VAGOTOMY & DRAINAGE FOR DUODENAL ULCER - AN EVALUATION & COMPARISON

With special reference to the use of gastric acid secretion as a basis for selection of surgical procedure

A THESIS SUBMITTED TO THE
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M a r c h 1 9 7 2

TO OUR PATIENTS

MAY OUR ENDEAVOURS BE OF BENEFIT TO THEM

TO MY TEACHERS

TO PAM & CHRISTOPHER

PREFACE

The early and late results of elective surgery for duodenal ulceration have been published from many eminent surgical and gastrointestinal centres in the world. There is not always complete agreement in these studies on the ultimate results, and regional differences in population structure may be important in this regard. In addition, there are relatively few five year studies available in the literature, and of late acid secretory studies in the selection of one or other surgical procedure have fallen into disrepute. One might cautiously claim that the present surgical approach to duodenal ulceration is somewhat confused.

It therefore seemed timely to have a "second look" at the results in general and in particular the results at Groote Schuur Hospital, and in the local population of Cape Town.

Cape Town was and is committed to pre- and postoperative acid secretory studies and is perhaps one of the few centres today with a wealth of past and present acid secretory data. This has thus logically formed a large section of my thesis, particularly with regard to a re-evaluation of acid studies in the selection of operative procedures.

It must be emphasised that a retrospective study of this nature cannot hope to compete with a prospective one. In addition, logistic difficulties in South Africa render the near complete patient return as reported from Europe and America almost impossible. However, I hope that the data collected will be of value in the planning of a controlled prospective study.

ACKNOWLEDGEMENTS

The eventual production of a series of results of this nature requires a tremendous amount of work, and this would have been impossible to accomplish without the immeasurable assistance that has been provided by so many people in such a wide variety of ways. To all concerned I would like to express my profound gratitude.

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To my wife and family must go the credit of providing a major proportion of the motivation to successfully complete this work, and I thank them for their interest and encouragement.

Finally, Dr. J.G. Burger, Medical Superintendent of Groote Schuur Hospital, receives my grateful appreciation for allowing me free access to the hospital records.

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P A R T I

INTRODUCTION & REVIEW

CHAPTER 1

APPLIED ANATOMY & PHYSIOLOGY OF THE STOMACH

I INTRODUCTION

The clinico-pathological entity of duodenal ulceration was only recognised in the early 19th century, when Abercrombie[1] described the pathology, complications and clinical features of this disease. The incidence was probably very low at the time and it was not often entertained as a preoperative or antemortem diagnosis. The first major articles appeared[1] in 1893, and interest has gathered momentum over the years. One is today overwhelmed by the battery of literature on the subject of what has now become a common disease, with considerable morbidity.

In 1910 Swartz[1] coined the dictum "no acid - no ulcer" and this has stood the test of time. Peptic ulceration has never been recorded in patients with gastric pH. persistently above 6 after maximal stimulation. In addition, the gastric proteolytic enzyme, pepsin, must be present in association with acid in order for duodenal or jejunal ulceration to occur, and this is secreted as the inactive precursor pepsinogen. Activation occurs in an acid medium (optimum $pH._2$) and at akaline levels peptic activity ceases (pH. 4.5 to 5.5).

Treatment of duodenal ulcer is therefore aimed at reducing the ulcer aggressive factors, acid and pepsin, or increasing the defence mechanisms, mucus and mucosal resistence. To date, there are no known universally effective methods of aiding the defence mechanisms so that in practice, the treatment of duodenal ulcer is directed at reducing the acid-pepsin component of the equation. The value of medical therapy in this regard is well known, but surgical correction is often desirable in patients with advanced disease or complications. Current surgical treatment utilises three main methods of combating the acid-pepsin mechanisms, namely:

(1) Vagus nerve section (vagotomy) accompanied by a "drainage" procedure to obviate side effects.

(2) Resection of a substantial part of the acid bearing area of the stomach as well as the gastrin-producing area (partial gastrectomy).

(3) Vagotomy plus resection of the gastric antrum (gastrin-producing area) thus attempting to remove the major physiological stimuli to acid production.

The search for an ideal operation continues unabated. Sleeve and tube resections, Finsterer operations and mucosal ablation, invagination procedures and the like have fallen by the wayside,

while highly selective vagotomy of the parietal cell area without a drainage procedure is at present being suggested.

AIMS OF STUDY:

(a) To compare the effectiveness of vagotomy and drainage, vagotomy and antrectomy and gastrectomy with regard to the incidence of recurrent ulceration.

(b) To compare the operations in regard to post-operative sequelae other than the recurrent ulcer rate.

(c) To evaluate the effect of the three operations on gastric acid secretion.

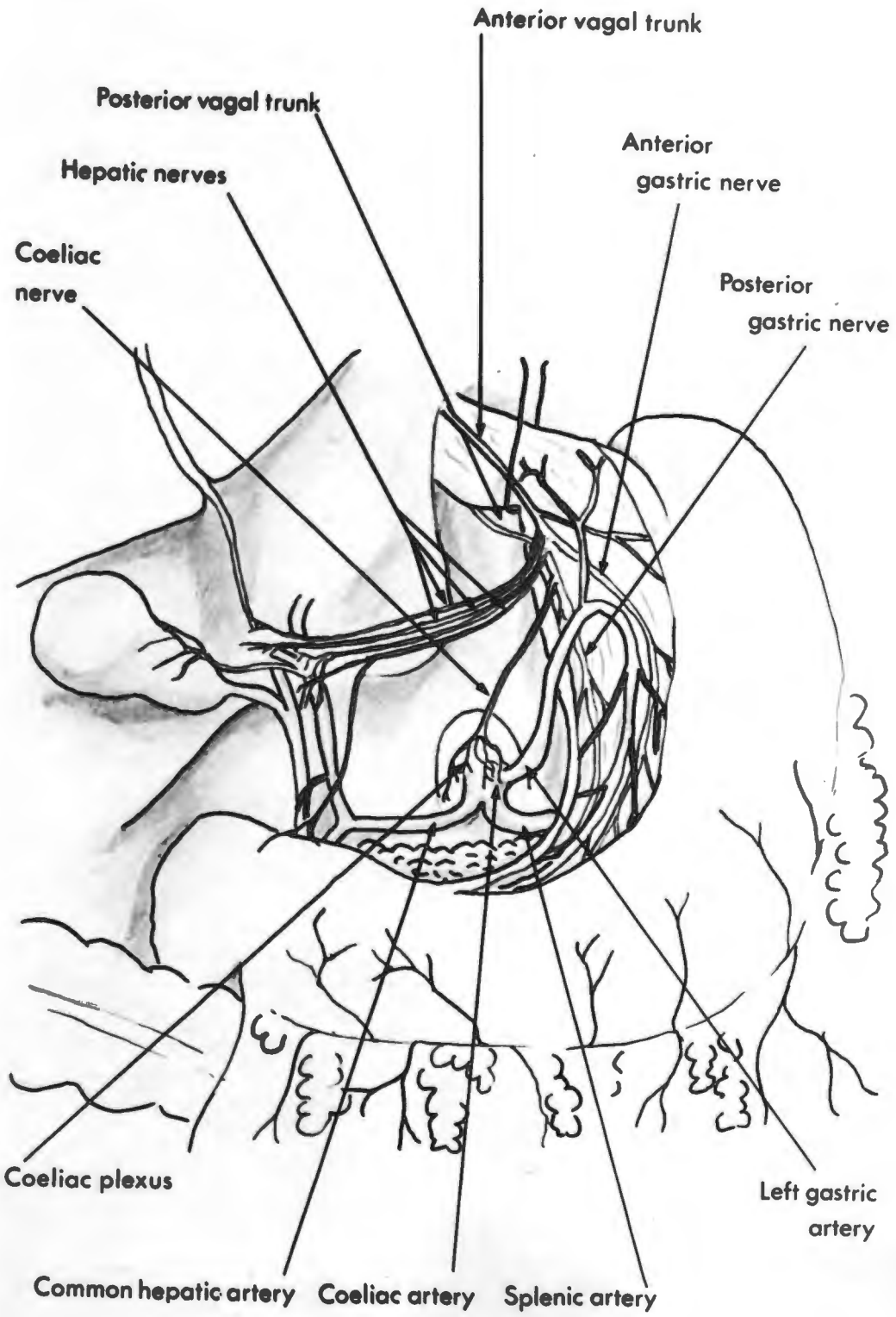
(d) To evaluate the completeness of vagotomy in the vagotomy and drainage and vagotomy and antrectomy groups.

(e) To assess whether preoperative measurement of gastric acid secretion has any part to play on the selection of the type of operation.

II APPLIED ANATOMY

A brief outline of the anatomy of the vagal innervation of the stomach, and the gross physiological anatomy of the stomach applicable to surgical concepts, and relevant to the discussion, will be presented:

FIG.1 ANATOMY OF THE VAGUS NERVE



(a) VAGUS

The vagus nerves are the sole source of parasympathetic supply to the foregut and midgut in man[2]. Left and right main nerve trunks, as they exist in the cervical and upper mediastinal regions, are distributed to the abdominal viscera via three constant components. These are the oesophageal plexus, the two main trunks and the four truncal divisions (Fig.1).

Three or usually four branches from each main nerve form the oesophageal plexus below the lung roots, but the complexity of this varies in each individual case. In spite of the variability in the plexus, the branches always ultimately unite to form two vagal trunks, one anterior and the other posterior to the oesophagus. The four truncal divisions, namely the hepatic, coeliac and anterior and posterior gastric nerves arise from these main trunks.

There is no embryologic or anatomic relationship of the vagus to the diaphragm and therefore the nerve may pass through the hiatus as the oesophageal plexus, the main trunks or as the truncal divisions. Ruckley et al.[3] reported on vagal anatomy at the level of the hiatus in a series of one hundred consecutive cases and found that 33% had more than one anterior trunk which usually united at the cardia (91% of

cases). Only 5% had multiple posterior trunks and in 47% small additional nerves were present on the distal oesophagus.

By the time the main abdominal nerve trunks have formed there is complete admixture of fibres from the original right and left nerves, which are diffusely distributed throughout the stomach. However, the anterior gastric division from the anterior trunk supplies only the anterior wall of the stomach while the identical set of circumstances apply to the posterior gastric division. The anterior and posterior gastric divisions continue along the lesser curvature beneath the anterior and posterior layers of the lesser omentum as the greater anterior and posterior gastric nerves. Terminal branches of the latter innervate the stomach from cardia to pylorus, and each of these branches supplies only its localised segment of stomach (4).

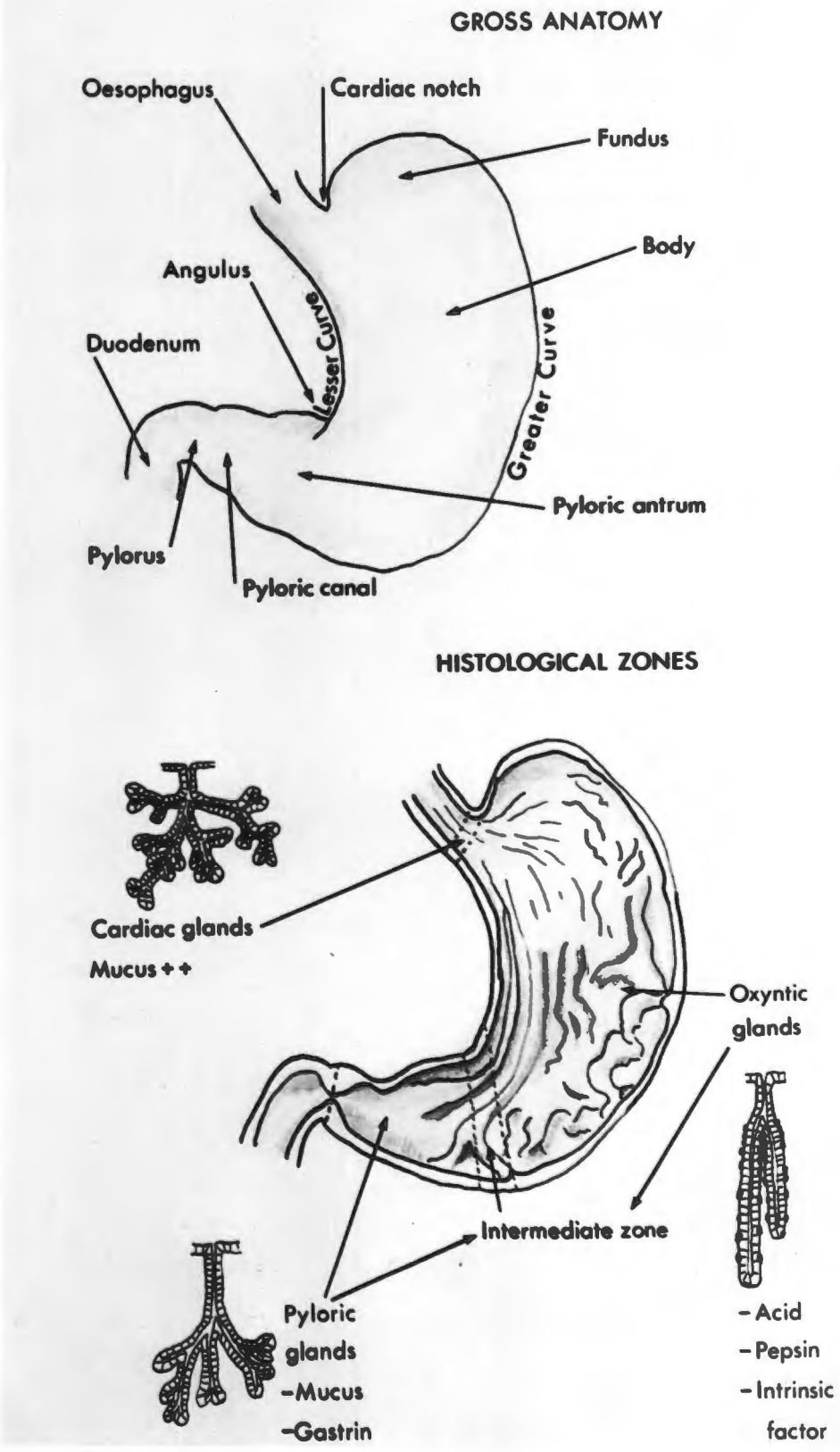
The hepatic and coeliac divisions innervate the midgut structures. The former consists of a collection of fibres running within the lesser omentum just below the liver to the hepatic plexus, which constitutes an autonomic plexus surrounding bile ducts and hepatic arteries (218). Identified as a single bundle in 35%

of cases the hepatic branch is seen to run as slightly separated multiple branches in 38% and widely separated (by more than one centimetre) in 28% of patients[3]. When the main anterior trunks are multiple and separate each one usually gives rise to hepatic branches. A large accessory hepatic artery, branching from the left gastric artery may accompany the nerves in their course.

From the hepatic plexus some fibres ascend into the liver, while others descend via the right gastric and gastroduodenal arteries to the extrahepatic biliary tree, distal antrum, pylorus, duodenum and head of pancreas[5-10, 218]. The function of hepatic branches to distal antrum and pylorus remain unknown but Burge [11] has demonstrated contraction of the pylorus and duodenum when these are electrically stimulated. There is no apparent secretory response to stimulation of these fibres.

Best regarded as the continuation of the posterior vagus, the coeliac is the largest of the truncal divisions. The nerve descends within the gastro-pancreatic peritoneal fold to reach the coeliac and superior mesenteric autonomic plexuses. In association with postganglionic sympathetic fibres, preganglionic coeliac vagal fibres innervate pancreas, bowel as far as distal transverse colon and possibly the biliary

FIG. 2 THE STOMACH



tract[12] via the superior mesenteric artery. No evidence exists that suggests gastric innervation via the coeliac nerve.

(b) STOMACH

The stomach is divided roughly into various regions, namely the cardia, fundus, body (parietal cell area), pyloric antrum (pyloric gland area) and pyloric canal. Fairly accurate macroscopic delineation can only be made of the pylorus and fundus however. Histologically distinct zones are the cardia (1 - 2 cm. wide); the fundus and body, which are identical; and the pyloric antrum. There is a narrow intermediate zone between the latter two areas (transitional zone)[13] (Fig.2).

Columnar mucus-secreting cells line the entire mucosal surface (surface cells) and enter and line the glands of all regions. Cardiac glands[14] have short ducts into which open tortuous branching tubular glands. These are simple mucus-secreting glands.

Oxyntic glands occupy approximately four fifths of the area of the gastric mucosa, from the cardia down to the transitional zone[15]. Between three and seven of these long tubular glands open into a single

duct. The lining is composed of four different cell types. Mucus-secreting (neck) cells line the isthmus of the gland, while in direct continuity with these, chief cells form the rest of the lining, and secrete pepsinogen.

Parietal (oxyntic) cells, so called due to the position they occupy on histology, are the source of hydrochloric acid[16]. These cells are numerous in the neck and isthmus of oxyntic glands.

Pyloric glands form a tightly coiled mass in the mucosa and open into long ducts[14,17]. Similar to cardiac glands, they are lined by mucus neck cells. The hormone gastrin[18] is secreted here as well as a small amount of pepsinogen[19].

A few argentaffin cells are found scattered throughout the glands of the gastric mucosa but their function remains uncertain[20].

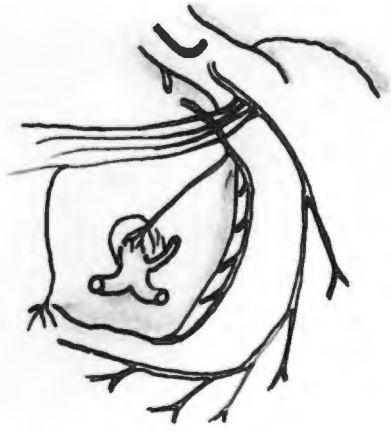
(c) THE PARIETAL CELL MASS

For a number of parenterally administered stimuli, after a certain dose level, the rate of gastric acid secretion does not increase as the dose increases. This is termed the "maximal response" for that stimulus.

By measurement of the surface area and thickness of the mucosa, and counting the number of parietal cells per unit field in histological sections of gastric mucosa, an accurate estimate of the number of parietal cells in the stomach can be made. Card and Marks[21] were the first to establish a correlation between the maximal histamine response and the parietal cell mass. The maximal histamine response of patients undergoing partial gastrectomy was measured before and after operation. After estimating the number of parietal cells in the resected portion they were able to discern a correlation between the number of parietal cells and the output of acid. A linear relationship, such that 10^9 parietal cells corresponded to a maximal secretory rate of 20 mEq./Hr. was shown.

Marks et al.[22] repeatedly ascertained the maximal histamine response in dogs with gastric fistula. Total gastrectomies were done and the total number of parietal cells were estimated. The line was again found to have a linear relationship, with the identical result i.e. 10^9 parietal cells corresponded to a maximal histamine response of 20 mEq./Hr.

FIG. 3 TYPES OF VAGOTOMY

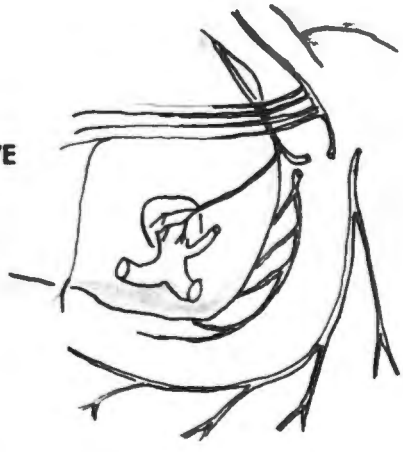


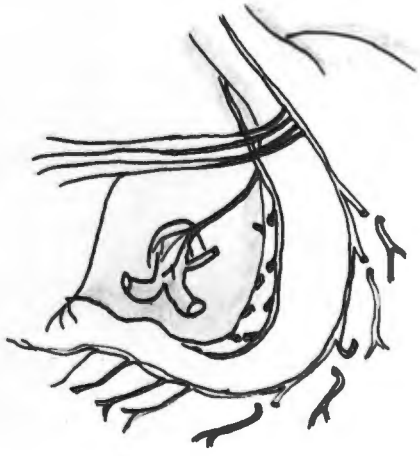
1. TRUNKAL

Main abdominal vagal trunks transected at or just below the level of the oesophageal hiatus

2. ANTERIOR & POSTERIOR SELECTIVE

Anterior & posterior gastric nerves sectioned at their origins leaving hepatic & coeliac branches intact





3. HIGHLY SELECTIVE

Only branches of the anterior & posterior gastric nerves, which supply the parietal cell mass, are sectioned leaving antral innervation intact

Although histamine is found in high concentrations in all tissues of the body, and is also a powerful stimulus to acid secretion, the evidence for this being the final common mediator is inconclusive and conflicting[23,24].

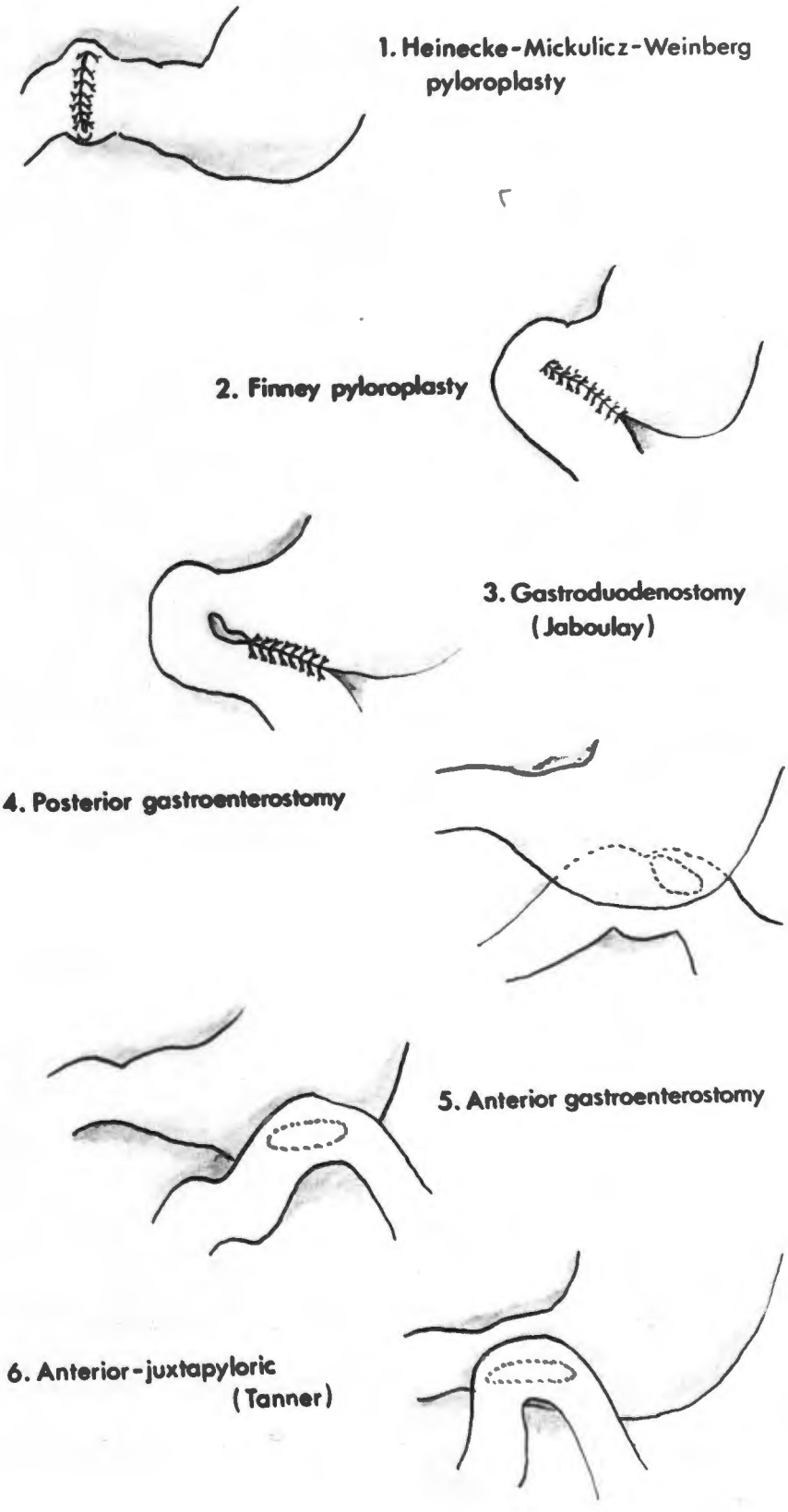
(d) OUTLINE OF OPERATIONS UNDER DISCUSSION

Detailed description of surgical technique is beyond the scope of this work, but the various types of vagotomy referred to in the following discussions are diagramatically illustrated in Figure 3.

Truncal (total) vagotomy involves section of the major nerve trunks, both anterior and posterior, as they enter the abdominal cavity via the oesophageal hiatus.

Selective vagotomy may be subdivided into anterior selective and posterior truncal; posterior selective and anterior truncal; or anterior and posterior selective. In the anterior selective procedure, the hepatic branch is left intact and only the anterior gastric nerve is sectioned at its origin from the main trunk. Posterior selective vagotomy involves division of only the posterior gastric nerve at its origin from the main vagal trunk while the coeliac branch is left intact.

FIG. 4 CURRENTLY PRACTISED DRAINAGE PROCEDURES



Unless otherwise specified the anterior and posterior selective procedure is the one referred to whenever "selective vagotomy" is mentioned.

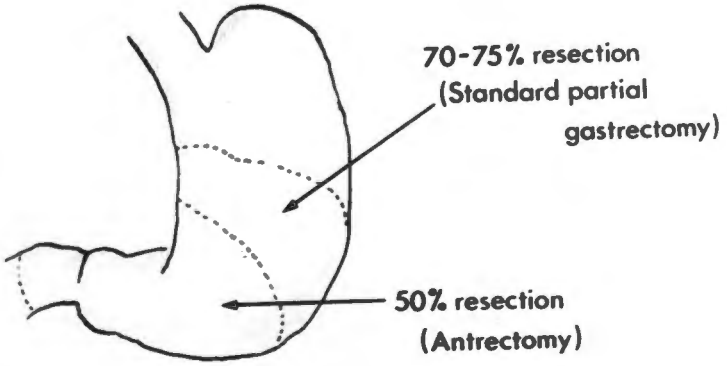
The most recent development, as yet experimental and currently the subject of limited clinical trials is the practice of highly selective (superselective; parietal cell) vagotomy. In this operation the main trunks of the gastric nerves are left intact while the branches supplying the parietal cells are selectively sectioned, leaving the nerve supply to the antrum intact. Accurate delineation of the antrum is effected by instillation into the stomach of the dye Congo red, which is only taken up by the acid secreting parietal cell area.

Drainage procedures, unless otherwise specified are either gastroenterostomy, or pyloroplasty of the Heinecke-Mickulicz-Weinberg type (Fig.4).

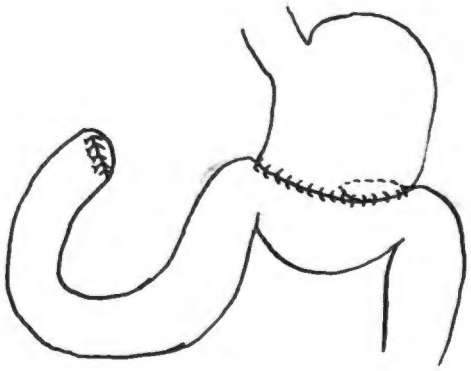
Antrectomy, always associated with some form of vagotomy, refers to hemigastrectomy (i.e. 50% resection).

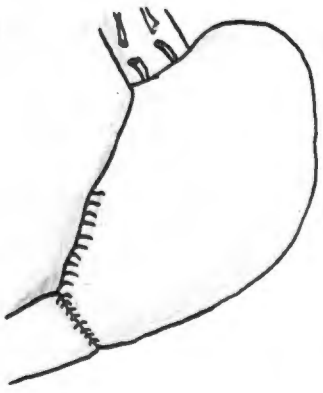
Partial gastrectomy involves a 70 percent, or more, resection of the stomach, without deliberate vagisection. After antrectomy, reconstruction is usually of the Billroth II (Polya) type, but some surgeons, where technically feasible, use the Billroth

FIG. 5 CURRENTLY PRACTISED GASTRIC RESECTION PROCEDURES FOR DUODENAL ULCER



Billroth II type reconstruction — universally practised after standard 70-75/ partial gastrectomy





Billroth I type reconstruction — only used after antrectomy in conjunction with vagotomy. Many surgeons favour Billroth II reconstruction after antrectomy.

I anastomosis. Routine partial gastrectomy for duodenal ulceration is always followed by a Billroth II reconstruction (Fig.5).

III CONTROL OF ACID SECRETION

The phases of gastric secretion are classically divided into unstimulated (basal), and stimulated. The latter is further subdivided into cephalic (vagal), gastric and intestinal phases. It must be emphasised that this indicates only the site at which the stimulus acts and that each phase is not dependent upon a single individual mechanism.

(a) UNSTIMULATED (BASAL) SECRETION

This is measured with the subject at mental and physical rest, 12 hours after the last meal i.e. no stimuli to secretion are in operation. The values obtained are extremely variable in any one individual from day to day and in different individuals (mean range 1.3 to 4.2 mEq./Hr.). It is of interest that basal achlorhydria can be obtained by training in the dog and man.

To abolish basal secretion vagotomy as well as antrectomy must be performed. Either procedure alone will result in reduced values but will not

abolish it. This has been shown in dogs with Heidenhain pouches[25] (i.e. vagotomized pouches of the oxyntic gland area). Therefore vagal, hormonal (gastrin) and probably local factors are involved.

(b) STIMULATED SECRETION

CEPHALIC (VAGAL) PHASE

Vagal stimulation is entirely responsible for this phase and secretion is completely abolished by vagotomy. Physiological stimuli to secretion, classically demonstrated by Pavlov, are the sight, smell and taste of food as well as conditioned stimuli connected with feeding.

The vagus may be artificially stimulated in various ways to elicit a secretory response. Insulin hypoglycaemia[26] and Tolbutamide[27] will bring this about via the anterior hypothalamus. Deoxy-D-glucose[28] has been shown to produce the identical effect, and probably acts by causing hypoglycaemia at cellular level, thus impairing glucose utilisation. Vagal nuclear receptors can be directly stimulated by barbituric acid derivatives (5 $\gamma\gamma$ dimethylallyl)-5-ethyl barbituric acid)[29].

Direct cholinergic stimulation of the oxyntic cells has been shown to be the mechanism of vagal action. Pevsner and Grossman[30] removed the gastric antrum and small bowel of an experimental animal, and rendered it hypoglycaemic. Acid production occurred in the absence of all known sites of gastrin production. Close arterial injection of small doses of acetylcholine by the same workers caused acid secretion.

Vagally mediated release of gastrin by the antral mucosa was demonstrated by Pe Thein and Schofield[31], confirmed by Grossman[32].

Several dogs with oesophagostomies, vagally innervated antral pouches, and Heidenhain pouches of the oxyntic gland area were sham fed. This caused acid secretion from the Heidenhain pouch which was prevented by acidification or vagotomy of the antral pouch.

GASTRIC PHASE

The existence of the hormone gastrin was first suggested by the work of Edkins in 1906[33], who experimented with simple hog antral mucosal extracts. This was heavily contaminated with histamine and it was not until 1961 that Blair and his co-workers[34]

were able to separate histamine from the extracts, but only on a small scale. Gregory and Tracy in 1964[35] evolved a method of extracting pure gastrin from antral mucosa on a large scale. The final product comprised two peptides, gastrins I and II (GI and GII) which are almost identical chemically.

Using the identical method Gregory et al.[36] have isolated from human antral mucosa two peptides (HI and HII) which are closely similar in structure, and with identical properties to the hog preparations. Similar peptides have been isolated from sheep and from the dog.

The same workers[37] have described the physiological properties of a series of synthetic peptides structurally related to Gastrin I. They showed that of the 17 residues of the molecule only the C-terminal tetrapeptide sequence (found in both gastrins) is required for the full range of physiological effects produced by the natural hormone. No physiological activity except for enhancement of the potency of the covalently attached tetrapeptide has been ascribed to the initial 13 amino acid residues of gastrin. Working with Tracy and Gregory, Morley[38] synthesised a number of peptides

and found that several pentapeptide derivatives were particularly active in their effects. Commercially available, these are now used in clinical tests of gastric acid output. Gastrin is the most powerful known stimulant of gastric acid secretion.

Direct immunoflurescent techniques with flourescein-labelled antibodies made against HI have been used by McGuigan and his colleagues [39,40] to examine human and porcine mucosa from the antrum and body of the stomach. Gastrin was isolated in or on granules that pack the cytoplasm of differentiated epithelial cells interspersed along the course of antro-pyloric mucosal glands. These cells have structural similarities to enterochromaffin cells, i.e. members of the argentaffin class of cells. However, the use of silver stains has not confirmed this. Probably gastrin is released from the cytoplasmic granules and gains access to the peripheral circulation in response to appropriate stimulation. Precise mechanisms of packaging and release of hormone remain undefined.

Gastrin is released directly from the pyloric gland area in response to distension[41] and local chemical stimuli. In dogs denervated fundic pouches were found to secrete acid in response to antral distension. The same stimulation of a transplanted antral pouch yielded similar results and shows that the release of gastrin is independent of extrinsic antral innervation. Nyhus et al.[42] confirmed this on dogs on which "antroneurolysis" had been performed. By this procedure the mucosa and submucosa are surgically separated from the muscular layers and therefore all extrinsic innervation is removed, although local nerve plexuses remain intact.

Other workers[43] have shown that the acid response to antral distension after "antroneurolysis" is abolished by local cocaine application, by 0.25 percent atropine locally applied, and by the injection of ganglion blocking agents. This suggests that mechanical stimulation releases gastrin via a cholinergic reflex within the mucosal and submucosal layers.

Local application of acetylcholine onto the antral mucosa releases gastrin[43,44]. This is blocked by local application of atropine or antral

acidification, but is the only form of chemically induced gastrin release not blocked by local anaesthesia[43,45,46]. Acetylcholine is therefore assumed to act directly on the hormone-containing cell.

Choline, which is contained in a variety of foods (e.g. meat and liver extracts) has a marked stimulatory effect on the acid output of a Heidenhain pouch when introduced into an innervated antral pouch[47].

Olbe and Elwin[48] studied the effect of local application of nicotine on the innervated antral pouch. In a concentration of 0.1 to 0.5 percent, an acid response was elicited in a Heidenhain pouch. A one percent solution did not cause an acid response. This resembles the effect of the drug on autonomic ganglia and may indicate that it interferes with release of gastrin by acting on intramural ganglionic cells.

Five to 10 percent ethanol stimulates gastrin release when it is topically applied to the antral mucosa[49]. By similar experiments to those outlined above local anaesthesia of, and topical application of atropine to, the mucosa of the antrum blocked the action of ethanol. Elwin and

Uvnäs[50] found that the gastrin releasing property of alcohols is confined to those with two or three carbon atoms, without branching of the carbon chain.

The powerful secretogogue action of meat and liver extracts on the antrum, and that the effect can be blocked by local anaesthetics or atropine has been known for years[47,51-54]. The acid secretory response to exogenously administered gastrin was not interfered with by topical atropine, which supports the concept that cholinergic neural mechanisms are responsible[54].

Heidenhain pouch responses to antrum irrigation with various amino acids has been studied[50] and it was found that the stimulatory activity was confined to amino acids with two or three carbon atoms. Glycine and β-alanine showed the most marked stimulatory potency.

The most powerful inhibition of gastrin secretion is acidification of antral content. Uvnäs[55] has shown that a powerful inhibitory effect occurs at about pH.3 and that maximal inhibition occurs at pH.1.5. He also clearly demonstrated that these pH. levels occur physiologically in both man and the dog. Argument has arisen as to whether the inhibitory effect is the result of suppression of

gastrin release or whether an inhibitory hormone is released from the antrum. Evidence for and against this is discussed under the heading of "inhibitory mechanisms".

In summary, the local chemical stimulation to gastrin release by nicotine, ethanol, choline, meat and liver extracts and amino acids are probably the result of local intramural nervous reflexes mediated by acetylcholine.

In the absence of the antrum, distension of the oxyntic gland portion of the stomach will stimulate production of acid and pepsin[56]. Afferent impulses have been detected in the vagus while the distending stimulus is applied[57]. In addition, stimulation of the afferent cut end of the vagus causes acid secretion if the other nerve is intact. This evidence indicates the presence of vago-vagal reflexes. The mechanism is probably one of direct action on the oxyntic cells.

In the absence of vagal innervation distension of the same area will produce the same, though much diminished result. Local (intramural) relex action is cited as the mechanism for this.

There is general agreement on the concentration of serum gastrin in normal fasting individuals.

Hansky and Cain[58] found a mean fasting level of 113 ± 11 pg./ml. in 40 patients. Others[59] noted a mean fasting gastrin level of 165 ± 28 pg./ml. in 102 patients without recognised gastrointestinal disease. The latter group found a direct correlation between age and fasting serum gastrin, that is, that the fasting level rose with increasing age. This they explained on the basis of there being atrophy mainly in the body and fundus of the stomach, without affecting the antrum to any great extent, with increasing age. Diminished acid production resulting from this would remove a major antral inhibitory factor in the production of gastrin. The identical mechanism is postulated for the elevated resting serum gastrin levels found in patients with pernicious anaemia.

Attention has since turned to the levels of fasting serum gastrin in patients with duodenal ulcer. The same two groups of workers were unable to demonstrate a significantly elevated serum gastrin level in patients with peptic ulcer disease.

Burns, Young and Chisholm[60] have recently reported that their patients with duodenal ulcer had consistently elevated fasting serum gastrin levels. The responses of duodenal ulcer patients

to stimuli known to cause gastrin release have yet to be studied and the role of gastrin in the pathogenesis of the disease has yet to be clarified.

INTESTINAL PHASE

Gastrin has been extracted from intestinal mucosa but it is uncertain whether this is identical to the gastric hormone. Differences also exist as to whether the potency of the substance is the same from both sites. The highest concentration comes from the duodenum, and smaller amounts from the jejunal, ileal and colonic mucosa.

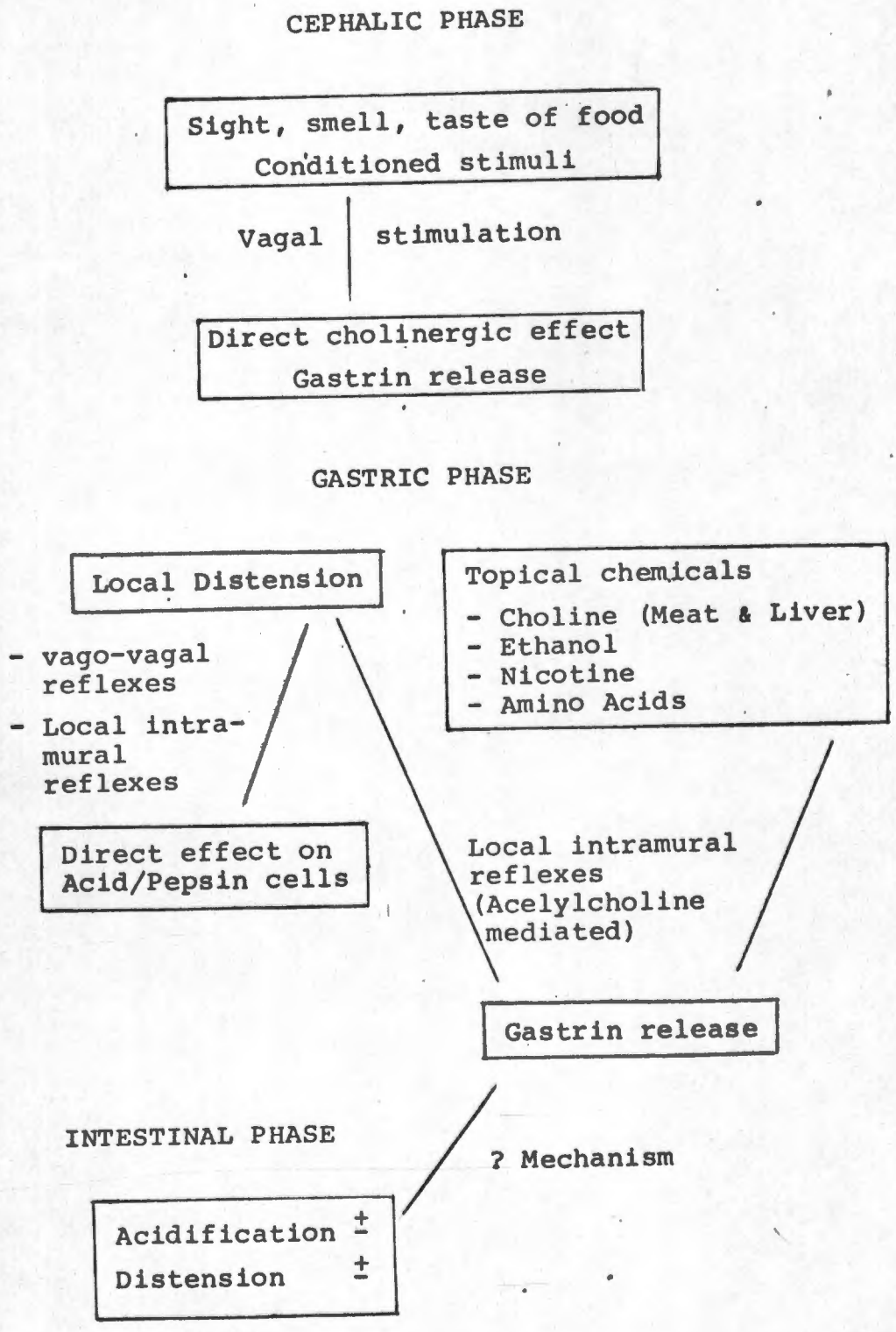
The mechanism of extragastric gastrin production is not clear. Conflicting experimental evidence has been presented. Acidification of the intestine can cause stimulation or inhibition of gastric acid production as can distension[61]. Most workers[62,63] indicate that duodenal acidification will inhibit, and jejunal acidification will stimulate gastric acid production. The ileum apparently has no influence on acid secretion.

INTERACTIONS OF STIMULATORY FACTORS

It has been well shown experimentally that each individual mechanism is dependent upon interaction with the other to bring about its maximal effect.

FIG.6

STIMULATION OF GASTRIC ACID SECRETION



Sham-fed dogs with oesophageal fistula and Pavlov (vagally innervated) pouches[64] responded with moderate acid secretion. Isolation of the vagally innervated antrum resulted in an enhanced response by the Pavlov pouch, due to removal of the inhibition caused by antral acidification. Irrigation of the antrum with acid gave the same moderate initial response. Vagal denervation of the antral pouch resulted in the same response as acidification thereof. Antrectomy led to the lowest values of acid production of all. Amounts of gastrin too small to cause secretion of acid alone, if given in conjunction with sham feeding gave the same results as when the isolated antrum was vagally innervated. This experiment serves to illustrate how physiologically artificial the rigid phasic division of stimulated gastric secretion is. The factors responsible for stimulation of gastric acid secretion are summarised in Figure 6.

(c) INHIBITORY MECHANISMS

INTRAGASTRIC MECHANISMS

As mentioned previously antral acidification with HCl or any other acid sufficient to drop the pH. to a value of less than 3 will cause gastric acid

production to cease[55]. Inhibition is progressive as acid strength increases. Responses to intragastric stimulation with meat extract are strongly inhibited, while the sham feeding response is inhibited to a much lesser degree. This is therefore effective mainly against local chemical stimulation of the antral mucosa.

Good evidence exists for this inhibition being due to suppression of gastrin release. Sham feeding an animal with a vagally denervated oxyntic cell pouch (Heidenhain) can only bring about a secretory response via vagally released gastrin from the antrum. Acidification of the antrum inhibits this response[65].

The release of gastrin by chemical stimulation is blocked by local anaesthetic and therefore probably a local nervous mechanism is responsible. Acid inhibition is not blocked by local anaesthesia and is thus thought to have a direct action on gastrin releasing structures[66].

An antral inhibitory hormone has been postulated (chalone) by Harrison[67] but there is no real conclusive evidence for this. Acidification of the antrum will not cause a diminished response of fundic glands to parenteral gastrin[68], which

mitigates against the presence of an inhibitory hormone.

pH. sensitive receptors have been shown to exist in the antral mucosa[69]. Vagal afferent impulses increase with a drop in antral pH., suggesting that neurogenic reflexes play a part in this inhibitory process.

DUODENAL MECHANISMS

Various substances introduced into the duodenum will cause inhibition of gastric acid secretion.

Duodenal acidification is a well known inhibitory influence. Pincus[70] showed that progressive acidification brought about progressive inhibition. 50% inhibition at pH.2.5 and total inhibition at pH.2 was demonstrated in dogs. Some experimental evidence exists that an intact vagus is necessary for this to occur suggesting a permissive neural action[63].

Humoral transmission has been well demonstrated by a large number of experiments. Acidification of the duodenum resulted in a diminished acid secretory response from vagally denervated fundic pouches[71, 72,73] and this effect was unaffected by sympathetic denervation[74]. Responses to exogenous gastrin administration are inhibited by the same acid

stimulus[73,75].

Duodenal bulb pouches in dogs were constructed by Anderson and Uvnäs[76] who showed that powerful inhibition was elicited by acidification of the bulbar mucosa. Other workers demonstrated that acid irrigation of lower duodenal loops had no effect on gastric acid secretion. It has been shown in dogs that the duodenal pH. never drops to a level lower than 4 after a meal, but that pH. 2.5 is required to stimulate inhibitory hormone release. In both man and dog duodenal bulb pH. values of 2.5 have been measured, which gives support to the hypothesis of Anderson and Uvnäs[77,78].

The presence of fat in the duodenum has been shown conclusively to inhibit acid secretion. To be effective this must be present in absorbable form, as shown by Sircus[79]. Olive oil failed to produce inhibition in isolated loop preparations unless pre-incubated with pancreatic juice. Also, inhibition resulting from duodenal introduction of fat or fatty acids has been correlated with their rate of absorption[62,80]. This effect has been produced from all levels of the small bowel, but is greatest from jejunal loops, coinciding with the fastest rate of fat absorption.

The hypothetical inhibitory agent was named "enterogastrone", which has not as yet been purified. Definite evidence exists for the presence of a humoral mediator. Greenlee et al.[81] injected secretin intravenously in Heidenhain pouch dogs, secreting in response to antral irrigation with liver extract, with resultant demonstrable inhibition. The question is whether this is due to secretin, or impurities in the extract (possibly enterogastrone). Recent studies with secretin of varying degrees of purity[64,73,82] showed that the degree of inhibitory activity correlated with the secretin activity of the preparations. The conclusion reached is that secretin and enterogastrone are probably identical.

Crude extracts of cholecystokinin have also demonstrated inhibitory activity[82], but the precise physiological significance of cholecystokinin/secretin in the control of gastric acid secretion remains inconclusive.

Hypertonic solutions in the duodenum cause gastric acid secretion inhibition[83], but this does not function as powerfully as fat and acids do and an osmoreceptor mechanism is postulated. Responses to transplanted fundic pouches suggest that humoral factors are responsible. Again, the physiological

INHIBITION OF GASTRIC ACID SECRETION

INTRAGASTRIC MECHANISMS

Antral acidification (pH.<3)

- Direct action on cell
- Vagal reflexes
- ? Inhibitory hormone

↓Gastrin release

DUODENAL MECHANISMS

Acidification (duodenal bulb) to pH.< 2.5

Fat (Absorbable forms)

Hypertonicity

? Permissive vagal action

Osmoreceptor mechanism

Humoral factor released
? Enterogastrone
? Secretin

significance of this phenomenon is uncertain.

Factors responsible for inhibition of gastric acid secretion are summarised in Figure 7.

IV OTHER SECRETORY FUNCTIONS

PEPSINOGEN

Pepsinogen depends for its major action on the presence of water and hydrochloric acid. The pro-enzyme is stored in secretory granules in the cell, for release when appropriate stimuli are applied. Synthesis is dependent on adrenal and pituitary factors[84-86].

Basal secretion is continuous in man[87-89].

Stimulated. The strongest mechanisms for pepsinogen secretion are vagal and all methods for stimulating the nerve will cause secretion. Vagotomy leads to significant depression of secretion[90,91].

Gastrin stimulates production of pepsinogen but probably does not play a dominant role in the normal mechanisms controlling secretion of the enzyme.

