SOME PHYSIOLOGIC PRINCIPLES INVOLVED IN THE SURGICAL TREATMENT OF GASTRIC AND DUODENAL ULCER

LESTER R. DRAGSTEDT, M.D.

CHICAGO, ILL.

FROM THE DEPARTMENT OF SURGERY OF THE UNIVERSITY OF CHICAGO

THE problem of the cause of gastric and duodenal ulcer is of constant interest to the physician who has to deal with these lesions and to the biologist who recognizes in it a part of the more general question of the resistance of the gastro-intestinal tract to the digestive action of its own secretions. From the time of John Hunter various men have interested themselves in this problem and the view has steadily gained headway that ulcer of the stomach is in some way due to a local loss of resistance on the part of the mucous membrane to the digestant activity of the gastric juice. The term peptic ulcer is an expression of that view. The occurrence of the lesion in those parts of the alimentary tract that are exposed to gastric juice (lower esophagus, stomach, first portion of duodenum, jejunum adjacent to a gastro-enterostomy stoma, and ileum adjacent to the entrance of a Meckel's diverticulum containing gastric mucosa) and nowhere else may be taken as strong confirmatory evidence. But under normal conditions the mucous membrane of the stomach is not digested away.

During the past 15 years there has been a renewed interest in the problem and many significant observations made. As a direct result of various experimental procedures the disease has been caused to develop in the lower animal and to duplicate in almost every particular the lesion encountered in man. The gross and histologic appearance of the experimental ulcer exactly resembles the clinical lesion, and it has been observed to perforate, to cause profuse hemorrhage, and to heal under a type of medical management which resembles that found effective in man. In addition, the alterations in the physiology of the alimentary tract under which experimental ulcers may be expected to develop and become chronic are well understood and the factors involved may be fairly accurately appraised. Indeed, there are not many diseases whose immediate pathogeneses seem at present to be better established. It is the purpose of the present paper to offer a brief analysis of a part of this newer information and to present a summary of some of the experimental work carried on with various associates in my laboratory on this problem during the past few years.

The early literature is replete with unsuccessful attempts to produce a chronic progressive lesion in the gastric or duodenal mucosa of dogs. This effort has served, however, to make evident the great capacity of the gastric mucosa of these animals to heal in the presence of the usual gastric content and after the most extensive mechanical and chemical traumas. Exalto (1911) and Mann and his associates (1923) must be credited with being

the first to develop methods which regularly lead to the production of chronic ulcers without the use of external destructive agencies.

The normal resistance of the gastric wall to the digestant action of gastric juice has been explained as due to a general vital principle (Hunter), the protective action of gastric mucus (Pavy), the neutralizing effect of the alkaline blood in the mucosa capillaries, or to the presence of anti-pepsin in the stomach mucosa (Weinland), *etc.* It has been a fairly common assumption that the mucosa lining the gastric wall has some specific resistance to such digestion not possessed by other living tissues and entirely absent after death. In 1924, together with Vaughn,[1] I made an attempt to secure experimental evidence regarding the resistance of various tissues to gastric digestion. Large openings were produced in the stomach of dogs

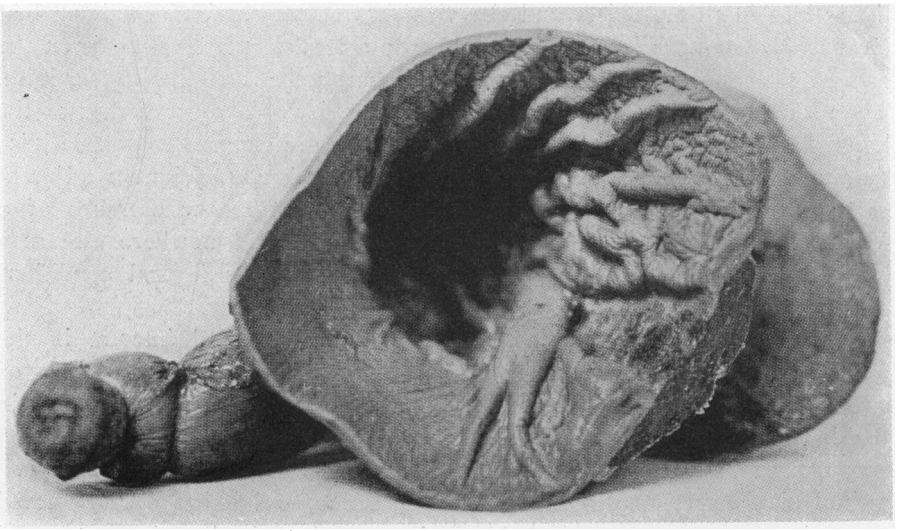


FIG. 1.—Implantation of the spleen in a window made in the anterior wall of the stomach, with exposure to gastric digestion for two weeks. The capsule of the spleen was removed before implantation so that the gastric content had direct access to the splenic pulp. The blood supply to the spleen was not interfered with. The spleen was not digested, although tests indicated that the gastric juice was normal. (From Dragstedt and Vaughn, Arch. Surg., vol. 8, p. 791, 1924.)

and into these defects were carefully sutured segments of duodenum, ileum, colon, and such organs of the spleen, kidney, and pancreas. In the latter case the capsule of the organ was first removed so as to permit the gastric content access to the parenchyma. In no case were these tissues digested away. The exposed surfaces of the spleen and kidney were soon covered by a layer of newly formed gastric mucosa while the mucosa of the duodenal and intestinal implants remained entirely normal for periods of at least nine months (Figs. 1 and 2). In subsequent experiments[2, 8] similar defects were produced in the first part of the duodenum and the free portion of the pancreas sutured in place so that its parenchyma would be exposed to digestant action of the duodenal content. Digestion did not occur. It is thus evident that there exists a widespread resistance to the corrosive and solvent action of the gastric and duodenal content on the part

of tissues and organs whose blood supply is not interfered with. It should be emphasized that these experiments yield data only on the resistance of tissues to the normal gastric content but not to pure gastric juice. There is a significant difference between the two with respect to both acid and enzyme content. The concentration of free HCl in the stomach contents of normal man examined one hour after the administration of an Ewald meal varies between 30 and 60 clinical units, whereas that in the pure gastric juice secreted by the isolated stomach of the dog remains practically con-

