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The gastric analysis

Warner F. Bowers
University of Nebraska Medical Center

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THE GASTRIC ANALYSIS

Senior Thesis by

Warner F. Bowers, A.B., B.Sc. in Med.

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THE GASTRIC ANALYSIS

The modern gastric analysis had its origin in the quaint experiments of Spallanzani (60) (91) in 1780, although Reaumur (60), prior to 1757, had recovered gastric contents from a pet kite and had demonstrated its solvent action on various articles of food.

Spallanzani, 1729-99, carried his work much further and was the first to demonstrate the digestive action of saliva, acidity of the gastric juice and prevention of putrefaction by gastric juice. He also showed that gastric juice would stop putrefaction and dissolve food particles outside of the body. Spallanzani concluded that gastric digestion depended partly on chemical changes in the food but he failed to recognize the cause of acidity of gastric juice. While Spallanzani used vomited material in some of his experiments, he usually employed other means. For example, he used a sponge attached to a string and then pressed out the juice thus obtained. Various types of foods were placed in perforated wooden capsules and these were recovered at different times during the digestive cycle by means of a string. Some capsules were allowed to be eliminated with the feces and their contents then examined. Spallanzani gained some knowledge of the force of contractions of the gastro-intestinal tract by feeding chickens glass balls from which needles protruded.

He found that on being eliminated, the needle points were always broken off.

The next development of significance was made by Beaumont (60) (91), 1785-1853, a French Medical Army Officer, who had the opportunity to observe an accidental gastric fistula in Alexis St. Martin, a Canadian. Beaumont observed the nature of gastric juice, the process of digestion in the stomach, and the early stages of gastritis. He showed that secretion took place only when food was present in the stomach and that mechanical stimulation caused only a slight local secretion. His experiments with gastric juice on different foods form the basis of modern diet tables and scales. Beaumont succeeded in isolating and recognizing free hydrochloric acid from gastric juice.

While Von Leube (91) was the first to introduce a catheter into the stomach, it remained for Ewald, 1845-1915 (60) (91) and Boas (91) in 1855 (57) to refine the technique. They used a constant stimulus and withdrew the entire contents of the stomach at the end of one hour. This work was continued by Hayem (57) but he made no particular contribution to it.

From this time on, developments came very rapidly. In 1906, Eakins (57) brought out his ideas on hormone control of gastric secretion (46). He demonstrated that gastric secretion could be produced by subcutaneous or intravenous

injection of extract of pyloric mucous membrane. He determined that this substance was not present in the mucous membrane of the fundus and that atropine did not diminish the effect of the pyloric extract. He concluded that this substance was not an enzyme because it was not found to be thermolabile.

Fuld (57) in 1908 was the first to introduce chromoscopy in the study of gastric secretion. He used such dyes as neutral red and methylene blue. At about this same time, Meunier (57) applied cryosecopy to the analysis of gastric secretions. He used the fractional type of analysis and stated the biphasic theory of secretion, by which he meant that there was a psychic and later a gastric phase in secretion. This same period is marked by the work of Barbera & Bernard (57) who endeavored to show the specific effects of various foods on the gastric mucosa. They showed that stimulation depends partially at least, on solubility or osmotic order and consequently fats inhibit while alcohol excites secretion. Albuminoids, all substances containing nitrogen and to a lesser degree, those containing sugar, were found to be gastric stimulants. Factors of taste were found to be important and purely mechanical stimulation gave no secretion.

The remarkable work of Pavlov (111), published in 1910, shed much light on the physiology of the stomach. By a series of experiments on dogs, he showed that initial sec-

retion is caused by purely psychic factors while later secretion is under chemical control by the stomach itself. He, with Heidenhain, developed the gastric experimental pouch which bears their name. Pavlov also demonstrated what he called conditioned reflexes by showing that dogs, accustomed to hear a bell ring at meal time, could finally be caused to secrete gastric juice by simply ringing the bell, although no food was presented to the animal.

Gross (91) in 1893 used a small flexible tube, in contrast to the large Ewald tube but it was not until 1914 that Rehfuß (91) (122) (123), used a modified Einhorn duodenal tube. The work of Rehfuß at this time firmly established the fractional method of gastric analysis in England and America. It is interesting to note that Rehfuß (122) and Einhorn (47) (49) (50) (51) both revert to the original work of Spallanzani in their use of gastric capsules and analytical buckets. Einhorn (91) formerly used two tubes, one in the duodenum with constant suction to prevent regurgitation, the other in the stomach and through which the samples were withdrawn. Von Leube (91) attempted a fractional examination but the large tube was too difficult to pass often and it could not be left in place long.

The original method of examination (91) consisted in complete withdrawal of gastric contents at the end of one hour after the ingestion of the meal. This method, although it is still used somewhat, has aroused considerable con-

controversy. The fractional method was evolved because of slowly elaborating stomachs which do not reach their peak in one hour. Here, samples are taken at regular intervals until no food particles remain or until the acidity has returned to the fasting level. Ewald (91) attempted fractional examination of the gastric contents by giving the patient an identical meal on different days and then withdrawing the contents at various times during the digestive cycle. This may yet be found to be the best method of fractional analysis (139). Many authors (29) (55) (54) (139) (61) (74) (109) (130) (102) (133) (35) (68) (91) (12) (13) (113) (31) prefer the Rehfuess fractional method and Henderson (68) enumerates the following advantages for this procedure; 1. The amount and character of the fasting juice is determined 2. Acidity is determined at various periods, thus permitting the plotting of a curve of secretion 3. The time of appearance of bile may be accurately noted. McCracken (91) mentions these points and in addition he believes that other advantages allowed by the fractional method are; 1. Determination of persistence of starch 2. Observation of such things as blood, bile, pus, charcoal and debris in the samples 3. Determination of the amount of two hour residue 4. Observation of general appearance of samples. He (91) criticises the Ewald method because the fasting acidity is not determined. The churning motion of the stomach does not mix the contents and the solid particles tend to layer

out of suspension. The merit of the fractional method rests in the fixed position of the tube and not on the mixing of the contents. This fixity of position was demonstrated by roentgenogram. Even so, the tip rests at various levels in different stomachs, so that the results are not strictly comparable. Smirnoff and Lavsky (130) state that the fractional method gives a better conception of the actual conditions in the stomach and they stress the fact that motor activity may also be studied. Wills (142) goes further and states that fractional analysis gauges motor function more accurately than secretory function, although the motility depends on the secretion of hydrochloric acid almost entirely. Andresen (3) says that too much emphasis is placed on secretion and not enough on motor function in the ordinary analysis. Chemical, physiological and psychic factors may also be examined (91). Smirnoff and Lavsky (130) list the following advantages of the fractional method; psychic and chemical phases are considerably influenced or disturbed because of 1. The indifferent character of the test meal 2. Introduction of the meal by the tube and not by the normal process 3. Unphysiological meals of substances not usually taken as foods 4. Amount of recovered contents following a fluid meal is less than with the Ewald type because of the loss of the important physiological act of mastication. They (130) believe with Garbat (59) that the Ewald examination is simple, physiological and easy for the

general practitioner but state that it fails to give a complete picture of the course of gastric secretion and does not give the maximum acid values. Galli (57) found that the fractional method during fasting was not reliable due to abnormal conditions, inhibitions and duodenal reflux. Still other objections to the Ewald method are raised by Strauss and Steinitz (133) who mention opacity and irregular structure of the contents, lumps which confuse the microscopic picture and the fact that the contents contain albumin and chlorides. Petrowa (112) feels that an examination of the fasting content is necessary whereas this is not usually done in the Ewald analysis. Germain (61) objects to the large tube, the mixture of gastric juice with food and the unphysiological aspects of the old methods. Ioffe (73) prefers the Ewald procedure, stating that it is physiological and excites profuse secretion. This preference is also shown by Garbat (59) who says that the single specimen gastric test fully suffices for general diagnostic purposes as an index of gastric secretion and digestion. It may also be argued that the single specimen meal is not subject to psychic inhibition because secretion has already taken place before the tube is introduced whereas fractional analysis depends on gastric secretion subsequent to intubation and the mere passage of the tube may inhibit this secretion, psychically. Debenedetti (37) feels that due to psychic factors, to the poor adaptation of test meals and

to the fact that the stomach is continuous with the intestine, the fractional method is no improvement over the original method of Ewald. White (151) says that the fractional method is based on the fallacy that the gastric contents is a homogeneous mixture. Carrega-Casaffousth (29) and Frenkel (54) maintain that the Ewald type of analysis may not show the actual maximum since the contents may not be withdrawn at the peak of the secretion whereas the fractional examination will show the highest as well as the lowest levels. Friedrich (55) states that the fractional method is of considerable theoretical and clinical significance in that it affords exact judgement of secretory disturbances as well as dysfunction of gastric motility. Results by the two methods do not always coincide but Lickint (88) believes that this may be due to differences in aspiration technique. Hess (69) indorses the fractional method because he feels that the degree of acidity is not so important as the entire course of acid secretion. Frenkel (54) notes that in many instances the large Ewald tube fails to recover fasting juice and may give difficulty in recovering the contents after a meal but he rarely finds this difficulty with the small fractional type of tube. Von Leube, Ewald, Riegel, Rosenbach & Reichmann (54) stated that the fasting stomach is always empty but this was with the use of the large tube. In fifteen cases Lickint (88) found no fasting juice with the large tube

but in each instance, he recovered fasting juice with the small tube on the following day. Lesnik (87) states that the small tube always gave a higher acid value and fewer empty fasting stomachs. In their early work, Rehfuss, Bergeim & Hawk (123) do not mention any special points of advantages not already quoted.

The size of the tube has also been a matter of considerable debate and some authors refuse to accept the work of others who used the large tube and vice versa. Knapp (81) reflects that the small tube is swallowed, whereas the large tube must be introduced. The large tube secures better mixture and gives a more homogeneous sample while the small tube shows an annoying tendency to clog. The large tube often will be found to coil around in the stomach so that the tip is above the fluid level. This may cause the investigator to believe that the stomach is empty. The small tube does not show this tendency to such a degree. The accuracy of any gastric analysis is questioned by various authors (139) on the ground that acid concentration varies at different levels in the stomach and so tests on different days may be from different levels and so are not comparable nor are those on different individuals comparable, for the same reason. Garbat (59) in 1931, noted a striking variation in acidity in the same individual on different days and found this lack of agreement mainly in the normal and hypoacid patients. The results

in hyperacid and anacid patients were more uniform. Duthie (44) found a marked variation on different days and he also noted considerable variation in free hydrochloric acid in the different portions of the stomach. There was also a marked variation in the time of appearance of free acid at the various levels. Using the xray to determine the level of the tube, Ramond (120) took samples of gastric juice from the bottom, middle and top at fifteen minute intervals and found the greatest acidity at the top and along the lesser curvature. Bell & MacAdam (10) (11) also found a variation in the same patient on different days. McCracken (91) points out that other glands are not absolutely constant in function but that in gastric analysis, this is minimized by attempting to use the same time, meal and method. Gerham (64) removed the entire gastric contents, forty-five minutes after the meal, in ten cubic centimeter samples, at different levels and showed a definite variation in free acid. Butcher (25) obtained similar results and noted a difference of ten points in acidity of pyloric and fundic regions. Other writers do not agree on these results and McCracken (91) states that gastric analyses at different times on the same individual show identical curves except at the end due to variations in duodenal regurgitation. He states, however, that either the gastric contents must be a homogeneous mixture or else the samples must come from the

same part of the mucosa. Different levels showed a variation in acidity of as much as 40%, the average variation being 17%. The lowest variation was in the fasting juice but this increased up to the height of digestion. Mixture was secured by suction and reinjection through the tube. This is a serious criticism of the fractional method which has not, as yet been answered. He (91) found the individual emptying time to be quite constant. Porges (117) favors the Ewald meal and large tube, claiming good clinical results. He feels that skill in passing the tube is an important factor in successful analysis. Another investigator who finds individual difference on successive analyses is Gukacian (65). Barkhash (7) and Andresen (3) agree and state that one gastric analysis is no more conclusive than one temperature reading in case of fever. Conflicting results were obtained by Ehrenreich (6) who showed a definite curve type in the same patient at long intervals. Kopeloff (84) states that a single determination is insufficient as a basis for conclusions, due to individual daily variations. Bennett and Ryle (12) (15) succeeded in obtaining identical curves on different days with slight variations toward the end, due to duodenal reflux depending on momentary changes in pyloric tonus which varied from day to day and meal to meal. Garbat (59) also found that analyses on successive days gave results which coincided within ten points. The variation in results of some authors is explained by Korneef (85)

on the basis of differences in acid concentration in various portions of the stomach. Roberts (124) does not feel that the daily variation is of sufficient magnitude to influence the results. He states that the samples cannot be said to represent the acidity of the whole stomach content.

By whatever method the samples may be obtained, there are certain determinations which are usually made, chemically, and of these the quantitative estimation of free and total hydrochloric acid is perhaps the most important and universally used. The most common method is the titration of a ten cubic centimeter sample against tenth normal sodium hydroxide, using Topfer's reagent and phenolphthalein as indicators. Topfer's reagent indicates the neutralization of all free acid by a canary yellow color and after continued addition of base, the phenolphthalein turns pink, thus showing neutralization of the total acid content (33) (91) (68) (139). There is some discussion of the use of Topfer's reagent but this is not valid because the organic acids are too dilute to affect the test. Other methods of determination of hydrochloric acid have been used but they are too complicated and involve the use of highly specialized laboratory equipment. Kahn & Stokes (76) comparing electrometric and colorimetric methods, state that the colorimetric method is accurate enough when the Ph is less than 2.1 but above that point, dialysis must be used. They favor the electrometric method but

caution against the loss of dissolved carbon dioxide if the Ph is greater than 5.5. Barkhash (7) also favors colorimetry and electrometry in acid determination. Taccone (135) takes two cubic centimeters of gastric filtrate, adds one half a cubic centimeter of hydrogen peroxide, two cubic centimeters of sulphuric ether and three to six drops of potassium bichromate. Hydrochloric acid gives a blue color and lactic acid a green color.

