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THE DUMPING SYNDROME

I. FACTORS RESPONSIBLE FOR THE SYMPTOMS

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The dumping syndrome is one cause of an unsatisfactory result after the operation of subtotal gastrectomy. Symptoms come on towards the end of or shortly after meals, the main features being feelings of abdominal distension, often accompanied by borborygmi, and of extreme exhaustion with faintness, dizziness, sweating, and palpitations. These symptoms, which are exacerbated by standing and relieved by recumbency, last for some 30–45 minutes. A severe attack may culminate in the passage of a loose motion. The onset or fear of symptoms restricts the size of meals, and many patients notice that carbohydrate food is particularly apt to produce symptoms. The true incidence of the condition is difficult to assess, because in the first few weeks after gastrectomy many patients experience these symptoms to a greater or less extent, but in the majority a spontaneous improvement occurs. The syndrome may also, but less often, develop after gastro-enterostomy.

It was shown by Machella (1949) that in patients with the dumping syndrome the symptoms could be reproduced by the ingestion of hypertonic glucose, sucrose, laevulose, and casein hydrolysate solutions, and that similar symptoms could be produced in the normal subject by the introduction of hypertonic glucose into the jejunum. Roberts *et al.* (1954), studying 14 patients who had undergone gastrectomy (10 total, 4 subtotal), showed that a suitably adjusted oral dose of any one of several hypertonic solutions produced with the dumping symptoms a simultaneous fall in plasma volume, and this was thought to be the main cause of the symptoms. They postulated that this fall in plasma volume was due to a transfer of fluid into the gut as a result of the osmotic attraction of the hypertonic solutions. They suggested that in the absence of the pylorus the unduly rapid passage of hyperosmotic food and its derivatives into the small intestine causes a shift of fluid from the vascular compartment with a fall in circulating volume, and this in turn causes the dumping symptoms.

If this hypothesis is true it is difficult to understand why all patients do not experience dumping symptoms after partial gastrectomy. Accordingly, to clarify the role of a fall in plasma volume in the production of symptoms we have not only investigated the effect of hypertonic glucose in the production of symptoms and a fall in plasma volume, but have also observed the individual's response to a reduction in circulating volume produced by the application of thigh cuffs. These investigations were carried out in two groups of patients: (a) 16 patients upon whom the test was

performed before and at intervals after partial gastrectomy, and (b) 11 patients with the dumping syndrome. In some of these patients certain additional tests were also performed.

Plasma Volume Studies

The test was performed in the morning, with the patient semi-recumbent on a couch after eight to nine hours without food or drink. A 7-ml. sample of venous blood was taken, followed by intravenous injection of 4–6 g. of 0.5% aqueous solution of Evans blue. Further venous samples were taken 60 and 80 minutes later and immediately after the latter the subject drank, within one minute, 175 ml. of 50% glucose. Venous samples were taken at 10, 20, 30, 40, 60, 90, and 120 minutes thereafter, though in some cases the later samples were taken at slightly differing intervals.

The venous samples (7 ml.) were taken without stasis into siliconed syringes, and immediately transferred to tubes containing 7 units of dry heparin. The haematocrit of each sample was measured in a Wintrobe tube spun for 30 minutes at 3,000 r.p.m. in a governed centrifuge with an arm of 15 cm. radius to the bottom of the tube (1,500 g.). The remainder of each sample was spun to separate the plasma, in which the concentration of Evans blue was estimated in duplicate by a modification (Hobsley and Dew, 1958) of the extraction method of Korner *et al.* (1954). The apparent plasma volume at the time of each sample was calculated from the following formula, the standard being 1:500 dilution of the Evans blue solution:

$$\text{Pl. vol. (L)} = \frac{\text{standard reading} \times \text{dose given (g. 0.5\% E.B.)} \times 0.5}{\text{reading of sample}}$$

FIG. 1.—Haematocrit and apparent plasma volume in a normal man at rest. Evans blue injected intravenously at time zero. After 60 minutes Evans blue disappears from the plasma at a steady rate, giving a linear increase in the apparent plasma volume. Stagnation occurred while taking the 125-minute sample, giving a slightly inaccurate reading.