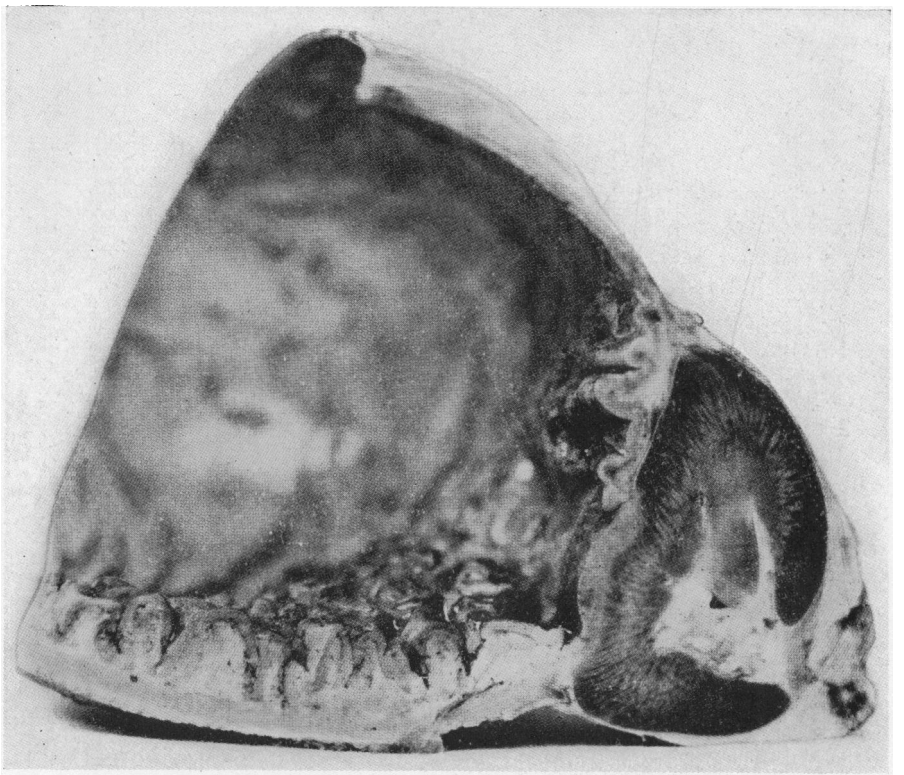
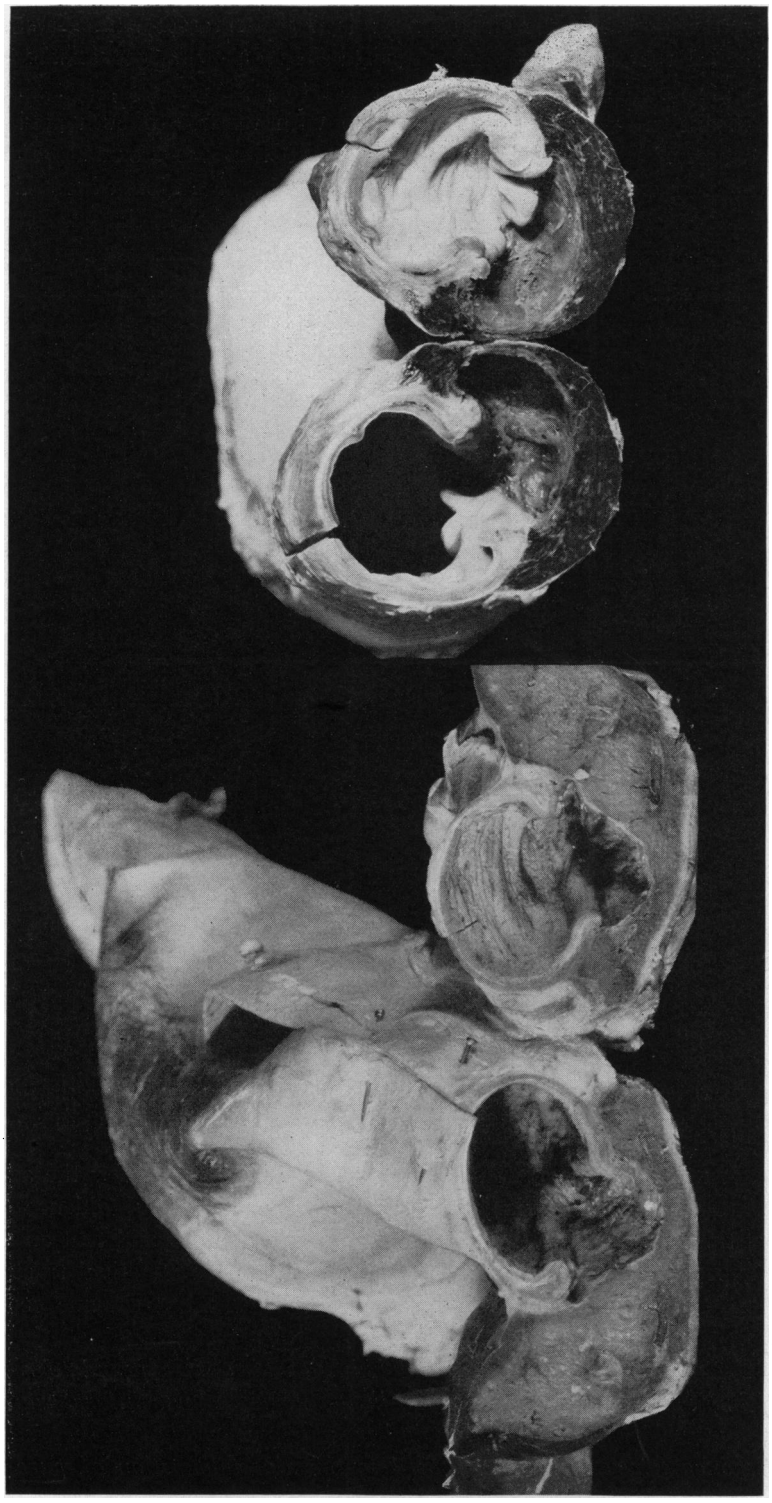


FIG. 2.—Implantation of the kidney in a window made in the anterior wall of the stomach, with exposure to gastric digestion for 14 days. The capsule of the kidney was first removed so that the parenchyma was directly exposed to the gastric content. There was no digestion of the kidney. (From Dragstedt and Vaughn, Arch. Surg., vol. 8, p. 791, 1924.)

stant at about 135 units. Carlson[3] has given a similar figure for the acidity of the pure undiluted gastric juice of man. The following evidence indicates that this pure gastric juice can digest any living tissue and that an ulcer may be expected to develop in any portion of the gastro-intestinal tract that is long exposed to a content that resembles it in acid and enzyme concentration.

