NOTES ON THE TREATMENT OF ACUTE PNEUMONIA BY A CONVALESCENT SERUM.

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"PNEUMONIA, one of the most widespread and fatal of all acute diseases, has become the Captain of the Men of Death, to use the phrase applied by John Bunyan to consumption." Such are the opening words of Osler when treating of the incidence of this disease. There is an impression, imprinted more deeply on the lay than on the professional mind, that pneumonia is a disease of the cold winter and early months associated, perhaps, with adverse conditions of climate. A study, however, of the records of the Citadel Military Hospital, Cairo, for the years 1929—1933, where the climate is hot during May and June and very warm and humid during July, August and September, will show that pneumonia tends to be a disease of the summer months, the greatest incidence occurring between May and September and the maximum number of admissions in any one month happening either in June, July or August. For example, in 1933, there were 53 cases out of the yearly total of 68 admissions between May and September, with a maximum of 22 cases admitted during June. In Cairo, therefore, pneumonia has been more prevalent during the summer months. The cause of this reversal of the general impression is not easy to discover and is still under investigation. Regarding the mortality in Cairo in 1933 the number of deaths among a civil population of 1,233,500 was 5,139 (4·16 per 1,000). In the same year among troops in the Cairo area, whose average strength was 6,439, the number of deaths from pneumonia for the whole year was 7 (1·08 per 1,000 strength), a case mortality of 10·3 per cent. Between May and September, the period of greatest incidence, the case mortality was 13·2 per cent. The annual reports on the Health of the Army show that the case mortality among the Regular Army serving at Home and Abroad lies between 9 and 10 per cent. It will be seen, therefore, that the opening words of Osler quoted above are almost as true to-day as when he wrote them. This being the case, every effort should be made to discover some means whereby the incidence and mortality of this widespread disease may be lessened. The number and the variety of the forms of treatment that have been suggested are legion and their very number indicates that no great measure of success has attended any one of them. Be this as it may, no apology is needed for suggesting yet another mode of therapy. In May of 1934 the summer wave of admissions
for acute pneumonia commenced and on examination it was learnt that the *Diplococcus pneumoniae* recovered from the sputa of all these early cases belonged to Type II, Armstrong's rapid method of typing being used in all instances. Sabin's method of typing did not prove a success, possibly because guinea-pigs were used instead of mice, none of the latter being available. It was only late in July that a change of type occurred in a patient whose sputum produced Type I. It was at the period when patients who were very ill continued to arrive in fairly rapid succession that it occurred to me that the giving of the serum from the convalescents would be perhaps more beneficial and helpful to the fresh pneumonia patients than the administration of the available stock serum. It is not claimed that the treatment of acute pneumonia by convalescent serum is new but I could find no reference to this form of therapy in the literature at my disposal and so, as no data were available, I had to proceed carefully by trial from the beginning, instead of being able to go ahead from a stage where others had left off. Some difficulties in obtaining sufficient serum presented themselves: firstly, the pneumonia patients were very exhausted for a few days after the temperature had been normal and one was reluctant to disturb them; secondly, as soon as convalescence was established, i.e., from about the fifth or seventh day after defervescence, it seemed unfair to ask them to part with twenty or more ounces of blood. In this investigation, therefore, one had to be content with as much blood as could be removed from each convalescent by a twenty cubic centimetre syringe. At the next opportunity it may be possible to obtain a larger quantity without harm or causing alarm to the patients in their debilitated condition. Blood was taken from a total of eleven convalescents on or as soon as possible after the seventh day after the temperature had fallen to normal. In each instance the medical history sheet was perused for evidence of antecedent disease. The blood was examined for malarial parasites. The serum was pipetted off after twenty-four hours and was placed in the water bath at 56°C. for half an hour for three or more days in succession, depending upon the day the serum was required. The Kahn test was carried out on all sera. At this point it should be mentioned that the sera of Type II convalescents agglutinated their own organism but not the pneumococcus Type I isolated from the sputum of a patient who was admitted late in July, thus demonstrating the presence of some specific antibody in the convalescent serum.

