plates were streaked at daily intervals for 4 days. Under these conditions, in occasional instances, it was possible to obtain typical III S colonies on plates streaked from cultures which had been incubated for 24 hours. In these experiments it was again impossible to demonstrate the occurrence of R forms during any phase of the transformation process. Furthermore the conditions provided were those most unfavorable for the development of R forms. However it is not possible to affirm that during the transformation the S organisms may not have passed through a phase comparable to the R form. In any case a new procedure for the transformation of pneumococcal types is presented.

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The Influence of Liver Extract and Acute Infection on Reticulocytes and Bone Marrow of Pigeons.

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The exact mechanism of the action of the potent material effective in pernicious anemia is still obscure. Certain facts are firmly established, however, such as the prompt reticulocyte response which this material induces, and that infection can inhibit this reaction to varying degrees. The potent material does not influence the peripheral blood of normal rats, rabbits, and dogs, nor, as a rule, does it effect anemias experimentally produced in these animals. However, pigeons seem to be peculiarly sensitive to the potent material. Relatively pure liver extracts injected intravenously, as well as commercial liver extracts fed by mouth, will cause a typical reticulocyte response in normal pigeons.[1] It has been tentatively suggested that this reaction is due to the partially megaloblastic type of bone marrow found in these birds.

To elucidate further the action of liver extract on the red blood cells in the bone marrow, and to obtain some possible explanation for the failure of an adequate reticulocyte response in pernicious anemia patients suffering from infections, the following experiments

[1]Vaughan, J. M., Muller, G. L., and Zetzel, L., *Brit. J. Exp. Path.*, 1930, **11**, 456.

have been carried out: Three groups of pigeons, kept under standard laboratory conditions, were given, (1) a *staphylococcus aureus* infection intramuscularly, (2) liver extract No. 343, (N.N.R.) by mouth, and (3) both infection and liver extract. Reticulocytes were followed in the peripheral blood, and, at various stages, tissues from the hematopoietic system were studied for any histological changes. The radial bone marrow was compared throughout, as this, as a rule, is mainly fatty, and extension and hyperactivity when present, is therefore more marked.

The *Staphylococcus aureus* was obtained from a fatal case of human septicemia. After infection, there was, in many animals, a drop in the reticulocytes from normal, about 10%, to about 5% or lower, the lowest level being obtained from the 3rd to the 5th day. There followed a gradual rise of reticulocytes to a maximum of 25 to 30% between the 12th and 17th day after infection. Twenty-four to 48 hours after infection, active mitosis was observed in the primitive red blood cells lining the sinuses of the bone marrow, as well as in the leucocyte series of cells; and in about 5 to 7 days the red blood cell centers had enlarged enormously, many of them consisting of conglomerations of megaloblasts, with numerous mitotic figures. At a later stage, with the increased number of reticulocytes in the peripheral blood, the white blood cell hyperplasia had subsided considerably, while the red blood cell centers were large and contained cells in various stages of maturity.

Normal pigeons fed liver extract showed the characteristic reticulocyte response.[1] The bone marrow obtained after feeding liver extract daily for 4, 7, 11, and 15 days showed no extension of the hematopoietic tissue. The megaloblasts, however, were diminished in number. There was a decrease of hematopoietic activity and of number of mitotic figures. The red blood cell centers were smaller than normal, and most of the cells were in the late erythroblastic and normoblastic stage.

In the third group of birds the infection was superimposed after 3 to 7 days' administration of liver extract. The results in this group were, as was to be expected, somewhat mixed; but both in the peripheral blood and in the bone marrow, the reaction to the infection, as described above, seemed to predominate.

It therefore seems as if the physiological results on the hematopoietic organs from infection is the opposite of the effect of liver extract. Thus, acute infection in pigeons can produce a bone marrow analogous to the one seen in pernicious anemia, *i. e.*, with red blood cell hyperplasia, while liver extract given pigeons produces a picture very similar to the one observed in patients with pernicious anemia after the administration of liver (Peabody[2]). Whether chronic infection acts in the same manner as acute infection is being investigated.

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Reticulocyte Response to Glutamic Acid in Pernicious Anemia.

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The clinical trial of glutamic acid in cases of pernicious anemia as an antianemic substance was suggested by the following experimental observations. According to Abderhalden[1] glutamic acid may be condensed into pyrrolidonecarboxylic acid. Hemin, the iron porphyrin, synthesized by Hans Fischer[2] is composed of pyrrole rings. West, Howe and Dakin[3] have recently isolated substances from liver tissue which are exceedingly active in pernicious anemia. These substances, identified by them as B-hydroxy-glutamic acid, δ-hydroxyproline, and as a tri-basic acid containing the pyrrolidone ring, are potential pyrrole percursors. More recently, Drabkin[4, 5] and Miller[4] found glutamic acid and certain other amino acids and compounds effective in the treatment of the anemia of rats caused by an exclusive milk diet.

Those substances which produce remissions in the blood picture of pernicious anemia, known to contain potential pyrrole percursors, are probably liberated from certain protein foods by normal gastric digestion[6] and then decomposed so that their products are available after absorption for the synthesis of hemoglobin and erythrocyte stroma. In pernicious anemia the necessary substances and their de-

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1 Abderhalden, E., and Kautzsch, K., *Z. f. physiol. Chem.*, 1910, **68**, 487.

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