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EDITORIAL

SURGICAL TREATMENT OF DUODENAL ULCER

Some cases of duodenal ulcer are best left to the surgeon, and many people go further and state frankly that partial gastrectomy is the standard treatment of the condition. There is of course the surgical alternative of gastrojejunostomy, with or without vagotomy. While the benefits of the vagotomy procedure have probably still finally to be assessed, long experience is available of the gastrojejunostomy operation, which was introduced by Moynihan in 1908. In fact, it was through the successful treatment of the commonest complication of this procedure, viz. stomal ulceration, that partial gastrectomy came into vogue. After unchallenged mastery of the field for 2 decades, simple gastrojejunostomy finally gave way in the thirties to partial gastrectomy and, as a general rule, little else is performed for duodenal ulcer nowadays. The universal popularity of partial gastrectomy does not, however, mean that it is of necessity the best treatment or the last word in the matter, and recently an eminent Scottish surgeon, E. L. Farquharson, expressed his 'doubts and misgivings that such an irrevocable and seemingly mutilating operation should be accepted as the standard treatment of duodenal ulcer today'.[1]

Four-fifths of duodenal ulcers are said to be 'cured' by partial gastrectomy, i.e. no long-term complications or alimentary upset are encountered, while 20% of cases suffer various disabilities that Farquharson calls collectively the malabsorption syndrome. In these cases it seems as if the patient merely exchanges his ulcer for postprandial symptoms and nutritional disturbances that are frequently more unpleasant than the ulcer itself. Most are the outcome of the appreciably diminished capacity of the stomach. Restricted intake leads to loss of weight and initial loss of intrinsic factor to anaemia; whilst too rapid emptying causes immediate postprandial symptoms such as bilious vomiting and the dumping syndrome. The term 'intestinal hurry' is no misnomer; in some cases barium reaches the hepatic flexure *within* 5 *minutes* of being swallowed.[2] Defective absorption is therefore bound to occur, causing further alimentary upset, e.g. diarrhoea or steatorrhoea. Since all these complications stem from

VAN DIE REDAKSIE

CHIRURGIESE BEHANDELING VAN DUODENAALSEER

Dit is beter as sommige gevalle van duodenaalseer aan die chirurg oorgelaat word en baie mense gaan nog verder en verklaar onomwonde dat gedeeltelike gastrektomie die standaard behandeling van die toestand is. Daar is natuurlik die chirurgiese alternatief van gastrojejunostomie, met of sonder vagotomie. Terwyl die voordele van die vagotomie prosedure heelwaarskynlik nog finaal bereken moet word, is lang ondervinding met die gastrojejunostomie-operasie, wat in 1908 deur Moynihan ingestel is, beskikbaar. Om die waarheid te sê, is dit deur die suksesvolle behandeling van die mees algemene komplikasie van hierdie prosedure, nl. stomale ulserering, dat gedeeltelike gastrektomie in swang gekom het. Ná onbestrede heerskappy van die veld vir 2 dekades, het eenvoudige gastrojejunostomie finaal in die dertigerjare vir gedeeltelike gastrektomie gewyk en as 'n algemene reël, word selde 'n ander operasie vir duodenaalseer deesdae uitgevoer. Die universele populariteit van gedeeltelike gastrektomie beteken egter nie dat dit noodwendig die beste behandeling of die finale woord in die saak is nie, en onlangs het 'n uitmuntende Skotse chirurg, E. L. Farquharson, sy ‚doubts and misgivings that such an irrevocable and seemingly mutilating operation should be accepted as the standard treatment of duodenal ulcer today'[1] uitgespreek.

Dit word verklaar dat vier-vyfdes van duodenaalsere ‚genees' word deur gedeeltelike gastrektomie, d.i. geen lang-termyn komplikasies of spysverterings-ontsteltenisse word aangetref nie, terwyl 20% van gevalle verskeie gebreke, wat Farquharson gesamentlik die gebrekkige absorberingssindroom noem, ondergaan. By hierdie gevalle skyn dit of die pasiënt slegs sy seer vir na-ete simptome en voedingssteurnisse verruil, wat dikwels meer onaangenaam as die seer self, is. Die meeste hiervan word veroorsaak deur die aansienlik verkleinde kapasiteit van die maag. Beperkte opname lei tot gewigsverlies en die aanvanklike verlies van inwendige faktor lei tot bloedarmoede; terwyl die té vinnige ontleding simptome onmiddellik na ete veroorsaak, soos byvoorbeeld mislike braking en die ophopingssindroom. Die term ‚ingewandshaas' is geen verkeerde benaming nie; by sommige gevalle bereik barium die lewerboog *binne* 5 *minute* ná dit gesluk is.[2] Gebrekkige absorbering sal dus stellig voorkom en verdere spysverteringsontsteltenisse, soos byvoorbeeld diaree of steatoree, veroorsaak. Aangesien al hierdie komplikasies van die afname in die grootte van die maag afstam, is dit natuurlik om voor te stel dat 'n kleiner gedeelte van die maag

