AGGLUTINATION PHENOMENA IN LOBAR PNEUMONIA.*

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Numerous investigators (1 to 11) have noted that when pneumococci are grown in immune serum the organisms exhibit unusual characteristics. Certain observers have also shown that the sera of animals immunized to pneumococci are able to cause agglutination of these organisms when the ordinary agglutination technique is employed.

In 1900 Besançon and Griffon (12) noted the presence of agglutinins in the blood of patients ill of and convalescent from lobar pneumonia. They found that often the homologous strain (the strain derived from the patient) was agglutinated when a heterologous strain was not. This fact suggested that the various strains of pneumococci might possess biological differences which could not be detected by ordinary cultural methods. Eyre and Washbourn (13) and Gargáno and Fattori (14) also noted such differences, but Neufeld and Händel (15) were the first to study thoroughly immunological variations in pneumococci. They worked, however, with relatively few strains of pneumococci.

Dochez (16) and Dochez and Gillespie (17), working with a large number of strains of pneumococci, isolated from patients suffering from lobar pneumonia, were able to differentiate pneumococci into four groups on the basis of cultural and immunological reactions. The three main groups were distinguishable by agglutination and animal protection experiments with a fourth group which includes all strains of pneumococci which cannot be otherwise classified.

More recently Lister (18) in South Africa, approaching the problem from another standpoint, has differentiated into four groups eighteen of twenty strains of pneumococci isolated by puncture of the lungs of patients having lobar pneumonia. This he was able to do by cross agglutination tests with cultures of these strains of pneumococci and the sera derived from these patients at about the time of crisis. Two strains he found to be non-agglutinable.

The present study has been carried out with the purpose of determining the time of appearance and disappearance of agglutinins in the blood of patients suffering from pneumonia, and of learning more concerning the specific character of these agglutinins, especially their specific relation to the various groups of pneumococci.

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METHODS.

Neufeld (19), Jehle (20), Kindborg (21), and others have found that pneumococci are agglutinated by the serum of immunized animals when this is diluted to 1 to 60 or even 1 to 100,000 (21), and that the serum of patients diluted even to 1 to 160 may cause such agglutination when the homologous strains are used. We have found, however, that the reaction is highly specific even as regards the various groups of organisms, so that for the purpose in view the use of diluted serum seemed unnecessary. This is especially true since normal human blood does not contain agglutinins for the pneumococcus, and spontaneous agglutination of pneumococci does not occur with the method employed. Therefore, in making these tests equal parts (0.3 of a cubic centimeter) of a broth culture of the organism to be tested and of the patient's serum were mixed together and macroscopic readings were made after two hours in a water bath at 37° C. and after twenty-four hours in the ice-box. In practically every case agglutination was apparent at the end of the two hour period, if it occurred at all.

The cultures of pneumococci were obtained from culture of the heart's blood of a mouse inoculated intraperitoneally with the patient's washed sputum, or from direct blood culture, or from culture of material obtained by puncture of the lung of the patient.

Certain observers (22) have noted that cultures fresh from the human host are occasionally not agglutinable. Therefore, all cultures were grown for several generations on artificial culture media. To make sure that the cultures employed were agglutinable, they were all tested with antipneumococcus serum specific for groups I and II, before they were used for the agglutination tests with human serum. At each examination the patient's serum was tested against the homologous organism and also against stock cultures belonging to groups I and II.

The blood to be tested was drawn aseptically from an arm vein of the patient. It was allowed to clot, was centrifuged, and the clear serum was pipetted off. The tests were made with serum as fresh as possible, for it has been found that agglutinins in human blood disappear quickly after it is stored. This is especially so if the serum has not been separated from the clot. With highly im-

mune horse serum this is not the case. Serum two years old has been found still to possess strong agglutinative properties.