A.—*Organs such as the spleen and kidney, which were found to remain intact if implanted into windows made in the normal stomach, are promptly digested away if implanted into similar windows made in the isolated stomach pouch where they are exposed to the digestant action of pure gas-*



FIGS. 3 and 4.—Implantation of the spleen into a window made in an isolated pouch of the stomach. The parenchyma of the spleen exposed to the pure gastric juice of the Pavlov pouch was extensively digested.

tric juice. In two dogs, a large Pavlov accessory stomach was made employing for this purpose approximately two-thirds of the entire fundus. The pouch was connected to the exterior by means of a tight fitting metal cannula so that gastric juice could be retained or permitted to escape at will. A large window was then made in the accessory stomach and into this was carefully sutured the spleen, exactly as was done in the experiments with the normal stomach. For the first week or two the gastric juice secreted in the pouch was promptly drained away, the juice remained fairly clear

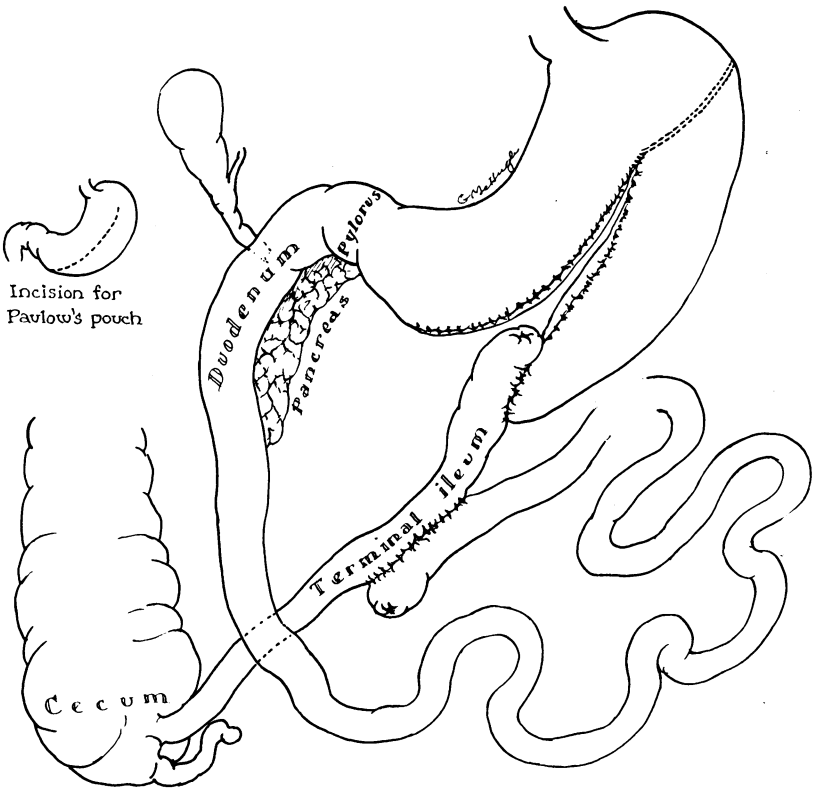


FIG. 5.—Diagram showing the method used to expose the mucosa of the ileum and jejunum to the digestant action of pure gastric juice. (From Matthews and Dragstedt, Surg., Gynec., and Obst., vol. 55, p. 265, 1932.)

and the condition of the animals excellent. The cap was then screwed over the cannula causing a retention of gastric juice in the pouch for daily periods of three to four hours. Care was taken not to permit the accumulation of sufficient secretion to distend the pouch and thus produce mechanical damage to the implant. The gastric juice draining from the pouch became immediately tinged with blood and in a few days repeated severe hemorrhages occurred. The dogs became markedly weak and cachectic. The specimens (Figs. 3 and 4) show the extensive digestion of the spleen by the pure gastric juice in striking contrast to the almost complete absence of such digestion by the normal gastric content.

B.—*If pure gastric juice be caused to flow into the empty jejunum or ileum, the mucosa is digested away and an ulcer is formed.* This experiment was performed in the following way (Fig. 5). A small isolated pouch of the dog stomach was made, in some cases with the vagus innervation intact (Pavlov pouch), in others with the vagi cut (Heidenhain pouch). The open end of these accessory stomach pouches was then sutured into the jejunum or ileum. Gastric juice secreted in the isolated stomach in response to meal taking passed immediately into the as yet empty intestine. In six animals in which the gastric juice was made to pass into the ileum an ulcer developed in the adjacent area in every case (100 per cent) and in the jejunum in 11 of a total of 13 experiments or 85 per cent[4] (Fig. 6). The ulcers always developed in the intestinal wall adjacent to the line of anastomosis with the stomach, but never in the gastric mucosa. They presented

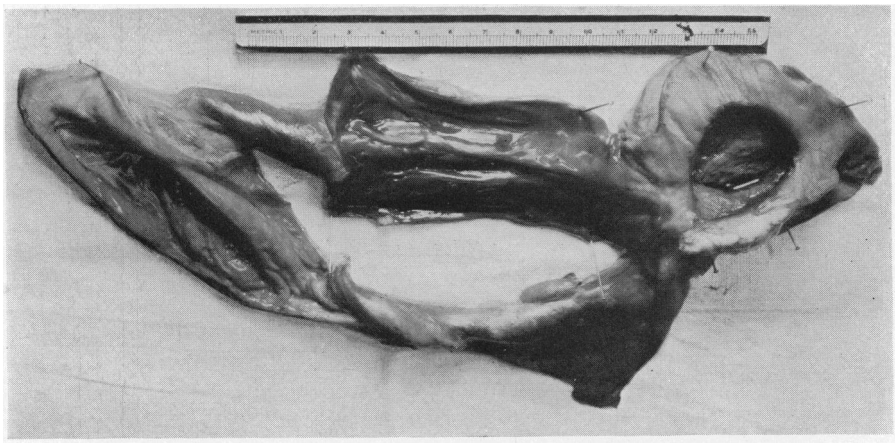


FIG. 6.—Showing a large ulcer in the jejunum near the anastomosis with the Pavlov pouch, as in Fig. 5. The unmixed gastric juice secreted by the isolated stomach has digested the jejunal mucosa. (From Matthews and Dragstedt, Surg., Gynec., and Obst., vol. 55, p. 265, 1932.)

the same clean, punched out appearance of the lesion in man. Several caused profuse hemorrhage, many perforated, and none showed any tendency toward spontaneous healing.

Nature performs an experiment similar to this in the so called Meckel's diverticulum ulcer, an example of which has recently come under my care.[5] Aschner and Karelitz[6] and Lindau and Wulff[7] have collected a number of cases in the literature in which an ulcer has been found in the ileum adjacent to the entrance of a Meckel's diverticulum. In these cases the diverticulum has been found to be lined with heterotopic mucosa which in some instances has been proved to secrete acid and pepsin.

