

of the disease than is the case in New York. In this series the serum treatment of Types I. and II. infection was commenced, so far as we can ascertain, within 48 hours of the onset of the illness in 16 cases; within 72 hours in 7 cases; within 96 hours in 10 cases; within 120 hours in 6 cases; within 144 hours in 2 cases. Two of the Types I. and II. patients who died received serum within 48 hours of the onset and one within 72 hours.

BIBLIOGRAPHY.

- Blake, F. G.: Methods for the Determination of Pneumococcus Types, *Jour. Exper. Med.*, 1917, xxvi., 67.
- Bullowa, J. G. M., and Schuman, A. H.: A Rapid Method of Using the Sabin Slide Microscopic Test, *Amer. Jour. Pub. Health*, 1930, xx., 878.
- Cooper, G., Edwards, M., and Rosenstein, C.: Separation of Types among the Pneumococci hitherto called Group IV., *Jour. Exp. Med.*, 1929, xlix., 461.
- Dochez, A. R., and Avery, O. T.: Elaboration of Specific Soluble Substance by the Pneumococcus during Growth, *Jour. Exper. Med.*, 1917, xxvi., 477.
- Glynn, E. E., and Digby, L.: Bacteriological and Clinical Observations on Pneumonia and Empyemata, *Med. Res. Council Spec. Rep. Ser. No. 79*.
- Griffith, F.: Significance of Pneumococcal Types, *Jour. Hyg.*, 1928, xxvii., 113.
- Lister, F. S.: Specific Serological Reaction with Pneumococci from Different Sources, *Pub. South African Inst. Med. Res.*, 1913, No. 2.
- Sabin, A. B.: Stained Slide Microscopic Agglutination Test, *Amer. Jour. Pub. Health*, 1929, xix., 1148; *Proc. Soc. Exper. Biol. and Med.*, 1929, xxvi., 492; *Microscopic Agglutination Test in Pneumonia*, *Jour. Infect. Dis.*, 1930, xlv., 469.
- Whittle, C. H.: Identification of Pneumococci, *Jour. Hyg.*, 1928, xxvii., 200.
- Austin, J. H., and Cullen, G. E.: Hydrogen-Ion Concentration of the Blood, *Medicine*, 1925, iv., 275.
- Barach, A. L., and Woodwell, M. N.: Studies in Oxygen Therapy, *Arch. Int. Med.*, 1921, xxviii., 394.
- Binger, C. A. L., Hastings, A. B., and Neill, J. M.: Oedema Associated with Moderate Bicarbonate Administration during Convalescence from Pneumonia, *Arch. Int. Med.*, 1923, xxxi., 144.
- Cushny, A. R.: *Pharmacology and Therapeutics*, London, 1918.
- Greenwald, J.: Studies on Metabolism in Pneumonia, *Jour. Biol. Chem.*, 1930, lxxxv., 447.
- Haldane, J. S., Meakins, J. C., and Priestley, J. G.: Respiratory Response to Anoxæmia, *Jour. Physiol.*, 1919, lii., 402.
- Haldane, J. S.: *Respiration*, Yale University Press, 1922.
- Harrop, G. A.: Behaviour of the Blood towards Oxygen in Influenzal Infections, *Johns Hopkins Hosp. Bull.*, 1919, xxx., 10.
- Leyden, E. von, and Klemperer, G.: *Handbuch der Ernährungstherapie*, Leipzig, 1914.
- Meakins, J. C., and Davies, H. W.: *Respiratory Function in Disease*, Edinburgh, 1925.
- Meyer, H. H., and Gottlieb, R.: *Experimental Pharmacology*, London, 1926.
- Palmer, W. W.: Acidosis and Acid Excretion in Pneumonia, *Jour. Exper. Med.*, 1917, xxvi., 495.
- Peabody, F. W.: Oxygen Content of Blood in Lobar Pneumonia, *Jour. Exper. Med.*, 1913, xviii., 7.
- Stadie, W. C.: Oxygen of the Arterial and Venous Blood in Pneumonia and its Relation to Cyanosis, *Jour. Exper. Med.*, 1919, xxx., 215.
- Binger, C. A. L.: Anoxæmia in Pneumonia and its Relief by Oxygen Inhalation, *Jour. Clin. Invest.*, 1928, vi., 203; *Construction and Management of an Oxygen Chamber*, *Modern Hospital*, 1925, xxiv., 186.
- Binger, C. A. L., and Davis, J. S.: Relation of Anoxæmia to the Type of Breathing in Pneumonia, *Jour. Clin. Invest.*, 1928, vi., 171.
- Bullowa, J. G. M.: Serum Treatment and its Evaluation in Lobar Pneumonia, *Bull. N.Y. Acad. Med.*, 1929, v., 328; *Pneumococcus Pneumonias and their Control*, *Med. and Surg. Yearbook*, Physicians Hospital, 1929, i., 3.
- Bullowa, J. G. M., and Jacobi, M.: Fatal Human Anaphylactic Shock, *Arch. Int. Med.*, 1930, xlv., 306.
- Bullowa, J. G. M., Rosenbluth, M. B., Park, W. H., and Cooper, G.: Use of Anti-pneumococcal Refined Serum in Pneumonia, *Jour. Amer. Med. Assoc.*, 1928, xc., 1349.
- Beil, R. L.: The Prevention and Treatment of Pneumonia, *N.Y. State Jour. Med.*, 1930, xxx., 210.
- Bole, R.: Serum Treatment in Type I. Lobar Pneumonia, *Jour. Amer. Med. Assoc.*, 1929, xciii., 741; *Acute Pulmonary Infections*, De Lamar Lectures, Baltimore, 1928.
- Davis, J. S.: Effects of Morphine on Respiration in Pneumonia, *Jour. Clin. Invest.*, 1928, vi., 187.
- Felton, L. D.: A Study of the Isolation and Concentration of Specific Antibodies of Anti-pneumococcus Sera, *Boston Med. and Surg. Jour.*, 1924, exc., 819; 1925-28, *Jour. Infect. Dis.* xxxvii., 199 and 309; xlii., 248, 256; xliii., 543; *Jour. Amer. Med. Assoc.*, 1930, xciv., 1893.
- Ferguson, F. R., and Lovell, R.: An Investigation of Primary Lobar Pneumonia, *Manchester*, 1925-27; *Quart. Jour. Med.*, 1928, xxii., 73.
- Furchison, C.: *The Continued Fevers*, London, 1884.
- Park, W. H., Bullowa, J. G. M., and Rosenbluth, M. B.: Treatment of Lobar Pneumonia with Refined Specific Antibacterial Serum, *Jour. Amer. Med. Assoc.*, 1928, xc., 1503. Rockefeller Institute Monograph, 1917, No. 7, *Acute Lobar Pneumonia, Its Prevention and Serum Treatment*.
- Stadie, W. C.: Construction of an Oxygen Chamber. The Treatment of Anoxæmia in Pneumonia, *Jour. Exper. Med.*, 1922, xxxv., 323.