These values for the plasma volume were plotted against time. Under normal circumstances, between 60 and 200 minutes after the injection of Evans blue the plasma volume apparently increases in a linear fashion owing to the disappearance of dye from the plasma (Fig. 1). In our observations this line could be drawn by joining the first two and the last two points plotted, and any alteration in plasma volume after the ingestion of glucose was represented by a deviation of the other points away from this line. The size of the fall as a percentage of the resting plasma volume is given by the expression:

$$\frac{\text{apparent fall}}{\text{expected apparent plasma volume}} \times 100$$

An approximate estimate of the size of the change in plasma volume could also be obtained from the haematocrit readings by the application of the formula

$$x = \frac{H_{t_1}}{100 - H_{t_1}} \times \frac{100 - H_{t_2}}{H_{t_2}} \times 100$$

where x = the percentage of the original to which the plasma volume is reduced, H_{t_1} the initial haematocrit reading, and H_{t_2} that at the time of maximum fall of plasma volume.

Reduction of Circulatory Volume by Thigh Cuffing.

—With the patient sitting upright in a chair, pneumatic tourniquets were applied to both thighs. Pulse and blood-pressure were recorded in one arm at five-minute intervals until they were stable. The thigh cuffs were then inflated to a pressure 20 mm. Hg below the brachial systolic pressure. Ten minutes later the pressure in the cuffs was raised a further 10 mm. Hg for 10 minutes and then the cuffs were deflated. Pulse and blood-pressure were recorded throughout and thereafter until they returned to normal; any abnormal symptoms occurring were also recorded.

Clinical Material

Series 1 consists of 16 patients studied before and after operation. These patients were admitted for subtotal gastrectomy and, save for excluding those with pyloric stenosis, were unselected. In each case the test involving the application of thigh cuffs was performed at some time during the week before operation. The effect of oral hypertonic glucose on the plasma volume was estimated before operation, at some time during the period 7–14 days after operation, again about six months later, and in two patients on an intermediate occasion as well about three months after operation. The pre-operative test was omitted in three cases, and the late post-operative in three others. Details of the patients in this group are given in Table I.

Series 2 consists of 11 patients with the dumping syndrome after previous gastric surgery. Details of these patients, who were investigated similarly, are given in Table II.

Throughout the remainder of this paper the estimation of the plasma volume after the oral administration of 175 ml. of 50% glucose is referred to as a "plasma volume study," the various tests being described respectively as pre-operative, and early, intermediate, and late post-operative plasma volume studies. The term "fall in plasma volume" refers to the maximum fall, which always occurred 10 to 20 minutes after the ingestion of the glucose solution. The test involving the inflation of pneumatic cuffs around the thighs is referred to as cuffing.

TABLE I.—*Details of 16 Patients in Series 1, and the Tests Performed on Them*

Case No.	Age and Sex	Lesion	Operation	Cuffing	Plasma Volume Studies			
					Pre-operative	Early	Intermediate	Late
1	54 M	D.U.	A.P.	Yes	Yes	Yes	No	Yes
2	65 F	G.U., D.U.	B.	"	"	"	Yes	"
3	52 M	D.U.	A.P.	"	"	"	No	"
4	32 M	D.U.	A.P.	"	"	"	"	"
5	32 M	D.U.	A.P.	"	"	"	"	"
6	39 M	D.U.	A.P.	"	"	"	"	"
7	50 M	G.U.	B.	"	"	"	"	"
8	50 M	D.U.	A.P.	"	"	"	"	"
9	58 M	D.U.	A.P.	"	No	"	"	"
10	61 M	D.U.	A.P.	"	Yes	"	"	"
11	64 M	G.U.	B.	"	"	"	"	"
12	40 M	D.U.	A.P.	"	"	"	"	"
13	46 M	Carc.	R.P.	"	"	"	"	No
14	70 M	D.U.	A.P.	"	"	"	"	Yes
15	20 M	D.U.	B.	"	No	"	Yes	Yes
16	46 M	G.U.	A.P.	"	"	"	No	"

A.P. = Antecolic, Polya. R.P. = Retrocolic, Polya. B. = Billroth I. All the Polya operations were performed with the afferent loop to the lesser curve and a valve on the lesser curve.

TABLE II.—*Details of 11 Patients in Series 2, and the Tests Performed on Them*

Case No.	Age and Sex	Lesion	Operation	Time after Operation	Cuffing	Plasma Volume Test
17	52 F	Ac. G.U.	B.	2.2 years	No	Yes
18	42 F	G.U.	P.	3 "	Yes	"
19	49 M	G.U.	B.	15 months	"	"
20	58 F	D.U.	A.P.	12 "	"	"
21	48 M	D.U.	A.P.	5 "	"	"
22	62 F	D.U.	G-E	9 years	"	"
23	45 F	Ac. G.U.	A.P.	18 months	"	"
24	36 M	G.U.	B.	13 "	"	"
25	64 M	D.U.	A.P.	3 years	"	"
26	47 F	D.U.	A.P.	4 "	"	"
27	35 F	?	G-E	7 "	"	"

A.P. = Antecolic, Polya. B. = Billroth I. G-E = Gastro-enterostomy. The position of the loop in Case 18 was not known. See text for details of Case 27.

