

## A LOW FAT DIET IMPROVES METABOLIC CONTROL IN INSULIN DEFICIENT RATS

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It is widely recognized that the composition of the background diet plays an important role in both the pathogenesis and treatment of non insulin-dependent (type 2) diabetes. However, the effects of diet on metabolic control in insulin-deficient (type 1) diabetes are poorly understood. Since high fat, low carbohydrate diets have been shown to impair glucose tolerance and lead to decreased insulin sensitivity in normal healthy subjects, (Himsworth 1935) the aim of the present study was to determine the effects of such diets on metabolic control in insulin-deficient diabetes.

Male Sprague Dawley rats (100 g) on a laboratory chow diet were fasted overnight. Streptozotocin (60 mg/kg body wt) or an equivalent volume of vehicle (0.1 M citrate buffer, pH 4.0) was injected intravenously into the rats previously anaesthetised with ether. They were then randomly allocated to either a high fat (HF) or low fat (LF) diet of the following composition: HF; carbohydrate 12%, protein 22%, fat 66% of calories, LF; carbohydrate 66%, protein 22%, fat 12% of calories. After at least two weeks on the diet, the rats were fasted overnight, anaesthetized with sodium pentobarbitone (60 mg/kg body wt). A fasting blood sample was taken and the rats were given an intravenous glucose tolerance test (0.5 g glucose/kg body wt). Blood samples were collected from the tail tip at 5, 10, 15, 30 and 60 minutes and glucose and insulin concentrations were determined.

The weight gain of both HF and LF rats was greatly reduced by streptozotocin (STZ) treatment. The fasting plasma glucose concentrations were not significantly affected by the HF diet. (HF;  $6.6 \pm 0.3$ , LF;  $6.2 \pm 0.3$  mmol/L). In contrast, the fasting plasma glucose concentrations in the HF-STZ rats were markedly elevated relative to LF-STZ rats (HF-STZ;  $14.5 \pm 1.3$ , LF-STZ;  $7.8 \pm 0.9$  mmol/L). Glucose tolerance was significantly impaired in the HF rats relative to the LF rats at all time points. This may be due in part to the lower insulin concentrations in the HF rats. HF diets were associated with a more severe impairment of glucose tolerance in the STZ treated animals.

These results show that a high fat diet was associated with a significant worsening of metabolic control in mild insulin deficiency induced by streptozotocin. The effect of the HF diet was most marked on fasting plasma glucose which may be indirect evidence that HF diets stimulate hepatic glucose production. Finally, these results provide strong evidence that the composition of the background diet can significantly influence metabolic control in insulin-deficient diabetes.

HIMSWORTH, H.P. (1935). Clin. Sci. 2 : 64.