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# Diagnosis of Gastric Cancer in Early Stage — The Clinical Ob-servation of Operated Cases\*

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## Abstract

1. An attempt has been made to find the diagnostic criteria for early gastric cancer. It is most important to detect the evidences or suspected features of the malignant growth in incipient stage in order to attain the radical cure by surgical operation. 2. Twelve patients with early gastric cancer (groups A and B) were selected out of 476 patients who had undergone gastrectomy during the past three years in the Okayama Saiseikai General Hospital. The other 6 patients in the “pre-cancerous group” (group C) were also studied, who had abnormal epithelial proliferation in the resected stomach membrane during the same period. 3. The processes of discovery of early cancer have been described. Fairly precise diagnosis can be made in the mucosal carcinoma, but it is not in the ulcer-carcinoma. It was generally difficult to estimate the degree of the malignancy and the extension of the growth preoperatively. 4. The details of the diagnostic aids are as follows. i. Negative occult blood of stool does not always mean the definite diagnostic aid. ii. The malignant gastric change may occur even in non-acidity. Further investigations should be followed up on gastric ulcer patients if malignant alteration is under the consideration. iii. Minor roentgenological findings, such as the absence or irregularity of mucosal folds, rigid and/or overlapped contour, localized absence or decrease of the peristaltic waves and absence or bow-shaped deformity of the angulus, are of important significance. Such changes should be minutely sought for by X-ray film examination. iv. On gastroscopy and gastrocamera photography, such changes as erosion or irregular granular thickening of the membrane with abnormal reddening and edematous appearance, irregularity of ulcer edge, uneven swelling on ulcer margin with reddening and unsharpness of the edge of adherent coat on ulcer floor, must be noted in the early gastric cancer. v. It is not safe to leave a patient having stomach ulceration under a mere conservative management because it is often quite difficult to dissolve the question of malignancy of the lesion with all sorts of examinations. vi. So far as clinical examinations have indicated malignancy, histological examination must be carried out immediately at the time of operation, even when malignant lesion is absent in inspection and palpation on the exposure of the stomach. vii. On the gross observation of the resected stomach, a particular attention must be paid to erosion, depression or atrophy, irregular granular thickening and abnormal reddening on the restricted areas of the mucosal surface.

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**DIAGNOSIS OF GASTRIC CANCER IN EARLY STAGE**  
**—THE CLINICAL OBSERVATION OF OPERATED CASES\***

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It has long been believed that surgical operation is the prime important treatment to attain a radical cure of gastric cancer. The prognosis has been, however, not satisfactory<sup>1,2</sup>, despite numerous efforts and research works in this field. On the other hand, antitumor chemotherapy offers a bright prospect toward cancer treatment in future<sup>3,4</sup>, but at the present stage it is still believed that radical treatment of gastric cancer must depend on surgical operation. An early diagnosis and discovery of cancer are, therefore, essential in order to obtain better results by the early surgical operation<sup>5</sup>. Although mass-examination for finding the early gastric cancer patients has been attempted for this purpose<sup>6,7</sup>, an effort toward accurate diagnosis and discovery of it is also demanded in the clinic on any patients who have not any characteristic complaints.

Up to the present time there are numerous case reports as well as histological and histogenetical studies of gastric cancer in early stage available<sup>8-22</sup>. But a vast uncultivated field still remains for the studies of clinical aspects on the early gastric cancer. Scrutinizing each case from the standpoint of physical examination, X-ray investigation, gastric analysis, gastroscopy and gastrocamera photography, many obstacles have to be encountered to get accurate diagnosis. An attempt has been made to analyze the clinical data accumulated in our hospital for the past three years in the course of the gastric cancer treatment in order to get a certain criterion and proposal toward the diagnosis of the early gastric cancer.

MATERIALS

Among 534 patients subjected to gastric operations, 476 cases who had

\* The outline of this study was read at the 46th Annual Meeting of the Gastroenterological Society of Japan, 1960 and at the Second Annual Meeting of Japan Gastrocamera Society, 1960.

undergone gastrectomy were diagnostically classified as follows; 119 cases with gastric cancer, 151 with gastric ulcer, 46 with gastro-duodenal ulcer, 88 with duodenal ulcer, 47 with chronic gastritis, 15 with gastric polyp and 10 with other gastric diseases.

Though the general concept of "early gastric cancer" is disputable, it must satisfy both morphological and biological conditions. At present, however, we must be contented with establishing morphological criteria. Therefore, with a due consideration to the reports by various investigators<sup>12,13,23,24</sup> the following patho-histological criteria for determining the cancer in early stage have been established. Primary mucosal carcinoma of gastritis in origin: Cancerous tissue is, in this case, localized only in the gastric mucosa and does not exceed the muscularis mucosae regardless of its extension and size (group A). Ulcer-carcinoma: Cancerous tissue is localized only in the margin and on the scar surface of the bottom of peptic ulcer (group B). It is to be noted that both groups do not show any metastasis. Precancerous and unrest changes: In a few of the cases that had been operated on the diagnosis of gastric cancer or ulcer, precancerous changes were histologically found. The precancerous changes are defined as follows: Mucosal epithelial cells show strong atypicality, proliferating with irregular arrangement, with excessive numbers of mitotic figures and with hyperchromatism of protoplasm. But the barrier of the basement membrane is never passed, and invasive or destructive proliferations of cells are never found. Unrest changes are defined as the condition showing abnormal proliferation similar to precancerous changes with less atypicality of cells (group C).

According to these criteria, 12 cases of gastric cancer in early stage consisted of six cases of group A and six cases of group B are to be presented. There was no polyp-carcinoma. Six cases of group C are composed of 3 cases each of the precancerous and the unrest changes. During the same period, 40 cases of gastric cancer, 103 cases of gastric and duodenal ulcer and 15 cases of chronic gastritis selected at random were observed as control and the findings were compared with those of 3 groups.

#### OBSERVATIONS AND RESULTS

The birds-eye view of ages, sex, examinations of occult blood, R. B. C. and serum protein, gastric analysis, X-ray examination, gastroscopy, gastro-camera photography, and the site of lesion, of all cases is shown in Table 1. The course of the typical cases of each group is reported in the following.

##### Group A: Primary mucosal carcinoma

Case No. 1 O. K. 56-year old female.

She consulted in our clinic at first on September 23, 1959. She had frequently complained

of nausea for the previous two or three years. Recently she had complained of heart-burn, anorexia and slight loss of weight. There were observed slight tenderness and resistance at the deep palpation in the upper midepigastrium. R. B. C. : 3,000,000. Hemoglobin index: 66 per cent (Sahli). Serum protein: 4.8g per deciliter. Occult blood in stool was regularly proved positive by benzidine method.

Table 1. Examinations-Data of the Cases

Group	Case No.	Age and Sex (years)	Occult Blood in Stool*	Gastric Analysis	Clinical Diagnosis**				Site*** of Lesion	Addendum****
					Roentgenologic	Gastroscopic	Gastro-camera	Final		
A	1	56 F	+	Hypoacid	Canc.	Canc.	Canc.?, Pol.	Canc.	Ci & AT	Associated with Chr. U.
	2	59 M	+ or -	Hypoacid	Canc. ?	Canc.	Canc. ?	Canc.	ATI	
	3	53 F	+ or -	Hypoacid	Canc. ?	Canc. ?	Gastr. Supf.	Canc. ?	AG	
	4	54 F	-		Ex. v. T.			Subph. Absc.	Ci & AT	
	5	66 F	+ or -	Hypoacid	Canc. ?	Canc.	Canc.	Canc.	AG	
	6	60 M		Hypoacid	Canc. ?	Canc.	Canc.	Canc.	ATI	
B	1	75 M	+	Anacid	U. V.			U. V.	Cial	Duplicated Carcinomas
	2	60 M	+	Anacid	M. U. ?	U. V.	M. U. ?	M. U. ?	AG	
	3	53 M	-	Anacid	M. U. ?	Canc. ?	Canc.	Canc.	1) AG 2) Ca	
	4	37 M	-	Anacid	U. V.			U. V.	Cial	
	5	45 M						U. V. ?	ATI	
	6	56 M						U. V. ?	Cp	
C	1	55 F	+ or -	Hypoacid	Adh., Ptos.	Canc. ?	Canc. ?	Canc. ?	AG	Pr—G
	2	40 M	+ or -	Hypoacid	U. V.	U. V.	U. V. ?	U. V.	ATI	Pr—G, Associated with Chr. U.
	3	48 M	+ or -	Hyperacid	U. V. D.			U. V. D.	Cial	Pr—UM.
	4	40 M	-	Hyperacid	M. U. ?	U. V.	U. C. ?	Canc. ?	AG	Un—UM.
	5	46 M	-	Hyperacid	U. V. D.	Gastr. Supf.		U. V. D.	Cp	Un—UM.
	6	58 M	+ or -		U. V. D. ?			U. V. D. ?	AG	Un—G, Associated with Chr. U.

\* + : constantly positive, + or - : sometimes positive.  
 \*\* Ex. v. T. : extraventricular tumor, Pol. : polyposis, Gastr. Supf : gastritis superficialis, Subph. Absc : subphrenic abscess, U. V. : gastric ulcer, U. V. D. : gastroduodenal ulcers, M. U. : malignant alteration of gastric ulcer, Adh. : perigastric adhesion, Ptos. : ptosis.  
 \*\*\* AG : angulus, AT : pyloric antrum, C : corpus, i : inferior part, a : anterior wall, p : posterior wall, l : on or near the lesser curvature.  
 \*\*\*\* Chr. Ulc. : chronic ulcer, Pr—G : precancerous change in the area with gastritis, Un—UM. : unrest change in ulcer margin.

*Gastric analysis* revealed four degrees of free HCl and fourteen degrees of total acid (Katsch-Kalk's method). X-ray investigation of the upper G. I. tract gave the impression of such changes, as rigid contour, interference with peristaltic waves on both curvatures and absence of normal rugae, just from the lower part of corpus to the antral portion, and cancer was diagnosed (Fig. 7).

