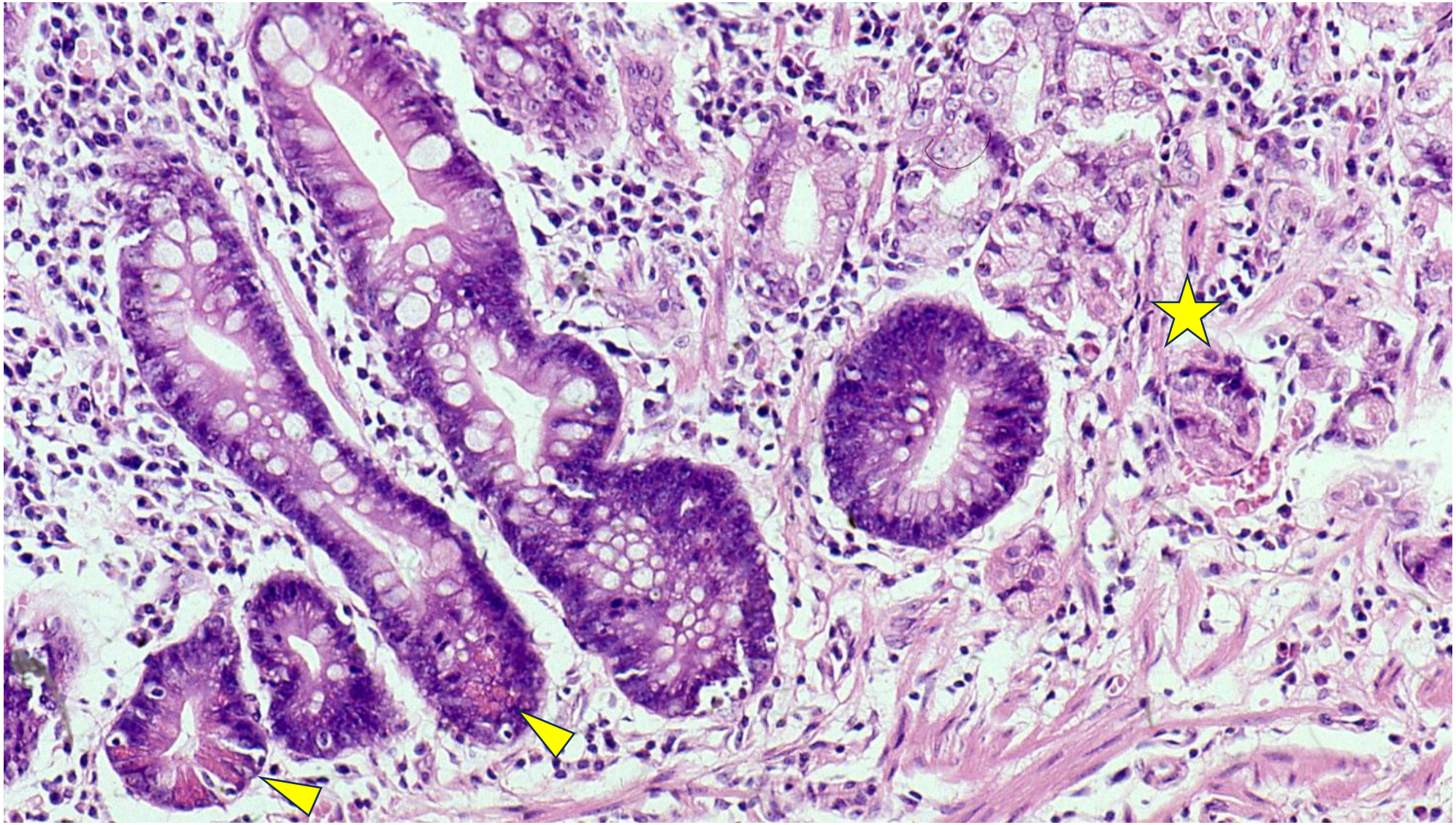
Pathophysiology of intestinal metaplasia of the gastric mucosa

・Non-intestinalized gastric mucosa with evident inflammatory changes shows weak immunoreactivity of secretory component (SC) at the generative cell zone. Enhanced immunoreactivity of SC with evidence of transepithelial transport of IgA and IgM, but not of IgG, is demonstrated in intestinalized glands of either complete or incomplete type. The number of inflammatory cells and lymphoid follicles are decreased in intestinalized mucosa when compared with that in non-intestinalized gastritic mucosa. J chain-negative IgG plasma cells and T cells, both of which are fairly abundant in the non-intestinalized mucosa, are remarkably decreased in the intestinalized mucosa, whereas the decrease of J chain-positive IgA or IgM plasma cells is slight or equivocal. In either mucosa, IgA is the most popular immunoglobulin class in plasma cells. IgD plasma cells are very rare. In the germinal centers of lymphoid follicles which are preferentially distributed in non-intestinalized gastritic mucosa, IgM or IgG germinocytes predominate over IgA germinocytes. Intraepithelial lymphocytes with a T-suppressor phenotype are detected in intestinalized glands. Intestinal metaplasia should be an adaptation to long-standing chronic gastritis. *(*Helicobacter pylori infection is never seen on the surface of the intestinal metaplasia.)*

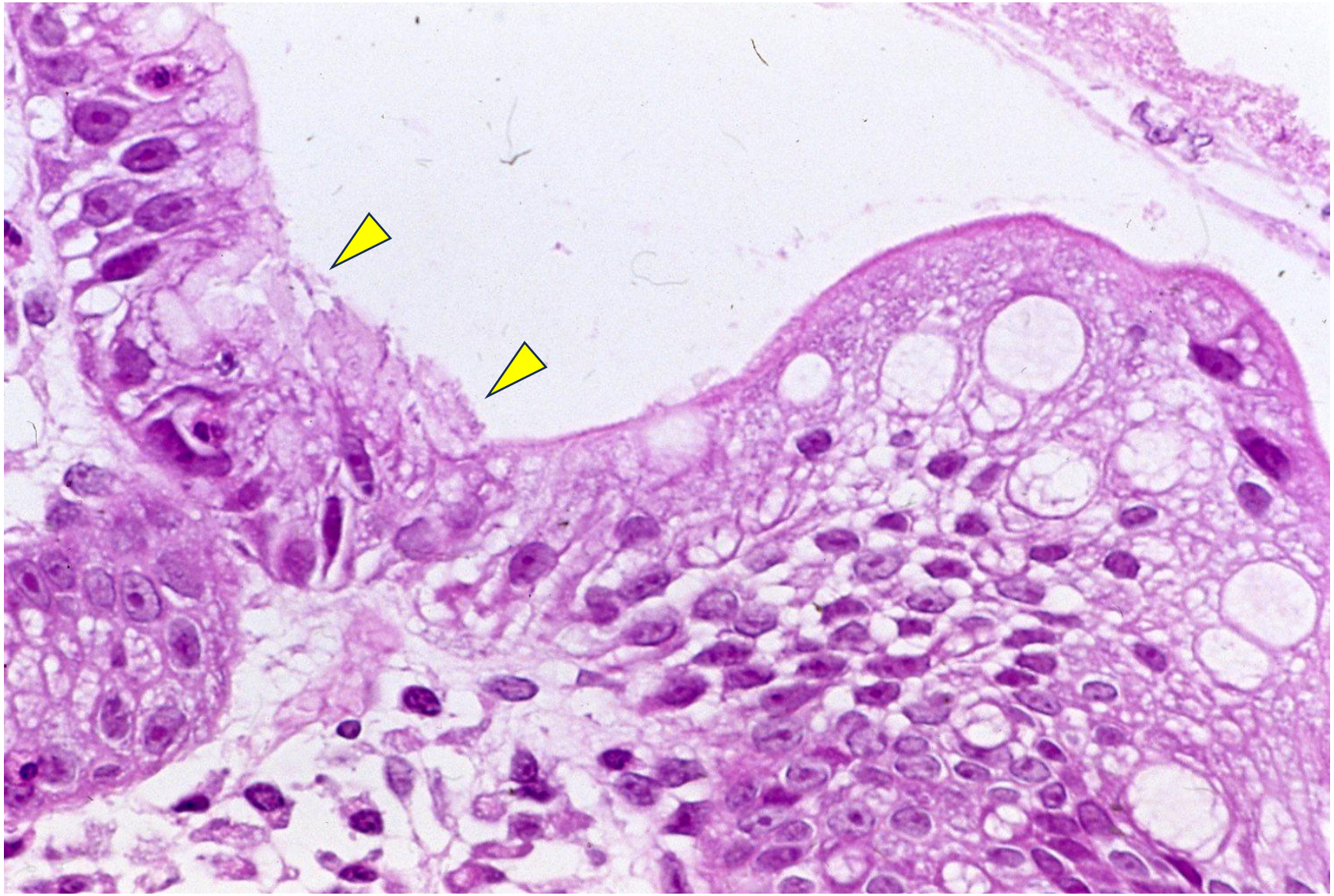
Ref.: Tsutsumi Y, et al. Immune aspects of intestinal metaplasia of the stomach: an immunohistochemical study. Virchows Arch [Pathol Anat] 1984; 403: 345-359. doi: 10.1007/BF00737285

・Intestinal metaplasia of the stomach can be grouped into 3 subtypes (A, B and C) according to the degree of pyloric gland involution which is judged from patterns of paradoxical Concanavalin A staining after Katsuyama and Spicer. The appearance of neuroendocrine cells is evaluated with immunohistochemical and silver methods. Type A metaplasia with slightly atrophic pyloric glands corresponds to the incomplete type in the previous classification, while Type C showing complete disappearance of pyloric glands corresponds to the complete type. Type B with moderately atrophic pyloric glands is an intermediate. This subtyping reflects the cell kinetics in the intestinalized mucosa well. Regarding the neuroendocrine cells, their total number varies in the order Type A＞Type B＞Type C. The selected populations of the endocrine cells including glicentin-containing cells, Grimelius-positive argyrophilic cells without argentaffinity and intestinal-type enterochromaffin cells frequently form hyperplastic foci in the intestinalized areas, where the other gut-type and proper gastric-type endocrine cells are scarcely noted. Immunoreactivity of glucagon or bovine pancreatic polypeptide are occasionally identified in a subpopulation of the glicentin-containing cells.

