HYPOGLYCAEMIA FOLLOWING PARTIAL GASTRECTOMY

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During a routine follow-up of 45 consecutive patients on whom a partial gastrectomy had been performed for peptic ulcer we noted symptoms of dizziness, palpitation, sweating, epigastric discomfort, and a feeling of weakness—progressing in several instances to complete loss of consciousness—in 17. These symptoms, coming on in from one-half to one and a half hours after food, were rapidly relieved by taking sugar or other easily assimilated carbohydrate. In this series they were far the commonest complication of partial gastrectomy, being greatly in excess of stomal ulcer and anaemia, which receive such a prominent place in the literature on the subject. Five of the patients were in consequence so severely disabled that they had become totally unfit for employment. Many of them, however, did not associate their symptoms with their operation, as their sensations seemed to be quite unconnected with the previous dyspepsia. In a follow-up of patients who have had a partial gastrectomy this syndrome may therefore be overlooked unless leading questions are asked.

Such symptoms have been noted previously, chiefly in the German literature by Lapp and Dibold (1933), Beckermann (1933), Koranyi (1936), and Wöhrle (1936). Evensen (1942) found that in 34 out of 95 cases of partial gastrectomy the blood sugar fell on occasion to less than 65 mg. per 100 ml. Adlersberg and Hammerschlag (1947), investigating the "post-gastrectomy syndrome," demonstrated a hypoglycaemic type of blood-sugar curve in all their 14 cases. There is a curious absence of reference in British literature to post-gastrectomy hypoglycaemia; the "dumping syndrome," however, is often mentioned, but is usually attributed to vagotonia, the result of jejunal distension from precipitate gastric evacuation.

TABLE I.—*Incidence of Hypoglycaemic Symptoms*

	Hypoglycaemic Symptoms		Asymptomatic		Total
	Male	Female	Male	Female	
No. of cases	12	5	24	4	45
Site of lesion:					
Duodenal ulcer	7	2	16	0	25
Gastric ulcer	5	3	8	4	20
Operation:					
Polya	12		18		30
Hoffmeister	5		10		15
Free acid in post-operative test meal	7		10		17
Age (years)	30–65 (average, 45·58)		32–65 (average, 42·61)		
Post-operative period (months)	4–84 (average, 33·29)		9–121 (average, 48·5)		

Table I shows the incidence of hypoglycaemic symptoms among our patients. It will be noted that their presence or absence bore no relation to the site of the previous ulcer, to the type of operation performed, to the presence or absence of free acid in the post-operative test meal, or to the age of the patient. On the whole the symptoms were more pronounced during the earlier months of the post-operative period.

Glucose tolerance tests were performed on all 45 patients. On the morning of the test a sample of fasting venous blood was withdrawn. The patient was then given 50 g. of glucose in 180 ml. of water orally, and samples of venous blood were withdrawn at 30, 60, 120, 180, and 240 minutes. In the latter half of the series an additional specimen was taken at 15 minutes. The sugar content of the blood specimens was estimated by the Hagedorn–Jensen method. Concomitant with the taking of the specimens the bladder was emptied and the urine was examined for sugar.

Illustrative Cases

Case 1.—The patient, a man aged 60, had been employed as a gardener until his operation (Polya) for a gastric ulcer eighteen months previously. For four or five years immediately

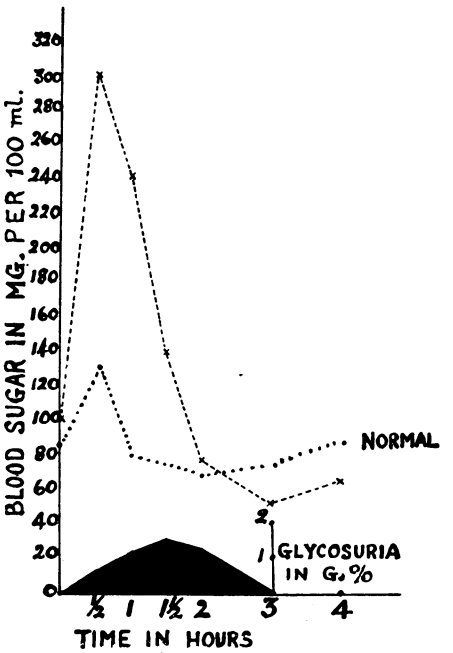

FIG. 1.—Case 1. Glucose tolerance curve. Note the sharp rise in blood sugar to 301 mg. and the fall to 53 mg., also a glycosuria of 1.6 g. during the peak of the blood-sugar curve.

