The Role of Brunner's Glands in the Intrinsic Resistance of the Duodenum to Acid-Peptic Digestion*

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IN 1951, DRAGSTEDT, Oberhelman, and Smith[2] reported that acid-peptic ulceration of the proximal jejunum occurred more frequently and rapidly than in the proximal duodenum. Following transplantation of the gastric antrum to the colon (for stimulation of the stomach remnant), gastro-intestinal continuity was re-established in ten dogs by gastroduodenostomy, and in another ten dogs by gastrojejunostomy. Only two of the gastroduodenostomy group developed duodenal ulcers, while eight of the gastrojejunostomy group developed jejunal ulcer.

In 1954 Harkins, Schmitz, Nyhus, Kanar, Zech and Griffith[9] confirmed these experimental results. In addition, we showed that following resection and discard of the gastric antrum, ulceration of the jejunum after gastrojejunostomy occurred more frequently and more rapidly, with histamine stimulation, than did ulceration of the duodenum after gastroduodenostomy. It is important to point out that short afferent loops were present in all dogs with gastrojejunostomies.

These observations are in keeping with the axiom that the tendency towards acid-peptic ulceration of the intestine progressively increases as the distance between the pylorus and gastroenterostomy increases (Matthews and Dragstedt,[14] McMaster[15]). From these experimental results, there is reason to believe that following a given subtotal gastric resection in a given patient, recurrent ulceration is more apt to occur with a Billroth II gastrojejunostomy than with a Billroth I gastroduodenostomy. Before fully appreciating this conclusion, however, we might first discuss why jejunal ulceration is more apt to occur than duodenal ulceration. In our previous report referred to above, the following reasons were presented.

1. *Duodenal Inhibition.* Day and Webster[1] showed in dogs that acid chyme in the duodenum suppresses secretion of gastric acid. This phenomenon is referred to as duodenal inhibition. Pincus, Thomas, and Rehfuss[18] demonstrated that duodenal inhibition in dogs does not occur unless the pH of the acid placed in the duodenum is 2.5 or less. This degree of acidity is most probably present in the duodenum of the dog whose entire acid secreting stomach remnant is anastomosed to the duodenum, and is stimulated by either an antral transplant to the colon or by histamine. Under the same stimulation, but with the stomach anastomosed to the jejunum, it is doubtful that a comparable degree of acidity is obtained in the duodenum by reflux through the afferent loop. Therefore, we have postulated that there is a greater effect of duodenal inhibition in these dogs with gastroduodenostomies than in dogs with gastrojejunostomies. To support this thesis, we presented evidence that gastroduodenostomy dogs secrete less acid from a Heidenhain pouch than do gastrojejunostomy dogs. At present we are confirming this finding in our laboratory.

