INDUCTION OF GASTRIC ULCERS BY ACID FEEDING IN THE TOAD, *BUFO MELANOSTICTUS* SCHN.

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THE ætiology and pathogenesis of gastric ulcer is not clearly established. The most favoured hypotheses are gastric hypersecretion, decreased tissue resistance and vascular occlusion.[1] Ulcers induced by polymyxin-B,[2] histamine[3] or 'Shay' operation[4] may be due to hyperacidity. However, in steroid-induced ulcers there is decreased acid and mucous secretions in the stomach.[5] As there is no direct evidence to show that hyperacidity causes ulcers, this problem is investigated.

The toad, *Bufo melanostictus* Schn., is chosen for experimentation, because of its slow response, increased resistance to stress and easy availability. Animals weighing 30 to 50 gm. were starved for two days, later 0·5 ml. of 0·25 N to 1·25 N hydrochloric acid (HCl) (BDH) was administered *per os*, per toad twice a day for five days. The controls received equal amount of distilled water for the same period. All toads were autopsied 12 hours after the last feed, the stomach was dissected out, the number and severity of the ulcers were noted.[6] The ulcerated portion was fixed in Bouin's fluid, sectioned and stained in Harris' hæmatoxylin-eosin and Mallory's triple stains. A total of 70 female toads were used.

The stomach of the control toad shows normal gastric mucosa, muscularis mucosa, submucosa and muscularis externa (Fig. 1). Administration of 0·25 N HCl causes inflammation of the stomach and interstitial hæmorrhages in the superficial gastric mucosa. With 0·5 N HCl there is erosion of superficial gastric epithelium exposing gastric glands (Fig. 2). Definitive ulcers, with the erosion of entire gastric mucosa, are seen with 0·75 N HCl treatment (Fig. 3). Acute and deep ulceration results with 1 N HCl wherein there is complete erosion of gastric mucosa and muscularis mucosa with perforations in the submucosa and muscularis externa (Fig. 4). The severity of ulceration increases to a maximum with 1·25 N HCl treatment (Table I).

TABLE I

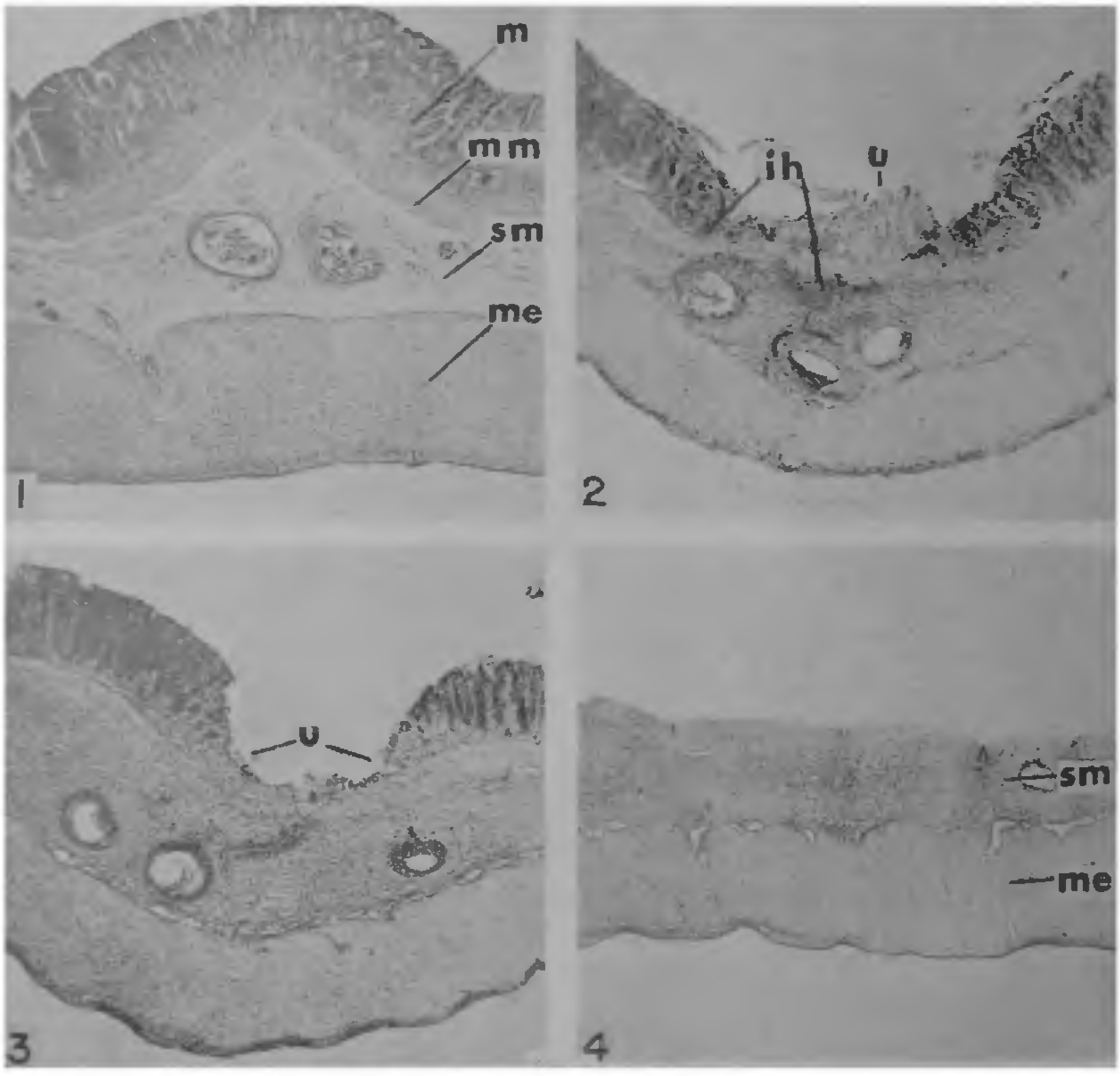
Effect of graded doses of hydrochloric acid on the induction of gastric ulcers in the toad

