

Progressive Hyperglycemia: The UKPDS Experience

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Abstract: The United Kingdom Prospective Diabetes Study (UKPDS) is now being conducted to determine whether intensive control of blood glucose to near-normal levels can reduce type II diabetes-associated morbidity and mortality. The study is not yet complete, but 6-year results suggest that type II diabetes is a relentlessly progressive disease characterized by an increasing decline in pancreatic β -cell function. Only patients with newly diagnosed type II diabetes were eligible to participate, yet about 50% had evidence of diabetes-derived tissue damage at entry, and 21% displayed signs of retinopathy. Although intensive treatment with insulin, a sulfonylurea, or metformin initially reduced fasting plasma glucose and glycosylated hemoglobin levels during the first year, glycemic control progressively deteriorated over the next 5 years despite escalating drug dosages. Insulin sensitivity was unaltered by sulfonylurea treatment and improved by metformin, but β -cell function declined in all treatment groups, regardless of the patient's initial weight and regardless of whether the patient was receiving intensive or conventional drug therapy. These results suggest that agents whose mechanism of action relies on continued β -cell function are likely to become less effective over the long term. Acarbose has been added to the UKPDS protocol, since it can attenuate the magnitude of postprandial glucose excursions. Final data will be available in 1998.