of immediate benefit to a gastritic mucosa or to a gastric ulcer. It might reduce the acidity in a man with a duodenal ulcer, but he suspected that there would be an increased morbidity in ten to twenty years' time.

Many citizens of the United States were now undergoing this method of treatment, and he believed that those on this side of the Atlantic would be wise to act as the unfrozen control series until the Americans reported, as he was sure they would, the long-term effects of the method.

Operations in the upper abdomen were not easy in patients with ankylosing spondylitis. High dissections of the stomach, as in carcinoma and operations on the hiatus, were particularly difficult and were certainly not cases for the tyro. He had carried out partial gastrectomy on 3 patients with this disease and had been impressed with the excellent way in which these unfortunate but courageous people had tolerated the post-operative period.

He quite agreed with Professor Ellis's decision to treat this case surgically.

Insulinoma with Symptoms for Thirty Years

R M Buckle MD MRCP
(for K O Black MD FRCP and M A Birnstingl FRCS)

R B, female, aged 72. Housewife

History: Thirty years previously the patient first developed attacks in which she felt 'far-away', noticed paræsthesiæ around the mouth and saw objects before the eyes. In the first attack and in several others she lost consciousness for twenty to thirty minutes. Most attacks occurred early in the morning; before them she would feel hungry and she found that they could be averted by taking sugar. The frequency and severity of the attacks have varied during the thirty years; in the last eighteen months they have been worse and during this time she developed profound weakness on waking up, being unable to get out of bed until she had eaten several glucose tablets. The patient gained 4 stone in weight, every attempt at dieting increasing the severity of her symptoms.

Spontaneous hypoglycæmia was suspected, but investigations in 1946, 1947 and 1950 showed fasting blood sugars ranging from 70 to 77 mg/100 ml, while the lowest values after 50 g oral glucose ranged from 55 to 71 mg/100 ml. In 1954, fasting blood sugars ranged from 58 to 68 mg/100 ml, and following twenty-four hours' starvation fell to 42 mg/100 ml. A six-hour glucose tolerance test suggested functional hypoglycæmia.

In September 1963, the patient was reinvestigated following two recent prolonged attacks of unconsciousness. Apart from obesity (weight 13 st 5 lb), physical examination was normal.

Investigations: Overnight fasting blood sugar (total reducing substance) 64–73 mg/100 ml (5 tests); blood glucose (glucose oxidase) 26–33 mg/100 ml. After starvation for forty-two hours the patient became disorientated, developed slurred speech and sweated profusely; the symptoms were immediately reversed by intravenous glucose. A blood glucose estimation during this episode was unsatisfactory (technical error). During a tolbutamide test (1g I.V.), the patient became comatose seventy minutes after the injection, but recovered consciousness rapidly following intravenous glucose, the blood glucose in the attack being 6 mg/100 ml. The fasting plasma insulin was 120 micro-units/ml (normal less than 30 micro-units/ml) (Dr J Ellis).

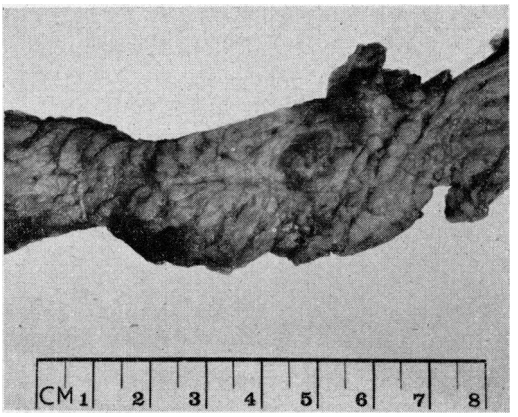

Fig 1 *Operative specimen showing the tumour*

Exploratory laparotomy 22.11.63 (Mr M A Birnstingl): Mobilization and careful examination of the head of the pancreas and the anterior and posterior surfaces of the body and tail failed to demonstrate any tumour; no ectopic pancreatic tissue was seen. Distal pancreatectomy was performed, two-thirds being removed. Serial sectioning through the specimen showed a small tumour 1 cm in diameter buried in its substance (Fig 1). Post-operatively, the patient developed hyperglycæmia for a few days, and required small doses of insulin. She is now on a normal diet, has lost 2 stone in weight and has had no further symptoms of hypoglycæmia.

Histology showed a benign islet-cell tumour; the cells were well differentiated and regular, and arranged in solid masses and columns; occasional glandular acini were present and most cells contained granules of the beta cell type (Fig 2).

