# GASTRIC SUBMUCOSAL GRANULOMA WITH EOSINOPHILIC INFILTRATION \*

J. Vanek, M.D.

(From the First Department of Pathology, Charles University, Prague, Czechoslovakia)

In view of the great interest aroused by recent work on the so-called eosinophilic or histiocyto-eosinophilic granuloma (Beck, 1943, Skorpil, 1946), I am presenting several cases showing in the submucosa of the gastric antrum granulation tissue of a peculiar type associated with eosinophilic infiltration.

#### REPORT OF CASES

#### Case 1

K. E., a male, 42 years old, had been suffering from "stomach trouble" for some time. He had lost weight and had symptoms pointing to pyloric stenosis. The gastric juice showed normal hydrochloric acid values. Roentgenograms showed pyloric stenosis with a thickening of the mucosa and some gastric retention. Gastric resection (Péan-Rydygier) was performed.

The surgical specimen (no. 6584/44) consisted of the pyloric part of the stomach and was 9 cm. in length. The mucous membrane showed no defect or scar and was freely movable. In the submucosa near the pylorus there was a soft, almost transparent, ill defined node, the size of a small plum, covered with normal mucous membrane. On section it was grayish white to yellow and the cut surface presented many small openings.

Microscopically, the mucous membrane showed atrophic gastritis with islands of metaplastic glands of intestinal type. There was considerable lymphocytic and also a moderate eosinophilic infiltration of the stroma. The lymphatic glands of the lesser curvature showed some hyperplasia.

The node in the submucosa of the pyloric part consisted of cells of the following types (Fig. 5): (1) Fusiform cells with ill defined plasma and oval nuclei poor in chromatin, obviously fibroblasts. Some of these cells were star-shaped. Between the cells a loose network of collagenous fibers could be seen. (2) Irregularly distributed lymphocytes, occasionally accumulated to form rudimentary lymph follicles. (3) Numerous eosinophilic cells of polymorphonuclear type, distributed evenly throughout the pathologic tissue.

The arterioles and capillaries were rather numerous. In addition there were small, round cavities lined with endothelium, obviously corresponding to the openings seen on gross examination. Some of them

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appeared empty while others were filled with a homogenous or foamy substance staining pink with eosin and containing a few lymphocytes. The larger cavities were surrounded by loose fibrous tissue. Undoubtedly all of these cavities were dilated lymphatic vessels.

The relation of the node to the neighboring structures was of interest. The muscularis mucosae was well preserved, in part, separating the abnormal tissue from the mucosa. In places, however, the tissue penetrated between its fibers, and at some points it reached the mucosa. Toward the duodenum it could be traced between the glands of Brunner. In the opposite direction it stopped in the submucosa. Everywhere its borders were ill defined, lacking any tendency to encapsulation. The mucous membrane covering this particular tissue was somewhat thinned out.

#### Case 2

O. Z., a woman, 64 years of age, had been complaining for about 6 months of pain below the processus xiphoideus, especially during meals. The pain was persistent, not accompanied by belching, and disappeared at rest. There was no hunger pain at night. Vomiting occurred once only, just after a meal. The patient lost 10 kg. of weight. She had not been treated previously. On palpation no resistance or tenderness of the epigastric area was found. Roentgenograms revealed a tumor of the prepyloric part of the stomach. At operation the stomach was found to be freely movable and small. In the prepyloric part a soft, elastic resistance the size of a plum was felt. Resection according to the method of Péan-Rydygier was performed and the patient left the hospital 19 days later in good condition.

In the resected stomach (no. 3991/45), about 2 cm. above the pylorus, there was found a polypoid growth, 2.7 by 1.6 by 1.4 cm. (Fig. 1). It was soft and elastic, and its smooth surface had a brownish violet color. The stalk was 1 cm. long and as thick as a quill.

Microscopically (Figs. 2 and 3), the bulk of the polyp was formed of a peculiar tissue localized to the submucosa. It consisted of fibroblasts and lymphocytes, partly arranged in formations similar to lymph follicles and of numerous, evenly distributed eosinophilic leukocytes. The whole tissue was rich in delicate capillaries and arterioles. Occasionally, cavities with endothelial lining were found, containing a pink substance; they obviously corresponded to lymphatic vessels. The mucous membrane covering the polypus was ulcerated and for the most part replaced by ordinary granulation tissue. The muscularis mucosae was preserved in the stalk only, from which its bundles radiated into the polypoid mass.

