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**THE ETIOLOGY OF PEPTIC ULCER WITH EMPHASIS  
ON THE ULCER DIATHESIS**

By

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the College of Medicine,  
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## HISTORY

Peptic ulcer in some respects is a disorder of modern times, for it was in the past and is at the present time unknown in the primitive and uncivilized races, and equally unknown in the animal kingdom.(1)

For the earliest record of a case of gastric ulcer we must go back to the year of 1586. (2) At that time a student of the sciences, one Marcellus Donatus, published in his "De Medica Historia Mirabili", the following case history: "Camillus Iacinus, a man of a bilious disposition, suffered at the age of 59 from a certain fever. When that was cured he was left with a bad colour, and was found to have a swelling of the spleen and an obstruction of the liver. While in this feeble condition, through careless regulation of his habits, he developed the fever once more and was reduced to a bad state of health. On the out-break of this malady he began vomiting, so that on the third day, after taking of food, for three or four hours he vomited what he had eaten and drunk, together with a great quantity of liquid matter, which was repeated on each subsequent day until his death. On every occasion he vomited no less than 3 pounds of phlegm, and frequently the amount reached as much as 5 pounds. During this time he never excreted

anything by the lower channels, although purgatives, both violent and mild, were injected, and he took laxative medicines through the upper channels; these, however, he vomited. Meanwhile, he complained of pain about the base of the stomach, and thus he continued, vomiting twice daily, till the fourth day, when he passed from life to death. The body was dissected by us with the consent of his wife and son, who were his heirs, and in the lower part of the stomach at the pylorus or lower orifice we found that the inner coating was ulcerated, and we had no doubt that this had been the cause of the malady."

There is no further reference in the medical literature to an ulcer until 1700, when Bonetus of Geneva, in his "Sepulchretum" quotes the history told by John Bauhin of a Doctor's wife, 18 years old, who had passed blood in her stools, and who died in the fourth day of an attack of peritonitis, which was shown at post-mortem to be due to perforation of a gastric ulcer.

Littre in 1704 was the first to describe a case in which death followed hematemesis from a gastric ulcer. It is in this account that we first find references made to a possible causative agent of gastric ulcer. Littre ascribed the ulcer to the strong medicines which had been given to the unfortunate patient by an inexperienced physician.

In 1729 Christopher Rawlinson presented, what he called, "Observations on a Preternatural Perforation found in the upper part of the stomach, with the symptoms it produced." "James Skidmore had complained for 3 or 4 years last past, of a violent pain in his stomach and bowels, never being able to rest in his bed at night 'till he had vomited up the greatest part of what he had eat or drunk the day before. He would often compare his pain to some great weight laying upon the region of the stomach, which he in some measure alleviated by pressing hard with his hand upon the part. He had no apparent tumour upon the part, nor was his belly more extended than usual." At autopsy he made some observations which the earlier workers had apparently neglected to record. He states, "We found the stomach perforated in its upper part, about the middle space betwixt the two orifices, wide enough to contain the end of one's finger. The whole stomach was a great deal thicker than usual: But that part next the pylorus was above four times thicker than in the natural state."

The earliest recorded description of a duodenal ulcer was written by Jacapo renada of Padua in 1793. ".....at autopsy was seen at the beginning of the duodenum a very singular oblong hole resembling an incision made with a knife. The external edge of this cleft was of considerable

thickness, to the touch it was sensibly hard and somewhat indurated and was turned in upon itself in a wort-like fashion; thus indicating that the peculiar local ulceration of the intestine was not of recent origin. The callous lips of this perforation were surrounded by a zone, which reached out for about an inch around the ulcer and shaded gradually into a lighter colour. Some blackish punctate markings were also noticed, scattered here and there in the reddish area. All the rest of the intestinal tube and stomach itself were free from morbid changes."

In 1799 Matthew Baillie, in his "Morbid Anatomy of some of the most important parts of the Human Body," gave the first clear description of the morbid anatomy and symptoms of gastric ulcer. He states that, "seldom do they resemble common ulcers in any other part of the body, but frequently they have a peculiar appearance. Many of them are scarcely surrounded with any inflammation, have not irregular eroded edges as ulcers have generally and are not attended with any particular diseased alteration in the structure of the stomach. They appear very much as if, some little time before, a part had been cut out from the stomach with a knife, and the edges had been healed, so as to present a uniform smooth boundry round the excavation which had been made." As to symptoms he

states that, "I have reason to believe that ulcers of the stomach are often slow in their progress. They are attended with pain, or an uneasy feeling in the stomach, and what is swallowed is frequently rejected by vomiting. This state continues for a considerable length of time, and is very little relieved by medicine; which may serve as some ground of distinction between this complaint and a temporary deranged action of the stomach." (2)

Although Cruveilhier of France is most generally given credit for the first clear description of peptic ulcer (3), John Abercrombie of Edinburgh anti-dated Cruveilhier by one year. In 1828, Abercrombie in his "Pathological and Practical Researches of Diseases of the Stomach, the Intestinal Canal, the Liver, and other Viscera of the Abdomen," gave an excellent account of the Symptoms of gastric ulcer. He states, "The disease may be suspected, when there is pain in the stomach occurring with considerable regularity immediately after meals, and continuing for a certain time during the process of digestion--especially if the pain be distinctly referred to a particular spot, and if there be at that spot tenderness on pressure. It may be further suspected if the pain continues severe until the patient is relieved by vomiting; but we have seen that the disease may go on to a very advanced stage without vomiting and, on the other

hand, that it is sometimes indicated by vomiting occurring occasionally, without any regular periods and with very little pain. Our chief reliance in diagnosis must probably be on a careful examination of the region of the stomach itself, with the view of discovering the existence of tenderness referred to a particular spot. We should not be deceived by the pain having remarkable remissions and the patient enjoying long intervals of perfect health, or by remarkable alleviation of the symptoms taking place under careful regulation of diet. The food must be in very small quantity, and of the mildest quality, consisting chiefly or entirely of farenaceous articles and milk. In early stages, little is probably gained by medicine given internally; in more advanced stages benefit may be obtained by some internal remedies, such as oxide of bismuch, lime water and nitric acid."

In 1855, Budd, Professor of Medicine at King's College, described the chief symptoms of ulcer in the duodenum as pain in the situation of the ulcer, which is seldom constant, and which in most cases, is felt only two or three hours after a meal.

During the last half of the 19th century, very little pioneer work was done on peptic ulcer. The malady was generally thought of as occurring rather infrequently. Occasional reference was made to it, however. In 1846



Rokitansky (4) pointed out that gastric changes could be caused by nervous lesions. From then onward, isolated observations of organic brain lesions associated with gastric hemorrhage and ulceration have been recorded (1). In 1875 Brown-Sequard showed that injury to the base of the brain produced gastric erosions. The association of subtentorial hemorrhage and brain injury at birth with gastric hemorrhage was also noted and commended upon.(5). Even as long ago as 1884, Stiller pointed out the relationship between gastric upsets and financial losses.(6)

It was not until 1901 and 1905 that Moynihan published the results of his pioneer surgical work. In these, he gave for the first, a complete account of the symptoms now known to be characteristic of peptic ulcer. (7)

The patient with gastric or duodenal ulcer nearly always gives a history of gastric disturbance, sometimes of some years' duration during which there have been remissions, often with complete absence of symptoms. The periodic character of the attack is a striking feature of the disease; the symptoms are rarely continuous. In certain cases there are no symptoms at all until signs of perforation appear or severe hemorrhage takes place. Moynihan states that, "the chief clinical symptoms of ulcer are pain, vomiting, and hematemesis, and of these the really important one is pain. The extremely significant feature with regard

to the pain is its punctuality. In the same patient, after the same meals it appears with the most exact regularity after the same intervals of comfort." In cases of gastric ulcer the pain, which after an interval follows the taking of a meal, gradually disappears before the next meal. In cases of duodenal ulcer the pain continues until the next meal or until food is taken to give ease to the wearisome pain. The rhythm of gastric ulcer is food, comfort, pain, comfort--of duodenal ulcer, food, comfort, pain--a quadruple rhythm in the former disease, a triple in the latter. (3)

## INCIDENCE

Although peptic ulcers are generally thought of as occurring almost exclusively in young adults and middle aged persons (20-50 years), the truth of the matter is that they are seen in people of all ages, in infants a few days old, and in the very aged (3).

Hurst, in reviewing 4000 autopsys at Leed's Hospital, found 117 cases of acute ulcers. Of this group he found 1 case occurring at the age of 7 months. 1.7% occurred in the age group from 1 year to 40 years. 4.3% occurred between the ages of 40 and 60. 3.8% occurred in persons between 60 and 75 years. He reported one case as occurring in a man 90 years of age. (2)

In case of chronic ulcers we do not see as wide a variation in age as seen in the acute type. The chronic ulcer is extremely rare before puberty. The average age of onset of gastric ulcer in women is 26 years, while in the male the average age of onset is 45 years.

In the case of chronic duodenal ulcers the average age of onset is approximately the same in both sexes, being 38 years in men and 39 years in women.

As a whole, however, Peptic ulcers must be considered as occurring predominantly in the younger age group. Russ (8) reports that, in a survey of the patients going

through the Mayo Clinic, of those suffering from peptic ulcer, 20% gave a history suggestive of ulcer symptoms before the age of 20. He further states that 61% of these patients had well developed ulcer symptoms before 30.

Contrary to the idea formerly held in Germany, peptic ulcers occur with much more frequency in the male of the species. Robinson (9) in his study of the subject states that the male sex is more susceptible to peptic ulcers in a ratio somewhere between 5:1 and 10:1. Hurst (2) in his work, is more conservative than this. He believes that acute gastric ulcer is 1.5 times as common in the male as in the female; while chronic gastric ulcer is only 0.8 as common in the male as in the female. In the case of acute duodenal ulcers, he finds that they occur in men 2.6 times as often, and that the chronic duodenal ulcer occurs 3.5 times more often than in women. Thus for all ulcers considered collectively, his figures show that peptic ulcers occur 2.1 times more often in men than in women.

