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JUAN A. DEL REGATO, M. D., *Editor*

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SCHATZKI

MEISSNER

MODLIN

GASTRIC TUMORS

THIS CANCER SEMINAR on gastric tumors took place in Colorado Springs on November 11th, 1961. The attending radiologists, gastroenterologists, pathologists and surgeons were beneficiaries of the didactic presentations and genial discussions of our guest radiologist Dr. Richard Schatzki, our guest pathologist Dr. William A. Meissner and our guest surgeon Dr. John J. Modlin. The publication of these edited proceedings endeavors to extend to a larger reading medical public the fruit of these discussions.

A selection of these cases made the basis of SEMINARIO DE LESIONES GASTRICAS in Guadalajara, Mexico, on April 10th, 1962, during the *Second Mexican Congress of Radiology,* thanks to the generous initiative and hospitality of Dr. Manuel Riebeling, president of the Congress. The Spanish language presentations were made by Dr. Philip J. Hodes, Professor of Radiology, Jefferson Medical College, Philadelphia, and again by Dr. William A. Meissner: they proved to be as eloquent in Spanish as in English. In Mexico, the discussions were opened by Dr. Ignacio Chávez, Professor Emeritus of Surgery, University of Guadalajara. Translated excerpts of these discussions have been added to the Colorado Springs proceedings.

We are thankful to the innumerable colleagues of all specialties who annually contribute for presentation the cases which make the subject of these discussions. We owe a particular word of thanks to the participating diagnostic radiologists who have repeatedly consented to "play the game" and contributed their impressions on the basis of admittedly inadequate data, for they have made it possible for all of us to learn. We are thankful also to the pathologists who have faced with candor the embarrassment of difficult problems. We are all indebted to our guest speakers who have condescended to participate and given so much time and devotion to their presentations; and finally, to our faithful audiences whose interest has brought warmth to these exercises: to all of them goes the credit of the success attained by these CANCER SEMINARS.

With this issue CANCER SEMINAR enters into its third volume of annual publication and adopts a simpler format. The growing demand for this publication and the increasing expense of bringing it to our readers have led us to this change. We hope that it meets the approval of our correspondents everywhere.

J. A. del REGATO, M. D.
Colorado Springs, October, 1962

OUR GUEST SPEAKERS

RICHARD SCHATZKI, M.D.

Associate Clinical Professor of Radiology, Harvard University Medical School, Boston. Doctor Schatzki graduated from the University of Berlin in 1926. For over 25 years he has been an Associate in Radiology at the Massachusetts General Hospital. He is known as one of the outstanding teachers of Radiology in the United States and has made numerous valuable contributions to the literature of Diagnostic Radiology. He was the guest of the Penrose Cancer Hospital.

WILLIAM A. MEISSNER, M.D.

Associate Clinical Professor of Pathology, Harvard University Medical School. Doctor Meissner graduated from the University of Oregon Medical School in 1938. Since 1941 he has been Pathologist to the New England Deaconess Hospital in Boston. He is a recognized authority in Tumor Pathology. He was the guest of the College of American Pathology.

JOHN J. MODLIN, M.D.

Professor of Surgery, University of Missouri Medical School, Columbia, Missouri. Doctor Modlin graduated from the University of Nebraska Medical School in 1938. He was Chief Surgeon of the Ellis Fischel Cancer Hospital. He is recognized as one of the finest young cancer surgeons in the United States. He has made valuable contributions to the literature of Surgery of Cancer. He was guest of the Penrose Cancer Hospital.

1. Primary Malignant Melanoma of the Esophagus

Contributed by C. P. Schwinn, M. D., and W. K. Bullock, M. D., Los Angeles, California

THE PATIENT was a 47-year-old man in October, 1960, when he complained of dysphagia and substernal pain. Esophagoscopy revealed the presence of polypoid masses filling the lumen of the esophagus. There were 23,850 white cells per mm^3 with a normal differential and 11.7 gm per cent of hemoglobin. The esophagoscopy revealed the presence of multiple and large polypoid masses.

Dr. Schatzki: The esophagus contains a large lobulated mass which seems to arise on the left anterior wall. In the region of the mass, the esophagus is dilated, probably not due to expansion by the mass. Distal to the mass, the esophagus is of normal caliber, but surprisingly enough, not collapsed as if something were lying in it. No abnormal soft tissue mass is seen outside the esophagus. This rules out a tumor growing into the esophagus from the outside, like lymphoma of the mediastinum or bronchial carcinoma.

The differential diagnosis of large filling defects in the esophagus concerns predominantly three causes: 1. Food. 2. Large benign pedunculated tumor, usually arising high in the esophagus. 3. Carcinoma or carcinosarcoma. Food as an explanation of the defect is unlikely since the dilatation of the esophagus is asymmetrical. In addition, the barium does not run completely around the mass. The shape of the lesion rules out a pedunculated benign tumor.

The most likely diagnosis is a large malignant tumor. Rare tumors like plasmocytoma occur in the esophagus producing large lesions but they are so rare that it is not possible to make a diagnosis. A soft polypoid carcinoma certainly can produce this appearance, particularly the variation which has been called carcinosarcoma.

Dr. Schatzki's impression: CARCINOSARCOMA.

Roentgenologic Impressions Submitted by Mail

Carcinoma	33
Lymphosarcoma	21
Carcinosarcoma	10
Pseudosarcoma	9
Leiomyosarcoma	6
Benign Lesions	37
Others	15

Dr. Schatzki: The largest number of participants called this lesion a carcinoma and I certainly will not disagree with them nor with those who call it a carcinosarcoma. Sarcoma of the esophagus growing in from the outside is extremely uunsual, I do not know if it occurs at all. Practically all lymphosarcomas of the esophagus are secondary to a mediastinal tumor. Leiomyosarcoma I think can be ruled out because there is no mass on the outside. I confess I do not know what pseudosarcoma is. A benign lesion would be highly unusual: the lesion has a rather ragged appearance.

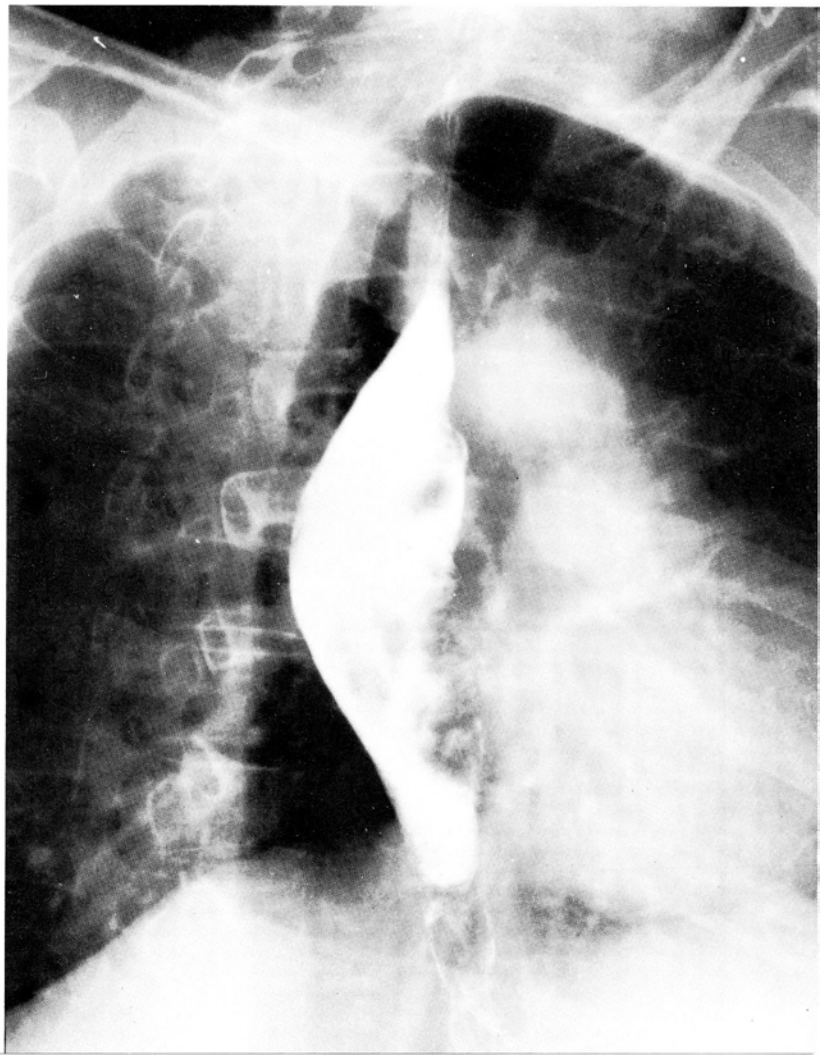
Dr. Regato: Dr. N. Glazer, of Akron, Dr. B. Felson, of Cincinnati, and Dr. J. A. Campbell, of Indianapolis, also suggested carcinosarcoma. Dr. F. Gorishek, of Denver, offered leiomyosarcoma.

Operative findings: On November 2, 1960, the patient was operated upon: the abdomen was first entered; there were no metastases or other abnormalities found. An abdomino-thoracic esophagectomy was performed followed by esophagogastric anastomosis. The esophagus contained three large pedunculated masses arising from the proximal third of the mucosa; they were ulcerated, necrotic and dark-brown in color, measuring 2, 4.5 and 6 cm. in diameter. Two of the nine nodes examined contained tumor.

Dr. Meissner: The low power field of the entire microscopic section shows an ulcerated polypoid mass arising from esophageal mucosa. The esophageal mucosa lies on either side of the stalk of the specimen, suggesting an extreme degree of pedunculation. The lesion is highly cellular and vascular and invades and infiltrates the adjacent structures as a malignant tumor. The tumor cells grow in solid sheets and invade not only the stroma, but the overlying esophageal mucosa as well. The individual tumor cells are mostly polyhedral; several mitoses are present in every high power field. A striking feature of the tumor cells is that many of them contain brown granular pigment. With an iron stain one sees that much of the pigment is not iron-containing, and we can presume then that it is melanin formed by tumor cells, and the diagnosis of malignant melanoma becomes certain.

With the diagnosis of malignant melanoma the only problem remaining is the differential diagnosis between a primary melanocarcinoma of the esophagus or a metastasis. In the intact esophageal mucosa adjacent to the tumor there

Fig. 1—Roentgenogram showing dilatation of the esophagus and large polypoid masses.



is an intimate relationship between remaining epithelium and tumor cells. This involvement of the mucosa could well be direct extension of an underlying tumor and might be seen either in a primary or metastatic melanoma. If one examines the mucosa away from an underlying tumor, there are nests of cells of the junctional nevus type which are definitive proof that the tumor is a primary melanocarcinoma rather than a metastasis. Allen and Spitz have emphasized the fact that one must find a junctional nevus adjacent to melanoma to be certain that the lesion is primary in that location rather than a metastasis.

Dr. Meissner's diagnosis: MALIGNANT MELANOMA.

Histopathologic Diagnoses Submitted by Mail

Primary melanoma	54
Malignant melanoma	45
Metastatic melanoma	8
Carcinoma	7
Hemangioendothelioma	6
Lymphosarcoma	5

Dr. Meissner: It is interesting that metastatic melanoma to the esophagus occurs rather rarely. We tend to forget that malignant melanomas may arise in mucous membranes. The more common sites are the mucous membranes of the anus and the buccal mucosa but it may occur in almost any mucosal surface. In 1954 Dr. Boyd and I reported a malignant melanoma of the middle third of the esophagus which we felt was the fourth verified case; since then there have been additional cases reported, but we could still say that there are less than ten primary malignant melanomas of the esophagus in the literature. Melanomas of any mucosal surface tend to be highly malignant, much more so than malignant melanomas arising from the skin, partly because they become large tumors before they are diagnosed, and partly because the treatment is much more difficult when the melanoma arises in the mucosa than when it arises in the skin.

Dr. Regato: Dr. Lattes, of New York, Dr. R. C. Horn, of Detroit, and Dr. L. V. Ackerman, of St. Louis, made a diagnosis of primary melanoma of the esophagus. Dr. R. M. Delcourt, of Brussels, detected signs of adjacent junctional nevus. Dr. R. Willis, of Leeds, suggested that other parts of the mucosa should be examined for signs of melanosis.

M. B. Dockerty, M.D., Rochester, Minnesota (by mail): I believe this to be a primary malignant melanoma. However, having seen several metastatic melanomas of the gastrointestinal tract, I trust that the contributors will provide data on color of the patient's nails, etc.

Dr. Modlin: I certainly would agree that the resection of the esophagus was indicated in this patient, regardless of whether this was a primary or metastatic lesion for palliative reasons, but I would expect that the prognosis would be rather grim. We have had one patient who had a melanoma arising in the buccal mucosa who developed lymph node metastases in the upper cervical region, treated by bilateral radical neck dissection, and who was well for a period of twelve years before she developed metastasis in the region of the sphenoid sinus; this is one apparently slow-growing melanoma that arose from the mucous membrane.

Dr. Regato: I would like to have Doctor Meissner comment upon this question: "How do you decide whether or not a malignant melanoma is primary in the esophagus or can you really do that?"

Dr. Meissner: The most important thing is the criterion set up by Allen and Spitz: the presence of junctional neval changes in the adjacent mucosa which this case showed very well. We saw this also in the case that Doctor Boyd and I reported. Without this I do not see how one can conclude whether it is primary or secondary. There is nothing that a metastatic malignant melanoma can do that a primary melanoma cannot do except show this junctional nevus change. In any patient with malignant melanoma, one should look for odd sites of primary lesions. The retina, the entire skin and the nail beds should be examined for a possible primary that is not obvious.

Dr. Schatzki: I do not see how anyone could make a radiologic diagnosis of melanoma of the esophagus.

Perry C. Martineau, M.D., Detroit, Michigan: Would Dr. Meissner comment on the diathesis in multiple versus single primary malignant melanoma.

Dr. Meissner: It is interesting that some patients do have a diathesis to the development of multiple malignant melanomas: patients with one malignant melanoma seem to be much more likely to have a second malignant melanoma. In addition, if a patient has one malignant melanoma, all his other nevi seem to become more active, what we call "pathologically active junctional nevi", which is another way of saying that they seem in their way to become malignant.

Fig. 2—Photograph of surgical specimen: large pedunculated dark masses are present at both extremes of the esophagus.

Fig. 3—Low power photomicrograph of edge of tumor mass. The overlying esophageal mucosa shows junctional nevus changes but no continuity with the tumor mass in this field (H & E x 40).

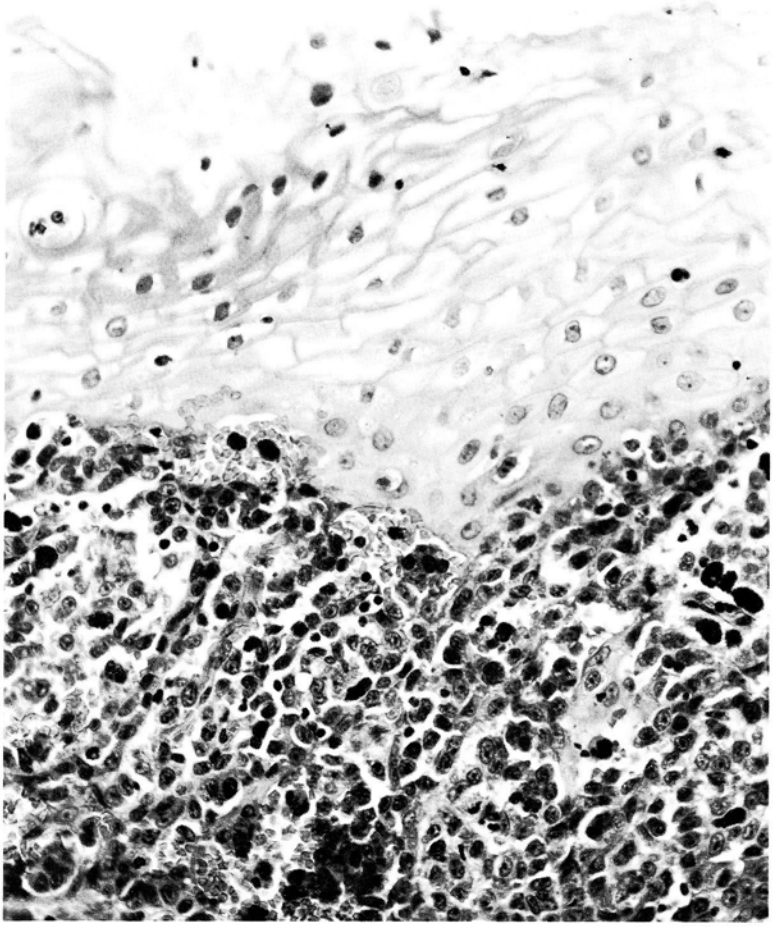
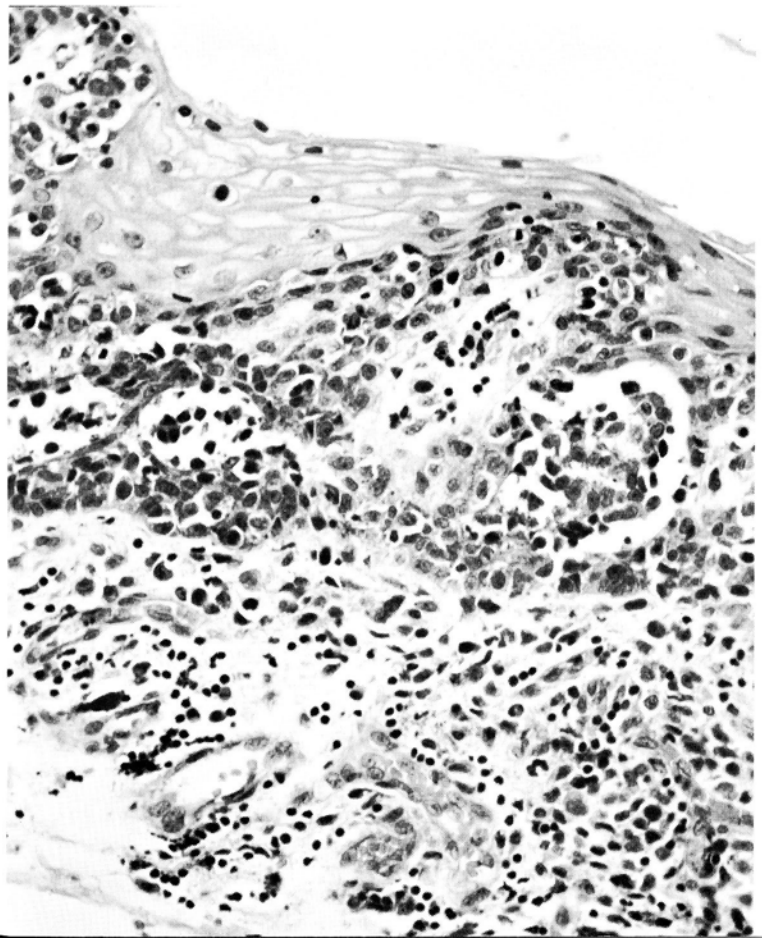


Fig. 4—In this field the darkly pigmented tumor cells extend to the epithelium but there are no junctional nevus changes (H & E x 300).

Fig. 5—Junctional nevus changes in esophageal mucosa near the periphery of the tumor proper. In this field inflammatory cells rather than tumor cells lie beneath the epithelium (H & E x 300).



Subsequent history: The patient did well after operation but four months later had to be admitted because of acute bowel obstruction. An exploration revealed multiple melanotic nodules on the viscera and peritoneum. On April 10, 1961, he expired: at autopsy, there was no recurrence in the region of the esophagus, but there were metastases in the pleura, myocardial sac, peritoneum, serosa of small and large bowel, liver, spleen and bone marrow.

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2. Hypertrophic Gastritis with Anastomosal Ulcer

Contributed by P. P. Newman, M. D., J. G. E. Barham, M. D., A. Ranier, M. D., and E. Cavin, M. D., Lake Charles, Louisiana

THE PATIENT was a 56-year-old man in May, 1959, when he complained of epigastric pain and weight loss. In 1940 he had had a subtotal gastrectomy for perforating duodenal ulcer; there had been subsequent episodes of hematemesis. There was palor but no other important physical findings; the hemoglobin was 8.2 gm per cent and the hematocrit 30%. There was no free hydrochloric acid and the bone marrow showed erythroblastic hyperplasia.

Dr. Schatzki: The difficult question to answer is where the stomach ends and where the anastomosed bowel starts. In addition to the film which the participants have seen I have been shown another film that makes me feel that the large portion of bowel which runs in continuity with the stomach on the patient's right is an abnormally wide anastomosed loop of jejunum, probably the afferent loop. If this is so, then it is possible that all the defects which are visible are caused by huge polypoid folds in a postoperative stomach. The history is that of an anastomosal ulcer. The radiological picture, especially the second film, is consistent with such a diagnosis.

Dr. Schatzki's impression: ANASTOMOSAL ULCER AND GASTRITIS.

Roentgenologic Impressions Submitted by Mail

Adenocarcinoma	48
Lymphosarcoma	39
Hypertrophic Gastritis	24
Others	19

Dr. Schatzki: The majority of the radiologists who interpreted this film made the diagnosis of malignant tumor, either adenocarcinoma or lymphosarcoma; I certainly cannot blame them, because it is just not possible to be sure whether this thing on the left side was stomach or not. If it was stomach, then one had to assume that the peculiar defect in the center was caused by tumor.

Dr. Regato: Dr. J. C. Lemon, of Denver, also suspected edematous abnormalities at the anastomosis; Dr. R. D. Moseley, of Chicago and Drs. J. J. Wolfson, of Albuquerque, Jose Aguilar, of Mexico City, Manuel Esparza, of Chihuahua, and G. Schwarz, of Denver, suggested post-operative hypertrophic gastritis.

Operative findings: In October, 1960, a subtotal gastrectomy was performed: an estimated 85 per cent of the stomach was removed. There was a 2 cm perforation in the smaller curvature area; the gastric wall was thickened to 3 cm in places; there were thickened rugae with polypoid appearance but no gross evidence of ulceration.

Dr. Meissner: The low power field of the section shows a thickening of the entire gastric wall. The thickening actually involves the submucosa and muscularis to a greater degree than the mucosa. The mucosa is not so much increased in thickness as it is thrown up into numerous prominent, enlarged rugae. The serosal surface is covered by an acute inflammatory exudate, and there are foci of chronic inflammatory cells scattered throughout the entire wall. With the trichrome stain at a higher magnification one can see again that the mucous membrane is not appreciably thickened, although there is some excessive formation of mucus in the superficial portions. The submucosa shows a considerable fibrosis and increased vascularity. The increase of mucus is in the necks of the gastric glands. The gastric mucosal glands are orderly and show no adenomatous hyperplasia.

This lesion then represents a thickening of the entire gastric wall due only in small part to mucosal changes and in larger part to a diffuse fibrosis of the submucosa and muscularis. The cause of such hypertrophy of the entire gastric wall, which we can justifiably call hypertrophic gastritis, is inflammation plus obstruction. In an additional slide which was sent to me for photographic purposes, there is something not seen on the routine sections. At one end of the block there is the edge of an active peptic ulcer which appears to be penetrating and probably even perforating through the serosa.

Fig. 1—Roentgenogram of the stomach with multiple filling defects apparently due to polypoid folds.

Dr. Meissner's diagnosis: Active PEPTIC ULCER and HYPERTROPHIC GASTRITIS.

Histopathologic Diagnoses Submitted by Mail

Hypertrophic gastritis	82
Menetriere's disease, Giant rugal hypertrophy	32
Others	6

Dr. Meissner: The nomenclature of this type of gastritis is a little bit confusing. It is a hypertrophic gastritis but it is often called by other names as well: gastritis polyposa, Menetrière's Disease, giant rugal folds, and they all add up to the same thing—that this is hypertrophy of the gastric wall, particularly of the mucosa and submucosa, without an abnormal proliferation of the epithelium. It does not seem to have particular precancerous significance and no one knows in most instances the true cause. This patient was said to have achlorhydria. I would question the validity of the diagnosis of achlorhydria in the presence of a functioning gastroenterostomy.

Dr. Regato: Dr. J. B. Frerichs, of El Paso, Dr. J. Stephenson, of Washington, and Dr. R. Lattes, of New York, all made a diagnosis of giant rugal hypertrophy or Menetrière's Disease. Dr. G. Gricouroff, of Paris, submitted polyposis with vascular hyperplasia and cystadenomatous hyperplasia. Dr. L. Lowbeer, of Tulsa, offered gastritis polyposa plus myoepithelial heterotopia and focal ulceration.

A. P. Stout, M. D., New York (by mail): Gastritis polyposa with marked intestinal metaplasia. There is pronounced hyperplasia of the muscularis mucosa with "Lattes fibers" (strands of smooth muscle fibers passing towards the lumen in the mucosa at right angles to the muscularis mucosa from which they spring). There are also microscopic cysts in the submucosa. This lesion is sometimes associated with carcinoma of the stomach.

Subsequent history: Three weeks after operation the patient complained of nausea for all foods and vomiting of liquids as well as ingested solid foods. On October, 1960, he was reoperated for release of adhesions and dilatation of the esophagus. Since then he has regained 20 pounds and tolerates food well.

Dr. Modlin: The problem which probably faced this surgeon in the operating room was whether or not this lesion was a benign ulcer, or whether it was a malignant process. In these cases the surgeon should always consider gastrotomy and biopsy of various areas within the stomach, and probably rely on his pathologist to help him out of a difficult situation. It is most important to establish the differential diagnosis between cancer and a benign condition because it will alter to a certain extent the type of operative procedure that would be done; the subtotal gastrectomy that was done here was the correct procedure, and I would agree with Doctor Meissner that it is almost inconceivable that this patient had an achlorhydria when he did have such a large peptic ulcer or anastomotic ulcer. It is interesting that this patient apparently required a dilatation of the esophagus. This brings to mind the question of a possible peptic esophagitis and possibly this patient still has problems in the future in regard to peptic ulcer.

Dr. Schatzki: I have long ago learned that it is impossible for the radiologist to differentiate between various forms of gastritis except in very rare ones. We sometimes see individual polyps which we can call "polypoid gastritis", and in very rare instances we see superficial erosions which we can call "erosive gastritis", but usually we have no way of knowing if this is just an acute swelling of the mucosa due to edema or an actual anatomical hypertrophy of the mucosa; so I do not make the diagnosis of hypertrophic gastritis. I have a little different opinion from Doctor Meissner about the various forms of large folds there. We see big folds in the post-operative stomach quite frequently without any evidence of obstruction and in wide open anastomosis we see very large folds. Some of these patients may not have gastritis, they just have big folds. As far as throwing hypertrophic gastritis, giant folds and Menetrière's Disease in one group, I have my objections. The giant folds of the stomach is a very definite entity described by anatomists several decades ago that has been forgotten. This is not a diffuse enlargement of all the folds of the stomach but a very localized area usually on the greater curvature side of the body of the stomach, a little bit above the middle of the stomach. This localized area of increased folds of the stomach may be present without any symptoms and in the cases which we have followed over many years it never changes, never gets worse, never gets better. I think that if gastritis is found in these cases, it is just secondary to the giant folds.

I have never read Menetrière's original article. What I just called "giant folds" is frequently now called "Menetrière's Disease".

Dr. Meissner: I would agree that what appears to the radiologist as giant folds or if you want to use the term, "hypertrophic gastritis", has often turned out to be nothing when the stomach is opened. These giant folds collapse and it looks like normal mucosa. I suppose in these instances one can say, as Doctor Schatzki suggests, that the prominent folds are due to edema. In this case at hand the folds are made prominent by the presence of fibrosis. That is why we can see them both grossly and microscopically; this is not always the case. We do not use the term "Menetrière's Disease" in our laboratory; I think it is unfortunate that people who have read his article have interpreted it in different ways. One recent review that I read says that Menetrière's described a "hypertrophic" type of hypertrophic gastritis and a "hyperplastic" type of hypertrophic gastritis; this confused me a little as to just what hypertrophic gastritis actually meant. Menetrière did describe a type of lesion which, as Doctor Schatzki says, is localized to one portion of the stomach as though one area of the gastric mucosa alone is involved in the process. In this there are giant rugal folds which remain more or less permanently and which may be associated with hypoproteinemia for reasons no one understands. Perhaps it is due to malnutrition. Perhaps it is due to loss of plasma from these giant rugal folds. Perhaps it is due to, as has recently been suggested, a faulty synthesis of protein or something which interferes with the storage of protein; but at any rate some of these patients have hypoproteinemia. The second type that Menetrière described involved the entire stomach and there were multiple polypoid projections throughout the entire stomach. If we use "Menetrière Disease" we should use it for both types, but they are quite different processes and I would like to comment on the second type of Menetrière's Disease when we come to Case 3.

H. J. Caes, M.D., Sioux City, Iowa: I would like to ask Doctor Meissner if he would handle the situation in the operating room. How would he arrive at a deduction that this is a case of hypertrophic rugae? Would he base it simply on the gross examination and the history? Would he base it on frozen sections?

Dr. Meissner: We do not like to do frozen sections to rule in or rule out gastric carcinoma. We will do it if the surgeon asks us to do it (we never refuse to do one if he asks) but it is true that many gastric carcinomas cannot be diagnosed without multiple sections and most of the surgeons I know do not wish to wait for multiple sections. I am never sure that I have ruled out carcinoma of the stomach by frozen section. Sometimes it takes eight to a dozen sections to find a focus of carcinoma in an ulcer. If we are presented with this lesion I think the gross appearance would be the most helpful single thing in the diagnosis.

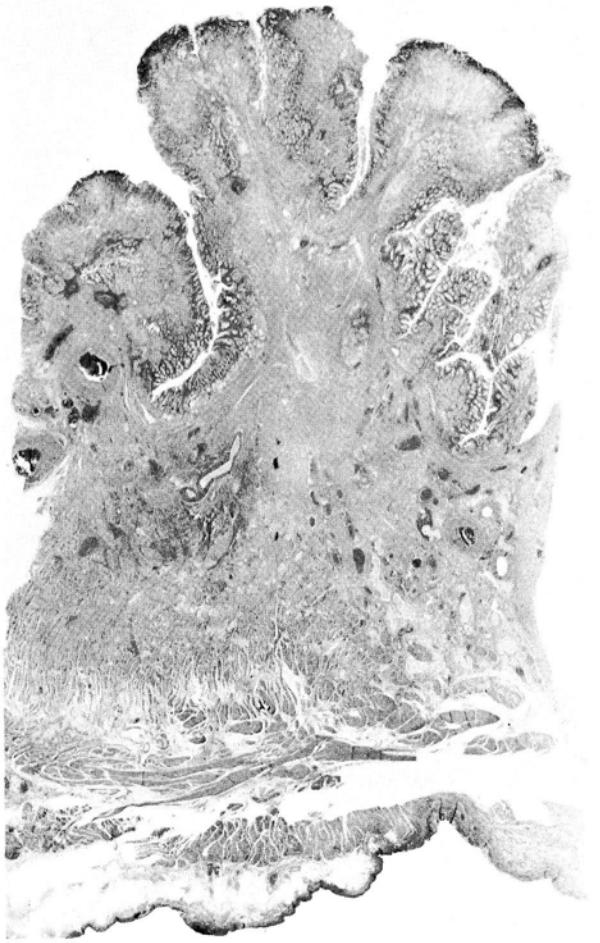

Fig. 2—Low power photomicrograph showing a thickening of entire gastric wall, especially of the submucosa and muscularis. The mucosa shows enlarged rugae (H & E x 5).

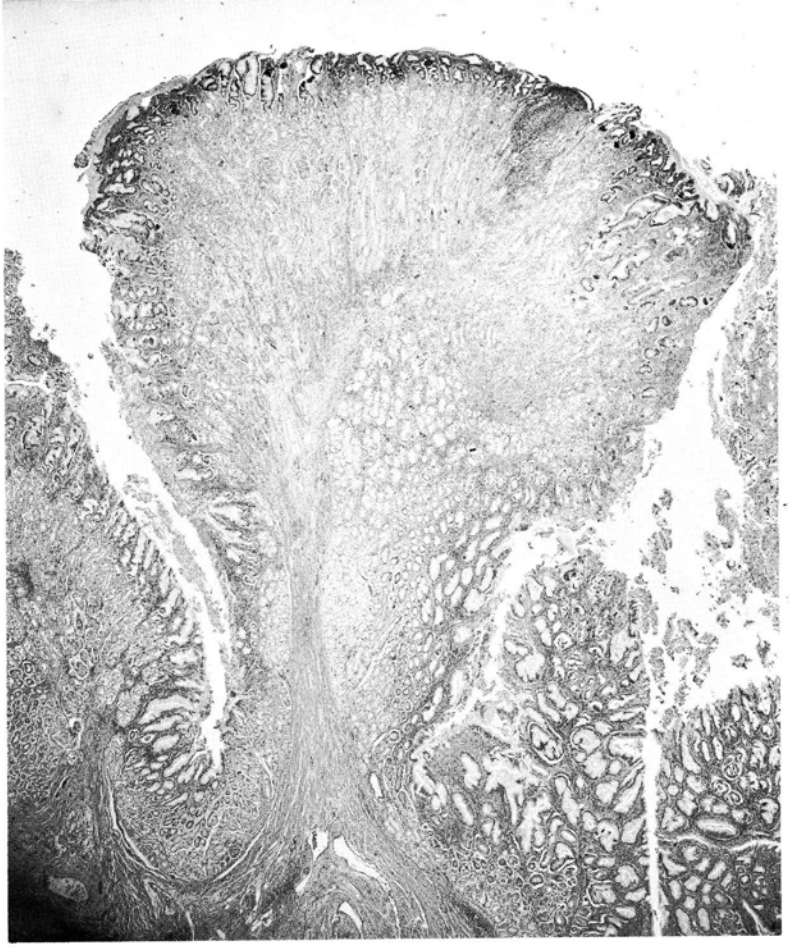

Fig. 3—Higher magnification of mucosal fold. The gastric glands are orderly but there is increased mucus production in the necks of the glands (H & E x 20).

Dr. Modlin: I would be of the opinion that it would take multiple sections to absolutely rule *out* carcinoma. On the other hand, a single biopsy of the edge of the ulcer or of one of these indurated areas might rule *in* the diagnosis of carcinoma.

Frank B. McGlone, M.D., Denver, Colorado: I feel that if there had been adequate workup by a good gastroenterologist, most of the answers could have been obtained preoperatively. This lesion is one lesion that can be seen very well through the gastroscope; I think this is one area where we can endoscopically rule out a malignant disease. Further study, if you have competent cell cytologists, may be helpful. Also of importance is that in many of these lesions the gastric secretions are very high in proteins, and if you do electrophoretic studies of the gastric secretions you may find the cause of hypoproteinemia. Also, the hypoproteinemia would be a very important thing to know preoperatively; it would contribute to the edema that resulted in obstruction postoperatively.

Lewis G. Allen, Jr., M.D., Kansas City, Kansas: Doctor Schatzki, do you subscribe to the postulate that the existence of a duodenal ulcer or history of such makes the possibility of malignancy rather remote?

Dr. Schatzki: It depends upon how radical the gastric resection was. If the gastric resection resulted in real anacidity of the stomach, this patient is definitely a candidate for carcinoma; and as you know, even if a patient still has acidity, he may have cancer of the stomach. It is almost a hundred per cent rule in a patient who has had a duodenal ulcer, that if you see something wrong at the anastomosis on the jejunal side, the chance is that it is a benign ulcer. If you see something on the gastric side, or anything in the stomach above, the overwhelming chance is that it is cancer. I think there was a series of cases of gastric cancer reported from the Mayo Clinic, in patients who had subtotal resection for duodenal ulcer.