# Case 3

S. K. was a male, 55 years old, who had contracted a syphilitic infection at age 30 and was treated with neosalvarsan. At about 35 years of age he noticed an indefinite pressure in the epigastrium, especially when his stomach was empty in the afternoons.

He had a feeling of fullness and suffered from belching and sour regurgitation. He often vomited recently taken or partially digested food and bitter-sour fluid. Gastric ulcer was diagnosed, and the complaints disappeared after treatment. Four years before the symptoms had recurred. An operation was suggested but not carried out. A year later he was admitted to the medical clinic owing to a lung complaint. Inflammatory infiltration of the left lung was diagnosed. Roentgenograms of the stomach, taken at the same time, gave the following result: "The stomach showed normal tonus; in the posterior wall of the antrum there was an immovable polypoid formation, the size of a cherry stone. The pyloric passage was free. No retention could be demonstrated, and pressure at the pyloric bulb produced no pain. Three and a half hours after the barium meal, a small remnant was still seen in the stomach while the bulk of the barium had passed into the small intestine." During the patient's further stay at the hospital he did not complain of stomach trouble. On December 10, 1945, the hemoglobin was 105 per cent; erythrocytes, 4,970,000; color index, 1.06; leukocytes, 7,800; differential count: segmented, 55.2 per cent; transitionals, 2.4 per cent; eosinophils, 1.6 per cent; basophils, 0.8 per cent; mononuclears, 8 per cent; lymphocytes, 31.2 per cent; plasmacytes, o.8 per cent; thrombocytes, normal in number; reticulocytes, 8 per 1,000. Gastric juice (free/total acidity): 32/50, 9/17, 4/13, 30/46, 48/60. The Wassermann reaction was repeatedly positive. Tests for occult blood were positive on several occasions. Blood sedimentation rates were 83, 101, 93, and 103 mm. per hour (Westergren). During treatment with potassium iodide the infiltration of the lung slowly receded and eventually almost disappeared. The patient was then admitted to the second surgical clinic. At that time, the state of nutrition was poor. Percussion of the lungs was normal but there were some ronchi and râles over the left apex of the lung.

In view of the roentgenologic findings, the medical consultants advised operation. A laparotomy was performed under local anesthesia. The stomach was of normal size but there were many thick, flat adhesions, especially on the posterior wall. The duodenum, particularly its bulb, was surrounded and slightly strangulated by firm adhesions which extended to the lower surface of the liver and to the gallbladder. The wall of the latter was not particularly thickened, and no calculi were seen. After separating the adhesions a rigid, localized thickening of the serosa was seen on the anterior wall near the lesser curvature and just above the deformed pylorus. Resection was performed according to Péan-Rydygier. In the submucosa of the prepyloric part a polypoid formation was found.

The postoperative course was uneventful. The patient left the hospital 17 days later. Blood count, taken at that time, revealed: Hemoglobin, 70 per cent; erythrocytes, 3,290,000; leukocytes, 7,600; color index, 1.06; differential count: segmented, 56 per cent; transitionals, 3 per cent; mononuclears, 2 per cent; eosinophils, 1 per cent; basophils, 1 per cent; lymphocytes, 37 per cent.

The patient was seen again 4 months later. He had no complaints, except for persistent coughing. Roentgenograms still showed a shadow over the left apex. Blood counts: Hemoglobin, 65 per cent; erythro-

cytes, 3,200,000; color index, 1.01; leukocytes, 11,800; differential count: segmented, 80 per cent; transitionals, 5 per cent; mononuclears, 0 per cent; basophils, 0 per cent; eosinophils, 0 per cent; lymphocytes, 15 per cent. In the sputum no eosinophilic leukocytes nor Charcot-Leyden crystals were found.