C.—*If the stomach be isolated from the gastro-intestinal tract in such a way that its blood supply and vagal innervation are but little interfered with and so that the gastric juice secreted is not promptly drained away but remains in contact with the gastric wall for a time, the gastric mucosa then*

becomes digested away and chronic progressive perforating ulcers develop that anatomically are not distinguishable from the clinical lesion.

In a study of the physiology of gastric secretion, Lim, Ivy, and McCarthy in 1925 isolated the entire stomach of dogs, and sutured the lower end of the esophagus to the open end of the duodenum. Although the vagus nerves to the isolated stomach were cut, from 300 to 400 cc. of highly acid

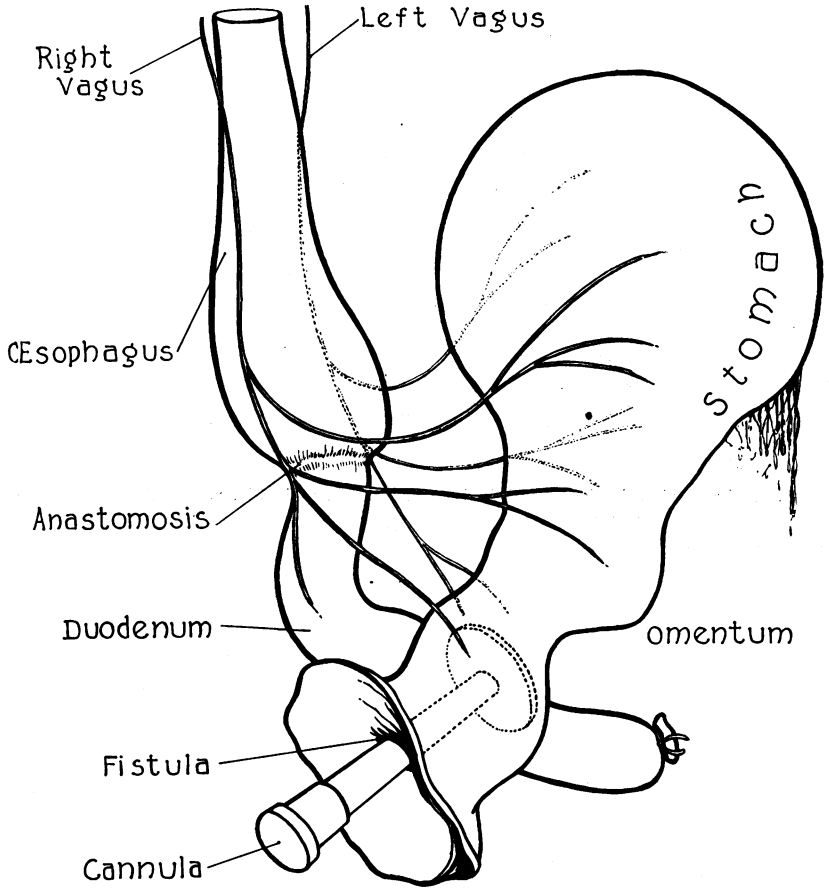


FIG. 7.—Diagram showing the method of preparation of the isolated stomach with vagus innervation intact. (From Dragstedt and Ellis: Am. Jour. Physiol., vol. 93, p. 407, 1930.)

proteolytic gastric juice were secreted daily. It occurred to us that a more physiologic preparation would be one in which the vagus innervation of the stomach was preserved, if possible, since the Pavlov pouch in which this is the case more nearly mirrors the activity of the normal stomach than does the Heidenhain pouch where the nerves have been severed. In a number of instances we were successful in so isolating the entire stomach that its blood supply and vagus innervation were left intact (Fig. 7). To our surprise, such an isolated stomach was found to secrete on an average about 2,000 cc. of gastric juice per 24 hours. The free hydrochloric acid of this secretion varied between 100 and 140 clinical units and its pepsin concentration

was approximately three times as great as that of the normal gastric content. The continued loss of this secretion produced dehydration, hypo-

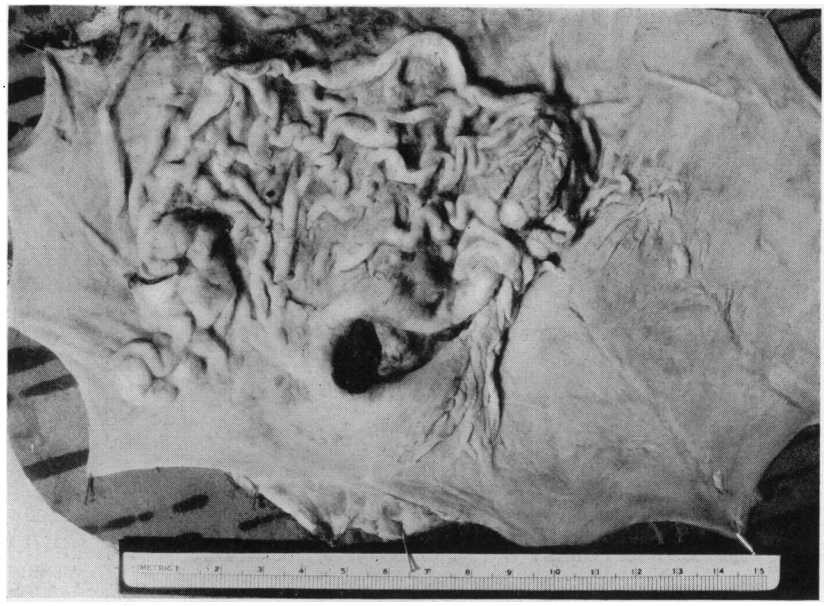


FIG. 8.—Large ulcer in the wall of the isolated stomach, as in Fig. 7. Death from perforation and peritonitis 20 days after original operation.

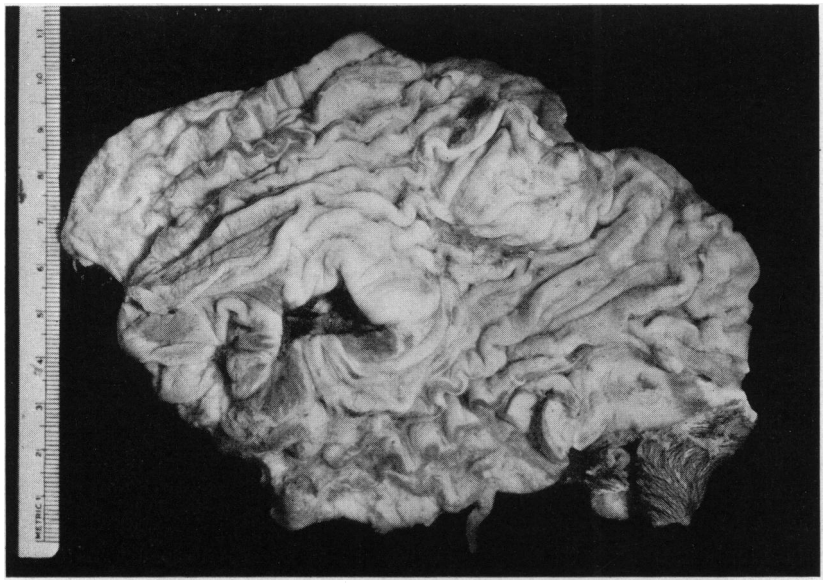


FIG. 9.—Large ulcer in the wall of the isolated stomach, as in Fig. 7. Death from perforation and peritonitis 43 days after original operation.

