

of the living esophageal mucosa in cats and dogs can be accomplished by bile, pancreatic juice, and mixtures of the two. (2) Bleeding from esophageal erosions attending the complete diversion of bile and pancreatic juice into the esophagus in the dog causes a severe

secondary anemia. (3) The development of the esophagitis and anemia in the dog is not altered by total excision of the acid secreting portion of the stomach.

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Effect of Inhaled Cigarette Smoke on Production of Peptic Ulcer in the Dog.* (18951)

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The effect of tobacco smoking on the etiology and course of peptic ulceration in man remains obscure. There is no reliable evidence that tobacco smoking causes peptic ulceration either experimentally or clinically. Barnett(1) failed to find a significantly greater proportion of smokers in 500 cases of peptic ulcer and gastric neurosis than in the general population. Gray(2) found 20% of ulcer patients failed to improve on medical management until tobacco was withdrawn. Batterman and Ehrenfeld(3) reported medical failures in 53.2% of habitual smokers and in 15% of non-smokers. Of the smokers who stopped of their own accord all responded satisfactorily to therapy; however when smoking was resumed, 85% had almost immediate recurrence of their disease. Trowell(4) found that men suffering from duodenal ulcer do not, on the average, smoke more tobacco than normal man but the practice of inhaling is twice as common in the ulcer group. Wolf and Wolff(5) reported no alteration in the motor and secretory activity of the stomach and

color of the mucosa by pleasurable smoking. The purpose of this investigation was to study the effect of inhaled cigarette smoke on the production of experimental peptic ulceration in the intact dog.

Method of study. Healthy adult mongrel dogs were used in all experiments. All dogs had been under observation for at least one month and were free of distemper. Permanent lateral tracheostomies were prepared in the following manner: Through a vertical midline incision in the neck the trachea was dissected free and delivered into the wound. The strap muscles of the neck were sutured together beneath the trachea to form a sling-like support. The anterior one-third of 3 tracheal rings was excised, leaving the underlying tracheal mucous membrane intact. From a central point in this square window, radial incisions were made in the tracheal membrane to the 4 corners of the window. This resulted in 4 triangular flaps of tracheal mucosa. The edges of the skin incision were sutured to the edges of the tracheal window so that the sutures passed through the tracheal cartilage and the mucosal flaps were approximated to the raw skin edges. After a recovery period of at least one month, the tracheostomy was fitted with an ordinary T-tube and a small cigarette holder was adapted to the tube. Lighted cigarettes were placed in the holder and the dogs were allowed to inhale the smoke directly into the bronchial tree. Inhalation

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1. Barnett, C. W., *Boston Med. and Surg. J.*, 1927, v197, 575.

2. Gray, I., *Ann. Int. Med.*, 1929, v3, 267.

3. Batterman, R. C., and Ehrenfeld, I., *Gastroenterology*, 1949, v12, 575.

4. Trowell, O. A., *Lancet*, 1934, v1, 808.

5. Wolf, S., and Wolff, H. G., *Human Gastric Function*, Oxford University Press, New York, 1943.

was intermittent to correspond to the human smoker. All animals tolerated this procedure well and seemed to suffer no ill effects. The daily number of cigarettes was administered over a 4-hour period. A daily intramuscular injection of histamine in beeswax was given in doses corresponding to 30 mg of base, according to the method of Code and Varco(6). At the time of injection, food pans were removed until the following morning. All animals, including controls, followed the same schedule of feeding, histamine injections, and time spent in the smoking room. All animals were fed a stock diet of vitamin enriched dog biscuit kibbles supplemented by daily fresh horse meat and milk.

Results. Series I. Effect of cigarette smoke alone. Five dogs were allowed to smoke 5 cigarettes daily for 6 months. When sacrificed there was no evidence of gastrointestinal ulceration or erosion. All animals remained in excellent health and showed a weight gain of 6 to 10 lb. Gross examination of the bronchial tree, lungs and coronary arteries showed no pathological changes.

Series II. Effect of histamine alone. A. In unoperated dogs. Ten dogs received a daily injection of histamine for 5 days and were then sacrificed. No lesions of the gastrointestinal tract were found. *B.* In tracheostomized dogs. A second series of 5 dogs had a lateral tracheostomy performed, and after a 30-day recovery period were given daily injections of histamine for 5 days. No ulcers or erosions were found in this group when sacrificed. All dogs showed a weight loss of one to 3 lb. In previous papers reported from this laboratory, the observed incidence of peptic ulcer following the daily administration of 30 mg of histamine base to healthy normal dogs over a 5-day period has varied from 10 to 20%. The longer observation period to allow the dogs to become completely adjusted to the laboratory environment may account for the complete absence of peptic ulceration in this series.

