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THE NERVOUS AND HUMORAL CONTROL OF GASTRIC SECRETION*

BY

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It is a well-established fact that food substances, or the products of their digestion, when in contact with the pyloric mucous membrane cause a secretion of gastric juice. The mechanism by which the gastric glands are stimulated to secrete during the chemical phase is still a subject of controversy. The importance of the pyloric region as a receptive surface for chemical substances is shown in experiments by Sawitsch and Zeliony (1913), of the Pavlov school, on dogs with an isolated pyloric pouch and either a gastric fistula or a Pavlov pouch. The introduction of chemical substances such as meat extracts, peptone, and acetic acid into an isolated pyloric pouch produced a secretion of juice from the glands of the fundus and corpus.

The Russian investigators further demonstrated that mechanical stimulation of the pyloric region also causes the cells to secrete acid and pepsin. If, however, the body of the stomach and the pyloric region are separated surgically and chemical substances are then introduced into the main stomach through a fistula no gastric juice is secreted either by the pouch or by the stomach. One of the theories advanced to explain this phenomenon involves the liberation from the pyloric region of a special hormone, "gastric secretin," as suggested by Edkins in 1906, later referred to as "gastrin." Edkins's idea was based on the observation that extracts from the pyloric mucosa when injected into a vein stimulate the gastric glands to secrete, while similar extracts from the fundus and body of the stomach have no such effect. Edkins regarded the action of gastrin on the gastric glands as analogous to that of secretin on the pancreas.

Among more recent workers Gregory and Ivy (1941) confirmed the operation of a hormonal mechanism in initiating gastric secretion, although they consider that the pyloric region is not essential in eliciting secretion of a transplanted fundic pouch on perfusion of the main stomach with secretagogues. In later experiments, however, Grossman, Robertson, and Ivy (1948) found that distension of the pyloric portion of the stomach stimulates the secretion of hydrochloric acid by the fundic glands. This finding is regarded by these authors as conclusive evidence for the existence of a pyloric hormone for gastric secretion.

Vagus Stimulation

In our laboratory, under the leadership of Uvnäs, the problem of gastrin was approached from a quite different angle. Stimulating the vagi to the stomach under proper conditions initiates secretion of gastric juice, which proceeds at a fairly high rate so long as stimulation of the secretory nerves is continued. In such experiments Uvnäs (1942) observed that if the blood supply to the pyloric region was obstructed the response of the gastric glands to vagal stimulation was reduced or nearly abolished. This observation indicated that the pyloric region might be instrumental not only in the chemical phase but also in the nervous phase of gastric secretion. The part played by the pyloric region in the nervous phase of gastric secretion was examined in experiments of varying types, as follows (Uvnäs, 1942).

In anaesthetized cats the main blood supply to the pyloric region can easily be obstructed by ligating the pyloric branches of the hepatic artery. After ligation of the arterial supply to the pyloric region the secretion of watery acid juice during vagal stimulation decreases considerably and abruptly, from 37 to 8 ml. in a typical experiment; the juice also changes in character and becomes highly mucous and poor in hydrochloric acid.

I have already referred to experiments by Sawitsch and Zeliony, who obtained secretion from the gastric glands by introducing chemical substances into an isolated pyloric pouch. These workers also observed that after cocainization of the pyloric mucosa there is no secretion in the main stomach on chemical stimulation of the pyloric region. In a typical experiment of this type on cats (Uvnäs, 1942) the vagi were stimulated for sixty minutes, which yielded about 16 ml. of acid watery juice. The stimulation was discontinued and the pyloric mucosa was rubbed with a 2% solution of cocaine hydrochloride. After a resting period of forty-five minutes the vagi were again stimulated: during three and a half hours of maximal vagal stimulation only a few drops of mucus were secreted; not until approximately six hours after cocainization did the rate of secretion return to normal. Cocaine does not inhibit the secretory mechanism by paralysing the acid- and pepsin-secreting cells, because histamine injected slowly into a vein or given intramuscularly evoked secretion in cats after cocainization of the pyloric mucosa. Cocaine given intramuscularly in doses sufficient to paralyse the respiratory centres did not significantly diminish the secretory response to vagus stimulation if the pyloric region was left functionally intact.

