# SYPHILIS OF THE STOMACH *

## A CRITICAL REVIEW OF REPORTED CASES FROM THE PATHOLOGICAL AND CLINICAL VIEWPOINTS

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Andral [1] reported two cases of supposed syphilitic disease of the stomach in 1834, and from that date to the present time, there has existed a controversy over many aspects of this condition. Andral based the diagnosis upon the existence of severe gastric symptoms in two patients known to be suffering from syphilis, who were greatly benefited or cured by the administration of mercury and iodide. Following his report, many other cases of a similar nature were published, but so far as we can find, no serious study from the pathological viewpoint was undertaken until 1891. Chiari [2] in that year published a comprehensive paper with a review of the literature, in which he emphasizes the rarity of syphilis of the stomach as demonstrated by histological evidence. He could find only seven reported cases that he was willing to accept as beyond question. To these seven cases he added two others which had come under his personal observation in the autopsy room. He definitely formulated the necessity of basing a diagnosis of syphilis of the stomach on histological evidence only. His analysis of all the previously reported cases in which the diagnosis rested on any other foundation, resulted in his rejection of such cases as unproved. This conclusion was reached by a study of 243 autopsy examinations of persons dying from syphilis, the disease being congenital in 145 cases, and acquired in 98 cases.

The influence of his work was very great, and his teaching was practically accepted by all writers until the introduction of the Wassermann reaction and of röntgenology as aids to our clinical study. Prior to this time a few isolated reports appeared, but the authors were very careful to question their own diagnosis because of the lack of histological evidence. Since this time the teaching of Chiari and those immediately following him, has been to a considerable extent lost sight of, and to-day in increasing numbers case reports are being published in which the diagnosis lacks not only histological evidence, but in an astonishingly large number, even sound clinical evidence (Fig. 12). A note of warning against this tendency has been sounded repeatedly, but apparently without producing the desired result. For this reason a critical review of the situation as it now presents itself may not be without value. Perhaps the most convincing form that such a review can take will be found in a detailed study of the comparatively few cases in which the diagnosis rests upon sound histological evidence, followed by an attempt to make those reported cases which rest upon other evidence conform to the former group, and failing this, to exclude them as examples

* Read before the New York Surgical Society, January 14, 1925.

of syphilis of the stomach. Unfortunately the number of reported cases in which histological evidence is lacking has increased so rapidly, and has now reached such a large total, that it would be an impossible undertaking to present their merits or demerits in detail. For this reason only those cases will be discussed which present substantial grounds for maintaining the diagnosis of syphilis of the stomach.

Chiari found but one case of the disease in the 145 congenital syphilitics on whom he performed an autopsy, and one case among the 98 subjects dying of acquired syphilis. In the former group 40 cases died soon after birth, and in one of these there was found a diffuse infiltration of the mucosa and submucosa of the stomach, which Chiari believed to be syphilis, but was unwilling to positively so class it. In 75 of this group living to later childhood, 27 showed marked circulatory changes in the stomach, such as hemorrhagic erosions, punctate hemorrhages, hyperæmia, and also œdema of the sub-mucosa. These he assigned as secondary to the syphilitic changes in the liver, but excluded them as actual syphilitic lesions of the stomach. In the acquired cases there were 37 that showed changes similar to those found in the older children, and in one case there was a true peptic ulcer, and in one the scar of a healed ulcer. The author was unwilling to accept any of these conditions as being the direct result of syphilis. Thirty-six of these cases occurred in patients who had died with the lesions of far-advanced syphilis. These observations are of the utmost importance, but have been lost sight of by many recent writers who have depended solely upon the

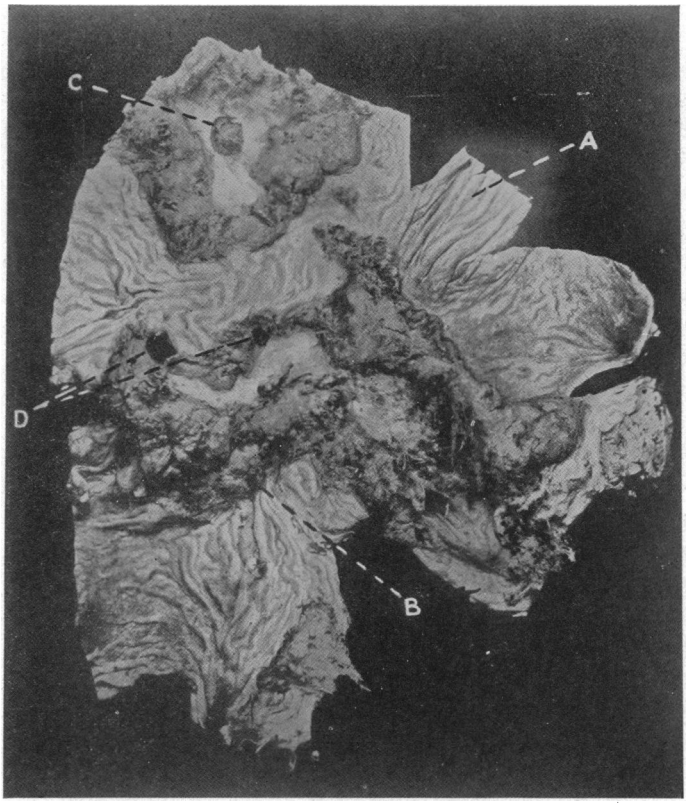


FIG. 1.—McNee's case from Quarterly Journal of Medicine, Oxford, 1921-22, vol. xv, pp. 215-226. A. Œsophagus. B. At pylorus. C. Similar to portion in which spirochætæ were found. D. Perforation.

therapeutic test in accepting the diagnosis of syphilis of the stomach. They demonstrate the presence of changes in the stomach, which are not actual luetic lesions, but which would beyond doubt be favorably influenced by the administration of anti-luetic agents.

Flexner,[3] in 1898, and Pappenheimer and Woodruff,[4] in 1906, each presented one additional case. They again reviewed the literature, and to Chiari's cases they were able to add five more, making a total of twelve cases. Pater,[5] in 1906, in a rather less critical review of the literature, adds seven cases which he accepts as histologically proved examples of gastric syphilis. The evidence is less convincing than in the cases accepted by the first-named

FIG. 2.—McNee's case from Quarterly Journal of Medicine, Oxford, 1921-22, vol. xv, pp. 215-226. Spirochætæ.

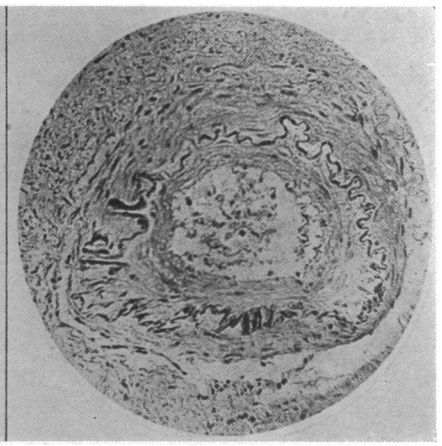

FIG. 3.—McNee's case from Quarterly Journal of Medicine, Oxford, 1921-22, vol. xv, pp. 215-226. Endarteritis obliterans.

writers, but one cannot find adequate ground for disregarding the diagnosis accepted by the reporters of Pater's cases.

In 1922, McNee [6] reported the only case in which the finding of the spirochæte proved beyond doubt the syphilitic nature of the lesion. Graham,[7] in the same year, adds one case in which the diagnosis rests on sound histological evidence. Brams and Meyer,[8] in 1923, report two more cases with acceptable histological findings. Our search to find additional cases has been unavailing.† The rarity of the disease where the diagnosis rests on histological proof is established by the fact that only these twenty-five cases are on record. Moreover, it is a fact of great importance that Chiari found his two cases in 243 autopsies on advanced syphilitics; that Pappenheimer's case was the only one in 4880 autopsies at Bellevue Hospital, of which number 316 (Symmers [9]) showed advanced syphilitic lesions; that Stolper found but one case in 86 autopsies on syphilitic subjects; that Turnbull [10] finds no case in nearly 13,000 autopsies and none in over 700 operative specimens

† Since going to press two additional cases have been found. Brams and Antoine [46] and Hemmeter and Stokes.[38] Some doubt that the latter is not tuberculosis may exist.

of stomach lesions coming to the Pathological Institute of the London Hospital. (v. i.) One is unable to explain away these figures in an endeavor to be credulous concerning the great number of reported cases resting on less secure ground than histological evidence. These twenty-five cases demonstrate beyond cavil that the spirochæte pallida does attack the stomach, that it sets up there lesions exactly similar to those found in other organs, and that the histological evidence of this is susceptible of proof.