A REPORT ON LOBAR PNEUMONIA : TREATMENT BY CONCENTRATED ANTISERUM

BY THE PHYSICIANS TO THE ROYAL
INFIRMARY, EDINBURGH.

In the latter part of 1929 a quantity of concentrated antipneumococcus serum was made available by the Medical Research Council for clinical trial in the Royal Infirmary.

In order to show that a remedy is of benefit in the treatment of lobar pneumonia, it would be necessary to demonstrate that it is capable of (a) reducing the case-mortality; (b) modifying the course of the disease; or (c) lessening the severity of the illness. For various reasons the matter is not as simple as it would appear at first sight. Effects on the case-mortality present special difficulty, since the death-rate in pneumonia may vary within wide limits not only in different places, but also in the same institution from year to year under apparently identical conditions. Deductions from small series of figures are always unsafe, and especially in such a subject as pneumonia, where the course of the disease is influenced by so many factors, such as the age of the patient, his previous health, habits, &c. The severity of the illness cannot be readily measured,¹ and experience shows that even those patients apparently extremely ill may recover without specific treatment.

Scheme of the Investigation.

At the outset of the investigation it was decided to give serum treatment without distinction to every alternate case of lobar pneumonia admitted to each of the eight medical charges in the Royal Infirmary. The remaining cases were to be treated in the usual way and were to serve as controls. This plan was carried out for about two and a half months and the cases belonging to this period are designated by the letter B. (before) in Table I. Later, owing to the small quantity of serum available, instructions were issued to choose the more seriously ill patients for treatment with the antiserum. The later cases are indicated by the letter A. (after). As has been pointed out, the subjects in the earlier period (B.) were quite unselected, so the serum and control cases are strictly comparable. In the second period the serum groups contain a larger proportion of the more seriously ill. The non-serum controls in this group (A.) include the less severe cases. Certain patients who were practically moribund when admitted to hospital were not given serum and are shown primarily amongst the controls.

