Letters to the Editor

Gastric and duodenal ulceration: differences

SIR,—The collective term peptic ulcer which has been used in experimental and clinical work to include ulceration of the stomach and duodenum becomes less descriptive as the different roles of the factors of causation in the two types of ulceration become clearer.

Hakkinen (1960), assuming injected histamine to be the sole cause of the ensuing experimental ulceration, suggested that the anatomical site of the lesion is related to the concentration of histamine in the blood. Thus, ulceration would be expected to occur predominantly in the stomach after high blood histamine levels are achieved, and in the duodenum after lower levels. However, this hypothesis appears to be based on experiments where a total of 12 guinea-pigs (groups of 8, 2 and 2) received different doses of aqueous histamine.

We have evidence which supports Hakkinen's hypothesis and which suggests that the causes of experimental ulceration at the two sites in the gut of the guinea-pig are different.

Healthy adult male guinea-pigs of one strain (strain T as used previously; Anderson & Soman, 1965a) were kept singly in cages which prevented access to sawdust and faeces; they were denied food during the 24 hr before and after injection. Three groups received respectively 1 ml/kg depot injections containing in 10% beeswax in arachis oil: histamine acid phosphate 10 mg/ml; atropine sulphate, 1 mg/ml; histamine acid phosphate 10 mg/ml plus atropine sulphate, 1 mg/ml. The drugs were sieved (200 mesh) before incorporation.

The animals were killed 24 hr after injection. Stomach and duodenum were removed, distended with water and ulceration was scored against transmitted light according to the scheme used previously (Anderson & Soman, 1965b). The results are in Table 1.

TABLE 1. ULCERATION IN THE GUINEA-PIG AFTER DEPOT INJECTIONS OF HISTAMINE, HISTAMINE PLUS ATROPINE, AND ATROPINE

No. of animals	Medication mg/ml, intramuscularly	Average ulceration (+ s.e.) gastric	Average ulceration (+ s.e.) duodenal
12	Histamine 10	1·4 ± 0·30	3·7 ± 0·11 } P<0·05
22	Histamine 10 + atropine sulphate 1 ..	1·3 ± 0·29	2·8 ± 0·26 }
12	Atropine sulphate 1	0	0

Atropine allowed the accumulation in the stomach of the gastric juice secreted under the influence of the non-lethal dose of depot histamine. Atropine is unlikely to confuse the present results because neither atropine nor vagotomy prevent the experimental histamine ulcer (Merkel, 1942; Baronofsky, Friesen, Sanchez-Palomera, Cole & Wangensteen, 1946), also the secretion-inhibitory effect of atropine in ulcer patients is controversial (Stein & Meyer, 1948; Kirsner, Levin & Palmer, 1948, Wyllie & Smith, 1965). Paton & Vane (1963) showed that atropine reduced histamine-induced motility of the guinea-pig stomach; Watt (1956) observed an increase in peristalsis in the guinea-pig stomach after histamine and also (Watt, 1963) greater duodenal damage following repeated administration of water which encouraged increased stomach emptying.

At the end of the present experiment, the stomachs were full of gastric juice and significant amounts of food, in spite of fasting, indicating delay in gastric emptying caused by atropine.

Table 1 shows decreased duodenal ulceration ($P < 0.05$) but unchanged gastric ulceration in the histamine plus atropine group. Duodenal ulceration is believed to be associated with the secretion of large volumes of acid gastric juice, and the decrease in duodenal ulceration observed could therefore be attributed to the less vigorous exposure to acid gastric juice occasioned by the decreased stomach motility. Increased damage to the stomach did not occur even when large volumes of juice were being retained for longer periods of time in contact with the gastric mucosa, supporting the view that, contrary to the supposed aetiology of the duodenal ulcer, the gastric lesion is not caused in the first instance by exposure to acid gastric juice. The severity of duodenal ulceration, which is not included in the ulcer score, was greater in the histamine group than in histamine plus atropine group, emphasising the association of the duodenal lesion with the acid gastric juice.

The acute gastric toxicity and subsequent devitalisation of the gastric mucosa produced by a sufficiently high, rapidly released, dose of histamine must precede the action of the gastric juice if ulceration is to follow (Anderson & Soman 1965a). This, taken with the fact that the relatively low, slowly released, histamine dose of 10 mg/kg i.m. in the present experiment caused ulceration primarily in the duodenum, indirectly supports Hakkinen's (1960) hypothesis.

This concept extends the belief (Dragstedt 1956, 1965) that gastric ulcer could be caused by hypersecretion following excessive antral activity. Further experimental examination of this point might be rewarding.

The direct approach of higher doses of depot histamine has been explored but antihistamine cover is required to protect the animals from the rapidly lethal effect of the histamine and a consistent gastric ulcer picture of 4+ grade cannot be obtained (Soman, 1963). We believe that this is due to interference by antihistamines with the gastric response to histamine (Watt, 1964; Anderson & Soman,1965a) together with rapid removal of the juice as a result of histamine-induced hypermotility of the stomach.

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