Progress report

Highly selective vagotomy

Highly selective vagotomy (HSV) is the first operation for peptic ulcer which both avoids gastric resection and keeps the antral 'mill' and pyloric sphincter intact¹. All the standard operations destroy, or at least severely impair, the functions of the antrum and pylorus. Truncal vagotomy with a drainage procedure (TV+D), once regarded as a conservative operation, has been shown to render the stomach 'incontinent' of liquids²⁻⁵, and to produce clinical results which are somewhat inferior to those of vagotomy combined with antrectomy^{6,7}. 'Parietal cell vagotomy' (PCV)⁸, which was introduced in Denmark at the same time as HSV was introduced in Britain, has the same rationale as HSV, but differs from HSV in that the precise extent of the antrum is 'mapped' at the time of operation. Highly selective vagotomy is a more empirical, but quicker, procedure, which involves the identification and preservation of the main vagal nerves to the antrum, the nerves of Latarjet. A forerunner of both these operations was selective proximal vagotomy (SPV), which also leaves the antrum innervated, but which is invariably accompanied by a pyloroplasty or by a limited form of antrectomy⁹. 'Proximal gastric vagotomy' has been proposed as a compromise term, but may not be necessary in my opinion, because it will become apparent before long whether either a pyloroplasty or antral mapping is required. Even if it is shown, however, that the addition of a pyloroplasty is not necessary, the use of SPV as the standard term would be a suitable tribute to the pioneering work of Holle and Hart in Munich⁹.

What matters to the patient, however, is not the name of the operation, but whether the hypotheses upon which it is based^{1,9-11} are correct. These are that the innervated antrum will expel the gastric contents efficiently through an intact pylorus but will not release excessive amounts of gastrin, that side effects such as dumping and diarrhoea will be reduced compared with the incidences which are found after conventional operations, and that recurrent ulceration will be no more frequent than after complete gastric vagotomy with a drainage procedure. It follows from this that any assessment of HSV at present must be incomplete, both because the maximum period of follow up in Leeds and Copenhagen is only five years and because the results of prospective random trials will not be known for many years. However, many of the salient questions have already been answered.

The first concerns operative mortality. There has been no operative mortality among 350 patients who have been treated electively for duodenal ulcer by HSV in Leeds and Copenhagen. When these numbers are added to the other series in the literature¹²⁻²¹, a total of over one thousand HSV operations has been reported without an operative death. There has been an isolated case report²², however, of an operative death after HSV, and the author has had one death among 45 patients who were treated by HSV for gastric ulcer. Clearly, HSV is an extremely safe operation, the safety being due, no doubt, to the absence both of a suture line and of an artificial 'loop' such as is

created in the performance of gastroenterostomy or of Polya partial gastrectomy. Postoperative recovery after HSV is usually smooth, ileus being very rare, and in Leeds we dispense both with the intravenous drip and with nasogastric suction from the end of the anaesthetic.

Do these undrained stomachs empty satisfactorily? The answer is an unequivocal 'yes'. Prolonged gastric stasis in the immediate postoperative period has not been reported. In Leeds, approximately 2% of patients have been troubled by vomiting of food within six weeks of operation, but in each of them this difficulty has resolved with time. Only 1% of patients in Leeds and Copenhagen have eventually required the addition of a drainage procedure for the relief of persistent gastric stasis²³. This incidence is no higher than that which is found after vagotomy with a drainage procedure. These favourable clinical findings in Leeds and Copenhagen have now been confirmed by many other workers¹²⁻²¹. In the laboratory, many hundreds of tests of gastric secretion, performed months or years after HSV, have shown that the resting juice in the stomach is not excessive and that it is free from food residues²⁴⁻²⁷.