Resection of Pyloric Region

In another series of experiments Uvnäs resected the pyloric region in cats and dogs. The resection included the distal part of the stomach from that closely proximal to

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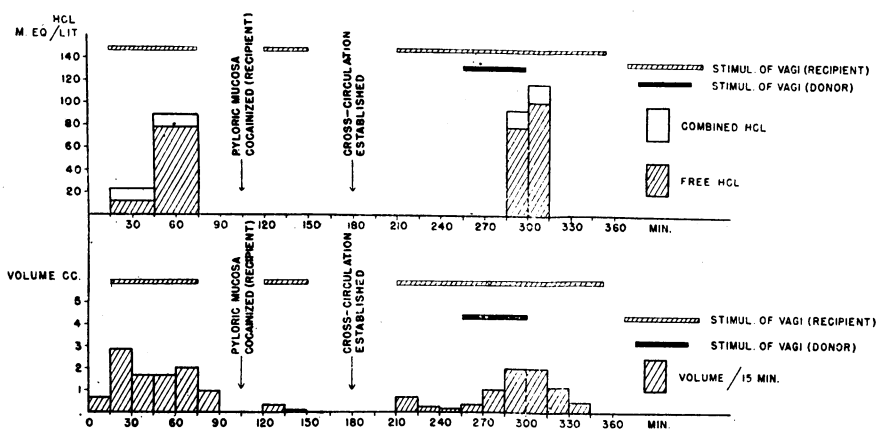
the incisura angularis to that just distal to the pylorus. In cats secretion decreases considerably after resection of the pyloric region. In dogs the effect of pyloric resection is still more striking. In one dog abundant secretion persisted during two hours of vagal stimulation. After resection of the pyloric region gastric secretion during vagal stimulation decreased to a negligible amount and the gastric juice completely changed character: the juice contained no free hydrochloric acid and was of a stringy mucous consistency.

All these experiments indicate that on stimulation of the secretory nerves to the stomach some active agent, or agents, is liberated in the pyloric region, and from here this agent is carried to the parietal cells. More direct evidence of a hormonal mechanism within the nervous phase of gastric secretion was obtained in cross-circulation experiments on cats (Uvnäs, 1942). The pyloric mucosa of the



Cats under chloralose. Pyloric region of the recipient functionally eliminated by cocaine. Cross-circulation experiment demonstrating the liberation of a hormone (gastrin) from the donor cat's pyloric region on stimulation of the vagi.

recipient was functionally eliminated by cocaine. The carotid artery of this cat was then anastomosed with the donor cat's coeliac artery, and the donor's superior mesenteric vein with the recipient's jugular vein. The portal vein and the hepatic artery of the donor cat were ligated. Since the superior mesenteric vein was ligated distally to the inflow of the gastro-splenic vein, the venous outflow from the donor's stomach and pyloric region was diverted to the recipient's jugular vein. Clotting was prevented by heparin. On stimulation of the recipient cat's vagi for forty-five minutes (see Chart) only a scanty flow of Congo-negative juice was secreted. If, however, the donor cat's vagi were also stimulated the stomach of the recipient started to secrete and free acid appeared in the juice. When stimulation of the donor's vagi was interrupted, gastric secretion ceased in the recipient cat even if its vagi were stimulated without interruption. Identical results were obtained in cross-circulation experiments where the pyloric region of the recipient cat was resected instead of being cocainized.

Production of Gastrin

These experiments suggest that, in cats, impulses from the brain, mediated by the vagi, cause the liberation in the pyloric mucosa of some agent which, carried by the blood stream, stimulates gastric glands to secrete acid juice. What is the nature of this secretory excitant and what physiological properties can be ascribed to this agent, which for the sake of simplicity we can refer to as gastrin? Ivy and his group (Sacks, Ivy, Burgess, and Vandolah, 1932) made a fresh attack on the gastrin problem in 1932. Using 80% acidified alcohol as a solvent they extracted from the pyloric mucosa of a hog an active agent which they identified chemically as histamine sulphate or picrate. These experiments were presented by Ivy and his co-workers as strong evidence that histamine may be a gastric secretory hormone liberated from the pyloric region and that histamine and gastrin are identical. I will come back to histamine, but will first turn to the work on gastrin carried out in Babkin's laboratory and in ours.