Slight responses to the same stimuli that cause acid production have been demonstrated during the intestinal phase of gastric secretion.

INTRINSIC FACTOR

This substance is believed to be secreted by the parietal cells[92]. Frozen sections of human gastric mucosa fixed in ammonium sulphate and incubated with 57 Cobalt labelled vitamin B_{12} ($^{57}Co\ B_{12}$) have shown radioactivity in the cytoplasm of parietal cells. Binding of the labelled B_{12} was inhibited by prior incubation with antibodies to intrinsic factor.

Control of secretion is identical to that of acid/pepsin. Intrinsic factor secretion just precedes the acid peak which suggests the presence of a mucosal store of the substance[93]. The chemical structure is as yet unknown but it is probably a mucoprotein.

V SUMMARY OF VAGAL EFFECTS ON GASTRIC SECRETION

ACID

(1) Direct cholinergic transmission of psychic stimuli to oxyntic glands.

(2) Seems to exert a permissive role allowing humoral non-vagal stimuli to be fully effective on the acid secreting cell.

(3) Vagal impulses are transmitted directly to the pyloric antrum to cause gastrin release.

(4) Local chemical and mechanical stimuli to antral gastrin release probably work more efficiently when the antrum is normally vagally innervated.

(5) May regulate inhibition caused by duodenal acidification.

(6) May influence potentiation of stimuli caused by distension of the fundic gland area.

(7) Vagal stimulation of gastric acid secretion may to some extent depend upon the permissive role of a background "tone" of gastrin secretion.

OTHER SECRETORY FUNCTIONS

(1) Pepsin secretion is largely cholinergic.

(2) Intrinsic factor secretion is affected by the vagus in a similar way to acid and pepsin.

From the foregoing discussion the major role played by the vagus in all phases of gastric secretion is quite evident. It is therefore obvious that from a purely physiological point of view vagotomy is a most effective way of decreasing acid/pepsin secretion, and so reducing the liability to duodenal ulcer.

VI GASTRIC MOTILITY

The major emphasis in the following discussion will be on the physiology of the pyloro-antral-duodenal cap area, and the possible influences exerted on gastro-

duodenal motility by the vagus nerves and the drainage procedures that accompany vagotomy.

Three major specific motor functions of the stomach can be delineated. These are storage and volume adaptation, mixing of the contents and propulsion of the contents. The fundus acts as a reservoir capable of large variations in size while the corpus also subserves a reservoir function but in addition mixes and propels its contents. The antrum acts mainly in propulsion and subserves little storage function. The most distal portion of the antrum is the pylorus, with its narrow pyloric canal measuring approximately one centimetre in length. Antrum and pylorus probably act as a single functional unit and in terms of motor activity form the most active and vigorous area of the stomach.

Various types of gastric contractions are described and the methods of elucidation of their nature are radiographic, using barium mixtures of varying consistency[94], or manometric. The most satisfactory results have been obtained using balloons of 3 to 4 centimetres in diameter and filled with 20 to 25 ml. of water. Antral pressure recordings have yielded the most satisfactory results by this method[95,96] and much of the experimental information

to be discussed has been recorded from this area, where the balloon can be securely wedged.

Contraction in the other areas of the stomach can only be measured if isolated pouches are prepared in animals. Attempts to measure pressures in the fundus and corpus in man result in the balloon being simply displaced into an adjacent area of low pressure.

(a) TYPES OF CONTRACTIONS

Muscle fibres involved in any form of contraction at any one moment extend circumferentially around the stomach but form only a narrow constricting band. The waves of contraction so produced may be stationary or migratory.

Tone contractions (type III contractions) occur over a band measuring 5 to 10 cm. in width and occur 10 to 30 percent of the time in the fasting stomach [97,98], range from 1 to 10 cm. of water in amplitude, [95,98,99] and have an average duration of 53 seconds. After feeding, the occurrence of the waves is unaltered but they last for 70 to 83 seconds with reduced amplitude.

Recordings made using isolated fundic pouches in dogs showed that tone waves occurred for 80 percent of the measuring time [100], but other areas

studied showed far less activity. No peristaltic waves have been measured in the fundic area.

Tone contractions occur as baseline pressure changes upon which are superimposed propulsive peristaltic contractions.

Peristaltic contractions involve the sequential passage of a band of contraction proximo-distally, and the width of the band is usually about 1 to 2 cm. Radiological studies in man, and direct observations on the dog stomach indicate that peristaltic waves originate in the cardiac region[101-103] and progress with increasing amplitude to terminate in the antrum. Frequently waves are seen to arise distal to the cardia but always move in a proximo-distal direction.

Two distinct wave types are described, namely I and II, according to the amplitude[95-97]. Type I waves produce pressures of 5 cm. of water or less in balloons of 3 cm. diameter, while during type II waves pressures in excess of this are recorded[95]. On X-Ray examination these waves produce characteristic patterns[96,97].

These peristaltic waves never occur together, but may alternate, and proceed to a basic rhythmic pattern. The maximum frequency is fixed at approximately three per minute in man, as described by

Carlson[104] and 4 to 5 per minute in the dog[97,100]. An irregular pattern may be produced by "dropped waves", but the basic background frequency of contraction is rhythmic.

It would seem that type I contractions are largely concerned with mixing and type II with mixing in addition to propulsion.

Terminal antral contractions follow three patterns. Waves of large amplitude may terminate abruptly at the pylorus, with active propulsion into the duodenum. Some contractions of smaller amplitude simply fade away in the antrum, but the commonest mode of termination is a simultaneous, vigorous, co-ordinated contraction of the antrum and pyloric canal[97]. The length of antral segment involved is variable and related to the strength of contraction. In dogs it is found to measure 3 to 4 cm. but no details are available in humans as yet. "Antral systole"[105], as it has been named, does not occur de novo but only follows strong (type II) peristaltic waves.

Radiographically it can be shown that the terminal antral contractions and pyloric canal closure occur simultaneously[97], and the pylorus, due to its narrower bore, remains closed throughout the continuation of the contraction.

However, on occasions the pyloric canal will narrow, but not completely close during the cycle, so that antral contents are propelled into the duodenum. The functions of antral activity are therefore to propel gastric contents and facilitate emptying of the stomach, as well as to mix and emulsify the chyme. The latter is effected by forcible retropulsion of the contents as the antrum contracts as a unit against the closed pylorus. In addition the antrum certainly plays a part in reducing food particle size by its vigorous activity[106].

Recently recordings of antral electrical activity have been made in man, together with intraluminal pressures[107]. Two types of activity were discerned. The basic electrical rhythm is characterised by a triphasic complex at a regular rhythm of 3 per minute, while spiking activity occurs superimposed upon this, consisting of bursts of fast spikes of unequal amplitude. These bursts are generally accompanied by a pressure wave and the degree of spike activity is proportional to the amplitude of the pressure wave.

(b) PYLORIC SPHINCTER AND DUODENAL CAP MOTILITY

Much controversy exists about the existence of a pyloric sphincter, and whether the pyloric canal is closed most of the time and opens momentarily to

let contents through, or is open most of the time and closes occasionally.

Four groups of workers have found that there is no tonic contraction of the pyloric ring comparable to the cardiac or cricopharyngeal sphincter[108-111] in man. Atkinson and his colleagues[108] measured pressures in this region using a chain of four air-filled balloons, slightly overlapping and each measuring 7 - 10 mm. in diameter. The chain was withdrawn stepwise from duodenum into antrum. They reasoned that in this way pressures could be recorded across the pyloric ring with certainty without necessarily having to localise it radiologically.

Using healthy fasting medical students as their subjects, as well as duodenal ulcer patients, they could in no instance demonstrate a band of sustained increased pressure. Similar results were obtained when the students were fed. When the experiments were repeated with a series of larger air-filled balloons, ranging from 10 to 20 mm. in diameter[112] it was found that on frequent occasions pressure increases were produced at the pyloric ring at balloon diameters in excess of 12 mm. The conclusion reached was that the pylorus presented no resistance to being stretched to a diameter of 7 to 12 mm.

The balance of evidence suggests that in man the pyloric ring is not a tonically contracted sphincter, opening occasionally, but that it behaves as a single unit as part of the thickened antral muscle mass, thus effecting closure of the pyloric canal.

Barium meal studies of duodenal cap (bulb) motility indicate that its contractions are independent of those of the antrum[113,114]. The bulb has a regular basic rhythm of 17 to 19 contractions per minute in the dog and 12 to 15 per minute in man. Bulbar contractions may commence at the apex, the pylorus or in the middle, or take the form of a concentric sleeve-like contraction of the whole bulb. It appears to have a reservoir function and may fill and distend without any barium passing into the post-bulbar region. Contractions may occur without any propulsion occurring, and when barium does spill into the rest of the duodenum the cap rarely empties completely. Barium may reflux through the pylorus, but only about 11 percent of bulbar contractions have been shown to occur when the pylorus is open[97]. Once the post-bulbar duodenum fills, contractions may be of the mixing segmentation type, or prograde peristaltic waves.

The weight of evidence indicates that the antrum and pylorus contract as a unit and that the duodenal cap forms a largely, if not wholly, independent unit [97,115-117]. That is to say, the one may contract without the other or both may contract simultaneously. However, it has been fairly constantly noted after feeding in dogs, that if contractions commence synchronously in the antrum and duodenal bulb, the latter appears to be suppressed [118].

(c) VAGAL INFLUENCES ON THE CONTROL OF GASTRIC MOTILITY

Reflexes that control gastric motility are initiated in visceral and somatic receptors. The most important visceral receptors are situated in the upper intestine and respond to the presence in the lumen of osmotically active substances [119], hydrogen ions [120], protein and fat digestion products [121,122] and mechanical stimulation such as increasing intraluminal pressure, physical contact or muscle stretch. Similar receptors are present in the stomach but detailed study of these has not been made.

Somatic and visceral pain receptors initiate reflexes that inhibit gastric motility.

The presence of vagal afferent fibres from the upper gastrointestinal tract is indicated by the

finding that certain reflexes originating in this area persist after sympathectomy, with the vagi left intact[123]. These afferent impulses do not give rise to pain or any other conscious sensation, but are concerned with autonomic regulation of gastro-intestinal function.

Agostoni et al.[124] made a count of the number of afferent and efferent fibres in the vagi of cats and found that approximately 90 percent of the nerve fibres are afferent.

Efferent vagal fibres that reach the stomach terminate in relation to cells of the myenteric plexus, which in turn innervate the gastrointestinal muscle. Gastric tone and peristalsis, which may be assumed to be dependent on the functioning of local reflex mechanisms, are temporarily suppressed after vagotomy, but ultimately recover, at least partially [125-128]. Direct activation of motor or inhibitory cells in the myenteric plexus probably explains best the prompt responses of gastric muscle to direct stimulation of the nerve.

Direct neural stimulation may result in either contraction of gastric muscle or relaxation. Most workers report that the gastric muscle is more likely to contract when fully relaxed and more likely to

relax when fully contracted[129]. In addition, strong stimulation favours relaxation, whereas mild or moderate degrees of stimulation produce a variable result.

Martinson[130] concluded that the efferent fibres caused relaxation of mainly the fundus and body, while the antro-pyloric portion of the stomach is much less sensitive to vagal inhibitory influences.

Consideration of available evidence indicates that the vagus exerts some influence on local reflex mechanisms.

Excitatory reflexes:

The existence of a cephalogastric reflex resulting in the initiation of active gastric motility in response to conditioned stimuli was initially reported by Cannon[106] working with cats. He found that vagotomy abolished this, but that if the vagi were sectioned once motility had begun, peristalsis continued normally.

In man Wolf and Wolff[131], on direct observation via a gastric fistula, reported that motility increased on exposure of the subject to conditioned stimuli associated with tasty food. Similar results have been reported by others[132] and demonstrate

that cephalic influences are involved in initiation and maintenance of gastric peristalsis.

There is no doubt about the existence of a gastric phase of stomach motility and that this is largely dependent upon vagal integrity[106]. Food in the stomach stimulates peristalsis provided that the vagi are intact but fails to do so in the recently vagotomized subject. However, within weeks or months of vagisection normal peristalsis returns and can again be stimulated by the presence of food, probably acting via local reflexes through the intrinsic plexuses. Temporary absence of these reflexes after withdrawal of vagal facilitation supports the conclusion that vagal reflexes are involved in the response to food in the intact subject.

Inhibitory reflexes:

Painful stimuli, both visceral and somatic are well known to give rise to generalised visceral inhibition[133], the stomach merely participating in this non-specific phenomenon, which has been convincingly shown to be largely a sympathetic reflex [134,135]. The vagus probably plays no part in this inhibition and almost certainly has no effect on the intesto-intestinal inhibitory reflex that follows rough handling of the viscera.

Cannon and Lieb[136] first described the receptive relaxation reflex which involves inhibition of the musculature of the body and fundus of the stomach as part of the swallowing reflex. The effect is to prevent a rise of intra-gastric pressure as the volume of the stomach contents is increased by swallowed food. Vagotomy abolishes this reflex and the work of Martinson et al.[130,137,138] suggests that the efferent inhibitory vagal fibres are involved.

Inhibition of gastric peristalsis via the entero-gastric reflex may be brought about by appropriate chemical and mechanical stimulation of the mucosa of the upper intestine[123]. The reflex is believed to play a major role in the control of gastric emptying, and substances found to initiate a response when present in the upper small bowel are fats, fatty acids, soaps, products of protein digestion, sugars, mineral acids, alcohol and hypotonic solutions [123,139-141].

The inhibitory response to some of these substances disappears after vagisection, but the effect of mineral acids and of fats persists to some degree [122,123].

Vagal influences on hormone responses:

Some humoral factor, as yet unpurified but named "enterogastrone"[142] has been shown to inhibit gastric peristaltic activity. This is released from the duodenum and jejunum by contact with fats and the products of fat digestion.

Vagotomy greatly diminishes the inhibition of the intact stomach[122,143] in response to fat in the duodenum, and the latent period is prolonged from a normal of approximately one minute to four minutes or more[144]. Local application of procaine to the intestinal mucosa abolishes the inhibition of gastric activity by fat.

The postulate has therefore evolved that a local reflex mechanism is responsible for release of the hormone and that the effects on gastric motility are facilitated by vagal impulses.

Gastrin and its synthetic analogues have been shown to increase gastric motility when administered intravenously[35]. This motor activity was diminished but not abolished by atropine which suggests that the cholinergic vagal stimulatory fibres may well influence the gastric motility response to gastrin.

Insulin, via hypoglycaemic stimulation of vagal

centres increases motility in the empty, vagally innervated, stomach of man and animals.

(d) SUMMARY

The stomach manifests a basic rhythmic pattern of motor activity. Tonic contractions are responsible for mixing and various types of peristaltic wave are responsible for both mixing and propulsion of gastric content.

The antrum constitutes the most active part of the stomach with regard to motility. Antrum and pylorus work as a unit mainly concerned with propulsion and retropulsion of chyme. The duodenal cap is largely autonomous but may possibly have some synchronisation with antral activity.

Control of gastric motility and emptying is largely the result of local intramural reflexes and hormonal factors. The vagus seems to exert some, though variable influence on most gastric reflexes and motor activity.

The effects of vagotomy alone, and vagotomy accompanied by a drainage procedure, or the drainage procedure alone, on gastric motility and emptying have been the subjects of many studies. These results will be reviewed and discussed later.

CHAPTER 2

EFFECTS OF VAGOTOMY - PATHOPHYSIOLOGY

The following discussion deals with the effect of vagal nerve section on various intra-abdominal viscera.

I OESOPHAGUS AND CARDIA

Symptoms attributable to gastro-oesophageal reflux (heartburn and regurgitation) and dysphagia have been reported in various series.

(a) Gastro-oesophageal reflux:

The normal physiological mechanisms which prevent this occurring are uncertain[145,146]. An intrinsic lower oesophageal sphincter can be identified manometrically as a zone of increased intraluminal pressure, although no anatomical sphincter exists. This is cited by some authors as the most important factor[146,147].

Varying degrees of importance have been attached to extrinsic mechanisms. The phreno-oesophageal ligament holds the gastro-oesophageal junction in place below the diaphragm. This also maintains the acute angle of entry of the oesophagus into the stomach which may serve as a valve mechanism. One

possibility is that it acts as a "flap valve", while another is the operation of the "flutter valve" principle, where the narrow flaccid tube closes as the outside (i.e. intragastric) pressure rises. The "pinch cock" action of the diaphragm and the "mucosal rosette" of oesophageal mucosa are also cited but regarded as unimportant[146].

In summary, the most important factor in maintaining competence is probably the physiological intrinsic sphincter, with a relatively minor role being played by extrinsic factors.

Vagotomy (abdominal) causes a definite decrease in sphincteric pressure[148,149]. It has been suggested that this might be the effect of surgical trauma during dissection. Evidence against this is the fact that the effect can be mimicked by anticholinergic drugs[150], and in dogs transthoracic vagotomy causes atony and reflux without interfering with the anatomy around the hiatus[151].

Traumatic damage to the extrinsic mechanisms, mainly division of the phreno-oesophageal ligament, allowing minor herniation and reflux to occur is difficult to prove radiologically or manometrically. Some workers[150,152-154] feel that this occurs uncommonly, while others found increased incidences.

Postlethwaite[155] states a figure of 11% of 135 cases, but none were symptomatic. Clarke and his co-workers [156] performed pre- and postoperative studies on 32 patients. Nine had intermittent gastro-oesophageal reflux preoperatively and 11 postoperatively, but 6 had more severe reflux when compared to the pre-operative state. However, the consensus is that the major cause of gastro-oesophageal reflux after vagotomy is functional due to denervation.

(b) Dysphagia:

Postvagotomy dysphagia usually starts one to two weeks postoperatively and usually resolves within three weeks to three months.

An "achalasia" mechanism has been postulated, i.e. the sphincter fails to relax with the peristaltic wave, directly attributable to denervation. Achalasia can be produced in dogs by performing vagotomy above the level of the hilum of the lung[157], and the suggestion was made that if the oesophageal sphincteric nerve supply comes off low down, truncal vagotomy may cause achalasia. Woodward[158] and Grimson[159] have shown normal peristalsis and sphincteric relaxation in man following vagotomy, using radiology and manometry. The same thing has been demonstrated in dogs[160].

Organic obstruction by transient postoperative oedema and haematoma is suggested as a possible cause [161]. Edwards [162] investigated 8 patients with severe postvagotomy dysphagia and found a radiological cuff of haematoma, with normal peristalsis of the body of the oesophagus and the involved, narrowed segment, which relaxed normally to a limited bore. He confirmed normal peristalsis and mucosa on oesophagoscopy and manometry.

However in the series of patients investigated at Groote Schuur Hospital [163-165], 66.7 percent were found to have a spastic condition of the lower oesophagus, relieved by Scopolamine, and 20 percent had associated hiatal hernia. Only in 10 percent was perioesophageal haematoma cited as the sole cause. It is of interest to note that 23.3% of cases had preoperative oesophageal dilatation on barium meal examination.

Peptic oesophagitis with secondary spasm, eventually proceeding to organic stricture formation is a definite possibility in some cases and supportive evidence is provided by the frequent finding of gastro-oesophageal reflux after vagotomy. There is no doubt that peptic stricture can be a cause of long-term dysphagia, first shown by Bruce and Small [161] in two

patients.

In summary, it would appear that vagal denervation per se does not result in dysphagia. The symptom is probably a direct result of trauma to the oesophagus at operation, resulting in reflex spasm, or organic obstruction in a minority of cases. Some long-term cases are due to peptic stricture.

II STOMACH

Detailed study has been made of the effects of vagotomy on motility, secretion and histopathology.

(a) Motility:

Undoubted motility disturbances occur following the vagotomy operations, but whether any gross long-term qualitative changes occur remains uncertain. Clinically, gastric stasis and vomiting are known to occur if no drainage procedure is performed[166,167].

Even with drainage, postoperative retention still occurs. Incidences reported in various series range from 6%[168] to 27.5%[169]. More recently[11,170] various series have been reported of selective and "highly selective" vagotomy operations without drainage procedures. No stasis problems occurred in any patients in these series. Although the follow up period is too short for proper evaluation, the results support the view that vagal innervation of the antrum

is important for efficient gastric emptying.

Part played by denervation:

Barium meal studies during the immediate post-operative period suggest that vagotomy causes diminished gastric motility and impairs emptying. The effect lasts for days, maybe weeks[169,171-173]. No difference in motility patterns between selective and truncal vagotomy have been discerned by these crude methods[174].

Pressure studies in dogs[175] using multiple implanted strain gauges, revealed that vagotomy altered the rate of muscle contraction. Normal peristaltic waves showed disturbance of propagation, and these changes were recorded for nine weeks, after which time the experiment was discontinued.

In man, Magee[176] showed that gastric contractions were weaker but that the pyloro-duodenal activity pattern remains unaltered after vagotomy. Using radiotelemetering capsules it has been shown that pressure-changes restart in the stomach approximately 30 hours post vagal section, and in the intestine after 6 to 18 hours, compared with post-laparotomy control values of 4 and 6 hours respectively[177].

Stadaas and Aune[178] found a resting response of flattened peristalsis in the vagotomized stomach (using balloons), with "autonomic contractions", that is,

there was no co-ordinated peristalsis. The defect in motility was corrected by intravenous administration of Metachlopramide. It has also been shown using similar methods that gastric pressure increases pari-passu with increasing volume in these subjects[179,180], indicating a disturbance of the normal "receptive relaxation" phenomenon. Everett and his colleagues[181] were unable to find any difference in the motility pattern produced by selective or truncal vagotomy.

These authors conclude that vagal action is responsible for co-ordinating "receptive relaxation", tone adjustments, and motility, and that vagotomy therefore results in "muscular rigidity" as opposed to complete atony.

Gastric emptying has been studied by a number of authors, comparing the effect of vagotomy and drainage[182-187] on emptying patterns after a fluid meal with that found in subjects with normal stomachs. All used the double sampling dye dilution technique[188] and found that emptying occurred more rapidly after vagotomy and drainage. Buckler[189] used a solid test meal of enteric coated barium granules and starch to compare rates of emptying of vagotomized stomachs without drainage with stomachs that had had drainage

procedures performed. Both group emptied more slowly than normal controls, with the "vagotomy alone" group significantly slower than the other groups.

Posture has little effect on the rate of gastric emptying in the healthy stomach. In vagotomized patients posture has a definite effect, and it has been shown that emptying is delayed in the supine position and significantly more rapid in the right lateral position[175,186,190,191].

Part played by the drainage procedure:

Theoretically gastroenterostomy should empty more efficiently than pyloroplasty. Gooddall[182] found that fluids emptied via the Heinecke-Mickulicz type of pyloroplasty at a significantly faster rate than through a gastroenterostomy. Griffith et al.[184] showed that the Finney pyloroplasty increased the rate of emptying while the Heinecke-Mickulicz delayed it (using a ^{51}Cr labelled solid meal).

McKelvey[186,187] studied the rates of gastric emptying for water and a liquid fatty meal, on patients who had had either selective or truncal vagotomy and pyloroplasty. His results showed that while there was a significant difference in emptying time between water and the liquid fatty meal in normal controls, there was no difference in the test subjects.

The type of vagotomy had no influence on the results. The conclusion reached was that the chemical control of the rate of gastric emptying was lost after vagotomy and drainage. Whether this is due to the vagotomy, or the drainage procedure is uncertain. The fact that there is no difference between the selective and truncal groups suggests that the pyloroplasty is responsible. He thus coined the concept of the "incontinent stomach".

It has been shown[192] that postoperative gastric retention, that is, the need to continue gastric suction for more than 48 hours, decreased in incidence (from 17% to 2% of patients) over a 5 year period with the adoption of a pyloroplasty technique which prevented any encroachment on the duodenal lumen by invagination of the bowel wall.

In summary, some gastric motility disturbance occurs after vagotomy, probably a loss of co-ordination of motility. Gastric retention is probably a combination of stomal obstruction and decreased motility and the latter makes mild degrees of obstruction more significant. The other effect on motility of vagotomy operations is the loss of chemical control of gastric emptying, most likely due to interference with normal pyloric closure by the drainage procedure.

(b) Secretion:

The evidence for, and a detailed account of, the role of the vagus in gastric secretion has already been discussed. In summary, the vagal effects on secretion which are probably abolished by vagotomy are:

(1) Direct transmission of psychic stimuli to fundic glands.

(2) Direct stimulation of gastrin release.

(3) Facilitation of the gastrin-releasing response to local stimulation.

(4) Permissive effect, possibly potentiating, on the response of the fundic cells to non-vagal stimuli.

(5) Possible background of tonic gastrin activity causing a permissive effect on the vagal action on the fundus.

(6) Possible role in inhibitory mechanisms on secretion.

(7) Pepsin secretion.

(8) Intrinsic factor secretion.

Effect on stimulated ACID/PEPSIN secretion:

Vagotomy will reduce the acid secretory response to all known forms of stimulation in man. Bank, Marks and Louw[163] established various patterns of secretion following vagotomy, in response to histamine stimulation.

Basal acid output (B.A.O.) manifested transient hypersecretion, eventually returning to a low level. Also shown was the fact that the B.A.O. may approximate maximal acid output (M.A.O.), but again diminish within a few months. This usually occurred when gastroenterostomy was used as the drainage procedure.

Complete section of the vagi seemed to result in four different patterns in M.A.O. results. (a) An early drop of 70% of the preoperative value. (b) Constant steady decline to this level. (c) Initial achlorhydria with gradual recovery to a low level, which gave rise to the concept of "parietal cell shock" lasting for two to three months[193]. (d) Total achlorhydria ab initio, which never recovers.

It was first shown by Payne and Kay[194], confirmed by others[195,196] that intravenous acetylcholine infusion at the time of histamine stimulation (subcutaneously) could restore the preoperative response. This provides additional evidence that changes in gastric acid secretory activity after denervation are due to removal of the permissive effect of the vagus on histamine stimulation of the parietal cells. Rosato[196] found that he was able to obtain post-vagotomy M.A.O. responses approaching preoperative levels by intravenously administering four times the

usual optimal dose of histamine acid phosphate. He also reported that the pepsin response, reduced after vagotomy, was not as effectively restored by using supramaximal histamine doses, and suggests that vagal tone is more important for pepsin than for acid secretion.

The response of oxyntic glands to gastrin and the synthetic gastrin-like polypeptides (pentagastrin) [38,197] has been shown to be identical to that caused by histamine[198]. However it has been shown by Bank and his colleagues[199] that histamine on a platform of pentagastrin before vagotomy and vice versa will stimulate acid production to an identical level, higher than the M.A.O. caused by either acting alone. This value is taken as the maximal acid secretory capacity of the parietal cells. Following vagotomy pentagastrin had a synergistic effect when given on a histamine platform, but the reverse did not hold true. It was concluded that the postvagotomy cell was more reactive to pentagastrin than histamine.

Recently it has been found that following vagal denervation the gastric juice sodium ion concentration was much higher than that found in normal controls, when the hydrogen ion concentration was low. A similar pattern was seen in atrophic gastritis and pernicious

anaemia, and the conclusion was that this reflected back diffusion of hydrogen ions across a mucosa which was unable to actively resist the process. No difference was found when the concentration of hydrogen ion exceeded 100 mEq./L. i.e. at higher rates of secretion. This suggests that when low levels of hydrogen ion are found after vagotomy, the values may be false due to back diffusion[195].

However, the interest in preoperative M.A.O. levels in response to the various tests was justified by Rune[200,201] who demonstrated that the response to a meal was identical to histamine stimulated M.A.O. and therefore one might assume that the diminished postvagotomy histamine response reflects the physiological response.

Various experimenters[174,181,202-204] working with dogs, have compared the results of truncal and selective vagotomy and pyloroplasty on acid secretion. Heidenhain pouch (vagally denervated) secretion in response to pentagastrin stimulation is significantly greater after truncal vagotomy (twice as great as the selective group). This suggests that the hepatic and coeliac vagi inhibit secretion in the dog.

In man, Bank, Marks and Louw[205] found that there was the same reduction in histamine/pentagastrin

stimulated response in both groups, although there was a higher incidence of complete vagotomy following the selective procedure. Their results indicate that the findings in the canine experiments regarding the possible roles of the coeliac and hepatic vagal branches probably do not apply to man.

Effect on gastrin secretion:

Byrnes, Young and Chisholm[60] demonstrated that patients with duodenal ulcer have a consistently elevated serum gastrin while in the fasting state, compared to normal controls. After vagotomy, serum gastrin levels were significantly lower in patients with complete nerve section (by insulin testing), compared with the incomplete vagotomy group. Those with incomplete vagotomy who had serum levels approaching that of the duodenal ulcer patients all developed recurrent ulceration. Dragstedts' original point that increased resting vagal tone is important in the pathogenesis of duodenal ulcer is hereby illustrated. The authors suggest that postvagotomy serum gastrin levels may be used as an index of "adequacy of vagotomy".

(c) Vagal nerve regeneration:

Bell[206] performed augmented histamine tests at ten days, one year, two years and three years after

vagotomy and found no appreciable difference in acid output, and concluded that the effects on histamine response last for at least three years.

Murray[207] has demonstrated that vagal nerve regeneration can occur both by gap-bridging and sprouting. This work has been confirmed by others [208-210] and the consensus is that although re-innervation in the short term is insignificant, the long term result is uncertain, and functional return may well take more than three years.

Stimulation of gastric secretion via central nervous system receptors, with the vagus acting as efferent pathway has led to the universal adoption of the insulin test to assess completeness of vagal nerve section after vagotomy[211,212]. Detailed discussion of tests for assessment of vagal denervation and their interpretation follows in a later chapter.

In summary, vagotomy reduces the acid output in response to all known forms of stimulation of gastric acid secretion, resulting in a number of definite patterns of secretion. The vagotomized cell is possibly more sensitive to pentagastrin than to histamine stimulation.

There is no difference in stimulated gastric acid secretion when responses after truncal and selective vagotomy are compared in man.

Serum gastrin levels are significantly reduced by vagal denervation.

Vagal nerve regeneration has been shown to occur after nerve section to an insignificant degree, but the long term effects (beyond 3 years) are as yet uncertain.

(d) Histopathology:

Very few studies have been undertaken to elucidate histological changes following on vagal denervation of the stomach.

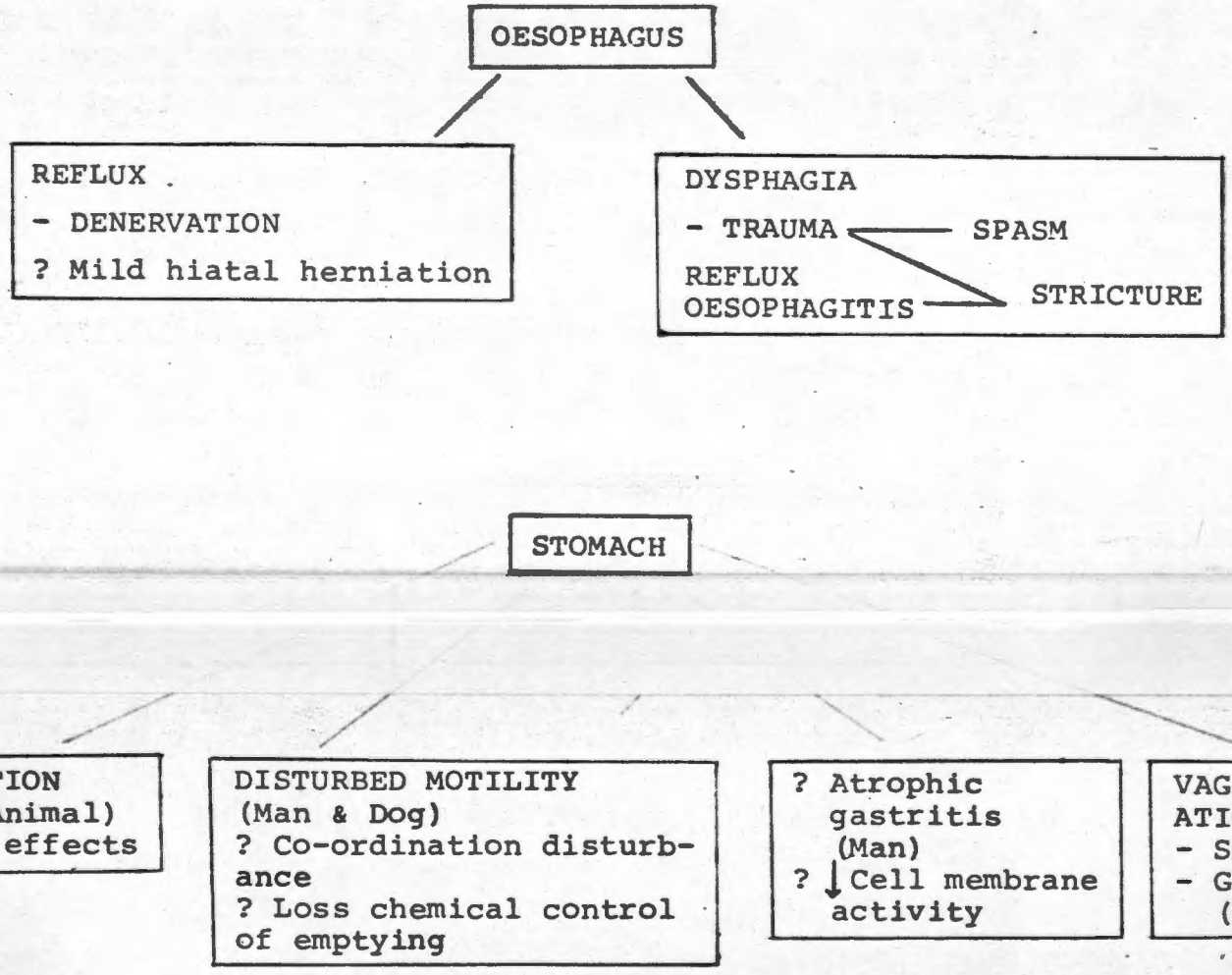
Working with rats, Crean et al.[213] examined gastric mucosa five weeks after operation and found a significant reduction in chief cells (33%) and in the fundic mucosal height (19%). The parietal cell population was also reduced, but not to a statistically significant degree. Ritchie and co-workers[214] compared parietal and chief cell populations in dogs who had undergone truncal vagotomy and pyloroplasty or antrectomy with preoperative examinations in the same animals. Biopsies were taken at one, three and six months, and at one year after operation. No significant difference was found. Vagotomy with

Billroth II reconstruction on the other hand resulted in marked mucosal changes within three months, with a diminished population of both chief and parietal cells. Histology showed an inflammatory infiltrate and the picture of atrophic gastritis. The same changes were seen within three months when a full thickness wedge of gastric corpus was implanted into the proximal jejunum. It seems therefore that vagotomy per se does not significantly alter histology in the canine stomach.

Cell membrane integrity has been examined in rats[215] in an attempt to explain the mechanism of diminished acid secretion. Phospholipid content and phosphorus incorporation into cell membranes was assessed by intra-peritoneal injection of ^{32}P. After two weeks the rats were sacrificed, and the phosphorus and phospholipid content of the gastric mucosa was estimated. A reduction (significant to $p < 0.05$) was demonstrated and the conclusion reached was that vagotomy resulted in a reduction of the specific activity of cell membranes in the glandular portion of the stomach. No relation between the degree of diminution of HCl secretion and phospholipid reduction was demonstrated, however.

FIGURE 8

EFFECTS OF VAGOTOMY



Bank et al.[216] have recently studied gastric mucosal histology in man after vagotomy. Gastric biopsies were done three months to four years after vagotomy and drainage operations. Half the patients had normal histology and none had gastric atrophy. The remaining group had superficial or atrophic gastritis, with the latter change being found more frequently in patients who had undergone truncal vagotomy and gastroenterostomy, than in those following pyloroplasty. Repeat biopsies taken on a group of the same patients three months, six months, and a year later suggested that there was a tendency for atrophic gastritis to develop with time. Melrose[217] showed a much higher incidence of atrophic gastritis in his series, but the biopsies were taken after a longer postoperative time interval (1 to 10 years). The conclusion reached in this study was that gastric atrophy probably did not occur after vagotomy and drainage, but that there is a tendency for superficial atrophic gastritis to develop with time.

Overall conclusions that can be reached are that vagotomy has marked effects on gastric motility and secretion. Histopathological changes which definitely occur in animals are less significant in man.

III BILIARY SYSTEM

(a) Hepatic bile flow and composition:

Vagal stimulation in dogs by hypoglycaemia resulted in a significant rise in bile volume and total solid output[219]. The increase in bile output was much less than that resulting from feeding and the effect was blocked by vagotomy or anticholinergic drugs. Baldwin et al.[220] repeated the experiments in humans after cholecystectomy, with a common bile duct catheter in situ, and stomach contents were prevented from stimulating secretion via duodenal acidification by constant suction. Hypoglycaemia resulted in an 86% rise over baseline levels in volume, and atropine abolished this effect. Solid output increase was not elicited but this was possibly due to interference with the enterohepatic circulation of the bile salt pool. McKelvey et al.[220] compared hepatic bile salt secretion following truncal and selective vagotomy in man. Bile salt secretion showed no difference after hypoglycaemia, and was abolished by both procedures.

Additional evidence for altered hepatic bile composition and concentration has been provided by several workers[219,221-225]. Fields and Duthie[221]

reported that there was an alteration in micellar fat formation in the small bowel, probably attributable to this.

Antrectomy was shown to virtually abolish the biliary response to hypoglycaemia[226] and it was therefore postulated that a humoral choleretic factor was responsible. Gastrin was thought to be the likeliest factor, and Zaterka and Grossman[227] were able to demonstrate that intravenous gastrin administration resulted in bile flow stimulation in dogs. Stimulation of antral pouches in dogs[228] causing gastrin release (as judged by gastric acid production), caused an increase in biliary volume and bicarbonate concentration. When the enterohepatic circulation of bile salt is maintained by constant intravenous infusion of taurocholate solution[229], gastrin produces much larger increases in bile flow than when the bile is diverted.

Further confirmation of the influence of gastrin on hepatic bile flow was provided by Beaugie and his colleagues[230] using isolated canine liver preparations.

The major effect of vagal denervation on bile secretion seems to be due to impaired gastrin release with subsequent reduction in bile flow.

(b) Effect on the gall bladder:

In man the fasting volume of the gall bladder increases steadily until it is double the prevagotomy value, as measured by means of cholecystography[231]. Incomplete vagotomy caused no increase in gall bladder size. Truncal vagotomy was shown to double the size of the organ, while anterior selective nerve section led to no significant change[222-225,232,233]. Cox and his co-workers[234] showed that dilatation was apparent within twelve days postoperatively, doubled by ten months and that there was possibly a slight volume increase in succeeding months.

Working with dogs Carter and Sawyers[235] found that at one year after vagotomy the gallbladders were smaller than at one month postoperatively (statistically significant at $p < 0.02$). However, there was no difference between the effects of selective and truncal vagotomy. They also reported that dilatation occurred to a far greater degree after vagotomy and antrectomy than after vagotomy and pyloroplasty, and suggested that gastrin plays a part in resting gall bladder tone. The observation by Cox et al.[234] that dilatation of the gall bladder occurred after gastrectomy was also attributed to this factor. However, in view of the work of Vigne and Grossman[236] the suggestion that

gastrin is a gall bladder activator can be rejected. They demonstrated convincingly that this hormone has poor cholecystokinetic action.

Tinker and Cox[237] demonstrated denervation hypersensitivity (Cannon's Law) of the gall bladder to subthreshold doses of carbochol and cholecystokinin after both truncal and selective vagotomy in man. There was no difference in the degree of response recorded between the two groups. They conclude that by present techniques of selective vagotomy the gall bladder is denervated, even though the hepatic branches appear to be grossly intact. This could possibly be a temporary effect due to a "neuropraxia".

The physiology of gall bladder emptying is complex. Since the discovery of the hormone cholecystokinin[238] it has been generally accepted that humoral mechanisms are more important than extrinsic neural mechanisms. Possibly the latter may modify the response to hormones. Jorpes and Mutt[239] have shown that pancreozymin and cholecystokinin are identical. Vagal stimulation in cats causes a protein rich output from the pancreas identical to the pancreozymin effect[240]. There is therefore indirect evidence for vagal stimulation causing pancreozymin/cholecystokinin release which

stimulates gall bladder contraction to a significant degree. Numerous stimuli, on local contact with duodenal mucosa, stimulate cholecystokinin release. Acid, peptone and fat act powerfully, and the latter has the most effective action. Release of the hormone from the duodenal mucosa of the dog involves stimulation of nervous receptors which are paralyzed by topical procaine, and at least one synapse (blocked by Hexomethonium)[241]. It seems likely that cholecystokinin-releasing cells and receptors are connected by a local nerve plexus and that this relays with long vagal fibres.

Postvagotomy rate of emptying of the gall bladder has been assessed by many workers, and conflicting results ranging from slower[232] to unimpaired[234, 242,243] to increased[244] rates of emptying have emerged. Rudick and Hutchinson[232] also demonstrated that truncal vagotomy resulted in greater impairment of emptying than the selective operation.

It became apparent that the rate of emptying was a function of the rate of gastric emptying into the duodenum, thus stimulating cholecystokinin release, and therefore depends on the nature of the drainage procedure[244]. In support of this, Glanville and Duthie[245] found that there was no change in gall

bladder emptying if contraction was timed from the passage of a meal through the pylorus.

The pattern of gall bladder emptying found by most workers was that normal gall bladder contraction expelled 70 to 80 percent of the contents within forty minutes. After vagisection the emptying pattern is probably unchanged except that the basal volume is doubled, leaving a residual volume of 20 cc., as opposed to the normal value of 6 to 9 cc.

Bile composition in the gall bladder has been found to be unaltered following vagotomy in dogs, either after truncal or selective nerve section, or pyloroplasty alone[222,223].

(c) Effect on the common bile duct:

An increase in diameter of the common bile duct occurs after truncal vagotomy. This has not been observed on any case following incomplete or selective nerve section[232]. In the dog Watts and Dunphy[246] showed a marked increase in intraductal pressure when the distal cut end of the vagus nerve was stimulated. The same effect was produced by parasympatheticomimetic drugs, and inhibited by atropine.

The vagus therefore has a similar effect on common bile duct tone to its effect on gall bladder tone.

(d) Vagotomy and gallstones:

Human gallstone will dissolve in the healthy canine gall bladder and also after selective vagotomy in the same animals. Following truncal vagotomy this does not occur[247]. Also working with dogs, Schein et al.[248] were able to produce the changes of chronic cholecystitis, with mucosal fibrosis, by simple truncal vagotomy. The animals also formed biliary sludge and pigment stones. Inserting a cholesterol stone into the normal gall bladder caused no changes, whereas the same manouvre after vagotomy resulted in 80% of the dogs developing acute cholecystitis. The authors suggest that vagotomy might precipitate acute inflammation in a previously asymptomatic calculous gall bladder. An additional suggestion is that vagotomy will result in gallstones in the dog.

In man, although there is no real evidence for it, the impression exists that gallstones occur more commonly after vagotomy than in the population at large[249].

There is a large residual volume with resultant stasis, even though gall bladder contraction is normal, after vagotomy. Therefore the vagus is important in maintaining resting tone. Also, the decreased flow and composition of hepatic bile may be an important

predisposing factor in the development of gallstones.

To establish whether vagotomy does in fact predispose to the development of gallstones in man will require more evidence, such as an adequate clinical follow up, and a trial of selective versus truncal vagotomy with this problem as the prime consideration.

(e) Summary:

Vagotomy results in the production of a diminished volume of hepatic bile, and alters its composition and concentration. Vagal stimulation of bile secretion is probably a result of antral gastrin release.

Truncal and selective vagotomy both abolish this to the same extent.

The evidence indicates that the vagus is important in maintaining resting tone of the gall bladder and gastrin plays no part in this.

Gall bladder emptying, mainly under humoral control, does not seem to be greatly influenced by vagotomy. There is some indirect evidence however, that the nerve acts as a mediator. Bile composition is unaffected.

Common bile duct tone apparently depends on vagal integrity, similarly to the gall bladder.

There is some evidence to suggest that vagotomy predisposes to the formation of gallstones and chole-

cystitis in dogs. No evidence exists for this in man, but undoubtedly some predisposing factors to gallstone genesis are a sequel of vagotomy.

IV PANCREAS

(a) Secretion:

Physiological control of exocrine secretion:

This is complex and a detailed account is beyond the scope of this study. Briefly, the response to a meal is divided into cephalic and hormonal phases. The cephalic phase, a response to the thought, smell or taste of food is vagally mediated, and results in the production of a small volume of enzyme-rich juice. Much more important than the cephalic phase, the hormonal phase results from the release of the hormones secretin and pancreozymin from duodenal mucosa. Secretin stimulates the production of a large volume of alkaline juice. Pancreozymin stimulates production of a small volume of enzyme-rich juice, that is, a similar response to direct vagal stimulation.

Hormone release from the duodenum is a response to chemical stimulation. Hydrochloric acid is more powerful for secretin release, while peptones, amino acids and fat are the main stimuli for pancreozymin release (250). The part played by the vagus in this phase is

indirect in that the gastric acid produced will cause duodenal hormone release. There is also a suggestion that the vagus may directly stimulate pancreozymin output. Another factor postulated in this phase is the possible existence of a gastric antral stimulatory hormone, as mechanical distension of the antrum results in pancreatic secretion.

Stimulated responses after vagotomy:

Truncal vagisection abolishes the response of pancreatic secretion to hypoglycaemia in man, dog and cat[251-254] but the importance of this finding is uncertain.

The effect on responsiveness to hormones has been investigated by various authors. Intravenous secretin has been shown to increase, decrease or have no effect on exocrine pancreatic function. Leminger et al.[255] working with dogs showed a diminished response, while others[253,256] showed enhanced responses.

In man, reduced function protagonists were Pfeiffer and his colleagues[252], while Dreiling et al.[251] reported that no change could be discerned. The latter results have been confirmed by others[257,258].

In dogs Routly[253], and Bastable[256] showed that exocrine secretory volume increased after pancreozymin administration. However, enzyme concentrations were

found to be increased or unchanged by each group of workers respectivly.

In man it has been shown by White[257] that little difference in pancreozymin response occurs following vagotomy and drainage. Billroth I gastrectomy with vagotomy resulted in a significant response reduction which suggests that an intact antrum is more important than the vagus.

Responses to a meal after vagotomy were extensively studied by Bastable[256] in dogs before and after truncal section. He measured the post cibal volume, bicarbonate, trypsin and lipase concentrations and found no significant disturbances except for a slight, though significant rise in lipase concentration. Pressure in the pancreatic duct was however found to be much lower. Frederickson and Rune[258] on the other hand, also in dogs, reported that an 85% drop in volume and bicarbonate, and a 57% decrease of protein secretion occurred in response to a meat meal. A cholinergic drug restored the volume and bicarbonate to prevagotomy levels, but not the protein. The result is probably due to a low acid output resulting in a low level of secretin production.

In man Holmquist and Colleen[259] used a tube to sample duodenal contents over the two hour period

immediately following a liquid meal. Trypsin concentrations showed no changes when compared with normal subjects.

Lipase activity has been shown to be significantly reduced[260] with some delay before the peak of activity was reached, when normal subjects were compared with subjects who had undergone vagotomy for duodenal ulcer.

Malabsorption of fat has been shown to definitely occur after vagotomy[261]. Fields and Duthie[260] found that this was accompanied by poor micelle formation, diminished bile acid concentration and reduced lipase activity.

Slightly dminished protein absorption has been reported in dogs[262,263] following truncal vagotomy. Similar experiments in man have failed to confirm these findings[264-266].

Although not entirely responsible, pancreatic vagal denervation seems to play some part in malabsorption after vagotomy.

Comparisons of pancreatic function after selective, as opposed to truncal vagotomy[267] have shown no significant differences. However, McKelvey [220] noted that pancreatic amylase secretion was abolished by truncal but preserved to a certain extent

by the selective operation.

Protein malabsorption was more significant after truncal than selective vagotomy in dogs[262,263].

