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

animals were pretreated with 3·0 g/kg GABA; and strychnine was administered administered 30 min, 1, 2, 3, 4, and 15 days after GABA and the CD50 values for these animals determined ($CD50_1$) according to Litchfield & Wilcoxon (1949). The CD50 values for strychnine were calculated at the same time intervals for rats not pretreated with GABA ($CD50_2$). The potency ratio (PR = $CD50_1/CD50_2$) and the $f_{P.R.}$ were calculated by the method of Litchfield & Wilcoxon (1949).

TABLE 1. THE EFFECT OF GABA ON CD50 OF STRYCHNINE

Weight (g)	Number of rats	$CD50_1$ with GABA mg/kg	Number of rats	$CD50_2$ without GABA mg/kg	Potency ratio $CD50_1/CD50_2$	$f_{P.R.}$
112–128	18	½ hr after GABA: 1·9 (1·7–2·1)	18	2·6 (2·3–2·9)	0·7 (0·6–0·8)	1·2
130–188	18	1 day after GABA: 2·9 (2·5–3·4)	18	2·4 (2·1–2·8)	1·2 (0·9–1·6)	1·3
124–152	18	2 days after GABA: 2·8 (2·5–3·1)	18	2·7 (2·4–3·0)	1·0 (0·8–1·2)	1·2
86–114	18	3 days after GABA: 2·5 (2·3–2·7)	18	2·0 (1·8–2·2)	1·3 (1·2–1·4)	1·1
117–134	18	4 days after GABA: 2·8 (2·5–3·2)	18	2·5 (2·3–2·7)	1·1 (0·9–1·3)	1·2
180–237	18	15 days after GABA: 3·3 (2·9–3·7)	18	2·7 (2·4–3·1)	1·2 (1·1–1·3)	1·1

The results are shown in Table 1. It is evident that 3 and 15 days after GABA administration the CD50 of strychnine was elevated significantly.

It has been established by Eccles (1956) that strychnine selectively blocks the inhibitory synaptic transmission in the central nervous system. Therefore it is of interest that the convulsant activity of strychnine is altered 3 and 15 days after a single dose of GABA.

At the present, however, it has not been established whether GABA blocks excitatory synapses or enhances inhibitory transmission in the central nervous system. Furthermore, it still remains to be determined if GABA alone or a metabolite of it is responsible for the postulated inhibitory effects of this amino-acid. If the elevation of the CD50 of strychnine 3 and 15 days after GABA is due to this amino-acid, the observations presented seems to indicate that GABA has a long onset of action as an inhibitory agent. Whether GABA alone or a metabolite of it is responsible for this phenomenon also remains to be determined.

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