Pepsin is secreted in the inactive mother zymogen form and this is activated by the free hydrochloric acid (139). From this, it is assumed (79) (71) (115) (91) (81) that the presence and amount of pepsin parallels the free acid. However some authors (38) (55) (105) (96) (53) state that there is no parallelism and it is known that in achlorhydria the enzyme is usually (79) (115) (81) present. Kemper (79) states that the normal parallelism is absent in disease. Methods of determining pepsin content are complex and not frequently used (52). Hirschberg (71) tests the degree of digestion of a definite length of macaroni by the colorimeter after a definite time of incubation at a known temperature. Rennin and gastric lipase are of no clinical significance and their determination is rarely undertaken (139).

The determination of neutral chlorides is not usually done (91) but may be accomplished by precipitation as an insoluble salt or by titrating, using an appropriate indicator.

Tests for starch, bile, mucus and blood are not usually run routinely but in most instances these determinations are rather important. Starch is indicated by a dark blue color with iodine (91), bile by a variegated display of colors with nitric acid, mucus by viscosity, and blood by the benzidine or guiac tests. Naked eye tests often suffice for blood, bile, mucus and motor substances as charcoal, raisins or rice.

Lactic acid is a distinctly abnormal constituent (33) (81) (52) of gastric juice and may be determined easily with a solution of ferric chloride. The positive test is the appearance of a lemon yellow color (139).

The determination of gastric mucus is rather infrequently made. Simchowitz (129) determines mucus by rapidity of filtration after a fluid meal, normally seven to eleven cubic centimeters of juice passing through the filter in thirty minutes. This mucus serves to protect the mucosa from thermal, chemical and mechanical injuries. Gastric mucus differs from other mucins in its poor ability to take stain, its occurrence in small floccules and its greater tenacity. Secretion of mucus is independent of acid secretion and occurs at no definite rate. Gastritis with hyperacidity is found more frequently than is supposed. Determination of mucus is of value in diagnosing gastritis but as gastritis accompanies both ulcer and carcinoma, it is not so valuable after all. Kelling (78) says that

gastric mucus is found usually in the lower portion of the stomach and is closely mixed with the food. He precipitates the mucus by electrolysis and then measures it after filtration.

The microscopic examination is of little value except in certain cases where debris, sarcinae, blood or Oppler-Boas bacilli may be found. The usual Ewald meal is too lumpy and turbid to permit of a very satisfactory examination. Pus, even if found, may be from the mouth or sinuses (91).

Certain other types of gastric examination, while used by a limited number of investigators, must be mentioned at this point. A purely motor investigation is carried on by means of Castle's capsules (138) and subsequent xray. The capsules are opaque and one sinks to the dependent portion of the stomach while the other floats. The amount of secretion may thus be roughly estimated and the process of emptying may be more accurately followed. Rehfuess in 1914, (122) harked back to the original work of Spallanzani in his use of a perforated capsule on a string. Rehfuess objected to the use of a tube on the ground that esophageal irritation produced a fluid which interfered with accurate results. The capsule was small and Rehfuess claimed that the esophageal irritation was thus minimized. He claimed the following advantages; 1. Any substance or medium could be introduced at any stage of digestion and could be with-

drawn when desired. 2. Acid residue after or between meals could be determined. The results were said to be comparable to those obtained with the Rehfuß tube. Later, Einhorn in 1928 (47) (48) (49) (50) (51) used what he called a bucket in gastric determinations. This small bucket contained in its walls, strips of paper soaked in substances which by color changes would show the presence of blood, bile and acid. He also worked out a method which would show Ph by shades of color on test papers. The quantitative method consisted of the use of standardized drops of base on the strips after they had been soaked in gastric juice. Einhorn gives as the drawbacks to the usual methods; 1. Frequent failure of the tube to reach the lower level of the stomach 2. Insufficient fluid obtained for the tests necessary 3. Necessity of making many time-consuming tests 4. Inability with blood in the stool, to determine the origin of bleeding by gastric analysis alone. Denis and Silverman (39) (40) (41) also use test papers for qualitative determinations.

In 1929, Cohen and Brock (34) brought out the idea of determination of gastric acidity without the use of intubation, but by utilization of changes in urinary Ph. Their idea, later substantiated by Matzner & Gray in 1931, (99) was that acid secretion in the stomach leaves less acid to be secreted by the kidney or stated in another way, when the stomach secretes acid, the kidneys must excrete less acid in order to maintain the acid-base equilibrium

of the body. This has been found to be true and achlorhydria gives a fixation of urinary reaction. It had been previously stated that gastric acidity might be estimated from a consideration of blood carbon dioxide tension but Matzner and Gray (97) state that the method is too complex and the results too variable to be reliable.

The subject of an adequate test meal has probably caused more controversy than any other phase of the question of gastric analysis and there are practically as many meals or variations of meals as there are investigators. Meals may be divided into two great groups - the liquid and the solid, with firm supporters on each side. The solid type of meal is the older of the two and it possesses the following advantages; 1. Psychic and mechanical factors are not sacrificed 2. The secretory response is more constant and in higher.

Ioffe (73) states that a dry meal shows slightly increased total acid, increased secretion in the first hour, and diminished emptying time. The disadvantages of the solid meal are (102); 1. Psychic and mechanical factors vary with the individual and should be completely excluded for the sake of uniformity. 2. Lumpy masses in the stomach seriously interfere with extraction of samples and there is a tendency to layer out. 3. Homogeneity of gastric contents is not obtained. 4. Duodenal regurgitation is often hard to recognize 5. Samples must be filtered.

The liquid meal is said to have the following

points in its favor (109) (102) (59) 1. Variable psychic and mechanical factors may be eliminated by injection of the meal through the tube 2. The liquid is easily recovered as samples are needed 3. The mixture of gastric contents is assured 4. Blood, bile mucus, debris and pus are easily recognized and a good microscopic examination is possible 5. Filtering is unnecessary 6. There is minimal salival admixture 7. No albuminoids or salts are present.

The disadvantages of the liquid meal are relatively few (59) (130) 1. Liquids leave the stomach before the test is completed 2. Maximal secretory response is not obtained due to lack of psychic stimulation.

A purely motor meal is rarely used but for this purpose a barium meal followed by fluorescopic observation is the most accurate (91). McCracken (91) states that in 1914 the Xray showed 70% more retentions than the gastric analysis. Russell (91) states that bismuth or barium is passed through the stomach sooner than the ordinary meal. It is usual to give some easily recognized substance (91) such as rice, raisins or charcoal, a number of hours before the test and if any of this material is recovered, a gastric retention is indicated. This is rather a rough method but is accurate enough for most purposes.

Two other motor methods (91) depend on the excretion of by-products after the meal reaches the intestine. By one method, salol is given and then the time of appearance

of salicylic acid in the urine is noted. The other method is similar and consists of giving iodoform with subsequent examination of the saliva for iodides.

Before discussing the various types of secretory meals, it would be wise to determine what factors are necessary to an adequate meal; 1. The meal must not be disgusting nor distasteful to the patient (69) (92) (110) 2. It must not be irritating to the stomach (92) 3. The meal must arouse strong secretory response by placing a load on the secretory mechanism (69) (92) 4. The meal must contain glucids, lipids, salts and water (92) 5. It must be out of the stomach in one hour (92). Barkhash (7) and Antoniak-Czyzewska (4) state that the meal must be free of protein, salt and acid if accurate results are to be obtained. Hess (69) adds that the meal must not hinder titration. Pollard and Bloomfield (20) (116) state that in order to be of value, the gastric analysis must be 1. applied under standard conditions 2. Must impose a load on the function under consideration 3. Must be capable of identical repetition 4. Must yield information which experience shows to be useful 5. Must be complete enough so that conclusions can be drawn. They give the following criticisms of test meals in general; 1. Appetite or distaste for the meal is not considered 2. Speed of eating and quantity of saliva are not regulated 3. The meal does not necessarily give maximal stimulation 4. The investigator is not dealing with pure

gastric juice 5. If the meal leaves the stomach rapidly, the remaining juice has a high acid value, but if there is delay, the buffer action of the food may mask the true acidity.

6. The investigator gets only a general idea as to the volume of the juice. Bloomfield and Keefer (18) and Pollard and Bloomfield (116) stress the necessity for the establishing of normal values for volume and acidity of secretion.

Some writers claim that the mere presence of the gastric tube will stimulate secretion as effectively as a meal but there is no general agreement on this point.

McCracken (91) Pavlov (111) Carlson (28) Cannon (26) and Orłowski (110) state that neither foreign bodies nor the tube will produce secretion, while Scimors & Riegel (57) Tiefensee (136) Galambos (56) and Germain (61) maintain that the tube is an adequate stimulus. Kahn & Stokes (77) carried on a very interesting experiment on a series of patients having gastric fistulae. Gastric contents was obtained through the esophagus by means of a tube and on alternate days through the gastric fistulae. They showed a marked decrease of titratable acidity with an increase in Ph due to the passage of the tube and this was most marked in the fasting juice. For this reason they conclude that no reliance can be placed on fasting juice findings, but after a meal, results are more accurate.

Von Leube (59) first used ice water as a secretory stimulant and he felt that the coldness was an im-

portant factor. According to Garbat, Heidenhain, Santotski, Pavlov, Foster & Lambert, Bergeim, Rehfuess & Hawk, Sawitch & Zelcony, Carlson & Orr, Brinkman (59) and Petrowich (113), water is a gastric secretory stimulant. However, Ivy (75) and Moffatt, Mitchell & Powell (103) cite the following objections to the use of water as a secretory stimulant; 1. There is a notable variation from day to day 2. Normal patients frequently show achlorhydria 3. Regurgitation of bile is more frequent 4. The rate of emptying is more difficult to determine. Barkhash (7) states that water is not a suitable meal for gastric analysis because there is no psychic phase but Vanderfy & Varady-Borbely (141) state that water, although a weak gastric stimulant, has a definite field of usefulness and Garbat (59) goes even further, saying that water is the most practical of the fluid meals. Orłowski (110) got no stimulation of normal stomachs by distilled water but irritable stomachs would respond. Tinker (138) noted that more water would not enter the duodenum until the previous portion had been neutralized. Normal saline left the stomach sooner than plain water but hypertonic solutions remained longer.

The Ewald meal, consisting of two slices of bread or toast and three hundred to four hundred cubic centimeters of weak tea or water (91) (139) is one of the oldest in use. A modern variation substitutes a shredded wheat biscuit in place of the bread because this eliminates the presence of yeast cells and lactic acid. The Boas meal has

also been commonly used (91) (139) and it is prepared by boiling a tablespoon full of oats in a quart of water, down to a pint of gruel. This meal also contains neither yeast nor lactic acid. Riegel (91) (139) thought that a more balanced meal should be used and so he advocated a meal consisting of four hundred cubic centimeters of bouillon, one hundred fifty to two hundred grams of broiled steak and one hundred fifty grams of mashed potatoes. The Fischer meal (139) was also designed to give a more balanced meal and it is the original Ewald meal plus a quarter of a pound of broiled hamburger. These latter two meals, like the modern Smithies balanced meal, are withdrawn in three to four hours instead of three quarters to one hour. McCracken (91) modifies the Beas meal by using double the amount of oatmeal. In all the fractional meals, the contents are withdrawn in ten to twenty cubic centimeters samples at ten to twenty minute intervals and then at the one and one half to two hour period, the remainder is withdrawn. Madariaga (92) uses a milk mixture as follows: pulverized milk 5 grams, distilled water 250 grams, soft water 15 grams, sugar 15 grams and five drops of vanilla. After the analysis they introduce sixty cubic centimeters of sodium bicarbonate solution. They claim that their meal is correct physiologically, chemically and psychically. They further maintain that it is practical and is given in normal quantity. Petrowa (112) in a series of experiments

on dogs with Heidenhain-Pavlov fistulae, tested the stimulating ability of a number of substances. He found that meat produces an unequal concentration and varied results. Absinthe (herba absinthii) gives a relatively slight stimulating effect. The Russian Maggi preparation gives a very small quantity of juice, but Hess (69) obtained higher curves with it than with alcohol. To continue with the results of Petrowa. A 5% decoction of dried mushrooms gave considerable secretion but Petrowa found that a 7% decoction of dried cabbage gave the best chemical and physiological stimulation. Orłowski (110) (109) found bouillon and meat extracts to be much better as gastric stimulants, than the Ewald meal. He found that the vegetable juices were far superior to other forms of meal but beets, potatoes and cauliflower had to be eliminated because of discoloration, after ingestion. The most satisfactory meal was found to consist of two hundred cubic centimeters of fresh crushed cabbage. A fractional examination was carried out and an Ewald examination was run in each case as a control. Orłowski found the following points of preference for cabbage juice; 1. Clearness and facility of recovery 2. Increased homogeneity and no layering 3. Easiness of filtration 4. Facility in recognizing mucus, pus, blood, bile and debris 5. Smallest residual particles are easily recognized 6. Fasting juice is not necessary 7. This meal is especially useful when the appetite is impaired,

psychic factors of digestion being inactive and chemical stimulation being necessary. He states that the results are explained by the chemical stimulation of the stomach by the nitrogenous substances in the vegetable juices. According to Allodi (1), vegetable juices make a very satisfactory gastric secretory meal. Antoniak-Czyzewska (4) uses three hundred cubic centimeters of a strained barley gruel. Ramond (120) uses a meal consisting of ten grams of peptone in five hundred cubic centimeters of water. Mirkin (102) experimented with a 5% lipoid mixture and while he secured adequate secretion, he objected to the opacity of the mixture and to the buffer substances which hindered titration. Frenkel (54) used a fish broth prepared without salt, pepper or onion but this would be rather distasteful to the ordinary individual. Strauss (133) in 1922 used three hundred cubic centimeters of mildly sweetened tea. He stated that it was physiological, easily digested, excited secretion and was distinguishable from gastric juice. Some liquid meals, he affirmed, have a weak stimulating power due to lack of mastication and psychic stimulation. Barkhash (7) feels that tea is not suitable for gastric analysis. Schaverin and Ostrovida (133) investigated variations in secretion by minor changes in the method of preparation of food and variations in sense of taste and lack of taste. They reached no conclusions.

