

THE HOSPITAL OF THE ROCKEFELLER INSTITUTE
FOR MEDICAL RESEARCH,
66TH STREET AND AVENUE A, NEW YORK

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April 4, 1914.

To the Board of Scientific Directors
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 in the hospital during the past quarter:-

Pneumonia:

During the past quarter thirty-five patients suffering from pneumonia have been treated in the hospital. This is not as large a number as it was hoped might be admitted during this season. During the past week, owing probably to newspaper publicity, there has been a marked increase in the number of admissions.

The study of the type of organism concerned in each case has been continued, and it has been found quite possible and fairly easy to determine readily the type of organism concerned in the individual case. During the present winter, of the fifty cases treated, only about twenty percent have been caused by organisms of type I, while almost forty percent have been due to organisms of type II. Whether or not this indicates a greater prevalence of pneumonia due to this latter type of organism during the present winter in New York than during last winter, it is difficult to say from our limited experience.

Our previous experience in regard to the relative severity of the condition in cases due to the different types has been confirmed. The cases treated with the type I serum have all done well, and the experimental and clinical evidence indicates that this serum is of therapeutic value. The effect of the type II serum, however, has not been so satisfactory, since four of the patients fully treated with this serum have died. The results were difficult to understand until further study of the serum used showed that its protective power in animals was much lower than that of the serum employed last year. All of the type II serum used for treatment has been obtained from the first horse immunized and from which all the serum used for treatment last year was obtained. It is not known why this horse, which was previously able to yield a potent serum, now fails to do so, but

it is known that horses yielding anti-toxic sera and also those producing other anti-bacterial sera may gradually lose their power to produce effective sera. The reason why no other type II serum was available for treatment was because the second horse, whose immunization was commenced last summer, developed a chronic joint infection and had to be sent to the farm. We also now have another horse in process of immunization with organisms of type II, and also a horse which is being immunized to organisms of both type I and type II. The serum of this latter horse now shows protective power against both types of organisms as high in each case as we have ever found with a monovalent serum. This serum is now ready for use.

Dr. Avery has continued his efforts to concentrate the serum on a large scale, but so far without very satisfactory results. The experimental work has shown that the protective substances are largely contained in the euglobulin fraction, as obtained by the salting out method, and also are present in the so-called insoluble globulin precipitated from the diluted serum by carbon dioxide. However, it has been found so far that the loss of immune substances in filtering, etc., when these methods are employed on a large scale, is too great to justify their use. Modifications, however, are being made and it is hoped that a satisfactory method may be worked out.

Dr. Dochez and Dr. Avery have carried on studies concerning the various types of pneumococci in relation to the mode of infection and epidemiology of the disease.

Dr. Dochez is carrying on a comparative study of pneumococci present in the mouths of normal individuals. A large number of strains have so far been isolated from the mouths of fifteen normal individuals. In only one instance has an organism of the fixed types I, II or III, been isolated. In this instance an organism of type II was isolated from the mouth of the wife of a patient with pneumonia due to an organism of this type. Further work, of course, may show that these fixed types occur in normal mouths much more frequently than the results so far would indicate. Rabbits are being immunized to various strains isolated from normal mouths, in order to learn more of their antigenic properties.

Dr. Avery is studying the persistence of the pneumococci of the various types in the sputum of convalescents. The evidence so far indicates that the pneumococci of fixed types can usually be found in the mouth or sputum no longer than a few weeks after recovery. Later only organisms of the type found in normal mouths are present. It is of great importance to learn whether or not the organisms present in pneumonia are simply displaced by these latter organisms, or whether possibly

a transformation may have taken place. In order to aid in determining this point, the antigenic relationships of/a number of the organisms isolated during the disease, to those found in the same mouths after recovery, are being studied.

Dr. Avery is also studying the behavior of the various specific type strains of pneumococci in the different carbohydrate media.

Dr. Chickering has been studying the time of appearance and disappearance of agglutinins in the blood of patients suffering from pneumonia. In untreated cases the agglutinins appear only about the time of crisis, though in some cases they may be delayed until a later period. In the treated cases the agglutinins appear much earlier. The presence of agglutinins, therefore, is not of much value in determining the type of organism concerned, but the demonstration of agglutinins may be of some importance in prognosis. Furthermore, this study will offer confirmatory evidence of the etiological relationship of the type of organism isolated in the cases where the organisms are only obtained from the sputum.

Dr. Zacharias is about to undertake a study of the hydrogen ion concentration of the blood in pneumonia by the electrometric method. The relation of the reaction of the blood to its oxygen and carbonic acid content will be studied. The relation of the degree of acidosis indicated by the increased ammonia excretion in pneumonia will also be considered, in order to determine whether the acidosis indicated by urine analysis really corresponds to an increased acidity of the blood.

The study of the production of methaemoglobin by pneumococci has been continued, and also the study of the toxins produced by these organisms. It has been found that by freezing the pneumococci and drying in vacuum while frozen and then making up in salt solution, the resulting solution is toxic for guinea pigs, and the same effects are produced as by the injection of the bile extract. Further evidence has therefore been brought that the toxic substance is pre-formed in the bodies of the bacteria and set free upon their dissolution. The method also permits large amounts of toxin being obtained and preserved, so that experiments may be carried on from day to day with toxins of equal strength.

Diabetes:

The following is a verbatim copy of the report received from Dr. Allen. ~~in relation to his work.~~ While in certain instances Dr. Allen has allowed his

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which are possibly
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enthusiasm to lead him to draw conclusions, not yet fully justified, yet it is very evident that he has a definite and most interesting point of view. The results obtained in the one patient so far treated are most striking and very promising.

Report from Dr. Allen

Work has been continued along the paths previously outlined. The progress along a few of the principal lines may be summarized as follows:-

I. Production of Diabetes.

A. By simple removal of pancreatic tissue:- The results in a long series of dogs are constant. The newly observed relation between pancreas and body-weight also holds good, i.e., large dogs have less pancreas in proportion to body-weight than small dogs, and become diabetic from removal of a corresponding smaller fraction of the pancreas. Large cats, on the contrary, have as much pancreas in proportion to body-weight as small cats, and similar fractions must be removed in order to cause diabetes. The "apparent" sugar tolerance is not an index of susceptibility to diabetes. For example, large dogs normally have as high a sugar tolerance as small dogs. Monkeys have a low sugar tolerance, and in pigs the apparent tolerance is almost nil, as Carlson reported. But if one attempts to maintain a continuous glycosuria in these animals, the organism responds by assimilating even the largest quantities of sugar, thus illustrating the difference between apparent and real tolerance. Even after removal of seven-eighths of the pancreas, a pig now under observation takes 500 gms. glucose daily with only slight glycosuria; but the glycosuria is now continuous and increasing, and true diabetes will probably be the result in such a predisposed animal. Pressure of other work has thus far prevented a satisfactory series of experiments with partial pancreatectomy in species other than dogs and cats, though the monkey and pig promise to be highly important (especially for the problem of acidosis) when time can be devoted to them.

B. By diet:- It is now safely established that dogs and cats can be predisposed to diabetes by removal of suitable portions of pancreas, and that carbohydrate-rich diet will then act as an exciting cause of diabetes. When the pancreas remnant is of certain size, the animal is glycosuria-free on meat diet, but