Differential Healing Periods of the Acetic Acid Ulcer Model in Rats and Cats

It is well known that submucosal injection of several agents, including silver nitrate, formalin, nicotine, and epinephrine can induce gastric ulcers in experimental cats and dogs[1-3]. These experimental lesions grossly and histologically resemble human gastric ulcers, although they heal rapidly in 2–3 weeks. However, one of the authors (S.O.) recently developed a chronic gastric ulcer model in rats which requires the gastric submucosal injection of acetic acid[4], and produces an ulcer which persists for 150 days. Thus, it was of interest to test the acetic acid ulcer procedure in cats, in which the gross anatomy of the stomach is similar to that of man, and compare the healing periods with the rat.

Materials and methods. Gastric ulcers were induced in male Sprague-Dawley rats (230–260 g) under ether anesthesia as described previously by TAKAGI et al.[4], by injection of 10% acetic acid (0.05 ml) into the submucosal layer of the stomach. After surgery the animals were fed normally (Purina Laboratory Chow) and sacrificed at 5, 60, or 200 days by an overdose of ether. Stomachs were removed and fixed according to the technique of BRODIE et al.[5]. Gastric ulcers were measured, and examined histologically (hematoxylin and eosin stain).

Male mongrel cats (2.3–2.7 kg) were subjected to a similar ulcerogenic procedure with the following variations. Cats were anesthetized by Surital (sodium thiamylal; 40 mg/kg, i.p.) and 20% acetic acid (0.5 ml) was injected into the submucosal layer of the gastric antrum on the lesser curvature. 10% acetic acid was not sufficiently ulcerogenic in the cat. The animals were maintained on a normal diet and 2 or 3 cats per period were sacrificed at 7, 14, 21, 28, 42, or 70 days after surgery by an overdose of Surital. After gross examination of the stomachs and measurement of ulcers, the gastric lesions were studied histologically.

Results. Both rats and cats withstood the procedure well, and adverse overt symptoms were not observed at any time during the experimental periods. The results for rats are delineated in Table I, and for cats are shown in Table II.

Gastric ulcer in rats. 5 rats sacrificed on the 5th day after the operation all had sharply defined, deep gastric ulcers (Figure 1a). Histological examination confirmed that the ulcers penetrated the entire gastric wall, and were characterized as confined perforations. By the 60th day the ulcers were markedly reduced in area and depth due to epithelial regeneration and connective tissue proliferation. However, at 200 days all rats had gross gastric ulcers of varying sizes (Table I). The gross appearance of a 200 day ulcer is illustrated in Figure 1b, and the histological character of this lesion is shown in Figure 2.

Gastric ulcer in cats. At 7 days after the operation, large and deeply excavated ulcers (4 mm in depth) were observed in the antrum of the stomach on the lesser curvature (Figure 3). The margins of the ulcers were overhanging and the floor was nodular and covered by necrotic debris, food residue and ingested hair. Histologically the lesion penetrated the entire gastric wall and in one of the cats the base of the ulcer consisted of omental fat adherent to the stomach (Figure 4). At 14 days the ulcer in the cat was smaller, but sharply defined (Table II), and granulation tissue in the lesion approached the level of the surface of the mucosa. The defect size was smaller at 21 days, and newly-formed capillaries were observed in the granulation tissue. By the 28th day, a small mucosal defect with nodular granulation tissue in the floor was found at the center of the area originally ulcerated. At 42 days after surgery the ulcer was completely healed, i.e., regenerated epithelia covered the entire surface of the ulcerated area. After 70 days the lesions remained healed, and there was no evidence of re-ulceration.

Discussion. The present experiments confirm the production of gastric ulcer in rats by submucosal injection

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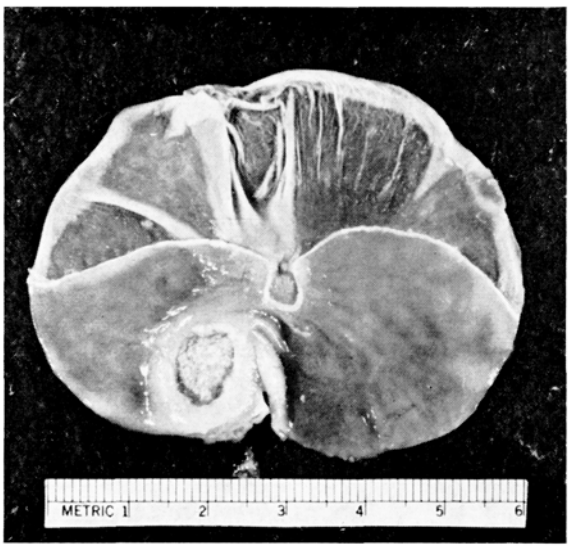

Fig. 1a. Experimental gastric ulcer in the rat at 5 days after induction.