Results of Plasma Volume Studies

Pre-operative Studies.—Plasma volume studies were carried out before operation in 13 of the 16 patients in Series 1. In no case did the oral glucose cause any symptoms. The greatest fall in plasma volume observed was 7%, but usually it was less than 5%. Details are given in Table III, columns 3 and 4.

Post-operative Studies

Thirty-two plasma volume studies were carried out at the various times after operation in the 16 patients in Series 1 (see Table III). On eight occasions in four patients the hypertonic glucose produced typical dumping symptoms, and on all occasions at the time of these eight tests the patients were experiencing similar symptoms after their ordinary meals. On each occasion the symptoms coincided with the fall in plasma volume, which averaged 13.1% (range 8–20%). At the time of the remaining 24 tests no patient was experiencing post-prandial dumping symptoms, and none developed such symptoms after the glucose: the average fall in plasma volume in these tests was 7.2% (range 2–15%).

Early post-operative plasma volume studies were performed in all 16 patients. Four developed typical dumping symptoms within 15 minutes of drinking the glucose, the average fall of plasma volume in this group being 14.6%. The remaining 12 patients, who developed no symptoms, showed an average fall in plasma volume of 7.1%. Considering the results in relation to the size of the fall in plasma volume produced, four patients showed a fall of 10% or greater

TABLE III.—Results of Various Tests Performed on Patients in Series I. See Text for Grading of Results of Thigh-cuffing Tests

Case No.	Thigh Cuffing	Plasma Volume Tests										
		Pre-operative		Early			Intermediate			Late		
		% Fall Plasma Volume		% Fall Plasma Volume		Symptoms	% Fall Plasma Volume		Symptoms	% Fall Plasma Volume		Symptoms
		E.B.	Ht.	E.B.	Ht.		E.B.	Ht.		E.B.	Ht.	
1	+	5.0	7.5	<3	4.0	0	—	—	—	7.0	7.5	0
2	++	<2	2.0	18.0	19.0	+	10.5	15.0	+	4.0	6.0	0
3	+	5.0	1.0	4.0	4.0	0	—	—	—	3.0	4.0	0
4	+	2.0	2.0	8.0	8.0	+	—	—	—	11.0	8.0	+
5	0	2.5	3.5	12.5	16.0	++	—	—	—	12.0	9.5	++
6	0	4.5	2.0	6.5	7.5	0	—	—	—	5.5	4.0	0
7	0	0	0	8.0	11.5	0	—	—	—	9.0	11.0	0
8	0	5.0	5.5	8.0	5.5	0	—	—	—	7.0	6.0	0
9	0	—	—	3.0	6.0	0	—	—	—	5.5	4.0	0
10	0	7.0	6.0	6.0	6.0	0	—	—	—	9.5	10.0	0
11	0	4.0	5.0	9.0	11.0	0	—	—	—	8.0	9.0	0
12	0	7.0	4.0	9.0	8.0	0	—	—	—	10.0	10.0	0
13	+	3.5	4.0	7.0	8.0	0	—	—	—	—	—	—
14	0	4.0	5.0	8.0	11.0	0	—	—	—	—	—	—
15	+	—	—	20.0	14.0	++	12.5	10.0	+	5.0	5.5	0
16	0	—	—	15.0	16.5	0	—	—	—	13.0	13.0	0

E.B. = Fall in plasma volume as measured by Evans blue. Ht. = Fall in plasma volume calculated from haematocrit.

and three of these had symptoms. In 12 patients the fall was less than 10%, and of these only one had symptoms.

A late post-operative plasma volume study was performed on all but two (Cases 13 and 14) of the patients. The test was performed on 10 of the 12 patients who had no symptoms at the early test: none had symptoms on the late test, and there was no significant change in the fall in plasma volume (correlation coefficient=0.80; regression coefficient=1.055). Of the four patients who had symptoms after the early test, two (Cases 4 and 5) had not improved clinically by the time of the late test; in both these patients the late test again produced typical dumping symptoms and a fall in plasma volume of the same magnitude as at the early test. The results in Case 5 are illustrated in Fig. 2. The remaining two (Cases 2 and

still definite symptoms with smaller falls in plasma volume (10.5% and 12.5%), and at the late test the glucose produced no symptoms and minimal falls in plasma volume (4% and 5%). The results of the plasma volume tests on one of these patients (Case 2) are shown in Fig. 3.