the reduction in size of the stomach, it is natural to suggest that a smaller portion of the stomach should be resected. It is generally held, however, that 'inadequate' resection—i.e., removal of less than 70%—is responsible for the 4% of cases in which ulceration recurs. Here Farquharson ventures an observation that may alter the entire approach to the treatment of duodenal ulcer. He states that in some cases of recurrent ulceration after partial gastrectomy observed in Edinburgh, the acid values of the secretion in the gastric remnant were found to be as much as 4 times the normal. If this observation is substantiated, the main purpose of performing a partial gastrectomy disappears.

The second pillar of Farquharson's thesis is this, that the satisfactory treatment of the malabsorption syndrome—i.e. every fifth case submitted to partial gastrectomy—is often impossible. Generally speaking the surgeon carrying out the operation relies upon the 80% chance of cure for his patient. If he fails to achieve it, there is little further that he can do.

Farquharson considers it to be a sad reflection upon present-day medicine that we should have to accept removal of the greater part of the healthy stomach as the best available method of reducing its acid secretion, and he quotes approvingly the remarks of a physician of the thirties: 'If any surgeon wanted to remove four-fifths of my normal stomach to cure a small ulcer of my duodenum, I should run faster than he'!

Is simple gastrojejunostomy the preferable and satisfactory alternative? The present-day objection to the procedure—apart from the often groundless bias in favour of partial gastrectomy—is based upon the liability of gastrojejunostomy to be followed by stomal ulceration. This complication, from casting no more than a shadow over the operation 40 years ago, has grown to be a spectre, and is, Farquharson maintains, 'seriously exaggerated'. The only statistical evidence of its incidence is contained in 5 large series comprising 5,170 cases of gastrojejunostomy performed in the decade preceding 1935. Over follow-up periods of never less than 4 years, only 180 stomal ulcers (3·5%) were recorded. Moreover, 25 years ago the operative mortality from gastrojejunostomy, in common with all major abdominal procedures, was considerably higher than it is today. Tanner, for instance, in 1954, recorded only one death in 107 cases of gastrojejunostomy—a mortality rate lower than that for partial gastrectomy.[3] It seems, therefore, that gastrojejunostomy has lost much of its former terrors. Besides, the surgeon does not burn his boats in performing it, for he can submit the 3·5 cases that subsequently go on to stomal ulceration to partial gastrectomy, which is usually a great success. In theory at any rate, simple gastrojejunostomy seems to be preferable to partial gastrectomy, but prejudice against it remains firm. 'For the unskilled surgeon on the unfit patient, it has much to recommend it', wrote Sir Heneage Ogilvie this year,[4] and in the face of such damning praise in high places it would be a bold surgeon who did not have second thoughts

uitgesny behoort te word. Dit word egter algemeen aanvaar dat ,onvoldoende' reseksie—d.i. verwydering van minder as 70%—verantwoordelik is vir die 4% van gevalle by wie ulserering hervat. Hier het Farquharson dit gewaag om 'n waarneming uit te spreek wat die algehele benadering tot die behandeling van duodenaalseer mag verander. Hy verklaar dat by sommige gevalle van herhalende ulserering ná gedeeltelike gastrektomie, wat in Edinburg waargeneem is, dit gevind is dat die suurgehaltes van die afskeiding by die oorblywende deel van die maag, so veel soos 4-maal die normale was. As hierdie waarneming gestaaf word, verdwyn die hoofdoel van die uitvoering van 'n gedeeltelike gastrektomie.

Die tweede steunpilaar van Farquharson se stelling is dat die bevredigende behandeling van die gebrekkige absorberingssindroom—d.i. elke vyfde geval wat aan gedeeltelike gastrektomie onderwerp word—dikwels onmoontlik is. In die algemeen gesproke, maak die chirurg, wat die operasie uitvoer, staat op die 80%-kans van genesing vir sy pasiënt. As hy nie hierin slaag nie, is daar weinig verder wat hy kan doen.