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3. *Gastric Adenomatous Polyposis*

Contributed by CARLOS PEREZ-MESA, M. D., Buffalo, New York

THE PATIENT was a 33-year-old woman, in March, 1957, when she complained of persistent anorexia, epigastric pain and weight loss. Four years previously a subtotal gastrectomy had been done for gastric polyposis. On physical examination there was a palpable 4 cm epigastric mass and slight edema of the lower extremities. The hemoglobin was 5.1 gm per cent; total proteins 5.5 gm per cent.

Dr. Schatzki: At the first examination four years ago, the stomach showed a long somewhat unusual filling defect with a reticulated surface and no apparent ulceration. Did the surgeon really find a tumor or was this perhaps a bezoar? Since he resected, we have to assume that this was tumor. Conceivably, the mass could consist of multiple, closely spaced polyps; it could have been a lobulated single tumor, possibly—from the surface appearance—a villous adenoma.

The film of the second examination shows a well-defined defect in the fundus of the stomach. It would be important to know whether this area was rigid. I doubt that it was since I have seen similar fundal defects in other postoperative stomachs and I shall disregard it. The remainder of the gastric stump shows an irregular, nodular surface. The appearance of the mucosa could be simply due to thick tortuous gastric folds as they are so commonly seen following gastric resection. Additional films would be very helpful in the differentiation of thick folds due to gastritis or due to tumor infiltration. I rather believe it is more likely that actual tumor infiltration is present.

Dr. Schatzki's impression: MALIGNANT TUMOR OF ANTRUM: 1. VILLOUS ADENOMA. 2. LYMPHOMA.

Roentgenologic Impressions Submitted by Mail

Benign gastric polyps	35
Gastric polyps and carcinoma	33
Adenocarcinoma	14
Lymphosarcoma	10
Others	11

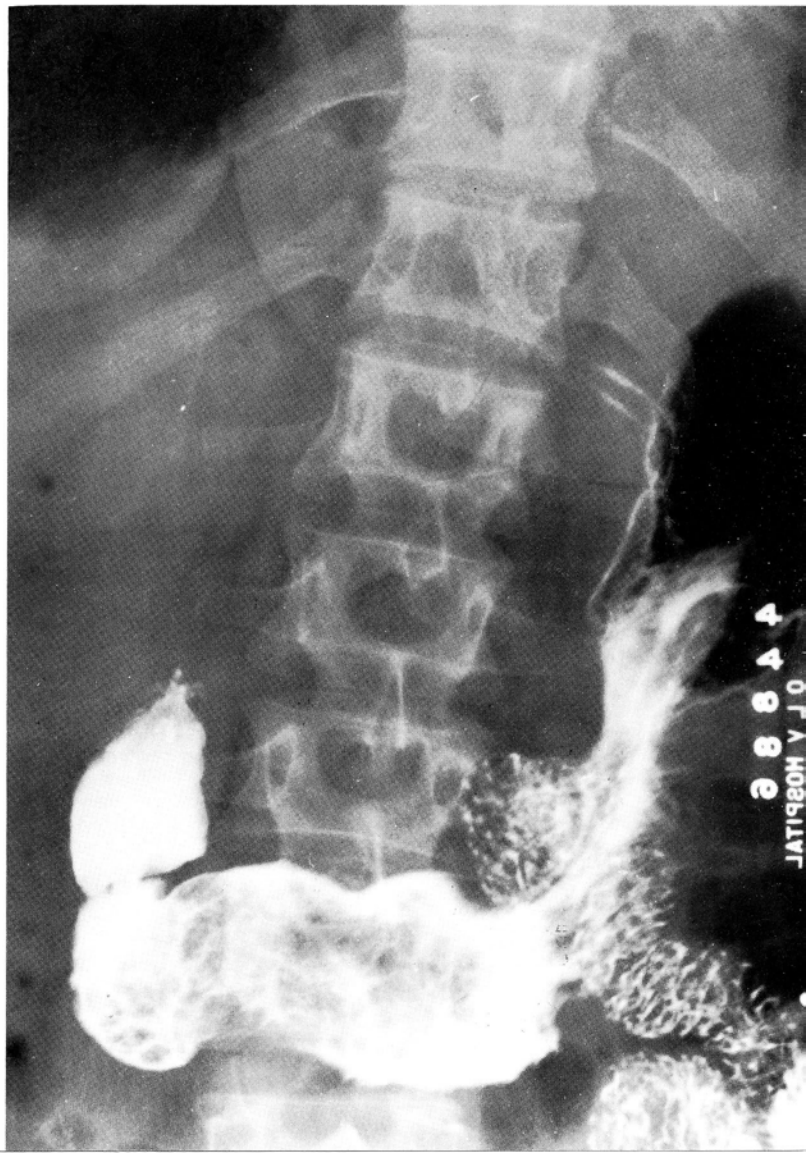
Dr. Schatzki: A great portion of the radiologists called this "benign gastric polyps". I assume that they thought that the original ones and also the later ones were benign gastric polyps. An equal number thought that these were mixed polyps and carcinoma which I suppose means that they thought the patient had first polyps and later carcinoma. I disagree a little with that because I am getting more and more convinced that polyps do not become cancer. They either are or aren't. Adenocarcioma, one cannot argue too much against; my diagnosis belongs in principle with this group. Lymphosarcoma I do not rule out completely because I am a little floating myself.

Dr. Regato: Dr. H. Hauser, of Cleveland, Dr. J. W. Barber, of Cheyenne, Dr. V. G. LaTourette, of Denver, and Dr. M. Ambia, of Mexico City, submitted benign gastric polyposis with malignant transformation; Dr. B. Felson, of Cincinnati, made a diagnosis of Menetrière's disease. Dr. N. Dorbecker, of Mexico City also made a diagnosis of poliadenomatosis of the Menetrière type.

Operative findings: On March 27, 1957, a total gastrectomy and splenectomy was done. Almost the entire gastric mucosa was covered by irregular polypoid masses up to 3 cm in diameter which stopped at the anastomotic and esophageal borders.

Dr. Meissner: The low power field of the section shows a normal gastric wall with the changes being limited exclusively to the mucosa. The mucosa is thrown up into several large polypoid folds, and I presume that the other sections of the mucosa show similar changes. The mucosa shows excessive mucus formation with numerous small accumulations of mucus in cystic spaces. I should like to point out particularly that these polypoid projections do not include a connective tissue stalk composed of the lamina propria or of the muscularis mucosae. This is an important observation because it shows that we are not dealing with giant rugal folds, but with a pure overgrowth of the epithelium of the mucous membrane. The higher magnification shows an overgrowth of the mucosal glands, predominantly involving the mucus secreting cells of the mucosa. The increase in mucosal glands is in an adenomatous pattern, but the cells appear orderly, and I found no points of invasion of the epithelial cell into stroma. The process is sharply delimited from the underlying gastric wall.

Fig. 1—Roentgenogram (1953) showing unusual reticulated filling defect and no apparent ulceration.



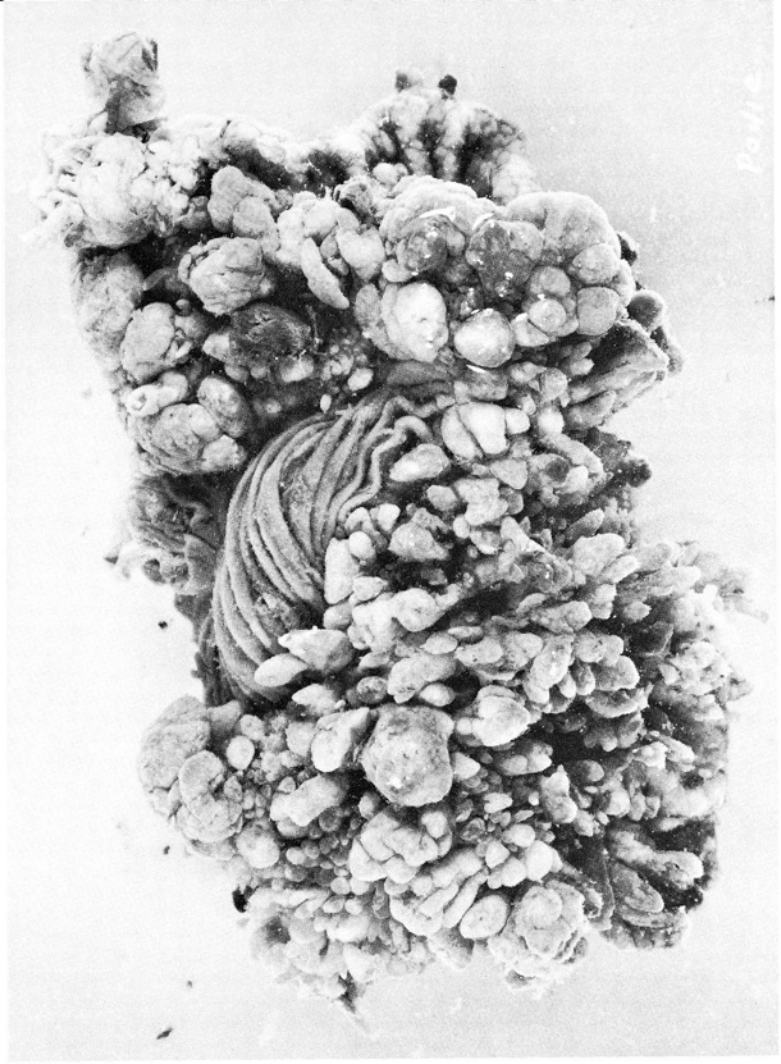


Fig. 2—Photograph of surgical specimen removed in 1953 and showing numerous polypoid lesions.

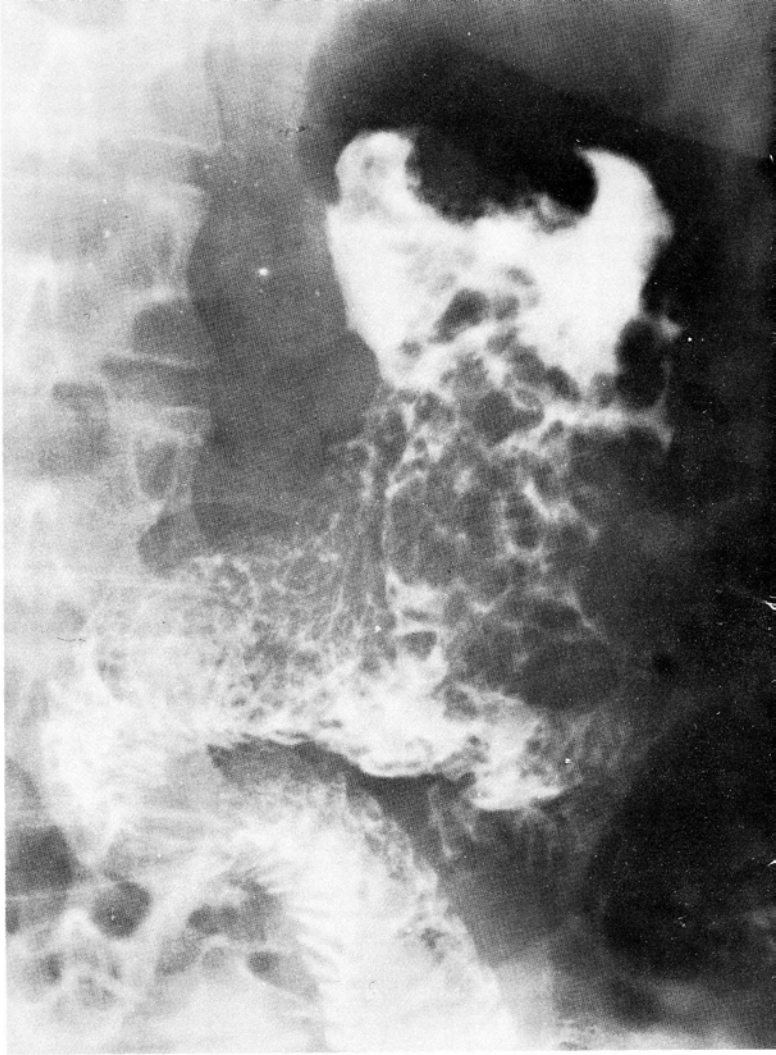


Fig. 3—Roentgenogram (1957) showing remainder of stomach with irregular apparently nodular defects.

This then is a case of polypoid adenomatous proliferation of the gastric mucosa and it is a process limited to the mucosa alone. There are several such polyps in this section, and we can assume that there are many additional ones elsewhere in the stomach. The first important problem in the differential diagnosis is to decide whether this lesion is benign or malignant. I found no invasion and no anaplasia of the epithelium, and I, therefore, believe that this is a benign proliferation. The second problem deals with the proper terminology for a polypoid epithelial proliferation such as this. Many years ago Menetrière described two types of polypoid mucosal lesions. One consisted of multiple epithelial proliferations arising independently, and the other consisted of giant hypertrophic gastric rugal folds with the overlying epithelium being hypertrophic as well. This latter type of Menetrière has been called by many names which include giant rugal hypertrophy, giant hypertrophic gastritis, adenopapillomatosis and so forth. It has also been called Menetrière's disease. We are not dealing with giant rugal folds in this case, however, since this polypoid projection is solely a proliferation of the epithelium. I believe there is enough evidence microscopically to suggest that this epithelium is neoplastic rather than hyperplastic. I feel, therefore, that the best diagnosis here is multiple gastric polyps or multiple polyposis of the stomach rather than hypertrophic gastritis.

Dr. Meissner's diagnosis: MULTIPLE ADENOMATOUS POLYPS.

Histopathologic Diagnoses Submitted by Mail

Adenomatous polyp	62
Hypertrophic gastritis	36
Polyp and Carcinoma	34
Others	11

Dr. Meissner: The majority voted for adenomatous polyps. The distinction between neoplasia and hyperplasia is often a difficult one. There is not much gastritis here, and I would hate to make the diagnosis of gastritis without some evidence of inflammation. I found no evidence of carcinoma in my section.

Dr. Regato: Dr. C. Pérez-Mesa, of Buffalo, submitted a diagnosis of Menetrière's disease; Dr. N. Puente-Duany, of Miami made a diagnosis of polyp with pseudoxanthomatous inflammation; Dr. W. J. Frable, of Chicago, noted concommittant histiocytosis; Dr. F. Bang, of Copenhagen, considered the lesion pre-malignant, Dr. E. Geever, of Bethesda saw focal cancerous changes and Dr. W. A. Meriwether, of El Paso, and Dr. C. P. Schwinn, of Los Angeles, diagnosed adenocarcinoma arising from adenomatous polyp.

A. P. Stout, M. D., New York (by mail): An extreme case of gastric polyposis with very marked intestinal metaplasia and microcyst formation. There is also a granuloma featuring both foam cells (histiocytes) and plasma cells.

M. B. Dockerty, M. D., Rochester, Minnesota (by mail): This condition is an example of benign adenomatous polyp with areas of gastritis and intestinalization. In the cases with pernicious anemia and atrophic gastritis the adenomatous polyps may have a background of inflammatory hyperplasia.

Subsequent history: On June, 1958, the patient underwent a colotomy for the removal of several large bowel polyps. In February, 1959, he had to be hospitalized again because of rectal bleeding and loss of weight; the hemoglobin was 4.7 gm per cent. Transfusions were given and additional large bowel polyps removed. In April, 1961, the

hemoglobin was 6.3 gm per cent; there were no gastrointestinal complaints and proctosigmoidoscopy did not reveal additional polyps. It has been learned that other members of the family have large bowel polyps.

C. Pérez-Mesa, M.D., Buffalo, New York: I thought that this type of case was a typical example of what Menetrière described as "polyadenome-en-nappe". There is a great deal of confusion about this disease; there is apparently a derangement in the turnover of the proteins. In this case, in spite of good treatment the hypoproteinemia persists in the patient.

Dr. Meissner: Multiple adenomatous polyps of this type may be associated with polyps of the small or large intestine, but not necessarily so. The question raised as to whether or not these polyps turn into carcinoma is still a very debatable one. Berg, at the Memorial Hospital of New York studied a hundred cases of gastric polyps and concluded that they were precancerous lesions and that he could find actual transition from the benign adenomatous polyp to carcinoma in a fair percentage of the cases. Others have said just as conclusively that there is no evidence for a gastric polyp of adenomatous type turning into carcinoma.. I must confess that I have never seen a convincing case of polyp of the stomach that was turning into carcinoma, but this I do not believe necessarily proves that it may not occur.

Menetrière did describe two types of polypoid lesions of the stomach. One was the localized type in which there were giant rugal folds, and the other was the type where there were multiple polypoid lesions. I believe that perhaps this represents his second type of gastric polyposis.

I think there is a tendency to make the diagnosis of "Menetrière's Disease" whenever there are polypoid lesions in the stomach associated with a low protein. Perhaps this isn't what Menetrière really wanted us to do.

Dr. Modlin: In the first resected specimen, it appeared that the polyps extended all the way to the edge of the resection, and one wonders if there were polyps in the proximal portion of the stomach. Extensive involvement of the stomach would necessitate a total gastrectomy. The majority of patients who receive a total gastrectomy have a very difficult postoperative course; if they are fortunate enough to survive they frequently have problems with malnutrition, and at least half of them, if they live long enough, will develop pernicious anemia. I think there are few indications for total gastrectomy but I suspect there was one here. It is also of interest in this case that multiple polyps involving the remainder of the intestinal tract have been discovered. This brings to mind the Peutz-Yeager syndrome and it would be of interest to know if this patient did have pigmentation of the mucosa of the lips and the digits.

Dr. Regato: The specimen was reported as showing polyposis almost of the entire gastric mucosa and extending to the point of anastomosis and the esophageal junction.

G. Zechel, M. D., Chicago, Illinois: Any tumor that protrudes over the surface of the skin or of the mucous membrane can develop by one of two processes: either the epithelium has grown out and the connective tissue was passive, and the whole show belongs to the epithelium and then we call it a *papilloma*. On the other hand, the epithelium can be perfectly passive and is being pushed above the normal surface of that area by a tumor that has grown underneath it. In this process the epithelium is perfectly passive; we call this kind of a growth a *polyp*.

E. S. Murphy, M. D., Mexico City: I do not think that a pathologist really has much difficulty in establishing that this type of process has or has not undergone a malignant change. In the slide that I received this change was so evident that there really was not any room for any discussion. I believe that this depends on the slide you get. Nonetheless, in the slide that I have I am sure that the lesion was originally benign and in one very small area there is definite invasion. I think about 34 others made the same decision and I doubt that we are all wrong.

J. Budinger, M. D., Chicago, Illinois: Doctor Meissner, how extensively do you feel we should section such a specimen as this?

J. J. Wolfson, M. D., Albuquerque, New Mexico: In the radiograph No. 2, in the fundus of the stomach there is a sharply delineated filling defect. Those of us who are radiologists are left a little unhappy now knowing how this may be related to the other polyps of the stomach.

W. Kern, M. D., Los Angeles, California: I would like to ask whether gastric cytology might have been useful in this case. We have bad experience with gastric cytology and perhaps Doctor Meissner would enlighten us.

Dr Meissner: The terminology of course is what we are all confused about very frequently in many medical problems. This is unfortunate, but I see no way out of the woods until we know the basic process of what is going on and understand it better. I don't know Dr. Murphy's criteria for the diagnosis of carcinoma, but I suspect that they are the same criteria that I use, and if he says he found a focus of definite carcinoma I will accept his opinion that he did

Fig. 4—Gross specimen of surgical intervention in 1957.

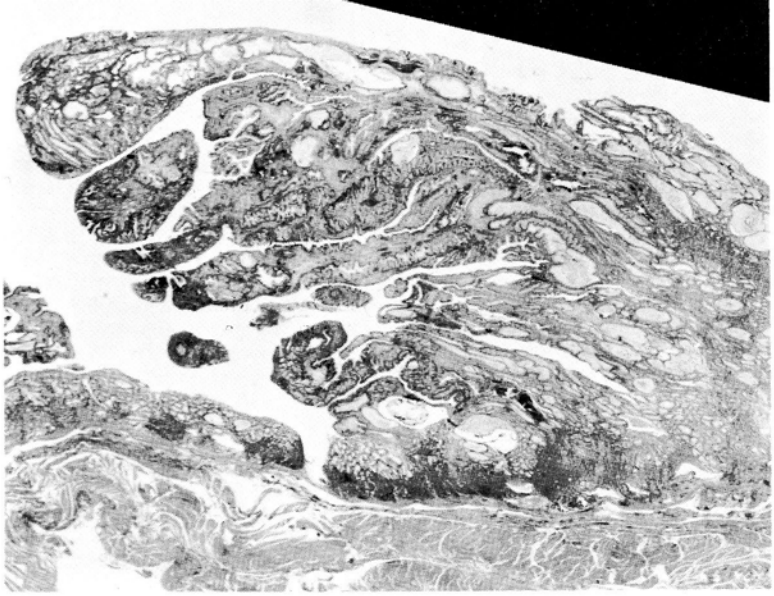


Fig. 5—The underlying submucosa and muscularis are normal, but the mucosa shows a polypoid adenomatous proliferation with the formation of numerous small cysts filled with mucus. This adenomatous growth is quite different from the enlarged rugae of case No. 2 (H & E x 5).

find a focus. I did not in my section, but I had only the one section. Certainly in a case like this we would want to look at multiple sections before we said there was no carcinoma or that there was only one focus or several foci of carcinoma.

Cytology for the diagnosis of gastric tumors may be very helpful in many instances. I do not know that it would be particularly helpful in this instance. Perhaps it would have if there is actual carcinoma here and if the carcinoma cells were sloughing. If it is just a small focus or carcinoma deep in the polyp I do not think the diagnosis of carcinoma could have been made by the cytology. But cytology is a good adjunct to the diagnostic routine in gastric lesions.

E. A. Deans-Barrett, M. D., Albuquerque, New Mexico: I should like again to re-ask or bring to mind the question Doctor Wolfson asked. This is a very disturbing filling defect.

Dr. Schatzki: I would start by saying that I would be just as interested as you are to know if that defect represented a polyp or not. I am afraid that it will be pretty difficult to orient the specimen and to be sure what area corresponds to what area in the film. I finally made up my mind to disregard this part of it because I have seen in stomachs which are a little bit changed in their attachment, as happens after gastrectomy, that they may sometimes have a peculiar incisura in the upper part of the stomach, I suppose due to muscular contraction there; it is fairly easy to be sure whether or not that is what it is during fluoroscopy.

T. Perrin, M. D., Omaha, Nebraska: I should like to ask Doctor Meissner if in his multiple sections he had found one small focus of carcinoma, what effect would that have had on the prognosis?

Dr. Meissner: I suppose this depends on the definition of "small focus". It is like the definition of sin!

In adenomatous polyps of the large intestine we often find a small focus of carcinoma out near the tip of the polyp. These patients rarely have metastases, and may be treated conservatively. If we found a similar small focus in one of these polyps from the stomach, we could say that the prognosis is almost the same as if we didn't find it at all. I think any carcinoma of any size is capable of metastasis, but of course the more of it there is, the more capable it is of giving rise to metastatic lesions.

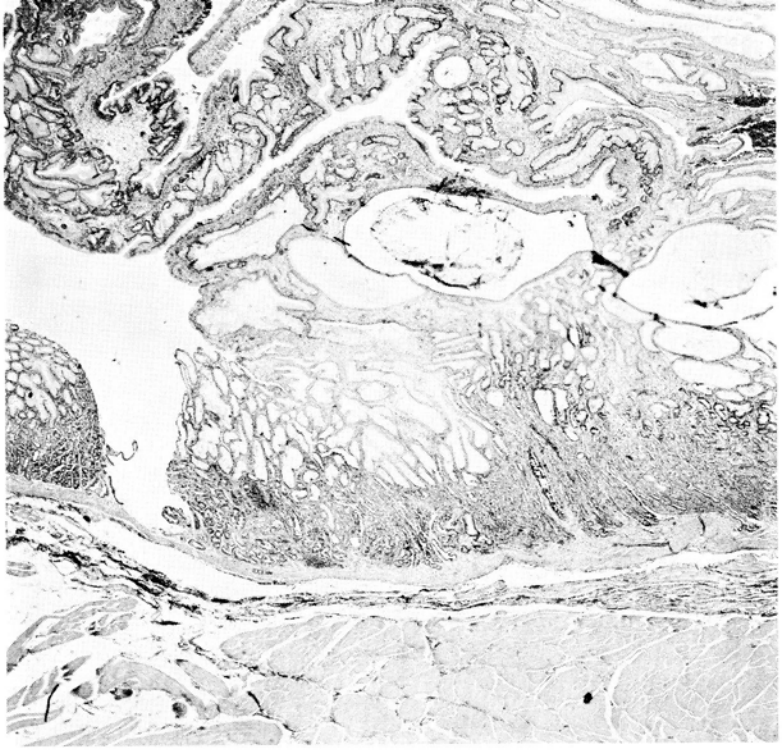


Fig. 6—Higher power magnification demonstrates cystic and adenomatous mucosal growth (H & E x 20).

I. Chavez, M. D. (in Guadalajara): In these cases we often call on the radiologists and pathologists to decide for us the question of adequate treatment, yet it is sometimes equally important to call on the patient to reveal details of the history that may be decisive. In this case, as a surgeon, I would ask myself how am I to decide on a subtotal or a total gastrectomy. I would think that if the process is to be treated surgically it should be extirpated *in toto*. How can we be sure that part of it was not left behind? I am not enthusiastic about total gastrectomies for the patients live rather uncomfortably thereafter, but I think that they should be carried out whenever this is clearly the only way to preserve life.

J. Estrada, M. D., Torreon, Mexico (in Guadalajara): Is that radiographic deformity of the fundus cicatricial?

P. J. Hodes, M. D., Philadelphia, Pennsylvania (in Guadalajara): I believe it is due to post-surgical adhesions.

M. Garcia-Sainz, M. D., Mexico City (In Guadalajara): Why do the pathologists continue to use the term "polyp" if they admit that it is a confusing term?

Dr. Antúnez, Mexico City (in Guadalajara): Because if we were to use other terms the confusion would be worse!

Editor's note: After the Seminar Dr. Kniseley, of Oak Ridge, sent his slide to Dr. Meissner who wrote: "This slide shows early invasive carcinoma in a polyp; this change was not present in my slide".

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4. Adenomatous Gastric Polyp

Contributed by WILLIAM A. MEISSNER, M.D., Boston, Massachusetts

THE PATIENT was a 75-year-old man in February, 1961, when he was admitted to the hospital for amputation of a leg affected by diabetic gangrene. Gastric analysis showed absence of free hydrochloric acid; there was occult blood in the stools. No abnormalities were found on physical examination.

Dr. Schatzki: The film shows three sharply defined small filling defects in the mid portion of the stomach. The stomach wall near the greater curvature appears somewhat contracted. It is impossible to say from this film whether the elasticity in this area is decreased. On this will depend to a great degree the nature of the lesion.

Dr. Schatzki's impression: Polypoid lesion of the stomach: 1. ADENOMATOUS POLYP. 2. METASTATIC CARCINOMA.

Roentgenologic Impressions Submitted by Mail

Adenocarcinoma	45
Benign Polyps	27
Leiomyosarcoma	13
Carcinoma of Pancreas	12
Leiomyoma	9
Others	6

Dr. Schatzki: The majority of the radiologists made a diagnosis of adenocarcinoma; there is surely not very much to say against this diagnosis. If you would take all pictures which show a similar filling defect, you would find more cancers than benign lesions. It would be highly unusual for a leimyosarcoma to have just these two little dots protruding into a lumen; you would have to assume the presence of two small leiomyosarcomas which would be very unlikely. A large leiomyoma may protrude like a polyp into the stomach, a small one would not. There is really nothing to make you think this is carcinoma of the pancreas, although carcinoma of the pancreas may involve the stomach and produce a polypoid lesion; it would be rather unlikely.

Dr. Regato: Dr. R. D. Moseley, of Chicago, diagnosed benign polyps; Dr. Martin E. Bischoff, of Denver, preferred polypoid carcinoma; Dr. J. Ceballos, of Mexico City, submitted leiomyoma.

Operative findings: On March 3, 1961, a sleeve resection of the stomach wall was done. There were two pedunculated lesions arising from the same point of the anterior gastric wall at the greater curvature; they measured 1 cm in diameter each. There were no other lesions found outside of the stomach.

Dr. Meissner: The low power section of one of the polyps shows that the changes are limited to the mucosa which projects outward on a stalk which is a prolongation of the submucosa. The adjacent mucous membrane shows chronic inflammation. There is no involvement of the gastric wall. The second polyp shows similar changes but the epithelium grows in a more jumbled fashion. Over the surface there is an excess of mucus and the vascularity of the entire lesion is quite evident. Under higher magnification excessive proliferation of the mucous glands of the polyp is clearly evident. Near the tip of the polyp the mucous glands show an adenomatous type of proliferation, but I could find no evidence of cellular anaplasia or of invasion to allow the diagnosis of carcinomatous change. The differential diagnosis in this case is similar to the previous one. This is a polypoid adenomatous growth involving the gastric mucosa and the main question is whether this is a benign or malignant lesion. In the absence of anaplasia of the epithelium and in the absence of invasion, I believe one must leave these lesions as benign adenomatous polyps.

True adenomatous gastric polyps may occur singularly, but often they are multiple. There is no clear line of distinction as to when one begins to use the term multiple polyposis, but I believe this latter term should be reserved for cases in which there are extensive mucosal overgrowths implying that at least a large zone of the mucous membrane is undergoing an abnormal proliferation. I do not feel that this case warrants the diagnosis of multiple polyposis. The indications for removal of a solitary or several polyps of the stomach are two-fold: one is that they may produce bleeding as was true in this case; secondly, they should be removed to determine the diagnosis since it is not possible to decide whether or not such a lesion is benign or malignant without histologic examination.

Dr. Meissner's diagnosis: BENIGN ADENOMATOUS POLYPS.

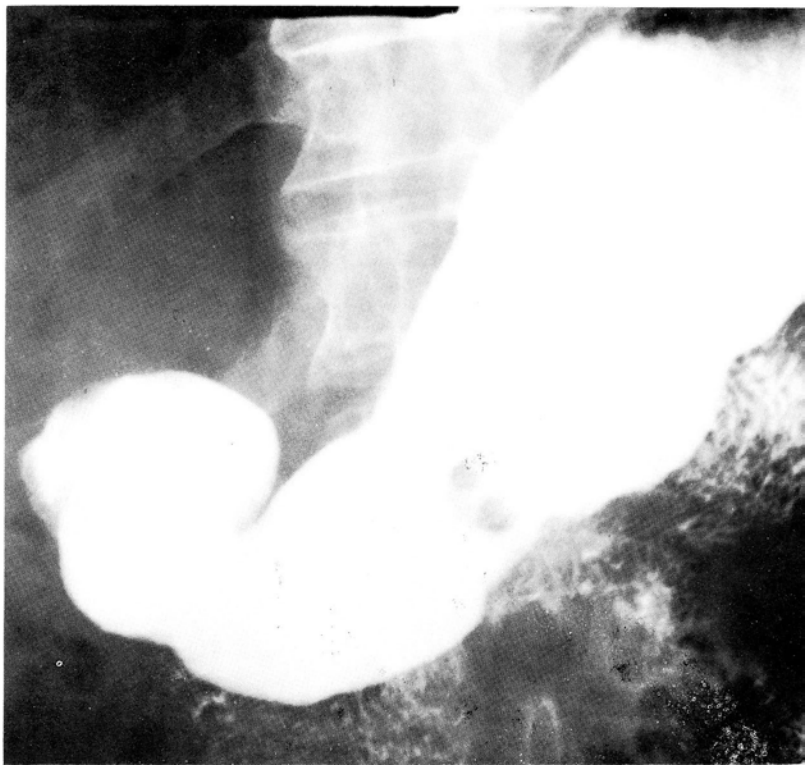
Histopathologic Diagnoses Submitted by Mail

Adenomatous Polyp	112
With carcinoma in situ	6
Gastritis	5

Dr. Meissner: Carcinoma in situ is a difficult diagnosis to make in lesions of the mucous membrane. Many polyps show a very active proliferation but I feel that they are still quite benign; I don't think one should make the diagnosis of carcinoma in situ just on the presence of mitoses and active proliferation. Sometimes mucosal polyps that are perfectly benign will show many more mitoses than most carcinomas of mucosal surfaces. I think this is more than gastritis for the reasons that we have enumerated before.

Dr. Regato: Without exception the experts recognized this as an adenomatous polyp. Dr. R. Willis, of Leeds and Dr. C. A. Hellwig, of Halstead also diagnosed carcinoma in situ; Dr. R. Font, of Pittsburgh and Dr. V. R. Khanolkar, of Bombay, noted evidence of intestinal metaplasia.

Fig. 1—Twin filling defects of the gastric wall with indentation of the greater curvature.



M. B. Dockerty, M.D., Rochester, Minnesota (by mail): Adenomatous gastric polyp in which chronic intussusception has resulted in partial infarction.

Subsequent history: In October, 1961, the patient was seen; he had no complaints.

Dr. Modlin: In all probability the surgeon in this case performed a gastrotomy. I would prefer to open the stomach near the lesion, and then make the decision as to whether to proceed with sleeve resection or subtotal gastrectomy or possibly only a wedge resection. In general if a polyp is 2 cm or less, the likelihood of malignancy is not great. I wonder in this particular case if one could not have proceeded with wedge resection without even going on to a sleeve resection. Certainly a careful inspection of the remainder of the stomach can be made through either of these incisions.

J. F. Dunkel, M.D., Lansing, Michigan: At the base of the polyp I saw clusters of cells with eosinophilic cytoplasm, some of which had the triangular shape of the parietal cells, but the others did not. Did you see such things and were you able to evaluate them in any way?

Dr. Meissner: I did not see those. I will look again, because if they were there I would like very much to see them. We have been looking for a long time for a tumor arising from the parietal cells of the stomach. We have looked at a good many hundreds or thousands of slides of the gastric mucosa to look for a mitosis in parietal cells. They apparently do not undergo mitosis. There has been one report of which I know, of a tumor arising from parietal cells. I have never seen one. I will certainly look at this slide again to see if those cells are there.

H. Braunstein, M.D., Cincinnati, Ohio: I would like to ask Doctor Meissner about the appearance of the adjacent gastric mucosa. It seemed to me there were parietal cells present. How do you reconcile this with the absence of free hydrochloric acid? This didn't look intestinalized at all to me.

Dr. Meissner: The presence or absence of parietal cells has no direct bearing on achlorhydria or the presence of acid. A person can have a perfectly normal looking gastric mucosa and still have achlorhydria.

