reduced to a figure as low as, or lower than, the best after gastrectomy.

We at one time thought that the incidence of changed bowel habit after vagal-nerve section might weigh in favour of gastrectomy. However, a study of these symptoms after gastrectomy reveals exactly the same problem, although to a somewhat less degree.

In trying to assess the place of vagotomy and gastro-enterostomy, we do not believe that it is indicated only in certain types of patient, as, for example, in women and elderly men. If it is to be used at all, then in our view it should be used in all cases where surgery is necessary. In the present state of our knowledge, based on this eight-year study, we believe that, given complete nerve-trunk section, vagotomy and gastro-enterostomy is the operation of choice. At one time we thought that a surgeon experienced in this operation could in every case achieve complete nerve-trunk section without the use of a test. Since such a test has been available we have satisfied ourselves that this is not true and that even an experienced surgeon will obtain better results with this help.

It will be interesting, in the future, to study the late results of this operation in cases in which complete nerve-trunk section has been proved at operation.

Summary

301 cases, of which only 6 are untraced, of duodenal ulceration treated by vagotomy and gastro-enterostomy are reported. All patients have been followed up for at least seven years. The proved recurrence rate was 4.25%, and this in spite of evidence of a high rate of incomplete nerve section. There has been no proved recurrence in this series since an earlier review in 1955.

The results of this operation are compared with those of gastrectomy, and it is concluded that vagotomy and gastro-enterostomy is a better operation so long as there is no great increase in the recurrence rate as shown by a long-term study. From the point of view of nutritional state, anaemia, maintenance of weight and ability for heavy work, vagotomy and gastro-enterostomy is more satisfactory than gastrectomy. The only less favourable symptom after this operation is some looseness of the bowels, which takes on the picture of occasional loose motions. This same symptom, with the same pattern though in somewhat milder form, is found to occur also after gastrectomy. No patient in this series seems to have sought advice for this symptom.

This high incidence of incomplete nerve section in the past is good evidence that this operation is better undertaken with the help of a test for complete nerve trunk section which can be used *during* operation. Such a test is now available (Burge and Vane, 1958).

It is concluded that vagotomy and gastro-enterostomy is the operation of choice in either sex and at any age when surgery is indicated for chronic duodenal ulceration.

This investigation has been made possible by the financial help of the Dan Mason Research Foundation of the West London Hospital Medical School. We thank all those surgeons who so kindly gave permission for us to follow their cases through all these years. We would thank the Ministry of Pensions and National Insurance for permission to study the war pensions cases. We are especially indebted to Mr. I. F. McNeill for the time and work he so kindly gave to these investigations.

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METHOD OF TESTING FOR COMPLETE NERVE SECTION DURING VAGOTOMY

BY

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The method described here was devised to allow the surgeon to test the completeness of vagotomy before the abdomen was closed. It consists in the application of a simple physiological technique to the human and, as such, was first validated on cats. It has now been applied successfully to patients, and is both safe and reliable.

Method

Cats.—Cats were anaesthetized with chloralose (80 mg./kg.). The blood pressure was recorded on a kymograph with a mercury manometer connected to a cannula in the left carotid artery. The intragastric pressure was also recorded on the kymograph, using a water manometer connected through the system, as shown in Fig. 1, to a tube

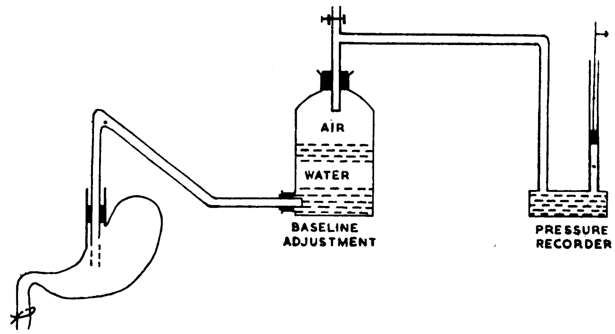

FIG. 1.—Diagram of recording technique. With the screw clip on the top inlet of the bottle open, the stomach can be filled with a known amount of water. The clip is then closed and the bottle moved up or down to bring the baseline on the pressure recorder to a convenient level.

passed down the oesophagus into the stomach. The oesophagus was sealed by an inflated cuff on the gastric tube and the pylorus was occluded by ligation. The stomach was distended with warm water. Platinum electrodes were used to stimulate the vagus nerves, either in the neck or on the oesophagus above or below the diaphragm with the chest open. Square wave pulses (0.5–25/second frequency, 0–50 volts, and 0.5–5 milliseconds' duration) were applied through the electrodes for periods of from 0.5–2 minutes. In some animals electrodes were made to encircle the oesophagus to correspond with the technique to be applied in man.

