chronic bronchitis, especially when hypercapnia is present.

60. THE EFFECT OF INSULIN ON THE METABOLISM OF THE PERFUSED IN SITU RAT LUNG
W. A. STUBBS, I. MORGAN and K. G. M. M. ALBERTI
Faculty of Medicine, Chemical Pathology and Human Metabolism, Southampton General Hospital

The metabolic potential of the lung has been generally unrecognized. As this organ receives half the cardiac output, small changes in its metabolism could have profound effects on whole body fuel homeostasis.

The lung has previously been considered to be unresponsive to insulin (Moxley & Longmore, 1975, Life Sciences, 17, 921). We have re-examined the effects of insulin using an improved in situ whole organ technique.

The lungs from fed or 48 h starved male Wistar rats were perfused through pulmonary artery and left atrial cannulae with Krebs-Henseleit buffer containing albumin, 4 mmoll⁻¹ glucose and insulin 0.01 µU ml⁻¹ without and with insulin respectively. Insulin increased glucose uptake and lactate release. At 4 h there were no significant changes in pyruvate, alanine and glycerol.

At 10 min, insulin concentrations were similar with or without prior addition of insulin. Subsequently, insulin increased glucose uptake and lactate release. At 4 h the mean (± SEM) glucose uptake was 57 ± 3 and 74 ± 6 µmol g dry wt⁻¹ h⁻¹ (P < 0.05) and the lactate production 76 ± 4 and 98 ± 1 µmol g dry wt⁻¹ h⁻¹ (P < 0.01) without and with insulin respectively. Insulin caused a small significant increase in glycerol production but had no effect on other metabolites. Similar effects were noted when the insulin concentration was increased to 500 µU ml⁻¹. In the fasted animal, the lower dose of insulin had no effect on glucose metabolism but with higher concentrations a similar increase to that found for the fed animal was noted.

This in situ lung perfusion technique offers advantages over previous methods. There was no evidence of cellular damage histologically and the dry wt/wet wt ratio was similar to that of the unperfused lung. It is technically simple, thus minimizing laceration damage; the myocardium cannot contribute metabolites to the perfusate; it produces physiological flow rates; and pulmonary oedema is avoided.

The demonstration of an effect of insulin suggests that the lung may have a non-respiratory metabolic role. Further study is required.

61. GLUCOSE CONTROL OF SECRETIN IN HEALTH AND DIABETES
K. D. BUCHANAN, E. R. TRIMBLE,* R. W. HENRY and J. C. MCLoughlin
Departments of Medicine and *Metabolic Medicine, the Queen's University of Belfast and the Royal Victoria Hospital, Belfast

Secretin may have metabolic actions outwith its recognized function in controlling pancreatic exocrine function. The hormone stimulates insulin release and high circulating levels are recorded during starvation (Henry et al., 1975, Lancet, ii, 202). A previous report indicated that oral glucose stimulated its release (Chisholm et al., 1969, Journal of Clinical Investigation, 48, 1453). We have therefore investigated the control of secretin release by glucose. Secretin was measured by a sensitive and specific radioimmunoassay.

Immunoreactive secretin (IRS) levels were suppressed significantly in normal subjects following 25 g oral glucose given after either 12 or 36 h fasting (P < 0.05 and P < 0.025 respectively) and 25 g intravenous glucose also given after either 12 or 36 h fasting (P < 0.05 and P < 0.025 respectively). However, reduced plasma glucose concentrations in nine subjects during 72 h starvation could not be correlated with rising IRS levels, and insulin induced hypoglycaemia in six normal human subjects did not stimulate IRS release.

In twenty-two untreated maturity onset diabetics, high circulating levels of IRS were recorded and this correlated with the fasting glucose concentration (r = 0.433, P < 0.025). The elevated IRS levels returned to normal following 6 months dietary control of the diabetes and the fall in the fasting glucose correlated with the fall in the IRS levels (r = 0.562, P < 0.01).