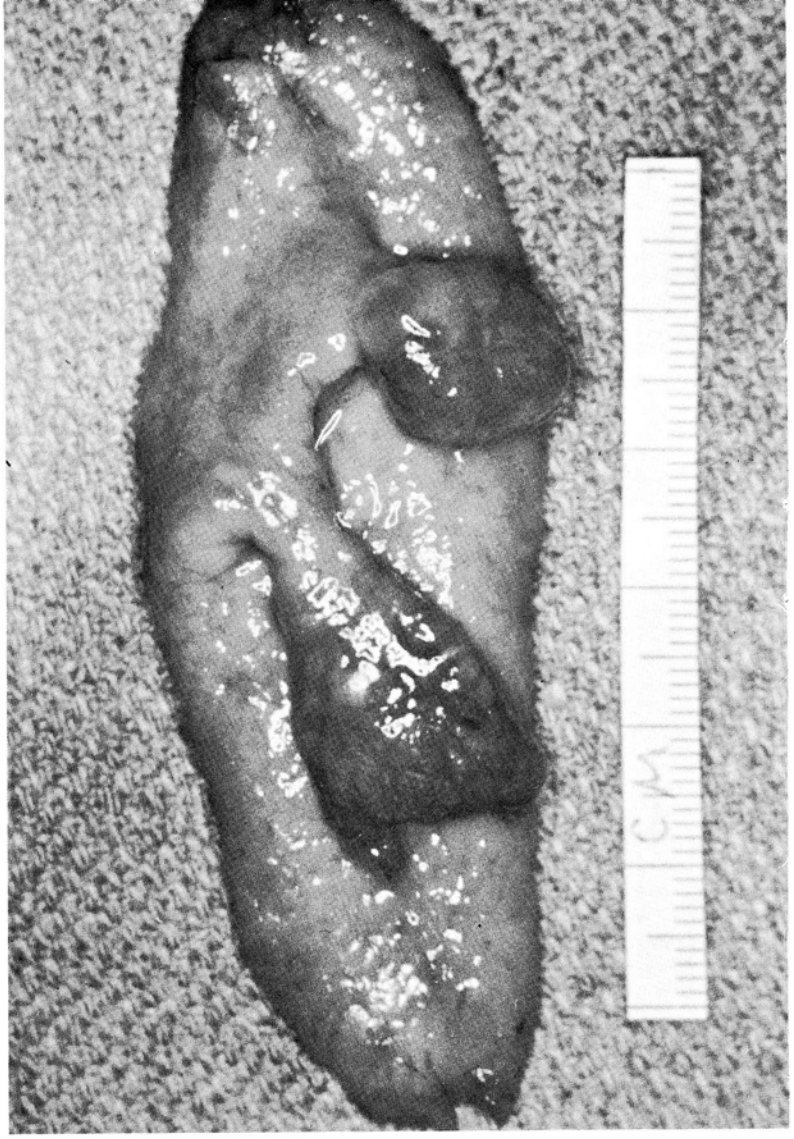


Fig. 2—Gross appearance of surgical specimen.

Fig. 3—Low power magnification of one of the polyps. Note the fibrovascular stalk and the adenomatous proliferation of the distal portion of the polyp (H & E x 5).

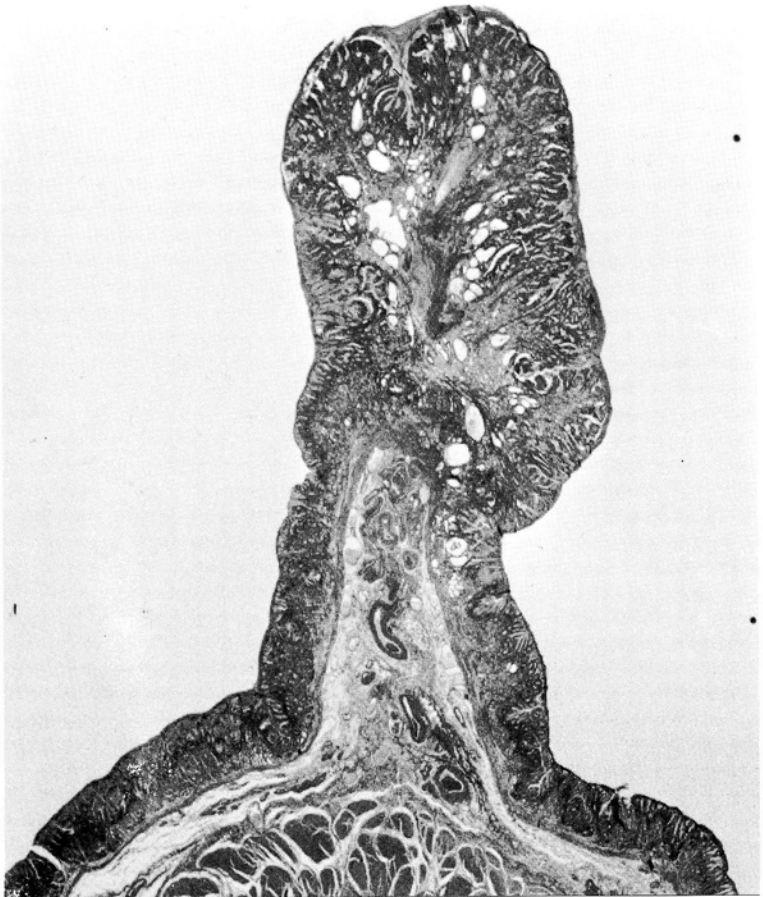
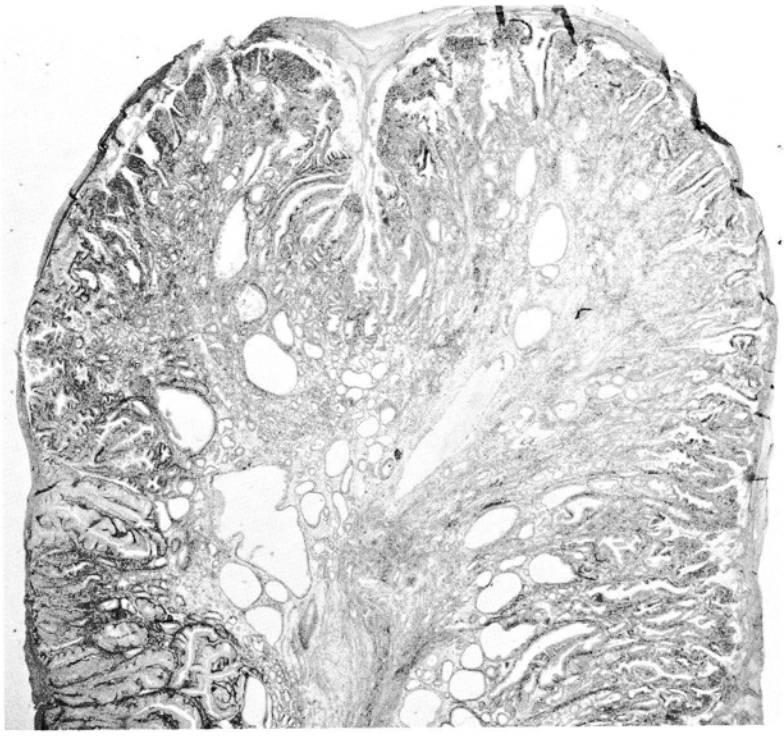


Fig. 4—Tip of adenomatous polyp: there is no anaplasia or invasion (H & E x 20).



5. *Syphilis of the Stomach*

Contributed by P. W. Gikas, M.D. and J. Bookstein, M.D., Ann Arbor, Michigan

THE PATIENT was a 39-year-old man in November, 1960, when he complained of epigastric pain unrelated to food intake and of 26 pounds weight loss in three months. There was a history of polycythemia treated with P^{32} and of two episodes of pulmonary infarction. There was occult blood in the stools; the hemoglobin was 13 grams per cent and the VDRL was reactive. On fluoroscopy the lower half of the stomach wall was stiffened, the mucosal folds were coarse and the pyloric canal elongated; a gastroscopic biopsy was done.

Dr. Schatzki: The first question to be answered is whether the deformity visible in the distal end of the stomach is caused by thickened folds or by wall infiltration. Mobility appears to be preserved on the films which we have at hand. The cap shows a deformity. I am not certain whether it is due to incomplete filling of the cap or due to scarring from an old ulcer. The first portion of the duodenum beyond the cap as well as the upper part of the second portion of the duodenum appear slightly stiffer than usual. There is normally distensible duodenum between these two areas.

From the evidence at hand, I believe that cancer of the stomach is unlikely. It is more likely that these changes are caused by a process which started in the region of the pancreas. This could be pancreatitis, possibly secondary to a gastric or duodenal ulcer (ulcer is quite common in patients with polycythemia). It could be lymphoma in the same area. Finally, but less likely, it could be secondary involvement of the stomach from cancer of the head of the pancreas.

Dr. Schatzki's impression: 1. PANCREATITIS. 2. LYMPHOMA. 3. CARCINOMA OF THE PANCREAS.

Roentgenologic Impressions Submitted by Mail

Syphilitic Gastritis	37
Adenocarcinoma	30
Carcinoma of Pancreas	15
Lymphosarcoma	13
Peptic Ulcers	12
Others	20

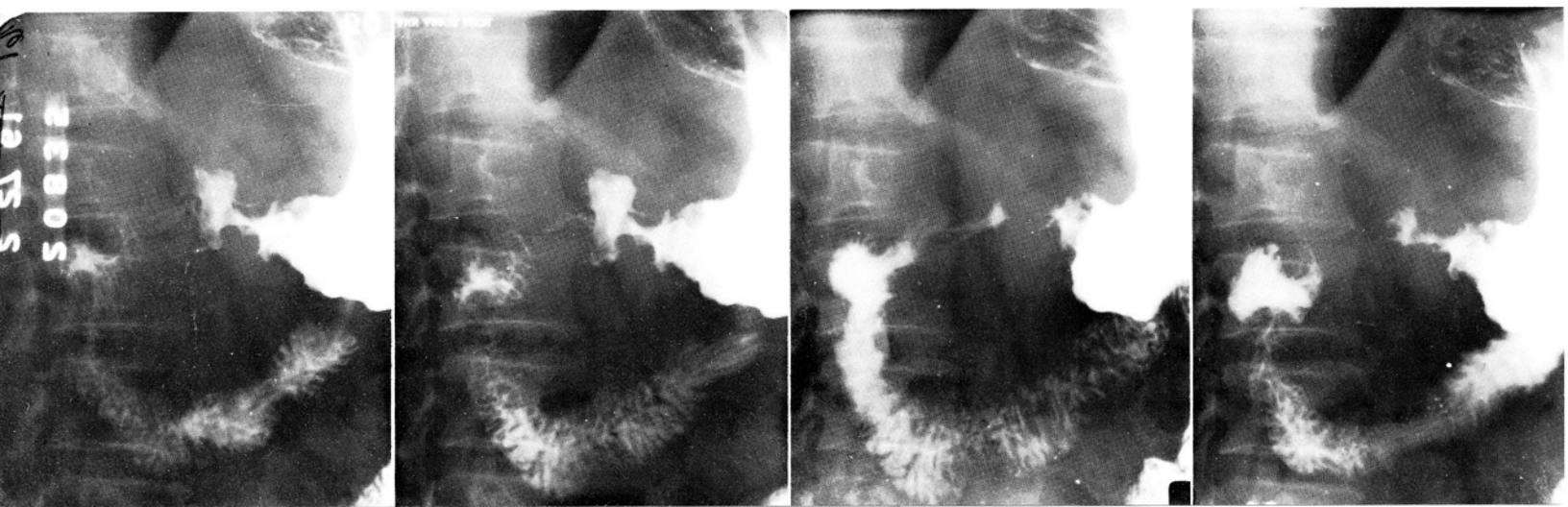
Dr. Schatzki: You will wonder why I did not mention the possibility of syphilitic gastritis in somebody who had positive serology. Because I have been bitten too often. I think I have seen just four cases which were finally diagnosed syphilitic gastritis and they all looked different from each other. I think the most striking character was that they looked different from any usual lesion. Some of them may look like cancer but not the ones I have seen. They just looked like peculiar cases of gastritis or something similar. Syphilitic gastritis is extremely rare, which should make it a good case for this conference. It simulates so many other diseases, particularly non-specific gastritis, and occasionally cancer, that if you make the diagnosis, unless you are in a different part of the world than where I am practicing, almost routinely your diagnosis will be wrong; therefore I teach my residents not to make the diagnosis, even in the presence of positive serology. As a matter of fact, it is very difficult for the students in medical schools to find a case of primary complex. I have asked fourth year students and the majority had not seen a case going through the medical school. The other reason why I stayed away from the diagnosis was that I had the impression there was something wrong in the duodenum as I have indicated. I do not see how anyone could make the diagnosis of adenocarcinoma of the stomach from the film. It just doesn't look like adenocarcinoma. Lymphosarcoma I would agree with if it originates outside the stomach, but not in the stomach. I do not think the patient has peptic ulcers of the stomach but the changes could be produced secondarily by pancreatitis secondary to ulcer.

Dr. Regato: Dr. J. J. Wolfson, of Albuquerque, submitted linitis plastica. Dr. M. Esparza, of Chihuahua, Dr. O. F. Prochazca, of Liberal, Kansas, Dr. E. Salzman and Dr. B. L. Pear, of Denver, all submitted a diagnosis of syphilitic gastritis.

Operative findings: The gastroscopic biopsy was reported as showing purulent gastritis, but because of the radiographic findings a celiotomy was done: The stomach wall presented patchy infiltration; the spleen, the gastrocolic ligamental nodes, as well as the celiac axis and paraortic nodes were enlarged. An incisional biopsy was done. The slides of the CANCER SEMINAR were processed from the scanty material of this and the gastroscopic biopsy; admittedly many of the latter slides were insufficient for a definite histologic diagnosis.

Dr. Meissner: This section shows gastric mucosa and a considerable amount of gastric wall; it is a very generous one because a portion of the specimen looks like serosa. A portion of the mucous membrane shows a mild inflammatory change, but much of it is involved, together with the underlying wall, in a diffuse process which has obliterated the gastric landmarks. The disease seems to involve primarily the submucosa, although it extends into the mucosa and also

Fig. 1—Spot roentgenograms showing elongation of pyloric canal.



to the serosa. Under higher magnification the cellular infiltrate is composed of eosinophils, lymphocytes, plasma cells and other inflammatory cells. I could find no mitoses in any of the round cells and for this reason, I believe that they do not represent a neoplastic infiltrate, but rather an inflammatory one. Of particular interest is the perivascular arrangement of many of these inflammatory cells, forming a cuff around blood vessels of varying size. In addition to the perivascular inflammation, some of the blood vessels show an obliterative endarteritis.

The differential diagnosis here is first between a diffuse inflammatory process and a neoplasm. The infiltrating cells do not appear microscopically neoplastic, they show no mitoses, and the infiltrating cells are of several types. To me this tends to rule out the possibility of neoplasm and I believe, therefore, that the process is basically inflammatory. The inflammation is more than the usual chronic gastritis which is generally limited to the mucosa. The involvement here appears to be basically in the submucosa and deeper tissues with a secondary involvement of the overlying epithelium. Since the inflammatory cells are predominantly lymphocytes and plasma cells and since there is perivascular inflammation together with an obliterative endarteritis, the changes are quite consistent with the diagnosis of tertiary syphilis. This diagnosis is also suggested by the reactive VDRL, and I believe, therefore, that the diagnosis is inflammation of the gastric wall, probably due to syphilis.

The pathologic diagnosis of syphilis of the stomach is a difficult one to make unless one can identify the spirochete. Many of the changes seen in syphilitic gastritis may be found in nonspecific inflammations. There is a great tendency to suggest the diagnosis of syphilis of the stomach when the patient has a gastric lesion and a positive serology, but it is probable, as has been pointed out many times, that the diagnosis of syphilis of the stomach is made too frequently when it is based only on these criteria. Gastric syphilis has always been a rare lesion and it is even rarer today than it was twenty or thirty years ago. The type of involvement described radiologically, however, is quite consistent with the diagnosis and the location of the lesion with the induration of the gastric wall is quite typical.

Dr. Meissner's diagnosis: INFLAMMATION of the gastric wall, probably due to SYPHILIS.

Histopathologic Diagnoses Submitted by Mail

Gastric syphilis	45
Inflammatory gastritis	37
Adenocarcinoma	17
Leukemia	8
Lymphosarcoma	5
No lesion seen	5
Others	22

Dr. Meissner: I am glad to hear that this was not just a gastroscopic biopsy because this includes the entire thickness of the gastric wall and some of the serosa. It is a temptation for the pathologist, just as it is for the clinician and radiologists to make the diagnosis of syphilitic gastritis when there is a positive serology. It has been pointed out many times that the only proof of syphilitic gastritis is to find the spirochete in the lesion, because this may be simulated by many other processes, even to and including the vascular changes that are seen here. I have only seen one other case of syphilitic gastritis, but I have seen the diagnosis made a good many times clinically and radiologically, when it turned out to be something different. Dr. Boyd says that syphilitic gastritis is probably quite rare.

Dr. Regato: Dr. W. A. Meriwether, of El Paso, Dr. R. Font, of Pittsburgh, and Dr. C. Perez-Mesa, of Buffalo, diagnosed gastric syphilis.

A. P. Stout, M.D., New York (by mail): There is marked inflammatory reaction with infiltrating lymphocytes, plasma-cells, histiocytes, eosinophils and occasional neutrophiles. It does not seem to be phlegmonous gastritis; if there were multiple ulcers I would guess syphilis.

M. B. Dockerty, M.D., Rochester, Minnesota (by mail): The endothelial proliferation, the inflammatory cuffing of the adventitia of certain large vessels combined with an infiltrate of plasma cells and lymphocytes lead me to a diagnosis of inflammatory ulcer which is not typically peptic; it could be luetic.

Subsequent history: In August, 1961, the patient had gained some weight under antiluetic treatment but suffered from general paresis and his mental condition had deteriorated.

Dr. Modlin: This case would give me some anxious moments, both before and at the operating table. This is the first case of gastric syphilis that I have actually seen; I would wish the pathologist to be bracing me from behind. I would certainly open the stomach and proceed with the biopsy. I am interested that the surgeon did not do a drainage procedure of some sort. From the radiograph the question arose in my mind about pyloric obstruction and the possibility that if it were not great at this moment that it might subsequently develop.

Paul M. Gikas, M.D., Ann Arbor, Michigan: This lesion was loaded with spirochetes; we did the Warthin-Starry stain and the organisms were numerous. This patient was presented to a board of gastroenterologists before his celiotomy. They failed to make a diagnosis; the diagnosis was suggested preoperatively by a surgical resident. That first biopsy was not obtained by gastroscopy; it was a blind tube biopsy; they pass a blind gastric tube down and apply suction; they got off a bite of mucosa which showed the purulent gastritis but the diagnosis was made from the surgical specimen. He had similar lesions in his rectum which were interpreted as granulomatous and no spirochetes could be demonstrated in these; the rectal lesions as well as the gastritis responded quite favorably to Penicillin therapy. The patient subsequently died and no autopsy was performed. However we have information that suggests he died from a pulmonary embolus resulting from thrombophlebitis.

Dr. Schatzki: I would like Doctor Meissner to say something about the extensive lymphadenopathy which was found and which was news to me in the case of syphilitic gastritis.

Dr. Meissner: Having seen only one case before and not remembering well I cannot answer the question, but lymphadenopathy does occur with lues.

Paul W. Gikas, M.D., Ann Arbor, Michigan: Lymph nodes showed marked reactive hyperplasia, which simulated a giant follicular lymphoblastoma; apparently this can occur with lues.

Dr. Meissner: Yes, but the giant follicular hyperplasia which might be confused with giant follicular lymphoma is more likely to occur with secondary lues than with tertiary.

Mark Wheelock, M.D., Chicago, Illinois: It is true that syphilis in the Boston area is lower than it is in other parts of the United States, but I saw there three cases of syphilitic osteitis, one of which was actually in a case of juvenile tabes. In early days when we used to see acute syphilis, one of the places where you looked for spirochetes was in the aspirations of lymph nodes. At the present time we are seeing a fair number of perianal chancres and actually syphilitic proctitis in the Chicago area.

I have been interested in pancreatitis; in some five hundred cases of lesions of the stomach, gall bladder, common bile duct and the pancreas; I have dissected all of the pancreas and made multiple sections of the structure, and in none of these instances, particularly when there was chronic pancreatitis, was there any way in which it en-

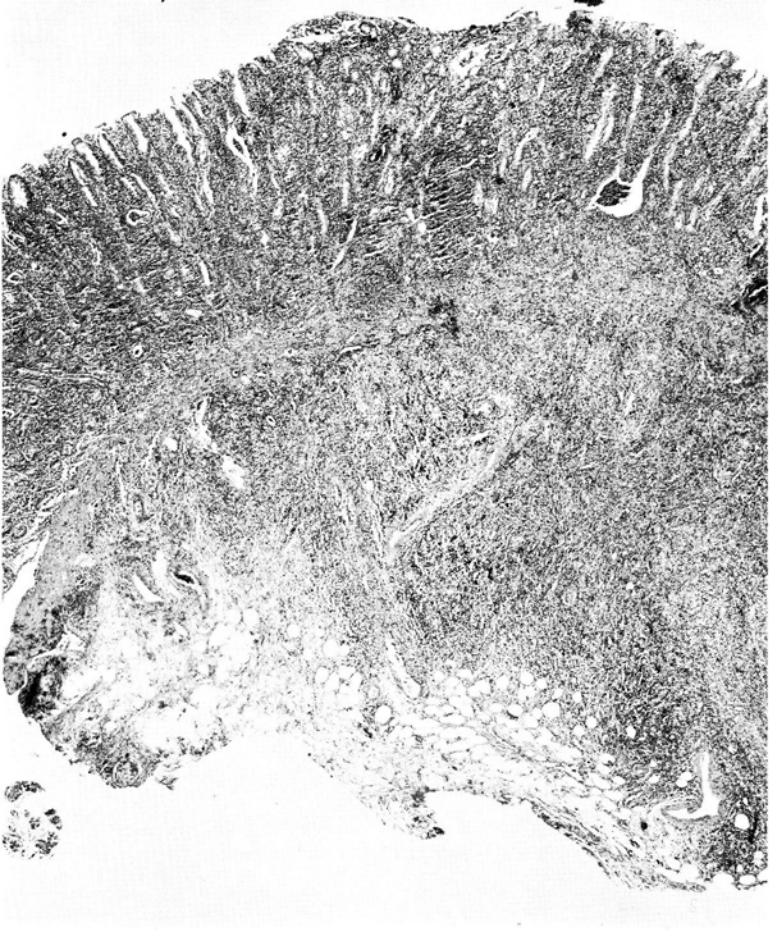


Fig. 2—Low power photomicrograph showing a diffuse inflammatory process which extends throughout enitre thickness of the mucosa and gastric wall (H & E x 30).

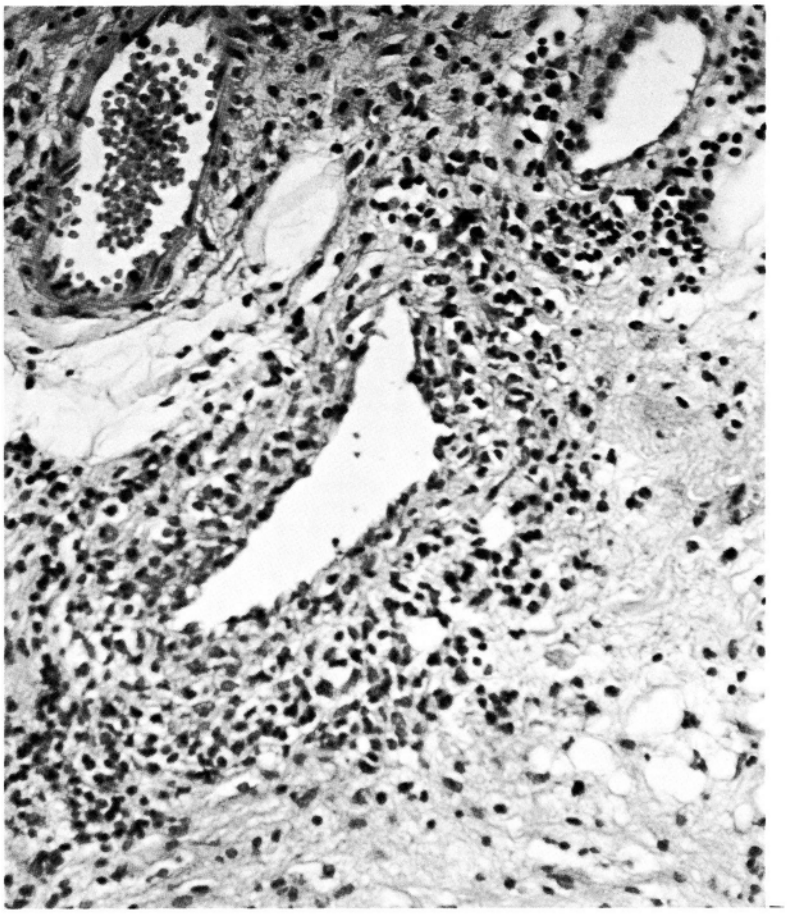


Fig. 3—The diffuse inflammatory infiltrate includes lymphocytes and plasma cells. Frequently the inflammatory cells show a perivascular arrangement (H & E x 300).

croached upon, produced distortion, or altered the structure of the stomach at all. Pancreatitis is a fibrosing lesion which causes the pancreas to shrink; even when it is in the head of the pancreas it does not cause any alteration that we could demonstrate in the stomach, and it did not involve the serosa of the stomach and it did not penetrate the stomach. On the other hand of course the gastric ulcer or duodenal ulcer both will definitely involve the pancreas.

Dr. Schatzki: I think that this only shows the limitations of the pathologist, who sees the specimen at one stage of the game; in this case, at the final stage. It is not at all uncommon in clinical pancreatitis enlargement to see a mass in the region of the pancreas which produces forward displacement of the stomach, and forward displacement of the duodenum, which will subside when the pancreatic acute episode has disappeared. It will produce changes in the third portion of the duodenum, in the antrum of the stomach and the body of the stomach. I would assume that many of these changes are just pressure changes from the enlarged pancreas, but I assume also that many of these changes are edema of the wall, which is a pretty difficult anatomical diagnosis to make. Of course this edema will only be present in the acute case of pancreatitis. There is nothing in the clinical history to really indicate that this patient had pancreatitis if I would not assume that he had a duodenal ulcer and from that a mild degree of chronic pancreatitis.

H. Braunstein, M.D., Cincinnati, Ohio: I would like to ask Doctor Gikas what stain was used to demonstrate the spirochetes in the gastric lesion.

Paul W. Gikas, M.D., Ann Arbor, Michigan: We use the Warthin-Starry stain; in Ann Arbor that is the only stain we use.

Henry J. Caes, M.D., Sioux City, Iowa: Ann Arbor is certainly known for its demonstration of spiorchetes with the Warthin-Starry stain. It was said, particularly in the old days, that they could demonstrate spirochetes in wood!

In our laboratory with a positive VDRL we are not satisfied that the patient does have syphilis and that other studies have to be made; particularly with sending specimens to other laboratories that can do Reiter's complement fixation tests or the spirochete immobilization test, before one is satisfied with the diagnosis of syphilis.

Paul W. Gikas, M.D., Ann Arbor, Michigan: We do some of these other tests in our own laboratory. The Ryder protein common fixation test was performed and was positive; the patient responded to the Penicillin therapy quite well; he was very ill before the celiotomy before the diagnosis was made. This material was sent to the Armed Forces Institute of Pathology and they also agreed that there were structures compatible with Treponema pallidum in the Warthin-Starry sections. He responded very well after that.

Isaac Costero, M.D., Mexico City (in Guadalajara): We should use this opportunity to insist upon the great importance of the histologic study of lymph nodes. In the gastric wall the neoplastic and inflammatory processes are often difficult to distinguish. The lymph nodes collect metastatic cells and also are the best places to find Treponema.

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6. *Adenocarcinoma of the Stomach and Duodenum*

Contributed by J. R. CLAY, M.D. and ROBERT DONNER, M.D., Lackland Air Force Base, Texas

THE PATIENT was a 40-year-old man in October, 1960, when he complained of bloating and vomiting following meals; there was also a slight weight loss. Physical examination revealed no abnormalities. The hemoglobin was 13.9 gm per cent. The hematocrit 42 per cent. Gastric acidity: 22 units; no free acid.

Dr. Schatzki: The film shows filling of the stomach and scattered filling of the bowel starting just beyond the region of the duodenal cap.

This patient did not have a complete pyloric obstruction; he had partial pyloric obstruction. Neither the film nor the history give any hint in regard to the cause of the pyloric obstruction.

Dr. Schatzki's impression: PARTIAL PYLORIC OBSTRUCTION, cause undetermined.

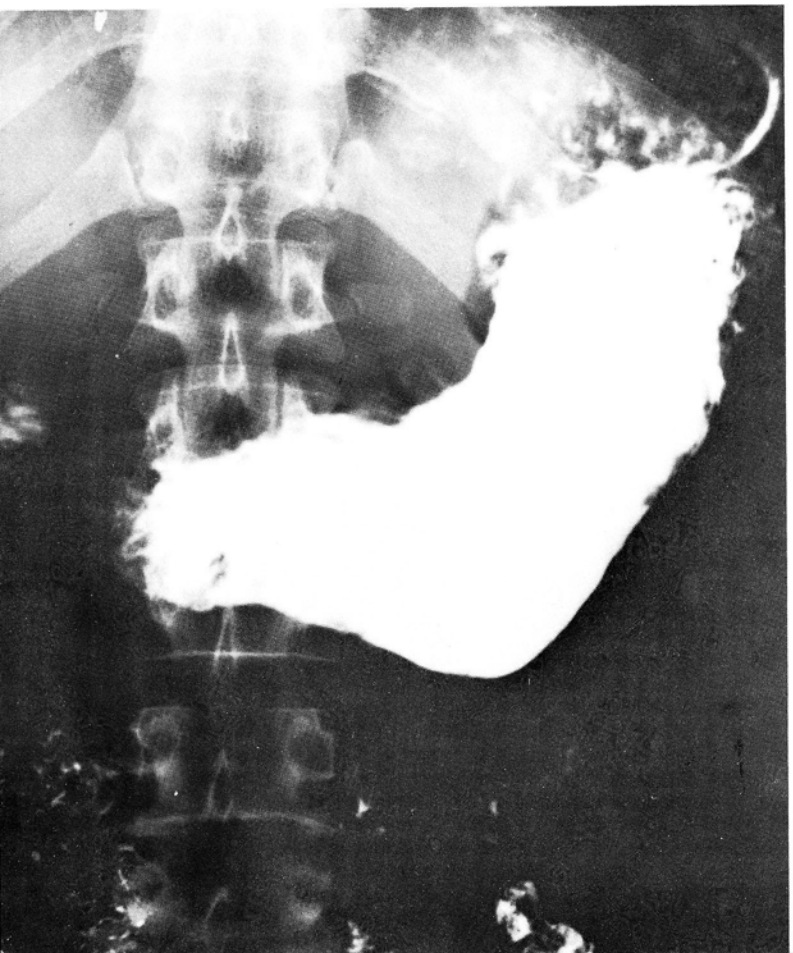
Roentgenologic Impressions Submitted by Mail

Peptic Ulcer	48
Carcinoma	31
No idea!	14
He is obstructed!	1
Others	5

Dr. Schatzki: Statistically there are obviously more pyloric obstructions of this degree due to peptic ulcers than due to cancer, but that doesn't help you in a given case. You have no idea what the obstruction is due to.

Dr. Regato: Dr. M. del C. Ambia, of Mexico City, Dr. R. R. McCarver, of Phoenix, and Dr. F. Gorishek, of Denver, made a diagnosis of carcinoma of the gastric antrum; Dr. W. Gunn, of San Francisco, favored a carcinoma of the pancreas.

Fig. 1—Roentgenogram of the stomach showing pyloric obstruction.



Operative findings: On November 3, 1960, a gastrostomy revealed a stenosed pyloric ring, admitting only the tip of a small clamp. A subtotal gastrectomy and bilateral vagectomy was done. The wall was thickened, there was a linear depression of the pyloric mucosa which extended into the muscularis and measured 3.5 by 0.5 cm; there was edema and congestion of the submucosa with slight hemorrhage.

Dr. Meissner: Under low power we see that this is a section of the pylorus with some stomach and duodenum attached. The mucosa of both stomach and duodenum appears normal, but there is a great enlargement of the muscularis of both structures. This appears then to be a process involving primarily the wall of the stomach and duodenum at the pylorus. Under high power the examination of the muscular coats show numerous small clusters of epithelial cells. These are more prominent in the wall of the duodenum than in the gastric wall. These cells often form a good glandular arrangement, but sometimes grow in a more solid fashion. Only a few of these epithelial cells show mitoses and there is very little pleomorphism. The cytoplasm of the cells is often foamy and suggests a mucus content which is verified by the PAS stain. The small clusters of cells do not stain as intensely as the mucus of Brunner's glands, but extend both to the serosa and into the duodenal mucosa surrounding Brunner's glands. There is no obvious connection between these clusters of cells and Brunner's glands themselves, but at one end of the section these clusters of cells extend up to and seem to erode the overlying duodenal mucosa. At this point the cells are quite similar to the mucus-secreting glands of the duodenal mucosa itself. Deep in the muscular wall where one finds nerves and ganglia, it is obvious that there are several clusters of these cells arranged about these structures, which, I believe, is ample evidence for the process being a malignant neoplasm.

The differential diagnosis here is between heterotopic epithelium growing diffusely in the gastroduodenal wall or low-grade carcinoma. The absence of better delimitation of the lesion and the presence of perineural invasion allows us to consider this as a carcinoma rather than heterotopic epithelium. The next point in the differential diagnosis is to decide the site of origin of the carcinoma. Because the tumor is primarily in the wall of the duodenum and at one point seems to be eroding the duodenal mucosa I think it is quite likely that this is a primary carcinoma of the duodenum, not of the Brunner's glands, but of the mucosa itself. A second possibility is that this is a carcinoma arising from heterotopic epithelium of the pyloric wall. I know of no way to exclude this possibility from the examination of one slide. I think it is even possible that this is a carcinoma which may be growing into the area from a carcinoma of another one of the viscera such as the pancreas. My impression, however, is that this is a primary carcinoma arising from duodenal mucosa.

Low-grade carcinomas such as this may infiltrate extensively without giving rise to serious signs or symptoms. Some such carcinomas are so low grade that it is difficult

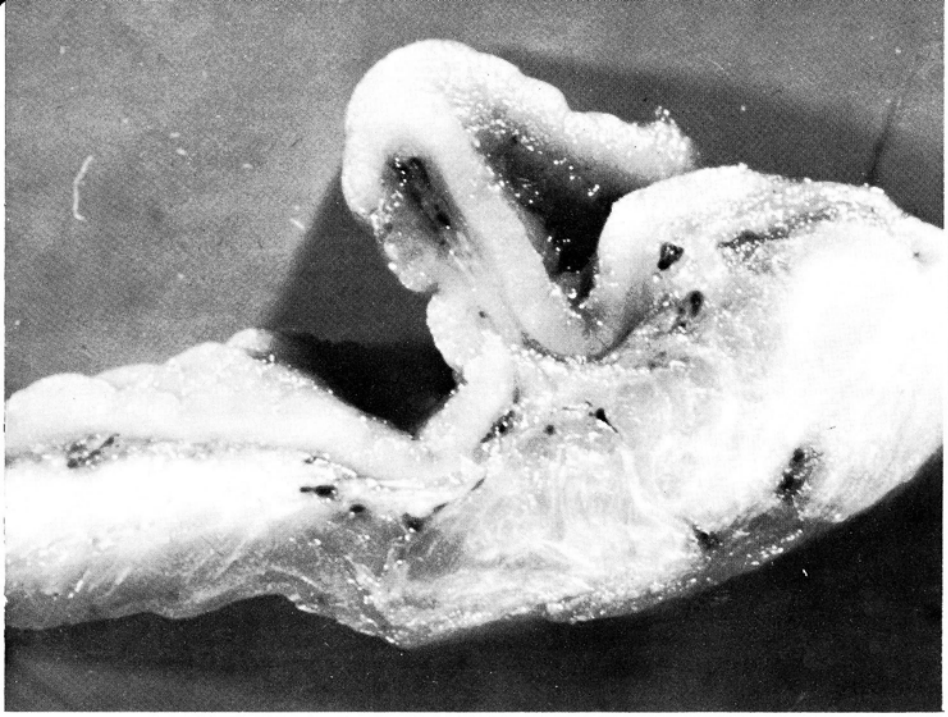


Fig. 2—Cross section of surgical specimen.

to be certain of the diagnosis of malignant tumor unless one finds definite evidence of invasion. In tumors in this region it is often very helpful to examine carefully nerves and ganglia for the presence of perineural invasion. The finding of this may be the only conclusive evidence that one is dealing with a carcinoma.

