THE DEPARTMENT OF THE HOSPITAL

Dr. Rivers, Director

STUDIES ON PNEUMOCOCCI. THE CAUSATIVE AGENT OF LOBAR PNEUMONIA

Dr. Avery and associates.

Dr. Avery and his associates have continued their work on the transformation of one type pneumococcus to another. Results of previous work showed that the essential transforming substance is desoxyribonucleic acid. If, under proper conditions, desoxyribonucleic acid derived from a smooth Type III pneumococcus is added to a culture of a rough variant of Type I pneumococcus, this variant becomes a smooth Type III pneumococcus. In addition to the essential transforming agent, other factors are required for transformation. In last year's report was a description of work on the accessory factors. At that time it was stated that rough variants, in order to be transformed, had to be clumped either by agglutinating antibodies or by some physical means; that a dialyzable factor in serum is essential; and, finally, that a globulin factor, which may be obtained from serum or certain organs, is required.

Work on the accessory factors has been continued during the past year and it has been found that sodium pyrophosphate can act as the dialyzable factor and that the nondialyzable factor previously thought to be globulin is actually albumin. Evidence that it is albumin instead of globulin has been obtained by using exceedingly small amounts of crystalline albumin obtained by methods recently described by Cohn of Harvard. As little as 300 micrograms of purified serum albumin per cubic centimeter of culture medium can under the proper conditions be the decisive factor determining prompt and typical transformation.

The idea, previously mentioned, that globulin instead of albumin was one of the accessory factors for transformation can be explained in the following manner. Before testing human sera or serous fluids for their ability to support transformation, it was customary to subject them to heating (60°C. for 30 minutes) at their normal slightly alkaline reaction. This was done in order to inactivate a serum enzyme, desoxyribonuclease, which would otherwise depolymerize and thus destroy the transforming activity of the specific nucleic acid present in the transforming system. It is not necessary to heat purified serum albumin for this purpose, but when it is heated under these conditions, the protein becomes more readily precipitable at lower concentrations of salt. Accordingly, it appears not unlikely that the activity previously observed in globulin fractions of the serum may have been due to such altered albumin.

Pneumococci exhibit marked variability in colonial forms covering a wide range of differences in contour, morphology and surface topography. The colonial variants display all degrees of smoothness and roughness from the glistening mucoid to the extremely granular and pebbled-surfaced colony. These physical features are in many instances reflected in recognized differences in biochemical and physiological properties of the cells. Considerable information is available with regard to alterations in the antigenic structure, serological behavior and virulence associated with these colonial changes. It seemed possible to Dr. Avery and his associates that the principles and techniques of transformation might afford a specific means of investigating the hereditary basis of this phenomenon. Work along these lines has progressed favorably and findings to date are summarized in the next two paragraphs.

The property of extreme roughness (ER) as opposed to moderate

roughness (MR) is apparently due to the lack of a factor or factors which can be experimentally introduced into the cells by the techniques of transformation. The MR factor is present in the desoxyribonucleic acid fraction of the moderately rough variant and of smooth Type III organisms as well. The factor MR, which determines the change from extreme to moderate roughness, can be introduced independently of the SIII factor. Indeed, the ER forms cannot be transformed to encapsulated Type III organisms until they have first been converted into MR cells, that is, the MR factor must be introduced first, the reaction being ER→MR→SIII.

This form of analysis is being pursued with three objectives in mind. First, it is hoped that some information may be gained on the nature of "competence", that property of cells which determines their capacity to respond to a given specific stimulus or factor in transformation. Second, such experiments may make possible further analysis of the nature of the specificity of the transforming substances. Third, the demonstration that two factors, one for moderate roughness (MR), the other for synthesis of capsular polysaccharide (SIII), each coexisting in the same preparation of nucleic acid, can be selectively taken up by pneumococcal cells and independently bring about development of the corresponding traits, justifies the hope that the pneumococcal cell may prove a delicate tool for the study of many hereditary characters at a biological level heretofore unrealized by geneticists.

ACUTE AND CHRONIC DISORDERS OF THE LIVER

Dr. Hoagland and his associates.

As stated in previous reports, Navy patients with infectious hepatitis or epidemic jaundice were admitted to the Rockefeller Hospital for treatment and study. Mention was made in last year's report that