The initial body mass index correlated inversely with both the fasting and post-glucose values ($r = -0.29$ and $-0.27$ respectively, $p < 0.002$). Low initial post-glucose values went with a larger decrease in weight in the first year ($r = 0.19$, $p < 0.03$). Growth hormone values were not correlated with glucose levels or the subject's sex.

A quantitative index of the sensitivity to vibration over the feet was obtained with the biothesiometer. The deterioration in this index during the first year correlated with the post-glucose hormone levels accounted for 5% of the total variance of the vibration change ($p < 0.001$). At 3 years from diagnosis, although a weaker zero order correlation remained ($r = 0.15$, N.S.), this was accountable by interactions with other, more strongly related factors.

### 133 RISK FACTORS FOR MICROANGIOPATHY IN TYPE I DIABETES

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Duration of diabetes and poor glycaemic control are established risk factors for the development of diabetic microvascular disease. We have ascertained two series of carefully characterised long duration Type I (insulin dependent) diabetic patients in order to examine genetic, immunological and clinical risk factors.

The two groups of subjects were collected consecutively from our clinics and were closely matched for age of onset and duration of disease. One group (n=133) had developed severe microangiopathy in the form of proliferative retinopathy. The other group (n=49) had no evidence of complications. There was a significant excess of males in the retinopathy group (M:F=91:42) compared with the group without complications (M:F=25:24), $p=0.046$. Phenotyping for HLA, A,B,C and DR and the acetylator polymorphism was performed. No association was found between these factors and susceptibility to microangiopathy.

Insulin binding capacity was similar in both groups of patients. However we found a significantly increased prevalence of raised immune complex levels measured by the Clq solid phase radioimmunoassay and polyethylene glycol precipitation methods ($p<0.05$). Glycosylated haemoglobin measured by a microscale chromatographic method was significantly higher in the retinopathy group, 12.0±1.9% (mean ± SD) than in the control group, 11.2±2.14% ($p=0.028$). An analysis of previous insulin regimens showed the patients with complications to have been treated with once daily insulin and raised levels of immune complexes are associated with microangiopathy. There is no evidence to implicate the HLA or acetylator polymorphism in diabetic complications.

### 134 INSULIN RESISTANCE AND DIABETIC RETINOPATHY IN TYPE II DIABETICS

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Type II diabetes results from a combination of decreased tissue sensitivity to insulin (insulin resistance) and decreased insulin secretion (insulin deficiency). The relationship between these two factors and diabetic retinopathy was studied by the 'euglycaemic' and the 'hyperglycaemic' clamp techniques.

In the 'euglycaemic' clamp a prime-continuous insulin infusion raises plasma glucose levels to 80 μM and keeps them constant for 80 min. The fasting plasma glucose (FPG) is maintained constant by a variable glucose infusion based on a negative feedback servoregulatory mechanism. Since the glucose system is at a steady state the mean glucose infusion rate equals the turnover rate (M). The ratio of M for the steady state insulin concentration (I), M/I, estimates insulin resistance. In the 'hyperglycaemic' clamp glucose levels are raised of 7 mmol/l above FPG and kept constant for 80 min. The endogenous insulin response estimates insulin secretion.

Ten diabetics without and 8 with retinopathy (matched for age, duration of known diabetes, weight, renal function) were studied. FPG, degree of diabetic control, measured by Haemoglobin A1, and fasting insulin levels were similar in the two groups. In the 'euglycaemic' clamp the steady state insulin (8.9±2.0 vs. 8.0±3.0 mmol/l) and insulin levels (7.1±6 vs. 8.2±22 μM) were similar in the two groups, but M (5.8±1.7 vs. 6.0±2.8 mg·min⁻¹·kg⁻¹, $p<0.001$) and M/I (7.6±1.8 vs. 13.8±2.4 mg·min⁻¹·kg⁻¹·μM⁻¹, $p<0.001$) were significantly smaller in patients with retinopathy. In the 'hyperglycaemic' clamp insulin secretion was similar in the two groups of diabetics, in both groups being smaller than in normals.

In type II diabetes an increased insulin resistance is associated with the presence of retinopathy.

### 135 CASEIN TOXICITY IN INTESTINAL ORGAN CULTURE


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There is considerable disparity between the results of previous studies on the mechanism of gliadin toxicity on coeliac mucosa in vitro and the dietary protein casein has usually been used as a reference protein. Our studies using this reference protein show that casein itself is toxic to intestinal mucosa in vitro. Normal jejunal biopsies were maintained in