In order that the serum cases and the controls should satisfy statistical requirements, the two groups should be of approximately equal size and as nearly similar as possible in such matters as the age of the patients (see Table III.), their physical state, the day on which they were admitted to hospital (Table IV.), &c. Owing to the selection of more severe cases for serum treatment during the second period, the non-serum cases in this group are not strictly comparable. The results obtained in the two periods (B. and A.) are so similar, however, that it would seem justifiable to group them together for purposes of analysis. This, of course, would tend to operate to the disadvantage of the serum results.

The concentrated antipneumococcal serum employed was that of Felton prepared by Messrs. Lederle, of New York. It was active only against organisms of Types I. and II., and contained 10,000 units in

TABLE I.

Group.	Day of crisis.								Lysis or over 9.	Deaths.	Age at death and remarks.	Totals.
	3	4	5	6	7	8	9					
S. I. { B.	—	1	4 (15)	—	1	—	1	1	—	—	—	8 } 12 4 } 12 } 17 } 29
A.	—	1	2	—	—	—	—	—	—	—	—	
C. I. { B.	—	—	2	2 (15)	1	2	—	1	4	27, 61, D. 62, 64, A. 60.	—	5 } 10 } 17 } 41
A.	1 (11)	—	—	1	1 (13)	1	—	—	1	—	—	
S. II. { B.	1	—	1	—	1	1	2	2	4	36, 38, A. 49, 52, K. 21, P.	—	12 } 17 } 41 5 } 10 } 24 } 14 }
C. II. { B.	—	1	—	1	1	—	—	2 (63)	6	34, N. 52, M. 57, M. 60, M. 62, M. 76.	—	
A.	—	1 (11)	1	2	1	2	1	2	4	24, B. 51, 54, U. 64, F.	—	
S. III.	—	—	1 (60)	—	1 (60)	—	—	—	—	—	—	2 } 2
C. III.	—	—	—	—	—	—	—	—	—	—	—	—
S. IV.	—	—	2	1	2	—	1	—	1	—	—	7 } 17
C. IV.	—	1 (14)	1	—	—	—	—	5 (15)	4	19, St. 60, 64, L.	—	10 }
Untyped { S.	—	—	1	1	3	2	1	3	1	17, M.	—	2 } 17
C.	—	—	1	1	3	2	1	3	4	50, M. 54, M. 68, M. 76, M.	—	15 }
<i>Summary of Types I. and II.</i>												
S. I. + S. II.	1	3	8	1	3	2	3	3	5	—	—	29
C. I. + C. II.	1 (11)	1 (11)	3	6	4	5	1	5	15	—	—	41

Group.—S.=Serum; C.=Control. B.=before; A.=after. Figures in italics represent ages.
 Remarks.—A.=alcoholic; D.=chronic bronchitis and diarrhoea. K.=meningitis and pericarditis; P.=pericarditis and extension; N.=nephritis; M.=died within 24 hours of admission; two were unconscious when admitted; B.=bronchitis and asthma; U.=ulcerative endocarditis; F.=auricular fibrillation; St.=mitral stenosis; L.=leukæmia.

each dose (5 c.cm.). As it has been shown that the earlier the serum can be administered the more favourable is the result likely to be, it was decided that the initial dose of serum should be given to the patients as soon as the diagnosis had been established and without waiting till typing of the organism had been completed. This resulted in a number of pneumonias of Types III. and IV. receiving one or more doses of serum before information regarding the type was available. This waste was more than outweighed by the advantage of being able to begin treatment earlier in the other cases. Table II. gives the number of doses received by patients in the different classes. Before serum was administered to a patient inquiry was made as to whether any

TABLE II.

	Number of doses of serum given.							
	1	2	3	4	5	6	10	12
SS. I. + } non-fatal	4	9	3	6	—	—	1	1
S. II. } fatal	—	2	2	—	—	1	—	—
S. III.	1	1	—	—	—	—	—	—
S. IV.	2	3	—	1	1	—	—	—
Untyped	—	2	—	—	—	—	—	—

serum had previously been given, and the presence of undue sensitivity was sought by placing a drop of normal horse serum in the conjunctival sac. During the period covered by the inquiry 106 cases of lobar pneumonia came under review. For various reasons (e.g., absence of sputum) typing was not carried out in 17 of the subjects. The remaining 89 cases were distributed as follows: Type I., 29; Type II., 41; Type III., 2; and Type IV., 17. The serological type of the pneumococci present in the sputum was determined by the usual macroscopic agglutinate method after mouse inoculation. Details of the technique and an account of the type incidence in Edinburgh during the years 1929-30 are being published by J. M. Alston and D. Stewart.²

LUNG PUNCTURE.