The resected part of the stomach was fixed in a 10 per cent formol solution and submitted for examination. On gross examination (no. 13118/46) no ulcer or scar was visible. In the antrum, 2 cm. from the edge of the specimen, a small polypoid growth was found. Microscopically, the gastric mucosa was practically normal. The polypoid formation was due to an accumulation of abnormal tissue in the submucosa. It had an edematous appearance and was composed of loosely arranged, delicate collagenous fibrils, and of cells with ill defined contours containing elongated, oval nuclei poor in chromatin. Numerous typical eosinophilic leukocytes were distributed in this tissue, particularly in its superficial layers. Lymphocytes, also rather numerous, occasionally showed an arrangement resembling lymph follicles. Besides arterioles and capillaries there were several cavities lined with endothelium. They contained homogenous material staining pink with eosin. The muscularis mucosae covered by the structures described was separated into bundles (Fig. 6), except the most superficial layer, which had preserved its normal parallel arrangement. The peculiar tissue could be traced between the muscle bundles as far as the bottom layers of the mucosa. Toward the surface of the mucosa the eosinophils decreased in number. and the most superficial layer appeared normal except for scattered eosinophils. The pathologic tissue itself showed no sharp lateral delimination from the normal submucosa. As the whole specimen could not be examined microscopically for technical reasons, the mucosa was carefully dissected from the muscularis, but no further foci of a similar appearance were found.

# Case 4

A. F., a man, 47 years old, had been in apparent good health until the age of 23, when a left-sided herniotomy was performed. At the age of 45 the same operation was performed on the right side. For 10 years he had been complaining of stomach trouble. Three years previously he reported burning and stabbing pains in the epigastrium, and a gastric ulcer was diagnosed. Seven weeks prior to admission he vomited sour fluid stained with bile. Over a short period he lost 8 kg. of weight. Carcinoma of the antrum was suspected and the patient was admitted to the hospital. The epigastrium was tender to pressure. The gastric fluid had normal acidity. The test for occult blood in the stools was negative. The evening temperature was 37.6° C. without any detectable reason. The Wassermann reaction was negative. Blood counts: Leukocytes, 3,100; erythrocytes, 4,800,000; hemoglobin, 90 per cent; color index, 0.93; differential count: segmented, 53 per cent; transitionals, 5 per cent; eosinophils, 3 per cent; lymphocytes, 39 per cent. Roentgenograms revealed stenosis of the prepyloric part of the stomach, believed to be due to an ulcer in view of the

long history and the normal peristalsis in the stenosed part. Delayed evacuation had not been observed. As cancer could not be excluded, operation was advised.

At operation the pyloric part of the stomach was found to be thickened but there was no sign of a malignant growth. On the lesser curvature typical signs of an ulcer were found. Resection of two-thirds of the stomach according to Billroth II was performed.

On gross examination of the resected part (no. 11/45), a deep ulcer was visible at the lesser curvature about 3 cm. above the pylorus. The stomach wall was considerably thickened and scarring extended as far as the pylorus. Near the edge of the ulcer a grayish white, sharply defined structure the size of a pea was found.

Microscopically, a typical deep ulcer with a calloused base was seen. The edges of the ulcer were partly covered with epithelium. The remaining mucosa was infiltrated by lymphocytes and contained many lymph follicles. The muscularis propria was interrupted by the ulcer, and both its ends were typically raised toward the mucosa. On one side the muscularis propria met the muscular layer of the mucosa, and both were directed toward the scar tissue at the base of the ulcer. On the other side the muscularis mucosae was divided into isolated bundles (Fig. 4). Between these and the muscularis propria a peculiar connective tissue growth was present, thrusting the muscular layers apart and reaching up to the mucosa and to the regenerated epithelium at the edge of the ulcer. From the base of the growth it was separated by a thin layer of connective tissue, rich in collagenous fibrils. It was sharply defined from the muscularis propria.

The structure of this pathologic tissue was almost a replica of that seen in the preceding cases, so that a detailed description appears superfluous. The collagenous fibers, however, were noticeably more numerous, and the cellularity somewhat less.

What makes this case particularly remarkable, however, was the fact that the eosinophilic growth was found in the immediate neighborhood of a peptic ulcer of otherwise trivial appearance. One may question whether the growth or the ulcer was pre-existent. The first possibility cannot be excluded although the ulcer was not situated exactly above the growth. If, however, we accept the view that the latter was secondary to the ulcer, it is necessary to stress the fact that the growth was by no means identical with simple granulation tissue such as is commonly seen at the base of ulcers and may contain a certain number of eosinophils.

