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Acute Splenic Tumor Produced by Non-Bacterial Antigens.

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It is well known that during the course of bacterial infections the spleen undergoes a change designated by the term "acute splenic tumor". The significance of this change has never been clearly understood. The essential microscopic characteristic of the condition is an increase in mononuclear cells which have not the appearance of ordinary lymphocytes. These cells appear first in the margins of the Malpighian bodies and spread throughout the pulp in advanced cases. Some are definitely plasma cells, but the majority have large vesicular nuclei and abundant basophilic cytoplasm, and there has never been any general agreement as to their nature or function. Some have described them as macrophages, some as lymphoblastic cells, but most writers have regarded them as young myeloid cells and have interpreted their presence as representing an activity of the spleen in the manufacture of granulocytes under the stimulus of the infection.

Although young myeloid cells may be found in the spleen (as in the blood) in bacterial infections, and although myeloid cell formation may undoubtedly occur in the spleen during the course of some infections, no acceptable evidence has ever been brought forth that the great body of newly formed mononuclear cells characteristic of acute splenic tumor are myeloid cells. They are non-granular cells, and the writer has never been able to observe any indication of their transformation into granulocytes. In view of the large amount of evidence that the spleen plays an important rôle in antibody production, and since acute splenic tumor and antibody production are factors that are common to bacterial infections of widely different nature, it has been suggested from time to time that acute splenic tumor may be an expression of the formation of protective substances active against the infecting bacteria and their products. Since experiments with bacteria and toxins introduce a variety of complicating factors, the present experiments were carried out to determine whether the essential characteristics of acute splenic tumor could be produced simply by inciting the formation of antibody in the absence of bacterial infection or bacterial substances or products.

Several investigators have examined the spleen histologically dur-

ing the course of experiments in which non-bacterial foreign protein was injected for various purposes but, so far as the writer is aware, none of the descriptions of the splenic changes following the injection of foreign protein can be clearly interpreted as a reproduction of those occurring in acute splenic tumor. Thus Cantacuzène's description of the cellular alterations that he observed[1] is totally different from that in acute splenic tumor; Epstein[2] observed various changes in the Malpighian bodies but described neither the production of the specific basophilic mononuclear cells nor any alteration of the pulp; Kuczynski[3] does describe "lymphoblastic" cells in the spleen of mice injected with or fed upon foreign protein, but the untreated mouse's spleen contains these cells to such a degree that in its normal state it resembles an acute splenic tumor. None of the above investigators studied the spleen from the standpoint of a comparison with acute splenic tumor.

In the present experiments, rabbits of approximately equal weight were used as the experimental animals, and sterile egg white, horse serum, dog serum or guinea pig serum as the antigen. Antibody formation was stimulated by (1) a single intravenous injection of 5.0 cc. or 10.0 cc. of antigen; (2) repeated intravenous injections of 1.0 cc. of antigen; (3) repeated intracutaneous and subcutaneous injections of 0.2 cc. to 1.0 cc. of antigen until sensitization of the Arthus phenomenon type was established.

Fourteen test rabbits and 14 controls were used in the experiments. Half were treated by intravenous injection and half by subcutaneous and intracutaneous injection. As a control for each animal that was injected with serum a rabbit of the same weight was injected in the same manner with normal salt solution. Test and control animals were killed at intervals ranging from 3 days to several weeks after the first injection but always within 3 days of the last injection. The temperatures of all the animals taken just before and the day following each injection remained within normal limits, and no intercurrent infection was found in any case at autopsy.

At autopsy, the average weight of the spleens of the animals in which antibody formation had been induced was 60% greater than that of the spleens of the controls, and the microscopic appearance of the spleens of all of the animals that received foreign protein was strikingly different from that of the spleens of the controls. In the

[1] Cantacuzène, J., *Ann. Inst. Past.*, 1908, **22**, 54.

[2] Epstein, E., *Virch. Arch.*, 1929, **273**, 89.

[3] Kuczynski, M. H., *Virch. Arch.*, 1922, **239**, 185.

test animals killed during the first few days there was a marked mitotic proliferation and enlargement of the mononuclear cells in the marginal zones of the Malpighian bodies. The nuclei became greatly enlarged and the cells developed an abundant basophilic cytoplasm and became identical in appearance with the specific large mononuclear cells of the acute splenic tumor of infection. There was no suggestion of a transformation of these cells into granulocytes in any of the animals. A precisely similar change constitutes the early stage of the acute splenic tumor occurring in bacterial infections. As the process advances, the specific mononuclear cells spread out into the pulp of the spleen of the antibody-forming rabbits precisely as in the acute splenic tumor of infection, and the histological picture becomes quite like that in a well developed acute splenic tumor.

Details of further studies dealing with the nature and characteristics of the specific cells as revealed by vital stains and motion pictures of tissue cultures, with the relation between the antibody titre and the degree of proliferation of these cells, with the lack of correlation between this reaction and granulocyte production in the spleen, and with a similar mononuclear cell reaction occurring in lymph nodes during infection and antibody formation will be presented in a separate report, together with a consideration of the literature. Here it is desired to point out only that the stimulus of foreign protein, uncomplicated by bacterial infection or bacterial substances or products, suffices to incite the specific mononuclear cell reaction characteristic of acute splenic tumor.

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Glycogen Formation After Various Fatty Acids.

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The transformation of the even-chained fatty acids into the acetone bodies has been demonstrated to be a quantitative one.[1] It was shown that such odd-chained fatty acids as propionic, valeric and heptoic did not give rise to appreciable amounts of the acetone

[1] Butts, J. S., Cutler, C. H., Hallman, Lois, and Deuel, H. J., Jr., *J. Biol. Chem.*, 1935, **109**, 597.