Man.—The patient was anaesthetized with thiopentone and nitrous oxide. Gallamine triethiodide was used to achieve muscular relaxation. Because the method depends upon recording the effects of vagal-nerve stimulation upon stomach motility, premedication with atropine or atropine-like drugs was avoided. Atropine was given during the operation after the test was finished. The abdomen was opened by a left upper paramedian incision; the left coronary ligament of the liver was divided to allow the left hepatic lobe to be retracted to the right. A small rubber tube was placed around the lower oesophagus for traction. There has been no difficulty in ensuring that the posterior vagus nerves were included within this tube. The upper part of the small omentum was divided between ligatures to give a better exposure of the lower oesophagus. A large-bore cuffed rubber tube was passed by the mouth until its

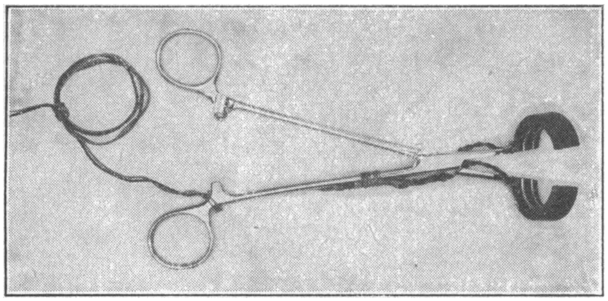

FIG. 2.—Electrodes.

tip was in the stomach. The electrodes designed for this operation (Fig. 2) were applied and the cuff on the tube was inflated. In this way the oesophagus was sealed and the vagus nerves were brought into contact with the electrodes. The pyloric antrum was occluded with a light intestinal clamp and the stomach filled with 0.5–1.5 litres of warm water, depending on its size. In early cases the recording apparatus was similar to that shown in Fig. 1, using a 2-litre aspirator for the baseline adjustment and filling-bottle. In the later cases an ink-writing bellows pressure recorder was used (Fig. 3).

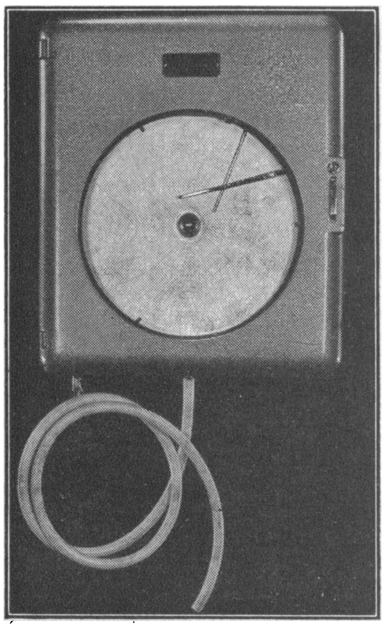

FIG. 3.—Ink-writing pressure recorder.

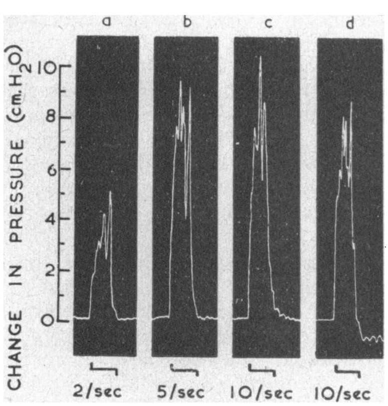

FIG. 4.—Kymograph tracing of gastric pressure responses to vagal-nerve stimulation in the cat. The stomach was distended with 50 ml. of saline. The vagus nerves were stimulated with platinum electrodes in the neck with 2 ms. shocks at 10 volts. (*a*) Both vagi stimulated at 2/sec for 1 minute. (*b*) Both vagi stimulated at 5/sec. for 1 minute. (*c*) Both vagi stimulated at 10/sec. for 1 minute. (*d*) Left vagus stimulated at 10/sec. for 1 minute.

