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NOCTURNAL AND POSTPRANDIAL METABOLISM IN DIABETES MELLITUS
- with special reference to lipid intolerance and the second meal effect

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Diabetes mellitus is a global health problem. Modern, intensified therapy prevents or delays the microvascular complications in both Type 1 and Type 2 diabetic patients. However, in Type 1 diabetes, nocturnal hypoglycemia is a serious side effect and an obstacle in the prevention of complications by intensive insulin therapy. In Type 2 diabetes, nocturnal plasma free fatty acid (FFA) levels are accentuated. This may be postulated as one possible mechanism behind the morning fasting and postprandial hyperglycemia and lipid intolerance. Moreover, ~40% of these patients have already established macroangiopathy at the onset of the disease. Thus, it is critically important today that early risk factors for cardiovascular disease are defined, and that stategies for effective treatment of both macrovascular and the microvascular complications of the disease are continously improved. The present study evaluated the profylactic effects of bedtime ingestion of a slowly digestable carbohydrate (uncooked cornstarch) on nocturnal and morning postprandial blood glucose control and lipid levels in Type 1 and Type 2 diabetic patients. Moreover, insulin sensitivity and postprandial triglyceride (TG) levels were studied in healthy, normoglycemic individuals with a massive heredity for Type 2 diabetes.
Bedtime uncooked cornstarch exhibited a lente release profile, the peak effect on blood glucose being similar to the nocturnal peak effect of NPH insulin, ie., after ~4-5 hrs. In Type 1 diabetics, ~20 g of bedtime cornstarch led to a 70% reduction of nocturnal hypoglycemia without significantly altering HbA1c or fasting lipids. In Type 2 diabetes, bedtime uncooked cornstarch ingestion led to sustained nocturnal insulinization and FFA suppression. This was associated with improved fasting blood glucose and glucose tolerance after breakfast, consistent with an overnight second-meal effect. The same effect was not obtained with similar amounts of rapid carbohydrates. The insulin secretory response at breakfast was improved. In contrast, postprandial lipemia was not corrected, probably because insulin resistance was not alleviated. It was also demonstrated, for the first time, that normoglycemic and normolipemic first-degree relatives of Type 2 diabetic patients, exhibit lipid intolerance in that the postprandial TG response to a fat-rich meal was 50% higher. This, in turn, is a risk factor for coronary heart disease. In conclusion, bedtime ingestion of uncooked cornstarch seems to be a feasable tool to balance the effect of NPH insulin and, thus, to prevent nocturnal hypoglycemia in intensively treated Type 1 diabetic patients. Moreover, modulation of nocturnal plasma insulin and FFA levels by slow-release cornstarch improved the morning glycemic control, possible due to relief of the "lipotoxic effect" of FFA on the ß-cell. Further, the finding of a lipid intolerance in healthy persons with massive heredity for Type 2 diabetes, is a clear marker of an atherogenic lipid profile which is present probably long before glucose tolerance is impaired.

Key words: diabetes, first-degree relatives, nocturnal, postprandial, glucose, triglyceride, metabolism, free fatty acids (FFA), insulin, insulin resistance, C-peptide, carbohydrates