CHRONIC GASTRITIS*

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IN THIS paper I shall confine myself strictly to the discussion of primary chronic nonspecific gastritis. After death the gastric mucosa disintegrates so rapidly that usually postmortem changes can only be recognized by gross and microscopic inspection. Therefore, the diagnosis of chronic gastritis was thoroughly discredited. Only when it became possible to observe the living gastric mucosa through the gastroscope was the frequency and importance of this disease rediscovered and described. Even so, the anatomic foundation of chronic gastritis is uncertain. We do not know very well the histology of the normal stomach of the adult. Material obtained at gastric resection does not give indisputable evidence of the preoperative condition of the stomach, as will be shown later. The normal gastric mucosa of the newborn is better known; it differs from that of adults, and there has been the tendency to make the microscopic diagnosis of chronic gastritis in every adult because of this fact. This is not permissible. There certainly are findings which are the remnants of the frequent acute gastritides of childhood; there is the physiological response of the gastric mucosa to the daily irritation by coarse, hot or cold food. These are the physiological changes the gastric mucosa undergoes. If we should call them pathological, then no adult would have a normal gastric mucosa, and such a definition cannot be accepted.

However, changes are sometimes found which evidently are proof of a disease. In the more severe cases we cannot doubt that a serious gastric disease is present. There is atrophy; the glands have disappeared; there is infiltration, and the epithelium has undergone a metaplasia into intestinal epithelial type; many goblet cells are seen. Such pronounced changes, however, are rarely seen histologically. The pathologist is usually unable to decide whether a gastritis exists or not.

The gastroscopic picture of gastritis is more easily recognized, as I shall endeavor to show you. Gastroscopic examination can be easily carried out repeatedly in healthy and in sick people. If the proper tech-

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nique is used, the patient does not experience any considerable discomfort and, therefore, we are able to examine many patients once a week up to thirty, or even sixty-five, times. Thus we can study normal and diseased stomachs at repeated examinations. The picture obtained by our modern, flexible, safe gastroscope is brilliant and sharp. It permits the visualization of much finer detail than even the inspection of the gross specimen. It is always amazing to see how difficult it is to find a small ulceration in the gross specimen, a lesion seen so readily at gastroscopy. This difference is due to the blood circulating at gastroscopy, absent in the gross specimen.

My conclusions regarding the gastroscopic appearance of the normal stomach were based on a study of healthy people of all age groups.[1] The gastric mucosa of the healthy adult looks smooth, and at the ridge of the folds, glistening, silk-like; it contains high-lights; its color is a uniform orange-red. It should be emphasized that older people also, up to sixty or sixty-five years of age, show the same picture, and we should dismiss the idea that at this age atrophic processes are frequent.

If we examine gastroscopically patients suffering from abdominal distress we often find pictures which differ from those found in healthy people. In almost 50 per cent of these patients we find diffuse alterations. The mucosa may show red patches and layers of adherent, glary, grayish mucus. Such red patches have been described by Beaumont in his famous observations made at the gastric fistula of his servant, Alexis St. Martin, and it is interesting to note that all the changes observed so beautifully by Beaumont and disregarded so entirely for a hundred years, now are rediscovered at the gastroscopic examination. Sometimes the secretion may even be purulent. Histologic checks are rare. However, I obtained the unique microscopic picture of a very outspoken superficial gastritis observed gastroscopically. At a laparatomy a biopsy was taken without the use of any clamps; microscopic sections revealed tremendous superficial infiltration by plasma cells.

If we watch the course of this type of gastritis, which I have called "chronic superficial gastritis," over a period of months or years, two different types of the course are observed. Either the changes disappear, the patient becoming entirely healthy; or chronic atrophic gastritis develops. In some areas of the stomach the signs of superficial gastritis are still seen; in adjacent portions, however, the mucosa becomes thin, mottled, grayish or greenish-gray in color. Atrophy may be patchy, or

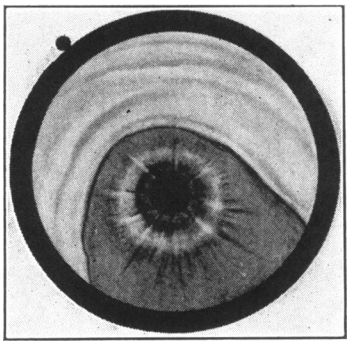

Fig. 1 a

Fig. 1, a and b

Gastroscopic (a) and microscopic (b) picture of the normal gastric mucosa. Gastroscopically the normal mucosa is smooth, silk-like. View of antrum, angulus and pylorus.—The microscopic section demonstrates the mucosa of the body of the stomach. Only few interstitial cells are seen.