In certain cases in this series—most frequently in those admitted at an early stage in their illness—no

sputum could be obtained for several days and occasionally not until actually after the crisis. By puncture of the lung substance over the affected lobe it was found that in the majority of such cases a pure

TABLE III.

	Age of pneumonia cases types I. and II.							Totals.
	10-19	20-29	30-39	40-49	50-59	60-69	70+	
S. I. + } non-fatal	4	5	9	2	4	—	—	24
S. II. } fatal	—	1	2	1	1	—	—	5
C. I. + } non-fatal	7	7	4	4	3	1	—	26
C. II. } fatal	—	2	1	—	4	7	1	15

culture of the pneumococcus could be obtained. The technique of this procedure and the results obtained have already been recorded.³

BLOOD CULTURE.

In 51 cases blood culture was performed. Ten cubic centimetres of whole blood was removed from the arm by venepuncture and was immediately transferred to flasks containing 50 c.cm. of phosphate broth (pH 7.6). The flasks were then incubated for 72 hours, being examined at daily intervals. A

TABLE IV.

	Day of disease on admission to hospital.								Totals.	
	1	2	3	4	5	6	7	8		Unc.
S. I. + } non-fatal	1	4	7	6	3	2	—	—	1	24
S. II. } fatal	—	—	2	—	2	—	—	1	—	5
C. I. + } non-fatal	—	4	6	5	6	4	1	—	—	26
C. II. } fatal	—	—	2	3	3	2	1	1	3	15

Unc. = Uncertain.

positive result was recorded in 6 of the 51 cases, in each case a pure culture of pneumococcus being obtained corresponding in type to that found in the sputum. No growth of pneumococcus was noted in 45 cases.

The majority of the blood cultures were done in cases that were admitted early in the investigation,

and it is interesting to note that death occurred in all cases where a positive culture was obtained; while no patient who survived showed a positive blood culture.

Analysis of Results.

CASE MORTALITY.

A summary of the findings is given in Table I. The total figures are so small that it hardly seems justifiable to express the results as percentages. The distribution of the deaths, however, is striking. It will be observed that amongst the Type I. cases none of those who received serum died, while there were five deaths in the control group. Similarly amongst the Type II. pneumonias there were considerably fewer deaths in those treated with serum. At first sight this would appear to be convincing evidence in favour of the serum, but closer scrutiny modifies this view. It is well known that the death-rate in pneumonia increases with age, rising from about 5 per cent. under 20 years, to about 100 per cent. over age 70.⁴ The serum cases and the controls are not closely similar in matter of age, since only the latter group contains subjects of 60 years and over (Table III.). In the first two groups all the patients of this age died with the exception of one. It will be noticed that though two cases of 60 years of age affected with pneumococcus of Type III. survived their illness, all the others of like age in Group IV. and in the untyped class ended fatally. In addition, it will be observed that several of the patients who did not receive serum died within a few hours of reaching hospital, two were moribund on admission, and others were extremely ill and may have been adversely affected by being moved to the infirmary late in the course of the disease. When consideration is given to these facts the smaller proportion of deaths amongst the serum cases would appear of less importance.

EFFECT OF SERUM TREATMENT ON THE COURSE OF THE DISEASE.

Duration of the fever.—As is well recognised, it is often difficult to ascertain exactly the day upon which the pneumonia commenced. A large proportion of the subjects in this investigation had suffered from some

TABLE V.—*Fall of Temperature in Relation to First Dose of Serum.*

Interval to crisis.	Day of disease on which serum given.							Totals.
	1	2	3	4	5	6	Unc.	
1 day and under .	—	1	2	3	3	—	—	9
2 and 3 days . .	—	1	2	2	—	3	—	8
4 days and over . .	1	1	2	1	1	—	1	7

“cold” or catarrhal condition for a week to a month before the onset of symptoms which could be definitely recognised as pneumonia. The earliest signs of the major disease may either be those of an abrupt febrile invasion, or local symptoms referable to the chest. There is thus often an element of doubt as to the exact duration of the illness, but every effort has been made to minimise this. The day of the disease on which the patients of Groups I. and II. came under treatment is shown in Table V. It will be observed that the majority of the patients were not admitted to hospital until after the third day of their illness.

