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Parietal cell antibodies in relation to basal serum gastrin in a normal population

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SUMMARY

Parietal cell antibodies, basal gastric pH and serum gastrin were determined in 544 normal non-achlorhydric subjects. Serum gastrin was significantly higher in subjects with parietal cell antibodies, both in the group with a weakly positive and in that with a strongly positive fluorescence score. The elevated serum gastrin level in subjects with circulating parietal cell antibodies was independent of gastric pH. It is suggested that parietal cell antibodies may interfere with gastrin receptors on the membrane of the parietal cell, thus influencing the feedback mechanism between the secretion of acid and gastrin, and resulting in an increase of the basal serum gastrin level at an unchanged basal gastric pH.

Keywords parietal cell antibodies gastrin basal gastric pH

INTRODUCTION

Circulating parietal cell antibodies are not an unusual finding among the normal population (Jacobs *et al.*, 1969; Strickland & Hooper, 1972). Parietal cell antibodies are frequently demonstrated in subjects with achlorhydria (Fisher & Taylor, 1965), and are present in the majority of patients with pernicious anaemia (Taylor *et al.*, 1962). These antibodies have also been demonstrated in subjects with a normal gastric histology on biopsy (Te Velde *et al.*, 1964), perhaps because of a patchy distribution of the gastritic lesion.

The pathophysiological role of parietal cell antibodies is not clear. It is uncertain whether they contribute to the development of chronic gastritis, or are merely an epiphenomemon of gastric mucosal damage (Taylor, 1976). Parietal cell antibodies react with antigens inside the parietal cell (Hoedemaeker & Ito, 1970), as well as with receptors on the parietal cell membrane (Masala *et al.*, 1980). It was also found, that acid secretion by parietal cells was affected by parietal cell antibodies *in vitro*, perhaps because of an influence on gastrin receptors (Loveridge *et al.*, 1980). *In vivo* parietal cell antibodies might also react with receptors on the parietal cell membrane and interfere with the feedback mechanism between gastrin secretion and acid production. This would result in a change in basal gastric pH or serum gastrin level. In order to study the influence of parietal cell antibodies on basal gastric pH and serum gastrin these parameters were compared in a normal population.

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Subjects with achlorhydria were excluded, because in them the feedback mechanism between gastrin secretion and acid production is not functional.

MATERIALS AND METHODS

Gastric pH, serum gastrin and parietal cell antibodies were determined after an overnight fast in 564 normal subjects aged 35–68 years. (366 males and 198 females, mean ages 50·5 and 48·9 years, respectively, described earlier (Bins *et al.*, 1982). A sample of the basal gastric contents was aspirated using the method of Hector (1968), and the pH was determined (Radiometer, Copenhagen). In all subjects with a basal pH higher than 6·0 the gastric secretion was maximally stimulated with pentagastrin (6 μg/kg i.m.) and aliquots of the gastric contents were sampled after 15 and 30 min. If after 30 min the gastric pH was still higher than 6, achlorhydria was assumed. This was found in 14 subjects, who were excluded from the study.

The serum gastrin concentration was measured by radioimmunoassay using antibody 2604, which binds the main gastrin components in serum with equal affinity (Rehfeld, 1976). The upper limit of normal in our laboratory is 85 pg/ml (mean + 3 s.d.), the limit of detection is less than 10 pg/ml. Parietal cell antibodies were estimated by the indirect immunofluorescence method (Coons & Kaplan, 1950), using fluorescein labelled horse anti-human antiserum on cryostat sections of a rat stomach. The sera to be tested were diluted 1:20 to avoid aspecific reactions by heterophil antibodies (Hawkins, McDonald & Dawkins, 1977; Strickland & Hooper, 1972). The resulting fluorescence was scored as negative, weakly positive or positive; no titration procedure was used to estimate the antibody concentration. Six subjects were excluded from the study because parietal cell antibodies were not determined, the remaining 544 persons were grouped according to parietal cell antibody fluorescence score and compared regarding the basal gastric pH and serum gastrin. In order to exclude any bias caused by differences in basal gastric pH subgroups with a basal gastric pH < 5 with and without parietal cell antibodies were compared as to serum gastrin level. Results were expressed as mean $\pm$ s.e.

The Student's t-test was applied to the results after logarithmic transformation of the serum gastrin concentrations in order to obtain a normal distribution.

RESULTS

In 515 subjects no parietal cell antibodies were observed, a weakly positive parietal cell antibody score was found in 21 and a positive score in eight. Serum gastrin concentrations were significantly higher in subjects with parietal cell antibodies, both in the group with a weakly positive score and in those with a positive score (Fig. 1). Differences in mean basal gastric pH between these groups were not statistically significant (pH $3{\cdot}31 \pm 0{\cdot}1$, $4{\cdot}17 \pm 0{\cdot}6$, $3{\cdot}41 \pm 0{\cdot}9$, respectively). In the group with PCA as well as in the group without PCA 29% of the subjects had a fasting gastric pH > 6 (eight of 28 and 150 of 515, respectively). The difference in serum gastrin level between the subjects with a weakly positive and a positive parietal cell antibody score was not statistically significant (Fig. 1).

