

17142. Effect of Cortical Extract and Other Agents on Eosinophilia of Mice Infected with *Trichina spiralis*.*

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An absolute reduction in the number of circulating eosinophiles occurs within a few hours following the stimulation of the human adrenal cortex with adrenotrophic hormone.¹ The same effect can be induced by the administration of cortical hormone, or epinephrine² which presumably stimulates anterior pituitary secretion of adrenotrophic hormone. Lymphopenia accompanies the drop in eosinophiles.³

A test animal in which eosinopenia can be readily determined for bioassay of adrenotrophic activity is desirable. In the mouse the normal level of blood eosinophiles is so low that normal animals cannot be utilized to good advantage. However, within 3-4 weeks after forcible ingestion of trichina-infected meat the mouse exhibits a decided eosinophilia which persists at a rather constant level for a matter of weeks. It was the purpose of this investigation to determine whether such infected animals might serve as a test object for hematologic assay of adrenocortical activity and/or function. The procedure was the following:

1. Young adult male mice were force-fed pectoral muscle from trichinous hosts (infected rats); ‡ eosinophilia of 4-20% was present

within 4 weeks and persisted for at least 5 weeks.

2. Total and differential counts, the latter on at least 100 cells, stained with Giemsa or Wright's stain, were made on the tail blood of unanesthetized animals.

3. The test material was then administered and counts were made after 6 and 24 or 48 hours.

The materials tested for their effect on the trichina-induced eosinophilia were whole adrenal cortex in oil, testosterone propionate, estradiol dipropionate, epinephrine, urethane, and peanut oil.§ Crystalline hormones were dissolved in peanut oil, urethane in water.

Within 6 hours after the subcutaneous administration of cortical extract (0.1 cc lipo-adrenal cortex—Upjohn) the percentage of circulating eosinophiles had dropped from 12.7 to 1.6 (average of 7 animals). In this series of animals the decline in total white blood cell count averaged 5700 cells/mm³, in eosinophiles 1800, and in lymphocytes 2900. The initial counts averaged 16,400. Preliminary findings on 4 intact and 2 adrenalectomized trichinous mice injected subcutaneously with sex steroids (70 µg testosterone propionate and 25 µg estradiol dipropionate) revealed that within 6 hours following injection, except in one animal, the percentages of the white blood cells were not significantly affected. This was true also for the one adrenalectomized and 4 intact trichinous mice which received injections of peanut oil.

The absolute number and the percentage of circulating eosinophiles were reduced in trichinous mice by the subcutaneous administration of epinephrine (0.02 mg/100 g hourly for 4 hours). The drop in eosinophiles (at

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¹ Thorn, G. W., Forsham, P. H., Recant, L., and Hills, A. G., *Program Assn. Study Internal Secretions*, 1948, 19.

² Recant, L., Forsham, P. H., and Thorn, G. W., *Program Assn. Study Internal Secretions*, 1948, 19.

³ Hills, A. G., Forsham, P. H., Finch, C. A., *Blood*, 1948, 3, 755.

‡ The author is indebted to Dr. Franklin Wallace of the Department of Zoology, University of Minnesota, for supplying rats infected with trichina.

§ The author is indebted to Dr. F. E. Houghton of Ciba Pharmaceutical Products, through whose courtesy the sex hormones were made available, and to Dr. L. E. Josselyn of Abbott Laboratories for supplying urethane.

6 hours) paralleled that produced by cortical hormone. The percentage of circulating eosinophiles dropped from 14.3 to 2.4, the per cent of lymphocytes remaining unaltered.

The absolute number of eosinophiles dropped from 2700 to 400 cell/mm³. In 2 adrenalectomized trichinous mice which received epinephrine, the total count had doubled within 6 hours. The percentages of eosinophiles and the other types of cells remained the same.

Urethane in aqueous solution (1 mg or 1/2 mg per g body weight) was injected into 6 intact trichinous mice. After 6 hours the absolute number of lymphocytes had dropped to approximately half, the eosinophiles to less than half the initial levels. Much greater decreases were obtained in 6 mice which survived 5 or 6 daily anesthetic doses of urethane. The percentage of eosinophiles dropped from 9.3 to 2.3, the absolute number from 1800 to 100. The absolute number of lymphocytes dropped from 12600 to 2200.

Urethane-induced lymphopenia has been observed in adrenalectomized as well as intact rats and mice.^{4,5} Urethane depressed the white blood cell count in mouse myeloid leukemia, but adrenal cortical extract was ineffective.⁶ These observations indicate that

⁴ Dury, A., and Robin, E. D., *Endocrinology*, 1948, **42**, 320.

⁵ Lu, C. S., Thesis, University of Minnesota, 1947.

⁶ Lu, C. S., Kirschbaum, A., *Proc. Internat. Cancer Res. Congress*, 1947, 105.

the effect of urethane on normal blood lymphocytes and leukemic myeloid cells is not mediated by the adrenal cortex. In the present experiments eosinopenia paralleled lymphopenia following the injection of urethane. Adrenalectomized trichinous mice did not tolerate anesthetic doses of urethane, and in these experiments it could not be determined whether depression of blood eosinophiles occurs as an effect of urethane in the absence of the adrenal cortex. Spink⁷ demonstrated that reduction in the eosinophile count of trichinous guinea pigs occurred with a superimposed bacterial infection. The eosinophile count was also suppressed in a patient developing bacterial infection during the course of trichinosis.

Summary. The number of circulating eosinophiles of trichinous mice was decidedly reduced by the administration of cortical hormone. The same effect was induced by epinephrine in intact, but not in adrenalectomized, trichinous mice. Sex steroids in the doses used did not significantly reduce the percentage of circulating eosinophiles in 4 intact and 2 adrenalectomized trichinous animals. Eosinopenia was induced by urethane in trichinous mice. Whether or not urethane-induced eosinopenia is mediated by the adrenal cortex has not been determined.

⁷ Spink, W. W., *Arch. Int. Med.*, 1943, **54**, 805.

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17143. Effect of Pteroylglutamic Acid and Vitamin B₁₂ on Growth of Rous Tumor Implants.

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Earlier work from this laboratory showed that pteroylglutamic acid was essential for the growth of implants of Rous sarcoma in young chicks.¹ The effect of other dietary

factors was much less pronounced.² A search was then made for additional dietary factors which might affect the growth of this sarcoma in chicks.

Day-old chicks in groups of 10 were fed

¹ Little, P. A., Sampath, A., Paganelli, V., Locke, E., and SubbaRow, Y., *Tr. N. Y. Acad. Sci.*, Series II, 1948, **10**, 91.

² Little, P. A., Oleson, J. J., and SubbaRow, Y., *J. Lab. and Clin. Med.*, 1948, **33**, 1139.