Draper (10), while accepting the fact that peptic ulcers are more common in men, seems to think that they are more common in the male because of his masculine characteristics, for he demonstrated a strong masculine component in those women who were susceptible to G-D ulcers .

He also found that in the members of his ulcer patients' immediate families, there was a sex distribution in the ratio of 138 males to 100 females. He concluded from this that, "there is a decided tendency for ulcer families to produce a preponderance of males."

Rivers (11) in attempting to discover if there was any relationship between peptic ulcers and different races, made a study of 200 negroes living in central Texas. All types were deliberately chosen so as to get as true a cross-section of the negro population as possible. He found no instance of ulcer complicated by perforation, obstruction or hemorrhage. He states that, "in only one instance was there sufficient evidence in the history to make a diagnosis of peptic ulcer. This instance occurred in a fretful, nervous, worrying negro, whose wife stated he was constantly worrying about himself, taking medicine and complaining." This investigation would tend to show that ulcers are a rarity among the colored population.

Adams (12) in writing on the same subject, says that racial immunity is not a fact. He believes that the lack of ulcer incidence in the Southern negro is due to psychological differences from the white race. In a series of industrial negro workers, a resume shows the frequency of ulcer to be similar to that in the white race, under

similar living and working conditions. It is only those negroes who are out of their agricultural environment and facing the complexities of life who have acquired the habit of worry and it is in this group only that we see an incidence comparable to that in the white race.

Dr. Bergsma (13) reports frequent ulcers in the colored race in Abyssinia. These he attributes to the native diet, which consists of sour bread and 50% capsicum or cayenne pepper--a mixture which was strong enough to cause blisters on Dr. Bergsma's lips. "The ulcers produced in these people are multiple and occur all over the stomach with the formation of fibrotic rings." However, Robinson (14) states that "there is absolutely no resemblance to the typical single ulcer in its common location along the lesser curvature and the first inch of duodenum,"--the type with which we are concerned in this paper. Neither is peptic ulcer found in the lesser pigmented races of the world, either before or after their contact with civilization. Hartman (15) while working among the Indian tribes of old Mexico, found them free from ulcer, although their hygienic conditions are extremely bad, and their diet is coarse and deficient.

Dr. McCarrison (16) reports that "in nine years of practice, he performed 3600 operations on primitive tribes

in the Himalaya Mountains and has never found ulcers, mucous colitis or appendicitis."

Generally speaking, occupation has little, if any, effect on the production of peptic ulcer. Though this is an idea held by most practitioners, Hurst, (2) finds that there is apparently a special liability among soldiers and sailors and to a lesser extent among the medical profession for the occurrence of ulcers. He points out that in the New Lodge Clinic in England he found that 42.2% of gastric ulcers occurred in soldiers and sailors, and 7.7% occurred in doctors. Of duodenal ulcers 15.5% occurred in soldiers and sailors and 16.5% in doctors. In this particular clinic, then, 18.1% of all cases are divided among all other occupations, while 81.9% of all cases are found among the medical profession and among the men of the military service.

Although it is very doubtful that these figures are a true representation of the occurrence of peptic ulcer throughout the civilized world, or even in England alone, they are sufficiently striking to impress upon one that occupations which involve more than the ordinary mental strain, worry and physical fatigue very likely show a preponderance of peptic ulcer cases.

The medical profession, as a whole, is well convinced that peptic ulcers develop far more often than they are

clinically recognized. The frequency of occurrence varies markedly in different countries, being recorded as 0.2% in Russia, 1.3% in North America, 5% in England and Germany and 16.7% in Denmark. Furthermore, this condition is less prevalent in beer-drinking southern Germany than in "Schnapps" drinking northern Germany. (3) One would gather from this that a nation's temperance habits might influence the occurrence of peptic ulcer; this I do not believe to be true, however. Rather, I would reconcile it with the fact that southern Germany includes the majority of the agricultural district of the country--the vineyards, farms, orchards, and market gardens, while northern Germany embraces the industrial centers, factories, mills, etc. In the former instance one will find the more easy-going type of individual, one less subject to strain, worry and emotional upsets. In the latter case one finds a person more subjected to the stress and strain of modern civilization--the job holders--the ones who must produce a certain amount daily, and who must meet a variety of emotional situations uncommon to the rural communities. The same line of reasoning would apply to Denmark also, a country where one acquainted with their social conditions would least expect to find a high incidence of peptic ulcers, and least of all to attempt to explain it on an



emotional basis. However, the Danish people as a whole are the constitutional type which is prone to develop the disorder, the doer rather than the dreamer, the active-- body and mind rather than the lethargic and more contented, contrasted with the more easy going type characteristic of the Southern European.

The same argument can be used to explain the frequency of the disorder in England, Russia and North America. In the United States, the preponderance of ulcer cases are seen along the Eastern seaboard, and in the large industrial centers of the west and middlewest. Furthermore, the disorder is not as severe in the person more or less common to the rural communities. Russ (8) reports that the important clinics in this country that deal with people from rural communities and small towns get about 90% satisfactory results in duodenal ulcer cases and about 80% in gastric cases. Other clinics equally good, dealing with a different type of patient show the most disappointing results. Clinics in Western and Southern cities show better results than--for example-- Mount Sinai Clinic in New York. In Mount Sinai the predominating types are distinctly vagotonic individuals. It is their temperament, physical make-up and training, and the environment in which they live, that determine their predisposition to the development of chronic peptic ulcer and are responsible for the

poor results of all treatment.

"Ulcer incidence is on the increase," says Davies(1). The number of deaths from ulcer has increased considerably since 1921, and since the mortality is relatively low, we can assume the number actually suffering from the disorder is also steadily rising. He reports that "in England & Wales in 1921 there were 2656 deaths from ulcer; in the same countries in 1931 there were 4235 deaths from the same cause." Comparable to this, also, is the increase in incidence in America. During the last decade, standards in America have changed. Competitive requirements have become more intricate, and better, keener, and more intensive methods are necessary for those who seek to succeed. Unfortunately, this speed and hurry and recklessness develop a momentum and pace which if it continues eventually is bound to produce a nation of nervously and physically exhausted persons.

Curiously enough, the desirable virtues of the modern, intensive, aggressive American, the characteristics which have been eulogized and designated as the cardinal marks of American successes, are precisely the characteristics so often reduplicated in the ulcerous type of patient.

Brown (3), writing in Cecil's book of medicine, is rather casual in his treatment of heredity as a factor in causing peptic ulcer. He states that "heredity plays only

an occasional etiological role."

Macklin (17) defines heredity as "those qualities, be they normal or abnormal, which are passed on in the germ plasm from parent to child." She states that, "it is entirely safe to go upon the assumption, that all diseases of the gastrointestinal tract which are not infectious (typhoid, dysentery, etc.) or due to injury (knife and bullet wounds, perforation by foreign objects, rupture, etc.) are inherited."

Robinson (9) found a definite hereditary factor in a large percentage of his cases. He says that, "all (i.e., the medical profession) have seen patients with fathers, brothers, mothers, etc., suffering from the same malady, and no element of chance could duplicate such familial susceptibility." It is easily measurable in the ulcer patient because the father or some distant ancestor transmits not only the ulcer "syndrome" to his son, but likewise his body build and diseased personality.

Hurst (2) in his extensive experience finds that patients with gastric or duodenal ulcers give a family history of indigestion much more frequently than patients suffering from other disorders. A history of ulcers or gastric disorders in parents, brothers or sisters of ulcer patients occurs at least 5 times as often as in patients with other disorders.

Draper (10) says that, "to scientifically study a disease it is necessary to uncover trends in the constitution of the family, and since total personality is an essential factor in causation of disease, it is necessary to observe the elements from which personality arises. Hereditary influences play a basic role in the final determination of the man, his morphology, psychology, strength, and his weaknesses in all systems of the body. These are strongly conditioned by his surroundings. The resultant between inherited qualities and the modifying influences from the world about him make up the finished individual." In his series of cases he found that in the ulcer families 62% were found with a heredo-familial weakness of the gastrointestinal tract; 15% of the families of healthy persons gave such a history. Assuming there is a hereditary influence, the tendency is in the form of a pathologic inferiority of the gastrointestinal tract. (Agrees with Macklin).

Ruhman (18) pointed out that definite ulcer is more frequent among the siblings and descendants of the patient, and indefinite stomach trouble is commoner among the ascendants.

Aschner (19) concluded from her studies of 120 ulcer families that the gene for stomach inferiority is a recessive, but is not sex-linked. In cases where both parents were affected, 50% of the off-spring also were affected.

If one parent is sick and the other has a sick heredity, 25% of the off-spring are affected. If both parents are well but show a sick heredity, 10% of the off-spring are affected.

Draper (10) does not agree with this; he says, "It is hard to conceive that a specific gene weakness is responsible for so complicated a disturbance of the vegetative Nervous System." Nor does he accept the condition as a recessive mendelian phenomenon in view of the variability of the external influences that may determine its expression. He found that, "ulcer families do produce a preponderance of males, and these males are of a long thin type." He states that in those maladies (such as peptic ulcer) in which one sex is definitely more often affected than the other, the selective susceptibility may very well be looked upon as a secondary sex character."

## ETIOLOGY

Since the turn of the century an important change in the phenomena of disease has occurred--the seriousness of infectious diseases has been undergoing a remarkable decline, and strains and stresses, especially affecting the nervous system have been on the increase. (20) The disorders resulting from this change may not lead directly to death and thereby affect statistics, but nevertheless they are capable of causing an immense amount of distress and pain.

Since bacterial agencies have become less potent and disturbances of nervous functions have become a greater liability, we should begin to recognize the change. Fears and worry, persistent hatred and resentment--what pathology have they? Teachings and practices of medical schools and hospitals make it difficult for the average practitioner to contemplate disease etiology on a basis of purely neurogenic factors. They have been taught to deal with concrete and demonstrable bodily changes, and are very likely to minimize or neglect entirely the influence of an emotional upset. Rather, such a patient, who complains of it, is dubbed neurotic. But emotional upsets have concrete and demonstrable effects in the organism.

