TUMOR GROWTH AND STROMAL POLYSACCHARIDES
IN GASTRIC CANCER (With Plates XIX—XXII)

ISAMU KIMURA
Department of Pathology, Shinshu University School of Medicine.
(Director: Prof. Z. Ishii)

Various histological patterns of tumor at the invading front into surrounding tissue are thought to be important in diagnosis of tumor malignancy. According to Willis, the infiltrative behaviors of tumor tissue are referred to autonomous proliferating and phagocytic activity, motility, production of toxic or histolytic substance of tumor cells and the correlative disorder of the surrounding tissue, and all are ascribed to the character of tumor cell itself. However, the antiblastic host reactions should be considered concurrently with tumor cell itself in analogous way to hostparasite relationship as in inflammation.

Imai, Tokoro, Okabayashi and others emphasize the importance of investigating the tumor in such a stereotypical manner. Imai, especially, studied the tissue architectonics of cancer using a large tumor section with the whole advancing margin included in it, and pointed out the significance of peritumoral tissue, in addition to the tumor itself, as the cause of tumor "Schub" or malignant change.

Numerous reports were published on "stromal reaction of tumor," but most of the studies (Ota, Machii, Kin, Yoshida, Tanaka, Kusuhara, Muto, Miyata, Imai, etc.) are concerned with fiber architectonics of host tissue. Recently the histochemical study is in progress associated with the connective tissue chemistry, but the pathomorphological studies of stromal ground substance of tumor are relatively few, except Gersh's study of basement membrane and Chiuma's study of cutaneous cancer stroma.

The author studied the polysaccharides of stromal ground substance by various histochemical methods both qualitatively and quantitatively, using surgical and autopsy specimens of gastric cancer, and detected the correlation between the tumor growth and the stromal polysaccharide reaction and also the histogenesis of scirrhus cancer.

MATERIAL AND METHODS

Materials used are 5 autopsy cases of gastric cancer, and 63 surgical specimens, 2 of which are stomachs resected as a whole. Simple gastritis and ulcer as well as normal stomach were also studied for control as follows: primary stomach cancer 34, gastritis 13, stomach ulcer 15 and normal stomach 6 cases. Stomach
tumors such as benign tumor, squamous cell cancer or sarcoma were not examined. The specimens were fixed in 10% formal as usual, some surgical specimens were also fixed in pure alcohol.

The histochemical methods applied for demonstration of polysaccharides* are as follows: Lillie's stain* (PAS), Hale-Rinehart's* colloid iron method, Ohno's toluidin blue metachromasia,* combination of Lillie's and H–R method of Ritter-Oleson. Used also are hematoxylin-eosin stain, Van Gieson's and Azan Mallory's stain for collagenous fibers, Weigert's elastic fiber stain, and in addition, Lillie's allochrome stain and combination of PAS method and anilin blue stain after phosphomolybdic acid mordanting in order to demonstrate the relation of stromal P. and various connective tissue fibers.

The histochemically proved P. are presumed chemically to be hyaluronic acid, algin sulphuric acid, glycogen, heparin in mast cells and so on, but a part of protein molecules should also be included in the group.

The stomach wall is divided into 7 layers: 1. epithelial layer, 2. basement membrane, 3. lamina propria, 4. muscularis mucosae, 5. submucosa, 6.

* L.: Lillie's stain.
M.: Toluidin blue metachromasia.
PSP.: Positive substance for polysaccharide reactions.
P.: Polysaccharides.
The quantity of positive substance for polysaccharide reactions* (PSP) in those layers except layer 1, was estimated and expressed as (−), (±), (+), (++), (+++). In tumor case however, the tumor cell was regarded as layer 1, and the stroma at the advancing tumor margin as layer 3.