(b) Histopathology

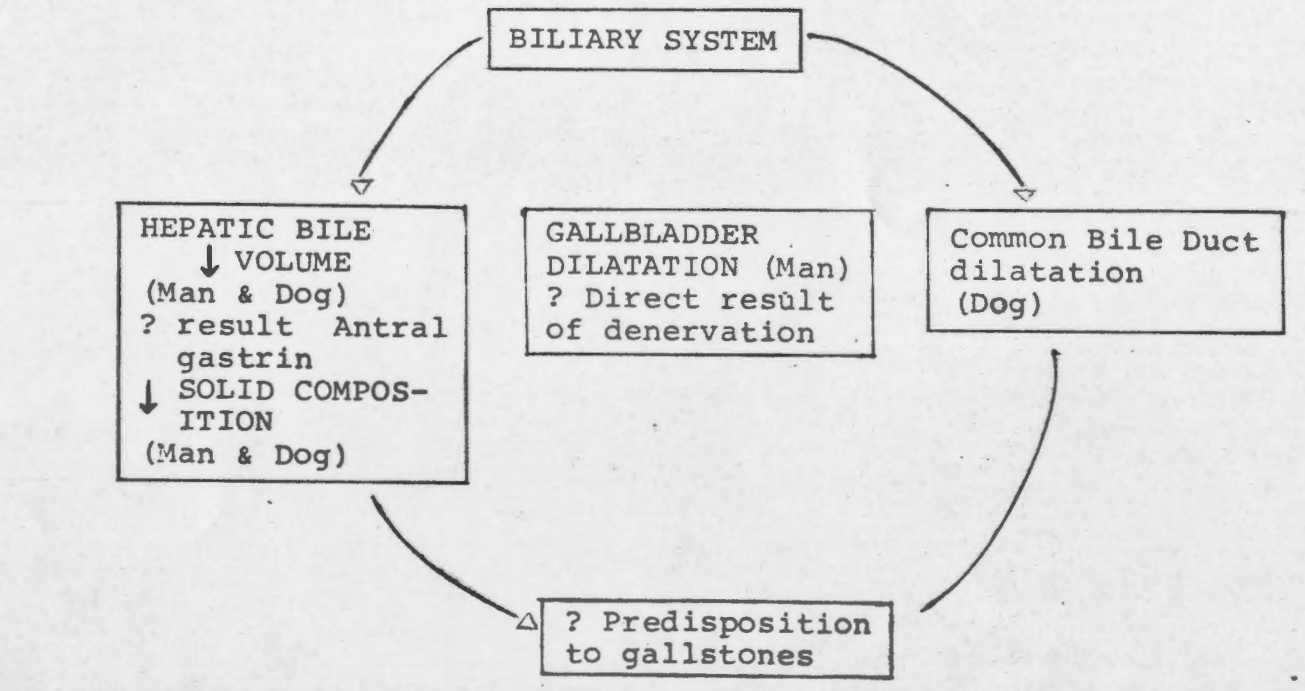
The only report in the literature on a study of histological changes in the pancreas following vagisection has come from Katsumi and his co-workers[268]. Electron microscopy in dogs revealed degenerative changes in the exocrine cells, with distension, vesiculation and vacuolisation of the cisternae of the endoplasmic reticulum. Also noticed was a diminution in the number of secretory granules, swelling and disruption of mitrochondria and the presence of inclusion bodies, while the islet cells appeared quite normal. Light microscopy revealed no obvious pathological changes. The same changes were seen in dogs after Billroth I gastrectomy but the changes were unequivocally more marked if a vagotomy was added to the Billroth I resection. All histological changes returned to normal after about three months. It should be noted that no controls were done, and that the changes may well be a non-specific result of laparotomy.

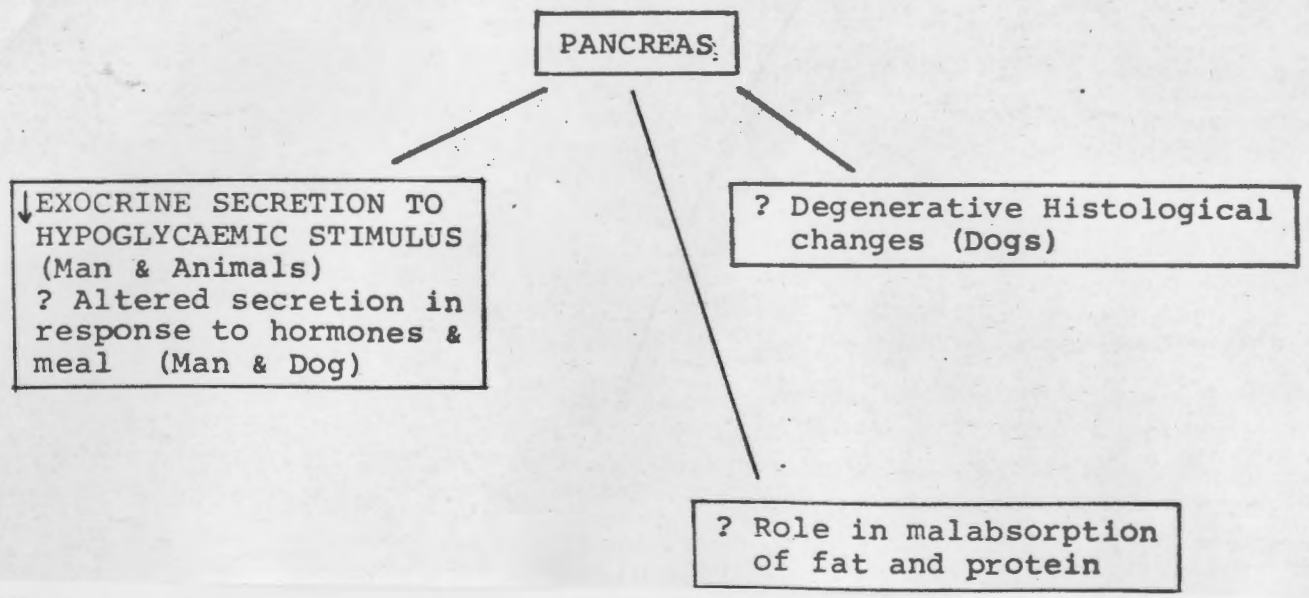
(c) Summary:

The only definite statement that can be made is that vagotomy abolishes the response of the exocrine

FIGURE 9

EFFECTS OF VAGOTOMY





pancreas to hypoglycaemia.

Conflicting reports have been presented regarding the effect of denervation on responses to hormones or a meal, either as regards volume and bicarbonate or enzyme production.

Pancreatic denervation may conceivably contribute to malabsorption which may occur following vagotomy.

Selective vagotomy seems to have no significant advantage over truncal vagisection with regard to effects on the exocrine pancreas.

Histology of the pancreas after vagotomy shows temporary degenerative changes which are possibly non-specific results of trauma.

V SMALL INTESTINE

The small bowel is undoubtedly innervated by the vagus but the precise function of this remains in doubt. Electrical stimulation of the coeliac division results in a massive contraction extending from proximal duodenum to mid transverse colon[269]. Fairly detailed study has been made of motility and histopathology following vagotomy.

(a) Motility:

Motility has been studied by means of radiology, radioisotope tracers, manometry and electrical

activity recordings.

Isaac et al.[270] performed the original radiological study, by barium meal examinations before and at intervals of up to six months after vagotomy. They reported definite changes in the small bowel pattern, namely dilatation, flocculation, and pooling of barium, especially in the duodenum. Also there was a delay in emptying of the small bowel into the caecum. The changes were all less obvious six months postoperatively. Roth and Beamis[271] found little delay in barium transit and it was concluded by some[272] that this phenomenon was the result of slow gastric emptying. The completely opposite view was held by Collins and his colleagues[273], confirmed by others[274], that transit time was more rapid. The only conclusion that can be reached is that a radiological abnormality occurs.

Radioisotopic studies in vagotomized rats[275] showed a 50% decrease in small bowel transit time compared with normal controls.

In man McKelvey and his colleagues[186,187] performed an excellent study on the relationship of gastric emptying to intestinal transit time and diarrhoea after vagotomy. Sixty-five patients, one year

after operation were compared with 20 preoperative duodenal ulcer patients. Eighteen of the post-vagotomy subjects had diarrhoea and 27 were asymptomatic. Gastric emptying time for a liquid milk meal labelled with ^{51}Cr. was measured by the double sampling techniques[188]. An intestinal transit time index was obtained by collecting stools and noting when the first appearance of the isotope occurred. An "index of motility" was recorded by measuring pressure in the rectosigmoid before and after a meal by means of a balloon.

Intestinal transit time and gastric emptying time was considerably more rapid in the group with diarrhoea, as well as among those with increased frequency of motions but without diarrhoea, when compared with the asymptomatic and preoperative groups. The "indices of motility" were also considerably greater in the former groups when a liquid meal was ingested but not with a solid meal. All patients with diarrhoea were thoroughly screened to exclude the presence of malabsorption states. The conclusion reached was that the increased rate of intestinal transit was a result of rapid gastric emptying and that the bowel was unable to handle the rapid flow of liquid. George[276] confirmed increased

gastric emptying time in patients with diarrhoea using similar methods.

By manometric means three types of pressure changes are seen in normal bowel. Rhythmic segmentations, of low amplitude occurring at a rate of about 12 per minute; peristaltic waves of larger amplitude, 30 to 120 seconds long occurring at irregular intervals; and spasms with a rise in baseline pressure lasting for between 4 to 15 minutes and occurring at irregular intervals, can be clearly demonstrated.

In dogs decreased motility was shown by this method[277]. Faik, Grindley and Mann[278] studied exteriorised loops of small bowel, and found that motor activity following the smell and sight of food was lost, and that the response to eating was very much diminished and delayed. Others have been unable to detect any change in dogs with terminal ileostomies after vagotomy.

Roth and Beams[271] recorded pressure patterns with balloons in man, for periods of up to several months postoperatively. Peristaltic waves were found to be less frequent but their amplitude and duration were unchanged. Spasms occurred with greater frequency while tone and segmentation waves were unaffected. No correlation was found in this study between the pattern

of motility and diarrhoea.

Postoperative ileus is prolonged following vagotomy[177] and by the use of a radiotelemetering capsule it was found that truncal vagotomy resulted in a period of postoperative ileus of 10 hours, as opposed to 4 hours after simple laparotomy.

Electrical activity in the small bowel muscle revealed slow waves, possibly the intrinsic electrical activity of the cell (B.E.R.), interspersed with periodic bursts of fast action potentials, associated with visible contraction[279]. The exact relationship of these recordings to pressure changes have not been demonstrated. There is a definite gradient of B.E.R. from upper to lower small bowel. Fifteen to 21 waves per minute occur in the duodenum, with 7 to 11 per minute being recorded in the terminal ileum. Atropine has little effect on B.E.R. and therefore it is probably myogenic and not extrinsically innervated. Binker and his colleagues[280] were able to discern a small reduction in slow waves after atropine administration, or vagotomy and suggest some vagal influence. However, this is probably not of great relevance to postvagotomy sequelae. The effect of vagal denervation on fast action potentials has yet to be studied.

No study has been reported as yet comparing small

bowel motility after selective vagotomy with that following truncal nerve section.

(b) Histopathology

Electron microscopic studies by Elliot et al.[281] on the jejunal epithelium of dogs before and up to one year after vagisection showed no changes in the mucosal cells, microvilli, mitochondria, Golgi apparatus, endoplasmic reticulum or terminal web area. Light microscopic studies gave similar results in man[263] and the rat.

Ballinger[283-286] reported diffuse inflammation followed by villus atrophy in the mid-ileum of vagotomized dogs. Changes were fully developed within 3 weeks of operation but had returned to normal within 20 weeks. Similar changes were seen in the jejunum of a patient at two weeks post vagotomy.

The suggestion was made that two types of mucosal change may occur. Firstly an increased intestinal bacterial flora causes an inflammatory response or secondly, villus atrophy occurs when the hepatic or coeliac branches of the vagus are sectioned, with no change in bacterial count. The latter is attributed to a diminution in intestinal blood flow.

The same authors[284] investigated changes in local blood flow after vagisection. In dogs mesenteric

flow was diminished by 42% following truncal vagotomy; 17% after coeliac vagotomy and 18% if the hepatic branch was cut. The ileum was shown to be more sensitive to ischaemia than the jejunum[287] and this might possibly explain the ileal changes seen by Ballinger which were not apparent in the jejunum at that stage. Delaney[288] however found no changes in canine small bowel blood flow 4 to 6 weeks after section of the vagus.

In a further attempt to elucidate the histological changes Silen et al.[289] examined epithelial cell turnover. Dividing epithelial cells in the bases of small intestinal crypts of dogs were labelled with tritiated thymidine. Increased rates of cell division were detected by increased rates of labelling, which was detected by means of a scanner. Six weeks after vagotomy there was increased labelling of cells in the duodenum and jejunum as compared to preoperative values. No changes were found in the ileum or colon and therefore vagotomy results in an increased rate of division of jejunal cells. The authors suggest that a rapid rate of degeneration occurs at a faster rate than replacement, so that the changes of degeneration are seen.

The significance of these transient changes described are uncertain. They are possibly related to the occurrence of transient postoperative diarrhoea, but no changes in intestinal epithelium were found by Bejar and his co-workers[290] who specifically studied a group of patients with this complaint.

Alterations in histochemistry have been demonstrated after vagal nerve section[285]. Succinicdehydrogenase, acid phosphatase, alkaline phosphatase and esterase were all reduced in the dog, but returned to normal within 11 weeks of operation.

Garcia-Paredes and Truelove[291] found normal small bowel disaccharidase activity in postvagotomy and pyloroplasty patients with diarrhoea.

(c) Summary:

Motility changes do occur after vagotomy as evidenced by radiological, manometric and electrical means but the precise interpretation of the changes remains doubtful. Most workers have reported patterns suggestive of diminished small bowel motility.

Some correlation may exist between postvagotomy diarrhoea and the rate of gastric emptying. Possibly the bowel is unable to absorb rapidly transported liquids and it is postulated that the latter effect may be a result of vagotomy.

Transient degenerative changes have been demonstrated in the epithelium of the mid-ileum, either the result of decreased blood flow or altered bacterial flora which causes inflammatory changes.

Some enzyme systems have been shown to be transiently altered in the dog as a result of vagotomy, but there are no apparent long-term changes in man.

There is as yet no study comparing the effects of truncal and selective vagotomy per se on small bowel motility and histopathology.

VI DIGESTION AND ABSORPTION

Having considered the effects of the vagotomy operations on the stomach, biliary system, pancreas and small bowel, attention can now be given to the effects on digestion and absorption.

(a) Fat:

Much work has been done on this topic and various methods have been used to assess fat malabsorption.

Intake versus output balance studies constitute the commonest method used.

Fox and Grimson[292] first studied 9 patients after vagotomy and found that all had steatorrhoea. Many others confirmed their findings[261,263,266,293-295], but some workers reported no difference in the incidence of steatorrhoea between patients with vagi-

section alone and those with an accompanying drainage procedure[292,293].

Others found that excessive faecal fat loss did not occur in patients with vagotomy alone[294]. Payne et al.[296] reported identical incidences of this complication when comparing the effects of pyloroplasty and gastroenterostomy in the vagotomized patient.

In all studies to date[264-266] there appears to be no significant difference when selective and truncal vagotomy are compared.

Identical studies have been done by various groups on dogs comparing vagotomy with other types of gastric operation[297-299]. All came to similar conclusions, namely that vagisection alone did not lead to steatorrhoea but subtotal and total gastrectomy caused macroscopically apparent faecal fat loss. The steatorrhoea of vagotomy and gastroenterostomy was significantly increased if subtotal gastrectomy was performed[298].

Wastell[295] found that pyloroplasty alone caused steatorrhoea, and that adding vagotomy to this increased the fat excretion. He found no appreciable difference between truncal and selective vagotomy.

Plasma turbidity increase following ingestion of

a standard (50G) fat meal was used to measure faecal fat loss by Williams and Irvine[266]. In patients with total or selective vagotomy and drainage, as well as patients with gastroenterostomy alone, the increase in lipaemia following this meal was significantly less than normal controls.

Multiple small bowel samples were taken by Fields and Duthie[260], at four different levels after a test meal containing a standard quantity of fat, and using polyethylene glycol as indicator. They compared results in normal and vagotomized patients. Samples were tested for concentration of bile acids, lipase, total fat and its hydrolytic products and pH. Definite decrease in bile acids and pancreatic lipase was found in the upper intestine. Increased quantities of intraluminal fat, with faulty micelle formation was apparent in the lower intestine. Gastroenterostomy caused more changes of the above nature than pyloroplasty.

Radioactive tracer substances have been used in animals to study fat absorption. Tucker and co-workers[131] fed Iodine-glyceryltrinitrate to dogs with selective/truncal vagotomy and pyloroplasty. There was no difference found when vagotomy alone was compared with pyloroplasty alone. It was found by

another group[263] that pyloroplasty with or without vagotomy increased the absorption rate but this was not statistically significant when compared with normal controls. Using 14 carbon-sodium octonoate Golding[300] found decreased fat absorption after vagotomy alone. Addition of pyloroplasty further suppressed fat absorption.

Undoubtedly steatorrhoea occurs with vagotomy and drainage operations. The precise mechanism remains uncertain, and the relative parts played by the effect of denervation on hepatic bile flow (diminished), or pancreatic lipase secretion (controversial) or histopathological changes of small bowel epithelium have yet to be elucidated. Evidence for the part played by the drainage procedure is conflicting, but it probably has some influence on fat absorption after these operations. The amount of fat lost, however, is probably not enough to cause major nutritional problems.

(b) Nitrogen:

Excessive faecal nitrogen losses after gastrectomy are well documented. Javid[298] measured stool nitrogen after total vagotomy in dogs and reported that vagotomy alone resulted in abnormal excretion. Vagotomy, when superimposed on subtotal gastrectomy

significantly aggravated the loss caused by the latter operation alone.

Two independent groups[262,300] fed dogs with ^{131}I labelled protein and measured peripheral blood radioactivity. There was a slight but insignificant impairment of protein absorption in dogs with pyloroplasty alone or vagotomy and pyloroplasty. Faecal nitrogen measurement in 72 hour collections in dogs eating standard laboratory diets showed a significantly increased amount in animals with truncal vagotomy when compared with those that had been selectively denervated.

Cox[301] reported on studies in patients with vagotomy and gastroenterostomy and he could find no significant increase in daily nitrogen loss compared with controls.

The overall conclusion reached is that some slight alteration in intestinal protein handling probably occurs but the relative parts played by gastric or pancreatic denervation again must be elucidated.

(c) Carbohydrate:

D-xylose absorption in dogs showed no differences between selective and truncal vagotomy or pyloroplasty alone[262,263] or in combination.

Earlier workers[302], however, showed enhanced absorption.

Williams and Irvine[266] found abnormal lactose tolerance in patients with total and selective vagotomy. Some of these patients had diarrhoea however, which may possibly have been due to lactose deficiency.

(d) Haemopoeietic factors:

Vitamin B_{12}

Four studies have been published to date of serum vitamin B_{12} values after vagotomy and drainage operations[303-306] and generally speaking there is a very small percentage of patients with subnormal values. Values were found to be significantly lower after gastroenterostomy than pyloroplasty[303,306].

Absorption studies in the dog[307] showed reduced uptake of ^{60}Cobalt B_{12} after vagotomy and pyloroplasty.

Cox et al.[261] showed in patients with vagotomy and gastroenterostomy that absorption was impaired (using the Schilling test). Adams and his co-workers[308] measured intrinsic factor secretion pre- and postvagotomy and found that after operation there was approximately 43% decrease in histamine stimulated intrinsic factor secretion.

There is a deficit in vitamin B_{12} absorption after vagotomy and drainage procedures due to reduced intrinsic factor secretion, and aggravated by a blind loop syndrome produced by gastroenterostomy. No definite evidence has been produced to elucidate the part played by vagotomy per se on small bowel with regard to this particular problem. Even in the presence of this mild vitamin B_{12} malabsorption no reports of megaloblastic anaemia, purely attributable to vagotomy and drainage have as yet emerged.

Serum folic acid studies in these patients have in turn been reported as unaltered[303,305] and slightly below normal levels (15% of males and 18% of females studied)[306]. In the latter study gastroenterostomy patients had higher average levels, and blind loop vitamin synthesis was postulated.

Iron:

Low serum iron levels have been found by several workers after vagotomy. The range of reduction after vagotomy and drainage procedures lay between 6% and 21% in follow up studies over 4 to 10 years[261,304-306].

Percentage saturation of total iron binding capacity (T.I.B.C.) was found to be lower as well after these operations. Cox and his colleagues[303] compared

patients 8 years after vagotomy and gastroenterostomy with patients awaiting surgery for duodenal ulcer, and they found a percentage saturation of 35.1 in the control group, while those who had had operations returned a mean value of 28.5 (statistically significant to $p < 0.02$). This confirmed the original report by Hopkinson[304] of 10% low values after vagotomy and drainage. Wastell[306] compared the same parameters in patients who had undergone vagotomy and either pyloroplasty or gastroenterostomy. Serum iron values were significantly higher after pyloroplasty than gastroenterostomy in both sexes. Percentage saturation was lower after gastroenterostomy in males and females, while the T.I.B.C. showed no significant difference.

Iron absorption was studied using a whole body counter (^{59}Fe) before and three months after vagotomy [309]. A statistically significant reduction in absorption when gastroenterostomy was used for drainage emerged (38.4%), but the reduction found in the vagotomy and pyloroplasty group was not statistically significant (25.9%). Patients undergoing minor operations who were used as controls showed a 7.5% reduction.

It would seem that iron malabsorption results

from vagotomy and drainage, especially when gastric drainage is effected via an enterostomy. The precise part played by the vagotomy is uncertain.

(e) Calcium and phosphorus:

No study on absorption of calcium and phosphorus following the vagotomy operations has, to date, appeared in the literature.

(f) Summary and conclusions regarding postvagotomy malabsorption:

Steatorrhoea definitely occurs after vagotomy and drainage, but there is conflicting evidence about the relative parts played by vagal denervation as opposed to the drainage procedure. Also the relative importance of changes recorded in pancreatic and biliary secretion is in doubt.

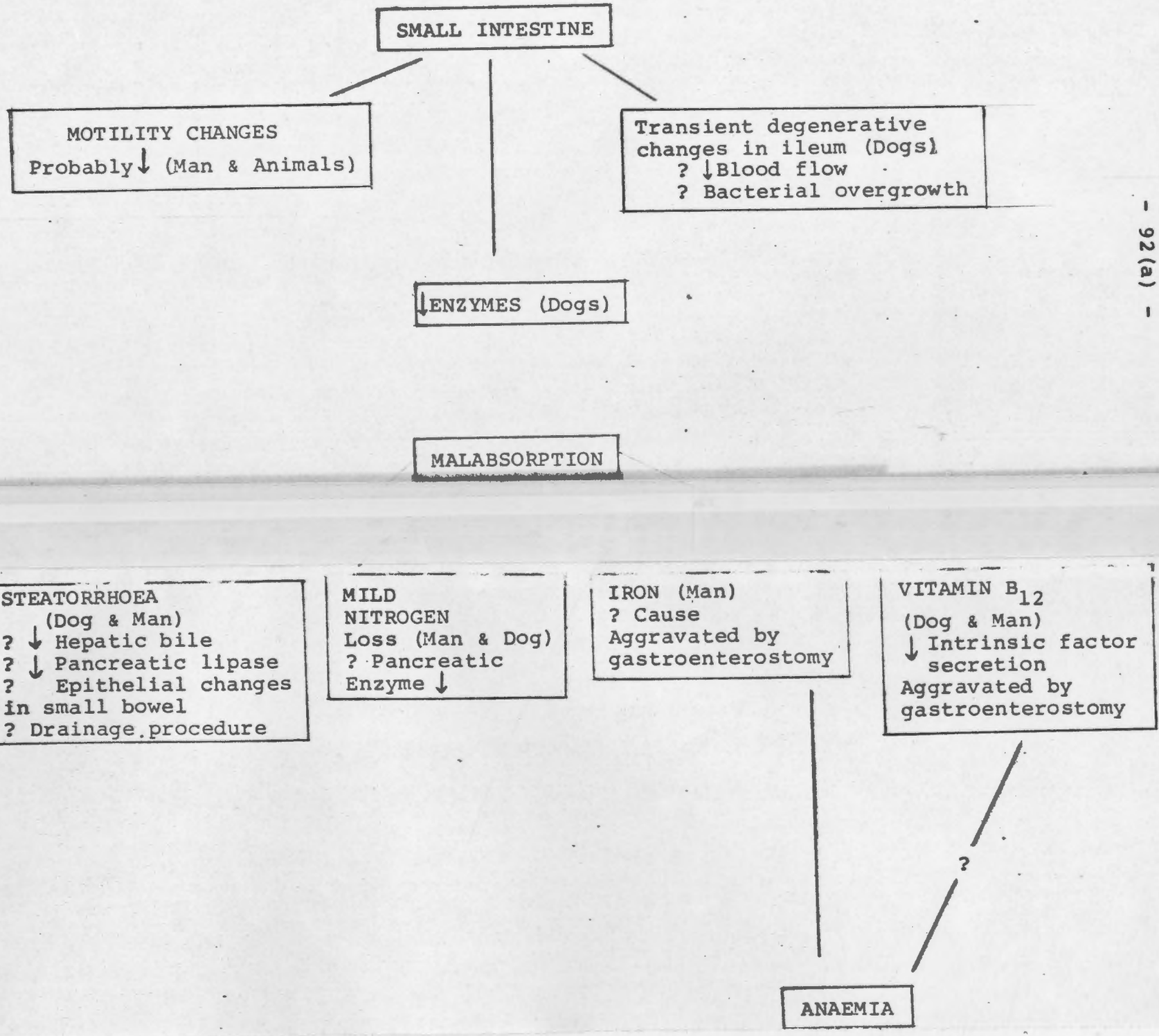
Some alteration in the handling of ingested protein results, but again the relative roles of the various factors remains to be elucidated.

Carbohydrate absorption appears to be unaffected. Vitamin B_{12} malabsorption occurs, as vagotomy causes a reduction in intrinsic factor production by the stomach. Probable blind loop syndrome following gastroenterostomy seems to aggravate this.

Iron absorption is also impaired, again aggravated by gastroenterostomy.

FIGURE 16

EFFECTS OF VAGOTOMY



Calcium and phosphorus absorption has not been investigated to date.

The overall conclusion is that the malabsorption that occurs is probably not of sufficient degree to give rise to significant sequelae.

VII METABOLIC AND SYSTEMIC EFFECTS

Presentation of data related to these effects is beyond the scope of this study. For the sake of completeness a brief review is included on findings regarding haematological changes and disturbances of calcium and phosphorus metabolism that may follow vagotomy.

(a) Anaemia:

Most studies indicate that anaemia occurs after vagotomy, however, it is important to exclude other causes such as haemorrhoids, menorrhagia, pregnancy, etc.

Pulvertaft et al.[310], limiting their study to males, compared 252 patients who had undergone vagotomy and gastroenterostomy (131 patients), polya antrectomy (63 patients), pyloroplasty (68 patients). A 5 year follow up was done on the antrectomy and gastroenterostomy group, while the pyloroplasty patients were seen for 2 years. The mean haemoglobin levels on the former group were assessed before

operation and at yearly intervals thereafter. Values for all groups (including vagotomy and pyloroplasty) fell appreciably during the first year, but then continued to fall at a slower rate during the next 4 years. This was slightly more marked after antrectomy, but the difference was very small. The drop during the first year for vagotomy and antrectomy was 9.8% vagotomy and gastroenterostomy 4.0% and for vagotomy and pyloroplasty 6.2%. Values were statistically significant for antrectomy and pyloroplasty ($p < 0.01$). During the period between 1 year and 5 years, the mean haemoglobin dropped 4.3% after antrectomy and 4.0% after gastroenterostomy (pyloroplasty had no 5 year follow up).

Complicating the issue was the fact that a certain percentage of the patients were treated for anaemia with oral iron. Details regarding precise amounts prescribed and ingested were impossible to obtain. Therefore, the proportions of men developing anaemia (haemoglobin less than 12 g.%) at any time within 5 years of operation were 22% of those with gastroenterostomy and 39% of those with antrectomy. This difference is not statistically significant, but one may conclude that antrectomy fairly commonly results in anaemia.

After 2 years 12% of the antrectomy patients, 5% of those with gastroenterostomy and none of the pyloroplasty group were anaemic.

Wastell[306] reported a 10 year follow up of vagotomy and drainage operations. It was found that the overall mean haemoglobin level was below normal values. Males had a significantly lower average haemoglobin after gastroenterostomy than after pyloroplasty. In females the difference, although not statistically significant was still apparent.

The overall incidence reported was a 10% anaemia rate for vagotomy and pyloroplasty, while 40% of the vagotomy and gastroenterostomy group were anaemic.

In both series the picture after investigation was one of iron deficiency, and no cases of megaloblastic anaemia, purely attributable to vagotomy and drainage, have as yet been reported. The aetiology of the iron deficiency state as discussed in the previous section is probably due to malabsorption.

Comparison of gastrectomy with vagotomy:

Gastrectomy is not infrequently followed by a degree of anaemia. Cox et al.[303] compared prospectively polya gastrectomy with truncal vagotomy and gastroenterostomy. After 8 years or more postoperatively the vagotomy and drainage operation

emerged with a distinct advantage. In comparing haemoglobin; packed cell volume; percentage saturation of total iron binding capacity and serum vitamin B_{12} a significant difference was found. Mean corpscular haemoglobin concentration; total iron binding capacity, serum folate and iron levels failed to show a significant difference.

Comparison between patients with vagotomy alone and subtotal gastrectomy showed that the mean haemoglobins and serum vitamin B_{12} were higher in the former group.

(b) Bone metabolism:

Osteomalacia occurs 8 to 10 years after gastrectomy, but there have to date been only two long-term studies of calcium metabolism on patients with vagotomy and drainage.

Wastell[306] performed serum calcium, phosphorus and alkaline phosphatase estimations on patients 10 years after their vagotomy and drainage operations, and found only one case out of 119 with decreased calcium and elevated phosphorus and alkaline phosphatase values. Wheldon[312], after a 15 year follow up of 255 patients, who had similar screening tests, found no evidence of osteomalacia in any patients. In a one to 5 year follow up of 266 patients with

vagotomy and gastroenterostomy Morgan and Pulvertaft [313] produced similar results. However, it should be mentioned that osteomalacia has been reported "many years" after simple gastroenterostomy [314,315].

There is a widely varying incidence reported of postgastrectomy metabolic bone disease. Williams [316] produced a figure of 20% while others [313] could find an incidence of only 0.4% in men and 4.5% in women.

The disease may result from either dietary deficiency or inadequate absorption of vitamin D. The loss of weight following gastrectomy is probably due to inadequate food intake [313], and calcium, with associated vitamin D ingestion is reduced in excess of other dietary constituents. This was found to be due to diminished intake of milk and milk products and eating fewer cakes (containing butter etc.). After vagotomy and drainage 0.6% of males and 2.1% of females had inadequate vitamin D intake. The proportion of postgastrectomy patients in the same category was significantly higher again, with a female predominance.

Moderate degrees of steatorrhoea are common after gastrectomy, and osteomalacia is attributed to this. [317-319]. Therefore, in view of the documented faecal

fat loss after vagotomy and drainage this complication should occur.

The incidence of osteoporosis after vagotomy and drainage operations has been assessed in only one published study to date[313] where normal controls were compared with patients who had undergone gastrectomy or vagotomy and drainage. The degree of bone disease was assessed by measuring the cortical width at the midpoint of the second right metacarpal.

No difference in incidence between patients over sixty years of age or under sixty was found in the control group. Similarly there was no significant difference between the three operation groups for patients under sixty. Over sixty years of age, there was no significant difference between controls (preoperative duodenal ulcer patients) and gastrectomy patients. The difference between controls and vagotomy and drainage patients was not significant. Attention must be drawn to the fact that the latter group has only been followed up for 5 years, and that the complication could still probably occur in the future.

Aetiology and pathogenesis of osteoporosis following gastrectomy has been attributed to diminished intake and absorption of nutrients with varying

emphasis[320-322], but there is little information as yet on vagotomy and drainage.

Morgan and Pulvertaft[313] studied the relationship of pre- and postoperative nutritional status to the problem. Using the ratio of total body fat to total body weight, expressed as a percentage, they compared nutritional status in the three operation groups with controls. They divided the postoperative patients into three groups, namely those who had maintained normal nutrition, those with slightly improved nutritional status and those with poor nutrition. The general distribution curve of the controls was similar to that of the vagotomy and drainage group while the partial gastrectomy group yielded a higher proportion with impaired nutrition. In all age groups there is a higher incidence of osteoporosis in patients with poorer nutritional status compared to adequately nourished patients. Whether this is due to generally poor nutrition or whether vitamin D deficiency plays the major part remains uncertain. Although the follow up of vagotomy and drainage patients is of less than 5 years duration, the figure suggests that the incidence of osteoporosis will be similar to that in the population at large.

(c) Summary and conclusions:

Anaemia occurs after the vagotomy operations. Antrectomy results in an incidence of approximately 40% while following vagotomy and drainage 20% of patients are anaemic.

When pyloroplasty is used as a drainage procedure, it seems to have an advantage over gastroenterostomy from this point of view.

The anaemia is always of an iron deficient nature, probably a result of poor absorption. Megaloblastic anaemia has yet to be reported.

Although the prerequistes for development of osteomalacia are present in patients who have had vagotomy and drainage, namely diminished intake and absorption of vitamin D, no cases have as yet been reported. The possibility exists that this complication may yet be found to occur with time.

Osteoporosis is not a problem in the short-term. This is due probably to the better standard of nutrition maintained by vagotomy patients compared to subtotal gastrectomy patients. Again, longer follow up may show a rising incidence.

VIII SELECTIVE AND TRUNCAL VAGOTOMY - COMPARISON OF EFFECTS

In an earlier chapter a brief description of the

anatomy pertaining to selective and truncal vagotomy has been presented, as well as the basic principles regarding technique. The most recent development in this field is the advocation of "highly selective" nerve section where an attempt is made to preserve innervation of the antrum, and thus the normal emptying mechanisms, while completely denervating the parietal cell mass[323-325]. So far all authors who have performed this type of vagotomy have done so without an accompanying drainage procedure, and all claim excellent results. However, it must be pointed out that the patient numbers are small and that the follow up to date is very short - a matter of months.

The preceding section has dealt in considerable detail with the pathophysiological effects of vagotomy on the various intra-abdominal viscera. In the following brief discussion the conclusions reached on comparing selective and truncal vagotomy will be presented.

No study comparing the effects of these operations on cardio-oesophageal function has been published to date.

Selective vagotomy per se may provide some theorectical advantages in preventing cardio-oesophageal reflux by preserving a few of the cardio-esophageal

branches, as only the small nerve filaments around the distal oesophagus are cleared at operation. This is in contradistinction to the truncal procedure where considerably more dissection, manipulation and hence division of fine neural twigs presumably occurs. As mentioned in the previous section, cardio-oesophageal reflux most likely results from paralysis of the intrinsic sphincteric mechanism[146,150].

Dysphagia, which is almost certainly a sequel of manipulation of the distal oesophagus, whether by a spastic mechanism or due to haematoma, oedema etc.[163-165] will probably occur to the same extent after the selective operation as after truncal vagotomy, but the trauma is possibly of a slightly lesser degree following the former.

The consensus regarding gastric motility is that standard selective holds no advantages over truncal vagotomy. The superselective vagotomists claim normal gastric motility and emptying without resorting to a drainage procedure, but only patients without duodenal stenosis were submitted to this operation. Gastric secretion in man is apparently affected to the same extent by truncal, standard selective and highly selective denervation[205,323,324,327]. Strong argument against the latter operation is the fact that

the antrum remains innervated and can therefore secrete gastrin in response to local stimulation. Johnston[323] measured the acid output in response to a meal of meat extract, and compared the maximal acid output (M.A.O.) with that produced by pentagastrin stimulation. Preoperatively, meat extract instillation resulted in an acid output equivalent to 55% of the M.A.O., which dropped to a figure of 20% after operation. Similarly, local acetylcholine stimulation produced figures of 27% and 3% of the M.A.O. pre- and postoperatively respectively. This served to demonstrate that whatever gastrin was being produced was stimulating cells with a diminished capacity to respond. The authors also state that the acid produced will inhibit gastrin production to a large extent. In addition, the preservation of normal antral motility and gastric emptying would theoretically not stimulate the production of excessive amounts of the hormone by stasis of gastric content.

There is fairly good documentation for truncal vagotomy causing an alteration in hepatic bile composition and flow[219,221,224,225], as well as dilatation of the gall bladder[231,234] and extrahepatic duct systems[232]. Conflicting reports have been published as to whether selective vagisection

prevents these changes[223-225,232,264,266]. However, the major practical issue, as yet unresolved, is whether the vagotomy operations predispose to gallstones and whether selective nerve section will provide protection against this.

Comparisons of exocrine pancreatic function in both vagotomy groups have shown no significant difference[251,257,328].

Protein and fat malabsorption studies, which reflect to some degree pancreatic function, have all been shown to yield identical results after either operation in man[260,264,266].

Changes in pancreatic function after vagotomy are however probably not very important.

Diarrhoea is generally regarded as being a major complication of vagotomy operations, and much of the interest centred around the development of the selective procedures has been in whether this symptom can be prevented by preserving small bowel innervation.

Some authors[266,329-332] report a significantly lower incidence in the selectively vagotomized group while others[163,333] report no difference from the truncal group.

Research into effects of vagal denervation on the small bowel again provides conflicting evidence regarding

both motility[177,186-188,270-280] and histological changes[263,281-286]. There is as yet no published study comparing the changes found in the two vagotomy groups. Most workers will agree that the changes are not gross and therefore probably not permanent.

Digestion and absorption of fat, protein and carbohydrate[262-266,291,295,300,326] is probably affected to the same degree after both procedures. Vitamin B_{12} and iron absorption[303,306-309], probably impaired by truncal denervation has never been assessed on the selective vagotomy patient, but there is unlikely to be any significant difference.

Iron deficiency anaemia[303,306,310,311], although it occurs after the total vagotomy and drainage operations, is seldom a problem. Similarly, although theoretically mechanisms exist for development of metabolic bone disease no cases have yet been reported[306,312-322]. Selective vagotomy will almost certainly not influence the issue regarding metabolic sequelae.

From the purely pathophysiological point of view, all the experimental evidence is confusing when the selective and truncal operations are compared. It would seem that in general standard selective vagotomy has no distinct advantage over the truncal procedure.

The point to make with regard to the effects of vagal denervation on the digestive organs, is that this relatively simple procedure, based on sound physiological principles as far as reduction of gastric acid secretion goes, has a tremendously wide range of unwanted effects. Although the clinical sequelae of the vagotomy operations have been well documented, the precise aetiopathogenesis of these is still far from clear and much of the significance of the foregoing experimental evidence has yet to be elucidated.

CHAPTER 3

EVOLUTION OF SURGERY FOR PEPTIC ULCER[335]

Having completed an account of the applied anatomy and physiology of the stomach and duodenum as well as a fairly detailed discussion of the effect on gastric physiology of the more modern methods of surgical treatment, the introductory section will be completed with a brief historical outline of the evolution of surgery for peptic ulcer. From the time of the earliest successful attempts at gastric surgery it is remarkable to note that the entire evolution has occurred over a period of approximately eighty years.

I DRAINAGE PROCEDURES

(a) Pyloroplasty:

Pyloroplasty was initially performed by Heinecke in 1866, and consisted of a longitudinal incision through all layers of the gastroduodenal wall across the pylorus, which was then closed transversely. Mickulicz described an identical procedure in 1888 and it has become known as the Heinecke-Mickulicz pyloroplasty.

Multiple modifications soon followed, including excision of a window of tissue bearing the ulcer[336].

Horseley (1919)[337] tried a similar manouvre, but advocated suturing only through the seromuscular coat on the gastric side of the incision.

Pyloromyotomy, described by Ramstedt in 1912, consists of simple longitudinal division of the pylorus, allowing full protrusion of the mucous membrane. Originally employed in the treatment of congenital hypertrophic pyloric stenosis it is also used today by many surgeons to facilitate drainage in association with oesophago-gastrectomy.

Jaboulay (1892) devised a gastroduodenostomy, with side to side anastomosis of the second part of the duodenum to the distal stomach. Finney's modification in 1902[338] consisted of a horseshoe-shaped incision extending across the distal part of the stomach and into the first and second parts of the duodenum.

As originally practised, pyloroplasty was used mainly in the treatment of congenital hypertrophic pyloric stenosis and in 1947, with the advent of clinical use of vagotomy in the treatment of duodenal ulcer, Weinberg (1947)[339] suggested a modification of the original work of Heinecke. He advocated using only a single layer of full thickness through and through silk sutures for closure, instead of the original multilayered technique, thus reducing the

liklihood of duodenal stenosis at the site.

Since Weinberg's description, numerous surgeons have described various techniques which, it is claimed, obviate the danger of "dog ear" formation and thus leaks from the pyloroplasty site, and also the liklihood of duodenal stenosis due to tissue invagination into the lumen. Moschel (1958)[340] described a V-Y plasty, while Wangensteen in the same year removed his tissue wedge without opening the mucosa. The most recent innovation is that described by Ballinger (1966)[341], of a serosal patch pyloroplasty. This constitutes a loop of proximal jejunum being laid over the open pylorplasty wound and sutured to its edges with interrupted or continuous silk.

Pyloroplasty per se has never been used in the treatment of duodenal ulcer but has become the drainage procedure of choice when vagotomy is performed. In spite of the tremendous amount of ingenuity and energy that has gone into trying to "improve" the procedure, the original Heinecke-Mickulicz operation, with a minor modification by Weinberg remains the technique most widely used in modern practice.

(b) Gastrojejunostomy:

Anton Wölfler, assistant to Billroth, performed the first gastrojejunostomy in September 1881. This

was done as palliative bypass procedure for an irresectable pyloric tumour, and the anastomosis was placed anterior to the colon on the anterior stomach wall. Posterior gastrojejunostomy was first done by Courvoisier two years later and the loop was brought up in a retrocolic position.

It was soon realised by these pioneer surgeons that vomiting frequently complicated the procedure and numerous innovations were suggested to counter the symptom. This included isoperistaltic anastomosis instead of the original antiperistaltic procedure, and also more dependent placement of the jejunal stoma.

Then attempts were made to drain duodenal contents into the jejunum distal to the stoma. Lauenstein (1891) was the first to suggest a bypass procedure between the afferent loop of jejunum and the distal jejunum. Jaboulay followed with a duodenojejunostomy a year later (duodenum to efferent jejunum), but Braun in 1892 evolved the most widely used bypass in the form of an enteroanastomosis between the two loops at a point equidistant from the gastrojejunostomy stoma. Roux (1897) popularised his "en-Y" anastomosis in which the jejunum was transected and the distal end anastomosed to the anterior wall

of the stomach, in front of the transverse colon, and the proximal end anastomosed with the side of the jejunum at a convenient point distal to the gastric anastomosis.

It was soon learned that these latter procedures resulted in gastrojejunal ulceration due to diversion of alkaline juice, first reported by Braun in 1899, and the length of the proximal jejunal loop became the focus of attention. There was a variance of opinion regarding optimum length, and Mickulicz recommended 20 inches for the posterior anastomoses. W.J. Mayo cited figures of 14 and 10 inches respectively. In 1900 Petersen, an assistant to Czerny, pointed out that the anastomosis was usually sited at a much lower level than the duodenojejunal flexure and attributed the low incidence of bilious vomiting in Czerny's patients to the use of a posterior "no loop" technique i.e. siting the ostium at a point close to the D-J flexure thus preventing the formation of a long loop between these two fixed points. This became common practice and was adopted by Mickulicz. W.J. Mayo in America and Moynihan in Britain popularized this principle, which has stood the test of time, in the English-speaking world.

The complication of internal bowel prolapse was overcome by the innovation of Meyer, who sutured the edges of the opening in transverse mesocolon to stomach wall when performing posterior gastro-jejunostomy.

Gastroenterostomy was originally practised to overcome malignant pyloric obstruction. Ludwick Rydgier in Poland (1884) and Doyen in France (1893) were the first surgeons to treat stenosis secondary to duodenal ulceration in this manner. Initial good results led to the operation becoming standard treatment for all duodenal ulcers and was used extensively by men of the calibre of W.J. Mayo and Moyinhan.

As time passed, a high peptic ulcer recurrence rate was noted and the operation fell into disrepute. Zubiran (1952)[342] investigated canine gastric acid secretion following gastrojejunostomy. He found a 31 to 140 percent increase in Heidenhain pouch secretion when the stoma was situated in the gastric body or fundus. If the stoma was placed close to the pylorus no increase in acid secretion occurred. The results have been confirmed by others and the general consensus is that gastrojejunal anastomosis, under certain circumstances will increase gastric acid secretion[343,344]. This hypersecretion is abolished

by antrectomy. With present day knowledge of antral gastrin production this is hardly surprising. The effects are probably due to antral stimulation whether by stasis, draining away of inhibitory acid gastric juice, or circus movement of gastric contents through the duodenum into the stomach. The latter is aggravated by the alkalinisation caused by the passage of pancreatico-biliary secretion.

Exclusion of duodenal inhibitory mechanisms or overstimulation of bowel stimulatory mechanisms may also play a part.

II GASTRIC RESECTIONS

Partial gastrectomy was initially performed in the treatment of neoplasms and ulcers of the stomach. It was only during the period 1914-18 that surgeons began treating duodenal ulcers in this way.

(a) Billroth I:

Gastrectomy with end to end gastroduodenal anastomosis had been successfully performed on dogs by Karl Theodore Merrem in 1810. Gussenbauer and Von Winwarter in 1874, followed by Kaiser and Czerny 4 years later, all assistants to Billroth, repeated the experiments.

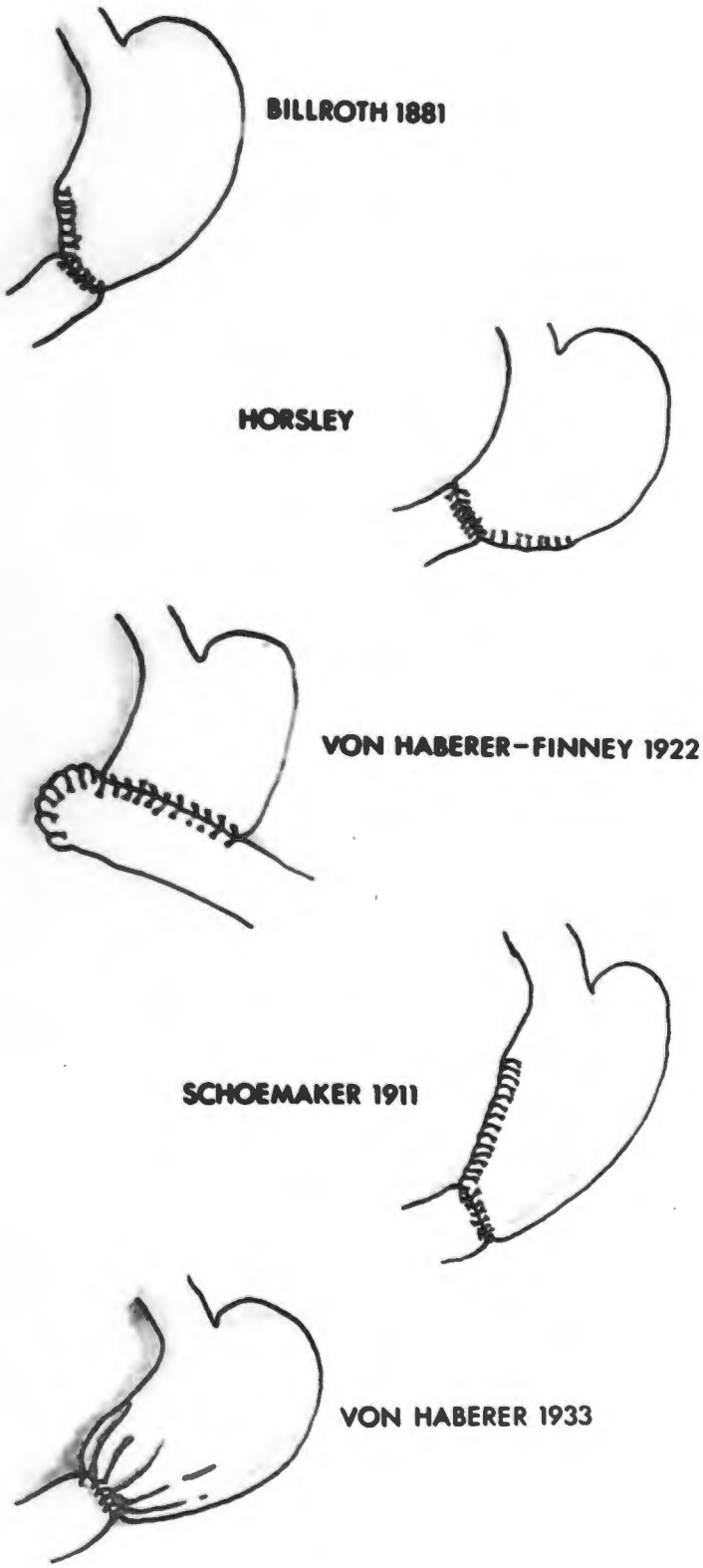
April 1879, saw the first attempt at pylorectomy, performed by Péan of Paris on a human, but the patient

died five days later. A year later Rydgier reported a similar unsuccessful operation. Theodore Billroth in January 1881, is accredited with the first successful pylorectomy for a carcinoma in that region. He is thus fittingly hailed as the father of gastric surgery[345,346].

