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PEPTIC ULCER
HISTORY, ETIOLOGY, AND SYMPTOMS

ERNEST EARL WISE

-HISTORY-

According to Leube, Galen mentions ulcer of the stomach, and Celsus lays down rules for its treatment. In his translation of the works of Paulus Aegineta, Adams asserts that both Rhases and Avicenna describe ulceration of the stomach very accurately.

With the more common practice of postmortem examinations this condition was occasionally noted as the cause of death. Thus, Grassius, in 1695, gives an account of a perforated gastric ulcer, and in 1704 Littré found the source of a severe fatal gastro-intestinal hemorrhage in an "ulcus rotundum," five lines broad and half a line deep. Duodenal ulcers also received casual mention, for example, by deMuralto who, 1688, described two perforations in the duodenum of a soldier. However, Morgagni in 1728, while describing in some detail cases showing gastric ulcers and even perforation by them, barely mentions erosions of the duodenum. It is quite evident that little recognition was given to duodenal conditions, whereas other lesions, including ulcers of the stomach, were well known. Indeed Matthew Baillie in his work on pathologic anatomy in 1793, devotes a special chapter to the subject of gastric ulcer (Leube) without mentioning the duodenum.

Nevertheless, about this time, Penada is said by Lenepveu to have mentioned a case of duodenal ulcer, and in 1802 Neumann described a perforation of the duodenum in a man with strangulated hernia. A second case is reported by Gerard in 1804. The ulcer was four lines below the pylorus, and resulted in a fatal peritonitis. Travers, 1817, published data concerning two instances of perforated ulcer of the duodenum. In 1825 Broussais, gave the details of a further case, and others were added by Rayer in 1826, Robert in 1828, Lenepveu in 1839, Holscher, and Bainbridge in 1842. In spite of these, Cruveilhier, who gave the first clear cut anatomic differentiation of cancer and ulcer of the stomach, and defined the "ulcus ventriculi simplex," does not mention duodenal ulcer. In 1828 Abercrombie wrote, "Although we do not have any extensive observations as yet, still it is probable that the duodenum is the site of various diseases that one can easily confuse with diseases of the liver or stomach." Hence it is not surprising to find this same author reporting, in 1826 a perforating ulcer of the duodenum.

But it was not until 1839 that any statistics were collected with reference to either duodenal or gastric ulcers. Rokitansky in that year reported observations on seventy-nine peptic ulcers, six of which were in the first part of the duodenum. About the same time Andral collected ninety-two cases of gastric, and

two, of duodenal ulcers.

In 1842, Curling reported in some detail twelve cases in which duodenal ulcers or inflammation had followed severe burns. This relation of ulcers to burns had first been noted by Dupuytren and was confirmed by numerous later writers, among others, Long, Erichsen and Hewett.

Mayer, in 1844, was the first to publish a monograph on the duodenum. More clinical than anatomic, his discussion includes ulcers both perforating and healing. He emphasizes burns as an etiologic factor. No comparison with gastric ulcers is given, although he regards the duodenum as a sort of second stomach. Cancer and tuberculosis have etiologic significance, but he concluded that "nothing is as yet known with respect to the diagnosis of duodenal lesions."

Bardeleben, in 1853, in reporting a case of perforated duodenum, said, "Of all parts of the intestinal canal the duodenum shows ulcers least often, as Andral had already pointed out." He agreed with Rokitansky that they resembled the ulcers found in the pylorus of the stomach. However, Virchow, in the same volume of his famous Archives in which Bardeleben reviewed his case, gives his views on the etiology of gastric ulcer but makes no mention of ulcer of the duodenum, in this or any other of his writings.

In a review of the postmortem work in the Pathologic In-

stitute at Prague, extending from February 1, 1854 to March 31, 1855, out of a total of 1,146 postmortem examinations, Willigk noted gastric ulcers in 225 (forty-six men and one hundred seventy-nine women) (19.6 per cent), and duodenal ulcers in only six (three men and three women) (0.5 per cent) a proportion of 37.5 to 1.

It is interesting to note that Brinton, who, in 1856, wrote a very comprehensive account of ulcers of the stomach, and collected considerable literature, reviewed the results of 7,226 postmortem examinations and concluded that gastric ulcers occur in an average of about 5 per cent of all persons, dismissed with the comment that "its situation, cause and appearances alike seem to me essentially distinct from ulcer of the stomach." In this same period appeared studies by Claus, Frank, Nick and Murchison, all of whom concerned themselves with the phenomenon of perforation in individual cases, although in 1859 Ranking, in describing a fatal case of hemorrhage from a duodenal ulcer, remarked on the comparative rarity of the presence of an isolated ulcer of the duodenum.

Muller's work in 1860, often quoted, added practically nothing to the subject of duodenal ulcers, and his data on ulcers of the stomach were hardly equal to Brinton's admirable study.

During the following decade single cases, sparsely scattered in the literature, were reported by Bouchaud, Kneeland, and

Haldane in 1862, Larcher in 1864, Malherve in 1864, Feierabend in 1866, Clark, in 1867, Cuthbertson in 1867, Ebstein in 1867, Barclay in 1870, Wadham in 1871, and Chauffard in 1871. Billroth in 1867, related that when Professor Arnold of Heidelberg was performing a postmortem examination, he found a duodenal ulcer which had apparently caused no symptoms during life.

Another phase of the subject was introduced by Hecker and Buhl in 1861, who reported eight cases of gastric or intestinal hemorrhage in infants, one of whom had a duodenal ulcer. Spiegelberg added two similar cases in 1869, and since then studies of this subject have been given, among others, by Kündrat, and Landau in 1874, Rhn in 1875, Veit in 1881, and Helmholtz in 1909.

Influenced perhaps by Brinton's and Muller's admirable studies on gastric ulcers, there arose similar efforts with reference to ulcers of the duodenum. One of the earliest of these was published by Klinger in 1861, who noticed ten cases in the literature, and added three of his own. Forster in 1861, and Falkenback in 1863, also contributed analytic reviews.

One of the most thorough of the earlier studies was made by Trier in 1864, who analyzed the postmortem records of the Frederic Hospital at Copenhagen from 1842 to 1862. In a total of 261 simple ulcers, only twenty-eight (10.9 per cent). Were

in the duodenum. He confirmed the usual observation as to the relative frequency of gastric ulcers in women, quoting Brinton's figures of 440 women to 214 men, and compared these to his collection of fifty-four cases of duodenal ulcer, forty-five of which were in men and only nine in women. He was the first to describe in detail the distortion of the duodenum, caused by the healing of ulcers.

In the following year the much more widely known work of Krauss appeared. He gave statistics of eighty cases noted in the literature, and is usually given credit for the first comprehensive survey of the subject. Of sixty-four of his cases, fifty-eight were in men and only six in women. Many recent writers on duodenal ulcer date the modern study of this subject from the time of Krauss' work. In this same year a thesis by Morot gave details of twenty-two cases, eighteen in men and four in women. He quotes Brinton as authority for the statement that duodenal ulcer is five times more common in men than in women.

Following the example of Krauss, papers on duodenal ulcers appeared in rapidly increasing numbers, many of them in the form of theses by German or French students. Thus Treibmann, in 1867, reported fourteen cases. He agreed with Krauss that "vollständige Heilung ist wohl selten." Teillais, in 1869, found sixteen cases, and discussed the various theories as to origin of the ulcers. From 384 postmortem examinations, Starcke, in 1870, discovered thirty-nine examples of simple ulcers or scars, but only three were in the duodenum.

