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Effect of Cortisone on the Serum Gamma-Globulin

Nicol and Snell[1] showed that cortisone depresses the phagocytic activity of the reticulo-endothelial system during the first two weeks of treatment, and that if the cortisone injections are continued the reticulo-endothelial system apparently recovers during the third and fourth weeks. Nicol and Bilbey[2] reported that cortisone also produces changes in the blood. They showed that when 10 mgm. of cortisone is given daily intramuscularly for one or two weeks, the total leucocyte count falls, due to reduction in the number of lymphocytes and polymorphs; but if the cortisone is continued for three or four weeks the total leucocyte count returns to normal, due to increase in the number of polymorphs, although the lymphocyte count remains low.

The present communication deals with the effect of cortisone on the antibody-level in the serum, the serum γ-globulin-level being taken as the measure of the antibody-level, since most antibodies are found in association with the γ-globulin fraction of the serum protein. In this investigation the γ-globulin-level was estimated by first separating the γ-globulin fraction by paper electrophoresis, then treating the electrophoretic paper with dyes and estimating the optical density of the protein dye complex by means of a photoelectric cell. In this manner the percentage of γ-globulin in relation to the total protein in the serum could be assessed.

Twelve male guinea pigs, aged about one year, were used for this investigation. Blood samples were first taken from each animal by heart puncture and the γ-globulin-level of normal serum estimated as described above. Each animal then received a daily dose of 10 mgm. of cortisone intramuscularly for five weeks, the blood samples were taken at weekly intervals and the γ-globulin-level of the serum estimated. More than forty estimations of this kind were made during the five weeks of cortisone treatment.

In all the animals the γ-globulin level became markedly reduced during the first two weeks of the cortisone injections and thereafter remained at a low level. In two of the animals, however, it increased slightly during the fourth and fifth weeks. These findings are in agreement with Bjørneboe, Fischel and Stoerk[3], who showed that cortisone inhibits the production of antibodies during active immunization and also after immunization is well established. They are also in line with the other blood changes recorded by Nicol and Bilbey[2]. Further, they emphasize the profound depression of the body defences produced by cortisone, and the great necessity to protect patients from intercurrent infection especially during the early stages of cortisone therapy.

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Action of Ribonuclease on the Multiplication of the Influenza Virus

Recent work of Ada and Perry[1] on the nucleic acid composition of influenza virus has shown that the infectious particles lack deoxyribonucleic acid, and that they contain about 0·8 per cent of ribonucleic acid. The degree of infectiveness is, in fact, a function of the ribonucleic acid content; the 'incomplete' form of the virus is characterized by a low infectivity/hæmagglutination ratio, and its ribonucleic acid content is lower than that of the standard form[2].

Indirect evidence for the importance of nucleic acid in the virus constitution is also given by the inactivation curve of virus infectivity by ultra-violet light; maximum effect is obtained[3] at a wave-length of 2652 A.

In the case of the tobacco mosaic virus, Casterman and Jeener[4] have observed a marked inhibition of synthesis of the virus by ribonuclease. The present work was undertaken with the hope of further defining the role of ribonucleic acid in virus growth, by studying the inhibitory action of ribonuclease on the multiplication of influenza virus.

Virus of strain *PR8* was cultivated in the allantoic cavity of the embryonated egg, or in test-tubes on a fragment of chorioallantoic membrane suspended in 1 ml. of diluted Hanks solution (method of Tamm *et al.*[5]). The hæmagglutinating power was assayed with chicken red-blood cells, by serial dilution of the culture medium. The infectivity was estimated by the method of Reed and Muench[6], after inoculation of embryonated eggs.

The enzymatic activity of the ribonuclease (G.B.I. or Armour) in the culture medium corresponded to concentrations of 0·1–0·7 mgm./ml. Tubes containing oxidized (inactive) ribonuclease served as controls. The following results have been obtained.

(1) The presence of ribonuclease in the culture medium inhibits completely the synthesis of the influenza virus cultivated on fragments of chorioallantoic membranes. In the controls, the hæmagglutinating titre rises regularly during incubation.

(2) Ribonuclease added to the culture medium at various times after introduction of the virus inhibits