women, a total of 1,413, or 27.5 per cent; between the ages of 31 and 40, 464 men and 233 women, a total of 697, or 13.6 per cent; between the ages of 41 and 50, 206 men and 117 women, a total of 323, or 6.4 per cent; between the ages of 51 and 60, 100 men and 81 women, a total of 181, or 3.5 per cent; between the ages of 61 and 70, 49 men and 30 women, a total of 79, or 1.5 per cent; between the ages of 71 and 80, 3 men and 1 woman, a total of 4, or 0.08 per cent.

The greatest number of cases of appendicitis occurs between the years of 11 and 20, when the percentage of mortality is next to the lowest of the whole group. The smallest number occurs between 61 and 70. In every decade the males outnumber the females considerably, but they seem to have more resistance to the disease.

2008 Walnut Street.

TYPE I LOBAR PNEUMONIA TREATED WITH CONCENTRATED PNEUMOCOCCIC ANTIBODY (FELTON)

THE CLINICAL COURSE *

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A primary consideration in evaluating a specific therapeutic agent for the treatment of lobar pneumonia is the determination of its effectiveness in saving life. A large amount of data has been accumulated by investigators who sought to determine the effect of Felton's concentrated pneumococcic antibody on the mortality from the disease. Table 1, which contains the fatality rates from type I lobar pneumonia obtained in controlled clinical therapeutic trials in New York and Boston, shows that this antibody has a consistently beneficial effect. It is noteworthy that, as with other immune specific measures, the best results are obtained following treatment early in the disease.

Since the individual physician often bases his use of a therapeutic measure on his own experience and that of his friends, the statistical method, as it is used in large hospitals, is for him of little value. This is particularly true in a disease such as type I lobar pneumonia, of which but relatively few cases are seen by him during the course of the year. The effect of therapy on the clinical course of the disease is the practitioner's best available method for gaging the value of a method of treatment. Thus, the nature and degree of the symptomatic effects of a specific antiserum are of great importance and, while they are mentioned by the observers quoted in table 1, it seemed worth while to treat a properly controlled group of patients with type I lobar pneumonia with specific antibody, particular stress being laid on the clinical effects of treatment.

At the Boston City Hospital [1] during the period from Nov. 15, 1929, to June 30, 1930, essentially all patients having, or suspected of having, lobar pneumonia were examined clinically and bacteriologically. Whenever a determination of type I pneumococcus was made, that case was entered as one of the series to be studied. Each alternate patient in this series received Felton's concentrated pneumococcic antibody. Twenty-eight of a group of fifty-nine patients with type I lobar pneumonia were thus given concentrated antibody administered according to a plan calculated to secure the maximum clinical effect, and all fifty-nine patients were carefully observed with the question of symptomatic improvement in mind.

METHODS

In the great majority of instances the type of pneumococcus was ascertained within six hours of the time sputum was first obtained. The Sabin [2] stained slide agglutination reaction with peritoneal exudate withdrawn by capillary pipet from the live mouse was used for the rapid determination of the pneumococcus type. In addition, sputum from each patient was examined one or more times by the usual eighteen hour mouse method. Blood cultures were made as a routine on admission and at intervals throughout the febrile course of the disease. When sputum was difficult to obtain, a sterile cotton throat swab was passed over the patient's posterior pharyngeal wall and washed off in 2 or 3 cc. of sterile broth medium, which was, in turn, treated as if it were sputum. The direct precipitation test, the clear urine being used against the usual typing serums, also gave a rapid result in a number of instances.[3]

Concentrated bivalent antibody, potent in mouse protection tests against pneumococcus types I and II, was used for treatment. Part of the serum was concentrated by Dr. L. D. Felton [4] in the laboratories of the Department of Preventive Medicine and Hygiene of the Harvard University Medical School.[5] The larger part of the serum was concentrated in the Anti-toxin and Vaccine Laboratory of the Massachusetts Department of Public Health [6] by Felton's method, and a few preparations were made in the same laboratory by Goodner's [7] method. The potency of the concentrates, as measured by the method of Felton,[8] ranged

TABLE 1.—*Mortality of Type I Lobar Pneumonia Treated With Concentrated Antibody (Felton) Compared With the Mortality of Simultaneous Control Series Without Specific Therapy*

