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Research Article

THERAPEUTIC SERUM FOR PNEUMOCOCCUS TYPE V (COOPER) PNEUMONIA[1]

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The characteristics of the pneumonias caused by pneumococcus Type V (Cooper) will be described elsewhere. This type was originally designated Type IIA by Avery. It is frequently mistaken for Type II, but by means of the Neufeld technic it is readily distinguished from that type. In general, pneumococcus Type V causes a less severe pneumonia than pneumococcus Type II. In the last seven years 249 cases of pneumonia due to Type V were observed at Harlem Hospital among adults. There were 34 deaths among 163 cases in which serum was not used, and the mortality rate was 20.8 per cent. If we add to these the 6 cases who came in with an overwhelming blood invasion and who died before they received a dose of serum adequate to affect the outcome, the mortality would be even higher. The 163 patients, who were not treated specifically and the other 6 cases who entered the hospital with overwhelming bacteremia constitute 169 cases; among them there were 40 deaths, a mortality of 24.4 per cent.

Therapeutic serum. Selection of cases

Pneumococcus Type V was responsible for seven and one-half per cent of the pneumococcus pneumonias observed in adults at Harlem Hospital during the past seven years. During the year 1934–1935, the incidence of this type was 10.8 per cent among 521 cases of pneumococcus pneumonias. Because of the frequency of pneumonias caused by pneumococcus Type V, and their considerable mortality, it, among other types, was selected for treatment with specific serum.[2]

When serum was available, the cases were alternated for serum treatment. At first, the serum was administered every eight hours. When our experience with this and other types showed the advantage of more intensive treatment, larger doses were administered, and the time between doses was shortened to three, or even two hours. Eighty-six patients received serum in the seven years covered by these observations, and 163 served as controls and received no serum. Nineteen of the patients who received serum have been excluded from the statistical evaluation because of inadequate treatment. Of these, 11 died and 8 recovered. The cases were removed from the series as inadequately treated if they were bacteremic and received less than 200,000 units within 24 hours, and if they were non-bacteremic and had received less than 100,000 units within 24 hours. They were not removed from the series even though less than these amounts of serum had been given, if sufficient had been administered to show agglutinins for Type V pneumococcus in the blood. Among the recovered cases, 4 were excluded because the temperature was already descending at the time the serum was given, and it was felt that the serum had had no demonstrable influence on the disease.

Effect on death rate

There were 67 cases adequately treated with serum. Of these, 5 died, a mortality of 7.5 ± 3.2 per cent. There were 163 cases treated without serum, of whom 34 died, a mortality of 20.8 ± 3.2

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[2] The horse serum was prepared by the Department of Health at the Municipal Farm, Otisville, New York, with funds provided in part by the City of New York; in part by the Altman Foundation, Inc.; and, by the Littauer Pneumonia Research Fund. It was also prepared by the Lederle Laboratories at Pearl River, New York. It was refined at the Department of Health Laboratories at first by Banzhaf and later by Falk. At Pearl River it was refined by Joseph Greene. At first the serum contained only 500 units per cc. Later serum containing as much as 8000 units was produced.

TABLE I

Pneumococcus Type V (Cooper) pneumonia

Years	Patients adequately treated with serum			Patients not treated with serum			Average units of antibody in serum
	Number of cases	Deaths		Number of cases	Deaths		
		Number	Per cent		Number	Per cent	
1928 to 1933	26 11*	3 2*	11.5 18.1*	108 28*	23 15*	21.3 53.5*	782
1933 to January 1936 †	41 6*	2 2*	4.9 33.3*	55 15*	11 11*	20.0 73.3*	3163

* Indicates bacteremia.

† During six months from January 1st to June 30th, 1936, there were 25 cases treated with serum with one death (bacteremia) or 4 per cent and 10 cases not treated with serum with one death (bacteremia) or 10 per cent.

per cent. The ratio of the difference to its error in this instance is 2.7, which indicates that the chances are 993 in a thousand that the difference in mortality rate was due to the difference in the treatment and not fortuitous.

