Section of Medicine

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DISCUSSION ON POST-GASTRECTOMY SYNDROMES

Mr. R. B. Welbourn (Liverpool): We recommend subtotal gastrectomy with increasing confidence for the relief of peptic ulceration, and the operation is being performed more and more frequently. At the same time the results of more extensive types of gastrectomy for carcinoma of the stomach and œsophagus are continually improving. But there are a number of patients who have symptoms and signs which are directly attributable to their gastrectomies, and it is these who return to hospital most frequently and who may give a false impression of the results of operation.

My own experience, which is based on a detailed study of well over 300 cases in the Department of Surgery at Liverpool, leads me to suggest the following as the overall picture in subtotal gastrectomy for ulcer. 90% are free from pain and well satisfied with the results of their operations. These do not return, unless specially followed up, and they present the *true* post-gastrectomy syndrome. In about 5% of cases we fail in our primary objective—that is to say the patients either die from the operation or develop recurrent ulcers. And a further 5%, although cured of their ulcers, develop severe post-prandial symptoms or deficiency states which make them feel that the operation has not been worth while. It is their complaints which we usually *refer to* as the post-gastrectomy syndromes. Of the 90% there are a fair number who present the syndromes in a mild degree—dumping, anæmia, vitamin-B deficiency, loss of weight and so on—but even so they are sure that they are better off than they were before operation.

I propose to discuss these syndromes, not primarily as clinical states, but as reflections of the ways in which the normal physiology may be upset by the different operations. I take it for granted that we are discussing *subtotal* gastrectomy, for any less procedure fails to control acid secretion and results in a high proportion of recurrent ulcers. In this operation we aim at removing three-quarters of the stomach, including all the body which secretes most of the hydrochloric acid, and the pyloric antrum which produces gastrin. Only the cardiac end, or true fundus, is left, and this is anastomosed either end-to-end with the duodenum, as in the Billroth I operation, or end-to-side with the jejunum as in the Polya operation and its modifications. Most surgeons bring the afferent loop to the lesser curvature, and many make a valve to direct food into the efferent loop. A few still favour bringing the afferent loop to the *greater* curvature. Œsophago-gastrectomy and total gastrectomy need no special description.

There are 4 fundamental physiological effects of these operations, and all the syndromes can be attributed to one or more of them. They are:

(*a*) Rapid emptying of the gastric remnant, which gives rise to various "small stomach sequelæ". I shall discuss these in some detail.

(*b*) "Stasis and reflux", which refers to the behaviour of bile and of food in the afferent jejunal loop and in the gastric stump after the different types of anastomosis. Several different syndromes can be distinguished (Wells and Welbourn, 1951).

(*c*) Achlorhydria, which follows in a high proportion of cases. It is the probable cause of the iron deficiency anæmia, which we see frequently, and of the vitamin-B deficiency states in which we have taken a particular interest in Liverpool (Welbourn, Hughes and Wells, 1951).

(*d*) Removal of the intrinsic factor which is the probable cause of the megaloblastic anæmia which occasionally develops, especially after total gastrectomy.

Let us consider now the small stomach sequelæ, that is to say the effects of the rapid passage of food into the intestine. The most important function of the stomach is that of a reservoir which prepares food for the small intestine and ensures that it leaves the stomach in a suitable condition and at a suitable rate for digestion and absorption to occur optimally. The properties of food which have been chiefly studied from the point of view of its suitability for the small intestine are its bulk and its osmotic pressure. Normally solid foods are broken up and dissolved in gastric juice to form liquid chyme, and many foods, especially sweets (which contain sugar), form hypertonic solutions in the stomach. These,

as we shall see, are unsuitable for the jejunum and are rendered isotonic before they get there by dilution in the stomach and duodenum. The rate of gastric emptying is adjusted by an elaborate mechanism to bring this about.