RESULTS

1. Polysaccharide reaction positive substance in ground substance. In most specimens of formol fixation, there is inclinationally a pararellism in grade between L. and H–R. method, some portions are more reactive by the latter infrequently. The collagenous fibers themselves are stained in negative or faintly. PSP in ground substance is precipitated on the surface of collagenous and reticulum fibers, taking the appearance of agglutinated irregular mass of various sizes or interfibrilar rosarylike agglutinated droplets, the interspace of which is entirely unstained. Combination of both methods revealed that PSP above described are subdivided in alpha, beta and gamma substances as Aoki named them. Alpha substance is positive by both methods, beta and gamma are positive by either one method. PSP agglutinated on the surface of fibers is alpha in character, while the collagenous fibers themselves are beta-like in colour, but where the collagenous fibers taper off finely and P. of matrix are relatively aboundant, gamma positive coagulative substance is increased frequently in place of alpha substance.

When both reactions are applied to the specimens fixed by pure alcohol, PSP in matrix is not agglutinated on the surface of connective tissue fibers as in case of formol fixation, but stained diffusely in fine granules between fibers.

They are more intensively stained than in case of formol fixation in general, especially by H–R method and alpha substance is tinged with deeper blue, gamma substance is more or less abundant in quantity. The collagenous fibers are also reactive to some extent by either L. or H–R method, and are beta positive approximating to gamma colour tone or entirely gamma positive in nature by the combined method infrequently.

By application of toluidin blue, heparin granules of mast cells are stained red metachromatically at pH 2.5, 4.1, 7.0, while dark red coagulative mass is found interfibrilar at pH 4.1, 7.0, and the whole fiber surface can be diffusely and faintly stained infrequently in case of formol fixation. The positive grade of this mass by this method seems, in comparison with other methods, to be parallel with the increase of gamma substance generally, but it is difficult to identity them morphologically. There is no difference in the appearance of M. depending upon pH fluctuation between the specimens of formol and pure alcohol fixation, but in the latter, the colour tone is shifted toward the short wave length principally and the latitude of positivity becomes wider, and therefore not only collagenous fiber,
cell nucleus, and mucus, but also a part of cytoplasm become clearly metachromatic. Fine granular metachromatic substances are filled in intercellular or interfibrilar ground substance as was seen by L. method. There are further positive substances in mucous epithelial cells, duodenal excret (beta positive and no reaction by H–R), colloidal mass or blood vessel wall.

2. **Quantitative estimation of stromal polysaccharides in tumor.** The modes of tumor growth are classified into 4 types according to Imai as follows:
   a) **Hypertrophic type:** Growth by the increase of thickness or volume of cancer alveoli or duct lumina.
   b) **Elongating type:** Growth by elongation of cancer alveoli or duct lumina, the thickness of which must attain to some extent.
   c) **Sprouting type:** Growth by shooting out as cell strands or free individual cells of cancer into surrounding tissue.
   d) **Intracanalicular type:** Growth by permeating lymphatics or blood vessels in loco, especially the former.

The histological pictures of gastric cancers are classified in various aspects by many authors such as Borrmann and others, but here the classification of Imai and Tanaka is adopted, where the growth pattern of tumor and the nature of tumor cells are arranged in good performance as follows:

1. **Adenocarcinoma (A)**
   a) Microfollicular adenocarcinoma (Am)
   b) Columnoepithelial adenocarcinoma (Ac)
   c) Papillary adenocarcinoma (Ap)
2. **Solid carcinoma (S)**
   a) Columnoepithelial solid carcinoma (Sc)
   b) Globoacellular solid carcinoma (Sg)
3. **Diffuse carcinoma (D)**
   a) Globoacellular diffuse carcinoma (Dg)
   b) Mucocellular diffuse carcinoma (Dm)
4. **Colloid carcinoma (C)**
   a) Adenomatous colloid carcinoma (Ga)
   b) Solid colloid carcinoma (Gs)
   c) Diffuse colloid carcinoma (Gd)

The number of specimens used are classified according to the above principle as follows: Am 14, Ac 11, Sg 4, Sc 2, Dg 8, Dm 3, Gs 3 cases.