The major problem encountered at this stage was leakage from the site of anastomosis, where this joined the site of closure of the lesser curvature, and modifications followed in an attempt to prevent this. Kocher (1891) completely closed the gastric stump and performed end to side anastomosis of duodenum to posterior gastric wall. The most important contribution came from Schoemaker in 1911, who advocated oblique resection down the lesser curve, thus removing the latter. Once this was closed the gastric remnant had a tubular configuration, with a bore at its distal end similar to that of the transected duodenum. Von Haberer in 1933 used the entire circumference of the gastric remnant and narrowed it down by using several layers of interrupted mattress sutures.

Technical problems in performing gastroduodenal anastomosis are posed by duodenal scarring with stenosis. Von Haberer (1922) and Finney (1923)

FIG. 11 EVOLUTION OF THE BILLROTH I RECONSTRUCTION



described a technique of end to side reconstruction in which the duodenal end was closed off and the full circumference of the transected stomach anastomosed to the side of the proximal duodenum.

Most modern surgeons practise the original technique of Billroth with some form of Schoemakers modification. The manner in which this procedure has evolved is illustrated in Figure 11.

(b) Billroth II:

Billroth in 1885 described for the first time gastrojejunal anastomosis after partial gastric resection (Billroth II). Initially an anterior gastrojejunostomy was done and then this was followed by resection of the pyloric end of the stomach. In 1888 Kronlein reported end to side anastomosis of the entire circumference of the gastric remnant to the jejunum, with an antecolic location of the stoma.

Problems which emerged were overshadowed by the phenomenon of bilious vomiting and subsequent attempts aimed at overcoming this. The first modification came from Von Eiselsberg (1889), who reduced the size of the gastric stoma by partially closing the gastric opening, beginning at the lesser curvature, and anastomosing jejunum with the greater curvature end of the incision. The proximal loop lay uppermost,

and the loops all lay anterior to the transverse colon.

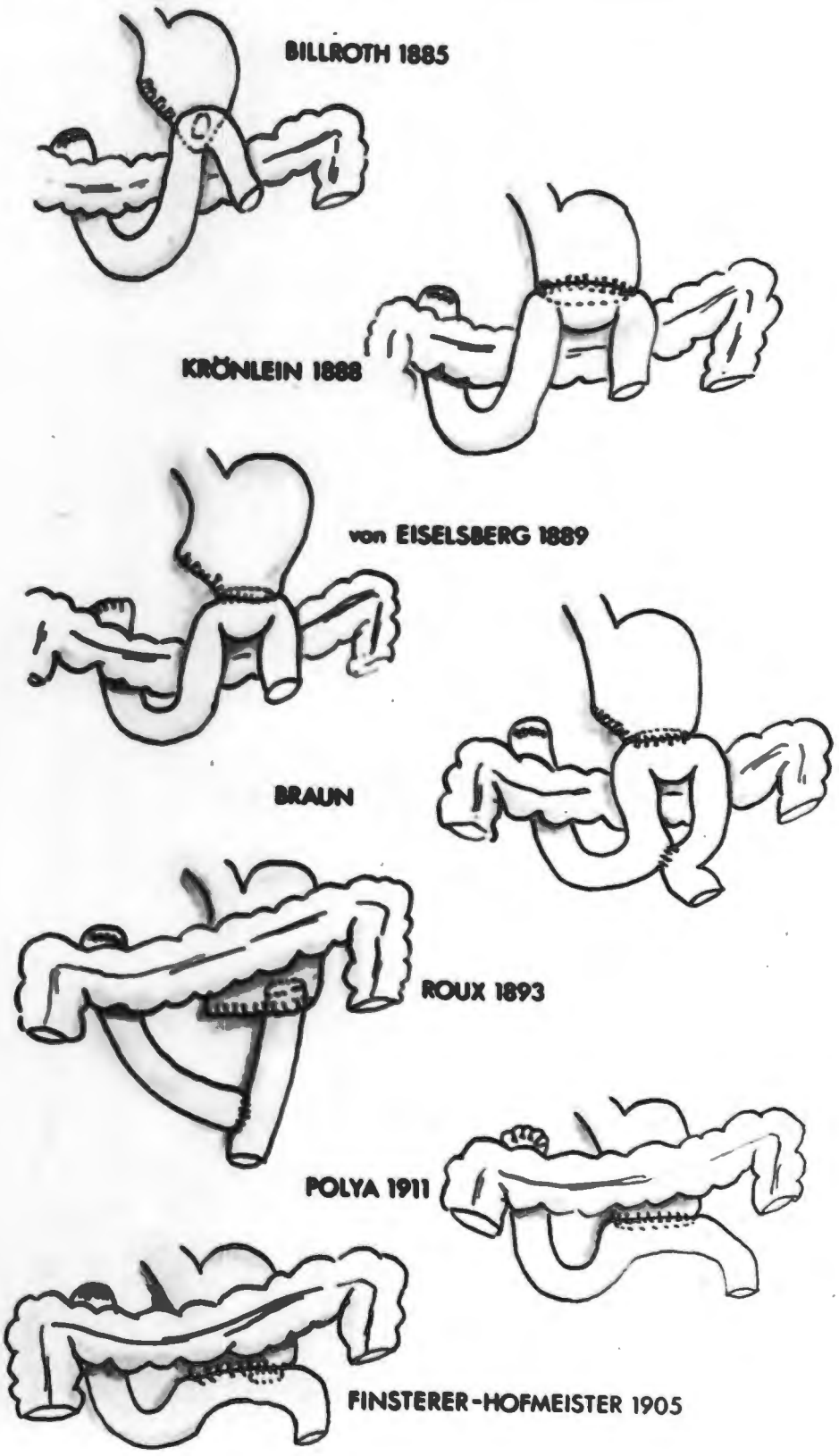
Many enthusiastic workers then "climbed onto the bandwagon" and reported every conceivable variation in the arrangement of the jejunal loops and stoma.

Eugene Polya (1911) working in Budapest, popularised Kronlein's original operation of anastomosing, end to side, the entire circumference of stomach remnant to jejunum, which he modified by using a retrocolic jejunal segment.

Hofmeister in 1905 described his "afferent loop valve" addition to Von Eiselsberg's operation. The closed portion of the gastric stump, beginning at the lesser curve was covered with the afferent loop of jejunum, even though only a small stoma was employed in the lower part. The second point of difference from the original procedure was the retrocolic location of the jejunal loop. Finsterer simultaneously developed a similar modification to that of Hofmeister, athough this remained unpublished until 1914.

As mentioned earlier partial gastrectomy as a form of treatment for duodenal ulcer was first recommended at about the time of the First World War. Advocates for this were Von Haberer in Germany and the Americans Strauss, Berg and Lewisohn, who led the

FIG. 12 EVOLUTION OF THE BILLROTH II RECONSTRUCTION



swing away from simple gastrojejunostomy. This principle rapidly gained support and is still practised in some centres as the routine operation for elective treatment of duodenal ulcer. The operation is physiologically sound, as the gastrin-producing area and a substantial proportion of acid-bearing mucosa is excised (approximately 70 to 75% resection). Partial gastrectomy results in low ulcer recurrence rates, especially if a Billroth II reconstruction is used, but problems arise with the development of sequelae attributable to afferent loop stasis and rapid gastric emptying into the efferent loop, as well as metabolic after effects which occur in the long term.

The basic technique as practised today remains that of Von Eiselsberg with regard to stomal site, and many surgeons utilise the Hofmeister valve principle (Fig.12).

(c) Other forms of gastrectomy:

In 1895 Von Eiselsberg described the antral exclusion operation. To deal with irresectable masses in the pyloroduodenal area, he transected the stomach proximal to the mass, closed the cut ends and performed a gastrojejunostomy with the proximal remnant. He applied the same technique to non-obstructive duodenal

ulcer in 1910, which Devine (1925) modified by employing a retrocolic polya-type reconstruction with the proximal stomach.

Antral exclusion resulted in a high incidence of recurrent ulcer, which, in retrospect, is not unexpected. This prompted Finsterer to add partial proximal gastrectomy to the antral exclusion. When the recurrence rate failed to fall significantly, coring out of the antral mucosa later became the third component of this operation.

Wilmanns (1926), Drüner (1931) and Bancroft (1932) decided to perform simple antral exclusion, after Devine, and to core out the antral mucosa without resorting to gastric resection. At this stage the physiological justification for this was Edkins' (1906) report on the existence of the hormone gastrin.

Routine practice of this operation in elective treatment of duodenal ulcer has fallen by the wayside due to the poor results obtained. In some centres, use is made of antral exclusion as part of a two-stage gastric resection where it is not possible to remove an inflammatory duodenal ulcer mass at the initial laparotomy. Gastrectomy and reconstruction are performed during the first stage and the antrum is removed later, once inflammation has subsided.

In the palliation of irresectable carcinoma this remains an acceptable form of treatment.

Segmental resection of the stomach was initially suggested by Mickulicz in 1898 and Erwin Paye of Liepzig (1910) and used for gastric neoplasms and ulceration. Duodenal ulceration was first treated in this way by Connell in 1929. He removed a wedge of fundus and hence a proportion of the acid-bearing area of the stomach. Wangensteen followed in 1940 (347) with the introduction of his tubular resection, in which a large portion of acid secreting stomach mucosa was removed from cardia to antrum. This was abandoned fairly soon in view of the high incidence of recurrent ulceration.

III VAGOTOMY

In 1892 Kehl reported the first observations on the effects of vagotomy. He compared the results in dogs of interrupting the vagi in the neck and in the supradiaphragmatic position. He observed diminished gastric acid secretion but was more interested in the motility of the stomach and oesophagogastric junction. Pavlov's classical work appeared 3 years later.

The first abdominal vagotomies in man are attributed to Exner in 1911, but he performed the

operation in the belief that it would relieve the pain attributable to tabetic crises. He also drained the stomach using a tube via the stomach and duodenum, as he was concerned about gastric atony. In 1922 Latarjet reported on 24 patients treated by vagotomy. Only 6 of these had peptic ulcer, the remainder being sufferers from tabes dorsalis, tuberculosis, carcinoma and unspecified "gastropathies". All six of the ulcer patients had gastroenterostomies but the reason for this is not clear. Although he noted that decreased secretion and motility were the main features of the operation, the original rationale again was to relieve their pain. Nevertheless, to this surgeon must go the credit for having performed the first deliberate vagotomy for peptic ulceration.

Total vagotomy became a permanent surgical entity after the report of its use to successfully reduce gastric acid production in two patients, by Dragstedt and Owens in 1943, who performed nerve section without an accompanying drainage procedure. Dragstedt later realised the need for gastric drainage and this became universally accepted[166]. Selective section of the gastric vagal supply, leaving either the hepatic, or coeliac, or both

branches intact was reported independently by Jackson (1947)[348] and Franksson (1948)[349]. While both agreed that the coeliac vagi should be preserved they were at variance regarding the value of preservation of hepatic branches. It is of interest to note that Laterjet's pupil Pierre Wertheimer, had reported the use of selective vagisection in dogs and in man.

Both of the former authors abandoned this operation (without drainage) due to problems with gastric stasis. When the need for gastric drainage became recognised and widely practised in conjunction with vagisection, support for the use of this composite operation increased. The selective procedure, largely due to the opposition of Dragstedt who believed that it would result in a high incidence of incomplete nerve section, was forgotten.

In 1957 an experimental study by Griffith and Harkins[350] reactivated interest in selective vagotomy. Griffith and Burge, working independently, started popularising the operation in the early 1960's. The latter advocated the use of an intraoperative electrical stimulation test to ensure completeness of vagotomy. Although for a time the argument arose once more as to whether the coeliac or hepatic branches, or both, should be preserved, the current consensus seems to advocate the latter alternative.

Associated procedures performed with vagotomy are a gastric drainage manouvre, or antral resection. Drainage as outlined earlier is effected either via gastrojejunostomy or pyloroplasty. Pyloroplasty is the most widely practised and the original technique of Heinecke and Mickulicz, modified by Weinberg, is most commonly employed.

Based on the reports of Edkins (1906) on gastrin, and physiological observations and experiments by Bircher and Borchers (1920 and 1921 respectively), Klein in 1929 followed by Berg (1938), and Winkelstein (1942), performed the operation of vagotomy and antrectomy, which is currently very popular amongst contemporary surgeons.

Consideration of gastric secretory physiology as previously described and the role of the gastric antrum confirms the fact that the performance of this procedure is based on sound physiological principle. This is borne out by the excellent results yielded by vagotomy and antrectomy for duodenal ulcer, apparently surpassing those of vagotomy and drainage or subtotal gastrectomy.

The most recent innovation in the never-ending story of duodenal ulcer surgery is the report by Amdrup and Griffith in 1969[351] of an operation on

animals designed to section only those branches of the vagus that supply the parietal cell mass and leaving the antral nerve supply intact, in an attempt to preserve emptying mechanisms and acid secretion inhibitory mechanisms. Several surgeons have to date performed this "superselective" (highly selective; parietal cell) vagotomy, without an accompanying drainage procedure, on a limited number of duodenal ulcer patients, and have reported excellent short term results[323-325]. The physiological justification for this operation has been discussed in an earlier chapter.

It is thus an interesting exercise to follow the swing of the surgical pendulum related to the surgical management of chronic duodenal ulceration. Starting with the relatively minor operation of simple gastroenterostomy, it swung to the opposite extreme of near total gastric resection as anaesthetic techniques improved. In modern practice the operation of 70% partial gastrectomy is still widely used, but it is probably correct to state that very few surgeons use it as a routine elective form of therapy.

At the present time opinion lies in approximately the middle of the arc of swing, with widespread routine use of vagotomy, whether accompanied

by a drainage procedure or antral resection. Whether selective vagisection holds any advantages over the truncal operation continues to be argued about with unabated intensity.

The pendulum may well return to occupy its original position on the conservative side of the surgical spectrum if current clinical experiments with selective parietal cell denervation prove fruitful.

PART II

METHODOLOGY

CHAPTER 1

MATERIAL AND METHODS

I CLINICAL MATERIAL AND FOLLOW UP

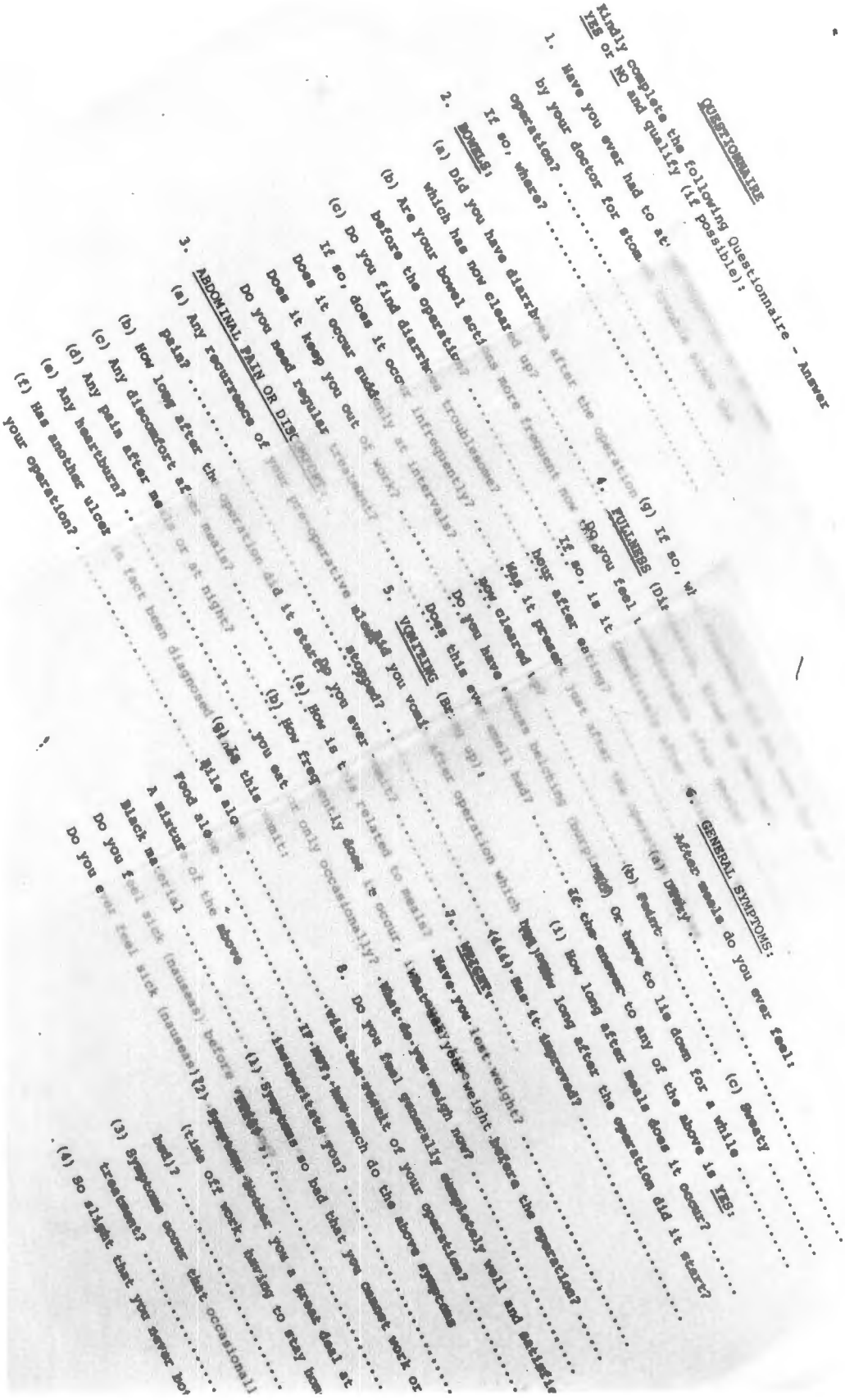
The aims of this study have been presented in detail in the introduction to Part I.

Patients who had undergone elective surgery for duodenal ulcer at Groote Schuur Hospital, Cape Town, during the period extending from June, 1960 to December, 1967 inclusive, formed the subject of a retrospective study. This therefore constitutes a clinical follow up of a minimum of four years and a maximum of ten years. Names of the patients were obtained from the operating theatre record books, and all were circularised with a simple, though fairly detailed and comprehensive questionnaire (Fig.13).

Those who returned the completed questionnaire and were therefore contactable, were re-circularised and requested to attend for further follow up at the Gastroenterology Clinic. All assessments were carried out by the author.

As many as possible of the subjects followed up were subjected to augmented histamine tests (A.H.T.),

FIG.13 QUESTIONNAIRE



or pentagastrin stimulation tests. The evidence for the identical results yielded by both these tests has been presented. For the sake of convenience therefore all future reference to the A.H.T. refers to the pentagastrin test as well. Eighty percent of all patients in the series had had preoperative A.H.T. performed.

In addition, as many as possible of the post-vagotomy subjects had insulin tests carried out, in order to assess completeness of gastric denervation.

A random control group of 185 apparently healthy adults was requested to complete the questionnaire. It was hoped that in this way a further index of questionnaire reliability could be obtained. In addition, it would be of interest to accumulate some clinical data on the incidence and prevalence of the various symptomatology such as diarrhoea, heartburn, post prandial nausea and vomiting etc., known to occur after the various gastric operations in individuals with intact stomachs.

Altogether 783 patients were operated upon electively for duodenal ulceration over this period (Table 1). Only 470 (60.0%) of these were traced, of whom 437 were alive and 85 percent of the latter were able to return for interviews and postoperative tests.

TABLE 1

ANALYSIS OF THE TOTAL NUMBER OF ELECTIVE OPERATIONS PERFORMED FOR DUODENAL ULCER BETWEEN JUNE 1960 & DECEMBER 1967 & THE PROPORTION FOLLOWED UP IN THIS STUDY

OPERATION	TOTAL NUMBER	NUMBER OF PATIENTS TRACED			% FOLLOW UP
		ALIVE	DECEASED	TOTALS	
VAG. & DRAIN.	518	311	19	330	63.7
VAG. & GASTY.	138	65	7	72	52.2
PARTIAL GASTY.	127	61	7	68	53.5
GRAND TOTALS	783	437	33	470	60.0

TABLE 2

PATIENTS NOT TRACED

CHANGED ADDRESS	267
ADDRESS KNOWN - REFUSE TO CO-OPERATE	46
TOTAL	313

Of the 313 patients not traced 267 had changed address, that is, all circulars were returned by the postal authorities or present tenants as "address unknown" (Table 2). Through the efforts of our departmental social worker 72 patients in this group, which had initially numbered 385, were traced. However, in view of the poor return for the number of man hours employed it was decided to no longer pursue this avenue. There remained 46 patients, the addresses of whom were known, who were not interested in responding to any circulars or requests to attend follow up clinics.

Race distribution was approximately equal (Table 3). Of the total number 50.9% were of the white race, and 49.1% belonged to the non-white group, which consists of Cape Coloured, Malay, Indian and Bantu patients. The group followed up comprised 52.0% white and 48.0% non-whites, indicating a marginally better follow up in the former.

Overall sex incidence for all races and all operations was 79.5% males and 20.5% females in those followed up.

The types of operation employed were vagotomy and drainage; vagotomy and antrectomy or partial gastrectomy. Drainage was effected by a pyloroplasty

TABLE 3

RACE DISTRIBUTION AMONG TOTAL NUMBER OF PATIENTS SUBMITTED TO ELECTIVE SURGERY FOR DUODENAL ULCER, & AMONG THOSE IN THIS GROUP WHO WERE FOLLOWED UP

ALL PATIENTS INITIALLY SUBMITTED TO OPERATION			PATIENTS TRACED		
NUM-BER	WHITE (%)	*NON WHITE (%)	NUM-BER	WHITE (%)	*NON WHITE (%)
783	50.9	49.1	467	52.0	48.0

*Includes Cape Coloured, Malay, Indian and Bantu patients

usually of the Heinecke-Mickulicz type, or gastro-enterostomy. The gastroenterostomy was sited for preference at the most dependent part of the stomach. Wherever technically possible pyloroplasty was done.

Antrectomy comprised a 50% gastric resection with a Billroth II type reconstruction, although a few had a Billroth I anastomosis performed. Usually the ulcer was included in the resection. All patients who underwent routine partial gastrectomies (two-thirds to three-quarters resection), without deliberate vagotomy, had Billroth II reconstructions. The vast majority of operations were performed by consultant surgeons on the staff of the hospital, a small number being done by surgeons in training.

For the purposes of this study, the results in the gastroenterostomy group have not been reported separately but together with the pyloroplasties forming a composite vagotomy and drainage group. Of the 311 cases followed up 78 had gastroenterostomies and the remaining 233 had pyloroplasties. Vagotomy and drainage accounts for the majority of operations done.

The 33 patients traced who were found to be deceased, died from causes which had no definite relationship to their surgery. Table 4 provides a detailed account of this group. It might well be

TABLE 4 CAUSES OF DEATH IN PATIENTS TRACED BUT REPORTED DECEASED

TRAUMA	(5)	Road accident	4
		Stabbing	1
DROWNING	(2)		2
CARDIO-RESPIRATORY	(12)	Coronary Thrombosis	5
		Chronic Cor Pulmonale	2
		"Pneumonia"	3
		Hypertensive Heart Failure	2
MALIGNANT DISEASE	(6)	Bowel	2
		Breast	1
		Ovary	1
		Disseminated	2
CEREBROVASCULAR ACCIDENT	(2)		2
UNKNOWN	(6)		6
		GRAND TOTAL	33

postulated in considering the various causes of death that certain complications, such as the hypoglycaemic syndrome, may be incriminated in the accidental death, myocardial infarct and cerebrovascular accident groups, which comprise 39% of the total.

The control group consisted of 185 randomly selected employees of a large insurance company, to whom the questionnaire was given. All references to the word "operation" were deleted. There is certainly a fairly large element of selection in this group. The vast majority (85%) were white and all in the group were clerical workers who are inclined to be more introspective than manual workers. Males constituted 70% of the sample and their ages ranged from 19 to 60 years.

Difficulties encountered:

In attempting to perform a study of this nature in this country one is faced with what at first sight appears to be an insurmountable task, and various reasons are put forward by way of explanation for the poor follow up.

The major obstacle is a geographical one. Groote Schuur Hospital is one of few major referral centres in a vast, relatively sparsely populated country. Patients of all races arrive from remote areas and

FIG.14

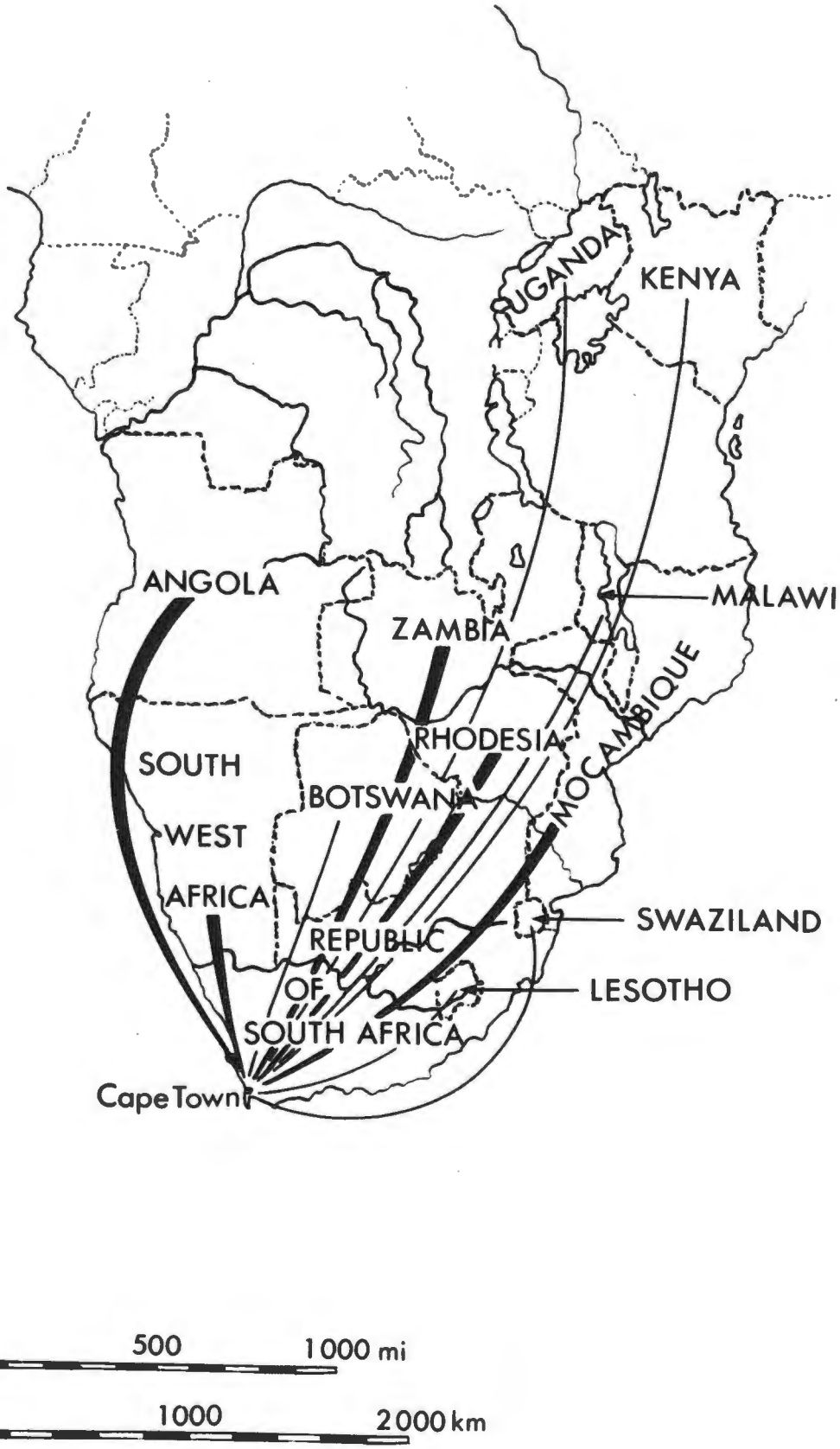

UGANDA
KENYA
ANGOLA
MALAWI
ZAMBIA
MOCAMBIQUE
RHODESIA
SOUTH
WEST
AFRICA
BOTSWANA
SWAZILAND
REPUBLIC
OF
LESOTHO
SOUTH AFRICA
Cape Town
0
500
1000 mi
0
1000
2000 km

FIGURE 14

MAP OF SOUTHERN AFRICA SHOWING WIDELY SCATTERED AREAS, BEYOND THE BORDERS OF THE REPUBLIC, WHENCE PATIENTS PRESENTED FOR SURGERY.

even from areas outside the borders of South Africa such as the Portuguese Territories, Rhodesia, Zambia, Botswana, Malawi and the East African States (Fig.14). Many of these leave local addresses without a precise forwarding address.

Cape Coloureds provide the major agricultural labour force in the entire Cape Province. They also tend to migrate and many are illiterate. 144 patients in this series can be classed as falling into this category, of whom only 36 (25%) were traced.

Many Cape Coloureds, Malays and Indians living mainly in the urban areas have been affected by recent implimentation of the Group Areas Act in which various local geographical areas are reserved for specific race groups. All those domiciled within areas declared exclusively white have been resettled and many of these old houses have been demolished. This group also is difficult to trace. Most earn too little to pay income tax and there is no way of ascertaining precise forwarding addresses.

The Bantu form a migrant labour force, and spend varying periods of time in urban areas before returning to the African homelands for varying periods of time. Tracing these people constitutes a difficult problem as they seldom return to the same local

employment or address. Duodenal ulcer is not a common disease in the Bantu however, and only 22 cases required elective surgery, of whom only one was traced.

It is of interest to note, however, that even considering all the unfavourable factors regarding follow up in the non-white group, there is an almost identical distribution of whites (50.5%) and non-whites (49.5%) in the address unknown group. The vast majority of whites who, during the period under review, underwent treatment at Groote Schuur Hospital belonged to that group of the community who were unable to afford private medical treatment. Apparently this group also leads a fairly nomadic sort of life in this country.

Having attempted in a variety of ways to trace as many as possible of the "address unknown" group it would appear that a 60% follow up is the best obtainable under the circumstances, which is a poor figure when compared with published series from Britain, the United States, and elsewhere. Almost certainly, the long term natural history of the unsophisticated nomadic postoperative ulcer patient, the majority of whom cannot be found, will differ from that of the better educated individual who enjoys a much higher

standard of living, the majority of whom can be found. Therefore the patients followed up are to a certain extent a selected group.

It is hoped, however, that even with the above reservations a large enough number of patients have been followed up to establish a pattern and provide an index of what the clinical results of elective surgery for duodenal ulcer have been at this hospital.

II THE AUGMENTED HISTAMINE TEST (PENTAGASTRIN STIMULATION TEST)

(a) EVOLUTION: This test evolved in an attempt to find a means of assessing the size of the parietal cell mass (P.C.M.) which was known to determine the magnitude of the acid secretory response of an individual[352-354].

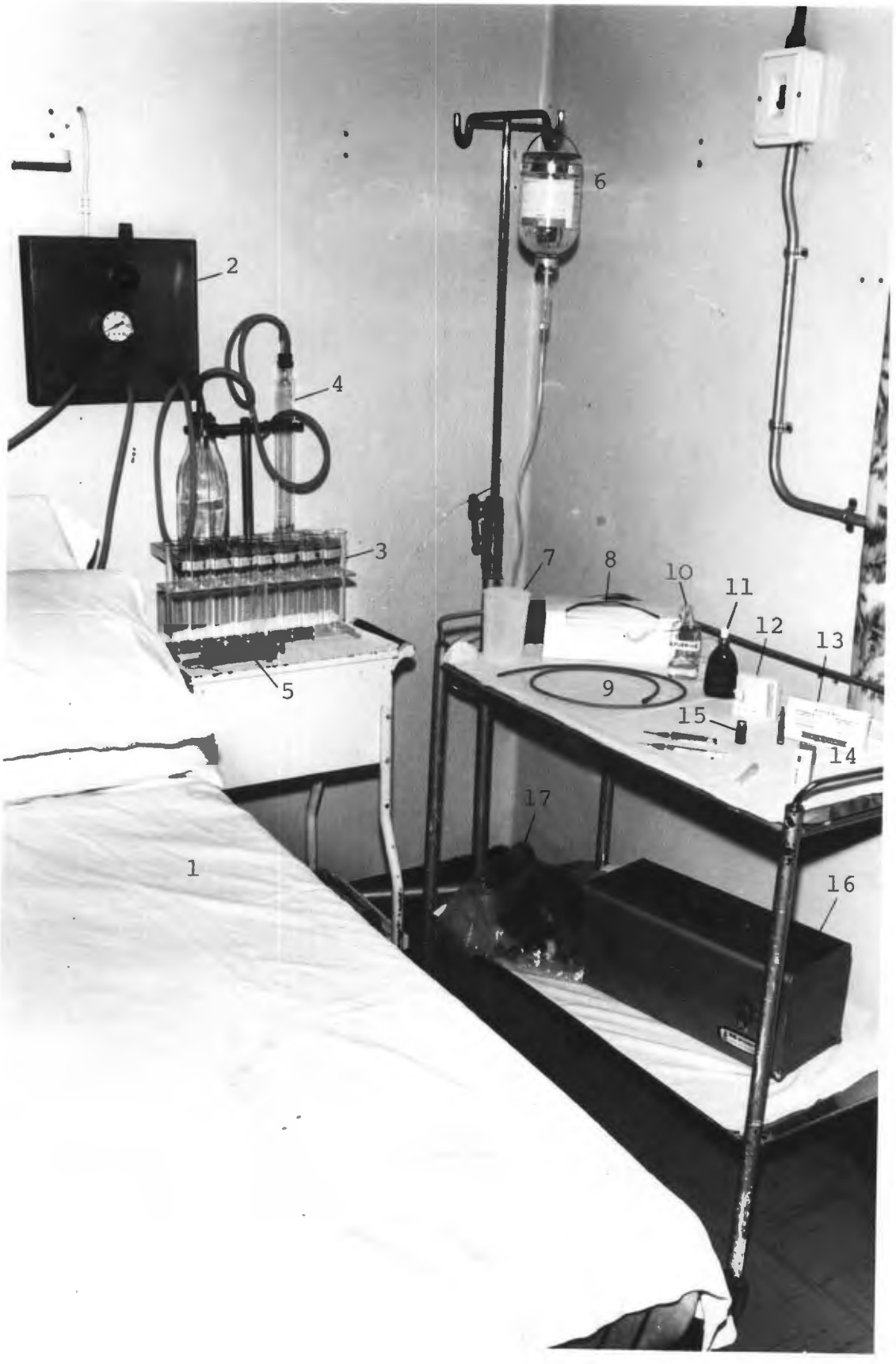
Popielski in 1920[355] reported on the marked stimulatory effect of histamine on gastric acid secretion and much controversy has ranged around what physiological role, if any, histamine occupies in mediating acid secretion. Halpern[356] demonstrated that the parenteral administration of antihistamine drugs antagonised the systemic effects of histamine, but did not influence its action on the stomach. Accordingly it became possible to measure the effects of graded doses of the drug, administered subcutaneously, on acid secretion[357]. Kay found that the

smallest dose of histamine acid phosphate necessary to produce the maximum secretory response of the P.C.M. was 0.04 mg./kg. body weight[357,358].

The same author, and others[357,359-362], have popularised the test and established its reproductibility in the same individual.

That the A.H.T. provides an accurate clinical measurement was demonstrated by Card and Marks[21] in humans, and Marks subsequently confirmed this in the dog[22]. They discerned an excellent relationship between acid output following histamine stimulation and the P.C.M. The experimental method and findings have been described in an earlier chapter.

Since the isolation and synthesis of gastrin[18] and the discovery that the powerful secretogogue action of the hormone resides in the terminal three amino acids of the molecule, Morley, Tracy and Gregory[38] have synthesised a pentapeptide (pentagastrin) comprising the terminal part of the molecule. The subcutaneous administration of pentagastrin in a dose of 6.0 /ug./kg. has been found to produce a secretory response identical to that of 0.04 mg./kg. histamine acid phosphate given the same way[198]. The pentagastrin stimulation test has therefore now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16
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FIGURE 15

APPARATUS REQUIRED FOR THE A.H.T.
(PENTAGASTRIN STIMULATION) AND INSULIN TESTS

1. Couch with adjustable headrest
2. Suction pump (low pressure)
3. Labelled specimen tubes in rack
4. Measuring cylinder - in series with pump to collect gastric samples
5. 50 cc. syringe
6. Intravenous administration equipment (10% Dextrose in water)
7. Sputum mug
8. Tissues
9. Nasogastric tube (size 14-16 Levin tube)
10. Glycerine
11. Xylocaine spray
12. Pentagastrin
13. Antihistaminic
14. Soluble insulin
15. Histamine
16. Emergency resuscitation box
17. Ambu bag

supplanted the A.H.T. as a routine test. Advantages of pentagastrin over histamine are the fact that to date few side effects or adverse systemic reactions have been reported and that only one injection is required.

In almost all the preoperative tests and in a fair number of the postoperative tests histamine was used. At present all routine testing in this unit is done with pentagastrin.

(b) TECHNIQUE:

FASTING - The test is preceded by a fast of approximately 8 to 12 hours, usually overnight. However, when tests had to be performed in the afternoons, patients were permitted to partake of a light breakfast consisting of tea or coffee and toast before 8.00 a.m. The test was then scheduled for 2.00 p.m. on the same afternoon. Under these circumstances the resting juice sample was carefully examined for food debris and if any was present the test was abandoned.

INTUBATION - After having the procedure carefully explained the patient clothed in trousers and hospital dressing gown is seated in a chair. All corsets and possible radio-opaque items of clothing having been removed. A radio-opaque Levin nasogastric tube (Rüsch), size range 14 - 16, is then well lubricated

with glycerine and passed through the nose. It has been found that the position of the tube in the stomach is much more accurately maintained in this way. If passed via the per-oral route, the tube is more likely to move due to the continual action of the tongue and buccal muscle in spitting out accumulated saliva.

The faucial pillars and oropharynx are routinely lightly sprayed (5-6 sprays) with 2% Xylocaine to prevent gagging. A cardboard mug and tissues are supplied for collecting saliva.

Slight extension of the neck facilitates passage of the tube by straightening out the curvature of the naso-and hypopharynx. Once the tube has entered the oropharynx, which can still just be felt by the patient due to the light nature of anaesthesia, the patient is told to swallow continously. With gentle manipulation the tube almost always passes into the stomach quite smoothly. Any coughing or stridor occurring during intubation indicates that the tube is entering the trachea, and it should be removed immediately and the entire procedure repeated after the subject has had time to recover.

The proximal end of the Levin tube is marked at 4 inch intervals. Once the first mark reaches the nostril, the patient is screened to ascertain position of the distal end of the tube.

SCREENING - The patient stands behind the machine facing the examiner, and the position of the tube is visualised on the fluoroscopic screen. Correct position for the tip of the tube on the screen lies to the left of and adjacent to the vertebral column, and it occupies a gentle curve from the cardia as it lies along the greater curve. The terminal portion of the tube thus lies just proximal to the antrum. It might occasionally be necessary to position the patient on the right side if the tube persists in coiling up in the fundus of the stomach. Usually, if this happens all that is required is to gently withdraw the tube as far as the cardio-oesophageal region and to reinsert it.

Postvagotomy and drainage patients present little difficulty. In those who have had gastroenterostomies care must be taken not to insert the tube through the stoma. This becomes evident by the nature of the aspirate as well as the fluoroscopic appearances.

Gastrectomized individuals sometimes present a difficult problem as much biliary reflux occurs into the gastric remnant. It has been found that a good working rule is to position the tip 2 - 3 inches below the left hemidiaphragm.

Once the tube has been satisfactorily positioned,

it is firmly fixed to the patient's cheek and the subject reclines comfortably on a couch with shoulders elevated about 40 degrees from the horizontal plane. The individual is advised to spit out all saliva into the provided container and to attempt not to swallow any during the course of the test.

COLLECTION OF SAMPLES - The Levin tube is connected to the calibrated collecting flask, which connects in series with an overflow flask (Fig.14). This unit communicates in turn with the suction pump. A vacuum of approximately 5 mm. mercury is maintained in the system.

Seven collections of gastric juice are made.

(a) Fasting juice

(b) 2 x 30 minute basal secretion

(c) 4 x post histamine (pentagastrin) collections

(i) 15 minutes

(ii) 30 minutes

(iii) 45 minutes

(iv) 60 minutes

Throughout the test continuous suction of 5 mm. Hg. pressure is applied. Every 5 to 10 minutes a little air is gently injected into the tube to ensure continuous patency of the tube and to prevent blockage of the laterally situated openings in the

tube by contact of the latter with the gastric mucosa.

All samples are placed in 200 cc. capacity test tubes provided for the test, contained in a rack. The rack is of course clearly marked with the name of the patient and on each tube the time of the collection is recorded.

(i) Fasting collection:

This usually contains swallowed saliva, mucus and bile due to reflux. A small amount of fresh blood may be present as a result of mucosal trauma during intubation.

Fasting collection continues until no more than a trace of bile, at most, is present and a relatively clear aspirate is obtained. Persistent aspiration of heavily bile stained fluid necessitates more proximal repositioning of the tube, preferably under fluoroscopic control.

The fasting sample usually takes between 5 and 15 minutes to collect and the volume varies from no juice at all to 200 ml.

(ii) Basal collection:

Two specimens are collected at half hourly intervals. At the time of collection of the first basal sample, if histamine is to be administered,

an intramuscular injection of an antihistamine is given (Anthisan 50 mg.).

(iii) Post histamine (pentagastrin) collection

At the end of the basal hour 0.04 mg./kg. of histamine acid phosphate is administered subcutaneously, but about 0.2 ml. is added to the calculated dosage to compensate for dead space in the syringe and needle. The injection is usually moderately painful and may result in transient flushing. Slow administration seems to obviate this to a certain extent. Minimal side effects have been encountered in our experience but occasional dizziness, palpitations and sweatiness may occur with a feeling of faintness. Simple horizontal positioning of the patient with elevation of the legs always corrects these symptoms and no tests have ever had to be abandoned.

Pentagastrin is administered in a dose of 0.7 mg./kg. body weight via the subcutaneous route. An extra 0.2 ml., as described above is added to the calculated dose. No reactions to this drug have to date been encountered.

After administration of the stimulatory drug four separate specimens are collected at accurately timed 15 minute intervals.

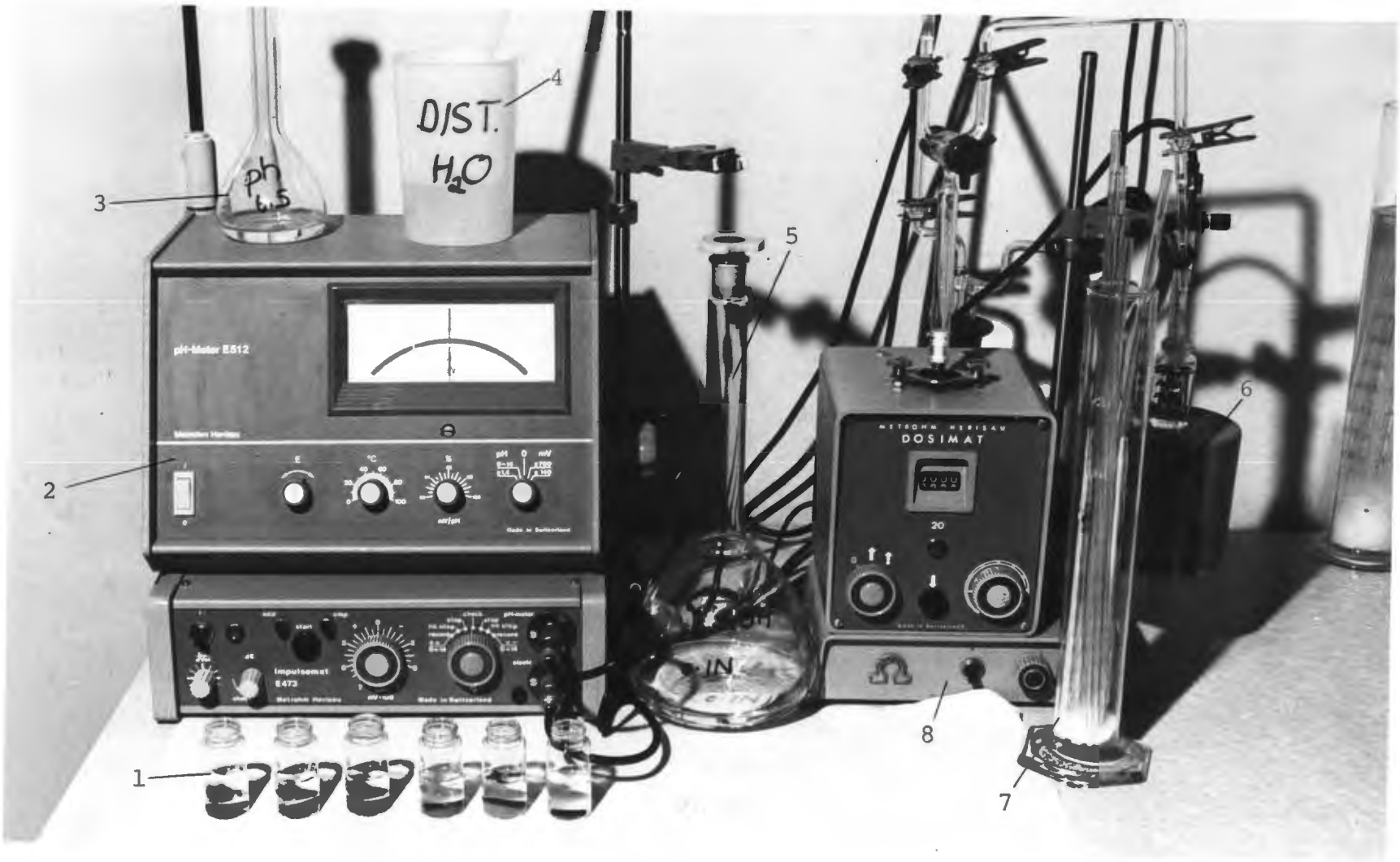

DIST.
H2O
pH
6.5
pH-Meter E512
Impulsomat
E473
DOSIMAT
20
1
2
3
4
5
6
7
8

FIGURE 16

AUTOMATIC TITRATOR & pH. METER

1. Glass bottles containing 5 ml. distilled water and stirring magnets
2. pH. meter
3. Standard pH. solution (pH.6.5)
4. Distilled water
5. NaOH (0.1 N).
6. Magnetic stirrer
7. Pipettes
8. Automatic titrator

(c) TITRATION AND CALCULATIONS:

Values used in this unit are basal acid output (B.A.O.), constituting the two half hour basal samples, and the maximal acid output (M.A.O.). Both are expressed in terms of milliquivalents of hydrochloric acid per hour and the figures used constitute the "total acid" in the specimen. Results are obtained by titrating collected specimens against N/10 sodium hydroxide using an automatic titrator (Metrohm Herisau Impulsomat E473/Dosimat) (Fig.16).

The volume of each collection is carefully measured and recorded. In addition a description of the juice is noted with reference to the presence of bile, blood, mucus or debris which may give falsely low values, especially when little acid is present in the sample. Into each bottle a small magnetic stirrer is inserted.

One ml. aliquots of each collection are measured into glass bottles containing 5 ml. of distilled water.

