Further Studies on the Pathogenesis of the Postgastrectomy Syndrome *

GEORGE H. PEDDIE, M.D., GEORGE L. JORDAN, JR., M.D.,
MICHAEL E. DE BAKEY, M.D.

Houston, Texas

From the Cora and Webb Mading Department of Surgery, Baylor University College of Medicine, and the Veterans Administration Hospital

SURGICAL PROCEDURES which alter the normal passage of food from the stomach into the intestines may produce physiologic or anatomic changes which cause symptoms not present prior to operation. In 1913, Hertz [1] noted postprandial symptoms in some patients treated by gastroenterostomy, but his observation stimulated little interest at that time. In 1922, Mix [5] described pooling of barium in the small bowel following gastroenterostomy and coined the term "dumping." As he described it, "dumping" referred to a roentgenographic observation, but this expressive term was rapidly incorporated into medical terminology, and currently it is often used as an inclusive term for all postgastrectomy symptoms. However, recent investigations have led to the delineation of several different postgastrectomy syndromes, so that it is necessary to use more specific terminology. There has been a tendency to limit the term "dumping" to that syndrome which occurs in the immediate postprandial period and is characterized by nausea, fullness and churning in the epigastrium, weakness, sweating, pallor and tachycardia. In severe cases, vomiting and diarrhea ensue. To differentiate it from a similar symptom complex which occurs two to four hours postprandially and is the result of a rebound hypoglycemia, this symptom complex has also been designated the "early postgastrectomy syndrome."

Many theories have been advanced to explain the pathogenesis of this most common of all postgastrectomy sequelae. There is little objective evidence to indicate that gastritis, achlorhydria, active disease in the afferent loop, hyperglycemia, hypoglycemia, distention of the gastric stump, toxemia, jejunitis or adrenal malfunction can be incriminated. Some physicians maintain that the symptoms are psychologic and that it is possible to predict which patients will have this difficulty prior to operation. The evidence to be presented does not support the importance of psychologic factors in pathogenesis. However, it is true that patients with psychoneurotic tendencies are those most likely to be incapacitated when symptoms occur, for such patients tend to magnify all symptoms while the stoic individual must experience considerable discomfort before he complains.

Currently the theories which have some objective evidence to support them concern alterations in postprandial fluid and electrolyte patterns. Smith [8] was one of the first to demonstrate that a fall in the serum potassium concentration of 0.5 to 1.5 mEq./L. may occur in the postprandial period. He also observed that electrocardiographic changes take place during the symptomatic period which are similar to those which occur in the presence of hypopotassemia. It was postulated that rapid absorption of glucose, leading to the deposition of glycogen, caused the movement of potassium into the cells and this sudden drop in the

* Submitted for publication April 25, 1957.

serum concentration produced symptoms and electrocardiographic changes.

Machella [4] suggested that undigested food passing directly into the jejunum may exert an osmotic pressure which caused the rapid influx of fluid into the bowel. This resulted in distention of the bowel and thereby initiated neurogenic reflexes which produced the vasomotor symptoms. Wells and Welbourn [9] agreed that a rapid influx of fluid into the bowel occurred during the symptomatic period, but they were unable to demonstrate distention of the gut. Instead they found increased motility and postulated that hypermotility rather than distention was responsible for reflex vasomotor symptoms.

Roberts [7] and her associates pursued this concept one step further and reported that an acute drop in blood volume occurs coincident with the passage of fluid into the bowel. Thus, while there was agreement that fluid passes rapidly into the bowel, it appeared that where it went was less important than where it had been, insofar as the production of symptoms was concerned.

Previous studies in this laboratory support the concept of a fluid exchange during the symptomatic period and our findings agree with those of Wells and Welbourn that the bowel responds with hypermotility rather than distention. However, it is not always possible to correlate the period of hypermotility with the symptomatic period, and the present study was undertaken to gain additional information concerning the fluid and electrolyte changes described by Smith and Roberts.

