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A Function for Tissue Mast Cells

Abstract. Experimental elimination of mast cells from the peritoneal tissues of the rat by distilled water treatment inhibited the increase of vascular permeability which normally follows a passively induced antigen-antibody reaction in peritoneal tissue. Thus mast cells may contribute to the initiation of inflammation which follows antigen-antibody reactions.

The tissue mast cells have been shown to contain histamine, 5-hydroxytryptamine, heparin, and hyaluronic acid—substances having significant physiological action (*1*). However, functions for the tissue mast cells have not been demonstrated clearly. Information concerning their function should be obtainable by determining whether phenomena conceivably controlled or influenced by the mast cells in normal tissues are altered in tissues made substantially free of mast cells. This report is concerned with such an approach which uses the alterations in the permeability of blood vessels that have been observed to follow antigen-antibody reactions in tissue (*2*).

The serous tissues of the peritoneal cavity of Sprague-Dawley rats weighing about 150 g were studied. The mast cells of these tissues were destroyed by the intraperitoneal injection of 20 ml of distilled water. This treatment causes the immediate disruption of mast cells, the debris of which is phagocytized during the next 3 to 5 days. Thereupon the serous tissues of the peritoneal cavity are quite normal in appearance except that they lack mast cells (*3*). The effects of antigen-antibody reactions on vascular permeability as determined by the method outlined by Ovary (*4*) in normal rats (having an intact mast cell population in the serous tissues of the peritoneal cavity) were compared with rats treated with distilled water 3 to 8 days previously. In these tests, a dilution of antiserum (rabbit anti-egg albumin) was injected intraperitoneally in volumes of 1 or 5 ml. (No estimates were made of the activity of the antiserum in terms of antibody N per milliliter.) This was followed 3 hours later by the intravenous injection of 10 mg of crystallized egg albumin in 1.0 or 1.5 ml of a 1-percent solution of Evans Blue dye in 0.9-percent sodium chloride. The animals were killed 15 to 20 minutes later by ether anesthesia, and the peritoneal tissues were washed free of exudate with water and examined for leakage of the dye into the perivascular spaces. Corresponding dilutions of normal rabbit serum were used as the control for the antiserum. An arbitrary grading system was employed for visual evaluation of the degree of coloration of the tissues against a background of white cardboard. The notations 0 and 1+ to 4+ were used to cover the observed range of dye leakage.

The mesentery and parietal peritoneum had a 2+ or greater coloration in normal rats treated with rabbit anti-egg albumin serum and egg albumin. This coloration was markedly attenuated (1+) or absent (0) in rats receiving the antibody, antigen, and dye but previously treated with distilled water. No extravascular blue coloration was seen in these tissues in either normal or water-pretreated animals into which normal rabbit serum was injected instead of the antiserum. These observations are summarized in Table 1.

Table 1. Effect of distilled water pretreatment on the leakage of dye following an egg albumin–rabbit anti-egg albumin reaction in the peritoneal tissues of the rat.

Treatment	Rats (No.)	Degree of coloration (No. of rats)				
		0	1+	2+	3+	4+
Distilled water, antiserum	18	10	8			
Distilled water, normal serum	11	11				
Antiserum only	20			3	3	14
Normal serum	13	13				

* All animals received a subsequent intravenous injection of egg albumin and dye.

Substantially the same results were obtained when the skin was used as the site of the antigen-antibody reaction, the mast cells having been previously destroyed by the local intradermal injection of distilled water. Four to six animals were included in each experimental group in individual experiments. The above findings have appeared consistently in six repetitions of the experiment. Preliminary experiments suggest that results similar to, though less striking than those described above, may be found in rats in which mast cell destruction has been effected by the injection of antimast cell serum prepared in rabbits (*5*) or by repeated administration of the histamine liberator, compound 48/80.

We interpret the findings of the experiments reported here to indicate that the increased permeabiliy accompanying the antigen-antibody reaction depends, in part at least, upon the presence of the tissue mast cell, the release of its histamine or 5-hydroxytryptamine, or of both, being directly responsible for the alteration in permeability. The mechanism by which the release of these substances is brought about is not clear. It is known from previous experiments, however, that mast cells disrupt and release their granules into the surrounding tissue in passive anaphylaxis (*6*), and recently, Archer (*7*) has reported that a heat-labile substance is formed during an antigen-antibody reaction which causes the disruption of rat mast cells in vitro. That mast cells may initiate inflammatory processes following other tissue injury in rats is suggested by Sheldon and Bauer (*8*). The present results indicate that the mast cells may be of primary importance in initiating the inflammatory response accompanying antigen-antibody reactions (*9*).

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