Komarov (1938a, b), in Montreal, approached the problem from a new angle, and so did Uvnäs and his group in Lund. Whereas their predecessors, like Ivy and his group, had extracted the non-protein substances from the pyloric mucosa, eliminating the protein fraction so far as possible, the Canadian and Swedish workers searched for gastrin under the assumption that it might chemically be related to secretin, which, as shown by Hammarsten and Ågren in Stockholm, is a protein-like body. Komarov in 1942, using several methods of extraction, obtained preparations from the pyloric mucosa which on intravenous injection stimulated gastric secretion both in anaesthetized and in unanaesthetized animals. Komarov's preparation contained no histamine.

In our laboratory Uvnäs (1943, 1944, 1948) and his group obtained a preparation of gastrin having a degree of purity which compares favourably with the best commercial preparations of secretin. The active principle is a protein-like water-soluble substance iso-electrically precipitated at a *p*H of about 4 to 5.5. Chemically, gastrin shows great similarities to secretin. Both substances are contained in the sodium chloride and the trichloracetic acid precipitates. They are alike in their solubility in some organic solvents and in their degree of stability in acid and alkaline solutions. But they differ in some other respects—e.g., in their solubility in ethyl alcohol.

Activity of Gastrin Preparations

The activity of gastrin preparations is assayed in our laboratory on cats anaesthetized with a mixture of chloralose and urethane. Comparisons are made on the following standard: the activity of the extracts is measured as the quantity of gastric juice secreted in the hour following the beginning of the injection, which is made in the iliac vein at a rate of 0.4 ml. per minute for thirty minutes. One secretory unit of gastrin is the quantity which produces a secretion of 1 ml. of acid juice per hour in a cat weighing 2–3 kg. (Gastrin, like secretin, is effective only when injected direct into the blood stream; intramuscular injections induce a very scanty secretion.) Purified preparations of gastrin do not contain histamine in detectable amounts.

On intravenous injection of gastrin, secretion usually begins in about five minutes, gradually increases for five to ten minutes, and then proceeds at a more or less constant rate. When injection is interrupted, secretion continues for ten to fifteen minutes at maximal rate, then gradually declines and reaches the basic level approximately thirty minutes after the end of injection.

Table I (Uvnäs, Munch-Petersen, and Rönnow, 1944) illustrates the activity of the preparations during the different stages of purification. Crude preparations from the pyloric mucosa of pigs obtained by precipitation of hydrochloric acid extracts with 20% sodium chloride contain one secretory unit in 45 mg., whereas with the purest

TABLE I.—*Gastric and Pancreatic Secretion after Intravenous Administration of Crude, Alcohol-washed, or Purified Substances from the Pyloric Mucosa of Cats and Pigs*

Active Material Stage of Purification	mg.	Gastric Secretion	Pancreatic Secretion
A. A crude trichloracetic acid precipitate from cat	75	12 ml.	11 drops
The trichloracetic acid precipitate from the above washed with 80% acid alcohol	65	10 ml.	0
B. A preparation from pig precipitated with 20% NaCl and 10% trichloracetic acid	50	9 ml.	5 drops
A preparation from pig precipitated with 20% NaCl and washed with 80% acid alcohol	40	7·5 ml.	0
A preparation from pig purified by the tannic acid method	40	14 ml.	0
Secretin	5	0	41 drops

preparations one secretory unit is contained in 2.3 and 2 mg. respectively. Comparison with the activity of a commercial preparation of secretin, "pancreotest," considered to be of a high degree of purity, showed that at least 3 to 5 mg. of this preparation must be introduced into a vein of a cat to produce a definite pancreatic secretion.

The gastric juice secreted on injection of purified preparations of gastrin was always strongly acid, the total acidity usually exceeding 150 milliequivalents per litre. The peptic power of the juice declined to a very low level during the course of the secretion, indicating that gastrin activates only the parietal cells.

