MYELOID INFILTRATIONS OCCURRING IN THE ADRENALS OF ANIMALS BEARING CERTAIN TUMORS

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In my studies on dibenzanthracene tumors in mice of pure inbred strains it was found that the presence of growing malignant tissue brought about an increase in the number of polymorphonuclear cells in the peripheral blood and blood-forming organs of the host, the severity of the resultant neutrophilia being characteristic for the particular tumor (Lewis, 1937). Of the 80 tumors induced in pure inbred strains of mice by means of one injection of 0.8 mg. of 1:2:5:6-dibenzanthracene, 14 proved to be of the type whose growth throughout many serial passages was always accompanied by a pronounced neutrophilic leukocytosis and a myeloid hyperplasia of the spleen and bone marrow of the host. Repeated grafting of these tumors into mice of an alien strain brought about in some of the animals an alteration that permitted the growth of some of the grafts (a total of 174) of tumors to which they had previously been resistant, and also brought about some change in ten of the tumors, by which they became thereafter transplantable into mice of more than one strain (Lewis and Lichtenstein, 1936; Lewis, 1937). The growth of these experimentally altered tumors was accompanied by an exceedingly severe myeloid hyperplasia in their alien-strain hosts. The hematopoietic disturbance increased with the growth of the tumor and subsided in those animals in which the tumors regressed.

Parsons (1935, 1936) found a similar condition in mice bearing certain tumors induced by a water-soluble dibenzanthracene, and described it as a myeloid leukemia "coincident with and transmissible by a spindle-celled sarcoma." The condition found in our mice seemed to resemble a severe neutrophilia rather than a leukemia, although in animals bearing certain of the tumors some myeloblasts and myelocytes were present in the peripheral blood, and myeloid hyperplasia occurred in the spleen and in certain lymph nodes. In some instances infiltrating cells were seen in other organs, particularly in the adrenals.

McEuen and Selye (1935), in a study of 130 rats bearing the transplanted Walker rat carcinosarcoma, better known as the Walker rat tumor No. 256, described the presence of infiltrations composed of lymphocytes and leukocytes in the adrenals of one-third of the animals; and Paunz (1923) encountered a similar condition in some instances in cancer of man. It seemed of interest, therefore, to extend our own study of the adrenals of tumor-bearing animals to include an examination of these glands in rats grafted with Crocker tumors Nos. 10, 95, and 1548, and Walker tumors Nos. 319 and 256, and also in mice bearing spontaneous mammary-gland adenocarcinoma.

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FIG. 1. SMALL INFILTRATION EXTENDING THROUGH THE CORTEX INTO THE MEDULLA OF THE ADRENAL OF A MOUSE WITH A PRIMARY DIBENZANTHRENE SARcoma NO. 142. X 60

FIG. 2. SAME PREPARATION SHOWING THE MYELOBLASTS, MYELOCYTES, MITOTIC FIGURES, AND POLYMORPHONUCLEAR LEUKOCYTES. X 1560
FIG. 3. LARGE MYELOID INFILTRATION IN THE MEDULLA AND TWO SMALL ONES IN THE CORTEX OF THE ADRENAL OF A MOUSE WITH THE EXPERIMENTALLY ALTERED SARCOMA NO. 54.  × 60

FIG. 4. SAME PREPARATION SHOWING THE CELLS AND MITOSES.  × 1560
The polymorphonuclear leukocytes that occurred in great numbers in animals bearing one of the myeloid stimulating tumors were large cells whose nuclei contained more than the normal amount of chromatin, distributed into many lobes. They resembled the giant neutrophils described in pernicious anemia by Musser and Wintrobe (Plate III).

The myeloid infiltrations observed in the present study of tumor-bearing animals (Figs. 1 and 2) consisted of a few myeloblasts, one or more of them in mitotic division, surrounded by myelocytes and polymorphonuclear leukocytes (Figs. 3 and 4). The larger areas of infiltration had several centers of dividing cells and myeloblasts (Fig. 6), while some of the smaller ones were composed almost entirely of myeloblasts (Fig. 5). A few of the infiltrations were made up of eosinophilic granulocytes, as was observed also by McEuen and Selye. In these there were some mature eosinophils as well as juvenile forms, eosinophilic myelocytes, and some cells in mitosis.\(^2\)

The study of the rat tumors comprised 23 rats. Of these 7 bore Walker tumor No. 256, 4 tumor No. 10, 4 tumor No. 95, 4 tumor No. 319, and 4 tumor No. 1548. The 7 animals bearing Walker tumor No. 256 were the only ones that developed a neutrophilia. Myeloid infiltrations were found in the adrenals of three of them. The 16 rats bearing the other four tumors exhibited only a mild increase in the proportion of polymorphonuclear cells in the blood during the growth of the tumors. Infiltrations were not found in the adrenals of these animals. A comparison of the figures given by McEuen and Selye with Figs. 5 and 6 in this paper indicates that the infiltrations described by those writers were likewise composed of myeloid cells.

