

**Concerning the cause and treatment of increased deposition of triglycerides in the diabetic liver.**

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The many differences of opinion on the behaviour of the deposition of fat in the diabetic liver, the cause of which is frequently to be looked for in the various techniques employed to estimate same, gave us cause to carry out quantitative investigations of the deposition of triglycerides in liver punctates. The triglyceride content was studied in normal-weight and overweight maturity-onset diabetics during starvation as well as during regular intake of food. The results were compared with those obtained in healthy control persons. The observations have shown that deposition of fat in the diabetic liver is not to be regarded as an expression of the diabetic disorder of metabolism but as a result of the overweight.

No influence of either administration of insulin or oral hypoglycaemics was observed on the deposition of fat in the liver of overweight maturity-onset diabetics. On the other hand, a reduction in body weight led to a reduction of the triglyceride content of the liver. The increased storage of fat in the liver of overweight maturity-onset diabetics is probably induced by disturbed elimination.

**Changes of carbohydrate metabolism in disorders of thyroid function.**

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Thirty four patients with hyperthyroidism and 12 patients with hypothyroidism were investigated. Intravenous glucose loading was performed under basal metabolic conditions in all hospitalized patients using 0.5 g of glucose per kg of body weight and the glucose assimilation coefficient  $k_G$  was determined. At the same time blood samples were taken to determine the nonesterified fatty acids (NFA) and the insulin levels (IMI). Eighteen patients with hyperthyroidism and 8 patients with hypothyroidism showed reduced glucose tolerance. Patients with hypothyroidism exhibited low serum insulin levels and reduced NFA levels. On the other hand these values were markedly elevated in patients with hyperthyroidism compared with healthy persons.

It was also observed that the serum insulin levels increased less markedly in patients with disturbed glucose tolerance than in patients with normal  $k_G$  values.

The decrease of glucose tolerance and the delayed and diminished increase of serum insulin during i.v. glucose tolerance tests in hypothyroidism are due to the overall decreased metabolism rate in this disease. The behaviour of insulin, NFA and glucose tolerance in hyperthyroidism is of complex nature and concerned on the one hand with the disturbed glucose assimilation because of high levels of NFA, on the other hand a result of direct toxic effects of thyroid hormone on the islet cells.

**Contribution to the pathogenesis of diabetic complications.**

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With the help of the Schilling test idiopathic pernicious anaemia was demonstrated in four out of 80 diabetics and symptomatic vitamin B<sub>12</sub> malabsorption was demonstrated in a further four patients. Furthermore diabetes mellitus was diagnosed in four out of 110 patients with essential pernicious anaemia.

By means of the xanthurenic acid determination after a tryptophan load, B<sub>6</sub> avitaminosis was diagnosed in eight of 37 patients.

Of 15 diabetics studied, seven showed a markedly reduced vitamin E and beta-carotin level in the serum.

Three out of 36 diabetics showed hyperthyroidism.

A brief report is presented on a patient with diabetes mellitus, polyneuropathy, pernicious anaemia and hyperthyroidism.

**Diagnosis of renal glycosuria.**

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During the mass screening programme carried out in Frankfurt for the early detection of diabetes, 15 patients showing glycosuria of between 2 and 30 g per day with repeatedly normal blood sugar values were further studied by ourselves. An intravenous glucose tolerance test and a tolbutamide tolerance test in accordance with Lange and Knick were carried out in all patients. The changes of the blood sugar and the serum insulin were evaluated diagnostically. The  $k$ -value after Conard, the T<sub>3</sub>-value of the tolbutamide test and the increase of the serum insulin were normal in all patients. In order to study further the cause of the glycosuria, a careful nephrological examination followed. From the investigations it is evident that moderate glycosuria may not only be the expression of hereditary enzymatic renal tubular dysfunctions but also of a previously masked chronic pyelonephritis.

**The influence of chronic gonadotropin on glucose tolerance and insulin secretion.**

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The clinical observation that pregnancy has a diabetogenic effect and the fact that a higher incidence of diabetes is to be observed in patients with Turner's syndrome caused us to carry out the following experiments: rats received 0.1 mg HCG daily for a period of 8 and 28 days respectively. The behaviour of the blood sugar and the serum insulin after glucose tolerance tests was continuously studied.

The results show a higher glucose assimilation and a more marked rise in insulin values in the blood of the treated group than of the control animals. The increased insulin secretion leads to exhaustion of the functional reserves of the pancreas, which increases from pregnancy to pregnancy.

**The influence of lactic acid on lipolysis.**

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Issekutz and Miller reported in 1962 on an antilipolytic effect of lactic acid in experiments *in vitro* in the dog. We likewise observed a marked fall in fatty acids on commencement of investigations of muscle metabolism in the human which was time-related to the highest production of lactate. To study the question of a direct effect of lactic acid on lipolysis, epididymal adipose tissue of the rat was incubated with lactate in increasing concentrations. Lactic acid induced a dose-related inhibition of lipolysis as measured by the liberation of nonesterified fatty acids and glycerol. With increasing lactate concentration in the medium the output of pyruvate and the lactate-pyruvate quotient increased continuously. Hence one cannot determine whether inhibition of lipolysis is induced directly by lactic acid or is a result of the increased liberation of pyruvate or a result of the increase of the lactate-pyruvate quotient. If one applies the results to conditions obtaining *in vivo* it appears that within certain limits the working muscle is able to regulate the uptake of fatty acids itself