

Histo-Clinical Classification and Follow-Up Study of Gastric Polyp

KOTARO UENO,* SABURO OSHIBA, SHOICHI YAMAGATA, FUKUJI MOCHIZUKI, MASANOBU KITAGAWA and SHIGERU HISAMICHI

The Third Department of Internal Medicine, Tohoku University School of Medicine, Sendai

UENO, K., OSHIBA, S., YAMAGATA, S., MOCHIZUKI, F., KITAGAWA, M. and HISAMICHI, S. *Histo-Clinical Classification and Follow-Up Study of Gastric Polyp*. Tohoku J. exp. Med., 1976, 118 (Suppl.), 23-38 — Gastric polyp was found in 1,616 cases or 0.23% of 711,455 persons through the gastric mass-survey. They were classified into 3 groups; hyperplastic polyp in 61%, gastritis polyposa in 34%, and polyp composed of metaplastic epithelium with marked atypism (ATP) in 5%. Gastritis polyposa was subclassified into 5 groups according to its histo-clinical features. Malignant degeneration was suspected in 5 or 2.1% of 236 hyperplastic polyps operated, while no polyp which had changed into cancer was experienced among 974 polyps followed-up by biopsy during the time course of 6 months to 11 years at the longest. On the other hand, coexistence of gastric cancer was found in 13% of cases with ATP. In polyps composed of metaplastic epithelium, there are two kinds of polyp: metaplastic polyp in hyperplastic proliferation and neoplastic polyp. In the follow-up study of 1,104 polyps, the growth of polyp was seen in only 14, and 12 of which were hyperplastic polyp. No change from gastritis polyposa to hyperplastic polyp was observed. The increase in size in 14 polyps was seen mostly 3 to 4 years after they were found and was always transient. From these results, it is considered that most of gastric polyps clinically detected have already completed their growth.
—— gastric polyp

Although most of gastric polyps are thought to be benign, the malignant potential of polyps over 2 cm in size or of those composed of more primitive metaplastic epithelia continues to be a subject of considerable discussion (Castleman and Krickstein 1960). To this subject, it will be an effective aid to know the actual incidence of gastric polyp among people who never come under clinical observation because of no complaints, and to know how each type of these gastric polyps develops and how many of them may actually turn to malignancy in their course.

The purpose of this paper is to describe the results of the clinico-histological observation of gastric polyp detected in the gastric mass-survey from the above point of view.

MATERIALS AND METHODS

During the past 11 years, a mass-survey for gastric diseases has been conducted on a total of 711,455 persons in a prefectural district population of about 2,000,000. The

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* Present address: The Second Department of Internal Medicine, Yamagata University School of Medicine, Yamagata.

screening test by means of indirect fluorophotography was primarily done in all of the subjects, and gastroscope or direct x-ray examination was then indicated for further study in about 20% of them. In cases in which some abnormality was found, fiberoptic examination and biopsy were done to make definite diagnosis. Consequently, gastric polyp, which is defined as a benign discrete mucosal elevation due to epithelial proliferation, was found in 1,616 cases. Inflammatory fibroid polyp and submucosal tumors were excluded from the discussion.

The gross appearance of gastric polyps was observed endoscopically, and the size of the lesion was measured indirectly by using FGS-BLG (Maruyama et al. 1972) or a scale attached to the biopsy forceps and by x-ray picture if necessary. In 1,104 polyps, the follow-up observation of the polyp in the clinical course has been done by fiberoptic examination and by biopsy during the time course of 6 months to 11 years at the longest. The interval between examinations was mostly 3 to 6 months at the beginning, and once or twice in a year in the later course.

To study the relationship between gastric polyp and cancer, histologic specimens of 236 polyps and 61 polypoid cancers, which had been detected through the mass-survey and operated, were reviewed.

Histologic specimens taken from polyps by biopsy or polypectomy were stained with hematoxylin-eosin and the multiple staining of alcian blue-PAS-Masson's trichrome method in order to study the mucin productivity of the epithelial cells composing polyp. Cell proliferation kinetics of the mucosa of some polyps was also investigated by means of in vitro autoradiography using ^3H -TDR.

RESULTS

Histo-clinical types of polyps detected

Gastric polyps so far diagnosed are classified as shown in Table 1, according to the endoscopic findings and histologic findings of the biopsy or resected specimens.