Extensive erosion, abnormal redness, dirty discoloration, unevenness and disappearance of peristaltic waves were recognized in the same area on gastroscopy, to determine diagnosis of the cancer. Polyposis-like irregular swelling, and thickening and stiffness at the angle were revealed on gastrocamera photography at the same area as to give rise to suspicion of cancer (Fig. 1). Operation was performed on October 12, 1959 under the final diagnosis of the cancer. Surgical exploration revealed slight thickness at the pyloric area and swelling of lymphnodes along the greater curvature. A subtotal gastrectomy with clearing of regional lymphnodes was performed. The resected specimen showed a belt-like erosion with sharp margin, measuring 4.5 by 9.3 cm. and covering the lower part of the corpus and the prepyloric area. There were islet-like remnants of mucous membrane in it and an irregular nodularity was seen at its margin. A polyp was found adjacent to the erosion on the lesser curvature of the prepyloric area (Figs. 8, 9). Histological examination showed superficial involvement of the mucosa by carcinoma simplex. The surface of the mucosa was widely eroded (Fig. 10). The polyp was proved to be benign adenoma. Metastasis was not found in the lymphnodes.

Case No. 2 T. H. 59-year old male.

He consulted in our clinic at first on November 6, 1959. For half a year he had suffered from dull pain in the epigastrium occurring about two hours after meals, anorexia, heart-burn and belch. He had once experienced tarry stool about five months previously. Recently he had been released from pain, heart-burn and belch. On physical examination there was tenderness in the epigastrium. R. B. C.: 3,300,000. Index of hemoglobin: 66 per cent (Sahli). Occult blood in stool was positive in two out of three examinations.

*Gastric analysis* showed sixteen degrees of free HCl and thirty-two degrees of total acid. Fluoroscopy and roentgenography showed rigid contour on the lesser curvature of the antral portion (Fig. 11). A polisogram showed weak peristalsis. By these findings cancer was suspected. Gastroscopic examination showed an irregular, uneven, edematous swelling with redness at the angle. The posterior wall of the pyloric area showed an edematous, uneven area with dark-red discoloration to suggest a diagnosis of the early cancer. Gastrocamera photo showed an area with edematous swelling and redness on the greater curvature of pars pylorica. Edematous redness was found at the angle, and its posterior wall appeared rigid with slight unevenness and then diagnosis of the cancer was also made (Fig. 2). Thus the patient was operated on December 10, 1959. Abnormal changes of stomach and lymphnodes could not be found by inspection and palpation at the exploration, but gastrectomy was performed. The resected specimen showed excessive granulation in pars pylorica. A small area on the lesser curvature appeared irregularly uneven with dark-red discoloration, measuring 2.0 cm in diameter (Figs. 12, 13). At the center of the area, within a *Leistchen*, a small cancerous focus was found by observing several sections.

It was so small that could be visible only microscopically. The epithelial cells were proliferated, forming numerous tubular cavities with irregular cellular arrangement, and marked atypicality. The basement membrane was found to have disappeared. A diagnosis of adeno-carcinoma was thus histologically made (Figs. 14, 15). The mucous membrane generally showed atrophy or disappearance of glands and fibrosis of the interstitial tissues between muscularis mucosae and surface epithelium. The metastasis of lymphnodes was not found.

Case No. 5 I. Y. 66-year old female.

She consulted in our clinic at first on June 5, 1961. She had complained of dull pain in epigastrium and slight loss of weight for about two weeks prior to it. There was tenderness in upper midepigastrium. R. B. C.: 4,390,000 per cu. mm. Index of hemoglobin: 92 per cent (Sahli). Serum protein: 7.3 g per deciliter. Occult blood in stool was positive in two out of four examinations.

*Gastric analysis* showed six degrees of free HCl and thirty degrees of total acid. Roentgenographic investigation of the stomach gave such changes as bow-shaped deformation of angulus, rigid and overlapped contour and interrupted rugae at angle (Fig. 16). Absence of peristalsis was shown on polisogram. Cancer was then suspected. Gastroscopy revealed an ulcer with indistinctly defined irregular border as well as uneven floor and edematous reddish margin at the angle. By the examination of gastrocamera on the side of posterior wall at angulus, an irregular, shallow excavation was found on the side view. There were a small adherent coat and a localized swelling with reddening adjacent to it. Cancer was finally diagnosed (Fig. 3). Operation was performed on June 13, 1961. On careful palpation the angle was felt like induration, and soft nodes were palpated along *A. gastrica sinistra* and *A. gastroepiploica dextra*. A subtotal gastrectomy with clearing of the regional lymphnodes was done. The resected specimen showed an erosion at the angle, measuring 1.4 by 2.4 cm. The margin was partially in irregular unevenness. There was found a shallow depression of the mucosal surface in the antrum adjoining the erosion. The whole area with such gross appearances measured 4.0 by 4.5 cm. (Figs. 17, 18). Microscopic examination showed that adenocarcinoma was well defined to the area showing the gross changes. High cylindrical neoplastic cells were proliferated along the superficial part of the mucosa, closely arranged and formed irregular tubular cavities (Fig. 19). Erosion was found in several parts after exfoliation of neoplastic tissues. Lymphnode metastasis was not recognized.

Case No. 6 K. K. 60-year old male.

His first visit was on August 1, 1961. For half a month the patient had suffered from dull pain with distension following meals in the epigastrium, heart-burn, anorexia and general weakness. There was slight tenderness on deep palpation in upper midepigastrium. R. B. C.: 3,500,000. Index of hemoglobin: 68 per cent (Sahli). Serum protein: 6.8 g per deciliter. Occult blood in stool was not tested.

*Gastric analysis* showed nine degrees of free HCl and twenty-five degrees of total acid. X-ray examination showed absence of the angle, rigid and overlapped contour, interrupted rugae and an ulcer crater on the lesser curvature near angulus. Cancer was suspected (Fig. 20). Rigidity of the wall, abnormal redness and ulcer with irregular margin were found on the side of the posterior wall of the angle on gastroscopic inspection, giving an impression of malignant alteration of ulcer. By gastrocamera examination, an ulcer with edematous red swelling on a part of its margin was recognized on the side of the posterior wall of the angle. A diagnosis of cancer was made (Fig. 4). Operation was performed on August 16, 1961. Despite the absence of any palpable abnormalities except a slight induration at the angle at exploration, a subtotal gastrectomy with clearing of the regional lymphnodes was performed. The resected specimen showed two ulcers, one on the angle and another on the posterior wall of corpus adjoining the lesser curvature. In the pyloric area near the ulcer at the angle there was an erosive lesion, measuring 1.0 by 1.5 cm. An edematous, irregular, granular elevation was observed on the pyloric side of the margin of the erosion (Figs. 21, 22). Microscopic examination showed that both ulcers were of typical chronic nature. Proliferated cancerous tissues along the superficial part of the mucosa were found in the site of the erosive lesion. Metastasis could not be found in the cleared regional lymphnodes (Figs. 23, 24).

#### Group B: Ulcer-carcinoma

##### Case No. 2 H. K. 60-year old male.

The patient consulted in our clinic on December 22, 1959. He had been suffering from epigastric pain at hunger for the 10 years previous. Pain was exaggerated for the last 2 months and heart-burn, cardialgia, belching, anorexia and melena were also complained. He had been once examined at our hospital two years previously. Duodenal ulcer was then radiographically suspected, but ulcer was not recognized by gastroscopy, and gastric analysis showed normoacidity. Anemia and remarkable tenderness in epigastrium were noticed at this consultation. R. B. C.: 2,500,000. Index of hemoglobin: 49 per cent (Sahli). Occult blood in stool was examined thrice repeatedly to be positive.

*Gastric analysis* showed zero degree of free HCl and thirty-four degrees of total acid. A big niche was observed above the angle and an asymmetric and rigid crater was found on X-ray examination. Cancerous change was suggested from these findings (Fig. 25). The gastroscopic examination showed a callous ulcer. On the other hand, gastrocamera photography revealed swelling on the margin of the ulcer, uneven bottom and unsharpness of the edge of the adherent coat on the floor to suggest a cancerous change (Fig. 5). Because of the possibility of malignancy, surgical resection was performed on January 13, 1960. A penetrated ulcer was found at the angle. The resected specimen showed an ulcer at the angle, measuring 1.0 by 2.0 cm. and a red colored and granular nodularity on the margin of cardiac side (Fig. 26). A localized cancer tissue was



histologically observed in the margin of the ulcer, but invasion into the submucosa or scar tissue of the ulcer floor was not found (Figs. 27, 28). The regional lymphnodes were histologically examined which proved to be quite free from metastasis.

#### Group C: Precancerous Change

Case No. 1 T. T. 55-year old female.

She was first examined on December 7, 1959. She had complained of dull epigastric pain after meals and anorexia for the past week. Physical examination revealed nothing remarkable. R. B. C.: 3,400,000. Index of hemoglobin: 74 per cent (Sahli). Occult blood in stool was positive.

*Gastric analysis* showed sixteen degrees of HCl and thirty-six degrees of total acid. The fluoroscopic findings of the stomach, such as resistance, stiffness of wall and normal rugae on the antral portion, suggested cancer. Perigastric adhesion was observed on X-ray film (Fig. 29). The gastroscopic inspection showed a remarkable edematous swelling with erosive redness at the angle. The photo taken by gastroscope showed that antral portion on the lesser curvature in contact with the angle presented an erosion with remarkable redness. These findings were enough to suspect gastric cancer (Fig. 6). Laparotomy was done on December 24, 1959. Although no abnormal changes of the stomach and lymphnodes could be found by both inspection and palpation at the exposure, a gastrectomy was performed. The resected specimen showed a sharply bordered depression of the mucous membrane, measuring 2.0 by 3.0 cm. and its posterior edge was found to be in slightly irregular granulated swelling (Figs. 30, 31). So-called "precancerous" changes were histologically observed in this area (Figs. 32, 33). The normal gastric glands had almost disappeared. Mucosal epithelial cells showed remarkable proliferation, forming irregularly branching and twisted tubular cavities. These cells were quite different both in size and shape. Nuclei were markedly swollen with clear membrane, rough chromatin and big nucleoli, and many mitotic figures were found. These cells showed extraordinarily atypical, without explosive or destructive proliferation enough to be diagnosed as cancer.

#### STATISTICAL CONSIDERATIONS

##### 1. Frequency

The 12 cases of the early cancer utilized for this report were 8.3 per cent to the total number of 145 cases of the operated gastric cancer and 10 per cent to 119 cases of the resected gastric cancer. The frequency of 6 cases in group A was 5 per cent and the one of 6 cases in group B was 5 per cent to the resected gastric cancer. The 6 cases of group B were 3.1 per cent to 197 cases of the resected ulcer, and 6 cases of group C were 1.7 per cent to 357 cases of the

benign gastric abnormalities subjected to gastrectomy.

### 2. Age

The average age was 56.2 years old in the series of the early cancer, 58.0 in group A, 54.5 in group B and 51.5 in group C. The age was mostly in the fifth decade in group A, and in the fourth decade in group C. On the other hand, it ranged from 37 to 75 years in group B.