Results in Cats

Stimulation of the vagus nerves is well known to cause a generalized contraction of the stomach, leading to a rise in intragastric pressure. The strength of the contraction depends on several factors, such as the frequency and voltage of stimulation and the initial distension of the stomach. Previous work (Paton and Vane, 1956) had defined some of the conditions necessary for obtaining maximal contractions of the isolated guinea-pig stomach in response to vagal stimulation; the response of the cat stomach *in situ* was found to vary in a similar way.

To obtain a maximal contraction in the cat it was found that stimuli of 2 ms. duration and up to 20 volts in strength were sufficient. The optimal frequency of stimulation was between 2 and 5/seconds in most animals (Fig. 4). Stimulation of one vagus nerve in the neck for one to two minutes produced an increase of pressure which was equal to, or nearly equal to, the maximal response elicited by stimulation of both vagus nerves.

The vagus system was dissected on the lower oesophagus with the chest opened and four to six nerve trunks were found. When all but one was divided and the vagus nerve stimulated in the neck, an increase in gastric pressure could still be recorded. In one cat, with the chest opened and the diaphragm divided, the circular electrodes were used to stimulate the vagus nerves just above the stomach. In this cat there were only two nerve trunks at this level. It was found that section of one of these two trunks failed to modify the response to stimulation. The remaining anterior trunk was then partially divided so that about one-half remained intact. On stimulation, a good response was obtained. What remained of the trunk was again halved, leaving now only a fraction of the whole nerve intact. In spite of this division, changes in gastric pressure were clearly recorded on stimulation. It this way we were able to conclude that the test was sensitive enough to record even small undivided nerve trunks.

Results in Man

It was not possible to study the parameters of stimulation in man to the same extent as in the cat, but in the first two cases various frequencies of stimulation were used. In each instance a frequency of 10/second gave a maximal contraction. Lower frequencies gave smaller contractions, whereas frequencies higher than 10/second had no greater effect. This frequency was therefore chosen for subsequent operations. The voltage of stimulation was also varied in the first two patients, and it was found that between 10 and 20 volts was sufficient to induce a maximal response in a one- to two-minute period of stimulation. It must be remembered, however, that the voltage needed depends not only upon the design of the electrode but also upon the amount of connective tissue covering the vagus nerves. It is therefore better to use a voltage of stimulation which is likely to be supramaximal, and in subsequent cases the voltage was set at between 40 and 50 volts.

The amount of fluid in the stomach is also important, for the magnitude of contraction depends upon the initial volume. In the first patient the vagus nerves were stimulated at the same frequency (10/second) with 0.5, 1, and 1.5 litres of water in the stomach. At 0.5 litre no contraction was obtained, but at both 1 and 1.5 litres the pressure increase was about 10 cm. of water. In subsequent patients the amount of filling was adjusted to give a basal pressure on the recorder of about 3 cm. of water This was usually achieved with 0.5–1 litre in the stomach.

After recording the change in gastric pressure in response to stimulation with all nerves intact, the electrodes were removed and one nerve trunk was cut. About 2 in. (5 cm.) of the nerve was removed and a ligature tied to the peripheral end so that it could be kept away from the electrode. The test was repeated after section of each nerve trunk until stimulation no longer produced a contraction, indicating that all the nerves had been found and sectioned. The surgeon found it more convenient if the stomach was emptied after each stimulation. The operative area was also more available to the surgeon if the stomach tube was withdrawn from the lower oesophagus.

In one patient, after a control stimulation, all the nerves that could be found were cut. The electrodes were then replaced and the area was stimulated to ensure that no nerve remained in continuity. It is this procedure that is to be used routinely.

Fig. 5 shows a tracing obtained from one of the patients. Between each part of the tracing a nerve trunk (later proved by histological examination) was removed. It can be seen that the contraction remained quite large until the third and fourth trunks were sectioned. In all patients frequent blood-pressure readings and E.C.G. records were taken.

