

of medicine, surgery, obstetrics and public health. The colleges will be asked to pay less attention to courses in special branches during the undergraduate term, and devote more time to the education of medical practitioners.

I believe that more attention to the subjects outlined in the foregoing paragraphs will equip men to render a service to the individual and the community which will eventually bring the practice of medicine to a level of achievement undreamed of in the past. I believe that men who have received such preparation will be ready after their graduation to practice medicine in cooperation with the many and varied agencies for social betterment, with a greater degree of mutual understanding.

CONCLUSION

Let me emphasize the belief that the higher ground toward which we are rapidly moving will afford to administrators of public health a steadily enlarging field of usefulness because of the better understanding by the medical profession of the proper relation between the prevention and the cure of disease, and the appreciation by it of the opportunity to take its proper place of leadership in this great movement toward social tranquility and the improvement of the race.

CLINICAL AND BACTERIOLOGIC STUDY OF ONE THOUSAND CASES OF LOBAR PNEUMONIA

WITH SPECIAL REFERENCE TO THE THERAPEUTIC
VALUE OF PNEUMOCOCCUS ANTIBODY SOLU-
TION: PRELIMINARY REPORT *

RUSSELL L. CECIL, M.D.

AND

NILS P. LARSEN, M.D.

NEW YORK

In the fall of 1920, an opportunity arose for conducting an extensive study of lobar pneumonia in the wards of Bellevue Hospital. Through the kind cooperation of the directors of the other medical services, all cases of lobar pneumonia admitted to the twelve medical wards were carefully studied from the bacteriologic standpoint with the idea of determining, if possible, the relationship between the exciting agent and the clinical course of the disease. The main object of the investigation, however, was to test the therapeutic value of a serum-free solution of pneumococcus antibody.¹ This product was first prepared by F. M. Huntoon,² who has described it at some length in a series of recently published articles.

The antibody solution is thus prepared by Huntoon:

Horses are injected at regular intervals with emulsions of Types I, II and III pneumococci. The serum after a number of injections develops protective antibodies. To obtain a serum which protects mice against 1,000,000 lethal doses or more of Type I is readily accomplished. It is more difficult to obtain as high a protective power for Type II, and against Type III a serum can seldom be obtained which protects against more than 100,000 fatal doses.

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¹ From the Second Medical (Cornell) Division and the Pathological Department of Bellevue Hospital, and the Hygienic Laboratory of the U. S. Public Health Service. This study also received financial aid from the Metropolitan Life Insurance Influenza Fund.

1. The pneumococcus antibody solution employed in this work was supplied by the Mulford Laboratories.

2. Huntoon, F. M.: *J. Immunol.* 6: 117 (March) 1921.

To this serum is added an equal volume of a heavy emulsion of living pneumococci Types I, II and III. The mixture is placed at 37 C. for one hour or 20 C. for twelve hours, and then centrifuged. The sediment is washed with salt solution to rid it of horse serum. The washed sediment is emulsified in salt solution containing 0.25 per cent. sodium bicarbonate and heated to 55 C. for from thirty minutes to one hour. This causes dissociation of the pneumococcus (antigen) and antibody. The mixture is centrifuged, and the supernatant fluid removed, chilled, recentrifuged and finally filtered through a filter candle. The final solution, which contains only 0.035 mg. of nitrogen per cubic centimeter, is in many lots able to protect mice against as many fatal doses of pneumococcus Types I, II and III as the original serum from which it was made.

This preparation is therefore a practically serum-free, aqueous solution of specific pneumococcus antibodies. It contains protective substances against pneumococcus Types I, II and III equal in amount to potent polyvalent antipneumococcus serum, yet is almost entirely free from the proteins of horse serum. It also contains, in addition to antibody, a small amount of pneumococcus protein which may conceivably act in the capacity of a vaccine and thereby induce a certain amount of active immunity.

In some experiments which will be published later, the therapeutic value of pneumococcus antibody solution has been tested in experimental pneumococcus pneumonia in monkeys. The results of these experiments are in agreement with protection tests on mice. The most striking results were observed in experimental pneumococcus Type I pneumonia. Following the injection of antibody, pneumococci immediately disappeared from the blood, and the animal made a rapid recovery. When antibody was administered to monkeys that had been inoculated with lethal doses of pneumococcus Type II, the results were not so striking. A certain number, however, were saved by this mode of treatment. In the case of experimental Type III pneumonia, no benefit whatever could be obtained by treating the infected monkeys with antibody solution. Since the antibody solution displays its highest protective power in mice against pneumococcus Type I, next highest against pneumococcus Type II and least against pneumococcus Type III, it would appear that the beneficial effect induced by its administration is, in large measure, proportional to the amount of protective substance present.

CLASSIFICATION OF CASES

An effort was made to determine the type of infection in every case of pneumonia in the series. For one reason or another this effort was unsuccessful in some instances, but in the majority of cases (92 per cent.) the exciting agent was isolated.

