had any serious bad results, it is necessary to discontinue the treatment promptly, in a small percentage of the cases, owing to the onset of the symptoms which I shall now mention.

From experience I do not now place a patient on the casein treatment unless I can see him daily for a week, or unless I can be daily informed of his condition by his medical attendant and have the urine sent to me daily.

I have met with unfavourable symptoms in about 20 per cent. of cases. A feeling of great weakness and exhaustion occurs in a few, and it is then desirable to discontinue the treatment on this account. Others become mentally depressed and irritable at what they consider a harsh treatment, and will not continue it. In a few it produces dyspepsia, or diarrhoea, or constipation. But in the majority of cases it can be followed quite easily and without unfavourable symptoms. When it cannot be taken the diet of cream, eggs, custard, beef-tea, already described, may be recommended.

Patients who are fond of the pleasures of the table and like nice foods will probably regard the casein treatment as monotonous, or as one of my patients expressed it, "not interesting." But many take it readily and without any dislike, and are delighted at the results as regards the sugar excretion.

In the casein treatment just described—

1. The amount of carbohydrates in the food is reduced to the minimum;
2. The total quantity of food is reduced to a very small amount;
3. The food is given in small quantities at frequent intervals—every two hours.

I am inclined to believe that the last two points are of much importance in the success of the treatment.

(Knowing the great pressure on the space in the BRITISH MEDICAL JOURNAL I have not added descriptions of cases. Such detailed accounts I hope to publish later in the *Medical Chronicle*.)

THE EARLY ADMINISTRATION OF VACCINE IN PNEUMONIA.*

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In the treatment of acute lobar pneumonia vaccines have been used, mainly as a last resort, in cases which were not doing well under other treatment. Some physicians advise that a vaccine should be prepared from the sputum early in an attack, to be used in the event of continued severity or relapse of symptoms, and in cases of slow resolution. This attitude is illogical. If a vaccine is of service at all, it should be used as soon as possible, in order to limit the intensity of the infection and prevent the occurrence of grave symptoms. A vaccine can give little or no assistance when the infection has been allowed to go on uncontrolled to the point of cardiac and nervous exhaustion. That they have principally been used late in the disease, and then usually in quite inadequate doses, is the reason that their value is not the subject of agreement. My own practice is to give a vaccine as early as possible after the onset of symptoms. The object of this paper is to give the results obtained in a number of cases which were injected not later than the third day of the disease.

Pneumonia is primarily a septicaemia, and it may prove fatal in this stage before there is any localization in the lungs. In laboratory animals injected with pneumococci septicaemia is the rule, unless they are immunized or the injected organisms are of low virulence. Man has a greater resistance than animals, and local lesions usually follow the septicaemia. The consolidation of the lungs must be regarded as a defensive process, an attempt to localize the infection. It is not true bacteriologically that infections attack the place of least resistance. They attack the place of greatest resistance. A fortress city suffers more than an open, undefended town. The chief defence against the pneumococcus is phagocytic,

and the lungs contain a larger number of leucocytes than any other organ, except the marrow, which is their birth-place, and the spleen, which is their grave. The emigration of leucocytes and the clotting of the fibrinous exudate in the alveoli prevent the spread of the germs but at the same time impede the access of antibodies from the blood. During the stage of firm consolidation little can be expected from vaccine treatment so far as the affected parts of the lungs are concerned; but inasmuch as other parts of the lungs are still patent the raising of the antibody content of the blood will be of some value. Further, by accumulating antibodies in the blood, we make them available for the time when unorganized ferments have liquefied the fibrin sufficiently for fluids to enter. But when vaccines are given late in the disease an increase of antibodies can have no effect upon the damage already done, and the patient may die of heart failure or nervous exhaustion. Elsewhere¹ I have shown the good results which can be obtained from using appropriate vaccines in septicaemia caused by the *streptococcus*, *staphylococcus*, *gonococcus*, or *Bacillus coli*. In spite of the pessimistic conclusion of Dr. Samuel West at a recent discussion that "in the acute general infections vaccine treatment offers but little prospect of benefit," I regard, after much experience of this class of case, the septicaemias as one of the best fields for the skilled employment of vaccines, and the septicaemic stage of pneumonia is no exception.