Their small number, taken in conjunction with the enormous number from which they have been isolated, emphasizes that for some reason the spirochæte does not find a favorable soil for growth in the stomach. Some writers have been inclined to argue that since practically no organ in the body is immune to the ravages of syphilis, and since both the oral and the anal segments of the digestive tract are known to be attacked, the relative immunity of the stomach must be apparent and not real. The argument is unsound, and cannot be used to controvert undeniable facts. First, because the rectum is not as frequently the seat of syphilitic lesions as formerly taught, many of the supposed syphilitic strictures being secondary to gonorrhœal infections, and second, because the intestines also are comparatively rarely attacked. Symmers [9] in 316 syphilitics found no lesions in the small intestine, and only 5 in the colon. The immunity of the stomach may with our present knowledge be unexplained, but it cannot be denied.

It is unfortunate that few of the reported cases are complete in clinical data. For this reason our knowledge of the disease, based on proved cases, is very meagre, except in pathological detail, while the clinical conception has been evolved from material which includes many conditions very doubtfully syphilitic.

Chiari's [2] excellent study establishes the characteristics of the syphilitic lesion as found in his own cases and those previously reported. Later writers have amplified this somewhat but nothing essential has been added.

His conclusions are as follows:

1. Syphilis produces actual changes in the stomach.

2. They may be direct or indirect.

3. The first are gummatous or simply inflammatory infiltration.

4. Gumma may occur in both hereditary and acquired syphilis. The infiltration was seen only in the former.

5. The indirect results are due to syphilitic changes in other organs, for example the liver, or in producing the hemorrhagic diathesis, so-called hemorrhagic syphilis, and are relatively frequent.

6. Gumma always apparently first starts in the sub-mucosa and extends from there into the other coats.

7. Through the breaking down of the gumma, particularly because of the action of the gastric juice, ulcer, and ultimately scars may form; then only by the finding of other gummata or the remains of gummatous tissue can the syphilitic nature be established.

In Stolper's [11] case, and in Flexner's [3] more fully reported case, the ulcer was formed by necrosis due to obliteration of the blood-vessels. The latter's report is worthy of quotation.

The patient was a man, aged fifty-two, who in December, 1891, suffered from an acute attack of vomiting followed by fever. In August, 1892, a physical examination disclosed a much enlarged and tender spleen. Ascites developed and a tapping was done on April 20, 1893. He was tapped altogether sixty-five times in the next year, and a cirrhotic liver became palpable. He died in June, 1894. The autopsy showed a large hepatic gumma, a perforated syphilitic ulcer of the stomach and acute peritonitis. The spleen was adherent to the site of the ulcer but the perforation had taken place immediately adjoining this. In the fundus of the stomach 4 cm. from the cardia along the greater curvature was an ulcer 5 x 5 cm. in the centre of which was a perforation 15 x 3 mm. in size. Just above the perforation the tissues presented a greenish and necrotic appearance.

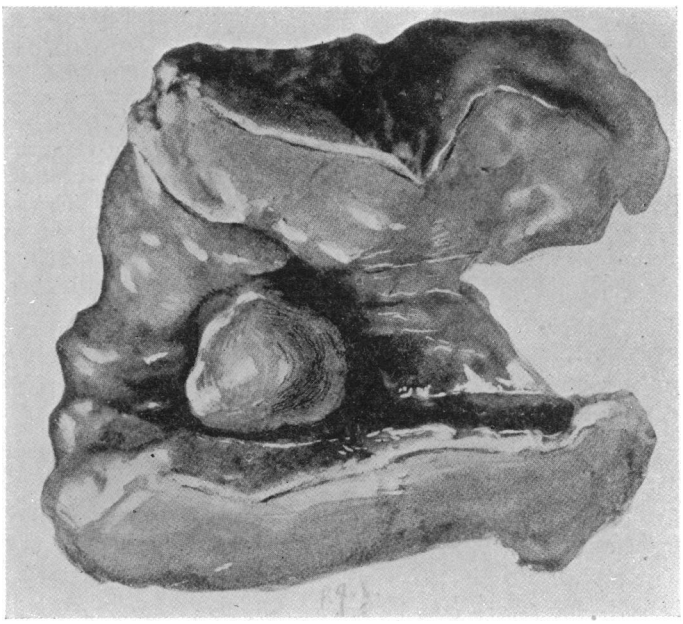

FIG. 4.—Graham's case from ANNALS OF SURGERY, 1922, vol. lxxvi, p. 449.

For the purpose of the microscopic study pieces of the ulcer from several different parts were subjected to examination. The principal microscopic characters are as follows: The pathological process is localized chiefly in the submucosa and exists in two distinct stages. The earlier stage is less frequently met with, and consists of a cellular infiltration of the submucosa, through which the tunic is rendered much thicker than normal. The cells belong, in general, to the type of granulation-tissue cells, many of which are large and epitheloid in appearance. They are interpolated between the old connective-tissue fibrils and collected into large, more independent foci. The infiltration extends from the submucosa into the muscular coat, and to a much less degree into the mucous layer. The muscularis mucosa is for the most part the limiting line above. Within the large cellular accumulations foci of necrosis occur. These are quite large and consist of centres of coagulation necrosis, in which much fragmentation of nuclei and emigrated polymorphonuclear leucocytes are prominent features. The form of necrosis is consistent either with tuberculosis or syphilis; in its acuteness it resembles that seen in the former disease. The necrotic foci extended freely into the muscle and not at all into the mucosa. The blood-vessels in this situation show a simple infiltration of the adventitial coat, except in the necrotic areas, where they are obliterated.

The later stage is more common, and is what is met with in all parts of the ulcer and the tissue forming its elevated boundaries. It consists of dense fibrous tissue, which again is developed chiefly in the submucosa, and then extends into the muscular tunic.

Scattered granulation-tissue cells are found among the developed fibrils. The blood-vessels are extensively diseased; endarteritis and endophlebitis obliterans, and hyaline thrombosis with organization are common. The serous coat, too, is thickened, and in some places about the adhesions greatly so.

The base of the ulcer is covered to some extent with mucous membrane, and only in its centre is it bare. The muscular coat is exposed in this part, and the more superficial fibres are quite necrotic. The elevated edges of the ulcer are clearly not the remains simply of the old mucosa and submucosa. This is proven by comparison with the surrounding intact mucosa, which is much less elevated. The microscopic examination shows the thickening to be due to a new development of dense fibrous tissue, such as was described in the later stages of the general pathological process.

There can, I think, be no doubt that the ulcer is of syphilitic origin; the character of the new tissue and the form of cell-death met with seem sufficient proof for this belief. But I think it much more improbable that it is due to the softening of a gumma. Indeed, I find very little evidence in support of such a view. On the other hand, the appearances described speak more for an indirect form of necrosis of the mucous membrane, brought about by the combined softening of submucous gummatous infiltration and the obstruction and obliteration of blood-vessels in the same situation. The mucous membrane thus deprived of its nutrition became necrotic, was removed, and the ulcer resulted. The submucosa suffered either directly through necrosis of the infiltrating cells, or, again, indirectly, owing to the vascular changes combined with the action of bacteria.

Pappenheimer's [4] case also is most instructive in that it gives undoubted evidence that when syphilis really attacks the stomach it produces lesions not to be mistaken for anything else. In general characteristics it follows closely the changes described by Chiari [2] and Flexner.[3]

Pater [5] adds to the gross lesions given by Chiari the condition of stenosis at the pylorus. In all these acquired cases there was to a greater or less extent the infiltrative process which Chiari reports as having been found only in hereditary syphilis.

McNee's [6] (Fig. 1) case being the only one in which the spirochæte has been demonstrated may be reported in detail. It also has an added significance in that at autopsy "aside from the stomach no other organ showed noteworthy pathological changes and nothing was found suggesting the presence of an antecedent syphilis." Syphilis had not been suspected and no Wassermann had been done. In all other cases studied at autopsy there were present syphilitic lesions in many parts of the body.

"On opening the stomach the first impression was that the condition was a gastric carcinoma of the scirrhous type. On closer observation, however, it was seen that the characters of the ulceration were peculiar. An examination of the lymphatic glands showed no evidence of cancerous invasion.

The lesser curvature of the stomach, from a point about one inch below the cardia to the pylorus, is completely ulcerated. The ulcer also extends over a large part of the greater curvature, and this portion has been cut in two in opening the stomach, so that part appears in the upper part of the opened-out specimen and part below. Two perforations are seen in the ulcer on the posterior wall of the stomach, fairly close together, while in two other adjacent spots penetration of the wall is almost complete. The chief characteristic of the ulcer is its irregular shape and greatly thickened borders. The floor is bare, but the margins are covered with shaggy shreds of necrotic tissue, mixed with shreds of tenacious mucus. Only about two-fifths of the stomach wall is free from ulceration.