	Specifically Treated			Not Specifically Treated		
	No. of Cases	Deaths No.	Deaths %	No. of Cases	Deaths No.	Deaths %
Cecil and Plummer: J. A. M. A. **95**: 1547 (Nov. 22) 1930	239	48	20.1	234	73	31.2
Cases of less than three days' duration	103	12	11.7	97	26	26.8
Park, Bullowa and Rosenbluth: J. A. M. A. **91**: 1503 (Nov. 17) 1928	58	13	22.0	54	19	35.0
Cases of less than three days' duration	29	6	21.0	28	10	36.0
Finland: New England J. Med. **202**: 1244 (June 26) 1930	80	17	21.3	70	22	31.4
Cases of less than three days' duration	42	4	9.5	16	6	37.5

* From the Thorndike Memorial Laboratory, Second and Fourth medical services (Harvard) of the Boston City Hospital and the Department of Medicine of the Harvard University Medical School.

* Acknowledgment is made of the assistance rendered by J. Kelley, M.D., and J. M. Bethea, M.D., who were, successively, Charles Follen Folsom Teaching Fellow in Hygiene of the Department of Preventive Medicine and Hygiene of Harvard University Medical School; by H. Stanford, student assistant, and by Mrs. Trousdale, technical assistant.

1. The staffs of the four medical services cooperated heartily in conducting the general care of the patients here reported.

2. Sabin, A. B.: The "Stained Slide" Microscopic Agglutination Test: Application to (1) Rapid Typing of Pneumococci; (2) Determination of Antibody, Proc. Soc. Exper. Biol. & Med. **26**: 492-494 (March) 1929.

3. Monovalent antipneumococcic serum for diagnostic purposes was supplied by Dr. W. H. Park.

4. Felton, L. D.: Concentration of Pneumococcus Antibody, J. Infect. Dis. **43**: 543-553 (Dec.) 1928.

5. Supplied through the courtesy of Dr. M. J. Rosenau and the Influenza Commission of the Metropolitan Life Insurance Company, which also rendered additional financial assistance.

6. Supplied through the courtesy of Dr. Benjamin White.

7. Goodner, Kenneth: Experiments on the Concentration of Antipneumococcic and Antimeningococcic Horse Sera, J. Immunol. **19**: 473-484 (Nov.) 1930.

8. Felton, L. D.: The Concentration of Antipneumococcus Serum, J. A. M. R. **94**: 1893-1896 (June 14) 1930.

from 2,000 units to 6,000 units per cubic centimeter against type I, and from 2,000 to 3,000 units per cubic centimeter against type II.

The effective dosage of Felton's concentrated antibody has been stated by various authors. Cecil and Sutliff [9] recommend 100,000 units during the first twenty-four hours of treatment. Park [10] recommends from 50,000 to 100,000 units during the first twenty-four hours of treatment. With this as a foundation, a procedure was used that gave promise of securing the maximum clinical effect. Since it has been commonly observed that treatment with specific serums in general and with antipneumococcic serum in particular is more effective early in the course of the infection in man, it was thought that the quantitative relationships observed by Goodner [11] in the treatment of pneumococcic skin infection in the rabbit might be applicable to the treatment of human lobar pneumonia.

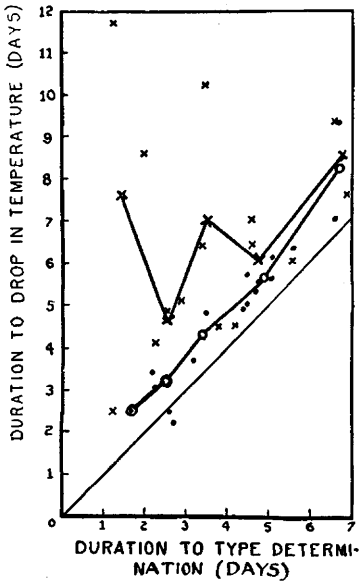

Chart 1.—The duration of type I lobar pneumonia as measured by the number of days before the occurrence of a marked and sustained drop in temperature to or nearly to normal. This and the following charts show on the left the duration of the disease in days and along the base line the number of days after the onset of the disease until the pneumococcus type was determined. The curves join points which represent the average of the duration of the acute disease in patients grouped according to the interval from the onset until the pneumococcus type was determined. The diagonal line beginning at O divides the portion of the disease before the determination of the pneumococcus type (below the line) from the portion of the disease after the determination of the pneumococcus type (above the line). Specific therapy was instituted in half the patients at the time represented by this line. Each dot represents a patient treated specifically and each cross a patient not given specific therapy.