1) **Hypertrophic growth type (Table 1)**

10 cases of this type, 12 portions of which were brought to study. 4 cases of Ac. and 1 case of G. cancer were included in them. The results in Table 1 are checked regarding 3, 5 and 6 layers (see Chart 1), the findings in the other layers were abridged for convenience. (The same rule applies to other tables that follow.)
As in Table 1, L. and H-R positive substances at the advancing margin of this growth type are insignificantly increased, poor in M. substance and collagenic fiber bundles are tortuous like thick wire with few active fibril formation. PSP are precipitated finely on the surface of collagenic fibers, and no such special localization as perivascular affinity was proved.

In case of No. 2184, the stroma at the advancing margin has a delicate capsular structure, but in spite of monocytic infiltration in tumor tissue due to bacterial infection, no extracapsular reactions take place, where the presence of PSP or M. is insignificant or failed. In 4 cases of Ac. carcinoma, the tumors are rather prone to project papillarly or cauliflower-like into stomach lumen than into submucosa or muscle wall, and there are neither increase of PSP nor proliferation

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Table 1. Results at the advancing margin of gastric cancers. (Hypertrophic type)

Table 2. Results at the advancing margin of gastric cancers. (Elongating type)
of collagenic fibers nor lymphocytic reaction, only mast cells migrate slightly in No. 2075 and No. 2806.

2) Elongating type (Table 2)

This type is frequently associated with the sprouting type in the studied cases, and 8 portions were selected where the former type is not so influenced by the latter. Both PSP and collagenic fibers are moderately increased in stroma.

There are 2 types of stromal collagenic fibers to be distinguished—the dense differentiated and the fine newly developed—the former arranged quite indifferent to tumor growth, whereas the latter tend to be entangled about or to envelope cancer alveoli. PSP are uniformly distributed on the surface of fine collagenic fibers adjacent to the invading front of tumor, and mottled in appearance in

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Table 3. Results at the advancing margin of gastric cancers. (Sprouting type)

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perivascular space occasionally (No. 2869). Between the tumor tissue and the PSP area, there is always a narrow free zone. The results by L. and H-R method run in parallel principally, but in No. 2869 H-R is intensively positive in contrast to faint L., where the fine fibrils are poorly developed and the dense fibers are tumefied.

M. substance is also increased especially in No. 2869. Cellular reactions take place in moderate degree, but mast cell reaction is variable in each case and not so marked in No. 2869.

3) Sprouting type (Table 3)

In 28 portions examined, the active proliferation of collagenic fibers, increase of H-R positive substance and M. are noticed in general.

When the collagenic fibers are not so extremely developed, positive grade by L. and H-R method seems to run in parallel, while it does not where the fibers proliferate actively and densely as in case of scirrhus or carcinoma fibrosum. In such a case, H-R positive substance is often strikingly increased in contrast to L. positive substance, where the fine collagenic fibers are irregularly entangled or dense differentiated fibers are tumefied. Such loosely meshed areas are enveloped by dense proliferative zone of differentiated collagenic fibers, where L-positive substances are distributed interfascicularly in wide area. PSP is increasing in mottled appearance as in case of the elongating type and often in close contact to tumor cells or in perivascular space. L. positive and H-R positive substances are distributed in antagonistic manner in the sprouting type. The relationship between H-R positive substance and collagenic fibers as described above is however inapplicable to some cases (No. 2669), where PSP is not so increased as the fine collagenic fibers (see the lower part of Table 3, and Figs. 7 8).

As to the elastic fiber, it proliferates mainly in muscularis mucosae and outer zone of submucosal layer near the advancing tumor margin regardless of any growth type and has no relation to PSP. condition.

3. Stromal findings of inflammative, ulcerative and normal stomach wall. 6 normal, 13 inflammative and 15 ulcerative cases were brought to investigation. In normal case, collagenic fibers are few and make dense bundles. PSP in ground substance is also scanty, precipitating on fiber surface. In case of acute and chronic gastric catarrh, there is no deeper bacterial invasion and no remarkable difference compared to normal case. In case of chronic ulcer, PSP is generally increased but very variable in quantity in each case compared with the constant presence of dense fibrosis.