The mouse method was used almost exclusively in the examination of sputum. Agglutination and precipitation tests were carried out with the mouse exudate, and at the same time cultures were made on blood agar plates from both the heart's blood and peritoneum of the mouse. Whenever the readings from the mouse exudate indicated pneumococcus Type IV or atypical pneumococcus Type II, colonies were fished from the plates and the pneumococcus was retyped from the broth culture. Typings from cultures were also made whenever the mouse exudate gave a doubtful reaction. Practically all fatal cases were checked with postmortem cultures.

All cases of clinical pneumonia from which a pneumococcus was isolated were included in the series.

Practically all of these were lobar in type. Cases with frank consolidation of one or more lobes were also included, even if cultures failed to reveal pneumococci. A few cases of *Streptococcus hemolyticus* pneumonia were encountered in which the signs were not absolutely frank, but in every other respect the patients presented the picture of a lobar pneumonia. They were therefore included in the series.

TABLE 1.—BACTERIOLOGIC CLASSIFICATION OF ONE THOUSAND CASES OF LOBAR PNEUMONIA

Organism	Number of Cases
Pneumococcus Type I.....	320
Pneumococcus Type II.....	150
Pneumococcus Type III.....	133
Pneumococcus Type IV.....	231
<i>Streptococcus hemolyticus</i>	52
<i>Streptococcus viridans</i>	22
<i>Bacillus influenzae</i>	3
<i>Bacillus of Friedländer</i>	4
<i>Staphylococcus aureus</i>	2
Unclassified.....	83
Total.....	1,000

In Table 1 the 1,000 cases included in the present study have been classified according to the type of micro-organism isolated. In cases of mixed infection the pneumococcus has been given the preference; that is, if the sputum showed both pneumococcus and streptococcus, the case has been classified as a pneumococcus pneumonia. Cases in which pneumococcus was absent and streptococcus was associated with the influenza bacillus have been classified as streptococcus pneumonia. It will be seen from this table that out of 1,000 cases studied, 917 could be classified bacteriologically. In eighty-three cases either no pathogenic organisms were found in the sputum, or for some reason or other the sputum was not examined.

Of the 917 classified cases, 834, or 90 per cent., showed some type of pneumococcus. The remaining 10 per cent. were mostly streptococcus pneumonias. There were three cases in which *Bacillus influenzae* was isolated in pure culture from the sputum; there were four cases of Friedländer bacillus pneumonia, and two cases of *Staphylococcus aureus* pneumonia.

TABLE 2.—CLASSIFICATION OF EIGHT HUNDRED AND THIRTY-FOUR CASES OF PNEUMOCOCCUS PNEUMONIA

	Number of Cases	Incidence, per Cent.
Pneumococcus Type I.....	320	38.4
Pneumococcus Type II.....	150	18.0
Pneumococcus Type III.....	133	15.9
Pneumococcus Type IV.....	231	27.7
Total.....	834	

Table 2 shows the incidence of the various types of pneumococcus pneumonia. Out of a total of 834 pneumococcus pneumonias, 320, or 38.4 per cent., showed pneumococcus Type I; 150, or 18 per cent., showed pneumococcus Type II; 133, or 15.9 per cent., pneumococcus Type III; 231, or 27.7 per cent., pneumococcus Type IV. When these figures are compared with the figures of Dochez and Gillespie,³ it will be seen that the incidence of Types I, III and IV pneumonia in the present series is slightly higher than theirs, while that of Type II is much lower. At the conclusion of the first year of this study, the incidence of Type I pneu-

monia was 42 per cent. of the total pneumococcus group. Type I pneumonia is therefore the commonest type of pneumococcus pneumonia, Type III the rarest.

Space will not permit a discussion in this paper of streptococcus pneumonia and the other more unusual forms. They will be considered in detail in a future article. Our interest was centered chiefly in pneumococcus pneumonia, since the agent which we proposed to test therapeutically was directed against this variety.

METHOD OF CONDUCTING ANTIBODY EXPERIMENT

In order to determine the therapeutic value of pneumococcus antibody solution, the twelve medical wards of Bellevue Hospital were divided into two groups. In six wards, all cases of lobar pneumonia were treated with the antibody solution. The other six were used as control wards. In these wards, patients with pneumonia received no antibody, but in other respects were treated in practically the same way as the patients receiving antibody. It was first determined that no selection of any kind was practiced by the admitting office in assigning patients to the various wards. In Bellevue Hospital, new patients are distributed by rotation, without regard to the character or severity of the disease. The control seemed, therefore, to be a fair one from every point of view.

RESULTS OF TREATMENT WITH ANTIBODY

Antibody treatment was started as soon as the diagnosis of pneumonia was made. The solution was given intravenously in most cases, the technic being similar to that of serum administration. The dose was from 50 to 100 c.c. given once, sometimes twice, occasionally three times a day.

The reactions produced by this solution have been one of the most striking features of the study, and deserve especial attention. The typical reaction may be thus described: There is no immediate reaction. From twenty to forty minutes after the injection, the patient begins to shiver and is soon in the midst of a hard chill. The cyanosis and dyspnea become more marked, and the patient often shows extreme anxiety. The chill lasts from fifteen to thirty minutes. At its conclusion, the patient complains of fever, and the temperature may have risen to 106 F. or even to 108 or 109. In rare cases, the temperature may rise to 110. In one case, the rectal temperature was too high to be recorded on the thermometer. When the thermometer was removed, the bulb was missing, and a careful reading of the mercury column recorded 113.1! The patient was wildly delirious during this period of hyperpyrexia, but ice packs were followed by a rapid drop, and on the next morning he showed a normal temperature and made an uncomplicated recovery.