In the cases here reported the total amount of serum administered was made dependent on the stage of the disease at which treatment was begun. The smallest amount was given to patients treated within twenty-four hours after the onset of the disease, and multiples of this amount were used in patients first treated on the succeeding days. The guide for dosage that was followed is given in table 2. In order to secure the full benefit of early administration, it seemed desirable to give all the antibody necessary in as short a time as was consistent with care and safety. Hence, the individual doses were administered at intervals of two hours. In other words, the administration of antibody was featured by the use of total dosages, as large as or larger than those of others, given as early and completed as soon as possible, and graded according to the duration of the disease before the time of treatment.

EFFECTS OF TREATMENT ON THE DISEASE

When one relies on clinical changes in a patient to judge of the effects of therapy, experience teaches the necessity for something more objective than the undocumented opinion of the physician. It is important to adopt certain facts as the indicators of improvement. Those that have seemed at once the most reliable and the most significant in cases of lobar pneumonia are: (1) the duration of the disease; (2) the course of the bacteremia, and (3) the presence or absence of pulmonary extensions of the infection.

Duration.—A comparison of the duration of the disease in specifically treated patients with the duration of the disease in patients not receiving any specific therapy should show most clearly whether or not a therapeutic measure produces immediate symptomatic improvement. This comparison can be expressed in a variety of ways. Since the temperature curve has the merit of objectivity, temperature changes alone are used to indicate the duration of the disease in charts 1 and 2. Symptoms, however, are not subject to exact measurement and may be variously estimated by different observers.

TABLE 2.—*Scheme of Dosage Used in the Treatment of Type I Lobar Pneumonia*

Duration of Disease	Cubic Centimeters of Concentrated Antibody: Individual Doses	Cubic Centimeters of Concentrated Antibody: Total	Total Mouse Protective Units in Average Preparation
1 to 24 hours	5-25	30	90,000
24 to 48 hours	5-25-45	75	225,000
48 to 72 hours	5-25-45-45	120	360,000
72 hours and more	5-25-45-45-45	165	495,000

In the present study, the daily notes of the pneumonia service were compared with those of the staffs of the medical services, and a composite and dependable picture was obtained. Because certain symptoms, such as pleural pain, prostration and delirium, may persist following a critical fall in temperature, symptomatic changes alone are used to indicate the duration of the disease in chart 3. In chart 4, the disappearance of fever and all symptoms is used to fix the duration of the disease.

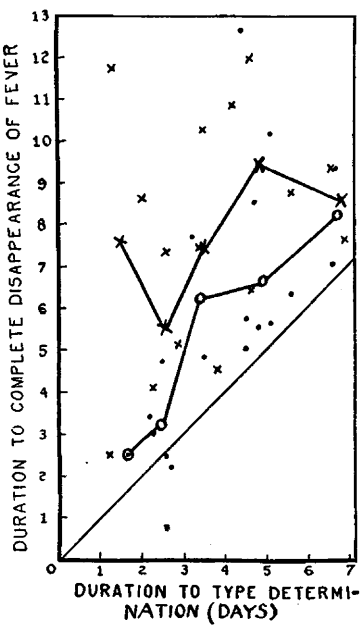

Chart 2.—The duration of type I lobar pneumonia as measured by the number of days required for complete disappearance of fever.

A general impression of the effect of specific treatment on the course of type I lobar pneumonia may be gained by observing the distribution on the charts of the points which represent individual cases. It is apparent from chart 1 that the specifically treated cases, represented by dots, showed improvement at a fairly regular and comparatively short interval after the pneumococcus type was determined and specific treatment was begun. It is also clear that in the cases in which concentrated antibody was not given, represented by crosses, improvement set in at irregular and usually much longer intervals after the determination of the

9. Cecil, R. L., and Sutliff, W. D.: The Treatment of Lobar Pneumonia with Concentrated Antipneumococcus Serum, J. A. M. A. **91**: 2035-2042 (Dec. 29) 1928.
10. Park, W. H.: Personal communication to the authors.
11. Goodner, Kenneth: Further Experiments with the Intradermal Pneumococcus Infection in Rabbits, J. Exper. Med. **48**: 413-429 (Sept.) 1928.

