

# EXCERPTA MEDICA

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No. 74

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## FIFTH CONGRESS OF THE INTERNATIONAL DIABETES FEDERATION

*5ème Congrès de la Fédération Internationale du Diabète*

*Toronto, Canada*

*July 20-24, 1964*

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*Toronto, Canada*

*July 20-24, 1964*

*Under the Patronage of*

His Excellency General GEORGES P. VANIER, D.S.O., M.C., C.D.  
Governor-General of Canada

## ABSTRACTS OF PAPERS

INTERNATIONAL CONGRESS SERIES NO. 74

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*Abstracts 1—30*

I

METABOLISM OF LIPIDS

Concert Hall

*Monday, July 20, P.M.*

Abstracts marked by an asterisk (\*) refer to papers read by title.



### **\*1. Tissu adipeux et rétention d'insuline et d'autres hormones**

ADEZATI, L. et PRANDO, R., *Clinica Medica Generale, Viale Benedetto XV, Genova, Italia*

Un pourcentage variable d'insuline hexogène peut être retenu au niveau du tissu adipeux, comme des pourcentages variables d'autres hormones protéiques.

L'augmentation ou la réduction du tissu adipeux total provoquent de remarquables variations de ce pourcentage.

Les résultats sont discutés du point de vue de la génèse de certaines formes cliniques de diabète pléthorique ainsi que d'autres syndromes dys hormonaux.

### **Fat tissue and trapping of insulin and other protein hormones**

Varying percentages of hexogenous insulin or other protein hormones may be trapped by adipose tissue.

The percentage so immobilised varies considerably as the total mass of adipose tissue increases or decreases.

The phenomenon is discussed with reference to the pathogenesis of some plethoric diabetic forms and of other hormonal disorders.

### **2. Effect of insulin upon adipose tissue electrical potentials**

BEIGELMAN, P. M. and HOLLANDER, P. B., *University of Southern California Medical School, 2025 Zonal Avenue, Los Angeles, Calif., U.S.A.*

Transmembrane or resting membrane electrical potentials (REP) may be demonstrated in rat epididymal adipose tissue. These adipose tissue REP's are significantly increased by insulin, a dose-response relationship being observed in the 1-1000 micro-units/ml. range of insulin. The REP response to insulin decreases in proportion to increase of rat weight. Omission of glucose or other exogenous energy source from the medium does not affect the REP values or REP response to insulin. Insulin antibody blocks the effect on adipose tissue REP of insulin. Gelatin, serum albumin, and insulin antibody do not alter adipose tissue REP. Epinephrine and nor-epinephrine, in concentrations as low as 0.1 gamma/L., may significantly increase adipose tissue REP. There is a significantly lower REP in high  $K^+$  — low  $Na^+$  medium as compared with high  $Na^+$  — low  $K^+$  medium.

### **\*3. Hyperketonemic response in man to orally administered medium chain triglyceride**

BERGEN, Jr. S., and VAN ITALLIE, T. B., *St. Luke's Hospital, 421 West 113th Street, New York 25, N.Y., U.S.A.*

In 1959 Schön et al. reported that ingestion of 100 Gm. of a mixed glyceride ( $C_8$ — $C_{12}$ ) was associated with a 35-44% rise in blood ketones. In an attempt to confirm and extend these observations, the effect on blood ketones of a synthetic medium chain triglyceride (MTS) (86%  $C_8$  and 14%  $C_{10}$ ) was compared with that of corn oil in fourteen healthy and three diabetic subjects. One hundred gram of MCT or corn oil was homogenized with casein and dextrose and administered orally as a liquid formula. Venous blood ketones and glucose were measured at 0,  $\frac{1}{2}$ , 1,  $1\frac{1}{2}$ , 2 and 3 hours after the test meal. The mean maximal increase in blood ketones among the fourteen nondiabetic subjects was  $4.3 \pm 0.45$  mg./100 ml. after MCT, and  $0.83 \pm 0.17$  mg./100 ml. after corn oil ( $P < 0.001$ ). After MCT three diabetics showed a mean rise in blood ketones of  $5.17 \pm 0.02$ . The nature of the fat in the test meal did not affect the blood glucose. Pretreatment of six subjects with 1 mg. glucagon I.M., three hours before formula administration, did not consistently alter the hyperketonemic response to MCT.

**\*4. Myocardial arteriovenous differences of individual free fatty acids in diabetics**

CARLSTEN, A., HALLGREN, B., JAGENBURG, R., SVANBORG, A. and WERKÖ, L., *Med. clin. II, University of Gothenburg, Gothenburg, Sweden*

The net myocardial extraction of individual plasma free fatty acids (FFA) has been studied by the determination of the differences in their concentrations in arterial and venous blood.

In diabetics the total FFA extraction was about the same as in healthy controls although the arterial FFA level was significantly higher in the diabetics. Arterial thresholds below which no fatty acids are extracted by the myocardium seem to exist both in diabetics and in healthy controls. The coefficient for the regression of the arterial level on the venous level of FFA was found to be closer to 1 in the diabetics than in non diabetics, i.e. the myocardial extraction of FFA was lower in relation to the arterial FFA level. After insulin these regression coefficients decreased.

