SERUM TREATMENT OF PNEUMONIA *

ROWLAND GODFREY FREEMAN, M.D.

NEW YORK

During the past few years many new methods for the treatment of that very fatal disease of infancy, pneumonia, have been instituted, but few of these have been markedly successful. Many of us believe that the use of out-of-door air has done more to limit the mortality of pneumonia than has been demonstrated for any of the treatments based on laboratory investigation.

Of the three treatments that come under this class one may mention the use of leukocyte extracts advocated by Dr. Hiss; the use of vaccines either commercial or autogenous, and, finally, the use of the serum.

The leukocyte extract of Hiss has produced some striking results, but has not as yet had sufficient use, I believe, to determine accurately its value. But in a report issued by Hiss and Zinsser¹ in 1908, they describe eight cases with recovery and with a reduction of temperature usually within two to four days after the injections were begun. These injections were repeated daily.

Vaccines, particularly autogenous vaccines, have been considerably used and some of the reports are quite favorable, but Stoner,² who has collected 155 cases of pneumonia, in which the patients were treated with vaccines, reports a mortality of 12.9 per cent. Howland and Hoobler report fifty cases, mostly in young children with bronchopneumonia, and some older ones with lobar pneumonia, treated with stock vaccines, but with no favorable results. A few cases also were treated with autogenous vaccines with similar results.

In going over the literature it has seemed to me that the results obtained from the so-called Romers' serum, a pneumococcus serum, have been in general very favorable. Thus Krikke³ reports ten cases in children from 9 months to 10 years of age in which he noted a distinct improvement after the administration of the serum and all the children recovered. May⁴ reports good results in twenty cases with increased leukocytosis.

* Read at the meeting of the American Pediatric Society, Hot Springs, Va., May, 1912.

1. Hiss and Zinsser: *Jour. Med. Research*, 1908, xix, No. 3, p. 321.

2. Stoner: *A Résumé of Vaccine Therapy*. *Am. Jour. Med. Sc.*, 1911, cxli, 186.

3. Krikke: *Zur Serumtherapie de krupösen Pneumonie*. *Med. Klin.*, 1908, iv, 1881.

4. May: *Ueber die Wirkung des Romerschen Pneumokokken-serums bei der krupösen Pneumonia mit besonderer Berücksichtigung der Leukocyten*. *München. med. Wehnschr.*, 1908, lv, 2140.

Monti⁵ used it in twelve cases with decided benefit, while Knauth,⁶ Linderstern,⁷ Tunher⁸ and Crux⁹ used it with favorable results. Brunning¹⁰ treated six patients with falling temperature, slowing of the pulse and general improvement after the administration of the serum. All these observers used a dosage of about 10 c.c. for children and 20 c.c. for adults.

Morse, in 1903, reported to this society eight cases in which the patients were treated with 5 c.c. of pneumococcus serum every four hours, or about 30 c.c. daily, and concluded that the treatment "had no effect on the duration of the disease, the course of the temperature, the rate of the pulse and respiration or the progress of the local condition. Complications occurred at least as frequently as is usual. Death occurred in an unusually large percentage. The serum, while it apparently did no good, certainly did no harm."

On account of the usually favorable results of treatment with anti-pneumococcus serum it seemed worth while to try it in a series of cases, using alternate cases as controls. This work was undertaken at an institution where the children have poorer reaction to disease than is usual in private practice, and where under any form of treatment many children go on after pneumonia with a condition of unresolved pneumonia which persists for week or months.

The cases admitted to this series were in patients showing a fairly high temperature with good signs in the chest. One of the injected patients had a severe pneumonia complicating measles, another measles-pneumonia being used as a control. This patient showed no good effects from the serum and finally died of general septic conditions and endocarditis. Three patients injected are not included in this paper; two that were moribund when injected and were injected simply to see whether the serum might help them. One of these was rigid and comatose and made no cry when the large needle was thrust into the abdominal wall and died within four hours after the injection. In the other similarly hopeless case the patient died within twenty-four hours after injection. I also injected an adult who recovered.