The correlation between the clinical severity of lobar pneumonia and the bacteriological findings has not only prognostic importance, but also considerable bearing on the effects of serum therapy. It has been learned that infections which are included in groups I and II are usually severe. The serum treatment of lobar pneumonia has been more successful in the cases included in group I than in group II, and experimentally it has been found that antipneumococcus serum I (a serum produced by highly immunizing a horse to pneumococci belonging to group I) possesses greater protective and curative properties than a serum similarly produced by organisms included in group II. It will be noted in the protocol that six of the fatal cases were group II infections, some of which were thoroughly treated with serum.

On the other hand, infections due to organisms in the heterogeneous group (group IV) are almost always mild and the prognosis is favorable. Infections due to *Pneumococcus mucosus* (group III) are often severe, but as this organism under ordinary cultural methods is non-agglutinable, this group may be left out of consideration for the present.

Bearing in mind these apparent differences in the type of disease produced by the different groups of pneumococci, we may make an analysis of the results of the agglutination reactions.

DISCUSSION.

The protocol of all the cases studied is briefly summarized in table I.

TABLE I.

Group.	No. of cases.	Agglutinins present at some time in the disease.	Never present.	Per cent. present.
I	16	16	0	100
II	13	7	6	53.8
III (*mucosus*)	2	0	2	0
IV (heterologous)	9	5	4	55.5

In all, sera from forty cases of lobar pneumonia, due to different types of pneumococcus, were examined. The sera of all the sixteen

cases belonging to group I showed the presence of agglutinins at some stage of the disease. Six of the thirteen cases in group II showed no agglutinins. In five of these negative cases the disease terminated fatally. Repeated examinations of the sera of these patients showed no agglutinins for their own organism or for stock cultures I and II. In all these cases there was no doubt as to the type of the infecting pneumococcus, for four had positive blood cultures and from the fifth an organism belonging to group II was recovered by lung puncture. This confirms the observations of Lister, who was unable to demonstrate the presence of agglutinins in the sera of four cases that terminated fatally.

The impression has been gained that the non-development of agglutinins in the sera of patients with severe infections is evidence of grave prognostic import. Exceptions to this observation have been noted, however, in which a feeble agglutination reaction developed late in two fatal cases. In one of these the patient's serum showed agglutinins on the thirteenth day (the day of admission to the hospital), the patient dying of a complicating meningitis and empyema on the seventeenth day. This case had no serum treatment. In the second case, which was treated with antipneumococcus serum, agglutinins were demonstrable on the thirteenth day of the disease. This patient had four lobes involved and died in extreme dyspnea on the following day.

Observations were made on only two patients infected with *Pneumococcus mucosus*. Hanes (23) has shown that members of this group are specifically agglutinable when treated according to the method of Porges (24), but that they do not agglutinate when subjected to the usual agglutination method. Since the latter method was employed in the present investigation, no agglutinins were demonstrable in the cases recorded.

In four of the nine cases belonging to group IV, no agglutinins were noted in the patients' sera. Two of these negative cases were mild in type, one was quite ill, having a positive blood culture, and the fourth was complicated with influenza. From this last case large numbers of *Bacillus influenzæ* were recovered from the sputum. Unfortunately a lung puncture yielded no culture. It is impossible to say absolutely whether *Bacillus influenzæ* or an atypical pneumo-

coccus or both were the etiological factors. In four of the five cases showing agglutination of the homologous organism, the reaction was feeble and lasted only one day, and in one case, which presented a very severe clinical picture, with positive blood cultures and spreading lesions, the serum developed strong agglutinative power for the patient's own organism on the day of the crisis (ninth day), which power persisted for eighty-four days. This patient later developed an abscess of the opposite lung and resolution of the original lesion was very slow. As the agglutinative power of this patient's serum was so strong and persistent, a few attempts were made to agglutinate with this serum other strains of organisms belonging to group IV, but all with negative results. It has seemed that in this case, as in two others in which agglutinins were demonstrated over a period of 117 days and 112 days respectively, the duration of the lesion (delayed resolution) had some relation to the persistence of agglutinins in the blood. In the other twenty-five cases showing positive agglutination at one time or another, the duration of this phenomenon was relatively short; the longest was twenty-one days, the average about seven days.