Treatment	Per cent. difference in Body weight	Per cent. Mortality	Ulcers			
			Number per toad (M ± S.E.)	Severity (M ± S.E.)	Per cent. incidence	Index *
Control (14)	+6·46	–	–	–	–	–
Hydrochloric Acid:						
0·25 N (9)	+5·24	–	1·0 ± 0·19	0·38 ± 0·01	75	8·88
0·5 N (16)	+9·35	–	2·6 ± 0·34	1·28 ± 0·27	93	13·18
0·75 N (10)	+9·52	10	5·8 ± 0·81	2·80 ± 0·40	100	18·60
1·0 N (13)	−4·25	23	6·7 ± 0·38	3·50 ± 0·07	100	20·20
1·25 N (8)	−8·43	50	9·0 ± 1·87	4·00 ± 0·00	100	23·00

Number in parenthesis denotes number of toads. M ± S.E. = Arithmetic Mean ± Standard Error.

* Ulcer Index[6] = Number of ulcers per toad + Severity (graded from 0 to 4+ based on the depth of ulcer) + Per cent. Incidence $\times 10^{-1}$.

Administration of adrenocortical steroids causes acute ulcers in rats without influencing the rate of gastric secretion.[6] The causative factors for ulceration appear to be decreased mucous secretion and tissue resistance.[5] Polymyxin-B[2] or histamine[3] treatment induces ulcers due to increased acidity in gastric secretion. The present experiment supports the view that hyperacidity causes ulcers, but whether it is due to hypersecretion of adrenals caused by the acid or by the release of histamine or serotonin by the connective tissue of the submucosa is not clear. This experiment offers an excellent method of inducing graded degrees



FIGS. 1–4. Transverse section of the stomach of the toad, × 45 (Harris' hæmatoxylin-eosin). *Fig. 1.* Control—showing normal mucosa and musculature of the stomach. *Fig. 2.* 0·5 N HCl treated—gastric epithelium is eroded exposing the gastric glands. *Fig. 3.* 0·75 N HCl treated—showing a definitive ulcer. *Fig. 4.* 1·0 N HCl treated—Acute ulcer showing loss of mucosa and muscularis mucosa with perforations in submucosa and musculature. (*ih*= interstitial hæmorrhage; *m*=gastric mucosa; *me*=muscularis externa; *mm*=muscularis mucosa; *sm*=submucosa; *u*=ulcer.)

of ulceration for testing anti-ulcerogenic drugs.

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1. Kirsner, J. B., *Ann. N.Y. Acad. Sci.*, 1962, **99**, 80.
2. Robert, A. and Nezamis, J. E., *Proc. Soc. Exp. Biol. Med.*, 1962, **109**, 698.
3. Hay, L. J., Vargo, R. L., Code, C. F. and Wangensteen, O. H., *Surg. Gynecol. Obstet.*, 1942, **75**, 170.
4. Shay, H., Komarov, S. A., Fels. S. S., Meranze, D., Gruenstein, M. and Siplet, H., *Gastroenterol.*, 1945, **5**, 43.
5. Robert, A. and Nezamis, J. E., *Proc. Soc. Exp. Biol. Med.*, 1963, **114**, 545.
6. — and —, *Ibid.*, 1958, **98**, 9.