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FIG. 1

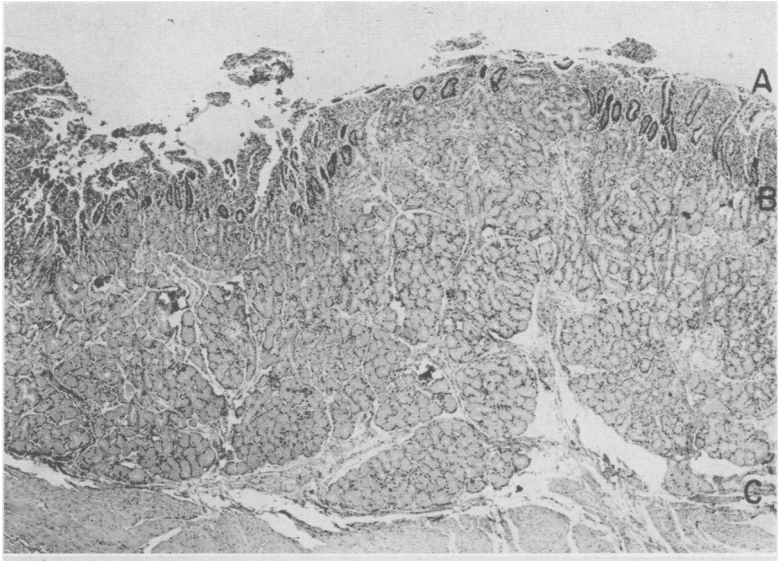

FIG. 2

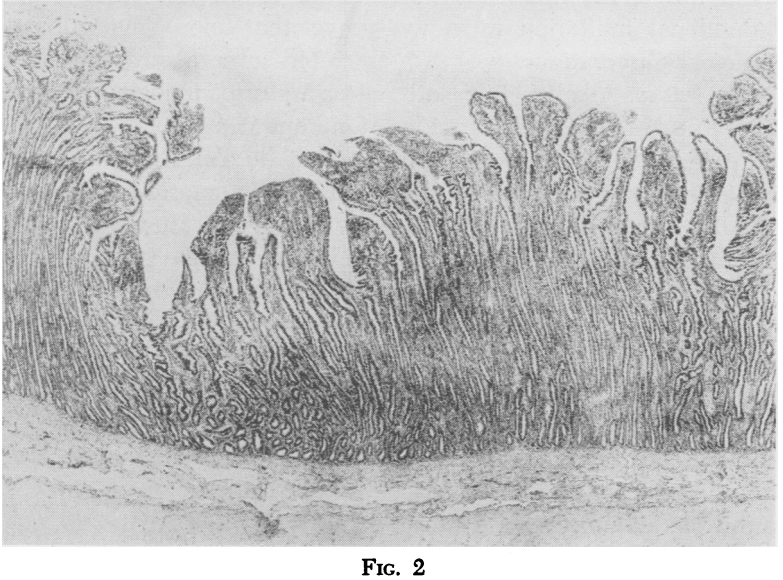

FIG. 1. Normal duodenum of man. This section was taken through duodenum 3 cm. distal to the pylorus. The epithelium (from A to B) is partially autolyzed. Brunner's glands are a thick, dense, continuous layer beneath the muscularis mucosa (from B to C). Brunner's glands in man are present as such from the pylorus to the ampulla of Vater. This section was obtained from a surgical specimen of a 48-year-old male, who underwent subtotal gastric resection for a benign gastric ulcer on the lesser curvature.

FIG. 2. Normal jejunum of man. This section was taken through jejunum approximately 8 cm. distal to the ligament of Treitz. The mucosa consists entirely of intestinal epithelium. In decided contrast to the duodenum (Fig. 1), no Brunner's glands are present. This section was obtained from a surgical specimen of a 33-year-old male who underwent reoperation for a stomal (jejunal) ulcer following an original subtotal gastric resection with a Billroth II anastomosis for duodenal ulcer.

However, it is unlikely that any similar effect of duodenal inhibition is present in the human following adequate subtotal gastrectomy. Although Griffiths (1936)[8] first demonstrated the phenomenon of duodenal inhibition in normal humans, Shay *et al.*

(1942),[19] found that to produce this duodenal inhibition, a degree of acidity must be present in the duodenum equal to the maximum degree of acidity obtained in the gastric juice secreted in response to a test meal. Furthermore, Shay *et al.* could not demonstrate duodenal inhibition in patients with duodenal ulcer, even though the concentration of acid placed in the duodenum was twice that obtained from the stomach after a test meal. Since an adequate subtotal gastric resection greatly decreases the acid output of the stomach, duodenal inhibition following this operation in the human is most probably negligible regardless of the type of anastomosis. Therefore, one cannot justifiably claim any superiority of the Billroth I operation over the Billroth II on the basis of duodenal inhibition in view of the above clinical observations.

2. *Neutralizing Juices.* Alkaline bile and pancreatic juice neutralize gastric acid. Kiriluk and Merendino[11] showed that in dogs "there is a progressive decrease in the pH and in the buffering capacity of the bowel contents as the distance from the pylorus is increased." There is, therefore, a greater capacity for neutralization of gastric acid in the proximal duodenum than in the proximal jejunum. Applying this fact to our experimental dogs, gastric acid entering the duodenum via a gastroduodenostomy is neutralized to a greater extent than is gastric acid entering the jejunum via a gastrojejunostomy. There is no reason to suspect that the same mechanism does not apply to the human, and therefore on this basis the Billroth I anastomosis should be followed by less ulceration than the Billroth II, provided, of course, that the extent of gastric resection in each instance is equal.

The same logic has been stressed by Merendino *et al.*,[16] and Wangensteen,[21] in their emphasis on the need for a short afferent loop when the Billroth II anastomosis is employed.

To sum up, the closer we anastomose the stomach to the source of neutralizing bile and pancreatic juices, the less recurrent ulceration will result. The Billroth I anastomosis is the closest we can get to these neutralizing agents.

3. *Secretion of Neutralizing Juices.* It has been repeatedly stated that the most physiologic restoration of gastro-intestinal continuity after gastric resection is by the Billroth I gastroduodenostomy. The Billroth II gastrojejunostomy shunts stomach content into the jejunum and by-passes the duodenum. The abundance of experimental and clinical evidence points to the fact that the humoral stimulation for bile and pancreatic juice and *succus entericus* is maximum in the duodenum. However, direct proof of this thesis is lacking. We know of no experimental or clinical studies which actually prove that more neutralizing juices are secreted after a gastroduodenostomy than after a gastrojejunostomy. Furthermore, the rapid and complete retrograde filling of the afferent duodenojejunal loop in some Billroth II anastomoses would tend to equalize any difference. However, we[9] (1954) have previously cited experimental and clinical evidence that there is better digestion and absorption of fats and proteins with a Billroth I anastomosis than with a Billroth II. Although the difference is small, and probably not clinically significant, any superiority in this respect must be given to the Billroth I operation.

INTRINSIC INTESTINAL RESISTANCE

This phrase refers to the ability of the intestine, by itself, to resist acid-peptic ulceration in the absence of any neutralizing bile, pancreatic, or intestinal juices. The experimental evidence for or against the existence of any differential resistance between the proximal duodenum and jejunum is contradictory. It is the purpose of this paper to present our experimental results showing that the proximal duodenum *does* possess more intrinsic resistance than the proximal jejunum. In so doing, we may

add this fact to the other advantages of the Billroth I over the Billroth II anastomosis. Before proceeding further in this regard, we might first discuss the anatomic difference between the proximal duodenum and jejunum which concerns the physiologic difference.