The sympatho-adrenal system, though organized for diffuse and widespread action, may influence excessively

separate organs or functions. An intense emotional shock, or prolonged emotional strain, may result in one or another of the viscera becoming so subject to sympathetic impulses that even slight perturbations in the daily routine will have noteworthy effect. (9) Emotional dyspepsia--so called--, including disturbances of the gastric secretion and motility, due to worry or anger; spasm of the cardiac and pyloric sphincters, readily understandable because both sphincters are tightened by sympathetic impulses; vaginismus, also explained by sympathetic innervation of the encircling smooth muscle are pertinent instances.

These emotional upsets, especially affect the disorders seen in the gastrointestinal tract, and particularly in the disease entity which we recognize as peptic ulcer. Though there appears to be little agreement on a single etiological cause of ulcer, most authors recognize a complexity of factors as being involved. Of the many exciting agents mentioned in the literature, there is one--the constitutional factor--which is more or less commonly emphasized by practically all writers.

As pointed out earlier in this paper, previous investigators had noted the occasional association between gastric upsets and emotional strain. Physicians and Surgeons have been impressed with this for over 90 years. Hauser(21) says that Siebert wrote on the subject in 1842, Grunsberg

in 1852, and as far back as 1828 Camerer produced ulcers in rabbits by injuring the vagus and splanchnic nerves. In 1846 Rokitansky (4) pointed out that gastric changes could be caused by nervous lesions. In 1875 Brown-Sequard showed that injury to the base of the brain produced gastric erosions. The association of subtentorial hemorrhage and brain injury at birth with gastric hemorrhage was also noted and commented upon (5). As long ago as 1884, Stilller pointed out the relationship between gastric upsets and financial losses(6). In more recent years Cushing (22) has pointed out that ulcer is rather commonly seen in patients dying with brain tumors and he reports 3 cases of perforated ulcer, following operation for brain lesions. Robertson and Hargis (23) observe that it is common in patients dying with exophthalmic goiter, a disease which is associated with great irritability of the nervous system.

- Many articles call attention to the role of emotional disturbances in gastro-intestinal disease. Patients often volunteer that emotional upsets at home or at work may initiate cramp-like pains, gas, fullness and eructations, or other dyspeptic symptoms. These motor, digestive, and secretory functions of the gastro-intestinal tract usually disappear when the mind is again at rest.

There is now increasing evidence which supports the contention that the "constitutional factor" has a direct



causal relationship to peptic ulcer, but in spite of this, hyperacidity still remains most widely accepted as the cause of this disease. Robinson(9) says that, "the prevalent therapy of the present day consists of acid neutralization-- a treatment essentially unaltered since the 16th century." Hyperacidity may be intimately associated with peptic ulcer as one of the important etiological factors, but in light of more recent observations the constitutional factor as a role has been grossly underestimated. The physiologic, the anatomic, and the neurogenic portion of the individual considered collectively, if not the primary etiological agent in the cause of peptic ulcer, is at least the most important factor and should be considered as such. Hypersecretion with resultant hyperacidity should be thought of as an associated complication of, and dependent upon, an exaggerated constitutional factor; for it is after the ulceration process has well begun, that the gastric acidity may play an important part.

Such is not the view of many investigators of the present day. Smithies (24) in 1920 said, "about 10 years ago I became convinced that any treatment of peptic ulcer based on fluctuating gastric chemistry was, as Leube, Rokitanski, Riegel and others have shown, more than half a century ago, little more than guesswork, unscientific, not justified by any known published records and might in fact prove harmful

to patients." While this comment does not refer directly to an etiological agent, it is safe to infer that Smithies did not consider hyperacidity of any particular significance as a causative factor. Black (25) asks, "Why should hyperacidity be an etiological factor any more in ulcer than achylia should be regarded as the cause of pernicious anemia?"

Conversely, there are men equally as well qualified who support the acidity theory as the primary cause of peptic ulcer. Probably the most outstanding one is A.F.Hurst, who says there is a general ulcer diathesis, which renders an individual liable to the development of a chronic ulcer, and a special diathesis which determine whether the ulcer develops in the stomach or duodenum (2). Part of this diathesis is believed to be a condition in which the reaction of the blood and tissues is more acid than normal. In 77 normal individuals it was found that the H-ion concentration of the blood varied between 7.54 and 7.64 with 7.59 as an average. In 89 patients with gastric or duodenal ulcer it varied between 7.46 and 7.60 with an average of 7.55.

If alkalis were given by mouth to the ulcer patients every two hours for several days, the urine finally became alkaline, but more slowly than in normal individuals,

as the tissues appeared to retain sufficient to neutralize their abnormal acidity before the excess was excreted.

As 22 patients, who had had a partial gastrectomy performed for gastric ulcer a year or more before, still showed an abnormal acidity of their blood and tissues, it seems probable that the latter constitutes the ulcer diathesis and is not a result of ulcer.

Balint (26) obtained some evidence that an abnormally acid reaction of the blood and tissues increases the exudation and exerts an unfavorable influence on the development of granulation tissue in experimental ulcers. He also showed that the blood from the veins in the neighborhood of varicose ulcers of the leg is abnormally acid, and that injection of alkali in the surrounding tissues greatly accelerated healing. An acute ulcer of the stomach or duodenum of an individual with the biochemical peculiarity constituting the ulcer diathesis tends to become chronic.

The other portion of this ulcer diathesis described by Hurst includes the actual anatomy of the stomach and intestinal tract. A large proportion of healthy men with hyperchlorhydria have also short stomachs. These are the individuals who Hurst says possess the hypersthenic gastric diatheses--an inborn variation from the average normal, which manifests itself in a short stomach with active peristalsis and rapid evacuation and in hyperchlorhydria

with digestive hypersecretion. Though this condition is compatible with perfect digestion, he believes this is the essential predisposing factor in production of duodenal ulcer. It is, like duodenal ulcer, more common in men, and is often present in several members of the same family. He found hyperchlorhydria in 61% of cases of duodenal ulcer in the New Lodge Clinic statistics. "The characteristics of hypersthenic stomachs are present in almost 100% of patients who develop duodenal ulcers."(2)

Bennett (27) found that the stomach contained food throughout the day, except for a brief period before lunch, when ordinary meals were taken at the ordinary times. The last traces of the evening meal do not leave the stomach until an hour or two before breakfast. The hypersthenic stomach is, on the other hand, empty for several hours each day. If 3 meals are taken a day at regular intervals, the stomach is empty 5 hours during the day and 8 during the night. In normal individuals it is empty perhaps 1 hour during the day and 5 during the night.

In most people a little gastric juice is continually secreted during the few hours when the stomach is empty, but Carlson (28) has shown that this is deficient in hydrochloric acid, unless a more abundant secretion, rich in acid, is called forth by hunger. In individuals with

hypersthenic gastric diathesis, however, there are several waking hours in which the stomach is empty, and in these the continuous secretion of gastric juice is probably more abundant as well as more acid than in most normal people. In the absence of food little peristalsis occurs in the stomach unless the individual is hungry. Then, in the average normal man, undiluted gastric juice rarely enters the duodenum and when it does, its acidity is low, but in people with the hypersthenic gastric diathesis the undiluted juice leaves the stomach for several hours out of 24. In a man with this diathesis there are several hours in every day during which the mucous membrane of the duodenal bulb is continually in contact with the undiluted and exceptionally acid juice, but this results in no harm except under certain conditions, so that such a man may go through life without even having the slightest digestive disturbance. The diathesis, however, renders the individual liable under certain conditions to develop duodenal ulcer. A duodenal ulcer, Hurst concludes, cannot develop in anybody who does not have this diathesis.

Hurst describes another gastric diathesis which he terms hyposthenic. In these individuals the acidity is above the normal, and hyperchlorhydria is present in 32.1% of these people. This diathesis, however, is never associated with a short and rapid emptying stomach, but

in the majority of cases is longer than average, but having normal tone.

In the person with a long stomach the condition known as orthostatic hour-glass stomach is observed, a condition in which the middle of the stomach forms a definite obstruction to the onward passage of food, so long as the erect posture is maintained. As a result the mucous membrane is subjected to much friction, especially on the lesser curvature, where most of the gastric ulcers occur. Chamberlain (quoted by Hurst) found short stomachs in 17% (all men) of 500 normal persons and 7% in women, while a long stomach was found in 3.6% of men and 15% of women. Since a short stomach is associated with duodenal ulcers and a long stomach with lesser curvature ulcers, these figures explain in part the greater frequency of duodenal ulcer in men and of gastric ulcer in women. Hurst also points out that it is not merely the motor and secretory functions of the stomach which differentiate hypersthenic diathesis from the hyposthenic type. It has been found that a short stomach with hyperchlorhydria occurs particularly in men of an athletic type with relatively short, broad chests, whereas a long stomach with hypochlorhydria occurs especially in men of less vigorous type with relatively long narrow chests.

Held (29) also allows the acidity theory an important place in the etiological role of ulcers. He states that peptic ulcers are most frequently accompanied by hyperacidity and when no hyperacid condition is demonstrable, symptoms of a higher acid are often present. Because in some there is normal acid, in others sub or an-acidity does not indicate that hyperacidity was not present before the ulcer started or during its early period. It may simply signify that some other factor was present, which brought about a diminished acidity. He is of the opinion that the hypersecretion and hyperacidity are the result of unbalance in the autonomic nervous system. Underlying vagotonia may produce these conditions without presence of ulcer, but where there is underlying tendency or diathesis to ulcer, such hypersecretion and hyperacidity greatly favor its occurrence. An imbalance in the autonomic nervous system may explain why existing hyperacidity changes to sub or an-acidity. At certain times, the vagus influence predominates; at other times the sympathetic. During early active life, the imbalance is on the side of the vagus. Later in life (phlegmatic period) the sympathetic predominates.