In a certain number of cases, morphin and atropin have been administered subcutaneously one-half hour before the injection of antibody, with the hope that such a procedure would mitigate the severity of the reactions. In general, it may be said that the reaction was somewhat less intense after morphin and atropin, but the effect was not striking. An effort was also made to determine what relationship existed between the severity of the reaction and quantity of antibody injected. In our experience, the reaction is not directly proportional to the antibody dosage. Ten or fifteen cubic centimeters of antibody have in some cases produced sharp reactions, while in other cases 100 or even 200 c.c. has excited no reaction whatever. As a rule,

3. Dochez, A. R., and Gillespie, L. J.: A Biologic Classification of Pneumococci by Means of Immunity Reactions, J. A. M. A. 61: 727 (Sept. 6) 1913.

however, the reactions are somewhat more severe and last longer when large doses are administered.

The high temperature usually persists for only a short time: from thirty to sixty minutes. The rapid fall is accompanied by a profuse perspiration, which often drenches the patient's linen, and which may continue for several hours. The fall may be slight, but is usually extensive, often reaching normal or even sub-normal limits. It may be temporary or permanent. It is more likely to be temporary if treatment is started early; permanent if the injection is given when the crisis is about due. In some cases, however, one or two injections appear to abort the infection completely, and the temperature remains normal on the third or fourth day of the disease.

These reactions have every appearance of the so-called "foreign protein reaction." They usually follow each injection of antibody, but tend to become somewhat less severe with each paroxysm.

In three cases, the reaction following injection with antibody appeared to be the immediate cause of death. In these three patients, the symptoms were very severe: chill, followed by high fever (from 106 to 109), delirium, cyanosis, dyspnea, rapid weak pulse, diaphoresis, congestion of lungs, coma and death. In two of these cases death was apparently due to cardiac

TABLE 3.—COMPARISON OF DEATH RATE IN TREATED AND CONTROL SERIES

Type	Antibody Wards			Control Wards		
	Cases	Deaths	Rate %	Cases	Deaths	Rate %
Pneumococcus I.....	158	21	13.3	162	36	22.2
Pneumococcus II.....	83	23	27.7	67	27	40.3
Pneumococcus III.....	73	29	39.7	60	24	40.0
Pneumococcus IV.....	110	18	16.4	121	29	24.0
Total.....	424	91	21.4	410	116	28.3
Streptococcus, etc.	48	24	50.0	35	12	34.3
Unclassified.....	36	14	38.8	47	20	42.5

failure. In the third case a long continued hyperpyrexia was probably responsible for the fatal termination.

Treatment with antibody was usually continued until the temperature of the patient came down and remained below 100 permanently. Occasionally, one injection was sufficient. More frequently, from three to six injections were necessary. The average number of injections was 3.6 for each patient, and the total amount of antibody administered averaged 225 c.c. for each patient.

The results of the experiment are shown in Table 3. It will be observed that 424 cases of pneumococcus pneumonia occurred in the antibody wards, and 410 in the control wards. Nearly all the patients in the antibody wards were treated with this solution, the only exceptions being patients that were convalescent or who showed signs of cardiac failure on admission. These exceptions, however, were counted as "treated" in the statistics given below. There was considerable difference in the mortality rate for Type I cases, 13.3 per cent. for the 158 treated cases, as compared with 22.2 per cent. for the 162 untreated cases. In the Type II groups the treated cases showed a death rate of only 27.7 per cent., as compared with the control death rate of 40.3 per cent. In the Type III series, the percentage of fatalities was practically the same for the two groups, 39.7 per cent. for the treated; 40 per cent. for the untreated cases. Strangely enough, a considerable difference in mortality rate was noted in favor of the

treated Type IV group, 16.4 per cent. against 24 per cent. Altogether, the treated pneumococcus cases showed a death rate of 21.4 per cent., while the control pneumococcus series presented a rate of 28.3 per cent.

Streptococcus pneumonia was not benefited in the least by antibody treatment. In fact, the death rate was higher for the treated series (50 per cent.) than it was for the untreated series (34.3). The number of cases, however, in the streptococcus groups is too small to permit of accurate conclusions.

In the small group of unclassified cases, the death rate was slightly lower for the "treated" wards (38.8 per cent.) than for the control wards (42.5 per cent.), but most of the former group did not actually receive antibody.

EFFECT OF ANTIBODY ON BLOOD CULTURES

Blood cultures were taken in 110 cases out of the total pneumococcus series. Of these, thirty-one cases, or 28 per cent., were positive. In several cases of pneumococcus Type I pneumonia, the blood became sterile after one administration of antibody. In one case of pneumococcus Type I pneumonia with 146 pneumococcus colonies to each cubic centimeter of blood and a complicating meningitis, three administrations of antibody of 100 c.c. each reduced the number of colonies to fifteen per cubic centimeter of blood, though the meningitis proved fatal. In two fatal cases of pneumococcus Type I pneumonia which were treated with antibody, blood cultures taken at the time of death were sterile. Postmortem cultures were taken in all but three of the fatal cases of pneumococcus Type I pneumonia. With two exceptions, these cultures showed living pneumococci in the lungs in spite of the previous administration of large amounts of antibody. In two of the fatal antibody cases, postmortem cultures showed that Type I pneumococcus had been entirely replaced by *Streptococcus hemolyticus*.