BRUNNER'S GLANDS

Florey and Harding[3-5] initiated experiments designed to elucidate the anatomic and physiologic significance of Brunner's glands. These authors found that the amount and distal extent of Brunner's glands varied greatly among many different animal species. Of perhaps greater importance, they demonstrated that Brunner's glands, in all animal species tested, secrete an abundant alkaline mucus in response to a "highly purified" preparation of secretin.* In 1940 the same group (Wright *et al.*[22]) showed that Brunner's glands secrete after vagal stimulation. Thus, like the stomach, the secretion of Brunner's glands consists of both cephalic and humoral phases.

In 1944, Landboe-Christensen[13] published a monograph concerning Brunner's glands in the human. His results were based upon 53 autopsies of 32 females and 21 males of all ages. Of extreme interest is his observation that in every instance the glands of Brunner extended distally as a continuous dense sheet to or beyond the ampulla of Vater (Fig. 1). In no instance did Brunner's glands extend beyond the ligament of Treitz (Fig. 2).

Applying these facts to subtotal gastric resection, we may conclude that the duodenum used for a Billroth I anastomosis has a dense continuous sheet of Brunner's glands capable of secreting an abundant alkaline mucus. In contrast, the jejunum used for a Billroth II anastomosis has no Brunner's glands, and therefore lacks this intrinsic source of alkaline mucus. Utilizing this fundamental anatomic and physiologic difference between the proximal duodenum and jejunum, our experiments were conducted to compare the intrinsic resistance to acid-peptic ulceration of these specific segments of intestine.

DUODENAL RESISTANCE TO ULCERATION

In 1939, Florey *et al.*[6] pointed out that the duodenum of the human and pig are similar in that the amount and distal extent of Brunner's glands are comparable. We have confirmed these observations. Brunner's glands in the pig are present as a continuous dense sheet from the pylorus to beyond the ampulla of Vater (Fig. 3). Just proximal to the beginning of the duodenum's retroperitoneal portion, Brunner's glands dwindle out and become scattered. A few islands may be found at the ligament of Treitz, but beyond this point the jejunum has no Brunner's glands (Fig. 4).

Florey *et al.*[6] isolated segments of pig duodenum (containing Brunner's glands) from the bile and pancreatic ducts, and anastomosed the proximal end to an acid secreting Pavlov pouch of the stomach. The distal end was drained internally into the small bowel. These segments of duodenum did not ulcerate. Segments of ileum (containing no Brunner's glands) were then anastomosed to Pavlov pouches in the same manner, and all ulcerated. Florey *et al.* concluded that the duodenum of the pig is protected from ulceration by secretion of Brunner's glands, and that the small bowel without Brunner's glands is not protected, and therefore ulcerates. These results indicate that the proximal duodenum with Brunner's glands is intrinsically more resistant to acid-peptic ulceration than the more distal small bowel without Brunner's glands. It is unfortunate regarding our

* Sonnenschein, Grossman, and Ivy[20] have concluded that the humoral stimulus of the secretion from Brunner's glands is not secretin itself, but is another related hormone present in the crude secretin product.

FIG. 3

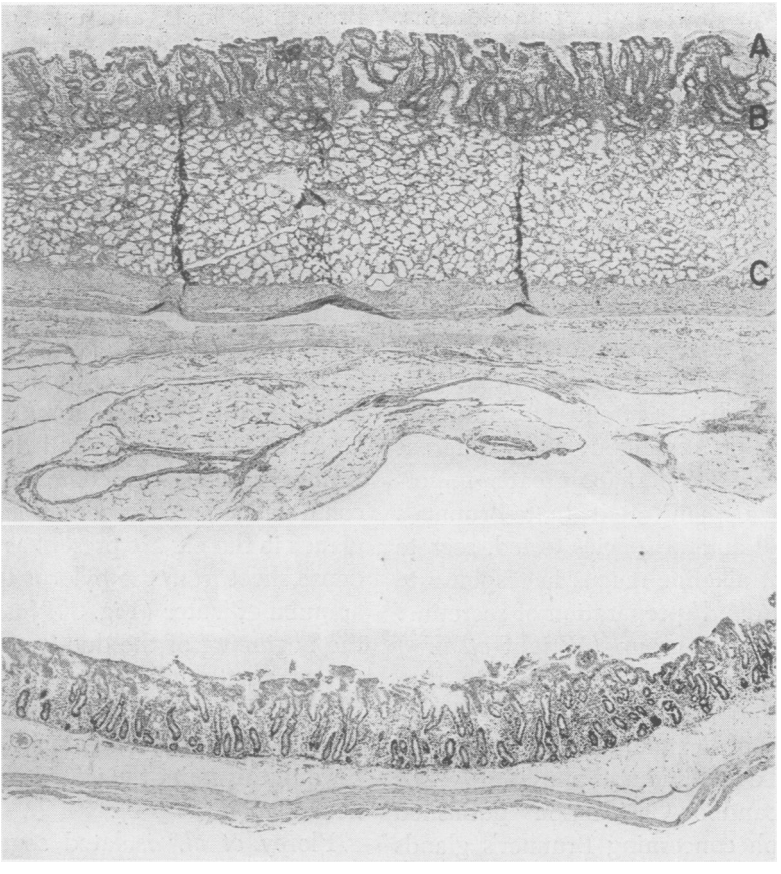

FIG. 4

FIG. 3. Normal duodenum of pig. This section was taken through duodenum 4 cm. distal to the pylorus. The dense, continuous layer of Brunner's glands (from B to C) is thicker than the overlying epithelium (from A to B). Brunner's glands of the pig are present as such from the pylorus to beyond the ampulla of Vater, and almost to the beginning of the retroperitoneal portion of the duodenum. Note the similarity of this section to Figure 1 (human duodenum) as regards the amount of Brunner's glands.