Another type of liquid meal is the caffeine solution of Katch-Kalk (59) which is two tenths of a gram of caffeine in three hundred cubic centimeters of water. Variations in results are reported in the use of caffeine. Petrowa (112) claims that it gave no more stimulation than distilled water while Smirnaff (130) published results after caffeine as identical with those after the Ewald meal. Mirkin (102) used intravenous caffeine and found it very satisfactory, bringing on a profuse secretion even after small doses. Emptying time was shortened and the ferments were not destroyed. In only one half the cases was the Ewald stimulus stronger than the caffeine. Mirkin therefore accepts caffeine as a good standard fluid test meal whose action is not directly on the mucous membrane but after absorption, directly through the blood stream. Antoniak-Czyzewska (4) and Barkhash (7) object to caffeine on the ground that it is not physiological. Lickint (88) used Ewald meals and Katch-Kalk meals on successive days in one hundred patients. He found agreement of results in one third of cases, a difference of ten points up or down in one third and incomparable differences in the other third. Tiefensee (137) also uses the Katch-Kalk solution. Garbat (59) states that coffee can not be used because it probably contains histamine in addition to caffeine.

The Ehrmann alcohol test meal is advocated by a number of experimentors. Petrowa (112) Antoniak-Czyzewska

(4) and Barkhash (7) agree that it is a strong stimulant but state that alcohol is not a normal physiological stimulant. Cheney (31) uses fifty cubic centimeters of a 7% alcoholic solution instead of the original one hundred cubic centimeters and finds it quite sufficient. He uses the fractional method and believes that the results are quite comparable to those obtained by other test meals. There is a greater ease of examination and interpretation of results, he says, Ishikawa (74) found ten cubic centimeters of alcohol to be more than sufficient to intoxicate some Japanese. He highly recommends this type of meal but says that it does not reveal the relation between acidity of gastric juice and the time of excretion. Sanders (130) found lower results with alcohol than with the Ewald meal but Retschild and Seddeg were not able to check his findings. Smirneff (130) got a rapid rise in acidity but the peak was not as high as with the Ewald meal. Galli (57) believes that Ehrmann's meal is practical, simple, accurate and complete. Markoff (94) favors the use of the alcohol test meal. Friedrich (55) states that it makes little difference what stimulant is used but he feels that alcohol is best because of its transparency and absence of chlorides, acids and proteins. He uses the Ehrmann solution for uniformity and comparability, the only variable factors being introduction and depth of the tube. Vandorfy and Varady-Borbely (141) ran a series of experiments comparing the efficiency of water and alcohol as gastric

secretory agents and they found; 1. All cases of hyperacidity showed a higher curve with alcohol 2. Normal cases showed a higher free and total acid with alcohol 3. Hypoacidity cases gave higher values with alcohol. Tiefensee (137) found that alcohol could not be used in women and children because of the resulting intoxication. He states that the pleasantness of alcohol to men patients caused stimulation whereas the unpleasant sensations experienced by women caused secretory inhibition. Garbat (59) recognizes the advantages already mentioned for alcohol and in addition he mentions the relatively sterile aspect of the solution. He found duodenal regurgitation to be more frequent with alcohol than with the Ewald or water meal. Alcohol was found to be a stronger stimulant than caffeine but Garbat (59) declares that alcohol is non-physiological, is irritating to the stomach and may cause intoxication. Orłowski (110) states that alcohol is not a suitable meal. McLean & Griffiths (90), Franks (53), and Delhougne (38) state that peptic activity is greatly stimulated by alcohol and that this is not necessarily parallel with the degree of stimulation of acid secretion. Kohn (83) believes that alcohol is superior to the Ewald meal except in men who habitually use alcohol.

The use of histamine, intravenously or intramuscularly, has attracted much attention and considerable investigation has been done, using it as a gastric secretory agent. Drouet (43) got no effect when the drug was given

by mouth, but after subcutaneous injection there was a profuse secretion in ten minutes, reaching a maximum in thirty minutes and then persisting for from one to one and one half hours. Moya (108) noted that the viscera and particularly the stomach showed marked vascular congestion after injection of histamine. He observed macroscopic blood in one case and therefore states that histamine is apt to increase the amount of hemorrhage in ulcer patients. He got a much greater stimulation from histamine than from the Ewald meal. A number of men (119) (20) (2) (63) (3) (116) (138) (17) (61) (140) (83) (62) feel that histamine is the best secretory stimulant now available. Kohn (83) says that histamine is used to test the maximum secretory ability of the stomach and that the results, reaching a maximum in thirty minutes, are higher than with any other form of stimulant. The drug acts by paralyzing the inhibitor fibers of the sympathetics. Gompertz (62) feels that as little as twenty-five hundredths of a milligram is sufficient and this quantity causes no undesirable results. Bloomfield and Pollard (20) had been using one tenth of a milligram per ten kilograms of body weight and Andresen (2) used one cubic centimeter of a one to one thousand solution. Ragle (119) states that histamine is the only positive stimulant to gastric cells, that the results are constant and give the true condition of gastric function at the time of examination. Cheney (32) believes that histamine is an abnormally powerful gastric stimulant but he states

that the increase in acid values is usually proportional to the acid values obtained by other methods of testing. Babkin (5) says that histamine increases volume and acidity of secretion but he states that the enzyme content is not increased. The general concensus of opinion (63) (21) (83) (140) (36) (32) (35) seems to be that the most important use of histamine is in the differentiation of the achylia. True achylia does not respond to histamine while pseudo-achylia gives a mild response. Beckus (21) states that histamine gives increased secretion in normals but that hyperacidity cases do not respond. He does not feel that histamine will supplant the Ewald fractional method now in use. One important point in favor of histamine is the fact that the investigator is dealing with pure gastric juice and not with a diluted mixture. This may account for the higher values obtained by the use of histamine. Matheson & Ammon (96) found that histamine stimulates the peptic activity earlier and to a more marked degree than the acid formation. Mogena (105) obtained similar results and states that there is no parallelism between the acid and peptic curves. Kemper (79) also found histamine to be an intense peptic stimulant. Cohen & Brock (34) believe that histamine secures maximal secretion by mobilizing all of the reserves of the stomach. The latest and most complete investigation with histamine is that of Comfort & Osterberg (35) who formulate the following questions; 1. Is histamine

so much more helpful in diagnosis that it should replace the Ewald meal? 2. Is there any field of gastroenterology in which histamine gives information of outstanding value other than in the differentiation of true and false achylia? 3. Are volume and acidity important enough to be made the basis for distinguishing between benign and malignant lesions? They reached the following conclusions; 1. With histamine it is possible to distinguish transitory secretory disturbances but it does not always give conclusive information as to the lesion or the prognosis. 2. Histamine does not always give maximal response and its constancy may be questioned. 3. It is not apparent that the response of gastric secretion to histamine is of greater value than the response to the Ewald meal in differential diagnosis. 4. There is a significant relationship between volume of secretion and free acid content. Volume varies widely in all types of lesions but the diagnostic value is limited and possible errors in estimation are too great. 5. Histamine is not of sufficient value to replace the Ewald meal. 6. The value of histamine after surgery lies in the disclosing of free acid masked by regurgitation. 7. There is evidence of the non-importance of the hormonal influence of the antral portion of the stomach in maintaining the secretory capacity of the stomach. Pollard and Bloomfield (116) using histamine, attempted to set a normal standard from which deductions might be drawn. They found that if the total secretion was collected at successive ten min-

ute periods, the greatest volume was obtained twenty to thirty minutes after stimulation. Half of the cases fell within the limits of twenty-one to twenty-five cubic centimeters, most of the larger volumes being in young people and the small volumes in people over fifty years of age. The upper limit of acidity was found to be in the vicinity of one hundred and fifty and this was approached by histamine.

A small group of investigators (69) (136) (55) (109) find that so long as there is stimulation of the stomach, the exact type of stimulant is not important and the results are comparable by any method. Orłowski (109) finds that the different test meals stimulate gastric function primarily by means of psychic factors and then by chemical stimuli, namely, by water, products of digestion and in the use of meat and bouillon - by extractive substances. He feels that the psychic factor is most important and so any meal is suitable if it is not repulsive to the patient. Friedrich (55) believes that it makes little difference what secretory stimulant is used but that it is desirable to use various meals in various cases due to individual differences in reaction to stimuli. Tiefensee (136) used various meals or mere mechanical stimulation and found that the nature of the stimulant had no influence on the curves obtained. Hess (69) used Ewald meal, Ehrmann meal, maggi cubes, Chinese tea, tincture of quinine and mustard water in his experiments and in 80% he obtained

the same curve despite the difference in stimuli.

Various other substances and drugs have been used in attempting to stimulate the gastric mucosa. Piersol & his co-workers (114) following the method of Finklestein, injected four cubic centimeters of a 1% solution of neutral red intramuscularly and then noted the changes in gastric function. Finklestein found that the dye appeared in the gastric juice as follows; in hyperacidity-seven to eight minutes, in the normal in ten to fifteen minutes and in hypoacidity in twenty to sixty minutes. The stain was deepest around the pylorus and so Finklestein concluded that the acid secreting cells were mainly concerned in the excretion of the dye. Piersol (114) confirmed these results but felt that a quantitative determination was of no value. He states that neutral red may be used to differentiate between true and false achylia. Animal experimentation showed; 1. Neutral red given intramuscularly, was eliminated by the entire gastric mucosa and the whole small intestine down to the caecum. 2. Elimination by bile and urine showed a greater concentration. 3. No dye was found in the saliva. 4. Lymph nodes took up the pigment. 5. The central portion of the stomach dyed most deeply but all the mucosa was colored somewhat. 6. A relatively small percent of neutral red was eliminated by the stomach. 7. There was a rough relationship between amount of dye secreted, time of appearance and degree of acidity.

No dye was excreted in true achylia. 8. Neutral red is an imperfect gastric secretory test and it gives no evidence as to motor function. Streicher (134) gave forty milligrams of neutral red intramuscularly and eight ounces of strained oatmeal gruel by mouth. He found that neutral red aids in the differentiation of the achylia not because of the dye but because of the long time needed to perform the test. The neutral red test may be used as any fractional test but the dye has no property of stimulating gastric secretion. Cheney (32) says that the beautifully shifting curves obtained over a two or three hour period represent changes in dilution more than in acid secretion. Clear solutions are preferable but the factor of dilution is still present. He believes that the best method is the use of dyes and determination by the colorimeter. Kohn (83) believes that findings with neutral red agree with results obtained by the use of histamine. Bockus (21) states that the failure of the stomach to secrete neutral red after intravenous injection, makes a reliable diagnosis of achylia.

Moffatt, Mitchell & Powell (104) obtained the following information with the use of atropine and pilocarpine. Atropine, hypodermically, in full doses, gave a diminished gastric secretion and by mouth it had a powerful local effect on the nerve endings. Diminution of acid by this means lasted longer than neutralization by alkalies. Atropine facilitated and speeded up the rate of emptying

of the stomach. Pilocarpine gave no marked increase in gastric acidity but this may have been due to the profuse salivation. Pilocarpine retarded the emptying of the stomach. Kerpola (80) gave one hundredth of a gram of pilocarpine hypodermically and noted an increase of secretion in the fasting stomach. Epinephrine was not found to be effectively in altering secretion but it caused the stomach to contract. This observation is also borne out by Tinker (138) who also noted that stimulation of the vagus nerve caused vigorous peristalsis, opening of the pylorus and increase in secretion. Sympathetic stimulation gave opposing results. No direct relationship between secretion and motility could be demonstrated. Atropine, pilocarpine and adrenalin gave results comparable to those obtained by Moffatt, Mitchell & Powell. Tinker (138) found that pituitrin increased peristalsis, increased pyloric tone and diminished secretion. Ergotamine paralyzed the sympathetic fibers and gave results opposite to those obtained by adrenalin. Butcher (25) confirms the results obtained with atropine.

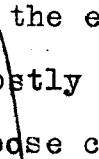
Ivy & Javois (172) found that hydrolyzed proteins had no effect when given subcutaneously but by mouth they gave a secretory stimulus which could be inhibited by atropine. Amino acids by mouth acted as secretory stimuli as did various amines, histamine being the strongest.

Ivy, McCarthy & Orndoff (173), in studying the effects of the roentgen ray on glandular secretion, reached

the following conclusions. Exposure of the thorax of Pavlov dogs to Xray sufficient to produce a first degree burn, gave no effects on gastric secretion and there were no symptoms. The same dosage over the lower abdomen gave temporary an-acidity or hypoacidity with anorexia. There was a gradual return to normal with progressive loss of weight and ca-
chexia. Autopsy showed chronic ulceration of the intestine. A human erythema dose over the lower abdomen gave hyper-acidity for one or two days, followed by anorexia, hypo-acidity and sometimes diarrhea with a return to normal by the fifth day. Seventy-five percent of the human erythema dose, used in the therapy of a malignant tumor, gave mild acute symptoms of the intoxication with anorexia, anacidity and hyposecretion. The intestinal mucosa was found to be twice as sensitive as the fundal mucosa of the stomach. The con-
clusion was that the Xray could not be used in the therapy of conditions needing a temporary reduction in gastric acidity.

Before discussing the various phases of the physiology and chemistry of the stomach, it might be well to briefly review the anatomy and more particularly the histology of this organ. The stomach serves a double pur-
pose in mammals, acting both as a reservoir and as a pre-
liminary agent in digestion. Here, food is thoroughly moist-
ened, softened and partly dissolved by the gastric juice, comminuted by the contractions of the muscular wall, and

transformed into a doughy mass called chyme. When a certain state of softness or acidity has been attained, the chyme is transferred to the duodenum in small portions (26) and thus the function of the stomach is in part mechanical and in part chemical. The first is taken care of by the muscular coat and the second by the various glands of the mucous membrane. In addition, special glands provide for the lubrication of the mucosa. The stomach is one of the most difficult organs of the body to preserve for post-mortem study, for as soon as circulation ceases, autolysis of the wall begins. Even the true macroscopical form of the stomach is not known exactly because at autopsy it is seen to be a large, flattened, curved sac whose shape does not agree with the J or hook shape so clearly shown by Xray examination of the stomach during life. The gastric cavity, especially in the empty state is hardly larger than that of the intestine. The conical opening from the esophagus is called the cardia and just to the left, the wall bulges upward and forms a pouch known as the fundus. Here gases tend to collect. The transition of the stomach into the duodenum is called the pylorus and it is guarded by a muscular sphincter. The incisura or isthmus tends to constrict the stomach at its mid-portion. Macroscopically, the surface of the filled stomach is stretched evenly, but in the empty, contracted state, it forms numerous high, mostly longitudinal folds, made possible by the very loose consistency of the submucous layer and the



muscularis mucosae. The whole thickness of the mucous membrane of all parts of the stomach is occupied by a multitude of glands, which open into the bottom of depressions in the mucosa, called gastric pits. The gastric glands are of different character in different regions of the stomach and on this basis the stomach is divided into three zones. The first zone, a narrow, irregular, ring-shaped area around the cardia, is called the cardiac area and contains glands of the same name. The second zone, the largest and most important, comprises the fundus and the proximal two thirds of the stomach and is called the fundic portion. The third or pyloric region occupies the distal third of the stomach. These regions vary with the individual and are never sharply delimited.

