LECTIN HISTOCHEMICAL STUDIES ON GASTRIC INTESTINAL METAPLASIA WITH ULEX EUROPAEUS AGGLUTININ-I DOLICHOS BIFLORUS AND PEANUT AGGLUTININS IN COMPARISON WITH GASTRIC AND SMALL AND LARGE INTESTINAL MUCOSA

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In order to find out which type of intestinal metaplasia, complete or incomplete, in the human stomach is more closely related to the small or large intestinal mucosa from the viewpoint of their glycoprotein content, we studied the lectin staining characteristics of the secreted mucin, luminal surface, apical and supranuclear cytoplasm, goblet mucin of both types of metaplastic glands and compared them with those of the small intestinal, ascending and descending colonic mucosa. Three types of lectins, *Ulex europaeus* agglutinin-I, *Dolichos biflorus* agglutinin (DBA) and peanut agglutinin, were used with and without prior neuraminidase digestion. Specimens were selected from 32 resected stomachs which contained both metaplastic and non-metaplastic glands. Six specimens were selected from the small intestine and 12 each from the ascending and descending colon.

Blood groups of the patients were also taken into consideration. Findings showed that both types of metaplastic glands possessed definitely different lectin binding properties from the non-metaplastic glands. They also differed from the small and large intestinal mucosa. However, no distinguishable difference was found between the lectin staining of the complete and incomplete types of metaplastic glands. When DBA, a group A antigen-specific lectin was used, patients with blood groups A and AB showed different lectin staining from patients with blood groups B and O. Also, goblet mucin of the metaplastic glands and small intestinal mucosa showed stepwise changes in lectin staining from the bottom to the upper portion of the crypts in accordance with the migration of these cells from the bottom of the crypts upwards.

Many plants and invertebrates contain agglutinins, called "lectins", that have the ability to specifically agglutinate erythrocytes and other types of cells (4). When they were first described, they were found to be specific for blood group antigens (5). Later, it became clear that they were specific for certain simple sugar moieties in the complex structures of glycoproteins and polysaccharides (28). These complex molecules are present not only on the cell surface, but also on the membranes of various cellular organelles. Therefore, this type of specific binding has been utilized for the histochemical demonstration of individual sugar residues at both the light and electron microscopic levels (17, 26).

It has been shown that intestinal metaplasia of the gastric mucosa is often associated with human gastric carcinoma and has been suspected to being its precursory change (9, 18, 24). Intestinal metaplasia has been classified into 2 types, complete and incomplete (1, 16, 18, 22). The complete type of intestinal metaplasia is characterized by the presence of sucrase, trehalase, leucine aminopeptidase, alkaline phosphatase, goblet cells and Paneth cells. On the other hand, the incomplete type, although it also contains sucrase, leucine aminopeptidase and goblet cells, lacks trehalase and alkaline phosphatase activities and Paneth cells (22). The relationship between these types of intestinal metaplasia and the development of gastric cancer is of great interest to us. In a previous study concerning intestinal metaplasia surrounding minute foci of gastric carcinoma, the incomplete type was more commonly associated with gastric cancer (22). However, no firm conclusion could be derived from this finding. The presence of intestinal marker enzymes would indicate that the complete type might be similar to the small intestinal mucosa. Since the incomplete type possesses goblet cells but lacks so many characteristics of the small intestinal mucosa, it might be closer to the colonic mucosa.

This study was aimed to compare each of these two types of metaplasia with the small and large intestinal mucosa by their lectin staining properties. Studies of lectin staining in the mucosa of the gastrointestinal tract are abundant for the colonic mucosa (2, 3, 7, 8, 15, 19, 25, 30, 31), but rather few for the oral (10) esophageal (27), gastric (14, 28) and small intestinal (12) mucosa. Another purpose of this study was to determine more precisely the lectin binding characteristics of the cytoplasmic contents of the gastric, small and colonic mucosa.

MATERIALS AND METHODS

1) *Specimens:*

Stomach: Paraffin-embedded sections of gastric specimens from 32 surgical patients were selected from areas with intestinal metaplasia as shown by hematoxylin-eosin staining. Intestinal metaplasia was recognized by the presence of goblet cells, with or without Paneth cells, and the striated border of the luminal surface. The age of the patients ranged from 37 to 85 years. The primary diseases leading to gastrectomy were both benign and malignant. There were 27 cases of gastric carcinoma; 14 of which were well-differentiated adenocarcinoma, 8 of moderately differentiated adenocarcinoma and 5 of poorly differentiated adenocarcinoma. Two cases revealed benign polyps and 3 perforated gastric ulcers. Eighteen patients were of blood group A, 6 of group B, 6 of group O and 2 of group AB.