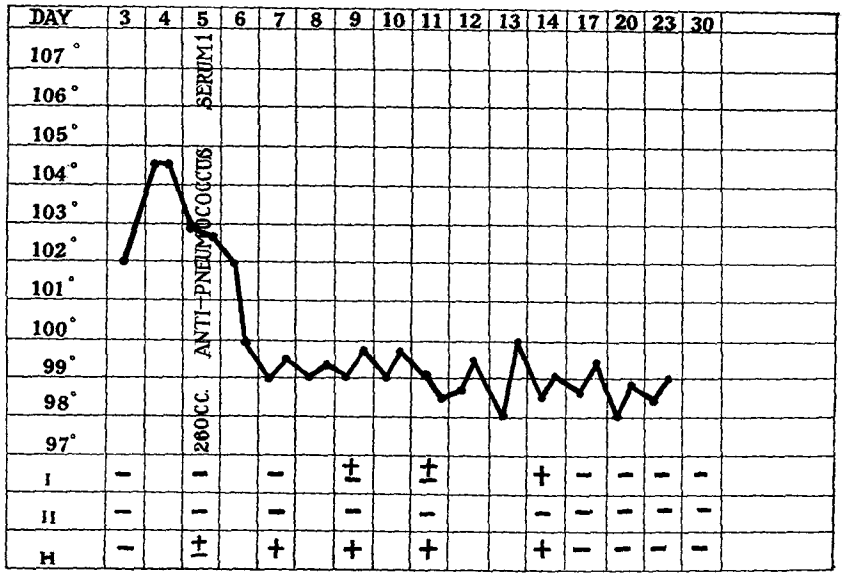
These findings are not wholly in accordance with the results of Jehle's investigations, who found that the sera of only a small number of patients agglutinated the pneumococcus forty-eight hours after the crisis and none after four days.

Agglutinins develop usually just before, at, or just after the crisis (table II, pp. 607–13). During this critical period of the disease Dochez (25) also demonstrated the presence of protective substances in human serum. Only two patients showed agglutinative power any appreciable time before the crisis; one showed it three days before, the second two days before the crisis. The former received antipneumococcus serum, the latter did not.

Too few cases have been studied to draw conclusions as to the effect of serum treatment on the appearance of agglutinins in the patients' blood. Of the sixteen patients in group I, agglutinins appeared in the serum of all. Eleven of these patients were treated with serum, and five received no serum. Of the thirteen cases in group II, agglutinins were demonstrable in the sera of seven cases, and in six cases no agglutinins could be demonstrated at any time.

Eight of the thirteen cases in this group were treated with serum, and of these three developed agglutinins and five did not. On the other hand, four patients showed agglutinins in the blood without serum treatment and none were demonstrated in one fatal case. Thus it would seem that serum treatment had but little influence on the development of agglutinins.

Probably the determination of the presence of agglutinins will have little practical bearing on the diagnosis and treatment of the disease. However, the fact that an organism derived from the



TEXT-FIG. 1. The relative time of development of agglutinins for homologous and stock organisms in a case of lobar pneumonia. I = stock culture of pneumococcus belonging to group I. II = stock culture of pneumococcus belonging to group II. H = homologous culture of pneumococcus, *i. e.*, that derived from the patient.

sputum is agglutinated by the patient's serum is corroborative evidence that this organism is the etiological agent concerned. In practically every case observed, in case the serum agglutinated any organism, it caused agglutination of the organism obtained from culture of the heart's blood of a mouse injected with the patient's washed sputum. Agglutination is of no help in the early recogni-

tion of the type of organism concerned, inasmuch as the appearance of agglutinins occurs relatively late in the disease.

In several instances it has been found that the first organism to be agglutinated was the homologous strain and only later was the stock strain agglutinated. This illustrates the great specificity of the reaction even when no dilutions are used. Clough (26) has noted this marked specificity of the serum of patients recovering from lobar pneumonia in his experiments, demonstrating the power of such sera to render virulent pneumococci phagocytable. One case on which observations were made at frequent intervals shows this group specificity clearly (text-figure 1).