An old scar tissue contains only sparsely distributed PSP occasionally, which is something different from tumor case. PSP is uniformly distributed and no local difference is present in non-neoplastic cases.

4. Topographic difference of stromal polysaccharides reaction in the same
tumor. The findings above described are concerned with the relationship of PSP and collagenic fibers of stroma at the advancing front of tumors of various types. But, since the growth type of the same tumor can be variable in many places, and is surrounded by different tissue structures, topographic difference of stromal response of the same tumor should be expected.

Some representative cases are demonstrated as follows:

Case 1. Colloid carcinoma (No. 2457) (Fig. 9)
Typical colloid cancer, the external surface of which is ulcerated and invades through muscle coat up to subserosa. At the invading front in muscle layer, goblet cells are floating in mucinous mass by which the surrounding tissue is compressed. Where the muscle tissue is adjacent to mucinous mass, PSP is poorly developed and restricted to interfascicular spaces, and a few non-mucinous secreting tumor cells sprout into the surrounding tissue. The interfibrilar deposition of PSP is few and restricted to the sprouting focus of non-mucinous secreting cells. The tumor cells are encountered by active deposition of PSP at subserosa and cease to grow outward. In submucosa on the other hand, non-mucinous secreting cells sprout in strands actively toward lateral direction, where PSP and M. increase strikingly in loco. It is characteristic in production of fine collagenic fibers and a few mast cells are in those areas. From the fact that there is considerable difference in P. reactions in two places, muscles and submucosal layer, it is presumed that the reaction is not the expression of host body as a whole against tumor, but is influenced by local conditions. It is also noted that the mucinous substance and the cells secreting it do not stimulate production of PSP so actively as non-mucinous secreting cells, and the influence of histological and chemical characteristics of muscle and submucosal layer upon P. reactions should be taken into consideration.

Case 2. Ulcerative cancer (No. 2918) (Fig. 10)
The mucle layer covered by thin coat of scar tissue is exposed to the ulcer ground and overhang the surrounding catarrhal mucous membrane at the right margin, from where the cancer seems to develop and spread over the ulcer surface and into submucosa permeating into lymphatics. The submucosal tumor on the right side (see the schema) develops in tubular structure (elongating type), a part of which penetrates muscularis mucosae and arrives at submucosa. At the advancing margin of tumor, the stromal H–R positive substance, M. subsaece and collagenic fibers are increased in moderate degree, a few mast cells are scattered among them.

In the ulcer ground opposite to the area above mentioned, the tumor cells poor in cytoplasm are sprouting in cell strands along the cicatrified muscle bundles. Here are PSP and M. insignificant as in normal stomach, and fine collagenic fibers are poorly developed among dense fiber bundles. P. reactions are only
faintly positive on fiber surface in scar tissue free from tumor invasion. Agglutinative precipitation on the fiber surface or in interfibrous space is entirely negative. The advancing margin in this area arrives at subserosa, where the tumor cells obtain rich protoplasm and form wide alveoli, and PSP also increases correspondingly. This case indicates that the growth type and the stromal P. reactions can be influenced by the local environment.

Case 3. Globocellular diffuse carcinoma (No. 2183) (Fig. 11)

The tumor cells, cubic or round in shape, form small alveoli and invade from submucosa into muscle layer (on the left half of the schema). PSP esp. H–R positive substance and collagenic fibers are increased surrounding the tumor cells infiltrating into muscle layer. Where PSP are abundantly produced, fine reticular structures are made up by precipitated mass interfibrarly, which show up apparently by van-Gieson’s and Mallory’s method. There are also capillary formations in those areas, and much PSP are deposited in perivascular spaces where the relatively dense fibrous elements are loosely meshed and run independently to each other and fine fibrils are developed on the other hand. In the muscle layer (on the right half of the schema), isolated tumor cells are infiltrating interfascicularly accompanying the slightly increased PSP and poorly developed fine collagenic fibers. M. is slight in the former but moderate in muscularis in degree, mast cells are also present to some extent in the latter.

