Effect of Cortisone on Serum Non-Specific Hyaluronidase Inhibitor Following Surgical Trauma. (18780)

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Investigators have recognized for some time the fact that the serum non-specific hyaluronidase inhibitor is elevated in many pathological and pathophysiological states. This elevation of the inhibitor has been observed in experimental animals following trauma(1,2) and in patients with active rheumatic fever(3), acute lupus erythematosus (4), and certain neoplastic lesions(5). When ACTH and cortisone were added to the therapeutic armamentarium for the treatment of some of the so-called "collagen diseases", it became of interest to determine what alteration might occur in the serum hyaluronidase inhibitor in patients with elevated inhibitor values undergoing treatment with ACTH or cortisone. Recently Adams and co-workers (6) submitted data which demonstrated a fall in the serum nonspecific hyaluronidase inhibitor in patients with active rheumatic fever receiving ACTH therapy. The decrease in the titer of the serum inhibitor paralleled the clinical improvement observed in these patients.

It was the purpose of the experimental work reported in this paper to determine if the elevation of the serum non-specific hyaluronidase inhibitor noted in animals following wounding was modified by cortisone administration. That a possible interaction between cortisone and the inhibitor might exist in wounding is suggested by the work of Ragan *et al.*(7) who observed a suppression of granulation tissue in healing wounds when cortisone was administered in large doses although aseptic surgical wounds healing per primam are apparently little affected when amounts of cortisone commensurate with those used in humans are employed(8-10).

Method. Healthy mongrel dogs were used throughout the experiment. They received a standard kennel ration. Four animals received cortisone and 3 served as controls. The cortisone was administered subcutaneously beginning one day prior to wounding and daily until the twentieth day following the initial surgical incisions. The dosage of cortisone was 2 mg per kilo of body weight. The wounds were made under aseptic conditions on the animal's back under intravenous nembutal. They consisted of linear incisions carried down through all tissue layers to the periosteum of the ribs and were sutured with interrupted No. 40 cotton sutures. Wounding was repeated on the third, seventh, and tenth day following the initial trauma. Blood samples were drawn prior to the initial wounding for determination of the serum inhibitor and 3 times each week thereafter during the period of experimental observation. The blood was taken from the external jugular vein and placed in sterile tubes and allowed to clot. The blood was then centrifuged and the serum decanted into sterile tubes and stored at −20°C until the determination of the inhibitor titers was

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made. Freezing of the samples until a complete series can be run has the advantage of doing the determinations of the various samples with the same hyaluronic acid substrate and the same enzyme solution, thereby avoiding day to day changes in concentration which may occur with storage of these solutions. Determination of the serum inhibitor was made viscosimetrically using the method of Hadidian(11) with minor modifications. All determinations were made employing the Ostwald type viscosimeter with a flow time of 25 seconds for 4 ml of distilled water and carried out in a constant temperature water bath at 25°C ± .05°C. Care was exercised to suspend the viscosimeter in the water bath in the same position for all readings. 0.1 ml of serum was used for the determinations. The serum non-specific hyaluronidase inhibitor values were expressed as per cent inhibition using the formula suggested by Wattenberg and Glick(12).

Results. The serum inhibitor values in the cortisone treated animals and the control animals showed a similar response to the repeated trauma varying only slightly in degree. The serum inhibitor increased postoperatively to a peak value which occurred between the seventh and twelfth day following the initial trauma and fell to pre-operative values between the seventeenth and twentieth postoperative day. (Fig. 1). An exception arose in the case of a control animal in which the titer remained elevated above the normal range on the twentieth day of the experiment.

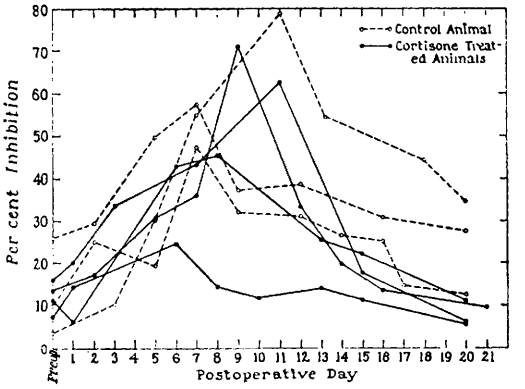

FIG. 1. Graph demonstrating per cent inhibition of hyaluronidase activity by serum of experimental and control animals during postoperative state.

One of the animals receiving cortisone showed a similar rise in the inhibitor following surgery but the level, although significantly elevated, did not attain the height observed in other experimental or control animals. Failure of cortisone to alter the inhibitor has been similarly observed by Glick(13).

Summary. Following repeated wounding of healthy mongrel dogs there is a rise in the titer of the serum non-specific hyaluronidase inhibitor which tends to return to normal preoperative values as healing occurs. This response of the inhibitor is unaltered by the administration of cortisone under the conditions of this experiment.

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