Diabetologia 4, 174-180 (1968)

British Diabetic Association

Abstracts

Medical and Scientific Section, Autumn Meeting

London, 6th and 7th October, 1967

1. Inorganic Plasma and Red Blood Cell Data in Diabetes Mellitus

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Plasma and red cell sodium, potassium, glucose and water estimations have been made on 59 insulin-dependent diabetic and 74 age-matched normal women, as part of a larger survey of sodium status in diabetes.

The diabetics' plasma (mean glucose 178 mg%) had a lower sodium concentration (mean diabetic 134.7, normal 137.6 mEq/kg, p < 0.001) and their red blood cells had higher water (mean diabetic 643.8, normal 634.2 g/kg, p < 0.01) and potassium (mean diabetic 93.6, normal 91.7 mEq/kg) concentration.

Multiple correlation analysis of the diabetic group showed a negative rectilinear association between plasma glucose concentration and potassium (mean diabetic 93.6, normal 91.7 mEq/kg) concentration.

It is suggested that this represents the redress of osmotic balance in hyperglycaemia, with egress of sodium from the plasma, not into the red blood cells, but through a final common pathway of variation in renal sodium excretion, upon which the more familiar glycosuric osmotic sodium loss is superimposed.

2. Intestinal Hormones and Plasma Insulin: Some Observations on Glucagon, Secretin and Gastrin

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The effects of equivalent small doses of glucagon and secretin (2-6 ~g) upon the blood sugar and plasma insulin levels of five normal human subjects were compared. Both hormones provoked a rise in the plasma immuno-reactive insulin level and glucagon caused a rise in the blood sugar as well. The pattern of the responses to the hormones differed, the insulin peak following secretin injection being sharper and more rapidly reached. In three of five subjects, there was a small fall in the blood sugar following secretin.

The effects of gastrin and pentagastrin infusions upon the blood sugar and plasma insulin levels were also investigated. In two subjects, neither gastrin nor pentagastrin altered the fasting levels of the blood sugar or plasma insulin. Gastrin also failed to augment the rise in plasma insulin during intravenous infusion of glucose in two further subjects.

3. Characteristics of Secretin - Induced Insulin Release in Normal Subjects

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The characteristics that distinguish the insulin response to ingested glucose from that to intravenously administered glucose are a greater rise in plasma insulin after oral glucose and inhibition of insulin release by adrenaline after intravenous, but not after oral glucose. This paper reports whether two preparations of secretin were able to reproduce these features.

In the fasting normoglycaemic state, the plasma insulin response to 75 units of secretin was variable. When hyper-glycaemia (of about 120 mg%) was produced by infusion of glucose (300 mg/min) secretin produced a consistent insulin response (mean maximal increment 45.6 ~U/ml).

When comparable hyperglycaemia was produced by adrenaline infusion (4-8 mg/min) secretin still produced a significant plasma insulin increment (28.5 ~U/ml), despite the continuing adrenaline induced inhibition of insulin secretion.

Further studies in hyperinsulin states (obesity and acromegaly) were similar to, but quantitatively larger than those observed among control subjects.

It is concluded that secretin-induced insulin release is augmented by hyperglycaemia and that it is not abolished by adrenaline, findings compatible with the thesis that secretin is one of the factors allowing the pancreatic islet to discriminate between oral and intravenous glucose.

4. The Metabolism of Glucose, Oxygen and Carbon Dioxide in Human Skeletal Muscle during Sustained Contractions.

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During mild sustained contractions, the actively metabolising muscle comes into equilibrium with its blood supply within 2-3 min. Venous blood samples were withdrawn, blood flow measured, and the Fick method used to calculate the metabolic activity of resting and contracting muscle in healthy young adults, most of whom had eaten a normal meal 1-3 h before the samples were obtained.

While oxygen uptake and carbon dioxide production both increased, the respiratory quotient sometimes rose and sometimes remained unchanged. Glucose metabolism was not affected to the same extent as that of oxygen and carbon dioxide and there was great variation in the change in uptake actually produced by local exercise.

5. The Effects of Insulin and Normal Human Sera on the Glucose Metabolism of Isolated Fat Cells.

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Crystalline insulin and dilute (10%) human sera were shown to stimulate the conversion of (14C)glucose to (14C)glycogen, (14CO2 and (14C)triglycerides by isolated fat cells. The stimulatory activities of normal human sera (obtained before and after oral glucose) were compared with the activities of human insulin. A potency in ~U/ml was allocated to the antibody suppressible activities of the sera. The non-suppressible activities were expressed in terms of glucose carbon incorporated into each metabolite.

A significant (P < 0.0005) linear correlation exists between serum IMI and the antibody suppressible activities of the sera on the conversion of glucose to CO2, glycogen and triglycerides. These activities have the same interrelationship as the activities of crystalline insulin when expressed as glucose incorporated into each metabolite. The non-suppressible activities do not increase after glucose load, and do not have the same interrelationship.
as the activities of crystalline insulin. The incorporation of glucose carbon into triglycerides is higher, relative to its incorporation into CO₂, in the presence of serum plus antibodies than in the presence of crystalline insulin. We conclude that these non-suppressible activities cannot be termed “insulin-like activities”.