Granted that HSV rarely produces gastric stasis, is the pattern of gastric emptying normal after HSV? The answer is that gastric emptying is not normal after HSV, but that it is closer to the normal than is gastric emptying after vagotomy with a drainage procedure. After HSV in man, gastric emptying of fluids is significantly faster than before operation^{5,28,29} (presumably because of impaired receptive relaxation by the denervated body of the stomach³⁰⁻³⁴) but it is significantly slower than gastric emptying after truncal or selective vagotomy with a drainage procedure, both of which render the stomach 'incontinent' of liquids²⁻⁵. Such gastric incontinence after vagotomy with drainage may be an important cause of so-called 'postvagotomy' diarrhoea^{2,3,35,36}, as McKelvey and his colleagues first suggested^{2,3}. Thus, when a hypertonic test meal is given orally to patients who have undergone either HSV or vagotomy with pyloroplasty (V+P), significantly more dumping and diarrhoea ensue in the patients who have undergone V+P than in the patients who have undergone HSV^{28,35-37}. Radiological studies of the gastric emptying and intestinal transit of a thick mixture of food and barium after HSV showed that the pattern of emptying was similar to that of preoperative patients with duodenal ulcer, and significantly slower than that of patients who had undergone truncal or selective vagotomy with pyloroplasty³⁸. Both Pederson and Amdrup³⁹ and Madsen, Kronborg, and Feldt-Rasmussen³⁶ found that gastric emptying of a 'nutritional contrast medium' was significantly faster after selective vagotomy and pyloroplasty than after highly selective vagotomy. A preliminary report has suggested that gastric emptying of solid food is within normal limits after HSV in man⁴⁰. In dogs and rabbits⁴¹, too, the evidence with the exception of one report⁴², suggests that HSV does not produce gastric stasis^{10,11,30,43}. Highly selective vagotomy in the dog leads to an increase in intragastric pressure and to accelerated emptying of liquids, whereas solid spheres leave the stomach at a normal rate³⁰.

Next, it must be asked whether HSV succeeds in its aim of diminishing the incidence of side effects. Recently, the clinical results achieved in 108 patients who had undergone HSV in Copenhagen and Leeds two years or more previously were reviewed²³ and compared with the results which had been recorded at a similar time after operation in previous series of patients

who had undergone selective vagotomy and pyloroplasty (SV + P) in Copenhagen or truncal vagotomy (TV) + P, TV + GJ or SV + P in Leeds. Episodic diarrhoea was recorded in only 5% of patients after HSV, compared with 15% of patients after SV + P and 25% of patients after TV + P. The incidences of severe diarrhoea were, respectively, 0%, 2%, and 5%. Early dumping was noted in 6% of patients after HSV, 32% after SV + P, and 11% of patients after TV with a drainage procedure. Biliary vomiting was recorded in 2% of patients after HSV, in 8% after SV + P, in 11% after TV + P, and in 16% of patients after TV with gastroenterostomy. Many authors, when reporting on their early experience with HSV, claim that the incidences of dumping and diarrhoea are low^{12,13,16,17,19-21}. In Leeds, diarrhoea was found to be no more frequent one year after HSV than one year after herniorrhaphy or operation for varicose veins³⁵. In Valladolid, De Miguel found that 40% of patients had diarrhoea after TV + P, 20% had diarrhoea after SV + P, and only 7% had diarrhoea after highly selective vagotomy. In Leeds and Copenhagen²³, it was found that other side effects of gastric surgery, such as dysphagia, flatulence, and heartburn, were no more common after HSV than after vagotomy with a drainage procedure. A disappointing finding in Leeds was that no fewer than 30% of patients after HSV experienced epigastric fullness after large meals and therefore preferred to limit the size of the main meal of the day. After vagotomy with drainage in Leeds, the incidence of this symptom was approximately 35%. Only 17% of the patients in Copenhagen experienced postprandial epigastric fullness after HSV (PCV). In summary, the use of HSV, rather than of truncal or selective vagotomy with a drainage procedure, leads to a large reduction in the incidences of early dumping, diarrhoea, and bilious vomiting, while the incidence of other side effects is not increased.

Both truncal (TV) and selective vagotomy (SV) impair gastric motility^{44,45} and when used alone produce gastric stasis^{41,46-48}. Myoelectrical activity in the stomach is disorganized after both TV and SV in man and dog^{30,49-51}. After HSV in man the regular three-per-minute rhythm of electrical activity in the antrum is maintained, with a normal wave form⁵¹. When HSV, then SV, then TV were performed successively in the same dogs, it was found that HSV produced less disturbance in gastric motility and emptying than did complete gastric vagotomy³⁰. All three types of vagotomy increased intragastric pressure in response to gastric distension and speeded gastric emptying of liquids³⁰.

The crucial questions about the effects of HSV on serum gastrin, on outputs of acid and pepsin, and on the incidence of recurrent ulceration are interlinked and will be considered together.

