

REPORT
OF THE
DIRECTOR OF THE HOSPITAL
TO THE
CORPORATION OF
THE ROCKEFELLER INSTITUTE FOR MEDICAL RESEARCH
OCTOBER, 1915

THE HOSPITAL.

The Director of the Hospital submits the following brief report of the work carried on in the Hospital during the past year.

At the beginning of the past year the staff consisted almost entirely of new men. This was due to the fact that several of the old men had been called to positions elsewhere, and others had left to take part in the war. The new men, however, very quickly took hold of the work, and all have proved to be capable workers. The work in the chemical laboratory has been reorganized under the direction of Dr. Donald D. Van Slyke. This has resulted in a marked improvement in the work being carried on in this department.

During the year several voluntary workers have been granted the privilege of working in the Hospital and assisting in the researches being carried on.

Dr. Gay, Professor of Pathology and Bacteriology in the University of California, acted as a voluntary assistant for several months, aiding in the studies concerning lobar pneumonia.

Dr. Henry F. Moore, (working under a grant from the National University of Ireland) has worked for several months in the hospital laboratories studying the effects of optochin in experimental pneumococcus infections in animals.

During the past summer Dr. J.T. Halsey, Professor of Pharmacology in Tulane University, has worked in the laboratories studying the effect of amyl nitrate on vagus tone.

At the close of the pneumonia season, Dr. Henry Chickering was given leave of absence for six months to work in the

Department of Pathology and Bacteriology in the University of California where he had been appointed a Research Assistant. He is assisting in studies concerning typhoid fever, and it is hoped that he will bring back new methods of value in furthering the work on pneumonia.

Very few changes are to be made in the personnel of the staff for the coming year. Two new Assistant Resident Physicians have been appointed: Dr. Walter W. Palmer, formerly Resident Physician at the Massachusetts General Hospital, Boston, Massachusetts, and Dr. Reginald Fitz, formerly of the staff of the Brigham Hospital and Harvard Medical School, Boston. Both of these men have already carried on investigations elsewhere, the former on the question of acidosis, and the latter on the subject of nephritis.

A brief report on the progress of the work along the various lines of investigation follows:-

PNEUMONIA

Epidemiology- Further studies of the pneumococci in the mouths of normal persons and in the mouths of patients during convalescence from pneumonia have shown that pneumococci of the fixed types I, II and III are found only in the mouths of those persons who have lately suffered from an infection with an organism of similar type, and in the mouths of normal persons who have been closely associated with infected persons, in which case the type of organism found is the same as that causing the infection. The organisms of the fixed types persist in patients, following pneumonia, only during a period of from a few days to three months. The organisms of the fixed types also spontaneously disappear from the mouths of contact carriers after a few weeks.

These new facts are apparently of great importance for our knowledge of the epidemiology of acute lobar pneumonia, but at present it is felt that much care must be taken in interpreting these facts, and at the present time no final conclusions should be drawn. They suggest strongly, however, that in the spread of acute lobar pneumonia, contact infection, either direct or through the intermediation of carriers, plays a very important role, and they give hope that the prevalence of the disease may be diminished by more strict isolation of the patients, though the probable large number of carriers may make this very difficult.

Frequency of Pneumonia due to the Different Types of Organisms- The type of organism concerned has now been determined in about five hundred cases, including the cases in this and other hospitals. The larger statistics confirm the previous observations that about one third of the cases are due to organisms of type I, about one third are due to organisms of type II, a considerably smaller number, 6 to 10 per cent. are due to pneumococcus type III, while the remainder are due to organisms of type IV. The mortality in the cases due to organisms of types I and II is about 30 per cent. In our experience cases due to pneumococci of type II are a little more severe than those due to pneumococci of type I. The mortality in the cases due to pneumococci of type III is considerably higher, from 45 to 50 per cent., while the mortality in the cases due to organisms of type IV is much lower, 10 to 12 per cent.

The method devised for the rapid determination of the type of organism concerned in any individual case has been de-

veloped so that it can now be carried out in any laboratory. The only difficulty which has arisen has been associated with the determination of type of certain organisms, small in number, which give an atypical or incomplete agglutination reaction with serum of type II. Ten such strains have now been found and have formed the basis of a thorough study made by Dr. Avery. His study has shown that all these organisms undoubtedly belong to type II, and all are acted upon by the type II serum. However these organisms differ somewhat in their immunity reactions from the typical type II organisms, and also differ among themselves, so that it has been possible to subdivide these organisms into several groups.

Specific Treatment.- The results obtained in the treatment with immune serum of cases due to organisms of type II have not been as good as we had hoped for. The serum treatment of cases due to pneumococci of type I, however, has proved very satisfactory. Forty-eight such cases have been treated with immune serum. Of these, four died. Of the four fatal cases, however, one died suddenly during convalescence from pulmonary embolism, an accidental complication, and two of the cases were only treated when they were almost "in extremis", a few hours before death. This leaves only one case that can be considered to have been treated with any hope of success, and this was treated only on the 5th and 6th days, the patient dying on the 6th day. The results obtained, therefore, are in marked contrast to the results in the untreated cases due to organisms of type I, in which the mortality is 25 or 30 per cent. While, therefore, the results obtained in the treatment of cases due to or-

ganisms of type I have been encouraging, nevertheless efforts are being made to improve the efficacy of the serum in this type of cases, and also to render immune serum effective in the cases due to other fixed types of organisms.

Concentration of the serum has not proved, at present, of practical importance. The attempts at concentration, however, especially the studies carried on by Dr. Gay and Dr. Chickering, have yielded results of great theoretical interest. By this method it has been possible to obtain the immune substances of the serum in a fluid containing an almost negligible amount of the other serum constituents. The preparation so formed also contains some of the bacterial substance, and may, therefore, be of value in stimulating active immunity. The therapeutic value of this preparation is not yet determined, but it is being tested in a small number of patients.