A great deal of information regarding the duration

of the febrile period in this disease is available as a standard for comparison. Many analyses have been published showing the proportion of cases which end by crisis on different days of the disease.⁴ From these it is evident that, while in the majority of pneumonias the temperature begins to fall from the sixth to the eighth day, there are many which run a shorter course. The accompanying chart compiled from twelve series of records shows the percentage distribution of the crisis in 7442 cases together with the limits of the figures given by the individual observers (shaded area). Taking the records of all the pneumonias of Types I. and II. together and omitting the fatal cases, it is found that 24 were treated with serum and 26 are available as controls. The average age of the non-fatal serum cases is 33.8 and that of the surviving controls 32.0 years, so that the two groups are fairly comparable. When the duration of the illness is examined, there is at once apparent a very marked difference between the two groups, especially in the case of Type I. No less than 50 per cent. of the serum cases ended critically on or before the fifth day, while the corresponding figure for the controls is only 19.2 per cent. (The value for the 7442 cases mentioned above is 26.0 per cent.) When it is considered that the later serum cases include some of the more severely ill patients, and that eight of the patients did not commence treatment until the fifth day or later, the result is even more striking. Experience has shown that abortive forms of the disease occur more frequently amongst young individuals, cases of three or four days' duration being not uncommon amongst children. In order to give weight to this point, the ages of all patients under 15 years of age are shown in italics in Table I. It is probable that the figures for the control group gain advantage from the inclusion of two patients aged 11 who had a crisis on the third and the fourth day respectively. The accompanying chart shows the percentage distributions of the serum cases and the controls according to day of crisis. Each group includes a single third-day crisis—a proportion to be expected from the published tables. The values for the fourth and especially for the fifth day in the case of the serum group are greatly in excess of expectation, while the later values are necessarily low. In the case of the control series, the figures lie fairly close to the average values within the limits expected. Of the 50 non-fatal cases of Types I. and II. it is well to notice that 18 who received serum and 15 controls were admitted on or before the fourth day, 3 serum cases and 6 controls on the fifth day, and 3 serum cases and 5 controls after the fifth day (Table IV.). Though the lateness in beginning specific treatment in certain cases would affect the total number of early crises, the two groups are fairly similar as regards time of admission to hospital. From the evidence submitted, it would seem a fair deduction that the administration of serum has definitely shortened the febrile period of the disease in a considerable number of cases. Table IV. shows the number of days which elapsed from the time of giving the first dose of serum to the onset of the crisis. No less than 9 of the cases who were admitted up to the fifth day of the illness had a definite crisis within twenty-four hours (second day, 1 case; third day, 2 cases; fourth and fifth day, 3 each). On the other hand, early administration of the serum is not necessarily followed by abortion of the disease. For example, the patient (Case 2) who commenced treatment within 24 hours of the onset of his illness and received 12 doses of serum did not have his crisis until the sixth day.

EFFECT OF SERUM ON THE SEVERITY OF THE ILLNESS.

Height of the fever.—Thermal reactions following the administration of serum have been reported.⁵ These have not been seen in this series of cases. In a number of instances the giving of serum has been followed by a slight temporary fall of temperature of one or two degrees, but variations of this magnitude are not uncommon during the course of pneumonia. One or two cases appear to have a pseudo-crisis, but where

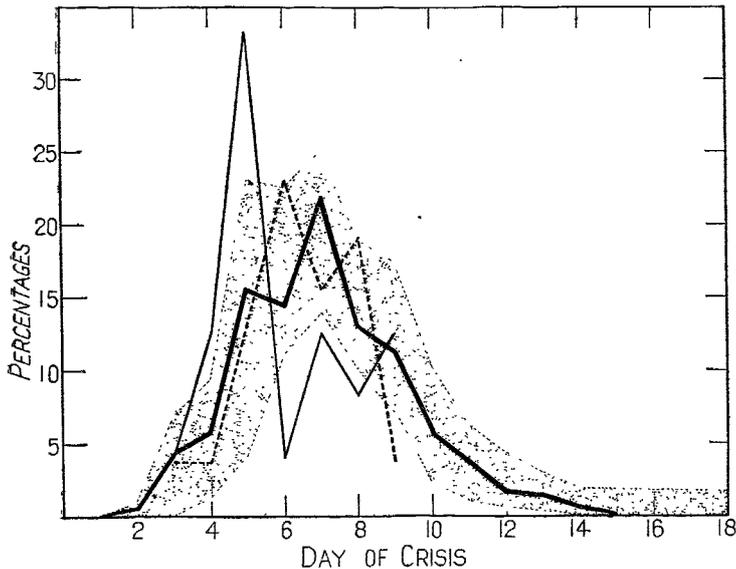


Chart shows the relative percentage distribution of the day of crisis in 7442 pneumonias which ended by crisis. The average values are shown by the heavy black line. The extreme limits given in the 12 different series from which the cases were drawn are shown by the shaded area. The control cases in this series (interrupted line) fall within expected limits. Serum cases (fine line) show a large percentage of crisis occurring on the fourth and fifth days of the disease.