All the cases of pneumonia described here have been treated with a stock vaccine made from a highly virulent strain of pneumococci. The diagnosis was made at first on clinical grounds and confirmed later by bacteriological examination and the progress of the case. The number of cases is small, as a physician does not get many opportunities, either in private consultations or in hospital, of seeing cases of pneumonia in their early stages. By far the majority of the cases which I have treated with vaccine were first seen on the fourth or later days. These are excluded from the scope of this article. Six cases received their first injection within twenty-four hours from the onset of symptoms, three were injected during the second day, and six during the third day.

Cases Injected within Twenty-four Hours of the Onset of Symptoms.

CASE I.

A lady, aged 25, at 1 a.m. on May 26th, 1913, had a severe rigor with vomiting. This was followed by pain in the left side

of the chest and a frequent restrained cough. She was seen by her doctor, who was a relative, at 3 a.m., and by myself in consultation at 11 a.m. The temperature was then 103°, pulse 120, respirations 38. She had the typical symptoms and appearance of pneumonia—hot dry skin, shallow breathing, grunting expiration, pain in the side. There were subdued breath sounds at the base of the left lung with a few fine crepitations. Sputum was already rusty; 25 million pneumococci were injected at once. This was followed by a fall of temperature, which reached normal during the following night. The respirations

Case I.—Female, aged 25. Injected ten hours after onset.

and pulse-rate fell with the temperature. Slight fluctuations of temperature occurred for three days, but after a second injection on the fourth day the temperature remained normal. In spite of the absence of symptoms there was well marked consolidation in the lower lobe of the left lung and a small patch in the right. The sputum contained large numbers of pneumococci. The lung rapidly cleared, and the patient was allowed out of bed in a week from the onset.

CASE II.

A man, aged 45. Several attacks of bronchitis during the previous year. A sharp rigor occurred on the evening of January 11th, 1914. Temperature rose to 105°, with a pulse-rate of 128 and respirations 38. When seen by me exactly twenty-four hours later he was somewhat cyanosed, his pulse was soft, and there was a mitral systolic murmur. Sputum was rusty. At both bases the breath sounds were subdued, with fine crepitations. Scattered rhonchi in both lungs. Herpes on lips. Considerable pain in right lower axillary region. The outlook seemed bad, and it was feared that his heart would not stand the strain. Twenty-five million pneumococci were injected. The temperature fell to 100° next morning, and, after a rise to

* The substance of this paper was given as a post-graduate lecture at the General Hospital, Birmingham, on April 28th, 1914.

102°, reached 98° on the 13th. Later on the same day it rose again to 103°; a second injection of 35 million was given on the evening of the 14th, and was again followed by a rapid fall of temperature. After the second day there was well-marked consolidation of both lower lobes, but this quickly resolved, and the patient's general condition was so good that he was sent away to the seaside a fortnight after the illness began. The sputum contained pneumococci and *Micrococcus catarrhalis*.

Case II.—Male, aged 45. Injected twenty-four hours after onset.

I saw her in the evening of the same day. There were labial herpes, pain in the left side, quiet broncho-vesicular breathing over the greater part of the left lung and at the right base. Pulse-rate 114, respirations 34. Twenty-five million pneumococci were injected. The temperature fell to 98.4° in about six hours. The pulse and respirations, however, remained quick, and there was much respiratory distress owing to the size of the abdomen. Labour occurred early the following morning, and she was delivered with considerable difficulty with the aid of forceps. For a time the outlook seemed hopeful, but there was consolidation of nearly the whole left lung and a large portion of the right lower lobe. Twenty-five million were injected again on the 8th, and 30 million on the 10th, but she died of heart failure on the 11th. In earlier years the patient had been asthmatic and suffered from attacks of cyanosis. The vaccine seemed to lessen the toxæmia, but the heart, in spite of oxygen and alcohol vapour and other stimulants, failed to stand the double strain of the labour and the pneumonia.

Looking back upon these three cases I consider the dose of vaccine was too small, and in Case III it should have been injected more frequently. In Cases I and III I should now give 50 million and in Case II 100 million.

CASE IV.