Series III. Effect of cigarette smoke and histamine. A. Thirty days or more after

lateral tracheostomy, 5 dogs were subjected to the smoke of 5 cigarettes and intramuscular injections of histamine daily for 5 days. Peptic ulceration of the duodenum was found in 2 dogs and a third showed a small superficial duodenal erosion. Two dogs showed no changes in the gastrointestinal tract. No perforation occurred in this group. All animals showed a weight loss of one to 6 lb. *B.* This series was similar to the preceding group except that the daily dose of inhaled smoke was doubled. Five dogs received the smoke of 10 cigarettes daily plus daily injections of histamine for 5 days. Peptic erosion or ulceration occurred in all animals. Duodenal erosion was found in 2, duodenal ulceration in 2, and both gastric and duodenal ulcers in one. There were no perforations. Four animals showed a weight loss of 1½ to 2½ lb and one gained 1½ lb. *C.* To test the thesis that the animals might develop a protective tolerance to smoke, 5 dogs received the smoke of 5 cigarettes daily for 30 days and then received both smoke and histamine for 5 days. In this group 2 animals were negative when sacrificed. One animal was found to have a duodenal erosion and 2 had multiple duodenal ulcerations, one of which was perforated (Fig. 1). In the animals with ulceration, a weight loss of 3 to 6 lb occurred during the smoke-histamine treatment. The other animals either maintained their weight or showed a weight gain.

Series IV. To determine how long dogs could survive the simultaneous administration of cigarette smoke and histamine, 5 animals received 5 cigarettes and histamine daily until death. Three dogs died in 5 to 12 days of typical chronic duodenal ulcers with perforation. One animal died of severe hemorrhage from a non-perforated duodenal ulcer on the 14th day. The remaining dog died of an acute gastric ulcer with perforation on the 51st day. The animals with duodenal ulcers all had a weight loss of 2 to 9 lb. The animal with gastric ulcer gained 2 lb before death.

Series V. The effect of "denicotinized" cigarettes ('SANO') was studied in a group of 5 dogs that received 10 such cigarettes daily plus histamine daily for 5 days and were then

6. Code, C. F., and Varco, R. L., PROC. SOC. EXP. BIOL. AND MED., 1940, v44, 475.

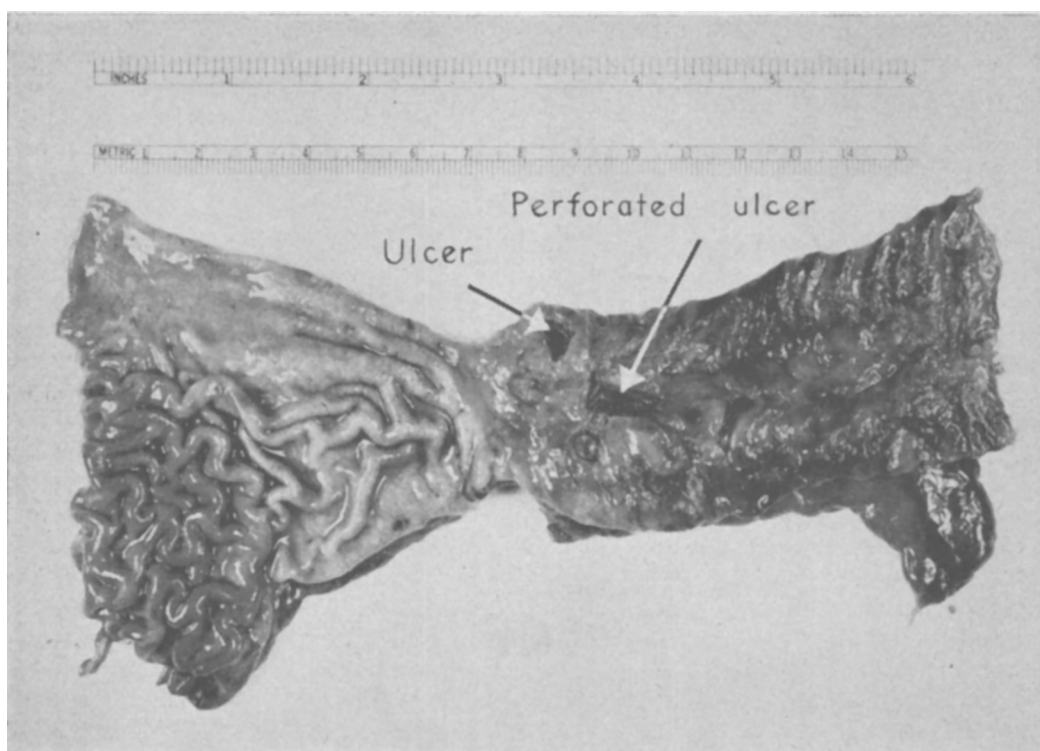


FIG. 1. Series III C, dog No. 4—Multiple duodenal ulcers with one perforation.

sacrificed. Duodenal ulceration without perforation occurred in one animal. The gastrointestinal tract of the remaining 4 dogs was negative. All sustained a weight loss of one to 5 lb.