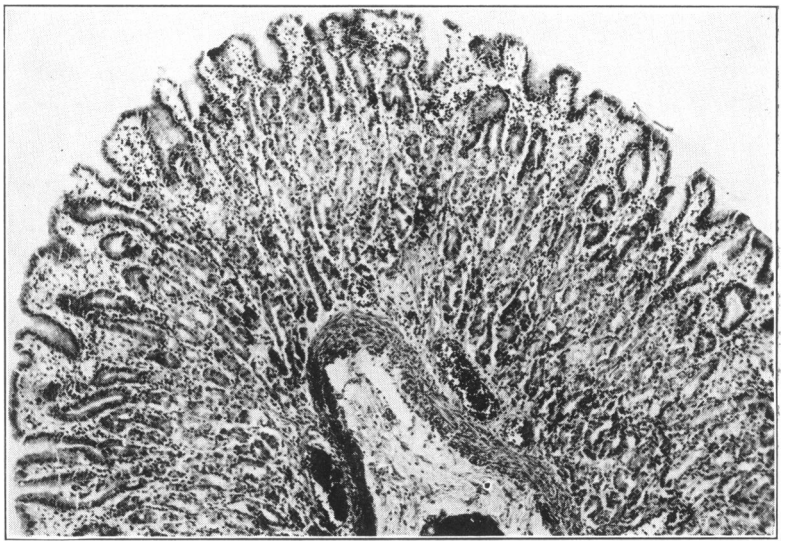

Fig. 1 b

more diffuse, or complete. Blood vessels, always absent in the normal mucosa, are seen. Here the question comes up whether such a condition may still be called inflammation, or do we have to deal with a merely degenerative process. However, this atrophy so often develops from an inflammation. We do not know if there are cases at all without preceding inflammation, nor do we know whether the inflammatory process is entirely gone. In cases of deficiency states, as in pernicious anemia, the first thing we can see gastroscopically is superficial gastritis. Brown has

seen definite inflammatory changes histologically in pernicious anemia; Jones and Benedict[2] observed hypertrophic changes in this disease gastroscopically. For these reasons it seems correct, in the light of our present knowledge, to call this disease an inflammation. Atrophic gastritis may develop within a few months, but then it remains stationary. Jones and Benedict were the first to show that in pernicious anemia following liver therapy, the atrophic gastric mucosa may regain its normal appearance. This observation has been corroborated since, and thus we know that atrophic gastritis is not unchangeable.

There is still a third gastroscopic picture of diffuse inflammation of the stomach which we call hypertrophic gastritis. The gastric mucosa looks swollen, velvety, dull; the high-lights are reduced; nodules and *verrucae* are seen. The folds sometimes look segmented, like a caterpillar. Mucosal hemorrhages are often present. If we have the occasion to examine such a mucosa microscopically, we find proliferation of the surface epithelium and of the glandular apparatus, with tremendous infiltration and enlargement of the lymph follicles. The proliferation may become fan-like or finger-like. Not infrequently superficial ulcerations are observed. These superficial inflammatory ulcerations never develop into true chronic gastric ulcer. The site of predilection of the gastritic changes is the body of the stomach; however, antrum gastritis occurs also, although ulcerative antrum gastritis is very rare.

What are the clinical aspects of chronic gastritis? How frequent is this disease? What is its etiology, its symptomatology, its diagnosis, its therapy? What is its relation to other diseases? European workers have called chronic gastritis one of the "central problems" of internal medicine, and from the observation of over 1,500 cases, I am inclined to agree.

In a statistical survey of gastric diseases as observed gastroscopically in 1,000 patients in the United States and in 255 patients in Germany, we found the incidence of chronic gastritis to be 41.8 and 45.0 per cent respectively.[3] For the clinical analysis all cases combined with some other disease had to be discarded. Even so, much care is needed to avoid faulty conclusions. I will try to summarize briefly the results of our analytical efforts.