In fatal cases of pneumococcus Type II pneumonia, pneumococci were recovered from the lungs in spite of the previous administration of large amounts of antibody. In two of these cases, antibody failed to affect the number of pneumococci in the blood. In one case of pneumococcus Type II pneumonia, blood cultures taken before, immediately after and three hours after the administration of 200 c.c. of antibody did not show any numerical change. On the other hand, in one control Type II pneumonia, the count on three successive days was forty-two, thirty and three colonies per cubic centimeter, respectively, and on the fourth day the blood was sterile. One week later, however, the patient developed pericarditis and died.

In serious Type III and Type IV pneumonias with positive blood cultures, the repeated administration of antibody failed to influence the colony count.

CASES ILLUSTRATING EFFECT OF ANTIBODY TREATMENT

The following cases, selected from the series of cases treated with antibody, will serve to illustrate the character of the reactions and the effect of this agent on the course of the disease. They have been chosen, not to illustrate the most striking results, but as examples of various types of reactions:

CASE 1.—J. S., a man, aged 31, with pneumococcus Type I pneumonia of the left lower lobe, at 1 p. m. on the second day of the disease received 50 c.c. of pneumococcus antibody intravenously. Twenty minutes later, he had a severe chill, and the temperature rose from 102 to 108 (Chart 1). This

sudden rise was followed by a rapid fall to 103, and by the following morning the temperature read 101. A second injection of 50 c.c. was given on the third day, and was followed by a less severe reaction. The temperature remained below 103 on the fourth day, and no antibody was administered. On the fifth day a third and final injection of antibody (50 c.c.) was given. This produced a mild reaction which was followed by complete recovery.

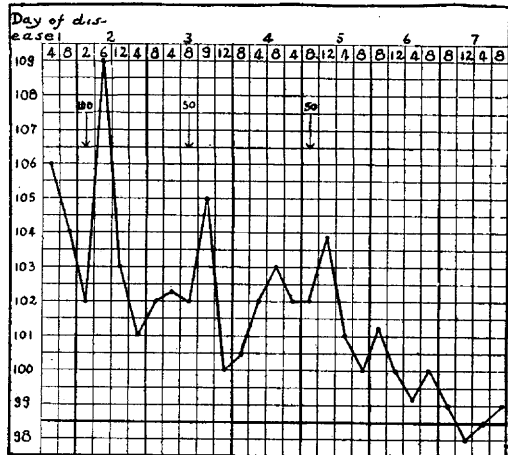


Chart 1.—Temperature in Case 1.

This case illustrates well the "stair-step" temperature curve which characterizes many cases of pneumonia treated with antibody. The first reaction is severe, and accompanied by a high shoot of temperature. With each succeeding injection the reaction is less marked, and the temperature steps down to normal.

CASE 2.—H. D., a boy, aged 15, with pneumococcus Type I pneumonia of the right upper lobe, received the first injection of antibody on the fourth day of the disease. Although he received 100 c.c. intravenously, he showed very little reaction to the antibody, and the temperature did not rise (Chart 2). During that day and the two days following, this patient received, in all, eight intravenous injections of antibody, seven of 100 c.c., the last of 50 c.c. No reaction of any consequence was noted after any of the injections, and the temperature maintained a fairly level plateau. Crisis occurred on the seventh day.

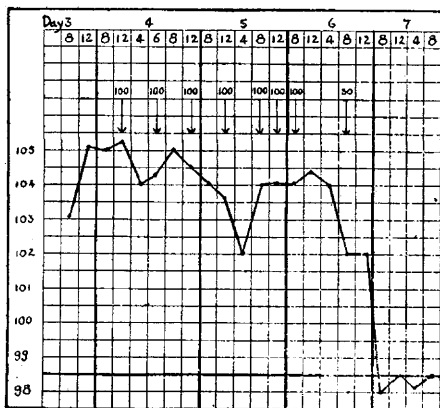


Chart 2.—Temperature in Case 2.

This case illustrates the comparatively rare type of case in which antibody produces little, if any, reaction. The antibody injections induced neither chills nor variations in temperature. In this particular case, however, the general condition of the patient appeared to be favorably influenced by the treatment.

CASE 3.—M. R., a man, aged 27, with pneumococcus Type I pneumonia of the right middle and lower, and left lower lobes, received his first injection of antibody on the fourth day of the disease. Altogether he received thirteen intravenous injections of 50 c.c. each. Most of these injections were followed by definite reactions, but the temperature never dropped to normal even temporarily (Chart 3). The disease ran a rather long course, with crisis on the eleventh day. Ten days later, the patient developed a pneumococcus Type I empyema. Thoracotomy and drainage were performed, and the patient eventually recovered.

This case exemplifies a group in which antibody is followed by reactions, but in which the temperature does not drop to normal. The antibody appeared to exert very little influence on the duration of the disease, though the patient usually appeared more comfortable after the administrations.