Material and Methods

A total of 33 adult male patients were studied at intervals varying from two months to four years following distal subtotal gastrectomy. Thirty-two patients were treated for benign gastroduodenal ulceration, while one patient was treated for a malignant gastric polyp. Fifteen of these patients were asymptomatic and able to ingest any food or liquid desired without postprandial distress of any type. The other 18 experienced postprandial symptoms consisting of weakness, elevation of pulse rate, and nausea in each instance. In the patients with severe symptoms there was pallor, sweating and diarrhea. Approximately 85 per cent of the patients in both the symptomatic and asymptomatic groups had gastro-intestinal continuity re-established with a gastrojejunostomy, while in the remaining patients a gastroduodenostomy was employed. The following tests were performed:

1. **Serial Determinations of Plasma Volume:** The method described by Roberts was used. Following the intravenous injection of 5 ml. of T-1824 dye, samples of blood were drawn at 30 minute intervals during a two-hour period to establish the disappearance curve of the dye. A liquid meal containing eight ounces of milk, six ounces of 40 per cent glucose and two ounces of Ediol® was then fed, and postprandial samples for blood volume determinations were drawn at intervals of ten, 20, 30, 45, 60, 90 and 180 minutes. This test was used in five asymptomatic and 16 symptomatic patients.

2. **Serial Determinations of Serum Potassium Concentration:** Samples of blood for serum potassium concentration were drawn in the fasting state and at the same intervals following ingestion of the liquid meal as noted for blood volume determinations. This test was used in seven asymptomatic and 11 symptomatic patients.

3. **Electrocardiographic Recordings:** Utilizing leads 1, 2 and 3, serial electrocardiographic recordings were made under the same conditions as were determinations for serum potassium concentrations in nine asymptomatic and eight symptomatic patients. All three tests were performed simultaneously in seven patients. Two tests were performed in an additional nine and only one in the remaining 17 (Tables 1 and 2).

TABLE 1. *Alterations in Plasma Volume, Serum Potassium Concentration and Electrocardiographic Tracings in Asymptomatic Postgastrectomy Patients After the Ingestion of a Hypertonic Liquid Meal*

Patient	Maximum Change in Plasma Volume (ml.)	Electrocardiographic Alteration	Maximum Change in Serum Potassium Concentration (mEq./L.)
1			0.84
2			1.56
3			0.52
4			0.25
5			1.44
6		+	
7		0	
8		+	
9		+	
10		0	
11	8	0	
12	61		
13	100	+	
14	100	0	0.85
15	191	0	0.70

TABLE 2. *Alterations in Plasma Volume, Serum Potassium Concentration and Electrocardiographic Tracings in Symptomatic Postgastrectomy Patients After the Ingestion of a Hypertonic Liquid Meal*

Patient	Maximum Change in Plasma Volume (ml.)	Electrocardiographic Alteration	Maximum Change in Serum Potassium Concentration (mEq./L.)
1			1.50
2		+	
3	0		
4	0		1.25
5	96	+	1.30
6	178	+	1.05
7	214	+	1.44
8	247		1.29
9	345		
10	348		0.85
11	471		
12	506	+	
13	520	+	0.52
14	528	+	
15	548		0.77
16	556		
17	636		0.50
18	697	+	0.71

Results

1. Alterations in Plasma Volume: A slight decrease in plasma volume was recorded in the immediate postprandial period in each of the five asymptomatic postgastrectomy patients tested, ranging from 8 to 191 ml. Two of the symptomatic patients demonstrated no postprandial fall in plasma volume, whereas in 14 there was a decrease ranging from 96 to 697 ml. (Fig. 1). In two of the latter patients, the fall did not exceed that observed in asymptomatic patients, while in 12 it exceeded 200 ml. The average fall for the entire symptomatic group was 368 ml.; with exclusion of the two patients having no change, the average decrease was 420 ml. In most instances the onset of the fall in plasma volume was recorded in the ten-minute postprandial sample, and always within 20 minutes. The maximum change occurred at 20 to 45 minutes after ingestion of the meal and a return to the preprandial level usually occurred within one hour. In each instance where a fall in blood volume occurred in a symptomatic patient, there was good correlation between the duration of the change in blood volume and the period of symptoms.

