

REPORT OF THE
DIRECTOR OF THE HOSPITAL
OF
THE ROCKEFELLER INSTITUTE FOR MEDICAL RESEARCH.

June 10, 1916

Since the last report the work in the hospital has
been chiefly in a continuation and completion of work stated in my last report to
show progress.

PNEUMONIA: The study of Dr Stillman in regard to epidemiology, some of the
results of which were given in our last report, is now about ready for publication. In
addition to the question of epidemiology an interesting study has recently been made
of a so-called house epidemic at Newburgh, N.Y. which was brought to our attention by
the State Board of Health. Dr Chickering went to Newburgh and obtained cultures from
a number of the patients and contacts. The family consisted of the father, mother and
four children, and a young baby. The mother was taken ill first and died. Following
her four children were taken down in succession. At the time of Dr Chickering's visit
two of these children were still ill and two were convalescent. Cultures were made from
all four children, from the father and from the woman caring for them. From the father
and two sick children, one of the convalescents and the nurse, pneumococci of Type I
were cultivated. The cultures from the other convalescent child were negative. These
findings seem very significant and suggest strongly the possibility of contagion in
pneumonia.

The study of Drs. Moore and Chickering in regard to optechin is also almost
ready to be published. This investigation has been important in determining the proper
dosage in order to confer upon the blood bactericidal power. So far the results of the
study indicate that bactericidal power of the blood gives a true indication of clinical
effect. Twenty-nine cases have now been studied, and among the eighteen receiving one
large dose followed by frequently repeated small ones only two have died, and one of
these received a dose which is now known to be too small, taking into account the patient's
body weight. The other patient was fairly well treated according to present standards
and the organism obtained at death proved to be relatively "fast". If the drug does
prove to be efficacious it seems that it will probably be because of this acquired

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fastness. By the present method it seems that in all cases the blood can be made bactericidal for pneumococci. A very recent case has been very instructive. The patient was an old man and there was difficulty in obtaining sputum. From the saliva a Type IV pneumococcus was cultivated. The patient was therefore given optochin and the dosage was correct according to our present conception. The patient, however, died. When the blood cultures were carefully studied, however, and also cultures made directly from the lung at the time of death, it was found that the infecting organism was not a pneumococcus but a streptococcus. The studies of the blood showed that it had acquired very prompt bactericidal power for pneumococcus, but, as is known, optochin has no effect on streptococci.

Studies concerning proper dosage of serum: At various times during the course of our work efforts have been made to devise methods which would enable us to determine the proper size and spacing of the doses of serum administered. Heretofore estimations of agglutinative power have not seemed to give much information, but lately the matter has been taken up again and very thorough studies are being made of the agglutination titre of the blood. The blood is being obtained very frequently both before and after the administration of serum. Those samples are all kept and at the end of the disease these samples are all studied under identical conditions and curves are made of the agglutination titre. In some cases it seems that there is too long a delay between the first and second dose. By studying a series of the treated cases in this way it is believed that the present methods of administration can be improved and the amount of serum used probably be reduced. One of our last cases received altogether 875 cc. of serum. The patient was an alcoholic, had very violent delirium, probably delirium tremens. We felt it inadvisable to stop the serum until we were quite sure that the pneumonic process was at an end. The patient has had severe serum sickness but is now quite well and, considering the severity of the disease, it is probable that the serum was life saving.

During the present season we have already had over 100 cases of pneumonia. Up to the first of June from the opening of the hospital 382 cases of pneumonia have

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been treated. Among the cases in which type has been determined, 112 were of Type I. Of these, 70 have been treated with serum, and of these 6 have died, a mortality rate of less than 9%. Of the six who died, two died of complications not of pneumococcal origin. Three were treated late in the disease, only on the day of death, and only one received serum treatment in a manner we now consider satisfactory. So far as serum treatment in pneumonia of Type I is concerned, therefore, we feel fairly safe in considering that it has a very definite therapeutic value.

