A complementary method for the quantitative evaluation of rat stomach with Shay-ulcer

The 'Shay' technique (Shay, Komarov & others, 1945) is widely used in pharmacological laboratories for testing potential anti-ulcer drugs. It would appear that most research workers evaluate the incidence of 'ulcers' appearing on the rumen part of the stomach, by the scoring method of Bonta (1961) which is based on an assessment of both the number and diameter of lesions present. Another way of quantifying these gastric lesions is based on the 'all or none' method of determining the proportion of stomachs with lesions to those without.

To date, the various methods of evaluating the severity of gastric mucosal lesions induced by the 'Shay' technique have only taken into account their size and diameter. The degree of damage in depth to the stomach wall has not been considered. The ulcerogenic processes decrease the tensile strength (TS) of the stomach wall and if the experiment is allowed to continue long enough perforations may occur. It is considered that the method now proposed will give more quantitative data on the conditon of the stomach of rats subjected to the 'Shay' technique. In order to establish its potential usefulness, the effect of known parasympatholytics was examined. These were atropine sulphate (Merck), propantheline and isopropamide (Chinoin), Gastrixon (EGYT, tropin-zanthene-9-carbonic acid ester-Br-methylate).

Wistar rats, of either sex weighing 120–150 g, were used in the experiments. The animals were fasted for 24 h but not deprived of water. Ligation of the pylorus was performed under ether anaesthesia and test drugs were given subcutaneously immediately after completion of surgery. The animals were killed 2, 4, 6 and 18 h after ligating the pylorus, the stomachs were removed and the contents sucked out through the oesophagus. The TS of the stomach wall was then measured according to the following technique. A polyethylene cannula which was tied into the oesophagus was connected to a U-shaped mercury manometer and a Griffin-type hand bulb inflator with 3 valves. The stomach was then placed in a 50 ml round flask filled with physiological saline and a reservoir vessel at 10° was connected into the system. Pressure was gradually increased in the stomach with the introduction of air, by pumping the hand bulb inflator, until the stomach wall was torn or a bubble appeared in its surface. This process required 20–30 s. Identical observations were made on control animals fasted for 24 h. The TS was determined as the pressure, measured in mm Hg, required to rupture the stomach wall. Animals which died during the course of the 18 h experiment because of spontaneous rupture of the stomach were scored with a zero TS value. The results were subjected to statistical analysis using Student's *t*-test. The TS of unligated rat stomachs was 145 mm Hg. The weakest

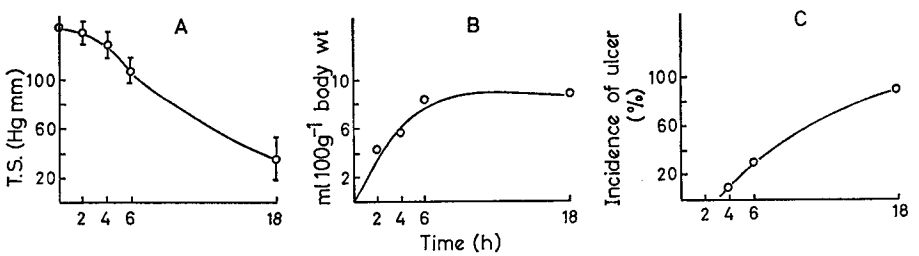

FIG. 1. Effects of the duration of ligation on the various gastric parameters. A. Change of tensile-strength (TS) of gastric wall. B. Change of gastric secretion. C. Incidence of ulcer (evaluation on the all or none principle). Each point represents the mean ±s.e. of a minimum of 10 rats.

Table 1. *Effects of various anti-ulcer drugs on the tensile strength of the gastric wall, after 18 h pyloric ligation.*

Treatment	Dose mg kg^{-1}	n	TS of gastric wall mm Hg
Control	—	43	39 ± 8·6
Atropine sulphate	5	10	54 ± 12·0
Propantheline	1·25	10	45 ± 19·0
,,	2·5	10	101* ± 13·0
,,	5·0	10	107* ± 4·2
Isopropamide	5·0	10	104* ± 2·8
Gastrixon	5·0	10	133* ± 5·0

* = $P < 0{\cdot}01$ when compared with control.

part of the normal stomach is in the rumen near the oesophagus. The TS value depends on the depth of the lesion and the area affected.

Changes observed in the TS of the stomach wall, the volume of gastric secretion, and the incidence of gastric lesions, which occurred after pylorus ligation are demonstrated in Fig. 1. The volume of the stomach contents reached a maximum level at 6 h, resulting in considerable dilation of the stomach and fatigue of its musculature over the course of the experiment. The latter feature was evident when the stomachs were placed in physiological saline at 10°. Normal stomachs gave strong contractions to the stimulus but the 'Shay' stomachs were unable to contract. This explains the low TS of the stomach wall after 6 h when gastric lesions began to appear.

It would appear, therefore, that the ulcerogenic process becomes progressively more intensive after 6 h, though it was noted that the initial appearance of gastric lesions was very variable in time and even after 24 h lesion-free stomachs were observed. The degree of damage to the connective tissue of the stomach, leading to tearing or bubbling, was not always related in depth to the size of the lesions present. In many cases quite small 'ulcers' penetrated deeply into the stomach wall.

Table 1 summarizes the protective effects of the various antiacetylcholine drugs examined using this technique in rats subjected to pylorus ligation for 18 h. Dose-dependent effects were demonstrated quite well. These drugs inhibit the formation of the gastric lesions by decreasing gastric acid secretion and the technique allows pH determinations to be made concurrently on the stomach contents. Gastrixon was found to be the most effective agent in protecting against the loss of TS in the stomach wall. This result is in close agreement with the findings of Kékes-Szabó & Thuránszky (1971). Atropine was almost without effect in this test but this can be explained on the basis of its short duration of action.

In our opinion the simple method described here offers complementary evidence to the 'Shay' technique in giving a more realistic picture of the extent of the overall damage caused to the connective tissue in the stomach wall.

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