FIG. 4. Normal jejunum of pig. This section was taken through jejunum 4 cm. distal to the ligament of Treitz. Like the human jejunum (Fig. 2), Brunner's glands are absent. The mucosa consists only of intestinal epithelium. Comparison of this section with Figure 3 (pig duodenum) offers a striking contrast, which may explain the different intrinsic sensitivity to acid-peptic injury between these two segments of intestine.

specific interests that Florey used the ileum instead of the proximal jejunum (distal to the extent of Brunner's glands) for comparison with the duodenum.

Before and since these important contributions of Florey and associates, many experiments have been done to investigate intrinsic resistance of various levels of the bowel to acid-peptic ulceration. None of the reports of these many experiments mention Brunner's glands. Furthermore, the majority of these experiments have been performed on dogs. In interpreting the results of such experiments, it is important to realize that the duodenum of the dog differs from the pig and human duodenum in a most significant respect. Brunner's glands in the dog are not nearly as dense as in the pig and human (Fig. 5), and furthermore, they extend distally for only 1 to 2 centimeters (Fig. 6). The mucosa of the proximal duodenum (beyond the distal limit of

FIG. 5

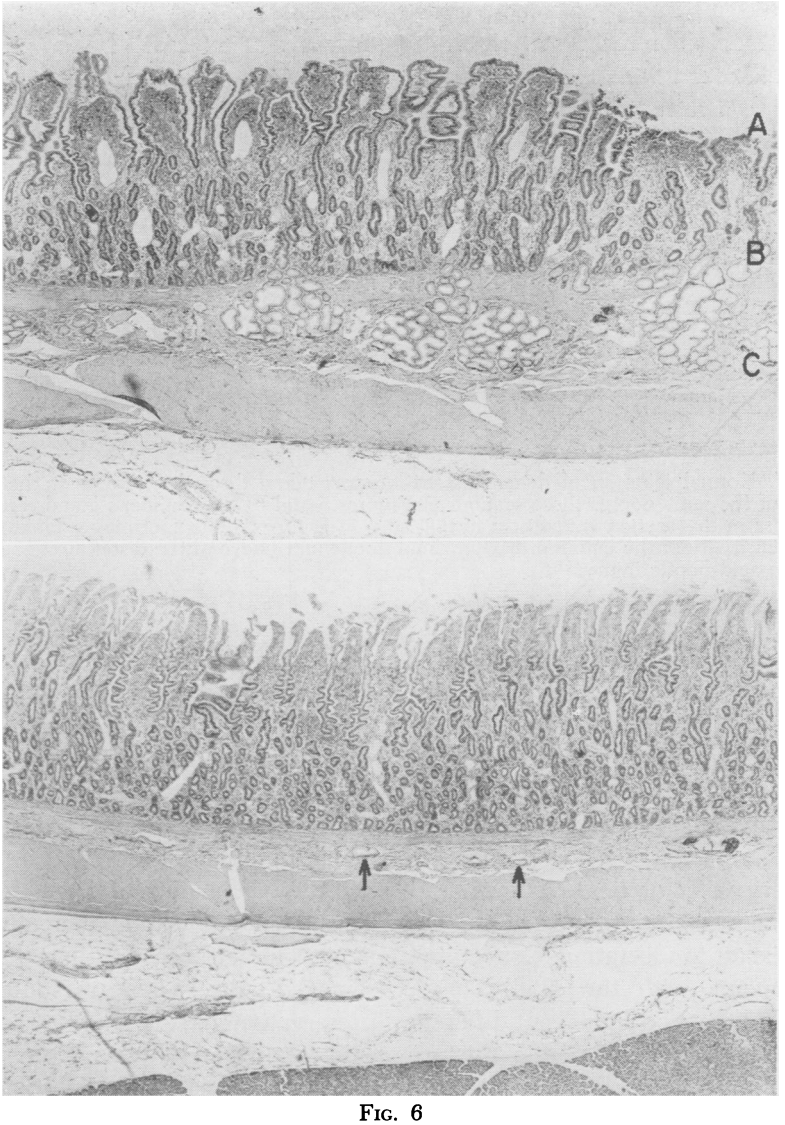

FIG. 6

FIG 5. Normal duodenum of dog. This section was taken through duodenum within the first centimeter distal to the mucosal gastroduodenal junction, which, in this animal, was 2.2 cm. distal to the pylorus. Brunner's glands (from B to C) are not nearly as dense or as thick or as continuous as in the human (Fig. 1) or pig (Fig. 3). The overlying epithelium is from A to B.

FIG. 6. Normal duodenum of dog. This section was taken through duodenum 1 cm. distal to that section shown in Figure 5. Brunner's glands (arrows) are practically non-existent. This finding is significant in that this section is from proximal duodenum only 2 cm. distal to the mucosal gastroduodenal junction. The absence of Brunner's glands here is a notable difference between the abundance of Brunner's glands in the human (Fig. 1) and pig (Fig. 3). A portion of pancreas is seen at the bottom of the section.

