

THE PROTECTIVE EFFECT OF HUMAN GASTRIC JUICE ON EXPERIMENTALLY INDUCED ULCERATION IN THE RAT

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In 1939 Brunschwig reported the presence of a substance in the gastric juice of achlorhydric patients which, when administered intravenously, diminishes the acidity and reduces the volume of gastric secretion in dogs.^{1,2} This substance was also found to be present in extracts of the antral mucosa of those patients and to a lesser extent in the gastric juice and saliva of patients with normal gastric function.^{3,4}

Subsequently, other workers confirmed Brunschwig's work and made interesting additional observations.⁵⁻¹³ It was shown that the inhibiting property of gastric juice is specific for water and hydrochloric-acid secretion, and is unrelated to pyrexia resulting from the injection of foreign proteins or mucinous substances.^{8,11,13} Smith and others found that this property is destroyed by boiling in an acid medium, thus signifying that it is of protein nature.

Smith further reported that if dogs are injected bi-weekly with dialysed and lyophilysed gastric juice they develop atrophic gastritis within 6 weeks.^{9,10} The histological changes in these stomachs were found to be strikingly similar to those which may precede gastric carcinoma, but were at least partially reversible after cessation of injections.

These findings led us to investigate the possibility of utilizing this property of gastric juice in the treatment of conditions which result from hypersecretion of the gastric glands. Thus, a series of experiments was undertaken to determine whether the development of experimentally induced ulceration could be prevented.

MATERIAL AND METHODS

Gastric juice was collected on ice at the Gastro-intestinal Clinic at Groote Schuur Hospital, immediately dialysed against distilled water for 24 hours at 5°C., and then

freeze-dried. The dry powder obtained in this way was stored at room temperature in airtight bottles. Immediately before use, the gastric juice was reconstituted in normal saline to a concentration of 10 mg. per ml.

The Shay rat preparation was used for the induction of gastric ulceration.¹⁴ Female albino rats weighing approximately 120 G. were starved for 48 hours to ensure that their stomachs would be completely empty. Under ether anaesthesia a midline abdominal incision was made and the pyloric-duodenal junction was ligated, taking care not to injure the gastric vessels or cause traction on the stomach. The abdominal incision was then closed with interrupted sutures. After 18 hours the rats were sacrificed. The volume and acidity of the gastric juice was measured and the stomach examined macroscopically for ulceration. Using this method ulceration develops in the rumen of the rat stomach within 18 hours, as a result of the accumulation of a large volume of highly acid gastric juice.

The inhibitory effect of gastric juice was tested on this preparation as follows:

The test animals received gastric juice intraperitoneally in 4-hourly doses of 5 mg., totalling 20 mg. of gastric juice per rat. The control rats received 0.5 ml. of normal saline intraperitoneally at the same times at which the test animals were given gastric juice.

Three experiments were performed:

1. In the first experiment, 16 rats divided into two groups were used: (a) 8 controls; and (b) 8 test rats which were each given a total of 20 mg. of gastric juice taken from a normal Bantu female.

2. In the second experiment, 18 rats divided into 3 groups were used: (a) 6 controls; (b) 6 which received injections of basally secreted gastric juice taken from a Coloured patient with gastric carcinoma; and (c) 6 which

received injections of histamine-stimulated gastric juice taken from the same patient.

3. In the third experiment, 26 rats divided into 3 groups were used: (a) 10 controls; (b) 6 which received injections of pooled gastric juice taken from normal European males; and (c) 10 which received similar injections of the same gastric juice after it had been boiled in a neutral medium.

RESULTS

1. In the first experiment the 8 rats used as controls all developed gastric ulceration as expected. In 3 rats ulceration was so severe that perforation of the gastric wall occurred. The 8 test rats in group (b) showed no signs of ulceration. There was a significant reduction of 35.8% in the volume of gastric secretion when compared with the controls ($p < .001$). The mean volume of the gastric juice of the controls was 5.7 ml. (SD = 0.30 ml.) and that of the test rats was 2.04 ml. (SD = 1.88 ml.).

2. In the second experiment all the control rats again developed ulceration. There were no signs of ulceration in groups (b) or (c). There was a noticeable reduction in the volume of gastric juice in both test groups, but the reduction was significantly greater in group (c) than in group (b). This interesting observation is being investigated further.

3. In the third experiment the 10 control rats all developed gastric ulceration. Ulceration was totally prevented in both groups (b) and (c).