A medical man, aged 52. He had felt rather unwell for a few days, until March 1st, 1914, when he shivered violently and went to bed. "feeling worse than he had ever done in his life." I saw him at 11.30 p.m. Temperature was then 105°, pulse 136, respirations 40. It was evident that a severe attack of pneumonia had begun. There was quiet, almost bronchial, breathing at both bases, with fine crepitations. Fifty million pneumococci were injected at once, and the response was very striking. Next morning, in less than twelve hours, all symptoms of distress had gone, temperature was normal, pulse 76, respirations 20. Herpes was beginning on the lips, the sputum was blood-stained, and contained pneumococci with *Micrococcus catarrhalis*. In spite of this great general improvement extensive consolidation developed in both lungs. The patient presented a striking picture of all the physical signs of pneumonia without any symptoms of toxæmia. He was allowed up in a week, and went to the seaside on the fourteenth day. All physical signs had disappeared by the twelfth day.

Case IV.—Male, aged 52. Injected during first twenty-four hours.

teenth day. All physical signs had disappeared by the twelfth day.

CASE V.

A girl, aged 6, complained of severe pain in the right side of the abdomen on February 6th. Temperature rose to 103° to 104°, pulse 140, respirations 42. Appendicitis was suspected, and a surgeon who was called in advised operation. Before this was finally decided upon I was asked to see her, and found signs of pneumonia in the right lower lobe. The abdomen was generally tender, but especially on the right side. There were also meningeal symptoms—headache with screaming, retraction of the head, and slight opisthotonos. Kernig's sign was present. It was decided to treat the case with vaccine, and

5 million pneumococci were injected. Next morning consolidation of the right lung was more marked, but there was considerable general improvement, the headache, screaming, and head retraction having disappeared. A second dose of 10 million was injected on the 8th, and temperature fell by lysis.

CASE VI.

A boy, aged 11½, after a few days' slight feverishness, complained, on the evening of February 15th, of great pain in the left side of the chest. Temperature next morning was 104°, pulse 120, and respirations 32. Commencing consolidation was found in the left lower lobe. Twenty-five million pneumococci were injected and repeated the next day, after which the temperature fell to 99°. After the first injection there was great general improvement and a fall in the pulse and respiration rate, although consolidation was more marked. The temperature remained irregular for a few days before finally settling down.

Case VI.—Male, aged 11½. Injected during first twenty-four hours.

Cases Injected during the Second Day of the Disease.

CASE VII.

A boy, aged 6½, had three convulsions at 2 a.m., February 5th. His temperature rose to 104°, with a pulse-rate of 144, and respirations 52. The physical signs of pneumonia developed in both lower lobes, with severe pain on the right side. Twenty-five million were injected on the 6th, and 20 million on the 8th. Temperature began to fall after the first injection, and reached normal on the 9th. Convalescence was rapid and uninterrupted.

CASE VIII.

A woman, aged 29, admitted to hospital on September 29th. She began to be ill on the evening of the 27th with a rigor and severe pain in the left lower axillary region. On admission, respirations were 40 and pulse 128. Dulness in both lower lobes, tubular breathing and crepitations; sputum rusty and loaded with pneumococci. Fifty million pneumococci were injected on the 29th, about thirty-six hours after the onset of symptoms. Next day temperature had dropped to 101°, and there was considerable

Case VIII.—Female, aged 29. Injected on second day.

general improvement. A dose of 100 million on October 1st was followed by crisis. The lungs rapidly cleared.

CASE IX.

A soldier, aged 19, admitted to the 1st Southern General Hospital after an illness of thirty-six hours, commencing with a sharp rigor. Temperature was 103°, pulse 100, respirations 38. Great pain, in right side of chest. Consolidation of whole of right lower lobe. One hundred million pneumococci injected on October 2nd. Crisis immediately followed. A second dose of 125 million was given on the 8th, and he was allowed up on the 9th. He was discharged from hospital quite well on the 14th.

Cases Injected during the Third Day.

CASE X.

Boy, aged 10½. Fell ill on the evening of January 28th with shivering and pain in the left side. On the 30th temperature was 104°, and on the 31st 105°, with a pulse-rate of 134 and respirations 46. Consolidation of left lower lobe and portion of upper lobe. Fifteen million pneumococci injected on the 31st, followed by general improvement, and a crisis on February 2nd. A second dose of 15 million was given on the 4th. Convalescence was quickly established.