It is concluded that secretin cannot exert an insulinotropic action after glucose ingestion. The mechanism by which glucose suppresses secretin release is obscure and hypoglycaemia cannot explain the rise in IRS during starvation. The normal suppressive effect of hypoglycaemia on IRS levels is lost in untreated diabetes and the role of secretin in the diabetic syndrome merits further study.

62. THE EFFECT OF INSULIN ON PLASMA 3-HYDROXYBUTYRATE AND CYCLIC AMP RESPONSE TO GLUCAGON IN DIABETES
R. S. ELKELES, J. HAMBLEY and P. G. FROST
Northwick Park Hospital and Clinical Research Centre, Harrow, Middlesex HA1 3UJ

The role of glucagon in the metabolic derangement of diabetes is debated. The effects of intravenous glucagon have been studied in seven insulin requiring diabetics before, 1 week and 1 month after starting insulin, on blood glucose, serum insulin, plasma 3-hydroxybutyrate, FFA and cyclic AMP (cAMP). After an overnight fast, glucagon 10 µg/kg was given i.v. and blood samples taken over 60 min. Results were compared with tests done in six healthy controls. The controls showed a small but not significant rise in plasma 3-hydroxybutyrate after glucagon with a fall to below basal concentrations from 30 min onwards. The untreated diabetics showed a significant rise at 15 min with no subsequent fall below basal concentration. After 1 week on insulin no significant changes occurred during the test. After 1 month on insulin the pattern of response had changed so that there was a significant fall below basal concentration from 15 min onwards. There was no difference in fasting blood glucose between the second and third tests. The change in plasma 3-hydroxybutyrate response to glucagon 1 month after starting insulin could not be explained by inhibition of the lipolytic effect as judged by the rise in plasma FFA, or increase in endogenous insulin secretion. It would therefore seem to reflect inhibition of the hepatic ketogenic effect of glucagon by exogenous insulin. Basal plasma cAMP concentration and the response to glucagon were similar in controls and diabetics, and there was no change in the diabetics after insulin. This agrees with previous findings (Siddle, Davies, Shetty & Elkeles, 1976, Clinical Science and Molecular Medicine, 50, 487).
that the administration of exogenous insulin does not alter the rise in plasma cAMP following intravenous glucagon. Plasma 3-hydroxybutyrate may provide an index of longer term tissue responsiveness to insulin.

63. COMPARISON OF TREATMENT OF MILD DIABETES WITH A BASAL INSULIN SUPPLEMENT OR SULPHONYLUREA

R. R. HOLMAN, E. HARRIS, P. HARDING and R. C. TURNER

Nuffield Department of Clinical Medicine, Radcliffe Infirmary, Oxford

A raised, 'basal' plasma glucose is a predominant abnormality of diabetes, and is found in many patients who by usual criteria are 'well controlled' by diet. At the Edinburgh M.R.S. meeting we reported that basal normoglycaemia can be obtained by a basal insulin supplement provided by ultralente insulin (UL) without the risk of hypoglycaemia or the need for rigid diet. These patients have been restudied on treatment with chlorpropamide (C) with 24 h profiles, including glucose, C-peptide and triglyceride assay.

Patients with a basal plasma glucose of more than 10 mmol/l could be controlled with UL but not with C. Nocturnal normoglycaemia was obtained in thirteen less severe diabetics with both treatments (mean nocturnal glucose reduced from 7.4 to 4.5 and 4.4 mmol/l, respectively), but the dose needed cannot be predicted as easily for C as UL. The latter caused a 'base line shift' decrease in the plasma glucose concentrations throughout the 24 h, with no change in the incremental glucose or C-peptide response to meals. The response to C was similar, except that the incremental glucose response to the meals was also improved (mean daytime plasma glucose, pre-treatment 9.6, UL 7.1, C 6.5 mmol/l) together with an enhanced C-peptide response (0-60 min C-peptide to standard breakfast pre-treatment, 0.34, UL 0.37, C 1.13 pmol/ml).

