

EXPERIMENTAL STUDY OF 79 CASES SHOWING THE EARLY POST-GASTRECTOMY SYNDROME

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At the present time partial gastrectomy seems to be the standard procedure when peptic ulcer presents a surgical problem. All authorities are agreed on the satisfactory nature of results, but the unpleasant symptoms, termed the "post-gastrectomy syndrome," which sometimes occur after operation continue to attract considerable attention. Indeed, the symptoms may be so severe and disabling as to make the patient a "gastric cripple" (Custer, Butt, and Waugh, 1946).

Perusal of the existing literature reveals the following hypotheses which have been offered to explain the causation of the syndrome: (1) Rapid emptying of a small gastric remnant, with jejunal filling and distension, due to absence of a sphincteric mechanism between the stomach and small bowel (Hurst 1913; Mix, 1922; Reingold, Schwartz, and Necheles, 1942; Custer, Butt, and Waugh, 1946; Adlersberg and Hammerschlag, 1947, 1949; Irvine, 1948). (2) Delayed emptying of the stomach remnant (Snell, 1937). (3) Reflux of food into the afferent loop of the anastomosis and into the duodenum (Finsterer and Cunha, 1931; Ogilvie, 1935; Lake, 1937; Maingot, 1940; Marshall, 1944; Ingelfinger, 1944; Wangenstein, 1945; Monro, 1945; Mimpriss and Birt, 1948). (4) Coincident hyperglycaemia due to rapid absorption of carbohydrate (Glaessner, 1940). (5) Reactive hypoglycaemia subsequent to the initial hyperglycaemia (Lawrence, 1936; Evensen, 1942; Gilbert and Dunlop, 1947; Barnes, 1947; Adlersberg and Hammerschlag, 1947, 1949; Zollinger and Hoerr, 1947). (6) Coincident gastrojejunitis (Porges, 1947). (7) Absorption of fluid into the jejunum as a result of too rapid entry of hypertonic solutions (Machella, 1949).

Much confusion has been caused by failure to establish exact time relationships between the occurrence of the symptoms and the various features observed as possible causes. In the attempt to elicit the aetiological factors of the post-gastrectomy syndrome, the most valuable concept is that offered by Adlersberg and Hammerschlag (1947), and confirmed by Zollinger and Hoerr (1947) and Avery Jones (1948, personal communication). These authorities believe that there are two distinct syndromes—an early type coming on at the end of a meal, or within a few minutes of its completion, and a late variety, occurring during the second or third hour after a meal.

This paper presents the results of a study of the post-gastrectomy syndrome over the past three and a half years. From 660 cases of patients who had survived partial gastrectomy performed for benign peptic ulcer and who had been carefully sifted, 79 cases showing the early post-gastrectomy syndrome were collected. It is not without significance that although 102 of the 660 cases reviewed were of the Billroth I type gastrectomy, all

these 79 cases were of the Polya type. Up to the present time we have not seen a case of the early syndrome following the Billroth I operation. For the purposes of control, every fifth case without symptoms was also studied, thus affording 174 cases in all—79 with the syndrome and 95 controls. We have come to use the term "early syndrome" only with reference to those symptoms which occur during the first half-hour after a meal. The various symptoms so occurring and their relative frequency are shown in Table I.

TABLE I.—*Analysis of Symptoms in 79 Cases*

Epigastric fullness and distress	79
Pallor	76
Sensation of warmth	72
Nausea	64
Palpitations	50
Vomiting of bile-stained fluid	41
Eruclations	9
Borborygmi	8
Vomiting of food	5
Sensation of cold	3

The precise aim of the present study has been to reproduce these symptoms by experimental methods in order to identify the cause.

A. Experimental Distension of the Jejunum with a Balloon

In this particular test the patient swallowed a Miller-Abbott tube and bag until about 18 in. (45 cm.) of it was in the gastric remnant as confirmed by x-ray examination. To get the balloon through the stoma into the jejunum was a most difficult task, and the simplest technique was found to be the best. The patient swallowed the tube on the day before the tests were performed. During the rest of the day he or she was encouraged to take all meals, to drink freely, and to walk around as much as possible. On the following morning the patient was screened to locate the balloon. A mouthful of barium emulsion was given to be swallowed, and this showed if the tube had passed through the stoma. When the attempt to pass the stoma was successful the balloon was usually situated about 12 in. (30 cm.) beyond the anastomosis in the efferent loop of jejunum.