Dr. Meissner's diagnosis: ADENOCARCINOMA OF THE STOMACH AND DUODENUM.

Histopathologic Diagnoses Submitted by Mail

Adenocarcinoma (Pancreas, Brunner's)	70
Ectopic Pancreas	26
Adenomyoma (Myoepithelial Hamartoma)	24
Others	7

Dr. Meissner: We have more or less discussed all of these, except the possibility of carcinoma arising from Brunner's glands. This would be a very interesting carcinoma to see because I know of no reported case of adenocarcinoma arising from Brunner's glands, but I do think it may be of duodenal origin. Ectopic pancreas would be included under heterotopic epithelium, and adenomyoma is really another way of saying the heterotopic epithelium and as is this last diagnosis.

Dr. Regato: Dr. E. S. Murphy, of Mexico City, Dr. A. O. Severance, of San Antonio and Dr. L. V. Ackerman, of St. Louis, diagnosed adenomyoma. Dr. Mark Wheelock, of Chicago, Dr. R. C. Horn, of Detroit, Dr. G. Gricouroff, of Paris, and Dr. R. Lattes, of New York submitted a diagnosis of adenocarcinoma possibly arising from ectopic tissue.

Elson B. Helwig, M.D., Washington, D.C. (by mail): It is difficult to distinguish between myoepithelial hamartoma (aberrant pancreas) and carcinoma. However, in some areas the cells do not show a clear cut glandular pattern or regular arrangement and this is interpreted as carcinoma.

M. B. Dockerty, M.D., Rochester, Minnesota (by mail): My differential was between pancreatic heterotopia and well differentiated carcinoma. The presence of a scirrhous reaction, of an apparent perineural placement of the glandular cells and of occasional signets decided me in favor of carcinoma; the primary growth should be extragastric. I have seen carcinoma of the pancreas, which involved stomach and duodenum produce this picture.

Subsequent history: After surgery, the patient improved. On July 6. 1961, he presented a patent stoma and had no retention. A telegram received this morning from Dr. James R. Clay states that the patient is free of disease.

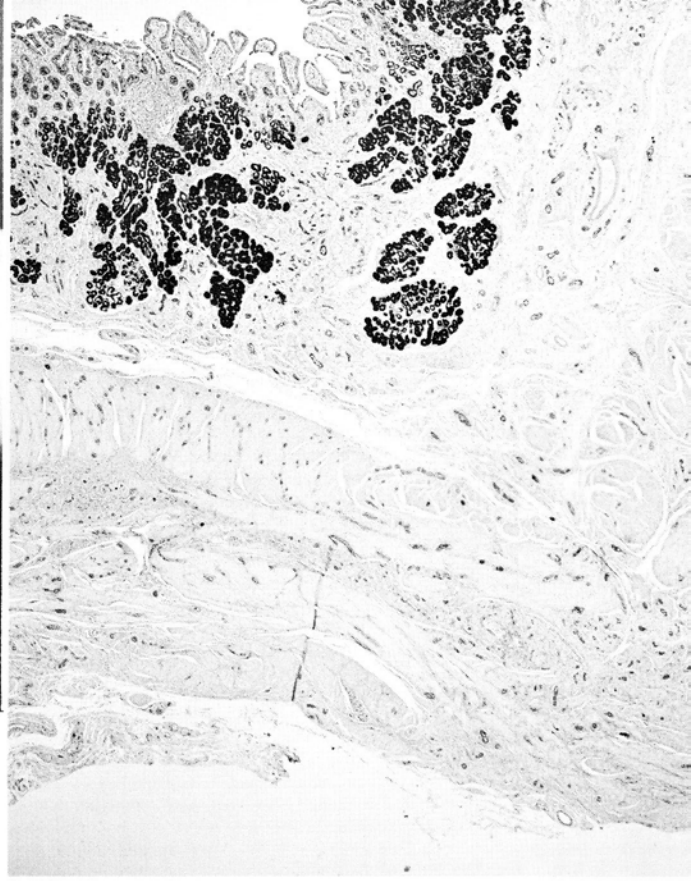
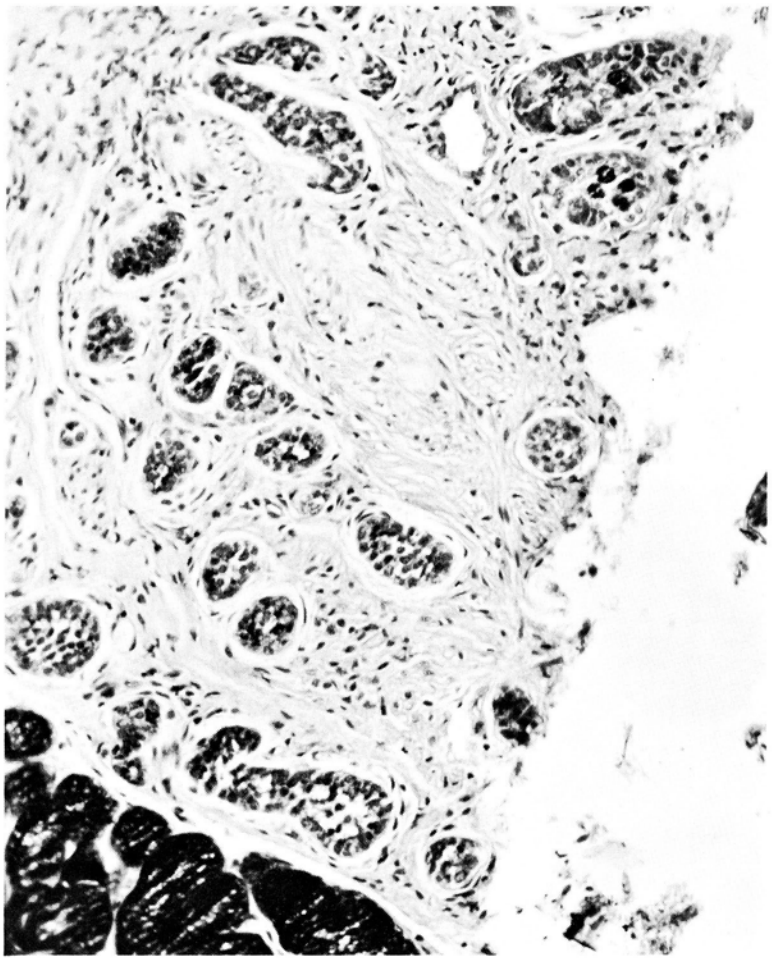


Fig. 3—Low power photomicrograph of entire duodenal wall stained with PAS. The duodenal epithelium and particularly the Brunner's glands (top left) are very conspicuous with this stain. Throughout the muscularis there are minute foci of PAS positive tumor cells (PAS x 20).

Fig. 4—At one point clusters of PAS positive tumor cells extend to the surface of the duodenal mucosa suggesting an origin from the duodenal epithelium. A portion of a heavily stained normal Brunner's gland is seen at the lower left (PAS x 250).



Dr. Modlin: I suspect that the surgeon in this case operated with the preoperative diagnosis of pyloric obstruction, and of course the most common cause of pyloric obstruction is the complications that arise from duodenal ulcer. It is interesting that a gastrostomy was done; and that the patient was then resected and a vagotomy done; so I assume that the surgeon probably felt that this was indeed an obstruction secondary to duodenal ulcer. I suspect that Doctor Meissner would agree that a biopsy would have been very difficult to interpret in this particular case by frozen section, particularly since the overlying mucosa was largely intact. In any event I don't think it made a great deal of difference because a subtotal gastric resection was the procedure of choice and certainly the surgeon is limited in his excursions in this area; certainly a wider resection, such as a Whipple type of operative procedure, is definitely not indicated. I doubt very much if the vagotomy made any difference.

Howard Ball, M.D., San Diego, California: I would like to ask Doctor Meissner if he did not feel that much of this infiltrate was possibly lymphangitic in type.

Dr. Meissner: I did not see any of the tumor cells in the lymphatics but I suspect they may well have been there. I do think I demonstrated them in perineural lymphatics but I didn't find them in others, but it may well be a diffuse lymphangitic spread of the tumor.

L. Lowbeer, M.D., Tulsa, Oklahoma: Doctor Meissner, you assumed an origin of Brunner's glands and I notice that you stained everything with PAS. Of course PAS is always found positive in Brunner's glands, but they do not stain with mucicarmine. Therefore, if you would stain this tumor with mucicarmine and you would find it to be negative, this would be supporting your idea that it originates from Brunner's glands, but if it were positive with mucicarmine it would indicate that it originates from glands other than Brunner's glands.

Dr. Meissner: I am sorry I didn't have additional sections to do this; I did only the PAS stain and I did a trichrome stain and by that time my extra slides were used up so I wasn't able to do the mucus stain.

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7. Lymphosarcoma of the Stomach

Contributed by D. Alcott, M.D. and J. J. McCort, M.D., San Jose, California

THE PATIENT was a 55-year-old man in January, 1960, when he complained of pyrosis and epigastric pain, severe at night and relieved by food intake; there had been a 25 pound weight loss. On physical examination epigastric tenderness was elicited on palpation; the hemoglobin was 13 gm per cent. The radiologic examination revealed pliable walls but no peristaltic waves were transmitted through abnormal zone.

Dr. Schatzki: There is marked irregularity of the lesser curvature with very thick folds being present in the stomach. It is difficult to say from this film alone whether there is an abnormal mass in the region of the lesser curvature. On some additional films which I have been shown, the outstanding feature is the presence of markedly thickened folds in the stomach with a possible area of ulceration. The folds in other areas of the stomach appear normal. The involved folds are unevenly thick. This makes gastritis unlikely. The appearance is that of lymphoma of the stomach.

Dr. Schatzki's impression: 1. LYMPHOSARCOMA.

Roentgenologic Impressions Submitted by Mail

Lymphosarcoma	43
Hypertrophic Gastritis	28
Carcinoma	12
Ulcer	11
Others	9

2. RETICULUM CELL SARCOMA.

Dr. Schatzki: You see that the differential diagnoses varied predominantly between lymphosarcoma and hypertrophic gastritis. These participants didn't have the advantage I had of an additional film; I would rather think that a large number of them would have jumped into my boat if they had had it. It would be a very peculiar gross appearance of carcinoma to give you this first picture. It looked as if there were foldlike structures and that is so much more common in lymphoma than it is in carcinoma. Ulcer I would consider a very unlikely diagnosis.

Dr. Regato: Dr. J. Ceballos, of Mexico City offered an impression of gastric hypertrophy; Dr. M. Bischoff of Denver, Dr. J. J. Wolfson, of Albuquerque, and Dr. G. Santin, of Mexico City, preferred lymphosarcoma; Dr. J. A. Campbell, of Indianapolis, and Dr. H. Glazer, of Akron, offered reticulum-cell sarcoma.

Operative findings: In January, 1960, the patient was operated upon: an ulcerated lesion was found and the frozen section was interpreted as showing lymphosarcoma. A gastrectomy and splenectomy were done; there was an 8 x 6 cm ulceration astride the lesser curvature; 30 lymph nodes were removed with the specimen.

Dr. Meissner: The low power view of the section shows a massive erosion of the gastric mucosa by a cellular mass which undermines the adjacent mucosa and invades extensively the gastric wall. The remainder of the mucosa appears essentially normal other than mild inflammatory changes. Under higher power the mass is composed of sheets of cells of fairly uniform type which invade the mucosa and muscularis. This is obviously a malignant neoplasm. The cells of the tumor show no structural arrangement to suggest epithelial origin; nor are there many mitoses. Some of the cells are multinucleated; some are small with a round, deeply staining nucleus.

The differential diagnosis here is first of all between a reactive process and a neoplasm. There seems to be little doubt that this is a malignant tumor with its extensive invasion and destruction of the gastric wall. The second problem is the decision as to whether this is an epithelial tumor or a lymphoma. There are no epithelial structures to suggest carcinoma. Furthermore the nature of the cells runs a spectrum from lymphocytes and lymphoblasts to reticulum cells. For this reason I believe this represents a lymphosarcoma of the stomach. I found no foci of necrosis and no Reed-Sternberg cells to suggest that this might be a Hodgkin's disease.

The differential diagnosis between lymphosarcoma and small cell carcinoma is always a difficult one and frequently cannot always be made microscopically. While as a rule the lymphomas are large, bulky tumors with extensive superficial ulceration, the gross appearance may be mimicked by carcinoma. The distinction between carcinoma and lymphoma is best made by the examination of multiple sections to search for foci which are either distinctively carcinomatous or lymphomatous. We have found that silver stains are not always of diagnostic value. In spite of the fact that the distinction between carcinoma and lymphoma is difficult to make, it is still an important one because the prognosis for lymphoma of the stomach is much better than carcinoma. A few years ago Dr. Marshall and I reviewed thirty-two cases of lymphoid tumors of the stomach which included Hodgkin's disease, reticulum cell sarcoma, lymphosarcoma and lymphocytoma. Twelve of the thirty-two patients had lived five years or longer without recurrence of the disease following resection. This relatively good prognosis of lymphoid tumors has been the experience of others as well and seems to hold true for lymphomas arising in viscera in general in contrast to the much poorer prognosis of lymphoid tumors presenting predominantly as a lymph node disease.

Dr. Meissner's diagnosis: LYMPHOSARCOMA.

Histopathologic Diagnoses Submitted by Mail

Lymphosarcoma	73
Reticulum-cell sarcoma	20
Hodgkin's	19
Pseudolymphoma	1
Others	15

Dr. Meissner: The only diagnosis I would strongly object to is the diagnosis of pseudolymphoma. I presume that it means that this is a gastritis growing like a lymphoma; I think we have ample evidence that this is a true tumor and not a pseudolymphoma.

Dr. Regato: Dr. R. G. Vernon, of Dubuque, made a diagnosis of Hodgkin's disease; Dr. M. R. Abell, of Ann Arbor, submitted lymphosarcoma; Dr. H. A. Van Ripen, of San Antonio, Dr. F. Bang, of Copenhagen, and Dr. A. P. Stout of New York, preferred reticulum-cell sarcoma.

This slide was examined at the Armed Forces Institute of Pathology (accession No. 992964) in March, 1961; the following report was rendered: "The staff interprets the lesion as reactive lymphoid hyperplasia or pseudolymphoma. This diagnosis is based principally on the mixed type of infiltrate as well as the presence of considerable reactive fibrosis." The report was made by Dr. Elson B. Helwig.

M. B. Dockerty, M.D., Rochester, Minnesota (by mail): I regard this an example of reticulum-cell sarcoma of the stomach. Just because the patient is cured of this condition (they are cured in over 60 per cent of cases) is no reason to assume that we are dealing with a pseudomalignant lesion.

A. P. Stout, M.D., New York, New York (by mail): Reticulum-cell lymphosarcoma. There is a considerable admixture of other cell types but it appears to me that the reticulum cell predominates. These tumors are among the mysteries of oncology because one can never be sure that they will behave like truly malignant tumors.

Subsequent history: In March, 1961, the patient was reported well and doing his daily work; there was no palpable lymphadenopathy.

Dr. Modlin: I think it is worthy of emphasis that the possibility of a given advanced or large gastric lesion being lymphosarcoma should be entertained by the clinician. This means that he would lean toward exploration and biopsy of the majority of patients with large gastric lesions. He will find that many of them are inoperable adenocarcinomas, but he should keep looking for this occasional case of lymphosarcoma which may have a much better prognosis, as has already been pointed out.

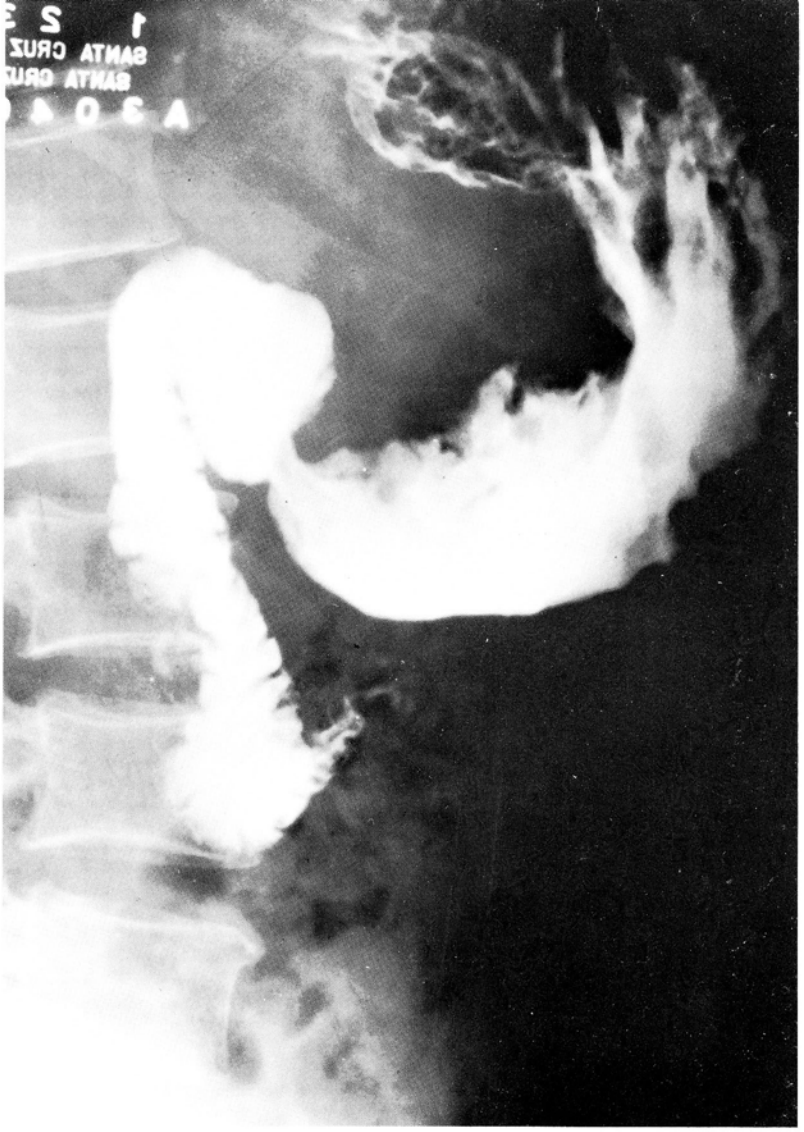


Fig. 1—Marked uneven irregularities of the lesser curvature.

I would be quite interested in asking Doctor Regato and Doctor Kramer and other radiotherapists in the audience how they feel about the management of these lesions. I think it is true that the majority of them have fallen into the clutches of the surgeons before they are seen by the radiotherapist, and usually the surgeon has performed excision of one type or another of the tumor; and then the question arises after the histologic diagnosis is made as to whether or not postoperative external roentgentherapy should be administered.

Dr. Regato: We have cases that have been operated on, in which the pathologist has reported that the tumor extended to the area of excision, and who have been given postoperative raidotherapy and remain well; but when they remain well, in hindsight this is said not to be a tumor, but a pseudotumor. If the patient dies no one will raise the question.

I think that in the field of malignant lymphomas we are just over-estimating the capabilities or trespassing the limitations of the morphologic diagnosis. We have tumors in the human economy that look benign and nevertheless metastasize. I think that in all instances in which a diagnosis of lymphosarcoma of the stomach is made, either by biopsy or after operation, and where there are either lymph nodes or tumor left behind, radiotherapy should be given; there are plenty of cases on record to prove that this is a fruitful procedure.

Simon Kramer, M.D., Philadelphia, Pennsylvania: There is an impression that lymphosarcomas of the gastro-intestinal

tract do better than lymphosarcomas elsewhere. I think this is fallacious; it has been our experience that most of them carry about the same prognosis: that is, a five-year survival of anywhere between thirty and forty per cent. I agree with Doctor del Regato. I think these patients should be treated. I would put it perhaps a little more strongly: I would prefer to see a rather less radical surgical interference if a diagnosis is made, because I think we stand a better chance of doing more good when the blood supply has been less interfered with; and I would stress that lymphosarcomas of the stomach be irradiated post-operatively and the irradiation be directed to the periaortic and upper abdominal lymph nodes. I also think that since these cases often are relatively localized it is important to give an adequate dose. There is a feeling abroad that lymphosarcoma is a very radiosensitive tumor and therefore a small dose is adequate. I think this is fallacious. I think if we are going to get good results we have to give adequate dosage.

H. Braunstein, M.D., Cincinnati, Ohio: I would like to defend the existence or potential existence of a lesion such as pseudolymphoma, without in any way claiming that it is always possible for the pathologist to make this diagnosis. We are not too anxious to go with the present trends in the field of lymphoma, yet we do believe that we have seen this entity and that there may be some validity in the conception that it exists. I think the argument offered that because a large portion of patients with apparent lymphoma survive this doesn't prove it is not lymphoma is perhaps a valid one. When an apparently malignant lesion has an excellent prognosis, as this seems to have, far out of proportion to what one would anticipate from the histologic nature of the lesion, then it is the function of the pathologist to reconsider his criteria, no matter how traditional they may have been and to re-evaluate some of the cases with an idea that perhaps the histologic pattern is fooling him. I must admit that the gross appearance of this one shook me. I had believed that this might be one of these pseudolymphomas.

Dr. Regato: Dr. Braunstein, do you think it would be right, in the re-appraisal of all cases as you suggested, that the pathologist be kept entirely uninformed as to the subsequent developments in the case, and that he makes this re-appraisal on the basis of pure morphology?

H. Braunstein, M.D., Cincinnati, Ohio: There are cases we cannot call pseudolymphoma, but perhaps there is such a lesion which is indistinguishable from lymphoma. There are criteria that have been applied that do appear to have some validity, but the problem is to distinguish all of these from the true lymphoma.

Dr. Meissner: I don't agree that the prognosis of visceral lymphoma is the same as lymphoma that arises in lymph nodes. I think the visceral lymphomas tend to be much more localized if they are primary in that viscera and that the treatment either by surgery or by a combination of surgery and radiotherapy can be curable in a much higher percentage than the lymphomas that present primarly as lymph node involvement. In the cases that Doctor Marshall and I reviewed, we were amazed to find that some of our five-year apparent cures were cases that had a tumor 10 centimeters in diameter that was diagnosable as Hodgkin's disease and had twelve or fifteen lymph nodes involved at the same time, and some of these patients were cured by surgery alone. I don't know of very many cases of lymph node lymphoma that have been cured by surgery alone, or even by a combination of surgery and radiotherapy; I know there have been a few. I think this is true in the lung. In the Cancer Seminar of a few years ago there was a case of lymphoma of the lung. In the thyroid I believe the lymphomas are more curable than the corresponding carcinomas. As far as there being an entity of atypical inflammatory hyperplasia and tumor-like formation, I think there is such a thing. We see this in lymph nodes and I think we probably see it in viscera, although it is harder to recognize in viscera. The last time I tried to make the diagnosis of inflammation of the stomach in contrast to lymphoma I found subsequently that the patient six years before had had a lymphoma removed from the lung which was called a benign reactive lymphoma. Six years later the same process occurred in the stomach and there was a real tendency to make the diagnosis of benign reactive lymphoma of the stomach, although as we look back at these two specimens

Fig. 2—Ulcerated lesion of the lesser curvature.

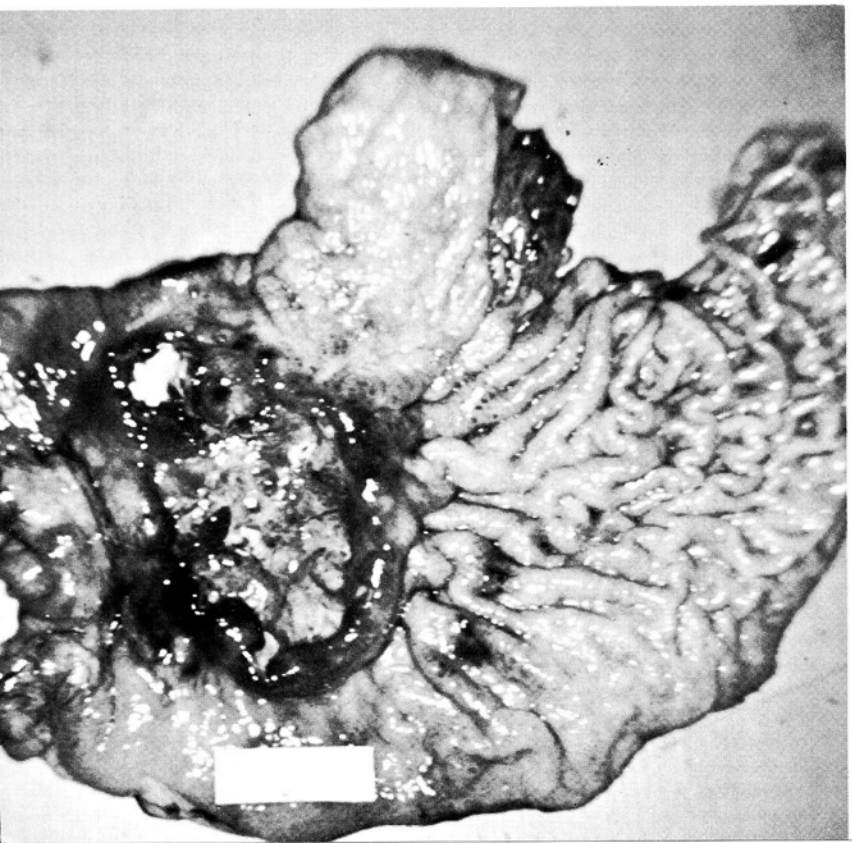
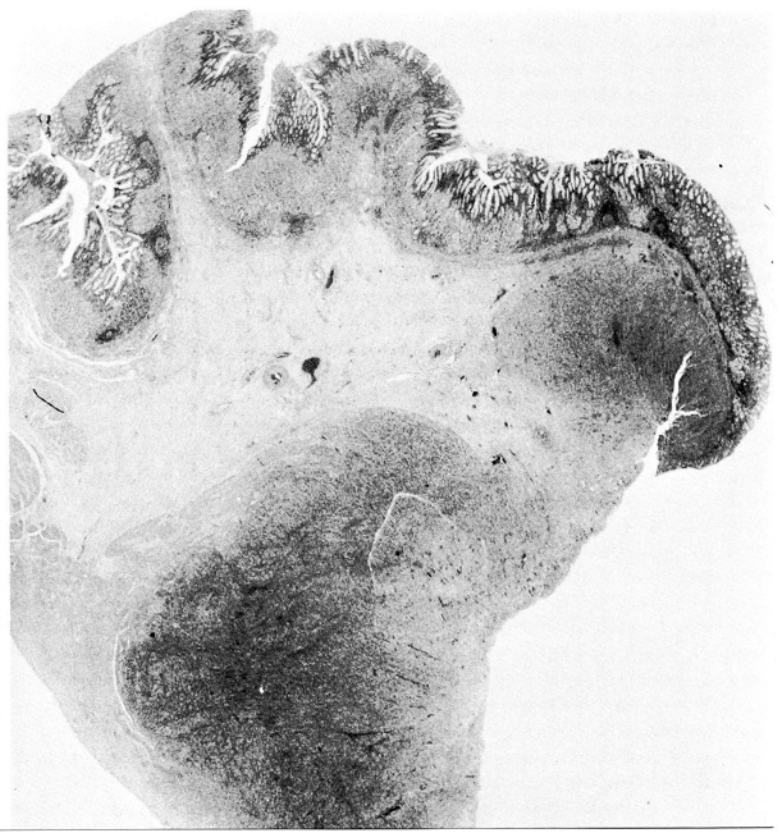


Fig. 3—Photomicrograph of mucosal erosion showing underlying cellular tumor mass (H & E x 5).



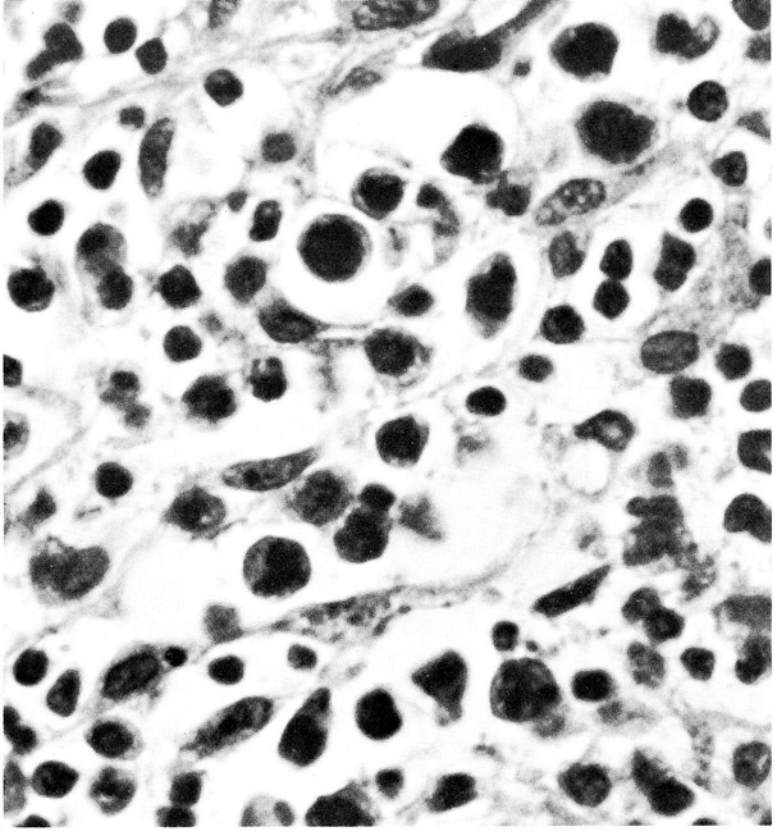


Fig. 4—High power magnification of typical focus of tumor. Many of the tumor cells resemble lymphoblasts (H & E x 1000).

from the same case I think we must conclude that they are malignant lesions.

R. C. Vernon, M.D., Dubuque, Iowa: I wonder if we could be privileged to hear from Doctor Alcott as to what the examination of the lymph nodes showed.

D. L. Alcott, M.D., San Jose, California: I had made the original diagnosis of lymphosarcoma. I have seen a set of slides of a Seminar on gastro-intestinal lesions presented by Doctor Helwig in Indiana; there was a case which was diagnosed as reactive lymphoid hyperplasia or pseudolymphoma. Apparently Dr. Helwig's group is restudying a series of over 130 cases of lymphoma of the gastro-intestinal tract and they are breaking them off into different groups; there are some of these lesions that grossly look like lymphoma and their enlarged nodes show no evidence of the lymphomatous process, just a mild reactive pattern. The spleen also did not show evidence of a lymphoma. Because of this Doctor Helwig and his group were making a detailed study and they have been able to find in the areas away from the ulceration and in the deeper areas, a polymorphic pattern with plasma cells, lymphocytes, granulocytes and histiocytes and fibroblasts, and particularly some nodularity and production of abundant collagen, these are the ones that are labeled as reactive lymphoid hyperplasia or pseudolymphoma. It seems to me in the cases that I have seen or read about, that in some of the cases they have resected across tumor and have not had irradiation and some of those have had prolonged survival; and that in other instances when the nodes were involved by tumor the course is the same as malignant lymphoma.

This patient was seen a week ago, he had gained weight following surgery and is back working every day. The lymph nodes were reactive. There has been no postoperative irradiation.

Dr. Regato: One must accept the fact that at one time a lymphosarcoma may not as yet have metastasized to the lymph nodes; this is the case in the nasopharynx, in the base of the tongue, in the nasal fossa, in the tonsil where lymphosarcomas may be found before they have metastasized, and properly treated and controlled. To say that these are all *probably* not lymphosarcomas is just simply enlarging too much the limitations of the morphologic diagnosis of tumors. Also one may accept the concept that there are degrees of malignancy in lymphomas as in osteosarcomas, leimyosarcomas, etc.

D. L. Alcott, M.D., San Jose, California: I think you are right. It may well be that we cannot diagnose these cases but I think it would be well that we try. Basically, the fact that some of these have prolonged survival does not prove anything and perhaps this is a bit of presbyopic thinking that is being used to call these things benign. Doctor Dockerty told us of a case that had been operated on and it took about fifteen years I believe for the lymphoma to manifest itself again.

Mark Wheelock, M.D., Chicago, Illinois: We have approximately 250 extranodal malignant lymphomas unpublished. I can tell you very definitely that there are several cases which have been missed by some of the finest pathologists in the United States; they have made the diagnosis of either nonmalignant lymphoma or of pseudolymphoma, and the disease has progressed and has killed the patient.

I was at that Indianapolis meeting and I can tell you very definitely that Doctor Helwig was very vigorously outvoted by the group. I don't think that he is necessarily correct and no one has any more regard for him than I do. In fact, a former resident of ours was diagnosed as a case of pseudolymphoma from the highest authority. Henry Rappaport and I thought it was malignant; at the present time he has disseminated lymphoma lymph nodes.

Leo Lowbeer, M.D., Tulsa, Oklahoma: To base a histologic criterion on the biologic action of a tumor is to put it bluntly, bankrupt pathology. It would be just as valid to call lymphatic leukemia a benign process since we know that it can last for twenty or twenty-five years. The same is true for what used to be called "benign follicular lymphoblastoma" and which we know now has a great longevity and is a malignant process. The presence of inflammatory cells like eosinophils and plasma cells is obviously explained by the ulcerative process which is present in these lesions and has nothing to do with a neoplastic character. Fibrosis we always find in cases of reticulum cell sarcomas of the fibrillar type where reticulum cells produce collagen and reticulin. In lesions such as this one where there is a complete absence of a follicular pattern, which we associate with malignant process, I cannot see how one can make a diagnosis of a benign process.

Dr. Meissner: The diagnosis of the benign process that looks similar to a malignant process to me is always a very dangerous pathologic diagnosis. I respect Doctor Helwig very much; I am sure there is such a thing as a benign atypical lymphoid hyperplasia which can look like a tumor but the thing that concerns me is that if this information is disseminated throughout all the pathology laboratories in the country the same thing is going to happen as what has already happened with juvenile melanoma: because the patient is between the ages of 1 day and 40 years, there is a great tendency to call all the melanomas that occur in that age group "juvenile melanomas" and consider them benign. Now, nothing could be further from the truth.

R. C. Vernon, M.D., Dubuque, Iowa: If patients with frank nodal lymphomas in axillary areas, inguinal areas, and so forth, undergo radical resection of these areas you will be surprised at how long these individuals may survive. In this regard I think it is most important to use localized or regional treatment, whether it is surgery or radiotherapy, rather than to go to the chemotherapeutic agents. These almost invariably shorten the patient's life in my experience.

Dr. Regato: As you know, when a pathologist is given a node he cannot tell whether that is a leukemic node or a lymphosarcomatous node; in some instances he might, but in many he cannot. If you tell me there is a patient who

has had peripheral lymphomatous nodes removed and got along well and his general condition is all right, I will propose that we re-study the patient, for the probability is that he has chronic lymphogenous leukemia that presented at the nodes first; what Conheim called "pseudoleukemia" and which he should have called "pseudolymphosarcoma". I know of such reports of lymphosarcoma that were cured by surgery, but actually this is not likely. The probability is that these were diagnosed as lymphosarcoma because morphologically they could not be differentiated.

H. Braunstein, M.D., Cincinnati, Ohio: From your last statement I would gather then that you accept the idea that something may look like a lymphoma and be a benign process, especially when it is treated by surgery and radiotherapy. Do I understand then that you do accept this entity?

Dr. Regato: I do not reject the entity "lymphoid hyperplasia", I only would not like to see this diagnosis made simply because a patient has remained well after treatment. Between lymphosarcoma and leukemia, both lethal, there is a difference in approach and expectancy. Our contention is that there is a great deal of confusion due to the belief that these things are clearcut histologically. We have two cases in our hospital that were referred to us after an operation had removed a considerable amount of nodes and a diagnosis of lymphosarcoma had been made. The eventual development of both cases through the blood picture and bone marrow manifestations proved that they were cases of chronic lymphogenous leukemia. The comfortable way out is to explain these cases as a transformation of one into the other but we object to this.

