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Effect of ACTH upon Artificially Induced Trichinosis in Rats with Special Reference to Eosinophilia. (21170)

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A few reports have recently been published dealing with the therapeutic possibilities of ACTH and Cortisone in the treatment of trichinosis. To study the problem further under controlled experimental conditions, it was deemed advisable to determine the effects of ACTH upon the course of an artificially induced Trichina infection in rats. Such an experiment afforded an opportunity to study the tissue reactions to the parasite in different sites in both treated and untreated animals. The magnitude of the effect of ACTH upon an artificially induced eosinophilia could also be determined(1).

As early as 1904, Opie(2), had described the peripheral blood leucocytosis with both relative and absolute increases of eosinophils and neutrophils in trichinosis in guinea pigs. He also noted myelocytic hyperplasia of the bone marrow and neutrophilic, eosinophilic, and lymphocytic tissue infiltration due to the encysted larvae in muscle(3,4). Luongo(5), *et al.*, reported the use of ACTH for cases of trichinosis in humans. In patients so treated there was observed a diminution in fever, loss of muscle pain, and a striking reduction of other subjective symptoms. Also reported in the same paper were observations on guinea pigs experimentally infected with *Trichina spiralis* and treated with ACTH. A drop in circulating eosinophils and a reduction in fever were reported, but the authors were unable to demonstrate any modification of the inflammatory response.

During our study a paper by Stoner and Godwin(6) appeared in which the effects of ACTH and Cortisone upon the susceptibility to trichinosis in mice was described. They found that these drugs increased the susceptibility of mice to trichinosis, but did not alter the course of the disease or the mortality to a lethal dose of Trichina. In these mice there was no significant change in the degree or type of inflammatory response in treated or untreated animals.

Experimental. Twenty young adult white male rats (Sprague-Dawley strain) weighing on the average from 60 to 80 g were used because of their susceptibility to trichinosis as well as the availability of blood for study. The animals were separated into 4 groups

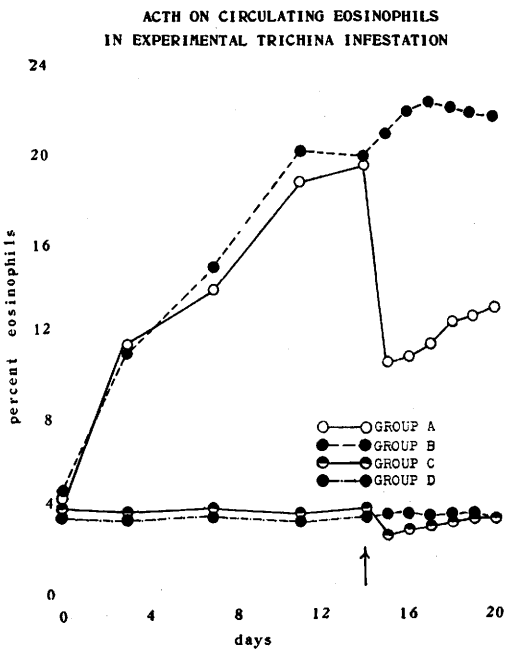

FIG. 1.

