A Sarcoma-Producing Factor Extractable from Transplanted Rat Fibrosarcomas*

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A number of investigators (Schabad, Menke, Kleinenburg, and Steiner) have reported the extraction of fat-soluble tumor-producing substances from human tumors and also from the liver of human beings afflicted with neoplasms. The injection of the extracted fatty compound into mice and rats, however, produced tumors in only a small percentage of the treated animals.

There were available a number of rat spindle cell and mixed cell sarcomas that had been induced by one of the carcinogenic hydrocarbons in the inbred albino rats of Dr. King's colony. These tumors had been transplanted through 20 to 40 passages, and had proved to be 100 per cent transplantable in rats of this strain. It seemed worth while to attempt to extract a tumor-producing factor from the transplanted rat sarcomas, for if such a factor could be obtained it might produce more tumors when injected into rats of the strain in which the tumors originated than had been obtained by other investigators in the animals injected with human material.

METHOD

Rat sarcomas that had grown in every one of the rats in the 20 to 40 passages through which they had been transplanted were excised from etherized rats. The tumors were ground into small particles, mixed with an equal volume of 95 per cent alcohol, and allowed to stand in the refrigerator at 4 °C. overnight. The tissue was then pressed through a gauze filter, ground into smaller particles, and pressed between sheets of absorbent paper to remove the excess fluid. After this partial drying the tissue was placed in 2 volumes of benzol in a flask to which was attached an extraction apparatus and extracted in an incubator at 42-45 °C. for 8 hours on 3 successive days. After this the extract was filtered off and concentrated in vacuo at 42-45 °C.

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1 Reagent benzene (Merck) thiophene-free.

The fat obtained in this manner was slightly tan colored, resembling vaseline. It was soft at room temperature, but became sufficiently fluid for injection when kept for a few minutes at 44-46 °C.

Twenty-eight inbred albino rats 21 to 40 days old were injected with the fat extracted from the rat sarcomas. Some rats received 0.12 cc. while others received 0.25 to 0.5 cc. About 4 months later these rats received into the same site 0.5 cc. of fat extracted in the same manner. During the following 6 months 5 of the rats developed tumors at the injection site. Three of them were transplanted and proved to be fibrosarcomas transplantable through many passages in rats of their strain of origin. The negative rats were kept for 10 months after the second injection. They were then autopsied. Two of them had tiny spots in their lungs. These were not considered sarcomas as they did not grow when transplanted into susceptible rats.

An attempt was also made to extract by means of benzol a tumor-producing substance from livers of rats bearing transplanted rat sarcomas. Twenty-four rats of the inbred albino strain 28 to 40 days old were injected with 0.12 to 0.5 cc. of fat extracted from livers. Four months later they received a second injection consisting of 0.5 cc. of a similar extract. Two of the rats developed sarcomas at the site of injection, one 4 months and the other 5 months after the second injection. One of the tumors was transplanted through 6 passages in rats of its strain of origin.

One female rat of the first group injected with fat from sarcomas, and one female rat of the second group injected with fat from liver, developed tumors in the mammary gland in the region that had been injected 9 months earlier.

Microscopical preparations of the tumors that arose following injection of the extracted fat showed that 7 of them were spindle cell sarcomas, 1 was a mammary gland adenoma, and 1 a colloid carcinoma.

In previous work with inbred rats of Dr. King's colony it was noted that they developed fewer neoplasms than rats of other strains. However, in order...
to ascertain the number of spontaneous tumors that arose in rats of the inbred albino strain during the course of this study 200 rats were autopsied when 10 to 12 months old. Every one of them proved to be free from neoplasms (sarcoma, lung tumor, adenoma, and lymphosarcoma). Therefore, we are led to conclude that none of the sarcomas that developed following injection of extracted fat were of spontaneous origin. On the other hand the 2 epithelial tumors may have been spontaneous growths whose development was hastened by the presence of the injected fat, since the majority of tumors induced by carcinogenic agents have proved to be sarcomas.

In studies on the susceptibility of rats of the inbred albino strain to the development of induced tumors, 120 rats were injected with one of the carcinogenic agents (dibenzanthracene, benzpyrene, or methylcholanthrene) and every one of them developed a sarcoma at the injection site.

The percentage of tumors induced in rats of the inbred albino strain by the injection of fat extracted from rat tumors and from the livers of tumor-bearing rats was slightly larger than that obtained by some of the previous investigators by means of fat extracted from human material; however, it was still small in relation to the number of rats treated.

CONCLUSIONS

Attempts were made to extract by means of benzo a tumor-producing factor from transplanted spindle cell and mixed cell rat sarcomas and from the liver of rats bearing this type of sarcoma.

The extracted fat was injected into young rats of the inbred albino strain. Rats of this strain had proved to be 100 per cent susceptible to the growth of grafts of the tumors used for extraction.

Sarcomas developed at the injection site in 5 of the 28 rats injected with the fat extracted from the tumors and in 2 of the 24 rats injected with the fat extracted from the liver.

In addition to the 7 sarcomas 1 adenoma developed at the site of injection of the fat extracted from the sarcoma and 1 carcinoma arose at the site of injection of the fat extracted from the liver.

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