The etiology of chronic non-specific gastritis is practically unknown. Most is speculation. Very few facts are proved. It seems to be certain that acute gastritis may develop into chronic superficial gastritis and finally into chronic atrophic gastritis. Chronic superficial gastritis is

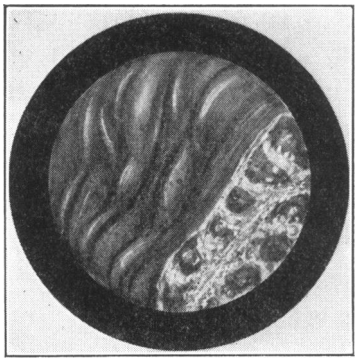

Fig. 2 a

Fig. 2, a and b

Gastroscopic (a) and microscopic (b) picture of chronic superficial gastritis. Gastroscopically red patches and layers of purulent secretion are seen. Microscopically there is tremendous infiltration with plasma cells only in the upper layers of the mucosa between the crypts and the necks of the gastric glands; one small erosion is seen.

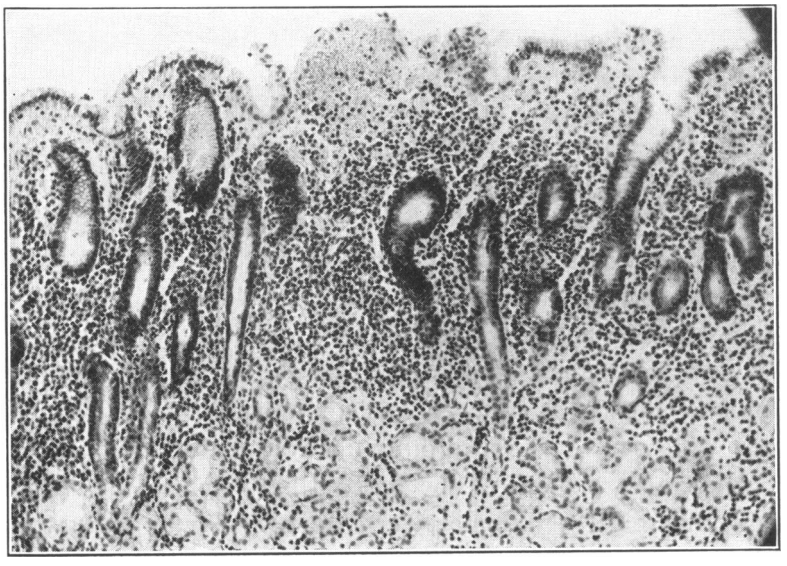

Fig. 2 b

frequently found together with infection of the sinuses and of the tonsils, or with chronic infectious diseases such as tuberculosis of the lungs. Alcohol does not play any role in my experience. However, it seems that the habitual use of hard liquor may lead to hypertrophic gastritis. All observers agree that nicotine may play an important role. Gastric retention, as found in pyloric obstruction, may lead to chronic gastritis. The continuous reflux of intestinal juice, as found sometimes in stomachs after operation, may produce a very severe form of gastritis. Since this

is a secondary form, it must be omitted from this discussion. Superficial and later atrophic gastritis may be found as a result of high voltage x-ray therapy of the stomach. That atrophic gastritis occurs in various deficiency states, as in pernicious anemia, is well known. With these few statements our positive knowledge of the etiology is almost exhausted. It seems that bacteriological factors play a minor role as compared with mechanical and chemical factors.

When we analyze the symptoms of an anatomical disease, we hope to find complaints so characteristic as to permit immediate diagnosis.[4] Attempts made by all gastroscopists in this direction have been so far without result. Neither case history nor physical examination, nor laboratory, nor Roentgen findings permit the diagnosis, although a few symptoms, especially in atrophic gastritis, are suggestive. In superficial gastritis the patients complain of epigastric pain, either of the delayed type or coming immediately after meals. Indefinite pressure, heavy feeling, fullness, belching, disagreeable taste in the mouth, nausea and vomiting are often present. At the physical examination sometimes, though unfortunately rarely, a sign is found which, in my opinion, is entirely characteristic. However, my description,[5] published in 1926, has never been confirmed. There is sometimes a tender zone to the left of the navel, which when checked fluoroscopically corresponds exactly with the silhouette of the stomach, and therefore cannot be mistaken for left-sided Head zones of the pancreas or the left kidney, and certainly not for a tender colon. The roentgenologic statement of a tenderness of the gastric silhouette is the only contribution x-ray can make in this diagnosis. Statement of the thickness of the folds, as seen in the x-ray relief pictures, is not diagnostic. Laboratory findings in superficial gastritis are inconclusive. Histamine proved anacidity may be found as well as hyperacidity. Occult blood may be found sometimes in the stools. Sometimes the aldehyde reaction in the urine is strongly positive, indicating participation of the liver.