Comment

The symptoms of hypoglycæmia are nonspecific and the diagnosis of insulinoma may be long delayed; in two collected series symptoms were present for five years or more in 25% of cases (Crain & Thorn 1949, Breidahl *et al.* 1956). The paroxysmal behaviour of insulinomas leads to a

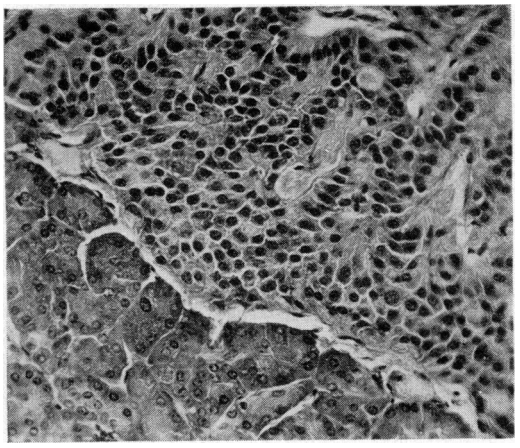

Fig 2 *Histological section showing tumour tissue*

great variation in the frequency and severity of the symptoms. Hypoglycæmia may result from several causes, but in insulinomas the symptoms typically develop during fasting, particularly during the night or in the early morning.

For diagnosis, the blood glucose is measured during an attack or after fasting. The blood sugar level, measured as total reducing power, is unreliable and glucose should be measured specifically by glucose oxidase. This patient was investigated for hypoglycæmia on several occasions over fifteen years, yet the fasting blood sugar levels were within normal limits. On the last admission fasting blood sugars were normal, whereas the actual glucose levels were abnormally low (26 to 33 mg/100 ml). Before spontaneous hypoglycæmia can be excluded the patient must be starved for seventy-two hours; it is rare for a patient with an insulinoma not to develop hypoglycæmia and symptoms within this time (Black *et al.* 1954, Breidahl *et al.* 1956). A prolonged six-hour glucose tolerance test is of little help in diagnosis of insulinomas (Crain & Thorn 1949, Breidahl *et al.* 1956) and is often confusing; it suggested functional hypoglycæmia in this patient. Provocative tests may be of value. The tolbutamide test (Fajans *et al.* 1961) causes a profound and prolonged lowering of the blood glucose and is useful in differentiating insulinomas from other causes of hypoglycæmia. In this patient it caused coma, with a blood glucose level of 6 mg/100 ml, which was reversed by intravenous glucose, so proving Whipple's triad. Glucagon also causes an exaggerated hypoglycæmia in insulinomas and its use may aid diagnosis (Marks 1960). The direct estimation of plasma insulin frequently shows high values and in this patient it was four or five times normal, but elevated levels are not always demonstrable (Yalow & Berson 1960).

Once the condition is diagnosed, surgery should not be delayed, for progressive mental deterioration and obesity may develop or the patient may die during a hypoglycæmic attack. The tumour, as in the present patient, may be difficult to find. The gland must be completely mobilized and all parts carefully examined, for the tumours are usually less than 2–3 cm in diameter, may be multiple and occur with equal frequency in the head, body or tail of the pancreas (Crain & Thorn 1949, Marshall 1958, Warren 1962). If no tumour can be found, ectopic pancreatic tissue must be excluded, for 2% of insulinomas develop in such tissue. In this patient distal pancreatectomy was performed and the tumour was found when the resected specimen was sliced. Only 10% of tumours are obviously malignant and, provided the insulinoma is identified and removed, the results of surgery are excellent (Marshall 1958, Warren 1962). Postoperative diabetes is only temporary and it is very uncommon for the patient to require dietary restriction or insulin after the first three to four weeks.

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Seven-year Survival after Bilateral Adrenalectomy and Oophorectomy for Carcinomatosis

P M Higgins MA FRCS
(for Hermon Taylor MCh FRCS)

It is generally accepted that a proportion of breast carcinomas are to a greater or lesser extent hormone sensitive, and therapeutic measures designed to take advantage of this sensitivity are well established. These measures are, however, regarded as being merely palliative, and the relief is frequently only of short duration. The present case is unusual in that relief of symptoms and objective evidence of regression of metastases have persisted for over seven years after bilateral oophorectomy and adrenalectomy.

Case Report

Mrs J P, now aged 47

In 1949, at the age of 32, one year after the birth of her second child (both breast fed) she noted a lump in the right breast. Right radical mastectomy was performed. Histology: 'Carcinoma of breast, partly intraduct, partly infiltrating, of a