H. Braunstein, M.D., Cincinnati, Ohio: I don't agree that the pathologist must be bound by his preconceived notions concerning the morphology of a lesion; he should review his material when he finds that the clinical outcome of these cases doesn't seem to coincide with his predicted prognosis. Many of the lesions that have lately been elucidated in surgical pathology in the last ten years have resulted from this very review; lesions such as the pseudosarcomatous fasciitis and some of the subcutaneous lesions described by Schumann, which simulate very malignant tumors and behave in a benign fashion, would not have been discovered if conventional morphologic criteria alone had been utilized.

Dr. Regato: I am glad to have you on the clinicians side, Doctor Braunstein. I believe that in the field of tumors the clinical character is sometimes very enlightening. This is true in tumors of the thyroid, parotid, and in other areas where the clinical developments are considerably more eloquent than the morphologic appearance. I don't believe in depriving the pathologist of worthy clinical information, but I am not willing to buy as morphologic diagnosis something that is not. The clinical differences should as you suggested spur a revision, but if morphologic criteria are found that explain them they should be found also independently and tested against the clinical behaviour.

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8. Inflammatory Fibroid Polyp of the Stomach

Contributed by S. A. Morton, M.D. and D. B. Claudon, M.D., Milwaukee, Wisconsin

THE PATIENT was a 63-year-old man in February, 1959, when he suffered from eructations, bloating and epigastric pain. There were no findings on physical examination except for tenderness of the epigastrium. The hemoglobin was 7.7 gm per cent and the hematocrit 26 per cent.

Dr. Schatzki: There is quite some discrepancy between the report of the first examiner and the film of the second examination two months later. For the purposes of this exercise, we shall assume that the first examiner was excellent. He found a duodenal diverticulum and ulcer and nothing wrong in the stomach. The second examination shows a sharply defined lobulated filling defect in the prepyloric area. Neither the duodenal ulcer nor the diverticulum are visible, possibly due to insufficient filling and distension of the duodenum. What causes the prepyloric defect which was not present at the first examination? It could be a blood clot. The shape of the defect is consistent with a clot, although the mass is considerably smaller than any blood clot I have seen in the stomach. This could be food collected proximal to a scarred duodenal cap. Another intriguing possibility came to my mind. Might it be possible for a duodenal diverticulum to invert itself and intussuscept backwards into the stomach? I have never heard of anything like this, and the solid retroperitoneal attachment of the duodenum makes such a happening highly unlikely. Finally, could this be a pedunculated polyp which at the time of the first examination was intussuscepted into the duodenum? It should have been visible there and our excellent first examiner would have discovered it. I, therefore, have to assume that the mass is due to blood clot or some swallowed foreign material which collected proximal to the pylorus.

Dr. Schatzki's impression: BLOOD CLOT or INGESTED FOREIGN MATERIAL.

Roentgenologic Impressions Submitted by Mail

Benign polyp	19
Foreign body	18
Ectopic pancreas	13
Carcinoma	10
Eosinophilic granuloma	2
Swallowed something!	1
Others	30

Dr. Schatzki: The radiologists are equally divided into pessimists and optimists; the pessimists thought that the first examiner just missed the lesion; the others are in my boat and thought he should have seen it and therefore since he was a good examiner, it wasn't there. There is occasionally a very large ectopic pancreas in the prepyloric area; this would be a possibility.

Dr. Regato: Dr. J. W. Barber, of Cheyenne, diagnosed a benign pedunculated polyp. Dr. B. Felson, of Cincinnati, and Dr. R. Mosely, of Chicago also had the impression of the presence of a foreign body. Dr. G. Schwarz and Dr. J. C. Lemon, of Denver, offered a diagnosis of ectopic pancreatic tissue. Dr. M. Castillo, of Mexico City, preferred polypoid carcinoma.

Operative findings: On April 21, 1959, a Billroth resection of the gastric wall with the polyp was done: a polypoid lesion, 1.5 x 4 cm was found in the region of the antrum with an ulceration that suggested carcinoma; the polyp homogeneous and resilient and was covered by thin mucosa.

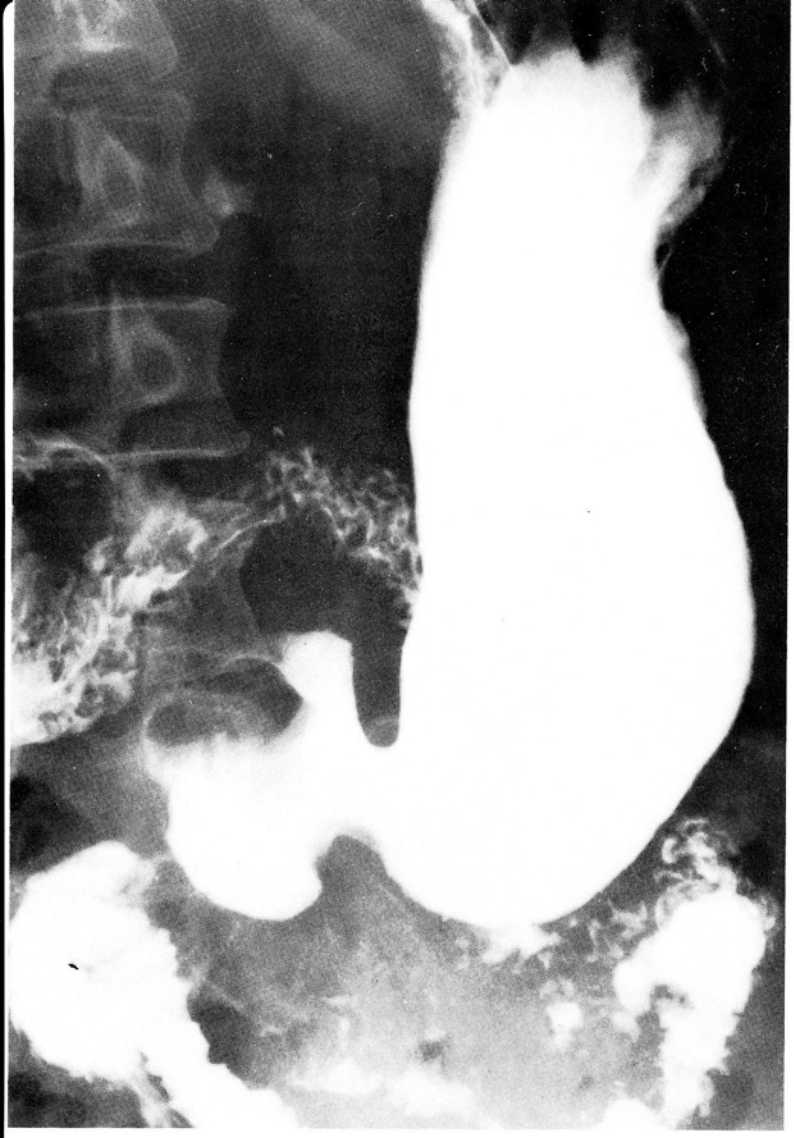


Fig. 1—Sharply defined filling defect in the prepyloric area.

Dr. Meissner: The low power view of the slide shows a polypoid neoplasm, which has eroded the mucosa and is ulcerating over an extensive area. The lesion appears to lie primarily in the gastric wall. The adjacent mucosa shows a mild inflammatory change, but nothing else. On higher power examination of the lesion there are several distinctive features: one is a prominent and diffuse infiltration with eosinophils; a second is the presence of numerous small blood vessels; and the third is the peculiar arrangement of stromal cells about the blood vessels. These changes are present throughout the lesion but in varying degree. In some foci the stromal cells predominate to give a tight, compact appearance. Near the base of the lesion there is a considerable amount of fibrosis. In other foci the vessels are particularly prominent and the peculiar concentric arrangement of the spindle cells about the blood vessels is striking.

The differential diagnosis of this lesion must recognize the presence of numerous blood vessels, a peculiar perivascular arrangement of spindle cells about the blood vessels, and the presence of numerous eosinophils. This is a lesion which has been described on numerous occasions under many different names. The difference in terminology depends largely on what aspect of the process one wishes to emphasize. For example some people have called this eosinophilic granuloma of the stomach, emphasizing the fibro-vascular granulomatous over-growth and the numerous eosinophils. Others have noted the great resemblance of portions of the lesion to a hemangiopericytoma and have labeled it as such. Still others have suggested the term fibroma, neurofibroma and so forth. Helwig and Rainer in 1957 described a group of these lesions and suggested that since the exact pathologic nature was still unknown it might be better for the time being to give a non-descript name to the process; the name they suggested was inflammatory fibroid polyp. This is the name I propose to use; I do so with the understanding that the lesion may justifiably be called by other terms such as hemangiopericytoma or eosinophilic granuloma equally well.

These benign inflammatory polyps characteristically occur in the antral end of the stomach, often causing obstruction and sometimes ulceration and hemorrhage. They occur in all adult age groups. Their course is that of a benign tumor without apparent pre-cancerous significance.

Dr. Meissner's diagnosis: INFLAMMATORY FIBROID POLYP.

Histopathologic Diagnoses Submitted by Mail

Eosinophilic granuloma	49
Inflammatory fibroid polyp	22
Leiomyoma	21
Granuloma	7
Neurogenous tumor	6
Hemangiopericytoma	3
Others	12

Dr. Meissner: Those who made the diagnosis of eosinophilic granuloma would emphasize the presence of the eosinophils. I don't believe these proliferating cells are smooth muscle cells and I have never seen a leiomyoma show this type of eosinophilic reaction.

Dr. Regato: Dr. E. S. Murphy, of Mexico City, made a diagnosis of eosinophilic granuloma of the Vanek and foreign body (crystalline) type. Dr. M. B. Dockerty, of Rochester, submitted fibrous inflammatory polyp "a la Bullock and Helwig" or vice-versa. Dr. W. A. Meriwether, of El Paso, preferred a diagnosis of pseudo-tumor, inflammatory fibroid polyp "of Ackerman".

Subsequent history: The patient was last seen in February, 1961, when he appeared in good health.

Dr. Modlin: I think that it would be incumbent on the surgeon to attempt to determine that it was indeed a benign lesion and save the patient the increased risk, small as it is, of a subtotal gastric resection. I would agree that a lesion this close to the pylorus would be difficult to remove locally. Not only would you be uncertain of removing the base of the attachment to the wall of the stomach, but also you would run the risk of possibility of cicatrix and pyloric obstruction. Probably the safest procedure, both from the standpoint of being widely around a polyp that could be malignant, and also from the standpoint of pyloric obstruction, would be a subtotal gastric resection. I wouldn't have done this however if the lesion were located at least another 3 or 4 cm away from the pylorus.

Mark Wheelock, M.D., Chicago, Illinois: I must admit that I called it a leiomyoma. At the same time if I can defend myself, the piece of tissue which we received didn't even include mucosa. I would like to ask Dr. Meissner if he did a Masson connected tissue stain to be absolutely sure that this was not muscle; and if he hasn't seen changes similar to this in necrotic leiomyomas in the uterus?

Dr. Meissner: I did a trichrome stain—there is not very much connective tissue in this, so the term "fibroid" is perhaps a misnomer too, but neither did the cells look like typical smooth muscle cells. I don't believe this is the type of change that I have seen in leiomyomas, with this diffuse eosinophilic infiltration, and the peculiar vascular arrangement. I think these blood vessels are particularly interesting; Dr. Stout mentioned several of these as hemangiopericytomas, but notes the fact that it is interesting that eosinophils occur along with them.

Dr. Schatzki: Dr. Meissner, do these lesions keep on growing? Have they grown visibly under observation, and how fast did they grow?

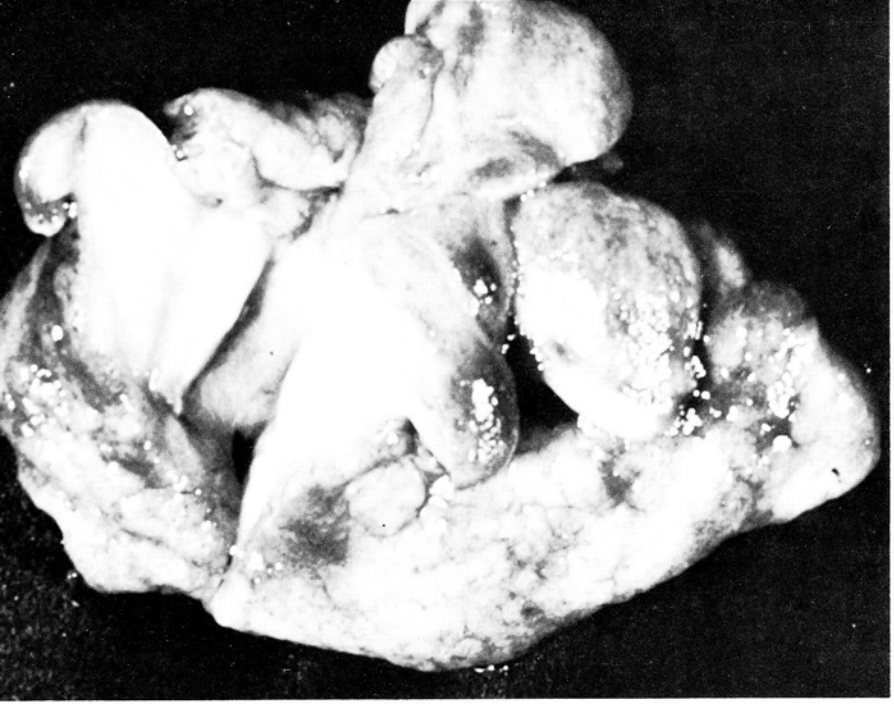


Fig. 2—Gross appearance of surgical specimen.

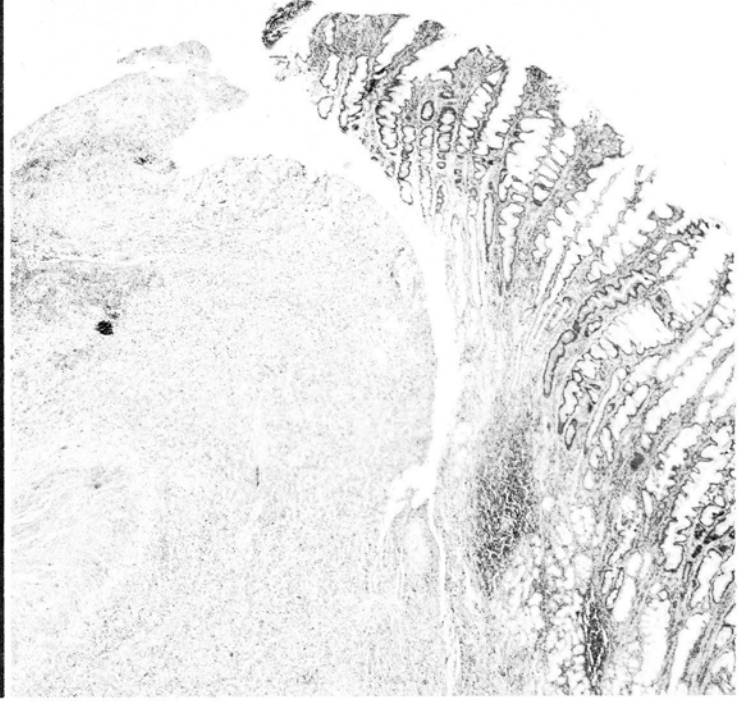


Fig. 3—Low power photomicrograph of polypoid mass compressing and eroding gastric mucosa (H & E x 30).

Dr. Meissner: I cannot answer that question—there have been so few reported that I don't think we know the rapidity of growth or whether they are capable of continued growth. In fact we don't even know if they are a tumor or not. I suspect, and most people who have written about these have implied, that they are probably inflammatory lesions of some type, perhaps an excessive proliferation of inflammatory tissue in response to something; which gets us back then again to the question of foreign body, and I don't think we should completely overlook that as a possibility for the stimulus of this entire inflammatory polyp.

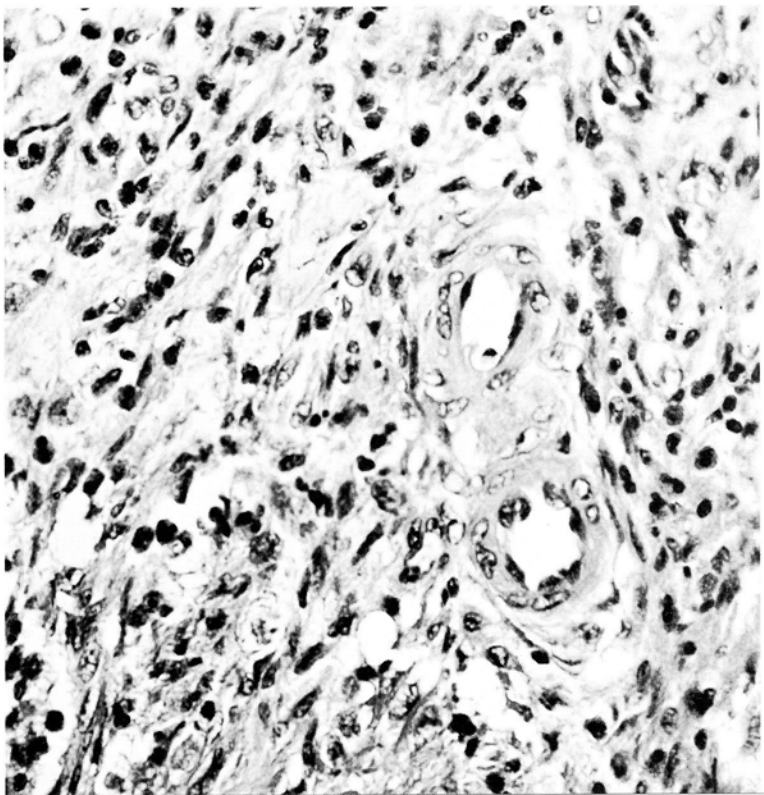
H. Braunstein, M.D., Cincinnati, Ohio: If these are not smooth muscle cells; if they are not fibroblasts, and they are not Schwann cells, and they are not pericytes, what are they?

Dr. Meissner: I wish I knew for then we would know the proper diagnosis. Doctor Stout believes they are hemangiopericytes, and I am not convinced that they aren't. When blood vessels proliferate they can carry several components along with them. They carry the endothelial lining of the blood cells; they carry the smooth muscle cells of the wall, and they carry hemangiopericytes along with them; so in any proliferating lesion that has blood vessels any of these may be seen and I suspect any and all are present in this case.

O. Rambo, M.D., San Francisco, California: We have encountered two almost identical lesions—one in the jejunum of a young person; the other in the colon of a woman who had been irradiated for carcinoma of the cervix. On the first one we were misled by the angry fibroblasts and we called it a low-grade sarcoma. I think the absence of collagens is probably a function of the youth of this particular tumor. We became a little more sophisticated on the second case and I think we diagnosed it correctly; these lesions apparently can grow rather rapidly.

J. Budinger, M.D., Chicago, Illinois: There is a very nice review of this whole subject in the American Journal of Surgery (Carlson). Apparently these lesions can exist not only singly in various parts of the gastro-intestinal tract, but also multiple ones all along the tract; they had no manifestations of systemic disease.

Fig. 4—Higher power magnification from center of polypoid mass showing prominent blood vessels, numerous spindle cells and inflammatory cells (H & E x 450).



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9. Kaposi's Disease of the Stomach

Contributed by E. ZONANA, M.D., Galveston, Texas

THE PATIENT was a 66-year-old woman in February, 1960, when she complained of vomiting and distressing epigastric and thoracic pains of nine months duration. For three years she had had an ulceration of the plantar region and maculo-papular lesions of the skin of the extremities; an ulceration of the rectum had been treated with radium; she had also received treatment for diabetes. There were 8,600 white cells per mm^3 with 9 per cent eosinophils.

Dr. Schatzki: This has been the most intriguing case of the whole group for me. Two sharply defined almost identical small defects are seen in the upper stomach. They have central dimples, most likely due to ulceration. Could these be benign ulcers? It is possible but unlikely from the extremely sharp edges of the surrounding mounds. Ulcerated cancers are definitely possible. It is, however, unlikely that two of them should look so much alike.

The fact that they are so much alike may indicate that they are of the same age, and may be blood born. It is tempting to bring them into relation to the skin lesions. Malignant melanoma metastasizing to the gastrointestinal mucosa is not uncommon. I should like to know a little more about the skin lesions, their color, etc. There is nothing to suggest from the story that the skin lesions are melanomas and the clinical course would be highly unusual for melanoma.

There is, however, one skin condition which could fulfill the description of the skin lesions and produce gastric metastasis. That is Kaposi's tumor. The rectal lesion could be due to Kaposi's. I never saw Kaposi's tumor of the skin ulcerate the stomach nor the rectum. These ulcerations may possibly be due to mechanical trauma.

Dr. Schatzki's impression: KAPOSI'S TUMOR.

Roentgenologic Impressions Submitted by Mail

Eosinophilic granuloma	25
Melanoma	15
Leiomyoma	13
Several benign lesions	32
Kaposi's	1
Others	27

Dr. Schatzki: There were 25 radiologists who thought of eosinophilic granuloma. I thought of this possibility also; one thing which got me going in that direction, which really shouldn't have, was the 7 percent eosinophils in the blood stream. Some of the eosinophilic granulomas of the stomach are reported to have shown eosinophilia in the blood stream, but the majority have not shown any eosinophilia; this was a rather superficial coincidence for any skin lesion may cause that much eosinophilia. The eosinophilic granuloma of the stomach are usually surprisingly sharply defined, as was this case and some of them have shown ulceration. I was impressed by the absolute symmetry of these two lesions, and therefore I finally decided to call it Kaposi's. I have given you my reasons why I did not call it melanoma. For a leiomyoma—we would have to assume again that two leiomyomas looked exactly alike, had exactly the same kind of ulceration and this is a little bit unlikely.

Dr. Regato: Dr. J. C. Campbell, of Indianapolis, and Dr. N. Glazer, of Akron, favored a metastatic melanoma; Dr. B. Felson, of Cincinnati, wrote that "it could not be anything else!" Dr. R. Raap, of Ann Arbor, suggested angiosarcoma; Dr. V. LaTourette, of Denver, offered a leiomyoma and Dr. O. F. Prochazka, of Liberal, Kansas, diagnosed this as a case of Kaposi's Disease.

Dr. Meissner: The low power field of the slide shows a thickening of the gastric wall with umbilication and ulceration of the mucosa, which appears to involve the muscular coat primarily. The higher power magnification shows two processes in the muscular coat: one is a focal dilatation of blood vessels suggesting a hemangioma; the other is a proliferation of spindle cells which extends up to and into the gastric mucosa. The bulk of the lesion is composed of the proliferation of spindle cell elements; in some foci these grow like smooth muscle cells; in others they look more like fibrous tissue. The spindle cell areas show no mitoses. The lesion is quite vascular and there is much evidence of old and recent hemorrhage.

This lesion is characterized by three elements: the presence of abnormal blood vessels, a proliferation of spindle cells and fibrosis. The differential diagnosis must, of course,

Fig. 1—Roentgenogram showing two sharply defined defects in the upper half of the stomach.

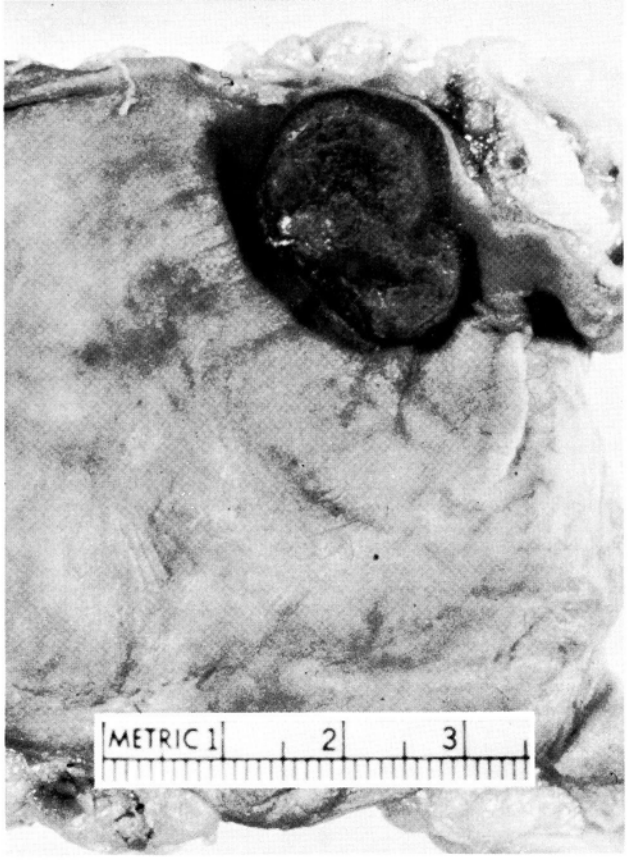

Fig. 2—Gross appearance of intestinal lesion found in postmortem examination.

include smooth muscle tumor or a connective tissue tumor, but this does not take into account the abnormal blood vessels which are present. I do not believe this is a fibrosis or a reaction to injury because the arrangement seems more purposeful than this. The one diagnosis which is capable of encompassing the various features of this lesion is Kaposi's disease, since here we expect to find an angiomatous component together with a proliferation of various types of mesenchymal cells. The history of lesions of the extremities and even the ulceration of the rectum are additional suggested evidence for this diagnosis.

While Kaposi's disease predominantly involves the skin, about ten percent of the cases show visceral manifestations as well. When there is visceral involvement, the gastrointestinal tract is one of the most common sites. The exact pathological classification of Kaposi's disease has always been a problem. Some of the cases appear only as a benign inflammatory proliferation of blood vessels and mesenchymal elements. Others look frankly sarcomatous and many cases show transition between the two variants. Whether one should use the term Kaposi's sarcoma or Kaposi's disease depends largely on individual preference. Certainly many of the cases show manifestations of a malignant tumor.

Dr. Meissner's diagnosis: KAPOSI'S DISEASE.

Histopathologic Diagnoses Submitted by Mail

Kaposi's sarcoma	84
Gastritis	13
Hemangioma	14
Leiomyoma	6
Others	18

Dr. Meissner: I asked Dr. Cesare Tedeschi, who wrote a monograph on the pathology of Kaposi's disease, two questions about this case: one was about the coincidence of Kaposi's disease in diabetes. He says that Hurlbut and Lincoln in 1949 did find an association of these two conditions: six of their thirteen cases of Kaposi's disease had diabetes. With regard to the high eosinophilic count he says that this is not a feature of Kaposi's disease to his knowledge and that "the only peripheral blood abnormality taking place in this

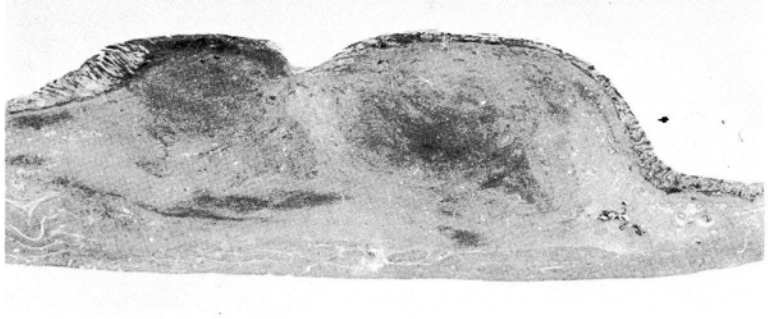

Fig. 3—Focal thickening of gastric wall with ulceration (H & E x 4).

condition is varying degrees of monocytosis, including atypical forms".

I don't quite understand the diagnosis of just "gastritis" here. There seems to be much more than inflammation alone with the proliferation of the stromal elements. I can see how the diagnosis of hemangioma might be considered if one saw only the vascular lesion. I think we have already discussed leiomyoma. I think perhaps this is partly leiomyomatous but not just an ordinary leiomyoma.

Dr. Regato: Dr. Carlo Sirtori, of Milan and Dr. C. F. Schwinn, of Los Angeles, also submitted a diagnosis of Kaposi's disease.

M. B. Dockerty, M.D., Rochester, Minnesota (by mail): This is a malignant spindle-cell neoplasm which resembles a fibrosarcoma with a matrix that is altogether too vascular; it is some form of hemangiofibrosarcoma, like Kaposi's.

Subsequent history: The patient received palliative roentgentheraphy but continued to worsen and on July 18, 1960, she expired. At autopsy lesions of Kaposi's sarcoma were found on the skin, stomach, colon, rectum, lungs, small bowel, trachea, mesentery and adrenals; an incidental thymoma was found in the mediastinum.

Dr. Schatzki: Was this ulceration or was this just dimpling of the lesion?

Dr. Meissner: No, there is actually erosion of the mucosa. It isn't what we would call a peptic ulceration; it is

Fig. 4—There is a cluster of small blood vessels resembling hemangioma at the periphery of the main mass (H & E x 20).

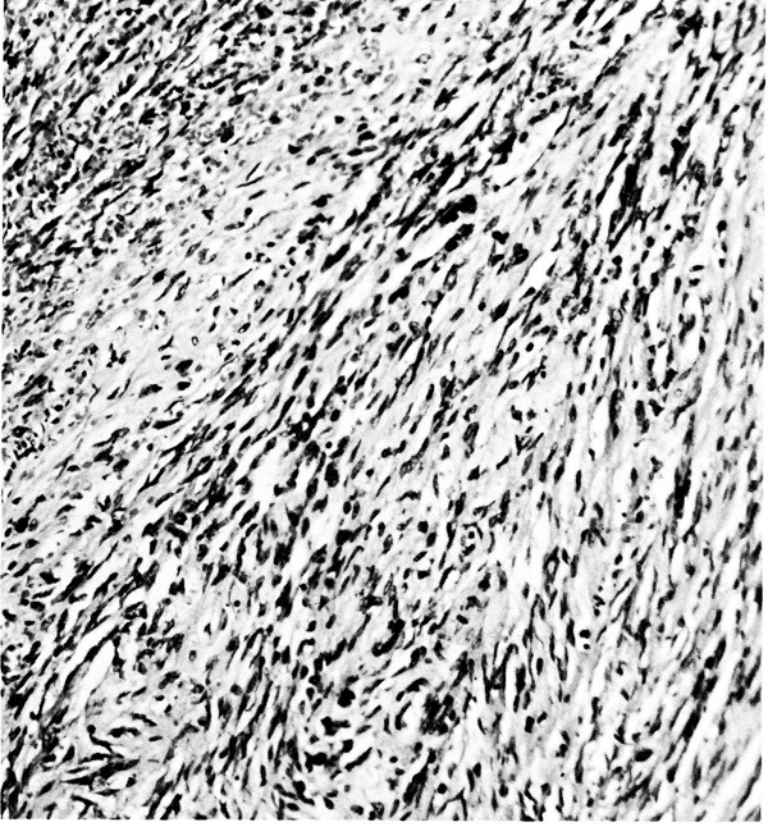

Fig. 5—Higher power magnification from center of intramural mass showing proliferation of spindle cells (H & E x 200).

more like the ulceration and erosion that occurs in a leiomyoma.

Dr. Modlin: I would like chiefly to congratulate Dr. Schatzki and Dr. Prochazka on a bit of brilliant detective work.

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10. *Gastric Plasmocytoma*

Contributed by R. LATTES, M.D., New York, New York

THE PATIENT was a 52-year-old man in August, 1960, when he complained of hematemesis; he was a heavy drinker and had had such episodes for 4 years, having required blood transfusions which led to homologous hepatitis. On examination there was a tender mass, 6 x 7 cm on the right side of the epigastrium; spleen and liver were not palpable. The hemoglobin was 8.8 gm per cent; cephalin flocculation and thymol turbidity were negative; there was a trace of albumin in the urine.

Dr. Schatzki: The single film of the stomach shows irregularity along the greater curvature side of the stomach which can be divided into an upper and a lower area. In the lower area I see normal folds, and the appearance of the stomach in this area is probably produced by pressure on the distended stomach by an outside organ, for instance, the spleen. The upper defect conceivably could be produced by a similar mechanism. The mucosal folds in this area, however are less definite and, therefore, it is very well possible that there is a tumor mass in this upper area. From this film alone, I do not dare to say whether this tumor is extrinsic to the stomach or in the stomach wall. Could gastric varices in the presence of a history of alcoholism and repeated episodes of hematemesis produce the appearance of the greater curvature? The location would be highly unlikely for varices, and the duration of the case and the description of the clinical findings makes the presence of cirrhosis unlikely.

Conclusion: Probable mass closely connected with the upper part of the greater curvature of the stomach. Most likely, the mass originates outside the mucosa. It may even originate outside the stomach, in the left lobe of the liver.

These conclusions do not explain the palpable mass on the right side of the epigastrium of which the film shows no evidence.

Dr. Schatzki's impression: Mass in the upper part of the stomach, most likely originating outside the mucosa.

Roentgenologic Impressions Submitted by Mail

Carcinoma	22
Lymphosarcoma	19
Benign ulcer	18
Hepatoma	15
Pancreatic pseudo-cyst	10
Hypertrophic gastritis	9
Others	15

Dr. Schatzki: Twenty-two of my colleagues called this carcinoma. I have nothing to say against this diagnosis or against the diagnosis of lymphosarcoma although for lymphosarcoma of this size one should see a little more ulceration.

I don't see any justification for a diagnosis of benign ulcer and I think the reason for this was a big inflammatory mound around the ulcer, but this would be a very peculiar appearing ulcer, and this thought did not come to me. I thought of hepatoma as a possibility. The patient was an alcoholic; this could be a hepatoma of the left lobe of the liver which was pressing down there, but actually if this bleeding was due to varices, he had been bleeding for four years, which I understand is quite a long time for a sclerotic to keep on bleeding and still be alive, so I finally concluded that it was probably not it. This thing is a little bit too irregular for pancreatic pseudo-cyst; otherwise this film could be consistent with it. I think the evidence is rather scant for such a diagnosis of hypertrophic gastritis.

Dr. Regato: Dr. H. Houser, of Cleveland, submitted an impression of hepatoma; Dr. J. Aguilar, of Mexico City suggested a pseudo-cyst of the tail of the pancreas. Dr. P. Hodes, of Philadelphia, and Dr. G. Santin, of Mexico City, diagnosed an ulcerated myoma.

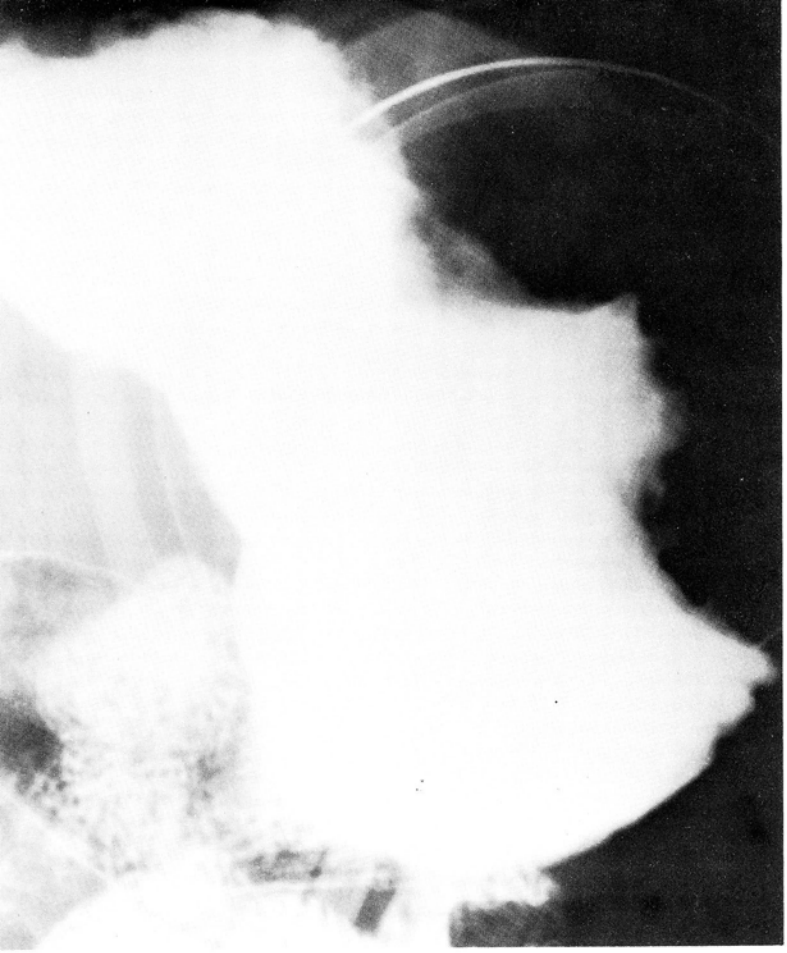

Fig. 1—Roentgenogram showing two adjacent defects of the stomach.