Subgroups of the subjects without parietal cell antibodies having a basal gastric pH below and over 5 differed significantly as to their serum gastrin level: 25·1 and 35·3 pg/ml respectively ($P < 0{\cdot}001$; Fig. 2). Subjects having a basal gastric pH below 5 were divided in two groups, one without and one with parietal cell antibodies, weakly positive as well as positive. Their basal serum gastrin level differed significantly: mean values were 25·1 and 41·7 pg/ml, respectively ($P < 0{\cdot}001$, Fig. 2).

No differences were found between the groups as to age or sex.

DISCUSSION

In an earlier study (Bins *et al.*, 1982) a relation was demonstrated between basal gastric pH and serum gastrin. This relation could be explained by the negative feedback mechanism which is active

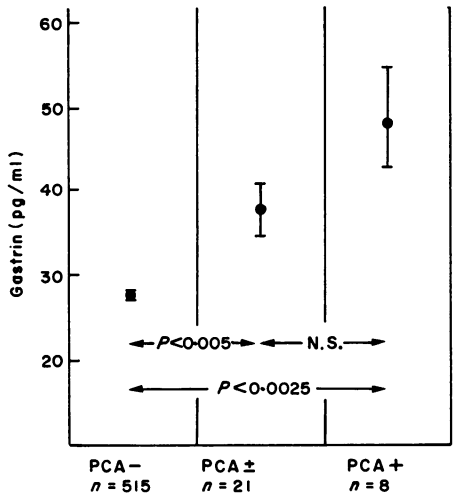

Fig. 1. Serum gastrin concentration in normal subjects grouped after parietal cell antibody fluorescence score (mean ± s.e.).

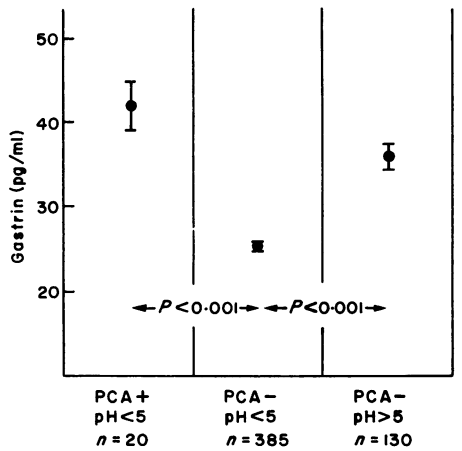

Fig. 2. Serum gastrin concentration in normal subjects grouped after parietal cell antibody fluorescence score and basal gastric pH (mean ± s.e.).

between gastrin secretion and acid production. As expected, this relation was also present in subgroups having a basal pH below and over 5 (Fig. 2). The differences in mean serum gastrin between the subjects with and without parietal cell antibodies were not dependent on basal gastric pH, which did not differ between the groups. A bias caused by differences in basal gastric pH was further excluded by the analysis of subjects having a basal gastric pH below 5, with and without parietal cell antibodies. In this pH range mean serum gastrin values do not differ significantly (Bins *et al.*, 1982). However, when subjects with and without parietal cell antibodies in this pH range were compared, a highly significant difference in serum gastrin was found ($P < 0{\cdot}001$, Fig. 2).

It is therefore likely, that the presence of parietal cell antibodies results in an increased serum gastrin level through a mechanism different from that mediated by gastric pH.

A possible explanation for this relation between serum gastrin and parietal cell antibodies might be that the feedback mechanism between gastrin secretion by the G-cell and acid production by the parietal cell is interfered with by these antibodies by blocking gastrin receptors on the parietal cell

membrane. This would cause an increase in serum gastrin level, since a higher serum gastrin would be required to reach the same acid production by the parietal cell. This hypothesis is in agreement with the *in vitro* findings that parietal cell antibodies are bound on the parietal cell membrane (Masala *et al.*, 1980), and with the study of Loveridge *et al.* (1980), who found a decreased acid secretion and carbonic anhydrase activity of parietal cells in the presence of parietal cell antibodies *in vivo*. They suggested a blocking of gastrin concentration as the possible cause. The increased serum gastrin concentration in subjects with parietal cell antibodies can be seen as an argument in favour of an *in vivo* influence of these antibodies on parietal cells. A cytotoxic effect, however, cannot be excluded.

It is difficult to interpret the unexpected finding, that both in presence and absence of PCA 29% of the subjects had a fasting gastric pH > 6. When we assume, that a fasting gastric pH > 6 usually is associated with a decreased maximal acid output and a loss of parietal cell mass, this seems to indicate that the prevalence of a small parietal cell mass (by chronic atrophic gastritis?) is not dependent on the presence or absence of parietal cell antibodies. Since data on gastric histology and function are not available in these subjects, it can only be speculated that the role of a humoral autoimmune mechanism mediated by PCA in the development of chronic atrophic gastritis is very modest or absent. This would be in agreement, however, with the finding that achlorhydria in a normal population usually is not associated with the presence of parietal cell antibodies (Bins *et al.*, 1983).

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