Farquharson beskou dit as 'n treurige refleksie op hedendaagse geneeskunde dat, om die suurafskeiding te verminder, ons verwydering van die groter gedeelte van 'n gesonde maag as die bes beskikbare metode moet aanvaar, en hy haal goedkeurend die opmerkings van 'n geneesheer van die dertigerjare aan: ,If any surgeon wanted to remove four-fifths of my normal stomach to cure a small ulcer of my duodenum, I should run faster than he'!

Is eenvoudige gastrojejunostomie die verkieslike en bevredigende alternatief? Die hedendaagse beswaar teen die metode—afgesien van die dikwels ongegronde vooroordeel ten gunste van gedeeltelike gastrektomie—is gebaseer op die onderhewigheid van gastrojejunostomie om deur stomale ulserering gevolg te word. Waar hierdie komplikasie 40 jaar gelede skaars 'n skaduwee oor die operasie gewerp het, het dit tot 'n spookgestalte gegroei en is dit volgens Farquharson, ,ernstig oordryf'. Die enigste statistiese bewys van sy voorkoms word gevind in 5 uitgebreide reekse waarby 5,170 gevalle van gastrojejunostomie, wat in die dekade vóór 1935 gedoen is, betrokke was. Gedurende opvolgingsperiodes van nooit meer as 4 jaar nie, is daar slegs 180 stomale sere (3·5%) opgeteken. Bowendien was die operatiewe sterftesyfer weens gastrojejunostomie 25 jaar gelede, in gemeen met alle ernstige maagoperasies, heelwat hoër as wat dit vandag is. Tanner het bv. in 1954 slegs een sterfgeval in 107 gevalle van gastrojejunostomie opgeteken—'n sterftesyfer laer as dié vir gedeeltelike gastrektomie.[3] Dit skyn dus of 'n groot deel van die vrees wat voorheen aan gastrojejunostomie verbonde was, nou nie meer bestaan nie. Buitendien verbrand die dokter, wanneer hy die operasie uitvoer, nie sy brûe nie, aangesien hy die 3·5 van gevalle wat daarna 'n stomale seer vorm, aan gedeeltelike gastrektomie, wat gewoonlik baie suksesvol is, kan onderwerp. In teorie in elk geval, skyn dit of eenvoudige gastrektomie verkieslik is bó gedeeltelike gastrektomie, maar die vooroordeel daarteen bly onwrikbaar. ,For the unskilled surgeon on the unfit patient, it has much to recommend it', het Sir Heneage Ogilvie hierdie jaar geskryf[4] en met hierdie veroordelende lof van hoë gesag voor oë, sal dit 'n dappere

upon performing a simple gastrojejunostomy. But Farquharson does not relent. We quote the concluding sentence in his paper. 'If I were to develop a duodenal ulcer resistant to medical treatment, such are my misgivings at present about gastrectomy that I think I would try to persuade my old chief to emerge from his retirement, to perform upon me a simple gastrojejunostomy, and to allow me to take my chance of a stomal ulcer.'

1. Farquharson, E. L. (1956): Lancet, **2**, 849.
2. Wells, C. (1955): Ann. Roy. Coll. Surg. Engl., **16**, 145.
3. Tanner, N. C. (1954): Postgrad. Med. J., **30**, 448.
4. Ogilvie, H. (1956): Lancet, **1**, 115.

dokter wees wat nie na verdere oorweging 'n eenvoudige gastrektomie uitvoer nie. Maar Farquharson gee nie skiet nie. Ons haal die slotsin van sy verhandeling aan: 'If I were to develop a duodenal ulcer resistant to medical treatment, such are my misgivings at present about gastrectomy that I think I would try to persuade my old chief to emerge from his retirement, to perform upon me a simple gastrojejunostomy, and to allow me to take my chance of a stomal ulcer.'

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CARBUTAMIDE AND TOLBUTAMIDE IN DIABETES

Although the existence of the insulin hormone had been known for many years, it was Banting and Best's discovery of means of isolating it from the pancreas of animals that made it possible to use it in the treatment of human diabetes. The discovery revolutionized treatment and completely changed the life and prospects of the victims of the disease, especially in its severer forms. Apart from thyroid therapy, which had been in use for a considerable time before, insulin treatment is the oldest of the hormone therapies. It has enabled many thousands of diabetics to live a normal and happy life and is rightly regarded as one of the triumphs of medicine.