Small and large intestines: For comparison with the gastric tissue, paraffin-

embedded sections were selected from normal appearing segments of the surgical specimens of the small intestine and ascending and descending colon. These segments were all found to be normal histologically. Six of the specimens were from the small intestine, 12 from the ascending colon and 12 from the descending colon. Specimens of the small intestine were resected from 2 patients with adenocarcinoma of the cecum and one from each patient with gastro-jejuno-colic fistula, necrotizing ileitis, non-specific localized small intestinal ulcer and Crohn's disease. Specimens of the ascending colon were resected from 11 patients with adenocarcinoma of the colon and one with Crohn's disease. Specimens of the descending colon were all resected from patients with adenocarcinoma of the colon or rectum.

Blood groups of patients in the small intestinal group were group A for 3 patients, group B for 2 and group O for 1. The ascending colonic specimens were obtained from 8 patients with blood group A, 2 with blood group B and 2 with blood group O. The descending colonic specimens were obtained from 4 patients with blood group A, 2 with blood group B, 4 with blood group O and 2 with blood group AB.

Thin histological sections were made from these paraffin blocks and stained with hematoxylin-eosin and lectins. Metaplastic glands of the stomach were divided into complete and incomplete types. The presence of Paneth cells and a distinct striated border of the metaplastic glands indicated glands of the complete type, while the absence of these two features in the metaplastic glands with goblet cells indicated the incomplete type (22).

2) *Lectin staining:*

Three types of biotinylated lectins, *Ulex europaeus* agglutinin-I (UEA-I), *Dolichos biflorus* agglutinin (DBA) and *Arachis hypogaea* or peanut agglutinin (PNA) were used with and without neuraminidase pretreatment. The biotinylated lectins were purchased from Vector Laboratories, Inc., California, USA, as a salt-free lyophilized powder. Stock solutions of 0.5% concentration in distilled water were prepared and kept until used.

The sections were deparaffinized and immersed in a solution of 0.3% hydrogen peroxide in methanol for 30 min and then washed in phosphate buffered saline. These were then incubated on glass slides with a 1 : 100 diluted solution of the stock solution of each lectin for 60 min at room temperature. After another washing in phosphate buffer saline, these were incubated for 40 min with avidin-biotin-peroxidase complex. Then the sections were stained with diaminobenzidine for 2-3 min and counterstained with methyl-green for 3 min. With this technique, the positive reaction with the corresponding lectin appears brown. The metaplastic glands, the non-metaplastic glands and the epithelial lining of the small and large intestines were examined for reactivity of the secreted mucin, luminal surface, apical cytoplasm, supranuclear cytoplasm and goblet mucin. The parietal and chief cells of the gastric glands were also examined for staining. Negative reaction was reported as — and positive reactions as + and ++ according to the degree of staining.

For control, the same staining procedures were carried out in the absence of lectin. Additional control sections were stained with lectin in the presence of an excess of the appropriate inhibitory carbohydrate: L-fucose for UEA-I, N-acetyl-galactosamine for DBA and D-galactose for PNA.

3) *Neuraminidase digestion:*

Neuraminidase from *Clostridium perfringens* (Type VIII) was purchased from Sigma Chemical Co., St. Louis, Mo., USA, as a purified powder and used immediately after dilution. For neuraminidase digestion, the deparaffinized sections were washed with 0.1 M sodium acetate buffer, pH 5.0, and incubated at 37°C for 90 min with neuraminidase at a concentration of 1 unit/ml in 0.1 M sodium acetate buffer, pH 5.0, and 0.04 M calcium chloride. They were then washed with water and lectin staining was carried out.

RESULTS

Most of the gastric mucosa that harbored intestinal metaplasia contained both complete and incomplete types of metaplastic glands. Reactivities with various lectins in the complete and incomplete types of metaplastic glands were compared carefully with each other in the same specimen as well as in specimens from different patients. However, no significant differences were found between the two types, although there were some variations in reactivity from case to case and even from area to area in the same case. The primary diseases of the patients also had no relation to lectin reactivity.

In the gastric mucosa, the metaplastic and non-metaplastic glands possessed definitely different lectin reactivities even in the same specimens and their differences seemed to reside mostly in the cytoplasm.