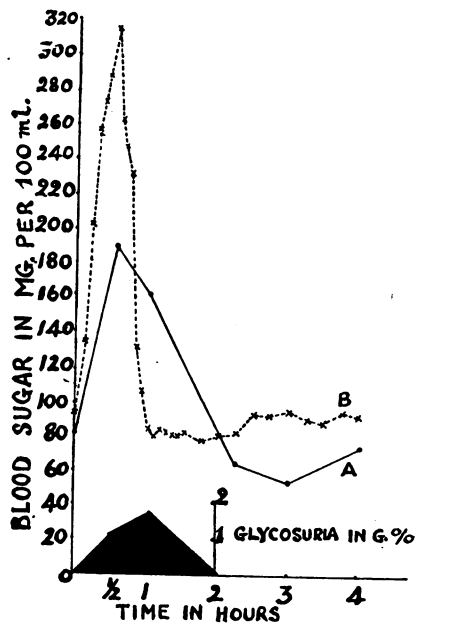

FIG. 2.—Case 2. Glucose tolerance curves. A=first specimen taken at 30-minute intervals: maximum level, 190 mg.; glycosuria, 1.8 g. B=specimen taken at five-minute intervals. The peak was missed in A.

before the operation he had lost one to two months' work each year because of pain and vomiting. Since the operation he has suffered from attacks of weakness, sweating, and dizziness one hour after food; these were intensified by taking exercise. Twice during such attacks he lost consciousness. He felt so weak and unsteady that he had not been able to return to work since his operation. A glucose tolerance curve is shown in Fig. 1.

Case 2.—A man aged 24 had had a Polya resection for duodenal ulcer nine months previously. Since the operation he had had severe attacks of hypoglycaemia half to one hour after meals. These were most pronounced after his afternoon tea, which consisted of tea with sugar, buns, and cakes. On one occasion, following a large carbohydrate tea, he boarded a bus, and instead of disembarking at his destination found himself at the terminus being wakened by the conductor. He was bathed in perspiration, felt very dizzy, and had extreme tachycardia. During a glucose tolerance test (Fig. 2, A) the highest reading was found to be only 190 mg. per 100 ml. in spite of a glycosuria of 1.8 g. %. It was therefore presumed that by taking specimens at 30 and 60 minutes the peak of the curve had been missed. On repeating this test, taking five-minute specimens, the peak was found to be 312 mg. (Fig. 2, B).

Discussion

Factors in the Production of Hypoglycaemia.—Three factors determine the production of hypoglycaemic symptoms—the maximum fall in blood sugar, the minimum level to which it falls, and the maximum rate at which it falls. These facts are illustrated in Table II, in which the figures

TABLE II.—*Average Readings of the Glucose Tolerance Curves*

	Hypoglycaemic Symptoms	Asymptomatic
No. of cases	17	28
Maximum fall	118·53 mg.	79·57 mg.
Minimum level	54·24 mg.	62·5 mg.
Maximum fall per minute	2·69 mg.	1·92 mg.
Maximum level	171·53 mg.	138·82 mg.
Glycosuria	52·82%	17·86%
Postprandial diuresis	47·05%	29·26%

given have been found to be statistically significant. It will be noted that the symptomatic cases show: (1) greater maximum fall, (2) lower minimum level, (3) greater maximum rate of fall, and (4) greater incidence of glycosuria and postprandial diuresis.

Physiological Basis for Post-gastrectomy Hpyoglycaemia.—It is a well-established fact that the gastric remnant after partial gastrectomy empties very quickly. This precipitous gastric evacuation is particularly marked following a meal rich in carbohydrate. Such food is rapidly absorbed from the jejunum, causing an abnormally brisk rise in blood sugar, sometimes to the extent of producing glycosuria. This in turn provokes an excessive secretion of endogenous insulin and a subsequent rapid fall in sugar concentration to an unusually low level. In nine of the cases showing symptoms of hypoglycaemia concentrations below 60 mg. per 100 ml. were noted. In the normal subject the stomach takes about three hours to empty. During this period food in small quantities is continually entering the jejunum, so that a less pronounced initial rise in blood sugar occurs. It must be confessed, however, that this theory does not explain the absence of hypoglycaemic symptoms following the rapid intravenous injection of glucose. Kalk and Meyer (1932) simulated post-gastrectomy conditions by intrajejunal intubation in a normal subject, and were able, by the administration of glucose through the tube, to produce the typical hypoglycaemic blood-sugar curve. A further observation by Evensen confirms short-circuiting to be the basis of the hypoglycaemia. He observed a high incidence of hypoglycaemia after gastro-enterostomy. In one such case the reconstitution of the normal alimentary tract immediately removed this abnormality from the glucose tolerance curve. A normal difference of the blood-sugar concentration in the capillaries and veins eliminates excessive tissue utilization or storage of carbohydrate as the cause of the hypoglycaemia. Further, in our cases a normal fasting blood sugar (average, 91 mg. per 100 ml.) and normal insulin tolerance curves rule out respectively excessive activity of the pancreatic islet tissue and undue sensitivity to insulin as causative factors.