The N/10 sodium hydroxide is prepared by adding sterile water to one ampoule of Titrisol (Taeuber and Corrssen), to make a total volume of one litre. The preparation should be sealed, as absorbed carbon dioxide may alter the concentration.

Principles of use of the automatic titrator (Metrohm-Herisau Impulsomat E473/Dosimat):

(a) Check and zero the pH. meter, using standard buffer solution (pH.6.5). Precautions taken before any readings are taken are firstly to ensure that the pH. meter is not recording while any manipulating or changing of samples is taking place. Secondly, the electrode bulb must be carefully wiped clean and dry, using a tissue, before changing samples and, thirdly, ensure that the electrode bulb is completely immersed before any recordings are made. In addition, the bulb must not be in contact with the stirrer or sides of the container.

(b) Ensure that the "Dosimat" NaOH reservoir is full and that no air bubbles are present in the burette system.

(c) Switch on the magnetic stirrer unit and measure the pH. of the sample, after allowing 30 seconds in order that thorough mixing may occur.

(d) After duly recording the pH. and burette reading on the standard test record sheet provided, titration is commenced. Check that the three-way burette tap is in the correct position, so that NaOH is actually dropping into the test sample. Titration continues until an end point of pH.7 is reached and then

G.S.H. 720H

GROOTE SCHUUR HOSPITAL

AUGMENTED HISTAMINE/GASTRIN TEST

GASTRO-INTESTINAL CLINIC

NAME: _____ FOLDER No.: _____

RACE: _____ SEX: _____ AGE: _____

DATE: _____ WEIGHT: _____ WARD: _____

PROVISIONAL DIAGNOSIS _____

Previous Tests: (1) Date: _____ Basal: _____ M.A.O.: _____

(2) Date: _____ Basal: _____ M.A.O.: _____

(3) Date: _____ Basal: _____ M.A.O.: _____

Specimen	Time	Vol	Bile RBC	Acidity mEq/L		Acid output mEq		pH
				FA	TA	FA	TA	
Fasting								
Basal 1.								
Basal 2.								
Post Histamine/ Gastrin 1.								
Post Histamine/ Gastrin 2.								
Post Histamine/ Gastrin 3.								
Post Histamine/ Gastrin 4.								

Basal Hour: _____ mEq/hr

Maximum Acid Output: _____ mEq/hr

Comment: _____

Cytology: _____

_____ Signed

Ann C.T.6/70/7,000

GSH 720 I

GROOTE SCHUUR HOSPITAL

INSULIN TEST

GASTRO - INTESTINAL CLINIC

NAME _____ Folder No. _____

Race _____ Sex _____ Age _____

Date _____ Weight _____ Ward _____

NATURE of operation, if any _____

POST-OPERATIVE SYMPTOMS: Dyspepsia, Dysphagia, Diarrhoea, Post-prandial fullness and vomiting

Pre-operative Basal Secretion _____ Post-operative Basal Secretion _____

Pre-operative M.A.O. _____ Post-operative M.A.O. _____

Specimen	Time	Volume	Bile RBC	Acidity mEq/L		Acid Output mEq/hr		pH
				FA	TA	FA	TA	
Fasting								
Basal 1								
Basal 2								
Post Insulin 1								
Post Insulin 2								
Post Insulin 3								
Post Insulin 4								

BLOOD SUGAR:
SWEATING:
HEADACHE:

1. Volume rise
2. Basal Hour ___ mEq/hr
3. Free Acid + 20mEq/L ___
4. Early rise in Free Acid YES/NO
5. L.A.O. ___ mEq/hr
6. pH fall YES/NO

COMMENT _____

SIGNED _____

McHunter CT/10137/8/70/7,000

automatically ceases. The burette reading is again carefully recorded once the end point is reached.

(e) The titration cycle is then repeated with careful attention to all the precautions as described above until all samples have been dealt with.

Calculation (Total acid):

Reference to the test record sheet (Fig.17) demonstrates that all the required information is recorded in columns.

Concentration of acid in mEq./Litre = ml./NaOH required to reach end point of pH.7 x 100.

Acid output in mEq./unit time = concentration acid (mEq./Litre) x volume of sample per unit time divided by 1000.

Basal acid output, expressed as mEq./Hour is therefore the sum of the values obtained for the two basal specimens.

Maximal acid output, in mEq./Hour is the sum of the values obtained for the four post histamine (pentagastrin) samples.

Secretory patterns in response to histamine/pentagastrin stimulation have been discussed in some detail in the section on pathophysiology.

III INSULIN TEST (Hollander)

(a) EVOLUTION:

The fact that hypoglycaemia causes increased acid production via central vagal connections has been known for a long time. Hollander in 1942 performed insulin tests on dogs in which vagally innervated Pavlov pouches were converted to denervated Heidenhain pouches.

He empirically determined that in dogs with an intact vagus, with a blood sugar of less than 50 mg. percent following intravenous injection of 15 units of regular insulin, a rise in the free acid level occurred. This was subsequently confirmed in humans[211,212].

Other methods of assessing completeness of vagal denervation after operation have been tried. Initially some workers[363,364] reported that a distinct decrease in gastric motility could be demonstrated after complete vagotomy. This has been refuted by others[90].

Others advocated the use of intravenous injections of amino acid mixtures[365] alcohol[366] and more recently deoxy-D-Glucose[28] to stimulate vagal centres.

However, in the long run the most satisfactory

results have been obtained with the insulin test.

The level at which the hypoglycaemic stimulus acts has been elegantly demonstrated in monkeys[367]. Electrical stimulation of the anterior hypothalamus caused an immediate gastric acid response which was abolished by vagotomy. Direct posterior hypothalamic stimulation gave rise to a delayed response, occurring after two hours and abolished by adrenalectomy. The latter response therefore depends upon an intact pituitary-adrenal axis. The authors were able to demonstrate the identical biphasic response to insulin hypoglycaemia. Stempien[368] demonstrated that the identical response occurred in man following insulin injection.

Questions which now arose in the evolution of the test were what dose of insulin was required to produce the optimum secretory response; whether the rate of fall of blood glucose level played an important role and whether there was any direct relationship between absolute level of blood sugar and secretory response.

Doses used for routine postoperative testing have arbitarily ranged from 10 to 20 units by intravenous injection, regardless of weight, in most reported studies[90,205,211,212,369-371]. In recently

reported experiments several workers conclude that the dose of soluble insulin producing the optimum result is 0.2 units/kg. body weight[372-374,376]. This was universally found to be the lowest dose of insulin which was guaranteed to provide an adequate hypoglycaemia, of sufficient duration to provide reliable results.

Demand et al.[375] found that the onset of acid secretory response always occurred when the blood sugar lay within the range of 33 to 73 mg. percent, irrespective of the dose of insulin used, and concluded that a threshold of initiation of the response which was therefore "all or none". The same conclusion was reached by Kronberg[377-380] who was unable to demonstrate an inverse relationship between blood sugar level and acid output. However, all the above experiments have been done on many different patients.

Baron[373,376] repeated thirteen separate studies on a single individual, and found that the rate of fall of glucose did not affect the response threshold in relation to blood sugar levels. However, the threshold differed in his subject from day to day and is obviously not the same for all individuals. Once the threshold was reached and a

secretory response initiated, as the blood sugar level dropped so the acid output rose. Dose-response curves comparing insulin dosage with acid output levels showed a wide scatter. This was explained on the basis that a varying dose of insulin was required to give the same blood sugar level in the same individual.

Once a blood sugar level of approximately 15 mg. percent was reached, inhibition of acid output occurred.

(b) TECHNIQUE:

Preparation of the patient by overnight fasting, intubation and screening are identical as described for the A.H.T.

Collection of specimens for the fasting and post insulin samples is done by the same technique, taking the same precautions as the A.H.T., but all samples are collected at half hourly intervals. One thus has at the end of the test seven samples, namely, one fasting, two basal, and four post insulin specimens and the entire test takes three hours to complete.

At the end of the first post insulin hour a capilliary blood sample (finger prick) is taken for blood glucose estimation. If the blood sugar fails

to fall below 45 mg. percent the results are declared invalid.

In this unit a standard dose of 15 units of soluble insulin administered intravenously has been used to date. As some of the data regarding results of the insulin test have been taken from earlier tests it was decided to proceed with this dose for the purposes of this study.

Results are expressed in mEq. per hour as basal secretion, first post insulin hour and second post insulin hour. Calculations are done as described for the A.H.T.

(c) COMPLICATIONS AND PRECAUTIONS:

In many reported series authors mention the occurrence of complications during hypoglycaemia. These seem to have a relatively low incidence, but fatalities do occur, albeit uncommonly. For example Kronberg[379] had the unpleasant experience of one death in a total of 177 consecutive tests.

Complications mentioned included coma, convulsions, cerebrovascular accident and myocardial infarction. Convulsions usually occur in predisposed individuals, that is, epileptics or those with a strong family history of the disease. All reported deaths have apparently followed myocardial infarction.

Almost all patients who reach blood sugar levels low enough to initiate gastric acid secretion experience symptoms of hypoglycaemia such as sweatiness, faintness, dizziness, hunger and sometimes nausea, palpitations and headache. They should be warned about this before the injection is given.

In my own personal experience with 57 consecutive insulin tests, 3 patients suffered generalised convulsions occurring at 30 to 60 minutes after the injection and one became semicomatosed at 45 minutes after insulin. All recovered completely after rapid intravenous infusion with 10% dextrose water. Of those who had convulsions one admitted to having had epileptic fits in the past and another to the fact that all his 5 sibs were epileptic. Both had denied this prior to commencement of the test. The third had never before experienced convulsions and gave no relevant family history. Unfortunately no accurate blood sugar estimations were done at that time. Blood glucose estimation in the semicomatosed patient, 45 minutes after insulin, was 46 mg./100 ml. Apart from the expected mild hypoglycaemic reactions no other untoward phenomena were noted, and it is interesting to note that the level of hypoglycaemia bears no apparent relationship to the severity of symptoma-

tology.

Recommended precautions in performing the insulin test are therefore as follows:

(a) Selection of patients for the test

(i) Age less than 60 years

(ii) Careful interrogation and examination with regard to myocardial, cerebrovascular or peripheral vascular disease, or significant hypertension.

(iii) Determine whether the patient is epileptic or has any family history of the disease.

(iv) Ensure that no factors are operative in the patient that may suppress or interfere with acid secretion e.g. fever, respiratory tract infections.

(b) Precautions during the test

(i) Careful monitoring of symptomatology, level of consciousness, pulse rate and blood pressure.

(ii) A 10% dextrose water infusion set should be available, prepared for immediate use.

(iii) The emergency resuscitation box should be at hand available for immediate use.

The point is therefore made that the insulin test, though easy to perform, is not without hazard and one should be fully aware of these problems when setting about the test.

(d) INTERPRETATION:

This is an extremely difficult problem and there is no universal agreement about interpretation. Most criteria postulated have been arrived at in a rather arbitrary way.

Hollander[211,212] showed that persistent vagal innervation to a canine gastric pouch resulted in increased acid secretion when compared to completely denervated pouches. He indicated that unless complete interruption of all nerve fibres was done, the test gave a positive result. In man he demonstrated that with unilateral vagotomy a positive response occurred. The point was thus made that the test merely indicated that some innervation persisted and was no reflection of the amount of residual nerve tissue.

Two years after this pioneer work he suggested that a positive response could be quantitated as a rise of 20 mEq./Litre over basal levels and 10 mEq./Litre if the basal sample was achlorhydric. These figures were entirely arbitrarily determined and were based on general experience with the test.

Waddell[371] demonstrated a definite volume decrease, compared with basal levels, following insulin hypoglycaemia after vagotomy in man. In

patients with intact stomachs and vagi a definite volume rise over basal levels could be demonstrated. No ulcer recurrences were found in patients thought to have complete vagotomy by this criterion at 6 to 12 months after operation.

Basal acid output was thought to be important by Bachrach[90]. All his patients who had positive insulin tests by Hollander criteria had basal levels of 2 mEq., or more, per hour. He also regarded a rise in acid, arbitrarily suggested, of 1 mEq. over the highest basal value as above the range of spontaneous fluctuation during the two post insulin hours, and indicating peristent innervation. This author suggested that the magnitude of this rise reflected the number of persisting vagal fibres.

It was then proposed by Stempien[370] that a rise of 0.5 mEq. or more of acid during the two hour period following insulin injection, over the level determined for a two hour basal sample was indicative of incomplete vagisection. This again was based on the fact that in his own group of patients, few proven recurrent ulcers or symptoms of recurrence occurred in the group in whom the post insulin rise was less than 0.5 mEq./2 hours.

Ross and Kay[369] attempted to relate the pattern of positive response to the amount of intact

nerve tissue. Twenty duodenal ulcer patients, before operation, were found to give positive responses (by the Hollander criteria) within 45 minutes of the insulin injection. One hundred consecutive patients had insulin tests postvagotomy. Of the 38% who had a positive result, two patterns emerged. One group, termed early positive showed a response within 45 minutes. The other group, termed late positive, responded between 45 and 120 minutes after insulin. Scrutiny of resting secretion, and M.A.O. after insulin, revealed that the early positive groups' results approximated those of the controls. The late positive group had results similar to those of the complete vagotomy group. These authors came to the conclusion that the later positive response indicated persistence of a few small vagal fibres and therefore indicated an incomplete though adequate vagotomy. Accordingly, early positive responses were taken as indicative of incomplete inadequate nerve section.

Some support of this suggestion came from Johnston et al.[381] who reported a 68% recurrent ulcer rate in their early positive group while the late positives had a 24% recurrence rate as opposed to a 2% recurrence rate in the complete vagotomy group. They however took 60 minutes after insulin

as their time interval when separating the groups. One must also comment on the fact that a 24% recurrence rate in the late positive group hardly indicates "adequate" vagotomy.

This whole concept was challenged by Burns and his colleagues[382] who found that in their experience 37 of 100 unoperated duodenal ulcer patients exhibited a late positive response. All of these patients had significantly higher basal acid outputs, but the difference was only significant when 60 minutes was taken as the dividing line. All positives occurred within 90 minutes of injection. They conclude that the division into early and late positive responders is artificial and suggest that patients with a high resting "vagal tone" require more prolonged stimulation before positive responses occur. Gillespie and Kay[388] have since produced evidence which corroborates the above.

Bank, Marks and Louw[205] considered that pure Hollander criteria were too insensitive to predict which patients were susceptable to recurrent ulceration, as many with positive Hollander tests remain asymptomatic. Therefore they suggest the use of multiple criteria as a means of predicting liability to recurrent ulceration.

These are:-

(a) Increase in free acid of 20 mEq. or more per litre over basal values (10 mEq./Litre if basal level anacid) (Hollander)[211,212].

(b) Basal level in excess of 2 mEq./Hour. (Bachrach)[90].

(c) Increasing volume after insulin (Waddell)[371].

(d) Whether the Hollander response (a) occurs within 60 minutes or not (i.e. whether vagotomy is "adequate" or not) (Ross and Kay[369], Johnston[381].

(e) A rise of 1.5 mEq./Hour of free acid or 2 mEq./Hour total acid, over basal hour secretion, occurring in any hour after insulin. This was suggested by Bank (unpublished data)[384] who considered this a more realistic value, using his own results, than those proposed by Bachrach[90] and Stempien[370].

In addition these workers showed in this paper that the range of M.A.O. (histamine) in patients with positive insulin tests was between 3 and 19 mEq./Hour. They suggest that patients with values below 3 mEq./Hour have complete vagotomy and that those with incomplete vagotomy have an M.A.O. of more than 19 mEq./Hour.

Further modification of the interpretation of Hollander's original criteria has been suggested by

Spencer et al.[385]. Females have been found to have a lower incidence of incomplete vagotomy than males. In a series of unoperated patients they found that males gave a significantly greater response than females. Males gave a mean maximal histamine response of 72 mEq./Hour as opposed to 60 mEq./Hour in females. Simple proportion calculations reveal that a 20 mEq./L. rise in males is represented by a figure of 17 mEq./L. in females.

Whether or not negative insulin tests become positive at a later date and what the optimum time lapse after operation should be has been the subject of recent study. Mason and his co-workers[386] made the point that of the negative responses occurring within the first 7 to 10 days postoperatively a "fair percentage" become positive "later on".

Gillespie and colleagues[383,387] performed repeat insulin tests on patients with vagotomy and drainage. Approximately 50% of patients with negative responses at the initial tests 10 days to 2 weeks after operation became positive on repeat testing 3 months to 4 years later. There was also a tendency for the late positive group to revert to early positive. The same team have subsequently

repeated the experiment in order to determine the stage at which this change in status occurs and found that 6 months after operation was the critical time and no further conversions occurred beyond this time. Short term reproductability of the test was found to be good when performed at 1 to 2 week intervals. They thus concluded that this increasing positivity could be explained on the basis of a recovering neuropraxia.

All tests in this series have been interpreted in terms of the Hollander criterion, as well as multiple criteria[205] in order to compare this data with earlier published series.

When considering volume changes one must ensure that excessive bile reflux has not occurred in the post insulin specimens, which will give false positive results.

The basal acid output is important, both from the point of view of assessing resting vagal tone and also for interpreting the significance of acid secretory response to insulin. It must be emphasised that at least one hour's resting secretion must be accurately collected. Care must be taken to ensure that fasting juice has been completely aspirated before commencing the test. There must also be no

evidence of gastric stasis or of the patients having recently taken food in the samples which would give high values due to chronic stimulation of the antral mucosa. Conversely, excessive bile reflux will give false low readings. If these criteria are not rigidly complied with the test results are vitiated.

Obviously the whole principle of the test revolves around the secretory response obtained when vagal nerve centres are stimulated. The precise magnitude of this response remains to be elucidated. In considering the results of all titrations one must carefully note the presence of bile, mucus and debris in the specimen which may neutralise or buffer acid, as relatively small volumes are being dealt with. Much larger volumes are being dealt with in the A.H.T. and therefore this is not as important. It does constitute a major problem in the interpretation of tests following vagotomy and gastric resection, as there is always a fairly large reflux of bile.

The concept of using multiple criteria for prognostic purposes i.e. to determine which of the Hollander positive patients are liable to recurrent ulceration is attractive, but adequate follow up is required to prove its validity.

In addition, whether or not the magnitude of the Hollander response, that is the magnitude of the rise measured in mEq./Litre, can be used as a prognostic tool has yet to be investigated.

IV INTRA-OPERATIVE TESTS FOR COMPLETENESS OF VAGOTOMY

Attempts have been made to measure completeness of vagotomy at operation.

The electrical stimulation test first described by Burge and Vane[388] works on the principle of measuring rises in gastric pressure in response to electrical stimulation of the vagus.

No drugs with anticholinergic properties, phenothizines or belladonna must be taken in the few weeks preceding surgery. Premedication must be limited to papaveretum, and anaesthesia maintained with thiopentone, gallamine nitrous oxide and oxygen only.

An electrode is placed around the oesophagus and a cuffed gastric tube seals the lower oesophagus and brings intact vagal nerve trunks into contact with the silver electrode. Across the prepyloric region a soft intestinal clamp is placed and the stomach is distended with air to a pressure of about

70 cm. of water. Even the smallest intact nerve trunk will evidently cause a pressure rise on stimualation. When nerve section is complete no rise in gastric pressure can be detected. Varied reports have emerged regarding efficacy of the test. Burge himself[389,390] reports a one percent recurrent ulcer rate in 200 cases. Twenty-five randomly performed insulin tests on these showed 100 percent complete vagotomy by the Hollander criterion. Others report similar favourable experiences[391], but some doubt exists about the interpretation and timing of their insulin tests.

Lythgoe[392] on the other hand found no difference in the incidence of incomplete vagotomy when comparison was made between the group on whom the electrotest had been used and that in which a routine vagotomy was performed without intraoperative testing.

Recently Coupland et al.[393] reported that when vagotomy was performed without the Burge machine 4.5% had early positive responses and 23.5% were late positives to insulin testing. When the Burge machine was used none gave early positive responses and 30% gave late positive results. The authors claim that use of the test results in a lower percentage of inadequate vagotomies. However,

if the division in early and late is discarded, there is an identical incidence of approximately 30% of positive Hollander tests in the two groups, and use of the electrotest therefore makes no difference.

Lee[394] described the use of the dye leuco-methylene blue to selectively stain small nerve fibres. The dye has a clear yellow colour but is oxidised to methylene blue. Small nerve fibres evidently oxidise the dye more readily than other tissues such as muscle and connective tissue but large nerve fibres, for some unknown reason do not. Several surgeons[395-397] have produced unfavourable reports regarding efficacy of this test. All found that in less than 30% of stained specimens could nerve tissue be demonstrated and the test has been abandoned for routine use.

Testing for completeness of vagotomy, whether intraoperatively or by use of the postoperative insulin test remains, in many patients, an intriguing and as yet unresolved problem.

CHAPTER 2

RESULTS

I OPERATIVE MORTALITY (Table 5)

Primary operative mortality refers to deaths occurring within one week of the initial (primary) surgical procedure.

Deaths due to delayed complications are defined as those occurring after this period, directly related to the primary operation or disease process, but unrelated to any secondary surgical procedure.

Secondary mortality refers to deaths following repeat operations for complications resulting from recurrence of the initial disease process or operation.

Primary mortality figures as presented are accurate and are taken from hospital records of all elective operations done for duodenal ulcer during the period under review. From Table 5 it can be seen that the figure for all three operations is low, at less than 1% in each case. In the present series, there is no statistically significant difference in the primary mortality between vagotomy and drainage and vagotomy and antrectomy ($p > 0.05$). The difference between vagotomy and drainage and gastrectomy

TABLE 5 OPERATIVE MORTALITY AFTER ELECTIVE SURGERY FOR DUODENAL ULCER

OPERATION		TOTAL NO. OPS.	NUMBER FOLLOW-ED UP	*PRIMARY MORT-ALITY	**DELAYED COMPLI-CATIONS	*+SECOND-ARY MORT.	**+RE-OPS.	MORT-ALITY OF REOP.	OVERALL MORT. (APPROX %)
VGY. & DRAIN.	NO.	518	311	1	1	3	41	3	
	%			0.2	0.3	0.9		7.3	1.4
VGY. & GY.	NO.	138	65	1	0	0	4	0	
	%			0.7				0	0.7
PARTIAL GY.	NO.	127	61	1	0	1	8	1	
	%			0.8		1.6		12.5	2.4

*Deaths occurring within 1 week of primary surgery
**Deaths occurring 1 week or more after primary surgery directly related to the initial operation, not related to reoperation
*+Deaths due to reoperation expressed as percentage of all patients followed up
**+Denotes number of operations not number of patients

is just significant, as the P value just equals 0.05.

Vagotomy and drainage can therefore be taken to be a significantly safer procedure than partial gastrectomy and marginally safer than vagotomy and antrectomy.

One patient died of delayed complications out of the 311 patients in the vagotomy and drainage group. No deaths in this group were recorded in the gastric resection or vagotomy and gastrectomy patients.

Among the 311 with vagotomy and drainage 3 (0.9%) died as a result of re-operation (secondary motality). There were none in this category in the vagotomy and antrectomy group and 1 (0.8%) in the gastrectomy group. Forty-one repeat operations were performed in a total of 32 patients (10.3% of those followed up), for complications resulting from the initial disease process or operation in the vagotomy and drainage group. Four patients (6.5% of those followed up) had to have repeat operations in the vagotomy and antrectomy group. Of the 61 gastrectomized patients followed up 5 (8.2%) had re-operations. The mortality of repeat operation is not statistically significant when comparing vagotomy and drainage and gastrectomy. No deaths occurred in

the vagotomy and antrectomy patients subjected to re-operation.

An approximation of the overall mortality has been arrived at by adding together the percentages for primary and secondary mortality and mortality due to delayed complications for each operation. It will be seen that vagotomy and antrectomy results in the lowest figure (0.7%) while partial gastrectomy has a markedly higher overall mortality than this operation or vagotomy and drainage (1.4%).

It would seem that although the primary mortality of vagotomy and drainage is lower than that of the other procedures, in the long run the mortality is probably not significantly different, with vagotomy and antrectomy resulting in a better long-term figure.

II CLINICAL COMPARISON OF VAGOTOMY AND DRAINAGE, VAGOTOMY AND ANTRECTOMY AND PARTIAL GASTRECTOMY

As mentioned earlier, 80% of the patients followed up were interviewed and examined. All assessments were performed and recorded by a single observer. The questionnaire has been found to be very nearly 100% reliable. Occasional discrepancies were encountered in the patient's interpretation of questions pertaining to diarrhoea and also those

concerning vasomotor dumping.

Comparison of the results following pyloroplasty and gastroenterostomy in this study showed almost identical incidences of all postoperative sequelae whatever vagotomy technique had been employed. These cases, as mentioned earlier, were therefore pooled into a composite vagotomy and drainage group.

In making the analyses differences have been regarded as statistically significant if the p value was less than 0.05.

(a) RECURRENT ULCERATION (Table 6)

Recurrent ulceration after operation has been grouped into duodenal (or jejunal) and gastric. In view of the difficulty in some instances in confirming the diagnosis of recurrent duodenal or jejunal ulceration, this group has been further subdivided into "proven" and "highly suspected" groups. Gastric ulceration occurring after these operations does not present as much of a problem and the diagnosis is usually fairly easily confirmed.

Proven recurrent ulcer refers to those which have been unequivocally seen, either at operation or gastroscopy.

The highly suspected recurrent ulcer group includes those patients in whom the majority of the

TABLE 6

RECURRENT ULCERATION AFTER ELECTIVE SURGERY FOR DUODENAL ULCER

OPERATION		DUODENAL/JEJUNAL			GASTRIC	TOTALS	
		PROVEN	HIGHLY SUSPECT	TOTAL	PROVEN	PROVEN	PROVEN AND SUSPECT
VGY. & DRAIN. (311 cases)	NO.	12	13	25	8	20	33
	%	3.9	4.2	8.1	2.6	6.5	10.7
VGY. & GY. (65 cases)	NO.	0	0	0	1	1	1
	%				1.5	1.5	1.5
PARTIAL GY. (61 cases)	NO.	1	1	2	0	1	2
	%	1.6	1.6	3.2	-	1.6	3.2

following criteria are fulfilled :

1. The patient presents with a clear cut history classical of peptic ulceration, and the general clinical impression is that the individual's symptomatology is unlikely to be functional.

2. Gastrointestinal haemorrhage.

3. There is a prompt response of the symptomatology to adequate and vigorous medical treatment.

4. Barium studies suggest the presence of recurrent ulceration.

5. Endoscopy findings are suggestive of recurrent ulcer.

6. The patient probably has an incomplete vagotomy assessed by means of insulin and histamine (pentagastrin) tests, or in the case of gastrectomy patients, when a fairly high M.A.O. is found on A.H.T. A value of more than 20 mEq./Hr. is taken as almost diagnostic of jejunal ulceration in this clinic.

7. Other disease (e.g. cholelithiasis) which may be responsible for the symptomatology has been excluded by full relevant investigation.

8. This group also includes those patients who have come to re-operation, for whatever reason, as suspected recurrent ulcer, but where no ulcer or other pathology which may give rise to the symptomatology is found. The possibilites entertained under

these circumstances are that either the ulcer has healed, or the surgeon has difficulty in confirming the diagnosis in view of the gross anatomical distortion resulting from initial surgery.

Proven recurrent duodenal/jejunal ulceration can be seen from Table 6 to have been demonstrated more frequently in the vagotomy and drainage group (3.9%) than among the gastrectomy(1.6%), or vagotomy and antrectomy patients. Indeed, no recurrent ulcers of this type have been demonstrated in the latter group. The difference between the vagotomy and drainage and gastrectomy groups is not however statistically significant ($p > 0.05$). Similar incidences can be seen in the "highly suspected" category.

The incidence of proven recurrent gastric ulcer after vagotomy and drainage is high in this series at 2.6%. One case was encountered in the vagotomy and antrectomy group (1.5%) which is not a statistically significant difference ($p > 0.05$). No gastric ulcers have to date been found after partial gastrectomy in this study.

When comparison is made between the three operations of the total incidence of proven ulceration i.e. both gastric and duodenal/jejunal statistical

significance is similarly not attained. Considering the total incidence of proven and highly suspected recurrence, vagotomy and drainage (10.7%) has a significantly higher figure than either vagotomy and antrectomy (1.5% $p < 0.025$) or partial gastrectomy (3.2% $p < 0.05$).

It would seem therefore that vagotomy and antrectomy emerges with an appreciable advantage over vagotomy and drainage from the recurrent jejunal/duodenal ulceration point of view. Similarly partial gastrectomy has a markedly lower incidence of recurrence than the former operation, but there does not seem to be much difference between the two gastrectomy operations.

(b) RECURRENT DYSPEPSIA - EXCLUDING PROVEN OR SUSPECTED RECURRENT ULCERATION (Table 7)

These patients have been divided into two main groups, namely, "severe dyspepsia" and "mild to moderate dyspepsia".

The "severe dyspepsia" group describes those in whom the symptomatology was severe enough for them to seek medical advice or treatment and in whom repeated investigation has yielded negative results, and also, those in whom all complaints would seem to be overtly functional. However, it must be emphasised that

TABLE 7

RECURRENT DYSPEPSIA -
EXCLUDING RECURRENT ULCER

OPERATION		SEVERE		MILD-MOD.	TOTAL	HEARTBURN
		*ABNORMAL INV.	NEGATIVE INV.	NOT INV.		
VGY. & DRAIN. (311 cases)	NO.	2	20	30	52	75
	%	0.6	6.4	9.6	16.6	24.1
VGY. & GY. (65 cases)	NO.	0	1	3	4	14
	%		1.5	4.6	6.1	21.5
PARTIAL GY. (61 cases)	NO.	0	1	6	7	7
	%		1.6	9.8	11.4	11.5

* Initially suspected to be gastric ulcers - not confirmed at operation

only those who have been fully investigated have been included in this group. There is of course a certain amount of overlap between these patients and the "highly suspected" recurrent ulcer group as some of the assessment is of necessity subjective.

It will be seen from Table 7 that two patients in the severe dyspepsia group after vagotomy and drainage have been labelled as having abnormal investigations. In both of these barium meal and gastroscopy revealed grossly distorted gastric anatomy and malignant gastric ulceration could not confidently be excluded. At laparotomy both were found to have fibrous adhesions binding the body and antrum of the stomach and the omentum to the under surface of the liver. Both had simple freeing of adhesions and both are at present asymptomatic at 5 and 3 months postoperatively respectively.

When the incidence of severe dyspepsia is compared in the three operations, vagotomy and drainage (7.0%) has a significantly higher incidence of this complication than vagotomy and antrectomy (1.5%) or partial gastrectomy (1.6%) ($p < 0.05$ in each instance).

"Mild to moderate dyspepsia" encompasses those patients who admit to occasional recurrence of preoperative duodenal ulcer symptoms, which necessitates

antacid therapy, but is never of sufficient duration or intensity for them to seek medical attention. There is no significant difference in the three groups in this complication, but when the total numbers of patients who have recurrent dyspepsia, but in whom recurrent ulceration is unlikely are compared, vagotomy and drainage (16.6%) has a significantly higher incidence than vagotomy and antrectomy (6.1% $p < 0.025$). Partial gastrectomy (11.4%) resulted in no significant difference in incidence from either of the other two operations.

Again vagotomy and drainage has a significantly higher incidence of this complication than vagotomy and antrectomy but there is no significant differ- between the gastric resection procedures.

(c) HEARTBURN

Reference to Table 7 will demonstrate that both the vagotomy operations have an approximately equal incidence of this complication ($\pm$ 20%) and that this is considerably higher than that in the partial gastrectomy group (11.5%). The difference is significant ($p < 0.05$).

For various reasons it has not been possible to accumulate sufficient data on the other oesophageal complications of the vagotomy operations, such as

dysphagia and reflux, in this study.

In the same clinic Bank et al.[163] have reported an incidence of transient dysphagia after vagotomy of approximately 30%. However, no obvious cases of organic oesophageal obstruction were encountered in the patients followed up in this series.

(d) ALTERATION IN BOWEL HABIT

Two broad groups of alteration in bowel habit, with reference to the patients preoperative status, have been recognised (Table 8).

Increased frequency of bowel action refers to the passage of a larger number of formed or softish stools but is regarded as a perfectly acceptable phenomenon by the patient.

Diarrhoea is defined for the purposes of this study as the passage of a loose watery stool, irrespective of the number of motions per day during attacks. The range was from three to eight stools daily, however.

Transient postoperative diarrhoea refers to the occurrence of this symptom within the first three months of operation which has subsequently resolved.

Patients in the "continued diarrhoea" group are those who still suffer regularly from the symptom. Further subdivision is made of these patients into

TABLE 8 ALTERATION IN BOWEL HABIT FOLLOWING ELECTIVE SURGERY FOR DUODENAL ULCER

OPERATION		INCREASED FREQUENCY	DIARRHOEA		
			TRANSIENT P.O.(≥3/12)	CONTINUED	TOTAL OVERALL
VGY. & DRAIN. (311 cases)	NO.	144	20	89	109
	%	46.3	6.4	28.6	35.0
VGY. & GY. (65 cases)	NO.	38	3	10	13
	%	58.5	4.6	15.4	20.0
PARTIAL GY. (61 cases)	NO.	14	5	12	17
	%	23.0	8.2	19.7	27.9

those with peristent diarrhoea, i.e. in whom diarrhoea is a regular daily occurrence, and those who suffer from intermittent attacks occurring at regular intervals, with variable periods during which the bowel habit returns to normal between attacks.

Any form of the continued pattern of diarrhoea was regarded as troublesome if the symptom interfered with daily work or recreation in any way and the patient was generally unhappy about it.

About half of the patients who have either vagotomy and drainage (46.3%) or vagotomy and antrectomy (58.5%) have increased frequency of bowel habit. The gastrectomy group has a significantly lower number of patients in this category (23.0%).

Transient postoperative diarrhoea was experienced by an almost equal percentage of patients after each operation. These formed a distinct group whose diarrhoea resolved within three months of surgery.

It will be seen from Table 9 that vagotomy and drainage (28.6%) has a significantly higher incidence of "continued diarrhoea" syndromes than either vagotomy and antrectomy (15.4% $p < 0.025$) or partial gastrectomy (19.7% $p < 0.05$). The incidence of troublesome diarrhoea, in all forms, followed almost the identical pattern to that described above (Tables 9 and 10),

TABLE 9

CONTINUED DIARRHOEA FOLLOWING
ELECTIVE SURGERY FOR DUODENAL ULCER

OPERATION		INTERMITTENT	PERSISTENT	TOTAL	TROUBLESOME
VGY. & DRAIN. (311 cases)	NO.	77	12	89	37
	%	24.7	3.9	28.6	11.9
VGY. & GY. (65 cases)	NO.	10	0	10	2
	%	15.4		15.4	3.1
PARTIAL GY. (61 cases)	NO.	10	2	12	2
	%	16.4	3.3	19.7	3.3

TABLE 10

ANALYSIS OF GROUP WITH TROUBLESOME DIARRHOEA FOLLOWING ELECTIVE SURGERY FOR DUODENAL ULCER

OPERATION	INTERMITTENT		PERSISTENT		TOTAL	
	NO.	%	NO.	%	NO.	%
VGY. & DRAIN.	25	8.0	12	3.9	37	11.9
VGY. & GY.	2	3.1	0		2	3.1
PARTIAL GY.	0		2	3.3	2	3.3

to exactly the same levels of significance. That is, comparison between vagotomy and drainage (11.9%) and vagotomy and antrectomy (3.1%) was significant to $p < 0.025$. Gastrectomy (3.3%) differed from vagotomy and drainage to a significance level of $p = 0.05$. Detailed analysis of the troublesome diarrhoea groups (Table 10) shows that all patients in this study who complained of persistent diarrhoea regarded the symptom as troublesome, but none of these came from patients who had undergone vagotomy and antrectomy.

General consideration of the whole question of diarrhoea shows that a similar pattern emerges to that shown in the other postoperative complication groups, namely, that a significant difference exists between vagotomy and drainage and the gastric resection operations but there is no difference between the latter.

(e) NAUSEA, VOMITING AND ERUCTATION (USUALLY ASCRIBED TO GASTRIC OR AFFERENT LOOP STASIS)

Table 11 illustrates the incidence of the symptoms of nausea, vomiting and excessive eructation after the various operations. These are symptoms which are generally ascribed to chronic gastric stasis in the vagotomy and drainage group or afferent loop stasis in the gastrectomy, and vagotomy and gastrectomy

TABLE 11 NAUSEA, VOMITING & ERUCTATION* AFTER ELECTIVE SURGERY FOR DUODENAL ULCER

OPERATION		TOTAL NO. PATIENTS AFFECTED	NAUSEA	VOMITING		ERUCTATION	
				NON-SPECIFIC	BILIOUS	EXCESSIVE	FOUL
VGY. & DRAIN. (311 cases)	NO.	109	88	22	12	81	31
	%	35.0	28.3	7.1	3.9	26.0	10.0
VGY. & GY. (65 cases)	NO.	20	10	5	6	16	4
	%	30.8	15.4	7.7	9.2	24.6	6.2
PARTIAL GY. (61 cases)	NO.	22	13	6	18	13	1
	%	36.1	21.3	9.8	29.5	21.3	1.6

*Symptoms usually ascribed to gastric stasis in the vagotomy & drainage group & to gastric stasis or afferent loop stasis in the gastrectomy & vagotomy & gastrectomy group

groups. The headings are self-explanatory.

Thirty to 35% of patients undergoing some form of surgery for duodenal ulcer develop symptoms in this category, with no significant difference between the procedures in this respect. Usually more than one symptom occurs concomitantly in any one affected patient, especially among the vagotomy and drainage group.

Not unexpectedly the symptom of pure bilious vomiting occurs more frequently, to a significant degree, in the partial gastrectomy patient (29.5%) when compared to those who have had either vagotomy and antrectomy (9.2%) or vagotomy and drainage (3.9% $p < 0.05$ in each instance).

It is also of interest to note the relative frequency (5 - 10%) with which the symptom of foul eructation occurs after the vagotomy operations. The difference is significant between vagotomy and drainage (10.0%) and gastrectomy (1.6% $p < 0.05$).

With the exceptions of the differences pointed out, there seems to be little to choose between these operations when they are compared from the above point of view.

(f) DUMPING SYNDROME

Two major groups are recognised, early and late, depending upon the time lapse between completing the

TABLE 12

DUMPING SYNDROMES AFTER ELECTIVE SURGERY FOR DUODENAL ULCER

POST PRANDIAL FULLNESS (EARLY DUMPING)

OPERATION		WITHOUT VASOMOTOR SYMPTOMS			WITH VASOMOTOR SYMPTOMS				
		TOTAL	TRANSIENT POSTOP. (3/12)	PERSIST-ENT	TOTAL	MILD*	MOD-ERATE**	SEV-ERE*+	GRAND TOTAL
VGY. & DRAIN. (311 cases)	NO.	84	27	57	72	49	19	4	156
	%	27.0	8.7	18.3	23.2	15.8	6.1	1.3	50.2
VGY. & GY. (65 cases)	NO.	20	10	10	10	7	3	0	30
	%	30.8	15.4	15.4	15.4	10.8	4.6	-	46.2
PARTIAL GY. (61 cases)	NO.	16	7	9	24	7	8	9	40
	%	26.3	11.5	14.8	39.4	11.5	13.1	14.8	65.7

meal and onset of symptoms.

Early dumping syndrome (Table 12)

This is defined, for the purposes of this study, as a marked sensation of epigastric distension and discomfort occurring almost immediately after eating or drinking. This symptom may be associated with certain "vasomotor" phenomena such as dizziness or faintness, sweatiness, palpitations and tachycardia. There may also be a feeling of thirst, and nausea, with or without vomiting. The symptom complex usually passes off within about half an hour.

Late dumping (hypoglycaemia) syndrome (Table 13)

The late dumping syndrome is defined as the onset of a sensation of dizziness, sweatiness, headache, and weakness coming on one and a half hours or so after taking food or drink.

An attempt has been made to grade the various degrees of severity of the symptomatology in the early vasomotor and late dumping groups. It proved very difficult to grade the group with post prandial fullness occurring without vasomotor symptoms and this was abandoned.

Severe dumping constitutes a fairly clear-cut entity. Symptoms occur after every meal, interfere with work and recreation and are not easily controlled by simple dietary means.

The classification into mild and moderate groups has been fairly arbitrarily decided. Mild dumpers are those who experience occasional attacks, related to dietary indiscretion, or those with more frequent attacks but who are not compelled to curtail their activities during an attack. Those with a moderate degree of the syndrome tend to have more frequent attacks but these can be controlled by diet, or who have symptoms severe enough to force them to curtail their activities during an attack. Obviously there is a large amount of overlap between the groups, especially in the mild - moderate categories.

It will be seen from Table 12 that 5 to 15% of all patients undergoing surgery experience post prandial distension transiently after their respective operations, which resolves completely within three months or so. The majority of patients who experience this symptom in the immediate postoperative period are left with various degrees of it in the long term. At 4 - 10 years after the respective operations there is no significant difference between them in the incidence of post prandial fullness.

Early vasomotor dumping however shows some significant differences in the frequency with which it occurs. Vagotomy and drainage (23.2%) has a

significantly lower incidence than partial gastrectomy (39.4% $p < 0.01$). However, the lowest incidence of the symptom was found in the vagotomy and antrectomy group (15.4%).

Severe grades of early dumping occur to a similar pattern. Gastrectomy (14.8%) has a significantly higher incidence of the severe grade than vagotomy and drainage (1.3% $p < 0.0005$). No cases of severe early vasomotor dumping were noted among vagotomy and antrectomy patients in this series.

Another interesting point that emerges is that approximately a half of all patients undergoing surgery for duodenal ulcer develop some form of early dumping syndrome at some stage after their respective operations.

Table 13 illustrates the incidence of late dumping syndrome and, the percentages are not significantly different. However it will be seen that the only cases with a severe grade of the syndrome both appeared among the vagotomy and antrectomy patients (3.0%).

The dumping syndromes are not fixed static entities once they become established, and with reasonably intelligent patients advice regarding diet etc. can alleviate the severity of their symptomatology. It can be seen from Table 14 that after the vagotomy

TABLE 13

HYPOGLYCAEMIA SYNDROME

(LATE DUMPING)

After elective surgery for duodenal ulcer

OPERATION		TOTAL	MILD	MODERATE	SEVERE
VGY. & DRAIN.	NO.	12	9	3	0
	%	3.9	2.9	1.0	-
VGY. & GY.	NO.	6	3	1	2
	%	9.2	4.6	1.5	3.0
PARTIAL GY.	NO.	3	1	2	0
	%	4.8	1.6	3.2	

TABLE 14

TABLE TO ILLUSTRATE HOW THE SEVERITY OF DUMPING SYNDROMES AFTER GASTRIC SURGERY TEND TO IMPROVE WITH TIME

OPERATION		EARLY				LATE	
		WITHOUT VASOMOTOR SYMPTOMS		WITH VASOMOTOR SYMPTOMS			
		TOTAL	*IMPROVED	TOTAL	*IMPROVED	TOTAL	*IMPROVED
VGY. & DRAIN. (311 cases)	NO.	57	31	72	32	12	4
	%		54.4		44.4		33.3
VGY. & GY. (65 cases)	NO.	10	5	10	5	6	2
	%		50.0		50.0		33.3
PARTIAL GY. (61 cases)	NO.	9	4	24	6	3	0
	%		44.4		25.0		

*Denotes improvement in degree of severity of symptoms NOT complete resolution

operations about a half of the early dumpers, and about a third of late dumpers improve to a significant degree. After partial gastrectomy a slightly lower percentage of early dumpers respond to treatment.

Partial gastrectomy undoubtedly emerges as the operation with the worst result, with reference to early dumping, while vagotomy and antectomy, for whatever reason, gives the best result. The order is reversed when late dumping is considered. On balance, partial gastrectomy has a high recurrence of severe dumping than the vagtomy procedures.

(g) WEIGHT CHANGE (Table 15)

Accurate data on alterations in weight were not available in all patients followed up. Persistent alterations in weight of 10 pounds or more, as an absolute value, were taken as significant. Table 15 is self-explanatory. No statistically significant difference can be demonstrated between any of the groups ($p < 0.05$).

(h) VISICK GRADING (MODIFIED)

Overall assessment of the current clinical status of patients in this series, with regard to their general feeling of well-being and satisifaction

TABLE 15 WEIGHT CHANGE (≥10 lb.)

AFTER ELECTIVE SURGERY FOR DUODENAL ULCER

OPERATION	GAIN		AVERAGE AMOUNT (lbs.)	LOSS		AVERAGE AMOUNT (lbs.)	UNALTERED	
	NO.	%		NO.	%		NO.	%
VGY. & DRAIN. (251 cases)	64	25.5	18.0	106	42.2	15.4	81	32.3
VGY. & GY. (52 cases)	12	23.1	24.0	24	46.2	18.4	16	30.8
PARTIAL GY. (53 cases)	18	34.0	20.6	25	47.2	19.3	10	18.7

with the result of their operation has been made using a modification of the Visick grading (Visick 1948). The modification used is identical with that employed by Goligher et al.[399-404].

Four grades of results are recognised:

Grade 1 (Excellent result)

The patient has absolutely no symptoms and the result is to all intents and purposes perfect.

Grade 2 (Very good result)

Interrogation elicits mild occasional symptoms easily controlled by dietary adjustments and not requiring any specific treatment. The patient considers the result perfect.

Grade 3 (Satisfactory)

Mild to moderate symptoms are present, not controlled merely by dietary means and requiring some medical therapy, but they do not interfere seriously with work or recreation. Doctor and patient satisfied with the result.

Grade 4 (Unsatisfactory i.e. surgical failures)

Symptoms are of severe enough degree to interfere considerably with work and leisure. Both doctor and patient are dissatisfied with the result.

This category includes all patients with proven recurrent ulceration and all those submitted to further

operation for complications of the initial disease process or of the initial operation. All these patients are automatically permanently placed into this group regardless of the result of any subsequent curative operation.

In making the assessments there is quite marked overlap between Grade 1 and 2 which can for all practical purposes be regarded as a single group. Similarly there is some overlap between Grade 3 and 4 but not to quite the same extent.

Assessment of current clinical status of patients in this series is summarised in Table 16. Vagotomy and antrectomy (83.6%) has a significantly greater proportion of patients in the Visick Grade 1 category than the vagotomy and drainage group (63.1% $p < 0.005$). Athough the percentage in this category is much lower in the gastrectomy group (69.4%) this fails to attain statistical significance when compared with vagotomy and antrectomy. Combination of the Grade 1 and 2 categories does not affect the statistical relationships between the operations.

The highest proportion of surgical failures (Grade 4 cases) was found in the vagotomy and drainage group (19.6%). This percentage was not however found to be significantly higher than that for vagotomy and

TABLE-~~16~~

VISICK GRADING (MODIFIED) IN PATIENTS AFTER ELECTIVE SURGERY FOR DUODENAL ULCER

OPERATION		GRADE 1	2	3	4
VGY. & DRAIN. (306 cases)	NO.	193	33	20	60
	%	63.1	10.8	6.6	19.6
VGY. & GY. (61 cases)	NO.	51	2	1	7
	%	83.6	3.3	1.6	11.5
PARTIAL GY. (59 cases)	NO.	41	5	4	9
	%	69.4	8.5	6.8	15.3

antrectomy (11.5%), which has the lowest incidence, or gastrectomy (15.3% $p > 0.05$). If the proportions of Visick Grade 3 and 4 are combined in each group, the difference between vagotomy and drainage (26.2%) and vagotomy and antectomy (13.1%) becomes statistically valid ($p = < 0.05$).

Although vagotomy and antrectomy produces the highest percentage of perfect results, significantly higher than the vagotomy and drainage group, the incidence of failures is equal in all operations. The trend however favours vagotomy and antrectomy.

The Grade 4 group has been further analysed in detail (Table 17) in terms of the total numbers of patients severely enough affected by a particular symptom to cause him or her to be placed in this category. There is however a certain amount of overlap of symptomatology.

In the vagotomy and drainage group 12 patients (20%) had more than one symptom of severe degree e.g. dumping with diarrhoea or dyspepsia with diarrhoea etc.