Case 4. Colloid diffuse carcinoma (No. 2669) (Fig. 12)

The tumor cells are separated from each other, distributed diffusely and uniformly in submucosa (on the left half of the schema), which is covered by relatively intact epithelium. All tumor cells contain in their cytoplasms L. positive red mucous droplets, some of them are changing into goblet cells. In this area the collagenic fibers proliferate actively and is demarkated definitely against the loose connective tissue area free from tumor cell invasion.

No increase of PSP, M. or mast cells in the tumor area. These facts seem to have some relations to the lack of non-mucous secreting cells.

**DISCUSSION AND CONCLUSION**

Before discussing the results above obtained, some problems on the histochemical procedures for P. should be considered. The results of histochemistry for P. depend upon the fixation of specimens. Aoki divided P. into alpha, beta and gamma by using Ritter-Oleson’s combined method, and thinks gamma substance, because of its water solubility, is impossible to prove histochemically by formol fixation. According to Ohneda, hyaluronic acid is prone to be transferred into water soluble fixatives, and Lison could extract it with water from the specimens fixed by acetone. He could also prove the glycogen to some extent histichemically by watery fixatives and supposed a part of glycogen combined with high molecules.
could be fixed to some extent when the protein is adequately fixed. The author compared the formol and pure alcohol fixatives applied to the same specimen in regard to the positivity of P. reactions, and found PSP precipitate in agglutinated status on the fiber surface in the former, in fine granules in the latter, but quantitatively there is no difference between them.

In addition, I could not find any reduction of these substances in deparaffinized sections rinsed in water for three days. Gamma substance is also well preserved, which indicates that PSP escapes little if any, when the specimens are fixed rapidly and completely by formol. It must be considered here that the formol does not permeate into tissue so fast as alcohol. From the aspect of chemical natures of L. positive and H-R positive substances, they should be always demon-

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Table 4 Estimation of PSP of tumor stroma. Numbers in parenthesis indicate percentage of case numbers when each method is applied.
The proliferation of collagenic fibers adjacent to the advancing tumor margin also runs parallel with P. reactions. In gastritis and in normal case, there is no increase of PSP in contrast to definite increase in ulcer case.

However, the inconstant presence of L. positive substance in comparison to the marked increase of collagenic fibers in ulcer case is noticed.

As regards the relation of PSP and histological pictures of cancer, Dg and Ac carcinomas are situated at both extremities as to the degree of P. reactions, other types are ranked between them. But in one and the same tumor mass,
there can be often found some variations or differences in growth type or histological picture topographically and also local stromal reaction correspondingly. When the results obtained from histological classification (Table 5) are compared with those from growth types (Table 4), many facts are revealed, for instance, Am carcinoma has tendency to be varied in growth type in different localities and the stromal response is dependent on each growth type, Ac carcinoma contains much PSP infrequently because of its predominance of hypertrophic type and Dg carcinoma invades tissue by sprouting mainly, as a result of which P. reactions are intensified.

Further it is presumed the stromal reactions are influenced also by the tissue conditions invaded by tumor as in case of muscle layer, ulcer ground, scar tissue, submucosa, etc.

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Table 5. Estimation of PSP in each type of cancer. Numbers in parenthesis mean the same as in Table 4.
There are often discrepancies between stromal response and growth type especially in the former.

On the problems of stromal reaction of tumor, various interpretations were postulated but no definite conclusion at present. It is because the reaction is influenced by many components, and a tumor as a whole is discussed. Imai demonstrated the histological difference of one and the same tumor both topographically and chronologically and could analyze the complex histology of cancer by application of prototypes of tumor growth designed by him to each advancing tumor margin.