The surface epithelium of the stomach is made up of tall, very regular, simple, columnar cells. These cells are very difficult to study but in the superficial portions, above the nuclei, pale round granules are closely packed. These granules are a particular kind of mucin and after having left the cells, these granules furnish the alkaline layer of mucus which lubricates the surface of the mucosa. Thin, thread-like mitochondria, the basis of all cellular activity, are prominently present in the basal portions of the cells. The outermost cells do not reproduce but mitosis takes place in the gastric pits and new cells are pushed out to the surface by growth pressure. The gastric

glands are of the simple, branched, tubular type and are densely arranged, perpendicular to the surface of the mucosa. The total number of these glands is estimated at thirty-five million.

There are four types of glandular cells found in these glands and many names have been applied to them. The zymogenic or chief cells are arranged in a single layer on the inner surface of the basement membrane and line the lumen of the lower half or third of the glandular tubule. They have the usual pyramidal form of glandular cells and disintegrate almost immediately after death. In the resting condition, the inner parts of these cells are full of coarse, brilliant granules but after intense secretory activity, the cells are smaller and contain but few granules. The granules are pepsinogen, the antecedent of the enzyme pepsin. Terminal bars protect the free surfaces and sometimes the lumen sends out short, conical prolongations between the cell bodies. Mitosis is never found and it is possible that the zymogenic cells arise from differentiation of the mucous neck cells, as described later. The parietal cells are scattered singly between the zymogenic cells throughout the whole length of the gland but more numerous toward the neck. These cells are spherical or triangular and occupy a more peripheral position between the zymogenic cells and the basement membrane. The cells contain many mitochondria but no distinct granules. Canaliculi are characteristically

present intracellularly, connecting externally with branches of the glandular lumen. Mitosis is common in these parietal cells whose function is the production of hydrochloric acid or its precursor - probably an unstable organic chloride. Mucous neck cells are found in the necks of the glands, arranged in one layer, filling the spaces between the parietal cells. They abruptly give way to zymogenic cells at an inconstant level. These cells are filled with very pale transparent granules which stain as mucin, different from that of the surface epithelium. Mitosis does not take place. Argentaffine cells are occasionally observed scattered singly and without visible order. Their function is unknown.

The pyloric glands open into very deep pits and have more branches than in the body of the stomach. The glands here are also of the simple, branched, tubular type but the divisions are more numerous, the lumen is larger and the tubules more coiled. Pyloric glands contain only cells resembling mucous neck cells with very occasional parietal or argentaffine cells. Cardiac glands are compound tubular glands and open into very shallow pits. Clear glandular cells are usually found but there may be parietal cells also. In the pyloric region, spherical accumulations of lymphoid tissue, called lenticular glands, occur normally. Under the mucosa lies the muscularis mucosae which consists of an inner circular and an outer longitudinal layer of smooth muscle. From the inner layer, smooth muscle

cells run between the glands toward the surface. Contraction of these strands compresses the mucous membrane and probably facilitates emptying of the glands. The submucous layer consists of loose, irregularly arranged connective tissue, which contains fat cells, basophiles, wandering lymphoid cells and eosinophiles. This layer contains the large blood and lymph vessels and venous plexuses. The muscularis externa consists of three layers - an outer longitudinal, a middle circular and an inner oblique. The outer layer is found only along the greater and lesser curvatures. The middle layer forms the pyloric sphincter which is open when the stomach is empty. The serosa is a thin layer of irregularly arranged connective tissue tightly attached to the muscularis externa and covered by mesothelium. On both curvatures of the stomach it is continuous with the large and small omenta. In the stomach the arteries arise from the two big arterial arches along the greater and lesser curvatures and pass to the dorsal and ventral surfaces. They pierce the muscularis and enter the submucosa where they form a large longitudinal plexus which supplies the muscularis and mucosa by capillary networks. Venous vessels follow a similar plan and are provided with valves in the submucosa.

Lymphatics of the stomach begin as well developed blind or looped capillaries in the submucosa, lying deep to the blood vessels. They anastomose freely and surround the glandular tubules. The innervation of the stomach

is by vagal and sympathetic fibers. The latter form the myenteric plexus of Auerbach between the muscular layers, and the submucous plexus of Meissner within the submucosa. Vagal fibers enter these plexuses and terminate in arborizations. Both motor and sensory elements are present but their distribution and relationship is indefinitely known.

After the fractional analysis began to be practised rather generally, many types of curves were described by different investigators. Rehfuss (6) in 1915 differentiated the following so-called normal types of curves;

1. The peak is reached in one hour, the level then descends and reaches the fasting level by the end of the second hour.
2. Continuous hypersecretion in the form of a uniform plateau.
3. A steep rise for thirty minutes is followed by a gradual fall.
4. A slowly rising curve.
5. The step-ladder type of curve.

Bennett (12) and McCracken (91) state that the curve depends on the amount of saliva swallowed, the amount of pyloric mucus secreted and the degree of duodenal regurgitation. McCracken (91) criticizes gastric analysis curves by saying that the curve for free hydrochloric acid leaves out the protein acid salts and the neutralized acid whereas the curve of total acid takes in the organic acids and dissolved carbon dioxide, so neither is strictly accurate. Two serious hinderances to accuracy are food contamination and duodenal regurgitation. He groups gastric curves into four large divisions; achlorhydria means no trace

of free hydrochloric acid, hyposecretion does not exceed ten percent free acid, normal shows high, medium and low values but does not go under ten nor over sixty percent, hypersecretion goes above sixty percent at one or more period during the examination. McCracken (91) holds that eighty percent of people fall into the so-called normal group. He says that the resting content of the stomach is very important and normally varies between twenty and one hundred cubic centimeters. Secretion is constant but varies from time to time. Variation in resting content may be due to variation in tonus and motility as well as in secretion. The composition of the fasting juice is more important than the quantity. A marked difference between the free and total acidity may mean a high organic acid content (91) because Fleischer (52) states that the presence of lactic acid is inversely proportional to the amount of hydrochloric acid. McCracken (91) states that the investigator must know the volume of secretion as well as the true percent acidity because there may be an increase in fluid content without a corresponding increase in acid although the two factors are usually comparable. In the usual analysis, the volume is diluted by food, saliva and regurgitated duodenal juice. Also an unknown amount of gastric juice may pass into the duodenum and the real acidity is masked by neutralization, by food, saliva, duodenal juice and pyloric antrum secretion. However, in digestion these factors

are normally present. Henderson (68) gives twelve to forty-nine cubic centimeters as the normal fasting content, with normal acid varying in the cycle from none to forty for the free and ten to fifty-five for the total. The usual result was free acid thirty-five and total fifty. The fasting level was regained at the two and one half hour period and the greatest motility was from the one and three quarter to the two and one quarter hour period. Bennett (13) feels that gastric analyses are inexact because of the normal variation in chemical composition of stomachs. This variation depends on the following series of factors which change from day to day; extrinsic-1. Composition of the meal 2. Fasting content - intrinsic-1. Stomach content is a mixture of food, gastric secretion, saliva and duodenal juice 2. Psychic factors such as difficulty with the tube, fear and initial inhibition 3. Errors in sampling resulting from lack of homogeneity. Close to the mucosa and close to the pylorus, the acid concentration is greater. The normal fasting juice varies between ten and one hundred cubic centimeters and averages about fifty-four. There is no free acid immediately after the meal but it usually rises to nearly fifty and then goes down again. Total acid is roughly parallel but ten to twenty points higher. Parallelism is never exact due to duodenal regurgitation. Orłowski (110) Petrowich (113) Ishikawa (74) Ioffe (73) and Barkhash (7) find that the acidity has reached its maximum one hour after the introduction of the meal and tube. Ishikawa (74), using

alcohol, gives the normal free acid value as fifteen to thirty and that for the total as twenty to forty. He states that secretion declines after three hours regardless of the condition of the stomach and that excretion of the test breakfast begins after two hours normally, when tested by the salicylate method. Smirnoff (130) gives the time of maximum secretion as one hundred thirty minutes, one hundred three minutes and seventy-six minutes with the Fwald, Katch-Kalk and Ehrmann meals respectively. Andresen (2) feels that the acid curve is not the most important thing to be determined but rather the motility and admixtures with such substances as blood, mucus, bile and pus. Ioffe (73) states that the amount of secretion depends on the amount of water in the body and when the blood is poor in water or when water is prevented from passing from the blood-vessels of the stomach into the glands, secretion is diminished. Intake of water increases gastric secretion only if the amount taken exceeds six hundred cubic centimeters. Casaffousth (29) believes that nothing standard has been established as yet and feels that the fractional merely allows the explanation of pain according to the time of highest acidity. Antoniak-Czyzewska (4) states that certain curves are repeatedly observed in various individuals and he differentiates the following secretory types; 1. A steadily increasing secretion 2. An abrupt increase followed by a plateau 3. Gradual increase and decline 4. Step-ladder increase 5. Rapid increase and step-ladder decline.

He states that traces of blood are normal but significance is attached to mucus and blood. Barkhash (7) says that there is no single normal type of curve but that after any stimulus, gastric secretion continues for from two to three hours. He says that investigators must ascertain the acidity, amount of fasting juice, amount after stimulation, amount after elimination of the stimulus and the emptying time of the stomach. Vandorfy & Varady-Borbely (141), in their comparison of results by stimulation with water and alcohol, got normal values as follows; water, free fifteen to thirty, total twenty to forty; alcohol, free twenty and total thirty. Their hypoacidity cases ran; water, free ten and total twenty, alcohol, free fifteen to twenty and total twenty-five to thirty. They believed that an anacidity with the water test might show free acid after a stronger stimulus. Hess (69) noted that the maximum values varied with the type of meal used. Kohiyar (82) believes that women run lower normal curves than men while Marriott and Davidson (95) and Pollard and Bloomfield (116) have shown that children, and especially infants, may not have sufficient free acid to give a red reaction to Topfer's reagent. Wright (191) found some free acid in the gastric contents of children aged six to fifteen and the total acidity was the same as that for adults. The position, size and shape of the stomach as determined by Xray, varied widely and more so toward puberty. There were no sex characteristics except after the age of eleven,

when the stomach tended to be lower in the female. Motility was uniformly greater than that seen in the adult stomachs.

Bennett (12) and Friedrich (55) found that a highly acid resting juice meant a high acidity to follow. Bennett (12) noted a marked absence of uniformity as to motility but ninety-four percent of patients showed a gradual climb-gradual decline type of acid curve. With cabbage juice, Orłowski (110) got normal values of free, forty-nine, total sixty-eight and combined eighteen, which are higher than with other types of stimuli. He states that one of the most frequent disorders was a prolonged secretion for three to four hours and in all cases, with marked disturbance, he used several different types of meal to rule out erroneous conclusions. Bolton & Goodhart (24) say that HCl rises to a certain height during digestion and then falls. The height of the curve varies with the individual and in normals due to regurgitation. This is said to be physiological. They believe that the curve is merely an index of behavior of the pyloric sphincter.

There are a number of variable factors which affect the type of curve which is to be obtained. Petrowich (113) declares that the function of the gastric glands may be differentiated into two phases. The first phase is reflex and is aroused by sight, smell, taste, chewing and swallowing. The second phase is chemical and is due to the stimulation of the gastric mucosa by protein salts, extracts and other

products of partial digestion. These factors are thought to act on the pyloric part of the stomach and they continue to act even after complete section of the nerves to the stomach. The importance of the nervous plexuses found in the stomach walls is not known. Petrowich assumes that all stimulation in the chemical phase is transmitted from the pyloric portion to the glands by means of the blood stream. He feels that both phases are closely related. This biphasic idea of secretion is rather generally accepted (113) (57) (91) (13). Mahler & Stary (93) find these two phases and in addition, a third or intestinal phase. They state that there is an unknown latent period before the manifestation of the stimulus. Pavlov (93) says that apparent feeding causes secretion in four and one half to ten minutes while psychogenic stimuli give secretion in six to ten minutes. Secretion is later following injection than after ingestion. Babkin (5) states that the humoral stimuli seem to wash out the secretion already present and then their activity ceases whereas the neurogenic stimuli cause actual secretion which continues for a longer period. McCracken (91) says that the varying rate of emptying causes a varying amount of stimulation in different cases.

The problem of superposition of gastric stimuli lead Mahler & Stary (93) to formulate the question - does superposition of stimuli lead to simple summation potentiation, or decrease in effect. They obtained the following

results. Repetition of the meal immediately after analysis was followed by a stationary condition of the stomach which was definite and characteristic for each stomach. The stomach tended to reach a certain volume as soon as possible and so emptied after the second meal, within the first few minutes. Water secretion was increased after the second meal. This rise in water secretion lead to a decrease in concentration of acid so that consecutive tests could not be run. A negative chloride wave appeared after each meal and as the course became more protracted, the wave became deeper. Moretti (106), after giving two hundred cubic centimeters of meat broth and two tablespoons of bread crumbs, followed by histamine, found that a summation of stimuli leads to decreased secretion. Galambos (56) showed that from one half to one hour after intubation without a test meal, there was a phase of exhaustion of the mechanism of gastric secretion, characterized by a reduction of volume and concentration of secretion. There was secretion of a heavy mucus and bile was regurgitated. This first phase of exhaustion lasted for ten to fifteen minutes and then after twenty to thirty minutes, there was a second phase of exhaustion which lasted for many hours following. Barkhash (7) feels, however, that secretion continues even after elimination of the stimulus.