chloremia, alkalosis, and eventually death unless sodium chloride was supplied in large amounts by intravenous injection. During the course of these experiments we came to the realization that if this pure gastric juice was

permitted to accumulate in the isolated stomach or if its drainage to the outside was not adequate, ulcers would develop in the gastric mucosa. To date typical chronic ulcers have been noted in seven animals (Figs. 8 and 9). In several instances these caused death from hemorrhage and in two cases from perforation. In one experiment, in which death occurred from pneumonia 48 hours after the operation, several superficial ulcers were found and the entire mucous membrane presented numerous small erosions, areas of round cell and leukocytic infiltration, and hemorrhages quite similar to those described by Konjetzny[14] as characteristic of ulcer gastritis (Figs. 10 and 11).

If we may conclude from these experimental observations that pure

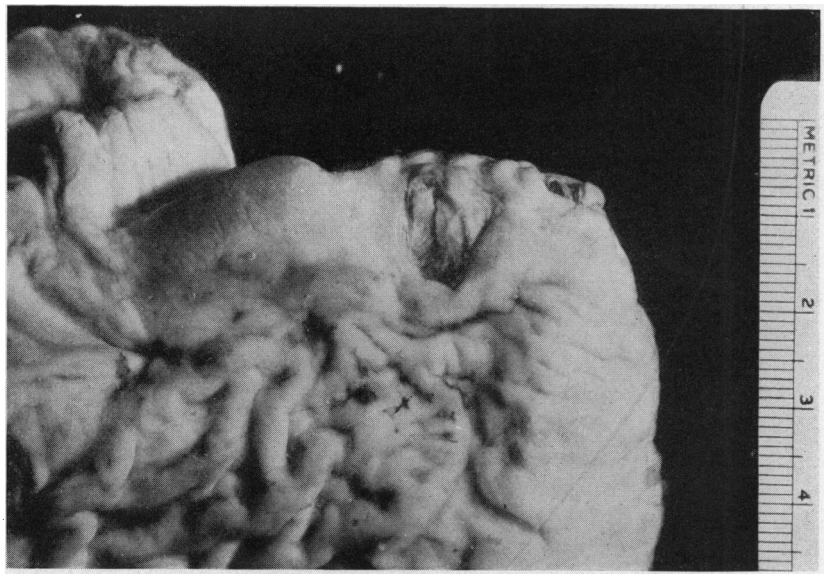


FIG. 10.—Large superficial ulcer and multiple erosions on the wall of an isolated stomach as in Fig. 7. Death from pneumonia 48 hours after operation.

gastric juice can digest away living tissues including the mucosa of the digestive tube, the question may be raised as to the substance in gastric juice responsible for this effect. Our inquiry in this respect has been limited to pepsin and free hydrochloric acid. If one can judge at all by the widespread use of the term peptic ulcer it would appear that many regard pepsin as the responsible corroding agent. In this connection it is perhaps pertinent to point out that trypsin is an even more active proteolytic enzyme but no ulcers have been reported in that part of the digestive tract exposed to pancreatic juice. The question is not entirely an academic one. The late Doctor Sippy based his method of treatment on the idea that pepsin was the principal agent that prevented the healing of ulcer and so endeavored to prevent the activation of the pepsinogen by preventing the appearance of free acid in the gastric content at any time. Very large amounts of alkalies were sometimes necessary to secure such complete neutralization.

Claude Bernard showed many years ago that the leg of a living frog

would be digested away if introduced through a fistula into the cavity of a dog's stomach. We have confirmed this observation in in vitro experiments[1] and have modified the method in an attempt to assay the relative importance of acid and of pepsin. The hind legs of living frogs were immersed in pure gastric juice, in pure pancreatic juice, and in gastric juice containing varying concentrations of free hydrochloric acid and pepsin. The legs immersed in pure gastric juice were gradually digested away so that in a few hours all that remained was a branching network of blood vessels surrounding the bones. Although usually the last to persist, the vessels were finally eroded and death from hemorrhage occurred. It is interesting that pure activated pancreatic juice had no such digestant effect and the skin remained intact though edematous even after 25 hours' exposure. Pure gastric juice of

FIG. 11.—Low power photomicrograph of one of the superficial erosions in the gastric mucosa of the isolated stomach of Fig. 10.

normal pepsin concentration but whose free acidity was reduced to 30 clinical units or less had no digestant or corrosive action, whereas juice having a concentration of free acid of 50 units or more had a very marked effect almost irrespective of the concentration of pepsin. When the concentration of free acid and of pepsin was varied in different samples, the extent of digestion of the living tissue was proportionate to the concentration of free acid and not at all to the concentration of pepsin. Somewhere beween 0.1 and 0.15 per cent of free hydrochloric acid was found to be the critical level at or above which living tissue was digested. At this concentration it made little difference whether the concentration of pepsin was 600 or 20 units per cc. It is doubtless significant that the acidity of the normal gastric content rarely rises above this level and that the high values which approach the acidity of pure juice are commonly found in ulcer patients.