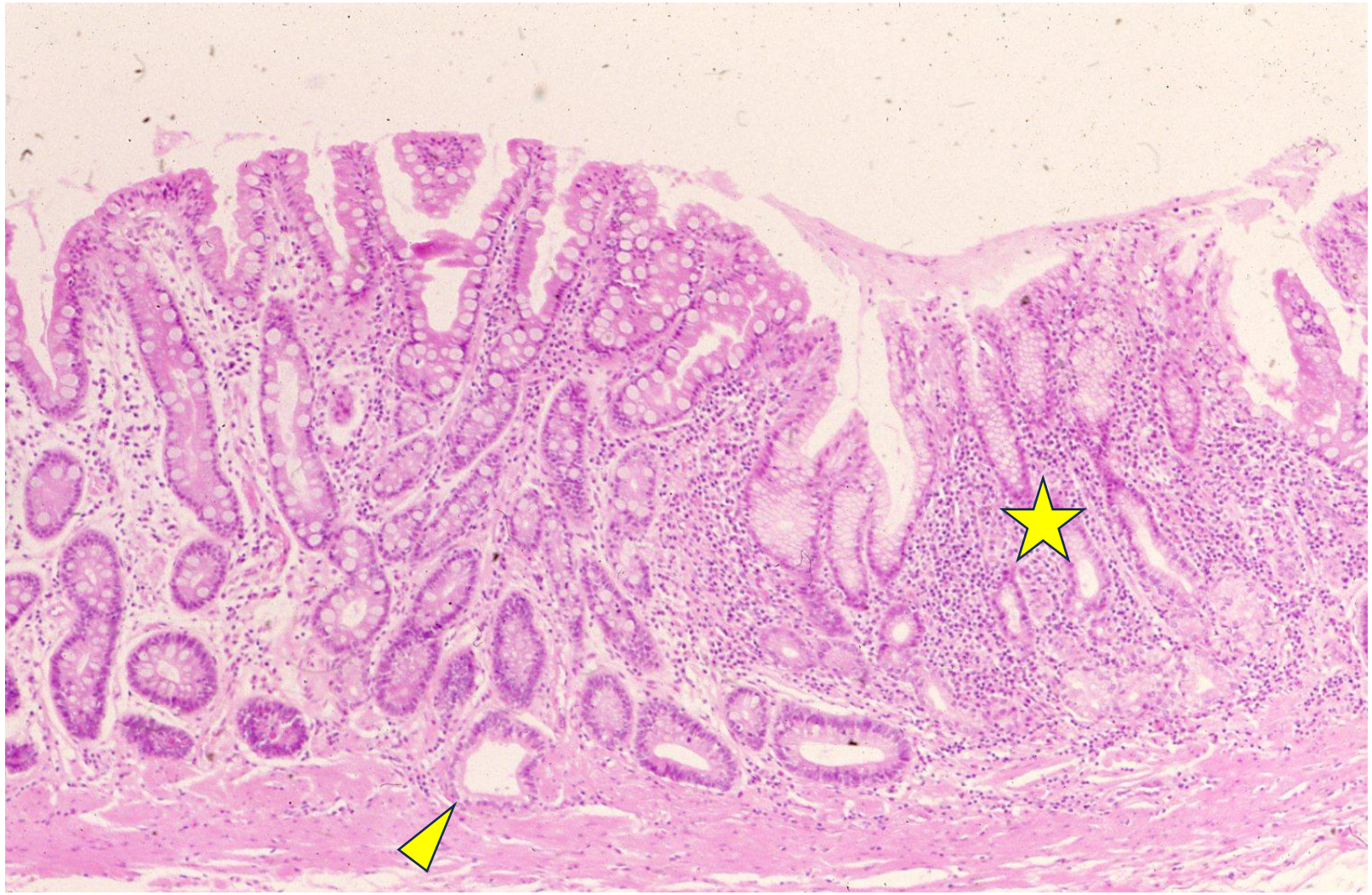
Ref.: Tsutsumi Y, et al. A novel subtyping of intestinal metaplasia of the stomach, with special reference to the histochemical characterizations of endocrine cells. Virchows Arch [Pathol Anat] 1983; 401: 73-88. doi: 10.1007/BF00644791



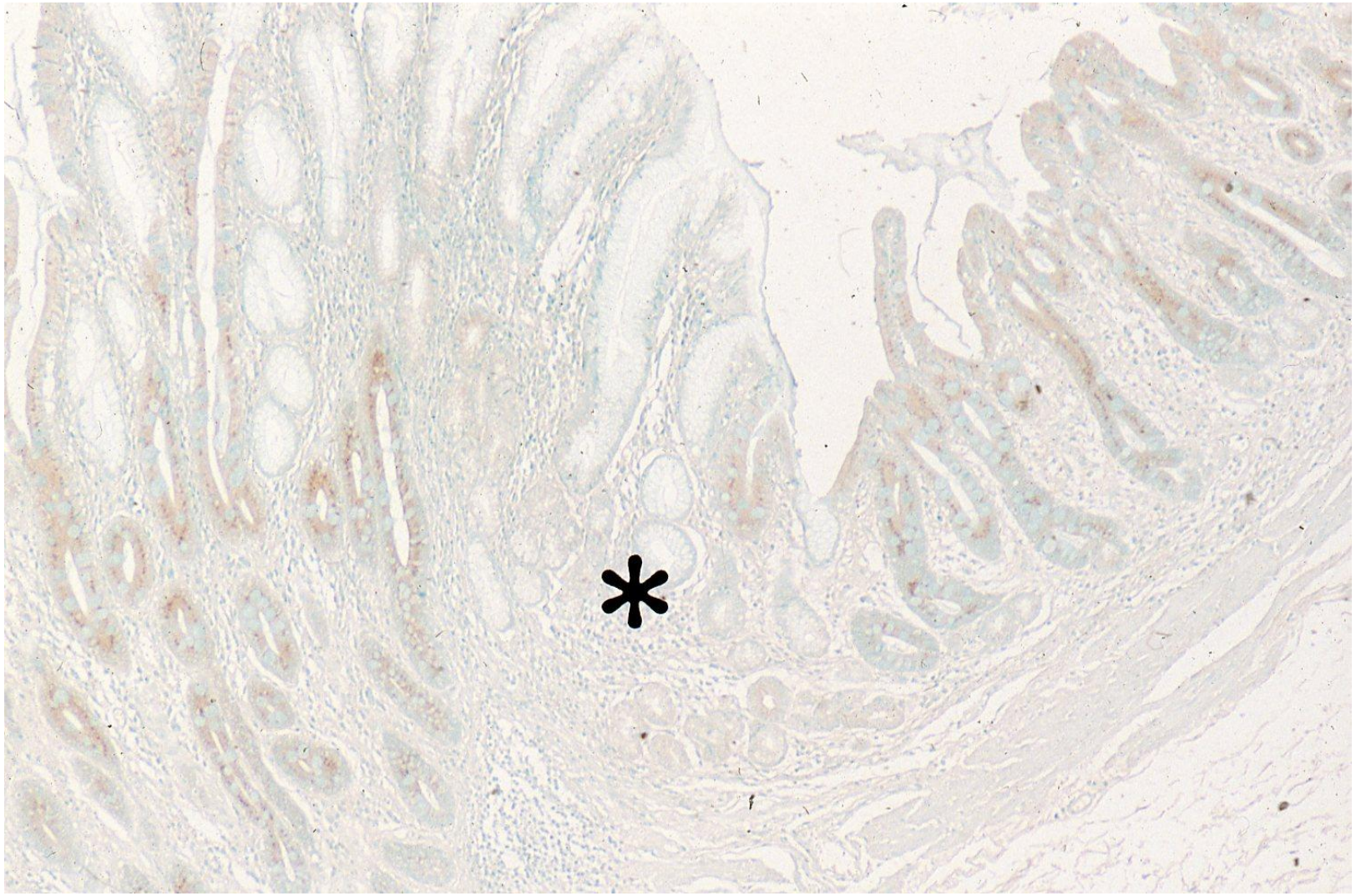
Intestinal metaplasia of the gastric mucosa (H&E). At the bottom of the intestinalized glands, Paneth cells are observed (arrowheads). Asterisk indicates non-intestinalized atrophic oxyntic mucosa.



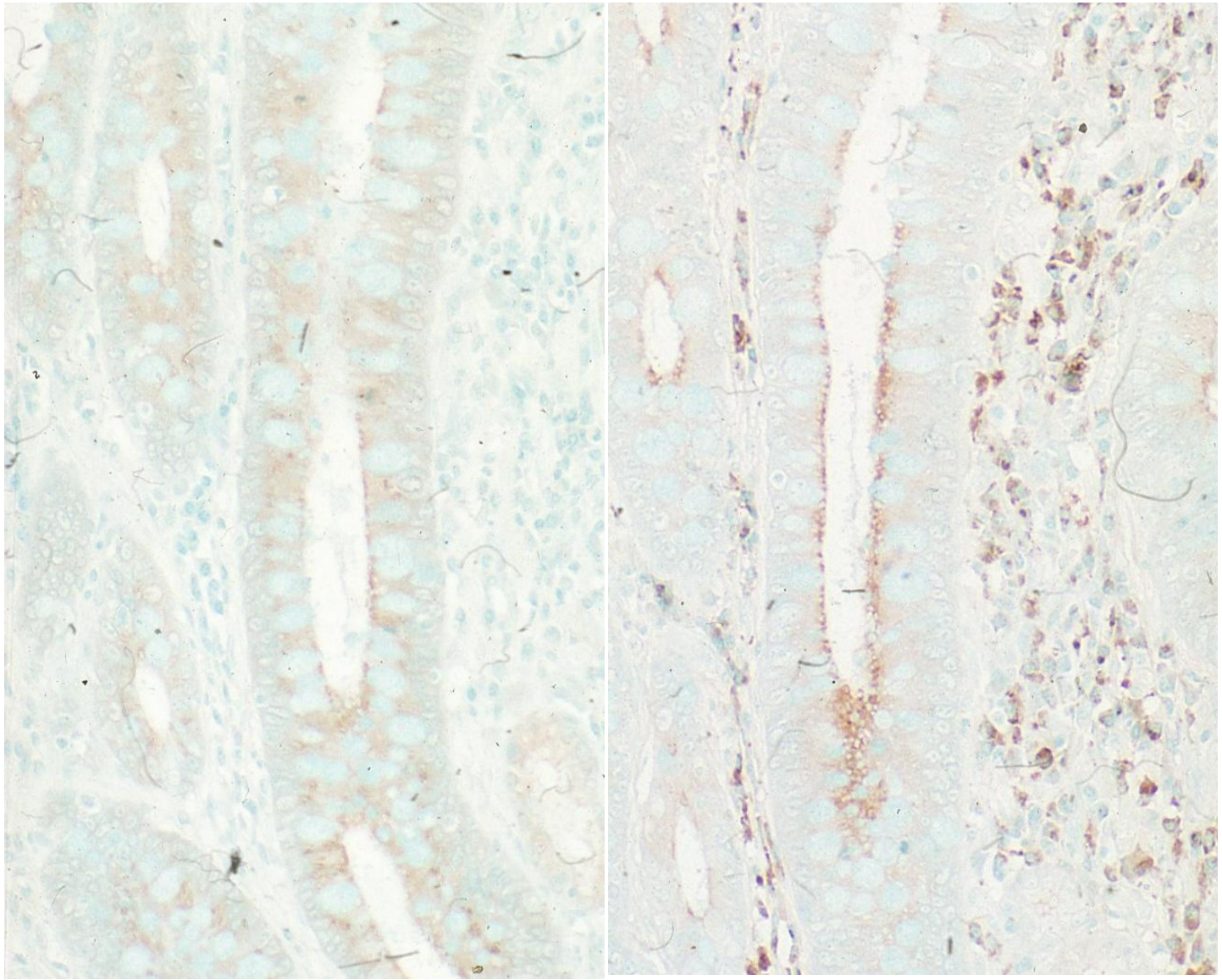
Intestinal metaplasia of the gastric mucosa (H&E). The intestinalized glands (right half) possess brush borders on the apical surface. *Helicobacter pylori* infection is seen on the surface of the adjacent non-intestinalized epithelial cells (arrowheads)