### 3. Sex

Out of 12 cases of the early cancer, 8 were male (67 per cent). Two were male in group A (33 per cent), all were male in group B, and 5 were male in group C (88 per cent). All of the male patients in group C were associated with chronic ulcer, and one female patient was not associated with it.

### 4. Duration of Complaints

As shown in Table 2, in the control groups the duration of complaints was more than one year in 29 per cent of the cancer cases, in 70 per cent of the ulcer cases and in 49 per cent of the gastritis cases. In 6 of the 12 cases with the early cancer (50 per cent), one in group A and 5 in group B, the duration exceeded one year. In one case without chronic ulcer of group C it was less than a month, and in the other 5, more than a year. Throughout the 3 groups, 10 of the 12 patients (83 per cent) associated with chronic ulcer in the lesion or in the distant region, had suffered over one year, and 5 of the six cases (83 per cent) without ulcer, less than a year. The duration was less than a month in 3 cases of group A (50 per cent), and more than five years in 5 from group B (83 per cent).

Table 2. Duration of Complaints

Group		~ 1 M	~ 3 M	~ 6 M	~ 1 Y	~ 3 Y	~ 5 Y	5 Y ~
Early Cancer	A (6 cases)	3	1		1	1		
	B (6 cases)		1					5
	% in Total	25	17		8	8		42
C (6 cases)		1				2		3
Control	Cancer (%)	10.6	7.2	24.0	28.6	20.5	6.2	2.9
	Ulcer (%)	3.3	8.7	2.2	15.2	21.7	6.5	42.4
	Gastritis (%)	9.8	11.8	17.6	11.8	16.6	28.4	4.0

### 5. Subjective Symptoms

As shown in Table 3, 33 per cent of the patients of the early cancer were free from abdominal pain. Anorexia and a slight loss of weight were more frequently complained of in the early cancer series than in the ulcer cases of the control group. In one case of each group A and group B, continuous heart-burn had disappeared in a short period before the first examination. Hematemesis

Table 3. Subjective Symptoms

Complaints	Early Cancer			Group C (6 cases)	Control Group		
	Group A (6 cases)	Group B (6 cases)	Total (%)		Cancer (%)	Ulcer (%)	Gastritis (%)
Epigastric Pain	4	4	67	5	84.5	81.3	73.7
Heart-burn	3	3	50	4	49.9	65.7	47.4
Epigastric Fulness	1	4	42		73.0	58.4	42.1
Nausea	3	3	50	1	53.8	47.9	26.3
Epigastric Pressure	4	1	42	3	42.3	37.5	42.1
Anorexia	3	3	50	2	68.2	39.5	35.3
Loss of Weight	4	4	67	4	90.8	60.4	52.9
Diarrhea			0		17.4	6.2	33.3
Melena	1	3	33	1	26.9	39.6	10.5
Hematemesis		2	17		11.6	16.6	21.1

and melena occurred just before admission in one-half of the patients of group B. Symptoms in group C did not show any significant difference from those of the ulcer or gastritis cases of the control. Thirty-three per cent of group A, 67 per cent of group B and 50 per cent of group C showed the ulcer-type symptoms, which are defined as the combination of three symptoms, i. e. epigastric pain related to food-taking, heart-burn and epigastric distension or pressure.

#### 6. Abdominal Signs

Tenderness was complained in 92 per cent of the early cancer group and in 67 per cent of group C. Tumor was palpated in one case of each group A and group C. It is, however, to be noted that the tumor of the former was of sub-phrenic abscess and the one of the latter was of callous ulcer (Table 4).

Table 4. Abdominal Signs

Group		Tenderness	Resistance	Tumor
Early Cancer	A (6 cases)	6	1	1*
	B (6 cases)	5		
	% in Total	92	8	8
C (6 cases)		4	1	1
Control	Cancer (%)	76.1	37.5	64.0
	Ulcer (%)	88.6	27.3	2.3
	Gastritis (%)	89.4	31.6	0

\* The tumor proved to be a subphrenic abscess.

#### 7. Anemia and Condition of Nutrition

As show in Table 5, R. B. C. was less than 3,000,000 per cu. mm. in 25

Table 5. Red Blood Cell Count (million per cu. mm.)

Group		$\leq 2.50$	$\leq 3.00$	$\leq 3.50$	$3.50 <$
Early Cancer	A (6 cases)		2	2	2
	B (6 cases)	1		1	4
	% in Total	8	17	25	50
C (6 cases)		1		5	
Control	Cancer (%)	7.4	44.5	33.4	14.7
	Ulcer (%)	11.4	18.4	36.8	33.4
	Gastritis (%)	6.2	43.8	25.0	25.0

per cent of the early cancer group and in 17 per cent of group C, and on the other hand, it was in 52 per cent of the gastric cancer, in 30 per cent of the ulcer and in 50 per cent of the gastritis of the control group.

Serum protein as a criterion of nutritional condition was measured by less than 6.0 g per deciliter in 36 per cent of the early cancer and in 40 per cent of group C. It was in 80 per cent of the gastric cancer, in 46 per cent of the ulcer, and in 26 per cent of the gastritis of the control group (Table 6).

Table 6. Serum Protein (g per dl.)

Group		$\leq 5.5$	$\leq 6.0$	$\leq 6.5$	$6.5 <$
Early Cancer	A (5 cases)	2	0	1	2
	B (6 cases)	1	1	1	3
	% in Total	27	9	18	46
C (5 cases)		2	0	1	2
Control	Cancer (%)	68.0	12.0	12.0	8.0
	Ulcer (%)	18.2	27.6	36.1	18.1
	Gastritis (%)	13.3	13.3	40.0	33.4

#### 8. Occult Blood in Stool Following Benzidin Method

In the early cancer, it was negative in 33 per cent and constantly positive in 33 per cent. In group C, it was negative in 33 per cent, and in none of the cases of the constantly positive. They are illustrated in Table 7.

#### 9. Gastric Analysis Following Katsch and Kalk

Classification of acidity was made with the free hydrochloric acid as follows; 0 degree: anacidity, 1 to 20 degrees: hypoacidity, 21 to 40 degrees: normoacidity, and over 40 degrees: hyperacidity. All of the five examined cases of group A showed hypoacidity and 4 cases of group B, anacidity. Out of the 5 cases of group C, two cases with chronic gastritis in origin showed hypoacidity and three cases with abnormal ulcer showed hyperacidity (Table 8).

Table 7. Occult Blood in Stool

Group		Negative	Positive (Constantly)
Early Cancer	A (5 cases)	1	4 (1)
	B (4 cases)	2	2 (2)
	% in Total	33	67 (33)
C (6 cases)		2	4 (0)
Control	Cancer (%)	6.3	93.7
	Ulcer (%)	35.2	64.8
	Gastritis (%)	47.4	52.6

Table 8. Acidity of Gastric Juice

Author	Group	Anac.	Hypoac.	Normoac.	Hrperac.
Mano et al.	Early Cancer { Group A (5 cases)	4	5		3
	Group B (4 cases)				
	Group C (5 cases)		2		
Ayabe	Mucosal Carcinoma (12 cases)	7	1	4	0
	Early Ulcer-carcinoma (16 cases)	4	2	7	3
Someya	Early Ulcer-carcinoma (per cent)	11.8	37.4	25.4	25.4
Stout	Superficial spreading carc. (10 cases)	3	2	5	0
Mano et al.	Cancer as Control (per cent)	74.5	15.0	5.5	5.0
	Ulcer as Control (per cent)	9.7	8.3	28.7	53.3
Kono et al.	Stomach Cancer (per cent)	67.6	17.3	10.0	3.1
	Stomach Ulcer (per cent)	9.3	13.2	35.6	41.9

### 10. X-ray Examination

This examination was mainly done by the barium fully filled or partially filled condition with occasional relief study in special attention. Both findings at fluoroscopic examination and at postfluoroscopic film study are given together in Table 9. It is important to recheck the X-ray film postoperatively to get the final correlation of preoperative X-ray diagnosis with postoperative diagnosis, but in this study an attempt was made not to change the preoperative X-ray diagnosis even if it was postoperatively found to have been a mistake. Such an attempt was followed in analyzing data in this report.

The important roentgenological evidences of delicate malignant alteration are indicated with interruption or disturbance of rugae, stiffness of the wall, overlapped contour of the stomach and the localized decrement or absence of the peristaltic waves. These changes are often found both at the angle and on the

Table 9. Roentgenological Findings.

Findings & Diagnosis	Group A		Group B		Group C	
	Fluoroscopy (6 cases)	Film Study (6 cases)	Fluoroscopy (4 cases)	Film Study (4 cases)	Fluoroscopy (6 cases)	Film Study (6 cases)
Tenderness	2	—	1	—	4	—
Resistance	1	—		—	1	—
Malignant Rugae		+1 ±3	1	+1 ±1	1	1
Absent Peristalsis	+1 ±2	+3 ±1		±1		1
Rigid Contour	+1 ±2	+4 ±1		+1 ±2	+1 ±1	2
Over-lapped Contour		+2 ±2		+1 ±2		+1 ±2
Absent or Bow-shaped Angulus	2	5	2	2		±1
Shortening of Lesser Curvature		2	1	3	1	3
Niche	1	1	+2 ±1	3	+2 ±1	+3 ±2
Filling Defect	±1					
Gastric Cancer		1				
Gastric Cancer ?	3	4		2	2	1
Gastric Uleer			2	2	2	3
Gastric Ulcer ?			2		2	1
Gastritis	2	1				
Others	1					1

lesser curvature in its vicinity, and the bow-shaped or absent angulus becomes of pathological significance. These changes are to appear in the case of small ulcer, linear ulcer, ulcer scar and adhesion. At this point the endoscopic examinations are attempted to differentiate whether these changes were malignant or benign.

Out of 10 cases of the early gastric cancer, three were diagnosed as cancer or suspected as cancer on fluoroscopy, 7 both on fluoroscopy and the X-ray film study. Most cases of group A showed the alterations and 5 out of 6 cases (83 per cent) were diagnosed as cancer or suspected cancer. Four cases of group B also showed these signs on the margin of the ulcer in a lower percentage. As to niches, Case No. 2 with asymmetry in shape and rigid margin, and Case No. 3 with flat and rigid contour, were solely suspected as cancer. But other 2 cases were considered as benign ulcers. Among group C, Case No. 1 was suspected to have cancer on fluoroscopy as mentioned in the case study. Case No. 4 was also suspected to have cancer by the finding of flat and rigid contour of niche. There were no significant findings in other cases.

