RHEUMATOID ARTHRITIS — AUTO-IMMUNE-DISEASE

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The timely release of the glucocorticosteroids by the adrenal cortex in response to an inflammatory agent is an essential key in understanding inflammation. These initial experiments have led us to propose the existence of a neuroendocrine control of inflammation. Ultimately these studies are leading the way for the development of new therapies in treating inflammatory-related diseases [1].

If there is a neuroendocrine control mechanism of inflammation, there should be a glucocorticosteroid response to an inflammatory agent. Consequently, the concentration of corticosterone was measured in rat blood plasma after an injection of carrageenan into the rat's paw. Corticosterone is the principal glucocorticosteroid in rats. The steroid concentration was measured using radioimmunoassay (RIA) [2].

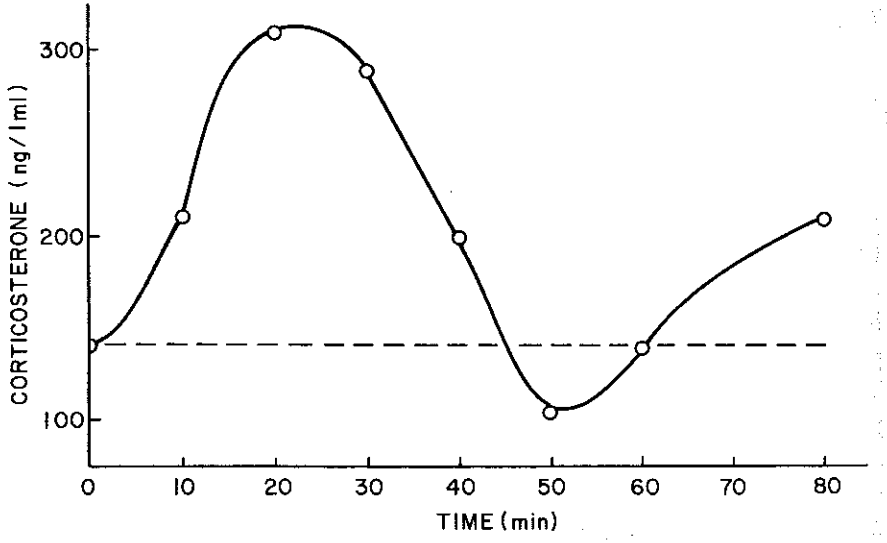

Figure 1. Corticosterone Concentration in Rat Blood Plasma Caused by Carrageenan.

A volume of 0.1 ml of carrageenan solution was injected into normal rats (32) Male Sprage Dawley Hap:(SD)f rats, weighing 220 to 250 grams. Each rat was anethesized. Blood samples were taken from the heart and collected with heprinized equipment. To remove the red blood cells, the samples were centrifuged and then frozen until use. The samples corresponding to the same elapsed time after injection of carrageenan were pooled. The pooled samples were diluted and run through the radioimmunoassay. The concentration of corticosterone versus time elapsed after carrageenan injection was plotted (Fig. 1). The data is consistent with the hypothesis of the neuroendocrine system controlling the inflammatory response.

From earlier data, the carrageenan-induced inflammation in hypophysectomized rats was more intense and persistent than in control rats. Although the hypophysectomized rats would not be affected by the stress of handling for lengthy periods of time, the control rat might (Fig. 2). If this stress were eliminated, the curve of the control rats might look more like that of the hypophysectomized rats.

The paw volume of control rats (37) were measured with a plethysmograph [3,4]. Each rat was injected in the right hind paw

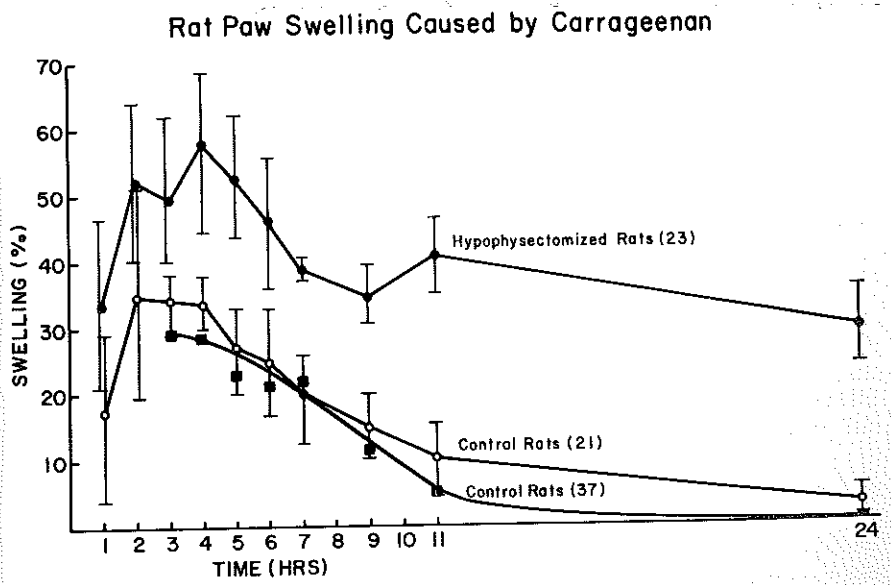

Figure 2. Rat Paw Swelling Caused by Carrageenan.

with a 0.1 cc aliquot of a 1% suspension of carrageenan in a 0.85% saline solution. After a specific duration of time, each rat was measured only once more with the plethysomograph. The average percent increase in paw volume was graphed with the actual range of values shown (Fig. 2). Thus, the original data was validated and hypophysectomized rats do indeed swell more intensely and for a longer duration of time to a carrageenan injection than control rats do.

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