Brunner's glands) is therefore comparable to the mucosa of the jejunum in that Brunner's glands are absent in both (Fig. 7). Therefore, assuming that Brunner's glands may be the source of the duodenum's increased intrinsic resistance to acid-peptic ulceration, the dog is not the best choice of experimental animal in which to prove it.

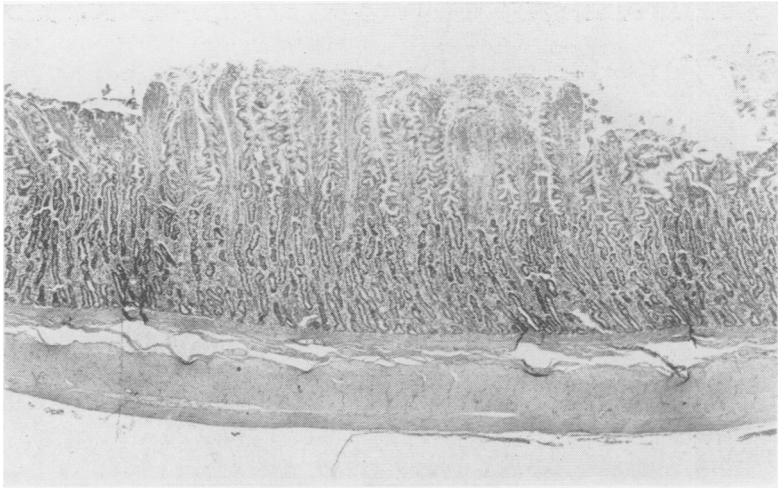

FIG. 7. Normal jejunum of dog. This section was taken through jejunum at the ligament of Treitz of the same dog as those sections in Figures 5 and 6. No Brunner's glands are present. The mucosa in this section is identical to that seen in Figure 6. This fact may explain the equal intrinsic sensitivity of the jejunum and proximal duodenum (beyond the distal limit of Brunner's glands) to acid-peptic injury.

Kolouch[12] introduced a simple method for determining intrinsic resistance of intestinal mucosa to acid-peptic ulceration. He exposed the mucosal surfaces of viable intestine, and allowed an acid-peptic mixture to drip onto them. Using this method, Kiriluk and Merendino[10] tested various portions of the alimentary tract of dogs. They found the stomach most resistant, and the esophagus least resistant to ulceration. Concerning their experiments with the small bowel, they concluded that "no significant differential sensitivity to the acid-peptic mixture was observed in the duodenum, jejunum, or ileum." However, the most proximal portion of the duodenum was *not* tested. Only the mid and distal duodenum was tested and compared with the jejunum and ileum.

Because the conclusions of Kiriluk and Merendino (based on dogs) are in direct contrast with those of Florey, *et al.* (based on pigs), and because these conclusions have a direct bearing on the rationale of the Billroth I gastric resection, we investigated the intrinsic resistance of the *proximal* duodenum and *proximal* jejunum to acid-peptic ulceration in both dogs and pigs.

METHODS

Six weanling pigs and nine mongrel dogs were used. Under intraperitoneal or intravenous nembutal anesthesia, the abdomen was opened. The distal stomach, pylorus, and proximal duodenum, and also the proximal jejunum just distal to the ligament of Treitz, were delivered from the abdomen. The common bile and pancreatic ducts were ligated and transected. The pancreas was removed entirely from the duodenum with preservation of the duodenal vasculature. The antrum, pylorus, and proximal duodenum, and also the proximal jejunum, were each opened longitudinally along the antimesenteric border. Both segments were then flushed with normal saline to remove their contents and cleanse the mucosa.

A solution of 0.1 N hydrochloric acid containing 2 per cent pepsin was dripped onto the two exposed mucosal surfaces from burettes placed 0.5 cm. above each mucosal surface. The rate of flow was adjusted to 15 to 20 drops per minute, and was continued for 30 to 90 minutes. The amount of acid-peptic mixture dripped onto each mucosal surface approximated 50 milliliters. In

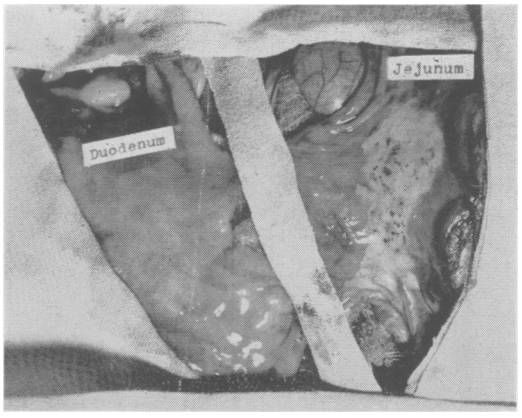

FIG. 8. Differential intrinsic resistance to acid-peptic ulceration of proximal duodenum and proximal jejunum of the pig. Each intestinal segment exposed to a total of 55 milliliters of 0.1 N HCl and 2 per cent pepsin solution delivered in drops for one hour. Injury to the duodenal mucosa is scarcely noticeable, but there is marked necrosis of the jejunal mucosa with hemorrhages.

each experiment, the rate of flow was carefully watched and kept constant, so that the duodenum and jejunum in each instance were equally exposed to the drip.

To prevent puddling of the drip solution on the mucosa, one end of each intestinal segment was elevated. The degree of tilting was slight, and kept constant in each experiment to equalize the contact of the drip solution with the mucosal surfaces. This encouraged an even flow of the drip solution over the mucosa.