Case IX.—Male, aged 19. Injected on second day.

CASE XI.

Woman, aged 54, admitted to hospital February 9th. Illness

Case XI.—Female, aged 54. Injected on third day.

was given on the 14th. Physical signs had disappeared on the 18th.

CASE XII.

Man, aged 72. Seen in consultation on the third day of the illness. He was then in a semi-conscious typhoid state with delirium. Extensive consolidation in both lungs. Temperature 100° to 101°, very septic mouth, much flatulence. A typical case of severe pneumonia in an elderly patient with poor reactive powers. Injected with 25 million pneumococci. There was no great change in temperature or physical signs, but general aspect improved in a few hours. A second injection of 30 million was followed by a fall in temperature to normal, and the patient quickly recovered.

CASE XIII.

Lady, aged 40. Rigor early on February 22nd. On the 24th consolidation of both lower lobes and part of left upper lobe. Considerable collapse and depression. Fifty million injected on the 24th and 26th. Temperature began to fall after the second injection and reached normal on March 2nd.

CASE XIV.

Lady, aged about 30, began to be ill on March 7th with shivering and very severe pain in the right side. She was seen by me on the 9th; her temperature was then 104.4°, pulse 152, and respirations 52. She complained of agonizing pain all over the right side of the chest, and examination showed consolidation of the greater part of the right lung with a small area in the base of the left lung. No sleep since the onset, sputum rusty, herpes on lips. Fifty million pneumococci at once injected. Within a few hours she was free from pain. Next morning the pulse was under 120 and respirations had dropped to 42. She was brighter and less anxious and said she felt wonderfully better. Two more injections of 50 million were given on the 11th and 13th, each being followed by general improvement. Temperature fell by lysis. After a few days' normal temperature, as the patient was feeling well and conditions at the nursing home were not very comfortable she was moved to a friend's house. This was followed by a rise of temperature and the development of a right-sided empyema. This was the only case which had an after complication. Although the chart does not show the striking changes seen in some of the others, those who saw the patient were struck with the great change in the appearance of the patient, from distress and danger to one of comfort and security which followed the first injection. I had

Case xv.—Male, aged 28. Injected on third day.

ing in left lower lobe. Pulse soft, general condition distinctly bad. Fifty million injected on the 28th and 30th. The second injection was followed by a crisis. As temperature was irregular for a few days, and there was some fluid in the right

pleura, 75 million were injected on June 2nd, and 100 million on the 4th. The fluid was absorbed, and the patient became quite well.

These cases were not selected in any way. There can be no doubt about the correctness of the diagnosis in each. All had the typical symptoms and appearance of acute pneumonia. Consolidation of the lung was present either at the time of injection or appeared later. The sputum contained large numbers of pneumococci. Most of the patients had no other treatment beyond ordinary nursing measures. To some a simple diaphoretic mixture was given. When severe pain was present at the onset a Dover's powder was prescribed. Only Cases III, XII, and XV required heart stimulants, and they were given oxygen with alcohol vapour and hypodermic injections of strychnine.

Of the 15 cases, only 1 died, and this case was complicated with pregnancy and labour, nearly always a fatal complication in pneumonia. Only 1 case developed an empyema, and this, I think, could have been prevented by continuing the vaccine treatment.

The most striking results were seen among those cases injected on the first or second day. In these there was little doubt that the course of the disease was greatly modified. In no case, even when the first injection was given ten hours after the initial rigor, was consolidation prevented, and in several the unusual picture was seen of a patient with a large portion of the lung solid, but with normal pulse, respiration, and temperature, together with an absence of symptoms. I formed the impression from these cases that vaccine treatment greatly hastened the evolution of the lung through its various stages. Consolidation, when absent at the time of injection, quickly followed, redux crepitations occurred early, and complete resolution was more rapid than usual. The general condition of the patient after the temperature had become normal was far better than that seen in uninoculated patients in the same stage. Several of the cases were allowed up in a week from the first onset, and two undertook a long railway journey in a fortnight. Even when there was no fall of temperature after an injection there was always an improvement in general symptoms, which was felt by the patient and was obvious even to the uninstructed observer. This improvement seemed to occur with some suddenness about six to eight hours after an injection. One doctor, writing about a patient, states: "Since six hours after the first dose of vaccine the patient, who was before very acutely ill, has been perfectly comfortable, and on the sixth day was on solid food."