1) UEA-I:

As shown in Table 1, staining of the non-metaplastic glands by UEA-I was

TABLE 1. UEA-I staining of the mucosa of the stomach (non-metaplastic and metaplastic glands), small intestine, and ascending and descending colon

	Stomach		Small intestine	Ascending colon	Descending colon
	Non-metaplastic	Metaplastic			
<i>Surface epithelium:</i>					
Secreted mucin	+ / ++*	++	+	—	—
Luminal surface	+ / ++	+ / ++	+	— (++)**	—
Apical cytoplasm	+ / ++	— / +	—	—	—
Supranuclear cytoplasm	+ / ++	— / +	—	—	—
Goblet mucin		+ / —	— / +	+ / —	—
<i>Glands or crypts:</i>					
Luminal surface	+ / ++	+	—	— (++)	—
Apical cytoplasm	+ / ++	—	—	—	—
Supranuclear cytoplasm	+ / ++	—	—	—	—
Goblet mucin (upper)		+ / —	— / +	+ / —	—
Goblet mucin (lower)		— / +	—	—	—
<i>Parietal cells</i>	+				
<i>Chief cells</i>	+				

* + / ++, + / — and — / + indicate that the intensity of staining varied considerably but the sign on the left of the bar predominates.

** + in parentheses indicates enhancement after neuraminidase treatment. No parentheses means no change after neuraminidase digestion.

FIG. 1a. UEA-I staining of non-metaplastic glands of the gastric mucosa. The luminal surface is positive. The apical and supranuclear cytoplasm show fine granular positive staining. $\times 300$

FIG. 1b. UEA-I staining of the surface epithelium and the upper portion of the metaplastic glands. The luminal surface is positive. The apical and supranuclear cytoplasm is stained variably and in a coarse granular pattern. The goblet mucin in this portion of the glands shows a weak or negative reaction. $\times 300$

FIG. 1c. UEA-I staining of the lower portion of the metaplastic glands. Only the luminal surface shows weakly positive staining; the cytoplasmic contents including goblet mucin are negative. $\times 300$

FIG. 1d. UEA-I staining of the small intestinal mucosa. The luminal surfaces of the villi and the upper portion of the crypts are positive. Some of the goblet cells in this portion of the crypts show weakly positive mucin. The apical and supranuclear cytoplasm show negative staining. $\times 300$

rather consistent. The secreted mucin as well as all cytoplasmic contents of the cells stained brightly with this lectin (Fig. 1a). Staining of the metaplastic glands, however, was more variable. The luminal surface was always positive, but the cytoplasm and the goblet mucin showed both positive and negative staining, varying from gland to gland. There was a slight tendency for the goblet mucin of the cells

FIG. 2a. DBA staining of the non-metaplastic glands of the gastric mucosa in a patient with blood group A. The secreted mucin, luminal surface and cytoplasmic contents are all positive. $\times 300$

FIG. 2b. DBA staining of the non-metaplastic glands of the gastric mucosa in a patient with blood group B. The secreted mucin, luminal surface and cytoplasmic contents are negative. $\times 300$

FIG. 2c. DBA staining of the metaplastic glands in a patient with blood group A. The apical and supranuclear cytoplasm show positive granular staining. Some of the goblet cells on the surface epithelium also contain positive mucin, while in some it is negative. $\times 300$

FIG. 2d. DBA staining of the metaplastic glands in a patient with blood group B. The luminal surface as well as the cytoplasmic contents show negative reactivity. The goblet mucin also is negative. $\times 300$

FIG. 2e. DBA staining of the villi of the small intestinal mucosa in a patient with blood group A showing positive staining of the luminal surface, cytoplasmic contents and goblet mucin. $\times 600$

FIG. 2f. DBA staining of the villi of the small intestinal mucosa in a patient with blood group B. The luminal surface and apical and supranuclear cytoplasm are negative. Some of the goblet cells show positive mucin while in others it is negative. $\times 300$

FIG. 2g. DBA staining of a crypt of the ascending colonic mucosa. The goblet cells in the upper portion of the crypt show positive staining of their mucin while those in the lower portion of the crypt are negative. $\times 300$

FIG. 2h. The same gland as in Fig. 2g. after neuraminidase digestion. All the goblet cells in both the upper and lower portions of the crypt show positive staining of their mucin. $\times 300$

on the surface epithelium and the upper portion of the metaplastic glands to be positive more frequently than those of the lower portion of the crypts (Figs. 1b, c). There was no difference between patients with different blood groups. Neuraminidase pretreatment did not enhance staining of any part of either the non-metaplastic or metaplastic glands.