In the 61 patients with the early syndrome who were subjected to this test the balloon passed into the jejunum 26 times, while in the control group success was obtained in 23 out of 53 attempts.

The effects of jejunal distension were tried in the morning before any food had been consumed. Initially, all the air in the balloon was aspirated, and then 80 ml., 100 ml., and 120 ml. of water was injected in turn, aspirating fully after each occasion and waiting half an hour or so between each injection to allow the effects of the previous distension to subside. The experiments were carried out first with the patient supine, then in the erect position. The results of these distension tests are shown in Table II, the figure in each case representing the number of patients in whom distension produced symptoms.

TABLE II.—*Effects of Jejunal Distension*

		Amount of Water in Balloon		
		80 ml.	100 ml.	120 ml.
Supine position:				
Cases with syndrome	.. 26	5	19	26
Cases without syndrome	.. 23	6	17	23
Erect position:				
Cases with syndrome	.. 26	5	20	26
Cases without syndrome	.. 23	5	18	23

The symptoms produced by this distension of the jejunum consisted of a vague sensation of fullness, on three occasions described as pain, and in every case the sensation was referred to the umbilical area. Three of the cases with the syndrome and two of the controls vomited bile during the performance of the tests in the supine position. In two cases only—one exhibiting the early syndrome and one of the controls—did the distension produce vasomotor effects—that is, tachycardia, pallor, perspiration—together with a sensation of nausea as well as fullness. The table indicates that posture does not affect the tests, the results of distension being almost the same in both the erect and the supine position. In addition, it seems that there is no difference in the sensitivity of the jejunum to distension, as both groups of patients appear to respond to an equal degree.

The effect of sympathetic splanchnic block was tried in some of these cases—in 20 with the syndrome and in 16 of the controls. With Kappis's technique 20 ml. of 1:2,000 solution of amethocaine was injected on each side of the first lumbar vertebra. The sensation produced by the balloon distension was abolished in 17 (85%) of the cases with the syndrome and in 11 (69%) of the cases of the control group.

Devine, of Australia (quoted by Aldersberg and Hammerschlag, 1947), stated that jejunal distension with a balloon in these cases produces no symptoms, while Machella (1949) believes that distension can produce them. The effect of balloon distension of the small bowel in normal individuals, however, has been observed repeatedly (Hurst, 1913; Barclay, 1936; Samson Wright, 1945). All these authors were especially concerned with the location of the sensations produced rather than their nature. In each case the raised tension within the jejunum caused by the distended balloon produced a sensation of fullness which was referred to the umbilicus.

As a result of these investigations, the following conclusions may be drawn: (1) jejunal distension produces a sensation of fullness referred to the umbilicus; (2) jejunal distension does not usually produce any other symptoms; (3) posture has no effect on the results of jejunal distension; (4) there is no difference in the sensitivity of the jejunum between cases with the early postcibal syndrome and those without it; and (5) sympathetic block (splanchnic) relieves the symptoms produced by jejunal distension.

B. Radiological Study

The aim of this study was to compare cases with and without symptoms in both the supine and the erect positions. In addition, since the early syndrome did not occur in 102 of the Billroth I cases reviewed, a series of these was studied also. The groups of cases were made up as follows: 72 Billroth I cases, 95 Polya cases without syndrome, and 61 Polya cases with syndrome. The number of cases with the syndrome was originally 79, but 18 of these did not attend for further observation.

In order to compare the findings in the supine and erect positions, screening was carried out in both, the stoma being occluded when the patient changed his position. In some cases the stomach was empty before the position could be changed. In the Billroth I series the position of the stoma was sometimes so high that occlusion was impossible. It was found that comparison of the state in the erect and supine positions was best achieved by a separate skiagram in each position showing all the vertebrae, the picture in each case being taken in the same phase of respiration.