The commonest single cause was proven or highly suspected recurrent ulceration (58%). This is followed by dyspepsia with negative investigation (27.0%), a group which contains a fair percentage

TABLE 17

VISICK GRADE 4 ANALYSIS

OPERATION		TOTAL NUMBER AFFECTED	PROVEN REC. ULCER	SUSPECTED REC. ULCER	DYSPEPSIA - NEG. INV.	STASIS SYND-ROMES	DUMPING EARLY & LATE	DIARR-HOEA	PTS. WITH MULTIPLE FACTORS
VGY. & DRAIN.	NO.	60	20	15	16	5	4	12	12
	%		33.3	25.0	27.0	8.3	6.7	20.0	20.0
			58.0						
VGY. & GY.	NO.	7	1	0	0	4	1	1	0
	%		14.3			57.1	14.3	14.3	
PARTIAL GY.	NO.	9	1	1	1	5	6	2	7
	%		11.1	11.1	11.1	55.6	66.7	22.2	77.8
			22.2						

whose symptoms are very probably functional. Stasis syndromes and dumping comprise the smallest proportion of patients in the vagotomy and drainage group.

Of the vagotomy and gastrectomy group the majority of the Grade 4 cases are due to stasis syndromes, i.e. afferent loop stasis (4 out of 7 - 57%) and there are none with multiple problems of severe degree.

In contrast it will be seen that the majority of the gastrectomy patients with failed primary surgery complain of multiple symptoms (7 out of 9 cases - 77.8%). The largest single problems are dumping (6 out of 9 - 66.7%) and afferent loop stasis (5 out of 9 - 55.6%).

Generally speaking, therefore, recurrent ulceration is the largest single cause of significant morbidity after vagotomy and drainage, while afferent loop problems and dumping are the major hazards of the gastric resections.

(i) REPEAT OPERATIONS FOR RECURRENT SYMPTOMS AFTER GASTRIC SURGERY

Tables 18 and 19 illustrate an analysis of the indications for repeat operations done for complications of the initial disease process or operation.

TABLE 18

REPEAT OPERATIONS FOR RECURRENT SYMPTOMS AFTER GASTRIC SURGERY

INITIAL OPERATION		FIRST REPEAT OPERATION						VISICK AFTER CURATIVE OPERATION			
		TOTAL NUMBER PTS.	PROVEN REC. ULCER	SUSP. REC. ULCER	STASIS SYNDROME (VOMIT'G)	DUMP-ING	MORT-ALITY	1	2	3	4
VGY. & DRAIN.	NO.	32	16	12	4	0	3	17	1	0	9
	%	10.3*	50.0	37.5	12.5		9.4	62.9	3.8		33.3
			87.5								
VGY. & GY.	NO.	4	0	0	4	0	0	2	0	0	2
	%	6.2*			100.0			50.0			50.0
PARTIAL GY.	NO.	5	0	1	2	2	1	1	0	3	0
	%	8.2*		20.0	40.0	40.0	20.0	20.0		60.0	

*% of total number submitted to each operation

TABLE 19 ANALYSIS OF PATIENTS WHO HAVE REQUIRED MORE THAN ONE OPERATION AFTER GASTRIC SURGERY FOR DUODENAL ULCER

INITIAL OPERATION		ADDITIONAL REPEAT OPERATION(S)						CURRENT VISICK STATUS			
		TOTAL NUMBER PTS.	TOTAL NUMBER OPS.	REC. ULCER	STASIS (VOMIT-ING)	EFFERENT LOOP OBSTRUCT'N	MORT-ALITY	1	2	3	4
VGY. & DRAIN.	NO.	5	9	5	4	0	0	3	1		1
	%	1.6									
VGY. & GY.	NO.	0									
	%										
PARTIAL GY.	NO.	1	2	0	0	2	0	1			
	%	1.6									

It will be seen from Table 18 that 32 patients (10.3% of those followed up) in the vagotomy and drainage group have had to undergo repeat operation. Five of these have required more surgery (1.6% of those followed up) to make a total of 41 repeat operations, 3 patients died after the first re-operation (9.4%).

Recurrent ulceration was the indication for operation in 87.5% of patients undergoing the first procedure. Five out of the 9 operations done subsequent to this were for the same reason.

Stasis syndromes constituted the only other indication, both for the first and for the subsequent repeat operations.

It is of interest to note that a third of patients who had undergone attempted curative surgery were still graded as surgical failures. Even after 5 of the 9 patients in this group had undergone further surgery, there still remains one who has a totally unsatisfactory result.

Four (6.2% of those followed up) vagotomy and antrectomy patients have been re-operated upon, all for afferent loop problems. Of these 2 are still categorized as Visick Grade 4.

Seven repeat operations have had to be done on

5 (8.2% of those followed up) of the gastrectomy patients. One death occurred as a result of the first re-operations, which were performed mainly for afferent loop problems (2 cases - 40%) and dumping (2 cases - 40%).

Visick grading of these patients after their operation shows 3 of the 4 remaining alive to be classified in the third category, i.e. a borderline satisfactory results.

One patient (1.6% of those followed up) in the gastrectomy group has had to undergo two subsequent repeat operations, both for efferent loop obstruction. He remains well to date 2 years after his last operation.

An important fact that emerges is that a fair proportion of patients having to undergo repeat surgery remain in the unsatisfactory result category irrespective of the nature of the original procedure.

III CLINICAL COMPARISON BETWEEN THE RESULTS OF SELECTIVE AND TRUNCAL VAGOTOMY IN THE VAGOTOMY AND DRAINAGE GROUP

One hundred and eleven of the vagotomy and drainage group were subjected to selective vagotomy. This comprised both anterior and posterior selective nerve section wherever technically feasible. The

drainage procedure was routinely pyloroplasty and gastroenterostomies were reserved for the cases in which the former was technically hazardous. The remaining 200 patients had routine truncal vagotomy.

(a) RECURRENT ULCERATION AND RECURRENT DYSPEPSIA (EXCLUDING RECURRENT ULCER)

It will be seen from Table 20 that in all categories there is an almost identical incidence of recurrent ulceration when the two types of vagotomy are compared.

The incidence of recurrent dyspepsia excluding recurrent ulcer also shows no significant differences between the two groups (Table 21).

(b) HEARTBURN

The incidence of this complication (Table 21) is significantly lower in the selective (17.1%) than in the truncal vagotomy group (28.0% $p < 0.05$).

(c) ALTERATION IN BOWEL HABIT

Table 22 shows that there is no significant difference between the two vagotomy types with regard to the incidence of increased frequency of bowel motions and transient postoperative diarrhoea. Differences become significant when the continued diarrhoea syndromes are considered, to a level of $p < 0.025$.

TABLE 20

RECURRENT ULCERATION - COMPARISON BETWEEN SELECTIVE & TRUNCAL VAGOTOMY & DRAINAGE

	DUODENAL/JEJUNAL			GASTRIC	TOTALS	
VGY. & DRAIN.	PROVEN	HIGHLY SUSPECT	TOTAL	PROVEN	PROVEN	PROVEN AND SUSPECT
SELECTIVE (Tot: 111) NO.	4	5	9	3	7	12
SELECTIVE (Tot: 111) %	3.6	4.5	8.1	2.7	6.3	10.8
TRUNCAL (Tot: 200) NO.	8	8	16	5	13	21
TRUNCAL (Tot: 200) %	4.0	4.0	8.0	2.5	6.5	10.5

TABLE 21

RECURRENT DYSPEPSIA - EXCLUDING RECURRENT ULCER
COMPARISON BETWEEN SELECTIVE & TRUNCAL VAGOTOMY & DRAINAGE

OPERATION		SEVERE		MILD-MOD.	TOTAL	HEARTBURN
		*ABNORMAL INV.	NEGATIVE INV.	NOT INV.		
SELECTIVE (111 cases)	NO.	0	6	14	20	19
	%		5.4	12.6	18.0	17.1
TRUNCAL (200 cases)	NO.	2	14	16	30	56
	%	1.0	7.0	8.0	15.0	28.0

* Initially suspected to be gastric ulcers - not confirmed at operation

TABLE 22 COMPARISON OF ALTERATION IN BOWEL HABIT BETWEEN SELECTIVE & TRUNCAL VAGOTOMY & DRAINAGE

VGY. & DRAIN.	INCREASED FREQUENCY		DIARRHOEA					
			TRANSIENT P.O.(3/12)		CONTINUED		TOTAL OVERALL	
	NO.	%	NO.	%	NO.	%	NO.	%
SELECTIVE (111 cases)	51	45.9	8	7.2	23	20.7	31	27.9
TRUNCAL (200 cases)	93	46.5	12	6.0	66	33.0	78	39.0

Troublesome diarrhoea can be seen in Table 23 to occur in 7.2% of selectively vagotomized patients and 14.5% of those who have had the truncal procedure. The differences are statistically significant ($p < 0.05$).

(d) NAUSEA, VOMITING AND ERUCTATION (USUALLY ASCRIBED TO GASTRIC STASIS)

It is of interest to note in Table 24 that a significantly greater proportion of the truncal vagotomy group (39.5 %) complain of excessive eructation, compared to the selective group (1.8% $p < 0.0005$). Similarly 15% of the truncal group suffer from foul eructation, as opposed to (0.9%) of the selectively vagotomized patients. The difference is also highly significant ($p < 0.0005$).

(e) DUMPING SYNDROMES

It will be seen from Table 25 that the majority of patients with the early dumping syndrome in the selective group have vasomotor symptoms. The 29.7% incidence of early vasomotor dumping in this group is significantly greater than the 19.5% found in the truncal group ($p < 0.0005$). All of these are of mild to moderate degree however and all those with severe early dumping belong to the truncal vagotomy group.

TABLE 23 CONTINUED DIARRHOEA AFTER VAGOTOMY & DRAINAGE
COMPARISON BETWEEN SELECTIVE & TRUNCAL VAGOTOMY

VGY. & DRAIN.		INTERMITTENT	PERSISTENT	TOTAL	TROUBLESOME
SELECTIVE (111 cases)	NO.	20	3	23	8
	%	18.6	2.7	20.7	7.2
TRUNCAL (200 cases)	NO.	57	9	66	29
	%	28.5	4.5	33.0	14.5

TABLE 24

NAUSEA, VOMITING & ERUCTATION* AFTER VAGOTOMY & DRAINAGE - COMPARISON BETWEEN SELECTIVE & TRUNCAL VAGOTOMY

VGY. & DRAIN.		TOTAL NO. PATIENTS AFFECTED	NAUSEA	VOMITING		ERUCTATION	
				NON-SPECIFIC	BILIOUS	EXCESSIVE	FOUL
SELECTIVE (111 cases)	NO.	34	32	9	4	2	1
	%	30.6	28.8	8.1	3.6	1.8	0.9
TRUNCAL (200 cases)	NO.	75	56	13	8	79	30
	%	37.5	28.0	7.5	4.0	39.5	15.0

*Symptoms usually attributed to gastric stasis

TABLE 25

DUMPING SYNDROMES AFTER VAGOTOMY & DRAINAGE
COMPARISON BETWEEN SELECTIVE & TRUNCAL VAGOTOMY

POST PRANDIAL FULLNESS (EARLY DUMPING)

	WITHOUT VASOMOTOR SYMPTOMS			WITH VASOMOTOR SYMPTOMS				
VGY. & DRAIN.	TOTAL	TRANSIENT POSTOP. (3/12)	PERSIST-ENT	TOTAL	MILD	MOD-ERATE	SEV-ERE	GRAND TOTAL
SELECTIVE (111 cases) NO.	16	5	11	33	23	8	0	49
SELECTIVE (111 cases) %	14.4	4.5	9.9	29.7	20.7	7.2		44.1
TRUNCAL (200 cases) NO.	68	22	46	39	25	12	4	107
TRUNCAL (200 cases) %	34.0	11.0	23.0	19.5	12.5	6.0	2.0	53.5

Late dumping (Table 26) is also significantly commoner in this group ($p < 0.01$).

(f) WEIGHT CHANGE

It is evidence from Table 27 that there is no significant difference between these groups with regard to this problem.

(g) VISICK GRADING

There is a slightly higher, though insignificantly so, percentage of Visick Grade 1 patients in the selective vagotomy group (Table 28). Similarly although there are 9% more Visick Grade 4 patients in the truncal vagotomy group, the difference fails to attain statistical significance.

Proven and suspected recurrent ulceration constitutes the largest single reason for surgical failure, significantly more so in the selective vagotomy group ($p < 0.05$) than in the truncal group (Table 29).

Stasis and dumping syndromes are conspicuous by their absence in the selective group. Diarrhoea, although accounting for a lower percentage among selectively vagotomized patients, in general, did not occur significantly less frequently among those who regarded the symptom as severe enough to place them into the Visick 4 category.

TABLE 26

HYPOGLYCAEMIA SYNDROME

(LATE DUMPING)

Comparison between selective and truncal vagotomy and drainage

VGY. & DRAIN.		TOTAL	MILD	MODERATE	SEVERE
SELECTIVE	NO.	9	7	2	0
	%	8.1	6.3	1.8	
TRUNCAL	NO.	3	3	0	0
	%	1.5	1.5		

TABLE 27

WEIGHT CHANGE (≥ 10 lb.)

COMPARISON BETWEEN SELECTIVE & TRUNCAL VAGOTOMY & DRAINAGE

VGY. & DRAIN.	GAIN		AVERAGE AMOUNT (lbs.)	LOSS		AVERAGE AMOUNT (lbs.)	UNALTERED	
	NO.	%		NO.	%		NO.	%
SELECTIVE (89 cases)	22	24.7	18.0	38	42.6	15.0	29	32.6
TRUNCAL (162 cases)	42	25.9	18.7	68	42.0	15.6	52	32.1

TABLE 28

VISICK GRADING (MODIFIED)
COMPARISON BETWEEN SELECTIVE &
TRUNCAL VAGOTOMY & DRAINAGE

VGY. & DRAIN.		GRADE 1	2	3	4
SELECTIVE (109 cases)	NO.	74	11	9	15
	%	67.9	10.1	8.3	13.8
TRUNCAL (197 cases)	NO.	122	16	14	45
	%	61.9	8.1	7.1	22.8

However, it would seem that if recurrent ulceration could be prevented, selective vagotomy and drainage would, in general, hold a marginal advantage over the truncal operation.

IV COMPARISON OF GASTRIC ACID SECRETORY PATTERNS IN RESPONSE TO HISTAMINE (PENTAGASTRIN) AND INSULIN STIMULATION AFTER VAGOTOMY AND DRAINAGE, VAGOTOMY AND ANTRECTOMY AND PARTIAL GASTRECTOMY

(a) GENERAL COMPARISON OF THE THREE OPERATIONS (Table 30) A.H.T.

The mean preoperative M.A.O. of all duodenal ulcer patients coming to surgery in this series was 32.9 mEq./Hr., with a mean B.A.O. of 7.1 mEq./Hr. The range of respective values found is illustrated in Figure 18.

The mean preoperative M.A.O. in the vagotomy and drainage group was found to be lowest at 27.3 mEq./Hr. (Fig.19) with a similar mean value for those subjected to gastrectomy (29.9 mEq./Hr.) (Fig.20).

Patients who underwent vagotomy and antrectomy had a very much higher mean preoperative M.A.O. (41.6 mEq./Hr.) than either of the other two groups (Fig.20).

Basal acid output (B.A.O.) preoperatively followed a similar pattern in the three groups.

TABLE 29 VISICK GRADE 4 ANALYSIS

VAGOTOMY		TOTAL NUMBER AFFECTED	PROVEN REC. ULCER	SUSPECTED REC. ULCER	DYSPEPSIA - NEG. INV.	STASIS SYND-ROMES	DUMPING EARLY & LATE	DIARR-HOEA	PTS. WITH MULTIPLE FACTORS
SELECTIVE	NO.	15	7	5	4	0	0	2	2
	%		46.2	33.3	26.7			13.3	13.3
			79.5						
TRUNCAL	NO.	45	13	10	12	5	4	10	10
	%		28.8	22.2	26.6	11.1	8.9	22.2	22.2
			51.0						

TABLE 31

GASTRIC ACID SECRETORY PATTERNS IN RESPONSE TO HISTAMINE (PENTAG.) & INSULIN IN THE POSTOPERATIVE RECURRENT ULCER/RECURRENT DYSPEPSIA GROUPS FOLLOWING VAGOTOMY & DRAINAGE

GROUP	TOT. NO. PTS.	NO. PTS. TESTED	A. H. T. MEAN PREOP mEq./Hr.		A. H. T. MEAN POSTOP mEq./Hr.		A. H. T. MEAN % REDUCTION		INSULIN TOT. NO. TESTS	INSULIN MULT. CRITERIA POSITIVE	INSULIN HOL-LANDER POSITIVE
			B.A.O.	M.A.O.	B.A.O.	M.A.O.	B.A.O.	M.A.O.			
REC. JU/DU PROVEN	12 3.9%	11	6.0	32.0	3.6	16.7	40.0	47.8	8	7 87.5%	7 87.5%
HIGHLY SUSPECT	13 4.3%	11	6.2	31.8	2.9	11.3	53.2	64.5	10	7 70.0%	7 80.0%
REC. G.U. PROVEN	8 2.6%	8	3.6	25.9	2.6	14.3	27.8	44.8	6	0	0
REC. DYSPEPSIA *SEV. - NEG. INV	22 7.3%	21	3.9	23.7	1.5	8.8	61.5	62.9	14	2 14.3%	6 42.9%
MILD - MOD. NOT INV.	30 9.6%	30	5.5	25.2	1.9	9.1	65.4	63.9	14	1 7.1%	5 35.7%

FIG.18

PREOPERATIVE A.H.T. RESULTS IN DUODENAL ULCER PATIENTS SUBMITTED TO SURGERY IN THIS SERIES (357 TESTS)

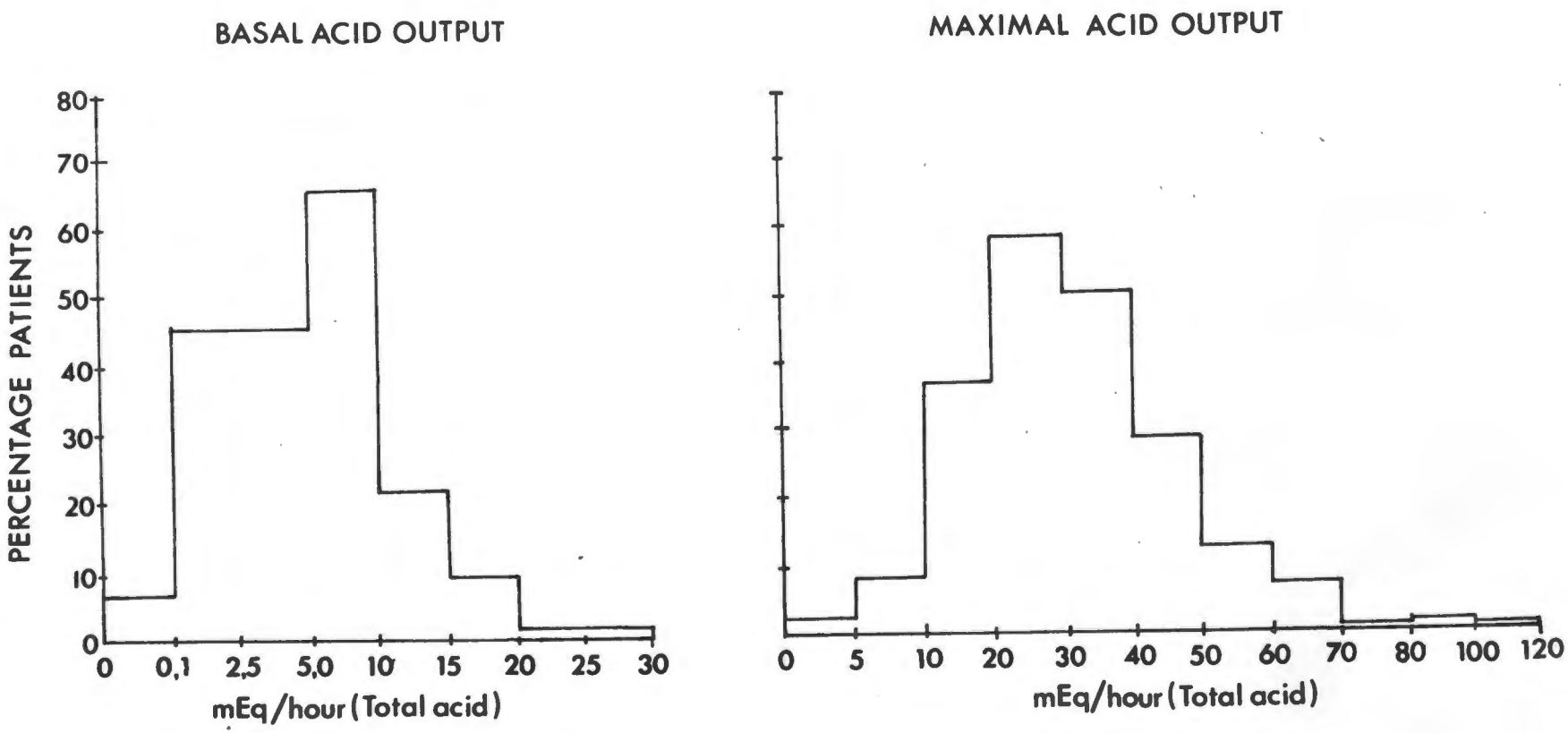


FIG.19

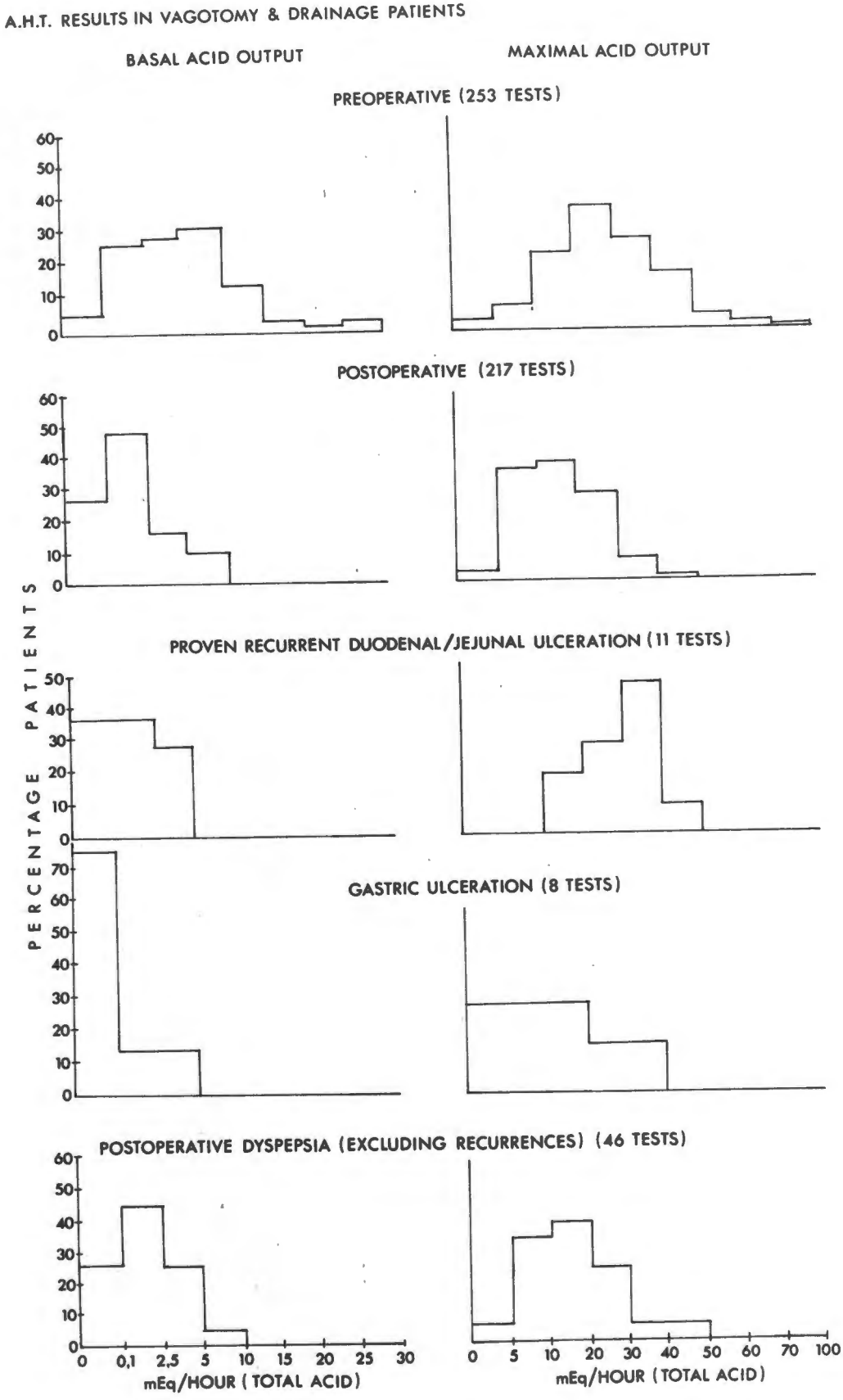
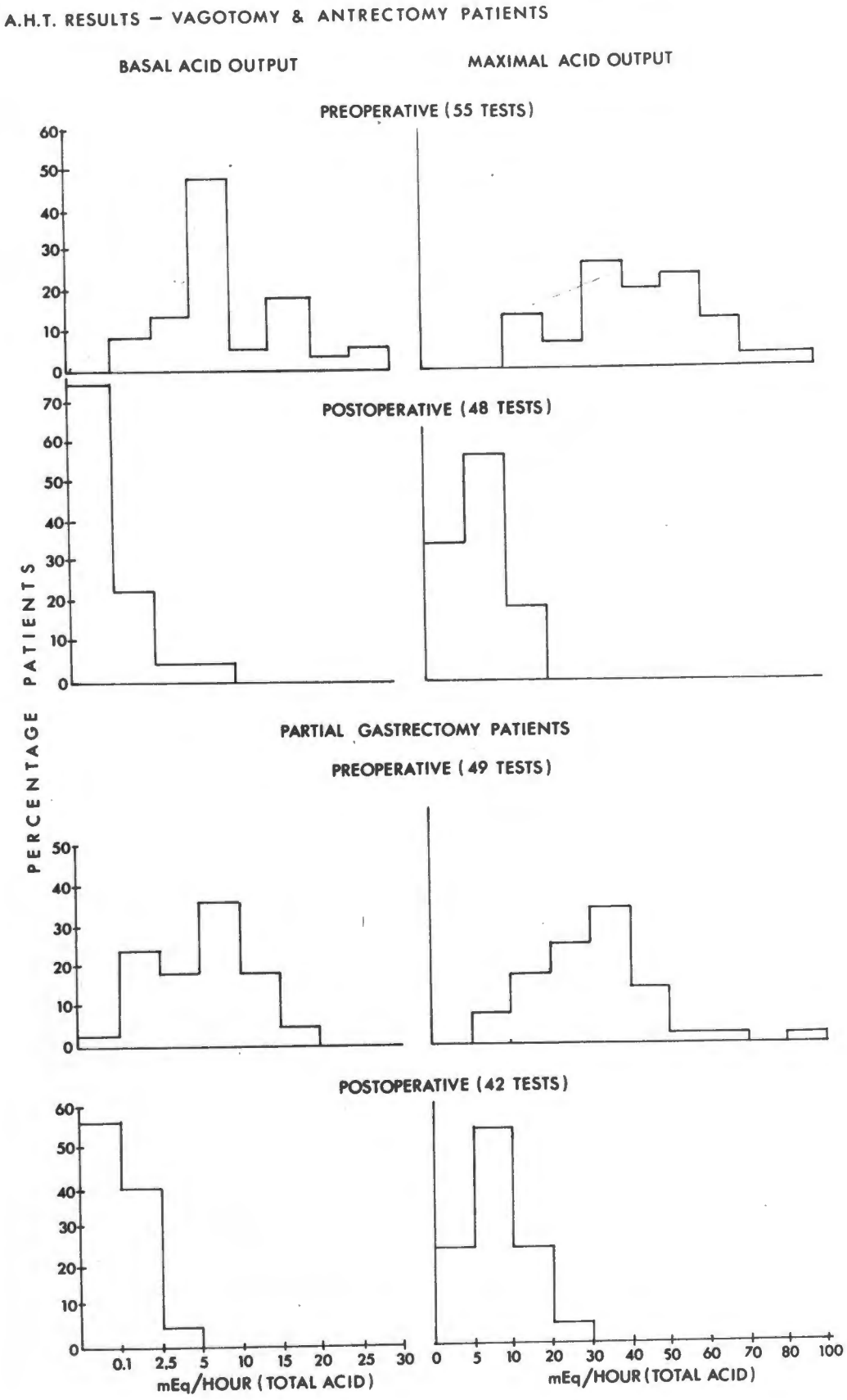

A.H.T. RESULTS IN VAGOTOMY & DRAINAGE PATIENTS
BASAL ACID OUTPUT
MAXIMAL ACID OUTPUT
PREOPERATIVE (253 TESTS)
POSTOPERATIVE (217 TESTS)
PROVEN RECURRENT DUODENAL/JEJUNAL ULCERATION (11 TESTS)
GASTRIC ULCERATION (8 TESTS)
POSTOPERATIVE DYSPEPSIA (EXCLUDING RECURRENCES) (46 TESTS)
PERCENTAGE PATIENTS
0 0,1 2,5 5 10 15 20 25 30
0 5 10 20 30 40 50 60 70 100
mEq/HOUR (TOTAL ACID)
mEq/HOUR (TOTAL ACID)

FIG. 20


A.H.T. RESULTS – VAGOTOMY & ANTRECTOMY PATIENTS
BASAL ACID OUTPUT
MAXIMAL ACID OUTPUT
PREOPERATIVE (55 TESTS)
POSTOPERATIVE (48 TESTS)
PERCENTAGE PATIENTS
PARTIAL GASTRECTOMY PATIENTS
PREOPERATIVE (49 TESTS)
POSTOPERATIVE (42 TESTS)
0.1 2.5 5 10 15 20 25 30
mEq/HOUR (TOTAL ACID)
0 5 10 20 30 40 50 60 70 80 100
mEq/HOUR (TOTAL ACID)

Percentage reduction:

Vagotomy and antrectomy resulted in a reduction of the preoperative B.A.O. and M.A.O. levels of over 90%. This reduction in acid levels is significantly higher than the 64.7% for basal and 67.0% for maximal acid output caused by vagotomy and drainage.

Partial gastrectomy, with values of just below 90% for B.A.O. as well as M.A.O. reduction is also shown to be considerably more efficient than vagotomy and drainage at reducing acid output, and marginally less effective than vagotomy and antrectomy.

Insulin Tests

Of 127 patients in the vagotomy and drainage group who had insulin tests done, 52 (40.9%) yielded positive results using pure Hollander criteria and hence are thought to have had incomplete vagotomies.

Eleven patients with vagotomy and antrectomy had insulin tests, 4 (36.4%) of which were Hollander positive.

When multiple criteria were used as the index of positivity of the test, that is, with three or more criteria positive, the proportion of incomplete vagotomies was much lower than when pure Hollander criteria were used.

Using this means of interpretation 22% of the

TABLE 30

EFFECT OF ELECTIVE OPERATIONS FOR DUODENAL ULCER ON GASTRIC ACID SECRETORY RESPONSE TO HISTAMINE (PENTAGASTRIN) AND INSULIN

OPERATION		TOT. NO. TESTS	A. H. T. MEAN PREOP mEq./Hr.		MEAN POSTOP mEq./Hr.		MEAN % REDUCTION		INSULIN TOT. NO. TESTS	MULT. CRITERIA POSITIVE	HOL-LANDER POSITIVE
			B.A.O.	M.A.O.	B.A.O.	M.A.O.	B.A.O.	M.A.O.			
VGY. & DRAIN. (Tot: 311)	NO.	253	5.1	27.3	1.8	9.0	64.7	67.0	127	28	52
	%									22.0	40.9
VGY. & GY. (Tot: 65)	NO.	55	10.3	41.6	0.7	2.3	93.2	94.5	11	0	4
	%									0	36.4
PARTIAL GY. (Tot: 61)	NO.	49	5.8	29.9	0.6	3.1	89.7	89.6	-	-	-
	%									-	-

vagotomy and drainage group were positive and none of the vagotomy and antrectomy patients were positive.

(b) COMPARISON OF THE POSTOPERATIVE ACID SECRETORY PATTERNS IN THE VARIOUS CATEGORIES OF RECURRENT ULCER DYSPEPSIA IN THE VAGOTOMY AND DRAINAGE GROUP (Table 31).

In view of the small numbers of patients in the vagotomy and antrectomy and partial gastrectomy groups, this analysis has been confined to the patients who have had vagotomy and drainage.

(i) RECURRENT DUODENAL/JEJUNAL ULCERATION

PROVEN RECURRENCE

A.H.T.

Eleven patients were tested pre- and post-operatively. It will be seen from Table 31 that preoperatively these patients had a higher mean basal and maximal acid output value than the vagotomy and drainage group as a whole, that is B.A.O./M.A.O. = 6.0/32.0 mEq./Hr. as apposed to 5.1/27.3 mEq./Hr. (see also Figure 18).

Percentage reduction

Conversely, the percentage reduction of pre-operative A.H.T. values by vagotomy and drainage is significantly lower in this recurrence group than in the whole group (B.A.O./M.A.O. = 40.0/47.8% as opposed

to 64.7/67.0% respectively).

Insulin tests

Out of 8 patients tested, one with a proven recurrent duodenal ulcer after vagotomy and pyloroplasty had a complete vagotomy using both pure Hollander as well as multiple criteria as parameters.

Otherwise it will be seen that there is an identical incidence of incomplete vagotomy using both means of interpretation of the test (7 out of 8 tests positive - 87.5%).

HIGHLY SUSPECTED RECURRENCE

A.H.T.

Table 31 shows that there are similar preoperative B.A.O. and M.A.O. levels to those found in the proven recurrent ulcer group among the 11 patients who had both preoperative and postoperative tests.

Percentage reduction

The percentage reduction of preoperative B.A.O. is slightly greater in this group than in the proven recurrence group (53.2% as opposed to 40.0%). Percentage reduction of the M.A.O. however approaches that of the mean value for the whole group (64.5% for highly suspected as opposed to 67.0% for the whole group).

Insulin tests

Of the 10 tests done, 8 were positive by pure Hollander criteria (80%) while 7 were positive by multiple criteria (70%), a difference not found among the proven recurrent ulceration patients.

The discrepancies in the A.H.T. and insulin data between the proven and suspected recurrent ulceration groups suggest that a fair number of the so-called highly suspected recurrences are in fact not true recurrent ulcers.

(ii) RECURRENT GASTRIC ULCERATION (G.U.) (PROVEN)

A.H.T.

All 8 patients had both pre- and postoperative tests. Mean preoperative B.A.O./M.A.O. (3.6/25.9 mEq./Hr.) values are slightly lower in patients with recurrent gastric ulcer, than the mean values for the vagotomy and drainage group as a whole, which has a mean figure of B.A.O./M.A.O. = 5.1/27.3 mEq./Hr.

There is also a fairly marked difference in this ratio between the recurrent gastric ulcer group and the recurrent duodenal/jejunal ulcer group where the values are B.A.O./M.A.O. = 6.0/32.0 mEq./Hr.

Percentage reduction

For this group this was significantly lower for both B.A.O. and M.A.O. than the mean values for

vagotomy and drainage as a whole, with similar values for those found in the proven recurrent duodenal/jejunal ulcer patients (refer Table 31) with regard to the M.A.O. The mean percentage reduction of preoperative B.A.O. was markedly lower than that for recurrent duodenal ulceration however (27.8% as opposed to 40.0%).

Insulin tests

It is of interest to note that of the 6 patients in this category who had insulin tests, none were positive by either pure Hollander or multiple criteria. All patients with gastric ulceration occurring after vagotomy and drainage in this series therefore probably had complete vagotomies.

(iii) RECURRENT DYSPEPSIA - EXCLUDING RECURRENT ULCER

A.H.T.

Considering those with relatively severe dyspepsia who have been fully investigated, with negative results, and those with relatively mild dyspepsia who have not been fully investigated, the mean preoperative M.A.O. values for both groups show only minor differences from the mean values for the whole vagotomy and drainage group (Tables 31 and 32). The levels are however quite markedly lower in these patients than in those who have proven recurrent

duodenal or jejunal ulcers, but not when compared with the gastric ulcer group.

Percentage reduction

It will be seen from Table 31 that a minimal difference exists between the percentage reduction in the "dyspepsia" group and the overall mean reduction in the vagotomy and drainage group. There is however a fairly marked difference from the proven recurrence groups, both duodenal/jejunal and gastric. No difference was found between these patients and the highly suspected JU/DU group except for a discrepancy in the B.A.O. values, a finding which is of questionable significance.

Insulin tests

Comparing the proven and suspected DU/JU and recurrent dyspepsia groups, it is of interest to note that there is a greater reduction in the proportion of patients with positive insulin tests in the latter group when multiple criteria are used for interpretation than when pure Hollander criteria are used.

Table 32 shows that the incidence of positive tests by both methods of interpretation as identical for proven recurrent DU/JU, at 87.5%. For highly suspected DU/JU recurrence however, there is a 10%

TABLE 32

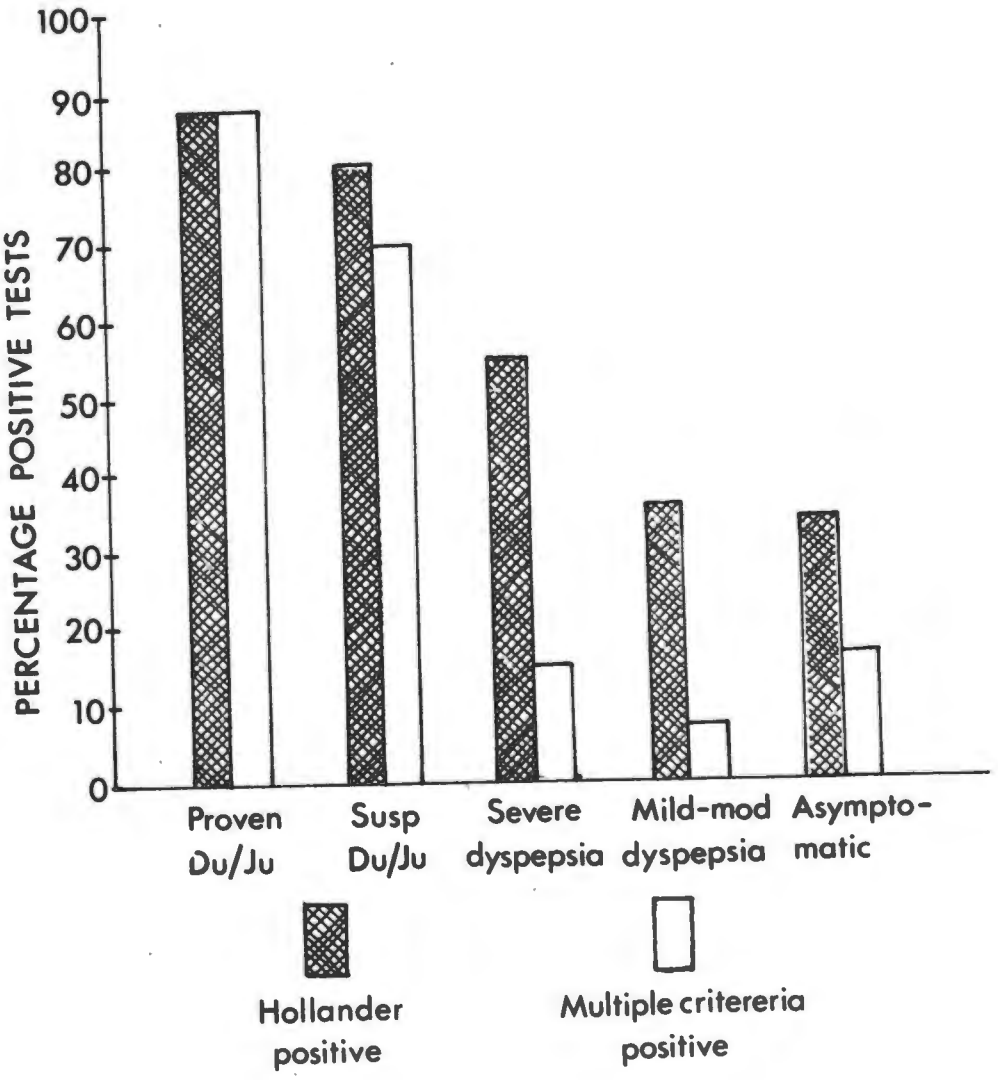
COMPARISON OF THE RELATIVE PROPORTIONS OF POSITIVE INSULIN TESTS WHEN THE RESULTS ARE INTERPRETED BY MULTIPLE CRITERIA OR BY THE PURE HOLLANDER CRITERION IN THE VARIOUS RECURRENT DYSPEPSIA GROUPS AFTER VAGOTOMY & DRAINAGE

GROUP	TOTAL NUMBER OF TESTS	MULTIPLE CRITERIA POSITIVE		HOLLANDER POSITIVE	
		NUMBER	%	NUMBER	%
PROVEN	8	7	87.5	7	87.5
HIGHLY SUSPECT	10	7	70.0	8	80.0
SEVERE DYSPEPSIA	14	2	14.3	6	42.9
MILD-MOD. DYSPEPSIA	14	1	7.1	5	35.7
ASYMPTOMATIC	75	11	14.7	26	34.6

*Excludes gastric ulceration

FIG.21

DIAGRAMATIC COMPARISON OF THE RELATIVE PROPORTIONS OF POSITIVE INSULIN TESTS WHEN THE INTERPRETATION IS MADE BY MULTIPLE CRITERIA AND BY THE PURE HOLLANDER CRITERION IN THE VARIOUS RECURRENT DYSPEPSIA GROUPS AFTER VAGOTOMY & DRAINAGE



discrepancy between the proportions of positive tests. This discrepancy then increases to between 20 and 30% when comparing the number of positive results among the asymptomatic and dyspeptic patients who are unlikely to have recurrent ulceration. Gastric ulcers occurring after vagotomy have been altogether excluded from this analysis, in view of the fact that a positive insulin test does not seem to play a consistent part in its aetiopathogenesis. These differences are diagrammatically represented in Figure 21.

(c) COMPARISON OF GASTRIC ACID SECRETORY PATTERNS AFTER TRUNCAL AND SELECTIVE VAGOTOMY AND DRAINAGE (Table 33).

A.H.T.

There are minimal differences between the two groups with regard to the preoperative acid values.

Percentage reduction

Comparing the reduction in preoperative B.A.O. (selective 71.7% and truncal 65.5%) and M.A.O. (selective 75.5% and truncal 66.3%) in the two groups it will be seen from Table 34 that selective vagotomy seems to be slightly more efficient than the truncal operation. This is probably related to the slightly lower incidence of incomplete vagotomy

TABLE 33

VAGOTOMY & DRAINAGE - ACID SECRETION DATA -
OVERALL COMPARISON BETWEEN SELECTIVE & TRUNCAL VAGOTOMY

VAGOTOMY	TOT. NO. PTS.	PTS. WITH A.H.T. DATA	A. H. T.						INSULIN		
			MEAN PREOP mEq./Hr.		MEAN POSTOP mEq./Hr.		MEAN % REDUCTION		TOT. NO. TESTS	MULT. CRITERIA POSITIVE	HOL-LANDER POSITIVE
			B.A.O.	M.A.O.	B.A.O.	M.A.O.	B.A.O.	M.A.O.			
SELECTIVE	111	88	6.0	27.7	1.7	6.9	71.7	75.5	45	8 17.8%	14 31.1%
TRUNCAL	200	165	5.5	28.2	1.9	9.5	65.5	66.3	78	19 24.4%	14 43.5%

in the former group.

Insulin test

Lower percentage for positive insulin tests were observed in the selective group when both pure Hollander (selective 31.1% - truncal 43.5%) and multiple criteria (selective 17.8% - truncal 24.4%) were used for interpretation.

The differences, however, fail to reach a statistically significant level ($p > 0.05$).

(iv) THE RELATIONSHIP OF PREOPERATIVE M.A.O. TO RECURRENT ULCERATION AND DYSPEPSIA IN PATIENTS WHO HAVE HAD VAGOTOMY AND DRAINAGE OPERATIONS

(Tables 34 and 35)

In examining the preoperative A.H.T. data on patients with vagotomy and drainage in an attempt to ascertain whether a critical M.A.O. value exists above which recurrent DU/JU, which is known to be a result of acid hypersecretion, occurs, the figure of 25 mEq./Hour emerged. No recurrent duodenal or jejunal ulceration occurred in patients with preoperative maximal acid outputs below this level.

One hundred and forty-three had a preoperative M.A.O. of greater than 25 mEq./Hour (mean 35.8 mEq./Hr.) and 110 had preoperative M.A.O. of less than 25 mEq./Hour (mean 17.9 mEq./Hour).

Recurrent ulceration (Table 34)

DU/JU

It will be seen from the Table that 11 recurrences (7.7%) occurred in the "over 25" group, while none were found among the "under 25" patients. This is obviously a significant result.

There is no significant difference between the two groups with regard to the incidence of suspected DU/JU, but when combined with the proven recurrences into composite groups, the "over 25" (18 cases 12.6%) and "under 25" (4 cases 3.6%) groups show a highly significant difference ($p < 0.01$).

Gastric

Gastric ulceration occurring after vagotomy and drainage showed the opposite trend to recurrent DU/JU, in that 2 cases (1.4%) occurred among the "over 25" patients and 6 cases (5.5%) were found in the "under 25" group. These differences are not however statistically significant ($p > 0.05$).

Recurrent dyspepsia

Table 34 illustrates that there is no significant difference in the incidence of recurrent dyspepsia, excluding recurrent ulceration, in the two groups.

TABLE 34

COMPARISON OF RECURRENT ULCER (PROVEN/SUSPECTED) RATES & OCCURRENCE OF POSTOPERATIVE DYSPEPSIA IN PATIENTS WITH PREOP. M.A.O. > 25 mEq./Hr. & < 25 mEq./Hr.

M.A.O. GROUP mEq./Hr.		TOT. NO. PTS.	RECURRENT ULCERATION			REC. DYSPEPSIA	
			DUODENAL/JEJUNAL		PROVEN GASTRIC	*SEV. NEG.INV.	MILD - MOD.
			PROVEN	SUSPECT			
> 25	NO.	143	11	7	2	12	18
	%		7.7	4.9	1.4	8.4	12.6
< 25	NO.	110	0	4	6	9	12
	%			3.6	5.5	8.2	10.6

* Includes two patients initially suspected of having recurrent gastric ulcer - not confirmed at operation

Insulin tests and A.H.T. results

It will be seen from Table 35 that the percentage reduction of the preoperative M.A.O. is similar among both groups, and there is a difference of less than 1% between them. There is a slightly larger difference (8.8%) when B.A.O. reduction is considered but this is not significant.

Twenty-six of the 60 patients in the "over 25" group who had insulin tests performed gave positive results using pure Hollander criteria (43.3%). Thirteen of 42 insulin tests in the "under 25" patients (30.9%) were Hollander positive. The difference is not statistically significant ($p > 0.05$).

When multiple criteria are used as the method of interpretation, the "over 25" group with 28.3% positive has a significantly higher proportion than the "under 25" group (9.5% - $p < 0.05$).

(e) COMPARISON OF ULCER RECURRENCE RATES IN PATIENTS WITH PREOPERATIVE M.A.O. OF GREATER THAN 25 mEq./Hour AFTER VAGOTOMY AND DRAINAGE; VAGOTOMY AND ANTRECTOMY AND PARTIAL GASTRECTOMY (Table 36)

Vagotomy and drainage

One hundred and fourty-three patients (56.5%) had a preoperative M.A.O. of greater than 25 mEq./Hour and among these 18 proven and suspected DU/JU

TABLE 35

VAGOTOMY & DRAINAGE

COMPARISON OF GASTRIC ACID SECRETORY RESPONSE TO HISTAMINE/PENTAG. & INSULIN IN PATIENTS WITH PREOP. M.A.O. > 25 mEq./Hr. & < 25 mEq./Hr.