**\*5. Diabetic lipid and glucose reflections of polyunsaturated fat feeding**

COCHRAN Jr., B., POUCHER, R. L., GILLILAND, J. A. B. and MARBACH, E. P., *Loma Linda University, 1200 North State St., Los Angeles, Calif., U.S.A.*

The response to high polyunsaturated (chiefly safflower oil) and high total fat formula feedings was followed in 33 hospital and clinic adult diabetic subjects. The liquid diet supplied 65% of calories as fat, 12% as protein and 23% as carbohydrate and was given initially as total isocaloric substitution for the existing diet. Subjects continued on formula only for periods up to three months. Subsequently a mixed diet was used with the formula supplying 1/3 to 2/3 of daily calories. In general patient acceptability was good.

Serum lipid, triglyceride, cholesterol and lipid phosphorous levels fell slightly during isocaloric total formula feeding. On the mixed diet, these reverted towards basal values. Serum esterified fatty acids, as analyzed by gas-liquid chromatography, showed a significant rise averaging about 79% in linoleic acid and a concomitant decrease in arachidonic and all other fatty acids while on full formula feeding. Of 13 subjects on insulin, 10 were able to decrease daily dosage by 30-100%, with three stopping completely. No deterioration of diabetic control was seen.

An intriguing, apparently coincidental, improvement in peripheral neuropathy occurred in three of these subjects.

**\*6. Aspects particuliers de la dynamique lipidique dans le diabète mellitus de l'adulte**

CUGUDDA, E., GRAGNOLI, G. et GIOVANNELLI, G., *Clinique Médicale, Piazza Duomo 2, Sienna, Italie*

Il résultait des recherches précédentes que même chez les sujets diabétiques avec activité insulino-plasmatique élevée, on peut observer dans la sang périphérique des valeurs d'acides gras libres supérieures à la normale et très peu influencées par les variations du contenu lipidique de la diète. Les connaissances actuelles de ces anomalies et d'autres altérations de la dyslipidémie diabétique nous portent à examiner le problème de ce désordre métabolique au point de vue dynamique directement chez l'homme.

Afin d'étudier la dynamique des lipides les AA. ont dosé le contenu des acides gras non-esterifiés et de ceux esterifiés dans les globules rouges et dans le plasma chez des sujets diabétiques examinés dans les conditions suivantes: a) jeune prolongé; b) alimentation avec diète à différents taux d'hydrates de carbon et lipides; c) charge de glucose; d) stimulation avec des hormones d'origine hypophysaire ou surrénalienne.

Les résultats de ces recherches ont montré l'existence de rapports particuliers entre les altérations de la lipolyse et l'utilisation périphérique du glucose dans le diabète sucré.

Les données acquises sont discutées en fonction des conceptions les plus modernes sur la pathogénie du diabète.

### **Particular aspects of lipid dynamics on diabetes mellitus in adults**

Previous studies had shown that even in those diabetics with a high plasma-insulin activity it is possible to demonstrate in the peripheral blood NEFA values which are in excess of normal and which are scarcely influenced by variations in the lipid content of the diet. In view of current knowledge of these and other derangements of lipid metabolism in diabetes we decided to study these metabolic phenomena directly in man and from a dynamic point of view.

In order to study the dynamics of lipids the authors determined the content both of esterified and non-esterified fatty acids in erythrocytes and in plasma of diabetic subjects under the following conditions: a) prolonged fasting; b) on diets of differing fat and carbohydrate content; c) following glucose loading; d) on stimulation with pituitary or adrenal hormones.

The results of the above investigations have shown the existence of specific relationships between the changes in lipolysis and the peripheral utilization of glucose in diabetic patients. The data obtained are discussed in the light of current concepts regarding the pathogenesis of diabetes.

#### **\*7. Les acides gras libres plasmatiques (A.G.L.) Courbes de leur évolution au cours de trois épreuves dynamiques dans les divers types cliniques de diabète**

DEUIL, D., DAVY, C. et LAURENT, C., *Hôpital Saint-Joseph, 7 rue Pierre Labrousse, Paris, France*

Les variations du taux des A.G.L. plasmatiques au cours de trois épreuves fonctionnelles (Glucose Tolerance Test — Insuline Tolerance Test et Tolbutamide Test) chez 25 sujets se situant diversement par rapport au diabète ont été étudiées. La méthode est exposée en détail et les résultats sont analysés et confrontés avec ceux des autres chercheurs. Les réponses obtenus dans chaque catégorie de malades sont comparées. Les hypothèses suggérées par les variations observées sont formulées. Les problèmes de l'unité du diabète, des rapports entre le taux des A.G.L. et 'l'insulin-like' activité du plasma, de la prophylaxie, sont en particulier abordés.

En conclusion, les auteurs pensent que l'étude du taux des A.G.L. au cours d'épreuves fonctionnelles et en particulier du G.T.T. présente un intérêt diagnostique et peut donner une indication thérapeutique.