It has been found that vagotomy of any type leads to an increase in serum gastrin⁵²⁻⁶⁰. This is true both of gastrin levels in fasting patients and of gastrin levels after a meal. There is no evidence that either fasting or postprandial gastrin levels are higher after HSV than after truncal vagotomy: indeed, Korman and Hansky's data⁵² suggest that gastrin levels are significantly higher after truncal vagotomy than after highly selective vagotomy. These results suggest that the main determinant of the concentration of serum gastrin is the pH of the contents of the antrum rather than the integrity or otherwise of the vagal nerve supply to the antrum. When the vagus nerves are stimulated by insulin-induced hypoglycaemia, gastrin release is demonstrable both in patients with intact vagi and in patients after HSV^{52,53,56,57}:

after truncal or selective vagotomy, no increase in gastrin levels was found by Korman and Hansky⁵², but Stadil and his colleagues found that gastrin levels still increased in response to insulin, even after truncal or selective vagotomy^{58,59}. The finding that truncal vagotomy increases rather than decreases serum gastrin in man is of great clinical importance, because it suggests that vagal denervation of the gastric antrum is unnecessary. It is also harmful to the patient because it leads inevitably to the need for a drainage procedure, to impaired function of the antral mill, and to loss of the pylorus as a sphincter⁶¹.

Basal and 'maximal' acid outputs have been shown to be reduced as effectively by HSV as by truncal or selective vagotomy²⁴⁻²⁷. Acid output increases slightly, but statistically significantly, in the course of the first year after HSV^{19,26,27}, but even more than one year after operation, basal, pentagastrin-stimulated^{26,62}, and insulin-stimulated²⁷ acid outputs were found to be no greater after HSV than after the other types of vagotomy. The insulin test which was performed one week after HSV in Leeds was positive by Hollander's criteria in only 3% of the first 100 patients treated (all three were late-positive)²⁷, but positive incidences as high as 28% at this time have been reported^{63,64}. Thus the inter-surgeon variability in the achievement of a complete vagotomy of the parietal cells, which has been demonstrated previously after truncal or selective vagotomy⁶⁵, is demonstrable also after highly selective vagotomy. Patients with positive insulin tests soon after truncal vagotomy (particularly those who have early positive responses) have been shown to be more likely to develop recurrent ulceration than are patients who have negative insulin tests^{66,67}, and it seems likely that a similar correlation will be found between insulin positivity soon after HSV and recurrent ulceration^{20,27,63,64}. It is now well known that many patients who are initially insulin-negative will show positive responses when tested later^{38,68-70}. Two to four years after operation in Leeds the insulin test has recently been shown to be positive by Hollander's criteria in approximately 90% of patients after HSV, 70% after SV, and 60% after truncal vagotomy. The acid output in response to insulin (minus basal output) is then significantly higher in patients after HSV than in patients after TV or SV, but the response is still small—a mere 10% of the preoperative acid response (P. J. Lyndon, unpublished observations). The reason for this difference between HSV and TV/SV is not known, but it might be due to vagal release of gastrin in the HSV patients⁷¹. Information on pepsin output after the different types of vagotomy is as usual much scantier than that on acid output, but our own unpublished observations suggest that pepsin responses to pentagastrin and to meat extract more than one year after HSV in man are similar to the pepsin outputs after truncal or selective vagotomy. Likewise, in the dog, it has been shown that both HSV and truncal vagotomy lead to profound, and equal, reductions in pepsin output in response to stimulation by pentagastrin and by histamine⁷². Acid responses to a test meal of meat extract were no higher in patients with an innervated antrum (HSV) than in patients with a denervated antrum (TV or SV)^{73,74}, which again suggests that gastrin release from the innervated antrum is not 'excessive'.

There has been no case of proven recurrent duodenal ulcer amongst the 350 patients who have been treated by HSV in Copenhagen and Leeds in the past five years. Recurrence was suspected clinically in 3% of these patients on account of pain, none having perforation or bleeding, but after full

