The functional 'G' cell mass in atrophic gastritis

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SUMMARY The serum gastrin response to a standard protein meal has been determined in achlorhydric patients with atrophic gastritis and contrasted with the response in normal subjects whose gastric contents were kept continuously neutral by intragastric bicarbonate instillation.

Five normal subjects showed a significant increase in serum gastrin from a mean ($\pm$ SEM) of 17 ± 3 pg/ml to 119 ± 10 pg/ml but their response did not approach that of four patients with atrophic gastritis and antral sparing (605 ± 133 pg/ml to 1418 ± 186 pg/ml). By contrast, in four patients with antral gastritis, there was no significant change in gastrin levels (24 ± 13 pg/ml to 55 ± 19 pg/ml).

These studies indicate that the gastrin-secreting cell mass is increased in atrophic gastritis with antral sparing and decreased in atrophic gastritis with antral involvement, as compared to the normal state. They provide further evidence for the existence in man of two distinct forms of atrophic gastritis.

Previous studies have indicated that the serum gastrin response to a standard protein meal provides an indirect measure of the mass of functioning gastrin-secreting ('G') cells (Korman, Soveny, and Hansky, 1971a; Korman, Soveny, and Hansky, 1971b). In health, the majority of these cells reside in the antrum of the stomach (McGuigan, 1968).

Estimation of the basal serum gastrin level in achlorhydric patients with atrophic gastritis has enabled two distinct groups of patients to be delineated. The first group, with hypergastrinaemia, has atrophic gastritis limited to the body and fundic mucosa with sparing of the antrum, and most have a positive test for the gastric parietal cell antibody. The second group, without hypergastrinaemia, has antral gastritis in addition to changes in the body mucosa and most are parietal cell antibody negative (Korman, Strickland, and Hansky, 1971c; Strickland, Bhathal, Korman, and Hansky, 1971).

In order to ascertain the 'G' cell mass in these two forms of atrophic gastritis, the serum gastrin response to a standard protein meal has been studied in each group and compared to that of normal subjects undergoing continuous intragastric neutralization.

Material and Methods

Eight patients, from a previously reported group with atrophic gastritis (Strickland *et al*, 1971), were selected on the basis of their antral mucosal histology. Four patients, three females and one male, aged between 43 and 67 years, had normal antral mucosal histology whilst the other four patients, two females and two males aged between 61 and 73 years, had antral gastritis with total or subtotal glandular atrophy. The clinical features, gastric mucosal histology, and response to the test for parietal cell antibody of these patients are shown in the Table.

Five healthy subjects, all volunteers aged between 21 and 25 years, were also studied. These subjects had normal gastric structure and the range of basal acid secretion for the group was between 2.1 and 5.0 m-equiv per hour. Informed consent was obtained from all participants.

After an overnight fast, a 19-gauge needle was inserted into a forearm vein, kept patent by frequent flushing with a solution of heparin (1 000 units) in 20 ml of 0.9% sodium chloride, and blood collected 30 minutes before, at the time of, and at 15-minute intervals for two hours after a standard protein meal (Korman *et al*, 1971a).

In addition the normal subjects underwent nasogastric intubation with fluoroscopic positioning of the tube in the antrum one hour before the meal. At zero time sodium bicarbonate (500 m-equiv per

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Group	Sex	Age	Gastric Acid (m-equiv/hour)		PCA ^a Status	Gastric Body ^a Histology	Clinical Status	Basal Serum Gastrin (pg/ml)
			Basal	Stimu- lated ¹				
Antrum spared	F	46	0	0	Pos.	Diffuse atrophic gastritis	Pernicious anaemia, hypothyroidism	690
	F	58	0	0	Neg.	Diffuse atrophic gastritis	Chronic hepatitis, thyroiditis	300
	F	63	0	0	Pos.	Multifocal gastritis	Pernicious anaemia in family	930
	M	68	0	0	Pos.	Gastric atrophy	Hashimoto's thyroiditis	500
Antral gastritis	F	61	0	0	Pos.	Diffuse atrophic gastritis	Hashimoto's thyroiditis	7
	F	69	0	0	Neg.	Multifocal gastritis	X-ray negative dyspepsia, osteoarthritis	0
	M	71	0	1.3	Neg.	Multifocal gastritis	X-ray negative dyspepsia	30
	M	73	0	0	Neg.	Multifocal gastritis	X-ray negative dyspepsia	60

Table Clinical details of patients with atrophic gastritis

¹Maximal stimulation with Histalog (betazole hydrochloride) 1.5 µg/kg body weight.^aPCA = Parietal cell antibody.^bBy peroral tube biopsy (Wood, Doig, Mottram, and Hughes, 1949)

litre) was instilled into the stomach at a rate of 50 m-equiv per hour. Frequent sampling of the gastric contents showed that the pH was above 7.0 throughout the study period.

Serum gastrin was estimated in duplicate by radioimmunoassay as previously reported (Hansky and Cain, 1969; Hansky, Soveny, and Korman, 1971b). Comparison of group means was by use of Student's *t* test (Snedecor and Cochran, 1968).