FIG. 2.—Case 5. Graphs showing the fall in plasma volume after hypertonic glucose on early and late post-operative testing. Shortly after operation this patient began to experience typical post-cibal dumping symptoms, which did not improve with the passage of time. On each occasion the hypertonic glucose reproduced identical symptoms, the duration of which is shown by the line above the plasma volume curve. The fall in plasma volume is the same on each occasion. In this and subsequent diagrams the vertical arrow denotes the time at which the glucose was drunk.

15) had spontaneously recovered from their dumping syndrome before the time of the late test, and in each an intermediate test was performed at a time when recovery was only partial. Results in both cases were similar. The early test produced severe symptoms and a large fall in plasma volume (18% and 20% respectively), the intermediate test had less severe but

FIG. 3.—Case 2. Graphs showing the fall in plasma volume after hypertonic glucose on early, intermediate, and late post-operative testing. Shortly after operation this patient experienced typical post-cibal dumping symptoms, which soon began to improve and had disappeared by the time of the last test. The hypertonic glucose produced a progressively smaller fall in plasma volume and progressively fewer symptoms as the clinical condition regressed.

Plasma volume studies were carried out in the 11 patients of Series 2 (see Table IV). In all but one (Case 25) the hypertonic glucose produced symptoms identical with those the patients were experiencing after meals. In all these 10 patients symptoms coincided with a fall in plasma volume, which in nine was at least 10% and

TABLE IV.—Results of Various Tests Performed on Patients in Series 2

No.	Cuffing	Plasma Volume Test		
		% Fall		Symptoms
		E.B.	Ht.	
17	—	16.0	15.5	+
18	+	12.5	12.0	+
19	0	16.0	14.5	+
20	+	11.0	10.0	+
21	+	11.0	9.5	+
22	++	12.0	6.0	++
23	+	10.0	13.0	+
24	+	10.0	9.0	+
25	0	11.0	11.5	0
26	++	7.5	12.0	++
27	++	14.5	10.5	++

in the 10th 7.5% ; the average fall was 11.8% (range 7.5–16%). A typical result from one of these patients is shown in Fig. 4.

Case 27 is of particular interest, as in this patient circumstances allowed us to observe the effect of closing a gastro-enterostomy. Seven years previously this young woman had undergone a gastro-enterostomy elsewhere, for unknown reasons. Since that time she had experienced severe dumping symptoms and had lost 20 lb. (9 kg.) in weight. Hypertonic glucose reproduced her symptoms, with a fall in plasma volume of 14.5%.

FIG. 4.—Case 18. Graphs showing the increase in haematocrit and fall in plasma volume after hypertonic glucose in one of the patients with an established dumping syndrome. The test produced typical symptoms, the duration of which is shown by the horizontal line. The fall in plasma volume as shown by direct measurement was 12.5% and as calculated from the change in haematocrit was 12%.

A barium-meal examination showed no evidence of any abnormality in the stomach or duodenum, apart from the gastro-enterostomy. At operation no evidence of a gastric or duodenal ulcer was found and the gastro-enterostomy was closed. Since then she has eaten normally with no post-cibal symptoms and has gained 10 lb. (4.5 kg.) in weight in seven months. Nine weeks after operation hypertonic glucose produced no symptoms, and a fall in plasma volume of only 4%.

In both series together, plasma volume studies were performed at varying times after operation on 43* occasions in 27 patients. Twenty-five times the test produced no symptoms and an average fall in plasma volume of 7.2% (range 2–15%) (S.D. 3.1). On only one of these occasions was the patient experiencing dumping symptoms after ordinary meals, and this exception (Case 25) is described in detail below. On the remaining 18 occasions the test produced typical symptoms with an average fall in plasma volume of 12.5% (range 7.5–20%) (S.D. 3.32), and all the patients were, at the time of testing, experiencing dumping symptoms after meals. The difference in the fall in plasma volume between these two groups is highly significant ($t=4.84$; $n=40$; $p<0.001$). It is to be noted, however, that there is a clear overlap between the two groups, with no absolute correlation between the occurrence of symptoms and the size of the plasma volume fall.