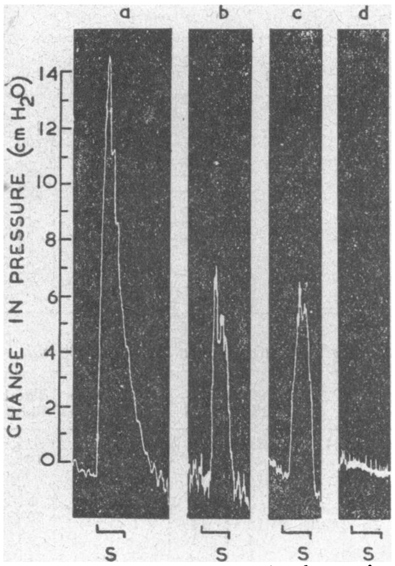

FIG. 5.—Kymograph record of gastric pressure responses to vagal-nerve stimulation in man. The stomach was distended with 0.7 litre of water. The vagus nerves were stimulated on the oesophagus below the diaphragm with 2 ms. shocks at 10/second and at 45 volts for 1½-minute periods. (*a*) Before nerve section. (*b*) After section of first major nerve trunk. (*c*) After section of second major nerve trunk. (*d*) After section of third and fourth major nerve trunks.

Stimulation of the vagus nerves had no effect on blood pressure, heart rate, or form of the E.C.G. In one patient stimulation of the vagus induced diaphragmatic movements, presumably by current spread. This movement was readily abolished by a further injection of gallamine triethiodide.

It is usual to record fluctuations in gastric pressure with each respiratory phase. To avoid these fluctuations, respiration was completely abolished during stimulation in the later cases.

After the test had demonstrated complete nerve-trunk section the operation was completed by making a posterior vertical isoperistaltic gastro-enterostomy. In the present work we have used this method of gastric drainage rather than pyloroplasty.

Recently an improved electrode has been developed which allows localization of the nerve trunks. Each semicircular band of silver was divided into two segments. In this way four pairs of electrodes were formed, and each was wired separately. Using a rotary switch, the stimulus was applied to the four quadrants in turn.

In this way the nerve trunks were localized to their quadrants before nerve section was attempted. Similarly, any small nerve trunk not found at the time of nerve section was not only demonstrated but also localized to its quadrant. The search for any such small nerve was made easier and more satisfactory in this way.

Discussion

Chamberlin and Winship (1947), Dragstedt *et al.* (1947a), and Jackson (1949) have all described the anatomy of the vagal-nerve trunks in the region of the lower oesophagus. From these papers it would seem that, at the site of subdiaphragmatic vagotomy, only two nerve trunks were present in approximately 80% of 160 cadavers. From the results of our study, using the test here described, 14 of 16 cases had three or more nerve trunks capable, on stimulation, of causing gastric contraction (see Table). The significance of this difference in distribution is uncertain, but may be related to the fact that the small group we have studied were all patients with peptic ulceration. It now seems likely that the majority of cases presented for vagotomy have, at the subdiaphragmatic level, more than two motor nerve trunks to the stomach, and it is

D

Number of Nerve Trunks Capable of Causing Gastric Contraction

Case No.	No. of Nerve Trunks		
	Anterior	Posterior	Total
1	1	2	3
2	2	1	3
3	3	2	5
4	2	2	4
5	1	2	3
6	1	1	2
7	1	2	3
8	1	2	3
9	1	1	2
10	2	3	5
11	4	3	7
12	1	2	3
13	2	2	4
14	2	1	3
15	2	2	4
16	2	3	5

therefore possible that in the past any vagotomy in which only two trunks were removed was incomplete.