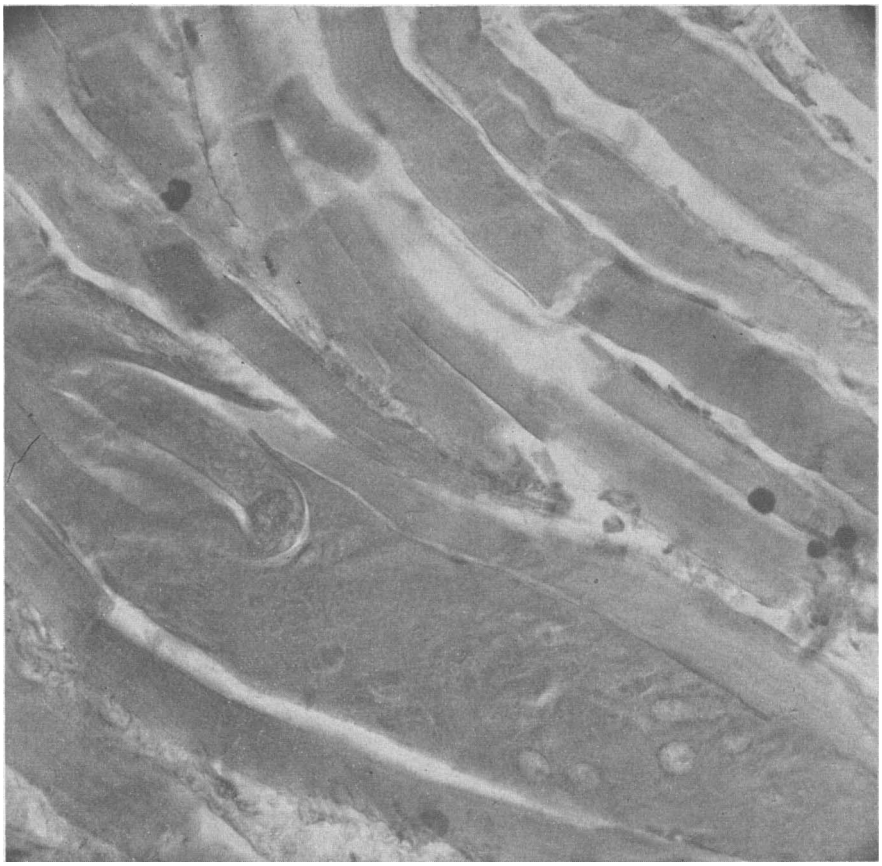

FIG. 2. 600×. Encysted larvae in striated muscle of rats treated with ACTH for 3-4 days.

(A,B,C, and D) with 5 rats in each group. Group A was infected with encysted Trichina larvae and treated with daily subcutaneous injections of ACTH (12.5 mg/day) from the 14th day of infestation until the 20th day. After the 15th day one animal was killed daily. Group B was infected with trichina and treated with daily subcutaneous injections of physiological saline from the 14th day of infestation and sacrificed at similar days as those of group A. The animals of groups C and D were not infected but on days of treatment corresponding to those given above for groups A and B, the rats of group C received ACTH alone and group D physiological saline. The rats were infected in the following manner. Infected rat muscle was fed to the animals following a 24 hour period of starvation. This infected muscle was assayed by counting the larvae in weighed samples and on this basis 3000 larvae were fed to each rat(7).

The course of the disease and the host response was followed by means of total white cell and eosinophil counts made on the 3rd, 7th, 11th, and 14th day of infestation, at which time treatment was instituted and thereafter counts were made every day until the rats were killed. Phloxine stain was used as a diluting fluid for the total eosinophil counts and proved most satisfactory in enhancing the recognition of eosinophils(8).

Histological preparations were made of the following tissues: the diaphragm, intercostal, and femoral muscles; bone marrow; liver; spleen; heart; intestine; and adrenal glands. The tissues were stained with hematoxylin-eosin except for the bone marrow which was stained by the Kingsley method.

