

a decision the medical practitioner should provide a statement covering the following points:

1. Name, age, address, and telephone number of invalid.....
2. Diagnosis of condition.....
3. Manifest symptoms.....
4. Severity of disability (mild, severe)*.....
5. Whether infectious or non-infectious.....
6. Where under treatment—if in a hospital or nursing-home.....
7. Nature of treatment.....
8. Whether treatment effectively controls symptoms.....
9. Whether treatment is necessary during the air journey.....
10. Whether an attendant is necessary.....
11. Whether patient can walk unaided.....
12. Whether patient can travel in sitting position.....
13. Any other points.....
14. In my opinion..... is fit to travel by air from..... to.....

Signature of doctor
 Address and Tel. No.

*Clinical findings referred to in a Table as possible limiting factors, including the systolic and diastolic blood pressures, should be recorded.

THE PHYSIOLOGICAL BASIS OF VAGOTOMY

BY

A. DAVIS BEATTIE, F.R.C.S., F.I.C.S.
Surgeon, Leicester General Hospital

The surgical treatment of peptic ulcer has recently become a matter of some controversy. The place held so long by subtotal gastrectomy in the treatment of all types of gastro-duodenal ulceration is now being challenged by vagotomy, and it is therefore of some importance that the physiological principles underlying the newer procedure should be generally appreciated.

Aetiology of Peptic Ulcer

There is little fundamental difference between the factors primarily responsible for gastro-duodenal ulceration and those producing similar lesions elsewhere. Trauma is probably the usual initiating factor; though toxæmia, localized vascular spasm, and even trophic neuritis may occasionally play a part in its onset. When an acute ulcer results from the action of one or more of these factors the natural reparative processes of the body attempt to produce healing, but their action is opposed both by the physiological peristaltic activity and by the digestive nature of the gastric secretion. Dragstedt (1942) has shown that these alone are not sufficient to delay physiological healing and to lead to chronic ulceration in a normal individual.

The stomach and duodenum are readily digested by pure gastric secretion, particularly if the latter has a high acid content, but they are rarely exposed to such action in a normal individual. The acid content of the stomach is relatively low unless provoked by the presence of food, which itself acts as a diluent, and it is still further lowered during digestion by the periodic regurgitation of duodenal contents. Moreover, all living tissues display a considerable resistance to digestion by the gastric juices owing to the

protection afforded by their mucous surface secretions. It is only when these protective mechanisms are overcome that a typical peptic ulcer develops in experimental animals.

Past Attempts at Physiological Surgery

Hyperacidity has long been recognized as the main factor responsible for the abnormal persistence of the ulcerative process and the consequent development of a chronic ulcer. From the introduction of gastro-enterostomy by Wolfier in 1881, successive attempts have been made to deal surgically with this problem along physiological lines. None of them has proved entirely successful, however; even the various modifications of subtotal gastrectomy, which have so far formed the most certain approach, being not without certain drawbacks and a proportion of failures.

The rationale of these operations is the resection of a sufficient area of the acid-secreting portion of the stomach to prevent subsequent hyperacidity, and, since this will obviously vary from individual to individual, their success depends on striking a correct balance in each case. To leave too much stomach will obviously defeat the whole object of the procedure, whilst the removal of too much may lead to possible anaemia and the development of "small stomach" symptoms afterwards. The latter are, in fact, responsible for the majority of poor results following modern techniques, as the tendency is towards over-removal of gastric mucosa in an attempt to prevent subsequent ulcer recurrence. Recent figures show that a surprisingly high percentage of patients who have had apparently successful gastric resections are unfitted for full economic life afterwards by the intermittent gastro-intestinal upsets which follow and the impossibility of returning to normal dietetic existence.

Gastrectomy has other disadvantages also. The operative mortality, though surprisingly low in expert hands, is necessarily higher in the older age groups—the very patients in whom the complications of ulcer have themselves such a high death rate. Moreover, it is a mutilating operation and, while a physiological proceeding so far as the ulcer problem is concerned, leaves an unphysiological and deformed upper digestive tract in its wake.

The Ulcer Diathesis

The relative failure of all past surgical attempts to deal really successfully with peptic ulcer has recently resulted in careful reconsideration of the problem of the ulcer diathesis and its underlying factors.