CONCLUSIONS.

1. Agglutinins are present in the blood of patients suffering from lobar pneumonia during some stage of the disease in a large percentage (73.8 per cent.) of the cases due to pneumococci belonging in groups I, II, and IV.

2. In most very severe and fatal cases agglutinins cannot be demonstrated, and it is probable that their absence during the later days of the disease may have unfavorable prognostic significance.

3. No agglutinins are demonstrable by the technique employed in the blood of patients suffering from infection with *Pneumococcus mucosus* (group III).

4. In certain cases agglutinins may be demonstrable for only one day, and in other cases they may persist for several weeks.

5. When agglutinins are demonstrable they usually appear at about the time of the crisis.

6. It has not been possible to demonstrate that treatment with immune serum has any effect on the appearance of agglutinins.

7. The agglutinins present in cases due to organisms of types I and II are always specific for the type of organism causing the infection. In certain cases the agglutination reaction may be more active or appear earlier when the homologous organism is employed than when other organisms of the group are used in the test. In cases due to organisms of type IV, the serum never causes agglutination of any organism except the homologous one.

BIBLIOGRAPHY.

1. Gruber, M., and Durham, H., *München. med. Wchnschr.,* 1896, xliii, 285.
2. Durham, H. E., *Jour. Path. and Bacteriol.,* 1897, iv, 13.
3. Metchnikoff, E., *Ann. de l'Inst. Pasteur,* 1891, v, 465.
4. Pane, N., *Riforma med.,* 1897, ii, 40; 1898, iv, 246; *Centralbl. f. Bakteriol., Ite Abt., Orig.,* 1897, xxi, 664.
5. Huber, F. O., *Centralbl. f. inn. Med.,* 1902, xxiii, 417.
6. Huber, F. O., *Berl. klin. Wchnschr.,* 1903, xl, 358.
7. Mosny, E., *Arch. de méd. expér. et d'anat. path.,* 1892, iv, 195.
8. Kruse, W., and Pansini, S., *Ztschr. f. Hyg.,* 1892, xi, 279.
9. Washbourn, J. W., *Lancet,* 1902, ii, 1301, 1378.
10. Besançon, F., and Griffon, V., *Compt. rend. Soc. de biol.,* 1897, vi, 551, 579.
11. Aoki, *Arch. f. Hyg.,* 1912, lxxv, 393.
12. Besançon, F., and Griffon, V., *Ann. de l'Inst. Pasteur,* 1900, xiv, 449.
13. Eyre, J. W. H., and Washbourn, J. W., *Brit. Med. Jour.,* 1899, ii, 1247.
14. Gargáno, C., and Fattori, C., *Riv. crit. di clin. med.,* 1903, iv, 177, 225.
15. Neufeld, F., and Händel, L., *Ztschr. f. Immunitätsforsch., Orig.,* 1909, iii, 159; *Berl. klin. Wchnschr.,* 1912, xlix, 680; *Arb. a. d. k. Gsndhtsamte.,* 1910, xxxiv, 167, 293.
16. Dochez, A. R., *Jour. Exper. Med.,* 1912, xvi, 680.
17. Dochez, A. R., and Gillespie, L. J., *Jour. Am. Med. Assn.,* 1913, lxi, 727.
18. Lister, F. S., *South African Institute for Medical Research* [*Publications*], December 22, 1913, p. 1.
19. Neufeld, F., *Ztschr. f. Hyg.,* 1902, xl, 54.
20. Jehle, L., *Wien. klin. Wchnschr.,* 1903, xvi, 917.
21. Kindborg, A., *Ztschr. f. Hyg.,* 1905, li, 197.
22. Meyer, F., *Deutsch. med. Wchnschr.,* 1902, xlii, 751.
23. Hanes, F. M., *Jour. Exper. Med.,* 1914, xix, 38.
24. Porges, O., *Wien. klin. Wchnschr.,* 1905, xviii, 691.
25. Dochez, A. R., *Jour. Exper. Med.,* 1912, xvi, 665.
26. Clough, P. W., *Bull. Johns Hopkins Hosp.,* 1913, xxiv, 295.