If the superficial inflammation leads to atrophy the clinical picture changes. The gastric symptoms become less marked, general symptoms being in the foreground of the clinical picture, so that these patients are always treated as psychoneurotics. Weakness and nervousness come in spells. The reason for this is unknown. Two physicians, both suffering from a severe gastric atrophy, told me that during such an attack, which may last several months, they are incapacitated. When Dr. Murphy of

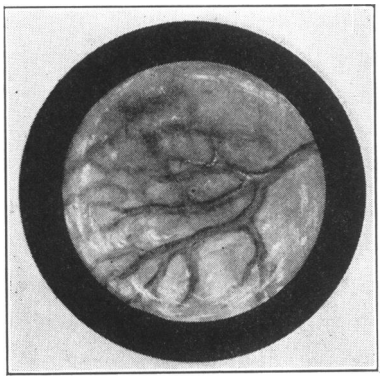

Fig. 3 a

Fig. 3, a and b

Gastroscopic (a) and microscopic (b) picture of chronic atrophic gastritis. Gastroscopically the mucosa is thinned so that the net of the submucosal blood vessels becomes visible. Microscopically the mucosa is thin, the glands have disappeared, the epithelial type has changed, many goblet cells are present.

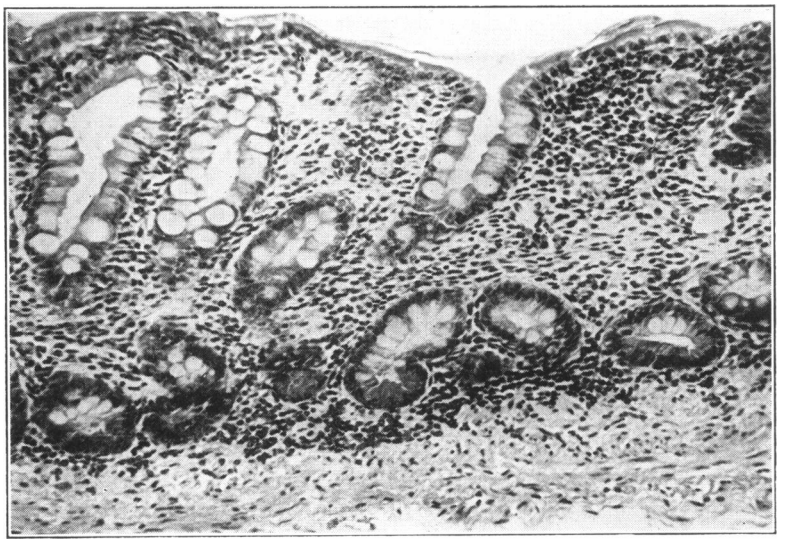

Fig. 3 b

Buffalo analyzed with me the records of forty-two patients suffering from uncomplicated atrophic gastritis, the question came up whether or not these general symptoms would be found also in other abdominal diseases. A subsequent analysis of a great number of cases of hypertrophic gastritis, ulcer, cholecystopathy, and similar conditions showed that only in pernicious anemia similar symptoms were found; so that the syndrome of epigastric pain, nausea, poor appetite, attacks of weakness and nervousness is highly suggestive of atrophic gastritis, especially if additional

complaints of sore tongue and numbness or tingling in the limbs are present. I believe that chronic atrophic gastritis is a very serious disease. It may incapacitate its bearer and, since it may be the precursor of gastric carcinoma, as will be shown later, it must be considered and treated as a major disease. Laboratory findings are of minor importance. Anacidity was found in fourteen out of forty-two cases; two-thirds of the patients did not have anacidity. Occult blood is found sometimes, and in three cases gross gastric hemorrhage was noted, evidently caused by a small inflammatory erosion. Benign obstruction of the pylorus may occur.