It has long been recognized that a true ulcer diathesis does exist. The typical ulcer patient belongs to Goldthwait's (1915) asthenic type. He is a thin, lanky, narrow-chested individual with a "lean and hungry look"—driving, ambitious, emotional, and tense. The psychic make-up accompanying these physical characteristics often determines the choice of occupation, with the result that certain professions and trades—such as engineering, law, and surgery—are particularly ulcer-prone. There are, however, quite a number of ulcer patients who do not fall into this main group. These individuals belong more to the sthenic type. They may exhibit a most deceptive external calm and seem to keep their nervous stress hidden well beneath the surface. It is interesting, as Moore (1946) points out, that this type of individual tends to suffer from ulcers which bleed rather than from typical ulcer pain.

To whichever group the ulcer patient belongs, however, he shows the same reaction towards his environment. Most intelligent patients can correlate definite exacerbations of their symptoms with such events as prolonged nervous stress, fatigue, overwork, or irregular meal hours. Sex also seems to play a contributory part in ulcer development.

The relative incidence in males is rising steadily in response to the greater stress of modern life, which normally affects men more than women. In a series of 9,000 necropsies performed on chronic ulcer cases up to 1923, Stewart (1923) found chronic ulcer to be twice as frequent in males, and approximately the same sex-incidence ratio was present in 4,000 necropsies disclosing acute ulcer; whereas the admission rate to E.M.S. hospitals of ulcer cases for operation in the period 1942-3 shows a 10:1 male preponderance in the 15-35 age group and a 4.6:1 ratio in patients over that age.

It appears that the ulcer diathesis is rather the result of nervous stress on a particular psychosomatic type than a mere accident of physical build. This is further supported by the evidence of Simnitzky (1926, 1927) and Fokin (1925), who showed the presence of parasympathetic hyperactivity in a high percentage of peptic ulcer cases.

Results of Recent Research

A considerable amount of recent research has therefore been directed to the investigation of the mechanism through which this vagotonia modifies normal gastric secretion.

A. Influence of the Vascular Supply

Little work appears to have been done on the relationship between vascular supply and gastric secretion, but it is reasonable to suppose, as Le Veen (1948) points out, that it is similar to that of other glandular structures which have been more carefully investigated, such as the salivary glands and the kidney.

It has been shown in fully denervated experimental preparations of these organs that their secretion is directly proportional to the volume of blood flow; and it is known from work on the voluntary muscles and heart that muscle contraction is similarly dependent on its vascular supply. Since gastric secretion is undoubtedly increased by hyperperistalsis, vasodilatation of the stomach vessels may therefore influence it by both these mechanisms.

B. Chemical Factors

It was first shown by Komarov (1945) that when extracts of the pyloric antrum and the first part of the duodenum are injected into the blood gastric secretion results. This secretion, which is identical with the juice of the chemical phase of gastric digestion, differs from that of the nervous phase by its high acid content and relative deficiency in pepsin. It is unaffected by atropine, and must therefore result from a purely chemical stimulus to the gastric glands. The extract responsible for this response does not contain histamine, and its causal component appears to be a polypeptide known as "gastrin." There seems little doubt that this is in fact the normal mechanism by which the chemical phase of gastric secretion is produced, and that the latter is the result of the action of the absorbed products of the early nervous phase of digestion on the glands of the pyloric antrum.

Contributory evidence of the purely chemical action of this mechanism and of its lack of dependence on any neurogenic stimulus is provided by the results of antrectomy. This operation, in which the mucosa of the pyloric antrum and first part of the duodenum is resected without any other surgical procedure, results in profound modification of the secondary phase of the gastric secretion; whereas complete gastric neurectomy affects the latter only relatively slightly.

C. Influence of the Nerve Supply

The detailed work of Swann (1834), Kollmann (1860), McCrea (1924), and Mitchell (1940) on the anatomy of the vagus nerves has not yet found its way into the standard textbooks on anatomy. They form an intricate plexus on the thoracic oesophagus from lung roots to diaphragm, and

re-form into their main abdominal trunks only at the latter level. They constitute the parasympathetic supply of the stomach, small intestine, and caecum, and give branches to the liver, spleen, and pancreas. As in the case of the sympathetic, they act on the bowel by modifying the tone of the two intestinal plexuses, which are primarily responsible for both movements and secretion.