The findings of this radiological study were as follows:

Billroth I Series (72).—Emptying of the stomach was complete within one hour in 65 of these cases (90%). In the remainder the stomach was empty in one and a half hours. Emptying was just as rapid in the supine position as in the erect. On occluding the stoma 17 (24%) of the series of 72 experienced a feeling of distension, but none had any vasomotor symptoms. The average width of the stoma appeared to be between 1.5 and 2 cm. In the change from the supine to the erect position the stoma descended, on the average, about 2 cm.

Polya Series without Symptoms (95).—The stomach was empty within 40 minutes in 91 cases (96%), whilst in the remainder a variable time between one and a half and two hours expired before emptying was complete. Afferent-loop reflux was seen in 21 cases (22%) in the erect position and in 25 cases in the supine position. The size of the stoma varied, of course, depending on the type of operation, and it ranged from 2 cm. to 8 cm. Occlusion of the stoma was difficult in these cases, but accumulation of barium in the stomach caused a feeling of distension in approximately one-third of the patients. Change from the supine to the erect position was associated with descent of the stoma, the average descent being about 2 cm. Although sometimes there was no descent apparent, on other occasions it was nearly 5 cm.

Polya Series with the Early Syndrome (61).—The emptying time in this series was 40 minutes for 57 (93%) of the cases. Afferent-loop filling was seen in 9 cases (15%). Again, as in group B, the size of the stoma showed variations according to the type of operation, but cases were equally scattered through the range. In this series 48 (79%) of the cases had symptoms during the examination. In all of them the symptoms occurred in the erect position, and in 17 (28%) it was observed that symptoms occurred while the barium emulsion was still in the stomach. The patients complained of fullness in the epigastrium, their pulse rate increased, they perspired, and two of them fainted. During screening, of course, pallor could not be seen, though it was obviously present when seen afterwards. In changing from the supine to the erect position the stoma was observed to descend on an average about 7 cm., the maximum being nearly 11 cm.

It was very difficult to evaluate this finding of descent, the degree of which appears to be greater in cases with the early syndrome than in cases without symptoms. In normal people there is considerable descent of the stomach in the change from the supine to the erect position. Thus, Moody and Van Nuys (quoted by Grant, 1946) have shown that the normal pylorus moves about 6–8 cm. with this change of position, whilst the lowest margin of the greater curvature moves a distance equivalent to the width of two vertebrae. The higher one ascends in the stomach the less is the range of movement. Moody and Van Nuys state that the most fixed position is the gastro-oesophageal junction. If this is so, the descent recorded may be interpreted as stretching of the gastric remnant. We were very careful to ensure that pictures were taken at exactly the same phase of respiration, so that the position of the diaphragm was constant. In this way descent relative to the diaphragm was measured. Figs. 1 and 2 show the descent in two cases with rapidly emptying stomachs. Although rotation of the gastric remnant around an axis through the gastro-oesophageal junction (the stoma moving downwards and to the left) would also account for apparent descent, this feature was not apparent in the radiographs. In any case, this rotation would be common to all cases except the Billroth I patients.

An observation common to about 70% of all the cases was as follows: The initial mouthful of barium, when

(b) On assuming the erect position, 57 patients (93%) complained of heaviness and fullness in the epigastrium—high in the costal angle. This was associated with nausea, and six patients began retching. All showed increased pulse rate, pallor, and sweating, whilst 24 complained of palpitations and a feeling of suffocation. Two patients fainted in assuming the erect position, and no further tests were carried out on them. On returning to the supine position these symptoms disappeared in five to ten minutes.

(c) Patients with retrocolic anastomoses required more mercury to produce symptoms compared with those with antecolic anastomoses (Table V).

TABLE V.—Comparison of Mercury-bag Test in Short Loop and Long Loop Anastomoses

	Retrocolic— Short Loop	Antecolic— Long Loop
Weight of mercury to produce symptoms (mean)	10 oz. (283 g.)	6-7 oz. (170-200 g.)
Amount of bile-stained fluid aspirated in supine position (mean)	6-10 oz. (170-284 ml.)	9-20 oz. (255-568 ml.)
Weight of additional mercury to produce symptoms (mean)	3 oz. (85 g.)	5-6 oz. (142-170 g.)