At the conclusion of each experiment, photographs were taken of the specimens in their viable state. The animals were then sacrificed after removal of the specimens for fixation and microscopic study.

RESULTS IN THE PIG

The results in all six pigs were the same, and were characterized by a remarkable resistance of the duodenum to the acid-peptic solution. In striking contrast, the jejunum was severely injured (Fig. 8). Specific differences between the results of the proximal duodenum and proximal jejunum were as follows:

1. Early in the experiments, the duodenal mucosa became coated with a layer of mucus. This mucus definitely protected the mucosa against the drip solution. In some experiments, the drops hit this mucus and ran off the surface like water off a duck's back. The jejunum did not produce such a protective coat of mucus. In some instances, the jejunum appeared to soak up the drip solution like a blotter.

In the first experiment, this mucus on the duodenum was so abundant that it was considered a spillover of mucus from the stomach. Accordingly, the operative field was inspected, and the pyloric canal and antrum were tightly repacked with sponges. Also, the distal end of the duodenum was elevated to prevent any such spillover. The drip solution was dropped onto the distal portion of the duodenal segment so that it flowed proximally. Under these conditions, abundant mucus secretion continued. This mucus was secreted by the duodenum itself, and almost certainly from Brunner's glands.

In a few instances, attempts were made to aspirate the mucus to allow the drip solution to contact the mucosa directly. These attempts were unsatisfactory because of the incomplete aspiration and trauma to the mucosa in so doing. The general impression gained, however, was that the drip solution did injure the duodenal mucosa more easily when the mucus was aspirated. Removal of the mucus is really begging the question. The mucus represents an intrinsic property of the duodenum not possessed by the jejunum, and makes for increased intrinsic resistance of the duodenum to acid-peptic ulceration.

2. The jejunal mucosa blanched more quickly (in some instances with the first drop) and severely than the duodenum. The duodenum blanched later in the experiment, and not nearly as much.

3. The jejunal mucosa took on a charred white appearance about 15 minutes after exposure to the drip solution. This charring became progressively more severe, and was accompanied by tiny hemorrhages from

the mucosal surface. The duodenum did not become charred or white, and mucosal hemorrhage was much less frequent and severe. The duodenal mucosa was injured, however. The mucosa in contact by the drip solution appeared grayer and more edematous than the surrounding mucosa (Fig. 8).

Microscopic Studies. The microscopic changes are not as striking as the gross. Sections of the injured jejunum show severe desquamation and coagulation necrosis of the superficial half or third of the epithelium. The injured duodenum shows only slight desquamation, and the most superficial cells show changes similar to cloudy swelling. Coagulation necrosis is minimal to absent. All microscopic sections serve to emphasize the presence of Brunner's glands in the duodenum, and their absence in the jejunum (Figs. 3 and 4).

One finding is of interest. In comparing all the slides, there seem to be more goblet cells (cells distended with mucus) in the duodenal epithelium than in the jejunal epithelium. These cells are not those of Brunner's glands, but are in the intestinal epithelium superficial to the muscularis mucosa. This difference is slight, and probably not significant.

RESULTS IN THE DOG

In contrast to the pig, the results concerning the duodenum of the dog as compared with the jejunum are much less striking. The difference may lie in the fact that much less mucus is secreted by the dog duodenum than the pig. The slightly greater resistance of the dog duodenum to the acid-peptic drip appeared to be directly related to the small amount of mucus present. Like the pig, however, the dog jejunum secreted little to no mucus in these experiments.

The reaction of the dog jejunum was essentially as described by Kiriluk and Merendino.[11] The mucosa blanched with the first drop, and mucosal hemorrhages appeared in approximately five minutes. These

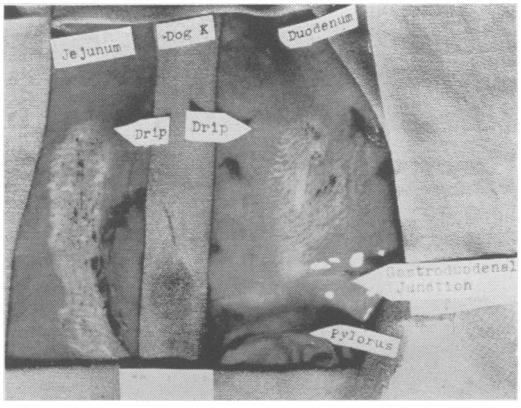

FIG. 9. In this experiment, the distal segments of the intestine were slightly elevated. The acid-peptic solution was dripped distally so that it flowed proximally. Forty milliliters were dripped onto the jejunum, and 60 onto the duodenum for 45 minutes. Despite the increased exposure of the duodenum, the most proximal duodenum shows less injury than the jejunum. The mucosal gastroduodenal junction is 1.8 cm. distal to the pylorus in this dog.

changes progressed, so that by the end of the experiment the mucosa appeared white and necrotic.

In general, the same changes took place in the duodenum. However, blanching did not occur for five to ten minutes, and hemorrhages did not appear for 15 minutes. At the end of the experiment, these changes were well developed, and like the jejunum, the duodenal mucosa was white and appeared necrotic (Fig. 9). However, the changes were a bit less severe in the duodenum.