pneumococcus type. Specifically, seventeen of eighteen treated patients showed a marked fall in temperature within thirty hours after the type of pneumococcus was determined and treatment was begun. Only one of the treated patients had a high fever for a longer period than the average untreated patient. While five of the untreated patients had a sharp drop in temperature within thirty hours after the type was determined and four showed the same change before the average treated patient, the remaining ten are scattered quite widely on the chart. The curves in chart 1, showing the average duration before the occurrence of a sustained drop in temperature, indicate perhaps even more clearly the difference in the duration of the disease in treated and in untreated patients. The patients that received concentrated antibody early in the disease had a fall in temperature to nearly normal, on the average, from 20 to 24 hours after they were typed and treated, while the untreated patients showed, on the average, a similar temperature drop from 48 to 144 hours after the determination of the pneumococcus type.

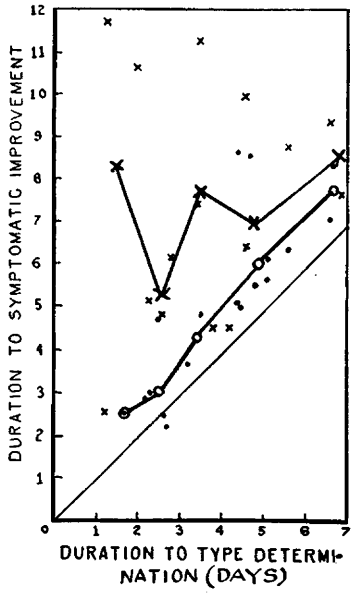

Chart 3.—The duration of type I lobar pneumonia as measured by the number of days of illness until a marked and sustained symptomatic change occurred.

In cases that came under observation after the fourth day from onset of the disease there was no great difference in the average course of the disease between treated and untreated patients.

A continuing low grade fever after a sharp drop in temperature occurred with equal frequency among the specifically treated and control patients. The number of days required for the complete disappearance of fever is given in chart 2. Fourteen of eighteen treated patients became afebrile before the average untreated patient, while only three of the fifteen untreated patients became afebrile before the average treated patient. The treated patients became afebrile, on the average, two days before the untreated patients if treatment was begun any day up to and including the fifth day of the disease.

Symptoms of the acute disease, such as cyanosis, dyspnea, pain in the chest and delirium, disappeared, and marked improvement was manifest, as is shown in chart 3 at approximately the time of a sustained fall in temperature. Thus, chart 3 is similar to chart 1 and does not need to be described separately. The regular and early symptomatic improvement following the administration of concentrated antibody before the fifth day of the disease and the irregular and delayed symptomatic improvement in corresponding cases not specifically treated are clear.

An inclusive definition of the end of the acute stage of lobar pneumonia and the beginning of convalescence includes a consideration both of temperature and of acute symptoms of the disease.

Although in the previous charts temperature is treated separately because it is an objective measurement, in chart 4 it is considered together with the symptoms, and the acute disease is taken to persist until all elevations of temperature as well as acute symptoms have disappeared. It is seen that eleven of the eighteen specifically treated patients were well within thirty hours after the pneumococcus type determination, which represents approximately the beginning of treatment. It is likewise apparent that twelve of the eighteen specifically treated patients were well before the average untreated patient. On the other hand, only four of the fifteen untreated patients were well within the first thirty hours after the pneumococcus type determination, and only five of the untreated were well before the average treated patient, three of the latter being patients first observed on the sixth and seventh days of the disease. As in the previous charts, the beneficial effect of antibody treatment is seen only in patients treated early; in this case, those treated on or before the fifth day of the disease.

TABLE 3.—*Incidence and Course of Bacteremia Among Serum Treated Type I Lobar Pneumonia Patients Compared to That Among Untreated Patients*

	Treated	Untreated
Number of bacteremic patients	7	10*
Patients with blood culture first positive, later negative	6	2
Patients with several blood cultures positive	0	4
Patients with blood culture first negative, later positive	0	4*

* One positive only from heart's blood at autopsy.