The actual mechanism by which these plexuses operate is still imperfectly understood, but the work of Tyrrell-Gray (1936) provides the most plausible explanation. He suggests that the primary movement of the bowel is a small recurrent rhythmical wave of contraction initiated by the ganglionated cells of the plexuses. The presence of a food bolus simultaneously stimulates Auerbach's plexus, producing a deep peristaltic contraction behind it, and also Meissner's plexus, resulting in a preceding wave of relaxation. Recent work on the "peristaltic gradient" of the intestine supports this hypothesis.

Modern research has added considerably to the knowledge of the function of the gastric nerve supplies. It was first suggested by Carlson (1913) and confirmed by McCrea that gastric peristalsis is governed entirely by the vagus, acting through the local plexuses, and that the muscle "tonus," upon which the peristaltic movements are superimposed, is separately controlled by the sympathetic. McSwiney (1931) has shown that the sympathetic nerves carry both stimulator and inhibitor fibres, and McCrea's work indicates that the former are concerned with the maintenance of gastric tone and the latter with peristalsis. The sympathetic is therefore not a true antagonist of the vagus, as is so often taught. The sympathetic supply to the stomach, as elsewhere in the body, controls the vascular tone, and it also forms the pathway for sensory impulses. Moore *et al.* (1946) have shown that painful stimuli can be produced by the inflation of an intragastric balloon after complete abdominal vagotomy. Latarjet's work proved that the pain of gastric crises, unaffected by vagotomy, ceases after complete gastric sympathectomy (Latarjet, 1922; Latarjet and Wertheimer, 1923). Grimson *et al.* (1947) have demonstrated that the vagus does not carry sensory tracts, and Dragstedt (1947) has shown that recurrence of ulcer pain can be reproduced after complete vagotomy by the ingestion of sufficient quantities of strong hydrochloric acid. This work is in keeping with that of Bentley and Smithwick (1940), who showed that many of the afferent pathways from the duodenum, gall-bladder, and biliary tract are via the sympathetic supply of these organs.

It therefore seems probable that the sympathetic supply of the stomach and duodenum plays little part in the aetiology of peptic ulcer, apart from any secondary action such as that which may be produced by the local anaemia resulting from an abnormally high sympathetic tone. The vagal supply, on the other hand, is known to be directly concerned with gastric secretion, in addition to any indirect effect on this which it may produce through its action on peristalsis. The psychic secretion which precedes the ingestion of food is due to vagal stimulation of the gastric glands. The same reflex occurs within 10 to 15 minutes of "sham feeding," apart from any psychological stimulation, and is probably the result of a vagal reflex from deglutition and mastication. The gastric secretion which results from this psychic or neurogenic stimulation is rich in both pepsin and hydrochloric acid, and persists for some time independently of the succeeding chemical phase.

Cushing (1932) showed the existence of a nerve pathway between the cerebral cortex and the upper gastro-intestinal region. From combined clinical and pathological evidence he showed that a definite nerve tract connected the vagal

centres with the cortex, and that irritative lesions along this tract resulted in ulceration of the stomach and duodenum. He demonstrated, further, that this was due to hyperactivity of the vagal centres and that the same result was produced by the action of psychic stimuli on the area of cerebral cortex at which this tract began. His important work, the full implications of which have only recently been realized, confirmed the investigations of previous workers on experimental dogs. Stahnke (1924) had already produced typical peptic ulcers in these animals as the result of the increased neurogenic gastric secretion following vagal stimulation. Hartzell (1929) had shown that complete vagal section resulted in permanent reduction of the gastric acidity, though this effect was only transient if section was incomplete; and Beaver and Mann (1931) had completed this chain of evidence by demonstrating that the only dogs to escape peptic ulceration after a Mann-Williamson (1923) physiological gastro-enterostomy were those in which complete vagotomy had also been performed.

The neurogenic secretion of gastric juice is not entirely limited to psychic stimulation, although Pavlov's (1910) original views to this effect are still regrettably present in many textbooks. Carlson (1923) showed, after intensive animal and clinical experiment, that there is normally a small continuous secretion of gastric juice even in prolonged fasting, and that this secretion is of the same type as that of the psychic phase of normal digestion though less in degree. Dragstedt and Schafer (1945) showed that this secretion was present to an excessive extent in the typical ulcer patient even during sleep, and that it was accentuated in emotional states and nervous stress. Wolf and Wolff (1942), studying a man with a permanent gastric fistula and complete traumatic oesophageal occlusion, have shown that the excessive acid secretion resulting from emotional conflict produces typical ulcer symptoms associated with definite changes in the gastric mucosa. When such physiological stimuli were prolonged the consequent hyperchlorhydria resulted in intense mucosal hyperaemia, with the development of small petechial haemorrhages, and the affected mucosa showed an increased tendency to macroscopic erosions through quite trivial trauma. If these erosions were then exposed to free hydrochloric acid small acute peptic ulcers rapidly developed.