CASE 4.—J. P., a man, aged 42, with pneumococcus Type II pneumonia of the right lower lobe, on the third day of the disease received 50 c.c. of antibody intravenously. This was followed by a sharp chill and rise of temperature to 107.4 (Chart 4). During the next few hours the temperature fell rapidly to 100. The following morning, a second injection of 50 c.c. was given. Again the patient reacted with chill and fever of 104.5, and, following this, was free from symptoms.

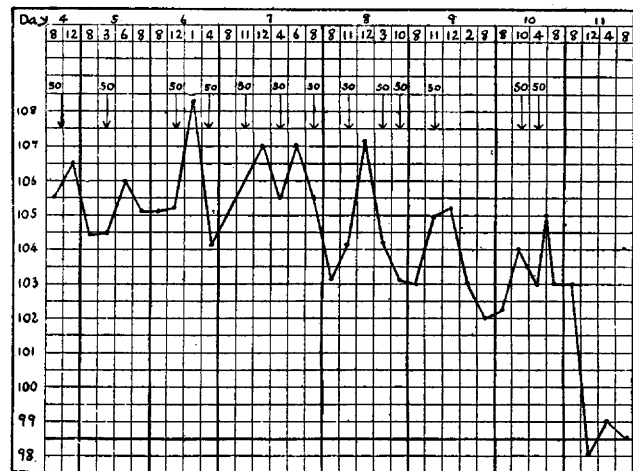


Chart 3.—Temperature in Case 3.

This case is a good instance of an abortive pneumonia terminating on the fourth day, a phenomenon so rare with pneumococcus Type II pneumonia that one is disposed to credit antibody for its occurrence.

CASE 5.—P. N., a woman, aged 60, with pneumococcus Type III pneumonia of the right lower lobe, received the first injection of antibody on the third day of the disease. She received three injections of 50 c.c. each on that day, and two injections of 50 c.c. each on the day following (Chart 5). There was a sharp reaction after the first injection, and there were definite reactions after each of the other four. Crisis occurred on the fifth day.

This case illustrates a pneumococcus Type III pneumonia that appeared to react favorably to antibody. Unfortunately, there were not a great many in this group. As pointed out previously, the death rate for Type III pneumonia was not appreciably affected by antibody treatment.

CASE 6.—F. H., a man, aged 44, alcoholic, with pneumococcus Type III pneumonia of the right and left lower lobes, received the first injection of antibody on the fifth (or sixth) day of the disease (Chart 6). He received altogether twenty-

eight injections of antibody over a period of eight days. The blood culture remained positive, and the patient died of a terminal pneumococcus Type III meningitis.

In this case, antibody appeared to have no effect whatever on the course of the disease. In spite of huge doses (a total of 1,650 c.c.) of antibody, pneumococci persisted in the blood stream, and the patient died of pneumococcus meningitis.

From these examples it will be seen that antibody does not always act in the same way. While reactions usually do occur, they may be entirely absent. A reaction may follow one injection and be lacking after the next. There may be a severe chill or a mild one. A rise of temperature may follow an antibody injection, even though the chill did not occur. Profuse diaphoresis is sometimes seen without any preceding chill. Finally, the antibody may produce a striking effect on the course of the disease, or it may produce no effect whatever. In experiments on mice, it is well established that while antibody often protects these animals against 1,000,000 fatal doses of pneumococcus culture, no amount of antibody will protect them if overwhelming doses of culture are injected. The same principle probably holds true for man.

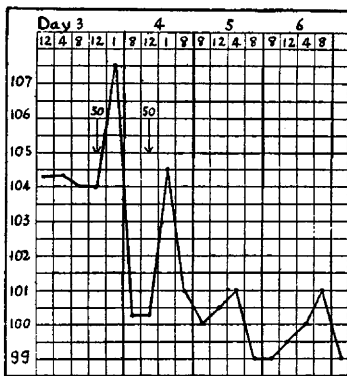


Chart 4.—Temperature in Case 4.

In Table 4 it will be noted that in a series of 118 patients treated with antibody on or before the fifth day, thirty-four, or 28.8 per cent., showed normal temperatures on or before the fifth day of the disease; while in 201 control patients admitted on or before the fifth day, only sixteen, or 7.9 per cent., showed a normal

TABLE 4.—DURATION OF PNEUMONIA IN PATIENTS THAT RECOVERED

	Antibody Wards			Control Wards		
	Tot. No.	T. 99	Per Cent.	Tot. No.	T. 99	Per Cent.
On or before 5th day.....	118	34	28.8	201	16	7.9
On or before 6th day.....	148	69	48.2	225	41	18.2
On or before 10th day.....	...	91	31.8	...	118	42.0

temperature on or before the fifth day. In a similar way, 48 per cent., or almost half, of the patients admitted on or before the sixth day, had a normal temperature on or before the sixth day of the disease; while only 18.2 per cent. of the controls reached normal in the same length of time. On the other hand, only 31.8 per cent. of the treated patients continued to have fever until the tenth day of the disease or thereafter, while 42 per cent. of the controls had elevated temperatures for ten days or more.