2. Serum Potassium Determination: A postprandial decrease in the serum potassium concentration occurred in each of the patients studied (Fig. 2). In the asymptomatic patients, the range was from 0.25 to 1.56 mEq./L. with an average of 0.88 mEq./L. while the range in the symptomatic patients was from 0.50 to 1.50 mEq./L. with an average of 0.97 mEq./L. The concentration began decrease at ten to 20 minutes postprandially. In some instances there was a return to fasting level within two hours, but in many instances there was a steady fall with the lowest volume being recorded in the one and one-half or two-hour sample. Correlation with the onset of the symptomatic period was good, but symptoms often abated while the serum potassium concentration remained low. There was

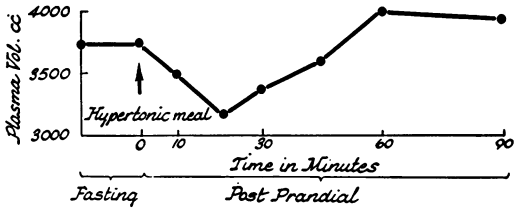

FIG. 1. Postprandial fall in plasma volume during symptomatic episode.

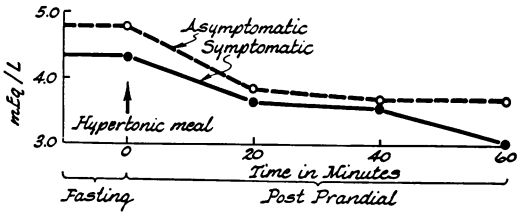

FIG. 2. Comparison of the postprandial fall in serum potassium concentration in asymptomatic and symptomatic patients.

an inverse relation of the magnitude of fall in serum potassium concentration to the magnitude of plasma volume decrease (Fig. 3).

3. Electrocardiographic Recordings: This test was performed in eight symptomatic patients, and each showed changes similar to those reported by others, consisting of sinus tachycardia, inversion of the T-wave, with a development of a U-wave in severe cases, and occasionally elevation or depression of the S-T segment. The electrocardiographic alterations correlated well in time, though not absolutely, with the changes in blood volume and the symptomatic period, but there was a return toward the preprandial electrocardiographic pattern while the serum potassium concentration remained depressed. Five of the nine asymptomatic patients exhibited no electrocardiographic changes, but there was an increase in heart rate in four, and three of these showed T-wave changes similar to those observed in the symptomatic patients (Fig. 4).

Discussion

In the original studies reported by Roberts and her associates, symptomatic patients had been subjected to a total gastrectomy and the asymptomatic control patients were those with an intact stomach. In the experiments reported herein, all of the patients, both the symptomatic and the asymptomatic controls, were treated by subtotal gastrectomy.

Our results in general support the concept that a postprandial fall in blood volume is an important feature in the pathogenesis of the dumping syndrome, for only in symptomatic patients were the plasma volume changes marked. Nevertheless, we feel that symptoms referable to the gastrointestinal tract are better explained as a result of fluid passing into the bowel rather than the fall in blood volume, and our concept of the pathogenesis of the dumping syndrome in most patients is as follows:

The passage of undigested liquids and foods into the jejunum stimulates in certain individuals a rapid passage of fluid from the blood stream into the lumen of the small intestine. The loss of fluid from the vascular bed results in a decreased blood volume which may be sufficiently great to cause symptoms of weakness, sweating and palpitation. The symptoms related to the gastro-intestinal tract, particularly diarrhea, are probably due to the filling of bowel with fluid, stimulating hyperperistalsis (Fig. 5). Studies of emptying of the gastric remnant indicate that the absolute emptying time is not the primary factor in initiating this train of events, for ingested liquids enter the jejunum within one minute in all patients with a normally functioning gastrojejunal stoma, and roentgenographic studies prove that some patients tolerate extremely rapid emptying of the gastric remnant without experiencing symptoms.[2] Rather, it is a response of the jejunum to undigested food that is significant. Nevertheless, in the symptomatic patient the speed of emptying of the gastric remnant does play an important role in that it governs the amount