Summarizing the effect of concentrated antibody treatment on the duration of type I lobar pneumonia, it may be said that definite improvement was quite regularly present in this group of treated patients within thirty hours after antibody administration and that such patients showed a shorter average duration of their illness than did the untreated patients. The difference in favor of the treated patients was greatest in those treated earliest in the disease and decreased progressively as treatment was delayed.

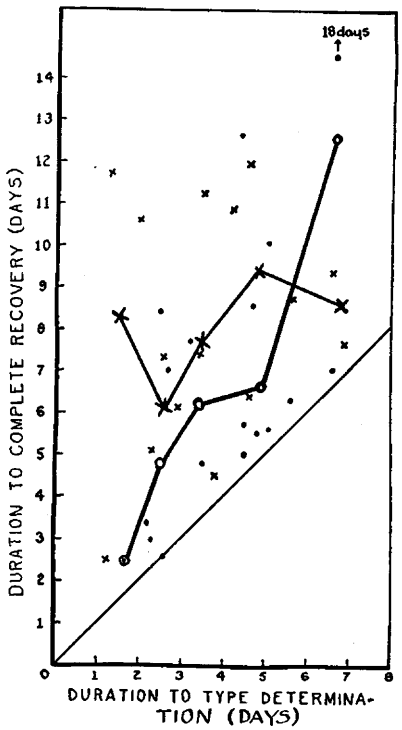

Chart 4.—The duration of type I lobar pneumonia as measured by the number of days required for complete disappearance of fever and symptoms.

Bacteremia.—The result of blood culture has been thought throughout the study of lobar pneumonia to be of considerable prognostic significance. The presence of bacteremia early in the course of the disease is considered an indication of a severe infection. The pres-

ence of a bacteremia on the fourth day or later in the course of the disease is an unfavorable prognostic sign. Seven of the treated patients had a bacteremia when they were first seen (table 3). The effect of specific treatment on the bacteremia was striking. All six of the patients who had more than one blood culture taken had negative cultures after serum treatment. These may be compared with the six untreated patients whose first blood cultures were positive. Only two of these untreated patients subsequently had negative blood cultures. Also the development of positive blood cultures was apparently hindered by the administration of antibody. In no instance did a treated patient with an originally negative blood culture develop a positive culture, whereas four of ten untreated patients whose first blood cultures were negative later had positive cultures (one was found positive on culture of heart's blood at autopsy).

Pulmonary Extensions.—The extension of the inflammatory process to a new area in the lungs is a clinical condition that is characteristic of a pneumonic process that is progressing unfavorably. All cases were carefully followed with this point in mind. The clinical signs of extension, such as continued bloody sputum and prolongation of the course of the disease or relapse, aided in making this diagnosis. No cases were considered as showing extension, however, unless the new area of consolidation was clearly demonstrated by physical signs and by roentgen examination. Among the treated patients no extensions were detected subsequent to the administration of specific therapy. Among the untreated patients, extensions occurred in four otherwise uncomplicated cases.

Summarizing the objective evidence of the effect of the administration of concentrated antibody on type I lobar pneumonia, it may be stated that (1) the duration of the disease was shortened on the average from one to two days in patients treated on or before the fourth day; (2) the blood culture became negative after serum treatment, while no patients developed positive blood cultures after treatment, and (3) extension of the infection to new portions of the lungs occurred among the untreated but not among the treated patients.

The total death rate in the untreated series (ten out of thirty-one patients, or 32.2 per cent) corresponds very well to that observed in much larger series of lobar pneumonia cases (table 1). There is only a slightly lower death rate in the treated group (seven out of twenty-eight patients, or 25 per cent). The number of deaths (one out of seven) among the treated bacteremic patients was less than among the untreated bacteremic patients (eight out of ten).

A comparison of the fatal cases in the treated and untreated series brings out points that are of interest:

First, among the patients of the treated group who died, the culture of the sputum was not confirmed in two instances, a type I pneumococcus being obtained only once out of several examinations. Pneumonia was present in both patients clinically. No autopsy was obtained in these cases. All fatal cases in the untreated group had confirmatory type determinations.

Second, among the fatal cases in the treated group there was only one case in which the blood culture was positive, either before or after serum, whereas in the untreated group every fatal case had a positive blood culture.