Cuffing Test

In Series 1 the cuffing test was performed on all patients. In 10 patients it produced no symptoms except locally in the legs. In the remaining six inflation of the cuffs produced, after a varying interval, faintness, drowsiness, and sweating, progressing in one case to complete loss of consciousness with disappearance of

the radial pulse, necessitating termination of the test. The results in each case are shown in Table III, column 2. For recording purposes the severity of the response was classified into three grades: grade 0 no symptoms; grade +, definite symptoms; grade ++, severe symptoms, necessitating termination of the test. No clear correlation was noticed between the development of symptoms and alterations in pulse-rate and blood-pressure. These latter were so variable both in those who did and in those who did not experience symptoms that they are not reported here.

In Series 2 the cuffing test was performed on 10 of the 11 patients (Table IV, column 2). In two patients it produced no symptoms: one of these is Case 25, discussed below. Five of the remaining eight patients had definite symptoms and three had severe symptoms.

In both series together, the test was performed on 26 patients. The result was negative in 12 and positive in 14. It is to be noted that of these 14 patients 11 had dumping symptoms after the hypertonic glucose, while only 2 of the 12 who had no symptoms on cuffing had symptoms after the glucose. The significance of these observations is discussed later, but of particular importance in this respect are the detailed findings in Case 25.

Case 25.—A man aged 64 underwent a partial gastrectomy for a chronic duodenal ulcer three years ago. Ever since, he has been restricted to small meals by a feeling of epigastric distension, followed by exhaustion, causing him to lie down and sleep for 15 to 20 minutes. These attacks follow all but the smallest meals, and after severe attacks he passes a loose motion. 175 ml. of 50% glucose by mouth produced a fall in plasma volume of 11.5%, but no symptoms. However, 225 ml. of 50% glucose also given with the patient in a semi-recumbent position reproduced his postprandial symptoms and caused a fall in plasma volume of 14.5%. Cuffing did not produce symptoms, neither did 175 ml. of 50% glucose taken sitting in a chair. However, when this quantity of glucose was taken sitting, with the simultaneous performance of a cuffing test, marked symptoms of faintness and exhaustion, worse than those following a meal, came on after 12 minutes. These symptoms were quickly relieved by deflating the cuffs and raising the patient's legs.

Plasma Volume Studies After a Meal

In two patients in Series 2 (Cases 20 and 26), in whom the fall in plasma volume after hypertonic glucose was respectively 11% and 7.5%, changes in plasma volume were also measured after a meal. In each instance the patient was sitting at a table throughout the procedure, which was the same as that previously described except that a meal was taken instead of hypertonic glucose. The meal was of the breakfast type (cornflakes, toast, tea, sugar, fruit juice, milk, marmalade) with carbohydrate predominating. In each case the size of the meal was the maximum that the patient could eat,

FIG. 5.—Case 20. Graph showing a fall in plasma volume of 11% after eating a meal containing 75 g. of carbohydrate. After the standard dose of hypertonic glucose this patient had a fall in plasma volume of 11%.

*This total includes only the first of two tests performed in Case 27, as the second was done after closure of the gastro-enterostomy.

and in each case it produced marked symptoms. The patient in Case 20 took a meal containing 75 g. of carbohydrate in 15 minutes, and in Case 26, 55 g. in 10 minutes. After the meal each patient experienced typical marked dumping symptoms, which coincided with falls in plasma volume of 11% and 8% respectively. Fig. 5 shows the results obtained in Case 20.

Replacement Infusion Experiments

On four occasions in three patients from Series 2 an intravenous infusion was given after the ingestion of 175 ml. of 50% dextrose. All three patients had had typical symptoms during a standard plasma volume study. The volume infused was equal to the fall in plasma volume observed during this previous study. The infusion was started immediately on drinking the glucose and was completed in 10 to 15 minutes, a Martin pump being used to obtain the necessary infusion-rate.

In Case 17, on the first occasion 250 ml. of normal saline was infused in 10 minutes without affecting the symptoms. When the experiment was repeated four days later using dextran ("dextrans") instead of normal saline the patient experienced no systemic symptoms such as dizziness, sweating, and exhaustion, only slight nausea and upper abdominal discomfort. Case 19 was given 400 ml. of dextran in 15 minutes and experienced no symptoms. The third patient (Case 22) was given 300 ml. of dextran in 10 mins, resulting in partial but definite alteration of symptoms, especially in that she experienced no palpitations, sweating, or tiredness.

Discussion

Many observers have reported that in patients with the dumping syndrome the symptoms can be reproduced by the oral administration of hypertonic glucose. Our observations have confirmed this, and a standard dose of hypertonic glucose has been used as the basis of an investigation designed to test the hypothesis that the major factor in the production of these symptoms is a temporary fall in the plasma volume.