This mechanism is hardly disturbed by gastro-enterostomy or by limited partial gastrectomy, and even after subtotal gastrectomy with a Billroth I anastomosis there is little disturbance—presumably because the food still passes through the duodenum before entering the jejunum. But after a Polya subtotal gastrectomy, when food is poured at once into the jejunum, there may be considerable disturbance, and after total gastrectomy the disturbance may be even greater. It usually takes the form of the common, early post-prandial, efferent loop "dumping syndrome", in which immediately after the end of a meal the patient experiences a feeling of fullness in the epigastrium, is overcome by a desire to sleep, and may have other symptoms such as nausea, sweating, palpitations, and so on.

It should be made quite clear that this early post-prandial syndrome has nothing to do with the blood sugar curve. There *is* a hypoglycæmic syndrome which also depends on rapid emptying of the stomach, but it is much less common, causes symptoms two to three hours after a meal (i.e. late post-prandial), and is simply an example of alimentary hypoglycæmia (Muir, 1949).

The "dumping syndrome" has been studied in a number of ways. First, meals of varying composition have been fed, and their effects have been observed. It has been found that the greater the bulk of a meal, the more likely it is to produce symptoms (Muir, 1949). Rubber balloons have been passed into the jejunum and inflated, and in some patients *all* the features of the syndrome have been reproduced (Muir, 1949; Machella, 1949, 1950; Glazebrook and Welbourn, 1951). These observations have led to the suggestion that *distension of the jejunum* is responsible for dumping symptoms. The investigation has been carried a stage further by Machella (loc. cit.), who has shown that if *hypertonic* solutions of glucose, amino acids, magnesium sulphate, &c., are introduced directly into the jejunum, the same symptoms are produced constantly and in a marked degree. He has shown that, although the jejunum does not usually have to dilute hypertonic solutions, it can do so if necessary. But, if it has to dilute a large quantity of hypertonic solution quickly, the bulk of its contents is greatly increased, and Machella has concluded that distension of the jejunum by this diluting fluid is mainly responsible for the dumping symptoms.

I was dissatisfied with this distension theory for several reasons:

First, jejunal distension is rarely seen in barium meals after gastrectomy, and it is certainly not seen constantly in patients with the dumping syndrome.

Secondly, healthy bowel responds to an increase in the bulk of its contents, not by distending, but by contracting actively and passing its contents along.

And thirdly, those with severe dumping syndromes are often conscious of increased intestinal movement and sometimes have small bowel colic; and their symptoms may end in an attack of diarrhœa.

So, with Dr. A. J. Glazebrook, I decided to investigate these patients in two further ways. First, we fed a mixture of hypertonic glucose and barium—the glucose to produce dumping symptoms, and the barium to show us radiologically what was happening. In each of 5 patients we reproduced the symptoms, and in every one of them the barium showed unusual activity in the jejunum. In one an ordinary barium meal presented no unusual features, but the hypertonic meal raced backwards and forwards at great speed, and produced spasm in the jejunum. In another case a peristaltic rush was produced and the mixture reached the hepatic flexure of the colon in five minutes. These are two extreme examples, but in every case we saw an unusual degree of activity in the jejunum, and in no case did we see any distension while the dumping symptoms were present.

Secondly we made kymographic records of the small intestine. These confirmed that great activity was produced by hypertonic solutions, and also showed that the mere inflation of a balloon caused active contractions in the intestine, especially when dumping symptoms were produced (Glazebrook and Welbourn, 1951). It seems reasonable, therefore, to suppose that the dumping syndrome is due to *increased tension and increased motor activity* in the bowel, rather than to *distension.*

The question now arises "How does this stimulus give rise to the symptoms?" We cannot give a complete answer, but the fact that splanchnic procaine block (Capper, 1950), thoracolumbar sympathectomy (Ray and Neill, 1947) and the administration of ganglion-blocking agents such as hexamethonium bromide (C6) (Glazebrook and Welbourn, 1951) can abolish the symptoms, suggests that afferent stimuli are carried from the bowel by the sympathetic nerves, and that these cause certain effects. As a working hypothesis I suggest that the symptoms can be divided into two groups. In the first group are the feeling of fullness, the consciousness of bowel movement and the colic, which are true visceral sensations. In the second group are fatigue, nausea, sweating, palpitations, &c. These suggest irradiation of the stimuli throughout the nervous system, and are probably of a reflex nature.