Results

The Figure compares the serum gastrin responses to a standard protein meal in four patients with atrophic gastritis but a spared antrum, four patients with antral gastritis, and five normal subjects undergoing continuous intragastric neutralization.

ATROPHIC GASTRITIS

Antrum spared

Serum gastrin showed a significant rise ($P < 0.01$) from a mean $\pm$ SEM basal level of 605 ± 133 pg/ml to a peak of 1418 ± 186 pg/ml recorded 75 minutes after the meal.

Antral gastritis

Serum gastrin showed a rise from a basal level of 24 ± 13 pg/ml to a peak of 55 ± 19 pg/ml recorded 90 minutes after the meal. The rise was not significant ($P = 0.1$).

NORMAL SUBJECTS WITH CONTINUOUS INTRAGASTRIC NEUTRALIZATION

Serum gastrin showed a significant rise ($P < 0.001$) from a basal level of 17 ± 3 pg/ml to a peak of 119

± 10 pg/ml recorded 60 minutes after the meal. The gastrin response to intragastric neutralization alone, performed in these subjects on a separate day, showed a significant rise ($P < 0.01$) from a basal level of 16 ± 2 pg/ml to 36 ± 4 pg/ml at 20 minutes

Fig. Serum gastrin response to a standard protein meal in atrophic gastritis with a spared antrum (four patients), antral gastritis (four patients), and normals undergoing continuous intragastric neutralization (five subjects). Note the broken vertical axis.

after beginning bicarbonate instillation and the level remained steady whilst neutralization continued, being 38 ± 4 pg/ml at 60 minutes when the study was completed.

The peak rise above basal levels was significantly greater in patients with atrophic gastritis and a spared antrum than either patients with antral gastritis ($P < 0.025$) or normal subjects ($P < 0.025$). The peak rise above basal levels in the normal subjects was significantly greater than in patients with antral gastritis ($P < 0.001$).

Discussion

Basal hypergastrinaemia is well documented in pernicious anaemia (McGuigan and Trudeau, 1970; Yalow and Berson, 1970; Hansky, Korman, Soveny, and St. John, 1971a). This has been attributed to the presence of achlorhydria and hence the lack of normal inhibition of gastrin release by acid (Yalow and Berson, 1970). In a recent study of basal gastrin levels in patients with gastritis and achlorhydria, two groups were delineated. Most patients with atrophic gastritis seropositive for parietal cell antibody had hypergastrinaemia whilst most patients with atrophic gastritis seronegative for parietal cell antibody had normal gastrin levels (Korman *et al*, 1971c). Therefore achlorhydria alone could not account for the basal gastrin elevation and alternative explanations were sought. Subsequently the state of the antral mucosa proved to be the major factor. It was shown that antral sparing was associated with hypergastrinaemia whereas in antral gastritis gastrin levels were not raised (Strickland *et al*, 1971).

The present investigation, in addition to providing physiological confirmation of earlier histological studies in atrophic gastritis, also gives an estimate of the mass of 'G' cells in this disease. The observation of an eight-fold difference in serum gastrin response to a protein meal in gastritis with antral sparing compared to normal subjects in whom acid inhibition of gastrin release had been prevented by intragastric neutralization supports the concept of a greatly increased mass of 'G' cells in this form of atrophic gastritis. Conversely, the insignificant rise in serum gastrin after a protein meal in patients with antral gastritis indicates an extremely small functional 'G' cell mass in such patients. This is best explained by destruction of 'G' cells by the gastritic process in the antrum.

The 'G' cell hyperplasia is presumably a response to repeated stimulation of these cells by food in the absence of the normal inhibitory influence of acid. Study of basal gastrin in patients with atrophic gastritis who were seropositive for parietal cell antibody has indicated significantly lower levels in

younger compared to older patients (Strickland, Korman, and Hansky, to be published). With increasing duration of disease the degree of 'G' cell hyperplasia might progressively rise.

The inability to suppress fully elevated basal serum gastrin levels by acid instillation into the stomach in patients with pernicious anaemia (Hansky *et al*, 1971a) suggests that part of this increased population of 'G' cells is autonomous and incapable of responding to normal inhibitory influences. If this part of the 'G' cell population is also incapable of responding to the stimulus of a protein meal, then the total 'G' cell mass in patients in whom the antrum is spared from gastritis may well be higher than our present estimate.

Thus, two forms of atrophic gastritis can be distinguished from a functional and histological point of view. In the first the antrum is spared from gastritis and basal hypergastrinaemia, together with a large functional 'G' cell mass, occurs. Most of these patients are seropositive for parietal cell antibody and the majority of patients with pernicious anaemia fall in this group. The other form has antral gastritis, normal basal gastrin levels, a small functional 'G' cell mass, and the majority of these patients are seronegative for parietal cell antibody and neither have pernicious anaemia nor a predisposition to it.

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