#### 11. Observations by Gastroscope and Gastrocamera

Out of the patients with the early cancer, five in group A and two in group B were subjected to gastroscopy and gastrocamera examinations. Details of

Table 10. Findings of Gastroscopy and Gastrocamera examination

Group	A (6 cases)		B (6 cases)		C (6 cases)	
	GS (5 cases)	GC (5 cases)	GS (2 cases)	GC (2 cases)	GS (4 cases)	GC (3 cases)
abnormal reddening	5	3	2	2	1	+2 ±1
edematous appearance	3	5	1	2	1	3
absent peristaltic waves	+1 ±2	—		—		—
absence of rugae	1	1		1		
erosion	2				±1	1
unevenness	4	5	1	2	1	2
Ulceration	2	2	2	2	2	1
irregularity of the edge	2	2	1	2		1
uneven floor	1	1	1	1		
unsharply defined adherent coat			1	2		1
Deformation of angulus	5	+4 ±1	2	2	3	+2 ±1
Diagnosis						
Cancer	4	2		1		
Cancer ?	1	2	1	1	1	2
Ulcer			1		2	
Ulcer ?						2
Gastritis		1			1	
Others						

GS : Gastroscopy

GC : Gastrocamera Photography

observation findings by both methods are shown in Table 10. Characteristic findings in the seven patients are summarized as follows: Erosion as well as irregularly granular swelling of the mucosa, with abnormal redness and edema, was one of the most striking features. Irregularity of ulcer edge, such as zig-zag, uneven thickening on the margin and unsharpness of the edge of adherent coat on the floor of ulceration, was noticeable in gross observation. The lesions were mostly seen in the vicinity of the angular portion of the stomach.

Of the seven cases, four were diagnosed as cancer, two as suspicious cancer and one as benign ulcer on gastroscopy. On the other hand, from gastrocamera findings three were diagnosed to be cancer, three suspicious cancers and one superficial gastritis. Either of the two diagnostic methods showed a positive result of malignancy in 86 per cent.

An erosion-like area with redness and edema was observed in Case No. 1 of group C on both examinations. A reddish irregular swelling on ulcer margin and an unsharpness of the edge of adherent coat were found in Case No. 4 of

the same group. They were both suspected to be malignant. In the rest four patients no findings were obtained to indicate malignancy. Though the mucosal surface of the resected stomach did not grossly show prominent changes in Case No. 2 of group A and in Case No. 1 of group C, the gastroscopic and gastro-camera findings indicated malignancy.

### 12. Preoperative Diagnosis

Efforts to find out the early gastric cancer have been made in our hospital mainly by roentgenographic, gastroscopic and gastrocamera examinations. With the combination of these methods of examinations, seven of the twelve patients with the early cancer (58 per cent) and five of the six patients in group A (83 per cent) were diagnosed as cancer or suspicious cancer. In group B, however, four of the six cases (67 per cent) were considered to be benign ulcers. Two of the six cases in group C were suspected of malignancy, and the other four of benign ulcer (See Table 1).

Of the seven cases with early cancer that had undergone all of the three examinations, five were diagnosed as cancer and the other two as suspicious cancer. These seven cases were analyzed by the preoperative estimation of the degree of malignancy as follows: a wide-spread invasive cancer in case A-1, an early cancer in case A-2, a suspicious cancer in case A-3, the cancer, probably of the early stage in cases A-5, A-6 and B-3, and malignant change of ulcer in case B-2.

### 13. Operative Findings

In group A, induration was perceived scarcely in one case and was palpated slightly in two cases, and slight thickening of stomach wall was found in two, in one of which metastatic lymphnodes were found macroscopically during operation but the histological examination revealed no metastasis postoperatively. It was remarkable to note that one case of this group did not show any characteristic finding at palpation and inspection during operation. In group B,

Table 11. Operative Findings

Group		Serosal Scar	Thickening		Induration		Tumor	Metastasis
			+	±	+	±		
Early Cancer	A (6 cases)		2		1	2		1
	B (6 cases)	4	1		5			
	% in Total	33	25	0	50	17	0	8
Group	C (6 cases)	4		1	3			
Control	Cancer (%)	3.6	0		10.7		89.3	92.8
	Ulcer (%)	53.7	2.1		54.7		10.3	1.0
	Gastritis (%)	0	5.3		5.3		0	0



induration was perceived in 83 per cent which is of higher percentage than the gastric ulcer group of the control. There are not any notable findings in group C (Table 11).

#### 14. Gross Findings of the Mucous Membrane of the Resected Stomach

##### a) Location

Among six cases of group A, 4 cases had lesions lying from angulus to the lesser curvature of pyloric antrum and 2 cases from lower corpus to pyloric antrum in transverse belt. Lesion was often found at angle and lower part of corpus near the angle in 4 of 7 cancer cases in group B. It is to be noted that most of the early cancers were located near along the lesser curvature between the corpus and the pyloric antrum. Group C showed the same features (Table 1).

##### b) Changes of Mucous Membrane

The following results were obtained from immediate postoperative observation of the mucous membrane and examination of the color films.

All of 6 cases in group A were found to have erosion, depression or irregular granular swelling. Five of them presented erosion. Several observations are to be noted in 5 cases of the erosion type: the erosion boundary is sharply defined in 2 cases, an abnormal redness of the affected erosion in comparison with the surrounding mucous membrane is noted in 3 cases, a localized depression is associated in one case and the normal mucous membrane remains to be scattered in the erosion in one case. The largest erosion extends to 4.5 by 9.3 centimeters. There are 5 cases of the irregular granular swelling type: 4 of them are associated with erosion. It is noteworthy that not-sharply defined redness and hemorrhage on mucous membrane are observed in 4 cases of this type. It was possible to determine a diagnosis of cancer merely from findings of the mucous membrane in 4 cases, of which erosion was localized. The case No. 4 with multiply scattered small erosions and Case No. 2 with an irregular and granular swelling could not be diagnosed as cancer by gross observation.

The chief findings of group B were slight elevation of ulcer margin and erosion, and these findings were observed in seven lesions. Five of them were in elevation type showing strong redness, and a fine or coarse irregular granular swelling was observed in the 4 lesions and a smooth, edematous swelling in the one. The erosion type showed strong redness, and a proliferated cancerous tissue was found on the mucous membrane covering ulcer scar in the histological feature in two erosive lesions. Moreover these showed more depressive erosion than the surrounding membrane. Also there was one lesion to present a very small erosion, corresponding to an elevation margin. From macroscopical findings, only 2 cases were diagnosed as cancer; one case was suspected. From the standpoint of ulcer form, 5 were ovoid and 2 were kissing and linear, and average diameters were under 1 cm. (1), 2 cm. (4), 3 cm. (0), and over 3 cm. (2).

The areas which showed such gross appearances, especially erosions, generally corresponded to the ones showing histological malignancy. Further findings from histological investigation will not be discussed in this paper.

In two cases of the gastritis-origin out of the six cases in group C, a localized mucosal depression or atrophy was observed, and in one of the ulcer-origin, an abnormally-red granular thickening was seen on the ulcer-margin. No prominent changes were observed on the mucosal surface.

#### COMMENT

##### *Definitional Criteria of Early Cancer and Precancer of the Stomach*

###### (a) Early Gastric Cancer

The fore-mentioned morphological criteria of the early cancer were provided in order to analyze the materials for this study. It will be discussed with reference to literature whether or not the criteria are adequate before consideration of clinical findings. The definition of "early cancer" must be considered both in pathological conditions, such as extension of the lesion and the metastasis, and in postoperative prognosis. The growth could not be regarded as the early cancer in spite of its size if metastasis has already occurred. As to prognosis, it is believed that removal of early cancer must always result in a permanent cure. Of the twelve patients utilized in this report, there is one case who died of other disease 10 days after resection. There are eleven survivors at the time of writing who are almost free from symptoms: four have survived for the two or three years after the operation, four for one or two years, and three less than one year. It is inadequate to discuss the matter of the permanent cure by the data available with our materials at present.

AYABE<sup>23</sup> studied both metastasis and postoperative prognosis of the mucosal carcinomas, or so-called gastritis-origin, the early ulcer-carcinomas, and the minor cancerous tumors. He stated that, regardless of width, the superficial cancer which affects mucosa only or slightly invades into submucosa without metastasis may be treated as early gastric cancer, and the removal of the growth in such stage results in permanent cure by approximately 100 per cent. MUTO<sup>24</sup> has the same opinion as to the early cancer on the basis of his study on extension of the lesion in gastric wall, metastasis, peritoneal dissemination and prognosis following resection of gastric cancers. The rate of lymphatic metastasis of the non-ulcerative mucosal carcinoma which has already involved the submucosa is reported to be 53.4 per cent by TAKAGI<sup>18</sup>, which is of higher percentage than might be expected. Therefore, the mucosal carcinoma of the so-called gastritis-origin may be regarded as an early cancer when only mucosa is involved. The same condition may be thought incipient in the case of polyp-carci-

noma.

As to ulcer-carcinoma, it is sometimes impossible to distinguish strictly whether the lesion is involved beyond muscularis mucosae, for the muscularis mucosae is often unrecognizable in repaired mucosa at the margin or on the scar tissue of chronic peptic ulcer.

The rate of lymphatic metastasis ranges from 15.4 per cent according to TAKAGI<sup>13</sup>, to 19.4 per cent by SOMEYA<sup>12</sup> in the case of ulcer-carcinoma limited to the mucosa, and from 12.5 per cent by the former, to 24.1 per cent by the latter in the case of the submucosally invaded. The incidence of metastasis appears to be rather high in both stages, but there is no significant difference between them. A limitation of the growth only to the mucosa can not be a criterion to assure an ulcer-carcinoma to be incipient. It seems rather difficult to determine the incipient feature of it. Under the criteria settled in this study, the prognosis following resection of this type may be naturally somewhat worse than the early mucosal carcinoma so far as postoperative prognosis is concerned.

Even though cancer is limited within the mucosa, metastasis may take place when the lymphatics and the blood vessels are affected. Therefore, strictly speaking, carcinoma *in situ*<sup>20</sup> or preinvasive cancer, in which the basement membrane of the involved gland remains completely intact, can be always indicated to be curable. The true preinvasive cancer is, however, so rare in stomach that those definitional criteria should be taken into consideration.

#### (b) Precancer

Pathologists often refrain from using the term precancer or precancerous lesion<sup>25</sup>. From clinical standpoint several authors<sup>26-27</sup> have repeatedly stated the significance of precancerous lesions of the stomach such as polyp, chronic peptic ulcer, chronic gastritis and heterotopic pancreatic tissue.