Dragstedt *et al.* (1947b) stated that recurrence or persistence of ulcer symptoms may occur if even a small vagus fibre to the stomach had been overlooked. They stated: "In man, apparently, the persistence of a small vagus fibre after section of two of the large vagal trunks permits the excessive night secretion characteristic of the ulcer patient. The remaining vagus fibre appears to be able to activate the whole glandular apparatus." They also stated that "where the vagotomy has been complete, there is, to date, no evidence of regeneration of the fibres in the vagus nerves." A possible explanation of Dragstedt's results is provided by the recent work of Murray and Thompson (1957a), who studied the results of incomplete nerve section in the autonomic nervous system. They showed that, if 90% of the total pre- or post-ganglionic sympathetic supply to an organ is cut, the remaining intact nerve fibres sprout and grow in such a way that complete recovery of function may take place within six weeks. With only 1% of the nerve fibres left in continuity, substantial recovery took place over several months. They have shown, too (Murray and Thompson, 1956b), that the vagus nerve can sprout.

It seems possible, therefore, that after incomplete vagotomy the remaining intact nerve fibres may sprout and within a few months the functional nerve supply to the stomach will have returned to a high level. This concept is supported by the incidence of positive insulin test meals in vagotomized patients. Lloyd Davies (1956) found that a marked response to hypoglycaemia with very high levels of free acid was found in 29% of 87 cases of vagotomy tested by the insulin test meal.

That the method described here is sensitive is shown by the smallness of the nerve trunks that it will detect. Fig. 6 shows a comparison of the normal nerve trunk with

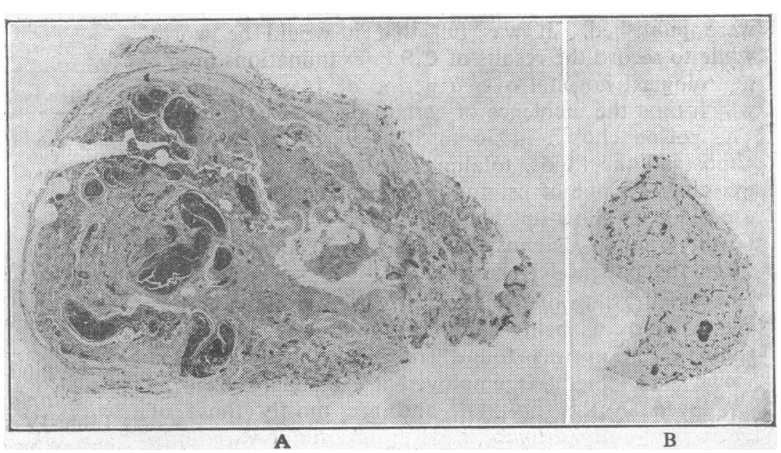

FIG. 6.—A: Section of a main posterior nerve trunk. B: Section of small nerve trunk (two bundles) which gave rise, on stimulation, to an increase of 1 cm. of water pressure. (Magnification in both instances ×21.)

a smaller trunk in transverse section which was found to be responsible for a rise of 1 cm. of water in gastric pressure on stimulation. If the motor and sensory nerves are randomly distributed in both these trunks then it appears that the method as at present used can detect a nerve trunk of about 1/50 the size of an average posterior vagus nerve.

Summary

A method is described which will detect the presence of even small vagal nerve trunks at the time of operation for vagotomy. If this method is used complete nerve-trunk section can be obtained.

We thank Professor Sir Lindor Brown for his advice; Dr. E. L. Harries for his help in the early stages of this work; Mr. H. Tennant and Mr. D. Green for their technical help; Spicers Ltd. for making the electrodes; Negretti and Zambra for making the pressure recorder; and Wm. Warne & Co. for making the gastric tube. We also thank the theatre sister and her staff of the West London Hospital for all their kind help in this work. This investigation has been made possible by the financial help of the Dan Mason Research Foundation of the West London Hospital Medical School.

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CEREBROSPINAL FLUID IN VARIOUS DISEASES

BY

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Greenfield and Carmichael in 1925 wrote a monograph on the cerebrospinal fluid (C.S.F.) which since that time has been one of the standard books of reference on this subject. The second part of that book was devoted to the results they found in various diseases seen during a period of five to six years. During the past 30 years innumerable papers and books have been written in which small series of results or even individual records were published. It was felt that it would be worth while to record the results of C.S.F. examinations in one neurological hospital over a period of 14 years, during which time the incidence of certain diseases has altered. The period chosen—1936 to 1949—was one in which almost all the fluids, totalling just under 12,000, were examined by one of us, and it also enabled us to obtain a period of follow-up should the need arise for revision of the original diagnosis, which had been determined when the patient left hospital.

