

*Brief Communication*

## Subcutaneous Sarcomas in Wistar Rats following Single 3-Methylcholanthrene Ingestion at Age 8-15 Days<sup>1</sup>

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**Summary.** Wistar rats were given a single intragastric dose of 2-5 mg of 3-methylcholanthrene at age 8-15 days. Five of 16 females and 6 of 10 males developed sarcoma, of which 5 were in the cervical and 4 in the axillary subcutaneous areas, and 1 each in the vaginal and thoracic region. Two of the 11 tumors contained liposarcomatous elements. There were no epithelial neoplasms of the breast, sebaceous glands, or skin, nor leukemias.

**Introduction.** The induction of mammary carcinomas in female rats following p.o. or i.v. administration of carcinogenic polycyclic hydrocarbons is known to be influenced by the age of the animal (4). The highest susceptibility is at reaching sexual maturity, with lower susceptibility in immature and older animals. Breast cancers are induced much less frequently in mature males, among whom appear carcinomas of the skin and sebaceous glands; the latter tumors are rarely seen in females (2). It became relevant to explore the effect of age, especially before maturity, on the induction of the neoplasms.

**Materials and Methods.** Single intragastric administrations of 2-5 mg of 3-methylcholanthrene (MCA) as a 1% solution in olive oil were given to rats 8-15 days of age. The rats weighed 12-20 gm, for a mean of 15 gm. The animals were observed for 1 year, with necropsies of all dead or killed animals, and histologic examination of relevant tissues.

**Results.** Of 10 rats that received 2 mg of MCA, 4 females and 2 males survived for a minimum of 8 weeks; of 52 rats given 5 mg of MCA, 12 females and 8 males survived this period.

Among 16 females that survived 8 weeks, 5 developed malignant connective tissue tumors. These included 1 subcutaneous fibrosarcoma of the right axilla at 18 weeks and 2 spindle-cell sarcomas in the neck at 14 and 22 weeks; the latter tumor involved the salivary gland. One female was found to have a fibrosarcoma that filled the thoracic cavity and invaded the lung at 16 weeks. In one animal a tumor arose at 47 weeks in the area of the vagina with invasion of the abdominal cavity; this was a spindle-cell sarcoma with an admixture of liposarcomatous elements. Three females died without tumors at 12, 20, and 44 weeks, and 8 were killed (and found free of tumors) at 52 weeks.

Among 10 males, 6 developed subcutaneous fibrosarcomas, at 7, 9, 17, 19, 31, and 42 weeks. Of these, 3 were in the axillary and 3 in the cervical areas. One cervical tumor, found at 9 weeks, replaced the salivary gland. One axillary tumor, found at 42 weeks, contained liposarcomatous as well as fibrosarcomatous elements. One tumor-free male died at 40 weeks and 3 were killed at 52 weeks.

In relation to dose, 2 tumors appeared in 6 rats that received 2 mg of MCA, at 9 and 42 weeks; 9 tumors appeared in 20 rats that received 5 mg of MCA.

Tumors were observed until they grew to a diameter of 1-2 cm, usually during 1 month of observation following detection. None of the 11 animals had more than 1 tumor. Grossly and histologically there was evidence of local invasion, but no metastases. No mammary, cutaneous, or sebaceous neoplasms or leukemias were found among the 26 animals.

**Discussion.** The finding of 11 Wistar rats with sarcoma among 26 that were given single p.o. administrations of 2 or 5 mg of MCA at the age of 8-15 days is in striking contrast with our experiences with hundreds of young but mature animals that received up to 1 gm of MCA over periods up to 1 year (2, 5). Dao (1) reported the appearance of mammary tumors in female offspring of Sprague-Dawley rats that were fed MCA before mating or during pregnancy, but not during lactation. Huggins and Fukunishi (3) obtained mammary carcinomas following the i.p. injection of 7,12-dimethylbenz(a)anthracene into newborn rats. Neither author observed the appearance of subcutaneous sarcomas.

It is suggested that young animals, 8-15 days of age, may be susceptible to connective tissue carcinogenesis following ingestion of MCA, and relatively resistant to neoplastic response of epithelial tissue such as the mammary gland, sebaceous gland, and the skin, as compared with the mature and, perhaps, newborn animals. The investigations are continuing.

### References

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