Crude preparations of gastrin were sometimes contaminated by secretin or some other agent which stimulated pancreatic secretion. The pancreatic excitant can be removed by washing with 80% ethyl alcohol.

As judged by present experimental evidence gastrin selectively stimulates the parietal cells. Salivary, pancreatic, peptic, or bile secretion, gastric motility, blood sugar, and blood pressure are not influenced by intravenous injection of doses which evoke a copious secretion of gastric juice. These observations indicate a specificity of gastrin as pronounced as that of secretin, which selectively activates pancreatic glands, causing the secretion of a sodium bicarbonate solution of low enzyme content.

In cats, dogs, and pigs the active agent, here referred to as gastrin, is predominantly present in the pyloric mucosa The confinement of the stimulating agent to the pyloric region in these animals, together with experimental evidence that the humoral mechanism of gastric secretion is chiefly related to this region, indicates that the active agent of pyloric extracts is identical with the gastric hormone, the existence of which was postulated by Edkins forty years ago.

When we discussed these problems with colleagues experienced in human gastric surgery we encountered useful criticism. We have been told that, in patients in whom the pyloric region has been removed in cases of peptic ulcer, acid gastric secretion is at a very low ebb for a couple of weeks or possibly months after the resection but that secretion then gradually returns to approximately normal. Komarov (1942) reports that a gastric secretory agent can be extracted from the duodenal mucosa of pigs. It was of course of special interest to study also in man the distribution of gastrin in the stomach and duodenum. For these experiments resected portions of stomachs from operated patients were transferred to the laboratory without delay. Post-mortem material was obtained within ten to thirty-six hours of death. The gastric mucosa was divided into three parts—the pyloric, the boundary, and the corpus regions. Table II (Uvnäs, 1945) gives the rate of secretion observed in cats on injecting extracts from the three different mucosal regions of human stomachs. So far only a small amount of surgical material has been

TABLE II.—*Rate of Excretion Observed in Cats on Injecting Extracts from Three Mucosal Regions of Human Stomachs*

No.	Case	Age	Sex	Mucosal Region: Pyloric Mucosa		Boundary Zone Mucosa		Corpus Mucosa		Final Precipitant
				Mucosa (wet) (g.)	Secretion (ml.)	Mucosa (wet) (g.)	Secretion (ml.)	Mucosa (wet) (g.)	Secretion (ml.)	
M4	Duodenal ulcer ..	33	M	12	6·8	—	—	11	1·4	Tr. ac
M6	,, ,, ..	36	F	10	16·1	21·5	1·2	10		Tr. ac
M7	,, ,, ..	55	F	12	4·0	9	2·1	13·5	0	Tr. ac.
M9	,, ,, ..	25	M	7	17·0	4	5·1	8	0	Tr. ac.
M8	Gastric ,, ..	55	M	10	6·5	—	—	19	0	Tr. ac.
M23	,, ,, ..	52	M	2	1·8	2	3·3	2	0	Ta. ac.
M26	,, ,, ..	35	F	3	10·2	—	—	3	0	Ta. ac.
M27	,, ,, ..	23	M	3	3·0	—	—	3	1·3	Ta. ac.
M29	,, ,, ..	45	M	—	—	3	9·2	3	0	Ta. ac.
M18	Malignant gastric ulcer	46	M	3	11·2	3	0	3	0	Ta. ac.
M19	Gastric carcinoma	75	M	3	3·0	6	0	—	—	Ta. ac.
M10	,, ,,	52	M	12	0	8	0	—	—	Tr. ac.

Tr. ac. = trichloracetic acid. Ta. ac. = tannic acid.

examined, but it definitely shows that the human gastric mucosa contains a gastric secretory agent. The observations are too few to permit definite conclusions about the distribution of the secretory principle, but they suggest that in man also the agent is chiefly if not entirely localized in the pyloric mucosa.

In man gastrin could also be extracted from the duodenal mucosa (Uvnäs, 1945). Of fifteen duodenal preparations from human cadavers six preparations were active, whereas nine were inactive. However, when we consider that gastrin is rapidly destroyed by trypsin it is surprising that the agent could be detected in such a large proportion of the examined material. The presence of gastrin in the duodenal mucosa of man might be a hint that the so-called intestinal phase of gastrin secretion, in line with the nervous and chemical phases, is controlled by a hormone, related to or identical with gastrin. Harper (1946) has reported that gastrin can be extracted from the mucosa of the hog's pyloric region and also from the upper part of the small intestine.