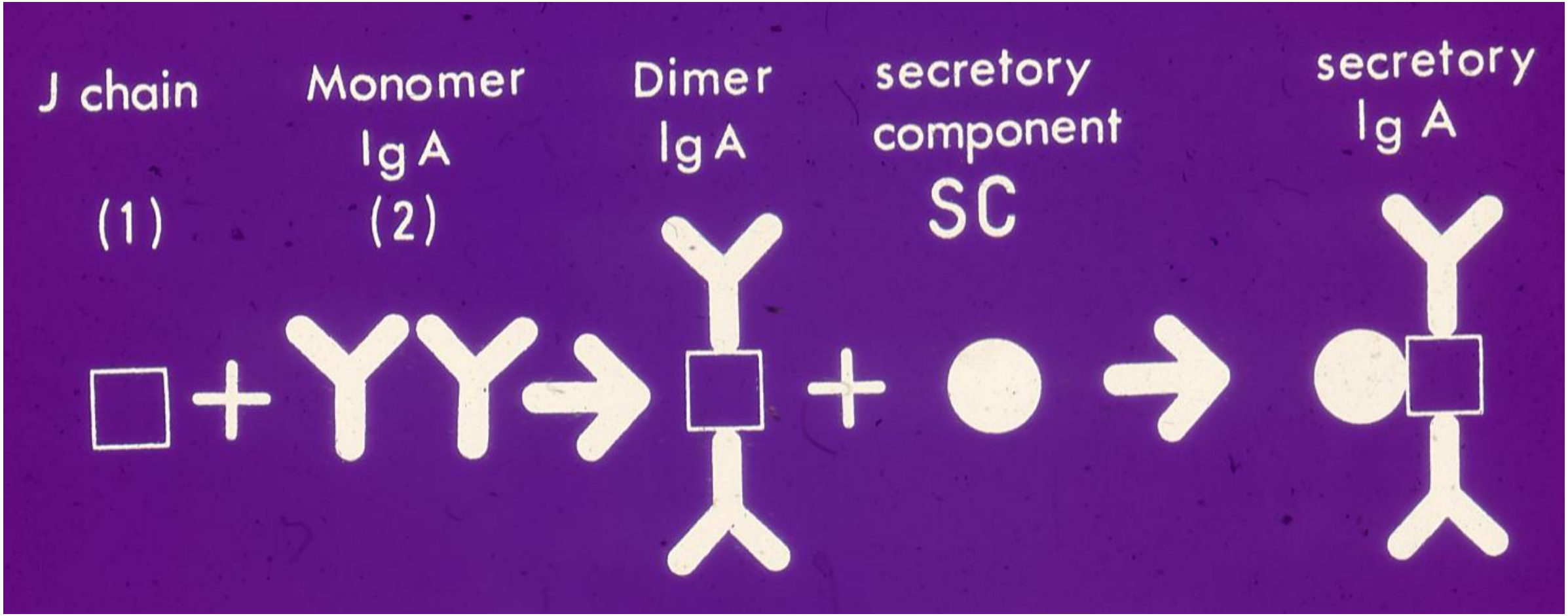
Intestinal metaplasia of the gastric mucosa (H&E). Chronic inflammatory reactions are milder At the bottom of the intestinalized glands, Paneth cells are observed (arrowheads). Asterisk indicates non-intestinalized atrophic oxyntic mucosa. Atrophic pyloric gland is shown by the arrowhead.



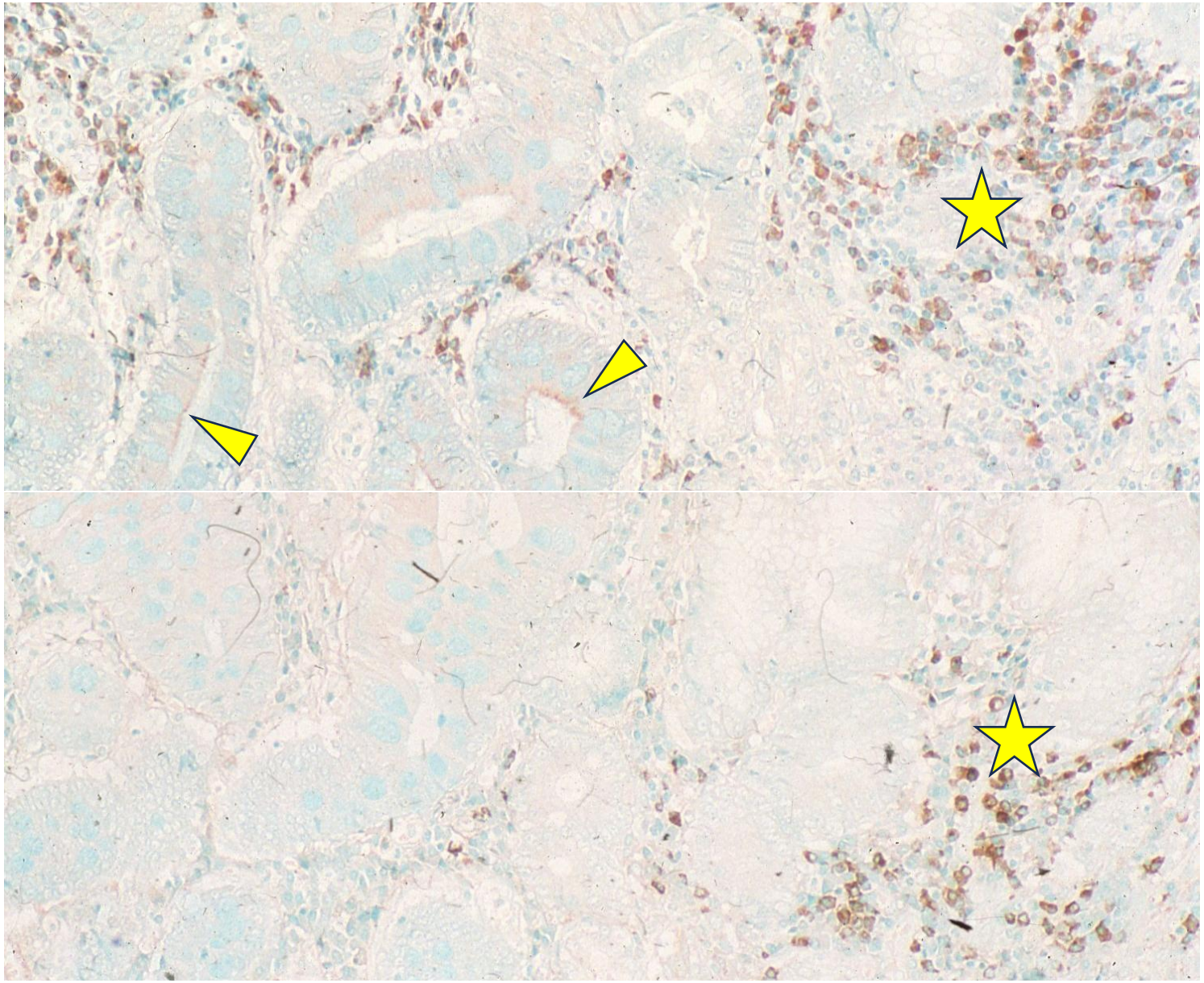
Production of secretory component (SC) in intestinal metaplasia.
Asterisk indicates non-metaplastic gastritis with paucity of SC production.