In this study, precancerous change or epithelial unrest is to be indicated by a sort of abnormal proliferation of the epithelium. As it is not possible to ascertain whether or not these epithelial changes are irreversible and they have potency to develop into carcinoma, it may be better to call them as atypical or abnormal proliferation of the epithelial cells. However, there is a probability that cancer may develop through such an abnormal stage in some cases. On the other hand, it has been generally admitted that gastric carcinoma may arise from repairing mechanisms of the damaged mucosa affected by chronic gastritis or chronic ulcer<sup>9, 14-18, 28, 29</sup>. Therefore, in case of group C, the abnormality resulted from such repairing mechanisms must be considered from cancerogenic standpoint.

Apart from such arguments about carcinogenology, the cases which fit into the histological criteria are grouped as the "precancer" in this paper, and the next problem is to make it clear whether or not any characteristic correlation

can be found with clinical data.

In group C, two cases showed the findings similar to those of the group of the early cancer on X-ray, gastroscopic and gastrocamera examinations; the mucosa of the three resected stomachs represented gross appearances similar to those of the early cancer. No other characteristics were found as compared with the control groups. The precancer group described here, therefore, cannot be grouped under a clinical entity, and it is natural to treat some of the cases under the diagnosis of gastric cancer and others as benign gastric ulcers or chronic gastritis till histological diagnosis is established after resection. No further comment will be made on the problem of precancer.

### *Analysis of Clinical Data*

#### (i) Frequency

The percentage of the early gastric cancers, including the one of submucosal involvement, is reported in numerous papers and illustrated in Table 12.

Table 12. Frequency of Early Gastric Cancer

Author	Classification	Percentage to Total Cancer Cases with Gastrectomy
Ayabe 23)	Mucosal Carcinoma without Metastasis	3.7
	Early Ulcer.carcinoma without Metastasis	4.9
	(Limited to the Mucosa, of Both Types)	4.0
Muto 24)	Mucosal Carcinoma	5.5
	(Limited to the Mucosa)	1.3
Takagi 13)	Mucosal Carcinoma	3.4
	(Limited to the Mucosa)	1.6
Someya 12)	Early Ulcer-carcinoma	3.1
	(Limited to the Mucosa)	1.6
Kurokawa 31)	Mucosal Carcinoma	3.1
Fukuda 2)	Carcinoma Limited to the Mucosa	2.5

Most of the reported percentage is approximately 3 per cent. The frequency of cancers limited to the mucosa ranges from 1.3 to 4.0 per cent. It is to be noticed that a higher percentage was obtained in our series. One of the reasons for this may be explained by the fact that the materials of this study were selected from the most recent cases resected during the past three years with a marked improvement in diagnostic measures of the early gastric cancer.

## (ii) Age

The average age of 56.2 years in this study, specially of 58.0 years in group A, is rather older than the ones in other reports. Significant comparison with other data, however, cannot be made, for the total number of this series is small.

## (iii) Sex

Of 8 male cases of early cancer, only one was not associated with gastric ulcer either in the affected area or in the distant area. According to Takagi's study on the mucosal carcinoma, the higher frequency is found in the group associated with ulcer than in the group without ulcer in male<sup>18</sup>. This may represent the following facts: stomach ulcer is more frequently found in male than in female, and cancer arises in ulcer with a higher ratio than in gastritis<sup>20</sup>.

## (iv) Duration of Complaints

It was reported that the duration of complaints was longer than 2 years in the majority of the cases with the early ulcer-carcinoma, and that the deeper layer of the stomach wall ulceration involved, the longer the complaints continued<sup>12</sup>. The duration of complaints was mostly long enough to exceed five years in group B. In contrast, it was less than a month in most of the cases of group A. From these facts, it may be suggested that the duration depends upon the presence or absence of chronic ulcer.

## (v) Subjective Symptoms

Though subjective symptoms are not necessarily determinative in diagnosis of cancer, attention should be paid to anorexia and slight loss of weight, which actually occur more frequently in early stage of cancer than in benign diseases, such as gastritis and ulcer, and also to spontaneous disappearance of heart-burn, for it may be correlated to a change in gastric secretion in the course of development of cancer.

It has been described in some reports that symptoms had lasted several years in the majority of the patients with the early ulcer-carcinoma<sup>12,21</sup>. In this series, 17 per cent of the cases in group A and 67 per cent of the cases in group B showed symptoms of the ulcer-type. Therefore, it can be concluded that such symptoms are rare in the case of early cancer not associated with chronic ulcer.

## (vi) Abdominal Signs

It is to be noted that there was not a single case in which the palpation could find the tumor of early cancer in our series.

## (vii) General Conditions

In this series, anemia and hypoproteinemia were usually in less degree than in the control group. The general conditions were maintained well.

## (viii) Occult Blood in Stool

Occult blood test was positive in most of the gastric cancer patients equally

as frequent as in gastric or duodenal ulcer and gastritis. Stool examination, therefore, is not definitive diagnostic measure to gastric carcinoma. Furthermore, 30 per cent of the early gastric cancer presents no evidence of positive occult blood in stool, so it must be kept in mind that carcinoma can be present even in the case of negative occult blood.

(ix) Gastric Analysis

It is interesting to note that group A shows hypoacidity and group B anacidity, but there are not enough cases to form an opinion about gastric acidity of the series. Table 8 illustrates the data of gastric analysis of Ayabe's early carcinoma<sup>23</sup>, Stout's early cancer<sup>21</sup>, Someya's early ulcer-carcinoma<sup>12</sup>, and Kono's gastric cancer and ulcer<sup>30</sup>. It is to be noticed that anacidity is not found in 25 per cent of our gastric cancer series, and it does not indicate the existence of the carcinoma. Anacidity is present in less percentage of the early cancer than the progressed cancer, but is more frequently obtained in the early ulcer-cancer than in benign ulcer. So, if benign ulcer is found to be associated with hypoacidity, its cancerous change must be suspected and further examination must be undertaken. Even in the case regarded as benign, the declining tendency of acidity in repeated gastric analysis might be the first valuable diagnostic finding of malignancy.

(x) Roentgenological Examination

The problem is how to find evidences of the delicate pathological changes caused by early gastric cancer. In our examination, the previously mentioned evidences were enough to be significant. They are, however, not characteristic to gastric cancer. It is important to note that roentgenological examination gives no decisive diagnosis of the presence of carcinoma. The X-ray film study in addition to fluoroscopy would afford a chance to discover the precise changes of cancer. The investigation must be carried out with careful fluoroscopy and film reading.

KUROKAWA<sup>31</sup> has analyzed the X-ray observations on the basis of the findings of the mucosal relief and the filled contour, and he states that there is roentgenologically no characteristic differences between mucosal carcinoma and progressed cancer. Most of our group A revealed the above-mentioned changes and its 83 per cent was diagnosed as cancer or suspected cancer. The relatively large extension of mucosal carcinoma makes its roentgenological diagnosis easy. Diagnostic rate was up to 94.1 per cent for cancer and suspicious cancer by YAMAGATA<sup>32</sup> and up to 84.6 per cent by AYABE<sup>23</sup>.

There is a difficulty in differentiating between the early ulcer-carcinoma and the benign peptic ulcer. In group B, the previously-mentioned changes were hardly found on the margin of the ulcer and cancerous changes were suspected only in two cases out of the four examined. On the other hand, difficulty in

differential diagnosis of the early malignant change from benign ulcer has been noted. KUROKAWA named several findings such as the rigid wall surrounding niche, the remarkably elevated margin of the crater, the papillomatous irregular change of the margin of the crater, the ragged, papuloid and asymmetrical niche<sup>31</sup>. And he stated that it is erroneous to diagnose any cancerous change by its size and that repeated examinations might lead to an erroneous diagnosis by the finding of the cancerous niche shrinkage. BROWN<sup>33</sup> studied 106 cases of the ulcer-carcinoma which had preoperatively been considered benign, 13 per cent of which had been roentgenologically diagnosed as healed ulcers. Eighty per cent of them had then been given conservative therapy for more than 3 months. It is, however, to be noted that the resectability and the survival rate were low in comparison with the ones of those who were surgically operated on without conservative therapy. His conclusion was as follows: if there is not a 50 to 75 per cent reduction of the ulcer in size roentgenologically after two weeks' intensive medical treatment, surgical operation must be resorted to and a strict observation is necessary to be followed up even if a niche diminishes in its size. This remark of BROWN suggests an important vision toward the effort to find the cancerous change of ulcer. Although we are apt to keep ulcers under conservative therapy if the gastric analysis does not show anacidity, a physician must keep in mind the fact that the early gastric cancer shows various acidity.

(xi) Gastroscopic and Gastrocamera Findings

The use of gastroscopy and gastrocamera photography as diagnostic methods of the early gastric cancer has been emphasized by many investigators. But there have been few reports which detailed the findings of the early cancer examined with gastroscope and gastrocamera. TSUNEOKA<sup>34,35</sup> stated that gastroscopy was better in differentiating the malignancy of gastric ulcerations than roentgenography, but gastroscopy was also often unable to detect minor changes of the mucosal surface. HAYASHIDA<sup>36</sup> and KIDOKORO<sup>11</sup> studied precisely the features in malignant ulcers with gastrocamera, and reported that it was rare to find out specific and typical changes in the early stage of malignant ulceration.

The gastroscopic and gastrocamera findings of this series have been already described. The gastroscopic and gastrocamera findings indicated malignancy in one case each in group A and in group C, in spite of no definite gross changes on the mucosal surface of the resected stomach.

SCHINDLER explained that gastroscopic diagnosis was inferior to histological diagnosis, and superior to the gross observation of the mucous membrane of the resected stomach. HAYASHIDA and KIDOKORO entertain the same opinion on gastrocamera examination because of the true nature of the mucous membrane, "blood-circulating" condition, in endoscopic observation. In comparing the two methods, gastroscopy is far more suitable to detect the delicate color changes of

the mucous membrane. Abnormal redness is more clearly shown on gastroscopy than on gastrocamera photography. And even if abnormal redness is caught on gastrocamera film, it needs some experience to differentiate it from normal redness, and it is usually difficult to detect an erosion by gastrocamera. Therefore, gastroscopy is superior to gastrocamera photography for the detection of the early gastric cancer. But it is desirable, of course, to attempt both of them, because there are several differences in the observatory range, the manipulatory difficulty on patients and the objectivity of the material.