A Pepsin-stimulating Agent

As I have already mentioned, purified gastrin does not stimulate the secretion of pepsin. If the pepsin present in the resting glands is washed out by a prolonged injection of histamine, which in itself does not stimulate peptic secretion, it can easily be demonstrated that gastrin given intravenously does not increase the peptic activity of the gastric juice, whereas subsequent vagal stimulation greatly increases the output of pepsin.

Sawitsch and Zeliony claimed that mechanical stimulation of the mucosa of an isolated pyloric pouch causes an increased secretion of pepsin in the main stomach. Pavlov showed that in dogs the peptic activity of the gastric juice varies with the composition of the food. All these facts suggest the existence of a humoral mechanism instrumental in the control of peptic secretion. Crude pyloric preparations, precipitated from acid mucosal extracts by trichloracetic acid, contain an agent which on intravenous injection augments the output of pepsin (Uvnäs, 1948). These experiments are incomplete, but they indicate the presence in the pyloric mucosa of an agent which stimulates the peptic cells.

Harper and Raper (1943), of Manchester, report that they have extracted from the duodenal mucosa a principle of protein nature which selectively activates the enzyme-producing pancreatic cells. This principle, called "pancreozymin" by them, they consider to be an ally of secretin

in the humoral control of pancreatic secretion. Further experiments will elucidate to what extent the pepsin-cell stimulating agent from the pyloric region is complementary to gastrin in the humoral control of gastric secretion.

Histamine

Where does histamine come into this picture? What functions, if any, can be ascribed to histamine in the control of gastric secretion? I have already mentioned that Ivy and his co-workers extracted histamine from the pyloric mucosa and identified it chemically in 1932. Influenced by this result some authors were inclined to classify histamine as a hormone liberated in the pyloric region and carried by the blood stream to the glands in the main stomach. However, Gavin, McHenry, and Wilson (1933) demonstrated that the fundic mucosa contained more histamine than the pyloric, only 20% of the total histamine extracted from the mucosa of the stomach being derived from the pyloric region. Under the impression that gastrin might be identical with histamine these authors felt that their result did not support Edkins's statements.

To my knowledge no experiments have been published demonstrating or even indicating the liberation from the pyloric region of excess histamine into the blood during the nervous or chemical phases of gastric secretion. Actually, it would seem rather unwise of Nature to resort for this purpose to a substance which in concentrations in the blood plasma sufficient to stimulate gastric secretion would produce a variety of other effects, such as general vasodilatation, increase in capillary permeability, contraction of smooth muscle, and, in hypersensitive persons, even headache. Obviously the role of histamine in stimulating gastric secretion cannot be that of a hormone carried in the blood stream to all parts of the body.

Histamine no doubt possesses admirable potentialities as a physiological excitant of acid gastric secretion. However, its mode of action on the parietal cells must be other than that of a blood-carried hormone. In cats and dogs histamine is contained in large amounts in the gastric mucosa, in concentrations approximately 1,000 times higher than in the blood plasma. Histaminase, a diamine oxidase present in the intestinal mucosa, is absent in gastric mucosa, as demonstrated *in vitro* by Best and McHenry (1930). This fact should not be stressed too strongly in favour of histamine as a gastric excitant, because it was demonstrated in our laboratory that in living tissues histamine is inactivated at a very much higher rate than *in vitro*. We have obtained evidence that *in vivo* histamine is destroyed rapidly by the lymph and in the interstitial spaces (Carlsten, Kahlson, and Wicksell, in press).

