The diminished effectiveness of insulin in stimulating glucose uptake in the forearm tissues of obese subjects provides indirect evidence for a relationship between adipose tissue mass, insulin resistance and carbohydrate intolerance. SALANS et al. reported that enlarged adipocytes are less sensitive than smaller ones to the stimulating effect of insulin on glucose utilization. This was confirmed by studies on fat cells from obese subjects with pathological carbohydrate tolerance and from spontaneously obese rats. According to BJÖRNTORP, insulin increased incorporation of glucose by adipose tissue in controls and obese non-diabetics, but not in obese diabetics.

The purpose of the present investigations was to assess the insulin-stimulated glucose uptake of fat tissue removed from normal weight persons with different stages of glucose intolerance.

MATERIALS AND METHODS

In 23 normal weight male subjects a 2-h glucose infusion test (12 mg/kg/min) (GIT) starting with a priming injection (0.33 g/kg) was performed to evaluate carbohydrate tolerance (CHT) and insulin secretion pattern. All had a previous history of diabetes (intermittent glycosuria) and were hospitalized at the Clinical Research Unit of the Central Institute for Diabetes.
INSULIN RESPONSIVENESS OF ADIPOSE TISSUE

Three days before testing they consumed a diet containing 50% carbohydrate, 30% fat and 20% protein.

The results were compared with those of 115 healthy normal weight subjects without family history of diabetes.

On the basis of a discriminant analysis two blood glucose criteria of the GIT were found to characterize CHT: (a) the area under blood glucose curve of the time interval 60-120 min of the test procedure (area BG 60-120 min absolute); (b) the blood glucose concentration at 150 min.

The normal range of each criterion was defined as the mean ± 1 SD. Values higher than the mean ± 1 and up to ± 2 SD were classified as borderline range. Values higher than the mean ± 2 SD were considered as pathological range. The existence of two criteria for characterization of CHT makes it necessary to define the following:

--- normal CHT: both criteria in the normal range or one in the borderline range;
--- borderline CHT: both criteria in the borderline range or one criterion ‘normal’ and the other ‘pathological’;
--- pathological CHT (chemical diabetes): both criteria in the pathological range or one in the borderline range.

Eleven subjects showed a normal, 3 a borderline and 9 a pathological CHT. Overt diabetics (WHO classification) were excluded. For characterization of the insulin secretion pattern the reactive areas above the IRI fasting levels of the time intervals 0-5 and 30-120 min were calculated.

Tab. 1 summarizes some relevant data regarding these groups.

Blood glucose was determined enzymatically (Beckman-Analyzer) and insulin radioimmunologically according to Ziegler et al. by the back titration method.

Three days after the performance of GIT and after an overnight fast, subcutaneous adipose tissue was removed by surgical biopsy from the anterior abdominal wall after careful intracutaneous anesthesia (1% lidocaine hydrochloride, VEB Jenapharm, GDR).

Fat tissue fragments were quickly excised and transferred to plastic vials.

Experiments with isolated adipocytes

Fragments of adipose tissue were cut with scissors into small pieces and disaggregated by collagenase (charge CLS 44 A 181, 238 U/mg, from Worthington Biochemical Corporation, U.S.A.) in Krebs-Ringer bicarbonate buffer (KRB). Fat tissue was divided into 200-mg portions and incubated at 37°C for 45 min in 3 ml KRB containing collagenase (2 mg/ml), 4% bovine serum albumin (Behring Werke AG, FRG, batch No. A 1001, electrophoretically pure) and 0.56 mM D-glucose. Following incubation with collagenase the cells obtained from 1.40 ± 0.13 g human fat tissue (mean ± SEM of 23 experiments) were pooled, filtered through nylon stockings and washed 4 times with 5 ml KRB, pH 7.4. Thereafter the fat cells were incubated for 2 hours in KRB in the presence of 2% bovine albumin (as controls) or with crystalline pork insulin (Novo, batch No. S 4769; concentrations used: 2.5, 12.5, 62.5 μU/ml). Immediately after the last washing, 1 ml of cell suspension was added to KRB yielding a final incubation medium of 2 ml. Insulin dilutions were prepared daily with KRB from a frozen insulin stock solution (1 U/ml HCl, pH 2.5). The fat cell suspensions were adjusted to 63,372 ± 6,582 cells/ml.