M.A.O. GROUP (mEq./Hr.)		A. H. T.						INSULIN		
		MEAN PREOP mEq./Hr.		MEAN POSTOP mEq./Hr.		% REDUCTION		TOT. NO. TESTS	MULT. CRITERIA POSITIVE	HOL-LANDER POSITIVE
		B.A.O.	M.A.O.	B.A.O.	M.A.O.	B.A.O.	M.A.O.			
>25 (Tot: 143)	NO.	6.8	35.8	2.2	11.3	67.6	68.4	60	17	26
	%								28.3	43.3
<25 (Tot: 110)	NO.	3.4	17.9	1.4	5.8	58.8	67.6	42	4	13
	%								9.5	30.9

TABLE 36

COMPARISON OF ULCER RECURRENCE RATES IN PATIENTS WITH PREOP. M.A.O. 25 mEq./1. AFTER ELECTIVE SURGERY FOR DUODENAL ULCER

OPERATION		A.H.T. DATA	M.A.O. > 25	A. H. T. MEAN PREOP mEq./Hr.		RECURRENT ULCERATION M.A.O. > 25		
						DUODENAL/JEJUNAL		GASTRIC
				B.A.O.	M.A.O.	PROVEN	SUSPECT	PROVEN
VGY. & DRAIN.	NO.	253	143	6.8	35.8	11	7	2
	%		56.5			7.7	4.9	1.4
VGY. & GY.	NO.	55	47	12.5	47.8	0	0	1
	%		84.5					2.1
PARTIAL GY.	NO.	49	33	7.4	38.2	0	1	0
	%		67.3				3.0	

were found (12.6%) and 2 gastric ulcers (1.4%).

Vagotomy and antrectomy

Fourty-seven (84.5%) of these patients belonged to the "over 25" group, and none of them had either proven or suspected DU/JU. One presented with gastric ulceration. There is an obviously significant difference between these patients and the vagotomy and drainage group with regard to recurrent DU/JU but not gastric ulceration.

Partial gastrectomy

Of the 33 (67.3%) who fell into the "over 25" category, one had a suspected JU but there were no gastric ulcers.

The differences are significant when compared with vagotomy and drainage, but not when compared with vagotomy and antrectomy.

P A R T I I I

DISCUSSION

CHAPTER 1

INTRODUCTION

The aim of this study was to evaluate the efficacy of elective vagotomy operations, especially vagotomy and drainage, in the treatment of duodenal ulcer as practised in this Clinic. Vagotomy and drainage has been the routine operation at Groote Schuur Hospital in the treatment of this disease for about the last eight years, and antrectomy has been added to the vagisection when the patient has been considered to be a gastric acid hypersecretor on preoperative testing. Partial gastrectomy initially occupied the place that vagotomy and drainage has now taken. Surgical treatment for duodenal ulcer has been in a constant state of flux, and numerous operations and modifications of these operations have been tried and rejected by different, and indeed the same, generations of surgeons. The problem has been to effectively reduce any liability to subsequent recurrent ulceration without subjecting the patient to a life of crippling morbidity due to other sequelae which may follow on the procedure. Thus the pendulum has swung from the conservative operation of gastro-

enterostomy as advocated by Moynihan, which resulted in acceptable morbidity but an unacceptable recurrence rate, to the radical operation of near total gastrectomy practised by Visick and others, where the reverse held true. With the advent of vagotomy, a far more conservative approach has become possible once more and current argument usually revolves around the relative merits of vagotomy and drainage and vagotomy and antrectomy; most series favouring the latter procedure. In the last year or two, with the advent of highly selective vagotomy without a drainage procedure, it seems that an even more conservative approach may be advocated in future should this operation prove to be as effective as its initial proponents suggest.

The evaluation of the various operations under review has been made with regard to the incidence of recurrent ulceration and of postoperative sequelae other than recurrent ulceration. In addition, a study has been made of the effects of these procedures on gastric acid secretion, and where relevant, on the incidence of incomplete vagotomy on insulin testing. Special reference has been made to the value of the measurement of preoperative gastric acid secretion for selection of the type of operation to be performed.

Discussion will be presented under four main headings :

I Mortality.

II Recurrent ulceration and its relationship to pre- and postoperative acid studies, and completeness of vagotomy as measured by insulin testing.

III Postoperative sequelae due to alimentary dysfunction.

IV General assessment of results based on a modified Visick grading.

V Conclusions.

MORTALITY

Modern standards of selection for operation, operative techniques, and postoperative management have made all forms of elective surgery for duodenal ulcer relatively safe. In this series the primary mortality for the three operations studied compare favourably with the figures for many published reports to date.

Vagotomy and drainage, in the experience of this hospital is significantly safer than partial gastrectomy, but has only a marginally lower mortality than vagotomy and antrectomy, in the short term. Once the

mortality of re-operation, which is significantly higher than the immediate primary mortality, and the deaths resulting from delayed complications are taken into account, vagotomy and drainage and partial gastrectomy have an approximately equal overall death rate, while vagotomy and antrectomy results in half this figure. It must be emphasised at this stage that only an approximation of the overall mortality can be made in this series in view of the discrepancy between the total number of operations initially performed and the number followed up. However, this pattern of mortality has been well documented by the results from other large prospective series[404-408].

The low incidence of re-operations and thus absence of deaths following re-operation is the reason for the lower overall mortality for vagotomy and antrectomy. This is very difficult to explain, as the conditions under which these procedures are performed and the technical difficulties faced at surgery should be almost identical for each re-operation, whatever the primary procedure. In this instance, however, one is dealing with small numbers and with more patients the figures may perhaps have approximated.

No deaths unequivocally related to remote complications of primary or subsequent surgery have come to light. It may well be postulated that some deaths due to apparently unrelated causes, such as road traffic accidents or coronary thrombosis or cerebrovascular accidents may have been related to early or late dumping symptoms and so on. At present, however, no definite evidence exists to support this postulate.

CHAPTER 2

RECURRENT ULCERATION AND ITS RELATIONSHIP TO PRE- AND POSTOPERATIVE A.H.T. AND POSTOPERATIVE INSULIN TESTING

(a) Incidence:

Recurrent dyspepsia does not necessarily mean recurrent ulceration, and when confronted with a patient who complains of recurrence of his pre-operative symptomatology one is often faced with a difficult problem.

In most reported series, recurrent dyspepsia is classified as being due to recurrent ulceration, either proven or suspected, and an incidence ranging from 5 - 10% is given for vagotomy and drainage [402-404,409,410], 0.8 to 2% for vagotomy and antrectomy and 2 to 4% for partial gastrectomy [399-401]. None of these reports however make separate analysis of whether the recurrent ulcer is gastric or duodenal/jejunal (DU/JU).

The proven and suspected recurrent ulcer rate in this series taking gastric and DU/JU as a composite group, fall within the expected range for the three operations studied. It must be

pointed out that a total of 17.7% of patients were investigated for recurrent symptoms after vagotomy and drainage, and that in about 40% of these no definite organic lesion could be demonstrated to account for their symptomatology, after a full routine work up had been performed. In addition, a further 10% of patients admitted to occasional recurrence of dyspepsia on direct questioning, but did not find this troublesome.

The average time of presentation of patients with proven or suspected recurrence was 2.0 years after vagotomy and drainage with a range of two weeks to five years. This is in distinct disagreement with the experience of J.A. Williams[410] who states that all recurrent ulcers occurred within one year of operation. It would seem therefore that at least a five year follow up is required to provide any index of the efficacy of an operation with regard to the recurrent ulcer rate. No doubt with longer follow up even more recurrences may come to light.

(b) Aetiology of recurrent ulceration:

The aetiology of recurrent duodenal/jejunal and gastric ulceration after vagotomy operations,

or gastrectomy, is probably best discussed under separate headings, as it seems that each forms a distinct pathogenetic entity.

Recurrent DU/JU

There is general acceptance of the fact that incomplete vagotomy, as shown by the insulin test, is the commonest cause of recurrent DU/JU after vagotomy[205,369,411-414], which results in persistent gastric acid hypersecretion.

However, it is a well documented experience that recurrent DU/JU can occur in the presence of a negative insulin test. Seven out of eight cases of proven recurrent DU/JU after vagotomy and drainage in this series had positive insulin tests by all criteria, while one had a negative test. It is postulated that patients who fall into the latter category probably have predominance of the antral phase of gastric acid secretion, so that vagotomy without antrectomy is insufficient to control the ulcer diathesis. Although Byrnes and his colleagues have been able to demonstrate significantly higher mean fasting serum gastrin levels in patients with recurrent DU/JU after vagotomy, all these patients had positive insulin

tests.—No study has to date been published on serum gastrin levels in patients with recurrent ulcers and negative insulin tests.

Inadequate drainage has been incriminated by some workers as being instrumental in causing a dominant and prolonged antral phase of secretion after vagotomy and drainage. Bryant, Klein and Griffen[412] showed that the one layer Heinecke-Mickulicz (H-M) pyloroplasty, which is almost universally practised in this hospital, had a significantly higher incidence of recurrence (22.9%) than the Finney pyloroplasty (10.9%). This has been confirmed by others[415,416]. The suggestion is that better drainage via the Finney type operation is responsible, and Griffith et al.[184] using a ^{51}Cr labelled solid meal demonstrated that the Finney pyloroplasty increased the rate of emptying while the H-M type delayed it. Our patient in fact had an H-M type of pyloroplasty, but no adequate information is available on her gastric emptying rate or serum gastrin levels.

Another important cause of recurrent DU/JU after all forms of surgery for duodenal ulcer, is a Zollinger-Ellison (Z-E) syndrome, missed at the

original operation. An indication of the presence of excess circulating gastrin is given by the ratio of basal acid output (B.A.O.) to maximal acid output (M.A.O.) on augmented histamine testing. If the ratio is greater than 60%, this is highly suggestive of Z-E syndrome[360-362]. Serum gastrin estimation, once it becomes routine practice, will have its greatest value in this regard. Grossly elevated serum gastrin levels have been noted in all case reports published to date[58-60]. The Z-E syndrome could not be incriminated in any cases of recurrent DU/JU in this series.

A small postoperative leak at the suture line may rarely result in a short fistulous track, and in this way predispose to recurrent ulceration on the basis of reduced mucosal resistance[512].

Gastric ulcer after vagotomy:

Gastric ulcer was recognised as an occasional complication of vagotomy without drainage after Dragstedt, Camp and Fritz[417] reported two cases. Since then sporadic reports have appeared in the literature. Burge[411] in a 10 year follow up after vagotomy and drainage for duodenal ulcer, reported an incidence of 0.8% after vagotomy and gastroenterostomy, and 2.3% when pyloroplasty was used for

drainage. The problem has been highlighted more recently by Bank and his colleagues[418] who reported on 9 cases of gastric ulcer after vagotomy and drainage. These workers have, to date, found 27 such cases in the past 5 years[512].

Atrophic changes are found in the mucosa of stomachs resected for gastric ulcer, especially in the region of the ulcer[419-422]. Du Plessis[422] found that 61 out of 75 specimens had atrophic mucosal changes. Acid production tends to be lower in patients with benign gastric ulceration[360-362], probably on the basis of an atrophic mucosa. Malignant ulceration may occur in the presence of achlorhydria, but it is probably true to say that acid must be present for benign gastric ulceration to occur, and healing of the ulcer will occur after gastric atrophy has been induced[423]. Vagotomy alone may also result in healing[424] in certain cases. The possibility does arise that false low levels of acid secretion are being measured in gastric ulcer patients due to back diffusion of hydrogen ions[425] through an atrophic mucosa, that is parietal cells are secreting more hydrogen ions than are being aspirated. However, it seems reasonable to assume that the gastric ulcer patient has an atrophic mucosa that is less resistant to acid/pepsin even if the

secretory capacity is diminished. The aetiology and pathogenesis of the decrease in gastric mucosal resistance to acid/pepsin is the unresolved question, and various authors have placed varying emphasis on a number of possible factors.

Gastric stasis is believed to be the major factor in the pathogenesis of gastric ulcer by many authors, initiated by Dragstedt and others[166,417,426,427], who reported on the occurrence of two gastric ulcers among 197 patients who had undergone vagotomy without drainage for duodenal ulcer, but none in 262 patients treated by vagotomy and gastroenterostomy. This author believes that antral stasis results in the prolonged and excessive production of gastrin, which in turn, results in sustained production of acid and pepsin. The resulting prolonged contact of the gastric juice with gastric mucosa leads to gastric ulceration.

Experimental evidence in support of this postulate has been provided by Storer et al.[428] who noted that stasis in the main stomach of patients with Heidenhain pouches resulted in acid hypersecretion in the pouch. Gastroenterostomy and vagisection prevented this from happening. Ligation of the pylorus in the dog[428] and rat[429] has produced

gastric ulceration. Similarly, Linares[430] could produce this type of ulceration in rabbits after vagotomy alone, but not if an accompanying pyloroplasty of gastroenterostomy was done.

Carman[431] first recognised that delayed gastric emptying occurred in association with gastric ulcer. Subsequently Dragstedt and his co-workers[427] have reported this finding in 25 to 100% of cases. Buckler[189] measuring the time taken for test meals of barium coated granules to leave the stomach, but was unable to show significant stasis in gastric ulcer patients unless gross scarring of the lesser curve was present. This has been confirmed by Griffith[432], who found that a solid meal left the stomach at a slower rate only in the presence of an associated duodenal ulcer. The opposite view is held by George[188] who reports a slower rate of emptying of a fluid meal in 60% of patients with gastric ulcer. Some evidence exists therefore in favour of gastric stasis playing some part in the aetiology of gastric ulcer in the intact stomach. On the other hand, the possibility exists that gastric stasis is a sequel to lesser curve ulceration in a proportion of patients, on the basis of "splintage" due either to muscle spasm or atonicity[512].

Gastric motility and emptying after vagotomy has been extensively studied, but the gross long term qualitative changes are uncertain. Work done on patients at varying times after their operations has yielded conflicting evidence. Motility studies by radiological methods[169,171-173] lend support to Dragstedt's concept. Pressure studies have shown disturbance of propagation of peristalsis[175] and abnormalities of co-ordination of gastric contraction and adaptation to volume increase[179-181].

Gastric emptying for fluids has been shown to occur more rapidly[182-187]. Solid test meals on the other hand have been found to empty from stomachs with vagotomy alone at a far slower rate than with vagotomy and drainage or normals[189]. Vagotomy and drainage still resulted in a slower rate of emptying than normal controls in the latter study however.

The various drainage procedures have been compared with reference to stomach emptying. Gooddall[182] found that gastroenterostomy delayed emptying to a far greater degree than pyloroplasty. Griffith[184] in turn reported that the Finney pyloroplasty was the most efficient drainage procedure and that the H-M pyloroplasty actually delayed emptying.

In general it seems that there is some gastric

motility disturbance after vagotomy, probably a loss of co-ordination of motility. Chronic gastric retention is therefore probably a combination of stomal obstruction and decreased motility, the latter making mild degrees of obstruction more significant.

Of the 9 patients with gastric ulceration after vagotomy in this series, including one patient who had an antrectomy, only 2 had symptoms suggestive of chronic gastric stasis, such as nausea, vomiting of unchanged food several hours after eating, or foul eructation, at the time of diagnosis of their ulcers. None had obvious gastric stasis or stenosis of the drainage ostium demonstrated on radiological examination. It must be pointed out that in the light of the evidence presented above, the use of the sophisticated techniques employed by these authors may well demonstrate significant motility disturbance and retardation of gastric emptying in our patients, but we can produce no gross evidence of gastric stasis having been a major factor in these cases. Bile reflux is postulated as the cause of atrophic gastritis and hence gastric ulcer by some authors. Capper et al.[433] demonstrated that reflux of duodenal content through the pylorus occurred more frequently in patients with stomach ulcers than in those with duodenal ulceration, to a significant degree (19 out of

29 with gastric and 9 out of 27 with duodenal ulcer). He used cineradiographic studies after the instillation of gastrografin into the duodenum as his experimental method for this study.

James and Pickering[434] reported the more frequent finding of bile in gastric aspirates of patients with gastric ulcer than in those with a duodenal lesion. Comparing the concentration of bile acid conjugates in the gastric juice of the 2 peptic ulcer groups and other dyspepsias, Du Plessis[422] showed a higher concentration in patients with gastric ulcer. This author believes that atrophic changes in the region of a stomach ulcer are due to reflux of bile along the lesser curvature of the stomach[435, 436]. His theories have found some confirmation in the work of others[437-439].

Recent work[440] however provides some evidence against reflux being responsible for the presence of excessive amounts of bile in the stomachs of these patients. Dogs with gastric fistulas were infused intravenously with submaximal doses of histamine, pentagastrin and 2 deoxy-D-glucose (2D-G). It was found that pentagastrin resulted in a four times greater bile content in gastric samples than histamine or 2D-G and vagotomy did not influence the

results. The author comes out in favour of Dragstedt's theory to account for the presence of bile in gastric ulcer patients, stating that the choleretic action of increased amounts of gastrin results in a relatively greater quantity entering the stomach through the pylorus, and he feels that the increased production of acid stimulated by gastrin is more important in the pathogenesis of gastric ulcer.

Bank and his co-workers[216], studied gastric mucosal biopsies from 75 patients at 3 months to 1 year after vagotomy and drainage. When the incidence of superficial and atrophic gastritis in this series was compared with a random control series of 1,000 biopsies[441] a greater percentage of normal biopsies was found in the former, with no cases of gastric atrophy. On repeated biopsies on the same patients 3, 6 and 12 months after the initial biopsies a tendency for atrophic gastritis to develop with time was noted. Melrose et al.[217] reported a much higher incidence of atrophic gastritis, which is expected in view of the much longer duration of follow up (1 - 10 years).

Superficial and atrophic gastritis has, however, been noted more frequently in patients with truncal vagotomy and gastroenterostomy, than in patients with

pyloroplasty[216], presumably due to reflux of duodenal juice. Various workers have shown that posture significantly increases the rate of gastric emptying of liquids in patients with pyloroplasty when they lie on the right side, due to destruction of the controlled emptying functions of the pyloro-antral region[186,187,190,191]. It seems logical to assume therefore that posture may well result in considerable reflux of duodenal content into the stomach. Bank et al.[216] however make the observation that reddening or "gastritis" is often seen around the gastroenterostomy stoma on gastroscopy, but that this appearance is unusual in the antrum after pyloroplasty.

One of the patients in this series had had a gastroenterostomy, and one an antrectomy. The remaining 7 had all been subjected to H-M pyloroplasty.

Of the 4 patients who subsequently had gastric resections for their ulcers, detailed histology is available on 3, which were shown to have the typical atrophic gastritic picture usually associated with gastric ulceration.

The well known association of <u>incomplete vagotomy</u> on <u>insulin testing</u> with recurrent DU/JU does not hold true for gastric ulcer after vagotomy[417,418]. All 6 of the gastric ulcer patients in this series who

had insulin tests performed gave a negative result by all criteria[205,211,212] and hence probably had a complete vagotomy.

There are several points to consider on examination of the histamine/pentagastrin stimulated acid secretory data on the above patients. Compared with the recurrent DU/JU group, the gastric ulcer patients have a markedly lower mean preoperative M.A.O. level and in addition, 6 of the 8 cases which followed vagotomy and drainage belonged to the group who had a preoperative M.A.O. of less than 25 mEq./Hour. The difference in incidence in the "over 25" and "under 25" groups is not statistically significant but the trend nevertheless seems to be for gastric ulceration to occur more frequently in the low secretor group following this operation.

On examination of the mean percentage reduction of preoperative B.A.O. as well as M.A.O. levels in the gastric ulcer patients it will be seen (Table 32, Fig.18) that there is a significantly lower figure for both when compared with overall mean values for patients who have undergone vagotomy and drainage, and the figures approximate those for recurrent DU/JU. It is of interest to note that basal levels are notably less reduced in the gastric ulcer group than in the recurrent duodenal/jejunal group.

The suggestion may be made therefore that in the patients who develop gastric ulcer after vagotomy and drainage procedures, complete vagal section is insufficient to reduce gastric acid secretion to the expected levels and that some factor is responsible for maintaining this relative hypersecretion. It is tempting to cite stasis, of a relatively minor degree and not detectable by routine crude radiological methods, resulting from the combined effects of vagal denervation and H-M pyloroplasty, with consequent gastrin hypersecretion. This may be construed as support for Dragstedt's theory[426,427]. It is of interest to note that a recently published study by Hansky and Cain[58] showed elevated serum gastrin levels in patients with gastric ulcer whereas opposite findings were published by Byrnes and his colleagues[60]. Refinement of assay techniques and accumulated data on a large series of patients may help resolve the issue.

Why this relative hypersecretion should result in ulceration in the stomach and not in the duodenum or jejunum is another question. The obvious suggestion of course is that mucosal resistance is compromised, whether by biliary reflux, or by prolonged contact of gastric content with the mucosa. It seems unlikely

that vagotomy per se results in any significant mucosal changes[213,214,216], but the fact that most of the gastric ulcer patients in this study belonged to the low secretor group (preoperative M.A.O. less than 25 mEq./Hour) does suggest that they may have had a degree of atrophic gastritis preoperatively which predisposed them to this complication.

The possibility exists that gastric ulceration after vagotomy may be a coincidental occurrence, or alternatively all these aforementioned factors may just tip the balance in a susceptible individual, whether determined by genetic or dietary factors. Circumstantial evidence for this is that 6 of the 8 patients in the vagotomy and drainage group were of the Cape Coloured race, a population group which is known to have a very high incidence of gastric ulceration. One of the 2 Whites in the series was a cirrhotic with known portosystemic shunting, which has a well documented association with gastric ulcer. The vagotomy and antrectomy patient, also of the White race, was on large doses of steroids to control his severe asthma, a drug with known ulcerogenic properties.

Another point made by A.P.M. Forest[442] in a survey of 18 published series of a total of more than 10,000 patients, between 2 and 53% of patients

with gastric ulcer had a co-existing duodenal ulcer. The rather remote likelihood of a gastric ulcer missed at initial surgery subsequently recurring may be entertained.

In conclusion it would appear that no single factor can be incriminated as the major one in the aetiology of gastric ulceration after vagotomy. Also, the mere fact that gastric ulcer occurs after vagotomy and drainage, in the presence of a complete vagotomy on insulin testing, indicates that the use of this operation in the treatment of gastric ulceration is questionable.

Investigation:

As has been pointed out, the investigation of the post surgical dyspeptic patient may present a vexing diagnostic problem. The routine work up of a patient who presents in this manner consists of an adequate history and examination, occult blood testing on the stool, barium meal and follow through, fibreoptic gastroscopy, A.H.T. and where relevant an insulin test. If these investigations prove negative, other possible causes outside the gastrointestinal tract are sought by cholecystography, specialised oesophageal motility/pressure studies and electrocardiography. Also in many cases barium enema and

pancreatic function tests (including hypotonic duodenography on occasions) are performed if the possibility arises that pathology in these sites is responsible for the patient's symptomatology.

The clinical history and examination are usually rewarding for the purposes of making a diagnosis of recurrent ulceration. In the presence of a battery of inconclusive investigative results, typical peptic ulcer symptomatology usually indicates that the patient does in fact have a recurrence.

Barium meal examinations after gastroenterostomy, with or without gastric resection fairly frequently allows a reasonably confident diagnosis to be made, especially if air/barium contrast studies are done (410,443,444). Difficulties are encountered however in those with some degree of stomal obstruction, or oedema of the jejunal folds. The entity of "jejunitis" with rigidity and narrowing of the jejunum also complicates the issue on occasions (445). The area of the pyloroplasty, in the experience of this unit presents a very difficult problem in interpretation, as reported by many other authors (443,446-448), even though in recent times detailed study has been made of the "normal" radiological picture of the pyloroplasty related to studies in the cadaver and asymptomatic postoperative patients.

Fibreoptic endoscopy plays an important part in the investigation of post surgical dyspepsia, in contra-distinction to the opinion of J.A. Williams [410]. In this clinic it has proved invaluable in the radiologically suspect case, especially with gastroenterostomy, when it is usually possible to pass the tip of the instrument through the stoma [449-451]. However, it is often difficult to interpret the findings around the stoma due to the almost invariable appearance of "gastritis" [216]. Occasionally it proves possible to pass the gastroscope through the pyloroplasty but a recurrent duodenal ulcer after vagotomy is seldom visualised in this manner.

In the present series endoscopy has proved invaluable in confirming a radiological diagnosis of gastric ulceration after vagotomy and drainage, and there are at present no cases classified as "suspect gastric ulcer". Two patients who had grossly distorted gastric mucosal patterns, both on barium meal and on gastroscopy and in whom the diagnosis of gastric ulcer, possibly malignant, was entertained were found at re-operation to have marked fibrous adhesions binding the stomach to surrounding viscera. Simple freeing of these adhesions has resulted in both being asymptomatic and well at 3 and 6 months posoperatively

respectively.

Augmented histamine testing of patients with postoperative dyspepsia has proved valuable as a diagnostic tool in this hospital. Bank et al.[360-362] reported on experiences with over 5,000 A.H.T.'s. After gastrectomy a basal secretion exceeding 5 mEq./Hour and an M.A.O. greater than 10 mEq./Hour favoured the diagnosis of jejunal ulceration. Basal acid output of 10 mEq./Hour and M.A.O. of 20 mEq./Hour was found to be almost diagnostic. Although this is less useful after vagotomy and drainage, an M.A.O. of over 20 mEq./Hour is nevertheless suggestive of recurrent DU/JU. After all forms of duodenal ulcer surgery, a maximal acid of less than 3 mEq./Hour mitigates against the diagnosis, and achlorhydria excludes it.

Scrutinizing the A.H.T. results of the vagotomy and drainage patients in this study, the mean post-operative values for the 11 with proven recurrent DU/JU were a B.A.O. of 3.6 and an M.A.O. of 16.7 mEq./Hour respectively. Six of these had post-operative M.A.O.'s greater than 20 mEq./Hour. These values are significantly higher than that of the mean for the whole group.

It is also suggested that a postoperative

reduction of M.A.O. of less than 10% is virtually diagnostic of recurrent DU/JU and that a reduction of less than 50% exposes the patient to the risk of such ulceration[362]. This is borne out by the results in this series where the mean percentage reduction of the M.A.O. in patients with proven duodenal or jejunal recurrence is less than 50%.

The pattern of acid secretory responses to histamine/pentagastrin in patients who have developed gastric ulceration after vagotomy has already been discussed in some detail. This follows a similar pattern to the recurrent DU/JU group, with regard to reduced percentage reduction of acid output, especially basal, but with generally lower absolute pre- and postoperative values.

Value of the A.H.T. in the diagnosis of the Zollinger-Ellison syndrome has also been previously discussed.

The insulin test remains the most widely accepted and satisfactory means of testing for completeness of vagotomy, although much difficulty is encountered in interpreting the results.

"Incomplete vagotomy", as evidenced by a positive insulin test, has been shown to be a major factor in the aetiology of recurrent DU/JU[205,369,411-414],

but not for gastric ulceration[417,418], after vagotomy and drainage.

Hollander's[211,212] original principle for interpretation of a positive response to insulin hypoglycaemia and hence incomplete vagotomy remains the only one that has been unequivocally demonstrated on the experimental animal. The precise magnitude of the response in humans has been arbitrarily suggested, based on general experience with the test. An increase over basal levels of 20 mEq./Litre within a two hour period (10 mEq./Litre if basal is anacid) after insulin injection, as originally proposed by Hollander, receives universal acceptance as a positive test result. Various authors have proposed additional or alternative criteria for assessment of whether vagotomy is complete, such as volume increases after insulin[371], the magnitude of basal acid output[90], increase in acid output after varying periods after insulin[90,370] or measuring the time interval after insulin at which the Hollander criterion is fulfilled[369,381]. The latter has recently been convincingly refuted as artificial, and abandoned[382,383]. All these various suggestions are however based either on their simultaneous occurrence in patients who fulfil the Hollander

criteria, or on findings in patients with recurrent ulceration who are assumed to have incomplete vagotomies. This further emphasises the rather arbitrary way in which conclusions regarding what constitutes a positive result have been arrived at. Obviously the whole basis of interpretation of the test must revolve around the magnitude of the secretory response to maximal vagal stimulation by insulin hypoglycaemia. The problem, therefore, is largely one of quantitation which will always remain difficult to resolve in man.

The poor discriminatory value of the Hollander criteria in assessing liability to recurrent ulceration prompted Bank et al.[205] to examine the value of multiple criteria. The 5 criteria used had been previously employed, on an individual basis, by various workers. They noted that three or more positive criteria suggested both an incomplete vagotomy and a high risk to recurrent ulceration (DU/JU).

The incidence of incomplete vagotomy, using both methods of interpretation exactly approximate each other in the proven recurrent DU/JU group. The discrepancy between the proportions of positive results when the two methods of interpretation are

used in the other dyspepsia groups (Table 33, Fig.20) suggests that there is probably some prognostic value in the use of multiple criteria for interpretation of the test.

However in interpreting the results of the insulin tests in the two groups of patients with preoperative M.A.O. values of greater than and less than 25 mEq./Hour, the difference between the two groups with regard to the incidence of incomplete vagotomy is insignificant by pure Hollander criteria, but highly significant when multiple criteria are used as the method of interpretation, with a lower incidence in the "under 25" group. No difference in the incidence of incomplete vagotomy would be expected between the two groups, as both have the identical proportions of truncal and selective vagotomy and all operations have been performed by the same surgical teams, to whom the patients have been allocated on a random basis. The difference suggests that the use of multiple criteria as an accurate index of the actual completeness of vagal section becomes unreliable in patients with a low M.A.O. on A.H.T.

Patients with a preoperative M.A.O. of less than 25 mEq./Hour had a mean postoperative value of 5.8 mEq./Hour, as opposed to 11.3 mEq./Hour in the

group with an M.A.O. of greater than 25 mEq./Hour on preoperative augmented histamine testing. In a preliminary investigation, insulin tests have been performed on a group of patients with intact vagi and stomachs and with pentagastrin stimulated maximal acid outputs of less than 6 mEq. /Hour. These patients show unreliable results, in the form of false negatives when both pure Hollander and multiple criteria are used for interpretation of the insulin response, especially with the latter. All earlier published work on the insulin test in patients with intact vagi has been done on patients with duodenal ulcer, who tend to be high acid secretors[369,383].

No recurrent duodenal or jejunal ulcers have occurred in the "under 25" group and this further substantiates that multiple criteria provides a more accurate index of liability to recurrent ulceration than the pure Hollander method, albeit empirically. The Hollander criterion would seem to be far more accurate with regard to whether the vagi are in fact intact or not. It is of interest also to compare the incidence of incomplete nerve section in the vagotomy and antrectomy patients with that in the vagotomy and drainage group. Admittedly very few (total 11) acceptable tests are available in the

former group, but the 36.4% incidence of incomplete vagotomy by the pure Hollander criterion is similar to that in the vagotomy and drainage group, but no tests are positive by multiple criteria among the vagotomy and antrectomy patients. As no recurrent jejunal ulcers have occurred in the vagotomy and antrectomy patients it provides further circumstantial evidence in favour of the empirical prognostic value of multiple criteria in the interpretation of the insulin test.

All patients who give a positive result by multiple criteria are also Hollander positive, so use of the former does seem to make the insulin test a little more specific. Attempts to further increase specificity so as to predict which patients were even more at risk of recurrent ulceration by adding up the number of criteria positive in each respective proven recurrence and dyspepsia group showed no definite pattern, that is, those with proven recurrent DU/JU did not have a higher proportion with all criteria positive than those who were asymptomatic, but fell into the "multiple criteria positive" group.

The overall incidence of incomplete vagotomy among the vagotomy and drainage patients of 40.9% lies at the upper limit of the range presented by

many authors in their respective series[269,452]. Almost all previously published data of this type has been on tests done within two weeks of operation. Reference is made to recent reports by Gillespie and his co-workers[383,387] of positive conversion of insulin tests found to be negative at the time of initial testing. When tests found to be negative at two weeks postoperatively were repeated three months to four years later, 50% of the initially negative results became positive (by Hollander criteria). They also state that six months seems to be the critical stage for this conversion. All tests reported on in this series were done at least three months, the vast majority over six months, after surgery. In fact the time interval was more than four years for 60% of these cases. Accordingly it may be suggested that routine postoperative insulin testing done at a much earlier stage would have resulted in a far lower incidence of positive results in this series.

The insulin test is therefore fraught with difficulties regarding its interpretation. The whole reason for the evolution of a test for completeness of vagotomy is to determine whether a particular patient falls into the group who are at risk of

recurrent ulceration when confronted with the problem of the postoperative dyspeptic. Multiple criteria seem to give a more accurate, although empirical index of which patients are "at risk" than the pure Hollander criterion. In view of the fact that all patients with three or more positive criteria are Hollander positive and that a greater proportion of patients with a low histamine/pentagastrin stimulated M.A.O. are Hollander positive and multiple criteria negative, it is suggested that this means of interpretation of response to insulin hypoglycaemia is more practial. In other words, it is more accurate to group patients as insulin test positive and "at risk", than as Hollander positive and therefore having "incomplete vagotomy".

Used in conjunction with the A.H.T. the insulin test probably has some value in diagnosis.

Considering the methods available for investigation of patients with recurrent dyspepsia after surgery for duodenal ulcer, and the difficulties encountered in interpretation of the various tests, it is hardly surprising that of the 3 to 17% who present with dyspepsia, there remain about 40% of these about whom no definite conclusions can be

reached regarding the cause of their complaints, even after full investigation.

Some are most likely psychosomatic on general clinical assessment, in fact, a fair proportion probably belong in this category. There remains a small number who probably have some organic lesion, but defy all attempts at diagnosis. One of these, who has been repeatedly investigated over the last 2 years, ultimately presented with a massive gastro-intestinal haemorrhage. At operation he was found to have a neuofibroma in the mesentery which had eroded through the wall of the duodeno-jejunal flexure. Although a rarity this case illustrates the difficulties which attend making a definitive diagnosis in this difficult group.

(d) Relationship of preoperative M.A.O. (histamine/pentagastrin) to the recurrent ulcer rate in patients with vagotomy and drainage:

Sufferers from duodenal ulceration have significantly higher mean maximal acid output values on A.H.T. than normal controls[163,205,360,361,453]. Also well substantiated is the fact that recurrent jejunal ulceration after gastric resection is dependent upon postoperative production of acid[205,362,454] and recurrence does not occur in the presence of achlordydria.

Card and Marks[21,22] demonstrated that histamine stimulated gastric acid output is directly proportional to the parietal cell mass. Based on this finding, Bruce et al.[455] suggested that patients who developed jejunal ulceration after partial gastrectomy had a high preoperative acid secretory capacity which was insufficiently reduced by "standard gastric resection". He thus suggested "tailoring" the operation according to the parietal cell mass as measured by the A.H.T. to avoid paying the "entirely ridiculous price" (Tanner)[456] of radical gastric resection for all duodenal ulcer patients.

From the same unit, Small and his colleagues[457] reported on the results of a programme of selective surgery for duodenal ulcer. Their policy of selection entailed submitting patients with M.A.O.'s in excess of 50 mEq./Hour to vagotomy and antrectomy, while those with lower M.A.O. figures than this were subjected to either standard two thirds gastrectomy or vagotomy and gastroenterostomy. A small group (17 patients) with M.A.O.'s of less than 30 mEq./Hour had gastroenterostomy alone performed. The majority of the "low secretors" were, however, subjected to gastrectomy. The whole programme was aimed at eradicating jejunal ulcer, but

the figure of 50 mEq./Hour was arrived at in a purely arbitrary way. Four hundred and sixty-four patients treated according to this policy and followed up for at least 5 years were compared with 575 patients treated mainly by partial gastrectomy before this means of preoperative selection became the routine. Comparing the overall jejunal ulceration recurrence rates in the two groups, there was no significant difference (2.5% selected; 3.8% unselected), but in the group with preoperative M.A.O.'s of greater than 50 mEq./Hour, treated by vagotomy and antrectomy, there were no recurrent ulcers. Similarly no recurrences occurred in those with preoperative M.A.O.'s of less than 30 mEq./Hour who had had gastroenterostomy alone. All jejunal ulcers therefore occurred in the group with an M.A.O. ranging from 30 to 50 mEq./Hour preoperatively, submitted either to partial gastrectomy or vagotomy and gastroenterostomy. Most recurrences (11 out of 12) were found in gastrectomized patients. Their ultimate conclusion is that the policy of selection has resulted in an acceptable recurrence rate with fewer side effects and that the results of gastrectomy are unreliable. The latter operation, they feel, should be replaced by vagotomy and gastroenterostomy.

Orr[458] also favoured a policy of selection based on preoperative A.H.T. results taking both basal and maximal acid outputs into account. The conclusion reached is based on a 12 year review of 1,494 patients. However he presented little real evidence to support his conclusions.

Some are of the opinion that preoperative acid testing has little significances. Clarke et al.[459] followed up 132 cases with vagotomy and gastro-enterostomy. Arbitrarily selecting a preoperative M.A.O. of 40 mEq./Hour as the level of hypersecretion, they found no difference in the incidence of recurrent ulceration in the two groups. Holt and Lythgoe[460], in their published series of 100 vagotomy and gastro-enterostomy cases, conclude that complete vagotomy provides adequate protection from jejunal ulceration irrespective of preoperative acid levels. This is baldly stated and no data on gastric acid secretion in their patients is presented in the paper.

At Groote Schuur Hospital a rather arbitrary policy has existed over approximately the last 10 years, in which vagotomy and antrectomy has been reserved for patients who have a preoperative M.A.O. of over 40 mEq./Hour. Those with lower maximal acid outputs (less than 40) have been subjected to vagotomy

and drainage, or partial gastrectomy which was the routine operation employed before 1962/3. The vast majority have had the former procedure. However, not all surgeons have rigidly applied the policy and a fair number of vagotomy and drainage patients belong in the hypersecretor category (overall M.A.O. mean for the group 27.3 mEq./Hour), and similarly some of those with vagotomy and antrectomy had M.A.O.'s of less than 40 mEq./Hour (overall mean 41.6 mEq./Hour). The gastrectomy group had a similar mean preoperative value to that of the vagotomy and drainage group (29.9 mEq./Hour) and the overall mean M.A.O. of all duodenal ulcer patients who have undergone surgery in this series is 32.9 mEq./Hour, (ranging from 9.6 to 110 mEq./Hour) which is almost identical with the average figures given for the series of both Bruce[455] and Small[457].

In view of the fact that proven recurrent DU/JU was still occurring in 3.9% of the vagotomy and drainage patients, the possibility was raised that a lower preoperative M.A.O. value than 40 mEq./Hour might be discerned as the "hypersecretor level" above which recurrent ulceration was more likely to occur. It will be seen from Table 35 that none of the 11 unequivocally proven recurrent duodenal or

jejunal ulcers occurred in patients with a pre-operative M.A.O. of less than 25 mEq./Hour. The lowest M.A.O. value among these patients was 26.9 mEq./Hour. Similarly when the incidence of "highly suspected DU/JU" in the "under 25" group is compared with that of "proven and highly suspected DU/JU" in the "over 25" group the difference remains highly significant to a P value of less than 0.025.

Vagotomy and drainage can be expected to reduce preoperative acid values, both basal and maximal, by 65 to 70% irrespective of their magnitude. The postoperative acid output of patients with low acids to begin with will therefore obviously be lower than those with high preoperative values. The mean postoperative M.A.O. in the "under 25" group suggests that a value in the region of 5 or 6 mEq./Hour is what one is, in effect, aiming for.

The results of insulin tests done on these two groups show that there is no significant difference between them in the incidence of incomplete vagotomy using Hollander's criterion for interpretation of the insulin test. Reasons for the significant difference between the "over and under 25s" when multiple criteria are applied to insulin test results have been discussed at length.

Re-examination of the data of Clarke et al.[459] reveals that of their 6 recurrent ulcers after vagotomy and gastroenterostomy only one falls into the "under 25" category, and it is also of interest to note that 4 of these had negative insulin tests. The report by Small and his colleagues[457] that no jejunal ulcers had occurred in their patients treated by gastroenterostomy without vagotomy, who had pre-operative M.A.O.'s of less than 30 mEq./Hour, further corroborates the findings in our patients. This must be regarded with some reservation in the light of the Mayo Clinic study[513], in which the average time interval for recurrent jejunal ulceration after simple gastroenterostomy for duodenal ulceration was approximately 11 years.

The trend is for gastric ulceration after vagotomy to occur in the low secretor group (M.A.O. less than 25 mEq./Hour) but not to a statistically significant degree, already fairly comprehensively discussed. Recurrent dyspepsia, excluding ulceration, of all degrees of severity occurs with equal frequency in the two groups. This suggests that the majority of these patients are probably not suffering from recurrent duodenal or jejunal ulceration.

To date no recurrent jejunal ulcers, proven or

suspected, have been found in patients undergoing vagotomy and antrectomy, the majority of whom (85%) have M.A.O.'s of greater than 25 mEq./Hour (mean 47.8 Table 30). Of the 56.5% in the vagotomy and drainage group with maximal acid outputs in excess of 25 mEq./Hour (mean 35.8 mEq./Hour) 12.6% presented with proven or suspected recurrent DU/JU. The gastrectomy groups figures lie somewhere in between those of the other two operations. The significantly better results in respect of recurrent DU/JU after the gastric resection operations are not surprising when one takes cognizance of the significantly greater percentage reduction of preoperative acid output, especially among the vagotomy and gastrectomy patients.

Taking the foregoing evidence into account it seems that a preoperative M.A.O. value of 25 mEq./Hour is a more realistic figure on which to base selection of patients for surgery than 40 or 50 mEq./Hour, if recurrent duodenal or jejunal ulceration is to be eradicated, or rather, if the incidence of this complication is to be drastically pruned.

When a rise over basal acid output of 20 mEq./Litre (10 mEq./L. if basal is anacid), as suggested by Hollander, is taken as indicative of a significant

degree of residual vagal innervation after vagotomy, it seems that in the presence of a preoperative M.A.O. of less than 25 mEq./Hour, residual vagal nerve fibres are relatively unimportant when vagotomy and drainage is performed. In fact it may even be suggested that these patients would have done as well with a drainage procedure alone, a statement which finds support in the findings of Small et al.[457] in their series. The similar incidence of incomplete vagotomy found in the "over 25" group who had the same operation, and among whom all recurrences occurred, indicates that residual vagal fibres assume greater importance under these circumstances. By the same token, insulin tests done on the vagotomy and antrectomy group suggest a similar incidence of incomplete vagotomy, not unexpected as the same surgeons, using the same techniques, are involved. The absence of recurrent jejunal ulceration in this group suggests that the addition of antrectomy to incomplete vagisection can sufficiently reduce the gastric acid output of a hypersecretor to provide adequate protection against recurrent jejunal ulceration. In general disagreement with Small et al.[457] standard partial gastrectomy offers a better result than vagotomy and drainage with regard to recurrent

jejunal ulcer in the M.A.O. 25 mEq./Hour, and over, group.

There still remains, however, a 2.6% incidence of gastric ulceration after vagotomy and drainage and a 1.5% incidence of this complication following vagotomy and antrectomy in this series. This does not seem to bear any definite relationship to pre-operative M.A.O. levels, although all had negative insulin tests. If recurrent DU/JU could be eliminated from the results of vagotomy and drainage presented here, the overall recurrence rate would be more than halved. Whether or not the use of more efficient drainage procedures would reduce the incidence of gastric ulcer occurring under these circumstances is a matter for considerable debate.

The major cause for unsatisfactory results (Visick 4) after vagotomy and drainage is recurrent ulceration. By the same token this is the major indication for repeat operation in this group. Technical difficulties encountered while performing repeat operations, directly attributable to the anatomical distortion produced by the initial procedure, can be incriminated as the major factor in the causation of two of the three deaths which followed these operations. It is this high secondary

mortality that brings the overall death rate after vagotomy and drainage to a figure which approximates that of the gastric resection procedures, even although the primary mortality of the former procedure is significantly lower.

Intraoperative testing for completeness of vagisection using the Burge machine[388-390,469] has not been found to be universally reliable, and it seems that in certain cases it is impossible to achieve complete vagotomy even in the hands of those experienced in its use. In addition, it is well documented that recurrent DU/JU occurs in the presence of a negative insulin test. It seems therefore that the surgeon must be satisified with a mean acid reduction of about 70% when using the vagotomy and drainage operations. On balance a policy of selection of patients for this operation, based on a preoperative M.A.O. of 25 mEq./Hour seems justified. Vagotomy and antrectomy is suggested for patients with a preoperative M.A.O. in excess of 25 mEq./Hour and vagotomy and drainage, or possibly gastroenterostomy alone should be reserved for the low secretors.

Many workers decry the routine practice of preoperative gastric acid measurement, and state that

its only value lies in the diagnostic screening for Zollinger-Ellison syndrome, in which respect the test is still not completely reliable. The results in this series justify this procedure however, and it would seem that if the knowledge gained from the A.H.T. in the individual patient is utilized when planning definitive surgical treatment, the surgeon will be rewarded with far superior clinical results.

(e) Selective or truncal vagotomy?

From the point of view of recurrent ulceration, both jejunal and gastric, and the incidence of various dyspepsias there is no significant difference between the two types of vagotomy and drainage in this series.

There is a slightly lower, but not significantly so, incidence of negative insulin tests among the selective vagotomy patients, which is a similar finding to that reported in other series (Kennedy et al. 1970). Most authors explain this on the basis of the more careful technique required for the adequate performance of this operation.

CHAPTER 3

POSTOPERATIVE SEQUELAE DUE TO ALIMENTARY DYSFUNCTION

Numerous symptoms other than recurrent dyspepsia occur after gastric operations, with various grades of severity. The clinical decision whether elective surgery is indicated for the chronic duodenal ulcer patient may on occasion prove a difficult problem. It is probably true to say that 100% of individuals submitted to gastric surgery will have some degree of alimentary dysfunction as a result, but it has been well documented that those with insignificant or atypical symptoms preoperatively, or those undergoing emergency resections, have a markedly higher incidence of significant postoperative symptomatology[462,463]. This indicates that fairly stringent criteria must be applied in selecting patients for elective surgery. In other words, the patient who has been incapacitated by his ulcer for a prolonged period of time and has therefore earned his operation, is far more likely to put up with any relatively minor complaints that may follow in the wake of operative intervention than one to whom this does not apply.

With regard to assessment of long term post-operative status, the patient acts as his own control, but in view of the fact that all scientific work demands that a control study be set up, it was decided to complete this study by including one. It must be emphasised nevertheless that the value of this is questionable, although the results summarised in Table 37 are interesting. Rather surprising is the proportion of individuals who regularly suffer from and take treatment for heartburn. Similarly, a fair percentage complained of feeling bloated after meals, even after small quantities had been eaten. One 18 year old female gave a history very suggestive of early vasomotor dumping! By and large the occurrence of these various problems in the population at large is negligible when compared with the figures obtained from postoperative patients, which will be pointed out as the relevant discussion proceeds.

To a large extent the aetiology of and mechanisms for many of these post surgery complications in relation to both vagotomy and gastric resection have been discussed in the section on pathophysiology (Chapter 2), where all the experimental evidence has been presented in some detail. The following discussion is concerned mainly with the clinical findings,

TABLE 37

CONTROL GROUP

ALL FIGURES REFER TO SYMPTOMATOLOGY
OCCURRING TO A REGULAR PATTERN

	TOTAL NUMBER OF CASES	DYSPEPSIA	HEARTBURN	DIARRHOEA	NAUSEA	VOMITING	ERUCTATION		POST PRANDIAL DISCOMFORT	SYMPTOMS SUGGESTIVE OF DUMPING
							EXCESSIVE	FOUL		
NUMBER	185	10	21	0	12	0	11	1	13	1
PERCENT		5.4	11.4		6.5		5.9	0.5	7.0	0.5

and where indicated brief summaries are presented of the earlier more detailed review.

(a) Oesophageal symptoms:

Gastro-oesophageal reflux, as evidenced by the occurrence of heartburn, was as frequent after each of the vagotomy operations, with a significantly higher incidence than that found among partial gastrectomy patients. The latter group, however, had the identical incidence of this complication to that found in the control group. This suggests that patients submitted to partial gastrectomy run a minimal risk of developing the complaint or, by the same token, of aggravating pre-existing heartburn as a result of their operation. Among the vagotomy and drainage group, those with the selective type of nerve section complained of heartburn with a significantly lower degree of frequency than those with truncal vagotomy, and with only a slightly though insignificantly higher incidence than after gastrectomy.

The integrity of the intrinsic lower oesophageal sphincter is regarded by most authors[146-150] as the most important physiological mechanism which prevents gastro-oesophageal reflux under normal circumstances. Extrinsic factors such as the phreno-oesophageal ligament, flap-valve and "mucosal rosette" mechanisms, and the pinch-cock action of the diaphragm-

atic crura probably play a minor role[145,146,150]. Sphincteric pressure has been shown to drop to a significant degree after truncal vagotomy[148,149], which can be mimicked in the normal patient by administration of anticholinergic drugs[150].