MacIntosh (1938), using the Bärsoum–Gaddum method of extraction and testing on the ileum of the guinea-pig, demonstrated in dogs that the gastric juice obtained by sham-feeding or by vagal stimulation contained a substance with the properties of histamine. We injected the gastrin obtained by Uvnäs into the blood stream of a cat and tested the gastric juice for its content of histamine. The juice contained histamine in a physiologically active form. At that time we thought that the histamine in the plasma and gastric mucosa was present in an inactive form, and that the function of gastrin might be to liberate, in the surroundings of the parietal cells, histamine in an active state and in concentrations sufficient to stimulate the acid-secreting cells (Emmelin and Kahlson, 1944). Babkin (1944) and MacIntosh (1938) have already presented a hypothesis that vagal impulses may be transmitted to the parietal cells not directly by acetylcholine but by histamine liberated locally by acetylcholine under the influence of the vagus nerves.

Histamine Concentration of Gastric Juice

Since in our experiments the gastric juice secreted in response to injection of gastrin contained free histamine it seemed worth while to examine the histamine concentration of gastric juice secreted as a response to a variety of stimuli. From dogs with an oesophageal fistula for sham-feeding and with a gastric pouch we collected juice during the nervous and chemical phases of gastric secretion. In both phases the histamine concentration of the juice was approximately the same. Spontaneously secreted gastric juice and juice obtained on vagus stimulation, on the injection of "priscol," and on injection of acetylcholine in the lateral cerebral ventricle all contained histamine in a physiologically active form. It is striking that the histamine concentration of the juice is rather independent of the nature of the stimulus employed to activate the parietal cells. It is also striking that the histamine concentration of the gastric juice is of the same order as in blood plasma.

The parietal cells are permeable to histamine. If the histamine concentration in the plasma is raised by prolonged intravenous injection of histamine this substance appears in the juice in higher concentrations than with physiological stimuli (Emmelin and Kahlson, 1944).

I am fully aware that these experiments do not prove that histamine is actually liberated in the mucosa under the influence of gastrin or other stimuli. Emmelin and I have spent a lot of time examining the histamine concentration in the venous plasma emerging from the stomach before and during stimulation of the parietal cells. We obtained no definite evidence of excess histamine in the venous plasma from the stomach during activity of the parietal cells. This obviously does not disprove the idea that histamine is locally engaged as an excitant, since histamine may be liberated in very close proximity to the parietal cells without diffusing in detectable amounts into the blood capillaries, or the liberated histamine may be destroyed before it reaches the absorbing blood vessels. It may be appropriate here to recall that we still lack generally accepted evidence of a liberation of histamine in any type of physiological reaction. With anaphylaxis and animal poisons, so far as histamine is concerned, the situation certainly is clearer (Gaddum, 1948). Unfortunately we know of no substance which inhibits the factors responsible for the destruction of histamine in the different tissues, and we know of no substance which specifically antagonizes the effect of histamine on the parietal cells. Those engaged in this field of endeavour, however, will remain confident that Nature has not embedded the parietal cells in copious quantities of the most potent gastric excitant so far known just to seep through the secreting cells to deceive physiologists.

Conclusion

If tentatively we try to link together the pattern of facts as they are seen so far, the contours above the horizon of unjustified speculation are as follows: Gastrin is contained in the pyloric mucosa, and in man and pigs in the duodenum as well. This agent is liberated by vagus impulses or when chemical substances such as food come into contact with the mucosal regions concerned. The liberated gastrin is carried by the blood to the fundic mucosa, where it causes some change so that histamine is liberated in quantities sufficient to stimulate the parietal cells. In this picture gastrin enters as a common factor in the nervous, gastric, and intestinal phases of acid gastric secretion.

Obviously much work remains to be done before this view can be accepted even by those who are suggesting it as a working hypothesis.

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RESULTS OF PARTIAL GASTRECTOMY FOR PEPTIC ULCER

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An attempt is here made to assess the merits of four types of anastomosis used in partial gastrectomy. The operations were performed for chronic gastric and duodenal ulcer during the six years ending Dec. 31, 1946. We have excluded all cases of carcinoma, those cases of peptic ulcer in which a previous operation other than suture of a perforation had been performed, emergency gastrectomies for haemorrhage, and a few operations in which the pylorus was not removed but was excluded. The series consists of 248 patients, and in reviewing the results we have paid particular attention to (*a*) the immediate post-operative course, with special reference to complications due to the type of anastomosis, and (*b*) the functional results. These have been divided into good, fair, and poor. The result is good if the patient is satisfied with the operation and admits to no significant side-effects. It is fair if the patient is satisfied with the operation but is found to have modified his diet or eating habits to avoid unpleasant symptoms. It is classified as poor when the patient is dissatisfied with the operation or when we have considered the functional result to be unsatisfactory.