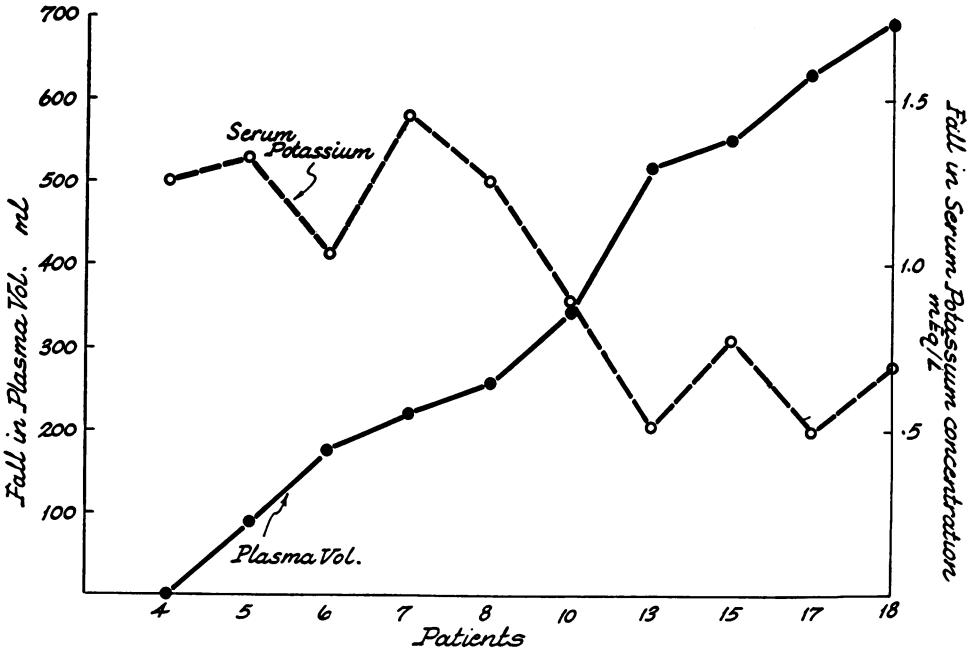

FIG. 3. Inverse relation of the magnitude of fall in serum protein concentration to the magnitude of the fall in plasma volume.