Results. Gross observation of the animals

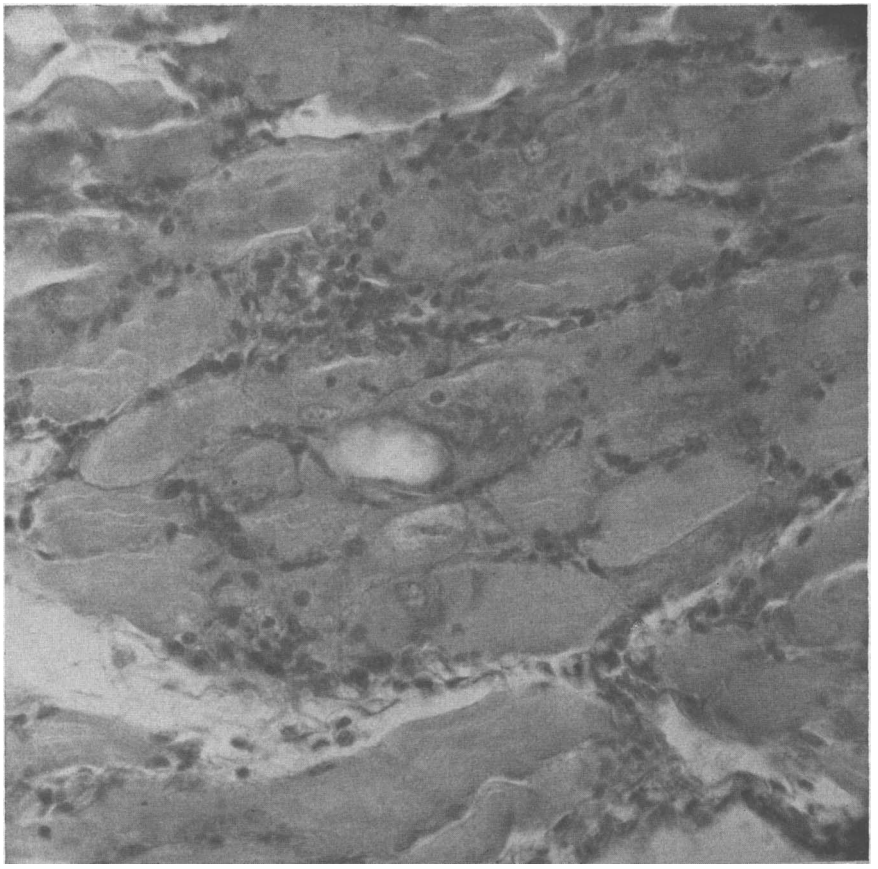

FIG. 3. 600×. Encysted larvae in striated muscle of rats which were untreated (physiological saline).

in the intestinal phase of the disease disclosed marked illness in the infected rats. The signs, although varying in intensity from animal to animal were marked weight loss, diarrhea, anorexia, and greatly reduced physical activity. The gastrointestinal signs decreased during the course of the infestation, but the reduced physical activity was progressive in all infected groups.

In group A the rise in eosinophils was constant and approximated that of group B until treatment was instituted on the fourteenth day (Fig. 1). The daily injections of ACTH had a profound effect on circulating eosinophils for animals of group A. Two distinct phases of the effect of ACTH on circulating eosinophils were demonstrated. The first or sensitive phase is from the 14th to the 17th day of infestation. During this phase there was a precipitous drop in circulating eosinophils from 19.4% to 10.5%. The second or resistant phase is from the 17th to the 20th day. This phase shows the rise in eosinophils even though the remaining animals of this group were still receiving ACTH. Histological sections of striated muscle from this group revealed the typical picture of encysted larvae in muscle of rats treated with ACTH for 3-4 days (Fig. 2). The inflammatory response of animals treated for only 3-4 days has been reduced in comparison to the response in rats treated for 5-7 days, and appears considerably reduced when compared to the response in the untreated animals of group B (Fig. 3). Sections of bone marrow from animals treated with ACTH for 3-4 days showed a myelocytic hyperplasia with great numbers of eosinophils and megakaryocytes

which is somewhat less than that in rats treated for 5-7 days and considerably less than that seen in untreated infected animals. Hyperplasia of the spleen and lymph nodes was noted in both the treated and untreated animals and treatment with ACTH seemed to have no modifying effect.

In group B the rise in eosinophils (Fig. 1) is typical of that found in untreated trichinosis. The injections of physiological saline from the 14th to the 20th day, as might be expected, had no effect on the circulating eosinophils. The normal response of eosinophils to ACTH in a normal animal is illustrated in the curve of group C (Fig. 1). In group D the graph illustrates the normal day to day variation in eosinophils which showed no change with physiological saline injections.

Conclusions. 1. The marked eosinophilia due to an experimental Trichina infection was greatly depressed but not abolished when ACTH was administered for short intervals. 2. The effects of ACTH in animals with artificially induced trichinosis were exhibited by (a) alterations of the inflammatory response to encysted larvae, (b) alterations in the bone marrow, and (c) the changes in the level of circulating eosinophils. 3. Although modification of the host response to Trichina infestation was obtained with ACTH there was no objective evidence that the infected rats benefited as a result of this treatment.

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Steroid-3B-OL Dehydrogenase Activity and Androgen Production in Adrenal and Interstitial-Cell Tumors of Mice.* (21171)

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It has been demonstrated(1) that all normal endocrine tissues which produce non-benzenoid steroid hormones contain an enzyme which will oxidize certain Δ^5-unsaturated steroids with a 3-β alcohol group to the corresponding α,β-unsaturated Δ^4-3 ketone, the latter structure being characteristic of the more active C_{19} and C_{21} compounds formed by these tissues. This enzyme system has not been found in non-endocrine tissues nor in significant quantities in tissues producing only the benzenoid steroids. The present communication reports the presence of this enzyme, 3 β-ol dehydrogenase, in neoplastic tissues arising from the mouse adrenal cortex and testicular interstitial cells, and relates its concentration to the steroid hormone production of these tumors.

Materials and methods. Carcinomas producing sex steroids develop regularly in the adrenal cortices of CE mice several months

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