Thirty-six agouti mice, descended from Strong's C\(_5\)H strain with spontaneous mammary gland tumors were studied.\(^3\) Some of these animals had one tumor, others had two tumors, and a few of them developed three. These spontaneous carcinomata grew slowly, and the mice were examined for infiltration in the adrenals forty to sixty days after the tumors were observed. Only 6 of them exhibited a distinct neutrophilia. Many of the others showed a slight leukocytosis, with an increase in polymorphonuclear leukocytes from 22 per cent to 46 per cent during the growth of the tumors. The spleens of the mice that developed a distinct neutrophilia were enlarged, and myeloid infiltrations were found in the adrenals of 3 of them.

In addition to the 80 tumors (Nos. 1-80) previously investigated (Lewis, 1937), a study was made of the blood and adrenals of 35 mice of pure inbred strains (16 of the BA and 19 of the C57 strains), each bearing a primary dibenzanthracene tumor (Nos. 125-160); also of the hosts of each of these tumors as it was transplanted through several serial passages. Examination of the 35 mice with these primary tumors showed that the neutrophilia that developed in them coincident with the growth of the primary tumors was less severe than in those bearing the transplanted tumors. On the whole, however, the blood pictures were characteristic for the particular tumors.

\(^2\) Every one of the tumors studied was free from bacteria, and all extracts, grafts and dead tumor tissue used were kept free from contamination, so that infections or abscesses such as described by McEuen and Selye did not occur in these animals. The Walker tumors No. 256 weighed about 30 grams; the others were larger, weighing around 50 grams.

\(^3\) I am indebted to Dr. H. B. Andervont, U. S. Public Health Service, for these mice.
Fig. 5. Small infiltration in the adrenal of a mouse with a spontaneous mammary gland adenocarcinoma. × 500

Fig. 6. Infiltration in the medulla of the adrenal of a rat with Walker carcinosarcoma No. 256. × 500

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That is, the primary tumors whose growth was accompanied by only a mild increase in the number of polymorphonuclear leukocytes continued to bring about a mild neutrophilia in the mice into which they were transplanted, while those whose growth was accompanied by a pronounced neutrophilia brought about a proportional though more severe neutrophilia during their growth in mice into which they had been transplanted. The spleens of the mice bearing the primary tumors were in most instances small, particularly in the C57 mice, or at most were only moderately enlarged, while those of the hosts of the grafted tumors increased in size as the tumors grew, some of them becoming several times larger (400–800 mg.) than normal (90–130 mg.).

Eight of the 35 primary tumors proved to be the myeloid stimulating type of sarcomata. Myeloid infiltrations were found in the adrenals of the 8 mice bearing these primary tumors and in the adrenals of the mice into which these tumors were transplanted. Areas of infiltrating myeloid cells were found in the adrenals of the mice bearing those tumors (previously described) whose growth brought about a severe neutrophilia in the hosts and also in the adrenals of the mice bearing any one of the 10 experimentally altered tumors, provided the tumors were permitted to grow to a somewhat more than medium size.

A number of mice were treated with extracts of tumor, large quantities of dead tumor tissue, or large amounts of living tumor tissue to which they were refractory. The inoculation of this material did not bring about a neutrophilia in the blood or myeloid infiltrations in the adrenals. Instead, it tended to increase the proliferation of the lymphocytes.

Parsons claims that there is present in the tumor an agent that stimulated the development of the leukemia, but it seems to me that the neutrophilia is brought about in the host as a result of the growth of the particular tumor, and that the blood pictures of the hosts furnish information in regard to biological differences in these malignant growths.

**Conclusion**

Areas of cell infiltration consisting of some myeloblasts, one or more of them in mitosis, a number of myelocytes and many polymorphonuclear cells, were found in the adrenals of certain tumor-bearing animals. The presence of these myeloid infiltrations was not a phenomenon common to all tumor-bearing animals; in our material it was limited to those bearing one of the tumors whose growth was accompanied by the development in the host of a severe neutrophilia in the peripheral blood and a myeloid hyperplasia of the spleen, bone marrow, and certain lymph nodes.

**Literature**

**Lewis, M. R.:** Myeloid hyperplasia brought about in mice by the growth of dibenzanthracene tumors and its relation to the transplantability of the tumors into mice of alien strains, Am. J. Cancer 29: 510, 1937.