investigation, which in three cases included laparotomy and careful inspection of the duodenal mucosa, the presence of recurrence could not be confirmed. Two patients in Copenhagen developed gastric ulceration, however. Hall has also reported one case of gastric ulceration in a series of 50 HSV operations in York⁷⁵. Although Holle always adds a pyloroplasty to HSV⁹, it is nonetheless of interest that he quotes an incidence of recurrence of less than 1% among 267 patients who had undergone 'selective proximal vagotomy' in the preceding five years⁷⁶. Even when allowance is made for the relatively brief period of follow up, these results from Munich, Copenhagen, and Leeds suggest that preservation of the vagal nerve supply to the antrum is 'safe'. The results of serum gastrin measurements quoted previously support this conclusion. Liavag and Roland¹⁹ report 250 HSV operations in the past three years, with no recurrent ulceration so far. Grassi and his colleagues report on 79 patients after HSV with only one recurrence¹⁸. Moberg and Hedenstedt followed up 48 patients for a minimum period of three years after HSV, and found three definite recurrences (6%), which all occurred in the first year after operation⁷⁷. Wastell and his colleagues report two recurrences (13%) after a short period of follow up of 16 patients after HSV, but the incidence of incomplete vagotomy soon after operation in their series was 28%¹⁴. Similar discouraging results after HSV have been reported by Madsen and Kronborg²¹, who in a brief follow up found three cases of recurrent duodenal ulceration and one case of gastric ulceration out of a total of only 30 patients. Liedberg and Oscarson²⁰ report an incidence of recurrence of 20% within 18 months of HSV in 20 patients. However, these authors also report that in this pilot series basal acid output (BAO) was reduced by only 40%, maximal acid output (MAO) by only 33%, while the insulin test was positive in 83% of the patients two months after operation and in 100% of patients after one year. Liedberg and Oscarson then proceeded to modify their surgical technique, and in the subsequent 60 patients obtained good results²⁰, the BAO being reduced by 80%, MAO by 58%, and no further recurrences have been found. It will be seen that the evidence concerning ulceration after HSV is conflicting, some centres reporting no recurrences, others incidences ranging up to 20%. Recurrence has usually been associated with incompleteness of the vagotomy. Thus already a pattern seems to be emerging which is familiar from previous experience with truncal and selective vagotomy: when vagotomy is complete, as shown by a negative insulin test soon after operation, recurrence is rare: when vagotomy is incomplete, and in consequence reductions in basal and maximal acid output are smaller, the incidence of recurrence is high^{66,67}. There is no evidence as yet that the incidence of recurrence after HSV is higher than that which is found after truncal or selective vagotomy with a drainage procedure. Under experimental conditions in the dog, HSV has been found to afford a protection against peptic ulceration which is as good or better than that which is conferred by selective vagotomy and pyloroplasty or by selective vagotomy and antrectomy⁴³.

As to the overall clinical results, 88% of patients in Copenhagen and Leeds were judged to have a perfect (Visick grade 1) or very good (Visick grade 2) result two to four years after highly selective vagotomy. Seventy-five per cent of patients in Copenhagen had achieved perfect results compared with only 58% in Leeds. This intriguing difference could be due to differences in diet or in the methods of assessment in the two centres, or it might be due to

the careful mapping of the extent of the antrum in Copenhagen which permits more of the stomach (mean, 9 cm) to be left innervated than is left innervated in Leeds (mean, 6.5 cm). The 5% incidence of failure (Visick grade 4) was attributable to proven (gastric) or suspected (duodenal) recurrent ulceration or to gastric stasis. In Leeds, 88% of male patients were in Visick grades 1 or 2 after HSV whereas only 68% of male patients were in Visick grades 1 or 2 after truncal or selective vagotomy with a drainage procedure. The apparent superiority of HSV was due largely to the reduction in side effects such as early dumping, diarrhoea and bilious vomiting, which meant that very few patients were in Visick grade 3 (the 'fair' or 'moderate' category) after HSV, whereas 20% of patients were in Visick grade 3 after complete gastric vagotomy with a drainage procedure. Although all patients in Leeds were assessed in 'blind' fashion at a special gastric follow-up clinic, it must be stressed that the comparison between HSV and vagotomy with drainage is not based upon prospectively randomized series of patients, and hence must be viewed with caution. Similar, very encouraging preliminary clinical results after HSV have been reported from other centres^{12,13,15-17,19,20}.