The experiments were then repeated on 59 patients—that is, excluding the two patients who reacted so markedly to the previous test. On this second occasion, however, the patients were instructed to lie supine half an hour before the test was begun. During this time the Miller-Abbott tube was still in position and aspiration was carried out. Bile-stained fluid was readily aspirated in amounts varying from 6 to 23 oz. (170 to 650 ml.). The same weight of mercury as in the previous test was then reintroduced into the bag, the patient still being supine. On adopting the erect position 10 patients had symptoms exactly as before. It was noted that these patients were those in whom small amounts of bile were aspirated. In four cases the patients complained of heaviness in the epigastrium, but there were no other symptoms—no vasomotor features. In the remaining 45 cases (76%), however, there were no symptoms until a further amount of mercury was added to the bag. This weight of extra mercury varied from 2 to 7 oz. (57 to 200 g.). To complete the test about 2 oz. (57 ml.) of barium emulsion was given to verify radiologically that the bag had not passed through the stoma during the course of the test.

Finally, the response to splanchnic block was observed. Of 53 patients on whom this was tried, 41 (77.3%) were free from symptoms when the loaded bag was in position. In seven patients, although there was a fall in blood pressure, indicating adequate nerve block, symptoms still occurred, but of reduced severity.

Throughout these tests two points were constantly checked. First, care was taken that the weight of the mercury was not taken up by the tube, so preventing full traction on the stomach. In each case about 18-24 in. (45-60 cm.) of the tube was allowed to coil up in the gastric remnant, and when the mercury was introduced the tube was held vertically so that all the mercury entered the bag or the immediately adjoining part of the tube in the stomach. Secondly, when the mercury was aspirated the same volume of saline was introduced into the bag. In no case did this cause symptoms. This was done to ensure that it was not the distension of the bag in the gastric remnant that caused symptoms during the tests.

It must be stressed that this test is very difficult to perform at times. The loaded bag often slips through the stoma and no symptoms are produced. Sometimes

the bag slips through the stoma after producing symptoms, and in these instances the symptoms disappear at once.

The average weight of mercury required to produce symptoms in this series was 8 oz. (227 g.). In the 95 controls this amount of mercury failed to produce effects in any of the cases, but 14 oz. (400 g.) produced identical symptoms in approximately 74%. In a series of six people who had never had a gastrectomy, 10% got symptoms similar to the early syndrome when 14 oz. was put into the bag.

Comment.—This seems to be the most significant test of the series. It indicates that a major factor in the production of the early syndrome is the weight of food in the stomach. It also indicates that the weight of the contents of the afferent loop and the weight of a meal in the stomach are complementary. If the afferent loop is relatively empty a greater bulk of meal can be taken before symptoms occur. If, on the other hand, the loop is heavy with temporarily retained contents a small meal increases the whole weight to the critical level required to produce symptoms.

E. The Therapeutic Value of Splanchnic Block

Splanchnic block by the posterior route (Kappis) was used many times during the whole series of investigations. Initially, successful block was obtained in less than half the cases to which it was administered. Recently, however, success has been obtained in about three-quarters of all attempts made. The effect of splanchnic block has been observed now on all 61 cases—some after one injection (that is, apart from splanchnic block in the experiments) others after two or even three injections. The success of the block was judged by the associated fall in the blood pressure.

In four cases the patients have had no further trouble—the longest period being seven months. In 46 cases the patients were relieved for periods ranging from two to nine days. During this time they were able to eat bulky meals, which they had not been able to do since the operation. In the remaining 11 patients the block failed to abolish the syndrome. This particular finding will be discussed in a later paper dealing with the nerve pathways involved. All that is necessary at the moment is to say that splanchnic block relieves only those cases in which all the afferent fibres involved pass through the splanchnic plexus. It is well known that in a proportion of cases some fibres go direct to the splanchnic nerves and lower thoracic ganglia. These cases will therefore not be affected by splanchnic block.