Operative findings: On August 26, 1960, an esophagogastrectomy, splenectomy and omentectomy were done. The gastric lesion was 12 cm in diameter, involving the entire fundus and coming within 3 cm of the esophagus and 6 cm of the pylorus; it was raised and bosselated but covered by intact mucosa. Cut section revealed a firm consistency and a gray-white color. Some of the nodules had a small central ulceration.

Dr. Meissner: The low power view of the section shows a large mass underlying the mucosa and causing a great enlargement of the gastric wall. The mass extends up into the muscularis musoca, and I suspect that in some areas the mucosa may have been ulcerated even though it does not show in our section. The mass is formed of sheets of cells which form no architectural arrangement. The cells show a moderate degree of pleomorphism, but basically seem to be of the same type. They have an acidophilic cytoplasm and the nucleus is often eccentrically placed. Some of the nuclei are very large, and an occasional nucleus shows mitosis. There are a few foci of lymphocytes which seem to merge with the great majority of these cells just described.

These cells with their pink cytoplasm and eccentric nuclei are plasm cells. While they are not all typical, they are usually identifiable as such. The differential diagnosis, therefore, is between an inflammatory process with massive plasma cell reaction or a plasma cell tumor. The size and extent of this lesion with its obvious invasive nature and the relative absence of other inflammatory cells allows the diagnosis of tumor quite readily.

Plasma cell tumors have rarely been reported in the stomach, but they may be seen involving any of the tissues of the body. When the tumor is solitary it is called a plasmacytoma; when there are multiple lesions, particularly with bone involvement, it is called a multiple myeloma. There is no reliable way of determining in any individual instance whether the lesion is solitary or just one of many similar lesions. If the tumor is a solitary plasmacytoma, the prognosis is much better than with multiple myeloma. The solitary plasmacytoma acts as a low-grade malignant tumor, often reaching a large size before treatment is instituted. Its gross appearance resembles that of a lymphoma. Many plasma cell tumors are associated with abnormal globulins in the serum and it is interesting to speculate whether or not the "trace of albumin" in the urine of this patient was truly albumin or an abnormal globulin secondary to the plasma cell tumor.

Dr. Meissner's diagnosis: PLASMOCYTOMA.

Histopathologic Diagnoses Submitted by Mail

Plasmocytoma	101
Myeloma	15
Lymphosarcoma	8
Hepatoma	6
Carcinoma	5
Hodgkin's	3
Others	5

Dr. Meissner: Apparently this lesion is much easier to diagnose for the pathologist than it is for the radiologist. The

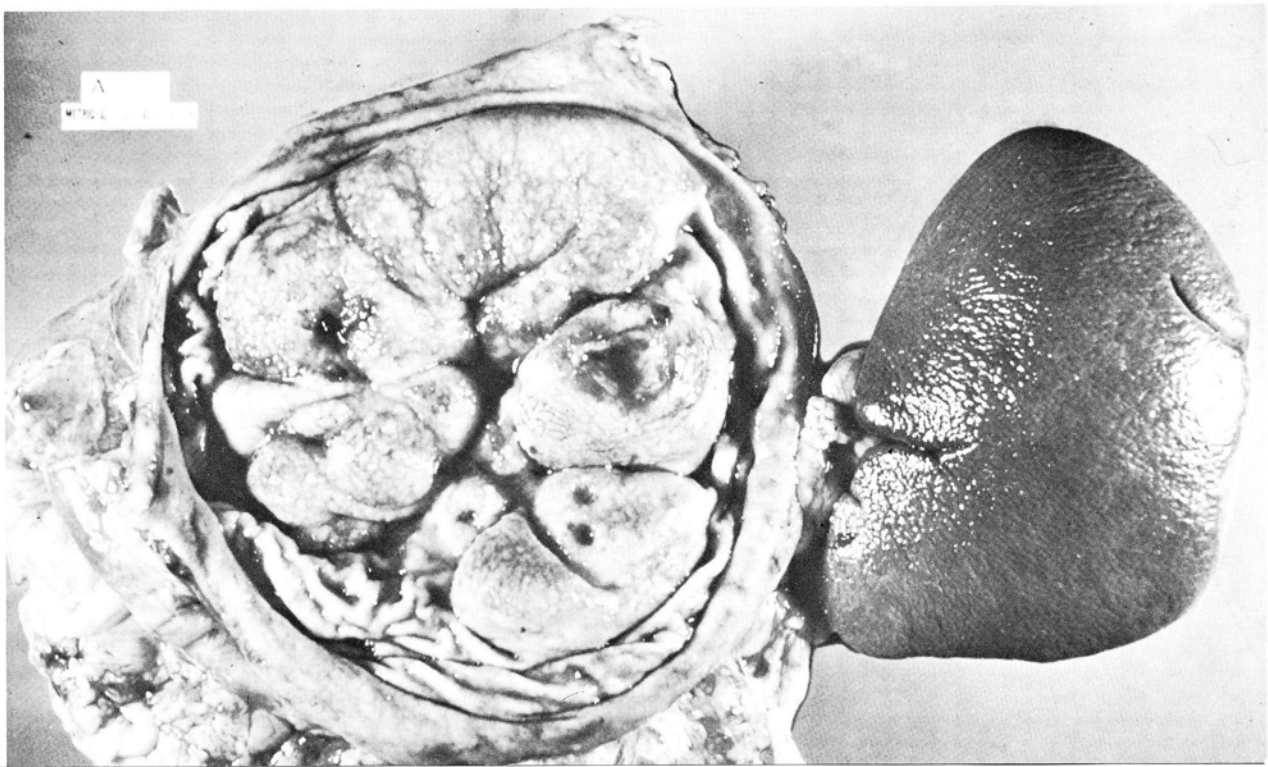

Fig. 2—Nodular masses with superficial ulceration occupying most of the surface of the stomach.

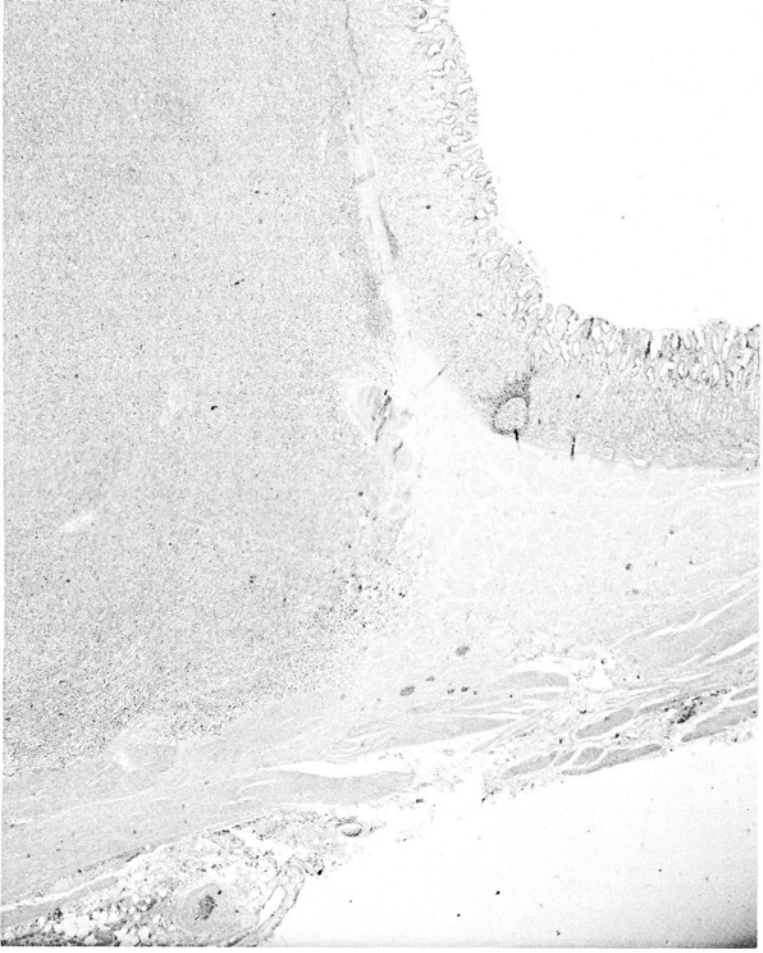

Fig. 3—Low power photomicrograph of homogeneous cellular mass underlying gastric mucosa (H & E x 20).

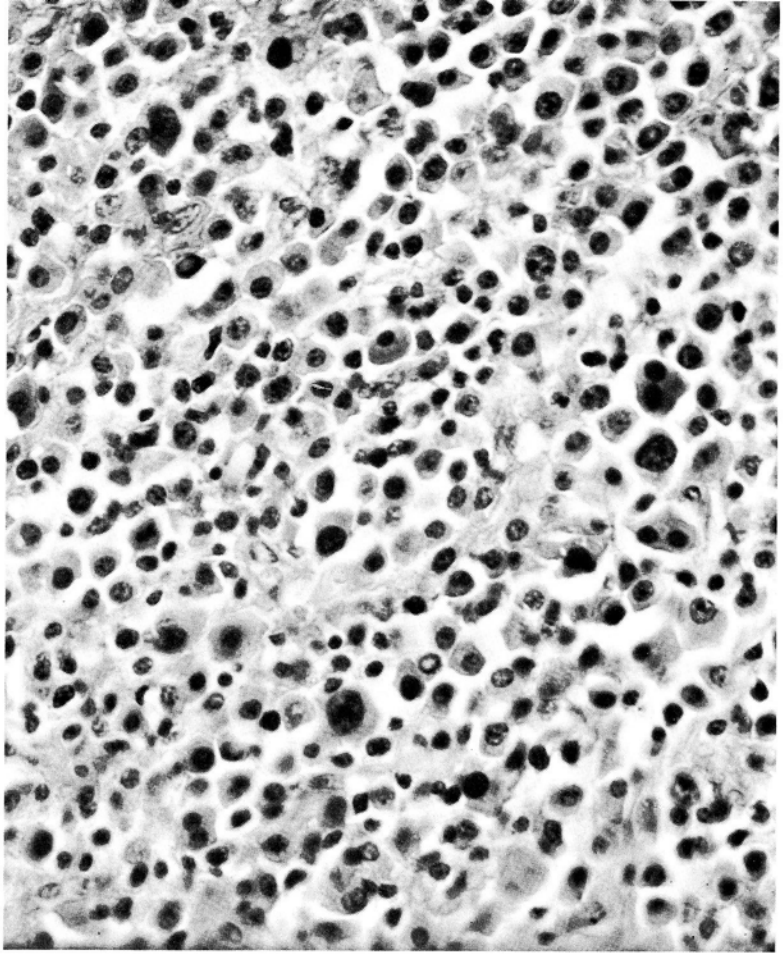

Fig. 4—Representative view of the cells composing the tumor. Some of the cells are typical plasma cells. Others show large hyperchromatic nuclei (H & E x 500).

slides I think are quite typically plasma cells and the great majority have voted either for plasmacytoma or for the diagnosis of myeloma which is certainly a related diagnosis.

Dr. Regato: There are no important differences of opinion among the experts. Dr. A. P. Stout, of New York, indicated that this is the second such tumor that he has seen in the stomach and that it might take an autopsy to settle whether or not primary is there. Dr. M. B. Dockerty, of Rochester, commented that these tumors are not always associated with multiple myeloma, that they are often a variety of malignant lymphoma and, not infrequently, are multicentric in the gastro-intestinal tract.

Subsequent history: On July, 1961, the patient had lost 22 pounds; the alkaline phosphatase was 8 King-Armstrong units, the serum calcium was 9.7 gm per cent and the serum phosphorus 3.4 gm per cent. The serum electrophoresis showed the following result:

	Normal Control Grams %	Patient Grams %
Albumin	4.6 (+0.2)	3.3
Globulins		
alpha—1	.2	.4
alpha—2	.6	1.1
beta	.7	1.0
gamma	.9	1.7
Total protein	7.0	7.5

Dr. Meissner: There are some abnormal globulins present, perhaps in the Alpha I, Alpha II, as well as Beta, and even Gamma. There are increased globulin certainly in all of the spectrum, which is somewhat helpful perhaps in making our diagnosis.

Dr. Modlin: I would want to see that patient myself and I still might have some doubt about whether or not this liver was palpable. I think the last thing in the world that the surgeon at the operating table would think of is a myeloma of the stomach, so he would be standing there with this huge tumor in his hand, running through his mind what it might be; one of the first things to come to mind would be a leiomyoma or a leiomyosarcoma. One would probably do the same procedure that was done here, and it would be only a few days later that you would be surprised to find the correct diagnosis.

Dr. Schatzki: May I just warn my friends the radiologists never to make the diagnosis of plasmocytoma of the stomach.

Dr. Regato: It has never been made according to the literature, but one will have to be the first.

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11. *Glomus Tumor of the Stomach*

Contributed by P. W. Gikas, M.D. and J. Bookstein, M.D., Ann Arbor, Michigan

THE PATIENT was a 74-year-old man in April, 1961, when he complained of nocturnal epigastric pain relieved by ingestion of food but recurring within 3 hours after meals; the patient also suffered from mild diabetes. On examination there was epigastric tenderness and an enlarged liver. The hemoglobin was 12 gm per cent; there was no free gastric acid.

Dr. Schatzki: A sharply defined oval filling defect is seen in the prepyloric area of the stomach. What is called "accentuated rugal folds" are probably the normal folds of the wall of the stomach opposite the lesion. I cannot see any evidence of ulceration.

This could be any of many lesions. It could be a polypoid epithelial tumor of the stomach, benign or malignant.

It could slightly more likely be an intramural submucosal tumor, like leiomyoma or any of the tumors which may arise in the stomach wall outside the mucosa. I have no way of making a differential diagnosis from the evidence at hand and I believe the history is of no help.

Dr. Schatzki's impression: 1. INTRAMURAL SUBMUCOSAL TUMOR. 2. EPITHELIAL BENIGN OR MALIGNANT TUMOR.

Roentgenologic Impressions Submitted by Mail

Leiomyoma, Lipoma, etc.	30
Ectopic pancreas	23
Benign polyps	18
Gastric carcinoma	16
Pancreatic carcinoma	9
Glomus tumor	1
Others	16

Dr. Schatzki: Any of these lesions is possible with the exception of carcinoma of the pancreas which would be highly unlikely; such a sharply defined lesion protruding in the stomach without any other evidence of a pancreatic lesion is conceivable but not likely. Benign polyp is possible. It could be ectopic pancreas; I have never seen a glomus tumor of the stomach but it could be that.

Dr. Regato: Dr. W. Stampfli, of Denver, suggested ademyoma; Dr. W. Gunn, of San Francisco, preferred an islet-cell adenoma of the pancreas; Dr. E. Salzman, of Denver, adenomatous polyp and Dr. O. F. Prochazka, of Liberal, Kansas, lipoma. Dr. G. Schwarz, of Denver, suggested a glomus tumor.

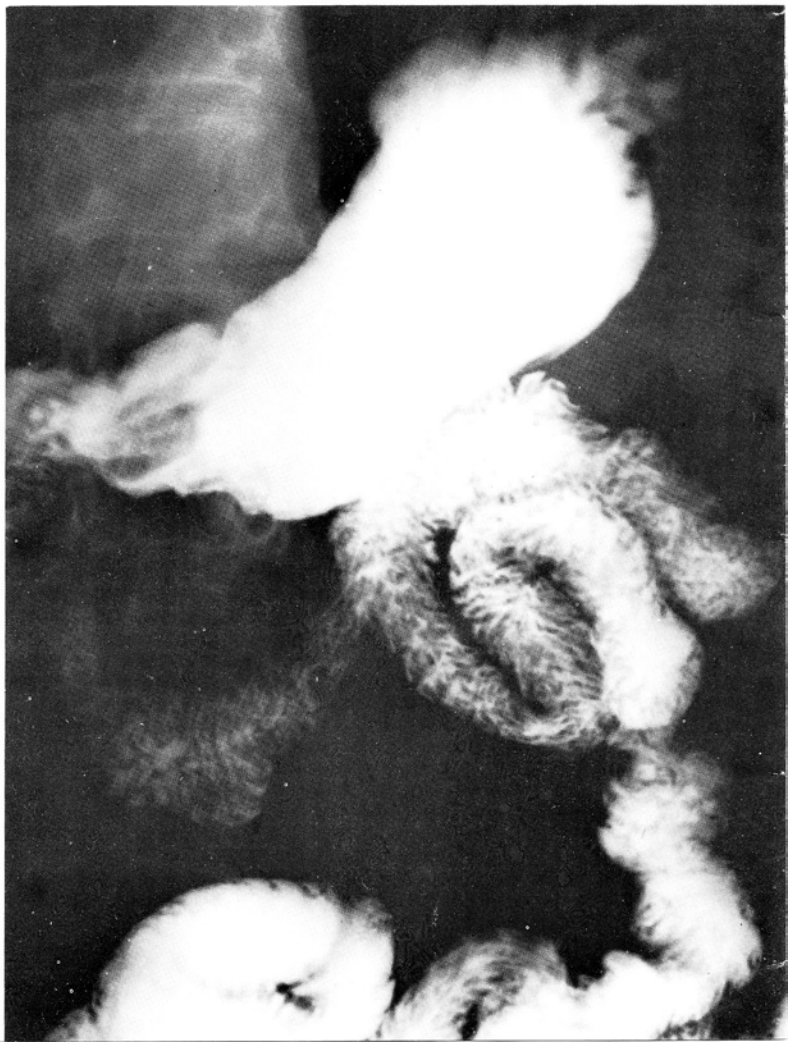
Operative findings: On May 2, 1961, a subtotal gastrectomy and cholecystectomy were done. A firm submucosal mass 2 x 2 x 1.5 cm was found 8 cm above the pylorus; the overlying mucosa was not invaded but the subserosal part of the tumor lied adjacent to the omentum.

Dr. Meissner: The low power view shows a mass which seems to be arising in the muscularis; no mucosal relationship is evident. The mass is well circumscribed from the adjacent muscular cells. The high power view shows the mass, especially at its periphery, to have numerous vascular spaces which extend into the adjacent muscle and carry about them some of the cells which make up the bulk of the lesion. The type of cell is of uniform size and shape and except for the vascular arrangement, shows no architectural formation. There are no mitoses and relatively little pleomorphism. Throughout the lesion there are numerous blood vessels, but these are not prominent at the periphery. These polyheldral cells have an intimate relationship to the blood vessel walls and in every instance seem to lie outside of the endothelial lining.

This is a mixed tumor which is characterized by two features: one is a considerable vascularity, especially about the periphery; the second is the presence of a uniform type cell which shows no particular arrangement except intimate association with the blood vessel walls. Some of these cells bear resemblance to a carcinoid tumor, but there is no suggestion of gland formation. Although occasionally the cells seem to bland with strands of smooth muscle they are quite different from the usual smooth muscle cells. I believe, therefore, that these cells are pericytes or glomus cells, and that this lesion is a glomus tumor.

The glomus is a peculiar structure composed basically of two elements: increased vascular spaces and specific cells called pericytes. The glomic tumors of the skin often contain nerves as well, but nerves are not usually present in the glomus found in the viscera. The function of the glomus is to serve as an end-organ for the regulation of temperature or of specific elements in the blood stream. About ten years ago Dr. Kay and associates reported three cases of glomic tumors of the stomach. Since that time eight or ten others have been reported and in this location. Most of them have arisen in the mucosa or near the gastric

Fig. 1—Sharply defined filling defect in the prepyloric areas.



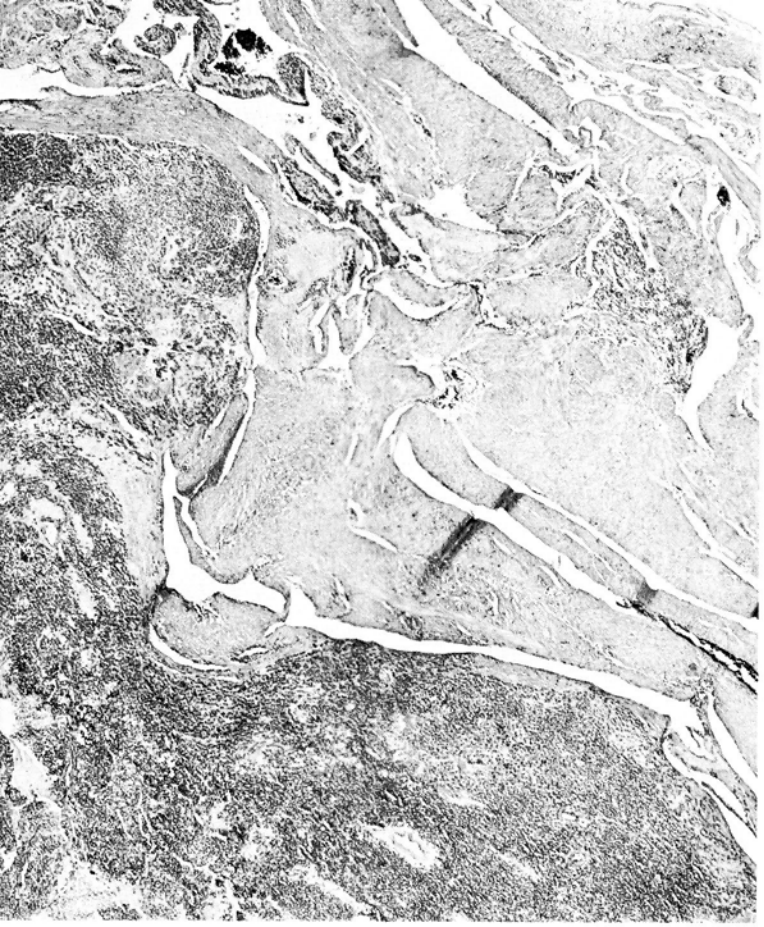


Fig. 2—Low power photomicrograph of lesion showing cellular foci at lower left and numerous vascular spaces at upper right (H & E x 40).

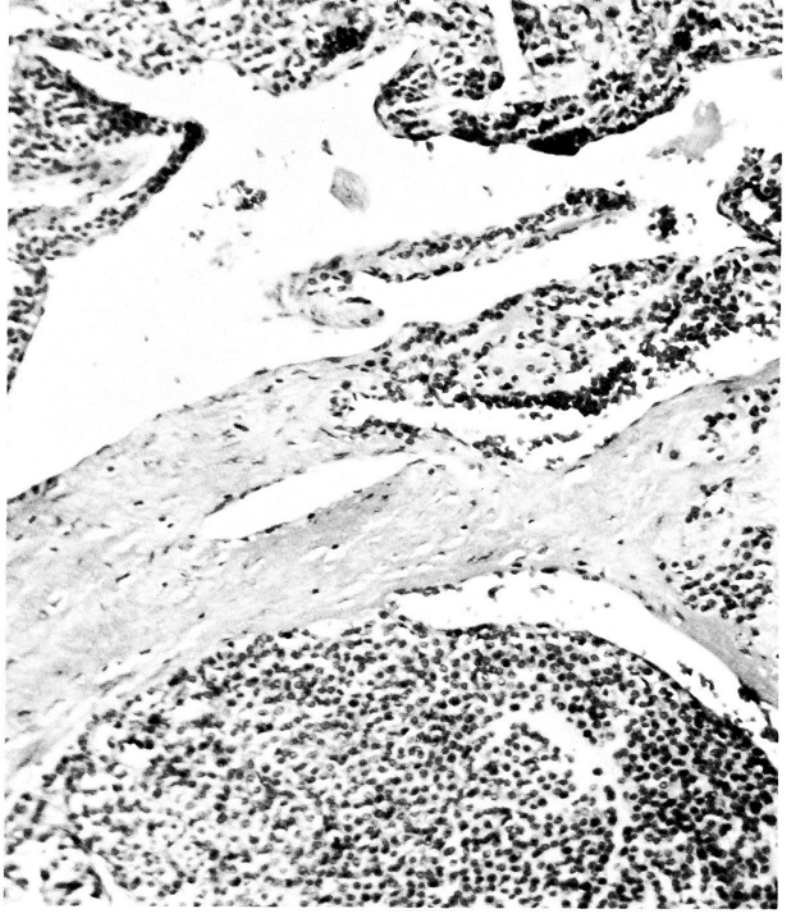


Fig. 3—The uniform cells composing the bulk of the mass show no structural arrangement but have an intimate relationship to the vascular spaces (H & E x 200).

antrum. Most of the reported cases with which I am familiar have all behaved as a benign neoplasm. According to the history, this patient has an enlarged liver. I suspect that this enlargement is due to other causes than a metastasis from the glomic tumor of the stomach.

Dr. Meissner's diagnosis: GLOMUS TUMOR.

Histopathologic Diagnoses Submitted by Mail

Glomus tumor	105
Islet-cell adenoma	6
Carcinoid	6
Lymphosarcoma	5
Others	11

Dr. Meissner: I have mentioned the carcinoid already and it is certainly true that some islet cell tumors have a configuration very similar to carcinoid tumors, and somewhat similar to glomus tumors as well. However the great majority favor glomus which I believe is the correct one. I don't see very much evidence for the diagnosis of lymphosarcoma.

Dr. Regato: Dr. R. M. Delcourt, of Brussels, suggested a neurogenous tumor of low degree of malignancy; Dr. F. Bang, of Copenhagen, preferred hemangiopericytoma; Dr. C. A. Hellwig, of Halstead, made a diagnosis of islet-cell tumor, Dr. M. B. Dockerty, of Rochester, offered glomangioma and commented that it is almsot too typical, and that this is the second case that he has seen in this location.

Subsequent history: On May, 1961, the patient appeared well and was being operated for cataracts.

Dr. Modlin: I would agree with subtotal gastrectomy; I suspect the surgeon was quite surprised at this diagnosis.

P. W. Gikas, M.D., Ann Arbor, Michigan: This tumor contained abundant calcium or lime salts and the white material in the poor photograph you saw was calcified material. There was so much calcium that a portion of the specimen was decalcified before sectioning. I wonder in retrospect if Doctor Schatzki could identify calcified material on the film.

Dr. Schatzki: I think if I had seen calcification in that mass I would have made a diagnosis of leiomyoma, because that is by far the most common lesion of the stomach which shows calcification.

O. Rambo, M.D., San Francisco, California: This patient complained of pain. I wonder if such a tumor will produce pain as it does under the skin, and if so, why would it be relieved by eating?

Dr. Meissner: The glomus found in the extremities do have nerves in them whereas the ones in the viscera usually do not. I know of only one report in which nerves were present in glomic tumor of viscera. I didn't see any nerves in this lesion. I suspect the pain may have been due to obstruction.

R. M. Knisely, M.D., Oak Ridge, Tennessee: I would like to say that my section did have nerves.

J. B. Frerichs, M.D., El Paso, Texas: This is a petty point and probably not worth transmission to posterity, but I think it should be recorded that the plural of "glomus" is "glomera", since it is a third declension neuter noun.

I. Costero, M.D., Mexico City (in Guadalajara): A glomus is an arteriovenous anastomosis by means of which the arterial blood may pass directly into a vein without passing through capillaries; the anastomotic vessel spins upon itself forming a coil or *glomus*. Apparently these anastomoses help in the adaptation to changes of temperature due to their association with very sensitive nerves; ideally they may be studied in the bat's wings. Glomus tumors arise from the epithelioid cells of the anastomotic segment or pericytes. Otologists talk of *glomus jugulare* because of histologic similarity but I do not think that these are glomus tumors because there is no glomi there. The true glomus tumor arises under the nails and also under the skin of the forearm. Tumors of the carotid body arise from chemoreceptors and for this reason they have been properly designated by Mulligan as *chemodectomas*. We have been studying these chemoreceptors which we like to call the *taste center* of the blood since they detect the proportion of oxygen and CO^2 in

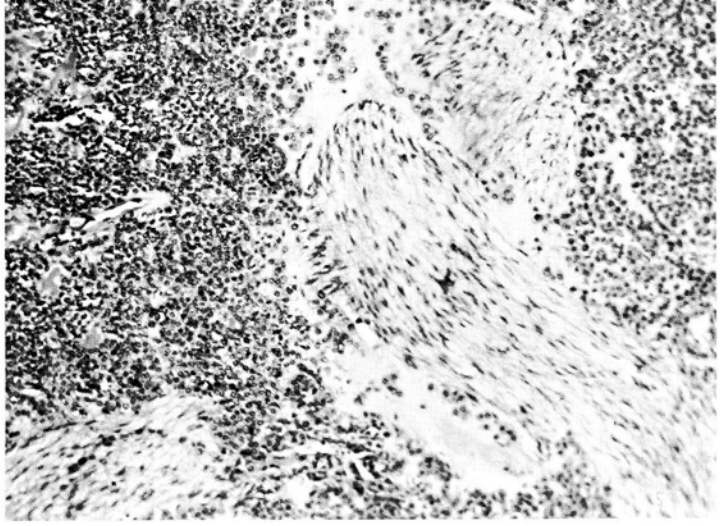


Fig. 4—A few of the sections prepared for the Seminar show bundles of nerves within the tumor. This photomicrograph showing nerves was prepared from the Seminar slide received by Doctor Ralph M. Kniseley (H & E x 100).

the carotidean blood and transmit their findings to the respiratory centers. The cells of glomus tumors are mesenchymatous perivasculates of the type of pericytes of Zimmermann whereas those of carotid body tumors and glomus jugulare are ectodermic sensory cells similar to the ones in the oral taste organs.

Editor's note: After the Seminar Dr. R. M. Knisely, of Oak Ridge, Tennessee, submitted his slide to Dr. Meissner who wrote: "This slide shows numerous nerves throughout the tumor, a fact infrequently described in visceral glomus tumors."

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12. *Carcinoid Tumor of the Stomach*

Contributed by L. A. Kidder, M.D., E. G. Shaumberg, M.D. and E. Wiege, M.D.,
Greeley, Colorado

THE PATIENT was a 67-year-old man in February, 1961, when he complained of postprandial pyrosis, tarry stools, slight dyspnea and nycturia. Examination failed to reveal any abnormalities except for unilateral induration of the prostate. Hemoglobin was 4.1 gm per cent and hematocrit 18 per cent.

Dr. Schatzki: The single film shows a mass in the lower portion of the stomach with irregularity which extends higher up. Within the mass there is a large irregular ulceration. In addition, there is a smaller ulceration simulating a benign ulcer seen in the upper part of the lesion.

The differential diagnosis lies between malignant tumor with or without an additional ulcer higher up and an ulcerated intramural extramucosal tumor. I was given an additional film which shows that the upper area of ulceration represents only a portion of the total larger area of ulceration.

In other words, this is a large irregular ulceration in a malignant tumor, most likely an ulcerated carcinoma.

Dr. Schatzki's impression: Ulcerated MALIGNANT TUMOR, most likely carcinoma.

Roentgenologic Impressions Submitted by Mail

Carcinoma	45
Benign ulcer	31
Lymphosarcoma	12
Bezoar with ulcer	11
Others	18

Dr. Schatzki: I do not see how one can call this just simply benign ulcer with that mass below. It is not uncommon that patients have a benign ulcer and cancer in the same stomach. I don't think I have seen an active duodenal ulcer and cancer of the stomach, but I have seen gastric benign ulcers with cancer of the stomach. Lymphosarcoma is a definite possibility for it can produce a deep ulceration. Certainly the large crater in these cases is an outstanding feature. I think the lower lesion doesn't quite fit the bezoar; there is a definite ulceration visible in the lower part of the lesion, even on the first slide. The second slide only reveals that the upper ulcer I think is part of the lower ulcer.

Dr. Regato: Dr. H. Hauser, of Cleveland, also suggested an ulcerated carcinoma. Dr. J. Ceballos, of Mexico City, and Dr. M. E. Bischoff, of Denver, both pointed at the probable coexistence of a large malignant tumor and a benign ulcer of the lesser curvature. Dr. H. Dorbecker, of Mexico City, offered lymphosarcoma.

Operative findings: On February 28, 1961, a subtotal gastrectomy was done with removal of two-thirds of the stomach; there was a deep ulceration of the lesser curvature with thickened wall. Numerous enlarged lymph nodes were present along the lesser curvature and nodularities of the liver were observed.

Dr. Meissner: The low power view of the slide shows a lobulated mass with no gastric mucosa attached. Under higher power the lesion is composed of solid masses of cells which vary somewhat in configuration from one area to another. In some regions the cells grow in solid sheets without any architectural arrangement. In these areas the cells are polyhedral and show only an occasional mitosis. In other areas the cells grow in a trabecular fashion with formation of long strands and cords; in still other foci there are gland structures and the cells appear to contain mucus. In these latter foci mitoses are found more readily.

This is a tumor growing in several different patterns, one of which is non-descript, one of which is serpiginous, and the third is glandular. This tumor is basically an adenocarcinoma and the main problem in the differential diagnosis is to determine its exact classification and site of origin. We get little help from the orientation of the slide because no mucosa is present. The enlargement of the prostate suggests the possibility that this man has prostatic carcinoma, and that there may be a metastasis to the gastric wall. This would be highly unusual; the tumor does not look like a typical prostatic carcinoma and I think this possibility may be excluded. The second possibility is that this is a lesion arising from pancreatic tissue, either from the main body of the pancreas and extending to the stomach, or from ectopic pancreatic tissue of the gastric wall. In favor of this diagnosis are the gland-like structures and the serpiginous arrangement of the cells which is often seen in islet cell tumors. I think this is a distinct possibility, but in order to be conclusive, one would need to show specific islet granules in some of the tumor cells, and this I was unable to do. The third possibility, and the one I prefer, is that this is a carcinoid tumor; individually the cells are quite consistent

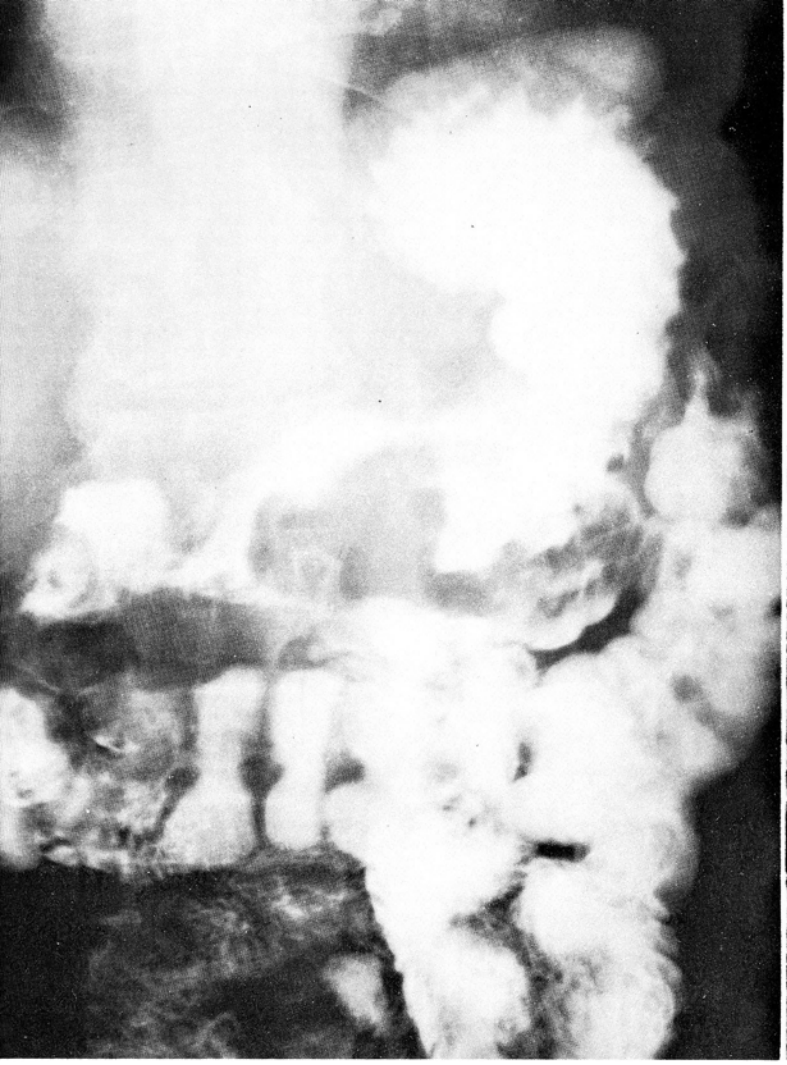

Fig. 1—Large irregular mass of lower portion of the stomach.

