Progressive increase in the functional G cell mass with age in atrophic gastritis

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SUMMARY Patients with atrophic gastritis but normal antral mucosa and achlorhydria were divided into three groups according to age—under 40, 40 to 70, and over 70 years. Serum gastrin, both basal and following a standard protein meal, was estimated in all patients by radioimmunoassay. There was a significant correlation between the magnitude of the gastrin response and age, the older the patient the greater the response. These results suggest that with increasing duration of gastritis and continued stimulation of a normal antrum in the absence of inhibition by acid, the functional G (gastrin) cell mass increases. However the possibility exists that each cell may secrete more gastrin in response to the same stimulus with age. This may be resolved by counting the number of G cells in the stomachs of subjects with atrophic gastritis and different ages.

Patients with pernicious anaemia or atrophic gastritis sero-positive for the parietal cell antibody in general show antral sparing from the gastritic process, basal hypergastrinaemia, and an increased gastrin-secreting (G) cell mass (Korman, Strickland, and Hansky, 1971; Strickland, Bhathal, Korman, and Hansky, 1971; Korman, Strickland, and Hansky, 1972). The degree of gastrin elevation is quite variable and there is a significant correlation between basal serum gastrin levels and age in these patients (Strickland, Korman, and Hansky, 1973). It was suggested that G cell numbers in the spared antrum increase with age and increasing duration of gastritis.

In the present study, the functional G cell mass has been measured in patients with atrophic gastritis and antral sparing and correlated with age.

Material and Methods

Fourteen patients with atrophic gastritis and a histologically normal antral mucosa were studied. All had histamine-fast achlorhydria which refers to failure to change pH by more than 1 unit after stimulation, and a positive test for parietal cell antibody. There were seven females and seven males, aged between 24 and 85 years.

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After an overnight fast, a 19-gauge needle was inserted into a forearm vein, kept patent by frequent flushing with a solution of heparin, 1000 units in 20 ml of 0.9% sodium chloride, and blood was collected 30 minutes before, at the time of, and at 15-minute intervals for two hours after a standard protein meal (Korman, Soveny, and Hansky, 1971).

Serum gastrin was estimated in duplicate by radioimmunoassay (Hansky and Cain, 1969; Hansky, Soveny, and Korman, 1971). The comparison of differences between group means was by use of Student's *t* test; the relation between magnitude of gastrin response to protein and age was assessed by regression analysis (Snedecor and Cochran, 1968).

Results

The patients were grouped according to their ages: four patients less than 40 years, six patients between 40 and 70 years, and four patients over 70 years.

Figure 1 compares the serum gastrin responses to protein in these three patient groups. In patients under 40 years, serum gastrin (mean $\pm$ SEM) rose significantly from a basal level of 157 ± 19 pg/ml to a peak of 330 ± 31 pg/ml, 60 minutes after protein ($P < 0.001$). In patients between 40 and 70 years, serum gastrin rose significantly from a basal level of 640 ± 79 pg/ml to a peak of 1345 ± 130 pg/ml, 75 minutes after protein ($P < 0.001$). In patients over 70 years, serum gastrin rose sig-

Fig 1 Serum gastrin responses to protein in 14 patients with atrophic gastritis grouped according to age; four patients over 70 years, six patients between 40 and 70 years, and four patients less than 40 years. Scale of vertical axis is 10^3 pg/ml. All values are mean $\pm$ SEM.

Fig 2 Absolute rise in serum gastrin in 14 patients with atrophic gastritis plotted against age. Correlation line is significant ($r = 0.8684$, $P < 0.001$).

nificantly from a basal level of 1830 ± 70 pg/ml to a peak of 5012 ± 100 pg/ml, 60 minutes after protein ($P < 0.0025$).

Figure 2 plots the absolute rise in serum gastrin in individual patients. There is a significant correlation between magnitude of the gastrin response to protein and age ($r = 0.8684$, $P < 0.001$).

Discussion

Creutzfeldt, Arnold, Creutzfeldt, Feurle, and Ketterer (1971) have provided direct evidence of G cell hyperplasia largely confined to the antral mucosa, together with increased secretory activity of these cells, in patients with pernicious anaemia. Similar conclusions were reached by Korman *et al* (1972) in patients with atrophic gastritis and antral sparing, with or without pernicious anaemia, using the rise in serum gastrin in response to a protein meal as an indirect measure of the G cell mass. The present investigation has documented that the magnitude of the gastrin response to protein in patients with parietal cell antibody positive atrophic gastritis and antral sparing varies greatly, the variation being age dependent.

The relatively small gastrin response to protein in younger patients indicates that the increased G cell mass so characteristic of older patients may not be present *de novo* and that with increasing duration of disease and continued stimulation in the absence of inhibition by acid, the G cell population progressively increases. This postulated mechanism is strengthened by serial basal serum gastrin estimations, over a period of two and a half years in a man, now aged 24 years, with pernicious anaemia seropositive parietal cell antibody and with antral sparing. Initially, this patient had a basal serum gastrin of 60 pg/ml, within the normal range for this laboratory (0-120 pg/ml). A more recent serum gastrin level is 140 pg/ml and perhaps this rise in basal serum gastrin, with time, reflects a progressive increase in G cell numbers.

The present finding of a correlation between the magnitude of gastrin response to protein and age in atrophic gastritis with antral sparing corresponds closely with that between basal serum gastrin and age in a larger series of patients (Strickland *et al*, 1973). Thus, basal gastrin levels in patients with atrophic gastritis and achlorhydria and a spared antrum provide an accurate guide to G cell numbers.

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