The stomach wall is greatly thickened in most parts of the floor of the ulcer, except at the points where perforation has ensued. The thickness is fully half an inch in most places, while in relation to the raised margins it is fully three-quarters of an inch. In section the thickened wall has everywhere a dense pearly-white appearance, such as is often seen characteristically in scirrhous carcinoma of the organ. Particular attention may be drawn to one particular area of the lesion where the process appeared to be more acute and recent than elsewhere. A similar small area was originally present on the extreme upper border of the specimen, but was removed for histological examination. The results of the examination of this portion of the ulcer are dealt with later.

Sections from the central portion of the ulcer for microscopic study gave the following findings. The floor of the ulcer is composed of a thin layer of necrotic fibrous tissue,

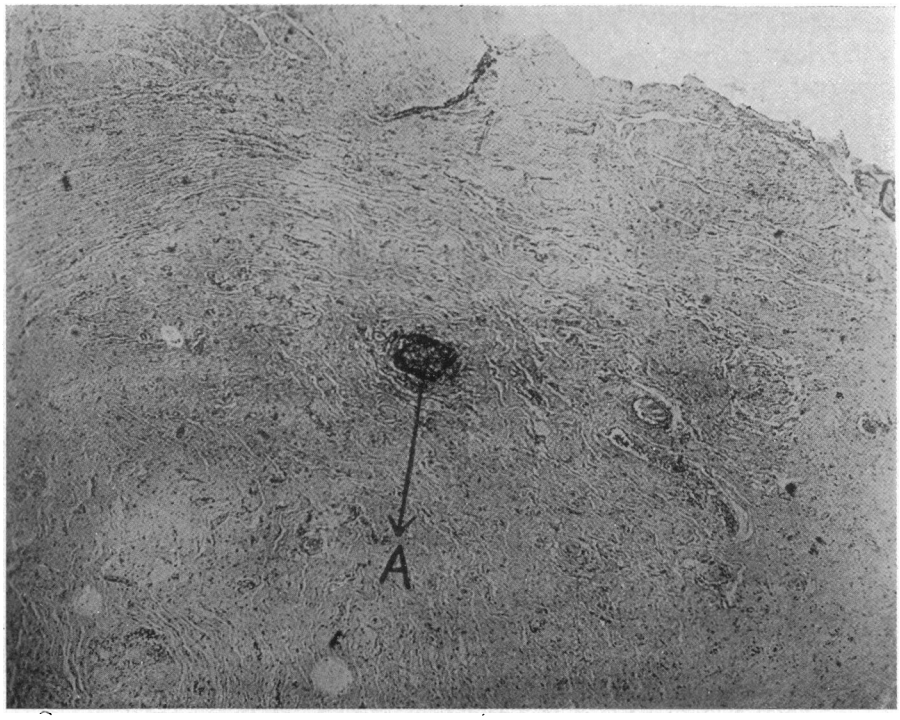


FIG. 5.—Graham's case from ANNALS OF SURGERY, 1922, vol. lxxvi, p. 449. Small gumma-like collection of round cells beneath the mucosa.

infiltrated with round cells. None of the mucosa or muscularis mucosa remains. Below this is a necrotic layer of dense adult scar tissue. In areas there is less adult connective tissue and numbers of small thin-walled capillaries; many surrounded with round cell infiltration. Arterial trunks are seen in the dense fibrous tissue, and their walls are thickened and show an advanced stage of endarteritis obliterans (Fig. 3), but no thrombosis. In sections from other parts of the ulcer, especially from the greatly thickened borders, the histological changes are of a much more active kind. The whole of the mucosa and submucosa is entirely replaced by an actively growing granulation tissue, which is necrotic and shaggy on its surface. There are abundant fibroblasts and thin-walled capillaries. The tissue is densely infiltrated with cells of lymphocytic type. The granulation tissue extends by branches along the larger blood-vessels into the muscular layers in some places, and in others the muscular coat is intact but round cell infiltration is seen around blood-vessels. The vessels in these parts are free from endarteritis. In a few places masses of granulation

tissue have necrosed and separated so as to expose even the deeper layers of the muscular coat. In this way perforation must have occurred, and since the blood-vessels have no endarteritis obliterans, the attacks of hæmatemesis are explained. No giant cells are seen. In sections from different parts it is possible to trace the pathogenesis from one stage to the other. Many sections were examined for the spirochætes stained by the Levaditi silver method. Eight blocks were so prepared, but in only one block were the spirochætes found (Fig. 2). So far as I have been able to follow the literature, this is the only positive case in which the spirochætes were demonstrated, though Wile [12] states that Warthin found them in a case operated upon at the University Hospital in Ann Arbor by Cabot, but he gives no details."

Graham's [7] accepted case is the first in which satisfactory histological evidence is found in a portion of the stomach removed at operation. There was a definite tumor about the size of a hickory nut along the greater curvature near the pylorus (Fig. 4). It was movable within the stomach and felt somewhat like an adenoma. A resection of the pylorus was done followed by a gastrojejunostomy by the Polya-Balfour method. Microscopical examination of the tumor showed numerous small gumma-like collections of round cells beneath the mucosa (Figs. 5 and 6).

Brams and Meyer [8] report two cases, also operative, which are so completely supported by histological evidence that the diagnosis is beyond question.

"The anatomical features of the resected specimens showed the characteristic changes which allowed the strongly presumptive diagnosis to be made at once. These were—the thickened submucosa, shallow, multiple and irregular ulcers, and the presence in Case II of visible miliary gummata. The entire pyloric portion of the stomach was thickened and infiltrated. Case I showed five irregular ulcers on the anterior and posterior wall (Fig. 7), while Case II had only three such ulcers on the posterior wall. The maximum diameters of the smallest ulcer were 15 x 5 mm. and 35 x 10 mm. in the largest. The average depth was 2 mm., and the comparatively smooth dark red base stood out in relief against the pale gray surrounding mucosa. The margins were somewhat raised and thickened, but there was no necrosis or caseation anywhere. Cut section showed the sub-mucosa to be thickened to about eight times its normal size in the region of the ulcers, and normal beyond them (Fig. 8).

"The chief feature seen on microscopical examination was perivascular infiltration which consisted chiefly of lymphocytes and a few plasma cells. There were many vessels involved in this manner, regardless of size, and both the veins and arteries were affected. Case II differed in that the vessels which showed changes in their walls were not so often seen to have this perivascular infiltrate. (Fig. 9.) Panarteritis and panphlebitis (Fig. 10), described by Fraenkel and considered by him to be solely characteristic of this condition when associated with such other conditions as the infiltrate, etc., were present. The process evidently began in the outer layers of the vessels, and then attacked the media and intima." * * * "Both specimens contained miliary gummata (Fig. 11), the number in Case II being greater than in Case I. These were located chiefly in the sub-mucosa, but some were present in the muscular layers as well." * * * "A few epithelioid cells were present near the periphery, and Case II showed one with giant cells of the Langhans type. The diffuse infiltrate consisted chiefly of lymphocytes with a few plasma cells and an occasional giant-cell. A careful search was made for spirochæte but none was found. There were a few long Gram-positive bacilli and Gram-positive cocci at the surface of the ulcer, but no tubercle bacilli were found."