It must be admitted that the experimental conditions under which the

ulcers described above have been caused to develop are highly artificial and with few exceptions their counterpart does not occur in man. If it be agreed that the evidence warrants the conclusion that a gastric content whose acidity and pepsin concentration approaches that of pure gastric juice will digest the wall of the stomach or duodenum and produce an ulcer and is in this sense its immediate cause, there still remains the question—under what conditions, if any, does such a content appear? This latter problem is obviously of greater practical significance and here unfortunately our information is far less precise. It seems clear enough from a consideration of the normal mechanisms that govern the secretion of gastric juice, that a pure undiluted and unneutralized secretion is not apt to accumulate in the stomach. The sight, odor, and especially the taste of food which serve as appropriate stimuli for the nervous phase of gastric secretion are followed so promptly by the ingestion of food that the juice is diluted and neutralized. Similarly the gastric secretion which results from the action of gastrin takes place only while food is in the stomach and upper intestine. Under normal conditions of motility the gastric content is passed on into the duodenum before its capacity to bind or neutralize the free hydrochloric acid is entirely overcome, so that we never observe in the digesting stomach a free acidity equal to that of pure juice and rarely an acidity above that at which gastric juice was found capable of digesting living tissue. When an abnormal retention of food in the stomach occurs, we should expect on theoretical grounds that the continuing secretion of gastric juice would gradually raise the acidity of the gastric content until it approaches the acidity of the pure secretion. There is, of course, plenty of clinical data to substantiate this view and the hyperacidity of the gastric content in cases of duodenal ulcer with pyloric obstruction has long been regarded as a significant factor in determining the chronicity of these lesions. It is not improbable that pyloric stenosis or spasm may operate also in another way to raise the acidity of the gastric content. It was found by Mann[9] and confirmed by ourselves and others that the experimental deviation of the alkaline pancreatic juice from the duodenum into the lower intestine or to the exterior is shortly followed by the appearance of chronic progressive ulcers in the duodenum. A few clinical cases have been described in which it appears that a failure of bile or pancreatic juice or both to reach the duodenum and neutralize the gastric content had been responsible for the occurrence of the duodenal ulcer. The practical significance of Mann's discovery, entirely apart from its theoretical importance, may, however, be much wider. According to the views of Boldyreff[10] a reflux of bile and pancreatic juice into the stomach normally occurs and serves to prevent the development of a high concentration of acid in the gastric content. Spasm of the pylorus and especially when associated with a stenosing duodenal ulcer might be expected to limit such regurgitation as well as cause retention and thus set up a vicious circle whereby the increasing acidity of the gastric content increases the pylorospasm. It seems reasonable to conclude that the major factor in determining the chronicity of ulcer

in the pyloric region is the resulting stenosis or spasm which acts thus in two ways to increase the acidity of the gastric content. The treatment of such a lesion, therefore, which does not return the emptying time of the stomach to normal may be expected to be followed by recurrence.

It is not easy to evaluate the rôle of the central nervous system and the undoubted effect of the stress and strain of modern life (Rivers[11]), in the pathogenesis of ulcer. Ulcers can be caused to form in portions of the gastro-intestinal tract entirely severed from any central nervous system connections so that I believe the immediate cause of the lesions is local. On the other hand, the vagi contain secretory fibers to the stomach and it is theoretically possible that these might be stimulated by other than the normal mechanism and there results a secretion of gastric juice in the empty stomach which if marked or persistent might cause ulcer. In 1927, Silberman[12] secured the secretion of gastric juice in the empty stomach by reflexly stimulating these secretory nerves. He performed double esophagostomy in dogs and gave these animals sham feedings for 40 to 60 minutes three times each day. Gastric or duodenal ulcers or erosions appeared in 18 of these dogs after periods of 16 to 49 days, and the acidity of the gastric content varied between 68 and 103 clinical units. It is possible that the acute ulcers and erosions observed by Dr. Harvey Cushing[13] in patients following operations for cerebellar tumor have an etiology similar to those in Silberman's experiments. It is not improbable that the operative trauma to the interbrain might stimulate the gastric secretory centers associated with the vagus center and cause a large secretion of gastric juice in the empty stomach, such as was secured by the sham feeding experiments. An examination of the gastric content after such cerebral traumas would be of great interest.

A continuous secretion of gastric juice into the empty stomach during the entire 24 hours occurs both in man and lower animals. The cause of this secretion (nervous or hormonal), its amount, and its variations under physiologic and pathologic conditions are but little understood. Normally the amount seems to be small and it is readily neutralized by the gastric mucus, swallowed saliva, and regurgitated bile and pancreatic juice. There is considerable evidence that in ulcer patients the volume of this continuous secretion is greatly augmented. Does this represent hyperactivity or hypertonicity of the vagus secretory mechanism as a result of continued mental strain? If so, vagus secretion may find a definite place in ulcer therapy. On the other hand, acute emotional stress definitely inhibits gastric motility and prolongs its emptying time and it is entirely possible that in this way may be significant in the clinical problem.

Considerable variation exists in the resistance of various parts of the alimentary canal and other tissues to the digestant action of pure gastric juice. When the secretion from an isolated Pavlov pouch was drained into the jejunum and ileum, several weeks were required before ulcers developed, whereas the exposed spleen was extensively digested in a few days. The ileum was found to be definitely more susceptible than the jejunum and in

every instance the gastric mucosa proved to be most resistant. This lessened resistance of the small intestine to the digestant action of gastric juice must always constitute an objection to all forms of surgical therapy in which an artificial opening is made between the stomach and jejunum. In those cases where the increased acidity of the gastric content is due to retention and where the operation corrects this defect the danger of jejunal ulcer should be minimal. The advisability of a large stoma to facilitate the emptying of the stomach seems indicated. The superior resistance of the duodenal mucosa as determined by experiment suggests that gastroduodenostomy or pyloroplasty, where conditions permit their employment, are preferable to gastrojejunostomy. On the other hand, when pyloric stenosis does not exist or where the increased acidity of the gastric content is due to excessive continuous secretion of gastric juice, the probability of recurrence or secondary jejunal ulcer is very real.

The development of typical ulcers in the wall of the isolated stomach proves that pure gastric juice can digest the gastric mucosa and makes it unnecessary to postulate a specific loss of resistance to account for ulcers in the stomach proper. The careful histologic examination of a large number of resected specimens in Konjetzny's[14] material failed to reveal evidence of local vascular injury, embolism, or thrombosis. It is not to be supposed that the resistance to digestion of the mucosa would always be uniform throughout or that a uniform exposure of the entire surface would always occur. Such variations should be of chief significance in determining the site of the resulting ulcer and its shape. The more general effect is manifested by the small erosions, hemorrhages, and cellular infiltrations in the neighboring more resistant or less exposed mucosa. According to this view the so called ulcer gastritis is of similar origin to the ulcer itself, is more amenable to medical treatment, and cannot be considered an indication for partial gastrectomy.

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DISCUSSION.—DR. EDWARD S. JUDD (Rochester, Minn.).—We are all greatly indebted to Doctor Dragstedt for this work. As you all know, he has investigated the pathogenesis of peptic ulcer for a great many years and has done a very good job. I hope we can make our surgical work conform to the principles that he has laid down and I think he has come closer to helping us out than any other research worker. The results which he has obtained from these experiments are strictly in accord with those obtained by Mann, Williamson and Bollman in the Mayo Clinic. It seems to me that we all feel that their experiments give sufficient evidence to show that a gastric content of sufficient acidity and concentration of pepsin can digest the normal mucous membrane of the stomach and duodenum and produce an ulcer. I think that it is, as Doctor Dragstedt says, unnecessary to postulate some local thrombosis, infection, or embolism, as has been suggested by some former investigators. When resistance is locally decreased, the digestive ability of the gastric juice undoubtedly will be more effective in producing and maintaining ulcer. I also fully agree with what Doctor Dragstedt says about gastritis as described by Konjetzny; namely, that it is attributable to the chemical action of the gastric content and that the condition is corrected when the acidity is controlled. I fully concur in his conclusion that, for this reason, the finding of extensive gastritis is not an indication for partial gastrectomy.