Neither treatment necessitates altering the patient's routine. Only long-term studies would determine if reduced diurnal glucose levels with nocturnal normoglycaemia, which can be obtained with either treatment, might prevent diabetic complications.

64. ATTEMPTED BETA CELL SALVAGE BY A REGULAR MEAL/INSULIN INFUSION REGIME IN NEW SEVERE KETOTIC DIABETICS

R. C. TURNER and R. R. HOLMAN

Nuffield Department of Clinical Medicine, Radcliffe Infirmary, Oxford

Following treatment of the sudden onset of severe diabetes, there is some beta cell recovery, and occasionally 'honeymoon' periods of minimal diabetes occur. It is possible that the high blood sugar 'exhausts' the remaining beta cells and that a period of normoglycaemia is needed to allow recovery of these cells. Normoglycaemia cannot be obtained in new severely diabetic patients with normal meals and appropriate subcutaneous insulin. Instead we give an insulin infusion from a portable pump at two rates, a high dose for the day to which is matched seven 2-hourly feeds of similar nutrient content, and a low dose infusion during the night. Normoglycaemia is achieved throughout the day in ambulant patients, and the necessary infusion doses are easily determined by two plasma glucose assays per day.

Five acute onset, ketotic patients provide a preliminary study. In four the dose of insulin required steadily dropped. Sufficient beta cell recovery was obtained that basal normoglycaemia was achieved with small doses (18-28 units) of Ultralente insulin. The C-peptide response to meals improved. Reasonable control could be obtained without restricting the patient's routine. The fifth continued to have high insulin requirements. Whilst such improvement might have occurred with other therapies, the regime is logical, simple to manage, and may assist in obtaining optimal control.

65. LONG-TERM STUDY OF NERVE CONDUCTION VELOCITY IN STREPTOZOTOCIN-DIABETIC RATS

C. FOX, C. LOWY and P. H. SØNSKJEN

St Thomas's Hospital, London

A colony of Streptozotocin-diabetic rats was maintained for 14 months in order to study structural and functional changes caused by long-term hyperglycaemia and the effect of different forms of treatment on these changes. The diabetic animals were allocated to one of four groups; (A) untreated; (B) fed a low carbohydrate diet; (C) given daily insulin; and (D) low CHO diet and insulin. The diabetic status of individual animals was monitored by plasma glucose concentration and urinary glucose excretion. Serial measurements of motor nerve conduction velocity (MNCV) were made in the tail nerve under Hypnorm anaesthesia.

Two months after the onset of diabetes, despite heavy glycosuria and hyperglycaemia (mean plasma glucose 34.7 mmol/l), MNCV was not reduced in untreated diabetics as compared with age-matched controls (38 m/s). MNCV in control rats then increased with age to a maximum of 46.2 m/s, while in untreated diabetics up to 7 months, MNCV did not increase with age and became significantly lower than in non-diabetic controls. Treated diabetics had intermediate MNCV values.

After 7 months, spontaneous recovery from hyperglycaemia occurred in a number of animals from all the diabetic groups and this improvement in diabetic status was accompanied by an increase in MNCV to the same as control values. At 10 and 14 months, mean MNCV was not significantly different in any of the groups. There was a significant negative correlation between plasma glucose concentration and MNCV.

66. BLOOD VISCOSITY AND METABOLIC CONTROL IN DIABETES MELLITUS

A. J. BARNES, P. LOCKE, T. L. DORMANDY and J. A. DORMANDY

Royal Postgraduate Medical School, Hammersmith Hospital, Whittington Hospital, and St James Hospital, Balham

In view of the close correlation between elevation of blood viscosity and the presence of diabetic complications, the relationship between blood viscosity and poor metabolic control was investigated in two groups of diabetic patients: Group A: ten insulin-dependent diabetics during recovery from keto-acidotic or hyperosmolar non-ketotic precoma. Group B: thirty out-