Schulze, in 1873, in his thesis, and in a case report endeavors to show the embolic origin of duodenal ulcers.

O'Hara, in 1875, in presenting the details of the first case of perforating duodenal ulcer ever given before the Philadelphia Pathologic Society said, "But little has been written of it," and that DaCosta had said in his "Medical Diagnosis," "Were it (duodenal ulcer) more frequent, it would be a constant source of error in diagnosis." In a similar presentation before the New York Pathological Society, Loomis, in 1879, remarked, "Perforating ulcer of the duodenum is not common," and in discussion Peters added that there were only ten cases in the records of this society. Moore, in 1883, reported two cases at the Pathologic Society of London, and asserted that from 1867 to 1882 only three cases were recorded on the postmortem records of St. Bartholomew's Hospital. Similarly, Siegel, in 1877, in a dissertation from Erlangen, in which he reported twenty cases, emphasized the lack of any extensive literature on the subject, and Clark, in 1881, in his discussion in Boston, said that duodenal ulcer is a comparatively rare disease occurring in the proportion of one to thirty gastric ulcers.

Nidergang, in 1881, produced the most complete review since Krauss. He directed attention to the greater frequency of the ulcer in men than in women, the reverse being true of gastric ulcers. This same point was emphasized by Lebert in 1878, who found that of thirty-nine patients with duodenal ulcers,

thirty-one were men, and eight, women. Nidergang noted only thirty-seven cases from the literature.

Grunfeld, in 1882, analyzed 1, 150 postmortems from Copenhagen, performed on men of more than fifty years, and women of more than sixty. Scars were found in the stomach in 124 instances (11 percent). In 578 men, scars were found in twenty-two (4 per cent), and in 632 women in 102 (16 per cent). He found them more frequently, if searched for carefully. In the entire series, however, only four scars were found in the duodenum, three in men and one in a woman.

Allouche, in 1883, in a thesis reports one case, and reviews forty-four noted in the literature. All but one of the patients were males.

Chvostek, in 1883, noted fifty-five cases in the literature since the collection of Krauss, and added eight of his own. He concluded that duodenal ulcers were more common in infants than gastric ulcers, but in adults occurred once in women to eight times in men. He said that complete scarring (denied by Krauss) was usually missed, because it was not searched for carefully. Distention or bulging of the duodenal wall in ulcer was emphasized by Turner, in 1864. Bucquoy, in 1887 said that the ulcers are more often present on the anterior wall, Krauss giving the proportion of fifteen anterior to six posterior. Johnson, in 1888, gave a very able review of the literature with-

out adding much to the subject. He says that Osler, in a review of 1,000 postmortems, found only nine ulcers of the duodenum. Pepper, in 1889, says that "all are agreed as to the rarity of duodenal ulcers..... it is doubtful if more than seventy authenticated cases are on record."

LeRenard, in 1891, found recorded in the literature, forty-two duodenal and 492 gastric ulcers; the former were more common in men than in women.

Perhaps the most thorough and valuable review the literature affords is that of Oppenheimer, in 1891. He reaffirms the view that duodenal ulcer is much rarer than gastric ulcer, but suggests that many small or healed duodenal ulcers may be overlooked. One other very important contribution is his observation that recurrences are very frequent, and not rarely are fresh ulcers found adjacent to old scars.

Perry and Shaw, in 1893, investigated the reports of 17,652 postmortems in Guy's Hospital, going back to 1826 in Dr. Hodgkins "Green Inspection Books" and ending with the close of 1892. They found that in seventy cases (0.4 per cent) there were duodenal ulcers, open or healed. In cases of burns there were ulcers of the duodenum in 33 per cent, and excluding these, the ulcers were found in forty-eight males and only sixteen females. They quote Brinton as affirming that gastric ulcer is twice as common in women as in men.

In an analysis by Vonqyl, of patients in the Zurich Medical

clinic from 1884 to 1892, of a total of 12,806 there were ninety-eight with gastric and only three with duodenal ulcers; the latter were all in men. Reckman, in 1893, discusses the diagnosis of duodenal ulcer as if a new clinical syndrome had been uncovered. Collin, in 1894, collected 257 cases, 205 in men and fifty-two in women. Dickinson, in 1895, says that according to the records of the duodenal ulcers in St. George's Hospital of London, fourteen were in men, and three in women (one a burn), and of gastric ulcers forty-two were in women, and only twelve in men. Maret, in 1895, very thoroughly reviews the current opinions concerning etiology. After an historical review with no new facts developed Darras in 1897, noted twenty cases in which laparotomy was done for perforation, with three recoveries. Burwinkel, in 1898, again affirms that in comparison with gastric ulcers, duodenal ulcers are observed "ziemlich selten." He quotes Berthold who analyzed the deaths noted in Charitennalen from 1868 to 1882, and found 262 gastric to twenty-duodenal ulcers. A similar review is given by Schwartz in the same year.

During the following twenty-five years we can find no article of importance on the subject of the incidence of duodenal ulcers. The reason for this state of affairs is rather difficult to comprehend. It may be that in this period the increasing occurrence of these ulcers directed attention chiefly to their diagnosis and treatment. One paper only appeared which gives data useful to our purpose. In 1923 Gruber and Kratzeisen gave a review

of 3,000 postmortem examinations made at the Mainz Hospital; 120 gastric and sixty-four duodenal ulcers were found. They also give Gruber's statistics from Strassburg from 1906 to 1910, in which out of 4,208 postmortem examinations, there were 2.1 per cent gastric, and 1.38 per cent duodenal ulcers. In Munich, from 1899 to 1912, out of 5,884 postmortems, scars and ulcers were found in the stomach in 6.57 per cent; but in the duodenum in only 1.56 per cent. These authors give figures from Hart and Musa and Holzweissig, who from 1913 to 1921 observed 211 (6.9 per cent) gastric, and 163 (5.3 per cent) duodenal, ulcers in 3,058 postmortem examinations at the Augusta Victoria Hospital in Berlin. They further assert that Sommerfeld at the German Alexander Hospital at St. Petersburg, in 19,200 postmortems from 1891 to 1911, found ulcers of the stomach in 1.77 per cent, and ulcers in the duodenum in 1.15 per cent. Lastly they give figures from Goldschmidt in Frankfort who in 1913 and 1914 in 2,309 postmortems found gastric ulcers in 2.1 per cent, and duodenal in 1.4 per cent. With respect to sex, these authors found a preponderance of both types of ulcer in men, more marked in the case of the duodenum. From these data one of two conclusions must be drawn: Either there was a distinct increase of the incidence of duodenal ulcers beginning about twenty-five years before, or else more accurate observation was revealing their presence. Considering how little escaped the wonderful eyes of Virchow and his well

trained scholars, the former is much the more reasonable hypothesis. However, it must be granted that when the attention is focused on finding ulcers (or anything else), they are likely to be more numerous than in the ordinary routine examinations.

- ETIOLOGY -

Age:- Ulcer of the stomach. It is claimed that more than one-half the cases in male occurs between the ages of thirty and fifty, while in the female three-quarters of the cases occur before thirty. The fact remains, however, that ulcer can develop at any time between the extremes of life and has been reported in a newborn babe as well as individuals of advanced years, but the great majority of ulcers begin between the ages of twenty and thirty.

Sex:- The acute ulcer is more likely to affect the female, and is generally recorded that gastric ulcer is more frequent in the female than in the male. Some authors give the incidence as three to one in favor of the female, a figure which may be too high.