To summarize briefly the results of other studies, it has been shown in man that neither HSV⁷⁸ nor selective vagotomy⁷⁹ leads to dilatation of the gallbladder, whereas the volume of the resting gallbladder is significantly increased after truncal vagotomy^{79,80}. Pancreatic enzyme output in man in response to vagal stimulation by insulin hypoglycaemia is significantly greater after both HSV⁸¹ and selective vagotomy⁸² than after truncal vagotomy⁸¹⁻⁸⁴, and faecal fat excretion is significantly less after HSV than after truncal or selective vagotomy with pyloroplasty⁸⁵. In the dog, both partial gastrectomy⁸⁶ and vagotomy with drainage⁸⁷ have been shown to lead to a significant increase in the bacterial flora of the small intestine, whereas after sham operation, pyloroplasty alone, and HSV the bowel flora did not change significantly⁸⁸.

Complications of Peptic Ulcer

Highly selective vagotomy has been used in the treatment of perforation, haemorrhage, and pyloric stenosis due to peptic ulcer¹⁸. It is obvious that patients with perforation must be selected for HSV with care, if good results are to be achieved. Highly selective vagotomy combined with direct suture of the bleeding point may be applicable to most cases of haemorrhage but when the operation has to be completed in the minimum time truncal vagotomy is preferable. When HSV is used, access to a bleeding duodenal ulcer can usually be obtained by means of a duodenotomy which stops short of the pylorus. Twenty consecutive patients with clinically manifest pyloric stenosis have been treated by HSV combined with digital dilatation of the stenosis through a gastrotomy. The stomach's compensatory mechanisms are thereby utilized rather than being sacrificed. Only one patient developed re-stenosis as the ulcer healed. This technique is not recommended for routine use at present, but its large measure of success so far suggests at least that the addition of a drainage procedure in patients who do not have pyloric stenosis is unnecessary.

Gastric Ulcer

In Leeds, 30 patients with gastric ulcer alone and 15 patients with combined gastric and duodenal ulcer have been treated by HSV plus excision of the ulcer through a gastrotomy^{89,90}. The cases were not quite consecutive,

a few patients having been excluded because of anticipated technical difficulties, suspicion that the ulcer was malignant, or on account of the patient's poor general condition. There was one operative death. Reductions in acid output one year after operation were profound, follow-up barium meal examinations revealed no evidence of gastric stasis or of recurrent ulceration, and the overall clinical results to date have been good. Similar encouraging results after HSV for gastric ulcer have been found by Hedenstedt⁹¹ and by Burge (personal communication). Again, it would clearly be wrong at this stage to advocate the use of HSV in the surgical treatment of gastric ulcer, but these preliminary results suggest that a prospective random trial of HSV versus partial gastrectomy is now desirable.

Summary

The experience of the past five years has shown that highly selective vagotomy without a drainage procedure (HSV) has a very low operative mortality and is applicable to nearly all patients who require elective surgery for duodenal ulcer. Gastric emptying has been found to be satisfactory. Gastric emptying has also been shown to be under better control after HSV than after operations in which the gastric antrum has been vagally denervated and 'drained'. Gastrin levels in the blood are no higher after HSV than after truncal vagotomy with a drainage procedure. Output of acid is reduced as effectively in the long term by HSV as by truncal or selective vagotomy. Studies of gall-bladder and pancreatic function and of fat excretion have shown that HSV produces less alteration than does truncal vagotomy with a drainage procedure. Early dumping, diarrhoea, and bilious vomiting are less frequent after HSV than after truncal or selective vagotomy with a drainage procedure. Among 350 patients who have been followed for up to five years after HSV in Leeds and Copenhagen, there has not been a single case of proven recurrent duodenal ulceration. Two of the 350 patients have developed gastric ulceration. Other centres report recurrence rates which range from nil to 20%, after brief periods of follow up. The overall clinical results (Visick grades) after HSV seem to be better than the results after truncal or selective vagotomy with a drainage procedure.

After a mere five years, evaluation of highly selective vagotomy is obviously still incomplete. However, the evidence which is already available suggests that the gastric antrum can be left vagally innervated with impunity and that the pyloric sphincter can be left intact, provided always that the parietal cell mass is efficiently denervated. If this be true, it is of great importance for the surgery of peptic ulcer, because it means that for the first time the principal functions of the stomach—those of a 'hopper' to receive the meal and of a 'mill' to grind it into chyme—can, in the main, be preserved. It means that 'drainage procedures' can be discarded and that side effects of gastric surgery such as early dumping, diarrhoea, and bilious vomiting are now largely preventable. In a further five years' time we shall know if the hypothesis is correct.

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DAVID JOHNSTON
*University Department of Surgery,
The General Infirmary, Leeds*

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