His analytical method is also applicable to the stromal P. reactions in many aspects. From the stromal P. reactions and the fiber formation in loco, cancer is classified in 4 types referring to Imai’s principle as follows:

1) Non-reactive type. Both PSP and collagenic fibers are poorly developed or failed. It is found in hypertrophic growth type, gastritis and a part of sprouting growth type.

2) Polysaccharide type. In this type, PSP is much increased in contrast to the poor development of collagenic fibers, which are characterized by fine fibers and often degenerating dense fibers. PSP is most reactive by H-R method, M. is most intensive in degree and mast cells emigrate actively. This type is found in stroma at the advancing front of sprouting or elongating growth type and further in pericapillary space near it. PSP is mottled in appearance and the loosely meshed fibers are stained like edematous swelling by the ordinary connective tissue stain.

3) Fibrous type. PSP is poor, collagenic fibers are predominant as in connective tissue callus of stomach ulcer. M. substances and mast cells are absent and collagenic fibers are densely bundled.

4) Polysaccharide-fibrous type. This is transitional type from 2 to 3. PSP is abundant and uniformly distributed on surface of proliferating collagenic fibers, M. is faintly positive, mast cells are not in appearance. The invading front of elongating and sprouting type or a part of ulcer cases belong to this type.

PSP patterns of the 4 types above described are intimately related to proliferation of collagenic fibers and growth types of tumor. The relationship of polysaccharides in matrix and collagenous fibers is being elucidated recently correlating with the problem of morphogenesis of collagenic fibers.

It is not concluded at present about the origin of collagenic fibers, intra- or extracellular. Porter or Miyata proved intra-cellular profibril formation by electron microscopy, Szent Georgi found plexus of profibrils arranged on the surface of fibrocytes. Chiuma, on the other hand, studied stromal P. reactions in experimental tumors and divided them into 5 stages. He explains that P. in matrix is depolymerized in his early stages, resulting in M. and then repoly-
merized as cancer develops, collagenic fibers change in parallel with PSP.

The stromal P. is thought to be induced from blood born component (Gersh) or from intraplastic production of fibrocyte excreted into intercellular space (Miyata).

Chiuma refers M. to the degree of polymerization of stromal P. When the author's classification above described is compared with Chiuma's stages, there can be found common chronological change of processes of stromal reactions.

When the tumor invasion takes place, the stromal P. is increased and deposited also in perivascular spaces and the already differentiated dense fibers are degenerated, which seem to be the same phenomenon that Tokoro and Kusuhara explained as "perifokale Mesenchymverjüngung," "Blastom-bedingte Mesoderm- auflösung" or "Demaskierung des Kollagens".

It is reasonable to think PSP about cancer alveoli as the result of depolymerization of local P. as Chiuma concludes, but that in perivascular space distant from cancer cells is difficult to be explained as the effect of depolymerizing enzyme of cancer cells. It is rather sound to derive them from blood born components as Gersh. Miyata distinguishes between the P. produced by fibrocyte and that originated from blood components and correlates the latter to serous inflammation. But in fact, it is difficult to distinguish them, and the exudate in serous inflammation is different in histochemical response. They may originate from blood vessels through some different mechanism.

The fact that PSP in perivascular space often spreads to considerable extent, whereas that about cancer alveoli does not increase to such an extent, makes them mainly referable to the blood born components. The blood vessel distribution must be also taken in consideration. In some cases (Case 2), the faint stromal reaction is already described in spite of the sprouting type of tumor developed in scar tissue, it may be responsible to the deficiency of blood vessels in scar tissue and the variance of positive degree according to each layer of stomach is thought to be related to blood vessel distribution to some extent. The spreading factor in tumor tissue and antispreading factor and its inhibiting factor are also proved in tumor patients, further is reported the presence of antitryptic substance in blood though their presence was denied by Kiriluk.

But the phenomenon of depolymerization at the invading front of tumor, the foreignness of tumor growth, localization of P. reaction corresponding to each growth type, some unexplainable facts in case of hypertrophic type or colloid cancer, all these facts seem to indicate the importance of the substances above mentioned.