In the small intestine, the luminal surface of the epithelial cells lining the villi and the upper portion of the crypts was positive, whereas that of the lower portion of the crypts was negative (Fig. 1d).

Most of the goblet mucin of the small intestine was negative but some reacted weakly with UEA-I. More than half of the goblet mucin of the ascending colon showed positive staining. On the contrary, descending colon stained negatively with UEA-I and the staining of the luminal surface of the ascending colonic mucosa was enhanced by neuraminidase pretreatment.

TABLE 2. *DBA staining of the mucosa of the stomach (non-metaplastic and metaplastic glands), small intestine, and ascending and descending colon*

	Stomach				Small intestine		Ascending colon	Descending colon
	Non-metaplastic		Metaplastic					
Blood group	A, AB	B, O	A, AB	B, O	A, AB	B, O	ANY	ANY

<i>Surface epithelium:</i>								
Secreted mucin	++	—	++	—	++	—	++	++
Luminal surface	++	—	++	—	++	—	—/+ (†)	—/+ (†)
Apical cytoplasm	++	—	+	—	+	—	—	—/+
Supranuclear cytoplasm	++	+	+	—	+	—	—	—
Goblet mucin			—/+*(†)**	—(†)	++	+/—(†)	—/+ (†)	—/+ (†)
<i>Glands or crypts:</i>								
Luminal surface	++	—	++	—	++	—	—	—
Apical cytoplasm	++	—	—/+	—	++	—	—(†)	—(†)
Supranuclear cytoplasm	++	+	—/+	—	++	—	—	—
Goblet mucin (upper)			—/+ (†)	—(†)	++	—(†)	+	+
Goblet mucin (lower)			—(†)	—(†)	++	—(†)	—(†)	—(†)
<i>Parietal cells</i>	—	—						
<i>Chief cells</i>	—	—						

*, ** See footnotes to TABLE 1.

2) *DBA:*

There appeared to be two distinct patterns of DBA reactivity of the non-metaplastic and metaplastic glands as well as the small intestinal mucosa (Table 2). It was noted that these patterns had a definite relationship to the patients' blood groups.

The first pattern of DBA staining was found only in patients with blood groups A and AB. It was characterized by strong positive staining in all the components of the cells lining the non-metaplastic glands, although the parietal and chief cells were negative (Fig. 2a). In the metaplastic glands of these patients, the secreted mucin, luminal surface and cytoplasm of the surface epithelium also showed positive staining with DBA. About half of the goblet mucin on the surface epithelium appeared positive (Fig. 2c). Staining of the cells in the crypts was more variable. Nevertheless, the luminal surface was always positive. Staining of the goblet mucin of the goblet cells in the crypts was less intense than on the surface epithelium, and goblet cells in the deepest part of the crypts were all negative. However, after neuraminidase treatment, all the goblet mucin became positive. This pattern of staining was found in 13 of the 16 cases (81.2%) with blood group A and also in the patient with blood group AB.

Patients with blood groups B and O and the remaining three patients with blood group A showed a different pattern which was characterized by negative reactivity for all components of the non-metaplastic glands except the supranuclear cytoplasm

which showed faint positive granular staining. The secreted mucin in this group, in contrast to the first pattern, was always negative (Fig. 2b). The luminal surface and all the cytoplasmic contents of the metaplastic glands were negative (Fig. 2d). However, after neuraminidase treatment, staining of all the goblet mucin was enhanced.

The small intestine also showed two distinct patterns. In patients with blood groups A and AB, all components of the cells, including the goblet and secreted mucin, were positive (Fig. 2e). In patients with blood groups B and O, only some of the goblet mucin in the surface epithelium was positive (Fig. 2f). After neuraminidase treatment, all goblet mucin, but not the other components, became positive.

The ascending and descending colon showed similar DBA reactivity without regard to the patients' blood groups. The secreted mucin, luminal surface and goblet mucin of the surface epithelium and the upper portion of the crypts were positive. The cytoplasm and the goblet mucin of the lower portion of the crypts were negative (Fig. 2g). After neuraminidase digestion, the staining intensity of the apical cytoplasm and the goblet mucin was enhanced (Fig. 2h).