#### Case 5

M. B. was a female, 56 years old, with a history of pneumonia in childhood. At the age of 34 she had icterus which reappeared at the age of 46. For 10 years she had been complaining of pressure in the stomach which usually increased after meals. She had suffered from heartburn and belching, and alternative diarrhea and consti-

pation. About 1 year before these symptoms had improved. For the past 2 years she had felt increasingly short of breath, chiefly at night, and complained of stabbing pain in the chest accompanied by a feeling of anxiety. During the past few years she had lost much weight. On admission, the liver was not palpable. In the middle of the epigastrium a resistance was felt which was only slightly tender to pressure. The patient left the hospital in a somewhat improved condition, but 2½ months later she was readmitted because of recurrence of pain and pressure in the epigastrium. Roentgenograms revealed a polypoid formation of the mucosa in the pyloric part of the stomach. In view of the normal acidity of the gastric juice and the normal blood sedimentation rate, cancer seemed improbable. At operation a movable polyp the size of a cherry, with a thin stalk, was removed from the pyloric part of the anterior wall of the stomach. At the same time the gallbladder containing calculi was removed. Four days after operation the patient developed diarrhea and a sharp rise in temperature (40.5° C.). She died with signs of peritonitis.

On gross examination the resected polyp (no. 896/44) was soft and gray. Microscopically, it was covered with normal mucosa. The bulk of the tumor consisted of a tissue showing the same pattern as in the preceding cases, but for minor differences. The network of collagen fibers was noticeably more dense, and infiltration with lymphocytes and eosinophilic cells was less intense. The muscularis mucosae was dissociated into small bundles at the whole periphery of the polypus by the pathologic tissue, which penetrated into the basal layers of the mucosa.

Autopsy (no. 1505/44) revealed a diffuse purulent peritonitis due to infection with *Staphylococcus pyogenes aureus*. In addition to the artefacts produced by the operation, early osteitis deformans of the skull and slight senile atrophy of the brain were found. No further tumor could be demonstrated in the stomach.

#### Case 6

P. A. was a female, 56 years old. For the previous 3 months she had complained of frequent spasms of pain in the gastric region, which radiated into the back and under the left scapula. The patient had lost 14 kg. of weight. Physical examination showed tenderness in the epigastric region, where a painful, movable mass was palpable, extending from the borderline of the enlarged liver to 3 fingerbreadths above the umbilicus. Roentgenograms revealed a hypotonic stomach. A dish-shaped, filling defect, 2.5 by 1 cm. wide, with sharply defined borders, was seen. This was situated in the lesser curvature, immediately above the angulus, and close to the anterior wall. The folds of the mucous membrane in the vicinity of the defect were somewhat roughened. Passage through the pylorus was free. A tumor and hypotonic elongation of the stomach were diagnosed.

At operation a tumor was found in the angular part of the lesser curvature, protruding into the lumen. A Péan-Rydygier resection was performed. After the operation the patient developed vomiting and diarrhea followed by dehydration and circulatory collapse. She died 2 days later.

On gross examination the surgical specimen (no. 12811/45) showed a tumorous mass the size of a small walnut, protruding above the level of the mucosa and sharply defined against the muscularis. It was yel-

lowish and soft. Microscopically, the tumor was composed of collagenous fibers with numerous fibroblasts and fibrocytes. Typical eosinophilic leukocytes were evenly spread over the whole tissue but their number was much less than in the preceding cases. Some lymphocytic infiltration was seen also, sometimes forming rudimentary lymph follicles. Occasionally, isolated plasmacytes were found. There were many capillaries and arterioles surrounded by concentrically arranged collagenous fibers and dilated lymphatics were seen as in the preceding cases. The tissue described was situated in the submucosa. It was separated from the muscularis propria by a thin layer of a rather dense and acellular fibrous tissue, and at the lateral borders the collagenous fibers of the submucosa took a course parallel to the surface of the tumor, thus forming a kind of capsule. Toward the mucosa the delimitation was less definite, the muscularis mucosae being separated into single bundles. The mucosa covering the whole area was much thinned out by superficial ulceration, and rather heavily infiltrated with inflammatory cells.