Some workers maintain that reflux follows damage to the extrinsic mechanisms which allows minor degrees of hiatal hernation to occur[155,156] while others present evidence which disputes this[150, 152-154].

The operative techniques involved in both selective and truncal vagotomy result in almost total disruption of the extrinsic mechanisms, with about the same amount of handling and trauma to the lower oesophagus. Results obtained in this series therefore provide strong clinical evidence that vagal denervation of the intrinsic sphincter is the major factor responsible for the gastro-oesophageal reflux that occurs. The fact that gastrectomy does not seem to result in this complication to a significant degree adds weight to this suggestion, though admittedly the routinely performed partial gastrectomy does not as a rule involve interference with the peri-oesophageal area.

Unfortunately insufficient data is available

on these patients with regard to the occurrence of dysphagia. However, no overt cases of lower oesophageal obstruction were found. This would corroborate the results of Bank, Marks, and Louw[163] who reported, from this clinic, that although approximately 30% of patients complained of the symptom in the immediate postoperative period, none were found to have persistent dysphagia at 18 months postoperatively. This complication is generally ascribed to oedema or haematoma with varying degrees of associated muscle spasm. Bruce and Small however reported on 2 cases with postvagotomy dysphagia in whom the cause was probably organic stricure formation secondary to peptic oesophagitis. This was thought to result from acid reflux through a hypotonic gastro-oesophageal sphincter[161].

(b) Alteration in bowel habit:

Diarrhoea has been cited by many as the major problem following vagotomy, but a marked variation in the incidence of the complication is reported from one study to the next. Undoubtedly this is attributable to lack of a precise definition of what constitutes the symptom. For the purposes of this study diarrhoea is defined simply as the frequent passage of loose watery stools, and its subdivision into

various clinical patterns has followed generally accepted rules.

The frequency with which these different patterns of alteration in bowel habit occurred in this study is similar to that reported in most series [399-404,464-467]. Many authors have stated that the occurrence of episodic diarrhoea as usually reported is probably an erroneously high figure, as some patients would be included who are merely suffering incidental attacks of gastroenteritis. This may well be true to a certain extent but the fact that no patients in the control group complained of regularly recurring attacks of explosive diarrhoea indicates that the error is probably very small.

In support of the findings of other authors [331,468] transient postoperative diarrhoea did not seem to have any prognostic significance with regard to the development of continued patterns of the symptom. Many of our patients who fell into the latter category had not experienced any significant degree of diarrhoea in the immediate postoperative period or in the first 2 or 3 months thereafter.

Current opinion indicates that selective nerve section reduces the incidence of diarrhoea [330,465, 469,470] after vagotomy and these results support

this view. An earlier report from this hospital[163] on the same groups of patients reported no significant difference between selective and truncal vagotomy at one year to 18 months after surgery. The finding that the difference is now significant supports the report of Kennedy and Connolly[471,472] that an almost identical incidence after both types of operation at one year, had become a significant difference in favour of selective vagotomy at 2 years after operation, in their prospective clinical trial on vagotomy and drainage.

Various hypothesis have been put forward for the aetiology of postvagotomy diarrhoea and the question is far from resolved. Colonisation of the stomach by pathogenic bacteria, a consequence of hypoacidity and atonicity, which in turn results in repeated bouts of infective enteritis was originally proposed by Dragstedt[473]. No difference in the concentration of faecal organisms in the stomach and jejunum could be demonstrated by some workers[474] who studied patients with vagotomy and gastroenterostomy and partial gastrectomy. Browning and his colleagues[475] investigated patients with transient diarrhoea following vagotomy and drainage, by taking samples from the upper jejunum preoperatively and

for 10 days after the operation. Preoperative colonisation was present in 11% of patients. On the second postoperative day 47% yielded positive cultures which then climbed to a figure of 69% by the eighth postoperative day. These figures were the same for both pyloroplasty and gastroenterostomy. The colonised group was found to have a higher mean postoperative M.A.O. (pentagastrin stimulated) than the non-colonised group. Sixteen percent of their patients developed diarrhoea, all of whom were colonised, as opposed to 76% colonisation among those who did not have diarrhoea. Bacterial colonisation may therefore be related to postvagotomy diarrhoea.

Small bowel motility disturbances have been demonstrated by various workers in the postvagotomy patient both by manometric[177,271,277,278] and electrical methods[279,280] but no correlation between the nature of these disturbances and the occurrence of diarrhoea has been noted.

Transit time of small bowel content after vagotomy has been studied with varying results. By radiological assessments some report decreased[270], others increased rates of intestinal emptying into the caecum[271-274]. The first study correlating the rate of intestinal transit with the occurrence

of diarrhoea was performed by McKelvey and his colleagues[186,187,276]. All patients with increased frequency of bowel action, or diarrhoea after vagotomy and pyloroplasty were found to have rapid rates of gastric emptying and short intestinal transit times. No difference was demonstrated in this respect between selective and truncal vagotomy and drainage. Accordingly, the conclusion reached was that the small bowel mucosa is unable to deal with the more rapid transit of its content attributable to rapid gastric emptying, which is in turn, largely a result of the drainage procedure, which destroys the normal mechanisms controlling this. Other authors have also incriminated the drainage procedure as a cause of diarrhoea, with the finding that patients with gastroenterostomy developed the complication more frequently than those with pyloroplasty[464,478]. However, the only published study comparing gastric emptying between pyloroplasty and gastroenterostomy showed that the latter resulted in a far slower rate of evacuation of stomach contents[182]. All forms of early dumping, almost certainly attributable to rapid gastric emptying[185] was significantly commoner among the selectively vagotomized patients in this series, compared to the

truncal group. In view of the fact that the same patients have a significantly lower incidence of diarrhoea after the selective procedure suggests that vagal denervation per se plays some part.

Histological changes in small intestinal mucosa, demonstrated by some[283,285-287], but refuted by others[281,282,288,290], whether due to diminished superior mesenteric blood flow when coeliac vagal branches are cut[284], or inflammatory changes resulting from bacterial overgrowth, have not been correlated with the occurrence of diarrhoea. The significance of these findings therefore remains uncertain. Similarly, the significance of Silen's[289] report with regard to increased cell turnover in the small bowel, or of the transient biochemical changes found by Ballinger[285], in relation to transient or chronic patterns of diarrhoea after vagisection are ill understood.

The fact that increased faecal fat loss occurs after vagotomy and drainage procedures finds general acceptance[260,261,263,266,292-295]. No definite relationship between faecal fat excretion and diarrhoea has been demonstrated by those who have investigated this possibility[264,266,267,293,474]. In addition, no difference has been found between selective and

truncal vagotomy in this respect[264-266].

Vagotomy induced carbohydrate intolerance, due to small bowel disaccharidase deficiencies has been discounted as a common cause of postoperative diarrhoea by the work of Garcia-Paredes and Truelove[291].

In conclusion it seems that selective vagotomy and drainage offers a better result with regard to the occurrence of postoperative diarrhoea than truncal vagotomy. The results in this study show that patients have the same chance of developing this complication after selective vagotomy and drainage as after partial gastrectomy and only slightly more so than after vagotomy and antrectomy. Why the latter procedure should result in lower incidences of diarrhoea than any of the others, when the patient is exposed to the problems of both gastric resection and vagotomy, truncal in all our cases, is difficult to understand. The suggestion may be made that this operation has been reserved for the bona fide ulcer sufferer in this series, on the basis of the policy of selection, and that fewer functional patients would be submitted to this procedure. It seems that rapid gastric emptying and hence rapid small bowel transit plays some part. In addition, it seems probable that a subtle mucosal change occurs, induced by parasympathetic denervation. These two

factors in conjunction provide an attractive explanation for the occurrence of increased frequency of bowel action and persistent diarrhoea. The commonest pattern of postvagotomy diarrhoea however, is one of intermittent precipitous attacks, usually of short duration, and invariably superimposed upon a background of more frequent daily bowel actions. It is obvious therefore that at least one variable factor must operate. Denervation is permanent, but although gastric emptying may vary with the consistency of the meal, the explosive, precipitous nature of these attacks would be far more logically explained on the basis of repeated bouts of infection, precipitated by upsetting a fine balance of factors. Much more investigation is required into this problem, particularly with regard to bacterial colonisation of the gastrointestinal tract after gastric operation.

(c) "Stasis syndromes" (nausea, vomiting and eructation):

This is a blanket term used in this study to describe that group of symptoms such as nausea, vomiting and eructation, usually ascribed to gastric stasis in the vagotomy and drainage group[166,417,427] and to gastric or afferent loop stasis in the

gastric resection group[478-481].

Approximately one third of all patients submitted to one of the operations under discussion complained of some component of the "stasis syndrome". The greatest proportion with multiple symptomatology, that is, with more than one component occurring to a significant degree is found among the vagotomy and drainage group.

Although symptoms such as nausea and eructation are apparently fairly common among normal controls the incidence of these various complaints following gastric surgery is 4 to 5 times that found in this group. Vomiting is recognised as a major complication of all the current operations for duodenal ulceration. Accurate definition of the type of vomiting, that is whether it consists predominantly of food (non-specific) or bile, is difficult, as much depends on the patient's own observations.

Bilious vomiting, it will be seen, was significantly more frequent following the gastric resection procedures especially after the 70% partial gastrectomy. In the vagotomy and drainage group, contrary to most reports[459,482] but in agreement with Goligher et al.[403,404] in their study, our results showed no difference in the incidence of either type

of vomiting when either gastroenterostomy or pyloroplasty was used for drainage. In addition, the type of vagotomy did not have any appreciable effect. Some degree of biliary reflux is invariably found in patients who have had any form of gastric surgery (216), but why some patients should tolerate this better than others is difficult to understand. There does seem to be an inverse relationship between the size of the gastric remnant and the incidence of bilious vomiting as evidenced by the results, but this is obviously not the entire explanation.

Non-specific (food) post-cibal vomiting occurred with slightly greater frequency after partial gastrectomy, which is what one would expect in view of the smaller gastric reservoir. Differences are not significant however.

Excessive eructation seemed to occur with equal frequency after each procedure, but foul eructation is a virtual sine quo now of chronic gastric stasis (166), occurred in one of every 10 patients submitted to vagotomy and drainage. This is a significantly higher incidence than that found in any of the other groups. Obviously a great deal of subjectivity is involved in eliciting this symptom, but the differences are clearly significant. Selective

vagotomy and drainage was complicated by this symptom much less frequently than was the truncally denervated group. Exclusion of all patients with gastroenterostomy from both selective and truncal groups made no difference whatever to the relationship between the two procedures.

It may be postulated therefore that the technique of routine selective vagotomy leaves some residual antral innervation, possibly from the hepatic or coeliac nerves, with better muscle tone and motility co-ordination and hence less gastric stasis.

Although an equal percentage of patients are affected by the "stasis syndrome" after each operation, vomiting remains the largest single cause for complaint and dissatisfaction, and the largest proportion of these patients is found after gastric resection, particularly two thirds partial gastrectomy. In general, on the other hand, after vagotomy and drainage these symptoms tend to be mild but multiple.

(d) Dumping syndromes:

Early dumping

Mix[483] first coined the phrase "dumping syndrome" when he observed radiologically the way in

which bismuth was "dumped" into the jejunum of a woman with a gastroenterostomy who had multiple postcibal complaints.

The definition of what constitutes the dumping syndrome is far from clear cut and for this reason comparison between the series of results from different centres is difficult. For the purpose of this study early dumping has been defined as a feeling of epigastric fullness and discomfort coming on almost immediately after meals. Those who, in addition to this, experience a syndrome of faintness, sweating, palpitations and weakness are classified as having early vasomotor dumping.

Uncomfortable postcibal fullness occurring after gastric surgery following the ingestion of even small quantities of foodstuffs is undoubtedly the result of excessively rapid emptying of the stomach or stomach remnant into the duodenum or jejunum, presumably with overdistension of the latter [478, 484]. This has been demonstrated both radiologically [485] and by the use of liquid test meals [185]. The demonstration of hypermotility in the efferent loop, which has been correlated with these postcibal sensations [485,486] provides additional evidence.

It has also been well documented that those who experience vasomotor symptoms in association with epigastric fullness have significantly more rapid rates of gastric emptying than asymptomatic post-gastric surgery patients[185,483,486-489]. Illingworth[478] provides further circumstantial evidence by his observations on the pathology of the proximal 8 to 10 inches of efferent loop, which is "somewhat enlarged, perhaps to twice its normal diameter, thick walled, vascular, congested, heavy with blood" when seen at laparotomy.

Why some individuals with rapid gastric emptying should develop vasomotor symptoms and others not is difficult to explain. Changes in the circulating plasma volume, constituting a 5 to 15% fall has been consistently demonstrated by several workers[487-490]. There is general agreement that this is the result of osmotic withdrawal of fluid from the interstitial space into the gut lumen by its hypertonic content of undigested food. Some workers have been able to correlate the amount of fluid sequestrated, that is the extent of the plasma volume change, to the intensity of symptoms[487-489]. Others have found no correlation and report that an equal number who do not have vasomotor symptoms exhibit comparable circulatory changes[491-493]. It seems therefore

that there is some inability to adapt to the plasma volume changes in those with vasomotor symptoms. Hinshaw and his colleagues[494] demonstrated that on digital plethysmography this group of patients significantly increased their peripheral blood flow compared to asymtomatic patients, who in fact responded in the normal way with peripheral vasoconstriction. Another possibility that has been raised is that there is excessive pooling of blood in the portal circulation during the phase of digestion in these individuals, and that this additional fluid sequestration cannot be compensated for by the normal homeostatic mechanisms. Some rather inconclusive evidence has been provided for this hypothesis[491,495].

Various other suggestions have been made in an attempt to explain the vasomotor phenomena. Intravenous administration of adrenaline mimicks these symptoms[496] and in addition increased levels of urinary catecholamines have been detected during attacks[497]. This has been variously thought to reflect reflex production of adrenaline[498] and sympathetic nervous system overactivity[497]. Liljedal et al.[498] provided evidence that this was a consequence of small bowel hypermotility, but this has been refuted[485]. Undoubtedly many of the

symptoms and signs of vasomotor dumping can be attributed to sympatho-adrenal overactivity, which are most likely part of the compensatory reflex activity for the well documented circulatory volume changes.

The rapid absorption of glucose, with consequent increase of blood sugar to hyperglycaemic levels, which is often found after gastrectomy has been implicated. Some authors have managed to correlate the rising blood sugar levels with early symptoms [496,499], while others have been unable to do so [491,500]. However, the fact that intravenous glucose does not cause the same symptoms [491,500], and that protein and fatty meals result in early dumping make this unlikely [501].

Smith [502] demonstrated electrocardiographic changes in patients with marked cardiac signs during dumping attacks, and suggested that these were probably due to hypokalaemia. This apparently occurred at intracellular level, as the serum potassium only fell some time after symptoms had abated although intravenous administration of potassium salts relieved or prevented these cardiac signs.

Considering all the available evidence, early dumping symptoms are certainly the result primarily

of rapid gastric emptying into the jejunum or duodenum. That an alteration in plasma volume results from this is also well substantiated. The most logical reason for the production of vasomotor symptomatology in some of these patients is that there is a failure of circulatory homeostatic mechanisms to adequately compensate for these changes.

According to Illingworth[478] 80% of those undergoing routine partial gastric resection will at some stage experience symptoms of dumping, if those with postcibal distension alone are included. Results in this study show a much lower figure than this among the gastrectomy group. About half of the patients in this series who were submitted to one of the vagotomy operations have experienced dumping at some stage since the operation, a significantly lower proportion than that found in the gastrectomy group. As one would expect therefore, in view of the much smaller stomach remnant patients with standard two thirds partial gastrectomy are far more liable to symptoms attributable to rapid gastric emptying and hence volume overload of the small bowel into which it drains, than are those with normal sized stomachs or alternatively, limited resections.

In the long term, that is at 4 to 10 years post-operatively, there is no significant difference

between the three operations studied with regard to the symptom of epigastric fullness alone. Grading of this into degrees of severity proved difficult and too imprecise to be of value, but the general impression gained was that postcibal fullness per se did not seem to result in a significant degree of morbidity.

Early vasomotor dumping was shown to be significantly more frequent after gastrectomy. In agreement with the reports of Goligher and his colleagues (400-404) vagotomy and antrectomy patients had a far lower incidence of this problem than those with either vagotomy and drainage or partial gastrectomy. These differences become significant when the relative incidences of severe grades of dumping are compared.

Forty percent of those routinely gastrectomized who have vasomotor complaints fall into the "severe" category. In distinct contrast, the majority of the early dumpers after vagotomy and drainage fall into the mild to moderate category, only 6% of these being labelled as severe. It is of interest to note that of the latter 4 patients, 3 had gastroenterostomies. One would expect dumping to be more of a problem after gastroenterostomy but not all authors

are in agreement on this point although some do report a lower incidence when this is compared with pyloroplasty[402-404,460]. Why vagotomy and antrectomy should provide a significantly better result in this respect than vagotomy and drainage can find no logical explanation, but the same reason may be suggested in this instance as for post-operative diarrhoea.

Patients with symptoms attributable to rapid gastric emptying after surgery seem to have a general tendency to improve with time. This is evidenced by the 10% or so who experience epigastric discomfort for a limited period after their respective operations, which then resolves completely. Similarly, among those with established patterns of early dumping after the vagotomy operations, about half improve. The percentage of postgastrectomy patients who improve is much smaller, however, especially among those with vasomotor symptoms. Improvement is most probably due to dietary adjustments, as the patient comes to realize what foods or fluids or combinations thereof are likely to aggravate or precipitate attacks.

There is general agreement that diet is effective in controlling symptoms in the vast majority of

early dumpers[478,479], and that the remaining patients, constituting roughly 10% of the total, who have a severe grade of the syndrome remain refractory to this form of treatment. Various success has been reported in the conservative treatment of this latter group using antispasmodics[503], oral administration of potassium salts[504], autonomic ganglion blocking drugs, alkalies, oral ingestion of local anaesthetics[505], and even injections of local anaesthetic into the paravertebral region[506], but these patients usually come to repeat operation.

Most of the patients in this series who developed early vasomotor dumping did so within three months to a year of leaving hospital. This moderate time lapse before symptoms develop is probably attributable to the individual's gradually gaining confidence after the operation and hence gradually increasing the bulk and variety of what was previously a bland and limited ulcer regime. What is difficult to reconcile however is how a certain proportion (in this series 20 to 30%) of patients only develop vasomotor symptoms for the first time a year or more later (range 14 months to 5 years). In these cases one may postulate that compensatory mechanisms for the circulatory changes,

which undoubtedly play a major role in the pathogenesis of the syndrome, gradually deteriorate to a certain critical level, possibly related to ageing, at which stage symptoms manifest. In certain cases it would seem that emotional stress plays some part in the development of this syndrome at this later stage.

Comparison of the two types of nerve section in the vagotomy and drainage group showed that there was no significant difference between them with regard to the relative proportions of patients affected by all forms of early dumping. Nevertheless significantly more of the selective group complained of mild to moderate vasomotor symptoms, and all the severe dumpers belonged to the truncal group. No logical explanation can be offered for these differences and their significance is uncertain.

Generally reviewing the significance of this problem after gastric surgery it seems that partial gastrectomy is far more likely to result in refractory degrees of the syndrome than the other operations.

Late Dumping

Imprecise definition again makes comparison of different reports difficult. Late dumping in this report describes a sensation of faintness, drowsiness, weakness and tremor coming on 1½ to 2 hours

after the last meal.

Lapp and Dibold[507] demonstrated that the oral ingestion of glucose by gastrectomy patients resulted in an abrupt rise of blood sugar to an abnormally high level, followed by a sharp fall to hypoglycaemic levels. They noted that the same changes could be produced in normal subjects if the glucose was introduced through a tube directly into the jejunum. This early rapid rise in the blood sugar is probably due to unduly rapid absorption from the jejunum consequent on precipitate gastric emptying. The subsequent hypoglycaemia is ascribed to delayed and excessive output of insulin following the rapid rise in blood sugar.

The relationship of hypoglycaemia to late dumping seems to be established, but although hypoglycaemia is common after gastrectomy, only a small proportion of patients develop the syndrome. It has therefore been suggested that the essential abnormality is probably a hypersensitivity to insulin in certain patients which aggravates the hypoglycaemia and makes it unduly prolonged[496]. However a simple explanation can be based on the well-known variability in tolerance to hypoglycaemia from patient to patient and even in the same individual from day to day.

In other words those with poor tolerance to low blood glucose present with symptoms.

Late dumping is uncommon and the incidence of about 5% found in this study is in accord with the usual published figures, with no significant differences between the various procedures. The only cases of severe degree were reported among the vagotomy and antrectomy patients, but this is difficult to account for and is of doubtful significance in view of the small numbers of patients involved. Most cases are therefore of mild to moderate degree and are readily treated by simple dietary measures, which include avoidance of carbohydrate-rich easily assimulable foods and liquids, and the taking of glucose or sugar by mouth when an attack seems imminent.

(e) Nutritional status after gastric surgery:

This is not strictly speaking entirely a result of "alimentary dysfunction" but for the sake of convenience is included in this section of the discussion. Detailed study of this aspect of gastric surgery sequelae is beyond the scope of this work. Weight changes reflect general nutritional status. No significant difference between the two vagotomy operations and postgastrectomy patients was found in

respect of weight changes. Similarly among the vagotomy and drainage patients selective vagisection did not influence the issue in any way.

Obviously the data in this study, where weight gain or loss is expressed simply as an absolute amount, which has been arbitrarily determined as being a probable significant figure, is not accurate as it takes no account of age, sex, race or what relationship the postoperative change in nutritional status bears to the patient's preoperative condition. For example, Johnston, Wellbourn and Acheson[508] for partial gastrectomy, and Cox et al.[261] for vagotomy and gastroenterostomy, have demonstrated that patients who had lost much weight before surgery tended to gain more after operation than those who had not.

Few studies have been published on weight changes following the vagotomy operations. Cox and his colleagues[261] found that 30% lost while 54% gained weight when gastroenterostomy was used as the drainage procedure. In the series of results reported by Schofield et al.[305], who studied weight changes after vagotomy and pyloroplasty, 7% lost and 60% gained weight. Both groups of authors compared post-operative alteration in weight with "best preoperative

weight" values. Wastell[509] also suggested in his review of the subject that vagotomy and pyloroplasty resulted in less weight loss than other procedures.

To compare the nutritional status of patients after vagotomy and drainage with that after partial gastrectomy, Pulvertaft and his co-workers[310,313] used the ratio of total body weight expressed as a percentage. They reported little change after vagotomy and drainage and that nutritional status changes were significantly greater following partial gastrectomy.

Inadequacies of dietary intake were considered to be most likely cause of this difference in view of the normal stomach size and hence greater capacity after vagotomy and drainage. Available evidence indicates that the average intake of food is not impaired for either vagotomy and drainage or partial gastrectomy patients[310,313,510]. All authors do agree however that there is a deficit in calcium and vitamin D intake compared with the recommended daily intake of these dietary constituents. Johnston, Wellbourn and Acheson[508] found a definite correlation between weight loss and deficient intake, but they admit that this is not the entire explanation. The poor nutrition seen in a few patients

is undoubtedly a consequence of poor intake resulting from fear of initiating postcibal symptoms.

Obviously, therefore factors other than deficient diet play a part in this problem. Recent literature regarding malabsorption, anaemia and metabolic bone disease has been reviewed fairly comprehensively in Chapter 2 and only the conclusions are summarised here.

After vagotomy and drainage, steatorrhoea undoubtedly occurs, probably to a lesser degree than after gastrectomy. Protein and carbohydrate malabsorption is found in some partially gastrectomized patients but is never a problem following vagotomy and drainage.

Vitamin B_{12} and iron malabsorption do occur after the vagotomy operations but anaemia is always of the iron deficiency type, never megaloblastic and usually of mild severity. Partial gastrectomy on the other hand is well-known for its anaemia, occasionally megaloblastic or of mixed type, and frequently presenting a refractory therapeutic problem. Distinct advantages, albeit short term, have been demonstrated for vagotomy and drainage over partial gastrectomy in this respect.

Clinically manifest metabolic bone disease is

a well documented though relatively uncommon complication of partial gastric resection. No reports of overt metabolic bone disease, directly attributable to vagotomy with a drainage procedure or antrectomy, have as yet appeared in the literature at the time of writing.

If all the accumulated evidence is considered, it would seem that from the point of view of the occurrence of nutritional and metabolic sequelae, vagotomy operations offer a better prognosis than partial gastrectomy. Relatively little work has been published on postvagotomy patients in relation to these problems, and in addition most current reports are based on information gleaned from short-term follow up studies. The results from this 4 to 10 year post surgery study, bearing in mind the reservations already mentioned concerning the data, may well indicate that in the long run there is no significant difference between the various operations. For the present however the relative absence of morbidity due to these sequelae remains a strong point in favour of persevering with the vagotomy and drainage procedures.

CHAPTER 4

GENERAL CLINICAL ASSESSMENT OF RESULTS (VISICK GRADING)

Most authors use a modification of Visick's classification for the purpose of assessing their overall clinical results. In this study, the precisely defined modification of the Visick grading used by Goligher and his colleagues[399-404] in their recently published clinical trial, which serves as a model of clinical research, have been adhered to.

Vagotomy and antrectomy has a significantly higher proportion of perfect results (Visick Grade I) compared to vagotomy and drainage. In addition, the former operation has a distinct, though insignificant advantage over partial gastrectomy. Combining the proportions falling into Grades 1 and 2, which can be designated as a "good result", the differences are much smaller, but the significance of the advantage of vagotomy and antrectomy is nevertheless just maintained. This general pattern with regard to good results is identical to that reported by Goligher et al.[402-404], and Cox in his extensive review of postvagotomy problems[511].

The percentage of unsatisfactory results (Visick Grade 4) is seen to be highest after vagotomy and drainage, but just fails to attain significance when compared with vagotomy and antrectomy, which has the lowest percentage. It should be noted, however, that the difference between truncal vagotomy and drainage and vagotomy and antrectomy is large enough in this respect to be significant. Partial gastrectomy occupies a position intermediate between the two other procedures in this respect. Differentiation between Grades 3 and 4 can be difficult in some patients where there is a narrow dividing line between an acceptable and unacceptable result. If these two categories are combined the relationship between the three operations is maintained, but the difference between vagotomy and antrectomy and vagotomy and drainage becomes statistically significant. Be that as it may, the Visick 4 category is the one that counts, and although perhaps some error exists, in that one is always more inclined to place doubtful cases into the more favourable group, no definite advantage can be demonstrated for any one procedure.

Analysis of the reasons for classification of patients into the Visick 4 category shows that in

the vagotomy and drainage group, the major reason for inclusion in this group was proven or suspected recurrent ulceration, which constitutes a significantly higher proportion than that found for the surgical failures after either vagotomy and antrectomy or partial gastrectomy.

Twenty percent of patients dissatisfied with the result of their vagotomy and drainage operation complained of combinations of symptoms, such as diarrhoea as well as dumping or "stasis" and dyspepsia. The impression gained with many of these individuals was that it was rather the cumulative effect of these multiple, relatively mild problems, than any particular symptom per se which led them to regard their operation as having been a failure.

It should be mentioned that although 7 of the 9 partial gastrectomy patients had more than one major complaint, the clinical impression in these cases was that each individual symptom on its own was incapacitating. This then raises the question of initial poor selection of patients for elective surgery. It has been fairly well documented by several authors that patients undergoing surgery who have had minimal preoperative symptomatology tend to be affected to a far greater extent than

those in whom the reverse holds true[462,463], a point that has been made in an earlier chapter.

This seems to be particularly relevant when those with dyspepsia in whom no apparent organic cause can be found are considered as a group. Many of these patients complain of vague dyspepsia, not typical of duodenal ulcer, and often identified as being identical to their preoperative complaints. Some, fortunately few, with this vague type of history had been submitted to surgery without having had what could be described as an adequate trial of medical therapy, on the basis of radiological evidence of duodenal ulceration. Two patients submitted to gastrectomy belonged unequivocally in the psychosomatic group and had relatively mild postoperative sequelae which had been exaggerated out of all proportion. The above serves to emphasise the point made by almost every author writing on this topic, namely, that patients must earn their surgery.

Diarrhoea is considered by many surgeons to be the bete-noir of vagotomy and drainage, but of 37 patients who stated that they found the symptom troublesome, only 12 cited it as a major reason for therapeutic failure. Although this is a slightly higher proportion than that found among the Visick 4's after either of the gastric resection procedures,

the difference fails to attain statistical significance, which is a similar finding to that reported by Goligher et al.[402-404]. It seems therefore that although in general diarrhoea occurs more frequently after vagotomy and drainage than other forms of gastric surgery, when attention is focused on the occurrence of really significant morbidity resulting from the symptom, there is no real advantage in using any one procedure. By the same token if post-resection patients develop diarrhoea they are far more likely to be incapacitated by it.

All of the postvagotomy and drainage patients in this category who complained of severe dumping stated that they would have been prepared to put up with the symptom if diarrhoea or dyspepsia had not complicated the issue. In distinct contrast to this, early dumping is the major single cause for dissatisfaction among the partial gastrectomy patients.

Only 5 vagotomy and drainage patients cited components of the loosely defined "stasis syndrome" as a major cause of disappointment with the operation, and 4 of these were mainly due to vomiting. Altogether these constitute a relatively small proportion of the Visick 4 category after this operation, as opposed to the gastric resections where this is a

major contributory factor.

Repeat operations:

Between 6 and 10% of all patients submitted to surgery for chronic duodenal ulceration have to undergo a subsequent operation, for complications related to the initial procedure. After each procedure a little more than half of those classified as Visick Grade 4 have had another operation, and the highest proportion of these patients belong to the vagotomy and drainage group.

The results show that recurrent ulceration is the major indication for reoperation, followed by vomiting, after vagotomy and drainage, and this follows a similar pattern to that reported by others[404,484]. If the number of patients with proven recurrent jejunal or duodenal ulceration is subtracted from the total number submitted to a second operation in this group, the incidence of repeat surgery is almost halved and the total percentage drops to the same level as that found after the other operation. By the same token the significance of the difference between truncal vagotomy and drainage and vagotomy and antrectomy in respect of the occurrence of Visick 4 category patients is invalidated. This also applies when

significances in the difference between the total number of Grade 3 and 4 results among the vagotomy and drainage group as a whole and vagotomy and antrectomy are recalculated. The eradication or probably more realistically, the significant reduction, in the incidence of recurrent DU/JU after vagotomy and drainage is a theoretical possibility if the selection of patients for this operation is based on their having a preoperative M.A.O. of less than 25 mEq./Hour.

Afferent loop problems and dumping are the most frequent causes of a second operation after any type of gastric resection. It may therefore be argued that if gastro-duodenal reconstructions (Billroth I) are performed, many patients will be spared this in view of the absence of an afferent loop, and the documented lower incidence of dumping after this procedure. The Billroth I type partial gastrectomy for chronic duodenal ulceration is known for its high recurrence rate, but it has been employed with remarkable success in association with vagotomy by several surgeons reporting on large series[405,406, 466]. It is of interest to note that in the current series, an initial gastro-duodenal reconstitution would theoretically have eliminated the need for re-operation after vagotomy and antrectomy. In addition,

this would have reduced the proportion belonging to the Visick 4 category to a significantly lower level than that found after both other operations, even if recurrent DU/JU is eliminated after vagotomy and drainage.

The mortality of the second operation is high and two of our four deaths can be directly attributed to technical difficulties, created by the initial surgery. Reducing the frequency with which these hazardous procedures have to be done therefore assumes great importance. It is of interest to note that between 30 and 50% of all those submitted to reoperation remain in the Visick 4 category, and 10 to 15% of these have more than one repeat surgical procedure. The marginal advantage of vagotomy and antrectomy and partial gastrectomy over vagotomy and drainage in respect of the relative proportions of unsatisfactory results is not materially altered by subsequent attempted curative operations. This rather sad state of affairs can undoubtedly be attributed in many of these patients to thorough disillusionment with, and what in certain cases amounts to open distrust of, the doctors' efforts to effect the originally promised cure.

Selective or truncal vagotomy?

Although more patients occupy the Visick 1 and 2 and fewer the Visick 3 and 4 categories after selective than after truncal vagotomy and drainage the differences are not significant.

Recurrent ulceration accounts for a significantly greater proportion of the unsatisfactory results following the selective operation, but elimination of recurrent jejunal or duodenal ulceration from both groups does not affect the issue.

Diarrhoea accounted for a lower proportion of the group classified as Visick Grade 4 after selective vagotomy but the difference fails to attain a significant level. It seems therefore that even although significantly more patients complain of troublesome diarrhoea after truncal vagotomy than after the selective operation, there is no difference between the two procedures when consideration is given to the proportion who suffer the symptom to a degree which forces them to regard the operation as a failure.

The complete absence of significant stasis problems or dumping after selective vagotomy presents an interesting phenomenon and the possible reasons for this have already been discussed.

Selective vagotomy with drainage therefore provides a marginally better overall clinical result than when the abdominal vagi are totally sectioned. In this study, the difference is centred around the relative absence of gastric stasis problems after the former, and not diarrhoea, which is usually quoted as the most important advantage of selective over truncal vagotomy.

CHAPTER 5

CONCLUSIONS

I MORTALITY

The primary mortality of elective surgery for duodenal ulcer carried out in this hospital is low, but vagotomy and drainage is generally accepted as having an advantage over gastric resection. When the final death rate is calculated to include those following repeat operations, there is probably no significant difference between these procedures. The majority of reoperations after vagotomy and drainage are for recurrent ulceration and deaths are largely due to technical difficulties created by the initial surgery. Eradication or drastic reduction of the recurrence of duodenal/jejunal ulceration in this group would undoubtedly favourably influence this mortality figure. Although no deaths occurred after repeat operations following vagotomy and antrectomy, it seems inevitable that with larger numbers of patients deaths would occur, as the hazards presented under these circumstances are identical with those of partial gastrectomy, which has a high reoperative mortality. It may be suggested that the elimination of afferent loop

problems, by using a gastroduodenal (Billroth I) reconstruction after vagotomy and antrectomy may considerably reduce the need for a subsequent surgical procedure among these patients.

II GENERAL COMPARISON OF THE CLINICAL RESULTS OF THE THREE PROCEDURES

Comparison of the incidences of postoperative sequelae severe enough for the patient to regard them as troublesome, or indeed, as a reason for regarding the particular operations as a failure, is summarised in Table 38. It will be seen that except for the incidence of recurrent ulceration, where vagotomy and antrectomy and partial gastrectomy demonstrate a significant advantage over both selective and truncal vagotomy and drainage, no dogmatic assertion can be made about the superiority of any one procedure.

Fairly consistently lower incidences of the various types of alimentary dysfunction among vagotomy and antrectomy patients, although not statistically significant in most instances, coupled with the significantly higher proportion assessed as having a good postoperative result, indicate a marginal superiority for this procedure.

Vagotomy and drainage on the other hand, although generally showing higher incidences of these various

TABLE 38

COMPARISON OF THE OVERALL CLINICAL RESULTS OF
ELECTIVE SURGICAL PROCEDURES DONE
FOR CHRONIC DUODENAL ULCERATION

OPERATION	APPROX. OVERALL MORT. %	TOTAL RECURRENT ULCER PR.&SUSP.	DYSPEPSIA %		DIARRHOEA %		GASTRIC & % AFF. LOOP "STASIS"		DUMPING % (EARLY & LATE)		OVERALL VIS. % GRADING	
			TOT.	VIS-ICK 4	TROUBLE-SOME	VIS-ICK 4	TOTAL AFFECTED	VIS-ICK 4	TROUBLE-SOME	VIS-ICK 4	1 & 2	4
SELECT. VGY. & DRAIN.	1.4	10.8	18.0	3.7	7.2	1.8	30.6	0	0	0	78.0	13.8
TRUNC. VGY. & DRAIN.		10.5	15.0	6.1	14.5	5.1	37.5	2.5	2.0	2.0	70.0	22.8
VGY.& GASTY.	0.7	1.5	6.1	0	3.1	1.6	30.8	6.6	3.0	1.6	86.9	11.5
PARTIAL GASTY.	2.4	3.2	11.4	1.7	3.3	3.3	36.1	8.5	14.8	10.2	77.9	15.3

symptoms emerges with no discredit when the occurrence of really significant problems is taken into account, even including diarrhoea which is cited by many surgeons as a good reason for abandoning the use of this operation. After selective vagisection the final clinical result almost parallels that of vagotomy and antrectomy. It is interesting to note that there is very little difference between the two operations in the proportions of unsatisfactory results, even when the significantly higher incidence of recurrent ulceration in the former is taken into account. Routine two thirds partial gastrectomy emerged in this study with results which generally lay intermediate between those of the other operations.

Evidence showing that nutritional and metabolic sequelae such as bone disease and weight loss, as well as anaemia, constitute an insignificant problem after vagotomy and drainage compared to partial gastric resection. This may be used as an added argument in favour of the former operation.

The point to be made in the light of this discussion is that the vagotomy and drainage procedures must be preserved with, especially if the proportion of reoperations necessary can be significantly reduced by the eradication of recurrent duodenal or jejunal ulceration.

III VALUE OF THE HISTAMINE/PENTAGASTRIN STIMULATION TEST OF GASTRIC ACID SECRETION

(a) Preoperative testing:

The mean percentage reduction in histamine/pentagastrin stimulated gastric acid output after vagotomy and drainage, in the presence of a 35 to 40% incidence of incomplete vagotomy, is between 65 and 70%. Under these conditions it seems that patients with a preoperative M.A.O. of less than 25 mEq./Hour are protected against recurrent DU/JU by this operation, and that the postoperative M.A.O. one is aiming at should not exceed 5 or 6 mEq./Hour. It may even be suggested in passing that these patients could possibly do as well with simple gastroenterostomy without vagotomy.

With the same apparent proportion of positive Hollander tests, the vagotomy and antrectomy group had a mean reduction in the M.A.O. of over 90%. As no recurrent DU/JU have been encountered to date after this operation among those with a preoperative M.A.O. in excess of 25 mEq./Hour, it seems that antrectomy can "cover" an incomplete vagotomy.

The suggestion is therefore made that those duodenal ulcer patients coming to elective surgery who have an M.A.O. of greater than 25 mEq./Hour

have antrectomy added to the vagotomy. Vagotomy and drainage should be reserved for those patients who secrete less than 25 mEq./Hour on A.H.T.

Generally partial gastrectomy does not offer any particular advantages over either of the other procedures, and in view of the mortality figures this operation does not seem to fit into the scheme outlined above. The point must be made, however, that this must not be interpreted to mean that the operation is being condemned as being the "worst" procedure.

With these points in view it would appear that there is ample justification for continuing with the routine practice of preoperative augmented histamine/pentagastrin tests in patients selected for elective surgical treatment of duodenal ulceration.

(b) Postoperative testing:

Used in conjunction with the insulin test, and other methods of investigation of postoperative dyspepsia, this test undoubtedly has some diagnostic value. Various parameters have evolved for the diagnosis of recurrent duodenal or jejunal ulceration, based on previous and current experience with the test.

(i) A postoperative M.A.O. greater than 20 mEq./Hour is highly suggestive of recurrent ulceration,

while an M.A.O. of less than 3 mEq./Hour mitigates strongly against the diagnosis.

(ii) Persistent postoperative achlorhydria excludes a recurrence.

(iii) If the M.A.O. is reduced by less than 10% of the preoperative level it is virtually diagnostic of recurrent ulceration, while a reduction of less than 50% exposes the patient to the risk thereof.

IV GASTRIC ULCERATION AFTER VAGOTOMY

Even although a therapeutic policy such as the one outlined above could in all probability significantly influence the incidence of recurrent DU/JU, gastric ulceration is still likely to occur after vagotomy. This constitutes an interesting if rather vexing problem, and no definite conclusions can be reached about its causation. Sustained relative hypersecretion of acid by a gastric mucosa of poor quality and resistance, resulting from antral stasis possibly caused by an inadequate drainage stoma, provides an attractive though probably oversimplified explanation for gastric ulceration occurring in a susceptible individual. This may serve to explain the tendency for this complication to occur in patients with a low preoperative acid output and low reduction of these levels, especially basal, even in the

presence of a negative Hollander test. Whether or not a drainage procedure which is known to result in significantly faster gastric emptying, such as the Finney pyloroplasty, would significantly affect the issue is a matter for conjecture.

V INSULIN TEST

In this hospital it seems that approximately 35 to 40% of all vagotomies will be incomplete, as measured by the insulin test, using Hollander's criterion for interpretation of a positive result. This holds true whether the vagisection is selective or truncal. That a positive insulin test is an important accompaniment of recurrent duodenal/jejunal ulceration is well documented and has been confirmed by this study, although recurrences do occur with a negative test.

Considerable difficulty is encountered with interpretation of what constitutes a positive insulin test result in view of the arbitrary nature in which various criteria have, of necessity, been decided upon. Many patients with positive insulin tests by the time-honoured Hollander method of interpretation remain asymptomatic, even at 4 to 10 years post-vagotomy. It would therefore be desirable to determine which of these patients are particularly at risk

of developing recurrent ulceration. For this purpose it seems that the use of multiple criteria for interpretation of this test is of some value although it works in a rather empirical manner. Among patients who have a low M.A.O. on histamine/pentagastrin stimulation, the results suggest that the insulin test becomes unreliable as an index of incomplete vagotomy per se, especially when multiple criteria are used. Accordingly it is probably generally preferable to describe a patient as being "at risk" than to speak of "incomplete vagotomy". Used in this way the insulin test, in conjunction with pre- and postoperative M.A.O. levels, and hence the percentage reduction of acid output may be of value as a diagnostic tool in the investigation of postvagotomy dyspepsia.

VI SELECTIVE OR TRUNCAL VAGOTOMY?

When selective and truncal vagotomy with drainage were compared, the results in the former group tended to be marginally superior although few stastistically significant differences were demonstrable. This slight advantage of the selective operation seemed to revolve around a significantly lower incidence of gastric stasis problems, but this is difficult to explain.

These results therefore serve to confirm the original conclusions reached on discussion of the theoretical advantages of the selective operation based on experimental evidence (Chapter 2).

Selective vagotomy cannot be unequivocally recommended as a superior procedure, but the suggestion made is that the operation be performed whenever technically feasible.

Although the study is a retrospective one, and a complete follow up has not been obtained, the pattern of clinical results that has emerged is comparable to that reported by most authors in their various series. This includes those from the model prospective clinical trials reported by Goligher et al.[399-404] and Jordan and Condon[405]. The point may be made however, that the results of gastric acid secretory data are not really influenced by whether this is collected in a prospective or retrospective manner.

With these considerations in mind it is hoped that the information gained from this study is of some value for assessing the results of elective surgery for duodenal ulceration at Groote Schuur Hospital, and may also serve to guide future policy

with regard to the efficient planning of a well-controlled prospective study.

The conclusions reached from this study could almost certainly favourably influence the overall results of the currently available surgical techniques employed in this hospital in the treatment of the chronic duodenal ulcer which cannot be effectively managed on a conservative regime. However, too many apostles have erroneously believed that they have found the answer to the problem of recurrent ulceration and one must of necessity have some reservations.

The whole fascinating subject is, as ever, in a constant state of flux and even now another "new" operation in the form of super-selective vagotomy is gradually capturing the imagination of all surgeons and physicians interested in the disease. This procedure has yet to be fully evaluated, but it seems that the surgical pendulum has slowly swung back to the position it occupied on the conservative side of the scale, when surgeons originally began to interest themselves in the problem.

The mere fact that this constant argument rages only serves to illustrate that a universally acceptable solution is nowhere near being achieved. One cannot help being left with the thought therefore

that with better understanding of gastric secretory physiology, particularly with regard to hormonal factors and the mechanisms of their control, advances in drug therapy may gradually reduce the surgeon's role in the treatment of chronic duodenal ulceration.

SUMMARY

This study was done in order to assess the clinical results of elective surgery for duodenal ulceration at Groote Schuur Hospital, to measure the effects of the various operations on gastric acid secretion and especially to evaluate gastric acid secretion in the selection of surgical procedure.

Four hundred and thirty-seven patients submitted to surgery between 1960 and 1967 inclusive, were retrospectively followed up by means of a postal questionnaire, followed wherever possible by personal interview and physical examination. As many as possible of these patients were submitted to histamine/pentagastrin stimulation tests, and where relevant, to insulin tests.

The postoperative results assessed were those of vagotomy and drainage, whether by pyloroplasty or gastroenterostomy, vagotomy and antrectomy and routine (65 to 70%) partial gastrectomy. Analysis was done with regard to mortality, recurrent ulceration and dyspepsia, the incidence of symptoms attributable to alimentary dysfunction such as cardio-oesophageal reflux, alterations in bowel habit, gastric or afferent loop stasis, and the

dumping syndromes. Additional analysis was made of general nutritional status as reflected by weight changes, and of the overall clinical results by means of a modified Visick grading.

Augmented Histamine/Pentagastrin Test (A.H.T.) data was analyzed with regard to percentage reduction of the preoperative basal (B.A.O.) and maximal acid output (M.A.O.) values, and the particular patterns that emerge in patients with recurrent ulceration and dyspepsia. Special reference was made to the relationship of the magnitude of preoperative M.A.O. to recurrent ulceration.

Insulin test results were used to ascertain the incidence of incomplete vagotomy, and the results using pure Hollander and multiple criteria methods of interpretation of what constitutes a positive result were compared.

The vagotomy and drainage group was the largest (312 cases) and was further subdivided into selective and truncal vagotomy groups. Clinical and gastric acid secretion results in these respective subgroups were analyzed in identical terms to the above.

Primary postoperative mortality was appreciably lower for vagotomy and drainage, but the overall long term mortality was equal in the three groups.

This is attributable to the relatively high re-operative mortality among the vagotomy and drainage patients. Most of these reoperations were for recurrent duodenal (DU) or jejunal (JU) ulceration.

Except for recurrent ulceration where vagotomy and drainage, irrespective of the type of vagotomy, had the highest incidence, there was no significant overall advantage in any one procedure. The results indicate however that vagotomy and antrectomy may emerge with a marginal superiority. Similarly it would seem that selective vagotomy and drainage gives marginally better results than truncal vagotomy and drainage.

Vagotomy and antrectomy provides the greatest percentage reduction of both B.A.O. and M.A.O. Vagotomy and drainage is least efficient in this regard. It would appear that patients submitted to this operation with a preoperative M.A.O. of less than 25 mEq./Hour are protected from recurrent DU/JU, but not from gastric ulceration. That is, all recurrent DU/JU occurred among those with a pre-operative M.A.O. in excess of 25 mEq./Hour, but for gastric ulcer occurring after vagotomy and drain-age, there was no definite pattern. The difference in incidence of recurrent DU/JU among the "over 25"

and "under 25" groups occurred in the presence of an equal incidence of incomplete vagotomy on insulin testing (by Hollander interpretation).

No recurrent DU/JU were found among vagotomy and antrectomy patients with an M.A.O. of greater than 25 mEq./Hour.

It is therefore suggested that a policy of selection of surgical procedure, based on the pre-operative M.A.O., might greatly reduce the incidence of recurrent DU/JU. Patients with a preoperative M.A.O. of greater than 25 mEq./Hour could be adequately treated by vagotomy and antrectomy, it is suggested that vagotomy and drainage be reserved for those with an M.A.O. below this figure. The major reason for persisting with vagotomy and drainage is the low mortality associated with the procedure, which would be maintained if the incidence of recurrent DU/JU and hence the need for reoperation is greatly reduced. Partial gastrectomy is not favoured, mainly in view of the mortality figures, and does not seem to fit into the above scheme.

Interpretation of the insulin test is difficult but the results indicate that multiple criteria is of value as a method of interpretation for prognostic purposes, with regard to recurrent DU/JU while the

Hollander method probably more accurately reflects the actual completeness of vagotomy. The test is certainly of value in the investigation of the dyspeptic patient when considered in conjunction with the A.H.T. and other investigations. It would seem that in patients with a low M.A.O. on histamine/pentagastrin stimulation (less than 5 or 6 mEq./Hour) the insulin test results are not consistently reliable, especially when multiple criteria are used for interpretation.

In the introductory chapters gastric secretory physiology, gastric motility, the pathophysiology of vagotomy and the evolution of gastric surgery were discussed.

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