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Age Factor and Latent Period in Production of Sarcoma by Methylcholanthrene in Rats.*

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It has been shown that the latent period for the production of epidermoid carcinoma in mice by tarring is not influenced by the age of the animals.¹ Recently Dunning, Curtis and Bullock² as a result of extensive observations on the latent period in the production of sarcoma by subcutaneous injections of dibenzanthracene and benzpyrene in rats and mice also concluded that the age of the injected animals was of no significance, although in some of the studies upon mice the latent period appeared to be definitely prolonged in younger subjects than in older ones.

Histologic study of the subcutaneous connective tissue in white rats at birth, at 2 to 3 weeks of age, at 2 to 3 months of age and in the adult animal reveal various stages in the maturation of this tissue. The following experiments were performed to observe, again, whether the age of the injected animal bore any relationship to the latent period for the development of sarcoma following the subcutaneous injection of a carcinogenic compound.

The animals used were all members of the same colony which has been inbred in this laboratory for the past 5 years, having originated from 3 males and 3 females procured from a dealer. One group of 13 young rats, injected at 3 weeks of age was compared with a group of 12 adults 1 to 2 years of age. The carcinogenic substance employed was methylcholanthrene. Single subcutaneous injections were made in the interscapular region and consisted of 2 mg. of the compound in 1/10 cc. lard.

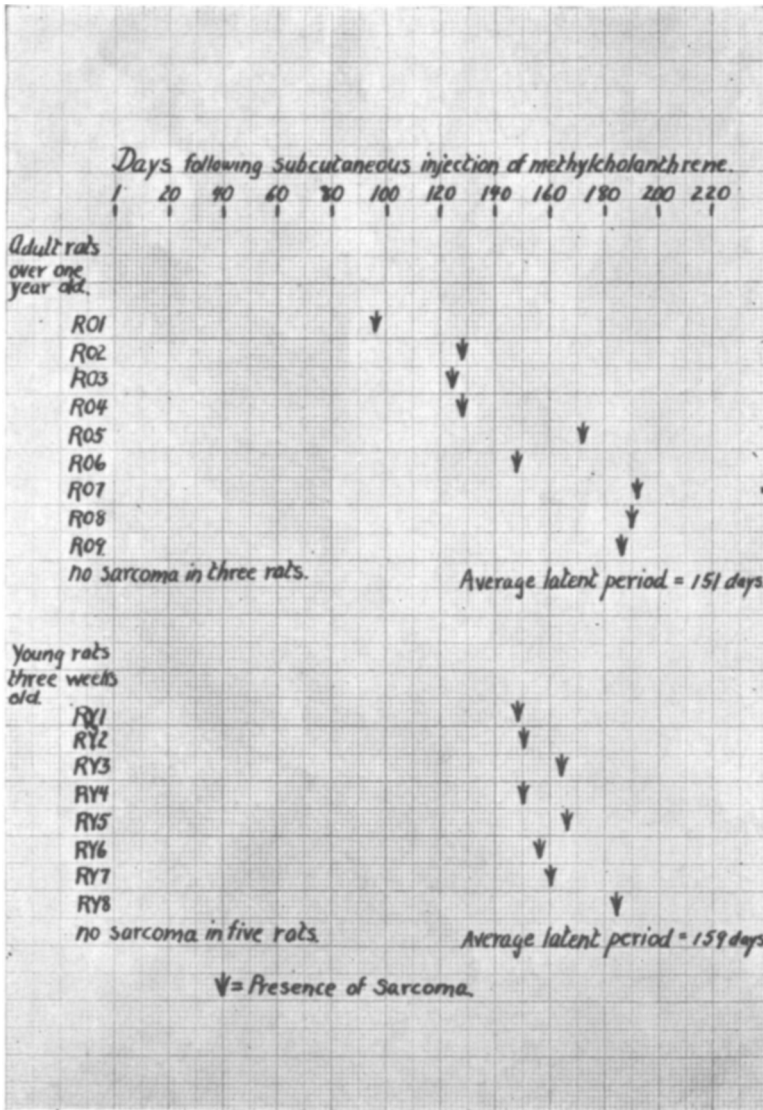
The presence of a tumor was recorded when it had reached about one cm. in diameter in order to avoid possible confusion with the injected mass. The results are summarized in Table I.

As shown, the shortest latent period was 96 days, the longest 192 days. Both instances were in the adult group. The latent periods among the young group varied between narrower limits, *i. e.*, 148

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¹ Woglom, W. H., *Arch. Path.*, 1926, **1**, 533.

² Dunning, W., Curtis, M. R., and Bullock, F. D., *Am. J. Cancer*, 1936, **28**, 681.



and 184 days. The average latent periods of the 2 groups were practically the same, 150 to 160 days. The experiment was terminated 220 days after the injections. Three animals did not develop tumors among the adult group and 5 had not developed sarcomas among the young group, during the period of observation.

The results indicate that maturing young, relatively less differentiated subcutaneous tissue in recently born and rapidly growing rats is not more prone to sarcomatous degeneration as a result of ex-

posure to a given carcinogenic agent than is adult subcutaneous tissue in the "static state" of a fully developed rat exposed to a similar dose of the same agent.

Thus, as in the case of epidermoid carcinoma produced by tar and sarcoma produced by the subcutaneous injection of dibenzanthracene and benzpyrene, the age of the animal bears little or no relationship to the latent period in the production of sarcoma by subcutaneous injection of methylcholanthrene.

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A Sensitive Method for Quantitative Estimation of Epinephrine in Blood.

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Meltzer and Auer¹ observed that epinephrine causes dilatation of the pupil much more readily after the corresponding superior cervical ganglion has been excised, in rabbits. By means of the "paradoxical" pupil reaction, Joseph and Meltzer² demonstrated liberation of epinephrine from the adrenals on stimulation of the splanchnic nerves. This was confirmed by Elliott,³ who found that dilatation of the pupil and retraction of the nictitating membrane, resulting from electrical excitation of the splanchnic nerve, do not occur in the absence of the adrenals.

Following these qualitative observations, Stewart and Rogoff⁴ employed the eye reactions (pupil dilatation, retraction of nictitating membrane and widening of palpebral aperture), sensitized by corresponding superior cervical ganglionectomy, for quantitative studies on the epinephrine output of the adrenals. A method of "auto-assay" was devised based upon reactions of the sensitized eye when adrenal vein blood was collected in a "cava pocket" for a given time and then released into the circulation. The intensity of the epinephrine reactions was measured by intravenous injections of appropriate amounts of epinephrine.

In our experience with various biological test objects used for

* Aided by the G. N. Stewart Memorial Fund and a grant from the Rosenwald Family Association.

¹ Meltzer, S. J., and Auer, C. M., *Am. J. Physiol.*, 1904, **11**, 28.

² Joseph, D. R., and Meltzer, S. J., *Am. J. Physiol.*, (Proc. Am. Physiol. Soc.), 1912, **20**, xxxiv.

³ Elliott, T. R., *J. Physiol.*, 1912, **44**, 374.

⁴ Stewart, G. N., and Rogoff, J. M., *J. Pharm. Exp. Therap.*, 1916, **8**, 479.