Seventeen of the cases treated with serum were bacteremic; 4 died, a mortality rate of 23.5 ± 10.3 per cent. Among 43 bacteremic cases not treated with serum there were 26 deaths, a mortality rate of 60.5 ± 7.4 per cent. The ratio of the difference to its error in this instance is 2.9. Of the 50 cases treated with serum and not bacteremic, only one died, a mortality rate of 2.0 per cent. Of the 120 non-bacteremic cases cared for without serum, 8 died, a mortality rate of 6.7 ± 2.3 per cent. The ratio of the difference to its error is 1.5.

If we divide our experience into that before and that after 1933 as shown in Table I, we find that before 1933 the mortality in cases treated with serum was approximately one-half of that in those not treated with serum. In the period before 1933 the average potency of serum was 782 units per cc. In the later period, the average potency was 3162 per cc. The death rate in the later period was still further reduced and became approximately one quarter of that in the cases not treated with serum. The death rate in the cases untreated with serum was approximately the same in both periods: 21.3 per cent in the first period and 20 per cent in the second period. With the increase in the strength of serum, the number of units given to the non-bacteremic patients was increased from an average of 152,000 units of 500-unit average potency per cubic centimeter in 1929–1930 to an average of 383,500 units of 6,649-unit average potency per cubic centimeter in 1935–1936. Larger amounts were given to bacteremic patients.

Influence of serum on bacteremia

Among the 67 cases adequately treated with serum, 17 were bacteremic, an incidence of 25.1 per cent. In the 163 cases not receiving serum therapy, 43 had bacteremia, an incidence of 26.4 per cent. After serum treatment was commenced, there was no invasion of the blood stream in any cases treated adequately.

It was possible to determine the day on which the blood was invaded in 22 cases. This occurred before the 4th day in 4 cases, and after the 4th day in 18 cases. Of the fatalities among cases treated with serum the blood was sterile in only one, and in this case treatment was begun on the 6th day.

Partition of the cases with respect to degree of invasion revealed that there were fewer cases with high colony counts in those who had adequate treatment with serum. The mortality rate was as low as 14.3 per cent if sufficient serum was given and the number of colonies in the blood was less than 50 per cc. The largest number of colonies in any culture was taken to designate the group to which a case belonged. It was found that the use of serum prevented increase in the number of colonies. From these data it seems fair to conclude that with adequate dosage of specific serum, not only is the blood protected against invasion, but also that the colonies do not increase after the serum is administered should the blood have been invaded already.

Duration of disease

Among the 67 patients who received serum, in 40, or 59.7 per cent, the fever terminated by crisis on the same day or the day following treatment with serum. Among the 163 cases not treated with serum such prompt defervescence after hospitalization occurred in only 13 instances, or 8 per cent. The termination of the disease seemed to be directly related to the administration of the specific serum.

There was one case, treated very late in the disease, where death may have been hastened through the administration of serum. This patient, a man aged 45, had bacteremia, was cyanotic, dyspneic and distended. His pulse was 120, and his respirations were 48. The patient received a dose of 5 cc. and a dose of 8 cc. serum without reaction on the 12th day. Two hours later the pulse was weak and distention had increased. After the third dose of serum, 5 cc. (7500 units), was injected he felt hot, retched, passed gas and feces, and was in collapse. Adrenalin was given without avail.

The following case exemplifies the value of specific serum when properly used in the treatment of a patient suffering from pneumonia due to pneumococcus Type V:

Case A. G., a plasterer, age 67, had a history of chronic bronchitis and emphysema lasting 40 years, with recurrent attacks of paroxysmal ventricular tachycardia. He was taken ill at 8 a.m. on March 21, 1936 with nausea, precordial pain, fever, and headache. The pain was not aggravated by cough or by deep inspiration. On March 23 the cough became worse, and was followed by the expectoration of white tenacious sputum which was bloody on one occasion. He had no chills and no vomiting. On March 23, at 9 p.m. he complained of severe headache and mild substernal pain. There was no pleuritic pain. The temperature was 104.6° F.