As experience with this method increased, it became obvious that the most proximal duodenum (the first 2 to 3 cm.) was a little more resistant than the more distal mucosa. Furthermore, beyond the first 2 or 3 cm. of proximal duodenum, the mucosa of the rest of the duodenum and proximal jejunum showed no difference in response to the drip solution (Fig. 9). Evaluation of differential response within the proximal duodenum cannot be appreciated without reviewing the gross and microscopic anatomy.

Careful inspection of the mucosa reveals that the junction of gastric and duodenal mucosa in the dog is *not* at the pylorus. The

gastric antral mucosa continues 1.5 to 2.5 cm. beyond the pylorus. At this point a gross line of demarcation in the mucosa marks the beginning of duodenal mucosa. These landmarks may be seen in Figure 9. Microscopic sections carefully correlated with these gross landmarks verify these observations. Thus the gross and microscopic *mucosal* gastroduodenal junction in the dog is 1.5 to 2.5 cm. beyond the pylorus. It should also be recalled at this point that Brunner's glands extend only 1 to 2 cm. beyond this mucosal gastroduodenal junction (Figs. 5 and 6), and that the duodenal mucosa beyond the distal extent of Brunner's glands appears the same as jejunal mucosa (Figs. 6 and 7).

If the pyloric and duodenal segment is exteriorized with the proximal end elevated slightly, the acid-peptic solution may be dripped onto antral mucosa just distal to the pylorus so that it flows distally. When this was done, no injury whatsoever was observed in the antral mucosa. Immediately distal to the mucosal gastroduodenal junction, however, the duodenal mucosa was injured. The most proximal duodenum was not injured as severely as the mucosa 2 or 3 cm. distally. Mucus partially protected the most proximal mucosa. On the basis that this mucus arose from the antral mucosa and flowed distally, other experiments were done in which the mucosal gastroduodenal junction itself was elevated, and the solution dripped just distal to the mucosal gastroduodenal junction so that it flowed distally. The results were essentially the same, although less mucus appeared with a corresponding increase in mucosal injury. Finally, as shown in Figure 9, the distal end of the intestinal segment was elevated, and the solution dripped onto the mucosa some 5 or 6 cm. distal to the mucosal gastroduodenal junction so that it flowed proximally. Injury at the site of the drip was the same as the jejunum, but lessened progressively in the proximal direction on up to the mucosal gastroduodenal junction, where it stopped abruptly and did not involve the antral mucosa. In these instances, the proximal duodenal mucosa was again partially protected by mucus, which not only was secreted in the area of Brunner's glands but also distal to them. The source of this mucus distal to Brunner's glands which was minimal but still more than was evident in the more distal duodenum and jejunum, must be from the duodenal epithelium itself (see below).

By this experimental method, we attempted to demonstrate that the most proximal centimeter or two of duodenum (containing Brunner's glands) is more resistant than the more distal duodenum without Brunner's glands. In general, these efforts failed, probably because the amount and extent of Brunner's glands in the dog are very small compared to the pig. However, the result of one such experiment (Fig. 10) suggests that Brunner's glands in the dog do afford some protection.

Microscopic studies. The changes produced by the acid-peptic solution are the same as seen in the pig. Desquamation and coagulation necrosis of the superficial mucosa are seen in both duodenum and jejunum. Little difference can be seen between the two intestinal segments. The difference of injury between the most proximal duodenum and more distal sections is not conclusive.

Many sections tend to show more mucus-distended goblet cells in the duodenum than in the jejunum. The difference is minimal, and does not seem to account for the greater mucus secreted by the proximal duodenum distal to Brunner's glands, as compared to the jejunum.

DISCUSSION

We feel that these experiments explain why various reports of intrinsic intestinal resistance to acid-peptic ulceration are contradictory. We have shown to our satisfac-

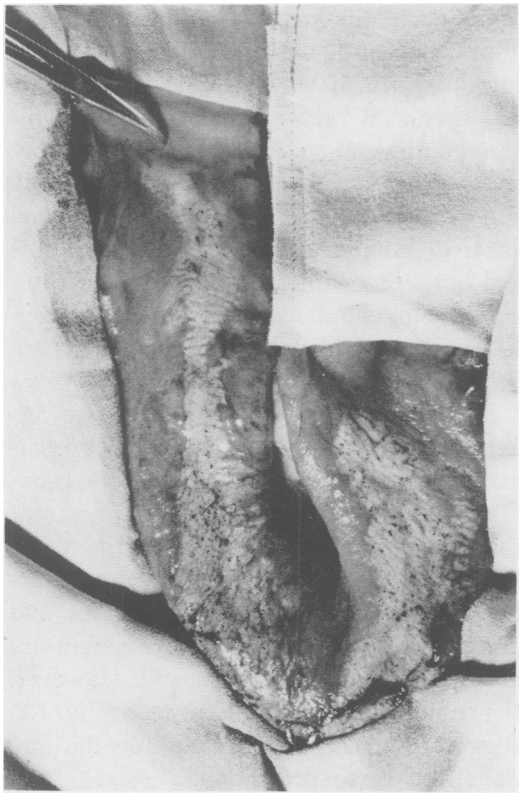

FIG. 10. In this experiment, the entire proximal duodenum (to the ligament of Treitz) was exposed to an acid-peptic drip. The forceps point to the mucosal gastroduodenal junction. The drape proximal to the forceps is placed across the pylorus to again demonstrate that the mucosal gastroduodenal junction is distal to the pylorus. The most proximal duodenum (less than a centimeter) shows less injury than the more distal duodenum, which in turn shows a more or less uniform injury. The less injured proximal duodenum is the only portion of duodenum containing Brunner's glands, in the dog.

tion that the duodenum of the pig is much more resistant than the jejunum. We also believe that this differential sensitivity is largely dependent upon the protection afforded the duodenum by the alkaline mucus secretion of Brunner's glands.