6. Flux of ¹⁴C-Glucose in the Forearm


Studies to determine the initial volume of distribution of glucose in man showed that this space is reduced in maturity-onset diabetes and this might possibly be due to alterations in the capillary wall impeding the outflow of glucose from the plasma. To investigate this hypothesis a mixture of ¹⁴C-glucose and Evans Blue — as a plasma marker — was infused intravenously into the forearms of six subjects, and the net outward flow of ¹⁴C-glucose measured for eight minutes from the recoveries of tracer and marker, respectively, in the plasma of an effluent vein, with and without the presence of insulin. Insulin had no effect either on ¹⁴C-glucose outflow or on the subsequent re-entry of the tracer. This reflex is evident from a flattening and progressive decrease in Evans Blue recovery as compared with that of ¹⁴C-glucose in the second half of the experiment. It is concluded that:
1. Insulin has no effect on capillary glucose transport;
2. Tracer glucose administered is in a state of two-way flux between the plasma and the rest of the body glucose mass until its equilibration is completed;
3. Peripheral equilibration of glucose newly added to the body glucose mass does not seem to be under insulin control.

7. The Movement of Insulin across the Liver Cell

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Thyroid, ovarian and adrenal hormones are broken down and conjugated by the liver and excreted into bile. Insulin, however, appears in rabbit bile in an immuno-assayable (so presumably physiologically active) form at a concentration higher than in venous blood.

In the experiments described here, bile was collected in 3 min aliquots from a catheter in the common bile duct of anaesthetized rabbits (the gall bladder had previously been tied off). Following an i.v. injection of 0.5 U of ox insulin, a maximum insulin concentration occurs in bile 24 min after (6 experiments). If this time is corrected for the dead space of the biliary tree and catheter, the insulin peak in bile follows about 15 min after injection. A similar result was obtained following the injection of D⁵-thr-insulin (a peak of radioactivity at 18 min) and in four rabbits who were given 0.5 U of rabbit insulin.

If the liver cells contain an active insulinase system it is interesting that the hormone should be able to pass quite so easily from blood into bile.

8. Carbohydrate-Induction of Hypertriglycerideraemia in Children


The condition of “carbohydrate-induced hypertriglyceridaemia” is known to be associated with impaired glucose tolerance and ischaemic heart disease. A rise in the fasting levels of serum triglyceride can, however, also be induced in normal adults by high carbohydrate diets but this has not previously been shown to occur in children. We have had the opportunity to observe the short-term effects of high carbohydrate feeding in six children aged 2—14 years with familial hypercholesterolaemia but with normal levels of serum triglyceride. A rise in serum triglyceride occurred in all the children, and highest levels were seen 3—6 days after commencement of the diet. The increase in triglyceride occurred predominantly (though not exclusively) in the very low-density lipoproteins. Analysis of the triglyceride fatty acids by gas-liquid chromatography showed an increased proportion of palmitoleic (C 16: 1) and palmitic (C 16: 0) acids during carbohydrate feeding, indicating that lipogenesis contributed to the rise in triglyceride. This study shows that in children, as in adults, carbohydrate-induction of a rise in serum triglyceride is not limited to patients with “carbohydrate-induced hypertriglyceridaemia”.


A study of subjects collected during a diabetes survey has been carried out to determine whether a group of people with a) normal glucose tolerance and glucosuria (“renal glucosuriains”) or b) a normal fasting blood glucose concentration but a failure to return to this 2h after 50g oral glucose (“delayed return”) showed any abnormality of plasma insulin or growth hormone concentration during the glucose tolerance test. The weight, sex and age of the individuals studied were found to affect the results and therefore comparisons were made between groups which had been matched to eliminate the effects of these variables. The renal glucosuriains showed an exaggerated early rise of blood glucose and plasma insulin concentration and a tendency to late hyperglycaemia. Abnormalities of the fasting plasma insulin and growth hormone concentration were also present. Non-obese subjects with delayed return showed a delay in the rise of plasma insulin concentration following oral glucose and some evidence of resistance to endogenous insulin. Obese subjects with delayed return showed a normal rise of plasma insulin after glucose.

10. Insulin Release in Response to Oral Glucose in Obesity: The Effect of Reduction of Body Weight.


Plasma levels of immuno-reactive insulin (I.R.I.) and plasma glucose concentration have been measured in a group of obese patients and in a group of normal subjects in the fasted state and after an oral glucose load. Measurements in the obese patients have been repeated after dietary reduction of their weight.

The basal concentration of I.R.I. in the plasma of the fasted obese patients was greater than that of the normal subjects; one hour after the oral glucose load the I.R.I. level was three times that found in normal subjects at the same sampling time. After weight loss I.R.I. levels in response to oral glucose were diminished. Concentrations of plasma glucose were also diminished after weight loss. The mean increment in plasma I.R.I. in response to the glucose load over a two-hour period before dieting was linearly related to the mean increment after dieting, and a similar relationship was found for plasma glucose increments.

Thus, insulin resistance in obesity is less after reduction of body weight.

11. The Renal Glucose Threshold in Diabetes.

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The assessment of control for most diabetics is based on the results of testing urine specimens for the presence of sugar. However, the value of this method depends on the