Psychic and emotional factors have been found to play a profoundly important role in gastric analysis (37). McCracken (91) found that the first analysis frequently

gave lower curves than subsequent ones (139) (87) and that a patient who took the tube easily was apt to show a higher acidity than one in whom the tube was passed with difficulty. Consecutive analyses were found to be most nearly comparable at the one and one half hour period. He (91) states that psychic factors are aroused by seeing, smelling, tasting and chewing and were largely eliminated in his series by the use of an insipid meal and by its injection through the tube. There is no psychic stimulation after the first fifteen minutes so that only the first sample would have been affected. Emotions such as fear and anger were found to inhibit secretion but pleasurable emotions gave no increase. This is ruled out in practice by using a meal which is neither pleasant nor unpleasant. Hypnosis (91) (137) was the mode of investigation of this phase of the subject. Tiefensee (137) records that the promise of a good meal or the telling of the patient of the importance of secretion of saliva, was followed by an increase in gastric secretion whereas if the patient was left alone, a scanty secretion with low acidity resulted. Carlson (28) feels that seeing, smelling and tasting are very important factors in influencing gastric secretion. Cannon (26) caused a dog to become angry by bringing a cat into its presence and at once the gastric secretion in the dog ceased. Bennett & Venables (16) noted that nausea, anxiety and hypnosis caused secretory inhibition but they could not demonstrate that pleasant sensations produced increased secretion.

Butcher (25) passed the tube and removed fasting juice in his series for ten days before the analysis to overcome the psychic influences. He then obtained constant normal curves. Psychic stimulation by chewing gave a rapid increase and high acid level with a rapid fall after the first half hour. Sight and smell were also found to be effective. Fleischer (52) agrees that psychic influences produce considerable quantitative and qualitative changes.

Chemical factors causing variations in gastric secretion have not been very extensively investigated. Ryle (128) found that a decreased salt intake had no effect on secretion after a standard test meal but it caused a diminution in fasting juice. Heelzel (72) investigated the effects of variation in protein intake and found that excessive quantities of protein caused a decrease in acidity of gastric fasting juice. Meat, fish, egg white, egg yolk, vegetable protein and casein were found to be effective. This decrease was explained on the basis of fatigue of the gastric secretory mechanism or to a limited but modifiable secretory capacity. Functional rest by fasting or by protein restriction raised the acidity again. It was suggested that the fatiguability of the gastric secretory mechanism might be a factor in regulating natural or instinctive intake of proteins by determining its limits. Various other types of foods have been found to influence gastric secretion. Ioffe (73) noted that bread exerted a stimulating effect,

between that of meat and milk but digestion with bread lasted longer than with either milk or meat. Carbohydrates were found to leave the stomach first, followed by a mixture of carbohydrates and proteins, then proteins, fats and last, a mixture of ~~fat~~ and proteins. Proteins left sooner in the presence of water, but when carbohydrates were present, no such effect of water on protein was noticed. According to Alodi (1) protein stimulation is due to absorption of extractive substances. Fats are said to depress (Cohnheim) at first and stimulate later but fats differ in their degree of action. Carbohydrates stimulate in an irregular manner.

Mechanical factors exert a definite influence. The work of Hamburger & Spork (66) must be mentioned here in order to get some necessary definitions before considering the mechanical factors. They stated that peptic digestion could not take place until the protein had become saturated with hydrochloric acid. They therefore added HCl to gastric contents until some free acid appeared and this added amount they called the "acid deficit". This acid deficit plus the total acid, equals the "acid binding power", if no free acid was present. If free acid was present, the total acid minus the free acid equals the acid binding power. This acid binding power is also called the buffer value or buffer capacity. Miles & Shohl (101) investigated the effects of dilution, Ph and buffer capacity on gastric sec-

retion. Dilute feeding mixtures were found to leave the stomach more rapidly than others and the Ph of the stomach increased more rapidly with dilute contents. There was also a decrease in total buffer capacity. Buffer capacity remained high until digestion was nearly completed and the stomach contents with high buffer value was found to have a low Ph and vice versa. Ph was relatively low when there was a short digestive period, slow digestion, large feeding or concentrated mixture. When large amounts of gastric contents were found to be associated with high buffer capacity, digestion was found to be incomplete. Standish, Cowgill and Shohl (132) carried out investigations of similar nature and found that the amount of gastric juice secreted was sufficient to increase the Ph between 4.1 and 3.9 for all meals. Therefore, the amount of HCl secreted depends directly on the volume and concentration of the meal. The Ph of the stomach tended to remain nearly constant until the end of digestion. Concentrated meals and meals of large volume took longer for digestion than small or dilute meals. The motility of the stomach therefore varies directly with the volume and concentration of the meal. A given meal was most rapidly digested when it was concentrated and of small volume. The buffer capacity, after an initial increase, stayed fairly constant. Large buffer capacity associated with relatively large volume indicates the beginning of digestion and conversely, small buffer capacity in small volume in-

icates the end of digestion. The effect of concentration on gastric secretion is important and was quantitatively measurable on both secretion and motility.

According to Bloomfield & Keefer (18) (19) and Bloomfield & Pollard (20), volume of secretion and acidity decrease with age. State of health is also found to be a factor.

Considerable investigation has been carried on with regard to the chloride content of the gastric juice. Probably the most complete and plausible work so far is that of MacLean & Griffiths (90), whose results follow. The gastric glands secrete sodium chloride and the concentration of this salt undergoes considerable change at various times in the digestive cycle. Duodenal regurgitation is not the prime factor in regulating the gastric acidity but there is evidence that the chlorine, brought to the gastric glands by the blood as sodium chloride, is secreted at a definite and fixed concentration, partly unchanged and partly as HCl, the extent of this change governing the acidity of the gastric juice. Thus, early in digestion, there is much acid and little NaCl but later and at a point varying in different individuals, the degree of transformation diminishes until more or less all of the salt is secreted unchanged. This gives a fall in acid and a rise in chlorides which corresponds to findings on resting juice which shows slight acidity with high chlorides.

Secretion from the isolated pouch of a dog's stomach during digestion is assumed to behave as a normal human stomach. Here, there is first a rise in acid concentration, followed by a definite fall. The total chloride value in the pouch remains approximately constant during the whole period of digestion. No regurgitation is possible and since there is a decrease in HCl and an increase in NaCl, it follows that regurgitation is not necessary to bring about reduced acidity in the normal stomach in the later stages of digestion but that the changes are due to altered transformation of blood sodium chloride. The total chlorides vary between the narrow limits of .11 and .12 N in fasting juice and rise to this level at the end of digestion. After the ingestion of a meal, the stomach strives by motor activity to empty itself and by secretory activity to bring the fluid contents back to the resting condition where there is little or no acid but a large amount of neutral chlorides. The administration of acid causes the secretion of a neutral fluid containing NaCl and so reduction of acid is mainly by dilution and not by neutralization. Peptic activity of the stomach rises parallel to the increase in neutral chlorides which occurs with diminished acidity. The peptic activity of the resting stomach has a high value comparable to that at the end of digestion. The association of peptic activity and neutral chloride content lies in the fact that the fluid which contains the enzyme also contains the neutral

salt and this accounts for the increase of peptic activity after introduction of acids into the stomach. Kemper (79) bears out this work in general and states that peptic activity is influenced by age and type of food but usually reaching its maximum in thirty minutes after the meal, before the acid peak and showing an average concentration of 1:160 or 1:320. Duthie (45) noted that the increase in HCl after histamine took place at the expense of the neutral chlorides. Roberts (124) feels that the total chloride value is a better guide of secretion than HCl because it includes the neutralized acid also. Matheson & Ammon (96) working with histamine, noted that peptic activity reached its peak before the acid and thereafter peptic activity was maintained at a fairly high level with but a slight tendency to fall. Rudd (126) while comparing gastric secretory response to meals of gruel and cream, came to similar conclusions. He found that the total chloride value was practically constant whereas the total acid and neutral chloride values varied widely. He states that the theory of formation of neutral chloride by neutralization of gastric acid by duodenal juice is incapable of explaining results and he, also, explains the variation in composition of gastric contents on the basis of changes in the amounts of HCl and neutral chloride secreted by the gastric mucosa. He feels that the total chloride value is the most significant finding. Bugler (35) found that the total chlorides

before and after stimulation by the water meal remained practically constant and so he argued that the secretion of HCl depended on the inhibition of secretion of base, rather than on an increase in secretion of chlorides. Comfort & Osterberg (35) however, say that there is such a high correlation between the total chloride value and the free HCl, that there is no need to run a chloride determination. Portis (118) using Pavlov pouch dogs after partial gastrectomy, showed the absence of free HCl but a high total chloride, whereas the secretion in the pouch, representing a similar part of the stomach, continued to show free acid. From this he reasoned that the factor of neutralization plays the most important role in explaining the presence of free hydrochloric acid. Gukacian (65), using the common bile duct-ligation dogs as prepared by Symnuitzky, found that a simultaneous examination of acidity and chlorides showed no parallelism. Roberts (124) states that achylia often follows partial gastrectomy.

This work brings up the question of the importance of duodenal regurgitation which according to Lesnik (87) is always present, and to Bennett (12) is present in 40% of cases. Markoff (94) approached the problem by a simultaneous fractional examination of the stomach and duodenum. His results follow. A simple gastric study was deemed insufficient due to regurgitation. Total chlorides of the stomach contained sodium and potassium salts from the duo-

denum. Occasionally there were more chlorides found in the duodenum than in the stomach and the chloride value was not found to be an absolute index to HCl secretion. The curve of neutral chlorides was thought to be a relative index of the entrance of duodenal contents. The less the volume of duodenal secretion, the more concentrated the chlorides.

The two tubes made possible the determination of the opening of the pylorus, expressed by the crossing of the curves of chlorides and acidity. The pylorus opened thirty, forty-five and seventy-five minutes after stimulation and the acidity was considerably decreased by the regurgitation. Two types of subacidity were differentiated - the actual, where the amount of chlorides was small and the apparent, where slight acidity is accompanied by considerable neutral chlorides. Bolton & Goodhart (24) and Spencer with his co-workers (131) state that duodenal regurgitation is a part of the normal sequence of events in the digestive cycle. McCracken (91) and Boldyreff (23) feel that duodenal regurgitation is an important factor in the self-regulating mechanism of gastric acidity. Boldyreff says that pancreatic secretion is the most important but saliva, bile, succus entericus and pyloric antrum secretion are of secondary importance. Iyen, Bartle & Ellison (89) state that frank macroscopic regurgitation of bile is abnormal except with retching or hyperacidity. Spencer, Meyer, Rehfuess & Hawk (131) say that there is an almost constant presence of

trypsin in the normal fasting juice. This was also noted by Beldyreff, Pavlov, and Ehrmann (131). This trypsin is highly resistant to acid and pepsin and is highest in conditions of low gastric acidity. A solution of 5% sodium bicarbonate was held in the stomach till neutralization to prevent irritation of the duodenum and was accompanied by a high tryptic value. Weak sodium bicarbonate speeded emptying and did not inhibit secretion. Free HCl was not necessary to open the pylorus. Regurgitation was thought to be a protective mechanism to spare the small gut from irritation by acids. Garbat (59) stated that duodenal regurgitation was a factor of importance. He added a few drops of methylene blue to all meals and got a green color even if the regurgitation was not macroscopic. Regurgitation was seen twice as often with fluid meals as with the Boas meal, probably due to the increased difficulty in recognizing it. Boldyreff (22), Cathcart (30) and Carlson (27) agree that the introduction of oil into the stomach causes regurgitation of bile and that the introduction of mineral acids causes regurgitation and neutralization until the fluid is not irritating to the intestine. Debenedetti (37) feels that regurgitation negatives results. Bashenow (8) found that duodenal regurgitation took place if the stomach contents became too acid but there was no regurgitation in the normal or hypoacid stomach. Patients who usually showed regurgitation did not do so, if given NaHCO_3 with the meal. Hyperchlor-

hydria may cause a constant regurgitation which will show an achlorhydria on analysis but all the symptoms will be aggravated by administration of hydrochloric acid. Knapp (81) feels that bile is normally present and is a physiological buffer. Stenosis causes a high acid value due to lack of regurgitation.

Theoretically, there are three types of secretory abnormality possible in the stomach - hyperacidity, hypoacidity and anacidity. These types will be considered in general before clinical entities are discussed.

Hypersecretion is usually assumed to mean hyperacidity, but it is possible to have increased volume of secretion without increased acid concentration. Hewlett (70) says that a vicious circle tends to form because increased acidity causes pyloric spasm with delayed emptying and there is then a greater accumulation of acid secretion. Lanz, Pavlov and Kleemann (6) found that the hyperacid stomach emptied more slowly than the subacid type. Hyperacidity (70) cuts short the salivary glucid-splitting activity and by digesting the proteins more thoroughly than usual, may play a role in chronic constipation. This increased acid content is of clinical importance because of its relative frequency in certain organic diseases and its direct or indirect production of gastric symptoms. Eggleston (151) feels that hyperacidity is due to a greater degree of acid secretion but Carlson (28) presupposes pyloric obstruction

gastric retention and a prolonged secretory response to foods. He states that hyperacidity is never demonstrable in any disease and that pathological deviation is always toward an anacidity. Immerman (171) gives the following causes of hyperacidity; gastritis, gastric ulcer, obstruction, duodenal ulcer, gall bladder disease, colitis, constipation, migraine, tabes dorsalis and abuse of tea, coffee, tobacco and alcohol. Barkhash (7) states that delayed emptying with consequent high acidity may be caused by perigastric adhesions, pylorospasm or gastroptosis with sluggish peristalsis. Boldyreff (151) states that the normal .2% free acid is secreted as .4% and then is neutralized and diluted. He states that in hyperacidity, there has been a failure of dilution and neutralization because of obstruction. His method was by total chloride determination. Eggleston (151) by Xray, could always demonstrate obstruction in cases of hyperacidity. He, with Carlson (28), says that hypersecretion with normal acidity is of motor origin, having a nervous basis. Immerman (171) insists on differentiating hypersecretion from hyperacidity and gives the following reasons for stating that pyloric obstruction is not essential to these conditions; 1. There is a continuous flow of juice 2. Food disappears from the stomach during fractional analysis 3. Bloomfield & Keefer introduced fifty cubic centimeters of alcoholic solution and five milligrams of phenolphthalein and could show dilution and diminution of

quantity by emptying 4. Ivy showed hypersecretion in a pouch dog with pyloric spasm due to the presence of food and products of digestion in the stomach and the contact of acid and digested food products in the intestine.

Hypoacidity is considered by some to be merely a step toward achlorhydria but this view is not generally held. The condition is discussed more fully later.