In general our results support this hypothesis. The average fall in plasma volume in those patients who had symptoms after the hypertonic glucose was significantly greater than in those patients who did not, though there was a distinct overlap between the two groups. Emphasizing this lack of correlation, Webber *et al.* (1957) concluded that a fall in plasma volume is not "a significant factor in the aetiology of the dumping syndrome." However, three of our observations make it difficult to accept this conclusion. First, in three patients experiencing typical symptoms after the test dose of glucose, the rapid intravenous infusion of an appropriate volume of a plasma expander prevented the development of systemic symptoms. Secondly, case 27, while experiencing dumping symptoms, had a fall in plasma volume of 14.5% after the test dose of glucose: after closure of her gastro-enterostomy, which cured her symptoms, this fall was reduced to 4%. Thirdly, in two patients the spontaneous regression of the dumping syndrome during six to eight months following operation was accompanied by a progressive diminution in the fall in plasma volume after the test dose of glucose. These facts suggest that the symptoms are indeed caused by a fall in plasma volume, and that a further factor must be sought to account for the discrepancies.

The results of the thigh-cuffing experiments suggest that this factor is the individual variation in the response to a sudden fall in circulatory volume. The application of pneumatic cuffs to the thighs traps 400–700 ml. of blood in the legs in 15 to 20 minutes, and this produces the same effect as the venesection of an equal quantity of blood (McMichael and Sharpey-Schafer, 1944). By the use of this test it was possible to assess the response of our patients to a sudden fall in circulatory volume of a size similar to that produced in many by the oral hypertonic glucose.

The application of thigh cuffs showed that 12 patients were insensitive to a sudden reduction in circulating volume. Twenty-one post-operative plasma volume tests were performed on these patients, the falls observed varying between 3 and 16%. Only two of these patients (Cases 5 and 19) had symptoms after the glucose, and, on the three occasions of testing, their fall in plasma volume was 12.5%, 12%, and 16%. Fourteen patients were sensitive to thigh cuffing, four to the extent that the test had to be cut short. Twenty-two post-operative plasma volume tests were performed on this group of patients, the falls in plasma volume varying between 3 and 20%. On 14 occasions the glucose produced typical symptoms with falls in plasma volume of 7.5–20%; on the remaining eight occasions the falls ranged between 3 and 7%. In other words, regardless of the patient's response to cuffing, a small fall in plasma volume (not greater than 7%) was never accompanied by symptoms, whereas if the fall was large (greater than 7%) symptoms always occurred in those sensitive to cuffing, and, except for two patients, never in those insensitive (Fig. 6). Presumably in these two patients the cuffing did not produce a fall in plasma volume as great as did the glucose.

FIG. 6.—Diagram showing the relationship between, on the one hand, the sensitivity of the patient to a sudden reduction in circulating volume (by thigh cuffs) and, on the other, the size of the fall in plasma volume and the production of symptoms after hypertonic glucose. Each symbol represents not a patient but a single post-operative plasma-volume test, and blocking of the symbol indicates that the test produced symptoms. The upper line represents the results in those patients insensitive to cuffing, the lower in those sensitive. When the fall in plasma volume is small symptoms never occur, irrespective of the response to cuffing. When the fall is larger (7%) symptoms always occurred in those sensitive to cuffing, but with three exceptions (in two patients) not in those insensitive.

It would therefore appear that the development of symptoms after hypertonic glucose depends upon the interaction of two factors, the size of the fall in plasma volume and the resistance of the patient to such a fall. This is illustrated well by two individual cases. In Case 16 the patient had no symptoms on thigh cuffing and no symptoms with his early and late post-operative plasma volume tests, despite falls in plasma volume of respectively 15% and 13%; he had no post-cibal

symptoms. In contrast, in Case 26 thigh cuffing produced definite symptoms within two minutes and had to be cut short at eight minutes as the patient was pale, sweating, and greatly distressed; a plasma volume test produced severe symptoms though a fall in plasma volume of only 7.5%; she had severe post-cibal dumping symptoms. This interaction between the size of the fall in plasma volume and the patient's ability to withstand such a fall is further emphasized by the studies in Case 25. This man was resistant to the fall in plasma volume produced by cuffing or the standard dose of hypertonic glucose, but when a large enough fall was achieved by a combination of these methods or by increasing the dose of glucose typical symptoms ensued.