The length of time since the operation ranges from one to six years, the average period being thirty-seven months. Fifteen patients have not been traced. The last known residence of eleven of these has been visited, but they had left the district and all attempts at follow-up have failed. Visits were not paid to the residences of the other four, as two were known to have left the country and two lived a long distance away.

The following four types of anastomosis were used: Type I: An end-to-side anastomosis with an antecolic proximal loop attached to the greater curve (Fig. 1). Type II: An end-to-side anastomosis with a long antecolic proximal loop attached to the lesser curve with a valve and a small stoma (Fig. 2). Type III: An end-to-side anastomosis with a short post-colic proximal loop attached to the lesser curve with a small valve and a small stoma (Fig. 3). Type IV: An end-to-end anastomosis of the Billroth I type, joining the duodenum to the greater curvature of the stomach (Fig. 4).

Type I: Antecolic Anastomosis

Average period since operation .. .. 61 months
Number of operations 45
Operative mortality .. .. 1 (duodenal ulcer)
Cause of death: Bronchopneumonia.
Traced 41
Good .. .. .. 18 (8 duodenal, 10 gastric)
Fair .. .. .. 18 (4 „ 14 „)
Poor .. .. .. 2 (1 „ 1 „)
Since died .. .. .. 3 (1 „ 2 „)
Causes of death: bomb injury (gastric), cardiac failure (duodenal), torsion of caecum (gastric).
Untraced .. .. 3 (1 duodenal, 2 gastric)
Male, duodenal ulcer. Very fit 4 months after operation. Changed address.
Male, gastric ulcer. Good 3 months after operation: changed address.
Female, gastric ulcer, changed address.

Post-operative Period.—The operation seemed to be safe and satisfactory. The only objection was that the stomach remnant was slow to begin emptying into the efferent loop. Accordingly a nasal suction tube was left *in situ* for several days until the stomach contents began to pass through into the efferent loop.

Late Function.—This operation is not really satisfactory. Many writers, including Ogilvie (1947), have pointed out that an anastomosis of this type leads to proximal-loop filling in many cases and consequent postcibal distress. Investigations show that proximal-loop reflux is present in most of the patients in this group. The barium meal can be seen to pass through the stomach remnant straight into the proximal loop; this contracts and gradually pumps its contents back through the stomach into the distal loop. In spite of the high incidence of proximal-loop reflux the results are quite good some years after operation. Most patients complain of side-effects for some months after the operation. Eighteen now claim to have a very good digestion. Eighteen are classed as fair: as a group these eighteen are very pleased with the operation and are living a reasonably normal life, but most of them like to rest for a period of half to one hour after their principal meal, and find that certain articles of diet, especially fats and fried food, should be taken with care. The results in the following two cases are poor:

Case 1.—A man, aged 35 at operation in 1942, had severe postcibal distress, including nausea and occasional vomits. In 1944 he was investigated at another hospital, and his troubles were attributed to proximal-loop reflux. Laparotomy showed no other abnormality, and an entero-enterostomy was performed. The patient says that he has had little relief from this operation.

Case 2.—A man, aged 44 at operation in 1943, has complained ever since of nausea and distension after meals. A barium meal shows considerable proximal-loop reflux but no other abnormality. He has worked continuously since operation and has maintained his weight, but the functional result is a poor one.

Although most patients are well satisfied, this anastomosis does not give first-class results. We suggest two reasons for this unexpected contentment with an operation which has given so high an incidence of proximal-loop reflux:

(1) All these patients were operated on at a time when only those with very large penetrating ulcers were recommended for surgery. The more severe the pre-operative symptoms the more tolerant is the patient of a moderate post-operative function. (2) All these operations were performed at least five years ago. The symptoms attributable to proximal-loop reflux become less severe with the passage of time.

We note that Watson (1947) has often used this anastomosis and has seldom detected proximal-loop reflux, but it