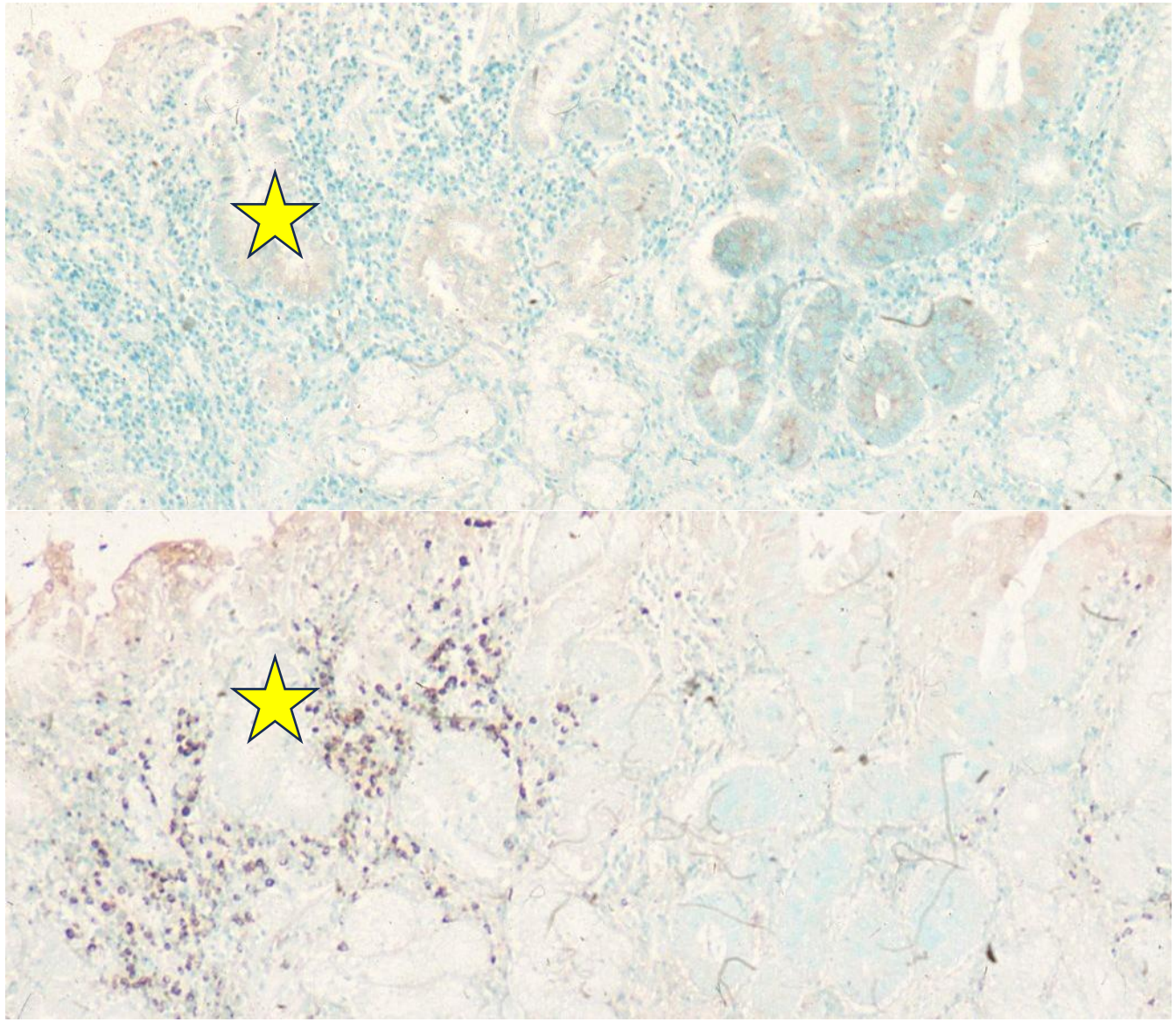
SC is produced in the intestinal metaplasia (left), and SC mediates transepithelial transport of secretory IgA (right). IgA plasma cells are rich in the lamina propria mucosae.



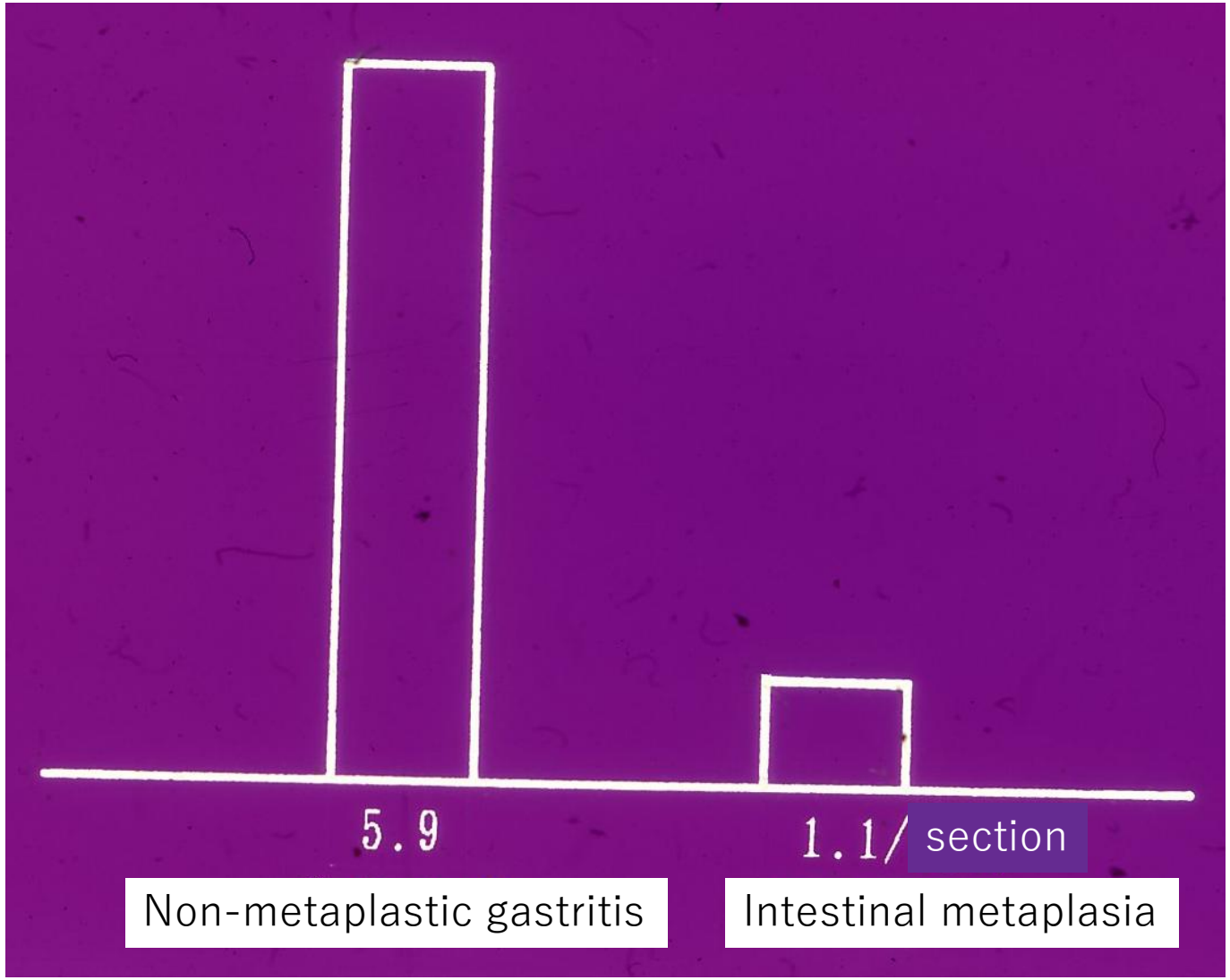
Schematic representation of formation of dimeric secretory IgA mediated by SC. Dimeric IgA is linked through J-chain. Secretory IgA functions as the main mediator of mucosal immunity.



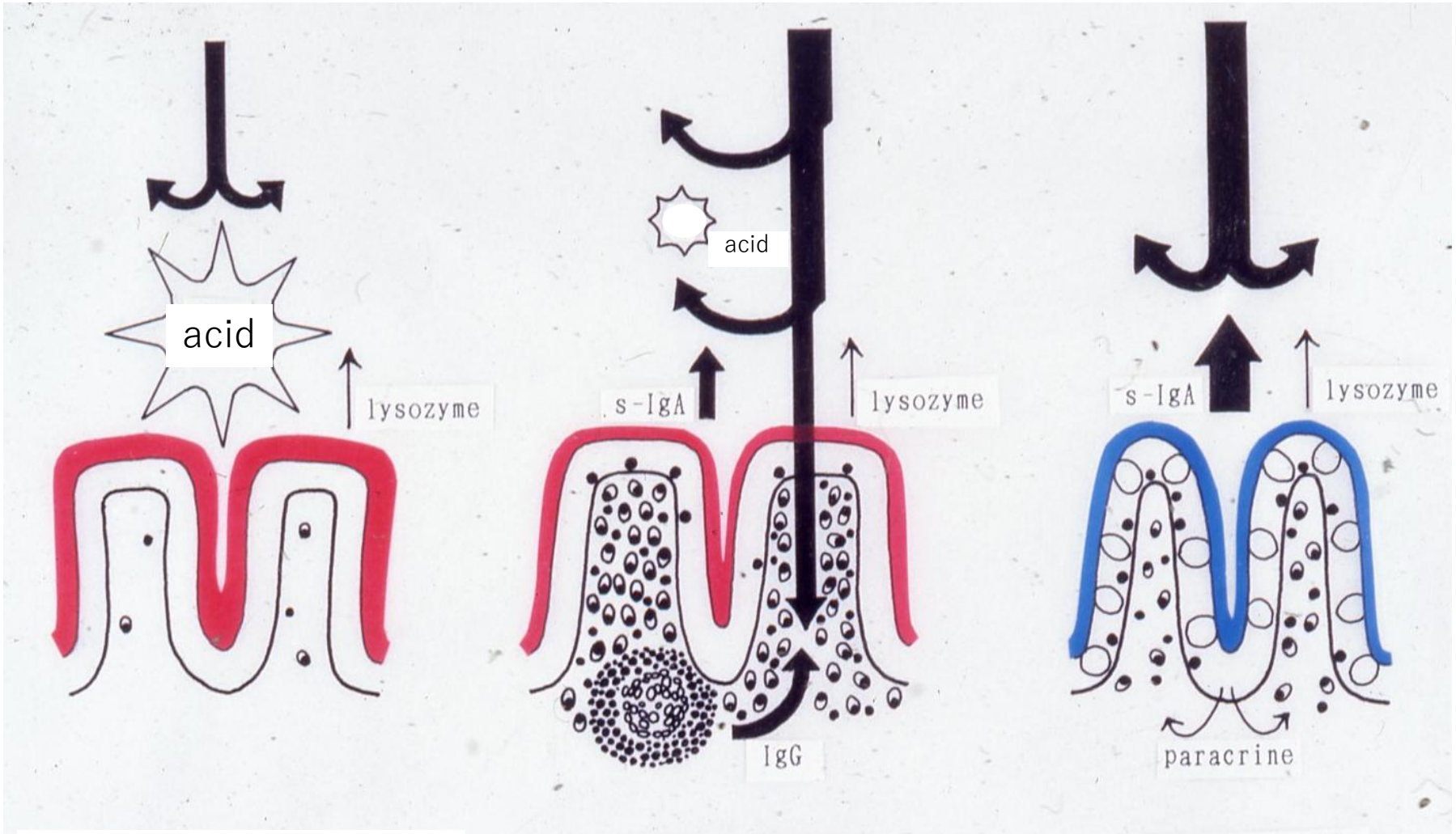
Distribution of IgA plasma cells (top panel) and IgG plasma cells (bottom panel). IgG plasma cells are clustered only in the non-metaplastic gastritis (asterisks). IgA plasma cells are seen in both metaplastic and non-metaplastic mucosa. Arrowheads indicate transepithelial transport of secretory IgA via metaplastic epithelium.