Neither can we ignore the fact that, working on the acidity theory, ulcers have been produced in lower animals. Mann and Williamson (30) produced ulcers in

dogs by severing the pylorus and connecting it with the duodenum or by connecting the stomach with the jejunum, and whenever the acid contents were allowed to flow freely into the duodenum or jejunum an ulcer resulted, even when the greater part of the stomach was cut away so that only a small part of the fornix, containing acid secreting glands, remained. They found that if the entire stomach was removed and the esophagus was connected with the jejunum or duodenum, no ulcer resulted. They also noted that the ulcers thus formed had a tendency to heal when acid was discontinued and that this healing tendency was disturbed when the secretions were again allowed to reach the ulcerated area.

Some doubt, however, is thrown on the validity of the results of these artificially produced ulcers. Robinson(14) in writing on the etiology of peptic ulcer states that, "peptic ulcer is never found in lower animals and its production artificially is debatable. Chronic peptic ulcers have never been consistently produced experimentally in the gastric mucosa by any method. By circuitious anastamosis, some chronic ulcers have been produced but their value is open to question. They are atypical and distort normal anatomy and physiological function to so great an extent as to make conclusions of doubtful value when applied to man."



Emery (31) in a survey of all peptic ulcer patients at Peter Bent Bringham Hospital up to January 1932-- a total of 1435 cases--minimizes the role of hyperacidity. It is generally believed that a high acidity is a definite complication to the treatment of peptic ulcer. However, in this survey, he was unable to determine any difference in the percentage of satisfactory results in patients with high, low, or moderate acidity. He also found that the incidence of complications was the same irrespective of the amount of acidity. It was found, however, that the patients with a hypersecretion responded very poorly to all treatment.

Durante(32) in a series of 75 experiments studied 17 possible ways of producing ulcer experimentally and arrived at the conclusion that, "disturbed innervation alone, without any additional trauma, or infection, will suffice to create in animals lesions presenting all the essential characteristics of acute and chronic ulcer in man."

Robinson (9) goes so far as to say that hyperacidity cannot be a factor of any great importance since 80 to 90% of all gastro-duodenal ulcers develop on the duodenum where the medium is essentially alkaline. Katsch (quoted by Robinson) in his experiments finds that the medium is alkaline promptly after secretion by Brunner's glands and that neutralization of the hydrochloric acid in the

stomach is not accomplished by regurgitation of duodenal contents as previously thought--therefore 9 out of 10 ulcers have their origin, reach maturity and disappear in an alkaline medium.

Conversely, it may be pointed out that nearly every gastric ulcer heals in an acid medium. If acid were the cause, one would expect the ulcer to heal with a lowered acidity. As pointed out before, Emery was unable to determine any difference in the percentage of satisfactory results with low, moderate, or high acidity. Also, the incidence of complications was the same, irrespective of the amount of acid present.

It is well known that many normal persons show high concentration and an increased volume of hydrochloric acid who do not have an ulcer or any dyspeptic symptoms. If hyperacidity and pepsin can produce ulcers why is approximately 80% of the mucous membrane of the stomach immune to ulceration? 95 % of chronic gastric ulcers are found in a narrow strip of the lesser curvature near the incisura. They seldom develop in the fundus or cardiac region or in the large posterior part of the stomach. This should be of some significance when one considers that the acid secreting cells are found in the fundus, where chronic ulcer seldom, if ever, occurs and fewer parietal cells are found on the lesser curv-

ature where most ulcers do occur.

Often patients present themselves with the complete symptomatology of gastro-duodenal ulcer, but with no X-ray evidence. Many have been operated and no ulcers could be found. But the hyperacid curve was identical with that of an ulcer patients. Therefore, we have a patient with hyperacidity, all symptoms and signs, and a normal mucous membrane in the stomach and duodenum. We must conclude that excess acid is unable to erode the stomach wall along the lesser curvature and duodenum in patients not only susceptible but suffering from the ulcer syndrome. Robinson (9) states that, "in view of this, one must assume that the pathology of the ulcer progresses independently of the acid-pepsin factor."

We may then, at this time, briefly set down some of the salient features of gastro-duodenal ulcers:

1. Peptic ulcers never occur spontaneously in lower animals, and their production artificially is debatable.
2. The pure negro, indian and the more primitive races are astonishingly free from gastro-duodenal ulcers.
3. There is a definite hereditary factor in a large percentage of cases.
4. Ulcer is principally a disease of the younger age group, and is in some way connected with modern life.
5. The male sex is more susceptible to peptic

ulcer, in a ratio varying somewhere between 2.1:1 and 10:1.

6. There is sufficient evidence to support the theory of an ulcer diathesis.

In studying the role of the emotions in peptic ulcer one must consider the constitutional make-up of the individual.

The investigation of a human beings constitution must include all the gross and subtle details of his environment. The problem would be much simpler if the visible universe comprised man's only environment. But because of his imaginative powers, his fears, his angers and worries, another vast yet entirely personal universe supplies an equally complex environment to which he must also make adjustment. To the pressure of the physical world he responds with consciously directed muscles. Such muscles are chiefly concerned with the life of his relation to environment. The other variety of muscle, nonstriated and not under conscious control, carries out the vital processes supporting the life of inner existence and procreation. This type of contractile tissue is strongly influenced by emotions. It is not necessary that the emotions be perceived in consciousness to be effective in modifying the function of organs equipped with smooth muscle. Ordinarily, if the organism is in good emotional equilibrium, the body machinery

moves easily at its work, quite automatically and unnoticed by the individual. But if there is a disturbance no matter how minute, of the balance between the human animal and either of its two universes, signs of that disturbance are immediately apparent. Consequently, we may say that disease is the expression of maladjustment between the organism and its surroundings--an overthrow of the delicate structure which Draper (10) terms the "Man-environment-unit."

The gastrointestinal tract is perhaps more than any other physiologic system exposed to blows from ponderable and imponderable worlds. Physical, chemical and thermal onslaughts alternate with the rapid fire of emotions, such as fear, anger, jealousy and sexual confusions. Yet no two stomachs and no two gastrointestinal tracts react similarly to any of these menaces; this is because the whole man is the digestive mechanism, and as the whole man responds to the pressure of his environment, so will any of his parts respond, for each cell and system within him is stamped with his special mark--the mark which is his personality.

Assuming that there does exist such a thing as an ulcer personality which predisposes certain individuals to the development of ulcers, we can best discuss this diathesis under the panels of personality, namely; anatomy, physiology and psychology.

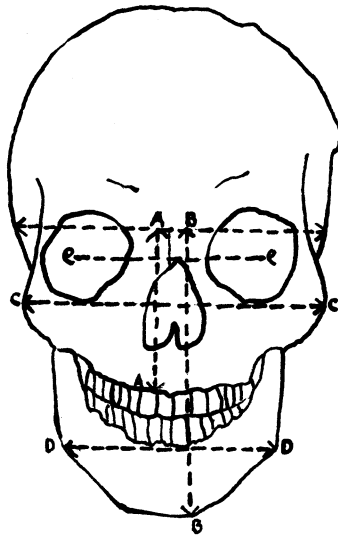
## ANATOMICAL PANEL

We have seen previously that Hurst (2) described an anatomical type which he called the hypersthenic gastric diathesis and intimated that it is an inborn variation from the average normal which manifests itself in a short stomach accompanied by active peristalsis and a rapid evacuation, and in hyperchlorhydria with gastric hypersecretion. Although he admitted that the condition is compatible with the perfect function of the digestive organs, he expressed the belief that it is one of the essential predisposing factors in the production of duodenal ulcers. He stated that persons with long stomachs, if exposed to the exciting causes of ulceration are likely to have gastric rather than duodenal ulcers.

It is believed by many investigators that the ulcer patient presents a typical facial design. Draper (33) has probably done more actual work along this line than any other man. By the use of special and very exact instruments he has made many facial measurements and has attempted to correlate these measurements with different diseases.

In analyzing the variation between human faces it is necessary first to define what constitutes the face. Anthropometrically, the face is limited superiorly by a

horizontal line drawn through the nasion. In this more restricted sense, the face is a more or less squat horizontal truncated oval; the facial diameter is always of greater length than the facial height.



Facial measurements: aa, nasion prosthion (upper facial height); bb, facial height; cc, facial diameter; dd, gonial diameter; ee, interpupillary space.

The measurements which Draper used are the following:

1. Nasion prosthion, from nasion to the maxillary alveolar point.
2. Facial height, from the nasion to the menton. (mental tubercle).
3. Facial diameter, the widest interval between zygomatic arches.
4. Bigonial diameter, the distance between angles of mandible.
5. Interpupillary space, taken to the center point of each pupil.
6. Infradental menton, distance from mandibular alveolar point to the mental tubercle.
7. Nasal height, from nasion to lower border of nose, where it meets the lip.

8. Nasal breadth, the distance between the outer surface of the alae nasae.
9. Palpebral length or length of eye slit.
10. Palpebral breadth, the greatest distance between upper and lower lids with the eyes fixed on a distant point.
11. Ponderal index, the relation of height to weight.
12. Subcostal angle, the angle of diverging costal margins.
13. Gonial angle, the angle formed by ascending and horizontal rami of mandible.

It is unnecessary to list here the actual measurements which Draper found to be characteristic of the ulcer group, since, from a point of clinical observation such measurements are useless. However, of the above examinations, he states that the ponderal index, the gonial angle, and the subcostal angle of the ulcer patient are so striking and so constant that they are of clinical significance. The average of the ponderal indices for the ulcer patient was found to be 33.3, an index considerably less than the average for the normal person. The subcostal angle averaged 34.1 degrees for these patients, which is much more acute than in the normal person. The gonial angle was found to be quite large and averaged 127 degrees in the ulcerous individual.

As to the facial characteristics, the good clinician sees more in the face of his patient than can be measured



by instruments. The element which first and most readily catches the eye is that produced by the distribution of the soft parts and by the muscles of expression. Almost any degree of form and expression may cloth the same bony framework. A second element which one should keep in mind is the strong impression produced solely by differences in actual size; and thirdly, one must consider the effect of relative size or in other words-- true proportional differences.

