Argyrophilic Reaction of Histamine-Containing Epithelial Cells in Murine Gastric Mucosa

The major portion of gastric histamine in the rat is contained in a system of epithelial cells tentatively named 'enterochromaffin-like' cells, which are numerous in the basal portion of the oxyntic gland area[1-3]. These cells have the capacity to produce and store not only histamine but also monoamines, such as dopamine and 5-hydroxytryptamine[4-6], although these fluorogenic monoamines can be demonstrated in the cells only when exogenous monoamine precursors are supplied[4,5]. The ordinary enterochromaffin (argentaffin) cells, known to store 5-hydroxytryptamine, occur exclusively in the antral region of the gastric mucosa[4,5,7-9]. These latter cells are rich in non-specific aromatic L-amino acid decarboxylase, also referred to as L-3,4-dihydroxyphenylalanine (L-DOPA) decarboxylase (E.C.4.1.1.26), but they lack both histamine and the 'specific' L-histidine decarboxylase (E.C.4.1.1.22) in contrast to the enterochromaffin-like cells[4,6].

The selective staining properties and thus the histological identity of the histamine-storing, enterochromaffin-like cells of the rat stomach is virtually unknown[2]. The distribution and morphology of these cells suggested that they might be identical with the system of argyrophil (but non-argentaffin) cells described by DAWSON[7]. This assumption has been confirmed in the present investigation.

Specimens from the stomach wall of untreated animals (rats and mice) and of animals given L-DOPA (50–100 mg/kg i.p. 1 h before decapitation) were first processed for the histochemical demonstration of histamine (non-injected animals) according to the technique of HÅKANSON and OWMAN[1] or dopamine (L-DOPA-injected animals) as described by FALCK and OWMAN[10], followed by silver-staining[11] for detection of argyrophil cells. The section was mounted in xylene and photographed in the fluorescence microscope. After removal of the cover slip the section was silver-stained for detection of argyrophil cells and re-photographed in a light microscope. Direct comparison of the photomicrographs thus taken from one and the same section (Figure 1) showed all argyrophil cells to correspond to fluorescent histamine-containing epithelial cells. This was further confirmed by experiments in which the enterochromaffin-like cells were induced to store dopamine by the injection of its immediate precursor, L-DOPA, and which showed the argyrophil cells to be identical also with the fluorescent dopamine cells as seen in photomicrographs of one and the same section (Figure 2). The direct fluorescence microscopic identity between the histamine-storing and dopamine-producing cells in the gastric mucosa of the rat has previously been described[1]. There was no evidence in the present study that the administration of L-DOPA or the histochemical processing of the specimens for fluorescence microscopy interfered with the silver staining reaction; the number of argyrophilic cells and their staining intensity were the same as in control tissues (fresh cryostat sections) from untreated animals.

It has been suggested that the argyrophil and argentaffin reactions of morphologically similar gastrointestinal cells reflect different functional states of one and the same cell type[12]. In conformity with this hypothesis, argyrophil but non-argentaffin cells are sometimes referred to as pre-argentaffin[13]. The present results suggest that such a conclusion is unwarranted. The arguments indicating that the argyrophil, argentaffin (enterochromaffin) cells and the argyrophil, non-argentaffin (enterochrom-

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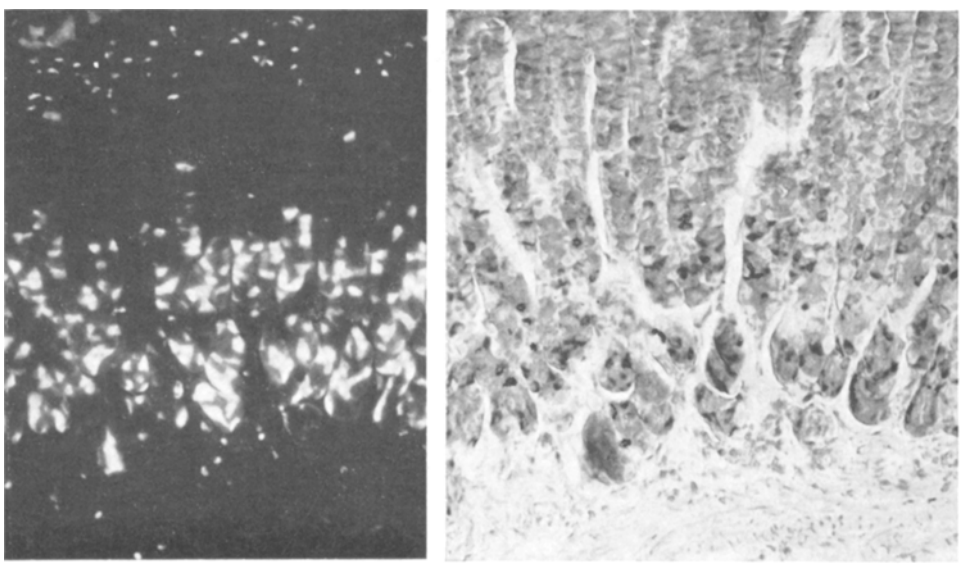

Fig. 1. Transverse section through the stomach wall in the oxyntic gland area from an untreated rat. Section first exposed to gaseous *o*-phthaldialdehyde for demonstration of histamine (left). Fluorescent mast cells near the mucosal surface. In the basal part of the mucosa an extensive system of histamine-containing enterochromaffin-like cells. Some few mast cells also in the submucosa. The section was subsequently silver-impregnated (right) to show the agreement between the enterochromaffin-like cells and the argyrophil cells. × 115.