Occupation:- As a predisposing cause, the idea being that cooks, for instance, who were exposed to the ingestion of hot and irritating foods, might more frequently develop the disease. The effect of high temperature in producing ulcer is shown by experiments of Dicker, who produced erosions and ulcerations in dozens ^{of dogs} by feeding gruel at a temperature of 50 degrees C.

These ulcers were not due to scalding, but to congestion of the mucous membrane with increased peristalsis. Heiser found that practically all patients with peptic ulcer gave a history of eating hot food. This idea has taken hold, and it is realized that the causative factors exist in a great diversity of occupations and, indeed, in those who have no occupations whatever. It is far more probable that any occupation which imposes a strain with irregular and inadequate feeding and general ill health might be predisposed to ulcer. Certainly the disease occurs at times in those who have been predisposed to a sedentary life and general ill health.

Trauma:- Mechanical injuries heal rapidly, and the instances in which ulcer can be clearly associated with trauma are anique and no greater than the association of any other symptoms complex with trauma. One should not ignore the experimental work which has produced acute ulceration simply because such acute ulcerations have no recognizable counterpart in chronic lesions as we meet them in practice. On the contrary, one should feel the real progress is being made only if we marshal the recognizable facts, and attempt to draw conclusions which might be of value in explaining any given case. Many of the etiological facts have been based on experimental study.

Circulatory Causes:- The importance of local disturbances in circulation in the etiology of gastric and duodenal ulcer appears to be a well established fact with the majority of those who have made a close anatomical study of this condition.

It may not be out of place, therefore, to restate the reasons advanced for the belief that gastric and duodenal ulcers arise primarily from vascular lesions.

Virchow first pointed out clearly the apparent relation of local vascular disturbances to gastric ulcer. He states that according to his experience the ulceration is preceded by a hemorrhagic necrosis of the mucous membrane and the disturbance in circulation which is its cause, he is inclined to attribute to vascular lesions. He mentions in particular disease and obstruction of arteries. He points out that only a local cause will account for such an exquisitely localized lesion and he is said to have pointed to the funnel shape of the ulcers as an additional argument of their relation to the vascular system.

Merhel seems to have been the first to publish cases of gastric ulcer in which vascular lesions was actually demonstrated. One of them was that of a woman of about one-hundred years of age with very marked atheroma and general arteriosclerosis, in whom he found at autopsy an acute perforated

duodenal ulcer due to a plainly visible thrombosis of the arteria pancreatico-duodenalis.

The most important work, however, was done by Hauser in 1883, and published in his excellent monograph on gastric ulcer and its relation to carcinoma. Hauser refers to Herhil's cases and recounts a case of his own of a recent gastric ulcer of a woman of fifty-four years of age. In the sections from the ulcer he found an arteriosclerotic artery filled with thrombus. After a careful analysis of the whole problem, he came to the following conclusions.

The hemorrhagic infarct which precedes the formation of the ulcer results always from a permanent interruption of the circulation in the small arteries which ascend from the submucosa into the mucous membrane. The disturbance in circulation may be caused by embolism or by autochthonous thrombosis or leaving of such an artery. The hemorrhage infarct is followed by a chronic ulcer, only when the disturbance in circulation follows local disease of the blood vessels of the stomach. In case of local disease of the gastric vessels, the ulcer assumes a chronic atonic character, because the development of blood vessels which is necessary to permit healing cannot occur normally from pathologic blood vessels. The degree of vascular disease,

determines the more or less chronic character of the ulcer.

The last statement in regard to the chronic ulcer of the stomach is of particular importance, because it is offered as an explanation of the failure to produce chronic ulcers by experiments which otherwise confirmed Virchow's theory. Panum in 1862 produced an acute gastric ulcer with all its anatomical characteristics by embolic obstruction of one of the arteries of the stomach. Cohnheim perfected the technique by injecting chromate of lead directly into one of the arteriae gastricae which arise from the splenic artery. Animals killed within a few days of the experiment show typical acute gastric ulcers, but all animals killed after the second week showed a normal mucous membrane as an evidence of the remarkable regenerative power of this structure, which has been brought out more and more clearly by later experimentation. It is impossible here to enter into the numerous attempts which have been made since to produce gastric ulcer experimentally. Suffice it to say that the latest endeavors in this direction by Pays and by Suzuhe are based on Cohnheim's idea. They have been somewhat more successful because in their experiments through the use of injections of hot salt solutions, dilute formaldehyde and dilute alcohol, or of silver nitrate, epinephrin or dilute solution of nicotin, more extensive local vascular lesions have been produced.

This practically confirms Hauser's statement in regard to the interdependence of the degree of vascular disturbance and the chronicity of the ulcer. But in these experiments even, the chronic ulcers so produced which may perforate and which may show extensive cicatrization with contraction in their surroundings, heal eventually. It is evidently impossible experimentally to reproduce exactly the conditions as they exist in man, but the resemblance of these experimental ulcers to those in man is very striking.

Hauser was also the first to call attention to the fact that gastric ulcer is frequently associated with general arteriosclerosis, which, of course, supports the vascular theory.

Apart from the peculiar funnel shape of many of the deep ulcers, there is one feature which to my mind points very strongly to a relation of the ulceration to the local disease of the arteries. This is the frequent erosion of arteries at the base of the ulcer, followed by severe arterial hemorrhage. If blood vessels were merely accidentally opened by a gradual extension of the ulceration into the tissues, there is every reason to believe that veins would be more likely to be opened than arteries. This point has really not received the attention which it deserves. One has taken this fact of the frequent erosion of arteries as a matter of fact, which it is not at all,

and it is astonishing how indefinite the statements in literature are in regard to this phase of the subject. The hemorrhage came from those arteries which supply that part of the gastric or duodenal wall in which the ulcers are situated; that is, in the usual position of these ulcers, the hemorrhage arises from branches of the arteria gastrica or gastro-epiploica dextro or of the arteria. Of the ulcer is the result of obstruction of such an artery, wither by disease or embolism, one understand at once why the necrosis should involve these arteries, and an opening results when the necrotic material is removed by digestion. The wonder is then, not that we have so many severe hemorrhages, but that we do not have them more frequent.

Much has been said about the abundant blood supply of the walls of the stomach and duodenum and about the numerous anastomosis between the arteries. As a matter of fact, anyone who takes the trouble to dissect the arteries of the stomach will be astonished how poorly supplied with arteries are these parts of the wall of the stomach and duodenum where we usually find ulcers. This is particularly true of the extreme pyloric end of the stomach, at the lesser curvature and on the posterior wall, and of the beginning of the duodenum at its convexity. In living, W. J. Mayo noticed the appearance of an anemic spot on the duodenum on the slightest traction.

He says:-

"The arrangement of the blood vessels immediately distal to the pylorus is such that the traction may interfere with the vascularization, and the local anemia thus produced causes a white spot to appear on the duodenum just below the pylorus."

