

October 16th, 1914.

To the Members of the Corporation
of the Rockefeller Institute for Medical Research,

Gentlemen:-

The Director of the Hospital has the honor to submit the following report of the work carried on during the past year.

When the Hospital was opened it was stated that one of its functions might be the training of men to take part and aid in the change which was likely to take place in the teaching of internal medicine. It is gratifying to know that the object has been, to a measure, attained, in that a number of the assistants in the Hospital have now been called to full-time academic positions in the teaching of medicine in various universities. Dr. Canby Robinson was called to Washington University of St. Louis, to become Assistant Professor of Medicine, and to aid in organizing the Department of Internal Medicine in the new hospital of that institution. Dr. Francis Peabody was called to the Harvard Medical School, and to the Brigham Hospital, Boston, to become Assistant in Medicine, and Resident Physician, respectively, in these two institutions. Finally, Dr. Swift, who has been Resident Physician of the Hospital, has received and accepted an appointment as Associate Professor of Medicine in Columbia University, and Dr. Fraser, who has also been a member of the staff, has been appointed an Instructor in Clinical Medicine in the same institution. All these men are now acting as full-time instructors in medicine. While these appointments add to the difficulty of maintaining the staff at all times on a most efficient basis, yet for the present, at least, such appointments are gratifying, not only because they show that the Hospital is able to occupy an important place in training such men, but also

because they offer an encouragement to the younger men who are working in the Hospital with the view of later making an academic career. In addition to the loss of Dr. Swift and Dr. Fraser, the Hospital has also lost Dr. Ellis and Dr. Zacharias, who have joined the English and German armies respectively. It is hoped that at the end of the war one or both of them may return to their work which was so suddenly interrupted.

Dr. A. R. Dochez, who has been a member of the Hospital staff since its organization, and was previously on the staff of the Institute Laboratories, has been advanced to the position of Resident Physician, to take the place left vacant by Dr. Swift. The following named men have been appointed to occupy the other vacant places on the staff: Dr. Alan M. Chesney, who formerly spent a year in the Hospital and during the past year has been on the staff of the Johns Hopkins Hospital; Dr. Ross A. Jamieson, who is a graduate of the University of Toronto, and has been for the past two years on the staff of the Bellevue Hospital in this city, and Dr. Franklin C. McLean, formerly professor of pharmacology in the University of Oregon. An important change in the organization of the Hospital staff has taken place during the past year by the appointment of Dr. Donald D. Van Slyke to take charge of the chemical laboratory. The organization of this department of the medical work has offered the most serious difficulties, and it has been very difficult to obtain a man of proper training and scientific inclination to act as director of this laboratory. It is felt and hoped that in Dr. Van Slyke the ideal man for such a position has been obtained.

In looking to the future development of the Hospital work, it is believed that, with the discovery of new methods which may be applied practically in the treatment of disease, definite organized efforts should be made by the Hospital, or by the Institute as a whole, to assist in putting these methods into more widespread and efficient operation. This can be done ^{either} by efforts to assist general practitioners in carrying out new methods of treatment or by assisting in the organization of other institutions for carrying out special methods of treat-

ment. The development of this idea could well be one of the functions of the department of Public Health, or the Third Section as suggested by Dr. Prudden.

During the summer months just past, owing to the work which was going on adjoining the Hospital, and owing to the fact that the staff was so materially reduced, a very small number of patients have been admitted and the work has been reduced so far as possible. It was not thought advisable to close the Hospital completely since, in order to obtain support from the public and medical profession, it is necessary that at all times the Hospital be open for the examination of patients and for the reception of suitable ones. The following is a brief review of work carried on in the Hospital.

Pneumonia.

During the period since the last report eighty cases of pneumonia have been treated. Numerous studies have been made on these patients from various points of view by Dr. Cole, Dr. Dochez, Dr. Avary and Dr. Chickering. The results obtained may be classified under the following heads:

Infection and Epidemiology. Studies have been made of the types of pneumococci occurring in normal mouths and in the mouths of patients convalescent from pneumonia. In the mouth of only one normal person have pneumocci of the fixed types I, II, and III been found. This person was the wife of a patient suffering from pneumonia due to pneumococci of type II. In her mouth pneumococci of type II were found. Studies of patients convalescent from pneumonia have shown that pneumococci of the type found during the disease usually persist in the mouths for from one to several weeks. Later than this they are not found. Only pneumococci of the non-specific type IV. are then present. During the present summer Dr. Lyle has carried out a study of the types of pneumococci present in the mouths of patients suffering from tuberculosis. Among fifty cases, in two, pneumococci of type I. were present. In no other cases were pneumococci of the fixed types found. These studies indicate that in cases of pneumonia, except possibly those due to organisms of type IV., infection probably occurs from without, though there are probably contributing factors in etiology.

In no case has direct evidence been obtained of transference of one organism of one type into those of another type. It is probable, however, that in the evolution of the pathogenic types such transformations have occurred. That this evolution may have been along different lines in different parts of the world is shown by the fact that in South Africa a type of pneumococci is present which has not been met with here, and this type is there fairly wide spread. A small number of organisms have been sent to us from South Africa. The four types found

here are among them and in addition a fifth type, as mentioned.