Formerly, true and false achlorhydria were not differentiated and all conditions of anacidity were spoken of as achylia, implying absence of enzyme also. We now know that the acid secreting cells are injured more easily than the zymogenic cells and so enzymes are found long after the stomach has ceased to produce acid (171) (169). False achlorhydria is a condition in which the stomach usually does not produce HCl, due to parietal cell injury but the mucosa is capable of forming some acid, under maximal stimulation as by histamine. True achlorhydria, as the name implies, refers to a condition in which the mucosa is not capable of producing HCl, regardless of the type of stimulation (83). Considering these new facts, and the variation reported in the percentage of achlorhydrias by the uses of the large as compared to the small tube, it will be seen that the conclusions of the older writers are of little value along this line. According to Kohiyar (82) achlorhydria is a frequent cause of an irritative form of diarrhea. Disintegration of food in the stomach is incom-

plete and this causes enterocolic irritation which is relieved by administration of HCl. Wilkinson (190) feels that achlorhydria may be due to the persistence of the infantile glandular state. Portis (118) states that achlorhydria may establish a different and possibly harmful bacterial flora of the gastrointestinal tract and with consequently greater abnormality but Deschiens (42) and Denis & Silverman (39) (40) (41) find that gastric hydrochloric acid is not bacteriacidal. Deschiens (42) found equal numbers of parasitic infections in hypoacid and hyperacid stomachs. Bacteria lived in different concentrations of gastric juice in the incubator without any inhibition being shown. Bockus (21) states that 53% of the achlorhydrias by the Rehfass method also show lack of acid by the histamine test. He and others (151) (152) feel that a diagnosis of achylia is impossible by the single extraction method. Eggleston (152) says that 10% of patients with digestive troubles have achlorhydria and that 18% of people show anacidity at the one hour period. He and others (28) (184) state that achlorhydria is not uncommon in normal individuals; at least these people are symptom free. The idea usually advanced (152) is that achlorhydria is due to a low grade chronic gastritis. The infection may be by means of food but is more usually hematogenous and is secondary to disease of some other part of the body. Achlorhydria is present before the glands are completely atrophic and this accounts for the false

achylia. Active treatment should be instituted at this stage in an attempt to prevent the patient from slipping over into the true type. It has been suggested that small stimulating doses of histamine might be of therapeutic value. In patients with a total acid under sixteen and no free acid, there is little if any response to histamine. Moschcowitz (184) states that the percent of individuals showing an anacidity increases with each decade. Hamrick (67) found achlorhydria twice as commonly in women as in men (28) and twice as commonly in whites as in negroes. The optimum age seems to be from forty to sixty years of age. Strangely enough, he finds that achylia may be characterized by epigastric distress, sour eructations and is relieved by soda. Achlorhydria is found in such conditions as; alcoholism (67) (83); tuberculosis (67) (83); diabetes mellitus (67) (83); nephritis (67) (83) (171); gastric lues (67) (83) (171); combined sclerosis (152) (190) (147); secondary anemia (152) (171) (184); gastrogenous diarrhea (152) (171) (190); chronic rheumatoid arthritis (152) (147) (190); chronic gall bladder disease (171) (152); colitis (190) (155) (147); acne rosacea (147) (190); urticaria (190); angioneurotic edema (190); sore tongue, lips and gums (190); acute infections (190) (171) (152). Carlson (28) quotes the following authors in connection with conditions found with achlorhydria. Infantile anorexia and atrophy-Wentworth, Sauer; gall bladder disease-Behm, Rydgard, Rhode, Blackford; chronic colitis-Boenheim; pellagra and beriberi-Kitamura, LaRue; acute fevers-Meyer, Cohn, Carlson.

The alkaline tide noted post-prandially in the urine is closely connected with gastric acidity and achlorhydria and has received increasing attention lately. Cohen and Break (34) simultaneously awakened stimulation of gastric secretion by Strauss tea which gives off no minerals or products of digestion to the blood, and subcutaneous histamine. They produced a very uniform initial Ph of the urine by an evenly prepared diet for several days. Determinations of the urinary Ph were by the Michaelis indicator method. On the evening before the test, at 7 P.M. the patient was given one egg, four Zweibachs with butter and two hundred cubic centimeters of Strauss tea. The next morning, in the fasting condition, urine was collected at six and seven o'clock. After the second voiding, the patient was given three hundred cubic centimeters of unsweetened Strauss tea and a subcutaneous injection of five tenths milligram of histamine. Urine was collected every thirty minutes for three hours, the seven o'clock sample serving as a basis for comparison. The normal and hyperacid cases averaged sixteen decimals difference, the maximum difference being noted in two hours. False achylia gave a difference of thirteen, with the maximum in one and one half hours while true achylia gave a difference of six, maximum in two and one half hours. The authors concluded that an increase in Ph by twelve decimals indicated the presence of some free hydrochloric acid. Matzner & Gray (98), using

twenty-five patients and about the same procedure as that just outlined, found an alkaline tide in only 50% of patients showing free HCl. This was ascribed to the use of histamine because it stimulates bile and duodenal juice and because it gives a maximal but short stimulation which may not be long enough to change the urinary reaction. The authors noted that the test could not be run for several hours after awakening, to avoid discrepancies caused by carbon dioxide stored during the night. It was concluded that histamine could not be used in the study of alkaline tide in urine so the authors (99) conducted another series of experiments using a Steere bouillon cube in a cup of warm water. The method and results follow. Urine was collected at 6:30 and 8:30 A.M. and the Ph was determined. The patient was intubated at 9:00 A.M. and the fasting juice was removed, after which the stomach was thoroughly washed. Two cups of the meal were then given and samples were taken every twenty to thirty minutes for three to five hours, urine being collected each time and making sure that the bladder was completely emptied each time. One duodenal ulcer patient with a high free acid did not show an alkaline tide but this may have been due to the constant maximal secretion of the stomach. Other factors were found to be impaired renal function and previous diet. All other cases except two, showed an alkaline tide. True achlorhydria showed a fixed urinary reaction. The authors feel that this combined test may be of value after gastrectomy or in

cases where the tube cannot be satisfactorily passed. They concluded that an alkaline tide could be demonstrated in 85% of cases. Kauders, Porges and Essen (175) state that a hyperacidity case is less apt to have an alkaline tide because the gastric acid value is at a maximum throughout the day and does not rise after a meal. This gives a fixed urinary reaction just as an achlorhydria. They used the method of determination of carbon dioxide tension of expired air but could not get satisfactory results.

The exact mechanism of pyloric sphincter control has been the subject of much theorizing but as yet there is no generally accepted hypothesis. The older idea was that the presence of acid on the pyloric side and base on the duodenal side kept the sphincter tightly closed. Then, when the gastric contents reached a certain degree of acidity, the sphincter opened, chyme spurted into the duodenum, neutralization took place, again the duodenum was alkaline and the sphincter closed. Another idea was based on motor activity and here it was thought that when waves of peristalsis from the stomach and duodenum met at the pylorus simultaneously, the sphincter relaxed momentarily and chyme was discharged into the duodenum in a small spurt. Other ideas were based on the fluid consistency of the chyme or the fatigue of the sphincter but none of these theories explain all of the phenomena and this probably means that no single theory is wholly correct.

While the minute details of the chemistry of digestion do not seem to be pertinent to a discussion of the gastric analysis, nevertheless, in order to bring out certain points in the clinical applications which are to follow, it was deemed necessary to present this phase of gastric activity (139) (180). Fats are not chemically changed by gastric juice but the acid may break down the protein covering the droplets and so destroy the emulsions. Muscular action tends to cause mixing of the fats and gastric lipase may begin the hydrolysis of simple fats as cream and butter. Carbohydrates undergo no change usually but there may be some hydrolysis of complex glucids by the hydrochloric acid. The most important chemical activity in the stomach is that on proteins which first react with the free acid to form acid metaproteins. Pepsinogen is activated by free acid and as pepsin, it begins hydrolysis of the metaproteins, known as acid albumin or syntonin. The next product is a primary protease, then secondary protease, peptones and amineacids. Other terms for these midproducts are used but they are confusing and will not be mentioned here. As the molecule becomes smaller and smaller, it reaches a stage where it can be absorbed by the mucosa and then a local secretory stimulating effect follows. This absorbed substance is the so-called hormone, gastrin, described by Edkins (46) and according to Berri (17) it is histamine or a histamine-like substance. The importance of the normal completion of this digestive process will be considered with the discussion of pernicious anemia.

The relation of gastric acidity to pernicious anemia is worked out more thoroughly than for any other clinical condition and for that reason, pernicious anemia will be discussed first. There is general agreement (152) (184) (171) (151) (150) (148) (154) (147) (169) (137) (67) (140) (83) that pernicious anemia is accompanied by a true achlorhydria; that is, no free acid can be demonstrated even after such stimuli as histamine. Further than this, there is considerable evidence to show that the achlorhydria may precede the development of pernicious anemia by a number of years (189) (145) (168) (179) (169) (184) (152) (150) (154) (185). Fenwick (150) in 1877 first discovered gastric atrophy in association with severe anemia and Cahn & Von Mering first noted the absence of free HCl in cases of pernicious anemia. Hurst (169) says that achlorhydria is the essential predisposing cause of pernicious anemia and following the work of Bartle and Harkins (143) on the bacteriacidal action of gastric juice, he accepts the idea of infection with absorption of toxins as the direct cause of the anemia. Weinberg (150) states that the relatives of a pernicious anemia patient may show a blood picture resembling the latent stage of the disease and Connor (150) cites a list of thirty-eight authors (28) who show a familial tendency in the disease. The familial tendency is also noted by Moschowitz (184). The present concept of pernicious anemia began to be evolved after the work of Minot

and Murphy (183) who found that all pernicious anemia patients improved on a diet of liver, fruits, vegetables and low fats. They ascribed this improvement to the presence of considerable iron and protein in the diet. Sharp (186) and Sturgis & Isaacs (188) showed that by the use of desiccated whole stomach or desiccated stomach defatted by petroleum benzene, a complete remission could be brought about. They felt that either there was an enzyme in the mucosa of the stomach which acted on the gastric protein during the drying process or else, the gastric mucosa, like the liver and kidney, contained a supply of active hemopoietic substance. This desiccated material was found to be more active than liver. Castle, Townsend & Heath (148) correlated and explained all these observations. They showed that the normal human stomach, by virtue of its content of secretions, could produce, by interaction with beef muscle, a substance effective in similar fashion to liver, in promoting prompt blood regeneration and clinical improvement in pernicious anemia. The patient was not able to form this substance. The validity of the hypothesis that the genesis of pernicious anemia is dependent on an inadequate gastric digestion of protein, thus permitting the development of a virtual deficiency in the presence of a diet adequate for the normal individual, was further examined and the nature of this postulated gastric defect was defined. The authors took two hundred grams of beef, incubated it for two hours with

seventy-five to one hundred and fifty cubic centimeters of fasting juice obtained after histamine, used this substance in treatment and got clinical improvement with blood regeneration in ten days. Pig gastric mucosa was found to be effective alone. From these results, the authors (148) arrived at the following conclusions. The active constituent or intrinsic factor of the normal human fasting gastric content is probably secreted by the mucosa of the stomach and is not present in the saliva or pure duodenal juice. This substance is probably organic in nature, is thermolabile, possibly an enzyme and is capable of interaction with protein, the intrinsic factor, or a closely related substance in neutral solution, resulting in the production of a material having a marked hemopoietic effect. This substance is not pepsin or rennin. The lack of this intrinsic factor is probably the essential defect in pernicious anemia. It is very interesting to note that Alledi (1) in his investigations of post-prandial leucocytosis, made some observations which fit in very well at this point. He stated that leucocytosis was caused by the stimulation of the hemopoietic organs by the absorption of products of digestion. He found the greatest leucocytosis after the ingestion of albuminoids and could get no variations with psychic stimulation. He got an increased white blood cell count after ingestion of HCl or injection of histamine and explained it on the basis of increased formation of this

hemopoietic substance. Eggleston (152) bears out the work of Castle but states that achlorhydria is not always followed by pernicious anemia. He also cites cases which resemble pernicious anemia, following subtotal gastrectomy. Achlorhydria may cause a secondary anemia which possibly is an early stage of pernicious anemia. Heath (152) feels that there may be a typical pernicious anemia in the presence of free acid and explains this on the absence of the hemopoietic substance from the gastric juice.

Gastric carcinoma is the only other condition, aside from chronic gastritis, which is accompanied by a true achlorhydria (67) (120) (83) (152) (170) (147) (140) (151) (171) (28) (68) (14) (139) (137). Hurst (170) never saw a case of carcinoma in which free HCl was present early, disappearing as the disease progressed. He states that carcinoma always shows chronic gastritis and he is upheld in this by others (137) (152). He says that carcinomata tend to develop in areas of friction as the pylorus. He gives the following figures as to etiology; chronic atrophic gastritis 75%, hypertrophic gastritis 1 1/2%, chronic gastric ulcer 20%, simple adenoma 4 1/2%. Henderson (68) in investigating gastric carcinoma, recovered two to eighty-seven cubic centimeters of malodorous, bloody fluid containing much mucus. Bile was present in 50% due to an incomplete pylorus. All findings were those of mechanical obstruction and retarded activity. There was an absence of free acid and only traces of total

acid (ten to twenty-five) later, but proportionately large amounts of lactic acid. Bennett (14) says that the gastric picture depends on the location of the tumor but that the gastric analysis is almost as diagnostic as the Xray. There may be some HCl and lactic acid is not invariably present. He differentiates three general types of chart which may be shown in gastric carcinoma. The benign achylia differs from pernicious anemia in that there is profuse mucus and blood in every sample and in that there is delayed emptying. With moderate pyloric obstruction there is low or absent free acid but moderate total HCl. An early case may show free acid and rapid emptying but the fasting juice shows no free acid and a high total acid. Wills (142) says that a diagnosis of carcinoma may be made on the analysis of the resting juice which is foul-smelling, thick and contains retained food, altered blood, pus, mucus and organic acid. Knapp (81) states that enzymes may be present but HCl is absent. Eggleston (152) states that the malignant growth is rarely so extensive as to give achlorhydria by actual destruction of glandular tissue. It may be due (152) to chronic gastritis. Immerman (171) found HCl in carcinoma cases as follows; inoperable 7%, resected group 51%, and malignant ulcer 82%. Hartman (164) (165) and Friedenwald (158) (159) found HCl in 50% of gastric carcinomata. Friedenwald (158) analyzed one thousand cases of gastric malignancy and reports the following data; Of gastric disturbances, 9.6% are carcinoma and 7.8% ulcer.