The outstanding increase of PSP in case of gastric ulcer also is full of suggestion in relation to gastric cancer from the viewpoint of histolytic enzyme. On the other hand, it is reported also the inhibiting factor in blood is P. itself, and the relation between the appearance of PSP and blood vessel distribution is of
much attractive interest.

**Summary**

34 cases of gastric cancer and control (gastritis, ulcer and normal stomach) were studied histochemically with regard to polysaccharides of ground substance.

1. At the advancing front of tumor, the stromal P. and the collagenic fibers are brought in intimate correlation.

   In this aspect, the stromal reactions of both cancerous and non-cancerous stomach wall can be divided into 4 types as follows: a. Non-reactive type. b. Polysaccharide type. c. Polysaccharide-fibrous type. d. Fibrous type.

2. In case of gastric cancer, the hypertrophic growth type at the advancing margin (Imai) corresponds to (a), while the elongating or sprouting type (Imai) to (b) and (c). Some relationships between the growth types of cancer (Imai) and the stromal P. reactions are confirmed.

3. The stromal P. in the same tumor is influenced not only by various growth types but also by different histological pictures. PSP at the advancing front of tumor does not mean the response of the whole host body, but the mutual relation between the local tumor tissue and the stroma.

4. The stromal P. is produced from the surrounding of the advancing margin of tumor and the pericapillary spaces near it, P. from the former is reasonably referred to the depolymerization of ground substance, whereas blood born components can also play an important role in producing it.

5. Toluidin blue metachromasia, which is thought to indicate the grade of polymerization, comes up most outstandingly in case of polysaccharide type than other types.

6. The proliferative stimulus of producing stromal P. is most referable to the histolytic enzymes produced by tumor.

7. The stromal reactions are influenced not only by tumor tissue, but also by environmental tissue structures. The capillaries near the advancing margin seem to play a role in the reaction.

8. P. in ground substance is precipitated on surface of collagenic fibers in agglutinated appearance in case of formol fixation in contrast to alcohol fixation. PSP in ground substance does not so easily disappear from ground substance by formol fixation as is usually believed.

Acknowledgment: The author is much indebted to Prof. Z. Ishii and assistant Dr. Y. Maruyama for appropriate advice and kind technical cooperation and to Prof. K. Maruta of Surgical Clinic of Shinshu University for offering surgical specimens.
REFERENCES


EXPLANATION OF PLATES XIX—XXII

Plate XIX

Fig. 1. The advancing front of hypertrophic growth (Sg) No. 2184.
Fig. 2. Colloid cancer of hypertrophic growth (Gs) M. 1.
Fig. 3. Intracanalicular growth (Am) No. 2289.
Fig. 4. Elongating growth (Am) No. 2328.
Fig. 5. Elongating growth (Am) No. 2075.
Fig. 6. Sprouting growth (Sg) No. 3098.
Fig. 7. Sprouting growth (Dm) No. 2669.
Fig. 8. Hale-Rinehart's stain of Fig. 7. Mucous secreting cells are intensively positive but PSP poor in ground substance. Fine collagenic fibers are actively developed with few cellular elements.

Plate XX

Fig. 9. Colloid cancer. No. 2456. Sprouting growth of non-mucous secreting cells in submucosa (upper left).
Fig. 10. Ulcerative cancer (Am) No. 2818. Elongating growth at the right and sprouting growth at the left. Lymphatic invasion at the right.

Plate XXI

Fig. 13—Fig. 20. Mallory's connective tissue stain, for demonstration of various proliferative...
status of connective tissue in accord with tumor growth.

Fig. 13. Normal stomach wall. S 111.

Fig. 14. Gastritis acuta. No. 2366. Submucous edema and capillary proliferation. No increase of fibrous elements.

Fig. 15. Ulcer. No. 3069. Connective tissue callus formation up to subserosa. PSP also increased in this case.

