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

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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

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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

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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

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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-
patient diabetics during their first 4 months of treatment with either diet alone, or diet and metformin, glibenclamide or insulin.

In both groups, blood viscosity was elevated when compared with age and sex matched non-diabetic subjects, falling significantly with improved metabolic control, irrespective of the diet and treatment administered. In Group A, the fall in blood viscosity was related to a fall in haematocrit, plasma fibrinogen and other proteins. In Group B, the fall in viscosity was related only to the fall in haematocrit, there being no significant change in the levels of plasma proteins.

Poor metabolic control in diabetic patients may result in considerable elevations of blood viscosity and in this way accelerate the progression of diabetic complications.

67. TRANSIENT GLUCOSE INTOLERANCE IN THE INTENSIVE CARE PATIENT
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(Introduced by E. Sherwood Jones)
The tolerance to glucose can be tested by giving dextrose as a continuous intravenous infusion. Heuckenkamp & Zollner (1972, Nutrition and Metabolism, 14, Suppl., 58–73), studied healthy subjects in this way and found that in the steady state, when the blood sugar was 8.2 mmol/l, the subjects could utilize 0.5 g kg⁻¹ h⁻¹; this was equivalent to 100% utilization of the dextrose. When the dose was doubled or even trebled (1.0 or 1.5 g kg⁻¹ h⁻¹) the utilization remained high at above 90%. We made comparable studies on intensive care patients to determine the incidence and severity of glucose intolerance. The twenty-nine patients (mean age 46 years) suffered from: acute pancreatitis (fourteen), self-poisoning (eight), multiple injuries (two), or miscellaneous illnesses (five). Glucose was infused as a 50% solution of dextrose at a constant rate of 25 g/h; the mean rate was 0.46 g kg⁻¹ h⁻¹, range 0.26–0.63 g kg⁻¹ h⁻¹. When, after 4 h, hyperglycaemia developed, the blood sugar was maintained in the range of 5.0–17.0 mmol/l by means of a continuous infusion of soluble insulin diluted in a gelatine carrier. Glucose intolerance was diagnosed when insulin, in a dose of 2.0 units/h or more, was necessary for a minimum period of 16 h. Of the twenty-nine patients, twenty-four showed intolerance and the dose of insulin for their control varied from 2.0 to 11.0 units/h (mean 4.6 units/h). Of these twenty-four patients, it was possible to demonstrate that the intolerance was transient in fifteen; of the remaining nine patients, one had previously unrecognized diabetes mellitus, four patients left the unit before completion of their study and four died.

The glucose intolerance was anticipated in the patients with injuries or widespread inflammatory disease, but was quite unexpected in uncomplicated cases of self-poisoning, among which four out of the eight showed intolerance. Both tricyclic antidepressants and barbiturates were associated with transient glucose intolerance. Nine of the twenty-four patients with intolerance had received drugs which might have contributed. The drugs were: a single dose of methylprednisolone in one case and glucagon given to eight of fifteen patients with acute pancreatitis; however, the glucagon is unlikely to have contributed as the other seven patients also showed intolerance.

This study was carried out in collaboration with Dr W. H. Taylor (Department of Chemical Pathology, Liverpool), and financed by the United Liverpool Hospitals Research Committee.

68. PROSTAGLANDINS (PGs) IN INTRINSIC BRONCHIAL ASTHMA
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Prostaglandin $F_{2\alpha}$ (PGF$_{2\alpha}$) constricts the normal human bronchus. Asthmatic patients appear to be up to 8000 times more sensitive to this effect than normal subjects (Mathé et al., 1973, British Medical Journal, i, 193). Sensitized human lung in vitro releases large amounts of PGF$_{2\alpha}$ on immunological challenge (Piper & Walker, 1973, British Journal of Pharmacology, 47, 291). In allergic patients, antigen inhalation caused an increase (up to five-fold) in blood levels of the primary metabolite of PGF$_{2\alpha}$ (Green et al., 1974, Lancet, ii, 1419). All of these data suggest that PGF$_{2\alpha}$ could be important in bronchial asthma.

In contrast, Smith & Dunlop (1975, Lancet, i, 39) and Rudolph et al. (1975, Lancet, i, 450) have been unable to alter the asthmatic response to exercise or to antigen challenge by giving large doses of aspirin or indomethacin which would reduce PG synthesis, and have inferred that PGs are not of major importance in bronchial asthma.

In order to make direct measurements of PG turnover

<table>
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<th>Patient No.</th>
<th>Sex</th>
<th>Age</th>
<th>Day 1 PGF-M excretion rate</th>
<th>PEFR (1 min⁻¹)</th>
<th>Day 5 PGF-M excretion rate</th>
<th>PEFR (1 min⁻¹)</th>
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</tr>
</tbody>
</table>

Table 1. Excretion of PGF-M (nmol/mmol creatinine) in five patients with bronchial asthma