

An adenocarcinoma of the true stomach was produced in 4 of 27 rats by application of a 5% solution of 20-methylcholanthrene to the gastric mucosa by means of an elastic wick from ampoules implanted into the stomach wall.

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Failure of experimental attempts to obtain tumors of the glandular portion of the rodent stomach is not entirely due to the increased resistance of this organ in the experimental animals to the action of carcinogens usually tested, but also to some extent to ineffectiveness of the methods used to apply the carcinogens to the gastric mucosa.

At the present time these methods may be divided into two main groups: application of carcinogens to the gastric mucosa (by mixing them with the food or administration through a tube) [2-4, 7-11], and injection of carcinogenic substances into the stomach wall (injection of solutions, implantation of pellets or threads containing the carcinogen) [3, 5, 6, 12].

The ineffectiveness of action of a carcinogen by contact on the stomach (methods of group 1) is due primarily to the specific features of this organ. The aqueous medium of the stomach, in which the carcinogens are practically insoluble, prevents sufficiently close contact, while their rapid evacuation with the food prevents sufficiently long contact with the mucous membrane.

The ineffectiveness of intramural administration of carcinogens is mainly due, as our own work and that of other investigators has shown [1, 5], to the speed of elimination of the carcinogens from the stomach wall.

In this investigation several methods of application of a carcinogen to the gastric mucosa were studied.

EXPERIMENTAL METHOD

Best contact between carcinogen and mucosa for the longest duration was obtained by the use of ampoules with an elastic wick (Fig. 1).

The ampoule was made of polyethylene tube with an external diameter of 5 mm, by drawing and blowing in a flame. After the ampoules had been filled with vegetable oil containing 5% 20-methylcholanthrene, a polyethylene capillary tube through which passed a silk thread (the wick) was glued into the neck of the ampoule.

The ampoules were implanted into the fundal region of the stomach so that the open end of the wick containing the carcinogen passed through the layer of moisture and rested on the gastric mucosa (Fig. 1). As a result of the great mobility of the stomach wall, constant rubbing of the mucosa against the end of the wick took place.

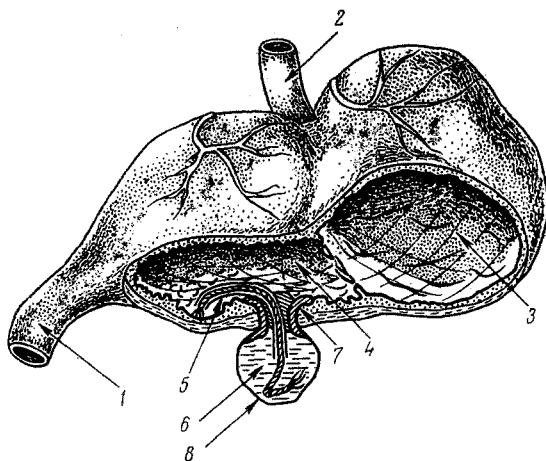


Fig. 1. Stomach of a rat with polyethylene ampoule implanted into wall of fundal portion (transverse section). 1) Duodenum; 2) esophagus; 3) proventriculus; 4) true stomach; 5) polyethylene capillary tube with silk wick; 6) carcinogen in vegetable oil; 7) neck of ampoule; 8) body of ampoule.

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Fig. 2. Adenocarcinoma (in center) of rat's stomach. Invasion of the serous membrane of the true stomach throughout its extent with tumor nodules (on the left). The proventriculus (on the right) is completely free from tumor.

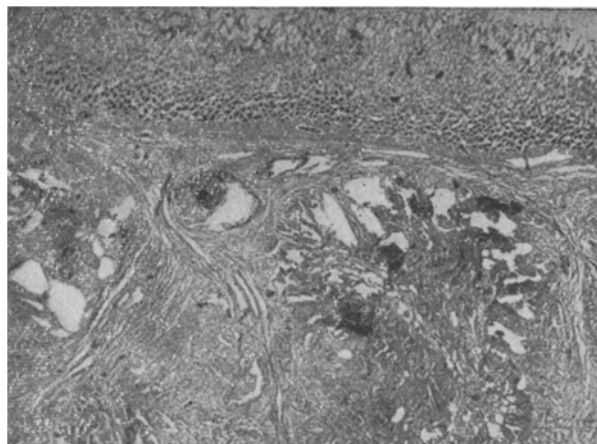


Fig. 3. Adenocarcinoma of the true stomach of a rat (endophytic form). Carcinoma tissue diffusely invading stomach wall. Tumor lined on inner surface with unchanged mucous membrane. Hematoxylin-eosin. 20 \times .

To implant the ampoules successfully, the body of the ampoule had to be completely stretched when filled (Fig. 1, 8).

The experiment were performed on 33 noninbred male rats weighing about 150 g.

EXPERIMENTAL RESULTS

One of the rats died on the day after operation (peritonitis developed and the ampoule escaped into the abdominal cavity), while 4 rats died in the 5th and 6th months without tumors. The remaining 28 animals remained under observation for 14 months. Observations were also made on 15 intact rats (control) throughout this period. The results of simultaneous weighing of the experimental and control animals showed that the implanted ampoules had no adverse effect on growth and development of the animals.

In the 15th month some of the rats died and the rest were sacrificed.

Despite their long stay in the stomach wall, the ampoules remained securely at the place of implantation. Only one ampoule had changed its position, and its wick lay in the proventriculus. In this case a malignant tumor of large size had formed from the squamous epithelium of the proventriculus, filling the proventriculus and protruding toward the diaphragm. In the true stomach no growth of tumor was found. In the remaining 27 rats the wicks of the ampoules turned toward the pylorus, the way in which they had been placed at the operation. Tumors of the gastric mucosa had developed in four of these animals. In none of these 4 rats was a tumor found in the proventriculus (Fig. 2). The tumors varied in size: 28 \times 18 \times 11 mm, 49 \times 35 \times 30 mm, 36 \times 31 \times 17 mm, and 34 \times 26 \times 14 mm, but their histological structure was similar*. The tumor tissue invaded the stomach wall diffusely (endophytic growth; Fig. 2), so that the wall was greatly thickened throughout its extent (10-30 mm). The normal relationships between the layers of the stomach wall and their continuity were disturbed, and on the inner surface, the tumor was covered only in some places by still intact mucous membrane (Fig. 3).

The histological picture (Fig. 3) was characterized by nodular heterotopic proliferation of the glandular elements, and by the stypia and polymorphism of the gland tubules, which in some places were invaginated with the formation of extensive cysts. Where the atypical glandular ducts and cysts were lined with stratified epithelium, it exhibited high mitotic activity. Side by side with extensive areas of necrosis, occupying a large part of the tumor, large areas of cancer cells could be seen, exhibiting marked polymorphism but still capable of producing mucin, which filled the numerous tiny, round cavities.

*Histological sections of the tumors were stained with hematoxylin-eosin and mucicarmine (to stain mucin).

All the tumors invaded the serous membrane of the stomach, an essential sign of malignant gastric neoplasms.

The method of application of 20-methylcholanthrene to the gastric mucosa of rats by means of a wick from ampoules implanted into the stomach wall, which we have developed, increases the effectiveness of this carcinogen, which does not produce tumors of the glandular part of the stomach in rodents when introduced into the stomach by the usual methods (with the food, through a tube).

The method described above for application of a carcinogen to the gastric mucosa requires further improvement, yet even as it stands it may be used in experiments requiring the production of carcinoma of the stomach.

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