The "Dumping" Syndrome (Dumping Stomach).—The symptoms of the so-called "dumping" syndrome are indistinguishable from those of postprandial hypoglycaemia, and it is probable that the two conditions are identical. There is no reason to believe that excessive vagotonia causes the syndrome, as is commonly held, since vagal stimulation would decrease the pulse rate, whereas tachycardia is present during the "dumping" syndrome. Again, atropine in full doses should inhibit the vagus, but it actually produces no alleviation of the symptoms. Lastly, Moore (1947) has recently reported a case of "dumping" following vagotomy in a patient with a subtotal gastrectomy. Upper abdominal discomfort and occasional vomiting, which have been reported as characteristic of the dumping syndrome, have been noted in some of our hypoglycaemic cases. It is well known that hypoglycaemia produces increased peristalsis; and a fall in blood sugar of sufficient magnitude to produce sweating, tachycardia, and faintness might produce not only increased peristalsis of the gastric remnant but actual spasm. Further, it is known that symptoms of the dumping syndrome often improve with time, and many of our hypoglycaemic patients gave a history of gradual improvement in spite of the persistence of hypoglycaemic blood-sugar curves, due no doubt to the gradual development of tolerance to low blood-sugar concentrations. We therefore believe that it is unnecessary to differentiate the two conditions, which are identical. If our theory is correct, that excessively rapid emptying of the gastric remnant into the jejunum is the primary cause of the dumping syndrome or postprandial hypoglycaemia, treatment should be directed to delaying the rate of gastric evacuation and jejunal absorption of sugar. We have in consequence, and with

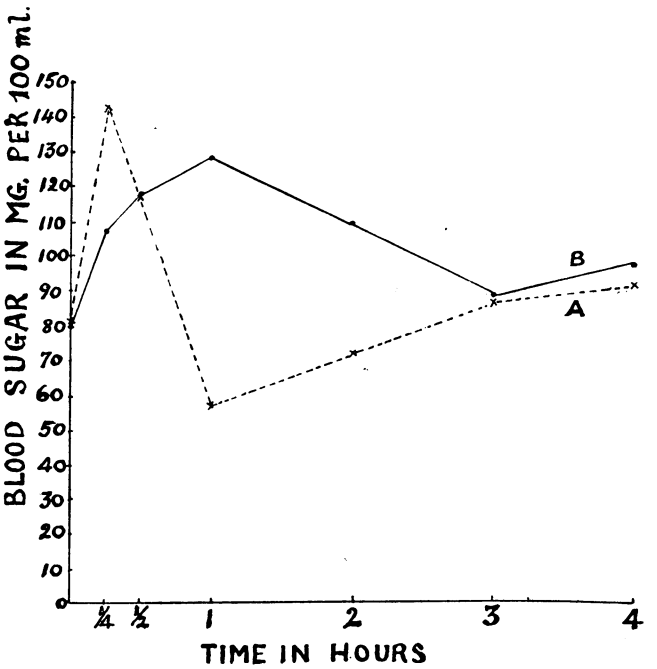

FIG. 3.—A = glucose tolerance curve without ephedrine. B = curve after 1/2 gr. (32 mg.) of ephedrine had been taken half an hour before the glucose.

some success, used high-fat diets or given 1 oz. (28 ml.) of olive oil before meals in the treatment of our hypoglycaemic cases. Ephedrine by its sympatheticomimetic action raises the blood sugar and has also proved useful in preventing reactive hypoglycaemia. It has been given in ½-gr. (32-mg.) doses half an hour before the three main meals. Fig. 3 shows its effect in a patient with moderately severe hypoglycaemia. Owing to their reduced gastric capacity these patients often feel better having six small meals a day instead of the usual three large ones.

Summary

Postprandial hypoglycaemia occurred in 17 out of 45 consecutive patients on whom a partial gastrectomy had been performed for peptic ulcer, and constituted the commonest complication of the operation in this series.

The symptoms produced were severe enough in five patients to preclude them from earning a livelihood.

It is suggested that rapid gastric evacuation is the basis of this hypoglycaemia, and that the "dumping" syndrome has identical clinical manifestations and an identical aetiology, so that the two conditions need not be distinguished.

The most effective method of treatment has proved to be a high-fat diet, six small meals a day instead of three large ones, and 1/2 gr. (32 mg.) of ephedrine before the three main meals.

