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THE SPLEEN

AND RED CELL DESTRUCTION

Studies in man of:

(a) the role of the spleen in the uptake of red cells altered by heat treatment and by treatment with a sulphydryl inhibitor;

(b) the use of such cells in the measurement of splenic sequestering function;

(c) the effect of noradrenaline on the splenic sequestration of red cells.

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In this study answers were sought to certain questions pertaining to the destruction of red cells by the spleen in man. These problems and the conclusions reached are broadly summarized below.

Do erythrocytes sequestered by the spleen manifest either a constant morphological appearance or a constant alteration in osmotic fragility? The investigations performed using heat or sulphydryl inhibition as the means of inducing red cell change establish that no such simple relationship exists. The spherocytic less fragile cells produced by heat treatment and the discoid less fragile type resulting from sulphydryl inhibition are, like the fragile spherocytic cells of hereditary spherocytosis, trapped in the spleen. Therefore a more subtle alteration in the erythrocyte membrane is probably the governing factor. Although red cell agglutination may predispose to hepatic trapping a similar less obvious surface change is probably operative when the liver is the major site of sequestration. As the heated spherocyte is more, and not less, resistant to osmotic rupture these studies also highlight the fact that erythrocyte morphology cannot be predicted merely from an examination of cellular osmotic fragility. With respect to the anaemia in cases of severe burns, it is suggested that erythrocytes are damaged at the site of thermal injury and subsequently trapped in the organs of the reticulo-endothelial system. This sequence probably accounts for the fall in haemoglobin in such instances.

Is it possible to measure the sequestering function of the spleen by studying the clearance rate of slightly altered erythrocytes? These investigations show that this is indeed possible using cells treated with a sulphydryl inhibitor though an accurate quantitation is not possible if heat damaged erythrocytes are utilized. With the former preparation the normal uptake function of the spleen has been delineated and it is shown that, whereas in most cases splenomegaly is associated with an increase in this parameter, in some cases, most strikingly in the condition of myelofibrosis, an enlarged spleen may be one with a reduced red cell sequestering function. Also even when increased this is not directly related to splenic size alone. The liver may in some cases manifest a "spleen-like" action and remove a proportion of the mildly damaged cells but the hepatic alteration in such cases is not merely brought about by an increase in the size of the organ, for in several instances hepatomegaly is not accompanied by the trapping of the cellular reagent. Results in this section relating to the dose of cells administered to the rate of splenic uptake in normal subjects show that with volumes up to 0.073 ml. red cells per kilogram body weight, there is no decline in the sequestering ability of the spleen. Therefore the immediate uptake capacity of the spleen is in excess of this quantity and larger volumes of such cells would have to be used to define the maximal phagocytic capabilities of the organ.

Can the measurement of splenic sequestration by such means be used to predict the value of splenectomy in subjects with haemolytic disease? There is no correlation between the life span of altered cells and that of autologous untreated cells in a particular subject and therefore the former preparation cannot be used to establish the presence of haemolysis. However the sites of sequestration of the two cellular preparations do correspond and the results in the cases reported make it likely that such an investigation may permit one to detect the major site of red cell destruction in a haemolytic state and predict more accurately the outcome of splenectomy.

In what way do corticosteroid hormones affect splenic sequestering function? The present investigations establish that these agents reduce the uptake capacity of the spleen for altered red cells. Though other actions of such steroids were not studied it is suggested that at least part of the benefit in patients with haemolytic disease is due to this role in depressing the ability of the reticulo-endothelial system to remove abnormal cells.

Are abnormal cells, when taken up in the spleen, retained in a "pool" from which they can be expelled by vasoconstrictor agents? It is conclusively demonstrated that the infusion of a vasoconstrictor, noradrenaline, does not prevent the splenic uptake of abnormal cells which are normally sequestered in this organ. Also though "pooling"

of untreated cells may take place in some cases associated with splenomegaly, abnormal cells are not trapped in such a compartment in the normal subject. Once taken up by the spleen the subsequent injection of noradrenaline will not bring about their reappearance in the general circulation.

This summary embraces the areas of the present study where it is believed a contribution has been made to present knowledge. As outlined previously certain problems raised in the course of the investigation are still unsolved. Amongst these are the ultimate nature of the erythrocyte surface changes governing organ selection of cells, the nature of the splenic and hepatic alterations that bring about enhanced sequestration, the magnitude of the maximal uptake capacity of the spleen as well as confirmation of the reliability in predicting the value of splenectomy by the study of the site of uptake of altered cells. It is hoped that there will be an opportunity to further study some of these problems in the future.