TABLE 1. *Histologic types of gastric polyps*

Polyp consisting of gastric epithelium	Polyp consisting of intestinal metaplastic epithelium (ATP)
Hyperplastic polyp	
Gastritis polyposa mainly composed of:	Metaplastic polyp in hyperplastic proliferation
Normal fundic mucosa	Neoplastic polyp
Pseudopyloric glands	
Epithelium of gastric foveolae	
Mere gastritis	
Lymph follicles within mucosa	

Hyperplastic polyp is the commonest type seen in 61% of all polyps, and corresponds to that previously called adenomatous polyp by Stout (1953), being mainly composed of large columnar epithelial cells which contained much mucin in the cytoplasm and formed cystic dilated glands intermingled with increased collagen and smooth muscle fibers originating from muscularis mucosae. This type consisted of sessile polyps as well as pedunculated polyps, and the surrounding mucosa of these polyps was mostly atrophic. Hyperplastic polyp is at present found most definitely not to be tumorous in nature, so that they are also called regenerative polyp (Ming and Goldman 1965; Evans 1966).

Among other polyps summarized as gastritis polyposa, five kinds are distinguished histologically. Type A is a polyp entirely consisting of normal fundic

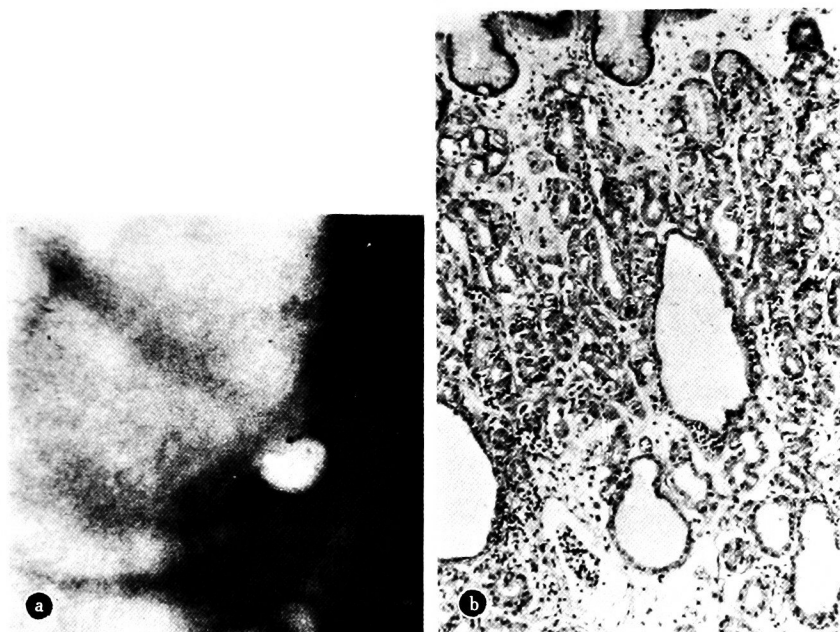


Fig. 1. Type A of gastritis polyposa. (a) Gastrocamera (GTF) picture of the polyp on the greater curvature of the upper portion of the corpus. (b) Its histologic picture consisting of normal fundic glands.

glands, rarely seen around the greater curvature of the gastric corpus, being usually solitary, sessile and small in size as shown in Fig. 1. Polyps of types B and C are due to focal hyperplasia of the gastric epithelium caused by erosive gastritis. This type was termed gastritis verrucosa by Abel (1954). The gross appearance of this type shows a characteristic feature like suckers of octopus, having a small depression due to an erosion on the top of the mucosal elevation. Type B is a polyp predominantly consisting of pseudopyloric glands in hyperplastic proliferation, showing rosary-like verrucous appearance, with characteristic multiple occurrence in the antrum (Fig. 2). Type C, on the contrary, mainly consists of regenerative epithelium of the gastric foveolae in hyperplastic proliferation, with characteristic multiple occurrence as polyposis on the portion of the fundic mucosa close to the border-line between the pyloric gland area and fundic gland area (Fig. 3). In 9.5% of the cases with gastritis verrucosa, pedunculated hyperplastic polyp was found concomitantly in the same stomach. The surrounding gastric mucosa of these polyps examined by biopsy was less atrophic. The gastric juice analysis revealed normo- or hyperacidity of gastric juice in 65% of the cases with type B and 12% of type C. In type D, no characteristic findings of polyp but solely gastritis were observed at gastric biopsy. Most of these consisted of small sessile polyps. Type E represents polyps with elevation around the lymph follicles within the gastric mucosa, rarely seen in the antrum as multiple polyposis. Most of these are sessile and small in size, but some are long and pedunculated, in which