When one becomes familiar with the detailed characteristics of the facial design, it is not difficult to recognize. In general ( based on Draper's measurements and clinical observations made by him and others) this face is broader in its upper half and tends to taper rather sharply to a small pointed chin. The eyes are separated by an interpupillary distance of from 60 to 62 mm. which is the average for the general population. The relation between the interpupillary space and the facial diameter is the most satisfactory from the standpoint of appearance of all the disease groups. The eyes are neither too close nor too far apart. The palpebral fissure is consistently wide, often enough to show the sclera above the iris. This character is especially interesting in view of other evidences of tension of the vegetative nervous system. This doubtless accounts for

the alert, watchful expression, which conveys a suggestion of continual apprehension, mixed with defiance, common to the ulcer type when the person is in good health. When gastric symptoms are severe and the entire organism is reduced from the effects of indigestion and a scant diet, then the wide eye slit produces the characteristic expression of exhaustion and despair.

Although the lower part of the face in general tends to be smaller than the upper, it presents significant details of structure in both the upper and lower jaw.

The dental ridge of the ulcer patient, usually forms a U-shaped oval, and the vertical cross section shows an arch of similar design. The incisor teeth extend in slight labial version from the anterior alveolar margin. The palatal arch sweeps up in back in a low slanting curve to the posterior edge of the palatine bone. The teeth are usually of a clear pearly quality. The lateral incisors are definitely narrower than the central, the biting edge is sharp and the profile curve of the bite line is waving, with low points at the molars and incisors.

Stenbuck (34) although not as scientific as Draper in writing on the facial characteristics of peptic ulcer, never-the-less gives a very graphic description of the facies which is much more practical for the

clinicians use.

He describes the general form of the face as being rugged and representing, apparently undeniable firmness. The lines are not gracefully rounded, but are straight and almost cruel in their fixity, the curves having been replaced by sharp angles. The facies is as if modeled roughly in clay with the thumb and as if no attempt had been made to smooth the edges. He further states that the resemblance to clay lies also in the apparently lifeless texture of the skin which, whether pale or ruddy, is uniformly lacking the variations in complexion that may be found in health.

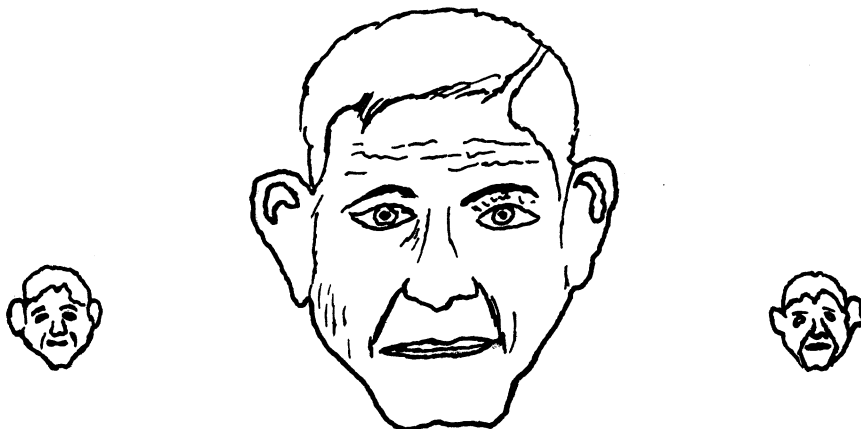
The forehead is described as being rather low and broad. When wrinkled, in spite of emaciation, the skin is thrown into thick heavy folds, due to its thickness and lack of elasticity.

The ears are large and protruding. They are not nicely molded and are rounded and lack well defined markings and lobules.

The mouth is very broad with thin lips which appear as if firmly pressed together. The cupid's bow formation is lacking. The mouth gives the general impression of a straight line with a slightly downward curve at either end.

The nasolabial fold is a very important feature. It

is not represented by a mere cleft, but is a substantial cord-like structure, so distinct that it often may be grasped and rolled under the fingers. It may even be pendulous. It does not taper down as it nears the corners of the mouth, but broadens abruptly to form a small nipple-like protuberance.



An ideal facies, combining all the characteristic features. The dominant wedge-like jaw is emphasized in A, and the hexagonal outline of the nasolabial folds and chin delineated in B.

A hexagonal figure is formed by the nasolabial folds, the chin and the nose as shown in the above diagram. This forms a literal and figurative keystone of the ulcer facies. The sides formed by the lower border of the chin and by the nasolabial folds are the most prominent. The hexagon is bisected horizontally by the straight wide line of the mouth.

If the face is viewed as a whole, we see the face of a fighter, a face which, through persistent severe pain and discomfort and self denial, has been modeled into

this definite mask that lacks softness and mobility. It shows undernourishment. It does not reveal whatever sensitiveness or emotional capabilities the patient may have, for the supple lines usually formed by the muscles of the face have been ironed out by an edema.

"The above description of the features" says Stenbuck, "were of the disease in its height, and the intensity of these signs runs parallel with the acuteness of the disease and does not depend on the mere chronicity or duration of the illness. With periodic cessation of symptoms or after successful surgery, the facies change strikingly, due to better nourishment and disappearance of the edema.

From the standpoint of anthropometry, the significant features of the trunk and extremities are the low anterior-posterior diameter chest index, the narrow subcostal angle, the relatively short arms and eunuchoidal trunk. The hands are often slender and long fingered, the nails are narrow, long and laterally curved and in the gastric group often display well marked lunulae. The duodenal cases present in general the same morphology, but almost every detail is slightly heavier or coarser. The trunk is thicker set, the subcostal angle is not so consistently narrow and the extremities are less lanky and eunuchoidal. The nails are flatter and squarer and show smaller or absent lunulae. The pilous system is

usually not very strongly developed in either group. Though in males, the hair distribution follows the so-called masculine distribution, lightness of growth and occasional absences occur in zones that are characteristically bare in the female.

The facial hair is almost always vigorous and abundant especially in the gastric group. There are also other subtle indications (besides hair) which emphasizes a female component in these patients--the slightly sloping shoulders, more marked in the duodenal group, short arms and fullness over the trochanteric region and above the gluteal masses, and the curve of the outer margin of the leg below the knee.

## PSYCHOPHYSIOLOGICAL PANEL

Due to the fact that the psychological and physiological panels of an individuals personality are so closely interwoven, these two factors can best be combined under one general heading.

Many investigators have observed that certain persons are particularly liable to the development of peptic ulcer. This has lead to the postulation that there must be some definite anatomic ( as previously described) and physiologic abnormality which increases the susceptibility of these persons to the development of ulcer.

There are certain biologic phenomina to which man alone is heir. During periods in which the general health of patients has been undermined, the liability to development or recurrence of peptic ulcer seems to be appreciably accentuated. The periodicity and intermittancy of symptoms in cases of ulcer are frequently determined by the variability of psychophysiologic influences incident to daily experiences of the patient. During periods of great emotional strain and of prolonged and unrelieved worry, and during long periods of mental or physical fatigue or of strain subsequent to catastrophies of any sort, the symptoms are likely to originate or to reestablish themselves.

Rivers (11) has pointed out that it is most difficult to accomplish the cessation of the manifestations of the lesion if the patients continue working under tension or if they are constantly disturbed, worried and restless while under a regime for ulcer in a hospital.

Occasionally patients who present a syndrome suggestive of peptic ulcer do not have peptic ulcers. These patients are of the same type as those who are likely to have ulcers. Similarly the pseudosyndrome of ulcer is likely to arise under comparable psychophysiologic disturbances. There is further similarity in that the pseudo-ulcer syndrome usually disappears promptly with the prospect of a vacation or cessation of active work and worry.

The pertinent analogy between these syndromes and the type of patients who experience them and their general behavior extending into the minutest details of symptoms suggests that the disturbance which is at the root of the entire syndrome is identical in both instances, and that this crucial derangement is in the nervous system. Factors which seem capable of influencing periodic reactivation of ulcers, which can prevent healing of ulcerous lesions and which at times are entirely capable of bringing forth symptoms mimicking the



apparent ulcer syndrome, although there are no demonstrable lesions, must be of pertinent significance in the cause of the syndrome. The variability of the degree and of the intensity of these psychophysiologic tendencies probably represents the fluctant which determines whether or not and when the syndrome will arise.

It is conceivable that when ulcer is absent or when the defense reactions of the tissues are normally intact, a syndrome similar to that experienced in ulcer and entirely dependent on the disturbed neurogenic factors may develop. In the event of prolonged persistence of nervous hyper-irritability and consequent accentuation of the aggressive factor, or in presence of increased vulnerability of gastric or duodenal tissues, it is suggested that ulcer may easily be the final result. Quiescence or activity of the ulcer syndrome could be an alternating condition dependent on fluctuating psychophysiology with its resultant mechanical and chemical gastrointestinal alterations. Marked elevation of the acid-pepsin values is often noted during periods of excitement and tension, and it may be that one of the mechanisms of reactivation during these periods is related directly to chemical conditions affected by the nervous system.

It is possible that the neurogenic factor is of significance because it produces other conditions, such

as markedly prolonged, persistent attenuation of the high values of acid and pepsin, and for this reason such patients are increasingly vulnerable to the development of peptic ulcer.

Muller (quoted by Hurst) in 1922 drew attention to the fact that patients with gastric ulcer were generally subjects of, what he called, the vasoneurotic diathesis, a congenital and often inherited condition of disharmony in the structure and function of the peripheral blood vessels. The arterioles, capillaries and venules of the skin and especially of the mucous membrane of the lips, when examined with the capillary microscope, show the greatest irregularity in their course, caliber and anastomosis, instead of the normal regularity. In some places they are contracted, in others dilated into varices. This spastic-atonie condition must result in great irregularity in the blood supply with a tendency to stasis. He suggested a similar condition of the blood vessels of the gastric mucosa with associated impaired circulation might be an important factor in the pathogenesis of peptic ulcer. In 1924, he brought forth evidence to show that the gastric mucosa was involved in the vasoneurotic diathesis, which was constantly present in patients with ulcer. He examined warm-fresh specimens immediately after partial gastrectomy for ulcer and found

the same abnormal structure and tendency to spasm and atony in arterioles, capillaries and venules of the gastric mucosa. The changes were present in all of the 32 stomachs excised for gastric or duodenal ulcers. They were most marked in the lesser curvature and pyloric vestibule, and especially in the neighborhood of the ulcer. The condition in patients with duodenal ulcer was equally constant but often less marked. He found the abnormality to be independent of the age of the ulcer, the degree of acidity or of the presence of gastritis.