Chronic hypertrophic gastritis is also a severe disease. Its symptoms are gastric symptoms highly suggestive of ulcer.[6] Night pain and delayed pain are frequent, but this pain often lasts only a few days; then the patient feels entirely well again; he quickly learns, however, that he must be careful with his diet to avoid a relapse. Gastroscopically one may see during an attack the gastric mucosa swollen with many scattered shallow gray erosions. A few days later all these erosions are gone but still some hypertrophic areas are seen. Complete cure seems to be rare. Gross hemorrhage as a complication has been observed by all gastroscopists. Fatal outcome is not rare. In some cases x-ray examination gives the picture of the so-called "cob-corn" or granulation relief picture. We found it in Chicago only twice in 300 cases. Flakes of mucus or remnants of food may simulate this picture of dark round holes. We have never succeeded in demonstrating by x-ray the definite localized alterations of the mucosa seen gastroscopically, such as single stiff folds or circumscribed node-formation.

We have seen that, with the exception of a few cases, gastroscopy is the sovereign diagnostic method for chronic gastritis.[7] Difficulties in the gastroscopic diagnosis of chronic gastritis, however, may be experienced also, especially in diffusely infiltrating forms, and the expert may face insurmountable difficulties. These cases, though rare, are important. In a thirty-five year old male the x-ray picture suggested carcinoma of the antrum, the gastroscopic picture was interpreted to be that of an ulcerative antrum gastritis. Through two years the picture remained essentially the same. Granular thickened mucosa with many ulcerations was observed. Finally, rather suddenly, atrophy of the antrum mucosa developed. One month later the patient developed fever and a retroperitoneal tumor. At operation a Hodgkin tumor was found; a biopsy was taken and a biopsy of the antrum was made. The excised stomach wall showed

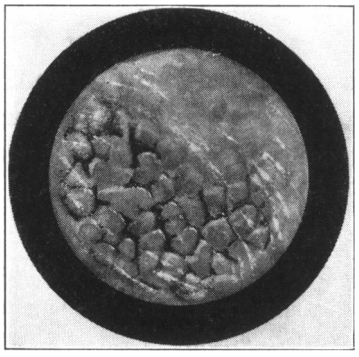

Fig. 4 a

Fig. 4, a and b

Gastroscopic (a) and microscopic (b) picture of chronic hypertrophic gastritis. Gastroscopically the mucosa is irregular with "cobblestone formation". Microscopically tremendous proliferation with edema and infiltration is seen.

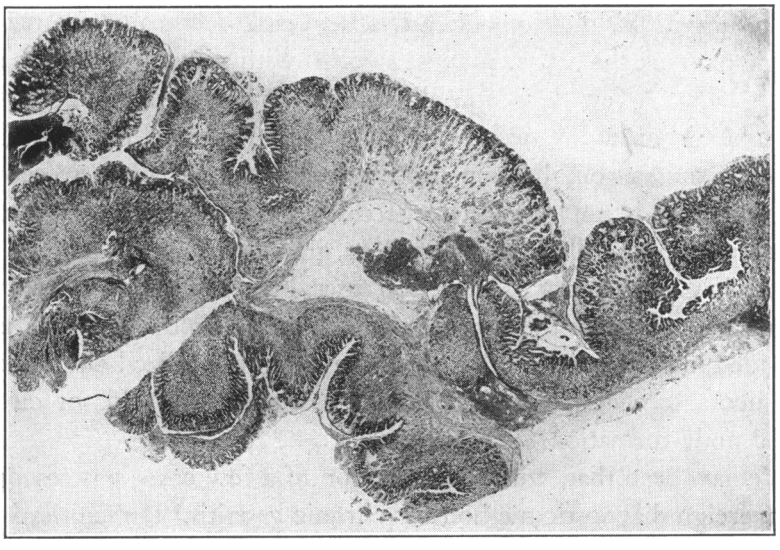

Fig. 4 b

the typical picture of atrophic gastritis as observed gastroscopically, but not the least sign of Hodgkin lymphogranuloma. In the case of a thirty-seven year old woman with anemia, x-ray suggested polyposis. She had been treated for a severe protein-deficiency state. One year later slight epigastric distress with vomiting developed. The gastroscopic picture was difficult to interpret; all types of diffuse infiltrations were considered. Pyloric obstruction led to immediate surgery, and in this case severe ulcerative antrum gastritis was present. The gross specimen showed

ulcers and inflammatory nodes. The microscopic section through the largest ulcer showed that it did not penetrate the muscularis mucosae. Cystic atrophic hyperplastic gastritis was seen. A section through the nodes revealed the inflammatory character.