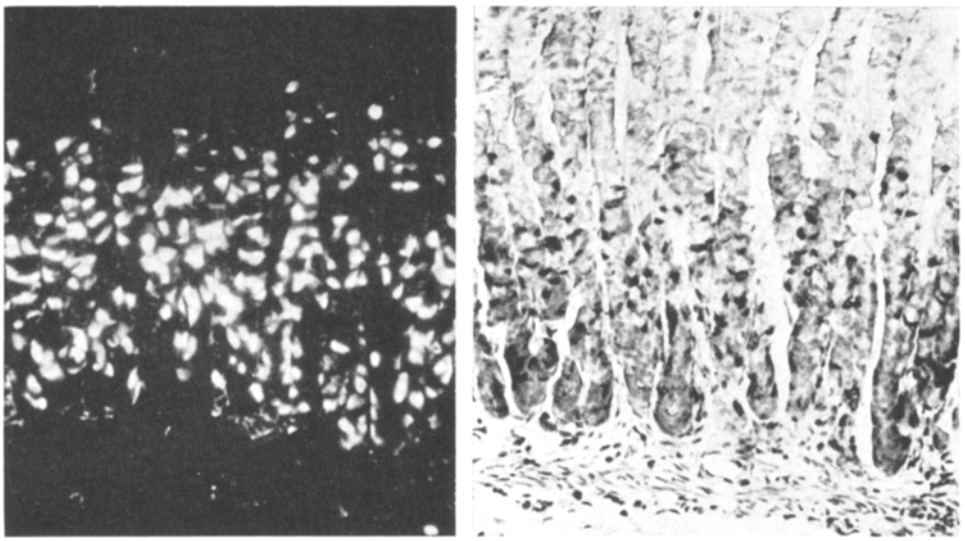

Fig. 2. Section from the same region of the stomach wall as in Figure 1, rat pretreated with L-DOPA. Formaldehyde-induced green fluorescence (left) in the enterochromaffin-like cells which have been induced to store dopamine. The argyrophil cells appearing after silver-staining are identical with dopamine-containing enterochromaffin-like cells. × 140.

affin-like) cells of the murine gastric mucosa are 2 different cell systems can be summarized as follows: (1) There is no evidence that argyrophil cells in this part of the gastrointestinal tract are ever transformed into argentaffin ones; the latter cell type is extremely rare in the oxyntic gland area, which on the other hand is very rich in argyrophil cells. (2) Argyrophil, non-argentaffin cells contain histamine and histidine decarboxylase; argentaffin cells do not. (3) Argentaffin cells are rich in DOPA decarboxylase; this enzyme is present also in the argyrophil, non-argentaffin cells but in considerably lower concentrations.

Nevertheless, the 2 systems of enterochromaffin and enterochromaffin-like cells have several properties in common – general morphology, all the characteristic features of protein-secreting cells, the capacity to produce and store amines – which may imply a similar function of these cells. It has been suggested that both the argentaffin and the argyrophil (non-argentaffin) cells of the digestive tract are endocrine in nature[14–18] and that they may be active in producing polypeptide hormones such as gastrin, secretin, pancreozymin-cholecystokinin and possibly also glucagon.

It should be pointed out that although the 2 endocrine cell systems of gastric mucosa are cytochemically different, the argyrophil but non-argentaffin cells observed elsewhere in the digestive tract may perhaps still be referred to as pre-argentaffin or as argentaffin cells temporarily devoid of their reducing cytoplasmic material[19].

Zusammenfassung. Durch fluoreszenzmikroskopische Untersuchung und nachfolgende Silberfärbung an ein und demselben Schnitt konnte gezeigt werden, dass das System argyrophiler, nicht argentaffiner Zellen in der Magenschleimhaut der Ratte mit demjenigen histaminspeichernder Epithelzellen identisch ist. Die histaminspeichernden Zellen, die argyrophil (aber nicht argentaffin) sind, bilden ein Zellsystem, das von dem der enterochromaffinen, serotoninhaltigen Zellen getrennt ist. Diese enterochromaffinen Epithelzellen sind im Gegensatz zu den histaminhaltigen Zellen sowohl argyrophil als auch argentaffin.

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The Investigation of *Xenopus laevis* Hemoglobins During Development by a Fluorescent Antibody

Analysis of hemoglobin solutions prepared from the blood of young tadpoles and mature adults of the South African Clawed Toad, *Xenopus laevis*, show that there are separate types of hemoglobin present in the tadpoles and adult animals respectively. Solutions of hemoglobin prepared from erythrocytes by osmotic shock were subjected to column chromatography on Whatman Chromedia CM52 carboxymethyl cellulose. The samples were eluted in a 0.01 *M* sodium phosphate pH gradient and eluent fractions were assayed for pH and optical absorption at 410 nm wavelength. Hemoglobin from *Xenopus* tadpoles emerges from the column in 2 elution peaks, at pH 6.50 and pH 6.82 respectively. The hemoglobin from adults emerges in 2 major and 1 minor peak at pH 7.41, pH 7.53, and pH 7.81 respectively. If an artificial mixture of hemoglobin solutions from adult and tadpole *Xenopus* is chromatographed, 5 elution peaks are seen, coincident with the 2 tadpole and the 3 adult peaks respectively.

Hemoglobin solutions from tadpole and adult *Xenopus* were also subjected to polyacrylamide gel disc electrophoresis in a *Tris*-Borate-EDTA buffer system at pH 7.8. The tadpole hemoglobin separated into 2 bands, one moving towards the anode more quickly than the other,