TABLE II.

Case No.	Age in yrs.	Day of disease.	Days.	Duration of agglutinins in dys.	Type of organism.	Treatment.	Remarks.
1867	56	1 2 3 4 5 6 7 8 9 10 11 12 13 14 15 16 17 18 19 20 21 22 23 24 25 26 27 28 29 30 31 32 33 34 35 36 37 38 39 40 I II H C	45 56 67 162 − + + + − − − − + + + −	117	I	495.5 c.c. serum I	Delayed resolution. Recovery.
1828	43	S S S S I − − + − II − − + − H + + + − C	113 −		I	995.5 c.c. serum I	Recovery.
1952	34	S S S I + + + + − − − II − − − − − − − H + + + + + − − C	...	7	I	525.5 c.c. serum I	Irregular heart. Recovery.
1980	7	S S S S S I − − − + + + ± − II − − − − − − − − H − − − + + + − − C	72 −	18	I	265.5 c.c. serum I	Empyema; otitis media. Recovery.
1843	35	S S S I − + + − − II − − − − − − H − − − − − − C	...	2	I	375 c.c. serum I	Recovery.

I = stock culture of pneumococcus belonging to group I. II = stock culture of pneumococcus belonging to group II. H = homologous culture of pneumococcus, *i. e.*, that derived from the patient. C = day temperature fell by crisis or lysis. S = days patient received antipneumococcus serum treatment.

TABLE II.—*Continued.*

Case No.	Age in yrs.	Day of disease. 1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	18	19	20	21	22	23	24	25	26	27	28	29	30	31	32	33	34	35	36	37	38	39	40	Days.		Duration of agglutinins in dys.	Type of organism.	Treatment.	Remarks.
1916	8	..	..	S	S	..	..	..	..	..	..	..	..	..	..	..	..	..	±	..	..	..	..	..	..	−	..	..	..	..	..	..	..	..	..	−	..	..	..	..	47	..	1	I	270 c.c. serum I	Empyema. Recovery.
		I	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	−	..	..	..	..	..	..	−	..	..	..	..	..	..	..	..	..	..	−	..	..	..	..	−	..					
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		II	..	−	..	−	..	−	..	−	..	−	..	..	−	..	..	−	..	..	−	..	..	−	..	..	..	..	..	−	..	..	..	..	..	..	..	..	..	..	..	..	9	I	260 c.c. serum I	Recovery.
		H	..	−	..	±	..	+	..	+	..	+	..	..	+	..	..	−	..	..	−	..	..	−	..	..	..	..	..	−	..	..	..	..	..	..	..	..	..	..	..	..				
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		II	..	..	..	−	..	..	−	..	..	..	−	..	..	..	−	..	..	−	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	−		7	I	0	Recovery.
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		..	..	..	C	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..				
1978	19	..	..	S	S	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..				
		I	−	−	−	..	..	..	..	−	..	..	±	..	..	..	−	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..				
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		II	−	−	−	−	..	..	..	..	..	..	−	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..		2	I	510 c.c. serum I	Died. Pulmonary embolism 16th dy.
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1882	22	..	..	..	..	..	S	S	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	76					
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Case No.	Age in yrs.	Day of disease;	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	18	19	20	21	22	23	24	25	26	27	28	29	30	31	32	33	34	35	36	37	38	39	40	Days.	Duration of agglutinins in dys.	Type of organism.	Treatment.	Remarks.
2083	24	I			−				−	+		−	+																	±												21	I	0	Recovery.
		II			−				−	−																				−															
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2044	38	I			−				−			−						−			−																					9	I	0	Recovery.
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1981	26	I			−				−			±		+			+					+																				10	I	0	Recovery.
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2008	24	I	S	S																											±												3	I	260 c.c. serum I	Recovery.
		II		−	−	−		−	−				−																		−														
		H		−	−	−	±		−				−																		−														
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1880	25	I									S																															47	0	II	100 c.c. serum II	Recovery.
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1827	40	I			S	S																																			129	7	II	175 c.c. serum II	Recovery.
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TABLE II.—*Continued.*

