the number of eosinophilic cells in the bone marrow. This is in accord with the observation that cortisone administration does not produce any diminution in eosinophils in the femoral marrow of mice(6).

The apparent increase in the eosinophilic cells of the bone marrow indicates that cortisone and ACTH may inhibit delivery of eosinophils from the bone marrow to the peripheral blood. However, the differential counts indicate no significant alteration in the percentage of the eosinophilic cells in relation to the nucleated cells of the bone marrow. It appears most probable that cortisone and ACTH increase the rate of removal of eosinophils from the blood without affecting their production by the bone marrow.

Summary. Eosinophil counts were performed on blood and bone marrow of 7 patients before and during either cortisone or ACTH therapy. At a time of marked diminution in the eosinophils of the peripheral blood, the eosinophilic cells of the bone marrow were not decreased.

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Influence of Tumors on Liver Concentration of Radioactive Stilbamidine.* (18326)

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(Introduced by J. H. Lawrence.)

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During the course of studies with radioactive stilbamidine, certain findings have appeared that are of sufficient interest to warrant a preliminary report. Kopac(1) reported that stilbamidine destroyed the neoplastic cells in cultures of rat mammary adenocarcinoma and transplanted lymphosarcoma. Snapper(2) further studied this drug and found inclusion bodies containing stilbamidine in the cytoplasm of plasma cells in patients with multiple myeloma. Accordingly, C^{14}-labeled stilbamidine was prepared and its metabolic distribution in normal mice and a patient with multiple myeloma was undertaken(3,4). These experiments established that the oxidation to $C^{14}O_2$ of stilbamidine by the body is negligible.

These studies suggested the possibility of investigating the localization and distribution of activity in mice with various types of tumors. Accordingly, normal and tumor bearing mice were injected intraperitoneally with 0.4 mg (4.50×10^6 dis/min) of stilbamidine-$C_2{}^{14}$ dissolved in 0.05 ml saline. The C^{14}-labeled stilbamidine used for this experiment was synthesized by Dr. J. C. Reid(5).

Procedure. Ninety-six hours after injection, the mice were killed with ether and autopsied. Liver, spleen, kidneys, pancreas and tumors were removed, dried in vacuum, weighed and burned over copper oxide and the resulting carbon dioxide was converted to barium carbonate and the radioactivity measured with a proportional counter(6).‡ The mice were kept in separate cages designed to prevent contamination of food and water with excreta.

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‡ Nucleometer, Radiation Counter Laboratories, Chicago, Ill.

TABLE I. Activity Found in the Livers of 16 Tumor Mice 96 Hours After Injection of Labeled Stilbamidine.

Strain	Sex	Age (mo.)	Mouse wt, g	Tumor wt, wet, g	Liver wt, dry, g	Total liver activity (% of inj. dose)	Type of tumor
A	♂	6	24	4.45	.272	40	Sarcoma
A	♂	6	23	2.09	.265	23	Mammary
A	♂	5	23	4.45	.321	23	Sarcoma
A	♂	5	21	3.39	.310	30	”
A	♂	5	22	4.26	.299	31	”
A	♂	5	24	4.76	.326	31	”
A	♂	6	21	large	.176	19	”
A	♂	6	21	large	.184	21	”
dba	♂	10	24	2.27	.407	19	Melanoma
”	♂	8	32	4.67	.559	12	”
”	♂	8	29	7.06	.547	11	”
McDowell	♀	6	26	0.06	.430	12	Lymphatic leukemia
”	♀	18	20	0.30	.296	35	Lymphatic leukemia
”	♀	6	19	0.16	.258	33	Lymphatic leukemia
C57	♂	6	30	0.58	.573	24	Myelogenous
”	♀	6	36	6.03	.659	41	Mammary

TABLE II. Activity Found in the Livers of 20 Normal Mice 96 Hours After Injection of Labeled Stilbamidine.