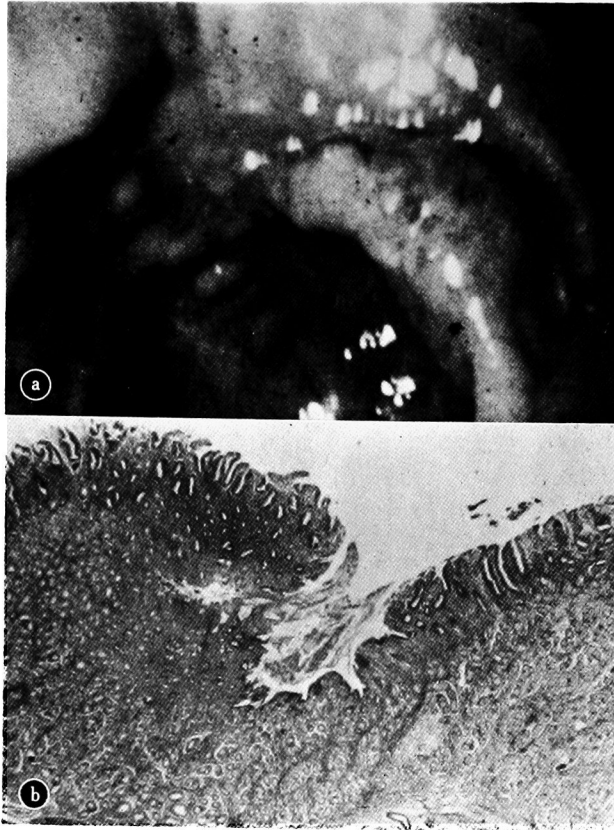


Fig. 2. Type B of gastritis polyposa. (a) Gastrocamera (GTF) picture showing large and small verrucous protrusions in the antrum. (b) Histologic picture of the large verrucous protrusion predominantly consisting of pseudopyloric glands in hyperplastic proliferation. An erosion was seen at the center of the lesion.

the basal portion of the polyp is presumably pulled by the peristaltic movement of the stomach (Fig. 4).

Polyps consisting of metaplastic epithelium occupied about 5% of all polyps. Sex ratio was 1:0.3. Multiple occurrence, which was 2 to 5 at most, was seen in 14% of 83 cases. The epithelial tubules in the polyps contain goblet cells and sometimes Paneth cells in a large number. The presence of brush border stained by alcian blue is also a feature of the intestinal epithelium. In most of them, marked atypism was seen in the superficial portion of the lesion, and was sometimes not readily differentiated from tubular adenocarcinoma (Fig. 5). The dense cells constituting the epithelial tubules have tall columnar cytoplasm with markedly increased eosinophilia, in which the amount of mucin content was reduced in inverse proportion to the increase of atypism (Fig. 6). The nuclei are short and spindle-shaped, pleomorphic and hyperchromatic with abundant mitosis, having sometimes lost their basal orientation (Fig. 7). In our experience, carcinoma was found in 13% of the cases with this type of polyp, either in the same lesion or in

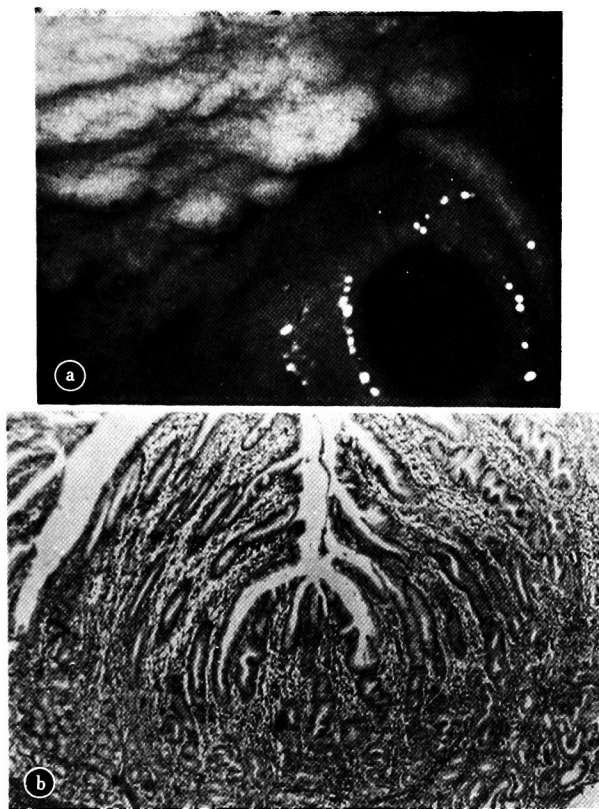


Fig. 3. Type C of gastritis polyposa. (a) Gastrocamera (GTF) picture reveals multiple gastric polyps on the anterior wall of the lower portion of the corpus. A red erosion is seen on the top of each elevation. (b) Histologic picture shows elongated gastric foveolae consisting of regenerative indifferent epithelial cells due to erosion which was seen at the center of the picture.

other parts of the same stomach. The commonest site of this type was the antrum where gastric mucosa showed severe atrophy with intestinal metaplasia. This type of polyps shows a low bank-like elevation with a broad base and a pale surface or a worm-like shape with unevenness of the surface, giving rise to a problem of differentiation from early gastric cancer type IIa (Fig. 8). Among these polyps, 3 lesions were pedunculated. The epithelial cells in these polyps showed more marked atypism (Fig. 9). Very rarely, on the other hand, there were some polyps showing no or little atypism of cells and glands even in this type.