a fall to normal occurred, the temperature usually remained down. In certain cases the impression was gathered that the serum, although it did not make the patient afebrile, kept the temperature at a lower level than is usual in pneumonia.⁵ Except where a definite crisis occurred the pulse-rate and respirations were not usually influenced by the giving of serum. The temperature-reducing effects of the serum appear to be more marked in cases of Type I. than in those of Type II.

Leucocytosis.—In a number of cases observations in the leucocyte count were made daily. The usual reaction appeared to be a fall in the number of leucocytes, roughly in proportion to the change in temperature; an increase in white cells was only found in one patient

Blood pressure.—No striking change in systolic readings was observed.

There is no doubt in the minds of those who were watching the patients that the antiserum was of considerable benefit in certain cases even although the course of the illness was not shortened. Many of the patients appeared to have improved rapidly, becoming more comfortable and less distressed shortly after the serum had been given. (See Case 2.) Clinical histories of cases illustrating some of the more striking results are given below.

Illustrative Cases.

CASE 1.—Youth aged 18. Gave a history of "cold, cough," "not feeling well," for seven days before admission. Continued at work till two days before admission. Pain in left side of chest, cough worse, vomiting, headache two days before admission; and spitting of blood one day before admission. Examination: Consolidation of the left lower lobe; well nourished; development good; acutely ill but no marked distress; temperature 102°, pulse 120, respiration

20–30. Blood culture—negative (twice). Sputum and lung puncture gave culture of pneumococcus I. Progress: Given one dose of serum on admission, at 8.45 P.M., on the third day of the disease. Conjunctival test negative. Following the injection the patient had a serum reaction like asthma, with urgent dyspnoea, cyanosis, and pain in the chest. One cubic centimetre of adrenalin eased the symptoms immediately. This injection was followed by a fall in temperature of 1° with consequent rise of 1.6° after six hours. Eighteen hours after admission there was sudden rise of temperature to 104.8° and he was given a second dose of serum. No anaphylactic phenomena followed this injection. After this the temperature came down steadily to normal, within 24 hours of admission and six hours after the second dose of serum. The fall in temperature was accompanied by all the typical signs of crisis. A very definite change was noted within a few hours of giving the second dose, not only in the temperature but also in the clinical condition of the patient. The ward sister, especially who has had considerable experience in nursing pneumonia patients, was impressed by the immediate improvement.

A similar asthmatic attack occurred in one other patient who had previously suffered much from bronchitis. He had never had asthma, and the preliminary eye test was negative.

CASE 2.—A man, aged 28, had had pain in left side of chest for one day before admission with slight cough, and shivering. He was admitted on the second day of illness. Examination: Consolidation of the left lower lobe. Patient extremely ill; collapsed; cyanosis marked. Temperature 101–103°; pulse 130–140; respiration 40–50. Blood culture negative (three times). Sputum, pneumococcus II. Progress: This patient was admitted within 24 hours of the onset of the illness, in a very critical condition. The prognosis was noted at the time as "almost hopeless." The white blood count was low, 8000. In all he received 12 doses of serum, injections being repeated every six or eight hours for five days. During that time "life hung in the balance." By the sixth day, however, definite signs of improvement were noticed, and by the seventh day it was obvious that the patient was going to live, all signs of crisis being present.

It is interesting to note that there was a gradual fall, both in pulse-rate and in respiration-rate, from the first dose of serum, although the patient did not seem to be making much headway. The ward sister, who also has had large experience in the nursing of pneumonia patients, attributed the recovery to serum. After the third and fourth doses of serum both doctors and nurses clearly noticed signs of improvement—less restlessness leading to natural sleep, less apathy, more coherent speech, sweating, and increased quantity of urine.