Recently we observed three cases of tumor causing gastritis. I shall describe only one of them. A tumor was diagnosed by x-ray; gastroscopically an extensive hypertrophic gastritis had been diagnosed and a bulging in of the lesser curvature had been interpreted correctly as an inflammatory tumor. Laparotomy revealed unusual inflammatory changes of the entire interior of the stomach and of almost the entire small intestine as well. The folds reached a height of 2 to 3 inches. A biopsy was made. Microscopically a tremendous proliferation of the mucosa was observed, with edema, hemorrhage and infiltration by plasma cells, leukocytes, and eosinophils. The last case of this series of difficult gastroscopic diagnoses shows that the microscopic difficulties may not be less outspoken. In a sixty-three year old man, complaining of relatively mild epigastric distress with moderate weight loss, clinical, laboratory and x-ray examination revealed nothing. Gastroscopy showed tremendous bleeding, nodular infiltration of the entire posterior wall with many small ulcerations and atrophic areas. The diagnosis of a diffuse infiltrative lesion was made and laparotomy was advised. The surgeon was unable to feel anything pathological in the stomach; however, he made a biopsy, and microscopically a most unusual section was obtained. There was no unity among the pathologists in the interpretation of this section. The majority made the diagnosis of lymphoblastoma, but the diagnosis of an unusual form of chronic atrophic gastritis has also been made. This unique case must be watched carefully.

The therapy of chronic gastritis, as derived from gastroscopic observation, will be discussed very briefly. The variations in the picture of such a multicolor disease, of eminently chronic course with many spontaneous remissions, render the judgment of the effect of any type of therapy very difficult. In all its forms chronic gastritis should be considered and treated as an important disease. Possible etiologic factors, such as infected tonsils, sinusitis, alcoholism, nicotine, should be eliminated. A bland diet is always advisable. The mechanical work of the inflamed mucosa should be reduced as much as possible. Raw cellulose should be eliminated; spices should be avoided in the superficial and hypertrophic forms, but are sometimes recommendable in atrophic forms.

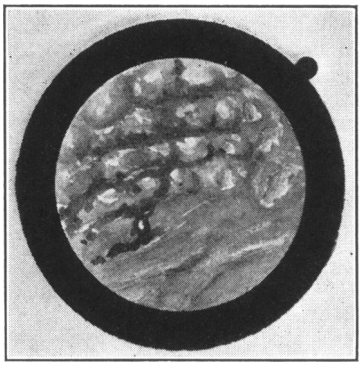

Fig. 5 a

Fig. 5, a and b

Gastroscopic (a) and microscopic (b) picture of a rare case of "lymphoblastomic gastritis." These severe changes were found neither by most refined x-ray relief studies, nor palpated at surgical interference, but only at gastroscopic and microscopic examination. Gastroscopically infiltration with erosions and bleeding is seen. Microscopically the mucosa is destroyed by a dense infiltration of lymphocytes.