Case No.	Age in yrs.		Day of disease. 1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	18	19	20	21	22	23	24	25	26	27	28	29	30	31	32	33	34	35	36	37	38	39	40	Days.	Duration of agglutinins in dys.	Type of organism.	Treatment.	Remarks.
1953	12	I	−	..	..	..	−	..	−	..	−	..	..	..	..	−	..	..	..	..	−	..	..	..	−	..	..	−	..	..	..	..	..	..	..	..	..	..	..	..	−	..	16	II	0	Recovery.
		II	−	..	..	..	−	..	−	..	+	..	..	..	..	−	..	..	..	..	−	..	..	..	−	..	..	±	..	..	..	..	..	..	..	..	..	..	..	..	..	−	..				
		H	−	..	..	..	−	..	−	..	−	..	..	..	..	−	..	..	..	..	−	..	..	..	±	..	..	−	..	..	..	..	..	..	..	..	..	..	..	..	..	−	..				
			..	..	..	..	C	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..				
1999	34		..	..	..	..	..	..	..	−	..	−	−	..	−	..	..	..	−	..	..	..	..	..	−	..	±	..	..	−	..	..	..	..	..	..	..	..	..	..	..	116	8	II	0	Empyema. Recovery.
			..	..	..	..	..	..	..	−	..	−	−	..	−	..	..	±	−	..	..	..	..	..	−	..	±	..	..	−	..	..	..	..	..	..	..	..	..	..	..	−				
			..	..	..	..	..	..	..	−	..	−	−	..	−	..	..	−	−	..	..	..	..	..	−	..	±	..	..	..	..	..	..	..	..	..	..	..	..	..	..	−				
			..	..	..	..	..	..	..	..	..	..	C	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..				
1820	31	I	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	10	II	0	Recovery.
		II	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..				
		H	..	..	..	..	..	..	..	..	..	..	..	+	..	..	..	..	..	+	..	..	..	+	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..				
			..	..	..	..	..	C	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..				
1871	33		..	..	..	..	..	..	..	S	S	S	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	122	112	II	405 c.c. serum II	Recovery.
		I	..	..	..	..	..	..	..	−	−	−	..	..	..	..	..	−	..	..	..	..	..	..	..	..	..	−	..	..	..	..	..	..	..	..	..	..	..	..	..	−				
		II	..	..	..	..	..	..	..	−	−	±	..	..	..	..	..	+	..	..	..	..	..	..	..	..	..	+	..	..	..	..	..	..	..	..	..	..	..	..	..	±				
		H	..	..	..	..	..	..	..	−	−	±	..	..	..	..	..	+	..	..	..	..	..	..	..	..	..	+	..	..	..	..	..	..	..	..	..	..	..	..	..	−				
			..	..	..	..	..	..	..	C	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..				
1969	19		..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	59	20	II	0	Recovery.
		I	..	..	−	..	−	..	..	..	−	..	−	..	..	−	..	..	−	..	..	..	..	..	−	..	..	−	..	..	..	..	..	..	..	..	..	..	..	..	..	−				
		II	..	..	−	..	−	..	..	..	−	..	+	..	..	+	..	..	+	..	..	..	..	..	+	..	..	+	..	..	..	..	..	..	..	..	..	..	..	..	..	−				
		H	..	..	−	..	+	..	..	..	+	..	+	..	..	+	..	..	−	..	..	..	..	..	−	..	..	−	..	..	..	..	..	..	..	..	..	..	..	..	..	..				
			..	..	..	..	..	..	C	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..				
1931	43	I	..	..	..	..	..	..	..	..	−	..	..	−	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	0	III	0	Recovery.
		II	..	..	..	..	..	..	..	..	−	..	..	−	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..				
		H	..	..	..	..	..	..	..	..	−	..	..	−	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..				
			..	..	..	..	..	..	..	..	..	Lysis																																		