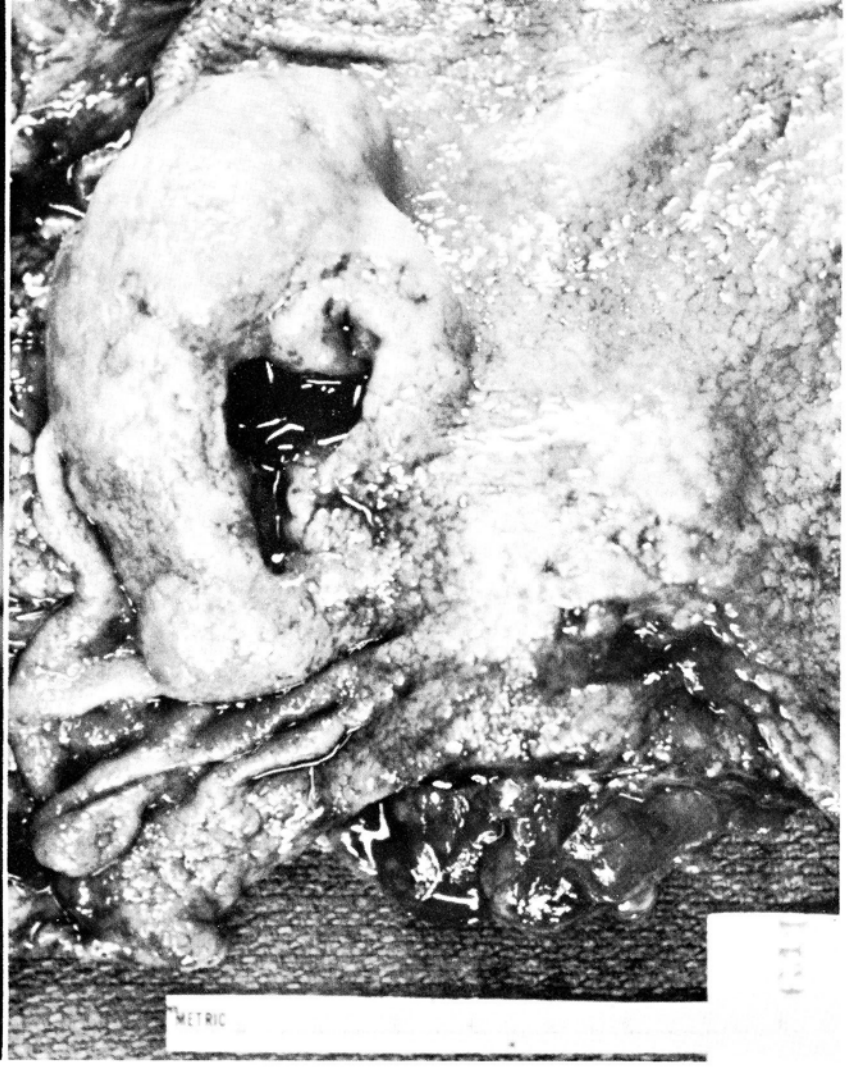

Fig. 2—Thickening of the wall and deep ulceration of the lesser curvature.

with the features of this tumor, and it is now well-appreciated that carcinoid tumors may in some foci produce glandular structures which secrete mucus. Here again this diagnosis could be definitely confirmed by an argentaffine impregnation stain to show the presence of characteristic granules in the tumorous argentaffine cells. In this type of lesion a pathologist wishes to have many slides for examination together with special stains.

Carcinoid tumors arising in the stomach are not as rare as some of the other tumors in the Seminar. Fredell in 1960 stated that forty cases have been reported and he added the forty-first. Many of the carcinoid tumors of the stomach show a low-grade malignancy and metastasize. It is interesting to point out that in the case Fredell reported, the patient's asthma was alleviated with resection. Many people consider the argentaffinoma or carcinoid as an endocrine tumor capable of secreting a substance identical with serotinin. An excess of this secretion may produce a patchy cyanosis, vaso-dilatation of the skin, tachycardia, asthmatic attacks and valvular defects of the right side of the heart.

Dr. Meissner's diagnosis: ADENOCARCINOMA (carcinoid type).

Histopathologic Diagnoses Submitted by Mail

Carcinoid	57
"Malignant" carcinoid	28
Carcinoma, carcinoid type	41
Metastatic carcinoma	11
Islet-cell adenoma	6

Dr. Meissner: I have mentioned the possibility of the metastatic carcinoma. I thought a great deal about islet-cell adenoma and even did an islet-cell stain on one of the two unstained sections that Dr. del Regato sent, but I could not show any Alpha or Beta cells within the tumor; it was partly because of this that I reached the diagnosis of carcinoid. Many participants had a little difficulty in terminology—they wanted to call this a malignant carcinoid and to imply that it wasn't just an ordinary carcinoid such as one sees in the appendix. The intestinal carcinoids of course are much more likely to metastasize than the ones in the appendix, which rarely give rise to metastasis.

Dr. Regato: Dr. G. Gricouroff, of Paris, made a diagnosis of adenocarcinoma; Dr. Robert C. Horn, of Detroit, suggested a mixed carcinoma and carcinoid; Dr. M. Wheelock, of Chicago, and Dr. N. Puente-Duany, of Miami, offered adenocarcinoma of the carcinoid type. Dr. M. D. Dockerty, of Rochester, also found an adenocarcinoma with a carcinoid component and said this had been seen once before in the stomach and once in the colon.

Subsequent history: The patient improved after operation but in October, 1961, he complained of loss of appetite and had a large indurated liver; he had developed hemorrhoids and the urine showed traces of albumin and bilirubin. A urine test for hydroxy-indol-acetic acid was negative.

Dr. Modlin: It would be interesting to know if there was any evidence of serotonin hyperactivity; perhaps Dr. Meissner would comment on whether or not he has had experience with frozen section in a tumor of this type. If the surgeon were alerted at the operating table that he had a carcinoid tumor, a very careful search of the appendiceal area and other areas for evidence of other carcinoids would be in order.

Dr. Meissner: I think it is possible to make a diagnosis of a carcinoid tumor on frozen section. We have never been presented with the possibility of doing this on a gastric lesion, but we have made the diagnosis on intestinal lesions.

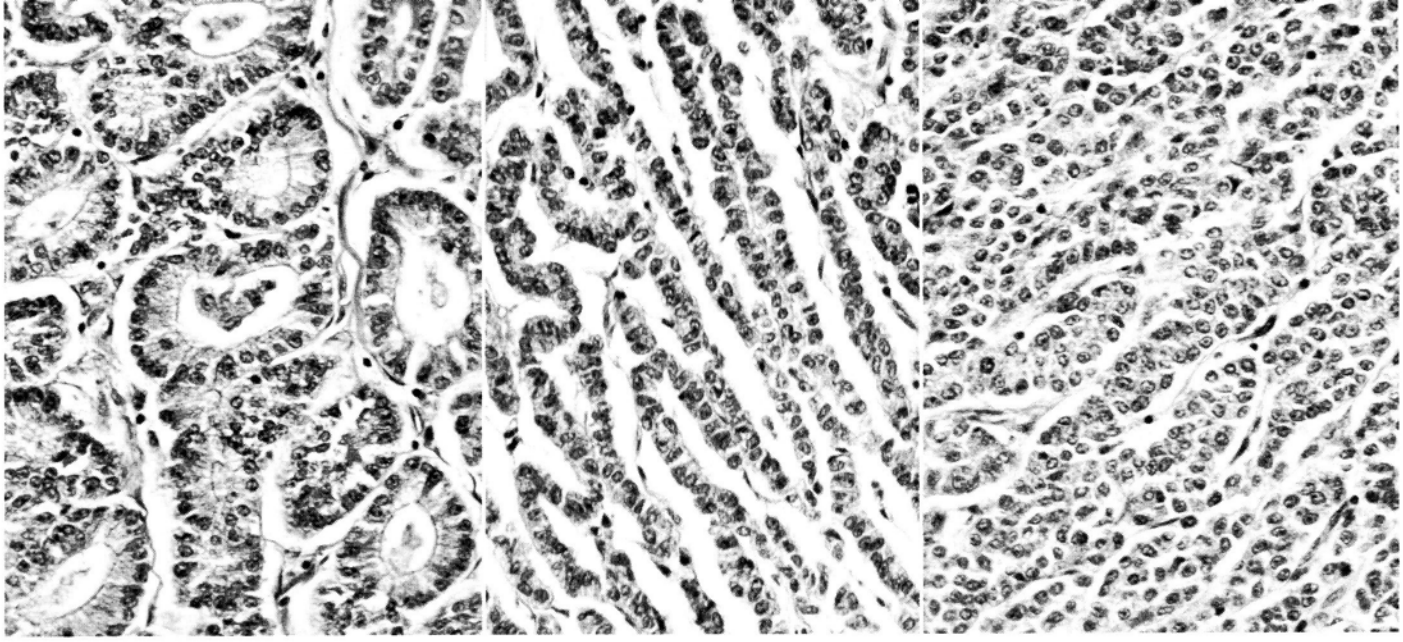

Fig. 3 (composite of 3)—Photomicrographs of three different growth patterns of the tumors: left shows typical gland-forming adenocarcinoma. Center shows a trabecular or serpentine pattern such as may be seen in islet cell tumors. Right shows a compact pattern similar to that of carcinoid tumors (H & E x 300).

On this one I think it would be quite difficult because there are foci that look like definite adenocarcinoma as well as foci that suggest carcinoid.

Dr. Schatzki: I had wanted to ask whether this patient had constitutional symptoms and if this patient had increased serotonin. Patients with marked liver involvement with carcinoid are very apt to have constitutional signs of carcinoid.

O. Rambo, M.D., San Francisco, California: Dr. del Regato mentioned that the excretion product of serotinin, 5-hydroxy-indol-acetic acid, was not elevated.

Dr. Regato: This was after the operation.

H. Braunstein, M.D., Cincinnati, Ohio: I would like to ask Doctor Meissner—did he do an argentoffin stain? Secondly, was an acid phosphotase determination done? I think prostatic carcinoma histologically may easily simulate carcinoid, and I would be extremely wary about ruling out that possibility in this patient, especially since the physical findings seem to indicate that he does have something going on in his prostate.

Dr. Meissner: I feel less secure about this diagnosis than most of the others. I was surprised that so many agreed that this was a carcinoid tumor; I thought there would be much more disagreement. One of my associates insists that this is a pancreatic carcinoma and I don't believe that I could prove that he is wrong. We tried a silver impregnation. I am sorry to say that the method failed because our control showed nothing either, so this doesn't help very much.

E. S. Murphy, M.D., Mexico City: In some recently published articles (Laird, Peskin), it is stated that there is no difference really between carcinoids of the rectum and of the appendix or any other place; it is only a matter of size and duration: when the lesions become more than 2 cm in diameter the majority have metastases. This has led to the conclusion that the most important thing in a carcinoid tumor is the size of the tumor and not its histologic aspect. I personally don't think that there is any evidence that the tumors which are called carcinoids in the appendix are any different from those in the rectum or any place else. It is just that before they get to be 2 cm in diameter they have caused some sort of symptoms and then the appendix is removed, so almost all of them don't give metastases; they are not there long enough.

E. A. Deans-Barrett, M.D., Albuquerque, New Mexico: I thought first, but later discarded this impression, that there may have been a gastrocolic fistulization because the visible part of the colon is considerably filled with barium. Then I decided that this was probably not a fistula but a hastily performed radiologic examination. If one considers fistula one may think of a fungating, soft type of tumor with a possible pedunculation, permitting the barium to go around the tumor and eventually collect within the colon.

Dr. Schatzki: Of course I agree with you. I think that is true as far as the picture which was given to you was concerned; it was not as clear as the additional one which I was given. I will have to confess that I didn't think on either case of a gastrocolic fistula.

Mark Wheelock, M.D., Chicago, Illinois: We are called on very frequently for frozen sections on these, and I think in most instances we have been fairly accurate. I think the color has been de-emphasized—most of these are yellow.

We had one case of carcinoid in which the lesion presented first in the ovaries as Krukenberg tumors. The patient died and we found quite a large carcinoid in her stomach. Incidentally, we don't need to worry about the prostate in this particular instance. I don't see how they can be confused with carcinoma of the prostate. I do think there may be a great deal of difficulty in distinguishing them from islet-cell adenoma and metastatic islet cell carcinoma to the liver.

G. Alvarez-Fuertes, M.D., Mexico City, in (Guadalajara): I saw in this slide portions which suggested pancreatic duct cells with adenocarcinoma, others suggested endocrine pancreatic tissue and, finally, others presented as carcinoid. I concluded to malignant carcinoid with hamartoma.

G. Alvarez-Fuertes, M.D., Mexico City, (in Guadalajara): correct diagnosis of carcinoid must be based on the finding of argentaffine granules or on the elevation of serotonin excretion products in the urine; otherwise, the diagnosis must remain in doubt. Dr. Barroso, in my laboratory has perfected our silver staining methods so that they can now be used with a high degree of reliability. If we obtain formalin fixed tissue before embedding in paraffin, we can stain with silver and reveal argentaffine granules very clearly.

Editor's note: This patient expired in January, 1962, with what was evidently an enlarged liver with apparent metastases, but no autopsy was done.

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13. *Hemangioendothelioma of the Stomach*

Contributed by A. Severance, M.D. and H. F. Elmendorf, M.D., San Antonio, Texas

THE PATIENT was a 66-year-old man in November, 1960, when he complained of increasing asthenia and tarry stools. On examination the patient appeared pale; there was epigastric tenderness but no palpable epigastric mass. The hemoglobin was 4.8 gm per cent and the hematocrit 14 per cent.

Dr. Schatzki: The patient has a bleeding ulcerated lesion in the stomach. Two films show the ulcer crater as well as the surrounding "mass". The mass is moderately sharply defined and has a slightly lobulated edge. The ulceration is rather small considering the size of the mass. This makes an ulcerated carcinoma comparatively unlikely and makes this much more likely to be an ulcerated intramural extramucosal tumor with ulceration, like leiomyoma, neurofibroma, hemangiopericytoma, or similar tumor or one of their sarcomatous variants.

From the evidence at hand, this is my first choice. I have seen, however, gastric ulcers with surprisingly sharply defined surrounding edema and infiltration. There is, therefore, a chance, although I would rather think an outside chance, that it is a benign ulcer with surrounding inflammatory mass.

Dr. Schatzki's impression: 1. ULCERATED INTRAMURAL TUMOR. 2. BENIGN ULCER.

Roentgenologic Impressions Submitted by Mail

Leiomyoma	34
Leiomyosarcoma	27
Carcinoma	12
Benign ulcer	9
Others	21

Dr. Schatzki: I think there is no way, as far as I can see radiologically to differentiate between leiomyoma and leiomyosarcoma. Both have a sharp edge; both may ulcerate in a similar way. I have no evidence that the leiomyosarcoma ulcerates more than the leiomyoma.

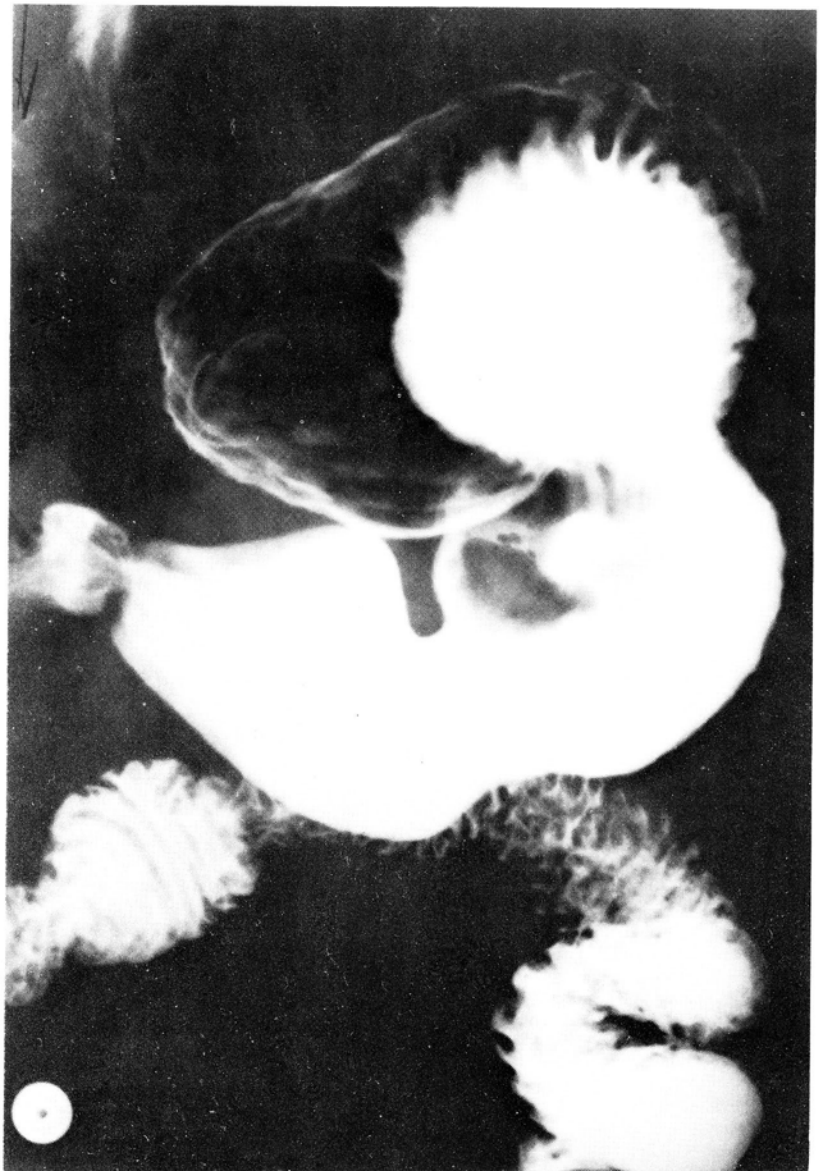
Dr. Regato: Dr. J. C. Lemon, of Denver, Dr. B. Felson, of Cincinnati, and Dr. H. Hauser, of Cleveland, all suggested an ulcerated intramural leiomyoma. Dr. C. E. Shopfner, of Grand Junction, Colorado, made a diagnosis of leiomyosarcoma.

Operative findings: On December 13, 1960, an exploratory intervention revealed a circumscribed tumor, 5 cm in diameter, along the lesser curvature with ulceration of the overlying mucosa; there was an adenopathy. An excision of the tumor with surrounding normal tissue was done.

Dr. Meissner: The low power view of the slide shows a massive growth in the gastric wall which undermines the mucosa and has caused extensive ulceration. At the junction of the ulcer the mucosa seems to be quite distinct from the underlying lesion; I believe, therefore, that it is reasonable to assume that the process did not originate in the gastric epithelium. Under higher magnification one is immediately impressed by the presence of numerous vascular spaces, some of which contain blood cells. The spaces are of different sizes and shapes, and the vascular walls are of varying degrees of thickness. Only a few inflammatory cells are present, and for this reason, the process suggests a neoplastic rather than a reactive change. Outside of the vessel walls there are numerous cells often spindle-shaped which bear a great resemblance in many instances to the endothelial cells lining the vascular channels. An occasional cell shows a mitosis. A silver stain fails to show a good demarcation of the wall of the vessel from the adjacent spindle cells, and even with the H & E stain there is a strong suggestion of a transition between the perivascular cells and the cells lining the vascular channels.

The differential diagnosis here must include lesions in which there is a prominent vascular component. I believe we can exclude a reactive change such as granulation tissue because of the absence of inflammation. The possibilities I should like to consider are hemangiopericytoma, vascular leiomyoma and hemangioendothelioma. I do not believe this is a vascular leiomyoma, because I could find no myofibrils in the perivascular cells and because of the intimate relationship of the perivascular spindle cells to the endothelial lining. For a similar reason I believe a hemangiopericytoma

Fig. 1—Moderately defined mass with crater and lobulated edge.



can be excluded since in this condition, the perivascular cells are distinctly separate from those of the vessel lining. This leaves us with a hemangioendothelioma as the best possibility, and this is the diagnosis I favor. The second question in the differential diagnosis is whether the tumor is benign or malignant; I know of no certain way in a lesion such as this to make the distinction. I believe the tumor is very low-grade, but nevertheless may be capable of producing metastasis.

Many hemangiomas are probably not true neoplasms, but represent malformations or hamartomas. Others represent blood vessel dilatation due to injury. The neoplastic hemangiomas may show excessive proliferation of any element of the vessel wall: the endothelium as in this case, the pericyte as in hemangiopericytoma or the smooth muscle of the wall as in a vascular leiomyoma. Many of the tumors classified as hemangioendothelioma behave as benign lesions, but some of them are capable of producing metastases.

Dr. Meissner's diagnosis:

HEMANGIOENDOTHELIOMA.

Histopathologic Diagnoses Submitted by Mail

Leiomyosarcoma	41
Leiomyoma	32
Rhabdomyosarcoma	19
Hemangiopericytoma	15
Neuro-fibrosarcoma	12
Hemangioendothelioma	3
Others	12

Dr. Meissner: I don't believe that the diagnoses of hemangiopericytoma or even of leiomyoma or leiomyosarcoma are too far removed from the basic concept that this is a vascular tumor in which the vessels themselves are the important part. This is not a typical leiomyoma of the stomach or a typical leiomyosarcoma of the stomach. I don't see any evidence for neurofibrosarcoma or for rhabdomyosarcoma.

Dr. Regato: Dr. M. B. Dockerty, of Rochester, made a diagnosis of leiomyosarcoma grade 3; Dr. R. C. Horn, of Detroit, discarded the diagnosis of rhabdomyosarcoma in favor of leiomyosarcoma; Dr. R. Abell, of Ann Arbor, Dr. Leo Lowbeer, of Tulsa, and Dr. G. Gricouroff, of Paris, suggested hemangiopericytoma; Dr. V. M. Arean, of Gainesville, Florida, submitted hemangioendothelioma.

A. P. Stout, M.D., New York (by mail): Leiomyoma. This is one of the bizarre forms in which a majority of the cells are rounded and often have a clear zone around the nucleus. I am reporting 69 gastric examples of this peculiar variety in the November issue of CANCER: only two of the sixty-nine had metastasized. This tumor has only one mitosis in 50 high power fields, which is almost a guaranty that it is benign.

Subsequent history: On August 21, 1961, the patient appeared in good health.

Dr. Modlin: I noticed in the history of the operation that an adenopathy was described and also that the lesion was treated by a local resection. I would be reluctant to perform a local resection for a tumor in a patient who exhibited a lymphadenopathy at the operating table. I would be afraid that this might indeed be a sarcoma or a leiomyosarcoma and I might feel a little conscience-stricken that I had done only a local resection; so the least I would do for this lesion would be a subtotal gastrectomy. Admittedly, none of the operative procedures that we do, even the ultraradical total gastrectomies, have been found to add to the salvage rate of carcinoma of the stomach; yet some patients with leiomyosarcoma have survived for considerable periods of time. Knowing the difficulties that the pathologists have in arriving at the distinction between a benign leiomyosarcoma and leomyoma, I would be inclined to be, I think, a little more radical in the procedure.

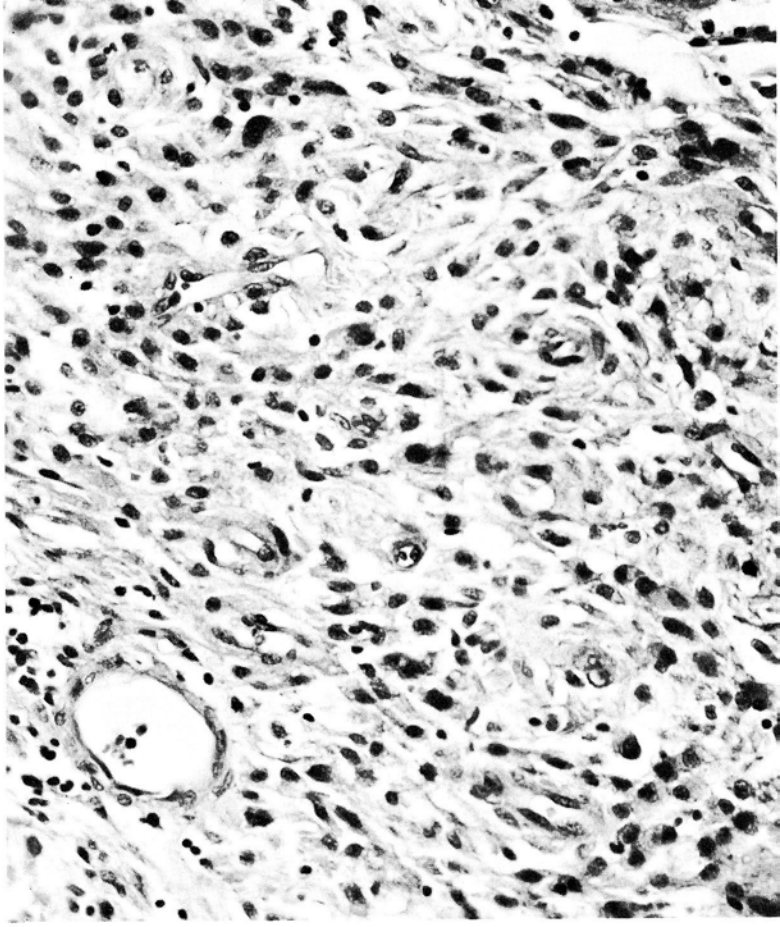


Fig. 2—Representative photomicrograph of the lesion showing numerous small, poorly formed vascular spaces and numerous spindle cells lying between and often intimately associated with the lining of the vascular spaces (H & E x 300).

Dr. Regato: Dr. Severance, would you tell us what that node showed, please?

A. O. Severance, M.D., San Antonio, Texas: The lymph nodes were thought to be inflammatory by the surgeon, and they weren't removed. We were given a small piece of this tumor for frozen section; my associate stewed around about this so long that when he went back and told the surgeon that it was a benign smooth muscle tumor, the surgeon had already excised it with a small margin and he was happy to stop at that and decided not to go any further. When we got the specimen and looked at it more carefully, our problem was: was it benign or was it malignant? We didn't entertain very much the idea of some other type of tumor except a smooth muscle tumor. We looked all around for mitoses and I didn't find very many. Dr. Meissner found one; we really had to look to find any, so we decided on that basis to call it a peculiar leiomyoma of the stomach. We did trichrome stains and they showed the cell cytoplasm taking a very red stain and that swayed us over; we thought the vascular component was perhaps a stimulation of the ulceration on the top, or again a vagary of the peculiar nature of this tumor.

Dr. Schatzki: I have always admired the accuracy of my pathological friends and the diagnosis of epithelial tumors anywhere, and I always wondered about the trouble they had with mesenchymal tumors, and particularly with the intramural tumors of the gastrointestinal tract. I have not been able to find that it makes very much difference what they call it because it seems to me that the benign type of whatever name you put behind it behaves just like the other malignant type, whatever name you put behind it. In other words, I have the impression what the only important thing really clinically and biologically to know is—is this a benign mesenchymal tumor or is it a malignant mesenchymal tumor? You don't have to fight so much about all these finesses. I am just wondering if really there are all these different

tumors as they appear to be histologically; if they are perhaps much more kin than their histological morphology might indicate.

H. Braunstein, M.D., Cincinnati, Ohio: I hate to agree with Dr. Schatzki on this subject. I suspect that most of these tumors are of the same origin; I don't think I have good evidence for it; however, I have studied ten spindle cell tumors of the alimentary tract histochemically by enzyme reactions. I believe that I can distinguish a fibroblast, a smooth muscle cell, a Schwann cell and an endothelial cell by histochemical means. So far every one of them, and of course, this is a very small number, even though they were called by different names by pathologists, whether these be called neurilemoma or leiomyoma or leiomyosarcoma, every one of them at least histochemically, appears to be of smooth muscle origin. This, of course, is a small group and I could not reach any sweeping conclusions, but I suspect that most of these tumors are indeed of smooth muscle origin and that they can show a wide variety of histological patterns, depending on whether the inflammation has caused disruption of the architecture as a result of the ulcer, or many other factors involved.

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14. *Gastric Liposarcoma*

Contributed by W. R. McPhee, M.D., L. M. Roberts, M.D., R. Gauer, M.D., and S. B. Chapman, M.D., Kansas City, Missouri

THE PATIENT was a 14-year-old girl in March, 1961, when she complained of headaches of several weeks duration and gave a history of recent tarry stools. There were no important findings on physical examination; the hemoglobin was 5.7 gm per cent and the hematocrit 18 per cent; there were 17,300 white cells per mm^3 with a normal differential.

Dr. Schatzki: This is certainly a weird lesion in a girl of 14. The question that I have to answer is whether the deep canal which separates the two lobulated masses protruding into the lumen of the stomach represent ulceration or normal stomach between two lobulated tumor masses. This depends primarily on whether this channel is rigid or not. From the appearance of this film I have the impression that certainly the part which is closest to the lumen of the stomach is not as rigid as I would expect it to be in ulceration, whereas the same thing cannot be said of the "cavity" at the bottom of the lesion. Could this be a benign ulcer with deep penetration and surrounding edema? I believe this possibility is highly unlikely both from the appearance of the "crater" and the edema. Could this be cancer of the stomach? In this age group, cancer of the stomach is so rare that even at a conference of this type I shall forget about this possibility.

Intramural extramucosal tumors like leiomyoma with deep ulceration could produce such an appearance, but my impression is that the channel at the beginning is not rigid enough for such an explanation, however, I still believe that this is a possibility. More likely, however, there are just two lobulated polypoid tumor masses close to each other with an area between them which fills and appears like a crater. This would be my first choice, with the possibility of a nonepithelial submucosal ulcerated tumor as my second choice. A third possibility is some weird congenital anomaly, e.g. reduplication of the stomach.

Dr. Schatzki's impression: 1. ADENOMATOUS POLYPS. 2. INTRAMURAL EXTRAMUCOSAL TUMOR.

Roentgenologic Impressions Submitted by Mail

Benign gastric ulcer	36
Lymphoma	15
Various sarcomas	12
Carcinoma	7
Others	22

Dr. Schatzki: I thought of benign ulcer at the beginning, but very soon ruled it out for various reasons. I think these participants thought that this channel between the two protruding things was an ulcer and that the protruding masses were the surrounding induration around the ulcer. Lymphoma could produce such a picture, extremely rare at this age. Various sarcomas include the intramural tumors, and as I told you, I think there is an outside chance. I think carcinoma is highly unlikely, both by the shape of the lesion and by the age group. I do not know of a carcinoma of the stomach in this age group.

Dr. Regato: Dr. R. Raap, of Ann Arbor, and Dr. E. Salzman, of Denver suggested a leiomyosarcoma.

Operative findings: On March 8, 1961, a subtotal gastrectomy was done. There were several submucosal masses, 0.5 to 2 cm, which on cut section had a "fish-flesh" appearance and a tan color.

Dr. Meissner: The low power view of the slide shows multiple lobulated masses lying in the gastric wall. Although ulceration was reported to have been present radiologically, it is not evident in this section. The overlying mucosa is thinned, but otherwise uninvolved. A tri-chrome stain shows collagen about some of the lobular masses in the mucosa. Under higher power one can see direct invasion of the cells of the masses into the muscle of the gastric wall. Under still higher power one is impressed by the several different growth patterns of the cells of the lesion. Some of them are large and irregular with an elongated cytoplasm. There are few mitoses in spite of the pleomorphism of the cells. Some of the cells suggest those of a striated muscle tumor, but I could find no cross-striations to confirm this impression. In other foci the tumor cells are small and of a nondescript nature. In still other foci there are numerous cells with a foamy cytoplasm which does not stain for mucus, and in these foci the nucleus is often pushed to one side as in a lipoblast. The tumor is highly vascular and some of the cells are growing within blood vessel spaces.

This again is obviously a tumor and a malignant one as is evidenced by its invasion of the muscle of the gastric wall. The presence of collagen in some portions of the tumor suggests the possibility that these cells are fibroblasts and that this may be a fibrosarcoma. In other foci the cells strongly suggest the possibility of muscular origin, although this could not be definitely confirmed. Still another type of cell with a clear cytoplasm suggests the formation of fat by the tumor cells, but this I believe then cannot be confirmed

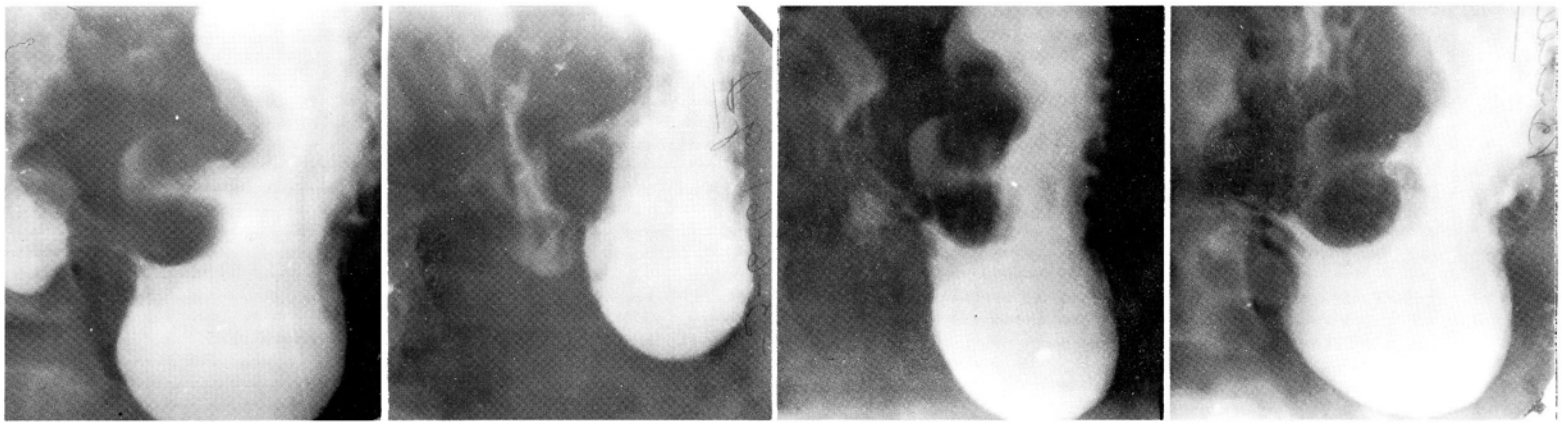


Fig. 1—Spot roentgenograms showing two lobulated masses arising from the lesser curvature.

without a stain for fat. I believe then that this is a sarcoma, probably composed of several mesenchymal elements. Because of the few mitoses present in this tumor, it would appear that it is of relatively low grade.