Duschl later confirmed Mullers work by the ordinary histological methods of tissue examination. (quoted by Hurst)

Held(29) thinks that ulcer may be due to an embolus or thrombus interfering with the local circulation and thus lead to infarction of the gastric area, supplied by a vessel, by exposing it to digestion by acid secretions. He also adds that a purely functional disturbance of the localized blood vessels may spastically so close the vessel as to interfere with circulation. Hauser (quoted by Held) in studying the relation of vascular emboli to infarction observed that an embolus generally occurs in a region where a very narrow vessel is given off by a vessel of a large caliber. Therefore, in most cases, emboli occur in terminal vessels. This is strikingly true in the stomach. The area in which ulcers occur

has the poorest blood supply of the entire stomach and the vessels are terminal. This however, does not explain why everyone doesn't develop ulcers at some time in their life. The probable explanation of this is spasm.

The neurogenic factor most logically explains this spasm. It is very possible that the nerves to this area are so disturbed as to cause marked spastic contractions of the vessels long enough to produce ischemia of the area, autodigestion and ulcer formation.

It is not exactly clear just what portion of the nervous system is at fault in the causation of this spasm. In reviewing the nerve distribution of this area it is well to remember that the lesser curvature of the stomach receives most of the innervation of this viscus. The vagus sweeps down on this ulcer bearing area and terminates the bulk of its fibrils into the serosa and together with the splanchnics, enter the stomach wall with the arteries, accompany their branches and are distributed to Auerbach's intra-muscular and to Meissner's submucous plexuses. Fibrils from the myenteric plexus extend to the tunica muscularis from the submucous plexus, to the vascular wall and to the secreting epithelium. They transmit motor, vasomotor, secretory and sensory impulses. Robinson (14) says that because of this, this is the portion of the stomach that will receive the blunt of psychic trauma with resultant hypermotility, secretion,

acidity, tonicity and vascular spasm.

von Bergman (35) says that stimulation of the parasympathetic nervous system causes three frequent precursors of ulcer--hypermotility, hypersecretion and pylorospasm--and that continuous irritability of this system will produce pyloric ischemia, then erosion and ulceration. Hartzell (36) contends that irritability or even actual neuritis of the vagus causes spasm, resulting in peptic ulcer.

Less known in its relation to peptic ulcer is the sympathetic system. "This if stimulated," says Adams (12) "would cause hypochlorhydria, gastric atony, lessened peristalsis, vasomotor and emotional stimulation, tachycardia and palpitation." The autonomic organs have this dual nerve supply which is involuntary and antagonistic. These mutual antagonistic actions, parasympathetic and sympathetic, provide a protection balance as long as their function is normal. Eppinger (37) believes that an imbalance between these systems is the origin of ulcer. If the nervous balance is disturbed, vagotonia or sympatheticotonia results. If vagotonia occurs, causing the prerequisites of mucosal erosion, the cycle of ulcer has begun.

Another factor is the reflex stimulation from lesions elsewhere in the abdomen causing pylorospasm.

Cholecystitis and chronic appendicitis and acute appendicitis are three main offenders. Excessive catharsis and intestinal allergy may produce the same thing according to Eppinger.

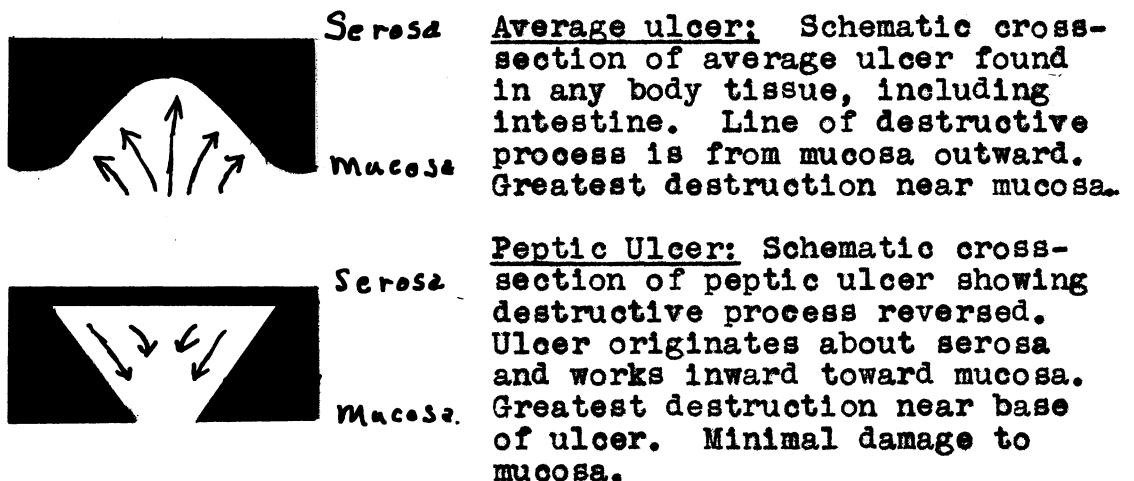
Crile (38) believes that the control of the body is through the sympathetic system--the suprarenals and thyroid all being guided to some extent by the forebrain. He contends that through worry, strain, infection and other causes, these controlling parts lose their normal relation, the results depending on the type of imbalance and manifesting themselves in hyperthyroidism, peptic ulcer, neurasthenia or hypertension.

Cushing (22) says that "from experimental works on animals is evidence to show that a parasympathetic center exists in the brain and that ulcers develop after prolonged stimulation in this region."

Vanzant (39) showed recently that ulcers are associated, on the average, with an acidity slightly lower than normal and that therefore factors other than acidity must enter the picture before an ulcer can form and be maintained." Neither can arterial degeneration be the cause of ulcer, for one would expect to find ulcer more in elderly people and not, as is the case, in young adults. He believes that arterial spasm is the link between the emotions and ulcer.

Robinson (14) believes that the pathology seen in peptic ulcers is conclusive evidence that this malady arises from a neurogenic factor with resulting spasm. Furthermore, he contends that vascular spasm means faulty innervation or vegetative imbalance which refers directly back to the personality study of the nervously unstable individual.

He found the destructive process of gastro-duodenal ulcer to be reversed from that of ordinary ulcer found in other body tissue. On cross-section, the greatest damage occurs near the serosa, in the muscularis and in the sub-muscularis with astonishingly little destruction of the mucous membrane itself, considering the chronicity of the lesion.



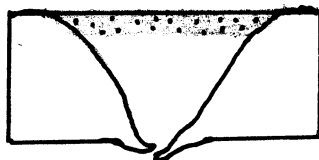
This reversal of destructive processes has been described by different pathologists. Morton (40) says, "the crater is often cone-shaped with the apex toward the mucosal surface and the submucosa is definitely

thickened, having in section the shape of a wedge with the thick part pointing to the crater and the point tapering off toward the mucosa. This is evidence of maximal damage to the stomach wall structures furthest away from the mucous membrane and shows that stomach contents play no part in initiating the lesion. If it did, the greatest damage would be to the mucosa."

In nearly every peptic ulcer, if careful study is made, especially beyond the ulcer bed, some evidence of obliterative arterial disease may be found. Schultz (41) in examining 30 specimens of ulcer found arterial obstructive lesions in every case. Stewart (42) and Delafield and Prudden (43) report these findings also. No embolic phenomenon could duplicate this picture. According to Robinson, spasm and thrombosis mean a destructive process that is dry and clean, which is precisely what is found in peptic ulcer. Deaver (44) says, "They appear as if punched out by a sharp instrument." Trout (45) reports that they are clean bacteriologically as well as histologically, and that the smears and cultures are steril.

Serosa

Mucosa.



Section showing overhanging edges of mucous membrane that are undercut; indurated and opaque serosa beyond ulcer bed; and thrombi.





Section showing ulcer as if punched out by some sharp instrument.



Section showing cone shaped apex toward mucosal surface, thick part toward crater or base.

As to the pseudo-ulcer mentioned previously, Robinson (14) finds that these patients are of the same build and have unstable nervous systems comparable to the true ulcer patient. Their stomach is hyperactive, and the pseudo-ulcer is chronic with exacerbations and remissions. They differ from the ulcer patient only in the degree of extension of the pathological process. Pathologically the serosa is thickened and indurated. The muscularis has round cell infiltration, is edematous and looks pale and ischemic. The mucous membrane in most cases he found to be intact. "Later, as the process extends," Judd (46) reports, "pin point defects may be noticed in a few cases."

Robinson, while operating on the stomach, has seen in the ulcer area pale ischemic areas due to local spasm. The area of ischemia persisted for several minutes followed suddenly by a return of circulation. Still no ulcer could be seen. He reports that these are the individuals who so frequently return within a few months after a futile exploratory, with symptoms and demonstrable X-ray signs. Held also reports (29) encountering these pale, almost

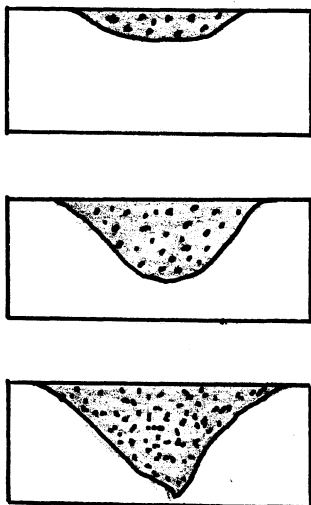
white ischemic areas in the ulcer area while operating.

The typical ulcer syndrome is produced by a pathological process in the submucous layers involving the serosa, muscularis and intervening structure up to the mucous membrane. Erosion of the mucous membrane is not a necessary part of the pathology and the classical picture can be obtained without it.

Robinson believes that mental strain and anxiety have produced in these cases of incipient ulcer, an unbalance of the vegetative nervous system about the lesser curvature and duodenum. Hydrochloric acid or pepsin or local trauma could not have initiated the lesion in view of the existence of a normal mucous membrane. Meyer (47) claims that the acid of the stomach could not produce the pain which accompanies this syndrome.