At a meeting of the Royal Society of Medicine in London, where Monod [13] presented a paper on "Syphilis of the Stomach," and at which

McNee's specimens were presented, Turnbull [10] of the Pathological Institute of the London Hospital, discussed the subject from the pathological standpoint most instructively. He stated that histological diagnosis of syphilitic inflammation was even more difficult in the case of the stomach than in that of other organs. Infiltration with plasma cells, lymphocytes, and eosinophilic leucocytes are characteristic of most of the syphilitic lesions. Such an infiltration was found, however, in chronic pyogenic inflammation and was constant in chronic progressive peptic ulceration. Endophlebitis and endarteritis are characteristics of more intense syphilitic inflammatory reactions, but they might occur in chronic inflammations caused by any pyogenic organism. They were very common in chronic progressive peptic ulceration. Again, multinuclear giant-cells occurred in the intenser syphilitic inflammation, but similar giant-cells were present in many other conditions. A few giant-cells were frequently seen in the base of progressive peptic ulcers. In some cases their relation to crystals or to granules of pigment showed that they were "foreign-body giant-cells"; in other cases they were clearly epithelial in origin and were comparable to the epithelial giant-cells so conspicuous in certain chronic pyogenic inflammations of the breast and of the testicle; in other cases the cause and mode of their origin were not indicated. In order to ensure that his memory was not at fault, he had examined the slides from the twelve last specimens sent from the operating theatres last year. Infil-

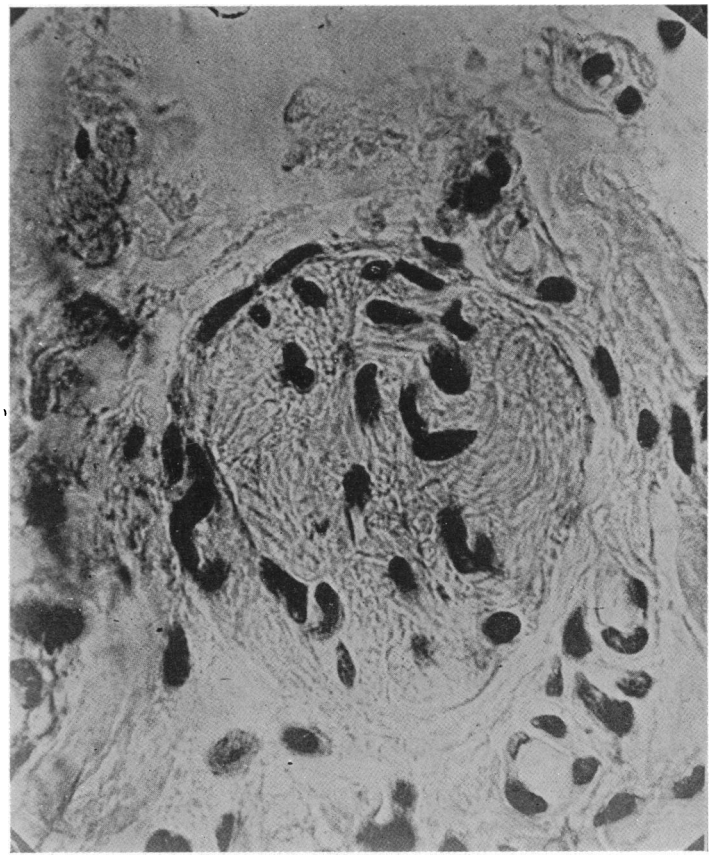

FIG. 6.—Graham's case from ANNALS OF SURGERY, 1922, vol. lxxvi, p. 449. Obliterating endarteritis.

tration of the above type was present in all; endarteritis was present in five; giant-cells were found in three. If the mere occurrence of the above histological phenomena were taken as evidence of syphilitic inflammation, then all, or almost all, progressive peptic ulcers must be accepted as syphilitic. But there was definite evidence against the majority of peptic ulcers being syphilitic. He then cited McNee's case, in which the spirochætes were demonstrated. Turnbull was glad to learn that in histology this specimen differed from ordinary progressive peptic ulcers. To the naked eye it was obviously no ordinary peptic ulcer. Had it resembled the usual chronic peptic ulcer, then it would have shown that the recognition of syphilis must rest entirely upon the discovery of the spirochætes. Since 1909, Turnbull had examined operative specimens from 713 stomachs. In these there had been found no syphilitic lesion. The stomach had been examined at necropsy in nearly 13,000 subjects since he had come to the Institute in 1907. Any obscure abnormality had been removed for microscopic examination; further, his colleagues and himself had been specially eager to find syphilitic lesions. There was only one stomach in which a tentative diagnosis of syphilis might prove to be correct. Histologically the lesion in the stomach had the characters of an intense gummatous syphilitic inflammation. There was syphilis in other organs of the body. Turnbull was unwilling to exclude tuberculosis, but he believed the case was syphilis. No spirochæte had been found up to the time of the report, but the case was still under study.

An analysis of the twenty-five cases shows that the general characteristics as laid down by Chiari [2] are present in all of them, and that the obliteration of the blood-vessels, as emphasized by Flexner [3] and Pappenheimer,[4] is not infrequently the cause of the necrosis leading to ulceration. The distribution of the lesions in the stomach shows that all parts may be attacked, but that the posterior wall near the lesser curvature and toward the pyloric antrum is possibly a favorite site. Seven cases showed multiple lesions; either ulcers or gummata, or often both. A rather striking characteristic is the large size of the ulcer in many instances; Chiari's [2] covering the whole breadth of the posterior wall, McNee's extending along the lesser curvature from the cardia to the pylorus and involving three-fifths of the entire stomach, Flexner's [3] being 5 x 5 cm. in diameter, and Stolper's [11] extending from the cardia to the mid-gastric region along the posterior wall. An irregular serpiginous border is mentioned by Pappenheimer [4] and McNee [6] and several ulcers are reported as having greatly thickened borders with a hard smooth base. In many descriptions the expressions vary, but it is apparent that there was an unusual amount of thickening and rigidity of the stomach wall, often extending a considerable distance from the principle lesion. This thickening is always most marked in the sub-mucosa, but often extends into the other layers. In no case is there mentioned any perigastric infiltration except where perforation had taken place. This was present in Chiari's acquired case and in the cases of Flexner and McNee.

The destruction of the blood-vessels was evident in Flexner's,[3] Pappen-

heimer's,[4] and McNee's [6] cases, and gave definite explanation of the hemorrhage that has taken place in several of the cases.

Thus it is found that grossly syphilitic ulcer of the stomach differs in no distinctive way from simple gastric ulcer. Neither by its position, its size, or its outline can it be positively diagnosed with the naked eye. Suggestive factors are—its tendency to be large, its irregular serpiginous border, its firm smooth base and the presence of demonstrable thickening in the stomach wall at a considerable distance from the ulcer itself. Multiple ulcers are apparently more common than with the non-syphilitic ulcer. The finding of unbroken gummata as in Graham's,[7] Stolper's[11] and Weichselbaum's[14] cases, may greatly strengthen the suspicion of a syphilitic origin.

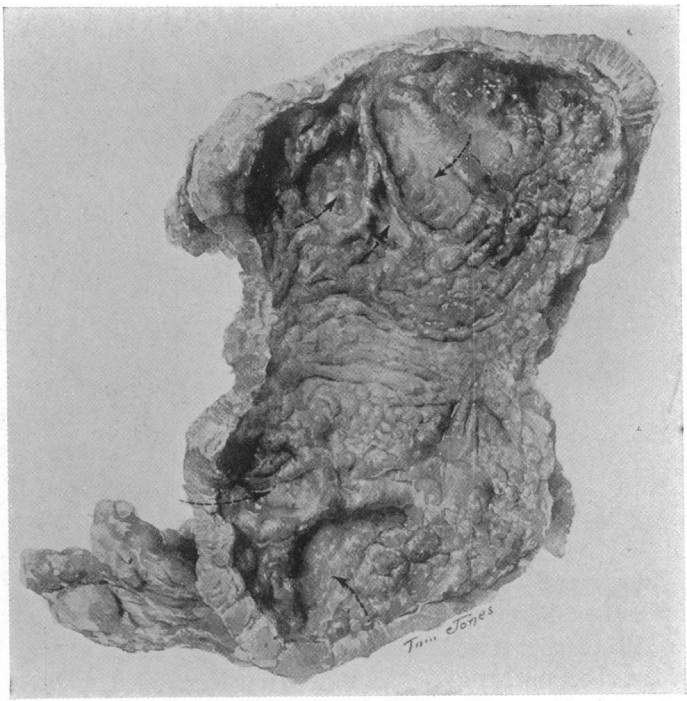

FIG. 7.—Brams and Meyer's case from Surgery, Gynecology and Obstetrics, Chicago, 1923, vol. xxxvii, pp. 127-133.

The clinical data given in connection with the proved cases is meagre except in Flexner's,[3] Stolper's,[11] McNee's,[6] Graham's[7] and Brams and Meyer's[8] cases. From these there can be drawn no facts on which a differential diagnosis from either carcinoma or simple peptic ulcer can be made.