Distilled water was used for the second injection in eight cases, but without effect.

It would appear that the early post-gastrectomy syndrome is transmitted via the sympathetic system. In a personal communication in 1949 Hastings-James stated that sympathectomy would relieve symptoms; and at the last Gastro-enterological Conference in the U.S.A. it was stated that "etamon" was also effective in relieving the symptoms.

Conclusions and Discussion

In view of the above we are able to draw the following conclusions:

1. The symptoms constituting the syndrome are not all due to the same cause. The sensation of central

abdominal fullness is due to the distension of the jejunum. The rate of emptying of the gastric remnant and thus of jejunal filling—that is, the x-ray observation that led to the use of the term “dumping”—is a factor in the production of the sensation of fullness, but is unrelated to the rest of the syndrome. Indeed, fullness is not the most distressing part of the syndrome. It is the vasomotor upset—that is, the feeling of warmth, sweating, tachycardia, palpitations—which really distresses the patients, and these symptoms were not reproduced by jejunal distension.

2. The vasomotor component can be completely reproduced by inert substances—that is, both barium and a mercury bag in the gastric remnant.

3. There is no difference in the blood-sugar curve of those with and without the early syndrome.

4. The afferent-loop reflux *per se* is not a cause of the symptoms, because, as has been shown, the incidence of this finding is equal in cases with and without the syndrome.

5. The syndrome can be reproduced fully by a mercury-loaded bag in the gastric remnant, where the weight of the mercury is roughly equal to the weight of a meal known to produce symptoms. This test also suggested that the weight of the gastric contents plus the weight of the contents of the afferent loop are complementary factors in production of the syndrome.

6. If the patient lies down the vasomotor symptoms produced by the mercury bag are abolished. On the other hand, posture had no effect on the sensation of fullness produced by balloon distension of the jejunum.

7. Splanchnic block suggests that the syndrome is mediated by the sympathetic rather than the vagus nerves.

As a result of these studies it appears that several different mechanisms are involved in production of the syndrome—namely, jejunal distension producing a sensation of fullness, and drag produced by the combined weight of the gastric and afferent-loop contents in the erect posture leading to vasomotor effects. Experimentally it has been shown that abolition of the effect of gravity abolishes the latter but not the former. This corresponds with the clinical observation that lying down during an attack causes the vasomotor symptoms to disappear within five minutes, whereas the sensation of fullness may persist for an indefinite period.

In a subsequent paper we hope to present a clinical study of the problem and attempt to correlate it with these experiments.

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THYROID ACTIVITY IN MENTAL PATIENTS

EVALUATION BY RADIOACTIVE TRACER METHODS

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The radioactive tracer method of estimating thyroid function used in these investigations has been reported elsewhere (Haigh and Reiss, 1950; Reiss *et al.*, 1951). Only small doses of radio-iodine are employed, and the method does not depend upon absolute measurements in the thyroid region. The index of thyroid function is calculated from measures of the uptake by the thyroid and of the urinary excretion of radio-iodine. With the particular units chosen, normal values of this function, I_t , have been found to lie in the range—males 1.8 to 8, females 3 to 12. The error in the measurements is about $\pm 20\%$, and there is evidence that the spread of the chosen normal limits is probably too great. It has been found useful to divide each normal range into an upper and lower normal range about the mean normal value.

The investigation can be repeated after two to four weeks without danger to the patient and without error due to the earlier injection. The radiation from the small dose (25 μ c.) of radio-iodine appears unlikely to influence thyroid function, which may be a source of error in methods employing large doses such as that published by Bowman *et al.* (1950) in his survey of 49 psychiatric cases.

Our series consists of 541 cases in an acute psychiatric admission hospital and out-patient clinic, embracing most of the usual psychiatric disorders. The series includes many cases of mental illnesses of recent origin and short duration, and is a fair cross-section of psychoneurotic and psychotic illness.

The Tables show the distribution of the psychiatric categories according to the degree of thyroid activity. Abnormal thyroid values do not seem to be consistently characteristic of any single psychiatric disorder,