The remaining gastric mucosa showed severe chronic gastritis with widespread metaplasia of the glands to the intestinal type.

At autopsy (24 hours after death) no signs of peritonitis were disclosed. The remaining parts of the stomach contained no tumor. The mucous membrane of the small intestine was covered with mucus.

#### DISCUSSION

In all 6 cases a peculiar lesion was found in the submucosa of the stomach. Histologically, it consisted of the following elements: (1) Basic connective tissue composed of mesenchymal elements, *i.e.*, fibroblasts or fibrocytes, and loosely arranged collagenous fibers. In the first 3 cases this tissue showed much edema. (2) Infiltration with eosinophilic leukocytes and lymphocytes, the latter being occasionally accumulated in rudimentary lymph follicles. (3) Arterioles, blood and lymph capillaries.

Clinically, all of the cases have many features in common. In case 1 the growth caused symptoms of stenosis and had to be removed by resection. In case 2 the pain under the processus xiphoideus, occurring especially after meals, was most probably due to the pull exerted by the stalk of the polyp which was seated 2 cm. above the pylorus. The third patient had been complaining for 20 years of symptoms suggesting a gastric ulcer, but in the resected stomach no ulcer was found. In case 4 a calloused ulcer had narrowed the gastric antrum, and the growth in the submucosa at the border of the ulcus may have been aggravating the stenosis. Case 5 was complicated by the presence of cholelithiasis and chronic cholecystitis, but the patient's complaints may have been due, at least partly, to the tumorous proliferation in the submucosa of

the gastric antrum. The sixth patient complained for 3 months of recurring abdominal pain which was obviously caused by the growth in the stomach. It is therefore evident that the process described is by no means a mere accidental finding, but may cause serious symptoms requiring operation.

The gross appearance of the lesion was similar in all 6 cases, although there were some minor differences. The tumor-like tissue was situated mainly in the submucosa, forcing the mucous membrane upwards either as a flat prominence (cases 1 and 6) or in the form of a pendulous polyp (cases 2, 3, and 5). In case 4, which is exceptional in this respect, it was situated at the border of a calloused ulcer. On section the tissue was grayish yellow and soft, having an edematous appearance (cases 1 to 3), or rather whitish, firm, and elastic. In some cases (case 1) the cut surface was studded with small openings which turned out to be dilated lymph vessels.

The microscopic findings in individual cases, though having the features in common as given above, showed variations, which, however, were largely quantitative. The differences concerned the amount of collagenous fibrils and the proportion of infiltrating cells. As a matter of fact, these 6 cases have not been grouped chronologically, but according to these differences. Thus in the first 2 the tissue in question was very loosely built, the collagenous fibrils being scarce, the nuclei of the fibrocytes for the most part vesicular, and the migratory cells, both eosinophils and lymphocytes, fairly numerous. On the other end of the series are cases 5 and 6 with much greater quantity of fibers, more mature fibrocytes, and a smaller number of migratory cells. The remaining 2 cases take an intermediate position.

To evaluate these differences it is essential to attempt a classification of the process. This may be considered as an inflammatory lesion of chronic granulomatous character, or as a neoplastic process, viz., a fibroma, with a secondary inflammatory reaction. If we accept the first point of view, it is clear that the differences may be explained on the basis of the different ages of the process, the highly cellular lesion poor in collagen being the more recent one. If, however, we regard the pathologic new-formation as a fibroma, the differences in cellularity would correspond to various degrees of maturity of the neoplasm.

Personally, I am inclined to consider the process as a granuloma. However, the fact should be stressed that it is by no means identical with the "eosinophilic granuloma," such as is found in bones, and may also occur in soft tissues (Škorpil). There are two main differences between these two lesions, not to speak of localization. In the eosino-

philic granuloma the basic cells are not fibroblasts as in my cases, but histiocytes or reticulum cells. Furthermore, the eosinophils in the first process are densely accumulated in some places while in others they are lacking, whereas in my cases they are evenly distributed throughout the lesion.