EFFECT OF ANTIBODY ON COMPLICATIONS

Table 5 shows the incidence of complications in the treated and control series. In 424 pneumococcus patients admitted to the antibody wards, empyema occurred thirty-one times, with eleven deaths; whereas 410 pneumococcus cases in the control wards were complicated by empyema thirty-two times, with fifteen

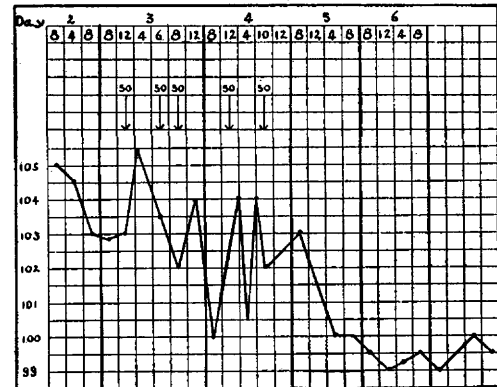


Chart 5.—Temperature in Case 5.

deaths. Meningitis occurred seven times in the treated series, and eleven times in the untreated. Endocarditis or pericarditis was observed six times in the treated

TABLE 5.—INCIDENCE OF COMPLICATIONS IN TREATED AND CONTROL SERIES

Complications	Antibody Wards 424 Pneumonia Cases		Control Wards 410 Pneumonia Cases	
	Total No.	Deaths	Total No.	Deaths
Empyema.....	31	11	32	15
Meningitis.....	7	7	11	11
Endocarditis, pericarditis.....	6	6	9	9
Arthritis.....	0	0	2	2
Total.....	44	24 (54.5)	54	37 (68.5)

cases, and nine times in the untreated cases. There were no cases of arthritis in the antibody series, and two cases in the control series. Altogether, there were forty-four severe complications in the antibody wards,

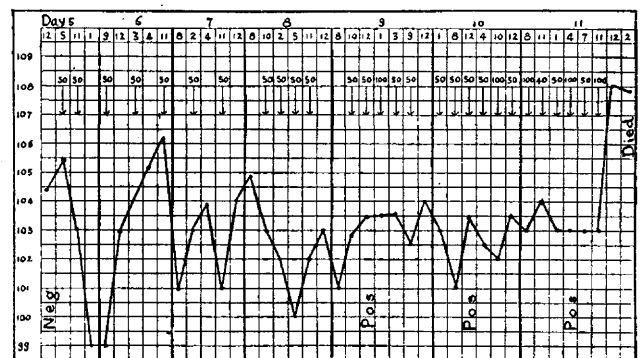


Chart 6.—Temperature in Case 6: Pos and Neg, blood culture positive or negative.

with twenty-four deaths (54.5 per cent.), and fifty-four severe complications in the control wards, with thirty-seven deaths (68.5 per cent.).

From these figures it will be seen that there is no evidence to show that treatment with antibody increases the incidence of empyema or any other severe complication. In the case of each of the severe complications,

the incidence rate was less for the antibody series than for the control series.

RESULTS

From the evidence presented above it may be concluded that pneumococcus antibody solution is a therapeutic agent of considerable power. The most striking results are undoubtedly obtained in pneumococcus Type I pneumonia. The results in pneumococcus Type II pneumonia are not so impressive, and in pneumococcus Type III cases the antibody solution seems to possess no benefit whatever. It would appear from these facts that antibody solution owes its therapeutic value chiefly to the amount of protective substance present. Just why a considerable difference in death rate has been observed between the treated and the untreated pneumococcus Type IV pneumonias, we are unable to say. The beneficial effect of antibody is probably not referable to the shock reactions, otherwise an improvement would be expected in pneumococcus Type III and in streptococcus pneumonia as well as in the other pneumococcus types. As a matter of fact, the reactions associated with antibody injections are often very uncomfortable and in certain cases are actually injurious to the patient. It has been claimed, of course, that foreign protein reactions have therapeutic value in pneumonia and other infectious diseases. There is little evidence, however, in the present study to support such a theory.

Patients treated with antibody have never shown any symptoms of serum sickness, and this is a great point in its favor. Furthermore, there is no danger of anaphylactic symptoms following the administration of antibody.

Perhaps the most important feature of antibody is its polyvalent nature. It contains protective substance against the three fixed types of pneumococcus. Furthermore, the statistics on Type IV pneumonia indicate that it has some therapeutic value in this type also, probably the result of cross protection. In the treatment of 424 pneumococcus pneumonias, the death rate was 21.4 per cent., while, in 410 control cases, the death rate was 28.3 per cent. In other words, the figures indicate that in every hundred patients with pneumococcus pneumonia treated there was a saving of seven patients. This difference between two almost equal groups of unselected patients, coming from similar environment, during the same seasons, and treated in the same institution, certainly must have some significance.

It is possible that considerable benefit could be derived from antibody by administering it subcutaneously. In the present study it has been employed in this manner on a number of occasions, and has never produced constitutional reactions. Our experience, however, with this form of administration is still too limited to permit of an opinion as to its practical value.

SUMMARY

1. In a series of 917 cases of lobar pneumonia in which a definite bacteriologic diagnosis was obtained, 90 per cent. were of pneumococcus origin. The greater part of the remainder were referable to *Streptococcus hemolyticus* or *Streptococcus viridans*.