Wilkie made a very careful study of the blood supply to the first part of the duodenum. He finds that the spot described by Mayo is supplied by a small artery of varying origin which is practically an end-artery. He also states that anastomosis between some other arterial branches which supply the first part of the duodenum are by no means free. He mentions in cases of duodenal ulcer the frequency of arteriosclerosis in the arteries which supply the side of the duodenal ulcers, and for all these reasons he believes that lack of blood supply is an important factor in the production of duodenal ulcer." (1)

Infection- Local or General:- "In previous paper I have shown that ulcers of the stomach in man and in domestic animals often is associated with streptococcus infection in the ulcerated area, that foci, such as in tonsils and teeth, harbor the streptococcus and predispose to ulcer, and from distant focus has elective affinity for the stomach, producing

ulcers, and their location, especially with regard to non-healing, resemble those noted in the spontaneous diseases. Among the difficulties encountered in my earlier work was the inability to maintain specific infecting power and specific immunologic properties in the streptococcus isolated. Specific infecting power disappeared on successive animal passage or aerobic cultivation. It has been found since that relatively anaerobic conditions and keeping the organisms in latent life, tend to preserve this property. Some of the strains were put aside under these conditions in hope that they would live and maintain specific characteristics for a long time. It is my purpose here to record the results of a study of the localizing power, the mechanism involved, and the immunologic condition of several of the strains isolated years ago, of a fresh strain from a recurrent ulcer in man, and of a series of similar strains from experimental ulcers in dogs.

LOCALIZATION OF A FRESHLY ISOLATED STRAIN

Through the cooperation of Dr. Eusterman of the section on gastroenterology in Mayo clinic, I have had the opportunity of studying the localizing power of the streptococcus, freshly isolated, from the tonsils of a patient with recurring ulcer. Ulcer of the duodenum was found, a gastro-enterostomy was

performed, and complete relief from symptoms of ulcer followed. No attention was given to foci of infection. Eleven months afterward symptoms of ulcer recurred, and the patient returned to clinic one month later. Roentgenograms revealed an ulcer at the gastrojejunal juncture, and one along the lesser curvature of the stomach. The tonsils were large and hyperemic, and from the crypts, a moderate amount of pus was expressed. A roentgenogram revealed four pulpless teeth, with well marked areas of rarefaction around the apexes of each. The tonsils and infected teeth were removed in four sittings. Coincidental with the removal of the foci of infection, and medical management of the ulcer, the patient's symptoms subsided, and marked evidence of healing accrued.

The suspension, of sodium chlorid solution of the pus expressed from the tonsils, directly injected, produced ulcer in the two rabbits enoculated. The primary culture, and the second, third, fourth, fifth, and sixth rapidly made subcultures produced ulcer in nearly all animals injected. The ulcers were often situated in the lesser curvature. Of the twelve rabbits injected with living streptococcus soon after isolation, ten developed lesions of the stomach, and only three had lesions elsewhere, one of which consisted of a few hemorrhages in the appendix, one of hemorrhages in the tricuped

valve, and one of a few hemorrhagic lesions in the tendinous ends of muscles and fascia. Ten rabbits injected with the strain after one animal passage, and after preservation in ascites - tissue - agar, stabs for from one month, developed ulcer with or without hemorrhage. Thus of a total of twenty-two rabbits developed gastric lesions. Four rabbits were given the killed cultures: of these three developed lesions of the stomach. Six rabbits were injected with filtrates of actively growing cultures, of these five developed hemorrhage of the stomach with or without ulceration. Two rabbits received the filtrate after shaking with animal charcoal, and two the dialysed filtrate. One of the former and both of the later developed hemorrhage and ulcer of the stomach, with no lesions elsewhere.

Mann and Williamson have developed a method of producing chronic ulcer in dogs. This consists essentially of transplanting the duodenum into the ilium and anastomosing the jejunum into the pyloric end of the stomach. The alkalization and other functions of the duodenum are thus circumvented. In dogs operated on in this manner, chronic ulcer develops with a good deal of regularity in the jejunum just beyond the line of anastomosis. The experimental ulcers have many of the features of chronic ulcers in man. A microscopic study of some of the experimental ulcers revealed circumscribed areas of leukocytic

and round-cell infiltration far from the ulcerated area in which gram-positive diplococci were demonstrable. On the basis of these findings, and the fact that I had previously found that spontaneous ulcer of the dog was due to the streptococcic infection, the hypothesis that this ulcer might be due to infection made possible through dysfunction induced by the operative procedure presented itself. It was thought worth while, therefore, to make a bacteriologic study of ulcers produced by the method of these investigators, and to determine the localizing power of the bacteria isolated. Moreover, since I had found that foci of infections in teeth and tonsils predispose to ulcer in man, and apparently in the dog and the cow, a thorough search for foci of infection was made in the dogs operated on, and if found, the localizing power of the bacteria was also studied.

Cultures have been made thus for in seven ulcers removed during exploratory operations or after death. In all cultures there have been streptococci resembling those previously isolated in spontaneous ulcer in the dog and in man. Cultures from the normal mucous membrane removed during the primary operation have not yielded the streptococcus in any of five instances. B Welchie and less commonly B Coli are usually found in small numbers in both the ulcers and the

normal mucous membrane. The streptococcus, generally is the second to the third subculture, from each of five of the ulcers, has been found to localize electively in the mucous membrane of the stomach, producing hemorrhage and ulcer. The infecting power of one of these strains was thoroughly studied. Seventeen rabbits were injected intravenously with living culture. Of each, all developed hemorrhage or ulcer, or both, of the stomach. Characteristic localization occurred following injection of the strain in the primary culture, in the twenty-ninth, thirty-second, forty-second, fiftyth, and fifty-third rapidly made subcultures. It followed injections of the acid glucose-brainbroth culture so well as after neutralization with sodium hydroxide, and occurred in the two dogs injected. Only four animals developed lesions in other organs, and these were slight. The heat-killed organism from the fifty-third rapidly made subcultures, suspended in sodium-chlorid solution, in amounts, representing the growth of from twenty to sixty C. C. of the broth culture, was injected into four rabbits. Of these, three developed lesions of the stomach and none lesions elsewhere.

The filtrate of broth in forty-second, fiftyth, and fifty-third subcultures was injected into thirteen rabbits in doses ranging from twelve to sixty C. C. Of these ten developed

lesions of the stomach, and none lesions elsewhere. Only one of eight rabbits injected with equivalent amounts of the same batches of broth, and of the broth brought to the same degree of acidity as the cultrue, developed hemorrhage of the stomach.

The results following injection of living organism of the other four strains were similar. Of the twelve rabbits injected, eleven developed lesions of the stomach, and only two had lesions elsewhere.

The findings in one of the dogs which had a perforating ulcer, are noteworthy. A search for foci of infection revealed marked pyorrhea, with retraction of the gums, and absorption of the alveolar processes of six lower incisors. All of the teeth were loose. From the pus aspirated from the pyorrheal pockets, from the apexes of two of these teeth, and from the corresponding alveolar sockets, a streptococcus was isolated which resembled the one isolated from the emulsion of the ulcer, and it produced hemorrhage or ulcer of the stomach in four rabbits injected". (3)

Trophic and Glandular ulcers; A different conception of ulcer formation has directed the great volume of work accomplished by the Italian school. They interpret the lesion as of a neurotrophic order, dependent on a defect in the nerve supply

to the stomach. Their researches have dealt chiefly with the influence of the vagi.