REFERENCES

Adlersberg, D., and Hammerschlag, E. (1947). *Surgery*, **21**, 720.
Beckermann, F. (1933). *Dtsch. med. Wschr.*, **59**, 683.
Evensen, O. K. (1942). *Acta med. scand.*, Supp., **126**, 148.
Kalk, H., and Meyer, P. F. (1932). *Z. klin. Med.*, **120**, 692.
Koranyi, A. (1936). *Dtsch. Arch. klin. Med.*, **178**, 353.
Lapp, F. W., and Dibold, H. (1933). *Klin. Wschr.*, **12**, 547.
Moore, F. D. (1947). *J. Amer. med. Ass.*, **133**, 749.
Wöhrle, M. (1936). *Dtsch. Arch. klin. Med.*, **179**, 411.

STATUS EPILEPTICUS COMPLICATING PREGNANCY

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Status epilepticus in pregnancy is uncommon, but a few cases have been reported, most of them fatal. The effect of pregnancy on idiopathic epilepsy is variable, increasing the frequency and severity of the fits in some cases, ameliorating them in others, and in many instances producing no change whatever. Status epilepticus may occur at any time during pregnancy, labour, or the puerperium. It may even be the first intimation that an epileptic tendency exists. Often, however, the condition is preceded by more violent and more frequent fits, in spite of adequate anticonvulsant therapy.

A fatal termination is almost the rule, though very occasionally patients recover. Sachs (1910) reported two cases in sisters, both fatal. DeLee (1938), Greenhill (1934), and Sachs all state that death is inevitable unless the uterus can be emptied, a procedure which offers a very slender chance of recovery. Jardine records a case in which pregnancy was terminated by manual dilatation of the os, but to no avail. Sachs has packed the uterus before dilating the os, with a similar result. Bachmann (1930) states that, as in eclampsia, improvement is likely to occur immediately the pregnancy is terminated, but there can be no doubt that status epilepticus, though much rarer, is far more deadly.

Burnett (1946), in an excellent survey of the literature, has summed up the relation between epilepsy and pregnancy and the prognosis in status epilepticus in the pregnant woman. He reports a case which recovered after induction of labour by low rupture of the membranes under thiopentone anaesthesia in the thirty-third week of pregnancy. Although the child was not born for a further five days, complete recovery of the mother resulted and a live child was obtained. Two months after delivery the patient was having fits at her normal frequency.

Bachmann advises sterilization for any patient who has once suffered from status epilepticus in pregnancy, on the grounds that the chances of recovery are negligible should an attack be repeated in a subsequent pregnancy. Having regard to the rarity of the condition and the high mortality rate it is not possible to forecast the chances of a recurrence, but there would appear to be good reasons for supporting his view.

The following case is of interest, since recovery took place without interruption of pregnancy.

Case History

The patient, a married woman of 23, was admitted to the Royal Infirmary under the care of Prof. E. J. Wayne on Dec. 29, 1946, in status epilepticus; she was then three months pregnant with her first child. At the age of 21 she began to have major epileptic fits, and after full investigation idiopathic epilepsy was diagnosed. There was no family history of convulsive phenomena. She continued to have occasional fits, which were controlled with phenobarbitone. After one year's treatment, however, she ceased to take the drug, with the result that she went into status epilepticus for a few hours eighteen months before the present admission. She had taken no phenobarbitone during pregnancy, which so far had been uneventful and free from fits. Three days before admission she was married to the father of her child. Continuous convulsions began at 1 p.m. on the day of admission.

On examination she was seen to be a well-developed young woman, comatose, with stertorous respiration and slight cyanosis. The pulse was rapid (120) and of good volume, the blood pressure 130/70. There were no localizing signs in the central nervous system; the reflexes were absent, the plantar responses extensor. There was no oedema. The optic fundi, heart, lungs, and abdomen were normal. Vaginal examination revealed pregnancy of approximately three months' duration. The urine contained a trace of albumin but no sugar or acetone. The temperature was 98.8° F. (37.1° C.). She was incontinent of faeces and urine; there was no urinary retention.

Further generalized epileptiform fits followed in rapid succession at intervals of ten to fifteen minutes and lasted one to three minutes. No response was obtained to intramuscular sodium phenobarbitone, and it became necessary to give intravenous thiopentone to prevent a continuous succession of fits. Oxygen was administered continuously.

Sodium phenobarbitone, 3 gr. (0.2 g.), was injected intramuscularly twice daily and 0.25 g. of thiopentone was given intravenously as required. A lumbar puncture was performed and 10 ml. of clear fluid at a pressure of 160 mm. of water was removed. This manœuvre produced little relief, but it is probable that the increased intervals between fits were due to the barbiturates. On Dec. 29 she had seventeen major fits, and remained unconscious. Next day she had only four fits, but still remained unconscious. To control dehydration fluids were administered per rectum, and into the stomach through a transnasal tube. There were no other physical signs and no evidence of rising intracranial pressure. A further lumbar puncture was normal in all respects. On the 31st her general condition was much the same, but the temperature rose suddenly to 103° F. (39.4° C.) and the pulse to 130 at 2 p.m. She was still unconscious. During the day she had