Neither the pain, the vomiting, hæmatemesis, nor evidence of perforation was in any way characteristic. The duration of the symptoms did not vary from that seen in other conditions. The radiographs where reported did not give conclusive evidence of other than a serious gastric lesion. In fact, both Brams and Meyer's[8] cases were diagnosed from the X-ray films as carcinoma, and Graham's[7] report simply states "Lesion of pars pylorica—probably luetic. Small residue in stomach at end of twenty-four hours." It is worthy of emphasis that these patients all presented much more the general clinical picture of carcinoma of the stomach than of an ulcer. They were emaciated, their pain was severe, vomiting was marked and gave relief. Alkalies did not give relief, and in two of them the radiograph showed

conditions which were interpreted as carcinoma. In addition the HCl. content of the gastric juice was low or absent. On the other hand, many of the cases which have been diagnosed as syphilis of the stomach on the strength of a positive Wassermann and the radiograph, have proved to be carcinoma. (White,[25] Downes and LeWald.[20] Probably Hoover quoted by Pappenheimer.[4])

Since it has proved impossible to draw any accurate diagnostic picture from the histologically demonstrated cases, the attempt has been made to do so from those cases in whom the diagnosis rests on the positive

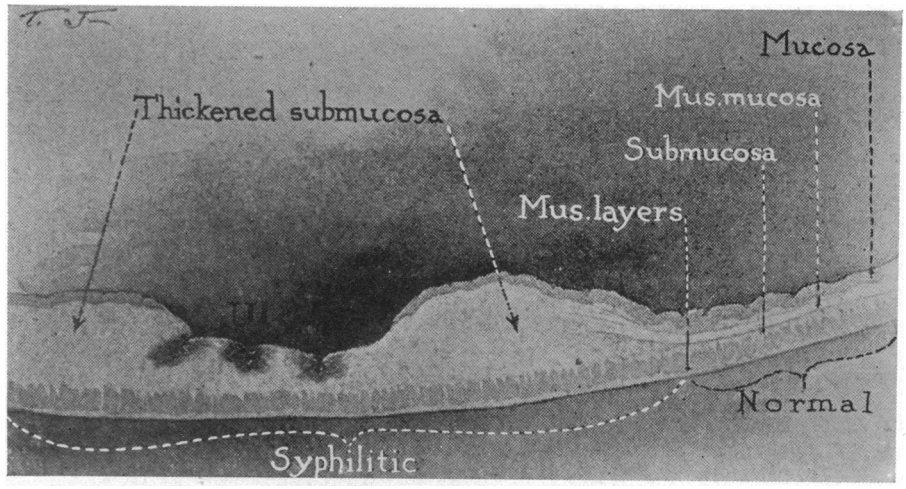


FIG. 8.—Brams and Meyer's case from Surgery, Gynecology and Obstetrics, Chicago, 1923, vol. xxxvii, pp. 127-133.

Wassermann reaction and a more or less satisfactory control of symptoms by anti-syphilitic treatment.

The earlier cases, reported largely by the French school, need not be considered because neither the Wassermann reaction, radiographic findings, nor chemical analysis is given in these reports. However, Hayem,[15] Fournier,[16] Fenwick,[17] Andral,[1] and Lancereaux,[18] with many others, have reported most striking cases over very considerable periods where the possibility of the condition being true syphilis of the stomach cannot be denied. There is nothing in the detail of these patients' histories which gives any basis for diagnosing the gastric lesion as syphilis, except that they were known to be suffering from that disease and accordingly the antisyphilitic treatment was undertaken.

In contrast to the rarity of syphilis of the stomach, as determined by positive histological evidence, its frequency as diagnosed without such evidence is very striking. This is in part due to the fact that the clinical reports are lacking in critical analysis. In part, however, it is due to the extreme difficulty of always proving by histological evidence the syphilitic nature of a lesion even when the material for examination is available. The statements by Turnbull,[10] already quoted, admirably explain these difficulties, and it

is accepted by all pathologists that many lesions may be syphilitic, even though the histology fails to reveal characteristic changes in the tissues. The fact that McNee [6] alone has been able to demonstrate the spirochæte in a syphilitic lesion, even where the microscopical evidence was convincing, shows that this final test of a positive diagnosis will be rarely found. It is noteworthy that McNee [6] found the spirochæte in only one portion of the lesion in his case, though a careful search was made for it in seven other areas. These difficulties have led the authors of reported cases to be less critical than they would be with other lesions, and it is a common occurrence in the literature to find accepted cases where the pathologist has only reported that the lesion is not malignant and has not the characteristics of a simple ulcer, or where he states that the lesion "may be syphilitic," or uses other expressions indicating uncertainty. Examples of this are found in Merril's [19] report, and in that of Downes,[26] LeWald,[21] LaFluer,[22] Eusterman,[23] Douglas [31] and others. Obviously it is unwise to exclude all such cases as being true cases of syphilis. On the other hand, it leads to a misconception unless one is most careful not to report cases as syphilis of the stomach where there is any lack of evidence from the clinical standpoint.

There are now recorded in the literature somewhat over 200 cases bearing the designation of syphilis of the stomach. A careful scrutiny of these shows that very many of them may be excluded without serious consideration. LaFleur [22] in 1903, Pater [5] in 1906, McNeil [24] in 1915, Downes and LeWald [20] in 1915, White [25] in 1917, have all reported cases which are worthy of serious consideration. On the other hand, reports of Tousey,[26] Weitzner,[27] 6 of Morgan's [28] cases, E. D. Holland,[29] many of LeWald's [21] cases, Kohn's [30] case, 2 of Graham's cases, Douglas' [31] case, Larimore's [32] 8 cases, and Merril's [19] 10 probable cases and 6 suggestive cases, do not seem sufficiently positive to enter into serious consideration. The cases of Niles,[33] J. Meyers,[34]‡ J. S. Myer,[35] and Morris,[36] as well as those of Fenwick [17] and Furno,[37] may be questioned. Eusterman reports forty cases as having come under his observation. It is impossible to draw sound conclusions as to the accuracy of the diagnosis in a majority of these. Operative material was obtained for microscopical study from ten. The reports are by no means convincing, and the microphotographs do not present the characteristic lesions demonstrated in the proved cases reported.

In view of the evidence given it is difficult to take seriously the statement by Castex and Mathis [39] that all cases of gastric ulcer are caused by syphilis, or the statement of Lang and Engel as quoted by Ewald [40] that 20 per cent. and 10 per cent. are so caused, or even the more moderate statement of Fenwick [17] that syphilis is the causative factor in 5 per cent. of gastric ulcer. Stokes and Brown [41] analyzed 200 syphilitic patients whose chief complaint was "stomach trouble." Twenty of these patients presented organic lesions of the stomach or duodenum; in only 8 did the

‡ The tabular analysis in the paper of Jerome Meyers is deserving of careful study.

authors think that true syphilis of the stomach was present, and they did not give sufficient data to determine the accuracy of their conclusion. White [25] found 44 patients with prominent stomach symptoms in a group of 600 cases of syphilis with strongly positive Wassermann reaction. In 35 of these 44 no definite lesion of the stomach was proved. In the remaining 9 there was a definite lesion, but two of these later came to autopsy and were proved to have cancer. White concluded that 5 suffered from ulcer of the stomach, but he was not willing to say that the ulcer was necessarily syphilitic. Two he believed to be suffering from true syphilis of the stomach, either induration or gumma. White makes this statement: "Since the free use of the

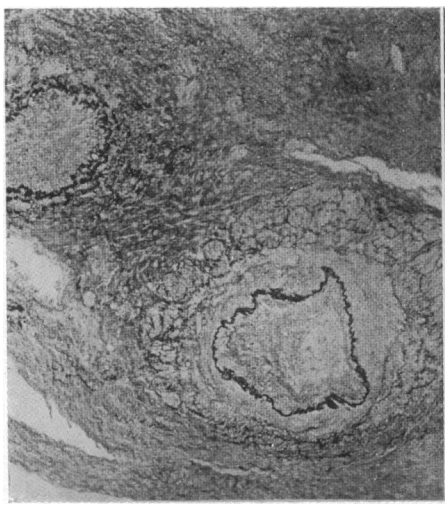

FIG. 9.—Brams and Meyer's case from Surgery, Gynecology and Obstetrics, Chicago, 1923, vol. xxxvii, pp. 127-133.

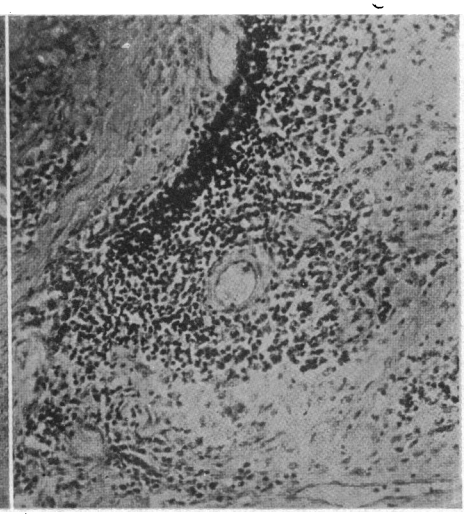

FIG. 10.—Brams and Meyer's case from Surgery, Gynecology and Obstetrics, Chicago, 1923, vol. xxxvii, pp. 127-133.