CASE 3.—A man, aged 39, had pain in the left side, with cough and insomnia for three to four days before admission. Examination: Consolidation of the left lower lobe. Blood culture negative. Sputum, pneumococcus I. White blood count 9000. Temperature 103°; pulse 100; respirations 40–50. Progress: This patient was chosen as a serum case because of the severity of his condition. Admitted on the fourth day, he was collapsed, cyanosed, and ashen-grey in colour—in short, extremely ill. He received one dose of serum two hours after admission, and within four hours his temperature had fallen to 99.5°. In another eight hours it had fallen to 97° F. A second dose was given 18 hours after admission, but by this time—that is, before the end of the fourth day—the crisis had occurred.

CASE 4.—Boy, aged 16, was feverish, with vomiting six days before admission; on the next day he had cough and pain and on the third day rusty sputum. Admitted on fifth day. Examination: Consolidation of right lower lobe. Well-nourished adolescent; no marked distress but severely ill. Temperature 103°; pulse 120; respirations 30. Blood culture negative; sputum, pneumococcus II. Progress: Admitted on the fifth day, one dose of serum was given at once. This was followed by a fall in temperature of 2°. A second dose of serum four hours afterwards was followed by relief, and by a fall of temperature to normal. A slight rise of temperature to 101° occurred eight hours afterwards, and a complete crisis took place 12 hours later. The recovery was uneventful.

CASE 5.—Man aged 30. Pain and cough for two days before admission; vomiting and rusty sputum for one day. The patient was moderately alcoholic. Examination: Consolidation of the left lower lobe; nutrition and development good; cyanosis; marked dyspnoea. Blood culture negative (twice), sputum, pneumococcus II. Progress: Reaching hospital on the third day of his illness, the patient was given a dose of serum, followed by further three doses at four-hourly intervals. Crisis occurred within 24 hours, with very marked improvement in general condition.

CASE 6.—Man aged 45. Indefinite "flu" 14 days before admission. Severe pain and vomiting three days before

admission, and headache; weakness two days. Examination: Consolidation of the right lower lobe; thin; nutrition poor; marked cyanosis; very marked distress; painful cough; rusty sputum; drowsiness marked. Temperature 104°; pulse 130; respirations 30-40. Blood culture negative (twice). Sputum, pneumococcus II. Progress: When admitted to hospital on the third day of the disease patient was in a collapsed condition. Three injections of serum were given within 24 hours followed by very marked improvement, and crisis occurred by the fifth day of the illness.

Summary.

The evidence submitted suggests that the administration of Felton's concentrated antiserum is of distinct benefit in the treatment of lobar pneumonia due to organisms of Types I. and II. Its action appears to be greater in the case of Type I. pneumonias. The records show that there were fewer deaths amongst the cases who received serum. Serum treatment seems to lessen the severity of the disease and undoubtedly shortens the febrile period in a proportion of cases. Many cases appeared to become less ill and more comfortable as a result of the injections. Anaphylactic phenomena were observed in two patients after the first dose of serum, although in both cases the preliminary eye test was negative. It is probable that the beneficial results would have been more striking had it been possible to commence treatment at an earlier stage in the disease, and if the supply of serum had permitted more frequent injections.

The writers wish to acknowledge their indebtedness to Dr. J. M. Alston and Dr. Donald Stewart and to Prof. Stanley Davidson for help in carrying out the investigations.

REFERENCES.

1. Bullowa, J. G. M.: Jour. Amer. Med. Assoc., 1928, xc., 1354.
2. Alston, J. M., and Stewart, D.: In the press.
3. Stewart, D.: THE LANCET, Sept. 6th, 1930, p. 520.
4. Lyon, D. M., and Lamb, W. L.: Edin. Med. Jour., 1929, xxxvi., 79.
5. Cecil, R. L., and Sutliff, W. D.: Jour. Amer. Med. Assoc., 1929, xci., 2035.

THE INFECTIVE FACTOR IN THE CAUSATION OF ACUTE MYELOGENOUS LEUKÆMIA.

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THE following observations on three cases of acute myelogenous leukæmia lend support to the opinion of Dr. F. J. Poynton and Dr. A. A. Moncrieff¹ that the tissues, and the blood-forming organs in particular, are capable of reacting to infective processes in a great variety of ways and in varying degrees. The main features of these cases are an intensely severe sepsis in the mouth, associated with a marked and increasing secondary anæmia, and a white count in the early stages showing a leucopenia affecting the granular cells, followed by the appearance of a leukæmic blood picture of myelogenous type.

CASE 1, a male aged 19, was admitted to hospital on Nov. 12th, 1928, with a history of increasing weakness, giddiness, and headaches, following the lancing of an "abscess in the mouth" two months previously. A severe epistaxis necessitated his admission for blood transfusion. There was nothing of importance in his previous history; he was an average, healthy male.