(xii) Preoperative Diagnosis

The final diagnosis was made chiefly by the combination of X-ray, gastroscopic and gastrocamera examinations. Including the diagnosis of the suspicious cancer, the final diagnosis was attained in 58 per cent of 12 cases of the early cancer, in 83 per cent in group A and in 33 per cent in group B.

It is difficult to discover the early cancer and to estimate the extension of the lesion preoperatively. An accurate diagnosis of the mucosal carcinoma can be easily done in comparison with the one of the ulcer-carcinomas. In determining the malignancy of ulceration in group B, difficulties were met with the following conditions: the endoscopic examinations were likely to be neglected under the over-confidence of X-ray diagnosis, and 2 cases or one-third of this series were subjected to an urgent operation without sufficient time for thorough examination because of acute severe hemorrhage. As to the nature of ulcerations, therefore, diagnosis should be made on the basis of as careful and sufficient examination as feasible, and in addition, the acidity of gastric contents should be carefully evaluated in the ulcer-carcinoma.

(xiii) Operative Findings

The cancer of early stage is difficult to be determined by macroscopic inspection and palpation alone during the operation. Thus surgeons should be thoroughly competent in judging those changes of the gastric mucosa that occur at an early stage of cancer, because it is necessary to make a direct observation of the resected mucosa and to examine minutely the mucosal surface of the resected stomach, especially in the case suspected of cancer by preoperative probe. What is more, even in the case not revealing any apparently marked changes in mucosa of stomach, since the histological diagnosis by preoperative examinations often proves to be more reliable, ample care should be exercised as to examine the biopsy material from the stomach to be operated on or quickly to conduct histological examination of the resected stomach.

(xiv) Gross Findings of the Mucous Membrane of the Resected Stomach

a) Location

According to TAKAGI<sup>23</sup>, the mucosal carcinoma without ulcer is located along the lesser curvature of the pyloric antrum in more than a half of cases,



but the cancer with ulcer is located along the same curvature of the gastric corpus. The same observations were made in our series. Lesions were located mostly at angulus and lesser curvature of pyloric antrum in group A, and on the other hand, they were found at angulus or at lower part of corpus in the vicinity of angulus in group B.

b) Changes of Mucous Membrane

Morphological changes of affected membrane are summarised in the following 3 groups: (1) erosion, (2) swelling (irregular and granular), and (3) depression. A localized erosion with irregular and granular swelling around it was chiefly found in group A. A clear-cut boundary was found around it if it was of large extension. Depression was found only in one case associated with erosion of this group. Only mucosal depression was observed in 2 cases of the precancerous group. An irregular and granular swelling of ulcer margin was found in most of the cases of group B; 2 cases of them which might be called the cicatricial cancer had depressed erosions.

According to TAKAGI<sup>13</sup>, chief findings of the cancerous mucous membrane in the mucosal cancer are the localized thickening (flat or nodular) and the localized erosion or depressive atrophy. In the case of the mucosal cancer without ulcer, thickening is noted, and in contrast, in the erosion or depressive type atrophy was observed in all of the mucosal cancer with ulcer. But none of the cases in group A showed flat swelling such as stated in his report, and there were a few cases in group B showing erosion.

There are few references on the changes of color tone. MURAKAMI<sup>17</sup> points out that redness is one of the most important findings, while TAKAGI<sup>13</sup> reports it only in three out of 52 cases of the early cancer, and most of them do not present differences in the color tone from surrounding membrane. BOCIAN<sup>19</sup> states that one case of gastric carcinoma *in situ* was pale. In our series, erosion and irregular granular swelling were red in color in most of the cases of granular groups A and B. The abnormal redness may be one of the characteristic macroscopic findings, though it does not appear constantly.

Among 12 cases of the early cancer, six (50 per cent) were diagnosed as cancer macroscopically (67 per cent in group A, and 33 per cent in group B). These determinations, however, were difficult and the differentiation of benign ulcer in group B was particularly uneasy. Clinical significance of the changes on the mucosal surface observed immediately upon opening the stomach lies in the fact whether or not these findings serve as the criterion to establish subsequent surgical procedures. The diagnosis of the early cancer may be easily established when there is a localized erosion combined with an irregular and granular swelling partially red in color. An utmost care should be given for the finding of irregular elevation or localized erosion which accompanies redness even

in part of the ulcer margin, and also for the finding of the localized granular swelling of gastric membrane with irregular granular change or redness.

#### SUMMARY AND CONCLUSIONS

1. An attempt has been made to find the diagnostic criteria for early gastric cancer. It is most important to detect the evidences or suspected features of the malignant growth in incipient stage in order to attain the radical cure by surgical operation.

2. Twelve patients with early gastric cancer (groups A and B) were selected out of 476 patients who had undergone gastrectomy during the past three years in the Okayama Saiseikai General Hospital. The other 6 patients in the "precancerous group" (group C) were also studied, who had abnormal epithelial proliferation in the resected stomach membrane during the same period.

3. The processes of discovery of early cancer have been described. Fairly precise diagnosis can be made in the mucosal carcinoma, but it is not in the ulcer-carcinoma. It was generally difficult to estimate the degree of the malignancy and the extension of the growth preoperatively.

4. The details of the diagnostic aids are as follows.

i. Negative occult blood of stool does not always mean the definite diagnostic aid.

ii. The malignant gastric change may occur even in non-acidity. Further investigations should be followed up on gastric ulcer patients if malignant alteration is under the consideration.

iii. Minor roentgenological findings, such as the absence or irregularity of mucosal folds, rigid and/or overlapped contour, localized absence or decrease of the peristaltic waves and absence or bow-shaped deformity of the angulus, are of important significance. Such changes should be minutely sought for by X-ray film examination.

iv. On gastroscopy and gastrocamera photography, such changes as erosion or irregular granular thickening of the membrane with abnormal reddening and edematous appearance, irregularity of ulcer edge, uneven swelling on ulcer margin with reddening and unsharpness of the edge of adherent coat on ulcer floor, must be noted in the early gastric cancer.

v. It is not safe to leave a patient having stomach ulceration under a mere conservative management because it is often quite difficult to dissolve the question of malignancy of the lesion with all sorts of examinations.

vi. So far as clinical examinations have indicated malignancy, histological examination must be carried out immediately at the time of operation, even when malignant lesion is absent in inspection and palpation on the exposure of

the stomach.

vii. On the gross observation of the resected stomach, a particular attention must be paid to erosion, depression or atrophy, irregular granular thickening and abnormal reddening on the restricted areas of the mucosal surface.

