

Connective Tissue Neoplasms Produced in Dogs by Methylcholanthrene.

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Passey¹ obtained cutaneous melanomas in 2 mongrel Airedale bitches by painting their skin with tar. Hueper, Wiley, and Wolfe² found carcinomas of the urinary bladder in 3 mongrel female dogs following the subcutaneous and oral administration of commercial beta-naphthylamine. Bonser³ fed pure beta-naphthylamine to 3 mongrel male Airedales which developed carcinomas of the urinary bladder.

In some recent experiments, in which methylcholanthrene was administered under nembutal anesthesia to dogs, a male white Scotch terrier mongrel (No. 53) about 3 years old and weighing 9.5 kg was injected (3/25/42) subfascially in the left flank with 50 mg of this carcinogen dissolved at about 45°C in 3 cc each of benzene and paraffin (M.P. 51.6°C). At the end of 297 days a nodular tumor in direct continuity with the injected material was found in the left lower quadrant of the ventral abdominal wall, where on the 327th day autopsy disclosed a neoplasm consisting of 6 nodules set close together, ranging from 10 to 22 mm in their greatest diameters, varying from white to dark red and white streaked to dark red in color, and firm to moderately firm in consistency. With hematoxylin and eosin stain the darker areas in the nodules were partly necrotic and suffused with recent hemorrhage. The lighter areas contained the best preserved parts of the neoplasm (Fig. 1), the constituent cells of which were spindle-shaped, possessed plasmodial pale acidophilic processes, and had indistinct borders so that they overlapped in syncytial fashion. The finely chromatinized diffusely vesicular nuclei of the cells were elongated or oval, varied greatly in size, and contained 1 to 4 basophilic nucleoli each.

Many tumor cells possessed 2 to 5 nuclei. A few mitotic figures were present. Some fine acidophilic intercellular fibrillæ were basophilic with Mallory's connective tissue stain, indicating their collagenous nature. The diagnosis was connective tissue neoplasm with the histologic characteristics of an immature fibrosarcoma. No metastases were observed.

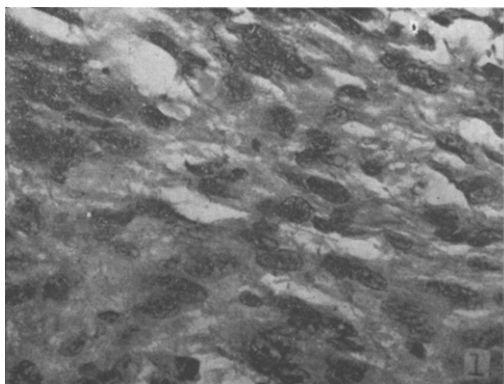
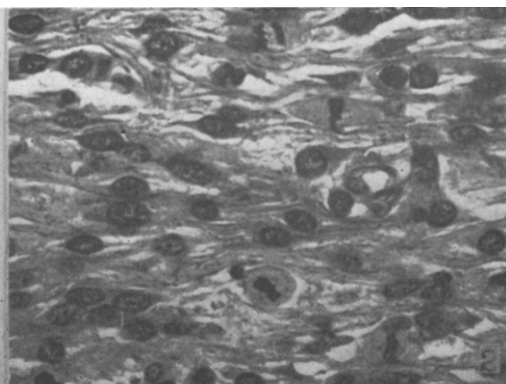
Another dog, a male black water spaniel mongrel (No. 52) about 1½ years old and weighing 8 kg, was injected (3/17/42) subfascially in the left flank with 40 mg of methylcholanthrene dissolved at about 45°C in 3 cc each of benzene and paraffin. On the 361st day, 100 mg of methylcholanthrene in a gelatin capsule were implanted subfascially through a small skin incision in the right side of the thorax over the 6th and 7th ribs. On the 735th day a nodule in direct continuity with the first methylcholanthrene given was found in the left lower quadrant of the ventral abdominal wall, where necropsy on the 791st day revealed a 23 mm firm, white, bulging neoplasm along the lateral border of the left rectus muscle. With hematoxylin and eosin stain the constituent cell was spindle-shaped, possessed tapering acidophilic processes, and had fairly distinct borders. The finely chromatinized nuclei of the cells were oval or oblong and contained 1 to 3 basophilic nucleoli each. Many mitotic figures (Fig. 2) were present. Some tumor cells showed 2 to 4 nuclei. The stroma contained pale basophilic material and toward the center of the tumor were areas of edema. Many capillaries were found. Numerous groups of acidophilic intercellular fibrillæ were basophilic with Mallory's connective tissue stain. The diagnosis was connective tissue neoplasm with the histologic characteristics of a mature fibrosarcoma. No metastases were observed.

The second methylcholanthrene implant revealed a 1.5 mm nodule of the carcinogen, but no neoplasm. This dog, the third dog

¹ Passey, R. D., *J. Path. and Bact.*, 1938, **47**, 349.

² Hueper, W. C., Wiley, F. H., and Wolfe, H. D., *J. Indust. Hyg. and Toxicol.*, 1938, **20**, 46.

³ Bonser, G. M., *J. Path. and Bact.*, 1943, **55**, 1.

FIG. 1. $\times 335$.FIG. 2. $\times 450$.

Connective Tissue Neoplasms Produced by Methylcholanthrene. Description in text.

described in a recent communication,⁴ was fed stilbestrol for the 280 days between the 34th and 314th days of the methylcholanthrene medication. On this 314th day, 500 mg of stilbestrol were implanted subfascially in the right upper quadrant of the ventral abdominal wall. The subsequent events and the clinical recovery of this animal have been reported.⁵

Methylcholanthrene was also administered in doses of 30 to 100 mg to 6 other mongrel dogs, 3 males (the 1st, 2nd, and 4th dogs

previously described⁴) and 3 females, about 1½ to 3 years old and weighing 7 to 14 kg at the start of the experiments lasting 150 to 618 days, but without the production of neoplasms demonstrable at autopsy at or near the site of injection or in other locations.

Summary. Connective tissue neoplasms with the histologic characteristics of fibrosarcoma were produced in 2 dogs by the subfascial injection of methylcholanthrene.

NOTE: Dog 53 was presented at the March 5, 1943, meeting and dog 52 at the May 26, 1944, meeting of the Rocky Mountain Section of the Society for Experimental Biology and Medicine.

⁴ Mulligan, R. M., *PROC. SOC. EXP. BIOL. AND MED.*, 1943, **54**, 21.

⁵ Mulligan, R. M., *Am. J. Path.*, 1944, **20**, 865.

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Effects of Fourneau 883 and Fourneau 933 on Late Renal Hypertension in the Rat.

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In a recent study of the effects of nembutal and yohimbine on the blood pressure of normal and hypertensive rats, Reed *et al.*¹ have shown that the blood pressure of *late* hypertensive animals is lowered by nembutal anesthesia and sympatholytic-adrenolytic doses of yohim-

bine, whereas the blood pressure of *normal* or *early* hypertensive animals is unaffected by these substances. These data were interpreted to signify a change in the mechanism of maintenance of renal hypertension in the animals used, the initial renal humoral disturbance which precipitates hypertension being superseded by neurovascular or other alterations which maintain blood pressure after the dis-

¹ Reed, Racheal K., Sapirstein, Leo A., Southard, F. D., Jr., and Ogden, Eric, *Am. J. Physiol.*, 1944, **141**, 707.