Central nervous system- Ebstein and Brown- Sequard, in the earliest studies on the central nervous system, obtained partial softening, erosion and formation of ulcer in the stomach following circumscribed destruction of the anterior corpora quadrigemina, and after burns of the cerebral surfaces. Schiff observed hemorrhagic infiltrations and ulcerations following intersection of the thalamus and cerebral peduncles. Greggio noted mucosal and submucous hemorrhages near the pylorus, associated with diffuse gastritis, in half of fifty cases subjected to unilateral and median compression of the cervical cord. He and Bolton cited the production of ulcer by Albertoni who cut off the cerebral hemisphere; Ewald and Kock who severed the cervical cord and administered 0.5 per cent hydrochloric acid daily; Schupfer, following bilateral lesions of the anterior and posterior roots of the fifth and eight dorsal segments, and Quincke and Dattwyler, who associated lesions of the cord with anemia.

Splanchnic nerves:- While Durante was studying the relationship of the splanchnic or sympathetic nerves to ulcerous changes, he repeated the work of della Vedova. He resected the splanchnic nerves by a lumbar approach, and found the section of the median splanchnic nerve produced circumscribed hemorrhagic or nonhemorrhagic necrosis of the gastric mucosa. The hemorrhagic area began

in the blood vessels of the muscular mucosae, destroying only the mucosa, and there was evidence of slow regeneration. The nonhemorrhagic type involved the mucosa and submucosa, but did not show signs of regeneration. He considered that the later type might have resulted from arterial spasm due to the action of epinephrine, because he observed simultaneous intense congestion with signs of hemorrhage in the suprarenal gland on the side of the resection. Section of the minor splanchnic nerve only transient congestion. Since both acute and chronic ulcers occurred, he did not consider that ~~this~~ was an important factor in their production. Koenecke observed that excision of the pylorus followed by a Billroth I or a Billroth II operation caused jejunal ulcer in one of five dogs, but bilateral division of the splanchnic nerves following the same procedure caused typical callous deeply penetrating ulcers in all dogs. He attributed the result to removal of an inhibition to secretion.

Celiac Plexus:- Gundelfinger, after extirpation of the celiac ganglion (by which the action of the sympathetic was removed from the stomach and duodenum, leaving only vagal influence) succeeded in producing gastric lesions. Latzel reported negative results after extirpation of the celiac plexus. Greggio, in his comprehensive review, reported ulceration of the gastric mucosa and hyperemia in the liver following extirpation of the celiac plexus by Pincus and Samuel, Lowin, Boer, and Popielski; other

have failed to produce them by this procedure in dogs and rabbits, for example, Adrian, Budge, Lustig, Lamansky and Peiper. Lesions of the plexus were found to produce ulcers and mucous hemorrhages by della Vedova, Kawamura, and Lilla and Gibelli. On the other hand, Donati, Kobagaski, Lorenzi, and Schminche observed negative results or only small hemorrhages by irritation of the plexus. Brancati found that ablation of the paravertebral lumbar sympathetic in a dog caused capillary dilatation necrosis of the mucosa and ulcers at the pyloric region of the stomach and in the adjacent part of the duodenum.

The vagi:- There has been a much more extensive investigation of the relationship of vagal influence to gastroduodenal lesions. Resection of both vagi in the neck of rabbits was found by Lorenzi to produce hemorrhage in the gastric mucosa fairly frequently. Saitta, after bilateral vagotomy observed multiple ulcers when he administered three per cent hydrochloric acid by mouth. Finzi noted that extirpation of one vagus yielded inconstant results, but that bilateral vagotomy produced, with greater regularity, circulatory disturbances, edema, echymosis, necrotic processes and atrophic ulceration. Keppish reported the formation of ulcer in five cases following resection of the vagus. According to Greggio, negative results following vagoatomy in the neck of a rabbit are reported by Donati, Kobayaski, Korte, and Martin, however, Midulla found that sectioning of the vagus in the neck of frogs and toads caused

gastric dilation, spasm of the pylorus, hypersecretion of the gastric juice and ulcers which showed a tendency to become chronic and perforate.

The thoracic approach to the vagus has been utilized by others. Zironie, after cutting the vagi around the esophagus of rabbits, observed ulceration in fifty-nine of one hundred experiments, Antonini observed ulcers in only seven of one hundred animals after the same procedure; the day following operation there was gastric disturbances and congestion, with the development of lesions possessing the same gross and microscopic appearances of peptic ulcer in man. Cicotrization was not observed. In lesions observed after, twenty-five and fifty days, there was no evidence of healing. Greggio frequently produced hemorrhagic infiltration of the mucosa after bilateral vagotomy, but in only one case did he find a chronic ulcer. This ulcer was two cm. in diameter and was situated on the greater curvature. He quoted negative results following this procedure by Krehl, Futsch, Kawamura, and Fiori, and inconstant results by Samuelson and Contejan.

Thorough studies have been carried out following resection of the vagi in the abdomen. Zironi claimed to have produced gastric ulcer in sixty-four of one hundred rabbits following sub-diaphragmatic vagotomy. Lorenzi duplicated these observations,

Van Yzeren cut both vagi subdiaphragmatically in twenty rabbits in ten of them he found chronic single ulcers, usually near the pylorus; the earliest was observed in five days and the oldest in two hundred and eighty nine days. Ophuls, repeated these studies with the same results, concluded that the lesions were neurotrophic, and that trophic influences are necessary to preserve the normal resistance of the mucous membrane to the digestive action of the gastric juice. Latzel noted hemorrhagic erosions and ulceration in ten dogs following subdiaphragmatic vagotomy. Zironi, after similar resection in guinea pigs, found lesions varying from 0.3 to 1 cm. in diameter in sixty-three per cent of his studies. Donati reported negative results after a thorough study by this method. Greggio quoted Gunsburg and Lunde and Kobayashi and Marchetti as having caused diffuse changes in the mucosa or actual ulcers by the procedure; Saitta, Gibelli and Vigliani reported negative results. Stimulation of the vagus has given contradictory results, Stahnke, in studying the effect of long continued vagal stimulation on gastric motility and secretion, faradized the vagi for forty minutes. At necropsy gastritis of the mucosa was found in some dogs, and superficial defects in the mucosa were found in others. He considered the ulceration to be a result of increased secretion and chronic gastritis. Kippish, by stimulating the vagi of rabbits with electrodes, produced

chronic gastric ulcers in ten of eleven surviving animals. Westphal believed that extreme vagal irritation explained the ulcers following the injection of pilocarpine. Hayashi interpreted similarly the lesions produced by muscarine. Gundelfinger was unable to produce ulcers by vagal irritation. Greggio cited Lalma and Lichenbeld as having produced lesions by excitation of the vagus; Lorenzi and della Vedova. After burns and alcoholic injections into the vagus, caused hemorrhage and ulceration of the stomach. Negative results were reported by Korte and Donati.

Glandular influence:- The effect of glandular activity on the formation of ulcer may be viewed as associated with some type of nervous mechanism. Durante, it will be recalled, noted that ulcers following median splanchnic resection were associated with lesions of the suprarenal glands, and concluded that the effect might have been produced by suprarenal activity.

The studies of numerous investigators have indicated a possible relation, between the glands of internal secretion and the ulcerative lesions of the stomach. There are reported in the literature five cases of ulcer of the stomach and duodenum in man associated with thickening of the suprarenal capsule, hypertrophy, fatty degeneration, congestion, and multiple hemorrhages into the glands. Latzel reported the occurrence of ulcers in the animals following destruction of the suprarenal capsule. Greggio quoted Gibelli, Onde and Aoffe as having produced ulcer by induced

suprarenal insufficiency. Mann observed acute ulcerations in ninety per cent of animals following the removal of both glands, but none associated with simple removal of the capsules. Hemorrhagic areas were found in the stomach in one animal which died in twenty-four hours; definite ulcers were found in another in twenty-two hours. If the ulcers were situated in the fundus usually the mucosa alone was involved; if they were found in the prepyloric division they penetrated the muscular mucosae.