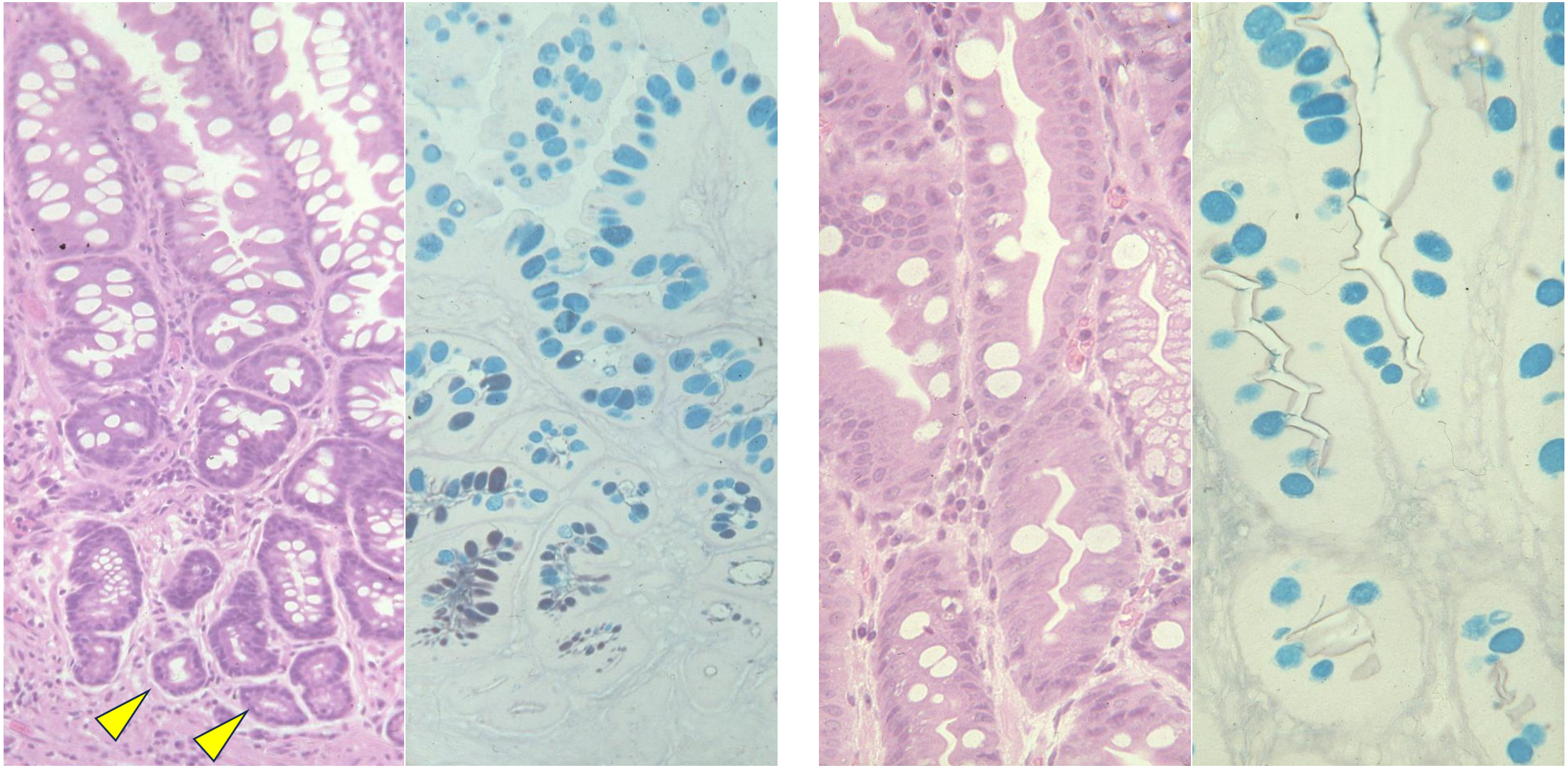
Epithelial cells in intestinal metaplasia produce SC (top panel), while IgG plasma cells (bottom panel) are clustered in the non-metaplastic mucosa (asterisk).



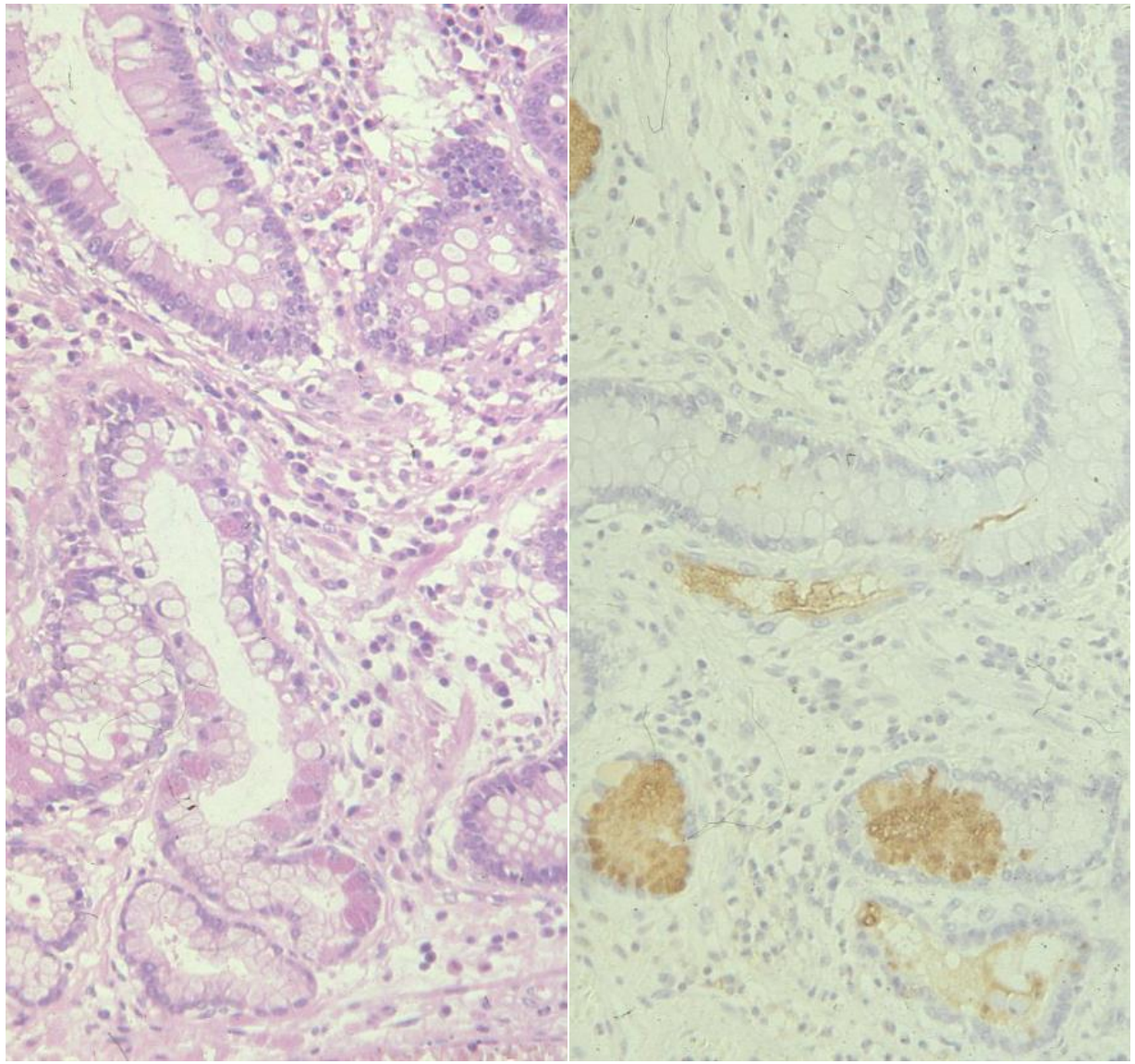
Numbers of lymphoid follicles in metaplastic and non-metaplastic gastritic mucosa. Lymphoid follicles are mainly distributed in the non-metaplastic gastritis mucosa. Surgical specimens were evaluated.



Schematic illustration of defense mechanisms in normal gastric mucosa, non-metaplastic gastritis and intestinal metaplasia. In normal state, acid, lysozyme and neutral mucin (red) function as important factors. In non-metaplastic gastritis, irritant (*Helicobacter pylori*) provokes lymphoid follicle formation and active IgG response. In intestinal metaplasia, secretory IgA response is the major tool for mucosal protection. The mucosal surface is covered with alcianophilic mucin (blue). Hyperplastic neuroendocrine cells provide a paracrine action.



Intestinal metaplasia and acidic mucin in goblet cells (H&E and high iron diamine-alcian blue=HID-AB). Left: type B (incomplete) metaplasia, right: type C (complete) metaplasia. Arrowheads indicate the remaining pyloric glands at the bottom. In type B (incomplete) metaplasia, goblet cells contain both sialomucin (blue) and sulfomucin (black). In type C (complete) metaplasia, the goblet cells contain blue-stained sialomucin alone. The surface coat is lined by black-stained sulfomucin.



Intestinal metaplasia, type B (left: H&E, right: Concanavalin A paradoxical staining for pyloric gland mucin. The pyloric gland remaining at the bottom of the metaplastic mucosa is clearly demonstrated colored brown. Paneth cells are distributed in this lesion.