3) PNA:

As shown in Table 3, secreted mucin of the gastric mucosa stained positively with PNA. The luminal surface of the gastric mucosal cells, both metaplastic and non-metaplastic, was always negative. Most of the cytoplasmic contents of the non-metaplastic glands were positive, while those of the metaplastic glands tended to be negative except for some weak fine granular staining of the apical cytoplasm on the surface epithelium (Fig. 3a). Goblet mucin of the metaplastic glands was negative with the exception of a few cells in some glands that showed weak positivity

TABLE 3. PNA staining of the mucosa of the stomach (non-metaplastic and metaplastic glands), small intestine, and ascending and descending colon

	Stomach		Small intestine	Ascending colon	Descending colon
	Non-metaplastic	Metaplastic			
<i>Surface epithelium:</i>					
Secreted mucin	++/+*	++/+	—	—	—
Luminal surface	—	—	—	—	—
Apical cytoplasm	+ / ++ / —	/ + —	—	—	—
Supranuclear cytoplasm	+ / ++	—	—	—	—
Goblet mucin		— (+ / —)**	—	—	—
<i>Glands or crypts:</i>					
Luminal surface	—	—	—	—	—
Apical cytoplasm	+ / ++ / —	—	—	—	—
Supranuclear cytoplasm	+ / ++	—	—	—	—
Goblet mucin (upper)		— (†)	—	—	—
Goblet mucin (lower)		— (‡)	— +	—	—
<i>Parietal cells</i>	—				
<i>Chief cells</i>	—				

*, ** See footnotes to TABLE 1.

of the goblet mucin. After neuraminidase treatment, the staining of the goblet mucin was enhanced while other components of the cells remained negative.

The goblet mucin in the lower portion of the crypts always stained darker than that in the upper portion and the surface epithelium after enhancement (Figs. 3b, c). Some of the goblet cells on the surface remained negative after neuraminidase treatment. Blood groups of the patients had no effect on PNA reactivity.

The small and large intestines were all negative with PNA staining. Only a few goblet cells of the small intestine gave a weak positive reaction with PNA before neuraminidase treatment. After the enzyme digestion, only the goblet mucin in the lower portion of the crypts of the small intestine was positive (Fig. 3d). Staining of the large intestine was not enhanced.

4) Controls:

All control sections, in which lectins were omitted or in which inhibitory carbohydrates were used, showed negative staining.

DISCUSSION

The epithelial mucosa and the secreted mucin of the gastrointestinal tract contain a large amount of different types of glycoproteins. Lectin binding sites in the mucosa of the stomach and the small and large intestines have been demonstrated by either the horseradish-peroxidase technique or fluorescence microscopic studies in both normal tissue and in those with benign and malignant changes (12, 13). It was shown that, for both the gastric and colorectal neoplastic changes, the carbohydrate content of the mucin (14, 19) as well as the lectin binding of the tissues (2, 8, 13) were different from those in normal tissues. It has also been shown that the ability of these cells to bind to lectins changes as the cells migrate from the bottom of the crypts towards the tip of the villi during the process of maturation of the intestinal mucosal cells (12). Furthermore, lectin-binding properties of the colonic mucosal cells and their secreted mucin were found to change during neoplastic transformation (3, 30, 31).

This study clearly shows that during the process of intestinalization of the gastric mucosa, not only changes in morphology and the activities of various marker enzymes, but also changes in the components of glycoproteins in almost every part of the cell, occur. Our results demonstrated that the patterns of lectin binding of

FIG. 3a. PNA staining of the gastric mucosa showing the transition between non-metaplastic and metaplastic areas. The non-metaplastic glands show positive reactivity of the cytoplasmic contents in contrast to the metaplastic glands which are negative. Note that the goblet mucin is negative with PNA staining. $\times 150$

FIG. 3b. PNA staining of the surface epithelium of the metaplastic glands after neuraminidase treatment, showing weakly positive goblet mucin. $\times 300$

FIG. 3c. The same glands as in Fig. 3b but at the bottom of the glands, showing strong positive staining of the goblet mucin with PNA after neuraminidase treatment. Compare this with the goblet mucin in the surface epithelium shown in Fig. 3b. $\times 300$

FIG. 3d. PNA staining of the small intestinal mucosa after neuraminidase treatment, showing positive staining of the goblet mucin in the bottom of the crypts but negative staining in the upper portion of the crypts. $\times 300$

the metaplastic glands were not identical to those patterns of either the small or large intestine. Moreover, the complete and incomplete types of intestinal metaplasia did not show significant or distinguishable difference in lectin reactivity. However, there was much variability in lectin staining of the metaplastic glands from case to case and from gland to gland even in the same case. These findings suggest that the process of intestinalization is not a homogeneous process and support the evidence found by Matsukura *et al.* (21), who showed that the expression of intestinal marker enzymes and the high-iron diamine staining properties of the metaplastic glands were rather heterogeneous even in the same specimen.