Physical examination. An acutely ill, aged man, dyspneic, tachypneic, apathetic, and slightly delirious. His tongue was dry and coated, the tissue turgor was poor. *Chest. Lungs.* Dulness, bronchial breathing, and bronchophony was heard over the left lower chest posteriorly. Slight dulness, bronchovesicular breathing and a moderate number of crepitant râles were present over the right lower chest posteriorly. Respirations were 44. Heart was normal in size, regular sinus rhythm with numerous ventricular premature contractions. Ventricular rate was 132, and pulse rate 126. There was cyanosis of the lips and nail beds. Abdomen was not distended.

Conjunctival and dermal tests with horse serum were negative. At 10 p.m. he received 8,000 units (1 cc.) of Type V serum. At 11 p.m. he received 80,000 units (10 cc.); at midnight, 160,000 units; at 2 a.m. 152,000 units; and at 5:30 a.m., 160,000 units. At 6 a.m. the temperature had fallen to 100.4° F. and the pulse to 92. From that time on the pulse and temperature were normal. All premature contractions disappeared. Before serum was commenced, there were no agglutinins in the blood of the patient. Before the 4th injection agglutinins in the blood were ± and at 8 a.m., after 56,000 units of serum had been administered the agglutinins were intensely positive. At this time he was clear mentally, had slight dyspnea, and requested food. The following day he was comfortable and requested a full diet; his dyspnea was gone.

This patient received the following during the night of treatment; chloral hydrate, grains 15; sodium bromide, grains 30; codeine sulphate, ½ grain. An oxygen tent was employed from 3 a.m. on March 24 until noon on March 25. On March 27 and on March 28 he received 1,000 cc. of 5 per cent glucose in saline intravenously. He was out of bed in a chair on March 31, ten days after the

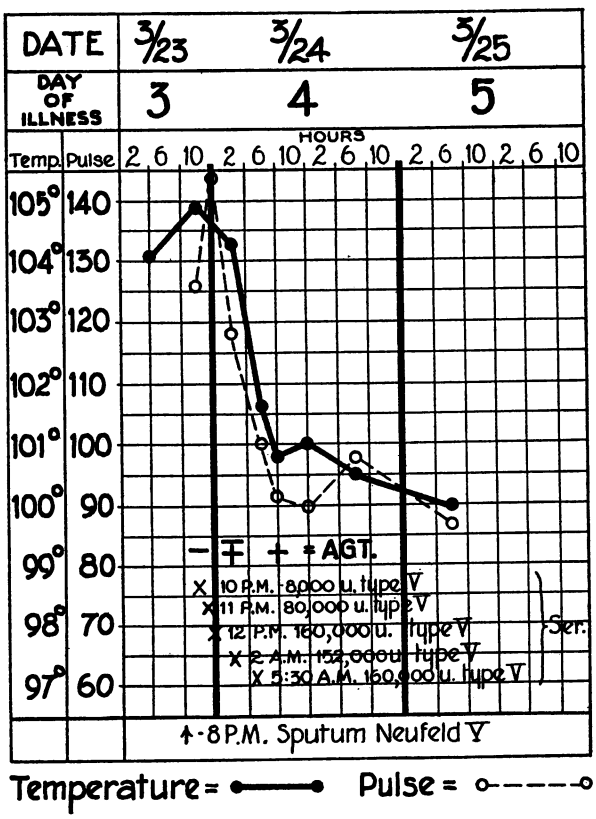

FIG. 1. EFFECT OF SPECIFIC SERUM ON PULSE, TEMPERATURE AND AGGLUTININS IN CASE A. G., PNEUMOCOCCUS TYPE V PNEUMONIA.

onset of the illness and seven days after the commencement of serum therapy. One week later he was at his regular work as a plasterer.

CONCLUSION

It seems reasonable to conclude that the available specific Type V serum not only promptly terminates the illness, but also protects and clears the blood stream of these pneumococci. The death rate in the cases observed was greatly reduced. In a later series treated with more potent preparations of serum more frequently administered, the mortality rate was reduced to one quarter of that in the contemporaneous controls. This mortality rate cut in half the mortality rate of the earlier serum series. The mortality rate in the first series was half that of the controls. The mortality rate in the controls of both series was the same. In the combined series there were sufficient cases for statistically valid conclusions.