The attempt to produce a better serum by employing a different method of immunization of the horses seems at present to be more promising than the method of improving its quality by concentration. By injecting smaller animals daily with mixtures of immune serum and bacteria, better sera have been obtained than could be obtained by the old method. These results are similar to those obtained during the present year by Dr. Flexner and Dr. Amoss in the preparation of antimeningitis serum. The method has not yet been tried on horses, but it is planned to immunize horses according to this method during the coming winter and to test the serum so obtained on patients.

Optochin.- Experimental studies concerning optochin (ethylhydrocuprein) have been undertaken to determine whether,

by combining this drug with serum, the results would justify the employment of this combined method of treatment in the cases due to organisms of type II in which treatment with serum alone has not proved satisfactory. This drug is a derivative of quinine, was discovered by Professor Morgenroth, and has been employed in Germany in the treatment of a limited number of patients with pneumonia. Judging from the reports, the results obtained from treatment with this drug have been suggestive, but not striking. The drug, however, has been said to have a definite specific action on pneumococci, both in the animal body and in the test tube. To control these observations Dr. Moore has carried on studies of this drug, first in the laboratory of Dr. Flexner, and later in the laboratory of the Hospital. He has found that the drug has a definite specific bactericidal action for pneumococci in the test tube, and that when administered to infected animals it has a definite curative value. This curative effect is not very satisfactory, however, since the curative dose is very close to the toxic dose. When the treatment with this drug is combined with treatment with immune serum, the drug is able to increase the curative value of the serum, i.e. a more intense grade of infection can be successfully treated when the drug is combined with the serum than when the serum alone is employed. Dr. Moore has studied various preparations of the drug and has made us quite familiar with the effect of the drug, so that now we are prepared to go ahead and test its value in increasing the effectiveness of immune serum of type II in cases of infection due to organisms of type II, and it is planned to do this during the coming winter.

The pneumonia studies also have yielded other results which are at present of only theoretical importance, though it is hoped to make practical application of certain of them. In the investigation of the mode of action of the immune serum, for instance, Dr. Dochez and Dr. Avery have shown that the immune serum has a depressing action on the metabolic activities of the bacteria. This is one of the actions of immune serum which has been little studied, but which may be of considerable importance. They have named this form of activity "antiblastic." Dr. Chesney has made studies concerning the rate of growth of pneumococci and has investigated further the question of the so-called "bacterial lag", or the delayed growth which occurs when pneumococci are transplanted to new medium. These studies are still in progress, but results have already been obtained which may be of general biological significance. Observations have also been made which indicate that inflammatory exudates induced by pneumococci have an inhibiting effect on the action of immune serum. These studies are also in progress.

SYPHILIS.

It was hoped that before this time a complete report of the studies concerning syphilis of the central nervous system could have been published in the form of a monograph. The departure of Dr. Ellis for the war, however, and the fact that Dr. Swift severed his connection with the Institute staff, have necessitated a delay in its appearance. However, during the past year the patients previously treated have been under observation, either returning here to be studied by Dr. Stillman,

or being admitted to the Presbyterian Hospital for study by Dr. Swift. The study of these patients, therefore, when it does appear, will be more complete than would have been the case, had it been published a year ago. During the year, Dr. Swift had little time to devote to the preparation of the material, but during the summer he spent most of his time at this Hospital, getting the material ready for publication and it is hoped that the monograph may appear this fall.

The method of treatment of tabes by intraspinal injections of salvarsanized serum has been quite extensively employed elsewhere. Many of the observers have been enthusiastic as to its value; others have been doubtful. It is felt by those who have carried on and observed the work in this Hospital that the reason for the adverse opinions which have appeared has been that the method has been very inadequately and unwisely employed. Instead of employing the method as described here, many have employed modifications, which have rendered it impossible for the observers to judge of the value of the procedure. It has always been realized that the method was technically difficult, and that it was necessary to carry out the treatment over prolonged periods of time, in order to obtain results. When the method is rightly carried out, the experience here indicates that the method is of very great value in the treatment of locomotor ataxia. It is believed that the publication of the monograph will permit an accurate estimate of the exact value of the method, and furnish a reliable guide for those who undertake this form of treatment.

DIABETES.

In the report to the corporation one year ago, it was

stated that the work on diabetes had consisted mainly in experimental studies on dogs, carried out by Dr. Allen, and in the treatment of a limited number of patients along lines suggested by the experimental studies. During the past year the number of patients treated has been largely increased. The direct care of the patients has been mainly under the immediate supervision of Dr. Stillman, while Dr. Allen has devoted his time largely to the continuation of his experimental studies. The method of treatment introduced by Dr. Allen has received very wide attention by the medical profession, and is being widely employed. Among those men in this country who have had the largest experience in diabetes, and are best able to judge, the concensus of opinion is that an important contribution to the method of treatment of diabetes has been made. The only question that has been raised in regard to the method of treatment devised here is as to whether or not the principle upon which it is based is new. This is of little importance, however, since, through the studies that have been made and through the new facts determined, it has been possible to apply the principle in a way that has not been done before, and in a manner to greatly improve the treatment of persons suffering from this serious disease. The patients admitted to this Hospital for treatment have been only those of the most severe type, mainly young people and children, and the results obtained have been very satisfactory.

Dr. Allen has continued his study of experimental diabetes in dogs in an effort to learn more of the essential nature of the condition. The effects of cold, exercise, feeding, etc. on the utilization of sugar, both by normal and by depancreatized