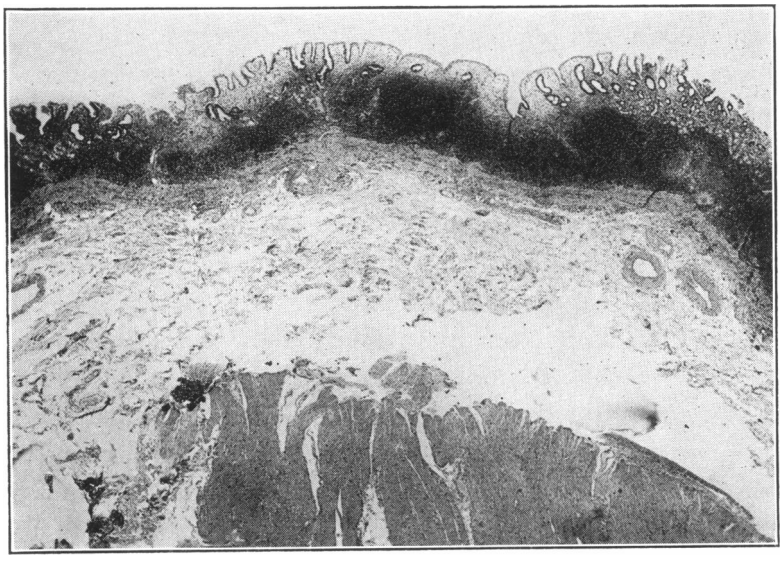

Fig. 5 b

Frequent small meals may be given. If ulcerations are seen, one should insist on rest in bed for a few days with hot applications. Longer rest in bed may be necessary after a gross hemorrhage. In my opinion, gastric lavage is often very useful in superficial gastritis. Lavage is less valuable in the other forms. Alkalis may be agreeable in some cases of hypertrophic gastritis. In atrophic gastritis hydrochloric acid and charcoal sometimes are appreciated. In cases of atrophy in which deficiency states may be suspected, liver may be tried, iron or vitamins, especially nicotinic acid.

Three of our patients with atrophic gastritis responded definitely to liver injections by regeneration of the gastric mucosa. High voltage x-ray therapy was tried first in a case of ulcerative hypertrophic gastritis observed over a period of ten years. The success was amazing, but one year later severe atrophy developed as a late effect of the irradiation. Newer observations confirmed the effectiveness of this type of therapy; however, the end results are still unknown. Surgical treatment, in my opinion, is justified only in the rare cases of gastritic pyloric obstruction. Gastritic gross hemorrhage is a definite contraindication to gastric surgery.

I come to the last chapter, to the complications and sequelae of chronic gastritis. The activity of the bowels is not impaired in uncomplicated gastritis. If diarrhea is noted, inflammation of the intestine may be assumed. The Argentine workers, Royer, Bur, and Montejano,[8] found (gastroscopically) gastritis in one-third of their colitis cases. In a case diagnosed clinically as Crohn's disease, I found (gastroscopically) severe hemorrhagic ulcerative gastritis. Chronic cholangitis together with chronic gastritis has been found frequently. In such cases the aldehyde reaction usually is strongly positive. The lesion may be an ascending or a descending one. The latter type with fatal outcome was observed once by myself.

The close relation of gastric atrophy to pernicious anemia is well known. Knud Faber,[9] Hurst[10] and others believed that chronic gastritis is the primary disease destroying the function of the pyloric Brunner glands, a possible source of Castle's[11] antianemic factor. Chester Jones, Benedict and Hampton[2] were the first to observe that liver therapy leads to regeneration of the gastric mucosa. This observation, confirmed by Chevallier and Moutier[12] and Lehmann,[13] speaks, in my opinion, against the correctness of the mentioned theory. Gastroscopic observations in twenty-three cases of pernicious anemia[14] led to the conclusion that there must be a primary dysfunction of those cells which produce the antianemic factor, and a secondary degeneration of the gastric surface epithelium with following genuine inflammation.

Konjetzny,[15] whose extensive surgical and histological work is of the utmost importance, has contended that chronic gastroduodenal ulcer develops from chronic gastritis, and in reality is a gastritic ulceration. This gastritic theory of gastric ulcer is widely accepted in Europe. Konjetzny described a macroscopically visible ulcerative antrum gastritis

in 50 per cent of all cases of duodenal ulcer he operated upon, and microscopically visible changes in all cases. In American hospitals these changes were not observed, and Walters and Sebening[16] therefore assumed geographical differences. Our gastroscopic observations have failed entirely to confirm Konjetzny's statements. Gastritic ulcerations have not developed into gastric ulcer, and ulcerative antrum gastritis has not been found in cases of ulcer. The relation of gastritis to gastric ulcer as noted in ninety-one cases of gastric ulcer has been studied by Dr. Baxmeier of Pittsburgh and myself.[17] Our findings did not support the gastritis theory. In 47 per cent of all ulcer cases, no inflammation was found. We therefore had the idea that differences in surgical technique may be responsible for this discrepancy. Gastric resections and other gastric operations were carried out in twenty-two dogs by Dr. H. Necheles, Dr. R. Gold and myself[18] with the following results. If a simple resection is made, the resected specimen does not show any pathology. If we filled the dog's stomach with N/10 hydrochloric acid and quickly excised it two hours later, we again found a normal mucosa. But if we filled the stomach with hydrochloric acid of the same concentration and made a resection, a severe ulcerative hemorrhagic antrum gastritis was seen, sometimes proceeding to extensive destruction of the mucosa. If we ligated the arterial blood supply of the left side of the stomach and then cut the stomach out, nothing was seen; but if the operation was performed and hydrochloric acid was used, ulcerative gastritis exactly corresponding with Konjetzny's pictures[15] was found only in the areas without blood supply, sharply demarcated from the other side of the gastric wall. Microscopically we see that the vicinity of the ulcerations is full of plasma cells, an astonishingly rapid inflammatory tissue reaction, which is entirely absent at some distance from the ulcer. These experiments seem to support our gastroscopic observations and to prove that chronic gastritis and gastric ulcer are two different diseases.