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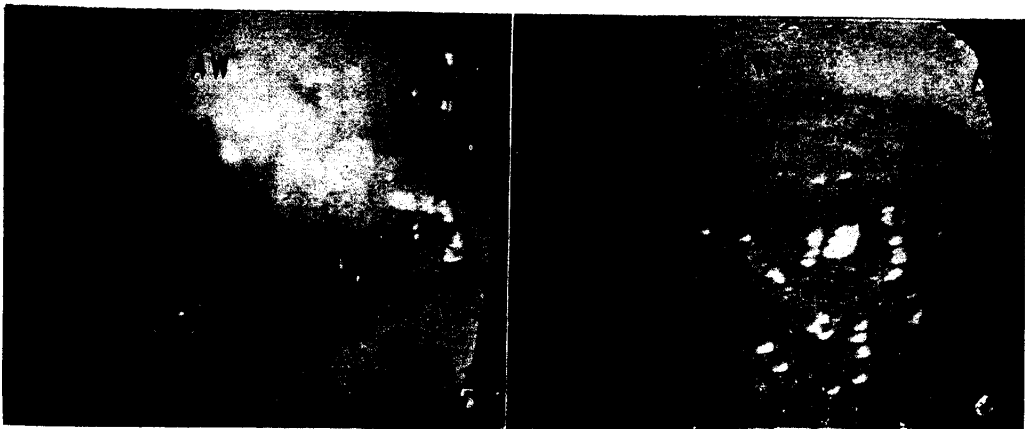
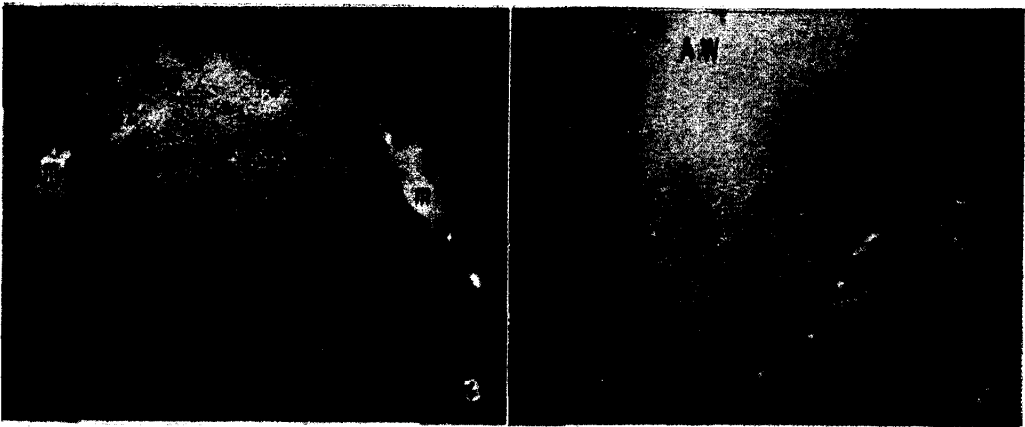
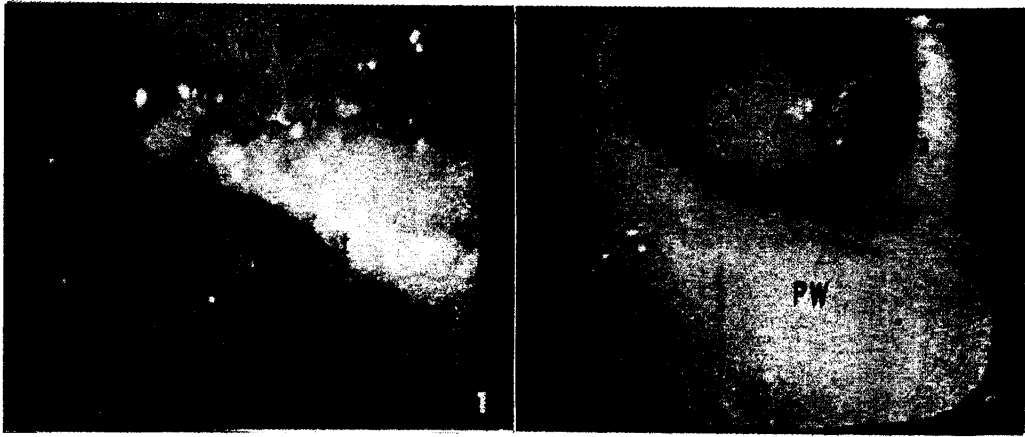
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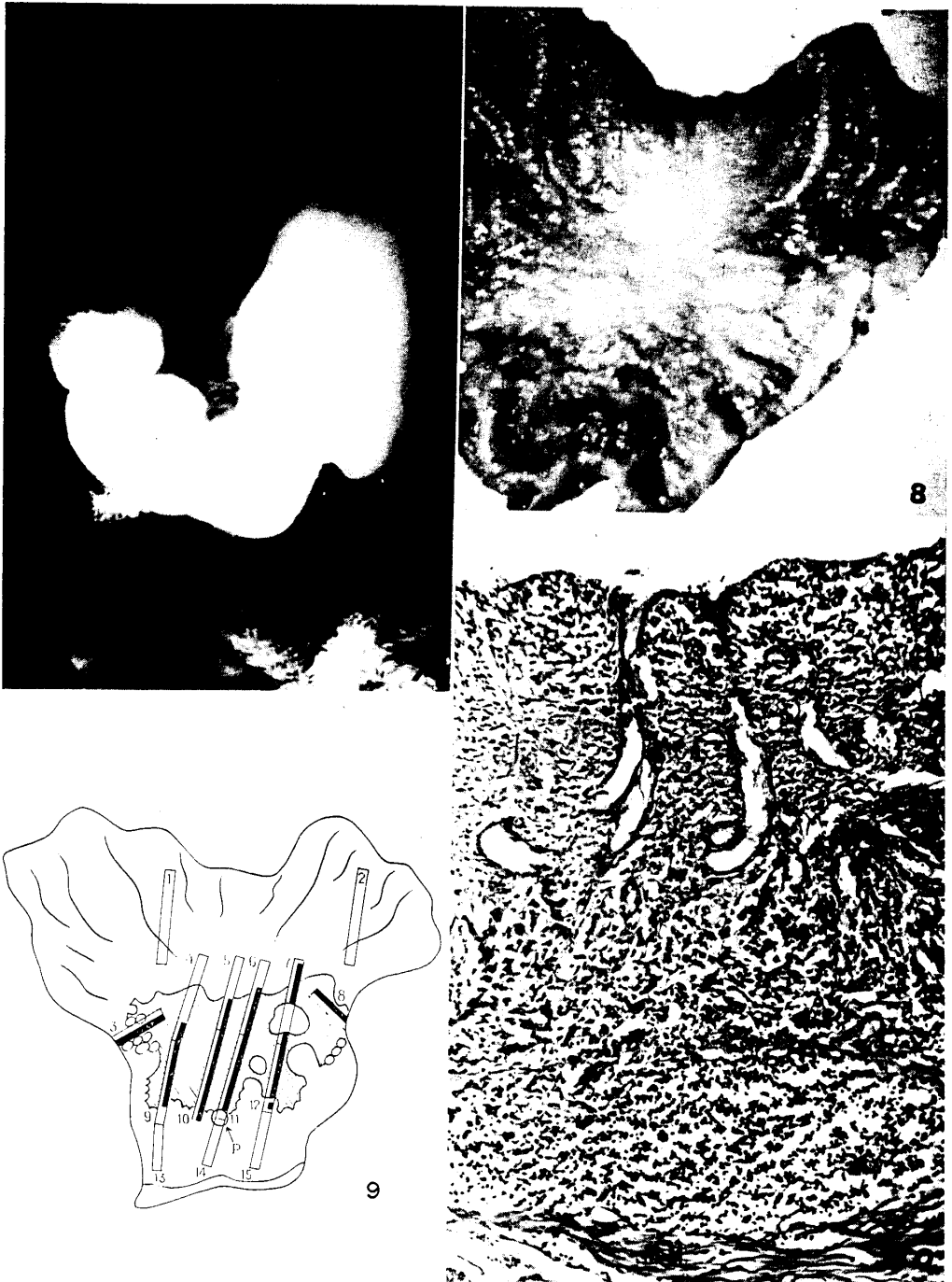
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Figs. 1—6. : Gastrocamera pictures of early gastric cancers.

A: antrum, AW: anterior wall, G: greater curvature, L: lesser curvature, PL: pyloric ring, PW: posterior wall.

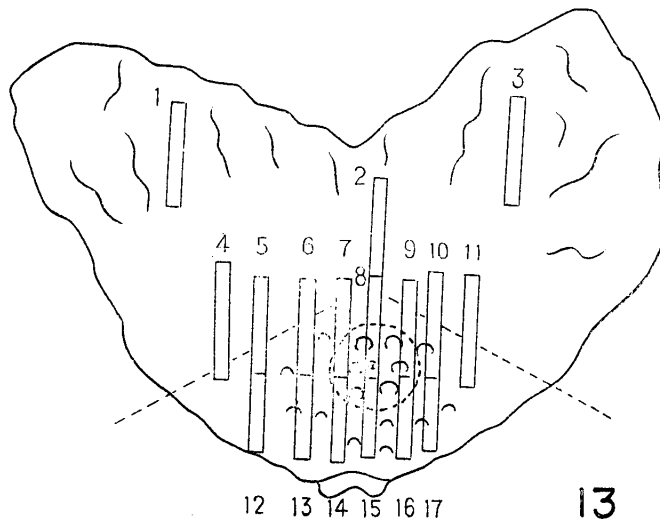
- Fig. 1. The picture of case A—1 shows thickened and rigid angulus (t) and polyposis-like swelling (p) on the anterior and posterior walls from the lower part of corpus to the antral region.
- Fig. 2. The picture of case A—2 shows edematous reddish granular swelling (s) on the greater curvature of the prepyloric region. Angulus is edematous and reddish, and its profile (a) near the posterior wall is slightly uneven and rigid. f: adherent foam.
- Fig. 3. In the picture of case A—5 profile of uneven shallow excavation (e) with adherent coat (c) and reddish uneven swelling (s) adjacent to the excavation can be seen at angulus. m: adherent mucus.
- Fig. 4. The picture of case A—6 shows an ulcer (u) and uneven swelling (s) with redness and edema at angulus near the posterior wall.
- Fig. 5. In the picture of case B—2 an ulcer crater (u) at angulus with uneven floor and margin and with ill-defined coat.
- Fig. 6. The picture of case C—1 shows an erosion (er) associated with remarkable redness on the lesser curvature in the antral region near angulus.



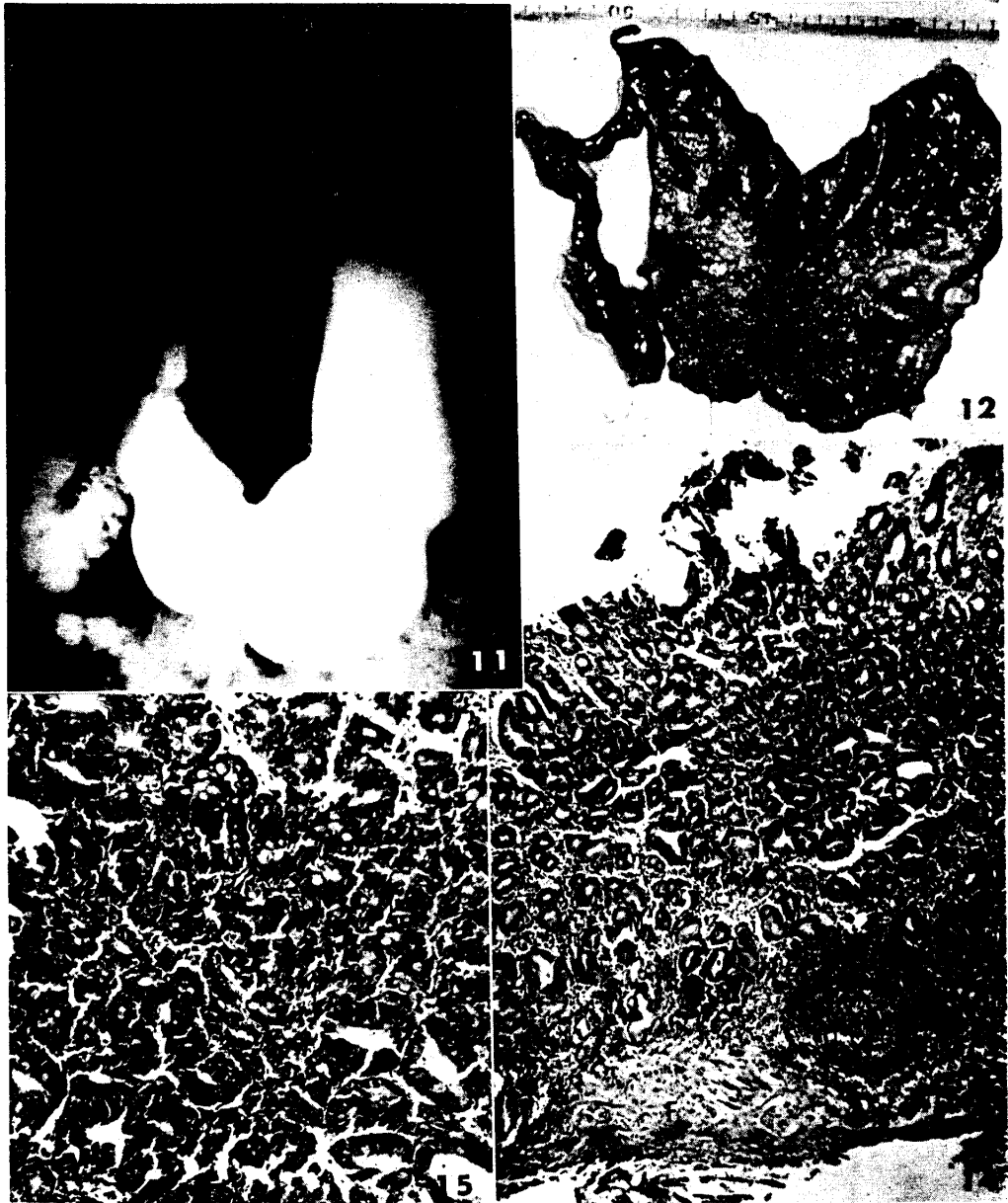


- Fig. 7. X-ray picture of the stomach of case A—1 shows rigid contour on both curvatures from the lower part of corpus to the antral region, and slight nodularity at angulus.
- Fig. 8. Gross appearance of the resected stomach of case A—1. A belt-like erosion covering an area 4.5 by 9.3 cm. from the lower part of corpus to antrum, with irregular slight nodularity in its periphery can be seen. There is islet-like remnant of the mucous membrane in it. A polyp can be seen on the lesser curvature in the prepyloric region adjoining the erosion.
- Fig. 9. A diagrammatic picture of sectioning the stomach of case A—1 for microscopic examinations. The hatched area shows erosion. Shaded bars show cancerous tissue.
- Fig. 10. The photomicrograph of section 5 appearing in Fig. 9. Carcinoma simplex proliferates diffusely in the superficial part of *lamina propria mucosae*;  $\times 100$ . CA: cancerous tissue, MM: muscularis mucosae.