The duodenum was generally injected. The suggested dependence of these lesions on bile and trypsin was ruled out by their continued appearance after the establishment of a biliary and pancreatic fistula. The acid appeared to be a factor as ulcers did not develop when sodium bicarbonate was fed to dogs on whom suprarenalectomy had been performed. Elliott noted acute gastric ulcers following the removal of suprarenal glands in cats, and cited it as proof of the full digestive power of the gastric juice. Finzi observed edema, congestion, hemorrhage, necrosis and ulceration with an effort to heal following suprarenal suppression. Friedman, while studying the interrelationship with other glands, also noted that removal of one suprarenal gland and one thyroid gland did not have any effect on the integrity of the gastric mucosa, but that intravenous thyroid medication associated with this procedure caused small ulcerations. Finzi also observed that the simultaneous

removal of one thyroid gland and one suprarenal gland failed to cause ulcerous changes; he assumed that suprarenal insufficiency can manifest its action on the stomach only with an intact thyroid gland, and that the correction of internal secretions may have a bearing on formation of ulcer. Hardt studies the relationship of the feeding of thyroid gland to acidity and found that with increasing thyroid administration, there was a decrease in acidity of the gastric secretion, while with its interruption there was a return to the normal status. Hayashi, by imitating the so-called mixed stigmatized constitution with the administration of thyroid gland, was able to produce spasmogenic ulcerous changes. Greggio reported ulcers following thyroidectomy as having been produced by Boccardi, Grofeddi and d'Amore. He reported ulcers following exclusion of the liver by Mueller, Kollicker, Bidder and Schmidt, Beati and others. They have been observed by Bollman and Mann following insufficiency of hepatic function induced by partial hepatectomy." (11)

Burns or scalds: " In a paper which has since become classical Curling called attention to the connexion between cases of burn or of scalds and acute ulceration of the duodenum. The term "Curling ulcer" has now obtained universal currency, and on account of duodenal ulcer has been written in recent years without conspicuous mention being made of the association of this lesion with burns or scalds.

Duodenal ulcer in connexion with burns is doubtless a toxic ulcer, and therefore analogous to the ulcer which occurs in septicaemia, uraemia, typhoid fever, erysipelas, and pemphigus. It is almost without exception the rule to find the ulcer only in cases where septic processes in the burnt skin have developed; and the frequency of duodenal ulcer in cases of burn or scald may well be due to the special liability to suppuration and to sloughing which these injuries display. A point which requires investigation in this connexion concerns the presence and possible influence of septic emboli, conveyed from the infected area to different regions in the body. In the alimentary canal they would produce haemorrhagic infiltration, which, immediately beyond the pylorus, would readily be converted into ulcers by the action of the gastric juice.

- SYMPTOMS -

Pain:- " That the question of genesis of gastric pain in pathologic conditions of the stomach and duodenum is still an open one can readily be seen from the diversified opinions of authors on the subject. The work of Gensbury, Tumpowsky, and Hamburger emphasizes the gastric tension and contractions of the stomach, together with the hyperirritability of the stomach, as the most important factors in the etiology of pain. According to the older view of chemical distress in gastric ulcer, there are certain facts which are not explainable on the basis of acid irritation. The only basis for this view at present is the alkali treatment in gastric ulcer, by which the pains are immediately relieved. Carlson concludes that the pain of gastric and duodenal ulcers are contraction pains, either in the stomach or in the pylorus and upper part of the duodenum. In order to confirm the contraction theory, analysis was made of three distinct types of cases:-

1. Carcinoma of the pylorus in which there are vigorous peristalsis and a moderate degree of pain.

2. Healed ulcer of the duodenum with cicatricial contractions, high grade obstruction and a very pronounced hyperperistalsis.

3. Typical peptic ulcer with vigorous peristalsis.

METHOD

The patients employed for this work were carefully examined and diagnosed clinically by Dr. B. W. Sippy and his assistants, after the diagnosis was made, the procedure was similar to that of Ginsbury, Lumpowsky and Hamburger. Kymographic tracings of the stomach contraction were begun immediately after the patient had a meal, and were continued until vigorous hunger peristalsis was obtained. The patients all cooperated very intelligently. In each case the patient swallowed two tubes, one a Rehfuß and the other an ordinary tube with rubber ballon attached. By means of the Rehfuß tube, acids and alkalis could be administered, or the stomach contents could be aspirated from time to time without disturbing the patient. When the tracings were started, the patient was told to tap the key to note the occurrence of pain. If the pains were mild, he tapped the key once; if severe, he tapped the key twice, and when intense, he tapped it three times. The lines below the tracings records the pain periods.

REPORT OF CASES

Case 1- A boy, aged 17, gave a typical history of gastric ulcer which began about eight years previous to admission. The pain had been present to irregular intervals for about five

years after the onset. But during the three years previous to admission, the pains had practically disappeared, and obstructive symptoms developed. When the patient entered the hospital, February 3, 1917, he had the symptoms compatible with a high grade obstruction at the outlet of the stomach. Practically no food could pass beyond the pyloric outlet. The stomach was found to be very much enlarged, the lower border coming to a level two finger-breadths below the umbilical line. Peristaltic waves were plainly visible through the abdominal wall. Repeated stomach analysis showed no evidence of blood, a free acidity ranging from forty to sixty-five and a total acidity from fifty to ninety. There was no blood in the stool.

Medical management seemed out of the question because the boy was rapidly becoming dehydrated in spite of medicinal and dietetic measures. An operation was performed and a cicatrix found at the outlet of the stomach involving a portion of the upper part of the duodenum and lower part of the pylorus. There was no evidence of an active process. Tractings were obtained previous to the operation, an vigorous peristalsis was recorded. In no instances were the peristaltic contractions associated with pain. The more vigorous were obtained when the stomach contained large quantities of food and liquid which could not pass beyond the pylorus. The contractions of the empty stomach were al

were also exaggerated, but not painful.

Case 2- The case described here is one which is typical of four others of the group. The patient, a man, aged forty-seven, entered the hospital March 5, 1917 with a typical history of gastric ulcer of about one year's duration. The distress came from two to four hours after eating and was relieved by the taking of food or alkalis. The pains were usually more severe in the afternoon, but occasionally the patient was awakened in the middle of the night by the distress. On careful questioning, we find that the pains were intermittent in character and not continuous.

Two complete series of tracings were obtained which were begun immediately after the eating of a large meal and continued until intense pains were experienced. The results of the two experiments were practically identical. No pains were experienced during the first two or three hours after eating, but fractional distillations of gastric juice at this time revealed a free acidity of from thirty to forty and a total acidity of from fifty to sixty. The digestive peristalsis was plainly visible on the records at this time, but nothing to indicate the painful pylorospasm or hunger peristalsis. Three hours after eating, the patient complained of severe pain. Sixty c.c. of 0.3 per cent hydrochloric acid was administered, which gave temporary relief.

Five hours after eating, the patient complained of a great deal of epigastric distress, which was a burning, gnawing character, and as the record showed also intermittent. The pains were more severe toward the end of a hunger contraction. The patient was aspirated, and twenty-five c.c. of thick mucus were withdrawn. No free acid was present, and only a trace of combined acidity. Immediately after aspiration, the pain disappeared for about ten minutes. The stomach was then washed, and the pains again disappeared. One and a half hours after it had been washed, the pains were quite severe and the stomach was again aspirated. The aspiration yielded fifty-five c. c. of fluid which had a free acidity of fifty-five and a total acidity of seventy. The pains were severe at ~~this~~ time but the contractions were also augmented.