There are two other major effects of rapid gastric emptying—diarrhœa and steatorrhœa. Diarrhœa may be a part of the dumping syndrome, but may also occur without it. In either case it is probably caused by peristaltic rushes initiated by hypertonic solutions. Possibly those in whom it is unaccompanied by other symptoms have a high symptom-threshold. It is probable that achlorhydria and bacterial growth in the small bowel also play a part (which is not clearly defined) in the production of diarrhœa.

Steatorrhœa is common after gastrectomy, but can usually only be detected by fat balance tests. 85–90% absorption of fat is often found, but sometimes (especially after *total* gastrectomy) the figure is much lower. It must be remembered that fat delays gastric emptying, and is normally delivered into the small intestine more slowly than other foods. It is not surprising, therefore, that the dumping of a whole meal directly into the jejunum should interfere with the digestion and absorption of fat.

There are three main ways in which the absorption can be increased: first by feeding the fat more slowly (Emery, 1935; Brain, 1950), secondly by using emulsifying agents such as "Tween 80" to help the intestine in its work (Jones *et al.*, 1948), and thirdly by slowing down the rate of intestinal passage by drugs such as C6. All of these have been used with varying success to increase the weight of patients after gastrectomy.

The only method which I personally have controlled with fat balance tests is the last. In those with slight steatorrhœa only, it has made no difference, but in 2 patients with marked steatorrhœa, it caused an increase in absorption over a three-day period of 11% and 15% respectively. When kept on C6 the first of these put on 9 lb. in six weeks, and the second put on 20 lb. in five weeks (Glazebrook and Welbourn, 1951). I should add that I have not found C6 of any *general* value in the correction of loss of weight after gastrectomy, but its further trial in patients with gross steatorrhœa seems to be indicated.

These, then, are the physiological effects of gastrectomy and the syndromes which may result from them. If my analysis is correct it is clear that the main problem in gastric surgery to-day is to find a method of controlling peptic ulceration without interfering with the reservoir function and normal emptying mechanism of the stomach.

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Mr. T. J. Butler (Bristol): *The ætiology of the early post-gastrectomy syndrome.*—The purpose of this short contribution is to present a review of an experimental study commenced in 1947 in an endeavour to find the cause of the early post-gastrectomy syndrome. This has unfortunately been called the "Dumping Syndrome" and is usually attributed to rapid emptying of the small gastric remnant with jejunal filling.

The material for this study was obtained by careful review of 660 patients who had survived partial gastrectomy for benign ulcer. This provided 79 cases of the syndrome (11·9%) for investigation. In addition every fifth case without symptoms was studied in the same way for control purposes—95 cases in all. Table I illustrates the various operative procedures involved and reveals that the syndrome does not occur after the Billroth I operation, and that the maximal incidence follows any modification of the Polya operation.

TABLE I.—ANALYSIS OF CASES

Type of operation		Cases with syndrome %
Billroth I	102	0
Polya-ante-colic-no valve	109	15 (13·7)
Polya-ante-colic-valve	168	27 (16)
Polya-retrocolic-no valve	104	14 (13·5)
Polya-retrocolic-valve	57	8 (14·0)
Polya-Moynihan	120	15 (12·5)
Total	660	79 (11·9)

TABLE II

No. of cases		No. with syndrome %
Billroth I	102	0
Total gastrectomy	56	1 (1·8)
Gastro-enterostomy	73	2 (2)
Polya gastrectomy	558	79 (14)

The syndrome is rare following gastro-enterostomy and total gastrectomy (Table II)—a surprising observation if one accepts the popular viewpoint of the cause of the condition.