Strain	Sex	Age (mo.)	Mouse wt, g	Liver wt, dry, g	Total liver activity (% of inj. dose)
A	♂	10	24	.356	2.5
A	♂	12	27	.496	7.7
A	♂	6	24	.535	7.7
A	♂	6	24	.539	7.5
A	♂	5	20	.336	4.4
A	♂	5	22	.380	4.8
A	♂	5	22	.389	2.0
A	♂	5	22	.408	3.0
Bagg	♂	10	32	.512	5.1
”	♂	10	34	.513	7.5
”	♂	10	32	.579	6.4
dba	♀	18	28	.336	8.0
”	♂	8	23	.473	4.6
”	♂	8	25	.517	5.0
C57	♀	6	23	.406	30.
”	♀	6	21	.420	17.
”	♂	6	24	.459	24.
”	♂	6	24	.443	34.
”	♂	13	32	.575	36.
”	♂	13	32	.57	30.

Results. Tables I and II show the total concentration of radioactivity present in the livers of normal and tumor mice 96 hours after injection. The total liver activity is given as percent of injected dose. It is evident that very much higher and distinctly abnormal concentrations of radioactivity are present in the livers of the tumor-bearing mice as compared to the controls for the *A* and *dba* strains. With the number of animals used no correlation between tumor weight and liver concentration of radioactivity can be established. However, there appears to be some correlation between mouse weight and liver concentration of radioactivity. Thus, there is a small increase in liver concentration in the normal group with increasing mouse weights. Conversely, there appears to be a drop in liver concentration in tumor mice with increasing mouse weights. The number of such mice is inadequate to definitely establish this correlation. The 3 mice with lymphatic leukemia were found to have elevated levels of radioactivity in the liver, but the significance of this group is not known since no control determinations have been made for mice of this strain.

It is of considerable interest that the normal C-57 strain mice have liver concentrations of radioactivity in the same range as mice with neoplasms. Whether this is unique for mice which develop spontaneous nonepithelial neoplasms or whether it is coincidental remains for further study. Here increasing mouse weights appear to be associated with increasing liver concentrations of radioactivity following the pattern of the other normals in this respect. More mice with tumors will need to be studied before the effect of tumors on liver concentration in this strain can be known.

The specific activity of liver for the tumor mice averaged 3,464 dis./mg/min. and for the strains A, dba and Bagg controls 498 dis./mg/min. For the normal strain C57 mice the specific activity averaged 2,726 dis./mg/min. No definite correlation could be established between tumor weight or mouse weight and specific activity.

The concentrations of activity in the kidneys and spleens of the tumor mice averaged 7.5 and 0.24% of injected dose respectively and are a little greater than in the normals, but the differences are not significant for the number of animals studied to date. The concentration of radioactivity in the pancreas was found to be intermediate between spleen and kidney and is in the same range for both control and tumor mice. None of the tumors contained more than traces of activity which compares with Snapper's qualitative results in which he found no evidence of localization of stilbamidine in transplantable lymphosarcoma and mammary carcinoma(7).

Kopac has shown that stilbamidine dissociates protamine-nucleate complexes with the release of partially denatured protamine molecules and the formation of an insoluble stilbamidine-nucleate complex(8). Snapper and his group have presented evidence that stilbamidine is capable of specifically combining with ribose nucleic acid in the cytoplasm of myeloma cells(2). Kelly and Jones(9) have found a considerable increase in turnover rates of desoxypentose nucleic acid in the liver, spleen and kidneys of tumor mice with transplanted mammary cancer as compared with turnover rates in normal mice. The behavior of ribose nucleic acid in this regard is not known.

It seems possible, then, that stilbamidine precipitates in the liver cells as an insoluble stilbamidine-nucleate complex and the increased amounts present in tumor-bearing animals are related to increased formation of certain nucleic acids in these livers. Studies are being made to determine the chemical natur of the stilbamidine complex or derivative that has concentrated in these livers and in what elements of the liver this material is located.

In a patient with multiple myeloma, who was injected with C^{14}-labeled stilbamidine, it was found that an unexpectedly high concentration of radioactivity was present in the liver at autopsy three months later(4). While this fits the pattern of the mouse results, more studies of humans with and without malignant disease will be necessary before significance can be attached to this isolated finding.

Summary. A series of normal and tumor mice were injected with stilbamidine-amidine-C_2^{14}. After 96 hours organs were removed and analyzed for radioactivity. Much higher and distinctly abnormal concentrations of C^{14} were found in the livers of tumor-bearing A and dba strain mice as compared to the controls. Some data for C57, Bagg and McDonnell strains are also given. The relation of this phenomenon to possible abnormalities in nucleic acids in tumor-bearing mice is discussed.

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