Fig. 16. Ulcerative cancer No. 2918. Adenocarcinoma arising from the ulcer margin. Lymphatic invasion of tumor in the middle part (compare Fig. 10).

Fig. 17. Solid cancer of hypertrophic type. No. 2184. Thin membranous capsule formation at the advancing margin. No extra-capsular deposition of PSP.

Fig. 18. (Am) carcinoma. No. 2075. Tumor mass to the upper right side. Elongating growth with sprouting growth in part. Active connective tissue proliferation in submucosa demarkated from intact submucosa.

Fig. 19. Colloid cancer. No. 2457. See explanation of Fig. 9.

Fig. 20. (Dm) carcinoma. No. 2669. See Fig. 12. PSP is restricted to the sprouting area.

要 旨

胃癌発育時における間質多糖類の態度

木村 勇
信州大学医学病理学教室 (指導: 石井藤一郎教授)

腫瘍組織の発育像はその悪性度診断の上に重要な所見とされているが、炎症におけると同様 Host-parasite Relationship 追究の要請されねばならぬことはすでに諸家の触れる所である。かかる二重の生物学的見知に立ち人胃癌発育の態度とともに同所間質内多糖類の所見を組織化学的に検索を行った。

腫瘍は同一例にあっても部位環境によってその組織像並びに発育型を異にするが、間質多糖類の所見もまた腫瘍の発育環境、発育型の変化に伴って変動し、この種反応が個体の腫瘍に対する全体的表現でなく、局所的な腫瘍、間質間の相互関係に規定せられると同時にまた該部位の膠原繊維の所見と密接なる関係を持つことが認められる。その個々の部位における反応態度を同所の膠原繊維の所見と併せ考えられれば次のごとく四型に分々これを整理した。

1) 無反応型；多糖類反応陽性物質 (PSP) の増量が顕著でなく、膠原繊維もまた増生を見ない。

2) 多糖類型；膠原繊維の新生は極めて乏しく、一部に既存繊維の膨化が見られ、かつ PSP の増量顕著なるもの。

3) 多糖類繊維型；前者と次の繊維型との移行型と考えられるもので、PSP 増量とともに
微細膠原纖維の増生が見られる。

4) 繊維型；膠原纖維の増生，生長著しく，PSP はむしろ減少している。

多糖類の重合度を示す異染性は多糖類型に強く，他の型に属すべき反応部にては極めて微弱であり，中馬の成績と比較考察し，これらの諸型は反応の時間的経過に依るものと考えられる。

以上の諸型を腫瘍の発育型（今井）に対応させると肥大発育型は無反応型を，延伸発育型および素出発育型にてはその時間的経過に応じて多糖類型，多糖類纖細型を示し，とくに素出発育部位ではしばしば多糖類型を示し，腫瘍の発育型と多糖類性反応の間には一連の関連を求めることができる。

これら PSP の増量は腫瘍発育先進部および近隣血管周囲より起り，前者については中馬の述べる如き局所基質の解重合に基づく PSP の増量とともに，血液成分由来の PSP の存在もまた考慮せめられ，発育部，筋層における多糖類性反応の微弱なる事は同所の血管保有量の乏しい事にも依るものであろうか。

之等 PSP の増量刺検として，腫瘍の異物性，腫瘍発育に伴う組織の破壊，並びに腫瘍物質の化学的刺検よりむしろ近時多数報告されつつある腫瘍組織の産生する諸組織纖解性酵素（Hyaluronidase, Trypsin 等）を重視したい。

最後に組織化学的な基礎的問題として，水溶性固定剤によっても青木の分類せる T 物質を証明し得たとともに，その成績から可溶性固定液を使用しても被検物質が巨大分子の一部を形成せる場合は基材の固定が同物質の固定に他ならないとの Lison の考えを支持したい。なおフオルマルイン固定液を使用せる場合は間質多糖類は結合繊維に附着凝集して認められ，純アルコール固定時の綿質な微細顆粒状像とその所見を異にする。
Fig. 9.

Fig. 10