With the exception of the one case in this series all the deaths in my inoculated cases of pneumonia have occurred in cases injected on the fourth or later days. I hope in a subsequent paper to discuss the vaccine treatment of the later stages of pneumonia.

Early Diagnosis.

Early administration necessitates early diagnosis. It may be argued that if a patient is injected during the first twenty-four hours there is no proof that he was suffering from pneumonia. Pneumococcal infection may cause a rigor with a high temperature lasting but a few hours. I have seen two patients who suffered from severe shivering fits in which the temperature rose to 104° or 105°. The attacks generally occurred in the evening, and next morning the temperature would be normal. Labial herpes always followed an attack, but careful examination never showed any lesion in the lung. Occasionally there was a cough lasting a few days, with scanty sputum containing pneumococci. Under vaccine treatment both patients completely lost the attacks, and have remained free for five and four years respectively. Such a case might be injected under the impression that the rigor marked the onset of pneumonia. If the attacks were caused by a pneumococcal infection the vaccine would do nothing but good, and if they were pneumonia, consolidation would develop. Only cases with lung consolidation must, of course, be recorded for statistical purposes.

In practice there seems to be a lack of confidence in diagnosing pneumonia before the onset of consolidation. A patient is taken suddenly ill with general febrile symptoms, high temperature, shivering, rapid respirations, but no sign of pulmonary disease. The case is loosely regarded as one of "influenza," and when physical signs

appear a few days later the pneumonia is said to have supervened upon influenza. This may sometimes be correct, but influenza is not now prevalent, and what is called influenza is the initial septicaemic stage of pneumonia.

When pneumonia begins in its most characteristic form with a rigor, high temperature, rapid respirations, flushed cheeks, hot dry pungent skin, and pain in the side, there can be little doubt about the diagnosis. When it begins insidiously, as in old people, patients with kidney disease, and occasionally in young adults, the diagnosis may be in doubt for a few days. Even before there is definite consolidation characteristic physical signs can generally be found in the lungs. Within a few hours of the onset there are peculiarly subdued and roughened breath sounds at one or other base, passing gradually into bronchial breathing. Crepitations may appear quite early.

In the majority of cases pneumonia can be definitely diagnosed within a few hours of the onset, and in such cases consolidation should not be waited for, but action taken at once. The events of the first few hours largely determine the course of the disease, and prompt action would save many lives. Of course, in many cases the patient is responsible for the delay, as medical advice may not be sought until three or four days have passed.

Stock versus Autogenous Vaccine.

For early administration a stock vaccine must be ready. It is commonly stated that a stock vaccine is useless because of the great variations in strain of pneumococci. But differences in strain chiefly concern the virulence, and if a stock vaccine be made from a highly virulent strain this should be efficacious against infections caused by pneumococci of less virulence. My own practice is to make a stock of vaccine whenever I obtain a pure culture from a case whose clinical course showed that the infection was a particularly severe one. For some time I have used one derived from a rapidly fatal case of pneumococcal meningitis.

The vaccine must be made from first cultures, and not from subcultures, which may have lost their virulence.

Pneumonia Caused by other Organisms than Pneumococci.

Another objection to the use of a stock vaccine is that pneumonia may be caused by Friedländer's bacillus, streptococci, staphylococci, *B. typhosus*, and *B. coli*. It is true that all these germs may cause consolidation of the lung, and therefore pneumonia, in the pathological sense; but their clinical features can rarely be confused with those of acute lobar pneumonia. I have never seen a case due to streptococci, staphylococci, or *B. coli* which did not at once give rise to suspicion that the infection was other than pneumococcal. Typhoid pneumonia may occasionally be a source of confusion. The cases of Friedländer pneumonia seen by me (four of which were successfully treated with a vaccine) were clinically different to cases of true acute lobar pneumonia.

Mixed Infections.

I admit the frequency of mixed infections. In some seasons the *B. influenzae* may be present with the pneumococcus. Last winter many of my cases showed *Micrococcus catarrhalis* in the sputum. But in these cases the pneumococcus is presumably the predominant organism in causing the pneumonia. In such cases a stock vaccine should be used at first, and an autogenous vaccine, including the secondary organism, can be made later if necessary. But a stock vaccine of known activity is of greater value than an autogenous vaccine of unknown activity.