UEA-I is a lectin which specifically binds L-fucose and has been shown to be specific to blood group O (H) antigen (23). It was shown by Fischer *et al.* (13) to bind to all parts of the cells of the normal gastric glands. Bur and Franklin (6) also demonstrated that UEA-I gave a positive reaction with the apical portion of the cytoplasm of normal gastric mucosal cells, but a less consistent reaction with the metaplastic glands, and there was no enhancement after neuraminidase digestion. Our findings confirmed their results in these respects. They also confirmed a previous finding (6) that UEA-I binding of the gastric mucosa does not have any relationship to the patients' blood groups.

Since UEA-I is specific to L-fucose residues which compose the non-reducing terminals of oligosaccharides (23), the results of this study suggest that the normal gastric mucosal cells possess more available L-fucose residues than the metaplastic cells. Yonezawa *et al.* (30) reported that UEA-I staining in goblet cell mucous was different between ascending and descending colon. Most of goblet cells of ascending colon showed positive UEA-I staining but those of descending colon were negative. Results of our study coincide with Yonezawa's report. Removal of the neuraminic acid residue with neuraminidase did not make more L-fucose available for UEA-I binding in any components except the luminal surface of the ascending colon.

DBA is a lectin that specifically binds to N-acetylgalactosamine and blood group A antigen (11, 29). By using fluorescence microscopy, it has been found to give a focal positive reaction with the apical cytoplasm of the foveolar cell vacuoles of normal gastric mucosa but to stain the cytoplasm of the metaplastic glands very weakly or negatively without relationship to the patients' blood groups (6). Contrary to their finding, in our present study, 13 (81.2%) of the 16 patients with blood group A and one with blood group AB expressed strong DBA binding to the non-metaplastic glands, surface epithelium of the metaplastic glands and the small intestinal mucosa. All patients with blood groups B and O and only 3 of the 16 patients with blood group A behaved differently; most of the cell components and their mucin were negative with DBA.

For DBA binding of the small intestine, previous reports (2, 12) have shown that its binding to the goblet mucin was rather variable, with more positive binding to the villi and upper part of the crypts. In the present study, DBA binding in the cases of blood groups B and O agreed quite well with their results while the A, AB group specimens stained constantly positively in all levels of the crypts. Our results of DBA binding of the large intestine were similar to those reported previously by Jacobs and Huber (15).

Since DBA is a blood group A-specific lectin, our findings suggest that the blood group A antigen might play a role in DBA binding to almost all components of the

gastric and small intestinal mucosal cells. The reason why the three blood group A patients behaved like blood groups B and O patients remains to be clarified.

After neuraminidase treatment, all the goblet mucin of the metaplastic glands and small and large intestinal mucosa were positive, indicating the presence of neuraminic acid residues in their structures which normally interfere with DBA binding.

PNA is a lectin specific to D-galactose and D-galactose- β -1,3-N-acetylgalactosamine and agglutinates human erythrocytes only after neuraminidase digestion (20). In normal gastric mucosa, PNA has been shown to react variably with the secreted mucin and cytoplasm (6, 28) although some observers (13) reported constant negative reactivity. Our results on PNA binding of the non-metaplastic glands also demonstrated variable staining of the secreted mucin and cytoplasm.

In the metaplastic glands, both Bur and Franklin (6) and Fischer *et al.* (13) reported that PNA staining was rather sparse or negative in every component of the cell including the goblet mucin and that only the staining of goblet mucin could be enhanced by neuraminidase. Our results agree with theirs. We clearly demonstrated that, after neuraminidase digestion, the goblet mucin of the metaplastic glands showed a stepwise change in reactivity from the bottom towards the upper portions of the glands according to the migration of the metaplastic cells from the bottom of the crypts just like those of the small intestinal mucosal cells.

The results of this study showed that neither the complete nor the incomplete type of intestinal metaplasia possesses the same properties as the small or large intestine from the viewpoint of lectin staining. Furthermore, lectin staining of the normal gastric and small and large intestinal mucosa was rather homogeneous, in contrast to the heterogeneity of the metaplastic glands. Moreover, lectin binding properties of the cells might have some relationship to cell migration along the crypts of the metaplastic glands and small intestinal mucosa.

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