Careful study of the organism isolated from each case of pneumonia coming under our observation has been made. The results confirm our previous report in regard to the relative frequency and severity of cases due to the different types of pneumococci. Studies concerning the occurrence of pneumococci of different types in cases of pneumonia have also been made with our assistance in the Brigham Hospital at Boston, the Pennsylvania hospital in Philadelphia, and the Detroit General Hospital.

Dr. Chickering has studied the agglutinating power of patients' serum for pneumococci of different types. The results afford further proof of the specificity of the different types and their relations to the disease. In the blood of patients with infections due to organisms of type IV. only the homologous organism is agglutinated. In the blood from patients with infections due to organisms of types I. and II. only organisms of the corresponding type are agglutinated. Agglutins have usually disappeared from the blood within a few weeks after the end of the disease. In the cases where they have persisted there has existed some specific complication, as delayed resolution or empyema.

Treatment with serum. Further studies in the treatment of cases have confirmed the opinion previously held in regard to the efficacy of immune serum in the treatment of cases due to organisms of type I. In regard to the serum effective against organisms of type II. our previous anticipations have not been entirely confirmed. During the past winter we had several very severe cases due to organisms of type II, in which the serum seemed to have little or no effect. A study of the serum then being used showed that it was much less effective, as tested by protective power in animals, than was the serum which had previously been used. While, therefore, the results were not necessarily discouraging, except as regards the statistical study being made, nevertheless,

when it is realized that it is very difficult to obtain and keep the serum of type II. at its highest efficiency it is evident that the complications in the way of carrying out effective treatment with type II. serum are bound to be considerable.

An attempt had been made to render this serum more effective by concentrating it, but the results as determined from experimental studies are not encouraging. It is quite possible to cause considerable concentration of the immune substances since all the protective substances have been found to be in the globulin fraction of the serum. When the protective power of concentrated serum is tested, however, the possibility of obtaining greater curative effects from its use does not seem probable. The reason for this is as follows. Serum of type I. protects mice against 0.1 c.c. of culture when 0. 2 c.c. of serum is used. It is found, however, that, no matter how much the amount of this serum be increased, even if 3 c.c. be used instead of 0. 2 c.c. , the amount of culture protected against can never be more than 0.1 c.c. This holds good for concentrated as well as not concentrated serum and has been found almost constantly true in a very large number of experiments. In the case of serum type II. this limit of dosage is still lower. 0.2 c.c. of serum never protects against more than 0.01 c.c. of culture, and no greater amount of culture can be protected against, no matter how large the amount of serum. In ^{case of} organisms of type III. even the smallest amount of culture cannot be protected against by immune serum, using even the largest amounts of serum.

The facts as stated render it evident that, in addition to the immune body, probably a second factor which must be supplied by the body itself, is necessary. In infections due to organisms of type I. this second factor is probably not required in large amounts. At any rate, by increasing the amount of immune body, the demand on the organism probably may be reduced. In the case of infection due to organism of type II. the requirement of this second factor is greater and even very large amounts of immune body will not supply this deficiency. In the

of infection due to organisms of type II. the requirement of this second factor is greater and even very large amounts of immune body will not supply this deficiency. In the case of infections due to organisms of type III. apparently the unimmunized animal is almost entirely unable to supply this deficient factor. The next step in obtaining a method of cure for this disease must consist in determining the nature of this additional factor and methods for stimulating the body to produce it.

The studies so far made of the groups of pneumococci causing pneumonia indicate the following arrangement as regards pathogenicity and immunity. First, group IV. in which the pathogenic effects are only slight; the patients infected practically all recover. Immunity against these organisms can very readily be obtained but the practical difficulty in the efficient use of the serum consists in the fact that these organisms differ among themselves, each one possessing specific immunological characteristics. Next come organisms of type I. which are found in cases of pneumonia of moderate severity and which constitute the etiological agents in the largest group of the cases of pneumonia. The organisms of this group are all alike immunologically and a high degree of specific immunity can be obtained in animals, the serum of these animals apparently being most effective in protection and cure. It is in this group of cases that it is felt that serum treatment is most effective. Next come organisms of group II. These organisms possess a still higher grade of pathogenicity; the infections caused by them are more severe and the mortality is higher. A high grade of active immunity may be obtained for these organisms but the passive immunity obtained by employing the serum of these immunized animals is considerably less effective in protection, and probably in cure, than is that obtained from the serum produced by the inoculation of organisms of type I. Lastly, organisms of type III. so-called *Pneumococcus mucosus* type, which probably possess the highest grade of pathogenicity of any of these organisms, causing infections in man of extreme severity and with a very high mortality. Active immunity can also be obtained by the inoculation of organisms of this type, but passive immunity in this

group is entirely lacking, the serum has no efficacy whatever.

The results of treatment indicate that much has already been accomplished with cases of type I. and it is hoped that this alone may make a material reduction in the total mortality from pneumonia. The chief effort is now being directed to improving the treatment of cases due to organisms of type II. Little can be hoped for, at present, as regards any form of effective specific therapy against organisms of type III.