Palmer (48) says that, "the increased acidity is an associated finding just as much as leucocytosis is in most infections. It would be as idle to focus one's attention on the leucocytosis instead of the invading organism as it is to regard hyperacidity as the 'sine quo non' of the ulcer and rest content with its neutralization."

Jaffe (49) says that, "the identical process stops the heart in coronary spasm and thrombosis and renders the kidney tissue impotent in nephrosclerosis."



These schematic diagrams serve to illustrate the pathological process in the ulcer syndrome. A potential ulcer, as shown in the last diagram may, if emotional conditions are satisfactorily under control, show remission with satisfactory healing. However, under mental strain, anger, fear or other emotional upsets, this may progress to the formation of a true ulcer.

Durante (32) says that he found acute and chronic ulcers in the same region of the same stomach, both originating at the same time--he assumes therefore that acute lesions do not take on the chronic form, but that both varieties occur simultaneously and start as specific entities. He believes that ulcers are produced by irritation of the splanchnic nerves which affect the adrenal medulla, in consequence of which greater quantities of adrenalin are secreted. The adrenal secretion stimulates the sympathetic nerve fibers controlling the non-striated muscles of the blood vessels, thereby causing the formation of hemorrhagic and spastic lesions. The hemorrhagic lesion, presenting the essential features of acute ulcer, heals by means of a scar; the spastic lesion becomes the starting point of genuine chronic ulcers.

Ulcer may be produced by any agent capable of damaging the sympathetic nervous system as it is on the integrity of this system, which controls circulation, secretion, and profound sensibility in the stomach, that the very life of the gastric cell may be said to depend.

The personality study of the neurogenic diathesis is very difficult to record. After studying some 500 patients, Robinson (9) says it has become apparent that a large percentage of them belong to a definite type with a similar emotional response to conflict. They display a relatively calm exterior and "do their worrying alone and within". The ulcer patient belongs to the active, driving group of the linear type, in contrast to the slow moving, slow thinking lethargic group. This is manifest both mentally and physically, but particularly in the former. Chronic ulcer is seldom found among the feebleminded. The ulcer patient is alert and intelligent with a quickened intellectual response. However, his mental, nor his physical activity is long sustained. He shifts from subject to subject, seldom finishing one at a single session. Draper (10) says that, "their capacity for long sustained effort is not great, they are of those persons whose intense activity is intermittent, because of easy fatigue. They recover energy promptly after short rest periods and the frequent ingestion of food".

Most ulcer patients admit that they do not concentrate well. They skim over a lot of subjects instead of devoting all their time to one and probing it. Yet for initial effort and for a given period of time, the concentration may be equal, if not better than average.

"Their memory is notoriously bad", says Robinson, and Draper says that in the average patient all the orderly, more logical qualities, such as planning capacity and executive and mathematical ability are not naturally highly developed, but often, by powerful compensatory effort they succeed in schooling themselves in executive work".

The average ulcer patient is not neurotic in the narrow sense of the word. He is not given to complaining. Some tend to minimize their symptoms. They may suffer for years with dyspepsia before seeking medical advice. They are very accurate and objective in describing their disease, often insisting that they do not even have pain. Instead they describe their symptoms as distress, or as an uncomfortable feeling. Robinson did not interview any whom he could classify under the syndrome of an anxiety neurosis or compulsion neurosis.

Schindler (quoted by Robinson) found that most of them have an apparent calm exterior and a good degree of composure as far as skeletal musculature is concerned. The emotional conflict inside is well concealed and pro-

tected from external gaze. From the first impression one would not gather that the psychological factor was foremost in the disease of this externally quiet individual.

On further study one will usually note a rather tense facies (34) with a worried look. The palpebral fissures are not necessarily widened, nor is there much of a staring appearance. The face muscles are set so as to produce an anxious, tense and worried expression. He is serious as if loaded down with many mental problems and is somewhat retiring. Behind this reserve there is often a challenging disposition. He accepts no strange situation and its uncertainty without some preparation for action in case it is unfriendly or hostile. All strange situations are to be viewed with suspicion. He may be glum as if he carried a grudge, until the atmosphere clears, but when he feels assured and safe he begins to unwind. As he becomes more at ease he may even wear a broad, whole hearted smile. He warms to persons quickly and shows appreciation for any interest in his baffling and long drawn out disease.

The dominant factor in the ulcer temperament is worry or the fear to meet some of the daily problems of life. They fret about little things all the time, and Robinson says that this inward aggravation is at the bottom of all their trouble. Draper (10) found it difficult to connect a conscious fear with the gastric symptoms.

such as hemorrhage and in some cases perforation. He believes it is reasonable to think that the original formation of the ulcer occurred long before one of these accidents. The fear has not been recognized consciously, however, in the earlier stages of the malady and it is usually denied by the patients. However, there seems to be two separate and independent sources of fear--one is subconscious and unrecognized by the patient. The anxiety from this level has been at work for a long time. The consciously perceived, on the other hand, is formed by the menacing episode that may threaten life, limb or ego.

The ulcer patient has no safety valve for pent up emotions. They carry their burdens, hates, angers and grudges and seldom lose their temper. They tend to fight it out against themselves for days instead of getting it out of their system. When they do it is violent and uncontrollable and associated with marked visceral disfunction. Broad problems of the future, such as family illness and economic security often do not cause as much worry and tension as little everyday problems.

Robinson found that fully 90% of the ulcer patients take everything too seriously. They may have an outward manner of assurance, but beneath there is a latent timidity which Draper believes may be the cause for their tendency

to over-preciseness in all they do and to be suspicious of people and situations. They are conscientious and cannot be casual about their routine work.

The ulcer patient is an individualist and prefers to go it alone. Seldom does he share his griefs and joys. He is very independent and would rather solve his own problems than to rely on the help of family or friend. Relatives and friends often speak of how hard it is to do things for the patient. He accepts favors grudgingly and returns them whenever and as soon as he can.

This strong independent nature probably arises from his sensitiveness. He is inclined to be obstinate and critical of others. He avoids partnerships or combined responsibility because of danger of disagreement. (This may account for so many ulcer patients in the medical profession. Robinson (9) found 40% of the staff in one clinic in this country suffering with the ulcer syndrome.)

A few pertinent facts about the ethical level increases our understanding of the ulcer patient. It is helpful to make this appraisal in every individual's personality. Riggs (50) found these patients to have a strong flair for justice. He may be cool and distant, but likes to see the game played fairly--at home, with friends and on a national and international scale. He is helpful, generous, considerate and soft hearted. He has a strange combination of



affection for his immediate circle, and apparently a strong compassion for humanity in general. They have more than a fair respect for other people and can not give anyone the short end of a deal; if no alternative arises, they tend to take it themselves. Although no survey has been made, Riggs believes that there would be more than a fair number of ulcer patients in liberal groups.

An exacerbation of the ulcer syndrome is precipitated by worry, heavy responsibilities and frustration, and release from these emotional upsets gives symptomatic relief.

Meyer (47) Davies (1) and Rivers (11) state that the symptoms of ulcer frequently reestablish themselves during periods of trouble and entanglements and become readily controllable when the patient ceases active work, evades responsibility and takes a vacation.

Cushing (22) says that, "highly strung persons are particularly susceptible to nervous indigestion and associated ulcer; that ulcers become symptomatically quiescent or even tend to heal when the patient is put mentally and physically at rest, and that the symptoms are prone to recur as soon as the former tasks and responsibilities are resumed."

In concluding, it is well to emphasize the necessity considering the neurogenic factor in the treatment of peptic ulcer.

Russ (8) states that he has had patients who were resistant to treatment by rest, diet and alkalies, but that they often recover completely and suddenly from their symptoms when they were made happy by some occurrence and when they were able to dispel their worries and fears.

Rivers (51) finds that by giving bromides, phenobarbatol and belladonna together with bed rest, he gets better results than by using the alkalization treatment.

Smithies (52) states that he does not use the alkalization method at all, and has not used it for several years. He insists on bed rest, and gives half an ounce of warm water by mouth every hour when the patient is awake. They are also given sweet orange juice or grape fruit juice. Also during the first few days he gives an enema consisting of 1 ounce of 50% alcohol, 1 ounce glucose syrup and 6 ounces of NaCl, every four hours. This is given at the rate of about 45 drops per minute. Tincture of opium is given for the first two days. The patient's diet is gradually increased to gruel, potatoes, beans, peas, milk, meat, etc. He states that he has treated 470 patients by this method and has gotten cessation of the process in 361 of them.

Adams (12) says, "It is necessary to completely control all of the factors involved in this malady to stifle the life cycle of the ulcer. In addition to relief by

alkalinization, dietary regime and anti-spasmodic drugs, one must correct the other factors by re-education in the manner of living and improve their daily routine and habits. The ability to get well is in the hands of the patient to a great extent.

#### Summary

Heredity plays a strong role in gastro-duodenal ulcers, as in most other diseases. An ulcer patient's body build and diseased personality is transmitted from some immediate or distant ancestor--this is manifested in a long thin individual with a more or less fixed behavior pattern, and associated with an innate ulcer diathesis or constitutional or individual susceptibility. The limited site selectivity of the ulcer to the lesser curvature of the stomach and the 1st portion of the duodenum is further confirmation of their inherited predisposition. There must be something defective in the psychosomatic background of the susceptible person which links up directly with the few inches of vulnerable stomach and duodenum. There is something wrong with this narrow strip of tissue or with the innervation reaching it. We are led to the latter conclusion because this area is more actively innervated than any other part of the stomach and therefore more sensitive neurologically. Hence any exogenous disturbance affects the autonomic Nervous System of the stomach

of the lesser curvature.