During one of the painful periods, a powder, containing thirty grains of each of bismuth and sodium bicarbonate, was administered through the tube and gave almost instant relief. No pains were experienced for the next hour and a half, and the stomach was practically quiescent. At the end of this period, the stomach was aspirated and fifty-five c. c. of a yellowish green material were obtained which had a free acidity of sixty-five and a total acidity of seventy-five. Ten minutes after aspiration, pains returned and were more intense than on any other previous occasion. The vigorous peristalsis of the

stomach returned, synchronous with return of the pain.

Case 3- A man, aged sixty-seven, was first admitted to the hospital, April 1, 1916 at which time a diagnosis of peptic ulcer of the duodenum was made. He left the hospital, June 13, 1916, apparently very much improved. At that time repeated stomach analysis showed a free acidity of seventy and a total of one hundred and ten, with an occasional weak positive weber test. The stools also showed a weak weber test. He returned again February 25, 1917, very much undernourished, and with all the classical symptoms of high grade pyloric obstruction. Peristaltic waves were visible in the upper abdomen and is low as half way between the umbilicus and symphysis. The patient was rapidly losing weight, and an operation was performed under local anesthetic. Carcinoma was found at the outlet of the pylorus. Gastro-enterostomy was performed, and the patient recovered. A number of tracings previous to operations were obtained which revealed the following facts:-

There was a hyperperistalsis of the stomach. The digestive peristalsis as seen in the normal individual was greatly augmented, and found to be painful. The pains, as the records showed, were most severe at the end of the peristaltic wave. In other words, when the peristalsis had reached the pyloric end of the stomach, the same type of peristalsis was also present when the stomach had been aspirated of its food contents.

The results further substantiate the theory that the pain is mainly due to the contraction or spasm of the upper end of the duodenum and pylorus, together with the peristalsis of the fundus, the acid playing only a secondary role. That the vigorous peristalsis in case 1 is not associated with pain is due to the ablituration of the upper portion of the duodenum and lower portion of the pylorus by scar tissue. The ulcer had healed and there was no longer an active hyperirritable process to produce a duodenopylorospasm. The increase in tension and the hyperperistalsis of the fundus were not sufficeint to produce typical gastric pains. The peristalsis is merely intensified digestive peristalsis, which is not subjective in character in the absence of an active hyperesthetic process.

DISCUSSION ON CAUSE OF GASTRIC PAIN

In the normal stomach, as digestion continues and the stomach gradually empties itself, there is an increasing tonus together with a low degree of hyperirritability, which culminates in hunger pains. When there is an active ulcer, or carcinoma at the outlet, these normal processes are intensified and we have distinct gastric pain. If the pains were due to acid corrosion, we would expect that when the stomach contents were sufficiently acid pain would be experienced; but the results in case 2 do not support this theory. When the stomach was relatively

quiescent and the stomach contents had a free acidity of thirty and total acidity of fifty, the patient did not have or complain of pain. Two hours later, with only a slight variation in acidity and with marked peristalsis, he complained of severe epigastric pains. These pains were temporarily relieved by a 0.3 per cent hydrochloric acid solution, and the contractions were slightly diminished. The action of the alkalis in relieving pain is due not merely to the neutralizing of the acid contents, but also to their inhibitory action on the contractions of the stomach. The alkalis act partly through a sedative effect on the stomach in which the vigorous peristalsis and painful pylorospasms are inhibited. The neutralization of the acid is probably a minor factor in the relief of pain as is shown by the charts. The alkalis relieved the pain for one and a half hour, after which the stomach was aspirated of fifty-five c.c. of fluid with a free acidity of sixty-five and a total of seventy-five. Ten minutes after fifty-five c. c. of acid had been aspirated, pains became more severe than on any previous occasion, and continued until the stomach was washed. The pains returned one hour after the stomach had been washed. The stomach analysis showed this time fifty-five c. c. of watery mucus with a free acidity of sixty and a total acidity of seventy. The ulcer pain is apparently independent of the variations in the acid concentration. There may be intense intermittent pains synchronous with the contractions with not free acid in the stomach. The stomach contents may be highly acid without causing pain.

Case 3- Represents a high grade of pyloric obstruction in which an active hyperirritable process is present. By means of the hystero-graphic tracing, it was demonstrated, previous to operation, that an active process was present at the pylorus or upper duodenum. The patient invariably recorded pain toward the end of a contraction. The fact that pains were experienced when the stomach contained from twelve to 1,500 c. c. of food material, and that the pains were felt only when the peristalsis had reached the pylorus, led to the conclusion that an active process was present at the outlet. Operation confirmed the conclusion.

CONCLUSIONS-

1. Ulcer pains may be present in the absence of free acid, and may be temporarily relieved by a 0.3 per cent hydrochloric acid solution.
2. Gastric ulcer pains may be absent in the presents of high acidity.
3. Any active process producing a hyperirritable condition may result in pain, but the pains are intermittent, being synchronous with the contractions of the stomach, pylorus or dudodenum, and bearing no relation to the degree of acidity.
4. Hypertension and hyperistalsis with high grade pyloric obstruction are not sufficient to produce pain in the absence of an irritable process.ⁿ (5)

Pain is perhaps the most constant and distinctive feature. It varies greatly in character; it may be only a gnawing or burning sensation, particularly felt when the stomach is empty, and relieved by taking food, but the more characteristic form comes on in paroxysms, in which the pain is only felt in the epigastrium, but radiates to the back and to the sides. In many cases the two points of epigastric pain and dorsal pain, about the level of the tenth dorsal vertebra, are very well marked. These attacks are most frequently induced by taking food, and they may recur at a variable period after eating. Except in severe attacks the pain does not usually last more than an hour and disappears before the next meal. In many cases it appears with greatest regularity as regards time after the same kind of meal. It occurs during the digestive process and disappears when the stomach is empty. It is usually stated that when the ulcer is near the cardia the pain is apt to set in earlier, but there is no certainty on this point. In some cases it comes on in the early morning hours. The attacks may occur at intervals for weeks or months and then disappear entirely for a prolonged period. In the attack the patient is usually bent forward, and finds relief from pressure over the epigastric region.

Perforation:- Is often preceded by definite exacerbation in the history of ulcer. It may contract a cold or influenza and perforation takes place within twenty-four hours. May be associated

with the lighting up of some focal infection, at least the association would seem to justify that belief. In some instances, it is unquestionably due to unusual muscular overwork. Infections, sudden trauma, coughing, sneezing, and twisting may induce this complication. In any event when perforation occurs there is a sudden onset of the most intolerable, agonising pain. The pain is hardly exceeded in severity by any that a human being can suffer; the extremity of agony is reached. So profound may the instant impression be that death results. Some of the so called "sudden deaths" are due to this form of perforation. The patient is always prostrate with agony; he looks pale and faint, his face wears a deeply anxious expression, the eyes are wide and watchful, beads of sweat stand out upon the brow, and lines are quickly graven on the cheeks. The patient breaths shortly and quickly; he cannot take a deep inspiration, the attempt to do so ends in a groan or shout of agony and a spasm of pain. The answers to one's questions are given in catches, and every expiratory phase ends abruptly in a catch. Collapse is certainly not present, however, when the patient is seen within an hour or two, if it is to be measured by the ordinary signs.