Case No.	Age in yrs.		Day of disease. 1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	18	19	20	21	22	23	24	25	26	27	28	29	30	31	32	33	34	35	36	37	38	39	40	Days.						Duration of agglutinins in dys.	Type of organism.	Treatment.	Remarks.
1876	7	I																																											1	IV	0	Otitis media. Recovery.
		II																																															
		H							C		+												−																									
2014	59	I								S	S																																		0	IV	185 c.c. serum I	Delayed resolution. Recovery.
		II																																														
		H								−	−	−	−													−																						
												C																																					
1936	22	I						−						−																														46			1	IV	0	Delayed resolution. Recovery.
		II						−						−																														−				
		H						−						+																														−				
								Lysis																																										
2032	20	I			−			−		−			−			−			−								−																		0	IV	0	Recovery.
		II			−			−		−			−			−			−								−																				
		H			−			−		−			−			−			−								−																				
										C																																							
2102	18	I						−		−			−			−			−								−																	46	63	68	93	100	0	IV	0	Abscess of lung. Recovery.
		II						−		−			−			−			−								−					−											−	−	−	−	−			
		H						−		−			−			−			+								+					±											+	+	+	+	−			
											+		+							+																													
2115	12	I						−		−			−			−			−								−																					1	IV	0	Recovery.
		II						−		−			−			−			−								−																				
		H						−		−			+			−			−								−																				
										C																																							

TABLE II.—*Concluded.*

Case No.	Age in yrs.	Day of disease.	Duration of agglutinins in dys.	Type of organism.	Treatment.	Remarks.
1857	31	I: 11 +; II: 11 +; H: 11 +; 24 −; 7 C	1	IV	0	Recovery.
2093	28	I: 6 −, 8 −, 9 −, 11 −, 13 −; II: 6 −, 8 −, 9 −, 11 −, 13 −; H: 6 −, 8 −, 9 −, 11 −, 13 −; 12 Lysis	0	IV	0	Recovery.
1904	16	I: 8 −, 11 −; II: 8 −, 11 −; H: 8 −, 11 −; 12 Lysis	0	IV	0	Recovery.
1930	50	I: 13 +, 16 +; II: 13 −, 16 −; H: 13 −, 16 −	3	I	0	Meningitis empyema. Died.
1839	37	4 S, 5 S, 6 S, 7 S; I: 5 −, 11 −; II: 5 −, 11 −; H: 5 −, 11 −	0	II	1025 c.c. serum II	4 lobes involved, Pericarditis. Died 10th dy.
1856	50	4 S, 5 S; I: 4 −, 5 −; II: 4 −, 5 −; H: 4 −, 5 −	0	II	375 c.c. serum II	2 lobes involved. Died 5th dy.

Case No.	Age in yrs.		Day of disease. 1 2 3 4 5 6 7 8 9 10 11 12 13 14 15 16 17 18 19 20 21 22 23 24 25 26 27 28 29 30 31 32 33 34 35 36 37 38 39 40	Duration of agglutinations in dys.	Type of organism.	Treatment.	Remarks.
1899	62	I	S S —	0	II	365 c.c. serum II	Died 6th dy.
		II	— —				
		H	— —				
1983	45	I	— —	0	II	0	3 lobes involved. Died 8th dy.
		II	— —				
		H	— —				
1835	36	I	S S S —	0	II	1125 c.c. serum II	4 lobes involved. Died 7th dy.
		II	— —				
		H	— —				
1858	43	I	S S S S S — — — — — — S —	1	II	1175 c.c. serum II	4 lobes involved. Died 17th dy.
		II	— —				
		H	— —				
1963	57	I	— —	0	III	0	Died 7th dy.
		II	— —				
		H	— —				