Results of clinical observation

In our mass-survey for gastric diseases, gastric polyp was found in 1,616 cases or 0.23% of 711,455 persons, with a yearly rate between 0.19% and 0.28%; on the other hand, gastric cancer was found in 0.2% in this series. The commonest site of these polyps was the antrum, occupying about 70% of all polyps. Females were more predominant than males with a ratio of 0.18:0.29 that is 1:1.6 (Table 2).

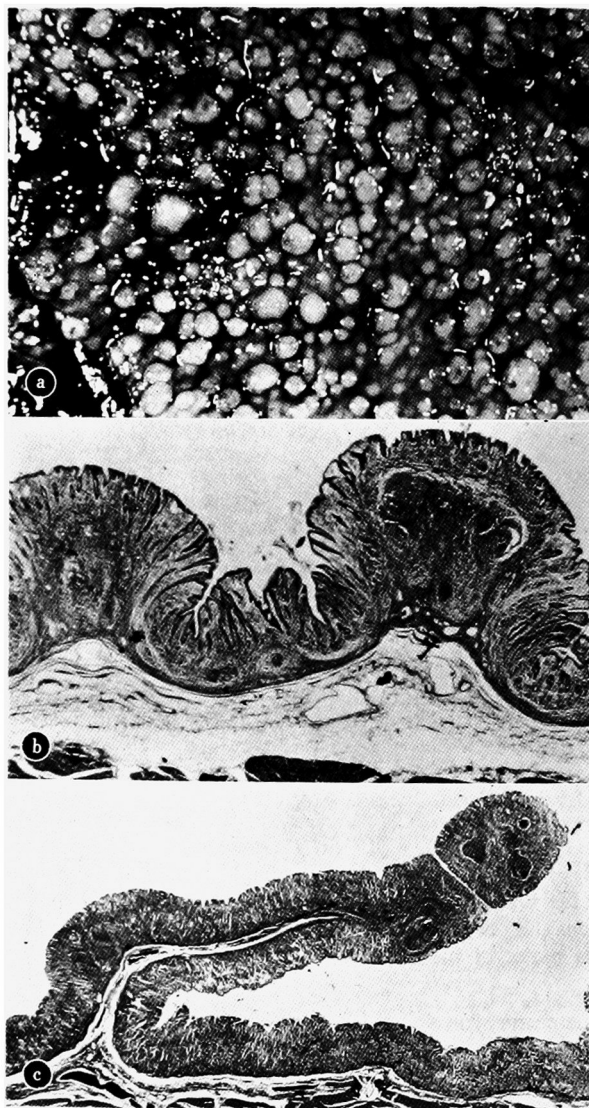


Fig. 4. Type E of gastritis polyposa. (a) Resected stomach of a 19-year-old male showing multiple polyposis in the antrum. (b) and (c) Histologic pictures of sessile and pedunculated polyps of the same case, composed of both proliferated lymph follicles and hyperplastic epithelium.

The survey of incidence of gastric polyp in different age groups revealed a tendency toward markedly increased gastric polyps with advancing age. When these polyps were classified into 4 gross pathological groups according to the shape of the lesion as shown in Fig. 10, sessile hemispherical polyp was most frequent in the young age group, whereas the increase of pedunculated polyp was most pronounced in older age groups.

