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Sarcomas Induced in Rats by Implanting Cellophane.

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In the course of experiments performed on rats to produce hypertension by wrapping regenerated cellulose film (cellophane) around one kidney, the accidental observation was made that several rats developed sarcomas in the neighborhood of the cellophane. As it was known that spontaneous sarcomas are a rarity in this Sherman strain of albino rats it was decided to investigate this question as an independent problem.

Method. The cellophane employed was regenerated cellulose film, the particular sample used throughout these experiments being known as Visking 5-1/2 H.S. ("high-stretch") cellulose sausage casing. Two strains of albino rats were used, the Sherman and the Wistar. The rats were fed on a mixture of Purina Laboratory Chow and Rockland Rat Diet in pellet form.

Cellophane was introduced by two methods into 110 male rats, 8 to 10 months old. In 55 of these, the left kidney was loosely wrapped with cellophane according to the familiar method introduced by Page.^{1,2} In the other 55 rats, a piece of cellophane 2-3 cm square was embedded subcutaneously in the abdominal wall, with a catgut suture passed through the corners to keep the film flat. At frequent intervals the site of the cellophane was palpated by an experienced technician to ascertain if any growth had started. The tumors were usually allowed to grow to a large size (2-5.5 cm in diameter) before the rats were sacrificed for histological examination.

Wherever possible, transplants were made from each tumor into 8-16 rats, usually males (but in some instances females), 6-8 months of age. A total of 422 rats were used for this

purpose, transplantation being carried out in some instances to the third, fourth and even fifth generation. Transplants were made by inoculating fragments of tumor tissue (0.003 to 0.006 g) subcutaneously into the anterior abdominal wall by means of a hollow platinum-iridium needle.

Results. As in the original accidental observation, a number of tumors were induced at the site of insertion of the cellophane. More than 11 months were required for their development. In the perirenal series the shortest time taken for the production of a tumor was 362 days from the date of wrapping to the development of a tumor 8 mm in diameter, whereas in the subcutaneous series the shortest period for development was 471 days.

Consequently, those rats that died from other causes within 11 months from the date of cellophane insertion were excluded altogether from the statistics, since they did not live long enough to develop induced tumors.

Among the rats with wrapped kidneys only 23 survived over 11 months, and of these 8 (34.8%) developed large well-defined tumors. Of the 55 rats in which the cellophane was embedded subcutaneously 42 survived beyond 11 months, and of these 15 (35.7%) presented tumors. The diagnosis of all these tumors was confirmed by microscopic examination.

The tumors resulting from transplantation appeared after 7 to 175 days. A total of 199 tumors were produced by transplantation from the primarily induced tumors, but this includes 126 instances in which well-defined growths subsequently receded, making microscopic examination impossible.

Types of Tumor. Of the 23 primarily induced tumors there were 17 fibrosarcomas, 2 liposarcomas, one rhabdomyosarcoma, one

¹ Page, I. H., *Science*, 1939, **89**, 273.

² Graef, I., and Page, I. H., *Am. J. Path.*, 1940, **16**, 211.

undifferentiated sarcoma, one osteogenic sarcoma and one plasmocytoma. Metastases occurred in 3 instances. Among the tumors derived by transplantation there were 63 fibrosarcomas, and a few other miscellaneous growths. Variation in differentiation and growth rate was noted in different generations.

Discussion. We have arrived at no conclusion as to the nature of the carcinogenic agent in these experiments. Attention is called to the fact that the procedure described is one of the simplest known for the production of sarcomas. In this connection the production of rat sarcomas by Turner³ by embedding disks of bakelite (phenol-formaldehyde) is of interest.

In the course of certain surgical procedures, cellophane has been used as a covering or sheath,⁴ and left in the human body. We are not acquainted with any reports of the devel-

opment of sarcoma in man subsequent to its use, but this possibility should not be forgotten.

Conclusions. 1. Sarcomas were induced in albino rats by the insertion of regenerated cellulose film either subcutaneously or by wrapping it around one kidney.

2. These tumors occurred in about 35% of the rats surviving the operation more than 11 months.

3. The tumors were transplantable.

4. This is a simple method for inducing sarcomas experimentally.

5. The foregoing results in rats should be taken into consideration in the surgical use of cellophane in man.

³ Turner, F. C., *J. Nat. Cancer Inst.*, 1941, **2**, 81.

⁴ Ingraham, F. D., Alexander, E., Jr., and Matson, D. D., *New Eng. J. Med.*, 1947, **236**, 403.

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Eugenol as a Stimulus for Gastric Mucous Secretion*†‡

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In the course of investigations in this laboratory on the characteristics of gastric mucus, various types of stimulation have been studied. These included subcutaneous injection of pilocarpine, gentle mucosal massage, and topical application of a number of aqueous solutions and emulsions including ether (saturated), ethyl alcohol (50%), isotonic NaCl (0.17 N), hypertonic NaCl (0.5 N), clove oil (5%), mustard oil (1%), and

distilled water.^{1,2,3} Among the several objectives of these investigations was the discovery of a mucus-stimulating agent which induces no parietal secretion and therefore might be adopted as a standard stimulus for further work on the physiology of mucus secretion. Of the nine stimuli already studied, the 5% clove oil-water emulsion was clearly the most suitable for the purpose, as evidenced by the following characteristics of specimens obtained after a single application of this agent: (a) high viscosity, (b) high pH,⁴ and (c) a large total volume relative

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¹ Hollander, F., Lauber, F. U., and Stein, J. J., *Am. J. Physiol.*, 1947, **149**, 724.

² Hollander, F., and Stein, J. J., *Am. J. Physiol.*, 1943, **140**, 136.

³ Hollander, F., Stein, J. J., and Lauber, F. U., *Gastroenterology*, 1946, **6**, 576.

⁴ Hollander, F., *J. Nat. Cancer Inst.*, 1945, **5**, 367.