Barber (5<sup>A</sup>) says that the lesser curvature forms a pathway for the vagus nerve trunks which are loosely incorporated in the serosa. Durante (32) says that the very life of the gastric cell depends on the sympathetic nervous system which controls circulation, secretion and motility. The enhanced motor and secretory physiology of this small portion of the Gastrointestinal tract is not due alone to the greater innervation to these parts. The axons only relay impulses. The power station is located essentially in the brain stem and hemispheres. Their individual or combined activity determines the quality and quantity of the impulses which are set forth in a continuous discharge along the nerves to the vascular bed, secretory cells and the musculature of the stomach and duodenum. The disturbances must not be sought here in the stomach's interior, but rather outside, higher up in the interior of the brain.

Cannon (20), Wittkower (54) and Herrin (55) agree that the central nervous system is important in the increased activity of the GI tract. The increased motor and secretory activity of the stomach and duodenum determine the dyspeptic symptomatology of the ulcer patient. Hypermotility, hypercontractility, hypertonus, spasm of the pylorus, rapid emptying time--all are classic features of

the ulcer picture and are disturbed motor functions of the Gastro-duodenum, produced by increased excitatory nerve impulses to the musculature.

The personality of the ulcer fits in well here. His emotional instability under conflict and his morbid and uncontrollable tendency to worry increases the excitatory nerve impulses to this region.

When the ulcer patient is removed from the strain and responsibility that causes this worry, his symptoms disappear. Ulcer itself lends itself pathologically to this theory. It is not an infectious thing. It is clean bacteriologically. There are thrombi--showing the effect of continued spasm.

The ulcer personality is shown to be a long and thin individual, chiefly of the male sex, and given to excess worry. Heavy responsibilities at work or social frustrations are shown to be factors causing exacerbation of the ulcer syndrome. Rest and release from worries bring symptomatic relief.

## BIBLIOGRAPHY

1. DAVIES, D. T.  
Some Observations on Peptic Ulcer  
Lancet 1: 521, 1936
2. HURST, A. F. and STEWART, M. J.  
Gastric and Duodenal Ulcer  
Oxford University Press 1929
3. BROWN, T. R.  
Cecil's Textbook of Medicine, Pg. 706  
W. B. Saunders & Co., Phila., Pa. 1937
4. ROKITANSKY, C.  
Quoted by D.T.Davies in, Some Observations on  
Peptic Ulcer.  
Lancet:1: 521, 1936
5. BROWN-SEQUARD  
Quoted by D.T.Davies in, Some Observations on  
Peptic Ulcer.  
Lancet 1: 521, 1936
6. STILLLEN, B.  
Quoted by D.T.Davies and A.T.Wilson in,  
Observations on the Life history of Chronic  
Peptic Ulcers.  
Lancet 2: 1353, 1937
7. MOYNIHAN, G. A.  
On Duodenal Ulcer and its Surgical Treatment  
Lancet 2: 1656, 1901
8. RUSS, W. B.  
Neurogenic factor in Chronic Peptic Ulcer.  
J.A.M.A. 97: 1618, 1931
9. ROBINSON, S.  
The Role of Emotions in Gastro-Duodenal Ulcers  
Ill. Med. Journ. 71: 338 April 1937
10. DRAPER, G. and TOURAINÉ, G. A.  
The Man-Environment-Unit and Peptic Ulcer.  
Archiv. Int. Med. 49: 616, 1932
11. RIVERS, A. B.  
Clinical consideration of the Etiology of Peptic  
Ulcers.  
Archiv. Int. Med. 53: 99, 1934

12. ADAMS, W. P.  
A Resume of the Etiological factors in Peptic Ulcer Syndrome.  
Virginia Med. Monthly 64: 191, July 1937
13. BERGSMA, S.  
Gastric and Duodenal Ulcer in the Black People of Abyssinia.  
Archi. Int. Med. 47: 144, Jan. 1931.
14. ROBINSON, S. C.  
On the Etiology of Peptic Ulcer  
Amer. Journ. Dig. Dis & Nutri. 2: 333, 1935
15. HARTMAN, H. R.  
Neurogenic factors in Peptic Ulcer.  
Med. Clinics of No. America 16: 1357, 1933
16. McCORRISON  
Quoted by S. Robinson in, On the Etiology of Peptic Ulcer.  
Amer. Journ. Dig. Dis. & Nutri. 2:333, 1935
17. MACKLIN, M. T.  
The importance to the Gastro-enterologist of Inheritance in Disease.  
Amer. Journ. Dig. Dis. & Nutri. 1: 480, 1934
18. RUHMAN, W.  
Quoted by Draper & Touraine in, The Man-Environment-Unit and Peptic Ulcer.  
Archi. Int. Med. 49: 616, 1932
19. ASCHNER, B.  
Quoted by Draper & Touraine in, The Man-Environment-Unit and Peptic Ulcer.  
Archi. Int. Med. 49: 616, 1932
20. CANNON, W.B.  
The Role of Emotions in Disease.  
Annals of Int. Med. 9: 1453, 1936
21. HAUSER  
Quoted by Alvarez in, Light from laboratory & clinic on Causes of Peptic Ulcer.  
Amer. Journ. Surg. 18: 207, 1932
22. CUSHING, H.  
Peptic Ulcers and the Interbrain.  
Surg., Gyn. & Ob. 55: 1, 1932

23. ROBERTSON, H. E. and HARGIS, E. H.  
Duodenal Ulcers; an Anatomic Study  
Med. Clin. No. America 8: 1065, 1925
24. SMITHIES, F.  
Significance of Etiological Factors in the  
Treatment of Peptic Ulcers.  
J.A.M.A. 74: 1555, 1920
25. BLOCK, L. & SERBY, A.M.  
Use of Alkalies in the Treatment of Peptic Ulcer.  
J.A.M.A. 92: 134, 1929
26. BALINT, R.  
Quoted by Hurst & Stewart in, Gastric and  
Duodenal Ulcer.  
Oxford University Press 1929
27. BENNETT, T.I. and RYLE, J. A.  
Normal Gastric function.  
Guys Hospital Report 71: 286, 1921
28. CARLSON, A. J. and LITT, S.  
Studies on the visceral nervous System.  
Archi. Int. Med. 33: 281, 1924
29. HELD, I.W. and GOLDBLOOM, A.  
Pathogenesis of Peptic Ulcer.  
Med. Clinics of No. America 14: 317, 1930
30. MANN, F.C. and WILLIAMSON, C.S.  
The experimental Production of Peptic Ulcer.  
Annals of Surg. 77: 409, 1923.
31. EMERY, E.S. Jr.  
Treatment of Peptic Ulcer based on 1435 cases.  
Amer. Journ. Dig. Dis. & Nutri. 1: 521, 1934
32. DURANTE, L.  
The Trophic Element in the Origin of Gastric Ulcer.  
Surg. Gyn. & Ob. 22: 399, 1916.
33. DRAPER, G. , DUNN and SEEGAL  
Studies in Human Constitution: Facial form and  
Disease correlation.  
Amer. Journ. of Med. Science. 169: 322, 1925



34. STENBUCK, J. B.  
A Description of the Type of Facies found in Cases  
of Ulcer of the Stomach and Duodenum.  
Amer. Journ. Surg. 38: 181, Aug. 1924.
35. VON BERGMAN, G.  
Quoted by Cushing in, Peptic Ulcer and the Interbrain  
Surg. Gyn. & Ob. 55:1, 1932
36. HARTZELL, J. B.  
The Effect of Section of the Vagus Nerves on  
Gastric Acidity.  
Amer. Journ. Physio. 91; 161, 1929
37. EPPINGER, H. and HESS, L.  
Quoted by Adams in, A resume of Etiological factors  
in Peptic ulcer Syndrome.  
Virginia Med. Monthly 64: 191, July 1937
38. CRILE, G. W.  
Recurrent Hyperthyroidism, Neurocirculatory Asthenia  
and Peptic Ulcer.  
J.A.M.A. 97: 1616, 1931
39. VANZANT, F.R. et al.  
Normal range of Gastric acidity from Youth to Old  
Age: an analysis of 3,746 records.  
Archi. Int. Med.:49: 345, 1932
40. MORTON, C. B.  
Observations on Peptic Ulcer.  
Annals of Surg. 85: 207, Feb 1927.
41. SCHUTZ, C. B.  
The Etiology of Gastric and Duodenal Ulcers.  
J.A.M.A. 96: 2182, June 1931
42. STEWART, M. J.  
The Pathology of Gastric Ulcer.  
Brit. Med. Journ. 2: 1021, 1923.
43. DELAFIELD and PRUDDEN  
Textbook of Pathology.  
Wm. Wood & Co. 1922
44. DEEVER, J.B. and REIMAN, S.P.  
Pathology and Treatment of Gastric and Duodenal  
ulcers.  
Amer. Journ. Surg. New series 3: 333, 1927

45. TROUT, H.H.  
The Treatment of Perforated Peptic Ulcers.  
J.A.M.A. 104: 7, 1935
46. JUDD, E.S.  
Pathological Conditions of the Duodenum.  
Lancet 41: 215, April 1921
47. MEYER, J. and KARTOON, L.B.  
The Effects of intravenous injection of Foreign Protein on Peptic ulcer.  
Arch. Int. Med. 46: 768, 1930
48. PALMER, W. L.  
Fundamental differences in the Treatment of Peptic ulcers.  
J.A.M.A. 101: 1604, 1933
49. JAFFE, R.A.  
Chicago Med. Soc.--Pathological Conference.  
March 15, 1935.
50. RIGGS, A.F.  
The Role of Personality in Psychotherapeutics.  
Annals of Int. Med. 10: 13, 1936.
51. RIVERS, A.B.  
Significant factors in the Course and Diagnosis of Peptic ulcers.  
Med. Clinics of No. America. 14:575, 1930
52. SMITH, F.  
The Non-surgical management of peptic ulcers by the Physiological Rest Method.  
J.A.M.A. 85: 674 Aug., 1925.
53. BARBER, W. H.  
Motility of the Stomach after local resection for Gastric Ulcer.  
J.A.M.A. 84:170, 1925.
54. WITTKOWER, E.  
Studies on the influence of Emotions on the functions Of Organs.  
Journ. of Ment. Science. 81: 533, 1935
55. HERRIN, R.C.  
Effect of Atropine and Pilocarpine upon Emptying time of Stomach.  
American Journ. of Physio. 115: 104, 1936.