- Fig. 11. X-ray picture of the stomach of case A—2 shows rigidity and slight nodularity on the lesser curvature of autrum.
- Fig. 12. Gross appearance of the resected stomach of case A—2. Pyloric antrum is markedly granulated. In the area encircled with dotted line in Fig. 13 dark-reddish discoloration and irregularity of granules are found.
- Fig. 13. A diagrammatic picture of sectioning the stomach of case A-2 for microscopic examinations. The black dot in block 8 shows the site of cancer.
- Fig. 14. Low-power photomicrograph of section 8 appearing in Fig. 13. Dense and irregular arrangement of atypical glandular cavities can be seen only in a restricted part.  $\times 40$ . CA: cancercus tissue, M: metaplastic glands, F: fibrosis. L: lymph follicle.
- Fig. 15. Photomicrograph of the area shown at the center of Fig. 14. Cells appear markedly atypical. The basement membrane can not be seen.  $\times 100$ .



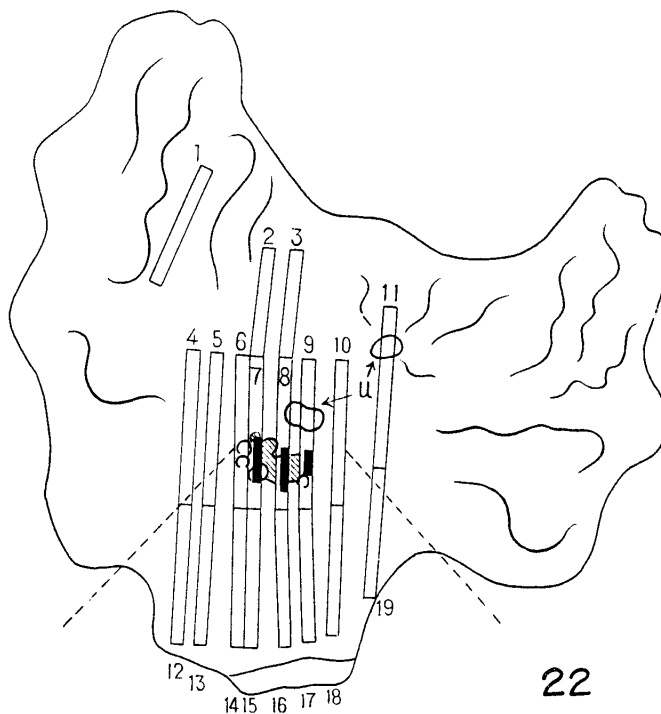


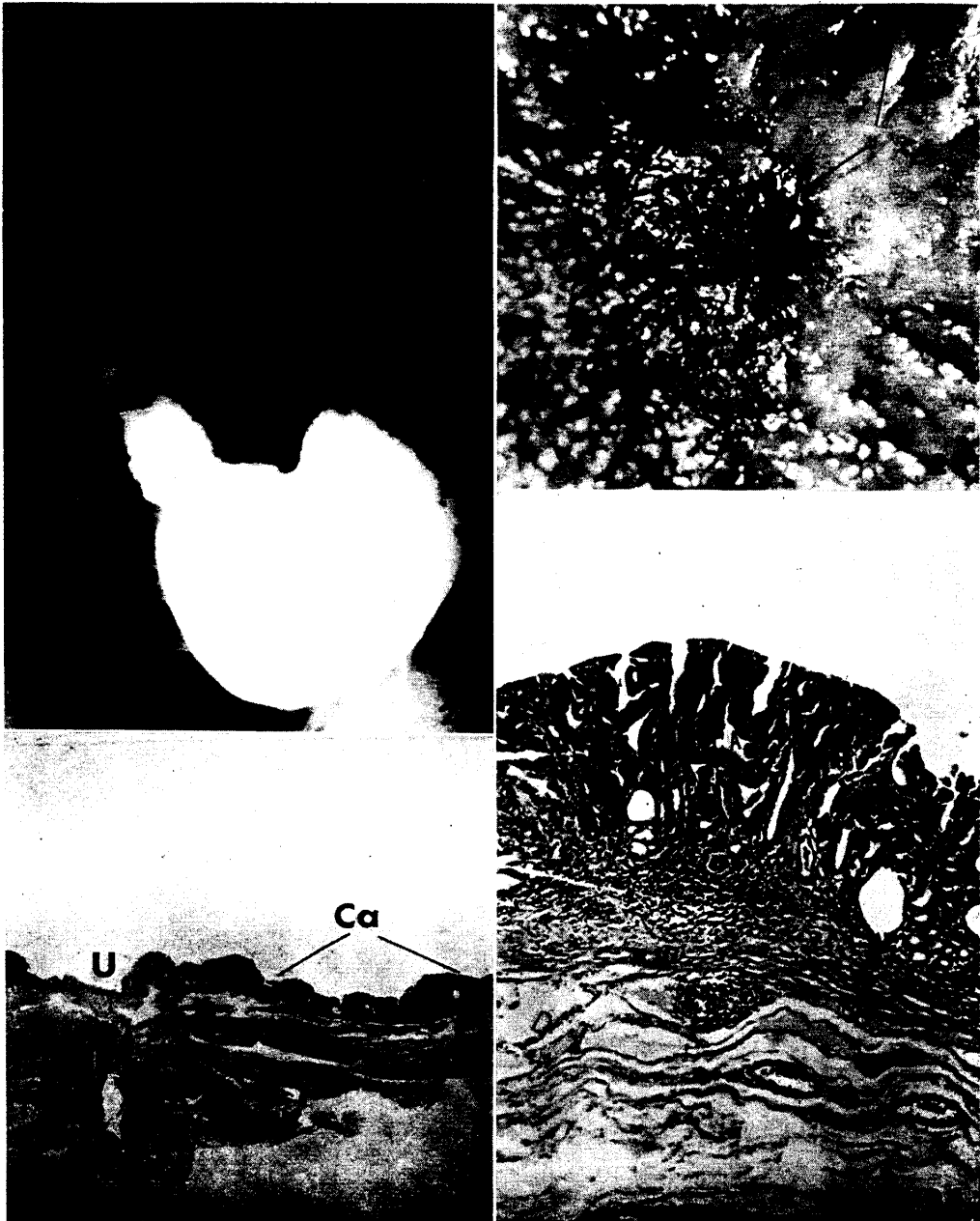




- Fig. 16. Rcentgenographic picture of the stomach of case A—5 shows bow-shaped deformation, rigidity and overlapped contour of angulus.
- Fig. 17. Gross appearance of the resected stomach of case A—5. An erosion covering an area 1.4 by 2.4 cm. can be seen at angulus, associated with slight unevenness in the cardia side of its periphery and with mucosal atrophy in the antral region adjacent to it.
- Fig. 18. A diagrammatic picture of sectioning the stomach of case A—5 for microscopic examinations. The hatched area shows erosion. Shaded bars show cancerous tissue.
- Fig. 19. Low-power photomicrograph of section 7 appearing in Fig. 18. High cylindrical tumor cells proliferate along the superficial layer of the mucosa, forming atypical glandular cavities.  $\times 40$ . CA: cancerous tissue, MM: *muscularis mucosae*.

- Fig. 20. X-ray picture of the stomach of case A—6 shows absence of angle, and overlapped contour, rigid contour and niche on the lesser curvature near the angle.
- Fig. 21. Gross appearance of the resected stomach of case A—6. There are two niches (u), one at angulus and another in corpus. A small erosion (e), measuring 1.0 by 1.5 cm., can be seen on the lesser curvature of antrum near angulus.
- Fig. 22. A diagrammatic picture of sectioning the stomach of case A—6 for microscopic examinations. The hatched area shows erosion. Shaded bars show cancerous tissue. U: ulcer.
- Fig. 23. The greater part of section 9 shown in Fig. 22 is illustrated. U means ulcer. Ca: cancer.
- Fig. 24. Low-power view of section 9 appearing in Fig. 22. High cylindrical tumor cells proliferate along the superficial layer of the mucosa, forming atypical glandular cavities.  $\times 40$ . CA: cancerous tissue, MM: *muscularis mucosae*.







- Fig. 25. X-ray picture of the stomach of case B-2 shows ulcer crater with asymmetric and rigid contour, and slight nodularity at the margin of it.
- Fig. 26. Gross appearance of the resected stomach of case B-2. A callous ulcer at angulus, measuring 1.0 by 2.0 cm. can be seen, the margin of which is finely granulated and reddish on the cardia side.
- Fig. 27. Low-power view of the ulcer margin of case B-2. Cancerous tissue is localized only in the marginal mucosa.
- Fig. 28. Photomicrograph of the part marked in Fig. 27 shows that the growth is localized in the mucosa only.  $\times 40$ . CA: cancerous tissue, MM: *muscularis mucosae*.

- Fig. 29. X-ray picture of the stomach of case C—1 shows no peculiar findings.
- Fig. 30. Gross appearance of the resected stomach of case C—1. Well-defined mucosal depression at angulus, measuring 2.0 by 3.0 cm. can be seen. The posterior boundary of it is slightly irregularly granulated.
- Fig. 31. A diagrammatic picture of sectioning the stomach of case C—1 for microscopic examinations. Dotted line encircles the mucosal depression. The hatched area shows precancerous change.
- Fig. 32. Photomicrograph of section 8 appearing in Fig. 31. Epithelial cells proliferate in the portion of the mucosa, forming atypical glandular cavities. Proper gastric glands have almost disappeared.  $\times 100$ .
- Fig. 33. High-power view of section 8. The epithelial cells are quite different in size and shape. Nuclei are swollen, with large nucleoli, clear-cut nuclear membrane, rough chromatin and mitotic figures. But the basement membrane is well held and there is no intensive or destructive proliferation enough to be regarded as cancer.  $\times 600$ .