In 1,104 polyps, in which the follow-up observation has been done by means of

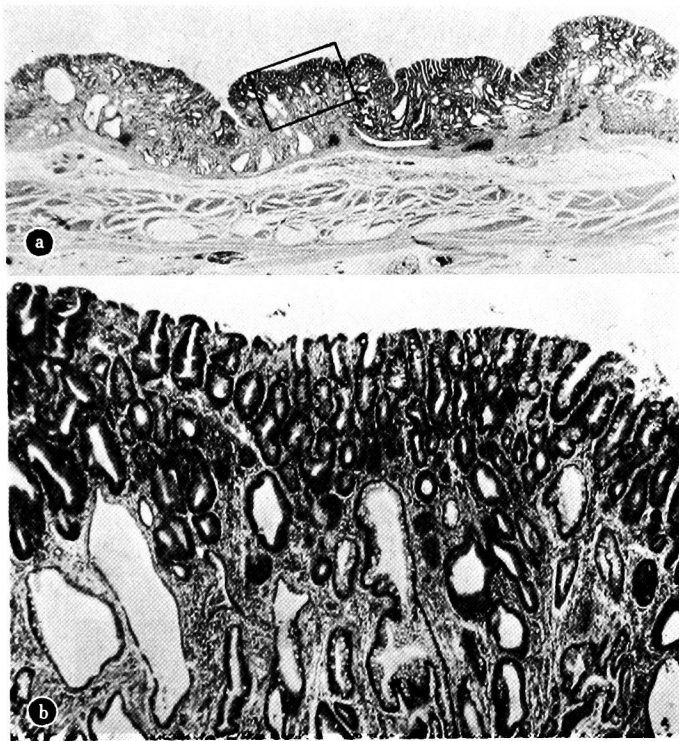


Fig. 5. Histologic pictures of polyp composed of metaplastic epithelium showing atypism. In Japan, this type is called atypical epithelium (ATP). (a) A typical picture of this type found in Japan. (b) A part of the same lesion magnified.

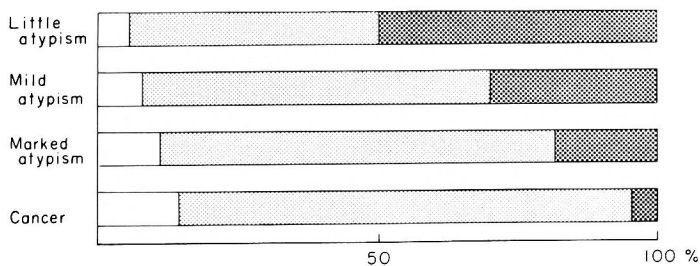


Fig. 6. Relationship between histologic atypism and the amount of cytoplasmic mucin contents of the atypical epithelium (ATP). □, alcian-blue staining of cytoplasmic mucin (—); ▨, (+); ▩, (++) .

fiberscopy and biopsy during a time course of 6 months to 11 years at the longest, a growth in the size and in the figure was seen in 14 polyps, 12 out of which were hyperplastic polyps diagnosed by biopsy (Table 3). In the remaining two, one was a pedunculated one, probably hyperplastic polyp though no biopsy was carried out

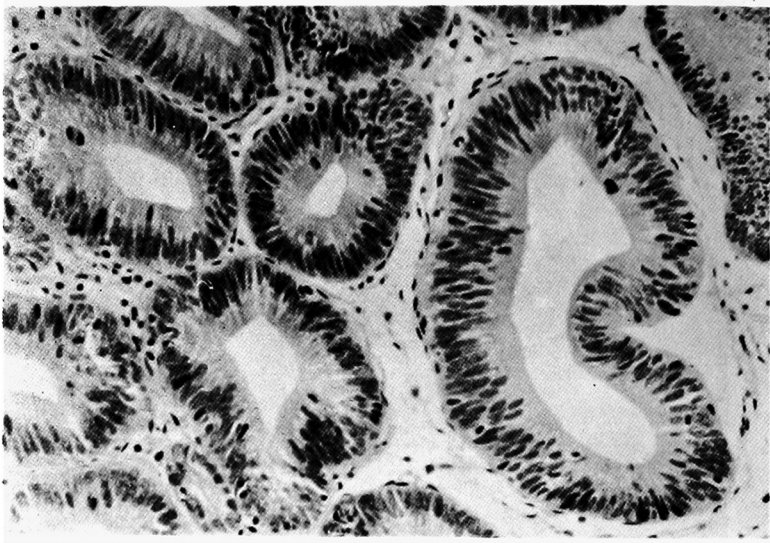


Fig. 7. Highly magnified histologic picture of ATP.

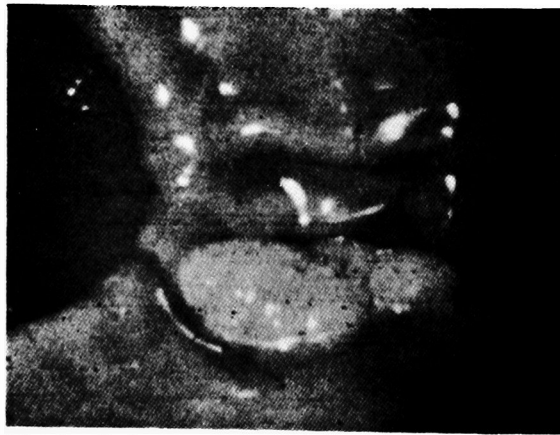


Fig. 8. Endoscopic picture of ATP taken by GTF-S.