He was markedly pale, with the right side of his face (around the mouth) puffy and swollen; he had difficulty in opening the mouth. There was a high temperature of swinging type (103°-100°), a pulse-rate of 120, and a respiration-rate of 30. There was a severe ulcerative condition of the mouth; the gums were swollen and cedematous, and oozed blood-stained muco-pus. The

cervical glands were enlarged and tender. The heart was dilated, and an apical systolic murmur was present. The spleen and liver were not palpable. There were a few scattered petechiæ over the trunk.

Blood Counts.

(1) Red cells. (2) White cells. (3) Hæmoglobin. (4) Colour-index. (5) Polymorphonuclear cells. (6) Lymphocytes. (7) Large mononuclear cells. (8) Myelocytes. (9) Leucoblasts.

	Nov. 12th.	Dec. 7th.	Dec. 17th.	Dec. 24th.	Dec. 31st.
(1)	738,000	2,172,000	1,824,000	2,016,000	896,000
(2)	800	27,200	66,400	24,000	10,600
(3)	15%	36%	28%	30%	18%
(4)	1.0	0.85	0.8	0.74	1.0
(5)	18%	18%	10.5%	17%	11%
(6)	82%	17%	3.5%	7%	7%
(7)	—	0.5%	—	—	—
(8)	—	35.5%	26.5%	18.5%	13%
(9)	—	29.0%	59.5%	57.5%	69%

Anisocytosis and poikilocytosis were present in all counts. Normoblasts were seen in the later counts.

Pathological Tests.—A culture from the teeth gave hæmolytic streptococci, but blood cultures were negative. A gastric test-meal showed complete achlorhydria. The van den Bergh reaction was within normal limits.

The patient had several blood transfusions, local dental and oral treatment, and an autogenous vaccine. The spleen became palpable about the beginning of December. His general condition improved considerably until towards the end of December. He died on Jan. 1st, 1929.

Necropsy.—The body was emaciated. There were petechial hæmorrhages scattered over the trunk and upper limbs. The lungs showed early diffuse broncho-pneumonia. The heart was dilated, flabby, and pale. The liver (5 lb. 2 oz.) was large, fatty, and a tawny-red colour. Free iron was present. The spleen (1 lb. 1 oz.) was large, soft, friable, and purple. The swollen pulp obscured the trabeculæ. The marrow of the sternum was a muddy grey colour; that of the tibia was reddish-grey.

Microscopical Appearances.—The spleen and the marrow from the long bones showed extensive myeloid hyperplasia. Many normoblasts were present in the marrow. Section of the liver showed severe fatty change around the portal radicles. Collections of immature myeloid cells were numerous in the portal spaces.

CASE 2, a female aged 28, was admitted to hospital on March 1st, 1929, with a four months' history of increasing lassitude and giddiness. Her teeth had been bad for some time, but her doctor told her that nothing could be done till she was stronger. A fortnight before admission she developed an acute feverish illness, which was associated with a sore-throat and swollen face.

Her appearance bore a striking resemblance to that of the previous case. The temperature was 103° and swinging in type, the pulse-rate 140, and the respiration-rate 30. Pallor was marked, and her face was so swollen around the mouth that the latter could only be opened with difficulty. There was noticeable fetor of the breath. The gums were swollen and cedematous and almost completely obscured the teeth. The discharge from the gums was serous rather than purulent. Severe stomatitis was present. The cervical glands were enlarged and tender. The heart was not noticeably enlarged; the sounds were feeble and tic-tac in character. Bronchitis was present. The spleen was palpable one inch below the costal margin and was rather soft.

Blood Counts.

	March 1st.	March 22nd.
Red cells	1,408,000	884,000
White cells	5,200	19,800
Hæmoglobin	32%	19%
Colour-index	1.1	1.12
Polymorphonuclear cells	54%	57%
Lymphocytes	43%	18.5%
Large mononuclear cells	3%	0.5%
Myelocytes	—	4%
Leucoblasts	—	20%

Anisocytosis and poikilocytosis were present in both counts. There were 140 normoblasts per c.mm. in the first count.

Pathological Findings.—A culture from the teeth yielded hæmolytic streptococci, but the blood culture was negative, the van den Bergh reaction normal.

In spite of rigorous local treatment and repeated mercuriochrome injections intravenously, the patient went downhill

¹ THE LANCET, 1930, ii., 787.