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Susceptibility of Mouse Strains to Lung Tumor and Sarcoma Induced by 1:2:5:6-dibenzanthracene.

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It has been shown that strains of mice differ in their inherited susceptibility to tumors both spontaneous and tar-induced.[1] Burrows, Hieger and Kennaway[2] and others have demonstrated the effectiveness of 1:2:5:6-dibenzanthracene in inducing sarcoma. The present paper is a preliminary report on the tumors induced by subcutaneous injection of 1:2:5:6-dibenzanthracene into various strains of mice.

Ordinary lard was filtered at 37°C. and the crystalline dibenzanthracene was dissolved in the filtrate by reheating to 140°C. Each mouse received a total dose of 4 mg. of 1:2:5:6-dibenzanthracene in 1 cc. of lard administered in 3 subcutàneous injections of 0.25 cc., 0.25 cc., and 0.5 cc. at biweekly intervals.

Of the mice receiving treatment 2 groups were from our branch of the Bagg albino strain. The 3rd was from our "Yellow" strain which is only pen inbred and probably not very homogeneous genetically but interesting because it produces yellow and brown mice. A 4th was from No. 1194—our highly inbred agouti or wild type strain; a 5th from Strain 5—an imported albino stock from McGill University. The 5th contained males only. The 6th was from Strain 62 which is composed of pink-eyed dilute brown mice, highly

TABLE I.

Percentage of Tumor after Subcutaneous Injection of 1:2:5:6-dibenzanthracene in Mice from Various Sources.

	Sarcoma			Lung tumor		
Strain	No. mice	No. with tumor	% tumor	No. mice	No. with tumor	% tumor
Bagg (previous experiment)	60	45	75.0	59	48	81.4
Bagg (Group I)	44	33	75.0	46	41	89.1
Bagg (Group II)	29	26	89.7	29	25	86.2
Yellow	32	29	90.6	30	10	33.3
1194	10	9	90.0	12	2	16.7
5	33	29	87.9	31	2	6.5
62	18	15	83.3	18	0	0.0

[1] Lynch, C. J., *J. Exp. Med.*, 1931, **54**, 747; PROC. SOC. EXP. BIOL. AND MED., 1933, **31**, 215.

[2] Burrows, H., Hieger, I., and Kennaway, E. L., *Am. J. Cancer*, 1932, **16**, 57.

inbred brother by sister. Another group of Bagg mice from a previous experiment may be legitimately included for discussion here.

The results are shown in Table I. The presence of lard makes it difficult to determine the time when malignancy supervenes in the injected tissue, and lung tumors are found only at autopsy. Therefore the percentages are based upon the populations surviving at the time the presence of the first tumor of each type was proven by microscopic sections. For the lung tumor, this date was the 66th day after the last injection; for the sarcoma, the 73rd day. No mice lived longer than 376 days after treatment, the majority less than 200 days. The table lists the subcutaneous sarcomas occurring at the site of injection and primary lung tumors of epithelial origin.

All groups show a high incidence of sarcoma. Though there is a distinct variation no strain can be clearly demonstrated to have a significantly different rate from any other.

The distribution of lung tumors is quite different, ranging from 0.0 to 89.1%. While the Bagg groups have about the same rate, each is significantly different from all of the 4 other stocks. The Yellow stock has an intermediate rate which is significantly different from all but Strain 1194. A detailed analysis shows that strain differences are not merely the result of variations in length of life after treatment. For example, by the 158th day when the mice of Strain 1194 were dead, with a lung tumor rate of 16.7%, the 71 mice that had died in the 3 Bagg groups showed 74.6%. Thirteen mice of Strain 62 lived well beyond this time but none developed a tumor.

If a comparison is made of the susceptibility to the 2 kinds of tumor exhibited by each stock it is found that the Bagg groups are highly susceptible to both. The greatest divergence, found in Group I, is not mathematically significant. But it is evident by inspection that the last 4 groups exhibit a marked difference in the reaction of subcutaneous connective tissue and pulmonary epithelium.

TABLE II.

Percentage of Spontaneous Tumors in Various Strains of Mice.

Strain	Total No. of mice	No. with sarcoma	% sarcoma	No. with lung tumor	% lung tumor
Bagg (1931-34)	207	0		66	31.8
1194 (1931-34)	327	1	0.31	8*	2.4
62	199	0		12*	6.0
5	50	0		2?	4.0?

* Includes questionable cases.

The data are based upon mice over 6 months old. Those for the Bagg strain and 1194 are from May, 1931, through December, 1934.

In attempting to explain these results reference may be made to the records of spontaneous tumor in 4 of these strains. (No data are available for the "Yellows".) The data (Table II) are based upon mice over 6 months old. Earlier records of the Bagg and 1194 strains have shown a small percentage of sarcoma (less than 2%). The later stock records given here are selected as being a closer control.

Only one spontaneous sarcoma occurred in these groups. No difference can be demonstrated between strains just as no difference was demonstrated between strains for induced sarcoma. However, as regards lung tumor the strains are dissimilar. The Bagg strain which here shows 31.8% gave 81.4 to 89.1% after dibenzanthracene. Evidently subcutaneous injection of dibenzanthracene induces lung tumor as well as sarcoma. The Bagg strain is also plainly more susceptible to spontaneous lung tumor than are the other 3 strains just as it was more susceptible to induced lung tumors than were the other strains.

These results confirm our earlier conclusions that strains differ in susceptibility to induced tumor and that susceptibility is organ-specific.

A number of other tumors occurred in these experiments but they will be treated more fully later. Mention might be made, however, that a mammary tumor occurred in a male in Strain 5.

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Skin Reactions in Sarcoid.

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Based on the hypothesis that sarcoid, like lymphogranuloma inguinale, might be a virus disease and that, like the latter, an antigen could be prepared from infected material for use for diagnostic purposes, the following work was done.

A sarcoid lesion of the skin, 2 cm. in diameter, was removed from the first patient described below. A portion of the tissue was taken for microscopic study, while the remainder was ground with the aid of sterile sand. To this, normal saline was added in a volume equal to 6 times that of tissue. This preparation was then sterilized