during the period of observation; another was a polyp consisting of metaplastic epithelium. Since this case is not operated yet, no conclusion can be drawn unless pathological confirmation is made. The reason is that two other lesions, which had been followed up as belonging to this type and increased in size in the clinical course, were found to be carcinoma after operation. A change from gastritis polyposa into pedunculated polyp or an increase in size in gastritis polyposa was never experienced. From these results, it can be said that most of the polyps with increase in size are hyperplastic polyps. In view of the frequency of 12 or 3.2% out of 380 hyperplastic polyps, however, the growth of hyperplastic polyp in the clinical course appears to be extremely rare. Most of hyperplastic polyps which



Fig. 9. A case of ATP which has a pedicle (a) showing so marked atypism as neoplastic in nature (b).

TABLE 2. *Frequency of gastric polyp in different age groups*

Age	Males			Females			Total		
	Examinees	Polyp	%	Examinees	Polyp	%	Examinees	Polyp	%
20-29	21,657	9	0.05	8,230	10	0.12	29,887	19	0.06
30-39	80,353	54	0.07	48,899	44	0.09	129,252	98	0.08
40-49	152,915	180	0.12	109,884	171	0.16	262,799	351	0.13
50-59	99,773	261	0.26	83,823	319	0.38	183,596	580	0.32
60-69	44,258	195	0.44	38,612	239	0.62	82,870	434	0.52
70-	10,662	63	0.60	7,491	62	0.83	18,153	125	0.69
Unknown	2,816			2,082	9		4,898	9	
Total	412,434	762	0.18	299,021	854	0.29	721,455	1616	0.23

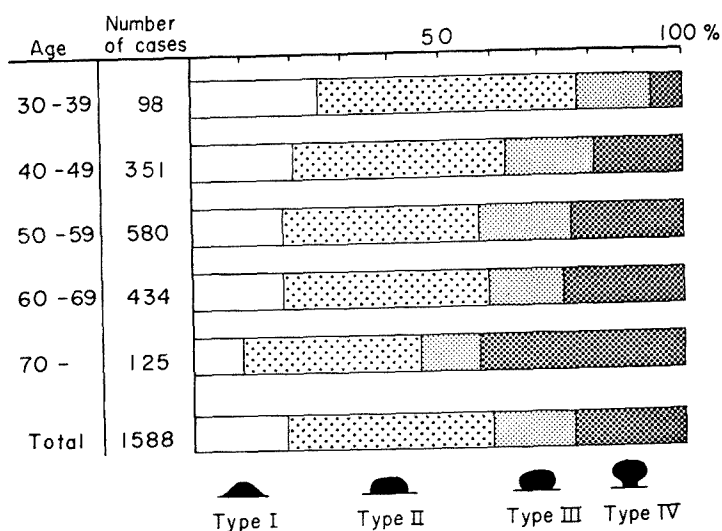


Fig. 10. Relationship between age and type of gastric polyp. □, Type I; ▤, Type II; ▨, Type III; ▩, Type IV.

TABLE 3. Results of follow-up observation of gastric polyps

Type of lesion	Follow-up period (years)							Total
	0.5	~1	~2	~3	~4	~5	5.1~	
Hyperplastic polyp	95(1)	56(1)	80(2)	49(3)	46(4)	30(1)	24	380(12)
Gastritis polyposa	71	43	35	13	8	10	14	194
Metaplastic polyp (ATP)	20	12	7	7	7	3	2	58(1)
Others in which biopsy was not done	187	100	93	62	11	7	12(1)	472(1)
Total	373(1)	211(1)	215(2)	131(3)	72(5)	50(1)	52(1)	1104(14)

Numbers in the parentheses show the grown-up polyp.

increased in size were small sessile polyps with marked surface reddening, appearing in the antrum (Table 4). The age of the patients averaged 53. The stage of the increase in size in 12 hyperplastic polyps was assigned to the beginning of the follow-up course in only one case, mostly to 3 to 4 years. The change in size was always transient, and a long-standing growth was never experienced. An increase in size seen in a few cases is, therefore, probably due to a secondary cause such as inflammatory change superimposed on these polyps.

Fig. 11(a) shows a polyp in the antrum, and Fig. 11(b) shows the gastrocamera picture of the same case 2 years before. On comparison of these two pictures, a reddening with small elevation was seen in Fig. 11(b) corresponding to the place of the polyp in Fig. 11(a). Since we have experienced 7 such cases, some of gastric polyps might occur as a "polypbud" with a histologic feature under the red color tone similar to that of hyperplastic polyp from the beginning. After actual

TABLE 4. 12 cases with hyperplastic polyp which increased in size during the follow-up period.