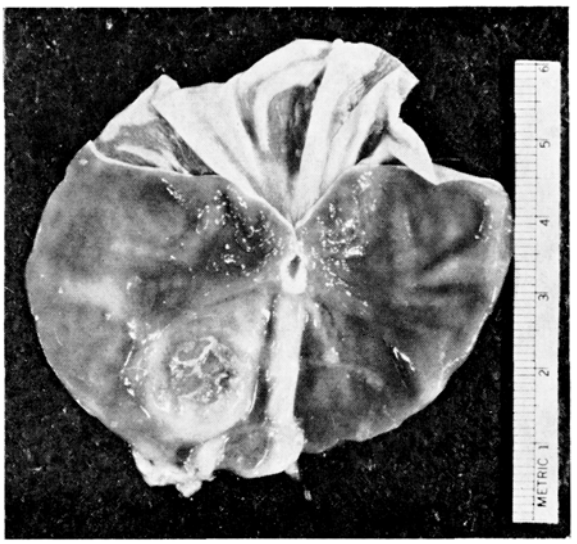

Fig. 1b. Experimental gastric ulcer in the rat at 200 days after induction.

Table I. Healing process of gastric ulcer in rats produced by submucosal injection of 10% acetic acid (0.05 ml)

No. of rats	Days after operation	Diameter of ulcer (mm)	Gross and histologic observations
12	5	10×9, 8×8, 9×9, 8×6 9×9, 9×9, 9×8, 8×8 6×5, 6×8, 4×6, 6×4	Punched-out deep ulcer adherent to adjacent liver (confined perforation).
5	60	3×3, 1×2, 1×1, 0, 0	Small, shallow ulcer. Well developed granulation tissue and limited epithelization. Healed ulcer in 2 rats.
4	200	12×12, 10×10, 2×1, 1×1	Clearly defined ulcer adherent to liver.

Table II. Healing process of gastric ulcer in cats produced by submucosal injection of 20% acetic acid (0.5 ml)

Cat number	Days after operation	Diameter of ulcer (cm)	Gross and histologic observations
1, 2, 3	7[a]	1.8×1.5, 1.9×1.1, 1.9×1.5	Sharply defined ulcer penetrating the stomach wall, and confined and adhered to liver. Necrotic, nodular floor.
4, 5	14	1.0×0.8, 0.9×0.7	Marked granulation tissue proliferation at the base.
6, 7	21	0.9×0.6, 0.6×0.4	Smaller, clearly defined, shallow ulcer with advanced proliferation of mucosal epithelium and connective tissue.
8, 9	28	0.5×0.4, 0.2×0.2	Small ulcer with necrotic material on surface.
10, 11	35	0, 0	Complete covering of regenerated epithelium on ulcer surface without interposition of muscularis mucosae and muscle layer.
12, 13	70	0, 0	Similar to 35 day response.

[a] Initially, gastric ulcers in cats were of similar size, in proportion to the entire stomach, as rat ulcers.

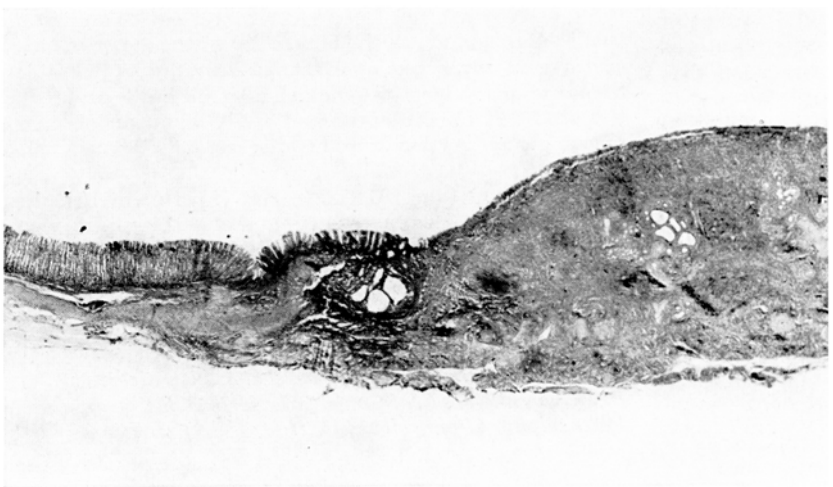

Fig. 2. Photomicrograph of the gastric ulcer in the rat at 200 days after surgery. ×18.