By using a stock vaccine promptly we may occasionally inject a case which afterwards is proved not to be pneumonia or even a pneumococcal infection. But in a case of suspected diphtheria we do not wait for the result of the examination of the throat swab before injecting antitoxic serum, and in this instance the injected substance is not entirely innocuous. Errors in the diagnosis of early pneumonia should be uncommon in the practice of an experienced clinician, but if an error is made I know of no harm which could arise from the injection of 50 or 100 million of pneumococcal vaccine into a patient suffering from typhoid fever or other infection. If the patient is

not infected with pneumococci he is not sensitized to the vaccine and cannot react.

Dosage.—With the first cases, treated years ago, I began tentatively with doses of 5 to 10 million. While occasionally effective in young children they were quite useless in adults. With further experience my doses increased and the cases here recorded show to some extent the evolution of my methods. I now regard 100 million as a suitable initial dose in an average adult man. In women and the less robust 50 to 75 million may suffice; 25 million is certainly too small a dose, and even when given during the first twenty-four hours rarely has that definite effect in cutting short the fever which is seen with larger doses. When a dose of 100 millions has no effect upon the symptoms the next dose should be increased, injections being given every day until an effect is obtained. When a definite improvement has followed the first dose, the next should be given in forty-eight hours. It is advisable to continue the injections until the lungs have completely resolved.

Sir A. E. Wright, in his recent work on the use of vaccines in pneumonia, found that inoculation in the form of small doses frequently repeated was absolutely ineffective, and that, on the other hand, inoculation in the form of a single large dose, administered in the incubation period, often arrested the disease and averted death. He thinks it reasonable that the results obtained during the incubation stage with doses of 250 to 1,000 million would repeat themselves if this treatment were applied in the early stages of pneumonia. We know the limit below which a pneumococcal vaccine is ineffective, but we do not know up to what limit of dosage it would be safe to go. I have not exceeded 200 million in acute cases, and find the results satisfactory. Much, however, depends upon the activity of the vaccines; 50 million of one vaccine might be more effective than 250 million of another. I believe that much lack of success in vaccine treatment generally is due to the use of vaccines of little activity. A mere enumeration of the organisms tells us little about the dose required, for the strength of the vaccine has still to be determined by its action upon the human patient.

The results obtained in the few cases here recorded have been confirmed by several practitioners to whom I have sent vaccine for use in their own practices, and who have kindly sent me charts and notes of their cases. The general practitioner alone has many opportunities of seeing pneumonia in its earliest stage, and upon him I would urge the importance of taking prompt measures to combat the infection and of seeking earlier consultations.

Owing to the hardships and exposure inseparable from a time of war, pneumonia is prevalent in military camps. Up to January 31st, 1,508 cases of pneumonia, with 301 deaths, had occurred among the British troops in the United Kingdom. I am confident that the early administration of a pneumococcal vaccine would save many lives and shorten the duration of the illness. In military practice it should be possible to discover cases of pneumonia sufficiently early to administer vaccine during the most favourable stage. If removal of the patient to a military hospital entails much delay, whenever possible the vaccine should be administered before removal and as soon as the case is diagnosed. As in early cases improvement occurs within a few hours, the patient would withstand better the journey to hospital. The rapid resolution of the lung and the short period of convalescence seen after the early administration of vaccine enable a soldier to return to active duty in a shorter period than with any other method of treatment.

REFERENCE.

¹ *Journal of Vaccine Therapy*, September, 1912; *Clinical Journal*, April 30th, 1913.

ON Tuesday next, at 3 p.m., Professor Sir J. G. Frazer will begin a course of two lectures at the Royal Institution on "The belief in immortality among the Polynesians"; and on Thursday Dr. Aubrey Strahan will commence a course of two lectures on "London geology."

KING EDWARD'S Hospital Fund has recently received a cheque for £500 from Sir John Ellerman, Bt., given as an annual subscription to be terminated a year or two after the war, when things become normal again, and thus to assist the hospitals over a period during which there is considerable fear of a material reduction in subscriptions and donations.