Carcinoma has its greatest incidence between the ages of forty and sixty and ulcer between twenty and fifty. Carcinoma is most frequent in the male and 9.4% show a hereditary taint for cancer. Eighty-two percent of the patients show anemia. In gastric analysis 89% showed anacidity, 3% were normal, 4% were hyperacid and 3% subacid. Lactic acid was present in 81%, Oppler-Boas bacilli in 79%, Sarcinae in 32% and old blood in 61%. Duration of life was greater than one year in 66% but all died within three years. Pain was present in 93%, anorexia and vomiting in 69%. Ninety-nine percent were primary in the stomach and 92.5% showed occult blood.

Chronic gastritis (139) is characterized by an early increased HCl and later by hypo or anacidity (83) (140). There may be traces of lactic acid and mucus in large amounts. There is also decreased motility and absorption. Hess (69) discovered that chronic gastritis gave the most instructive and distinctive curves. Eggleston (152) warns of the dangerous aftermaths of chronic gastritis and advocates vigorous treatment before the glands are completely destroyed. He advocates removal of foci, administration of dilute HCl and regulation of diet as to irritation, vitamins, alcohol, tobacco, drugs, speed of eating, heat of foods, sweets, and soda fountain products. He sees no rationale in giving pepsin or bitters but advocates a hot pad to the epigastrium for pain and gastric lavage for excessive mucus. Immerman (171) found chronic gastritis in all achylia.

Hurst (169) to be different, maintains that the gastritis is secondary to the achylia. Rehfuss (152) thinks chronic gastritis may result from continual swallowing of mucus in cases of chronic sinusitis.

Peptic ulcer, including the gastric and duodenal types, is characterized by hyperacidity (80) (8) (177) (176) (171) (151) (68) (14) (139) (55) (69) (142) (107) (20). Kerpola (80) explains all gastric pathology on the same basis; a spastic condition or paralysis of the blood vessels of the stomach. According to him, mild pathology causes the so-called nervous dyspepsia while stronger contraction gives subacidity or anacidity. The paralysis gives hyperacidity and hypersecretion. Spasticity and paralysis together, according to this theory, produce ulcer. Bashenow (8) feels that ulcers form as a result of high acidity with a failure of duodenal regurgitation to neutralize it. This explains the benefits of an alkali regime. The gall bladder is the safety valve to keep the duodenum alkaline and ulcers may be produced experimentally (8) by ligation of the cystic duct. Morton (107) found free acid in the duodenum only in cases of ulcer. He believes that chronicity is due to an imbalance between the acids from the stomach and the alkalies of the duodenum. This may depend on a faulty action of the pylorus. Carlson (28) (151) says that duodenal ulcer with no pyloric obstruction gives a normal acidity and Moynihan (151) found 50% of gastric ulcers showed subacidity while 72% of duod-

enal ulcers showed hyperacidity. Eggleston (151) substantiates these figures. Henderson (68) attempted to differentiate between duodenal and gastric ulcers by the results of gastric analysis. In duodenal ulcer, he found twenty-one to ninety-two cubic centimeters of fasting juice, due to retention and hypersecretion. Mucus was small in amount and the acidity was on an average, free thirty-five and total sixty. After the meal, the curve showed the peak or plateau type, depending on pyloric relaxation. The high point was reached and then bile began to enter, gradually reducing the acidity. Probably the high acid is the antecedent of the ulceration. The stomachs emptied in one and one quarter to three and one quarter hours. Gastric ulcer showed twenty-four to seventy-nine cubic centimeters of fasting juice, with an average acidity of, free twenty and total forty. There is less spasm if the ulcer is on the lesser curvature and the whole picture is interpreted in terms of a disordered pylorus. The nearer the ulcer is to the pylorus, the greater the spasm and the higher the acidity. The stomachs emptied in one and three quarters to two and one half hours. Bennett (14) feels that an acidity above fifty means definite pathology and probably ulcer. Rapid rise in acidity with rapid emptying usually means duodenal ulcer while he finds that a slow rise with high acid and spasm of the pylorus, indicates gastric ulcer. The plateau type of curve indicates obstruction. Friedrich (55) carried on some ex-

haustive investigation on ulcer patients and his results follow. The curve type was not pathognomonic for ulcer but was usually of the climbing type. The location of the ulcer modified the curve and it was possible to differentiate between gastric and duodenal ulcers. There were five secretory types associated with ulcer; 1. Ascending and descending with maximum at various times 2. Rapidly rising curve and plateau formation 3. Low ascending and descending curve 4. Constantly ascending 5. Climbing or ladder type of curve. Duodenal ulcers most often showed the plateau or ladder curves or combinations of them, whereas ulcers of the lesser curvature showed the ascending-descending type and never a ladder formation. Prepyloric and double ulcers gave non-uniform results. Gastric and duodenal ulcers could not be differentiated as to emptying time but those on the lesser curvature emptied most rapidly. Maximum acidity was higher in duodenal than in gastric ulcers. Fifty percent of duodenal ulcers showed no regurgitation and it was always after seventy-five minutes. In gastric ulcers, regurgitation was absent in thirty percent and in the others, regurgitation took place within sixty minutes. Neutral red was found in the stomach fifteen minutes after injection and appeared earlier with duodenal ulcers. It did not always parallel the acid secretion. Chloride excretion was also independent of HCl and was higher with duodenal ulcer. This was not pathognomonic but definite types were found and regurgitation

played a great part. There was no relation between the type of test breakfast and the type of curve or its acid value. There was no definite relation between the secretory type and symptoms and so the study of the curve is of no value in estimating the progress under therapy. Ramond (120) states that normally, there is free acid in the first samples but that in ulcer cases, free acid does not appear until after the second or third sample. Leriche (177) and Gosset (161) feel that hyperacidity is the cause of ulcers and state that post-operative ulcer is essentially a disease resulting from the anastomosis of a hyperacid stomach, but Hardt (163) got no hyperacidity of gastric juice after experimental production of ulcers. Post-operative ulcers follow gastroenterostomy in 1.5 to 5% of cases but rarely occur (177) (161) after excision followed by gastroenterostomy. They are particularly frequent (25%) after antral exclusions and are frequent after pyloric and trans-antral resection, which is often followed by hyperacidity and hypersecretion. Ulcers are rare following extensive pylorogastrectomies and are never found after operating on an achlorhydric stomach. Medical treatment of these ulcers is uncertain because of the tendency to perforation. Fogelson (157) found that from gastric mucus, he could prepare a neutral mucin having a high combining power for free HCl. This was found to be an ideal antacid because it did not excite secretion, was soothing, was protective and did not alter the body chem-

istry not disturb the gastrointestinal tract. It gave excellent therapeutic results. Now, it had been shown (174) that exclusion of bile from the intestine lead to spontaneous development of single or multiple duodenal or gastric ulcers in the dog. Kapsinow (174) diverted bile to the kidney pelves and got ulcers in 40% of cases. Berg & Jobling (144) obtained ulcers in 60%. Fauley & Ivy (156) got ulcers in 10% with common duct ligation, and 10% after pancreatic duct occlusion. They found also that ligation of the pancreatic duct in the Pavlov dog gave a temporary decrease in gastric secretion for a few days, followed by a hypernormal secretion for as long as six months, although occasionally it declined to normal in three or four weeks. The hypersecretion was due to an unexplained increase in the intestinal phase of gastric secretion. The emptying time of the stomach was found to be decreased and hunger was the main factor. They showed that acid in the duodenum is a minor factor in controlling rate of emptying. Mann and Williamson (181) diverted bile from the duodenum by various types of operation and got acute ulcers in 30% with chronic ulcers in 16%. Still and Carlson (187) working with obstructive jaundice, found that the rate of hunger contraction was diminished, the hunger periods were shortened, magnitude of individual hunger contractions was diminished, volume of secretion was diminished and concentration of acid in the gastric juice was increased. Kim & Ivy (176)

using all the facts just mentioned, believed that these ulcers could be prevented by the feeding of the mucin described by Fogelson. One gram of the mucin would combine with fifteen to eighteen cubic centimeters of tenth normal hydrochloric acid and each dog in the series received fifteen grams of mucin in each meal. The dogs did well on the mucin and after a month of observation, none had developed ulcers whereas the controls showed a 60% incidence of ulcer and some dogs had multiple ulcers. They concluded that the acid was a factor in ulcer formation and that mucin was a preventative.

The previous discussion has thrown some light on the relation of the gall bladder to gastric function but there has been additional work of a more direct character. Henderson (68) found that chronic cholecystitis gave an abnormally high volume of gastric juice with a slowly increasing acidity, rising to a hyperacid peak, late in the course. He found the same condition with a chronic appendix. Ballowitz (6) and Immerman (171) found a hyperacidity in acute cholecystitis and Alder, Hohlweg and Ohly (6) found a low acidity in chronic gall bladder disease. Eggleston (152) found gall bladder disease frequently associated with hypoacidity and he felt that chronic gastritis was a frequent cause of cholecystitis. This would explain the lowered acidity. It is possible that imperfect gastric digestion of protein with low acidity might favor biliary stasis and thus

cause gall stone formation.

According to Henderson (68) gastric neuroses or functional dyspepsias are characterized by a hypoacidity of the slowly ascending-descending type.

Other investigators mention a variety of clinical conditions which tend to cause a variation from the normal picture of gastric function. Bowen (146) states that diabetes mellitus, in long standing cases, causes hypoacidity or achlorhydria. Hardt (163), Green (162) and Chang (149) agree that a condition of hyperthyroidism is accompanied by hypoacidity whereas hypothyroidism or cretinism shows no definite change. This experimentation was carried on by forced thyroid feeding in pouch dogs, rabbits and in thyroid-ectomized rabbits. Dr. Alfred J. Brown (personal communication) after a careful consideration of the case records at the University Hospital, states very definitely that conditions of hyperthyroidism are accompanied by diminished or absent HCl in the stomach. Hypothyroidism showed no definite changes.

The findings on gastric analysis are not in any way diagnostic as yet, with but few exceptions. Carcinoma and pernicious anemia may be fairly definitely diagnosed by a gastric analysis but in all other conditions, the results are merely adjuvant (6) (68) to other findings. The examination, due to the many variable factors as previously explained, due to the variety of methods used and due to the lack of knowledge of standard normal values, must, as yet, be classed as a clinical and not as an exact laboratory determination.

Typical Case Records of Various Clinical Conditions

Showing Their Effects on Gastric Function.

The Gastric Analysis in Gastric Carcinoma

William Henry Sirrell, a colored, divorced, farmer, aged fifty-one, came into the University Hospital on Nov. 2, 1930 complaining of; 1. a dull pain in the epigastrium, aggravated by eating. Sometimes this pain did not come on for one to one and one half hours after meals. 2. Vomiting of a greenish to coffee colored material. 3. Constipation with tarry, black stools. 4. Loss of about forty pounds in weight in the last two months. 5. Marked loss of strength.

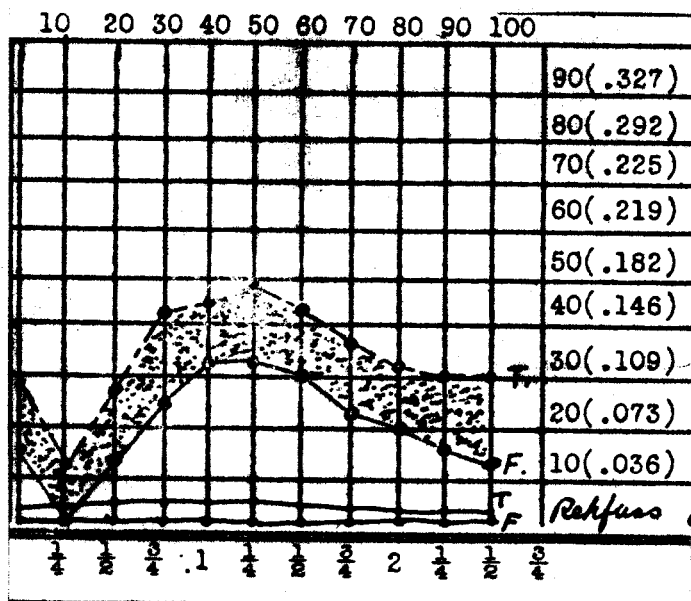
The appetite had always been good and constipation was only occasional up until two months ago, when the patient began to feel ill, having vomiting spells which were sometimes immediately after meals or after several hours. This latter was especially true of the evening meal. After about six such spells, he began to have pain with the vomiting and he noted some hematemesis. Soon a constant dull ache began in the epigastrium and one month ago the stools began to be dark. The rapid loss in weight had been accompanied by a marked weakness in the last two months so that the patient was unable to work. The pain was chiefly in the epigastrium but occasionally radiated to the lower right abdomen. Pain was relieved by vomiting and the quantity was often greater than the amount of food just eaten. Starchy foods seemed to cause the most pain and vomiting and as the appetite for meat had been lost, this was also excluded from the diet.

Gastric Carcinoma

Inspection showed a profoundly emaciated man with an emesis basin at hand, containing a coffee ground material. The mucous membranes were pale but not jaundiced. The examination revealed no masses but the epigastrium was tender. Therapy was instituted as follows; bed rest, morphine to splint the bowel, fluid diet in small feedings, normal saline solution by hypodermoclysis, intravenous glucose and calcium chloride.

A roentgenogram showed an inoperable carcinoma of the lower stomach, along both curvatures, and with an extreme degree of retention even after twenty-four hours. The erythrocyte count was slightly above two million and two transfusions were given. Stool examinations were always positive for occult blood and a gastric analysis gave the following information;

| | | | | | | |
|-------|----|----|---|---|-----|-----|
| R.J. | 1 | 2 | 3 | 4 | 5 | 6 |
| Free | 0 | 0 | 0 | 0 | 0 | 0 |
| Total | .5 | .5 | 1 | 1 | 1.5 | 1.5 |



Gastric Carcinoma

All of the gastric samples were positive for occult blood.

Surgical laparotomy was deemed advisable and revealed an extensive carcinomatosis. Anterior gastroenterostomy was performed and the patient died the same day.

Necropsy showed carcinomatous infiltration of the mesentery, gall bladder, liver and pancreas. The primary lesion was an ulcerated scirrhous type of carcinoma at the pylorus of the stomach.