2. In the pneumococcus series, pneumococcus Type I predominated (38.4 per cent.). Pneumococcus Type IV was next in frequency (27.7 per cent.); pneumococcus Type II (18 per cent.); pneumococcus Type III (15.9 per cent.).

3. In 424 cases of pneumococcus pneumonia treated with pneumococcus antibody solution, the death rate was 21.4 per cent. A control series of 410 cases in the same institution showed a death rate of 28.3 per cent.

4. Pneumococcus antibody produces its most striking effect in pneumococcus Type I pneumonia. In a series of 156 treated cases the death rate was 13.3 per cent.; while a control series of 162 cases showed a death rate of 22.2 per cent. A definite but less marked effect was observed in cases of pneumococcus Types II and IV pneumonia which were treated with antibody. The antibody solution had no effect whatever on the death rate in pneumococcus Type III pneumonia.

5. The death rate of streptococcus pneumonia was not favorably influenced by antibody treatment.

6. In the series of patients with pneumococcus pneumonia treated with antibody, 28.8 per cent. recovered on or before the fifth day. In the control series, only 7.9 per cent. recovered on or before the fifth day.

7. There were forty-four severe complications in the series of 424 pneumococcus pneumonias treated with antibody, while the control series of 410 pneumococcus pneumonias showed fifty-four severe complications.

33 East Sixty-First Street.

ABSTRACT OF DISCUSSION

DR. F. M. HUNTOON, Glenolden, Pa.: We utilize the principle that antibodies in serum will combine with the bacteria with which the animals were immunized. By exposing bacteria to these immune serums, one causes the antibodies to attach themselves to the bacteria. Then by heating the sensitized bacteria in an alkaline solution, one can cause the antibody to split off. That, in brief, is the method of preparation of these antibody solutions. I want to emphasize not only the large number of cases observed but also the adequate control used in this series. There is an advantage in the cooperation of institutions for scientific interest. Five different institutions had combined resources to gain something of possible scientific value. The aim from the start has been to find out whether this material was therapeutically efficient. If so, it represented a distinct biologic advance, since we had eliminated the horse serum from consideration. The production of serum protein-free solutions has enabled us to do some research on the chemical nature of the antibody. An antibody is a definite substance. It is not a globulin, and if it is a protein at all, it is a peculiar albumin which is not destroyed by alcohol. It is not a fatty substance, and it is not injured by trypsin digestion. We can say what it is not, but we cannot say what it is.

DR. NELLIS B. FOSTER, New York: This antibody extract is being tried experimentally in two institutions: in Bellevue Hospital under Dr. Cecil, and in the New York Hospital under Dr. Connor and myself, both services being parts of the Cornell Medical School. In an experiment of this kind it is necessary to have a large amount of data to prove anything at all. Last year we had a large number of cases, but at the end of the year we did not feel that we had results that justified making a statement, and at present we do not feel that we have perfect therapeutic measures for treating pneumonia; but we do feel that we are one step farther in developing a substance for treating pneumonia. There are statistics on mortality at the New York Hospital for more than a hundred years. The mortality has never been lower than 25 per cent. During the last two years, it has been materially reduced by the use of this antibody extract, because that is the only material change in treatment during the last two years. Still, in the aggregate of several hundred cases of true pneumonia, we do not yet feel certain where we stand. Pneumonia is a disease which changes from year to year, and in a city like New York it has a higher mortality than in a rural population.

DR. WILLARD J. STONE, Pasadena, Calif.: I should like to ask Dr. Huntoon whether he has reason to believe that the subcutaneous use of this product would be followed by good results.

DR. HUNTOON: I have no experience to decide the question. I know only the laboratory side.

DR. MARY FREEMAN, Perrine, Fla.: I should like to ask whether there were fatalities from the immediate reaction after the giving of that serum. The clinical or medical side is waiting too much for the laboratory. I appreciate the work the laboratory is doing, but if physicians will study and heed the symptoms of patients and keep the chest and the back of the arms well covered, remembering the relation of the brachial plexus to the thoracic and other nerves of the chest, many a time the giving of an opiate to check the cough will be unnecessary. A chill should never be allowed to strike the chest. I have the advantage of having a warm climate but, even in Florida, after the air cools off it is necessary to warm it. In my practice, I put a sweater over the nightgown and I apply a hot kaolin poultice. For elimination, in my practice I give castor oil and turpentine every day to an adult until resolution sets in. If he needs any liver medicine, he gets sodium bicarbonate. Atropin is the sheet anchor in pneumonia. I start its use in pneumonia before the crisis comes, so that the patient has a blood pressure that will hold him through an ordinarily difficult situation.