Heretofore the occurrence of symptoms has been correlated with changes in plasma volume, though the precise factor involved must be a change in total blood volume. The difference between these two is probably small, as shown by the haematocrit estimations. On the assumption that there was no change in the circulating red-cell volume, alterations in plasma volume calculated from changes in the haematocrit corresponded fairly closely to those derived from the Evans blue estimations. However, conclusions concerning alterations in the total blood volume based on haematocrit and plasma volume readings are difficult to interpret (Mollison, 1956). For these reasons the production of symptoms has been correlated with fall in plasma volume, which can be measured accurately.

Though hypertonic glucose is an artificial stimulus, it is clear from our observations on two patients after a normal meal that the meal and the glucose produce similar falls in plasma volume with similar symptoms. As shown, these symptoms can be largely prevented by a suitable replacement infusion, and it may be concluded that the systemic symptoms of the dumping syndrome as seen clinically are due to a temporary post-cibal fall in circulating volume in patients sensitive to such a fall. There can be no reasonable doubt that this fall is due to a transfer of fluid into the intestines as the result of osmotic forces, as there is direct proof that such a transfer occurs when hypertonic glucose is introduced into the human intestine (Abbott *et al.*, 1938).

As our pre-operative tests show, the introduction of hyperosmotic solutions into the stomach causes only minimal falls in plasma volume. The reason for this is twofold: first, hyperosmotic solutions are only diluted slowly while in the stomach (Hunt *et al.*, 1951); and, secondly, such solutions delay gastric emptying, as first shown by Carnot and Chassevant (1905) working on dogs, and confirmed in humans by, amongst others, Apperly (1926). The resulting slow depletion of the plasma volume is readily compensated by a passage of fluid from the interstitial space. It would therefore appear that interference with the normal control of gastric emptying is the essential factor in the causation of the dumping syndrome.

Our observations lead to the conclusion that the symptoms of the dumping syndrome are due to the passage of an hyperosmotic solution into the upper intestine, causing in some patients a rapid transfer of fluid from the vascular compartment into the gut; this results, on the one hand, in intestinal distension and, on the other, in an abrupt fall in circulating volume which, in subjects intolerant of such a fall, gives rise to the systemic symptoms. This hypothesis provides a clear

explanation of the well-established clinical features of the syndrome. The increase in fluid in the gut is responsible for the feeling of repletion and distension, with excessive peristalsis (Glazebrook and Welbourn, 1952) and, in severe cases, the passage of a loose stool. The fall in plasma volume is responsible for the faintness and exhaustion with pallor, sweating, and palpitations, thus explaining why these symptoms are relieved by reclining or lying, and are less prominent if the meal is eaten in a recumbent position. Obviously the greater the size of the meal the greater the osmotic load and so the worse the symptoms: it is for this reason that patients can take only small meals, and undoubtedly this is a major factor in their characteristic loss of or failure to gain weight. Apart from its actual size, the tendency of a meal to produce dumping symptoms also depends upon its osmolarity when in solution. This explains why carbohydrate, which is rapidly broken down into a large number of small glucose molecules with a corresponding rise in osmotic pressure, is particularly associated with the syndrome.

It remains to explain why, following a gastrectomy, only some patients show a fall in plasma volume after taking hypertonic glucose, and also why, in those who spontaneously recover from the dumping syndrome, this fall diminishes *pari passu*. These two facts are probably related to the rate at which glucose is absorbed from the intestine, and are considered in a further article.

Summary and Conclusions

The effects of oral hypertonic glucose in producing dumping symptoms and changes in plasma volume were observed in two groups of patients: (a) 16 patients undergoing partial gastrectomy, in whom the test was performed before and at intervals after operation; and (b) 11 patients with the dumping syndrome. In all but one patient the effect of a sudden reduction in circulatory volume by the application of thigh cuffs was also observed.

In all but one of the patients who at the time of testing were experiencing post-cibal dumping symptoms the hypertonic glucose reproduced these symptoms; the glucose never produced symptoms in those who were symptom-free after meals.

The hypertonic glucose produced a fall in plasma volume which was significantly greater in those with than those without symptoms, but there was a definite overlap between the two groups. The results of the thigh-cuffing observations showed that this overlap was due to the differences in the individual response to a sudden fall in circulatory volume.

Additional evidence linking the systemic symptoms of the dumping syndrome with the fall in plasma volume was provided by replacement infusion experiments, by observations on two patients who spontaneously recovered from the syndrome, and by observations on a patient before and after closure of a gastro-enterostomy.

It is concluded that the dumping syndrome is due to the passage of hyperosmotic solutions into the upper intestine, causing in some patients a rapid transfer of fluid from the vascular compartment into the intestine. This results in intestinal distension and an abrupt fall

in circulating volume, which, in subjects intolerant of such a fall, gives rise to the systemic symptoms.