Mann and Bollman have stated, in an article on experimentally produced peptic ulcers, that two types of ulcerative lesions of the gastric and duodenal mucosa are produced experimentally: "The ulcerative type most often produced has always remained acute; it is usually multiple and is more often distributed throughout the mucosa of the fundus than in the mucosa of the pylorus or duodenum. The exact site of occurrence of the lesions is never definite or constant. They start as a hemorrhage in the submucosa, and the lesion of the mucosa appears secondary to the vascular injury. This type of lesion is readily produced experimentally by various means. It occurs in the so called toxic conditions, after the injection of toxins, certain drugs and bacteria, and in some moribund conditions that follow the loss of the adrenal and parathyroid glands, as well as after section of the splanchnic nerves and other operative procedures. In our experience, this type of ulcer is always acute. If the animal survives the procedure, which was accompanied by the development of the ulcer, healing always occurs, and no trace of the lesion remains.

"The other type of ulcer is the one that we have observed more commonly. The conditions under which it develops are definite and limited. The ulcer is usually single, although two or, rarely, three (hardly more) ulcers may be present at one time. The site of the lesion is in the pathway of the outflow of gastric contents; it is never in the fundus. The exact site of its development is definite and constant. It starts on the surface of the mucosa as a grayish, circumscribed membrane. At first it is saucer-shaped, and later the usual appearance of peptic ulcer as seen in man develops. In the beginning the lesion is acute, but if perforation with peritonitis or fatal hemorrhage does not occur, it quickly becomes chronic. Grossly and microscopically, this type of lesion resembles peptic ulcer as found in man.

"Whether either of these two types of lesions corresponds to the type seen in man has not been determined, owing to the fact that the process of development of the lesion in man has not been determined. If the mucosal lesion in man which precedes the development of the characteristic chronic peptic ulcer begins as a hemorrhage into the submucosa, it would appear that many of the

results of our investigations would have little, if any, clinical bearing. On the other hand, if the lesion in man begins at the surface of the mucosa, the type of lesion we have studied would appear to be the only type of experimentally produced ulcer that may be of clinical significance."

I believe that the acute type of ulcer which Mann and Bollman described is similar to the acute ulcerative lesions which Silberman produced in dogs after performing double esophagostomy and feeding a secretion of gastric juice obtained from the empty stomach by stimulating the secretory nerve. I believe that these acute ulcers and erosions described by Mann and by Silberman are the ulcers which Cushing found occurred following operations for cerebellar tumor. I do not think that this type of ulcer need be considered as simulating the chronic gastric or duodenal ulcer which is observed clinically.

The medical treatment of ulcer should be based entirely on these physiologic principles. Sometimes a great deal may be accomplished by employing a medical and dietary regimen similar to that originated by Doctor Sippy. If the patient responds satisfactorily, this plan of treatment may be continued. However, if the patient does not improve within a reasonable period of time, surgery should be undertaken. In our experience the various local operations and gastro-enterostomy have given very satisfactory results.

Endeavoring to utilize the principles of the experimental work that has been done and to apply them clinically, I have employed direct anastomosis of the stomach and duodenum for the past several years. I have done this because it seemed to me that this operation left the structures so that they could function more in accord with the normal physiologic processes than would be possible if other procedures were used. The stomach and duodenum can be anastomosed much more readily than formerly was presumed possible. This operation has been employed particularly by Wilkie, in Edinburgh, and the results have been most encouraging. I have carried out such an anastomosis in many cases of duodenal ulcer and have reason to think that a new ulcer will not form in the duodenum subsequently. I realize that this is not in accord with the results obtained by some others. However, my experience has encouraged me to continue to employ the operation in selected cases. I have not carried out resection of the stomach for benign ulcer of the stomach and duodenum except under exceptional circumstances. Furthermore, it seems to me that I shall not be inclined to do so, as the experimental studies indicate that the principles involved in the treatment of gastric and duodenal ulcer do not support the contention that resection of the stomach is often required for solution of the problem of ulcer.

DR. ALTON OCHSNER (New Orleans, La.).—We, too, have attempted to evaluate the effect of acidity in experimental production of ulcer in three groups of experiments. We have attempted to reproduce ulcer in the stomach and the first portion of the intestine, as Doctor Dragstedt has done in a series of experiments.

In one series we formed pouches from the greater and lesser curvatures of the stomach, respectively. Although the acidity in the individual pouches varied but little, the incidence of ulcer was much higher (63.6 per cent) in the lesser curvature pouches than in those on the greater curvatures (0 per cent). Following histamine injections we also found the incidence of ulceration much greater along the lesser curvature than elsewhere in the stomach. This, we believe, is due to the fact that the "magenstrasse" is more susceptible to ulceration than other portions of the stomach.

In a second group of experiments the lesser and the greater curvature

pouches, respectively, were anastomosed with the proximal jejunum. Jejunal ulcers developed in all (100 per cent) of the animals with the greater curvature pouch-jejunal anastomosis, whereas but 71 per cent of the animals with lesser curvature pouch-jejunal anastomosis developed ulcers. In another group of animals with lesser and greater curvature pouches, respectively, and jejunal anastomoses, bile was diverted into the pouch by anastomosing the gallbladder to the pouch and dividing the common duct. The ulcer incidence decreased in the lesser curvature pouch-jejunal anastomosis to 50 per cent and in the greater curvature pouch-jejunal anastomosis to 28 per cent.

In further experiments performed by Doctor DeBakey, in our laboratory, the relative protective influences of bile, pancreatic, and duodenal juices were determined. Pyloric occlusion and gastrojejunostomies, similar to those advocated by von Eiselberg, were performed. Jejunal ulcers developed in 50 per cent of the animals. In addition to the pyloric occlusion operation the pancreatic juice was deviated away from the anastomotic site by anastomosing the pancreatic duct with the terminal ileum. The incidence of ulceration in this group was 70 per cent.

In another group the bile was deviated from the anastomotic site by anastomosing the gallbladder to the terminal ileum and dividing the common duct. Incidence of ulceration increased to 90 per cent. In animals with both the bile and pancreatic juice deviated from the anastomotic site the incidence of ulcer was 100 per cent. It may be concluded from these experiments that both bile and pancreatic juice are protective in preventing ulceration and that of the two bile is more protective than is pancreatic juice.