Third, in the treated group autopsy examinations showed an organism other than the pneumococcus in the lung in two instances. In one, the lung showed a pneumonia with abscesses, but cultures yielded a pure growth of staphylococci with no trace of the type I pneumococcus which had been found in the sputum two weeks earlier. In the other patient, pneumococcus type I was found in the lung associated with a hemolytic streptococcus. Three autopsy examinations in fatal untreated cases showed that the patients died of typical lobar pneumonia, and pneumococcus type I was recovered in pure culture from the lungs of each.

These three differences indicate an unfortunate division of cases between the treated and the untreated groups. Such differences demonstrate the inaccuracy of comparative fatality rates when a small series of cases is studied.

REACTIONS DUE TO SERUM

In connection with the administration of antibody and, in fact, the intravenous administration of any foreign protein, reactions of various kinds may occur. On the whole, pneumococcic antibody concentrated by the method of Felton seldom produces untoward reactions. The possible types of reaction may be listed as (1) immediate reactions with urticarial and asthmatic symptoms; (2) thermal reactions, and (3) serum sickness.

The immediate or allergic type of reaction is the greatest source of anxiety, because of occasional reports of fatalities that have followed immediately after serum was given. In this series of cases no asthmatic symptoms were encountered and only two patients developed mild urticaria shortly after the administration of antibody. The precautions that were used to determine hypersensitiveness included a careful questioning for symptoms of allergy in the patient and his relatives, and for a history of previous serum therapy, the skin test and the ophthalmic test. The skin test was performed by intradermal injection of 0.1 cc. of a 1:10 dilution of normal horse serum in 0.9 per cent saline solution. The ophthalmic test consisted of instilling 1 or 2 drops of a 1:10 dilution of normal horse serum or the therapeutic serum into the conjunctival sac of the patient. The therapeutic serum itself gives positive skin reactions fairly regularly in normal persons and so is unsuited for the diagnosis of skin sensitivity. The eye test has shown no bad local or general effects, such as have been reported with the ocular tuberculin reaction. If the history was positive for previous serum therapy or for any manifestation of sensitivity other than susceptibility to horse protein, or if the skin test was positive but the ophthalmic test was negative, serum was administered according to the usual plan and any sign of reaction was looked for carefully. No individuals were seen who had previously had symptoms due to sensitivity to horse emanations or horse protein or who showed positive ophthalmic reactions to horse protein.

Thermal reactions accompanied by chills occurred at periods ranging from forty to ninety minutes after five different administrations of serum in four different patients. Hyperpyrexia was not observed. The incidence was 2 per cent of serum doses and 12.5 per cent of patients treated.

Serum sickness occurred six times among twenty-one recovered cases (29 per cent). It varied in severity from mere temperature elevation to arthralgia of six days' duration. Only two patients (9.5 per cent) had serum sickness that was at all severe.

COMMENT

The direct method of determining whether the mortality of a given disease has been altered by the use of a specific agent is that used by the authors quoted in table 1. It has been shown by these investigators that Felton's concentrated pneumococcic antibody reduces the death rate of type I lobar pneumonia and that it is especially effective when used early in the course of the disease. To the average practitioner, however, the effect on the death rate is not obvious, because each man treats comparatively few patients with type I lobar pneumonia. In order to be convinced that a new agent is effective, the physician wishes obvious improvement to follow its administration. The experiences outlined lead one to believe that obvious and consistent benefit occurs in patients with type I lobar pneumonia who have been treated with antibody within the first four days after the onset of the disease. The clinical evidences of specific therapeutic action of the serum are a shortening of the disease, an immediate effect on the bacteremia that may be present together with the prevention of the development of a bacteremia and, finally, a diminution in the incidence of spreading areas of consolidation.

A consideration of what these observations mean when translated to the conditions under which the average practitioner works brings up a number of practical questions. In the first place, early diagnosis of lobar pneumonia becomes of the greatest importance. It is probable that, when emphasis is placed on early diagnosis by the physician and eventually by the lay public, many more cases of lobar pneumonia will be recognized within the first two or three days. It is also probable that the number of early cases discovered in homes will outnumber those that are seen in hospitals. Secondly, the question must be solved of determining the type of pneumococcus as quickly as possible. To do this requires that an adequate typing service be established in the laboratories of states, of cities, of hospitals and of private individuals. The medical profession should appreciate that it has at hand a useful specific remedy for type I lobar pneumonia and that early diagnosis of pneumonia, early determination of the pneumococcus type, and specific treatment are feasible and imperative.