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THE DUMPING SYNDROME

II. CAUSE OF THE SYNDROME AND THE RATIONALE OF ITS TREATMENT

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In the previous communication the role of a fall in plasma volume in the production of the dumping syndrome was described (Le Quesne *et al.*, 1960). It was shown that the fall in plasma volume following the ingestion of hypertonic glucose by patients who had undergone partial gastrectomy varies greatly from individual to individual, and in some with the passage of time. It was further shown that the development of symptoms depends not only upon the size of the fall in plasma volume but also upon the individual's response to a sudden reduction in circulating volume. In the course of these studies we noted that the coincident changes in blood-sugar concentration were far from constant. In the present paper we propose to examine the relation of the changes in blood-sugar concentration to those in plasma volume, and to describe further observations, made after the injection of insulin, which clarify this relationship. From these observations we have been able to devise means, by the use of insulin, of reducing the fall in plasma volume produced by hypertonic glucose or by meals, and thus of relieving the dumping syndrome.

Procedure and Material

Changes in plasma volume and blood-sugar concentration were estimated after the drinking of 175 ml. of 50% glucose. The test involved the taking of venous samples before and at 10 minutes after taking the glucose, and at varying intervals thereafter. Details of the conditions of the test have been given previously (Le Quesne *et al.*, 1960).

Observations were also made of the effects of the prior injection of insulin on the changes in plasma

volume following (a) 175 ml. of 50% glucose by mouth, and (b) a carbohydrate meal.

The change in plasma volume was estimated by the use of Evans blue: details of the methods involved are given in our previous communication. The blood-sugar concentration was measured by the method of Haslewood and Strookman (1939), as described by Varley (1958).

Changes in plasma volume and blood-sugar concentration were estimated on 35 occasions in 28 patients, who fell into two groups. Group A consists of 13 patients admitted to the wards of the department for subtotal gastrectomy for benign peptic ulcer. These patients are the same as those in Series 1 in our previous paper, in which full details concerning them are given; Cases 4, 11, and 12 are omitted here, as blood-sugar estimations in them are not available. In the 13 patients post-operative studies were performed on 26 occasions; on seven of these the blood glucose was not estimated, leaving 19 for analysis here. Group B consists of 15 patients admitted for investigation of their dumping syndrome: in 14 this followed partial gastrectomy and in one a gastro-enterostomy. Of these 15 patients, seven form part of Series 2 in our previous communication; Cases 17, 20, 23, and 26 are omitted because again blood-sugar estimations are not available. Details of the remaining eight patients are given in Table I.

TABLE I.—Details of the Eight Patients in Group B Additional to Those Described in Our Previous Communication

Case No.	Age	Sex	Lesion	Operation	Time after Operation
28	53	F	G.U.	B.	7 months
29	73	M	D.U.	A.P.	26 "
30	47	M	Carc.	T.G.	5 years
31	54	M	G.U., D.U.	A.P.	5 "
32	71	F	D.U.	B.	3 "
33	43	M	D.U.	A.P.	2 "
34	55	F	Chol.	A.P.	8 months
35	77	M	D.U.	P. & V.	5 "

G.U.=Gastric ulcer. D.U.=Duodenal ulcer. Chol.=Recurrent cholangitis, from cholechocho-duodenal fistula. B.=Billroth I gastrectomy. A.P.=Antecolic Polya gastrectomy. T.G.=Total gastrectomy. P.&V.=Pylorotomy and vagotomy.

The effect of the prior injection of insulin was observed in seven patients following the ingestion of 175 ml. of 50% glucose, and in three patients following a carbohydrate meal. Of these 10 patients, seven were drawn from those described in our previous paragraph. The remaining three (Cases 38, 43, and 44) were admitted for investigation of their dumping syndrome: in two (Cases 38 and 43) the fall in plasma volume was calculated from changes in the haematocrit (see previous paper) and not by direct measurement.

Observations on Blood Sugar and Plasma Volume

After ingestion of the test dose of 175 ml. of 50% dextrose it was noted that the greater the fall in plasma volume the more rapid and pronounced was the rise in blood sugar. Typical blood-sugar curves associated with a large and small fall in plasma volume are shown in Fig. 1.

The data on blood sugar and plasma volume for all the patients were analysed in various ways in an attempt to discover any correlation between the two. No correlation could be found between, on the one hand, either the greatest height to which the blood sugar rose or the time taken to return to its resting level, and, on the other, the fall in plasma volume. There is, however, a clear correlation between the fall in plasma volume