Clinically, the following features are relevant: (1) The bulk of the meal appears to be the chief factor in the production of the syndrome (Muir, 1949; Butler and Capper, 1951). (2) The syndrome can be prevented and relieved by lying down. (3) Vomiting of large amounts of bile-stained fluid, presumably from the afferent loop, enables the patient to take bigger meals without ill-effects. (4) When the syndrome disappears, the abdominal component fades first, followed two or three years later by the vasomotor features. (5) As a general rule, following the Polya operation, patients who have had a long antecolic anastomosis develop the syndrome with smaller meals than do those with short retrocolic anastomoses.

Experimental Studies

A. *Jejunal distension with a balloon.*—This was done in both the patients with the syndrome and the controls. Only in one patient in each group could the whole syndrome be reproduced in this way. In all the remaining patients only a sensation of fullness around the umbilicus was produced. There was no difference in the sensitivity of the jejunum to this form of stimulation between the two groups of cases.

B. *Effects of change of posture.*—It was observed in all cases that relief of symptoms occurred if the patients were allowed to lie down after meals. Further, when meals were consumed whilst lying down, none of the vasomotor features appeared. If the patients were instructed to lie down for a period before meals, amounts of bile-stained fluid up to 25 oz. could be aspirated via a Ryle's tube in the gastric remnant. After this, a larger meal could be taken without symptoms, illustrating a complementary relation between the contents of the afferent loop and the meal in the production of the syndrome.

C. *Radiological studies.*—There was no difference in the relative incidence of rapid emptying, delayed emptying, and afferent loop reflux between those patients with the syndrome and the control group (Table III). The rate of emptying was not altered by change of posture. Two features were observed in the group with the syndrome:

Table III

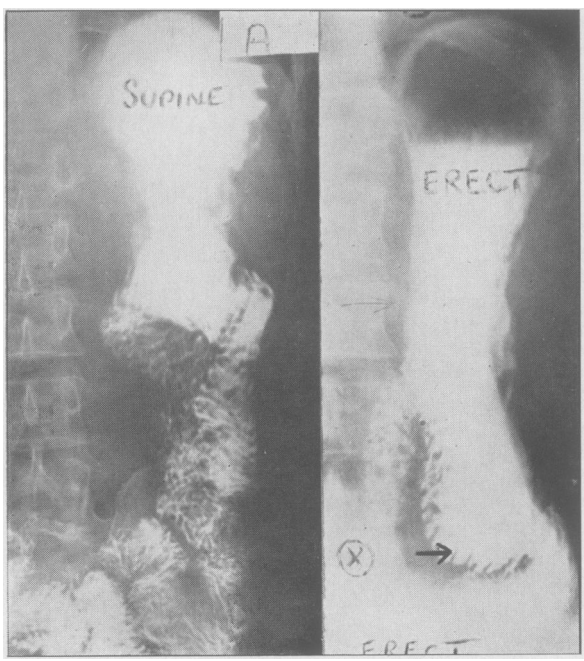
X-ray finding	Cases with syndrome 79 %	Asymptomatic controls 95 %
Rapid emptying	76 (96)	91 (95)
Delayed emptying	3 (4)	4 (4)
Afferent loop reflux	12 (15)	21 (22)

(*a*) The symptoms commenced whilst the bulk of the meal was still in the gastric remnant.

(*b*) There was a greater degree of descent of the gastric remnant—interpreted as stretching of the remnant—compared with the controls (Table IV and Fig. 1).

Table IV

Series	Descent
Billroth I	2 cm.
Polya—controls	2–5 cm.
Polya—with syndrome ..	7–11 cm.



← Fig. 1.—X-ray illustrating the descent and stretching of the gastric remnant by the weight of its contents in changing from the supine to the erect position.

