was particularly interesting because his pneumococcic asthmatic bronchitis complicated an asymptomatic minimal silicosis. The patient had been a coal miner from the age of 25 to 45 years, with no history of silica exposure in the seventeen year interval before he was seen at the clinic. His case was further of particular interest because of the bronchoscopic demonstration of tracheobronchial lesions from which the pneumococci were obtained.

In the case of septic arthritis, a type-specific pneumococcus was aspirated from one of the three joints involved, and the symptoms and objective findings entirely disappeared after one week of drug therapy.

No follow-up has been obtained on the one patient in whom a pneumococcus was felt to be complicating pulmonary aspergillosis (Aspergillis niger).

Chemotherapy was used for only one of the patients suffering from chronic suppurative sinusitis, all 4 patients having fundamentally maxillary infections, and the result was gratifying. The other 3 patients having pneumococcic suppurative maxillary sinusitis were treated only by saline irrigation of the involved antra via the natural ostia (the maximum number of irrigations being four), with apparent equal improvement and subsidence of the infection.

The patient with pneumococcic peritonitis died before chemotherapy could be used. He presented a most unusual problem in that his fundamental trouble was a perforated peptic ulcer. When brought to the hospital he was critically ill, and a laparotomy was immediately performed because of the suspected ulcer perforation. In addition to the ulcer perforation, the laparotomy revealed diffuse peritonitis, all cultures of which revealed pure Type III pneumococci. The patient died three hours postoperatively, and autopsy showed no evidence of pneumonia.

In the case of primary brain abscess caused by a Type III pneumococcus, death followed the establishment of the etiologic diagnosis before chemotherapy could be instituted.

In the case of extradural abscess of the spinal cord, also due to Type III, the infection was eradicated through a combination of chemotherapy and surgical drainage. It is problematical which treatment was of most value, although chemotherapy was felt to be as helpful as drainage in preventing any further complication. However, when the patient left the hospital, it was felt that he would probably have permanent cord changes because of the longstanding cord compression prior to the establishment of treatment.

In the case of postoperative thyroidectomy wound infection of pneumococcic origin, Type III, irrigations of the wound with sulfanilamide solution quickly eradicated the complication. The wound infection appeared on the third postoperative day. The temperature returned to normal within twenty-four hours after the institution of chemotherapy, and the convalescence was steady and uneventful from that time.

SUMMARY

Because of the advent of chemotherapy, it was felt worth while to review a series of 51 cases seen at the clinic during the past twenty-four months in which the pneumococcus was associated with conditions other than pneumonia. Chemotherapy was used in the majority of these cases as effectively as it is used in pneumonia. As apneumonic infections on the whole normally have a much lower mortality, the chief importance of chemotherapy was found in the reduction of the morbidity of the infection. Observance of the response to trial chemotherapy in certain cases was of much help in evaluating the etiologic importance of the pneumococcus found.

The therapeutic test was used because of the well-known fact that the pneumococcus may be harbored in many people in asymptomatic forms. The therapeutic test seemed to indicate that the pneumococcus prolonged and enhanced the symptoms, as well as being an important etiologic factor in certain cases, particularly of severe acute upper respiratory infection, chronic bronchitis in which no other etiology could be found, certain cases of asthma and asthmatic bronchitis, certain cases of chronic suppurative sinusitis and bronchiectasis.

The series of 51 cases was reviewed with reference to source of material for bacteriologic study, seasonal incidence, variety of types of pneumococcus, clinical diagnosis and response to treatment.