1. Fat and Ketone Metabolism in the Livers of Obese Hyperglycaemic Mice.

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A colony of obese hyperglycaemic mice (Bar Harbor) has been bred in Aberdeen. Fat metabolism and ketogenesis have been investigated in the livers of these obese mice, their non-obese littermates and also in normal mice. The obese mice had enlarged livers containing increased amounts of total fat. The triglycerides of the liver of the obese mice contained a higher proportion of oleic acid and a lower proportion of linoleic acid than was found in non-obese littersmates or in normal mice. Rates of lipolysis of tri- and monoglyceride were found to be similar in "obese" and "non-obese" livers. However, the rate of breakdown of monoglyceride by liver homogenates appeared to be markedly greater than that of triglyceride in both groups of animals. Lower levels of free fatty acids (FFA) were found in the livers of the obese mice, and can probably be explained by the reduced levels of FFA in the plasma. Ketone production by liver slices from obese mice was significantly lower than from normal mice. Ketone production by non-obese littermates was intermediate.

The difference in metabolism between the livers of obese and non-obese mice may be related to the hyperinsulism in the obese mice described by other workers, and also to the increased rates of lipogenesis in liver. Interesting parallels can be drawn between the metabolism of fat and ketones in these obese mice and that in human diabetes.

2. Metabolism of Adipose Tissue of the Golden Hamster with Chronic Hypoglycaemia and Hyperinsulinemia due to a Transplantable Islet-Cell Tumour.

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In previous papers, we have described some biological and histological characteristics of a transplantable islet-cell tumour of the golden hamster. Results concerning the insulin release by the tumour in vitro, the insulin release by the pancreas of the host and the ultrastructure of the insuloma have been published elsewhere. The fasted golden hamster bearing this transplantable...
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islet-cell tumour is markedly hypoglycaemic and hyper-insulinaemic. Lipolysis from adipose tissue is increased in these animals although NEFA release is reduced. This indicates an increased re-esterification of NEFA. In the presence of 100 mg/100 ml of glucose in the medium, glucose uptake and glycolol release are increased and NEFA release is reduced compared with the values obtained in the presence of 25 mg/100 ml of glucose.

Prostaglandin PGE; reduces basal glycolol release in the normal, fasted or fed hamsters and in the fed tumour-bearing animals. This compound has no effect on basal glycolol release in the fasted insulina-bearing animals.

3. The Role of Zinc in Adipose Tissue Metabolism.

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For many years zinc has been known to have an ill-defined relationship to insulin action and glucose metabolism. Zinc administration to rats over a long period increases glycogen stores and plasma insulin activity and decreases blood glucose levels. Urinary zinc losses are increased in diabetic in humans and experimental animals. At this Institute we have found that in zinc-deficient rats there is an increase in plasma free-fatty acid levels and a steady loss of adipose tissue.

Zinc has a direct effect on adipose tissue in vitro. When zinc is added in trace amounts (5 p.p.m.) to a bicarbonate medium containing epidermal fat-pads from zinc-deficient or zinc-normal rats, the uptake of glucose from the medium by the tissue is doubled. This action of zinc is independent of insulin and has features which distinguish it from insulin action. There is some evidence that the action of zinc is at the cell membrane. It has not been possible to show any effect of zinc on fatty acid metabolism in vitro and the relationship of these findings to the in vivo observations is obscure.

4. The Disposal of Orally Administered 14C-glucose in the Normal Rat.

S.L. Jeffcoate, and A.J. Moody, Novo Research Institute, Copenhagen, Denmark.

6-14C-glucose (specific activity 6.0 mCi/gm) was administered by oesophageal tube to fasted normal rats; the load was 1.5 g/kg. Rats were killed, in groups, at 0, 10, 20, 30, 60, 120 and 180 min after administration of the load, and the blood and liver sampled.

Scrub insulin and serum sugar peaked at 20 min. The radioactive serum glucose measured by the radioactivity in the dinitrobenzene derivatives of C-6 of glucose peaked at 60 min. At this time 92% of the serum glucose originated from the load. Liver glycogen started to rise after 10—20 min, reaching a maximum at 120 min. The incorporation of 14C-glucose into liver glycogen paralleled the changes in total glycogen.

These data are analysed. It is suggested that during the first hour following an oral glucose load there is a reduction in the hepatic release of glucose accompanied by an increase in hepatic glycogen synthesis. During the second hour there is a further marked increase in hepatic glycogen. Between 120 and 180 min there is a decrease in hepatic glycogen, and hepatic glucose release increases. The results emphasise the important role of the liver in the disposal of an oral glucose load.

5. Glucose Phosphorylating and Glucose-6-Phosphatase Activities of Mouse Pancreatic Islets.

S.J.H. Ashcroft, and P.J. Randle, University of Bristol.

Earlier studies have indicated that the glucose stimulation of insulin release may be mediated by a product of glucose metabolism and that the glucose receptor may be an enzyme or enzymes controlling the rate of phosphorylation of glucose by the beta-cell.

We have studied the glucose phosphorylating activities and the glucose-6-phosphatase activity in homogenates of pancreatic islets. The simultaneous operation of a hexokinase inhibited by glucose-6-phosphate and glucose-6-phosphatase inhibited by glucose was found to be a major factor in the control of glucose phosphorylation. Results suggesting the presence of islets of a high Km glucokinase were obtained. The activity of glucokinase was considerably lower than that of hexokinase but may be of prime importance in the response to high glucose.

6. The Incidence of Clinical Features in a Diabetic Population.

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This report describes the incidence of various clinical features in 420 diabetic patients attending clinics in Dundee.

Most patients had a duration of illness of less than 10 years, in 80 patients duration was 15 years or more. Patients were classified as far as possible into maturity-onset and juvenile types and an attempt was made to define control in terms of blood glucose levels. Proteinuria occurred in 9.1% and retinopathy in 29.3%; only 14.3% of those with diabetes for 20 years or more were free of retinopathy. There was a significant difference (P < 0.01) in the incidence of retinopathy in juvenile type diabetes, depending on whether diabetes appeared before or after the age of 35 years, 37.8% compared with 16.3% respectively.

7. Retinopathy at Diagnosis in Young Diabetics.

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The incidence of retinopathy present at diagnosis varies in different reports from 4% to 15%. From 1960 to 1967, 5,157 new diabetics were seen in whom retinopathy was present in 389 (7.5%). Retinopathy is acknowledged to be a late complication of diabetes, and when present at diagnosis probably results from asymptomatic longstanding mild diabetes.

There are 10 patients under 40 years of age in this group with retinopathy at diagnosis, and their clinical features are compared with those of their older counterparts. Only 1 patient presented with a classical symptom of diabetes-puritus vulvae. Two were diagnosed following crops of boils, 1 with a neuropathic ulcer of the foot and 2 were referred following ophthalmic examination. Four were found quite incidentally on urine testing. Two years was the maximum duration of evidence of diabetes, in 1 case only. No patients presented with acute diabetes. Of the 10 patients, 5 had at least one other abnormality (neuropathy, proteinuria, hypertension, claudication).

The evidence is in favour of these patients having had longstanding mild asymptomatic diabetes. Their subsequent clinical course was similar to that of other young diabetics with accelerated onset of complications. This was often related to uncontrolled diabetes, but sometimes occurred in association with normal blood sugars when patients were vomiting or starving. Other patients with severely uncontrolled diabetes had normal blood ketone levels.