CONCLUSIONS

Felton's concentrated antibody produces obvious symptomatic changes in patients with type I lobar pneumonia, treated during the first four days of the disease.

A Foodstuff Defined.—Nutrition is the sum total of those processes by which the living organism receives and utilizes the materials necessary for the maintenance of life. This includes growth, the repair of worn-out structures, and the liberation of energy. The energy thus set free appears in the form of heat, mechanical work, electric currents, and perhaps also in ways yet unknown. Food has been defined as a palatable mixture of foodstuffs. A foodstuff is a material capable of being added to the body substance, or which when absorbed into the blood stream will prevent or reduce the wasting of a necessary constituent of the organism. For the animal organism, these nutritive substances are water, inorganic salts, the organic foodstuffs, and certain other substances of unknown chemical nature. The union of oxygen with the organic foodstuffs or their cleavage products maintains life and warmth in the cells. Water is the most urgently needed of these substances, which need can be measured by the exceeding promptness with which symptoms of deprivation appear and their extreme gravity.—McLester, J, S.: Nutrition and Diet in Health and Disease, Philadelphia, W. B. Saunders Company, 1931.

MESENTERIC INVOLVEMENT IN BUERGER'S DISEASE (THROMBO-ANGIITIS OBLITERANS)

REPORT OF TWO CASES

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My purpose in this paper is to review some salient points of thrombo-angiitis obliterans, laying especial stress on the involvement of vascular areas other than the extremities and adding two cases that came under my observation, in which the blood vessels to the intestinal tract were affected.

In 1878, von Winiwarter [1] reported a case in which the arteries of the lower extremities were occluded and which appeared to him to be due to a chronic proliferative process, having its origin in the intima, and being associated with an inflammatory reaction of the wall of the blood vessels. As a result of this study he proposed the name "endarteritis obliterans" for this condition. Later, von Manteuffel [2] suggested that the occlusion of the blood vessels in this disease is due to a primary arteriosclerosis, and to him the veins did not seem to be involved in the process. In 1897, Bachard [3] established the thrombotic nature of the disease and concluded that it is a primary thrombosis of the arteries and veins and its identity is distinct from arteriosclerosis. However, it was not until 1908 that Leo Buerger [4] rescued this condition from the heap of confusion and placed it on a sound clinical and pathologic foundation. He gave it the name thrombo-angiitis obliterans.

ETIOLOGY

The disease occurs most frequently, though not entirely, in Russian and Polish Jews. Cases have been reported in Turks, Koreans, Chinese and Japanese. Buerger, in a series of 500 cases, found 7 gentiles. The disease is confined to males, though a few cases have been reported as occurring in females. Syphilis is not a cause of this disease. At first some observers believed that an excessive use of tobacco might be an etiologic factor, but the many instances encountered in which the typical disease develops in men who have never smoked has led to its being regarded as an undetermined factor.

Although no definite infectious agent has been found as yet which might be the cause of this strange malady, the clinical and pathologic evidence leads one to suppose that thrombo-angiitis obliterans is an infectious disease. Recently Buerger [5] succeeded in implanting clots from patients with "acute" thrombo-angiitis obliterans and thus produced typical lesions in the veins of inoculated persons. Barber asserts that a diplostreptococcus is the causative factor, while Rabinowitz reports the isolation of an organism which is capable of producing the disease; but their work has not been corroborated by other investigators.

1. von Winiwarter, Felix: Ueber eine eigentümliche Form von Endarteritis und Endophlebitis mit Gangrän des Fusses, Arch. f. klin. Chir. **23**: 202, 1878.
2. von Manteuffel: Ueber angio-sklerotische Gangrän, Arch. f. klin. Chir. **42**: 569-574, 1892.
3. Bachard: Beitraege zur primaeren Endarteritis Obliterans, Deutsche Ztschr. f. Chir. **39**: 130, 1897.
4. Buerger, Leo: Thrombo-Angiitis Obliterans: A Study of the Vascular Lesions Leading to Presenile Spontaneous Gangrene, Am. J. M. Sc. **136**: 567, 1908.
5. Buerger, Leo: Thrombo-Angiitis Obliterans: Experimental Reproduction of Lesions, Arch. Path. **7**: 381 (March) 1929.