The Development of Vagotomy

An analysis of all this evidence suggested that the most rational physiological approach to the problem was to be found in vagotomy, and a number of attempts had been made along these lines before Dragstedt and Owens's first reported successes. Most of these had been made through an abdominal approach and were reviewed by Hartzell (1929). The first transthoracic approach was made by Pieri and Tanferna (1930), but their cases were not uniformly successful, and it was left to Dragstedt and Owens (1943) to elaborate a suitable technique. A year later Dragstedt (personal communication) was also the first to evolve the modern abdominal approach, which he afterwards described in detail. Since then a voluminous literature from many sources has grown up on the technique and after-results of vagotomy, and a great deal of detailed research has been made into the physiological end-results of this operation. Nearly 1,500 successful cases have now been reported from the U.S.A., Scandinavia, and Britain alone, so that the operation can no longer be considered an experimental method of treatment.

The majority of surgeons employing vagotomy confine its use to the treatment of uncomplicated duodenal ulcer in the younger age groups, and of recurrent ulceration

following more radical procedures. But there is a strong case for carrying it out as a routine, as a concurrent procedure, whenever gastrectomy or gastro-enterostomy is performed for peptic ulceration; and I believe that it may also have a place as the sole treatment of some types of gastric ulcer. There is a justifiable tendency to avoid vagotomy in gastric ulcer through fear of later malignant change or of missing early carcinomata. But this does not apply in the same degree to small subacute lesions of the lesser curvature which fail to respond rapidly to energetic medical treatment, or to the high cardiac ulcers which are otherwise so difficult to deal with surgically. My own series of more than 160 vagotomies includes a number of successful operations in this type of case.

Apart from the effects on the stomach and duodenum, which are described below, division of the vagus nerves appears to produce few physiological sequelae in the other abdominal viscera. It has been shown by several investigators, including Ivy (1934), that vagotomy is followed by a slightly decreased secretion of bile and pancreatic juice; Pfeiffer *et al.* (1940) have described a temporary post-operative drop in blood calcium similar to that found to occur in experimental dogs; and the occasional occurrence of the "dumping syndrome" after operation suggests that there may also be some temporary alteration in the amount of insulin secreted. But all these are minor effects, and the absence of any more definite sequelae is in accordance with the clinical results following high subtotal gastrectomy and lower oesophagectomy, in which a concurrent complete abdominal vagotomy is almost always unwittingly carried out.

Clinical Results of Vagotomy

The most dramatic effect of vagotomy is the immediate relief of all pain and other ulcer symptoms, together with a rapid increase in weight. The psychological reaction of the patients after operation is highly satisfactory, and the majority of them are enabled to return to full economic life within six weeks.

There has been no proved case of ulcer recurrence following a complete neurectomy, as checked by insulin test meal. This test, first described by Hollander (1944), depends on the fact that the hunger pains consequent on hypoglycaemia are associated with excessive gastric secretion. This was originally demonstrated by Roholm (1930); and Okada *et al.* (1929) and La Barre and de Cespédès (1931) showed that the hypersecretion is dependent on the integrity of the vagal pathway. The acid response of the stomach is very great where this pathway is normal, but it is abolished after complete vagotomy. As might be expected, another effect of vagotomy is to lower both the total volume and the acidity of the gastric secretion. Thornton *et al.* (1946) and Grimson *et al.* (1946) have both drawn attention to these changes in the night fasting juice, which are similar to those previously described by Hartzell in the fractional test meal. I have shown that the free hydrochloric acid secreted during a fractional meal test is reduced to one-third of the pre-operative quantity, but that the general character of the curve remains otherwise unaltered (Beattie, 1948). This drop in acidity is undoubtedly the main factor responsible for the disappearance of the previous ulcer diathesis after vagotomy.