Nevertheless a search continued for other drugs which might be useful in the treatment of diabetes.[1] Perhaps the chief spur to this research was the desire for a medicine which might be taken by the mouth and thus relieve the patient of the burden of daily subcutaneous injection; but certain limitations to the effectiveness of insulin that are evident in some classes of diabetic patient have also provided a stimulus.[1] It is not until recently that any substantial progress has been made in this research. It was noted in 1942 by French observers[2] that the administration of certain sulphonamides resulted in severe hypoglycaemia in animals, associated in some cases with damage to the liver. Other sulphonamides, however, have since been discovered in Germany, which lower the blood sugar but are free from this dangerous toxic action. Two of these stand out prominently, viz. BZ 55 (Boehringer) or carbutamide (Invenol, Nadisan or Orabetic), and D 860 (Hoechst) or tolbutamide (Rastinon, Artosin, Orinase or Dolipol). It appears that these two drugs are alike in their action in diabetes, but that the prolonged use of BZ 55 has in some cases resulted in agranulocytosis,[3] while the use of D 860 has not been accompanied by this side-effect.

Investigations in the use of these two drugs in diabetes therapy have been carried out in Germany and the UK, and in the present issue of the *Journal* (pages 1222 and 1227) articles by Jackson, Linder and others are published reporting clinical trials of BZ 55 (carbutamide, Orabetic) in cases of diabetics admitted to Groote Schuur Hospital, Cape Town, and in the diabetic clinic of the same hospital. At the present time similar trials are proceeding of D 860 (tolbutamide, Rastinon). The Cape Town investigators confirm the results reported elsewhere, particularly (to put it very broadly) that BZ 55 is effective in controlling the hyperglycaemia and glycosuria in 'mild' diabetes (such as that seen in older people) but in the 'severe' form (more often seen in young people) its usefulness is mainly restricted to its action as an adjuvant to insulin therapy. They definitely conclude that the drug represents an advance in diabetes therapy, both in the 'maturity' type of the disease and in the 'severe' type. No toxic effects were observed in the cases treated, but the authors recognize that carbutamide is potentially dangerous and recommend that its use should at present be confined to hospitals where the patient can be kept under adequate observation.

The potential undesirable side-effects of BZ 55 administered over long periods are due to its action as a sulphanilamide (1) in causing blood changes (agranulocytosis), (2) in unfavourably affecting the gastro-intestinal bacterial content, and (3) in its allergic action. The newer product D 860 (tolbutamide, Rastinon) differs from BZ 55 in that the H_2N radicle in the latter is replaced by a H_3C radicle in the former. This molecular difference is held to explain the absence in tolbutamide therapy of the occasional side-effects noted with carbutamide. It has been estimated that throughout the world 35,000 patients have been treated with Rastinon and other brands of D 860, some for a period up to 14 months, and no cases of agranulocytosis have been reported.

As regards the mode of action of these adjuvant drugs in diabetes, it appears that the blood-sugar level is dependent on other factors as well as the quantity of insulin produced by the pancreas. For some time it has been known that there normally exists in the body an enzyme produced in the liver and known as insulinase, which inactivates insulin. Normally a balance is struck between the production of insulin and of insulinase. Diabetes may result from an under-production of insulin (as in the 'young' diabetic) or from an over-production of insulinase (as in the 'elderly' diabetic); and this is thought to be the reason why BZ 55 or D 860 is an effective remedy in the latter type, while by itself it may not control the hyperglycaemia in the former. With these new oral drugs the patient still depends on insulin produced by his pancreas or in-

jected by the physician; and, moreover, the possibility of hypoglycaemia resulting from an overdose, which is a property of insulin, does not exist with the BZ 55 and D 860. There are, of course, other factors concerned in sugar metabolism, and C. H. Best,[4] co-discoverer of insulin has remarked that, apart from their therapeutic possibilities, the study of these new hypoglycaemia-producing substances may disclose valuable information concerning sugar metabolism and its disorders.

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3. Jackson, W. P. U. and Herman, J. B. (1956): S. Afr. Med. J., **30,** 904.
4. Best, C. H. (1956): Canad. Med. Assoc. J., **74,** 959.