D. *Effects of a mercury-loaded bag in the gastric remnant.*—In this test, a Miller-Abbott tube and bag were introduced into the gastric remnant and a weight of mercury equal to the weight of a meal that normally caused symptoms was put into the bag. In 57 out of 61 patients the syndrome was reproduced fully and relief was afforded by lying down. When the gastric remnant was aspirated first with the patient lying supine, a much greater weight of mercury was needed to produce symptoms, the extra weight being proportional to the amount of aspirated bile-stained fluid. Corresponding amounts of mercury did not produce any symptoms in the controls. These tests confirm the close relationship between the weight of the meal and the contents of the afferent loop.

Conclusions

All the symptoms of the syndrome are not due to the same cause. The sensation of fullness is undoubtedly due to jejunal filling and both clinically and experimentally is unaffected by change of posture. The remaining features, especially the vasomotor symptoms, are due to the effect of gravity and are both relieved and prevented by lying down. Consideration of the extremes of incidence following partial gastrectomy and gastro-enterostomy indicates that simple short circuit with rapid jejunal filling cannot be the major causative factor.

The essence of gastrectomy as a technical procedure is adequate mobilization. There is a very definite impression that the syndrome has become more common since the operation became more radical. It is suggested that the key to the solution may lie in these facts. Fig. 2 illustrates the chief peritoneal supports of the stomach. In Fig. 3 the state after gastrectomy is shown. The loaded U-loop of the anastomosis exerts traction on the unsupported

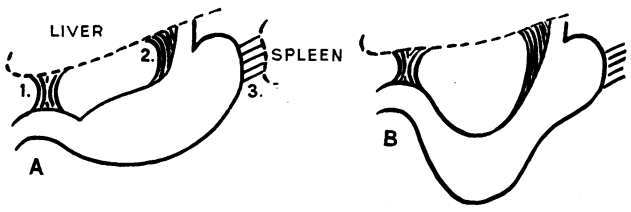


FIG. 2.—A. Diagram illustrating the supports of the stomach. 1. Right free edge of the lesser omentum. 2. Thick peritoneum around the left gastric vessels. 3. Gastrosplenic ligament. B. Illustrating sagging of the relatively unsupported part of the stomach.

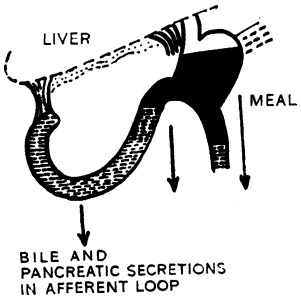


FIG. 3.—Diagram illustrating the state of affairs after gastrectomy. Traction effect is exerted by the weight of the meal and by the weight of the afferent loop on the stomach remnant deprived of its major supports.

gastric remnant. The added weight of food still further increases this traction effect and the complementary relationship of the weight of the contents of the afferent loop and the weight of the meal can be readily explained.

In order to prove the validity of this concept, a series of operations was commenced in 1948 in which a serious attempt was made to reconstruct the peritoneal attachments of the stomach. The effect was to reduce the incidence of the syndrome to approximately 1% in a series of 128 cases compared with 12% in a control series of 113 cases by the same surgeons in which no reconstruction was attempted. This difference in the incidence is significant.

Restitutio ad integram.

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Mr. W. M. Capper (Bristol): One of the things which creates the difficulty in interpreting the results of various observers lies in the fact that we have to rely on the subjective symptoms of the patient as a basis for argument, and these obviously vary from hour to hour and from day to day in such things as fatigue, nervous tension, and other factors which cannot be assess d. We have concluded that a mere description of his symptoms by the

patient as given in Out-Patients is not enough, and we think it is necessary to observe him in the attack. Furthermore, in the purely experimental side, we have tried not only to reproduce the symptoms, but to reproduce them with the same pattern and response to the same influences as observed in the clinical state.