The first seven of the patients were injected with a simple pneumococcus serum, a large dose, 100 c.c., being injected and in some cases repeated. The injection was done by means of a buret (Fig. 1) made for salvarsan injection and a rubber tube with a glass section near the needle

5. Monti: *Arch. f. Kinderh.*, 1908, xl, 45.

6. Knauth: *Deutsch. med. Wchnschr.*, 1905, No. 12.

7. Linderstern: *München. med. Wchnschr.*, 1905, No. 39.

8. Tunher: *Wein. med. Wchnschr.*, 1906, No. 11.

9. Crux: *Zwölf Fälle von Lungenentzündung im Kindesalter mit Romer's Pneumokokkenserum behandelt.* *Deutsch. med. Wchnschr.*, 1908, xxxiv, 16.

10. Brunning: *Kinderpneumonie und Pneumokokkenheil-serum.* *Deutsch. med. Wchnschr.*, 1911, xxxv, 42.

and a very large needle, this being necessary as the blood serum will not flow freely through a small needle. The injections were all made into the anterior abdominal wall and it was found that by keeping the end of the needle in the fascia below the skin and gradually advancing this rather long needle 100 c.c. could be readily delivered with one penetration of the skin. Pressure was made in addition to that of gravity by the use of a rubber bulb attached to the buret.

The first seven patients received 100 c.c. of pneumococcus serum, while the last eight cases received 50 c.c. each of pneumococcus and streptococcus serum. This serum was that of the New York Board of

Fig. 1.—Showing apparatus used for injecting antipneumococcus serum.

Health and I am indebted to Drs. Park and Nicoll of this department not only for the serum, but also for advice as to its use.

In none of the cases was there any evidence of irritation at the point of injection. The serum was rapidly absorbed and there was no inflammatory disturbance. In all of the cases, on the other hand, the injections were followed by urticaria, sometimes appearing on the following day, often ten days later, but without fever or general disturbance. In one case in addition to the urticaria an ankle joint was swollen, hot and painful, but this subsided in twenty-four hours and was accompanied by little rise in temperature.

The children injected varied in age from 2 months to $3\frac{1}{4}$ years, the average age being 20 months, while the controls ranged in age from $3\frac{1}{2}$ months to $3\frac{1}{2}$ years, with an average age of 11 months.

As to the effect of the serum, there was in many cases an immediate change in the appearance of the child. Children that looked septic, were apathetic, with anorexia and a pale blotchy complexion, in several cases after the injection, had a good color, were brighter, took the feedings better and seemed much improved, although the condition in the lung was usually unchanged or perhaps spreading.

Before going into the general effect of this treatment I would like to call attention to charts of several cases with marked results, to indicate that in some cases the serum seemed to be of real benefit.

Fig. 2.—Temperature curve in Case 1, showing effect of injection of antipneumococcus serum on second day.

Case 1 was a child that had appeared very sick, the temperature ranging from 103 to 105.8 F., and being 105.2 F. at the time of the injection (Fig. 2). The physical examination showed crepitant râles, increased voice and high-pitched breathing over the upper part of the right lower lobe and over the right middle and upper lobes. After the injection the temperature immediately dropped to 102 F. and then gradually to normal, reaching that point three days after the injection and remaining normal after the fourth day. This injection was made on the second day of the disease and on the following day the signs showed an involvement of the posterior portion of the right lung, while on the third

day after the injection and the fourth day of the disease the signs in the chest cleared up. This was fortunately the first injection case and made a very favorable impression on the people at the institution.

Another striking case was Case 6, in which the patient suddenly had a temperature of 104.1 F., with cough and cyanosis. On examination of the chest in the left subscapular region there was dullness, bronchial breathing, sharp subcrepitant râles, with harsh breathing and crepitant râles lower down, while on the right side there were sibilant râles. After injection the temperature dropped immediately to 99.6 F. (Fig. 3) and never rose, and the signs in the chest gradually cleared up. This seemed like a very wonderful result, but our control patient with no serum did exactly the same thing.

Fig. 3.—Temperature curve in Case 6. Injection of antipneumococcus serum on seventh day.