Capsular substance: Dr. Dochez has been making a study of this question and his report is as follows:

From the study of the different groups of pneumococcus it has become apparent that there are differences in the amount of capsular development by the organisms of the four groups. The virulence of the group as measured in human beings is directly proportional to the degree of capsule formation. Group IV shows some irregularity in the capsule formation. Group I has a well-defined capsule; Group II forms a heavy capsule and Group III, in addition to a very voluminous capsule, gives rise to a large amount of mucoid material in the exudates which it causes in animals. The fact has been noted that Berkfeld filtrates of pneumococcus cultures which contain no bacterial bodies contain in solution considerable amounts of bacterial substance which is precipitable by specific immune serum. One would at first think that this specifically precipitable substance arises from the disintegration or autolysis of the bacteria themselves. This, however, can be shown not to be the case inasmuch as it is present in considerable amounts before measurable bacterial disintegration has occurred as determined by the presence of soluble haemolysin and from the character of the curve representing the rate of growth. The substance is present in the early hours of growth (at the end of four hours in cultures of type III) and is of undoubted bacterial origin because of its specific precipitability, and cannot be entirely due to bacterial autolysis. The amount formed and the rate of formation corresponds exactly to

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the degree of capsular development of the different groups. Type III gives rise to the largest amount and Type I to the least. In cultures of type III there is present at the end of nine hours an amount of soluble bacterial substance which is roughly comparable to the total amount of living bacteria in the same amount of culture. The greatest formation of the soluble bacterial substance seems to occur during the period of active growth of the bacteria. The substance can be demonstrated in both broth and serum broth cultures and also in the filtered blood of heavily infected animals. From the facts stated it seems unlikely that the soluble bacterial protein present in the early stages of pneumococcus cultures is due to disintegration of the organisms, but more probable that it is a produce of growth. The close relationship in amount formed to the degree of capsular development suggests that the capsular function is a continuous one, and that capsular material is continually formed and thrown off into the medium of environment.

DIABETES - Dr. Allen, Dr. Stillman and Dr. Fitz : - Rapid progress is being made in the preparation of the monograph for publication. The preparation of graphic charts of the cases treated is not far from completion and the data of the animal experiments are also being collected and tabulated.

About a dozen diabetic patients are kept in the hospital, under care of Dr. Fitz. In addition to observations of the relation of acetone bodies in blood and urine to the clinical condition, Dr. Fitz is now paying special attention to the renal permeability, finding marked variations from the normal to be frequent in severe diabetes. One patient lately showed entirely normal urine, while sugar, acetone bodies and fat were remarkably high in the blood, and the alkalinity of the blood was low. Sodium bicarbonate caused a sweeping out of both sugar and acetone bodies abundantly in the urine.

Animal experiments, which still continue, show that diabetic lipemia and diabetic acidosis can be regularly and positively reproduced in dogs. By varying the conditions, it is possible to cause animals to go into coma on mixed diet and also animals to go into coma on fasting. There are also indications that the var-

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changes of renal permeability can be reproduced in diabetic animals under controllable conditions.

CANCER - Dr. Murphy, Dr. Montgomery:

Nine cases have been treated and observed in the hospital up to date. These, with two exceptions, are breast cancers which have been incompletely operated on. Treatment has been started shortly after operation. From the point of view of the lymphocytic increase following small diffuse doses of X-rays the results have been satisfactory. Clinically, the cases, with one exception, have improved markedly in general health and none have so far shown recurrences. But as the oldest cases have gone only four or five months after operation we can draw no conclusions as yet. The exception to this general statement is a case complicated by heart and kidney disease with extensive metastasis to the liver and lungs. This woman died shortly after admission to the hospital. In order to determine what effect this non-penetrating diffuse dose of X-ray has on the spleen in man we have treated by this method a patient with lymphatic leukaemia having a very large spleen. In this case the doses were repeated at frequent intervals. The blood count on admission was 50,000, and after a number of treatments rapidly fell to about 18,000. The spleen, besides a slight softening and the disappearance of tenderness and pain, has not been affected perceptibly in size. Treatment with penetrating doses over the spleen is now being employed.