DR. ALEXANDER LAMBERT, New York: My ward belonged to the control group of which Dr. Cecil spoke. The feelings of the patient and the result obtained produced an impression even more favorable than the figures show. There was, however, a peculiar variation in the different wards. Among the controls the percentage varied, and the death rate varied from 14 to 64 per cent.; but the general totals were exactly as Dr. Cecil gave them. There has been a great change in the pneumonias in New York City. When we had all the alcohol that was desired in life, in Bellevue Hospital one third of the 40,000 patients were in the alcoholic wards with or without delirium tremens. That made a strong alcoholic group among pneumonia patients, and the death rate was 66 per cent. for the alcoholic group and 23 per cent. for the non-alcoholic group. The type has changed. One does not see the thoroughly poisoned, chronically soaked alcoholic person in the hospital. The change in pneumonia has also been distinct. We had two wards of fifty patients each; in one group alcohol was given, and the death rate was 40 per cent.; in the other group alcohol was not given, and the death rate was 14 per cent. Oddly enough, the April pneumonias in New York usually have a higher death rate than do the pneumonias in the winter.

DR. RUSSELL L. CECIL, New York: I tried subcutaneous inoculation on some very ill patients to whom I was afraid to give antibody intravenously. The results were not striking, but I will try it more extensively, and I expect also to try subcutaneous treatment on monkeys. In monkeys with experimental pneumonia, our results with antibody treatment were best in pneumococcus Type I cases, next best in Type II, and worst in Type III. As to the fatal reactions: If a patient with pneumonia dies within a certain number of hours after an injection of antibody, the question naturally arises whether antibody killed the patient. In my series there were three deaths probably directly due to the antibody. In one case the cause of death was hyperpyrexia. In the other two cases, the cause was failing circulation. As a result of these unfortunate reactions, I have become cautious about giving antibody to older persons or to pneumonia patients late in the disease, when they are worn out. I have figures based on my series of cases which indicate that the results are much better when the treatment is started early in the disease. These patients feel better after the injection of antibody. If they have a pain in the side, it usually disappears, and they have a general sense of well-being which is quite noticeable. The change in the pneumonia death rate of which Dr. Lambert spoke is a striking thing. In Bellevue Hospital, the death rate before prohibition was from 40 to 55 per cent.; but the present death rate is only 28 per cent. With regard to the leukocyte reac-

tions following antibody injections, I have curves which show a decided leukocytosis, which, however, is seen shortly after giving the antibody solution, and is only temporary.

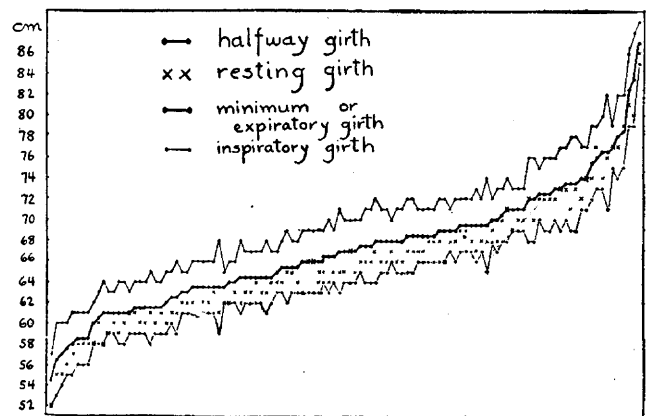
AGAINST MEASURING THE CHEST GIRTH AT REST*

HORACE GRAY, M.D.
BOSTON

Recent biometric evidence that body weight is more closely correlated with chest-girth than with stature¹ brings up anew the ancient questions as to technic.

The three levels cannot be entered on here save to state that the axillary has been generally discarded, the mammillary has been used by me in accordance with most medical men, and the xiphoid is very appealing for further study with reference to avoidance of the considerable pectoral muscle and gland tissue in men and women.

The moment of the respiratory cycle is the question aroused by the favor accorded by Dreyer² to the variously called resting, relaxed, talking, normally breath-



Chest-girth, nipple level, net, of 114 private school boys, arranged according to size of "halfway girth" (heavy line); note irregular position of "resting girth" (indicated by crosses) with relation to "minimum or expiratory girth" (circles); inspiratory girth, light line above.

ing, and not expanded chest circumference. The brief evidence so far presented³ to indicate the inferiority of the resting girth to the halfway girth (arithmetical mean between the inspiratory and expiratory girths) has seemed to need amplification.

The subjects studied composed two normal series, one of forty men, the other of 114 private school boys. The resting girth was greater than the halfway girth in 18 per cent. of the first series of men, equal in 17 per cent., and less in 65 per cent.; while in the boys' group the respective percentages were 2, 8 and 90. These figures signify that in men generally and in children nearly always the resting girth diverges from the mean girth in the direction of the girth deflated, as shown in the accompanying chart.

More important is the degree of divergence of the resting girth from the midway girth. In the men the average was 0.7 cm., or less than 1 per cent. of the mid-

* Read before the Philadelphia Pediatric Society, May 9, 1922.
1. Gray, Horace: The Relation of Weight to Chest-Girth, Stature, and Stem-Length, Judged by the Biometric Coefficient of Correlation, *Am. J. Physical Anthropol.*, to be published.
2. Dreyer, Georges, and Hanson, G. F.: The Assessment of Physical Fitness, London, 1920, reprinted by Paul B. Hoeber, New York, 1921.
3. Gray, Horace, and Root, H. F.: Weight Prediction by the Formulae of Bornhardt, of von Pirquet, and of Dreyer, *Boston M. & S. J.* 185: 28 (July 7) 1921.