The *late syndrome* is much less frequent and far less serious than the early variety. It occurred in 5·2% of 600 cases which we reviewed and it commences during the second or third hour after a meal. The commonest symptoms are: tremor of the limbs, giddiness, and profuse sweating, associated with anxiety and exhaustion. The onset of the symptoms coincides with a period of hypoglycæmia following the post-prandial hyperglycæmic phase. It may be that the high portal glycæmia inhibits glycogenolysis in the liver. The syndrome may follow vagotomy, and possibly this is due to the known effect of vagotomy in producing a marked initial hyperglycæmia. It is self-limiting and patients should be treated with frequent small meals. A small amount of ephedrine or a lump of sugar at the onset of the symptoms should give complete relief.

The *early syndrome* is a much more difficult problem. We believe that a large factor is due to the stretch of the unsupported gastric remnant as caused by the weight of the food entering it, plus the weight of the afferent loop. Machella, in a series of interesting experiments, was able to reproduce the symptoms with oral and intrajejunal hypertonic glucose, and hypertonic protein hydrolysate. The distending of the jejunum with a balloon also reproduced the symptoms which he considered were due to excessive intestinal secretion, induced by a hypertonic solution. He thought that the relief which occurred on lying down was due to the flow-back of the jejunal contents into the stomach. We feel that jejunal distension cannot be the whole story. If this is so, total gastrectomy should give a very high percentage of the syndrome, which it certainly does not. Professor Croot was only able to find one case in 56 total gastrectomies at follow-up. The incidence in gastro-enterostomy and the Billroth I operation would approximate to that of the Polya operation, which is not the case. Entero-anastomosis has been carried out in this condition with benefit. This manœuvre effectively lessens the drag of the distended afferent loop. If jejunal distension is the main factor, this operation presumably should not give relief. Machella, furthermore, found that balloon distension, sufficient to produce the symptoms, caused pain, which is not a feature of the syndrome.

It is the clinical impression of many of the older surgeons that "early dumping" is the result of more and more radical gastrectomy, and it is precisely the higher operation which will reduce the supports for the gastric remnant. The two worst cases of the syndrome which I have ever seen were able to eat a full-sized meal without any symptoms when they were lying down. Even a small meal taken sitting up in these 2 cases produced symptoms of such a nature that they were unable to carry on with their work.

We believe that the condition can be, to a large extent, prevented by paying careful attention to the support of the remnant of the stomach, so that there is no undue gastric stretch when the food enters the stomach. The measures consist of putting a strong silk ligature around the mass of tissue surrounding the left gastric artery, and leaving the ends long, so that at the end of the operation the lesser curve at the angle of the anastomosis can be drawn up to this point. It may, furthermore, be necessary to put in supporting sutures between the lesser curve and the upper free edge of the gastro-hepatic omentum, and this method of support should be extended to the afferent loop of the jejunum (in the right-to-left antecolic Polya operation). We were able to compare 113 Polya-Hofmeister operations, done by two of us, without attempting to reconstruct supports for the gastric remnant, with 128 similar operations where close attention was paid to reconstruction of the supports. The former showed 13% of cases with early dumping, and the last 128, where support was carried out, showed an incidence of 1%. Several people have made attempts to devise a method of dealing with the condition when well developed. Vagotomy has been tried, and on the whole makes the condition worse. Entero-anastomosis between the afferent and efferent loops has given relief in some cases. Perman has carried out an operation to change the Polya type of anastomosis to the Billroth I type, with considerable success in a number of instances. Murphy of Bath has also done 3 of these conversion operations with complete relief of symptoms. We have attempted to cure the condition by supporting the lesser curve and the afferent loop along the lines outlined above in reference to its prevention.

We have done 9 such cases in this way, and 8 of them have obtained complete relief. They are able to eat normal-sized meals without difficulty again; usually they rapidly put on weight, and most of them have returned to full work. One patient has been a complete failure. He found he could take larger meals, but complained of symptoms two hours later, which we have not been able to alleviate. In some cases, symptoms have been relieved by procaine infiltration of the sympathetic plexus.

In view of the evidence, it seems likely that gastric stretch is at least a factor in the production of the syndrome, which is itself undoubtedly mediated by the sympathetic.