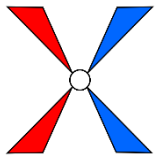


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<p><752/c></p>  <p>Key:</p> <p><u>Footprint</u></p> <p><u>ConEn1</u></p> <p><u>Footprint</u></p> <p><u>ConEn2</u></p> <p><u>Footprint</u></p> <p><u>ConEn3</u></p>	<p>association with endocrine cell hyperplasia, gastric carcinoid tumours have been observed in 1-7% of pernicious anaemia patients screened by gastroscopy. Procedures after the discovery of these tumours have varied from mere follow up to radical gastrectomy. The long term behaviour of small gastric carcinoids and results after their treatment need to be further observed. In this study we evaluated the findings of follow up gastroscopies performed three years after primary gastroscopic screening of pernicious anaemia patients. The aim of the gastroscopies was to detect possible new gastric tumours, to follow up known gastric carcinoids, and to observe the effect of sustained hypergastrinaemia on fundic endocrine cell changes. Patients and methods PATIENTS In 1986, 70 pernicious anaemia patients below the age of 76 years were screened by gastroscopy at the Second Department of Surgery of the Helsinki University Central Hospital. These patients had been treated earlier for pernicious anaemia in the same hospital between 1972 and 1985. The screening showed hyperplastic polyps in 12 patients (17%), a tubular adenoma in one patient (1%), and carcinoid tumours in five patients (7%). The lesions were found in the atrophic mucosa of the gastric corpus and fundus except for one antral carcinoid tumour. The carcinoids were associated with diffuse and nodular hyperplasia of fundic endocrine cells. Fifteen additional patients showed nodular hyperplasia of endocrine cells that was not seen in 14 normal controls. No cases of adenocarcinoma were found. The carcinoids were removed by hot biopsy forceps or electrocautery snare. In 1989, that is three years after the original gastroscopic screening, the same pernicious anaemia patients were called for a follow up gastroscopy. Fifty four of the original 70 patients attended the examination and two additional patients who had moved from the district had gastroscopy done elsewhere. The mean age of the patients (22 men and 34 women) was 60 years (range 27-78 years) at the time of the second gastroscopy. ENDOSCOPIC, HISTOLOGICAL, AND LABORATORY METHODS Several antral and fundic biopsy specimens were taken during the gastroscopies (Olympus GIF-Q 10). In addition to routine biopsy specimens all local changes such as discoloured spots, ulcerative lesions, and polyps were biopsied separately. The specimens were fixed overnight in neutral buffered 10% formalin and embedded in paraffin wax. The sections (4 µm) were stained with haematoxylin and eosin, Alcian blue (pH 2.5) - periodic acid Schiff, and Grimelius techniques. The diagnosis of carcinoid tumours was based on the typical histological morphology and positive Grimelius staining. The limit between <u>nodular hyperplasia</u> of <u>endocrine (argyrophil) cells</u> and carcinoid tumours was set at the size of 0.5 mm according to the classification of Solcia et al. <u>Hyperplasia</u> of <u>endocrine cells</u> was called <u>nodular</u> when there were <u>clusters of five or more endocrine cells</u> as suggested by Borch et al. Argyrophil (Grimelius positive) staining was supposed to detect most fundic <u>endocrine cells</u>. Morphometric calculation of <u>these cells</u> was performed using an ocular with a square raster plate (64 points) in the microscopic examination (magnification ×400). The technique has been described in detail previously. Briefly, the count of argyrophil cells and the count of raster points</p>
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	<p>coinciding on the mucosa were calculated in areas of standard length and whole thickness of mucosa. Thus it was possible to determine the density of argyrophil cells in arbitrary units of cell count per volume of the mucosa as expressed by the number of coinciding raster points. To reduce the risk of variable staining intensities, Grimelius staining was performed at the same time for all the specimens of one examination year. During both periods the same person (S-MS) did the countings blindly from the biopsy specimens which randomly represented the fundic (oxyntic) mucosa. Fasting serum gastrin was measured by a GASK-PR radioimmunoassay kit from Oris Company, France (normal range 5-50 pmol/l). According to the information provided, the antiserum used in the assay stained big-gastrin. Results</p> <p>ADENOCARCINOMA The follow up gastroscopies showed two cases of adenocarcinoma. The ages of the patients were 58 and 68 years, and the duration of pernicious anaemia was seven and three years, respectively. One of the carcinomas presented as an ulcer in the distal antrum and the other carcinoma was situated in the distal corpus in a tubular adenoma measuring about 3 mm in diameter. Both patients underwent subtotal gastrectomy without complications. One of the tumours infiltrated the submucosa and the other was confined to the mucosa. There was no spread to the lymph nodes. As for possible premalignant changes, all the patients had severe chronic atrophic gastritis in corpus biopsy specimens consistent with the diagnosis of pernicious anaemia, and four patients had slight atrophic changes in antral specimens. Corpus biopsy specimens showed intestinal metaplasia in 49 patients and all four patients with slight atrophic changes in antral specimens also had intestinal metaplasia in the antrum. In 1986 two patients had slight dysplastic changes in random biopsy specimens of the corpus area and six additional patients showed dysplastic changes in antral biopsy specimens. In 1989 the same two patients who had had dysplastic changes in the corpus specimens three years earlier again showed slight dysplasia. Of the six patients with dysplastic changes in the antral biopsy specimens in 1986, two did not participate in the follow up examination and the antral specimens of the remaining four patients were now interpreted as being devoid of dysplastic changes but in one case showing intestinal metaplasia. One additional patient showed slight dysplasia in the antrum. However, the random biopsy specimens in the patients with</p>
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