The serum was in all instances administered by injection under the skin of the flanks. Having no guide on which to base the dosage and in the absence of any means of estimating the antitoxic power of the serum, it was considered wise in this series to commence with small trial doses. The clinical results were briefly as follows:—

**Case 1.**—A very severe infection. He received 10 cubic centimetres of convalescent serum on the fifth, sixth and seventh days of his illness. After the third injection there was a distinct amelioration in his general
condition. Crisis occurred on the eighth and ninth day and the temperature came to normal on the tenth day. He was too ill at the time to remember anything and so could not say whether he felt better for the injections or not.

Case 2.—A less severe case who on the third and fourth days of illness received 10 cubic centimetres. It was noted that the temperature began to fall on the fourth day and reached normal by lysis on the eighth day. This patient said that after the second injection he felt "champion."

Case 3.—Was the best advocate of the treatment for, after receiving the first injection of 9 cubic centimetres on the fourth day of illness, he volunteered the statement that the injection took away the tight, blown-out feeling in his chest, and made his breathing easier and not so painful; the second injection (on the fifth day of 10 cubic centimetres), he said, cured him.

His temperature began to fall on the fourth day and continued to fall by gradual lysis and reached normal on the eleventh morning. After the fifth day the temperature did not rise above 100°F.

Case 4.—A very acute severe infection for whom, unfortunately, only 17 cubic centimetres of convalescent serum were available and this was administered in doses of 8 and 9 cubic centimetres on the seventh and sixth days of the illness. It cannot be said that the serum had any great effect upon his general condition, but it was noted that on the seventh day the temperature showed a big fall and reached 96.8°F. on the tenth morning. This fall in temperature, which, it should be noted, was seen in all four cases within twenty-four hours of the last injection, might have occurred in the natural course of the disease without the injection of the serum, therefore observations upon many more cases are necessary before one can say whether the defervescence was due to the serum or to coincidence.

There was no sign of serum reaction, local or general, in any of the patients.

The result of this investigation, although not dramatic, is encouraging and should a similar series of cases present itself this year it is intended to give this form of treatment a further and more extended trial by administration of larger quantities of serum either intravenously or subcutaneously. It is hoped also that by publication of these notes others will be induced to do the same so that as many observations as possible may be collected and compared. The injection of the whole blood of a man convalescent from malaria and free from syphilis into the muscles of an actively ill patient is also put forward as worthy of trial. In this series it was not possible to give the serum earlier than the third day, this being the earliest opportunity after the arrival of the patients in the acute medical ward. From the pathologist's point of view the investigation is obviously incomplete, but it was the best that could be carried out at this period. Still, some data were obtained and the clinical results would appear to justify a fuller
investigation this year when a small research laboratory, set apart from the general laboratory, could be arranged.

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A CASE OF AGRANULOCYTOSIS.

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The patient, aged 28, was admitted to the Queen Alexandra Military Hospital, Millbank, on August 29, 1934. He had returned from India five months previously, having served there for three and a half years. He had always been a healthy man and had had no previous serious illness. While in India he had suffered from occasional fever lasting for one day at a time, for which he had treated himself with esanofele; he had never been in hospital.

On August 20 he woke up with acute abdominal pain, he sweated profusely, had a rigor, and vomited twice. He was seen by his doctor, who said his temperature was 105°F. For the next four days he had severe headache and his high temperature persisted. He was then sent to a civil hospital, where it was noted that the rise in temperature occurred every other day. The Widal reaction against typhoid, Para A and B, was negative; nothing could be found to account for his pyrexia, and on the tenth day of his illness he was transferred to Millbank.

On admission, therefore, he presented the problem of "a pyrexia of unknown origin" of ten days' duration. He complained only of severe frontal headache, inability to sleep, and constipation. His bowels had only been open twice since the onset, each time with an enema. His temperature was 103.4°F; pulse-rate 88, and respiration 24. His tongue was furred and brown, his mouth very dry, and his throat injected; there was some enlargement of the cervical glands; no ulceration was present in the mouth or throat. He presented no other abnormal physical signs in any system, and his spleen was not palpable. The following investigations were carried out:—