A small group of diseases have been chosen for this special study as being common conditions, or because some variation was found from previously accepted views. The methods employed are standard ones as employed in this hospital, and are mostly those of Greenfield and Carmichael, with only minor variations.

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Results

Cerebral Tumour.—The results of the cell counts are given in Table I, and the protein levels are found in Table II. A

TABLE I.—*Cells in Cerebral Tumour per c.mm.*

Tumour	0–4	5–9	10–19	20–29	30–39	40–50	Over 50	Total Fluids
Cerebral glioma ..	299	10	7	4	5	4	6	335
Meningioma	136	4	—	—	—	—	1	141
Neurofibroma VIII ..	55	1	—	—	—	—	—	56
,, V ..	7	—	—	—	—	—	—	7
Brain-stem tumour ..	30	2	1	1	—	1	—	35
Cerebellar ,, ..	60	1	1	—	—	—	1	63
Intraventricular tumour	10	1	1	—	—	—	1	13
Choroid plexus ,, ..	10	—	—	—	—	1	—	11
Angioma	31	—	—	1	—	—	1	33
Pituitary tumour ..	61	7	1	—	—	—	—	69
Suprapituitary tumour	22	3	—	—	—	—	1	26
Secondary carcinoma ..	45	1	—	—	—	—	—	46

TABLE II.—*Protein in Cerebral Tumour in mg. per 100 ml.*

Tumour	0–40	45–95	100–295	300–495	500–1,000	Over 1,000	Total Fluids
Cerebral glioma ..	112	131	83	4	4	1	335
Meningioma	29	65	45	2	—	—	141
Neurofibroma VIII ..	—	11	27	12	5	1	56
,, V ..	—	1	5	1	—	—	7
Brain-stem tumour ..	12	14	9	—	—	—	35
Cerebellar ,, ..	26	20	15	1	1	—	63
Intraventricular tumour	7	1	4	1	—	—	13
Choroid plexus ,, ..	5	5	1	—	—	—	11
Angioma	13	9	10	1	—	—	33
Pituitary tumour ..	16	35	17	—	—	1	69
Suprapituitary tumour	8	13	5	—	—	—	26
Secondary carcinoma ..	14	21	8	2	—	1	46

total of 835 cases were examined, and all the results represent the findings at the first lumbar fluid examination. Greenfield and Carmichael record results in only 54 cases in their five-year period, so it will be seen that the incidence of such cases now treated in hospital has risen steeply. The features especially worthy of note are that, of the 835 cases, 766 (91.7%) showed no increase in cell count, and that any increase in cell count occurred chiefly in the glioma series. There were in all 69 cases showing a cell increase, and 36 of these (52.2%) were in cases of cerebral glioma, or 10.7% of all glioma cases. However, in only 242 cases (28.9%) was there a normal protein content. The cerebral glioma group showed a raised protein content in 66.5%, while in secondary carcinoma the figure was 69.6%, and in acoustic neurofibroma it was as high as 100%. The other tests employed did not show any features worthy of note.

It should be mentioned that care is needed if lumbar puncture is resorted to in cerebral tumour cases, and it should be performed only in selected patients and where neurosurgery is available.

Epilepsy.—The results are shown in Table III. As can be seen, in only 11 cases was the cell count raised, whereas the

TABLE III.—*Cells and Protein in Epilepsy*

Cells/c.mm.	No. of Fluids	Protein (mg./100 ml.)	No. of Fluids
0–4	893	0–40	559
5–9	7	45–70	290
10–19	3	75–100	53
20–30	1	105–150	2

protein was 70 mg./100 ml. or below in 93.9%. It was somewhat surprising to find that two cases had a protein above 100 mg./100 ml., and also that 25 cases showed a figure above 80 mg./100 ml.; but the records were carefully searched, and in no case had any of these patients returned to hospital for further investigation.

Multiple Sclerosis.—Some 690 cases were investigated, and Table IV shows the findings obtained. The cell count was normal in 589 cases (85.4%) and in only three patients was there a count above 50/c.mm. However, in six patients one or two polymorphs were present in the fluid, which is usually