Varying occurrence of gastroduodenal immunoreactive pancreatic secretory trypsin inhibitor

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SUMMARY Operative specimens from various parts of gastroduodenal mucosa were analysed for immunoreactive pancreatic secretory trypsin inhibitor (PSTI) using a peroxidase-antiperoxidase method. Normal gastric mucosa exhibited a varying degree of PSTI immunoreactivity, which was more pronounced in the foveolar cells of gastric mucosa of fundus type than in the non-pepsinogen producing antrum pyloric mucosa. With the exception of metaplastic Paneth cells and some goblet cells, the intracellular content of PSTI was low in gastric mucosa with intestinal metaplasia. These findings may indicate that a PSTI immunoreactive substance has a role in the normal defence of the gastric mucosa.

Pancreatic secretory trypsin inhibitor (PSTI), a product of the pancreatic acinar cells secreted into the pancreatic juice, was first described by Kazal et al.1 Physiologically PSTI has an inhibitory effect on trypsin, and increased serum and urine concentrations have been noted in pancreatic diseases, especially in pancreatitis.2–5 Increased serum concentrations of immunoreactive PSTI have also been noted in gynaecological malignancy,6 7 in different malignant8 and inflammatory9 diseases and after major abdominal surgery.9 10 Normal plasma concentrations of immunoreactive PSTI have been shown after total pancreatectomy, suggesting an extrapancreatic source of immunoreactive PSTI.10

Recently we found immunoreactive PSTI in Paneth cells of both normal and gastric metaplastic type.11 We have also previously shown this cell type to contain immunoreactive trypsin.12

Material and methods

Formalin fixed, paraffin embedded tissue blocks from various parts of the human stomach (cardia, fundus and corpus, antrum and pylorus) and the duodenum were cut into 4–5 μm thick histological sections, deparaffinised, and prepared for immunohistochemical staining according to Sternberger et al.13 using the PAP method but with slight modifications.14 Rabbit antisera to human PSTI diluted 1/2000 were used. Further sections from each block were used as controls using non-immune rabbit serum and antiserum previously absorbed with PSTI. Staining was completely absent when the antiserum was absorbed by PSTI above 1 μg/ml (of diluted antiserum 1/2000). Rabbit antisera against PSTI were produced at our laboratory,15 and PSTI was purified from pancreatic juice as described earlier.15 Swine antirabbit IgG, peroxidase-antiperoxidase complexes (PAP), and normal swine serum were obtained from Dakopatts, Denmark.

Results

NORMAL GASTRIC MUCOSA

A strong positive PSTI immunoreactivity was shown in gastric mucosa of fundus (corpus fundus) type (fig 1), especially in the upper parts of the mucosa corresponding to the foveolar cells of the gastric pits. A slight immunoreactivity was found in the lower parts of the mucosa. In gastric mucosa of cardia and antrum pyloric type PSTI immunoreactivity was found in the deeper parts of the mucosa, corresponding to the foveolar cells occupying both the upper and deeper parts of the mucosa. The cardiac and pyloric glands showed weak immunoreactivity (figs 2 and 3).

METAPLASTIC GASTRIC MUCOSA

In gastric mucosa with chronic gastritis and intestinal metaplasia there was a severe deficiency of PSTI immunoreactive material in the upper parts of the mucosa and only slight immunoreactivity in its basal parts, mainly concentrated in cells of Paneth type and in some goblet like cells in the basal parts of the crypts.

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Fig 1  Gastric mucosa of fundus type. High concentration of PSTI in upper (foveolar) part of mucosa. Lower two thirds mucosa contains oxyntic and chief cells, mainly lacking in PSTI.

Fig 2  Antral mucosa (with chronic gastritis). High concentration of PSTI in all parts of mucosa, especially in middle and upper one third, corresponding to foveolar cells.

(figs 4 and 5). Such focal metaplastic mucosal areas appeared as PSTI immunoreactivity defects in the gastric mucosa.

DUODENAL MUCOSA
In duodenal mucosa the PSTI immunoreactivity was very weak in the surface columnar epithelium and strong in the Paneth cell region and in the goblet cells in the basal parts of the crypts (fig 3). The Brunner’s glands of the submucosa exhibited a varying degree of immunoreactivity. Control sections exposed to non-immune rabbit serum or antiserum previously absorbed with PSTI yielded no staining reaction.

Discussion
PSTI is a trypsin inhibitor in the acinar pancreatic cells.16 We have previously shown the presence of PSTI immunoreactive material in Paneth cells in the small intestinal mucosa and in Paneth cells of metaplastic type in colonic mucosa.11 We also found immunoreactive PSTI in normal gastric mucosa.17 This finding has now been studied in detail and immunoreactive PSTI was shown in the foveolar cells in the gastric pits of the upper parts of normal fundus mucosa. A similar distribution of immunoreactive PSTI in normal gastric mucosa was independently reported from another laboratory while this paper was in preparation.18 One difference, however, was that in that report immunoreactive PSTI was not found in the Paneth cells of either metaplastic gastric mucosa or normal mucosa of the small intestine. Our finding of immunoreactive PSTI in the goblet cells of the small intestine was, however, confirmed.17

Why PSTI should be found in the hydrochloric acid-pepsinogen producing part of the gastric mucosa
is not known at present. It may be that the PSTI immunoreactivity represents a common protease inhibitor activity or that PSTI and a possible pepsin protease inhibitor are immunologically related. The PSTI-like material may also have a throphic effect on gastroduodenal mucosa similar to that shown for epidermal growth factor (EGF). EGF is structurally related to PSTI and has been shown immunohistologically in the Brunner’s glands in the duodenum and in the gastric glands but not in the foveolar cells in the stomach. The presence of PSTI-like immunoreactive material has, however, been shown in various parts of the stomach but rarely in the Brunner’s glands.

The PSTI immunoreactivity shown in this study may also be of interest in the discussion of the pathogenesis of peptic ulcer disease. Gastric peptic ulcers are usually situated in those parts of the mucosa that do not produce HCL-pepsinogen—that is, mainly in the antrum and the pyloric mucosa. Gastric peptic ulcers are also usually seen in elderly patients, often in combination with chronic gastritis which, in turn, is often combined with intestinal metaplasia. In this study we have shown a reduced content of PSTI-like material in normal non-acid-pepsinogen producing gastric mucosa and, in addition, in the mucosa in gastritis with intestinal metaplasia. Taken together, these findings may indicate that a PSTI-like immunoreactive protein has some as yet unidentifiable role in the normal defence of the gastric mucosa.

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