Since the duodenum of the pig and human are almost identical in regard to the presence of Brunner's glands, we believe that these observations on the pig can be applied to the human. That is, because of Brunner's glands, the human duodenum should possess a greater intrinsic resistance to acid-peptic ulceration than the jejunum. In this respect, the Billroth I anastomosis should be superior to the Billroth II as regards recurrent stomal ulceration. In this connection it is an interesting clinical observation that when dealing with the duodenal stump by the open technic, whether for anastomosis or for closure, there is always a considerable amount of clear mucus that wells up into the field from the duodenum. No such mucus comes from the jejunum when doing a gastrojejunostomy.

The anatomy of the proximal duodenum of the dog differs greatly from that of the human. On this basis, the mechanism of resistance to ulceration in the dog duodenum may be entirely different from the human. We therefore do not believe that experiments of intrinsic intestinal sensitivity in the dog are as applicable to the human as are those in the pig.

It has been stated that the secretion of Brunner's glands is under both vagal control and hormonal control. In performing an operation for duodenal ulcer, it is therefore desirable to retain the protective secretion of Brunner's glands. We have previously mentioned that the Billroth I anastomosis is more apt to stimulate the formation of secretin and related hormones than the Billroth II. The amount of such humoral secretion from the pancreas and Brunner's glands may therefore be greater with a Billroth I anastomosis.

These considerations may be carried further in respect to vagotomy. Not only does the usual technic of vagotomy eliminate the cephalic phase of gastric secretion but also the vagal stimulation of the pancreas, liver (bile flow), and intestine (Brunner's glands and *succus entericus*). It would therefore seem desirable when vagotomy is employed, that the vagal interruption be confined to the stomach, and that the vagal innervation to the remainder of the abdominal viscera be preserved. A method for accomplishing such a *gastric* vagotomy is considered in another report (Griffith, 1955).[7]

SUMMARY

1. Previous experiments by the authors have shown that following resection of the gastric antrum in the dog, and anastomosis of the stomach remnant to the duodenum or jejunum, more stomal ulcers occur at the site of gastrojejunostomy than at the site of gastroduodenostomy. Gastric stimulation in these experiments is afforded by transplanting the antrum to the colon or by histamine.

As measured by Heidenhain pouch secretions in this type of experiment, more gastric acid is secreted in dogs with gastrojejunostomies than with gastroduodenostomies.

Explanations of the difference in incidence of ulceration and secretion of gastric acid between these two experimental preparations include: (a) Increased neutralization of gastric acid in the duodenum. (b) Increased secretion of neutralizing juices with gastroduodenostomy. (c) Increased effect of duodenal inhibition with gastroduodenostomy.

2. Applying these experimental factors to the patient following subtotal gastrectomy, the most important appears to be the increased capacity for neutralization of gastric acid in the duodenum made available by a Billroth I anastomosis. Increased secretion of neutralizing juices and increased effect of duodenal inhibition as occurs with experimental gastroduodenostomies are most probably not clinically significant in instances of gastric resection where the lowered acidity does not permit duodenal inhibition to be activated.

3. A difference in intrinsic resistance to acid-peptic ulceration between the proximal duodenum and jejunum is another factor bearing on the rationale of the Billroth I anastomosis. This difference was evaluated in the dog and pig by exposing proximal duodenal and jejunal mucosa to an acid-peptic solution.

4. The pig duodenum is definitely more resistant to an acid-peptic solution than the jejunum. The difference between the dog duodenum and jejunum in this respect is minimal.

5. Brunner's glands are abundant in the pig duodenum, and secrete an abundant alkaline mucus which protects against acid-peptic ulceration. Brunner's glands are absent in the jejunum of the pig, which is therefore unprotected and ulcerated by acid-peptic action. Brunner's glands in the duodenum of the dog are present in only the proximal 1 to 1.5 cm. The remainder of the duodenum and jejunum do not possess the protective secretion of Brunner's glands, and therefore their resistance to acid-peptic ulceration is comparable.

6. Brunner's glands in the human duodenum are well developed, and extend as a continuous sheet to or beyond the ampulla of Vater. They are not present in the proximal jejunum. The proximal duodenum in human patients therefore possesses an intrinsic mechanism to resist acid-peptic ulceration which is absent in the jejunum.

CONCLUSIONS

1. On the basis of the comparative anatomy of Brunner's glands in dogs, pigs, and human beings, and on their secretion, the proximal duodenum of the human may intrinsically resist acid-peptic ulceration more than the proximal jejunum.

2. The Billroth I anastomosis may be superior to the Billroth II following a given gastric resection because: (a) More capacity for neutralizing gastric acid is present in the duodenum. (b) Gastroduodenostomy affords a more physiologic stimulation for secretion of protective and digestive juices. (c) The duodenum is better equipped to intrinsically resist acid-peptic ulceration on the basis of its Brunner's glands.

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