DISCUSSION

The rat stomach is divided into two histologically different portions. The glandular portion is anatomically and functionally analogous to the body of the stomach in man. The rumen, or non-secretory part, has a smooth mucosa covered by a thin, stratified, squamous epithelium. It is here that the type of ulceration described develops (Fig. 1). In the Shay rat preparation gastric ulceration develops within 18 hours in 100% of cases. The extent of ulceration depends on the volume of secretion and the acidity of the juice in the obstructed stomach. In the rats that received gastric juice intraperitoneally there was a definite decrease in the volume of gastric secretion as compared with the controls. Although the acidity of the gastric juice from the test animals was well below the normal level for rat gastric juice, a valid comparison with the acidity of the control group could not be made, since all the control

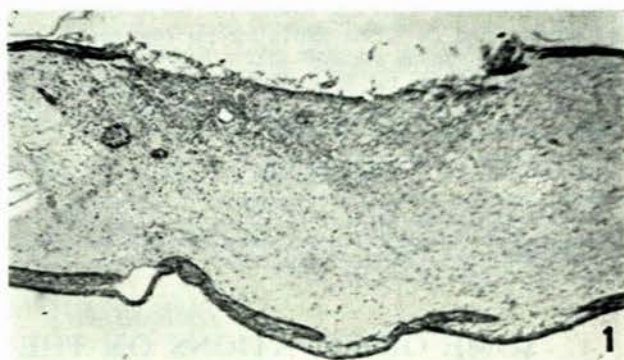


Fig. 1. Rumen of control rat showing ulcerative lesion. The mucosal break is characterized by a swarm of neutrophils.

rats had developed ulceration and the gastric juice was contaminated with blood with consequent buffering of the acidity.

Shay found that variation exists in tissue resistance to the action of gastric juice in individual rats. For this reason the severity and number of ulcers varied over a wide range in the control rats. In spite of this, in all the controls ulceration could be detected macroscopically (Fig. 2A), whereas in no test animals could even the beginnings of ulceration be found (Fig. 2B). Histological sections taken from the apex of the rumen, where ulceration usually develops first, failed to reveal any lesions in test animals.

The finding that boiling in a neutral medium has no effect on the property of gastric juice to inhibit gastric secretion confirms the reports of Smith *et al.*⁸ and of Menguay and Smith.¹¹

SUMMARY AND CONCLUSION

A series of experiments was undertaken in order to determine whether the property of human gastric juice to inhibit the acidity and rate of gastric secretion could be utilized in the treatment of conditions which result from hypersecretion of the gastric glands.

In order to induce gastric ulceration the Shay rat preparation was made on 60 female albino rats. Twenty-four rats acting as controls all developed ulceration. Gastric ulceration was totally prevented in the remaining rats by the intraperitoneal injection of freeze-dried human gastric juice. This protection was effected by inhibition of

the acid and rate of secretion.

It can be concluded from this investigation that gastric ulceration as exhibited in the Shay rat preparation can be prevented by the intraperitoneal injection of human gastric juice.

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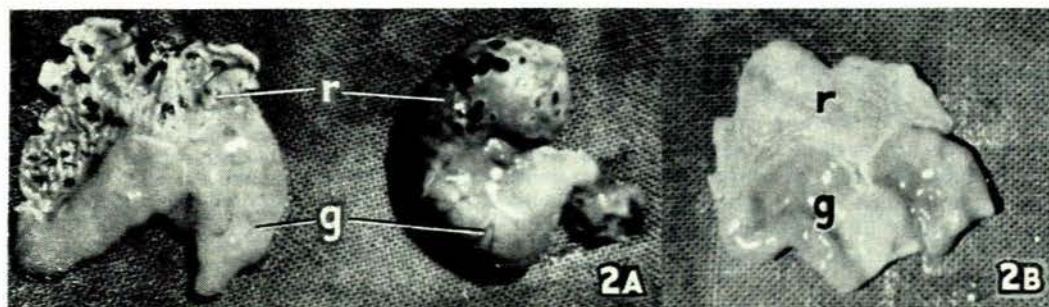


Fig. 2. A. Typical appearance of stomach of Shay rat preparation showing ulcerative lesions in rumen. B. Typical appearance of inner surface of stomach of Shay rat preparation after intraperitoneal gastric-juice injection. Key: r = rumen, g = glandular portion.

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