Case No.	Sex	Age	Location	Form	Observation period (years)							
					(0.5)	1	2	3	4	5	6	7~
1	F	59	Antrum	Small sessile	↓	●	↓					
2	F	66	Antrum	Small sessile	↓		●	↓				
3	F	60	Antrum	Small sessile	↓			↓	●			
4	M	55	Antrum	Small sessile	↓		↓	↓	↓	●		
5	F	60	Antrum	Small peduncu.	↓	↓	↓	↓	↓	↓		
6	F	64	Antrum	Small sessile	↓			↓	↓	↓	●	
7	M	50	Corpus	Small sessile	↓	↓						
8	F	58	Antrum	Small peduncu.	↓	↓	↓	↓	↓	↓	↓	
9	F	51	Antrum	Small sessile	↓				↓	↓	↓	
10	M	69	Antrum	Small peduncu.	↓	↓	↓	↓	↓	↓	↓	
11	F	59	Antrum	Small sessile	↓			↓	↓	↓	↓	
12	M	64	Corpus	Middle peduncu.	↓	↓	↓	↓	↓	↓	↓	

●: growing up was evidenced ↓: examination

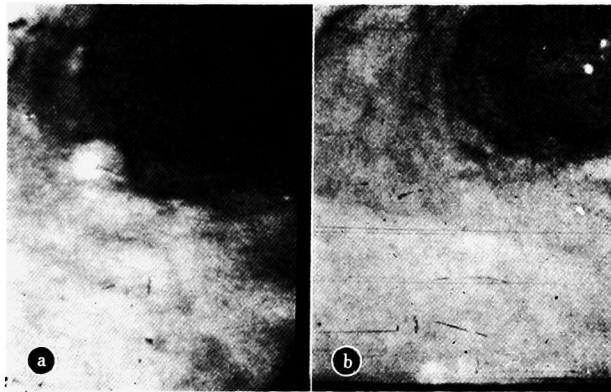


Fig. 11. (a) A polyp in the antrum. (b) Gastrocamera picture of the same stomach taken 2 years before.

observation of 12 such lesions newly detected, however, no tendency toward growth was noted in any case during the follow-up study of 1 to 3 years. Based on this observation, the period between the occurrence of polyp and the completion of its growth is rather short; and most of the polyps clinically detected have probably completed their growth even in such small polyps.

The assumption was substantiated by the result of autoradiographic study using $^3\text{H-TdR}$; labeling index of epithelial cells composing hyperplastic polyp was nearly 0%, while labeling indices of adenocarcinoma, ATP and the mucosa of atrophic gastritis were 13.6%, 10.8% and 10.3%, respectively (Fig. 12).

TABLE 5. *Histological classifications of gastric polyp.*

Polyp consisting of gastric epithelium			Polyp consisting of metaplastic epithelium
Borrmann	1926	Fibroadenoma	
Konjetzny	1928	Hyperplastic polyp	
Schindler	1950	Pseudopolyp	Hyperplastic polyp
Yarnis	1952		Adenoma*
Stout	1953	Gastritis polyposa	Adenoma
Berg	1958	Hyperplastic polyp	Adenomatous polyp
Monaco	1962		Adenoma
Tachadjian	1963		Adenomatous polyp
Nakamura	1964	II-type	I-type
Ming	1965	Regenerative polyp	III-type
Morson	1972	Regenerative polyp	Adenomatous polyp
Debray	1974	Differentiated polyp	Adenoma
Ueno	1975	Gastritis polyposa	Dedifferentiated polyp
			Hyperplastic polyp
			Metaplastic polyp

Types in these classifications which show common characteristics are arranged in the same column. Types with mixed characteristics of two types are put between the columns of the two.

* A type in a different sense from other types

common types and are just considered to be the result of regeneration. These must be distinguished from verrucous protrusion of gastritis erosiva due to inflammatory edema. The histologic feature, particularly of type C, is in continuity with that of hyperplastic polyp. In reality, coexistence of pedunculated hyperplastic polyp and gastritis verrucosa in the same stomach was found in 9.5% in our experience and in 11% of cases of this type by Takasu et al. (1974). Based on these facts, a possibility of growth from gastritis verrucosa to pedunculated hyperplastic polyp has been suggested (Sano et al. 1970). In our results, however, no change from this type into hyperplastic polyp or an increase in size of polyps in gastritis polyposa was experienced. Type D is just a polyp called pseudopolyp. Type E is a special type composed of both hyperplastic epithelia and proliferated lymph follicles. For the study of gastric polyp, therefore, it will be necessary to investigate each type of gastritis polyposa as well as other polyps.

