Further Observations on Skin Carcinogenesis by a Single Application of 20-Methylcholanthrene*

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The induction of skin cancer in a fraction of mice treated by a single application of a potent carcinogen—methylcholanthrene—has been demonstrated so far in two strains: the C57 brown strain used by Mider and Morton (2), and the Swiss strain used by Cramer and Stowell (1). A negative result was reported by Mider and Morton with C57 black mice (3). This note records the positive carcinogenic response to similar treatment with methylcholanthrene in New Buffalo mice, the third strain to be reported susceptible.

The experimental technic was the same as that used by Cramer and Stowell (1): a 0.6 per cent solution of the carcinogen applied on one occasion only to a large area of the back by means of 3 strokes of a No. 4 camel’s hair brush. In 12 effective mice (mice alive when the first tumor appeared) 3 malignant growths developed, 2 carcinomas and one sarcoma. Each of the 2 carcinomas, in mice 3213 and 3217, was preceded by a papilloma. In No. 3213 the papilloma appeared 5 weeks after the application, persisted for another 3 months, then began to grow deep. This animal was killed 4½ months after the application. Microscopically the tumor was a differentiated, heavily keratinized, squamous cell carcinoma.

In No. 3217 the papilloma appeared as a small warty growth 7 weeks after the application and persisted, without showing any distinct increase in size, for another 7 months, when it began to grow deep and the development of malignancy was suspected. The animal was allowed to live for another 2 months. It was killed 11 months after the application when an isolated, round, ulcerating growth about 1.25 cm. in diameter was present at the posterior end of the painted area. Enlarged lymph nodes were found in both axillae. Upon microscopic examination the tumor was found to be a highly anaplastic carcinoma showing numerous mitoses (Fig. 1). The cells varied greatly in size and shape, and keratinization was scanty. Both the lymph nodes were filled with metastatic growths having features characteristic of the primary tumor (Fig. 2).

The third malignant growth, in mouse 3219, was not preceded by a papilloma. It was first noticed 7 months after the application, as a tumor that appeared to have originated below the surface of the skin. It grew rapidly and the mouse was killed 1 month later, 8 months after the application. On microscopic examination it was found to be a spindle cell sarcoma. The epidermis was histologically nearly normal except for a slight hyperplasia where it covered the sarcoma.

The anaplastic carcinoma of mouse 3217 presents as an interesting feature the combination of a long period of induction with rapid growth and a high grade of malignancy as evidenced by the metastatic spread to lymph nodes. This disposes of the suggestion that carcinomas with a long period of induction grow more slowly and are less malignant than those with a very short period.

SUMMARY

It has been demonstrated for a third strain—the New Buffalo—that a single application of methylcholanthrene in benzene can induce malignant tumors. Of 12 effective mice 2 developed carcinomas and 1 a sarcoma. Of 4 different strains tested so far by a single application of a potent carcinogen only one has given a negative result. A positive carcinogenic response to a single application of a potent carcinogen is, therefore, not an exceptional phenomenon restricted to one particularly susceptible strain of mice. It is noteworthy that one of the carcinomas had a very long period of induction—9 months—and that both its morphology and its biological behavior characterized it as a very malignant type of growth.

REFERENCES


FIG. 1.—Mouse 3217. Primary skin carcinoma that developed 9 months after a single application of methylcholanthrene to the back of a New Buffalo strain mouse, showing the highly anaplastic character of the growth. At least 8 mitoses can be counted in this single high power field. Bouin fixation. Hematoxylin and cosin. Mag. X 580.

FIG. 2.—Mouse 3217. Lymph node invaded by the metastatic growth. Cells show the same features as those of the primary tumor of Fig. 1. Bouin fixation. Hematoxylin and cosin. Mag. × 90.
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