Wassermann test many cases with digestive symptoms and positive serum are classed as syphilis of the stomach, probably without reason. Even the relief of symptoms by treatment is not a sure guide in diagnosis, though if plaques, large indurated areas, hour-glass deformity, tumors easily demonstrated by X-ray or operation of a patient with positive Wassermann, have previously resisted treatment, and fade away under anti-syphilitic drugs, we have valuable evidence that the lesion was specific." This conservative statement made in 1917 has not received the attention that it deserves. Fowler [42] in 1921 presented a paper entitled "Benign Gastric Ulcer in a Syphilitic," in which he reported the case of a woman, aged twenty-six, who had a four-plus Wassermann, and at operation resection of the pylorus disclosed a simple ulcer. In this case neither a gastro-enterostomy or the administration of anti-luetics had been of benefit. Brams, in the discussion at the time the Brams and Meyer [8] case was presented, reported another case with four-plus Wassermann who had suffered from gastric symptoms for many months. At autopsy five days after admission, five superficial ulcers were found which proved not to be syphilitic. The one case which we present is added evidence

that the finding of a gastric ulcer in a patient suffering from syphilis or presenting a strongly positive Wassermann, is not of necessity a syphilitic ulcer. This has been recognized in the literature since the original report by Chiari,[2] and yet the tendency to disregard it is very strong in the writers of the present day. Our contribution to the subject has only a negative value, but this value is very great in that it demonstrates the need of extreme care in accepting the diagnosis of syphilis of the stomach.

The patient, a married woman thirty-nine years old, was admitted to Bellevue Hospital on October 10, 1924. She was married at the age of eighteen and never had been pregnant. Her menstrual history was normal until she was thirty-two, when for some reason not known, a double oöphorectomy was done. No history leading to a suspicion of syphilis could be obtained, and there were no relevant facts concerning previous illnesses.

In May, 1924, she first suffered from a gnawing pain in the epigastrium passing backward to the mid-lumbar region. This pain had persisted ever since and gradually vomiting became a constant symptom so that neither solids nor liquids could be retained. Alkalies gave no relief to the pain. There had been a steady loss of strength and weight, the latter amounting to forty pounds since the onset of the illness. Examination revealed an emaciated woman appearing chronically ill. Aside from the abdominal condition no abnormalities were found and there were no stigmata of syphilis either congenital or acquired. The abdominal wall is soft, relaxed and lacking in adipose tissue. No tumor is seen. Palpation in the epigastrium causes pain and an indefinite mass is palpable over the site of the stomach. A small discrete movable tumor is felt opposite the umbilicus on the left side. This was believed to be an enlarged mesenteric lymph-node. A gastric analysis from the fasting stomach returned 42 c.c. containing no free HCl, and a combined acidity of six. The blood on two separate examinations showed about 4,500,000 erythrocytes and 95 per cent. hæmoglobin, with 5100 white blood cells. The Wassermann reaction was four plus on October 22 and three plus on October 29.

The radiographic report was as follows: "Fluoroscopic examination shows an annular constriction of the pars media. Stomach is hyposthenic and deformed. There is a marked persistent irregularity of the lesser and greater curvature pars pylorica and media with decreased lumen. No gastric retention at end of six hours. *Diagnosis.*—New growth pars pylorica and media, scirrhus type." (Fig. 13.) This diagnosis was concurred in by the clinicians and accordingly an operation was done on November 7, 1924, with the following findings.

The stomach was moderately distended, not hypertrophied. It was quite mobile including the pylorus and first portion of the duodenum. In the lesser curvature of the pyloric antrum and extending into the pars media was a rather diffuse thickening involving an area of 2½ or 3 inches in diameter, the centre of which presented a palpable crater. On the serous surface there was evidence of some contraction and injection but no definite stippling. The pylorus seemed to be patent. There were several lymph-nodes about 1 mm. in diameter in gastrohepatic and gastrocolic omenta. Gall-bladder was small, of normal color and lay entirely outside the liver so that it practically had a mesentery of its own. Palpation of the pelvis revealed uterus present. Ovaries not found. In the small intestine exact location not determined but probably in lower jejunum was a mass about 2 cm. in diameter which seemed to infiltrate the wall.

An extensive pyloric resection seemed advisable and this was done and followed by a Polya-Reichel repair.

On opening the resected portion of the stomach the following lesion presented itself. There was a superficial ulceration on the posterior wall crossing the lesser curvature on to the anterior wall. It was about 2 x 3 inches in diameter its right margin lying about 2 inches from the pylorus. The outline was irregular and serpiginous. The edges were somewhat elevated and thickened, but not greatly so. The floor was composed of

smooth gray fibrous tissue and was clean. The stomach wall was thickened particularly in its submucous layer. Several minute normal appearing lymph-nodes were found in the mesentary. The small tumor felt on examination and thought to be an enlarged lymph-node proved to be a fibromyoma of the small intestine. This was excised.

The microscopical report on the stomach lesion made by Symmers was as follows:

"Microscopic examination shows the presence of a simple ulcer without evidences of tuberculosis, syphilis or malignant transformation. The tubules at the edges of the ulcer are hyperplastic and some of them are of the immature type. The base of the ulcer is lined by necrotic tissue, scattered through which are numerous polymorphonuclear neutrophiles and immediately under which are numbers of round cells of the lymphocytic type, imbedded in which are a few thin-walled blood-vessels. Immediately beneath this layer the muscle tissues are extensively replaced by scar tissue in which are moderate numbers of capillary vessels and arterioles, some of which are surrounded by a mantle of plasma cells. (Figs. 14 and 15.)

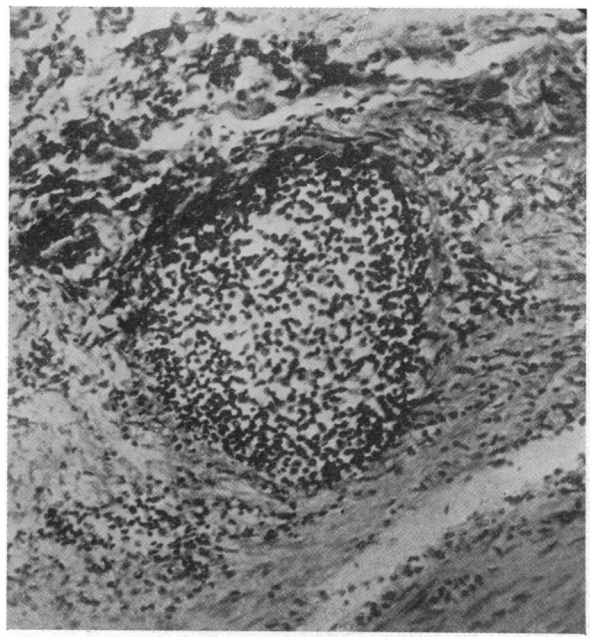

FIG. 11.—Brams and Meyer's case from Surgery, Gynecology and Obstetrics, 1923, vol. xxxvii, pp. 127-133.

"Sections stained by the older method of Levaditi and examined by three independent observers over a long period of time, fail to show the presence of spirochætes. In fact, there is nothing in the histology of the ulcer to suggest syphilis."

The patient made a prompt recovery, and now January 14, 1925, is free from all symptoms. She is receiving antiluetic treatment but the Wassermann is four plus. She has gained very considerable weight but is not yet back to her normal.

The summary is interesting. A woman, age thirty-nine, presents a four plus Wassermann, a marked deformity of the stomach is seen by X-ray, of the abrupt infiltrating type. No free HCl in the stomach contents, with a history of intractable vomiting and gastric pain extending over a period of five months. During this time she has lost forty pounds in weight and is correspondingly weak, but she is not anæmic and is not cachectic.

The picture is identical with many of the cases reported as syphilis of the stomach. Yet on resection of the diseased portion there is no histological evidence of syphilis and the case cannot be considered to be syphilis. The histology also is identical with that in many reported cases where the reporter has ignored the facts and accepted the diagnosis of syphilis.