Since Carey and Hay (1948) stated, based on the result of their follow-up study, that there was no direct relationship between gastric carcinoma and gastric polyp, gastric polyp is considered mostly to be benign. Yarnis et al. (1952) found polyp-cancer in 2 or 6.7% out of 30 cases, Sano (1968) in 5 or 7% of 69 pedunculated polyps, Sugano et al. (1968) in 5 or 9% of 53, and Nakamura (1968) in 3 or 4.8% of 62 polyps. In our result, malignant degeneration was suspected in 5 out of 61 polypoid cancers and 236 gastric polyps operated; that was 2% of 236 gastric polyps. The evidence of malignant degeneration in gastric polyp is that carcinoma is limited to a small part of the lesion showing mostly histologic features of benign gastric polyp. Even in this criterion, however, the original nature of these lesions cannot be known definitely; whether they were gastric polyp undergoing malignant degeneration or carcinoma from the beginning is uncertain. In reality, no case of polyp which changed into cancer was experienced in 1,016 polyps followed-up by biopsy.

Since the existence of gastric polyp composed of metaplastic epithelium was first pointed out with the special reference to gastric carcinoma by Morson (1955), this type of polyp has been separated from other polyps by Nakamura (1964) and by Ming and Goldman (1965). In Japan, this type is called ATP (atypical epithelium), and attention is focused on its relationship with cancer (Nakamura et al. 1966). Actually, coexistence with gastric cancer was found in 40% by Ming, in 75% by Berg (1958), in 15.6% by Nakamura and in 13.2% in our experience. In foreign countries, these are considered mostly to be neoplastic in nature for their marked atypism and for their special reference to carcinoma, and are called adenomatous polyp (Ming and Goldman 1965; Evans 1966) or adenoma (Morson et al. 1972a; Debray and Martin 1974), like adenoma of colonic polyp (Morson et al. 1972b). However, it is really difficult to know whether each of this type is neoplastic in nature or hyperplastic reaction in origin. The reason for this is twofold. First, no tendency of the growth was seen in this group of polyps during the clinical course of our follow-up observation. The growth of a neoplastic lesion may persist in the same excessive manner in the clinical course though it is not necessarily seen (Meissner and Warren 1971). Second, all grades of atypism were seen in every polyp of this type, showing histological continuity with one another; a polyp showing little atypism with many goblet cells, Paneth cells and a large mucin content in the cytoplasm may be safely said to be of neoplastic nature, while a polyp showing marked atypism with the reduced mucin content in the cytoplasm is not easily differentiated from carcinoma. The latter one might be called adenoma, if this could be exactly distinguished from carcinoma *in situ* or well differentiated tubular adenocarcinoma. In general, most of polyps composed of the metaplastic epithelium detected in our country revealed low flower bed-like elevation with a broad base, mostly within 2 cm in size, in which atypical epithelium was limited to the surface and the foveolar portion of the glands (Sugano et al. 1971). Sugano et al. (1971) suggested two possibilities for the outcome of these atypical epithelium: differentiation to intestinal metaplasia and transformation into cancer. These low flower bed-like lesions may correspond to those described by Ming and Goldman (1965) as "earlier lesion". On the other hand, 40% of adenomatous polyps reported by Ming and Goldman (1965) were pedunculated and 80% of them were those over 2 cm in size. The reason for this discrepancy between our country and foreign countries may be threefold. Firstly, the incidence of the lesion may be different in different races. Secondly, many small lesions as below 1 cm in size have been found clinically by routine endoscopic examination as well as biopsy in Japan. Thirdly, the histologic criterion for malignancy varies from one author to another and a consensus is not arrived at in this respect. Recently, Nakamura (1972) made a change on his classification reported in 1964, adding a new type which is pedunculated polyp showing more marked atypism and is considered to be neoplastic in nature. This type is rare in our country and 3 or 3.6% out of 83 cases in our series. Based on these facts, it can be said that there are probably two kinds of polyps in ATP: a metaplastic polyp of hyperplastic nature and the

other neoplastic in nature.

It has been known that the incidence of gastric polyp, especially of pedunculated polyp, reveals a tendency of increase with increasing age. However, no report is available on whether and how a small polyp really grows into a large one with advancing age. From the results of our follow-up study, it can be said that most of gastric polyps clinically detected have already completed their growth even in small polyps. The period between the occurrence of gastric polyp and the completion of its growth is rather short and every polyp reaches the different predestined final size in a short time after the appearance, probably within 3 months, and scarcely changes thereafter. Even if an increase in the size may be seen in a few cases (3% or so), it is probably due to a secondary cause superimposed upon the polyp.

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