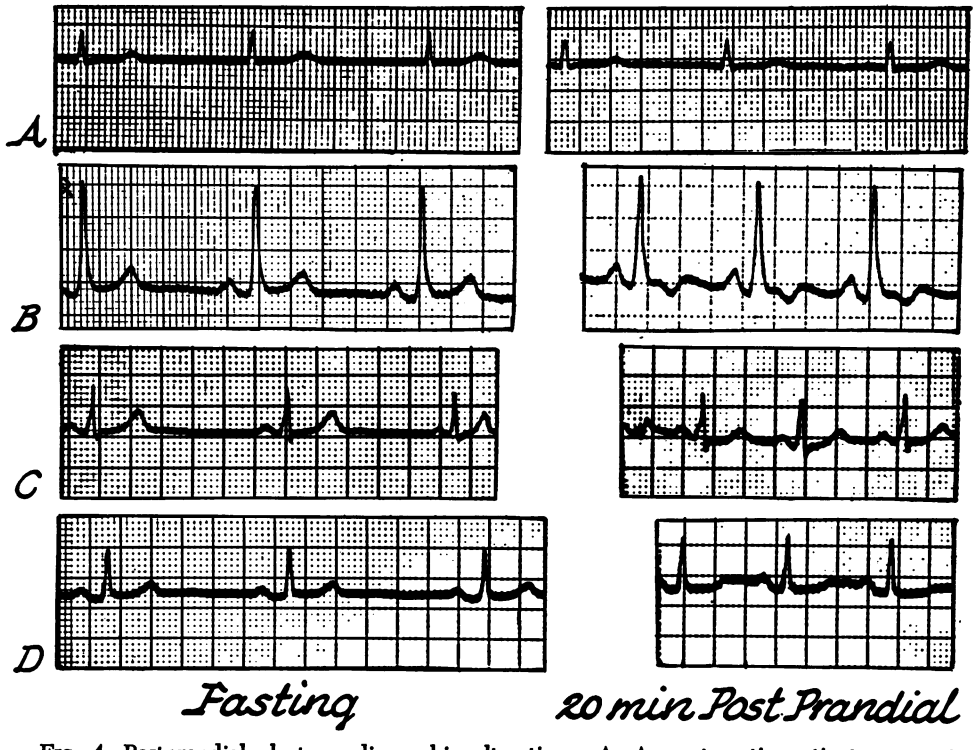

FIG. 4. Postprandial electrocardiographic alterations: A. Asymptomatic patient; no postprandial alteration. B. Asymptomatic patient; increased rate, depression of S-T segment and inversion of T-wave. C. Symptomatic patient; increased rate, lowering of T-wave. D. Symptomatic patient; increased rate, depression of T-wave, appearance of U-wave.

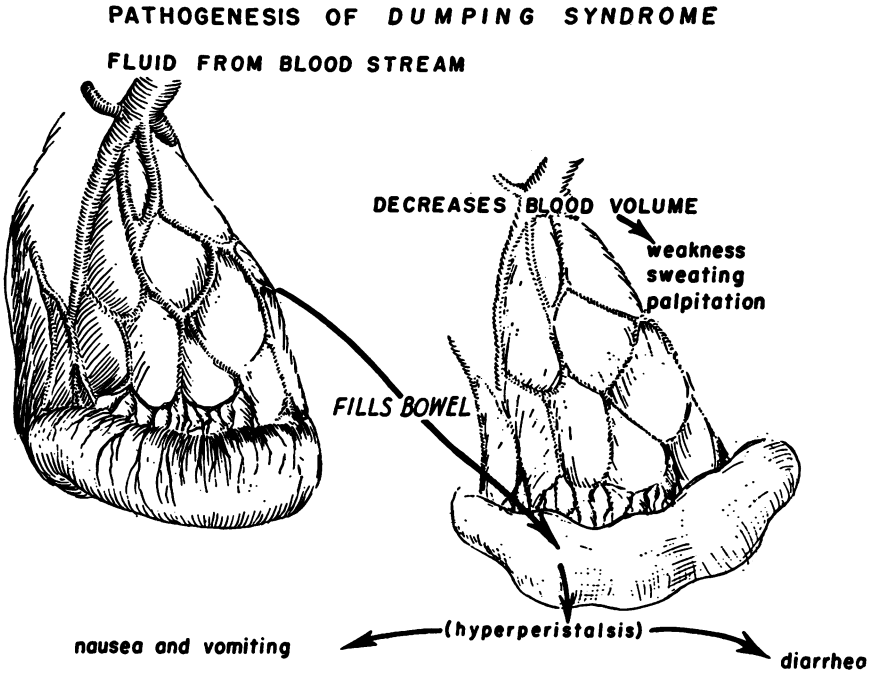

FIG. 5. Diagrammatic representation of the pathogenesis of the "dumping syndrome." This train of events is initiated by the presence of undigested food in the jejunum.

of stimulating material which will be present in the jejunum at any given period.

As noted above, we are unable to explain the symptoms experienced in all of our patients on the basis of this hypothesis, for two patients showed no change in blood volume despite classical symptoms. Therefore, we are led to the conclusion that, whereas the hypothesis presented herein probably represents the pathogenesis in most cases, certain patients may have similar symptoms from other causes. The fact that the fall in serum potassium concentration occurred in asymptomatic as well as symptomatic patients, originally led us to the conclusion that this change was of no significance, insofar as the production of symptoms was concerned. However, it was noted that the decrease in serum potassium concentration was to a large degree inversely proportional to the decrease in plasma volume in the symptomatic patients, so that in all four patients with a plasma volume decrease of less than 300 ml. the fall in serum potassium concentrations exceeded 1 mEq./L. A simple explanation may be that a relatively higher concentration of serum potassium will be recorded following a given loss of potassium from the blood stream if a fall in blood volume occurs concurrently; but, the studies on asymptomatic patients do not support this concept, and the possibility exists that an occasional patient may develop symptoms as a result of a sudden decrease in serum potassium concentration exceeding 1 mEq./L.