We have made a careful study of the detailed histories, the radiographic findings, and the chemical analyses of the greater part of the 200 cases or more reported as syphilis of the stomach where the diagnosis rests upon other

than histological evidence. Especial attention has been paid to those in which the evidence was sufficiently strong to make the diagnosis presumptively correct. This study convinces us that there are no characteristic subjective symptoms or objective findings upon which a diagnosis of syphilis of the stomach may soundly rest. The differentiation is much more difficult and much more uncertain than that between simple ulcer and carcinoma. There seem to be five principle factors that have influenced writers in making the diagnosis. First.—The positive Wassermann reaction. Second.—An anacidity or a markedly reduced HCl. content. Third.—A marked deformity of the stomach as shown by the X-ray, particularly of the "dumb-bell type," or with an abrupt margin between the healthy and the diseased portions of the stomach. Fourth.—A less marked cachexia, emaciation and anæmia than

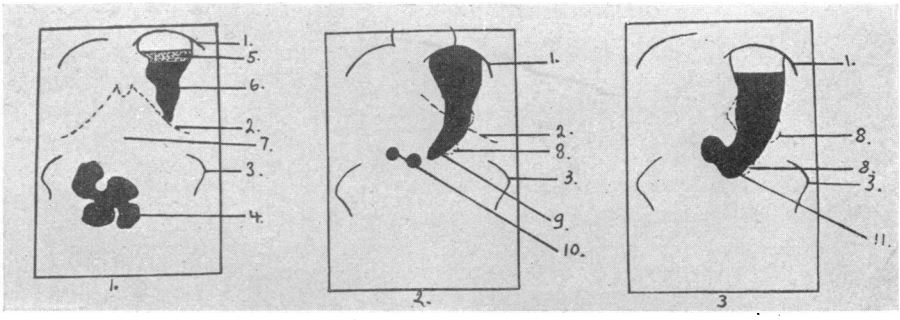


FIG. 12.—Brams and Antoine's case from U. S. Naval Medical Bulletin, vol. xviii, 1923, p. 305. This represents the use of antisyphilitic treatment in a patient who presented no evidence of syphilis and in whom the Wassermann was negative! It is not the histologically proved case of the same authors, cited in foot note on page 769.

would be found with such radiographic changes due to other than syphilitic lesions. Fifth.—Improvement under antisyphilitic treatment. It is not difficult to find ample evidence for considering all of these points as of doubtful value. (1) We have already discussed the danger of laying too much stress upon the presence of a Wassermann reaction. (2) In most of the positively demonstrated cases no report is given of a chemical analysis of the gastric content, except in those recently studied. This analysis is rarely given in any of the cases up to the time of Pappenheimer's report. Pater does not enter into a consideration of this phase. In Graham's [7] accepted cases the free HCl. varied between 3 and 6. In Brams and Meyer's [8] first case there was no free HCl. and a total acidity of 30. In their second case there was no free HCl. a total acidity of 2. In McNee's case there was no free HCl., but lactic acid was present; in the probable cases of LaFleur [22] and McNeil,[24] no acid was found in the former, and in the latter there was no free HCl. and a total acidity of 25. The low acid content is rather a constant finding in the clinically reported cases, but Smithies [43] found an anacidity in only 2 of 26 instances of dyspepsia associated with positive Wassermann Noguchi reaction. The average free HCl. of the whole group was 33 and the maximum was 110. Stokes and Brown,[41] in an analysis of 122 of their patients, found a hypoacidity in 50 per cent. and a normal acidity in 38 per cent., and yet only eight of

these cases at the most had true syphilitic stomach lesions. Other observers (Glasser [47]) have found that syphilis *per se,* without reference to the presence of the gastric lesion, tends to produce a marked hypoacidity, and finally many of the cases at first supposed to be syphilis have ultimately proved to be cancer, where, as is well known, hypoacidity is the rule. While, therefore, it is probable that true syphilitic lesions of the stomach produce, as a rule, a low

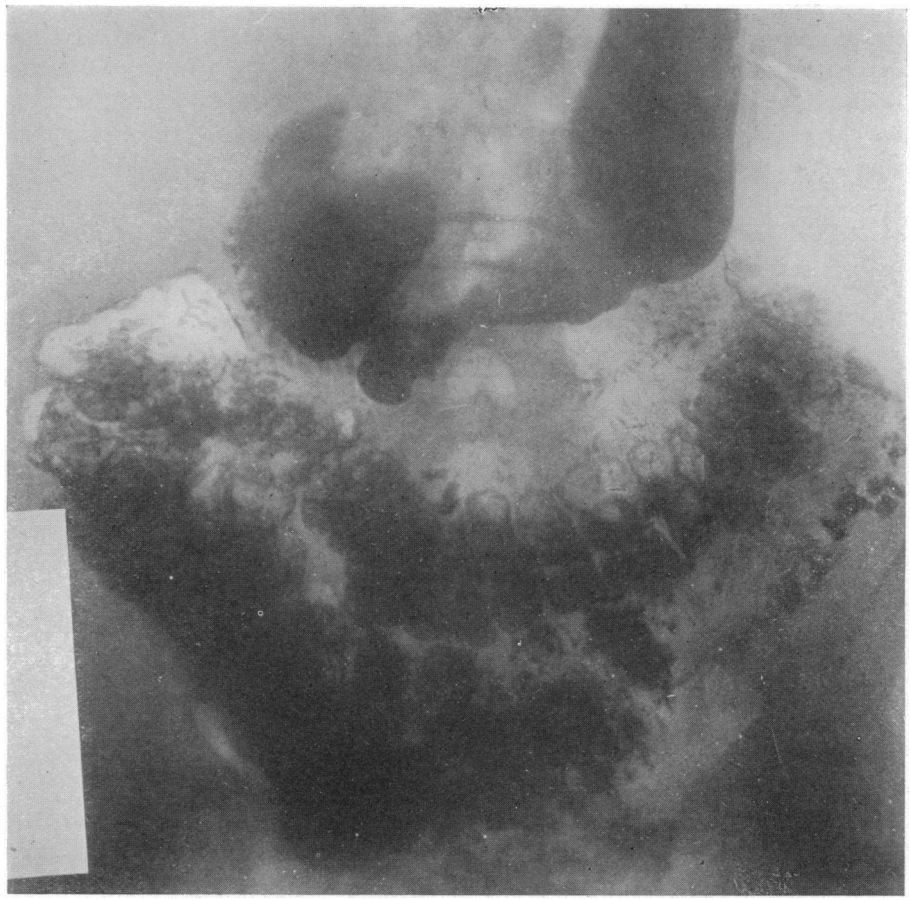

FIG. 13.—Simple ulcer of pars media and pylorica in a patient having a four plus Wassermann. Note abrupt line between normal and diseased portions. See report of case in text, page 781.

acid content, this finding is of no great value in making the diagnosis. (3) The radiographic findings have been given greatest consideration in arriving at the clinical diagnosis of gastric syphilis, and it is noteworthy that many of the papers on this subject are being written by the radiologists. Carman [44] discusses this phase of the work and comments on the opinion of Dewis and LeWald concerning the " dumb-bell type " of hour-glass stomach as being diagnostic of syphilis. He is not convinced that this deformity is sufficiently characteristic to be of great value. He names eight suggestive points in reading the radiogram.

1. Filling defect of the gastric outline, usually without corresponding palpable mass.

2. Shrinkage of gastric capacity.

3. Stiffening and lessened pliability of the gastric wall.

4. Absence of peristalsis from the involved area.

5. Pylorus gaping rather than obstructed.

6. Six-hour retention less common than in other gastric lesions (23 per cent.).

7. So-called hour-glass stomach; upper loculus expanded and bulbous, lower loculus tubular, due to extensive irregular concentric contraction.

8. Patient usually under cancer age and not ill in proportion to the extent of disease shown by the X-ray.

His summing up is as follows: "As a matter of fact, however, the röntgenologist's first suspicion of the lesion being syphilis rather than cancer, is usually aroused not by the Röntgen picture so much as by certain obvious clinical facts. There is an absence of palpable mass, the patient may be under the cancer age, he is anæmic rather than cachectic, and has not lost weight and strength in proportion to the extent of gastric involvement and the duration of the trouble."

Merril,[19] in the study of his 16 cases of probable or suggestive cases of syphilis of the stomach, says that there is a progressive course with marked loss of weight, unaccompanied by the degree of cachexia and weakness seen with cancer. Palpable tumor is uncommon. Notwithstanding these views, the cases of Flexner,[3] Pappenheimer,[4] McNee,[6] and others of the positive cases, showed very considerable loss of weight and cachexia. In many of the reports the statement is made that the patient was considered to be in the last stages of gastric cancer and operation was undertaken only as a palliative measure, or antisyphilitic treatment was instituted more or less empirically. Brams and Meyer's [8] case, and McNee's [6] case, both gave distinct palpable tumors. One may therefore be not a little skeptical concerning the ability of the röntgenologist to make a correct diagnosis of syphilis of the stomach. Differential characteristics are no more than suggestive, and Merril [19] sums the situation by saying: "Röntgen evidence is not characteristic, but is valuable in determining the location and extent of the lesion and should be used in conjunction with all other possible evidence in deducing the probable diagnosis." In regard to the fifth diagnostic characteristic, namely improvement under antisyphilitic measures, it is only necessary to refer to the uncertainty of this evidence unless it be carried over a very long period. There are records extending over such a period that are of true value. Among these may be named two cases of Hayem,[15] where the patients were brought from a state approaching death to perfect health and continued so for periods of many years, one approximately thirty years; several of the cases cited in Downes and LeWald's [20] original report and subsequently reported upon two and three years later by Downes.[20] Downes has been good enough to give me recently (December, 1924,) a final report on these cases.