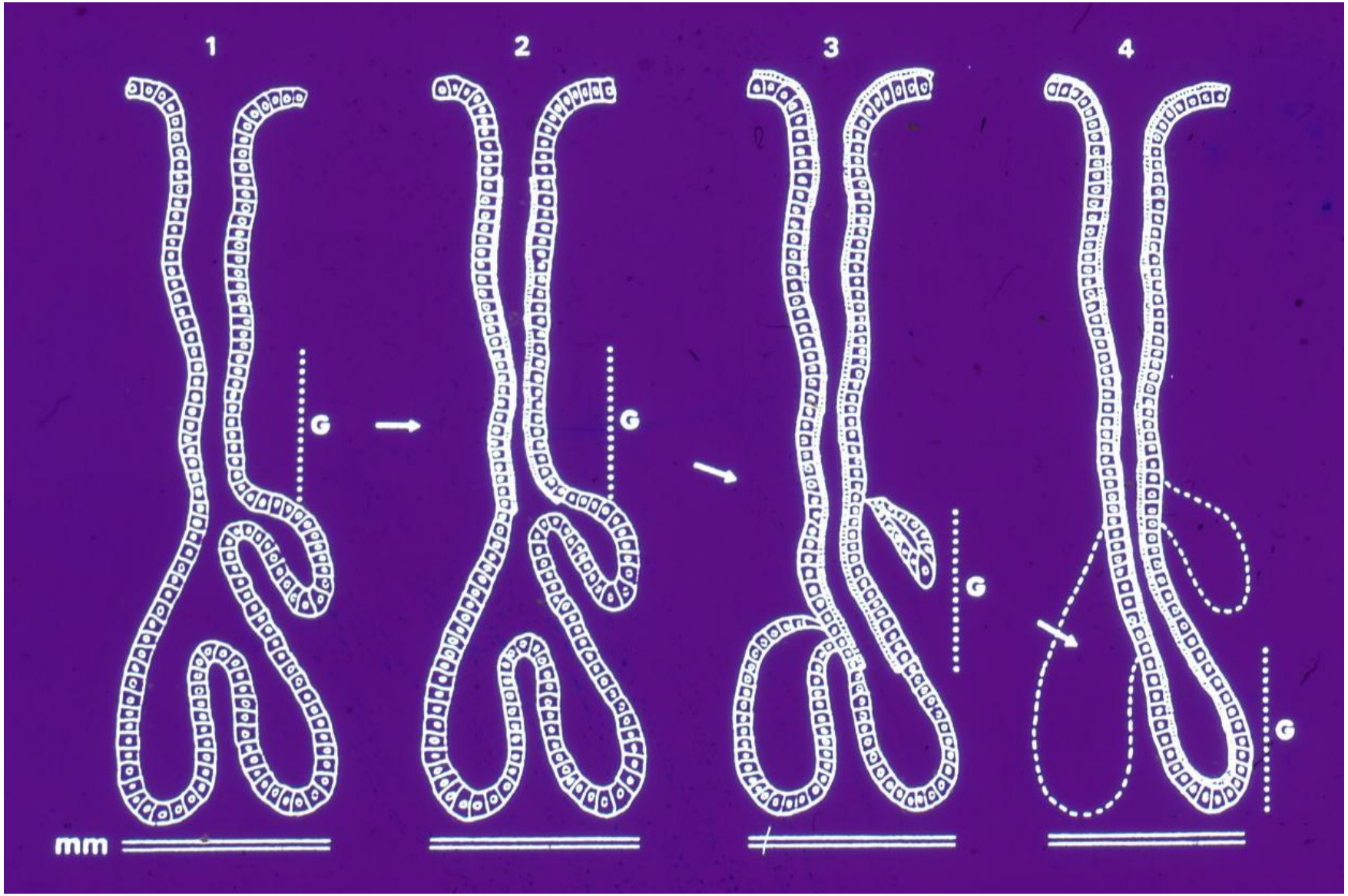


Diagram pf progression of intestinal metaplasia of the gastric mucosa (I).
1) Normal gastric mucosa, 2) type A metaplasia, 3) type B metaplasia, 4) type C metaplasia
G= generative (proliferative) zone, mm= tunica muscularis mucosae

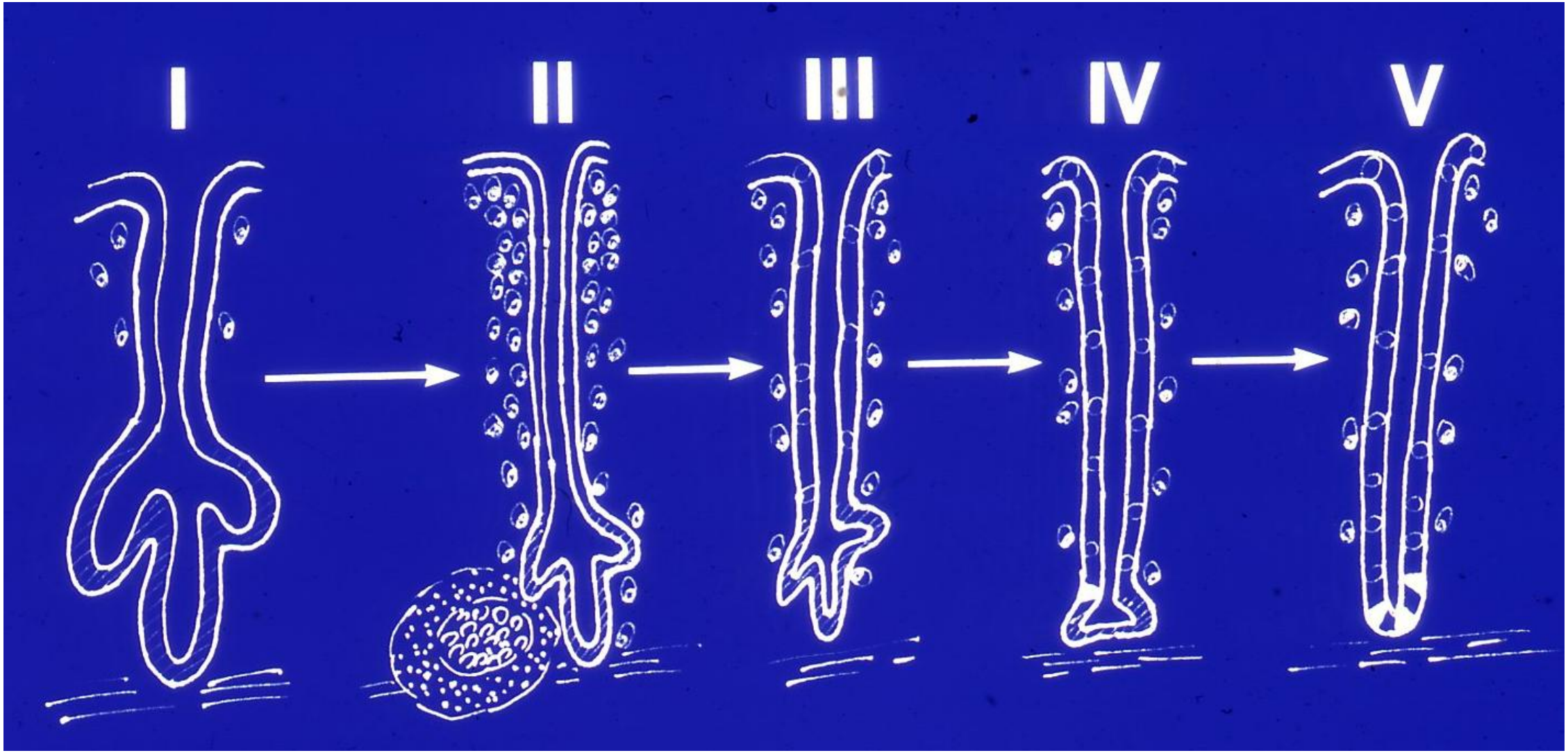
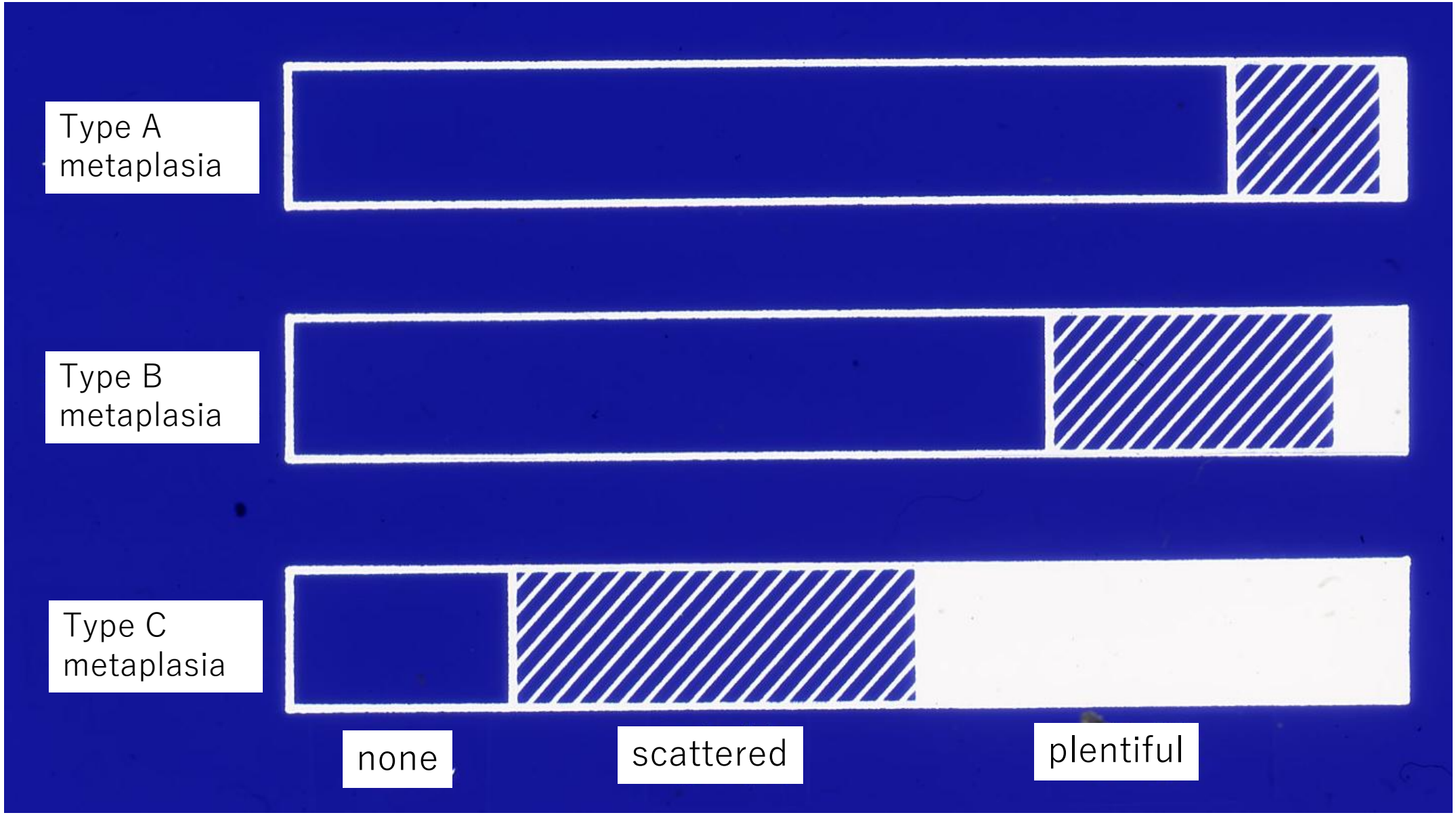
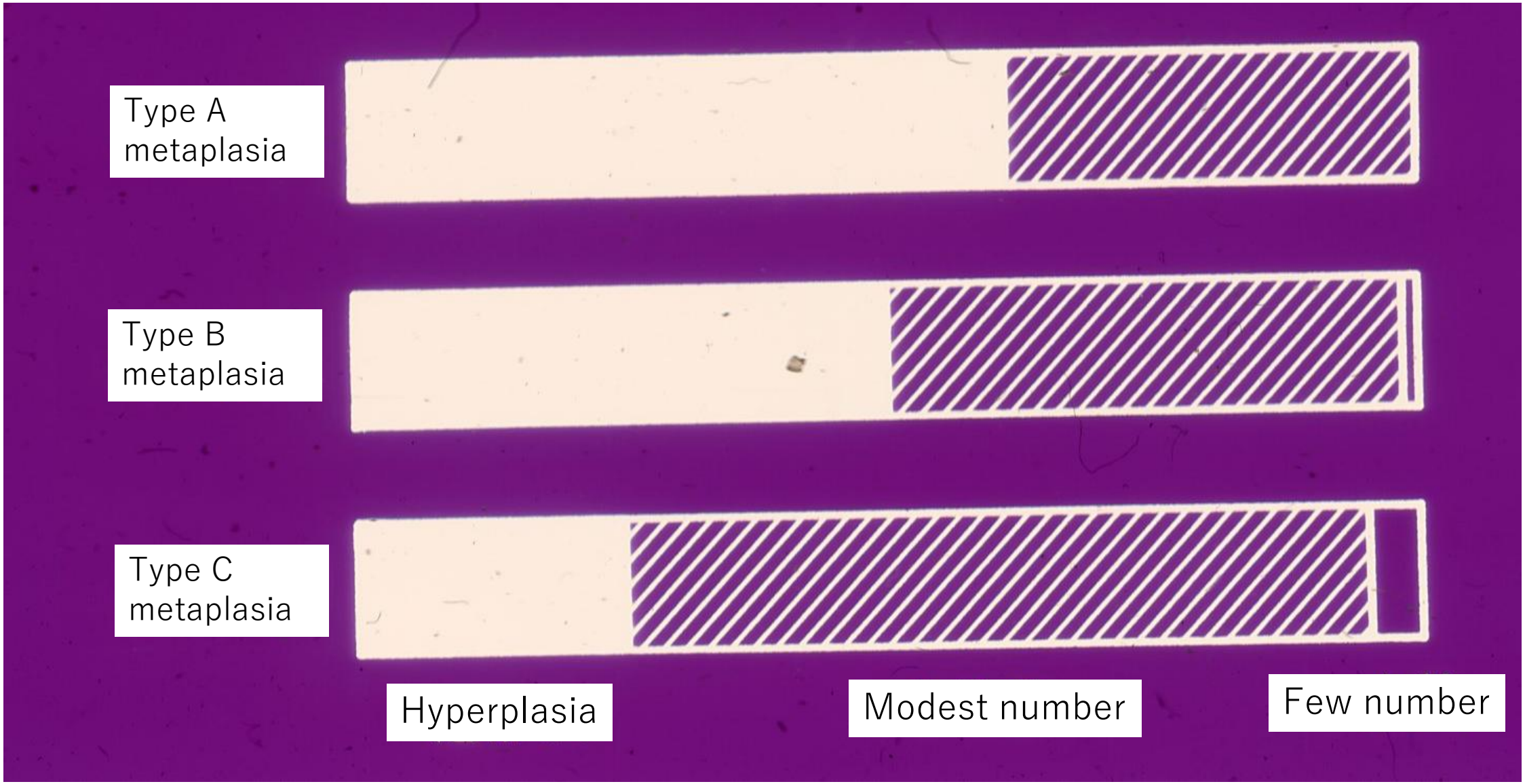