CARDIAC DISEASE - Dr. Cohn :

Since writing the last report, no additional problems have been undertaken. The experiments already reported concerning experimental cardiac hypertrophy are being continued.

The study dealing with the action of digitalis in pneumonia is about finished and was reported in brief in Washington before the Society for Experimental Medicine. It deals with the changes in the Q wave and in the P-R time in the electrocardiogram in pneumonia. A second paper, dealing with the cardiac irregularities in pneumonia is being prepared; it deals with the frequency (9.7%) of auricular flutter and fibrillation, the incidence and significance of the occurrence of ex-

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trasytolic irregularities, the occurrence of heart block, and certain alterations in the R wave in the curve, probably due to respiration and probably an exaggeration of usual alterations.

The collection of material for a third paper on digitalis dosage is almost concluded. As already reported, the problem is concerned with whether a large dose given in a small period of time (calculated on the basis of physiological (cat) units) is a satisfactory method of administration. From our observations, we believe that under these circumstances the digitalis is probably excreted in part, before a sufficient amount can be absorbed by the heart muscle.

The necessarily slow anatomical studies of hearts obtained in experiments and of others obtained from human autopsies are being continued. The latter include cases of bundle branch lesions, heart block, auricular fibrillation, and one of paroxysmal tachycardia.

NEPHRITIS, Dr. McLean : The study of the mechanism of urea retention in nephritis is being continued. In one patient the blood urea content has been varied from .200 to 2.500 grams per liter by changes in the nitrogen intake, without any symptoms, and without any significant change in the mode of excretion, the rate of excretion being parallel with the increased concentration in the blood.

Attempts to influence blood pressure in cases of hypertension, by varying the diet, have so far yielded negative results.

The study of chlorid excretion and the mechanism of its retention is being continued. In one patient with nephritic edema, not due to heart failure, salt feeding produced edema and salt retention without any change in the relation of the plasma chloride to the rate of excretion. It seems probable that salt retention and edema are rarely or never due to a primary inability of the kidneys to excrete salt, but to some cause which results in the retention of salt by the tissues.

CHEMICAL LABORATORY - Dr. Van Slyke : For the most part, the problems discussed in the April report are being continued along the same lines. The following advances may, however, be noted.

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Cullen and McLean are continuing work on the fate of protein digestion products, utilizing our recently perfected methods for determination of plasma proteins. They have as yet obtained negative results in looking for effects of protein digestion on fibrin, albumin, or globulin of the plasma. There is no evidence of the formation of any of the plasma proteins direct from absorbed digestion products. On the other hand, during the first two hours of digestion peptides as well as amino acids do appear to increase in the circulation, although after six hours only amino acids can be detected. It appears, therefore, that during the earlier stages of digestion it may be possible for some of the intermediate products of protein digestion to enter the circulation, although during the later stages only the amino acids do so.

The comparison of the proteins of human with those of cows' milk, begun by the chemical work of Dr. Vinograd-Villchur, has been broadened by the cooperation of Dr. Auer and Dr. Avery, who are comparing the respective caseins and albumins biologically. Dr. Auer is testing the identity of the cow and human proteins by means of the anaphylactic reaction, Dr. Avery by complement fixation.

For the further study of acidosis, especially in diabetes, we have been perfecting for use in further work a new method for the determination of B-oxybutyric acid in urine, former analyses being either time-consuming or too liable to subjective influence to trust for even approximate results in the hands of ordinary analysts. In the present method 2 to 10 cc. of urine are boiled for an hour in an Erlenmeyer flask under reflex condenser with a solution containing definite concentrations of sulfuric acid, mercuric sulfate, and potassium dichromate. The oxybutyric acid is oxidized by the dichromate to acetone, and simultaneously the acetone is precipitated as an insoluble mercuric sulfate compound, which at the end of the hour's boiling is filtered and weighed. The results are accurate, and the manipulations so few and simple that the danger of subjective error appears to be eliminated.