In Case 10 the child was injected on the fourth day after admission to the hospital, where it was brought on account of convulsions. At the time of injection it had bronchial breathing and crepitant râles over the right upper lobe and the temperature was 102.2 F. (Fig. 4). The temperature reached normal three days after injection. Some signs, however, persisted, but four days after the injection the chest showed only slight dullness at the right apex posteriorly and ten days later when the child was sent out of the hospital the chest was clear.

A very striking case was Case 11, in which the patient had run a steady temperature from 103 to 105 F. (Fig. 5) for four days before injection. At that time the temperature was 104 F., and over the right

lower lobe there was high-pitch respiration and fine râles, and pneumococci were obtained from a throat swab. After injection the temperature rapidly declined and reached normal in three days. In this case the leukocytosis, which was 15,000 at the time of injection, was the same on the following day, but on the second day was reduced to 8,800, while the polynuclear leukocytes changed from 41 per cent. at the time of the injection to 47 per cent.

These cases I have given simply to show that in some cases there was apparently a good reaction from the serum.

The improvement in the well-being of the children has been commented on by other observers and is not always followed by recovery.

Fig. 4.—Temperature curve in Case 10. Antipneumococcus and antistreptococcus serum on the fourth day.

The effect on the temperature in some cases was marked. In seven cases there was a reduction in temperature after injection, while in eight cases there was no evident effect.

The effect on the process in the lungs was interesting for, as I have said, in some cases in which there seemed to be an improvement in the general condition of the child, the lung condition either showed no improvement or spread. Where there was a marked reduction in temperature from the injection the lung signs did not spread materially and often cleared up quickly.

The effect on the leukocytosis was studied in eleven cases (see table), most of which were injections of combined pneumococcus and strepto-

coccus serum. These showed usually a reduction in the leukocytosis, although in one case the leukocytes increased from 10,000 to 18,000 with a reduction in the polynuclear leukocytes from 70 to 44 per cent. The average of the eleven cases was a reduction in leukocytes from 25,790 to 19,333, and a reduction of polynuclear leukocytes from 67 to 63 per cent. so that the average result is not very striking. A more striking result, but on too few cases to draw any conclusions, is found by examining the three cases in which the counts were made on the third day. These show an average reduction from 29,667 on the first day to 15,300 on the second day, and of 11,933 on the third day, while the polynuclear leukocytes averaged 51 per cent. on each of these days.

serum alone there were four recoveries and two deaths, while the controls showed five recoveries and one death. Of the nine patients injected with the pneumococcus and streptococcus serum five recovered and four died, while of the controls of these there were three recoveries and six deaths. Repeated injections in patients who had showed no reaction from the first injection were equally unsuccessful.

RESULT OF BLOOD EXAMINATION AT TIME OF INJECTION AND TWENTY-FOUR HOURS
LATER IN ELEVEN CASES

At Time of Injection		One Day Later	
Leukocytes	Percentage of Polynuclear Leukocytes	Leukocytes	Percentage of Polynuclear Leukocytes
58,000	84	18,400	64
17,800	75	11,000	69
24,400	42	21,760	79
14,000	75	14,000	74
15,000	41	15,500	47
26,000	86	17,400	48
34,000	85	36,000	95
10,500	70	18,000	44
16,000	27	12,000	40
40,000	73	21,000	70
28,000	76	27,600	71
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283,700	734	212,660	701
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*25,790	67	*19,333	63

*Average of the eleven cases.

In conclusion, I would say that the serum injections, while apparently affecting favorably the course of the disease in some cases, appears to have no result in others; that in most cases there appears to be a better reaction on the part of the child after injection than before. It was usually followed by some reduction in leukocytosis, and the percentage of the polynuclear leukocytes was also diminished. In these favorably influenced cases there was little spreading of the disease after injection, and in some a fairly rapid resolution.

The injected patients who lived had a much shorter average course than the controls, and the mortality of the injected cases was slightly less than that of the controls.

The pneumococcus serum presents a safe method of attempting to influence the course of pneumonia in children; the addition of anti-streptococcus serum seems to offer no advantage over the use of the pneumococcus serum alone.