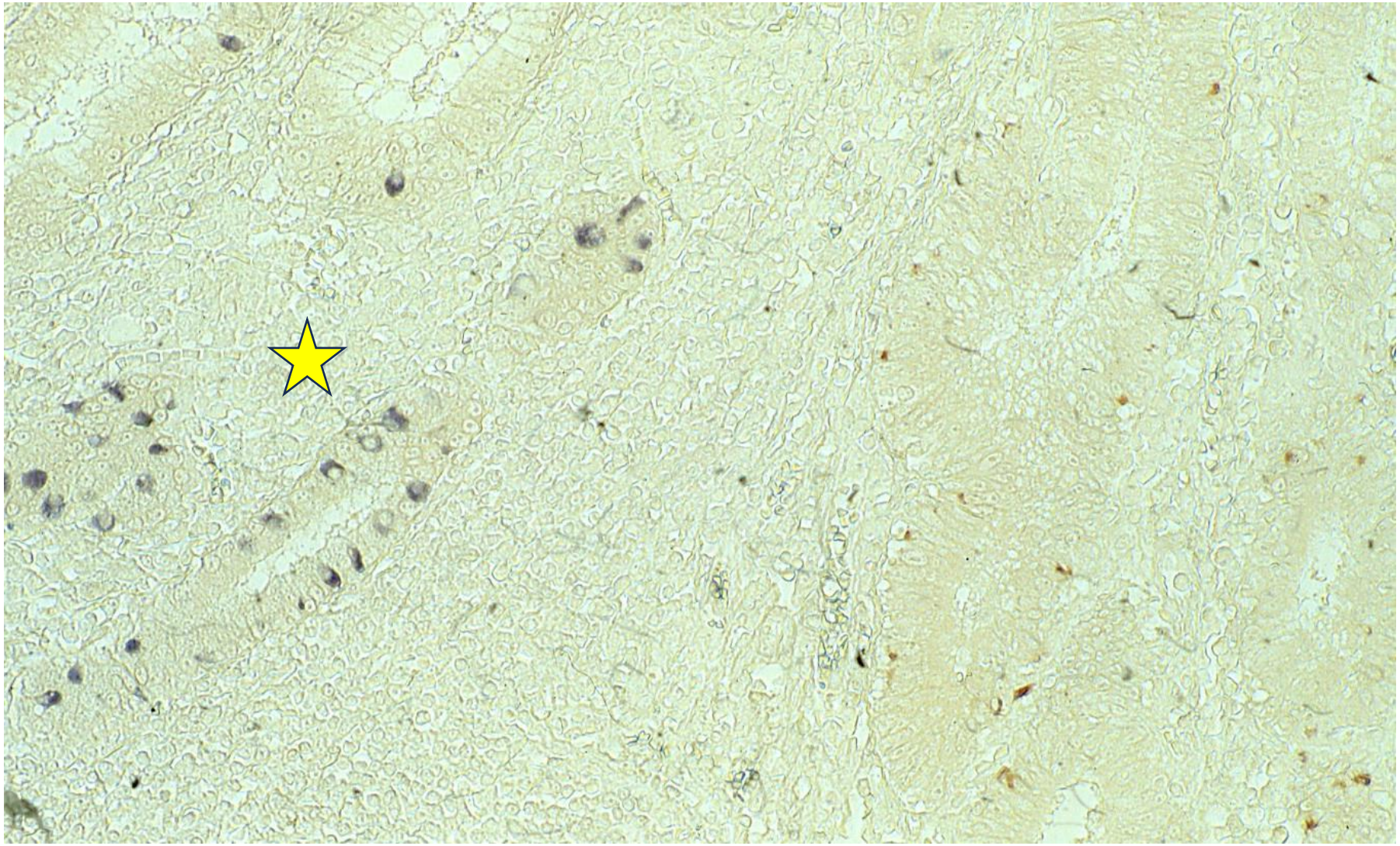
Diagram pf progression of intestinal metaplasia of the gastric mucosa (II).
I) Normal gastric mucosa, II) non-metaplastic gastritis with lymphoid follicle formation, III) type A metaplasia, IV) type B metaplasia, V) type C metaplasia with Paneth cells



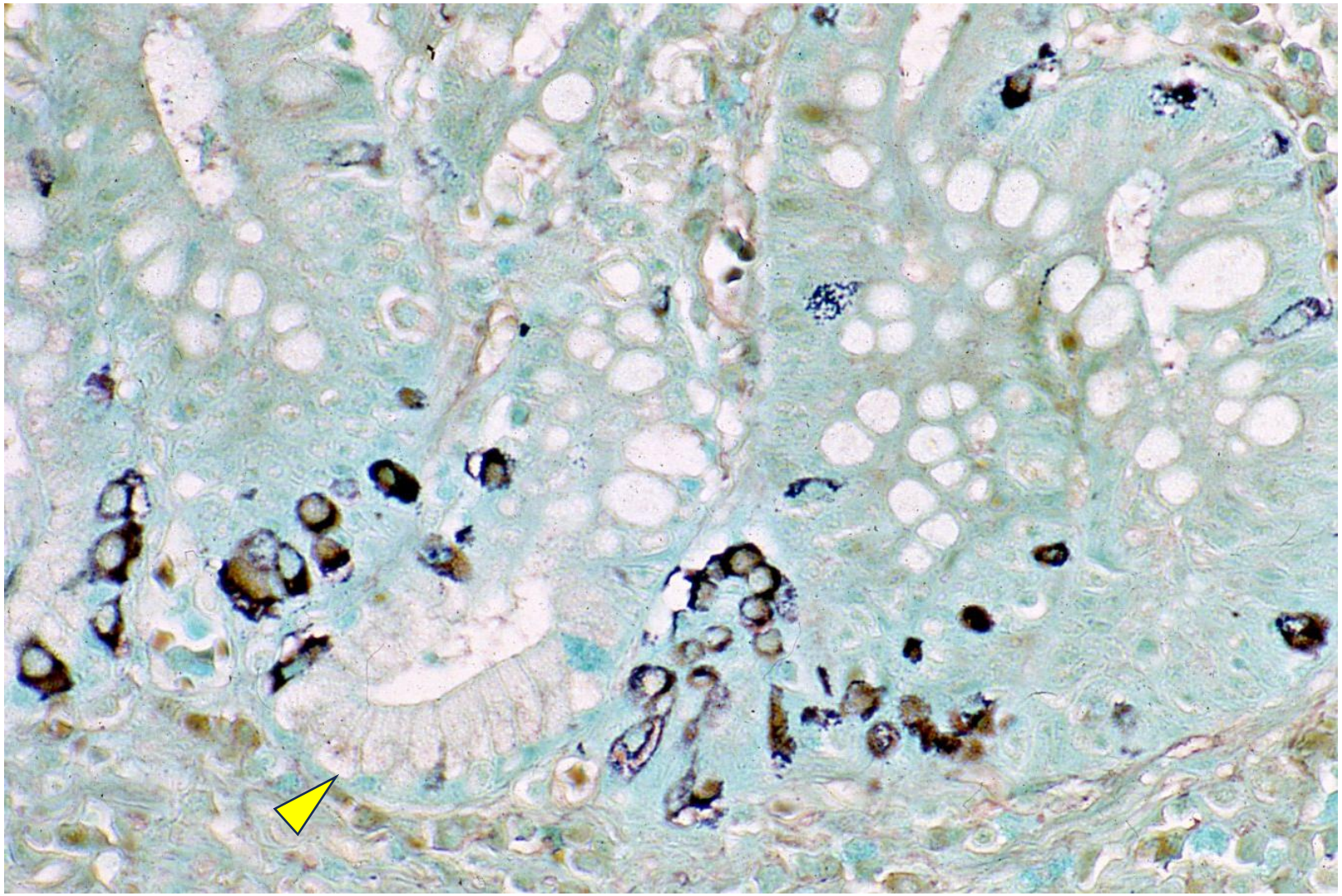
Intestinal metaplasia subtypes (A-C) and the appearance of Paneth cells