CASE I.—That of a congenital syphilitic, is perfectly well at the present time. A gastro-enterostomy was done when she first came under treatment, and its influence in restoring good health must not be overlooked. The histology of a piece of the stomach wall at operation was suggestive but by no means positive of syphilis. Case II.—Died in 1920, six years after the gastro-enterostomy; his physician stated that the symptoms were suggestive of cancer of the stomach. Case III.—Died of cancer of the lip and pulmonary tuberculosis in December, 1917, and the autopsy was performed by Ewing from whose protocol the following is a quotation:

"Opening from the inferior curvature of the stomach 6 cm. from the pylorus is a gastro-enteric fistula 1½ cm. in diameter. (Gastro-enterostomy stoma.) Pylorus much contracted exactly at pyloric orifice apparently running over into the duodenum. Here there is a defect in the mucosa reaching down to the muscularis 1½ cm. long, about which the tissues are fibrosed and deeply injected. Microscopical examination.—Sections from the pyloric mucosa and wall fail to show any definite scar of an old ulcer. The glands have been superficially removed by post-mortem digestion and trauma in some places, but no mucosal defect is found. There are occasional islands of atypical hypertrophic glands, and the mucosa is generally thin. At one point the muscularis mucosa is disordered and gastric gland alveoli appear deeper than normal over Brunner's glands. There is a diffuse interstitial myositis throughout the indurated area, with considerable replacement of muscle fibres with tissues."

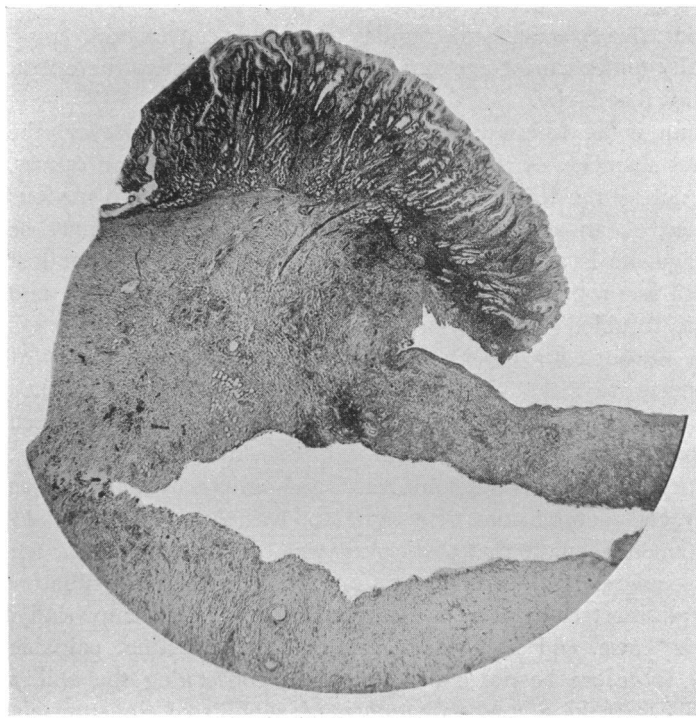

FIG. 14.—Section at border of ulcer in case reported in text. See page 782.

This lesion may well be the remains of syphilitic disease, but it equally may be the remains of a simple ulcer which had healed because of the gastro-enterostomy. Cases V, VI and VII are reported as well during the year 1923, eight, ten and nine years respectively, after the original report, and Case VIII was reported as well in 1920, six years after the first report. To sum up; of the eight cases one apparently had cancer of the stomach, one died of cancer of the lip and pulmonary tuberculosis with the stomach findings above given, and a third died of acute Bright's disease. The remaining five are in good health, but two of these received the benefit of a gastro-enterostomy, and this must be given due weight in determining the cause of their present good health. The other three are good examples of patients with a positive Wassermann and deforming lesions of the stomach who have remained in good health over long periods under antisyph-

ilitic treatment. There has been some but not striking change in the radiogram of some of these patients. (Cf. original LeWald.[21])

In contrast to the cases here cited many reports give only short periods of improvement under medical treatment, many have also received the benefit of surgical operation, and many after the initial improvement have subsequently died of cancer or other lesions of the stomach. Obviously such cases present no therapeutic test on which a diagnosis of syphilis of the stomach can properly be based. The most emphatic testimony against the placing of too great value upon the therapeutic test is found in the observations made by Chiari concerning changes in the stomach in the presence of syphilitic disease, which in no sense may be called syphilis of the stomach. The clinical testimony of Stokes and Brown, of White, and of others, adds emphasis to this. There can be no question that syphilitic patients suffering either from cancer or from simple ulcer of the stomach would be greatly benefited by a course of anti-syphilitic treatment, and this benefit would conceivably extend over a very considerable period. This, however, would not justify one in more than suspecting that the patient had a true syphilitic lesion of the stomach.

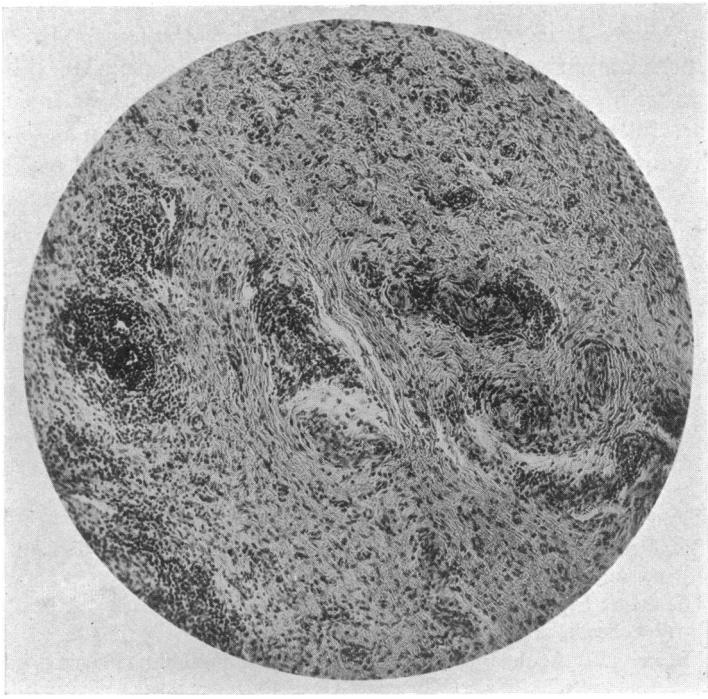

FIG. 15.—Microphotograph of simple ulcer reported in text (page 782). The changes are those so well described by Turnbull and are not characteristic of syphilis.

The importance of differentiating between "true syphilitic ulcer" and "ulcer in syphilitics" is thus manifest. If future reporters will endeavor to make such distinction and will only publish well-supported cases, we are firm in the belief that the discrepancy which now exists between the number of those cases which can be proved histologically and those cases which are presumptively positive from clinical evidence only, will no longer exist.

A careful study of the accurate pathological descriptions given by Chiari,

Flexner, Stolper, Pappenheimer, and McNee, on cases coming to autopsy, and by Brams and Meyer on operative specimens, would arouse skepticism in the mind of any operator when the pathological report on portions of the removed stomach fails to give very positive evidence that the causal factor is syphilis. It was on the basis of such a study that our one case was excluded in spite of the overwhelming clinical and gross evidence that it was true syphilitic ulcer.

From the educational standpoint, the necessity of such careful study will be apparent to anyone who will read the description of syphilis of the stomach given by Mills [45] in Nelson's *Loose-Leaf Medicine*. From the description there appearing the reader must draw the conclusion that syphilis of the stomach is a common disease, that its manifestations from every viewpoint are fully understood, and that the diagnosis rests upon as sound a basis as that of any frequently observed and distinctly differentiated pathological condition.

My appreciative thanks are given to Doctors Symmers, Ewing, and L'Esperance for their pathological studies and to Doctor Dudley for aid in reviewing the literature.

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