To avoid confusion, I therefore suggest—pending a better denomination—the somewhat clumsy term "gastric submucosal granuloma with eosinophilic infiltration" for the lesion described. However, I am aware that in some cases, in which the infiltration with migratory cells has greatly receded, the differentiation from a true fibroma may be rather difficult. In such a case even the criteria given by Hueck may be of little help. In fact, I venture to say that some of the alleged fibromas of the stomach actually were of inflammatory origin.

It is obvious that this question cannot be settled satisfactorily unless the etiology of the lesion is cleared up. In this respect, however, very little can be inferred from my own cases, except that the outstanding eosinophilic infiltration of the pathologic tissue is suggestive of some allergic phenomenon.

Kaijser, in 1937, reported 3 cases of allergic disease of the alimentary tract. Of these, the third case is of special interest as the lesion found in the stomach was studied microscopically. The patient was 53 years old and since his youth had been known to be allergic to onion; he had vomited after eating the smallest quantity. One of his brothers had suffered from attacks of migraine, and one aunt had bronchial asthma. At 23 years he had contracted a syphilitic infection, but the Wassermann test later became negative. He had since received no antisyphilic treatment. For 12 or 13 years he had been complaining of gastric trouble, especially in the spring. The diagnosis of gastric ulcer was made and he was repeatedly treated by diet. The gastric trouble increased during the last 18 months. He complained often of hunger pains which disappeared after a meal, but no hunger pains during the night were reported. Roentgenograms suggested an ulcer of the lesser curvature, about 3 cm. above the pylorus. At operation the pylorus was found to be largely adherent to surrounding structures and the serosa was thickened and scarred. A resection according to Billroth I was performed. A blood count taken 9 days after the operation revealed 26 per cent eosinophilic leukocytes. The resected part of the stomach showed diffuse thickening of the walls, particularly toward the pylorus, which was caused chiefly by edema of the submucosa. Neither gross nor microscopic examination revealed an ulcer. The submucosa of the pyloric part of the stomach was very edematous. In its superficial layer there was considerable inflammatory

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infiltration, consisting of neutrophilic leukocytes, lymphocytes, and very numerous eosinophilic leukocytes. This infiltration was most pronounced at the top of the folds of the mucous membrane and increased toward the pylorus. The muscularis mucosae was split up into single bundles. Between these, there was inflammatory edema and considerable infiltration consisting mainly of eosinophilic leukocytes. In places, the submucosa showed very many dilated lymphatic vessels, some of them filled with eosinophilic leukocytes, lymphocytes, and endothelial cells, which last were swollen and proliferating, so that they obliterated the lumen. There was much less inflammatory infiltration in the deeper layers of the submucosa. The muscularis propria showed very slight inflammatory infiltration composed again of eosinophilic leukocytes which were mainly situated along the vessels.

Through the courtesy of Dr. Kaijser I was able to study one original slide from that case. The splitting up of the muscularis mucosae, as described by the author, was clearly seen, but in addition to this there were fibroblastic nuclei, the number of which definitely exceeded what might be expected in pure edema. It therefore appears that the lesion has some similarity to that found in my cases, although in the submucosa there was infiltration with inflammatory cells only, which is at variance with my own findings.

In view of the allergic factor in Kaijser's case, I have carefully reviewed the clinical histories of my cases, but I could not find anything definite in this respect. Nor did the hemograms show anything particular, the number of eosinophils at most approaching the upper limit of normal values. Pending further observations, I therefore feel that the question of etiology is to be left open.

#### SUMMARY

In 6 patients who had suffered from stomach trouble of various kinds, a peculiar lesion was observed consisting of more or less loose collagenous tissue with fibroblasts, lymphocytes, and eosinophilic polymorphonuclear leukocytes. The pathologic tissue thus composed appeared as a circumscribed focus in the submucosa, spreading toward the mucosa of the stomach. Macroscopically, it caused a bulging of the mucosa, and in some cases even a polypous formation. In one case it was situated at the border of a chronic peptic ulcer.

The composition varied somewhat as to the proportion of the collagenous fibrils to the migratory cells, particularly the eosinophils. This seemed to be due to a different degree of maturation of the pathologic tissue.