Series VI. The effect of cigarette smoke inhalation on gastric secretory response was studied in 4 dogs with tracheostomies and total gastric pouches. In 16 trials there was either no effect or a slight decrease in volume and free acidity as compared to the standard fasting response for each dog. Schnedorf and Ivy(7) have reported similar results with Pavlov pouches.

Discussion. (1) Spontaneous peptic ulceration, rarely if ever, occurs in the intact dog. The daily inhalation of cigarette smoke over a period of 6 months failed to produce any gastrointestinal lesions in dogs. The animals all ate well during the experiment and either maintained their weight or showed an actual weight increase. After the first day or two

the animals exhibited no signs of irritation and remained very quiet during the inhalation of smoke. This was true only if the inhalation was intermittent; *i.e.*, alternated with breathing pure air in the manner of human smokers. Continuous inhalation of smoke led to prostration, and if allowed to proceed, the animal would die. Autopsy usually revealed pulmonary edema. (2) The ulcerogenic effect of histamine in beeswax on the dog's gastrointestinal tract has been well documented(8). In intact healthy animals the incidence is quite low when administered over a short time interval. In this series of unoperated dogs or 30 days after lateral tracheostomy, no ulcerations or erosions occurred over a 5-day interval. (3) The abetting factor of cigarette smoke was tested in dogs receiving histamine in beeswax. Of 15 dogs so tested 11 or 73% developed gastroduodenal ulcerations or erosions in 5 days. No ulcers or erosions were

7. Schnedorf, J. G., and Ivy, A. C., *J.A.M.A.*, 1939, v112, 898.

8. Hay, L. J., Varco, R. L., Code, C. F., and Wangenstein, O. H., *Surg., Gynec. and Obst.*, 1942, v75, 170.

found in 15 dogs on histamine alone. When the number of cigarettes was doubled the incidence of peptic ulcers or erosions increased from 60% to 100%. Under identical conditions denicotinized cigarettes did not provoke as high an incidence of ulcer-erosion as was obtained with ordinary cigarettes. Exposure to cigarette smoke for 30 days prior to the administration of histamine afforded little protection to the development of gastrointestinal lesions. In 5 dogs the continued simultaneous administration of cigarette smoke and histamine was uniformly fatal in 51 days. Four died of perforation and one of massive hemorrhage. According to Hay *et al.* (8) the

daily injection of histamine to fresh unselected stock dogs produced ulceration in 87.5% in 37 days. About 1/3 of these were perforated. The secretory response of total gastric pouches in dogs was either unaffected or slightly decreased by the inhalation of cigarette smoke.

Conclusion. (1) The daily inhalation of cigarette smoke failed to produce peptic ulcers in dogs. (2) Cigarette smoke abets the ulcerogenic effect of histamine in beeswax; this is believed to be a nicotine effect. (3) Cigarette smoke does not stimulate gastric secretion in dogs.

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Transplantability of Rabbit Ovaries in the Anterior Chamber of the Rabbit Eye.* (18952)

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Survival and growth of autologous, homologous and heterologous tissue transplants in the anterior chamber of the eye has been observed and confirmed by many investigators (1-7). By the use of this method, Goodman (4) transplanted immature rat ovaries into 60 female and 20 male rats and found the percentage of takes in non-castrated males and non-spayed females, 2 months after transfer, to be 90% and 89%, respectively. Takes

of transplants in females spayed concurrently and in those spayed 2 months after transfer were 100% and 33%, respectively, when examined 6 months after this operation. Continued growth of transplants in normal males castrated 2 months after transfer was evident in 80% of this group. Goodman utilized a Graefe knife for the corneo-scleral incision and curved, smooth, iris forceps to implant the tissue into the anterior chamber. Dunham, Watts, and Adair (6) studied newborn and adult rat ovaries transplanted into the anterior chambers of 137 rats. The percentage of takes was 74% in castrated males and 72% in spayed females, while those in non-castrate males and non-spayed females were 47% and 40%, respectively. A further group of spayed females and castrated males which had received chorionic gonadotrophin 3-14 days prior to tissue transfer yielded the highest percentage of takes (83%). The lowest percentage of takes was found when adult ovarian tissue was used. These workers used an angular keratome to make the ocular incision and donor tissue was inserted with a

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5. Goodman, L., *Anat. Rec.*, 1934, v59, 223.

6. Dunham, L. J., Watts, R. M., and Adair, F. L., *Arch. Path.*, 1941, v32, 910.

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