The Gastric Analysis in Gastric Ulcer

Edwin G. Hunnel, an American, white, single, carpenter, aged fifty-nine, came into the University Hospital on Sept. 26, 1931 complaining of; 1. Nausea 2. Pain in the epigastrium 3. Burning sensation in the chest 4. A yellow color of the skin 5. Burning on urination 6. Urinary frequency.

About seven years ago the patient became sick at the stomach and vomited a considerable quantity of blood. Since that time he has noticed a rather constant gnawing pain in the epigastrium, often becoming worse, one to two hours after meals and sometimes being relieved by taking food. Three years ago there was another similar attack of severe pain with nausea and vomiting but no hematemesis. For the past few months the patient has been living on crackers and milk. Six weeks ago a third attack came on and considerable green material was vomited but there was no hemorrhage. Jaundice began to appear about two weeks ago.

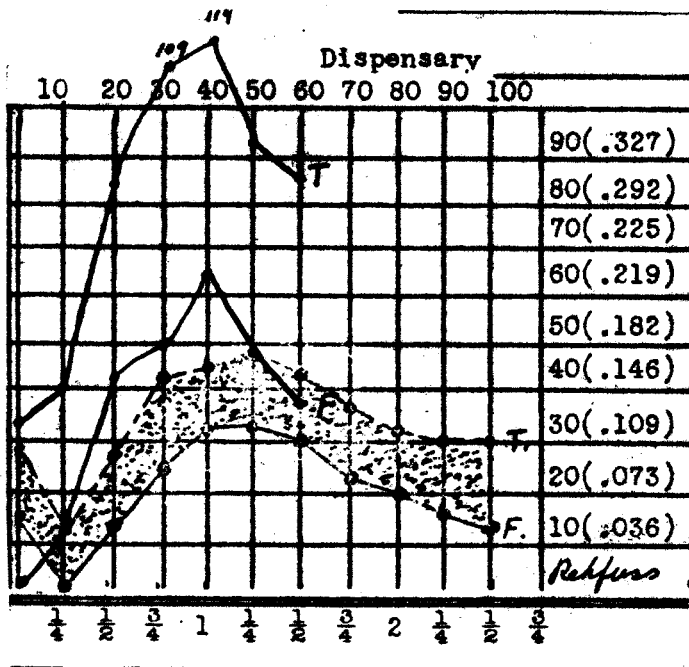
Physical examination showed considerable emaciation. The epigastrium was rigid, tender and an indefinite mass was palpated.

A roentgen film showed poor filling in the prepyloric and duodenal regions. The appearance was that of neoplasm and from this and the history, a diagnosis of early carcinoma on an old ulcer base was made.

Gastric Ulcer

The stools were tarry and positive for blood. The Van Den Bergh reaction showed a direct positive immediately. A gastric analysis by the Rehfuess method showed;

| R.J. | 1 | 2 | 3 | 4 | 5 | 6 |
|-------|----|----|----|-----|-----|----|
| Free | 0 | 12 | 42 | 50 | 65 | 48 |
| Total | 32 | 40 | 84 | 109 | 114 | 92 |



Surgical resection was advised but the patient refused and was dismissed on Oct. 9, 1931, slightly improved.

The Gastric Analysis in Duodenal Ulcer

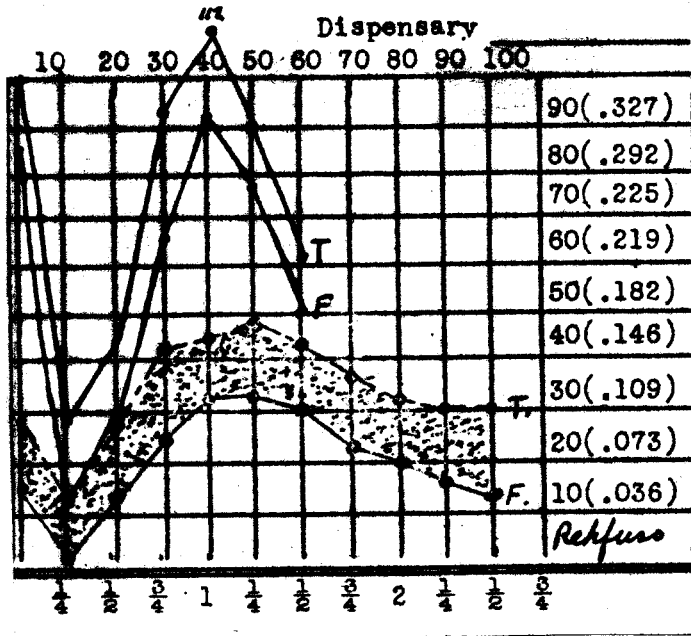
Lorenzo Lingle, a single, American, white, farm-hand, aged twenty-three, came into the University Hospital on Feb. 11, 1931, having had no complaints for the previous five days.

Four years ago in June, he had noted an unusual amount of distention of the upper abdomen after meals, relieved by belching or by soda. This distress was worst after eating cabbage or fat meats. He had never been nauseated nor had he vomited. This condition persisted for three years when the patient went to South Dakota and was relieved for four months. He came back to Nebraska and eight months later the same distress reappeared, followed in about a week by a burning sensation in the epigastrium. This burning came on one to two hours after every meal but was especially noticed while working. A doctor gave him some powders and put him on a diet but without results. Later the patient was on a diet of raw eggs and milk for ten days and was relieved for a short period. The recurrence was not so severe and now he is bothered by gas and an occasional sharp pain in the epigastrium.

Physical examination revealed slight tenderness over the epigastrium. A gastric analysis showed;

| | R. J. | 1 | 2 | 3 | 4 | 5 | 6 |
|-------|-------|----|----|----|-----|----|----|
| Free | 86 | 14 | 30 | 66 | 92 | 78 | 50 |
| Total | 100 | 28 | 42 | 84 | 112 | 90 | 60 |

Duodenal Ulcer



The gastric samples as well as the stools were always positive for occult blood. A roentgen film at this time showed the duodenal bulb to be large, with a relatively constant outpocketing on the lesser curvature just distal to the pylorus.

Sippy diet was instituted and gastric lavage was used at bed-time. The patient soon became symptom free and on Mar. 17, 1931 the patient was discharged and referred to the home doctor for continued ambulant management.

The Gastric Analysis in Cholecystitis

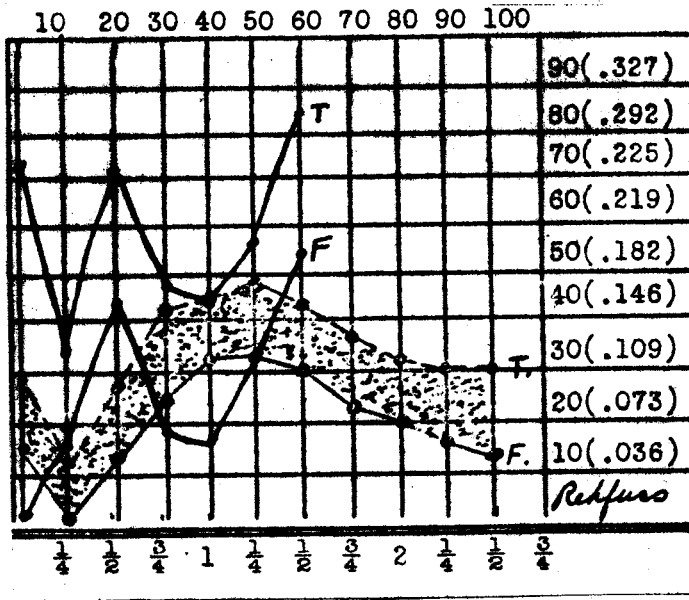
Mrs. Alma Martin, a married, American, white, housewife, aged fifty-one, entered the University Hospital on Aug. 4, 1931 because of a very severe chronic constipation.

She was quite well until about ten years ago when she had to quit eating cabbage, beans, and fat pork because of the belching and flatulence produced. About five years ago, constipation gradually became worse and in July of 1929 she had to be operated on for a fecal impaction. The constipation has continued since that time in spite of the use of Epsom salts, mineral oil and frequent enemas. Pain in the back and right side gradually developed and became moderately severe, often awakening her at night and requiring soda for relief. There were frequent cramps, gas pains and nausea but no vomiting.

Physical examination revealed tenderness over the epigastrium and Graham-Cole test failed to show any evidence of a normally functioning gall-bladder. A Rehfuess type of gastric analysis at this time showed:

| R.J. | 1 | 2 | 3 | 4 | 5 | 6 |
|----------|----|----|----|----|----|----|
| Free O | 16 | 42 | 19 | 17 | 31 | 53 |
| Total 73 | 32 | 72 | 48 | 43 | 58 | 84 |

Cholecystitis



Cholecystectomy and appendectomy were done and on Sept. 17, 1931 the patient was dismissed, much improved.

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The Gastric Analysis in Pernicious Anemia

Edwin R. Wilson, a white, married, painter, aged fifty-five, entered the University Hospital on Jan. 7, 1931 complaining of: 1. Progressive weakness of four years duration 2. Dizzy spells for the past four years 3. Pain in the abdomen, extending around to the back, especially on the left, and of a duration of two years 4. Numbness of the legs, feet and hands 5. Shortness of breath 6. Nocturia three or four times 7. Gas on the stomach.

In March of 1927 the patient had an attack of pain in the abdomen and soon became comatose, remaining unconscious for three days. He recovered after two months but was weak, had pain in the abdomen and a persistent diarrhea. He was fairly well until March of 1928 and then got gradually weaker, developed shortness of breath and lost his appetite. In September of that year, he noticed more abdominal soreness and more severe attacks of diarrhea. This persisted for two and one half years with remissions and exacerbations. Paresthesias of the hands and feet have developed in the past three months and are noticed most when the extremities have been kept quiet for a while. The nocturia developed in 1928 and got progressively more troublesome.

The gastrointestinal history revealed that he had not eaten beans, cabbage or eggs for the past twenty

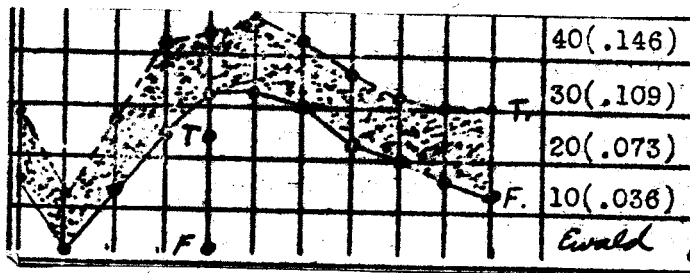
Pernicious Anemia

years because of the gas formation. For the past three years he had little appetite and so ate very little. He would often start to eat and would then become nauseated.

Inspection showed a lemon-yellow tint to the skin and palpation revealed a tender epigastrium. The tongue was smooth. The knee jerks were retarded and the vibratory sense was diminished. The patient was emaciated, listless and dyspneic. Blood counts were as follows:

| | 1/18/31 | 1/15/31 | 1/22/31 |
|-----|-----------|-----------|-----------|
| Hem | 68% | 85% | 86% |
| RBC | 2,880,000 | 3,640,000 | 3,790,000 |
| WBC | 8,400 | 6,400 | 5,800 |

Blood smears showed anisocytosis, poikilocytosis and reticulocytosis. A gastric analysis by the Ewald method on Jan. 13, showed at the end of one hour, no free acid with a total acidity of twenty-four.



The patient was put on dilute HCl and Ventriculin. He was dismissed on Feb. 3, 1931, with instructions to continue this therapy indefinitely.

The Gastric Analysis in Hyperthyroidism

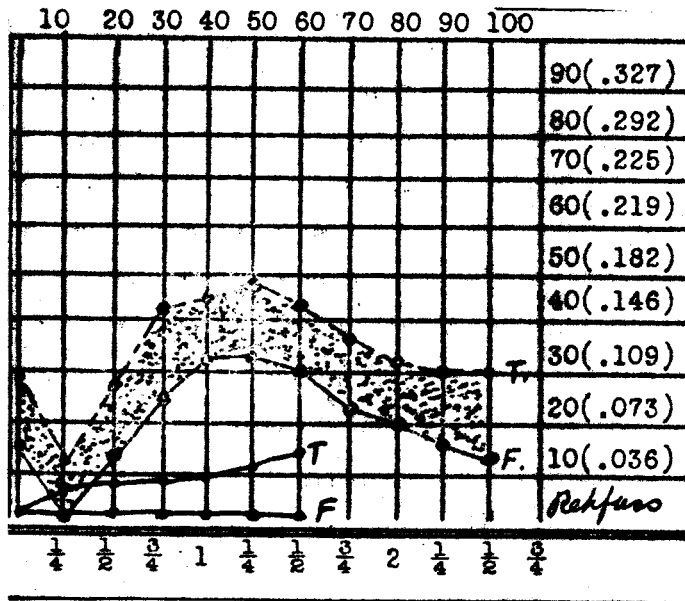
Mrs. Sara Higgins, a widowed, Irish, house-wife, aged sixty-three, came into the University Hospital on Dec. 19, 1929 complaining of: 1. A smothering sensation around the heart 2. Considerable loss of weight 3. Pain and swelling of the legs 4. Increasing nervousness 5. Progressive weakness 6. Voracious appetite 7. Small mass in the neck.

About eighteen years ago the patient had noticed a small mass in the neck and about the size of a pea. This very slowly grew larger but caused no symptoms until about five years ago when the patient noted that she was getting weaker and was always tired. Then she began to have painful swellings of the legs and feet. During this time there had been an increasing tendency toward belching, accompanied by sour eructations. There were occasional attacks of nausea with vomiting. Several of these attacks occurred during the last winter and were accompanied by sharp pain in the epigastrium, relieved by vomiting.

A diagnosis of toxic adenoma of the thyroid with myocarditis was made. The heart was fibrillating but the patient was at least thought to be in suitable condition for operation. A Rehfuess type of gastric analysis at this time showed:

| | R. J. | 1. | 2 | 3 | 4 | 5 | 6 |
|-------|-------|----|---|---|---|----|----|
| Free | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| Total | 0 | 7 | 8 | 9 | 7 | 12 | 14 |

Hyperthyroidism



Thyroidectomy was performed and the patient recovered uneventfully. She went home on Feb. 4, 1930, much improved but died the following September of heart failure.

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