of acetic acid, and demonstrate that these lesions persist for at least 200 days. It seems likely that the experimental ulcer in the rat undergoes partial healing and re-ulceration under chronic conditions since large ulcers were observed at 200 days. In contrast, gastric ulcers produced in the cat were similar in appearance initially, and of similar size in proportion to the stomach, but completely healed at 35 days. The difference in healing was not attributable to the different concentrations of acetic acid used in the rat and cat since a stronger concentration was used with the cat. Although it is possible that the differential healing periods related to the different regions of the stomach in which the ulcer was induced (cat antrum, rat fundus), this is not likely since preliminary studies in our laboratory[6] indicated that acetic acid ulcer healing (painting method[7]) is slower in the rat antrum than in the rat fundus. In the present study the antral region was selected in the cat because human ulcers situated on the antrum are frequently chronic lesions[8]. However, in the rat, which has a much smaller stomach, it is

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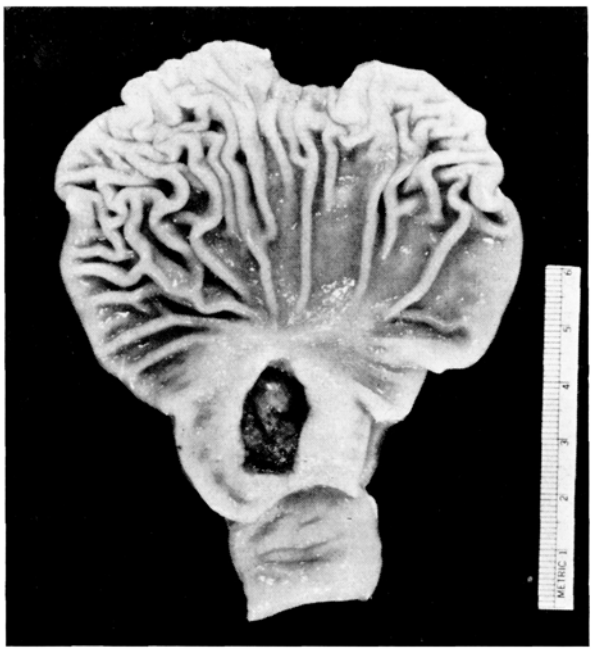

Fig. 3. Gross appearance of gastric ulcer in the cat antrum at 7 days after induction.

Fig. 4. Photomicrograph of the cat ulcer shown in Figure 3. ×18.

difficult to induce experimental acetic acid ulcers in the antrum by the injection method. The rapid healing of the gastric ulcer produced in cats by acetic acid observed here is similar to the rapid healing reported after nicotine, formalin and silver nitrate injection in cats[1-8], and after the mechanical induction of gastric defects in cats as described by GUNTER[9]. Thus, it can be concluded that the chronicity of the gastric ulcer in the rat is not necessarily related to the acetic acid itself, but to a special characteristic of the rat. Presumably, normal gastric mucosal regeneration times are similar for both species[10-13]. Inasmuch as the chronicity of the experimental, acetic acid ulcer model in the rat uniquely resembles human peptic ulcer, this model may be quite useful for the study of human ulcer and the evaluation of pharmacologic agents used for this disease.

Zusammenfassung. Methode zur experimentellen Erzeugung eines Magengeschwüres beim Tier, das weitgehend mit dem menschlichen Magengeschwür übereinstimmt.

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Photo-Orientation in the Larvae of the Waxmoth *Galleria mellonella* L. Reared Under Constant Dark and Constant Light Conditions

The larvae of *G. mellonella* live in the permanent darkness of the beehives, where they feed on wax. In the laboratory, they show distinct negative phototaxis. The present communication deals with the effect of constant darkness and constant light on the pattern of phototactic behaviour in these larvae.

The larvae were reared in the laboratory at 30 °C and 40% relative humidity under the two different lighting conditions mentioned above. The apparatus for testing the phototactic behaviour consisted of a black circular arena 50 cm in diameter. This was illuminated from one side by a projector lamp in such a way that uniformally decreasing light intensities were obtained on it opposite the source of illumination. The intensity at the centre of the arena was 3800 Lux.

During an experiment, 10 larvae were released, 1 at a time, in the centre of the arena. They crawled away either straight along the radius coinciding with the light axis, or often at a certain angle to it. The angle made by each of them with the light axis while crawling across the periphery of the arena was recorded. The angles to the right and left of the light axis were treated