## Degraded carrageenan and histamine-induced parietal cell hyperplasia in the guinea-pig

SIR,—Repeated administration of a depot injection of histamine acid phosphate to the guinea-pig will cause a parietal cell hyperplasia of the gastric mucosa (Cox & Barnes, 1945). Sulphated polysaccharides will reduce the volume and acidity of gastric juice secreted by guinea-pigs treated with depot histamine (Anderson, Marcus & Watt, 1962). The parietal cell is believed to be the acid secreting cell of the stomach and we report the results of an examination of the effect on the development of this histamine-induced hyperplasia in the guinea-pig of the sulphated polysaccharide degraded carrageenan (Ebimar, Evans Medical Ltd.) (Anderson, 1961) given at the same time.

Male albino guinea-pigs, 475 ± 50 g weight, maintained on a cube and cabbage diet were used in three groups: group A, control; group B received i.m. injections of histamine acid phosphate suspended in beeswax (10%)—arachis oil, 10 mg/kg thrice weekly for four weeks; group C received the same dose of histamine but had a 5% solution of degraded carrageenan *ad lib.* in place of the drinking water given to the other groups. At the end of the experiment the animals were killed and the stomachs removed.

Parietal cell counts were made by the method used by Cox & Barnes (1945) as modified by Marks (1957); staining was according to Marks & Drysdale (1957). During processing, shrinkage of the strips containing the parietal cells occurred, but this was assumed to be constant in both directions and in strips obtained from all three positions (greater curvature (posterior and anterior walls) and lesser curvature) and was, therefore, ignored. 18 to 24 counts were made and averaged for the number of parietal cells occurring from the surface to the base of the mucosa in the representative strips 0·1 mm wide and 8 $\mu$ thick. The nuclear diameter averaged 6·7 $\mu$ for all three groups. Parietal cell counts for each stomach were calculated in millions per kg total body weight. The results (Table 1) indicated that degraded carrageenan prevented the development of the histamine parietal cell hyperplasia, although there is still a significant rise in parietal cell numbers ($t = 2{\cdot}61$; $P < 0{\cdot}05$).

TABLE 1. THE REDUCTION OF HISTAMINE PARIETAL CELL HYPERPLASIA IN GUINEA-PIGS BY DEGRADED CARRAGEENAN

| Group | No. of animals | Average body weight g | Parietal cell count millions per kg | |
|---|---|---|---|---|
| A | 6 | 505 | 187 | $t = 27{\cdot}3$; $P < 0{\cdot}001$ |
| B | 6 | 495 | 238 | $t = 2{\cdot}50$; $P < 0{\cdot}05$ |
| C | 5 | 492 | 196 | |

Group A was control; group B received histamine i.m.; group C received histamine and 5% solution of degraded carrageenan in place of drinking water, consuming an average of 64 ml per animal per day.

In another control group of two animals which received only degraded carrageenan *ad lib.* (no histamine) the parietal cell count was unaltered after one month ($187{\cdot}0 \times 10^6$ parietal cells per kg; average daily intake of 5% solution of degraded carrageenan, 59 ml).

At death there was no evidence of peptic ulceration in any group. This absence of ulceration with a dose of histamine which produced peptic ulcers in fasted susceptible animals is, we believe, due to the continuous presence of food in the stomach. The stomachs in group B appeared to be larger *in situ* at death, although after fixation and preparation for photography, the stomach areas per kg body weight of the different groups were not significantly different.

Although the histamine hyperplasia is less when degraded carrageenan is administered the number of parietal cells is not reduced below the normal level in group C and the effect, therefore, appears not to be one of general parietal cell toxicity.

Evidence which suggests the possibility of a humoral action of degraded carrageenan has been found (Anderson & Soman, 1963) in guinea-pigs prepared by high duodenal ligation, where the sulphated polysaccharide, introduced distal to the ligature, diminishes histamine-stimulated gastric secretion. In the present experiments the same mechanism could operate.

Sulphated polysaccharides adhere to the stomach mucosa by combining with the protein and mucoprotein of mucin in acid conditions. During histamine stimulation the parietal cell will, in its hyperactive state, be associated with an unusually high hydrogen ion concentration which will favour such reaction in the vicinity or even on the surface of these cells, perhaps to an extent sufficient to interfere with their multiplication.

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## Effect of γ-aminobutyric acid upon strychnine convulsions

SIR,—It has been demonstrated that γ-aminobutyric acid (GABA) applied to the surface of the cerebral cortex of several animal species protects the animals from electrically or chemically induced seizures (Purpura & Grundfest, 1956; Purpura, Girado & Grundfest, 1957). Furthermore, several investigators have demonstrated that acute administration of GABA parenterally protects animals from electrically and chemically induced seizures (Hawkins & Sarett, 1957; McLennan, 1957; 1958).

In the course of our experiments, we found that parenterally administered GABA (3·0 g/kg) failed to afford immediate protection to rats from electrically induced seizures and also strychnine seizures. Pylkkö & Woodbury (1959) demonstrated that the CD50 of strychnine was increased in rats pretreated with GABA 72 hr before treatment with the convulsant. This observation prompted us to study further the time course of the protective properties of GABA against strychnine seizures.

Mature male albino Holtzman rats were used. γ-Aminobutyric acid and strychnine sulphate were dissolved in saline and given intraperitoneally. The