Fortunately we are able to support fully Konjetzny's ideas[15] about the origin of gastric carcinoma. Rarely, if ever, carcinoma develops in a normal gastric mucosa. Gastroscopically, as well as microscopically, carcinoma develops in an inflamed mucosa, sometimes in several places, multicentrically. Gastroscopic observation and clinical check prove that frequently atrophic gastritis is a definite forerunner of gastric carcinoma, a precancerous condition.[1] I myself, in 1933, suggested periodical x-ray and gastroscopic examinations of patients suffering from atrophic gastritis

as the most important weapon in the fight against the most frequent carcinoma. Minimal gastric carcinomas cannot be found otherwise than incidentally, and they will be found incidentally if we decide to carry out periodic x-ray and gastroscopic examinations in patients suffering from atrophic gastritis. The last three case reports will confirm this statement.

A fifty-seven year old patient suffered for more than one year from mild epigastric distress. In the last few months he had some loss of weight. X-ray revealed a prepyloric ulcer. Because of the long case-history, the presence of hydrochloric acid and good response to ulcer therapy, the ulcer was considered to be benign. The gastroscopic picture, however, was that of an extremely small pyloric carcinoma. Atrophic gastritis was found around the lesion. After resection, grossly, no signs of malignancy were discovered; but, microscopically, in full accord with the gastroscopic picture, a minimal carcinoma was found. Its width was 8 mm., the depth 0.5 mm. to 2 mm. It is unbelievable that this small carcinoma could have produced symptoms of one year's duration. These symptoms probably were due to the existing atrophic gastritis which also was found microscopically; and probably the discovery of the minimal carcinoma was incidental and due to the careful x-ray and especially due to the gastroscopic examination.

A fifty-four year old surgeon suffered for more than ten years from epigastric distress. Severe purulent cholangitis was found at a cholecystectomy, but the distress was not relieved. The patient developed a histamine proved anacidity, and in the last eight years had terrible attacks of anorexia, weakness and exhaustion. Within the last three years a filling defect of the greater curvature developed. This was thought due to spasm. The defect grew slowly, and when the patient finally submitted himself to the gastroscopic examination, a polypoid tumor was found to lie in an entirely atrophic mucosa. This diagnosis would have been possible two years earlier by gastroscopy. However, the patient recovered after resection. A microscopic section through the edge of the tumor showed the mucosa to be completely atrophic, and the transformation of the atrophic mucosa into tumor tissue was observed. It is a typical case: chronic cholangitis, severe chronic atrophic gastritis of ten years duration, slow development of a carcinoma which by periodic gastroscopic examination would have been discovered at least two years earlier.

The last case shows that such incidental diagnoses are possible in

reality. A fifty-nine year old man suffered from pernicious anemia and combined cord degeneration. Our roentgenologists were unable to find any pathologic change. Only for the sake of completeness, gastroscopy was undertaken. In the antrum atrophic gastritis was seen, but in the midportion of the stomach toward the greater curvature the ulcerated wall of a small gastric carcinoma appeared. X-ray examination repeated with compression and relief films was negative, but at operation a very small adenocarcinoma was excised.

Knowledge of chronic gastritis is of outstanding importance in our fight against gastric cancer. The following points are the obvious results of these observations: 1. Superficial gastritis should be prevented from turning into atrophic gastritis by thorough treatment. Therefore it must be diagnosed gastroscopically. 2. Atrophic gastritis, the precancerous condition, should be diagnosed. This is also possible only gastroscopically. 3. If atrophic gastritis has been diagnosed, the patient should be observed, but naturally not told the reason for this observation. Every six months x-ray and gastroscopic examination should be undertaken. With such a program we may hope to discover carcinomas of minimal size and to bring about cures in a percentage of cases not dreamed of until now, as shown by the presentation of the last three cases. Chronic gastritis—a severe disease in itself—derives its most outstanding significance because of its role in the fight against gastric carcinoma.

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