The lesion is apparently a granuloma, which, however, is definitely different from the "eosinophilic granuloma" of the bone or soft tissues. To point out this difference the provisory term "gastric submucosal granuloma with eosinophilic infiltration" is suggested. In view of a case described by Kaijser, an allergic etiologic factor has been considered.

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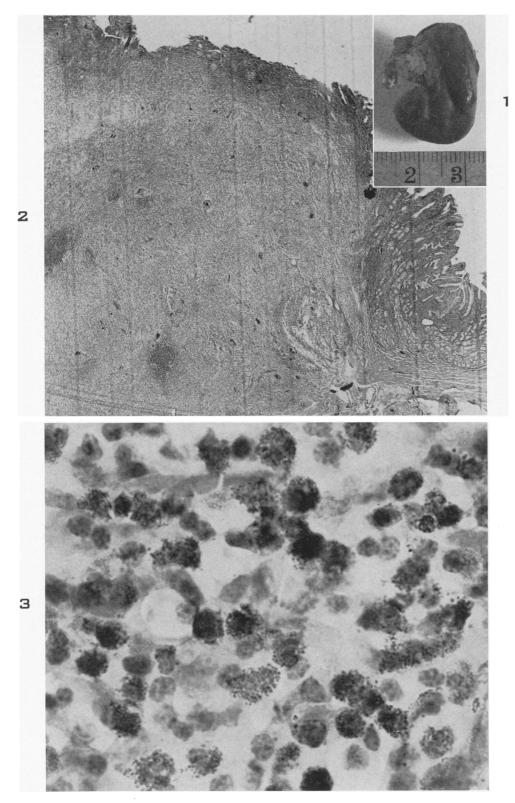
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[Illustrations follow]

# DESCRIPTION OF PLATES

# PLATE 56

- Fig. 1. Case 2. Gross specimen of the pendulous polyp found in the antrum.
- Fig. 2. Case 2. Granuloma enlarging the mucosa and infiltrating the mucosa. The dark areas in the granuloma are foci of lymphocytes.  $\times$  27.
- Fig. 3. Case 2. Higher magnification of the granuloma showing the relatively great number of eosinophilic cells.  $\times$  1000.

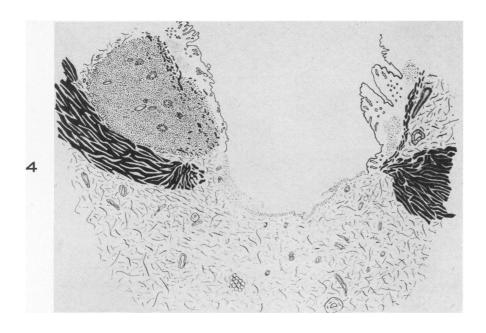


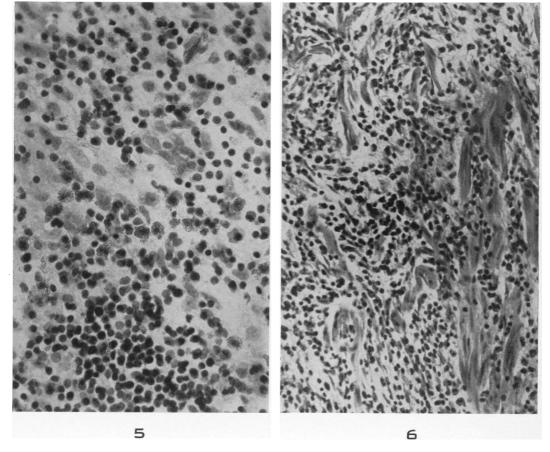
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### PLATE 57

- Fig. 4. Case 4. Drawing to show the topographic relations of the granulomatous tissue in the submucosa to the peptic ulcer. The muscularis mucosae is split into isolated bundles.
- Fig. 5. Case 1. Typical pattern of the lesion in the submucosa includes fibroblasts with swollen nuclei, eosinophilic leukocytes, and lymphocytes. The lymphocytes are grouped as a rudimentary lymph follicle in the lower portion of the field. Hematoxylin and eosin stain.  $\times$  260.
- Fig. 6. Case 3. Splitting up of the muscularis mucosae of the stomach into isolated bundles by the granuloma. Heavy infiltration of eosinophils and lymphocytes. Hematoxylin and eosin stain.  $\times$  180.





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