The commonest sarcomas of the stomach are the lymphomas and the leiomyosarcomas. Sarcomas of many other types occasionally have been described. I found only two cases of gastric liposarcoma reported.

Dr. Meissner's diagnosis: MIXED SARCOMA, partially liposarcoma?

Histopathologic Diagnoses Submitted by Mail

Leiomyosarcoma	51
Sarcoma, unclassified	17
Leiomyoma	15
Hemangiopericytoma	14
Neurogenous tumor	12
Reticulum-cell sarcoma	6
Rhabdomyosarcoma	5
Hemangioendothelioma	5
Liposarcoma	3
Others	12

Dr. Meissner: Well, many participants classified the tumor from the portions that do look like leiomyosarcoma, that strongly suggest this. I believe it is not a leiomyoma but it is a malignant tumor for the reasons that I have mentioned before. I don't believe this has for me the characteristics of hemangiopericytoma or a neurogenous tumor or a lymphoid tumor. Rhabdomyosarcoma I have mentioned as a possibility, and liposarcoma as a possibility.

Dr. Regato: Dr. L. V. Ackerman, of St. Louis, made a diagnosis of atypical leiomyoma and stated that he was not certain that it is benign. Dr. R. Willis, of Leeds, based on the widespread presence of nerves with excessive sheath cells, suggested sarcoma possibly arising from gastric neurofibromatosis. Dr. G. Gricouroff, of Paris, offered Schwannoma. Dr. R. B. Vernon, of Dubuque, preferred rhabdomyosarcoma; Dr. W. J. Frable, of Chicago, offered hemangiopericytoma and Dr. M. R. Abell, of Ann Arbor, liposarcoma.

A. P. Stout, M.D., New York (by mail): Without differential stains I cannot be sure whether this is a hemangiopericytoma or a vascular leiomyosarcoma. Since I have never encountered a hemangiopericytoma of the stomach in a child but have seen several leiomyosarcomas, I favor the latter. In spite of their malignant appearance and many mitoses, leiomyosarcomas in children seldom metastasize. (Dr. Stout had previously given an opinion on another slide of the same case; see below.)

M. B. Dockerty, M.D., Rochester, Minnesota (by mail): Very cellular myoma. I found no mitotic figures in my section but would buy the lesion for a low grade malignant myoma if mitotic activity were demonstrated in the block. (Dr. Dockerty was not aware that he had previously seen another section; see below).

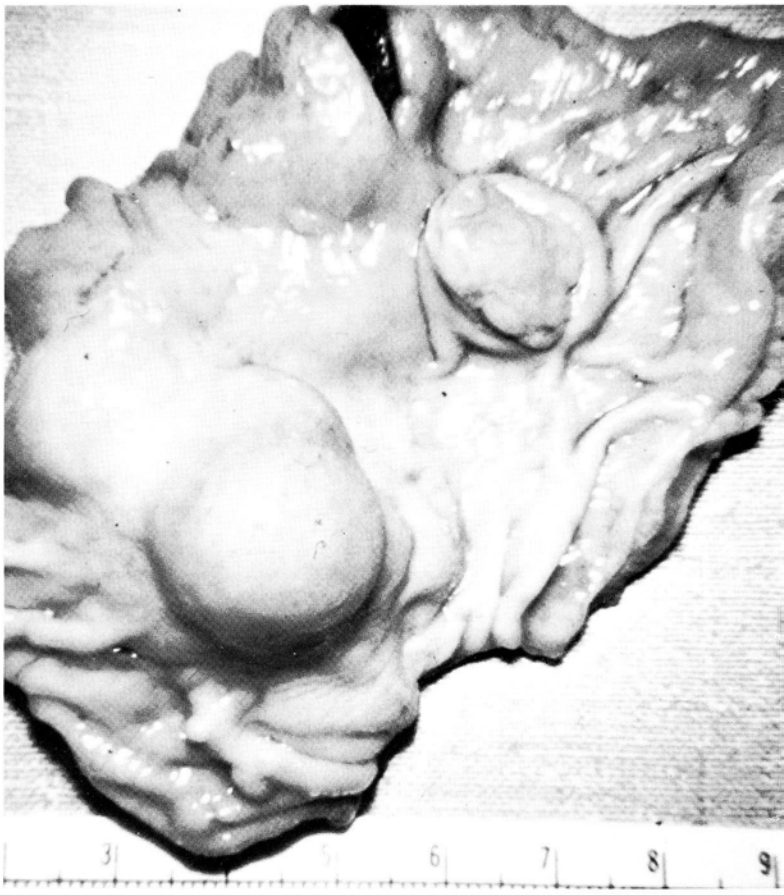
A. P. Stout, M.D., New York (by mail on April 10, 1961; P. and S. No. 67520): The tumor is most certainly a smooth muscle tumor characterized largely by founded cells but showing also in places elongated cells of the more usual myoblastic type. It is difficult to say whether the accessory nodules are independent or infiltrative growths; my opinion is that they are independent. The mitotic rate is 2 in 50 fields; if the rate was higher than 12 in 50 fields the tumor would be potentially metastasizing, but in this case the chances are greatly in favor of a benign lesion.

M. B. Dockerty, M.D., Rochester, Minnesota (by mail, March 13, 1961): "I believe this tumor to be a low grade leimyosarcoma on the basis of three findings. 1) The tumor cells are quite elongated and there appears to be a transition to smooth muscle elements. 2) In several other zones the nuclei are clearly palisaded, a characteristic feature of myomatous tumors of the gastro-intestinal tract. 3) There is finally a finely granular and somewhat eosinophilic character of the cell cytoplasm. Mitotic figures are difficult to find; I would not expect metastases to occur."

This slide was also seen at the Armed Forces Institute of Pathology (accession No. 996886): the report was made by Dr. H. B. Taylor: "The lesion is interpreted as myomatous but difficult to distinguish between leiomyoma and leimyosarcoma. Diagnosis of low grade leiomyosarcoma is favored."

L. V. Ackerman, M.D. (by mail, March 15, 1961): "This is a classic case for a Seminar and naturally I am not certain as to what it is. There is great variation in nuclear size but very few mitotic figures. The stroma is hyalinized in some areas. In a few areas a smooth muscle origin is suggested but I don't even know if it is benign or malignant. Since the lesion has been resected nothing further needs to be

Fig. 2—Gross appearance of surgical specimen.



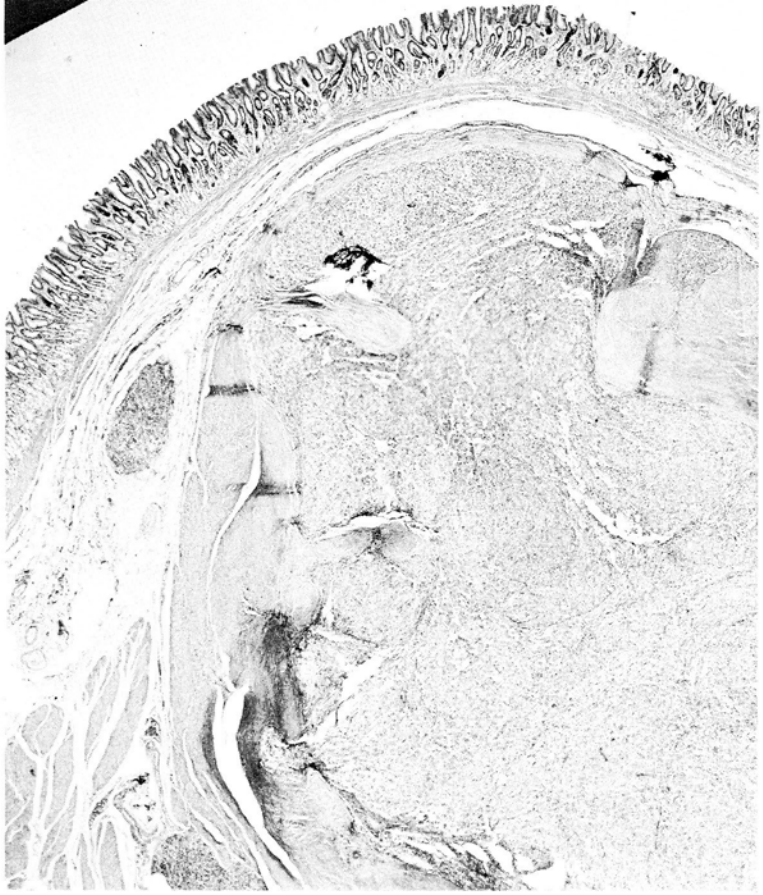


Fig. 3—Lobular intramural mass extending into and distorting the muscularis. The overlying mucosa is uninvolved (H & E x 20).

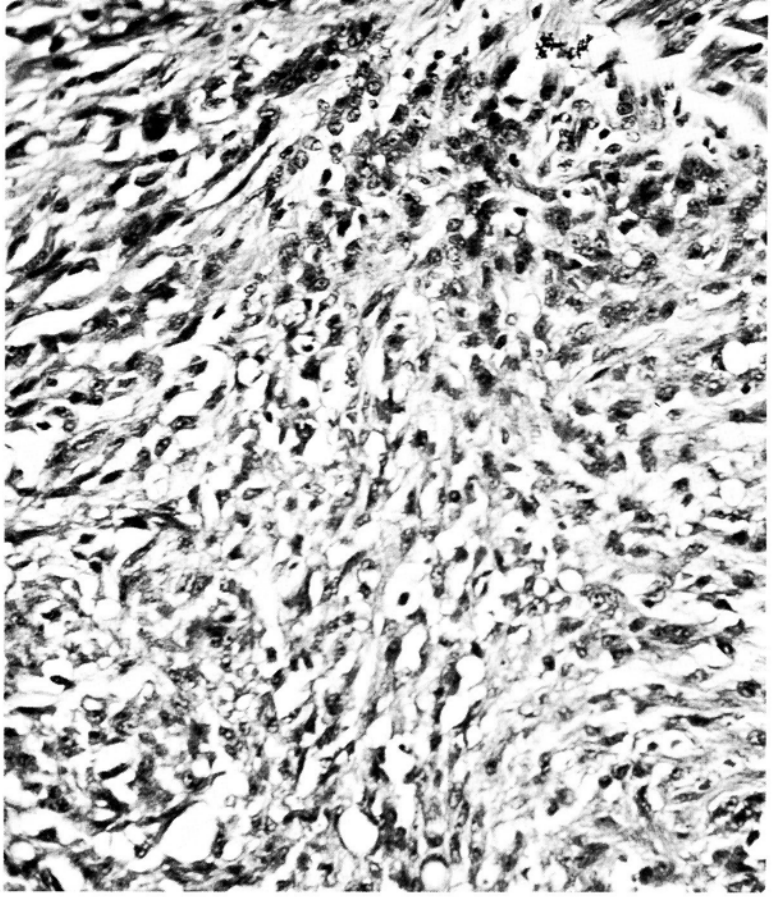


Fig. 4—Higher power view of tumor showing pleomorphic cells which are often vacuolated (H & E x 300).

done, except to worry! I would be against further surgery or irradiation but also against chemotherapy or any of the things that are usually suggested, particularly in children, under the reasoning that *we must do everything we can.*"

Subsequent history: On June, 1961, the patient had gained weight, but presented recurrent lesions of the cardiac end of stomach.

Dr. Modlin: This is certainly representative of the tragedy of cancer in children. The question comes up whether one would advise re-operation for this child, now that one knows that there is tumor in the proximal portion of the stomach. I can only say that I am glad that I don't have to make this decision. The contemplation of a total gastrectomy in a 14-year-old child is rather bad.

E. S. Murphy, M.D., Mexico City: I think very possibly there has been some mixup in the slides on the last two cases, because in the last case which I called rhabdomyosarcoma I don't remember having seen any lesion on my slide which was like the one we just saw. And then in this case I was sure it was leiomyosarcoma. I really think that it is easy, or at least possible, to tell the difference between leiomyosarcoma and rhabdomyosarcoma.

A. O. Severance, M.D., San Antonio, Texas: When I was looking at my own case No. 13 without knowing what I had originally diagnosed, I was worrying again about whether it was benign or malignant. So I got out all of the original slides and there is no mixup in the slide.

Dr. Meissner: I would like to add that we saw nine consecutive cases that we called leiomyosarcoma, and in each instance the patient apparently was cured by the gastric resection; so we questioned our ability to call something a leiomyosarcoma of the stomach. However, the next three cases that we saw, the patients all died within four or five months from metastases, and those three cases didn't look any different from the first nine cases.

Dr. Schatzki: One thing that interested me in this case was the appearance of a second lesion higher up; it is my impression that this was not metastatic, because all the metastases I have seen from leiomyosarcoma or similar malignant spindle cell tumors of the stomach have been outside the stomach and not inside the stomach.

Dr. Meissner: I pointed out the extension of little nubbins of the tumor out into the adjacent muscular wall and it might well be that this tumor has extended at the time of the original resection beyond the point of resection. I think extensive intramural growth of these tumors may occur. As far as the differentiation by the ulceration of a leiomyoma from a leiomyosarcoma, I believe this is mostly due to the size of the lesion rather than to whether it is benign or malignant.

L. M. Roberts, M.D., Kansas City, Missouri: I would like to point out that there were tumors present at the time of the primary resection in the proximal portion of the stomach. These have subsequently grown. Also, I am certain that the slides were not mixed up.

W. R. McPhee, M.D., Kansas City, Missouri: I would like to add my vote of confidence to the proper identity of the slides. These are the slides from our case labeled No. 14. I think that one of the gross points was missed here, and that is that this tumor extended in an hour-glass fashion into the mesentery of the lesser curvature, and I think that is the reason possibly for some of these clear cells which showed up so vividly on Dr. Meissner's preparation.

L. Lowbeer, M.D., Tulsa, Oklahoma: Smooth muscle tumors behave erratically and one has to recognize it.

Dr. Modlin: I would be interested in asking the gentlemen from Kansas City who had knowledge of this particular case if they have made any decisions about whether they feel that they would re-operate this child or not.

L. M. Roberts, M.D., Kansas City, Missouri: When I originally operated the patient the largest lesion was ulcerated and she was bleeding profusely. There were several areas in the remaining portion of the stomach. The resection was probably 25 or 30%. There was no evidence of

metastases to the regional nodes. The ones that are now remaining were 2 cm in diameter at the time of her operation; one was in the cardia adjacent to the cardio-esophageal junction. I hesitated to do a total gastric resection in a 14-year-old child. I have made no decision; I thought possibly this Conference might help me make that decision. I would like to hear your opinion.

Dr. Modlin: I would be inclined to re-operate this child; I think this is the one possibility that remains. Certainly one would not expect this to be a radio-sensitive tumor. The child will undoubtedly have further trouble and in the event that a re-exploration showed that the tumor was still localized to the cardiac region of the stomach, I think I would consider a total gastrectomy.

M. R. Abell, M.D., Ann Arbor, Michigan: Do we have any information as to whether these vacuoles contained lipid? Were lipid stains done in this case? If not, I would like to put in a plea that lipid stains be carried out on the resected specimen, so we can ascertain if this might have a liposarcomatous component.

W. R. McPhee, M.D., Kansas City, Missouri: Fat stains were done in this case and we found fat only in those areas where we would expect to find it; that is, in those areas in which there was direct involvement of the lesser curvature mesentery. I am still hopeful that it might be possible to remove all of these nodules in a local fashion, but it is a diminishing hope at the moment.

J. F. Dunkel, M.D., Lansing, Michigan: May I suggest tissue culture on the re-operated specimen might offer some information about the pattern of cell outgrowth.

Editor's note: Dr. A. P. Stout made a diagnosis of leiomyosarcoma in this case and there was a suggestion that again this was due to a mixup of slides. Since Dr. Stout had seen a previous slide of the same case before it was submitted to the CANCER SEMINAR we asked him to compare them. He wrote: "I am quite sure that there is no mixup of slides; it is the same tumor of the previous slide. I had trichrome stains on the previous slides and the case is certainly a leiomyosarcoma. I would not have suggested hemangiopericytoma if I had known it was the same case."

On December 8, 1961, Dr. McPhee wrote: "The patient was re-operated; three submucosal nodules were found near the lesser curvature and cardia. It was possible to remove them without resecting the stomach. Sufficient stomach was left to construct a sleeve type reservoir which should prove useful and prevent the patient from becoming a gastric cripple. There was no evidence of metastases in the adjacent lymph nodes or viscera."

In October 1962, Dr. McPhee reported that the patient is apparently with good function of her stomach and no evidence of recurrence of her tumor.

References

Hohf, R. P., Engel, K. L. and Kapos, N. J.: Liposarcoma of the stomach, Ann Surg, **142**: 1029-1033, 1955.

15. *Mucinous Carcinoma of the Stomach*

Contributed by Leo Lowbeer, M.D., Tulsa, Oklahoma

THE PATIENT was a 51-year-old man in April, 1960, when he complained of asthenia and loss of weight. In 1956 he had had a subtotal gastrectomy for pancreatic ectopic tissue in the wall of the stomach. On examination, he appeared pale and had soft enlargement of the prostate. The hemoglobin was 10 gm per cent; 157,000 platelets, with normal differential white count; calcium was 4.7 m Eq/1, and phosphorus 2.2 m Eq/1. There was a sclerotic appearance of numerous bones.

Dr. Schatzki: The earlier film shows a defect of the greater curvature side of the prepyloric area characteristic of an intramural extramucosal lesion. The lesion is quite consistent with the diagnosis of ectopic pancreas. On the later film, I cannot see the defects which are described in the summary of the patient. There may be some irregularity and infiltration along the lesser curvature. This is so questionable that I shall say that I cannot see anything wrong with the stomach. The region of the anastomosis is not densely filled, probably a happenstance finding, rather than due to tumor or due to rare retrograde intussusception.

The record mentions the sclerotic appearance of numerous bones. The later film seems to show some sclerosis in the lumbar spine. I cannot see any such lesion on the original film. If the bones really have become denser without becoming enlarged, and if no operation like removal of a parathyroid tumor has been performed, I assume that these lesions are metastatic, possibly from cancer of the prostate.

Dr. Schatzki's impression: 1. No abnormality seen in the stomach. 2. OSTEOBLASTIC BONE METASTASIS (Cancer of the prostate?).

Roentgenologic Impressions Submitted by Mail

Gastric carcinoma	25
Metastatic carcinoma	15
Carcinoid	6
Quien sabe?	1
Others	32

Dr. Schatzki: Twenty-five radiologists called this gastric carcinoma; I do not see on what evidence they made this diagnosis. Metastatic carcinoma, meant probably of the bone. Carcinoid I see no evidence of. I agree with the diagnosis of "quien sabe?".

Dr. Regato: Dr. R. R. McCarver, of Phoenix, and Dr. B. Pear, of Denver, made a diagnosis of carcinoma of the stomach. Dr. H. Hauser, of Cleveland, and Dr. J. A. Campbell, of Indianapolis, suggested metastatic carcinoma from a prostatic primary. Dr. R. D. Moseley, of Chicago, suggested gastro-jejunal intussusception and Dr. O. F. Prochazka, of Liberal, Kansas, ectopic pancreas.

Dr. Meissner: The low power view shows a thickening of the gastric wall without obvious mucosal changes. Furthermore, the section seems to be at the junction of the gastro-enterostomy because of the arrangement of the muscle fibers. There is even a suggestion of a small amount of intestinal epithelium at one end of the mucosa. The thickening of the wall is not due to muscle hypertrophy but to a diffuse infiltration with cells of a signet-ring type which do not form any glandular arrangement. The cells have a distended and clear cytoplasm and are diffusely infiltrating the entire wall of the stomach. Without a mucus stain it would be difficult to be certain whether these cells contain fat or whether they are epithelial cells distended with mucus. With the PAS stain it is obvious that the cells contain varying amounts of mucus, and we assume, therefore, that they are epithelial. The diffuse infiltration of the epithelial cells of the signet-ring type extends into the serosa. The malignant nature of the infiltration is evidenced by the direct invasion of a nerve by these cells. A section of the gastric mucosa shows cells of a somewhat similar type. These cells in the gastric mucosa, however, seem to be orderly in arrangement and I could find no specific evidence of neoplasm in the gastric mucosa. The resemblance of the mucus cells of the gastric glands and their staining quality to those of the cells

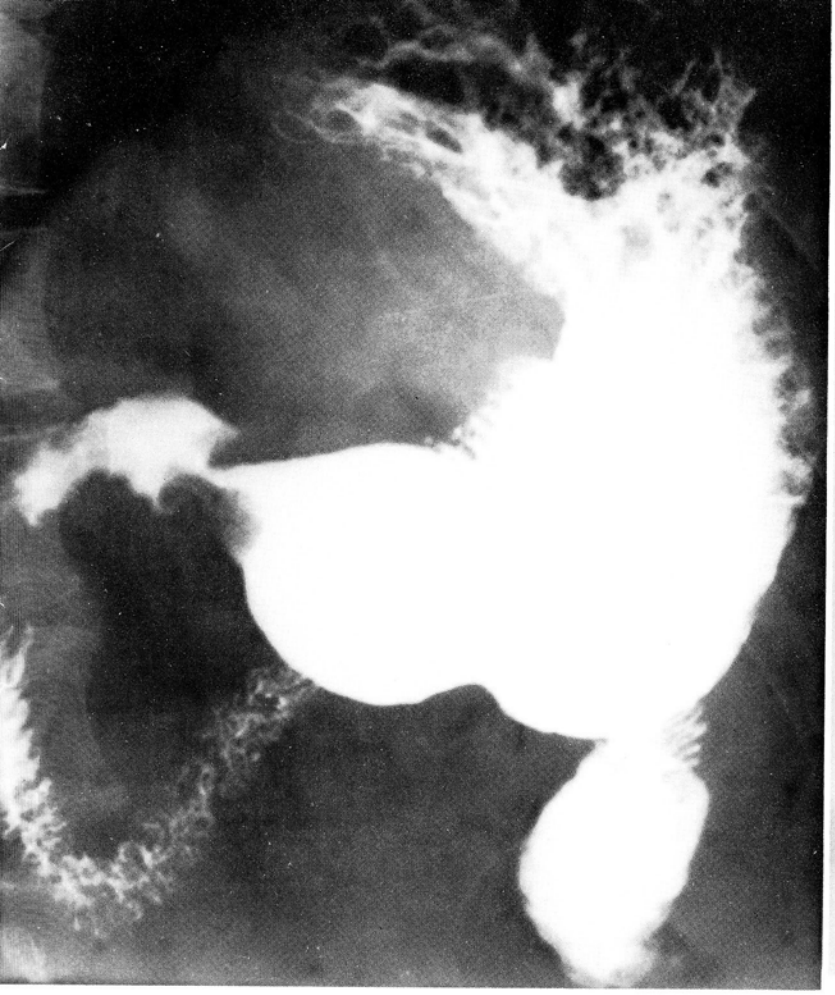


Fig. 1—Roentgenograms of the stomach (1956) showing defect caused by ectopic pancreatic tissue.

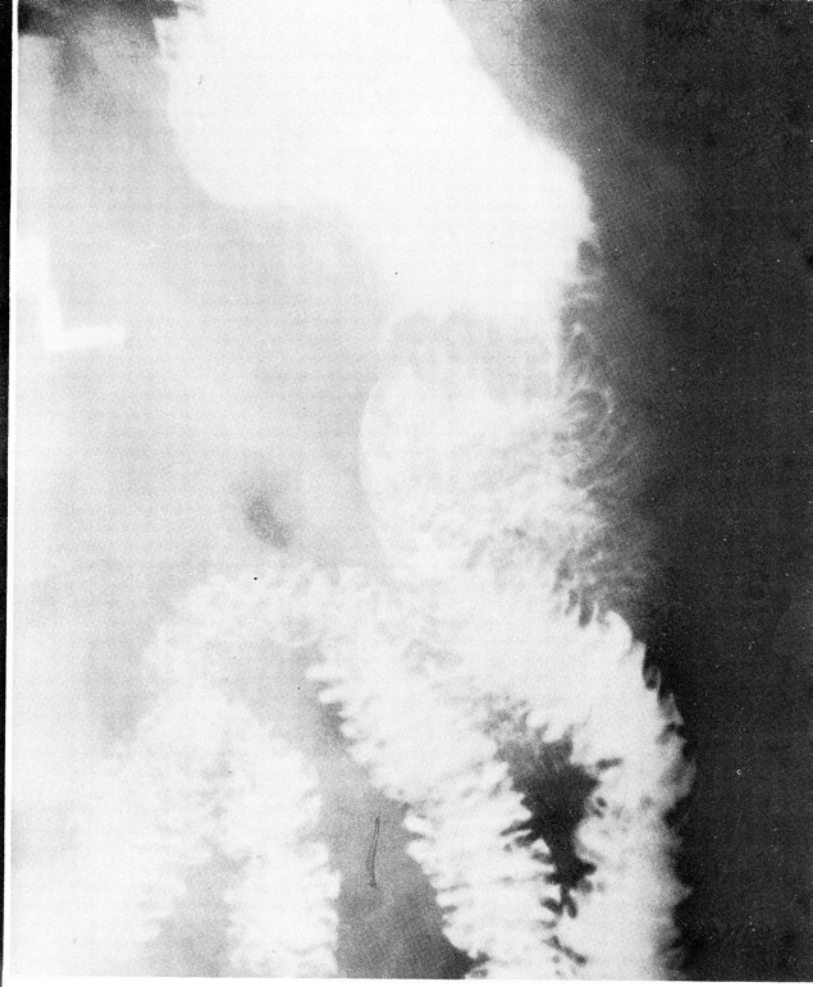


Fig. 2—Functioning gastro-jejunostomy with negative shadows in the remaining portion of the stomach.

infiltrating the wall is, however, striking and I believe, therefore, that we are dealing with a mucinous carcinoma, probably originating in the stomach and extending through the gastric wall and gastro-enterostomy.

Mucinous carcinoma of the signet-ring type is one of the common gastric cancers. It tends to metastasize widely in spite of its relatively slow growth rate, and I suspect that the sclerotic appearance of the bones may be due to multiple bony metastases. Without the opportunity to study the slides from the partial gastrectomy four years before, it is impossible to conjecture on the relationship to the previous diagnosis of heterotopic pancreatic epithelium. It is unlikely that the previous diagnosis was in error, although admittedly it is possible for a mucinous carcinoma to be of sufficiently low grade to be present for four years, particularly with a functioning gastro-enterostomy.

Dr. Meissner's diagnosis: MUCINOUS CARCINOMA OF THE SIGNET TYPE.

Histopathologic Diagnoses Submitted by Mail

Adenocarcinoma	36
Mucinous carcinoma	23
Linitis plastica	22
Signet-cell carcinoma	20
Metastatic carcinoma	18
Neuroma	6
Granular-cell myoblastoma	5
Others	17

Dr. Meissner: There is wide agreement among the participating pathologists. This is a signet ring carcinoma, it is also a mucinous carcinoma, it is also an adenocarcinoma, and if one uses the term "linitis plastica" for a diffuse carcinomatous infiltration of the wall of the stomach, then this could also be included in this general category of diagnoses. I suppose this could be metastatic carcinoma, since I found no primary site in the gastric mucosa. However, I believe it is quite consistent, and even highly suggestive of a primary gastric tumor.

Dr. Regato: Dr. R. M. Delcourt, of Brussels, Dr. R. Lattes, of New York, Dr. N. Puente-Duany, of Miami, and Dr. R. Willis, of Leeds, all agreed on a diagnosis of signet-ring cell mucinous carcinoma.

Subsequent history: Besides widespread osteoblastic lesions the patient also presented diffuse infiltration of both lungs. A bone marrow biopsy revealed evidence of metastatic carcinoma compatible with a prostatic primary; the patient was given transfusions and estrogens and an orchectomy was done but he became weaker and on May 12, 1960, he expired. At autopsy the prostate was normal but metastases were widespread.

L. Lowbeer, M.D., Tulsa, Oklahoma: The radiographic changes were so extensive that our radiologist did not think it was really compatible with prostatic carcinoma. The alkaline phosphotase was elevated and the acid phosphotase was elevated also; but the prostate was found to be rather small. In spite of this, an orchectomy was done. At the autopsy there were, in addition to extensive bone metastases only a few metastases to the lungs. The liver was large showing extramedullary hemopoesis. In very large members of sections through the prostate no tumor was found. The bone showed only adenocarcinoma: we re-stained it with mucicarmine, taking care to alkalinize the section; it is very difficult to demonstrate mucin with a mucicarmine stain in acid sections; that is the reason it is difficult to demonstrate in the stomach, and particularly difficult to demonstrate it in decalcified and rather acid bone sections.

The stomach appeared to be entirely normal, with the exception of the anastomosis which grossly appeared to be very bulky. The sections of this area revealed signet ring cell carcinoma of the anastomosis, but not of the remainder of the stomach.

R. Erdmann, M.D., Amarillo, Texas: I wish to ask Dr. Meissner his opinion of what I think has been emphasized

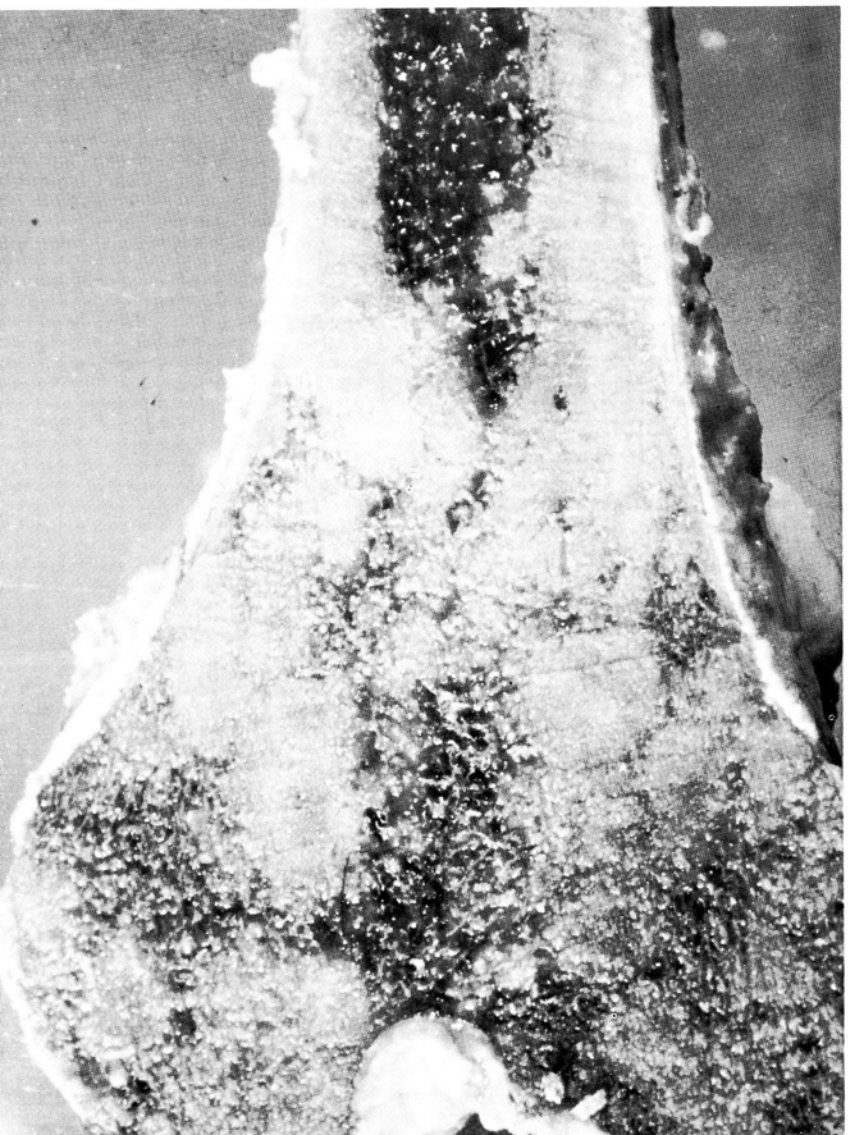
in the last two cases—cases 14 and 15—and which I believe would have little bearing in arriving to final diagnosis. This pertains to the use of fat stains. In Case 14, it was mentioned that fat stains should have been done to rule out liposarcoma. In Case 15, a similar statement was made. I question the validity of such a stain in any anaplastic tumor, particularly of mesenchymal origin, since degenerative changes may produce lipid cytoplasmic concentration with formation of vacuoles. I wonder what Dr. Meissner thinks regarding this standpoint.

Dr. Meissner: I agree that a positive fat stain shows many things other than fat; for example, the lipochrome pigments will stain, and I am sure that fat can be present because of degenerative changes. In this last case I don't believe the fat stain is necessary because the mucus stain was so strongly positive. I think this gives us our diagnosis; but if the mucus stain is negative, I think a fat stain might have been added assistance to us in our consideration of what else this tumor might have been.

M. R. Abell, M.D., Ann Arbor, Michigan: Any rapidly growing sarcoma will show lipid present. Lipid is usually in the presence of very fine droplets. Now if the fat stain reveals large globules, that displace the nucleus, then it is of some significance and only then.

R. P. Spurk, M.D., Denver, Colorado: I don't think that the osteoblastic metastases from mucus-cell carcinoma is really very rare; I have had two cases in the last three years, one of which was in the colon with an identical picture to this case. Did Dr. Schatzki make a remark that the osteoblastic metastases was one of the commonest things with carcinoma of the pancreas?

Fig. 3—Cross section of bone showing extensive involvement.



Dr. Regato: You will find that the osteoblastic metastasis is more related to the speed of development of any tumor than it is to its histologic character. You can have osteoblastic metastases from carcinoma of the breast from carcinoma of the prostate, as well as from the gastrointestinal tract, and it is only because the lesion is developing slowly that bone formation results. If the lesion is a rapid growing one, there is considerably more destruction than there is formation of bone.

R. P. Spurk, M.D., Denver, Colorado: The two mucus cell carcinomas I had were very rapidly progressive. We had films on one of them six months prior and there was no evidence of osteoblastic metastases and he died within four months of that time.

J. Budinger, M.D., Chicago, Illinois: It ought to be remembered that it is very easy to produce elevated acid phosphotase with a prostatic massage. This is a fact I think most urologists know.

H. Braunstein, M.D., Cincinnati, Ohio: Concerning the validity of the fat stain, we are currently engaged in a survey. We have studied about 300 to 400 tumors with fat stains of all varieties to see what the significance of this is. It is my impression that degenerative change in the tumor will not commonly produce fat in the tumor unless there is actual necrosis in the area. We have not been impressed that we can see fat in intact tumor cells that are not necrotic except in certain varieties of neoplasm and I believe the fat stain does have value in distinguishing certain types of neoplasms. With respect to the acid phosphotase, I don't think that I am ready to discard the acid phosphotase as a valuable adjunct in the differential diagnosis of carcinoma of the prostate. There is the factor of prostatic massage; it is, of course, not inconceivable that in rare instances acid phosphotase may occur in other tumors than prostatic for virtually all epithelial tumors possess acid phosphotase in fair quantity, although nowhere near as much as the prostatic tumor has.

O. Rambo, M.D., San Francisco, California: I think in cases like this we should desert the classic teaching and do the radiographs first, the laboratory second, and the physical examination third. Then we will find how valuable the phosphatase is.

Fig. 4—Low power photomicrograph with PAS stain showing a diffuse infiltration of PAS positive epithelial cells in the thickened gastric wall (PAS x 200).