As the result of the immediate paralysis of the stomach and small intestine, which only gradually recover their tone and power of movement, certain unpleasant retention symptoms occur. Almost complete gastric paralysis persists for two to three days and peristalsis then gradually returns, though it probably never reaches the same frequency and amplitude as previously. Moore *et al.* (1946) and Grimson *et al.* (1947) have investigated this subject

by means of repeated radiological examinations and pressure-recording intra-intestinal balloons. The latter workers have shown that there also is a gradual increase in muscle tone, which may reach two or three times its pre-operative strength within three years. Despite this, however, some degree of gastric dilatation often occurs—the probable result of pylorospasm from the unopposed action of the sympathetic nerve supply at the pylorus. This has been checked radiologically by Moore *et al.* (1946) and by Lawson (personal communication), and it has been shown by Grimson *et al.* (1947) that similar minor alterations in muscle tone and movement also occur in the duodenum and jejunum.

In addition to the immediate gastric paralysis there is nearly always some degree of temporary dysphagia following operation. This is the result of cardiospasm secondary to the trauma inflicted on the lower oesophagus and to interference with its nerve supply. It always passes off spontaneously within a few weeks, but while it exists it increases the tendency to gastric distension already present by the aerophagy which it encourages.

These retention phenomena, which present themselves clinically as occasional attacks of flatulence associated with eructation of foul gas towards evening or in the early hours of the morning, may be accompanied by mild regurgitant vomiting and followed by transient diarrhoea. In the majority of cases they are relatively mild and are regarded by the patient as of only minor importance, but they may be more severe and last for many months. They tend to subside eventually as the stomach recovers its tone and peristalsis, but may be so persistent that further operation becomes necessary. Dragstedt (personal communication) has pointed out that even in the milder cases there is a tendency for similar attacks of the same character to occur throughout the subsequent lifetime of these individuals. Such attacks occur during the same emotional crisis and nervous stress as would previously have produced ulcer exacerbations, and are probably due to the unopposed action of the sympathetic system in the new gastro-intestinal response to the nervous impulses consequent on psychic stimuli.

Recent work on certain choline derivatives has produced drugs which have a relatively selective action on the gastro-intestinal part of the parasympathetic system, and I have found the administration of these to be of value in reducing the severity of the retention symptoms in some cases. Unfortunately they do not yet appear to be equally effective in all instances, though it seems probable that further research in this direction may eventually prove more successful.

Conclusion

There seems little doubt that the final solution to the ulcer problem lies along medical lines. It should not be beyond the limits of future possibility for suitable drugs to be developed to control the vagotonia which is the underlying cause of the ulcer diathesis.

Till then, however, the failure of medical treatment in a certain proportion of cases will continue to result in chronic ulceration, which can be dealt with successfully only by surgical means. There is little doubt that vagotomy will ultimately come to be accepted as the routine surgical treatment for chronic duodenal ulcer and for the complications of anastomotic and jejunal ulcer after gastrectomy or gastro-enterostomy. It may even find a place in the treatment of some varieties of chronic gastric ulcer. It has a much lower operative mortality and post-operative recurrence rate than the more radical procedure of gastrectomy, and gives a higher proportion of full economic successes. But it is still relatively in its infancy, despite the

six-year post-operative records of the earlier cases that are now available; and it requires further technical development to eliminate its occasionally severe retention sequelae before it can be regarded with complete confidence.

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NOTES ON EXPERIMENTS ILLUSTRATING NORMAL TEMPERATURE REGULATION IN YOUNG MEN

BY

SAMSON WRIGHT, M.D., F.R.C.P.

John Astor Professor of Physiology, Department of Physiology,
Middlesex Hospital Medical School

It has been the custom for some years in the department of physiology for our students to carry out a series of experiments which illustrate some of the more important facts about body temperature and its regulation in man. The experiments are conveniently performed during the vacation in the student's own home, as they require no special apparatus but do need a good deal of time and access to a bathroom. In this paper brief particulars are given of these experiments for the benefit of teachers who might care to use them. Some illustrative results are also shown graphically; most readers may find these graphs more instructive than a statistical analysis of the results. All the observations on which this report is based were carried out on healthy young men during the summer vacation; the readings are given in °F. I am greatly indebted to the students whose results I have used.

Temperature in the Mouth, Groin, and Axilla

The subject, using a so-called "half-minute" thermometer, is instructed to read the temperature at half-minute