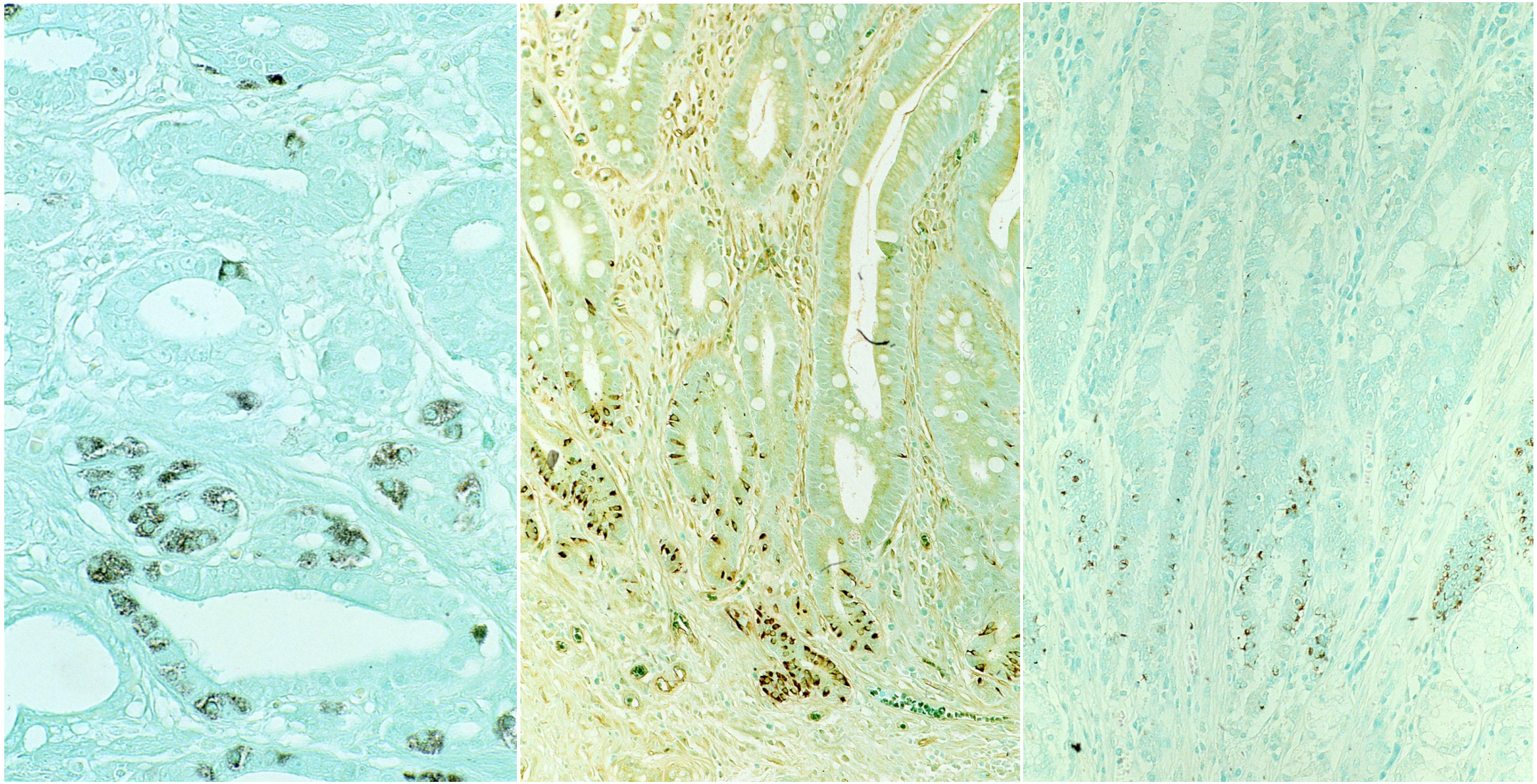
Neuroendocrine cell hyperplasia in intestinal metaplasia, types A, B and C:
Glicentin-immunoreactive cells and Grimelius-positive argyrophilic cells were evaluated.
Intestinal metaplasia, types A and B, often accompany neuroendocrine cell hyperplasia.



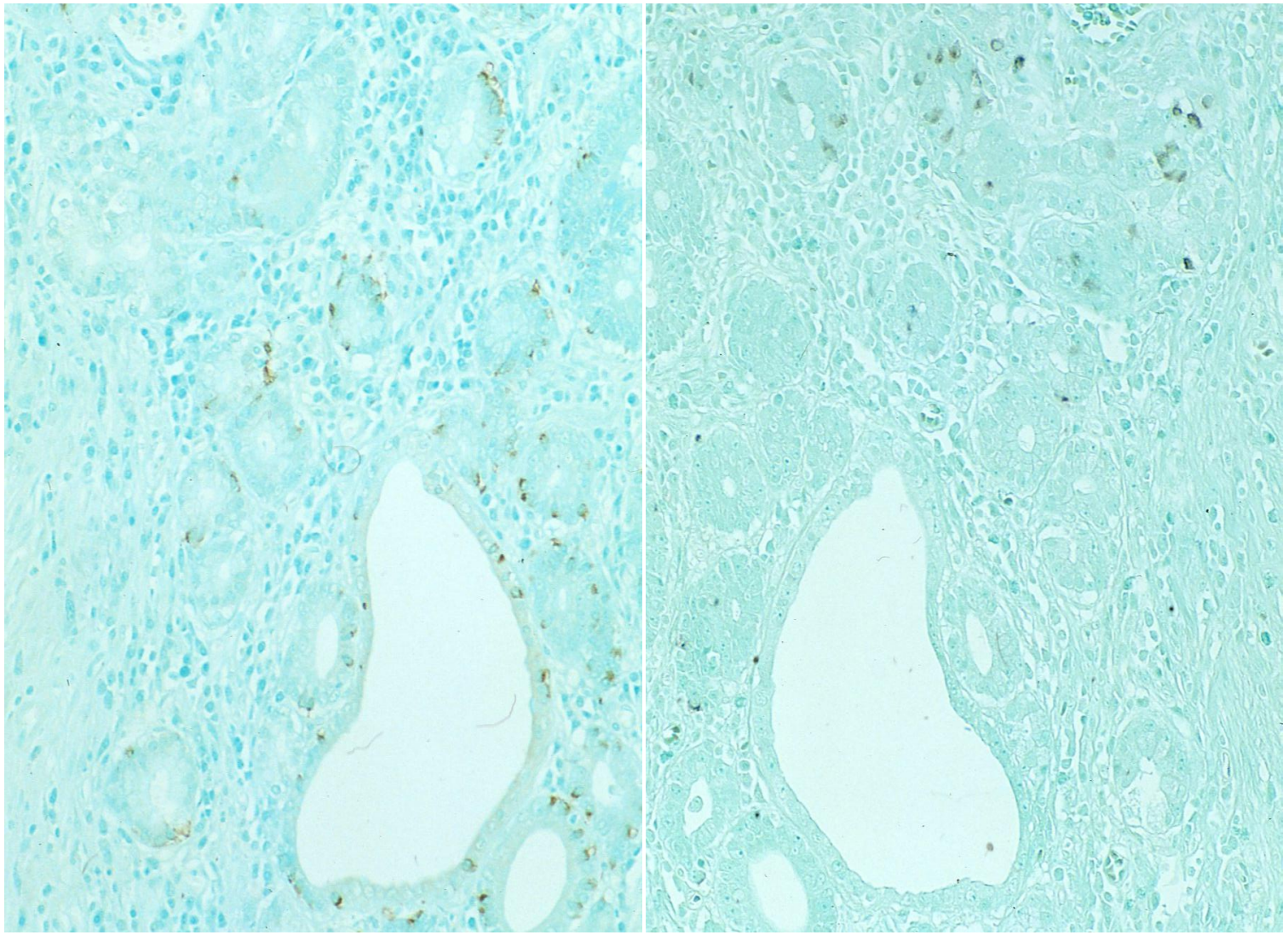
Double staining for gastrin (stained blue) and glicentin (stained brown) in the antral gastric mucosa. Non-metaplastic gastric mucosa (left half, asterisk) contains gastrin-immunoreactive cells, while in the intestinalized metaplastic mucosa (right half), glicentin-immunoreactive cells are distributed. Gastrin cells are totally lost in the metaplastic mucosa.



In intestinal metaplasia, type B, Grimelius-positive argyrophilic neuroendocrine cells show evident hyperplasia. Arrowhead indicates the remaining pyloric gland at the bottom of the mucosa.



In intestinal metaplasia, type B, hyperplasia of three types of neuroendocrine cells is observed. Left: Fontana-Masson-positive intestinal-type enterochromaffin cells, center: Grimelius-positive argyrophilic neuroendocrine cells, right: glicentin-immunoreactive L-cells.



Mirror sections of intestinal metaplasia stained for glicentin (left) and Grimelius' silver. Both cells comprise different cell populations. Actually, glicentin-immunoreactive cells are not argyrophilic.