Based upon those experiments and our clinical observation, we feel that there are three factors in the production of peptic ulcer as follows: first, and probably the most important one from the standpoint of therapeusis, is increased acidity; second is tissue predisposition, and the lesser curvature of stomach is, as we all know, more susceptible to ulceration than other portions of the stomach. The third, and probably the most important etiologic factor is a predisposition to ulcer formation; *i.e.*, ulcer diathesis.

As regards therapy the best we can do is to control the acidity by diet and by the administration of antacids or by operation. All operative procedures should be of such a type as to decrease the acidity. We feel that in the patient with normal or hyperacidity gastro-enterostomy should not be done, because with the patient's ulcer diathesis the chances of developing a jejunal ulcer are even greater than developing the original ulcer, because the jejunal mucosa is less resistant to the acid gastric chyme than are the duodenal and gastric mucosa. A pyloroplasty which will permit regurgitation of the alkaline duodenal secretions more readily is much safer, but in some instances subtotal gastric resection will be necessary. From our experimental and clinical observations, however, we are convinced that the acceptance of the ulcer diathesis is essential and that for the life of the individual it is necessary for him to abstain from those things which increase gastric acidity, especially smoking and drinking of alcohol.

DR. HENRY F. GRAHAM (Brooklyn, N. Y.).—I would like to take exception to one statement made by Doctor Dragstedt, namely, the recommendation for a large opening in gastro-enterostomy. There are certain individuals who have a gastro-enterostomy, who are unable to eat large meals, especially those containing large quantities of fluid such as a dinner accompanied by soup and several glasses of water, without a great deal of discomfort and inability for

rapid emptying of the stomach afterward. I think there is a good mechanical reason for it.

If you have a large opening, and the stomach becomes distended, you get a flattening of the jejunum against the stomach and in that way it closes up the entire opening. I think it is possible to make too large an opening and thus cause trouble.

DR. J. SHELTON HORSLEY (Richmond, Va.).—It is quite necessary for surgery on any portion of the body, and especially on the stomach, to have a firm foundation on biologic facts. The observations of physiologists have taught us more about correct fundamental principles of gastric surgery than have the operating surgeons.

The etiology of peptic ulcers may be divided into three classes, or a combination of these classes: (1) hyperacidity, which Doctor Dragstedt has so well brought out; (2) toxic influences such as from burns or from certain types of streptococcic bacteria, which Rosenow has demonstrated; and (3) the neurogenic origin, which has been brought into prominence recently by Harvey Cushing. Doubtless in many instances some combination of these three causes may act to produce a peptic ulcer. The presence of hyperacidity, for instance, may be due to excessive vagus stimulation. The affinity of gastric cells for certain bacteria or toxic products may also cause hyperemia and probably hyperacidity.

An important fact that physiologists have shown is that the susceptibility of the gastro-intestinal mucosa to the acid of the gastric juice increases with the distance from the pylorus. Consequently, in a Billroth II type of gastrectomy, particularly if done for a gastric or duodenal ulcer with high acidity, we are apposing to the stomach a portion of the bowel that is more susceptible to irritation by the gastric juice than would be the duodenum. When the gastric acidity is low, as it usually is in cancer, the danger of jejunal ulcer is not so great, but it cannot be entirely eliminated for after the malignant lesion has been removed it may be that the acid secretion of the stomach will be resumed. That this is not solely a theory is shown by an interesting case reported by Dr. Fordyce B. St. John, of New York; he removed a cancer of the stomach and did a Billroth II type of operation. Later the patient died from a jejunal ulcer. It seems apparent that when a partial gastrectomy is indicated some type of Billroth I operation should be employed whenever it is possible to do so. There are ulcers in the duodenum not because the duodenum is more susceptible to the gastric juice, but because it receives the first impact of the acid.

Doctor Ochsner has shown in experiments that there is some protective influence of the bile against the formation of peptic gastric ulcers in experimental work on dogs, but this is not so great as the alkaline influence of the pancreatic juice. Bile is very slightly acid, or even neutral, whereas the pancreatic juice is very strongly alkaline. If the presence of bile, then, tends to lessen the incidence of peptic ulcer, it is probably due to some other cause than to its chemical reaction. In the interesting experiments of Doctor Ochsner a peptic ulcer occurred more frequently along the lesser curvature than the greater curvature. The factor of more active peristalsis along the lesser curvature than along the greater curvature should be taken into consideration. Peristalsis is initiated along the lesser curvature and ordinarily it is far more active in this region, whereas if the segment of the stomach comprising the greater curvature is isolated, much of the impulse for peristalsis has been obliterated. The more vigorous and constant action along the lesser curva-

ture, other things being equal, would seem to predispose to ulcer formation far more than in the quiet, inactive segment of the stomach.

DR. LESTER R. DRAGSTEDT (Chicago, Ill.).—It is not possible in the time allotted to give proper credit to the large amount of excellent experimental work on the cause of ulcer done both in this country and abroad. I should like to emphasize that there is nothing in our experiments which precludes the possibility that mechanical factors, such as the motility of the stomach or pylorus or the abrasive action of coarse food, or infection, may operate to delay the healing of an acute lesion and induce chronicity. However, I do believe that of all the factors likely to play a rôle in young and otherwise healthy adults (the people who get ulcers) the chemical action of the gastric content when it approaches the acidity of pure juice is the most important. The concentration of free hydrochloric acid is more significant than pepsin, and hence the term "acid ulcer" is more accurate than "peptic."

I am not convinced that the theory of Aschoff that the cause of prevalence of ulcer along the lesser curvature is the mechanical effect of food passing along the "canalis gastricus" is correct. We created such a canal experimentally in a dog with a large Pavlov pouch. The mucosa of the canal remained normal but an ulcer developed in the isolated pouch. There is no doubt that an acute lesion near the pylorus is more apt to become chronic than a similar one in the body of the stomach. We have a special case in the fact, I think, that such lesions produce spasm of the pylorus, cause retention, and so raise the acidity of the gastric content until it approaches the acidity of gastric juice. A pyloric lesion will do this to a normal secretory mechanism. There are other cases in which we find a hypersecretion of gastric juice, ill understood, perhaps, but without pyloric obstruction, and it is in these cases, I believe, that we find a large incidence of jejunal ulcer following operation, whether it be a gastro-enterostomy or partial resection.

The protective action of bile and pancreatic juice has been clearly demonstrated in experimental ulcer and has been of great significance in determining the importance of acid in the genesis of these lesions. This factor is of less importance in the clinical problem.