The two symptomatic patients who exhibited only slight changes in blood volume are particularly interesting in that both had very low total blood volumes. It is possible that in patients with low blood volumes, minor changes may be sufficient to produce symptoms. One of these patients has been transfused so that his blood volume returned to normal and symptoms have been relieved in this manner.[8] This is taken to

be further support of the concept that changes in blood volume are important in the pathogenesis of this syndrome.

Our data confirm the observations of others that electrocardiographic alterations are uniformly present in patients with the dumping syndrome, and in general there is fairly good correlation in time between the electrocardiographic alterations and the alterations in blood volume. However, it has not been proved that these alterations are a direct result of the changes in blood volume. Pulvertaft [6] noted some electrocardiographic changes in patients during periods when they were not symptomatic. In our asymptomatic patients, electrocardiographic changes were recorded in one-third, and in one patient the changes were as great as those observed in many of the symptomatic patients. This patient had a normal blood volume, and the maximum change in plasma volume in the postprandial period was 100 ml. Consequently, it would appear that the pathogenesis of the changes in the electrocardiogram warrant further investigation.

Summary

1. The postprandial alterations in plasma volume, serum potassium concentration and electrocardiographic recording were studied in patients with the "dumping syndrome" following subtotal gastrectomy and in asymptomatic postgastrectomy patients.

2. Fourteen of the 16 symptomatic patients demonstrated a decrease in postprandial plasma volume averaging 420 ml. A decrease was also observed in five symptomatic patients averaging 92 ml.

3. A postprandial fall in serum potassium concentration was recorded in each patient studied, the average being 0.88 mEq./L. in the asymptomatic patients and 0.97 mEq./L. in the symptomatic patients.

4. Electrocardiographic alterations were observed in each of the symptomatic patients studied and in four of the nine asymptomatic patients.

5. It is concluded that the rapid passage of fluid from the blood stream into the intestine is an important feature in the pathogenesis of the dumping syndrome in most patients, but two of the patients in this study exhibited identical symptoms without demonstrating this phenomenon.

6. It is possible that alterations in the concentration of serum potassium may be important in the production of symptoms in the occasional patient.

Acknowledgment

The authors are indebted to Dr. W. Morse Hicks, Jr. for aid in interpreting electrocardiographic data.

Bibliography

1. Hertz, A. F.: The Cause and Treatment of Unfavorable After Effects of Gastroenterostomy. Ann. Surg., **58**:466, 1913.
2. Jordan, G. L., Jr., H. L. Barton and W. A. Williamson: A Study of Motility in the Gastric Remnant following Subtotal Gastrectomy. Surg. Gyn. & Obst., **104**:257, 1957.
3. Jordan, G. L., Jr., J. W. Overstreet and G. H. Peddie: The Use of Blood Transfusions in the Treatment of the Postgastrectomy Syndrome. (In press)
4. Machella, T. E.: The Mechanism of the Postgastrectomy "Dumping Syndrome." Ann. Surg., **130**:145, 1949.
5. Mix, C. L.: "Dumping Stomach" following Gastrojejunostomy. S. Clin. N. Am., **3**:617, 1922.
6. Pulvertaft, C. N.: Electrocardiographic Changes in the Dumping Syndrome. Lancet, **1**:325, 1954.
7. Roberts, K. E., H. T. Randall, H. W. Farr, A. P. Kidwell, G. P. McNeer and G. T. Pack: Cardiovascular and Blood Volume Alteration Resulting from the Intrajejunal Administration of Hypertonic Solutions to Gastrectomized Patients: The Relationship of These Changes to the Dumping Syndrome. Ann. Surg., **140**: 631, 1954.
8. Smith, W. H.: Potassium Lack in Postgastrectomy Dumping Syndrome. Lancet, **2**:745, 1951.
9. Wells, C. A. and R. Welbourn: Postgastrectomy Syndrome. Brit. Med. J., **1**:546, 1951.