For the pulse is not rapid, it is usually not more than eighty, and its quality is not much impaired. The surface of the body is perhaps a little cold, though not generally so, at first.

Any examination of the abdomen wall is tight; it is held

with a rigidity that never for one instant slackens. The abdomen is retracted, never at this stage distended, that comes later. The extreme tenseness of all the abdominal muscles cannot be induced to relax by any change in posture; the protective muscles splint is never removed; the muscles are never off their guard. When it is remembered that the diaphragm is also an abdominal muscle, the shallow respiration is at once understood. A careful examination of the abdomen will, always reveal an area of more exquisite tenderness, and if possible of even more abduurate resistance than the rest. For duodenal ulcer perforation the area will be found to the right of the mid-line and above the umbilicus. In cases of gastric perforation the area varies, according to the position of the ulcer. Vomiting may occur at first, but usually does not; doubtless its presence depends upon the state of repletion of the stomach. It will be observed in about twenty-five per cent of all cases; it is accordingly of no value as a diagnostic sign. The liver dullness is not impaired, but percussion of the liver, or indeed of any part of the abdomen, is deeply resented by the patient.

Vomiting is found in about two-thirds of the ulcer cases. It is intermittent at first, due to accumulated hypersecretion or persistent pain. It usually occurs after taking food and is most likely to occur at the close of the day, although if severe pain

be present, it may take place at any time. If the stomach is irritable or the food indigestible, vomiting is far more frequent. Later, as stenosis develops, vomiting is more and more persistent, until finally, in advanced stenosis, vomiting as an evidence of gastric dilatation may be a daily event, the material brought up consisting of not only the last meal, but frequently recognizable debris from former meals and hypersecretion. Vomiting usually relieves the pain of ulceration and in the acute stages of the disease it may occur immediately after the ingestion of food. A study of vomiting will reveal the fact that in many cases it occurs only with acute exacerbations accompanied by hypersecretion. This is particularly the case with ulcer at the pylorus.

Ulcer of the stomach is usually accompanied by a series of vagus manifestations. In the first place, there is a hyperesthesia toward food, so that the patient is conscious of his stomach. Again, with exalted vagus tone, particularly in the early stages of ulcer, there is a slight tendency toward gastric delay with a residual or terminal hypersecretion at the end of the meal. The patient complains of fulness, distention, heart-burn, and not infrequently sour eructations. Furthermore, there is often pronounced aerophagia, also a vagus symptom. Another series of symptoms associated with this group (reflex symptoms along the vagus distribution) are a sense of substernal constriction, globus, cardiac arrhythmia, tachycardia, and vasomotor symptoms which simply

express the general lack of stability of the autonomic system. Hyperacidity is described by the patient as the dull burning ache after meals which is synchronous with the pain of ulcer. In these cases no increase over normal standards of acid may be found, but simply evidence of reduced acid tolerance on the part of the stomach.

"Symptoms in ulceration of duodenum following burns and scalds, clinically the ulcer, which occurs twice as frequently in females as in males, may assert itself with a great variety of manner. In no small proportion of the cases the ulcer has been latent, producing no symptoms, and giving no hint of its presence, during the life of the patient. At the post-mortem examination one or two ulcers may be found, and the process of healing in some may be beginning, or may even be complete. In the majority of the cases either perforation or haemorrhage or both are the first warnings given. In 20 of the 29 cases followed by Perry and Shaw one or both occurred. The case of earliest perforation is recorded by W. C. Hills ("Jour. of Mental Sci.," in 1881, XXVI, 556); the patient was a girl of eighteen who was accidentally scalded to the second degree by hot water. Vomiting occurred the next day, and eighty-three hours later she dies collapsed. At the autopsy an ulcer the size of a shilling was found on the posterior wall of the duodenum two inches from the pylorus. The ulcer involved all the coats of the duodenum, was in part adherent to the pancreas, and perforation into the general peritoneal

cavity had occurred. A case of a death from haemorrhage, the pancreatico-duodenal artery being opened, occurring four and one-half days after the injury is recorded by Caesar Hawkins ("Path. Soc. Trans.," 1851, 11, 290). Perforation may occur between the fifth and the twentieth days, and is most common on the tenth and eleventh. It is very rarely preceded by symptoms, and ends speedily in the death of the patient.

There is no recorded case of surgical treatment being adopted, but there is no reason why it should not prove successful if the condition of the patient were not too exhausted by the extent or severity of the original injury. Haemorrhage is more common than perforation; in Perry and Shaw's twenty cases there were 7 of perforation and 13 of haemorrhage. It is sometimes preceded by a sense of heat in the epigastrium or by collapse and great prostration. It has proved fatal as early as four and one-half days and as late as thirty-seven days after the accident; the day of maximum frequency is the fifteenth. In the ulcer from which the haemorrhage comes no vessels may be seen laid open, the bleeding having occurred from several small points, or rarely a large artery, the pancreatico-duodenal, or a branch of it, may have its walls destroyed. In one case related by Keate ("Path. Soc. Trans.," 1850 1, 258) the patient, a girl of six, lived seventy-five days after being severely burnt; three ulcers were found in the duodenum. This is the longest period of survival mentioned in any of the records." (10)

-CONCLUSIONS-

1. The initial stage of ulcer formation is a local damage or devitalization of the gastric cell. The process is probably in no way specific, in as much as a variety of substances totally different in their physiological effects can all produce devitalization. Bacteria of many varieties, of which the streptococcus, colon, and other members of the pathogenic group, seem most prominent. Metabolic toxins as a result of disturbances in endocrine glands; circulating cytotoxins; circulating poisons from vitiated intestinal, renal, hepatic, and other sources, as well as ingested toxins, can all produce, under certain conditions, this devitalization. That this may occur through ingestion or through the circulation seems probable from experimental evidence.

2. This primary damage is followed by secondary digestion and usually hemorrhage of the mucosa.

3. Necrosis is not necessary to destruction of the mucous membrane; it is only necessary that the gastric cells be damaged.

4. Gastric secretion per se does not produce ulcer, but in the presence of the above factors it is capable of causing an extension and persistence of the lesion.

5. Any protoplasmic poison in itself too weak to induce a lesion can do so in presence of a blood poison or altered gastric states.

6. The gross effect of cell damage with toxemia and gastric secretion is an ulceration probably chronic.

7. Characteristic Symptoms.- 1. Pain in epigastrium definitely related to food; 2. Deep tenderness; 3. Muscular rigidity; 4. Vomiting; 5. Haematemesis and occult blood.

8. Mode of onset- Types:-

1. Latent. First symptom haematemesis or even perforation, especially in acute ulcers.
2. Dyspepsia may exist for years before definite symptoms.
3. Definite symptoms occur early.

9. Pain- Rarely absent.

Site- Epigastrium, frequently just below ensiform: usually localized. Also occurs in back, at tenth dorsal vertebra; pain may shoot through, or spread round left side. In adherent ulcers, often lower in epigastrium and more diffuse. Follows, or aggravated by, Food.- Recurring fairly regularly one-quarter to two hours after meal. Not so consistent as in duodenal ulcer. Worse after solids. Duration.- Varies: often one hour, eased by alkalis or vomiting. Is not continuous, though in severe cases discomfort may be persistent. In early stages not severe. May be burning, or heavy, or in severe paroxysms. May be freedom for weeks and then recurrence.

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