#### **Non esterified plasma fatty acids (N.E.F.A.)**

In 25 patients with varying clinical histories as regards diabetic illness, the plasma NEFA curve was recorded during the three following functional tests: Glucose Tolerance Test — Insulin Tolerance Test and Tolbutamide Test. The method of investigation is described in detail and the results are analysed and estimated in comparison with those of other investigators. The various answers obtained in each category of patients are compared. The various hypotheses suggested by analysis of the variations observed are formulated with special regard to problems concerning uniformity of diabetes, correlations between NEFA level and insulin-like activity in plasma, and prevention of diabetes. The authors conclude that a systematic study of the NEFA curve in the plasma during the various functional tests and especially the Glucose Tolerance Test is of diagnostic importance and may provide a valuable pointer as to the therapy to be employed.

#### **8. Fatty acid metabolism in the diabetic rat heart**

EVANS, J. R. and HOLLENBERG, CH. H., *Department of Medicine, University of Toronto, 101 College St., Toronto, Canada*

Isolated hearts from alloxan-diabetic rats were perfused in a closed recirculation system with C<sup>14</sup>-labelled fatty acids bound to albumin. Myocardial uptake of individual fatty acids was similar to that observed in hearts from fed and fasted rats but the principal fates were different. Less labelled fatty acid was oxidised and the contribution of endogenous lipid to respiration of the isolated diabetic heart was increased. Incorporation of labelled

fatty acid into tissue triglyceride was much greater than in control hearts but recovery of label in diglyceride, phospholipid and free fatty acid fractions of heart muscle was only slightly increased. Tissue triglyceride labelled during a preliminary perfusion with palmitate-C<sup>14</sup> was oxidised in a subsequent perfusion without exogenous substrate. The rate of disappearance of label from endogenous triglyceride was similar to control hearts but total triglyceride and the pool size of labelled triglyceride were greater in diabetic hearts and hence lipolysis appeared to be increased. The combination of increased synthesis and lipolysis observed in these experiments may be explained by accelerated turnover of tissue triglyceride in the diabetic heart.

#### **\*9. Serum lipids in human and experimental diabetes**

FUKUI, I. and YOSHIDA, H., *Department of Internal Medicine, Kyoto Prefectural University of Medicine, Kawramachi-hirokoji, Kamikyo-ku, Kyoto, Japan*

Disturbances of lipid metabolism relating to atherosclerosis are an essential part of the deranged metabolism in diabetes mellitus. This paper reports the results of investigations of serum lipids in diabetic patients and experimental animals.

In diabetic patients, the abnormalities of serum lipids are mainly in the elevations of fatty acids and triglycerides, with moderate or no increase in serum cholesterol and phospholipids. They are caused by two factors: (1) compensation of deranged carbohydrate metabolism, (2) presence of vascular complications. In serum fatty acid fractions (studied using gas chromatography) the palmitine fraction is lowered and L/O ratio is decreased. These changes are reversible by compensation of deranged carbohydrate metabolism and similar to those in atherosclerosis. The clearance of triglycerides from the blood stream depends upon the rate of carbohydrate metabolism.

In experimental diabetic dogs, the abnormalities of serum lipids, similar to those of patients stated above, can be controlled with adequate doses of insulin. When large doses of nicotinic acids are administered orally to the diabetic animals, the levels of serum cholesterol were lowered with occasional individual variations. These latter variations are unexplained. When a high fat diet was given, the serum cholesterol were elevated, with a low fat diet the serum cholesterol were lowered. Triglyceride levels were unstable.

Extensive experiments are being continued in our laboratory.

#### **\*10. The total plasma lipids, free fatty acids and lipoprotein electrophoretic pattern in diabetes**

GHAREEB, A. M. and ABD-EL-WAHAB, E., *Ain Shams University Hospitals, Abassia, Cairo, Egypt, U.A.R.*

Lipid patterns were studied in 70 patients with diabetes mellitus differing with respect to age, sex, duration of disease, diabetic control and presence or absence of complications. The total lipids and free fatty acids were estimated in the usual way. The lipoprotein electrophoretic pattern was estimated using the dye Fat Red 7 B. With this dye, as compared with that formerly employed by us (Sudan Black B), the bands were more distinct and new bands were recognised. The results are tabulated in relation to age, sex, duration of disease and type of diabetic control (whether by diet alone, diet and insulin or oral antidiabetics). Correlations were also sought with the major complications where present, i.e. diabetic ketoacidosis, neuropathy, nephropathy and coronary heart disease.

#### **\*11. Hyperlipemia in latent diabetes and in prediabetes**

GOTH, A., *Janos Hospital, Budapest, Hungary*

Out of thirty non-diabetic women aged 27-79 years with elevation of serum triglyceride level, the glucose tolerance was decreased in twenty-six. In these cases of latent diabetes

vascular lesions (ischaemic heart disease, thrombosis of the central retinal vein etc.) were often found. Diabetes occurred in the families of seven patients. Of twenty women in this group who had children, eleven had recorded both weights in excess of 4.5 kg, six had still-births, sixteen became obese during pregnancy, five had hyperlactation (signs of prediabetes). In another group of eight patients with familial and case histories characteristic of prediabetes, but with normal glucose-tolerance and thus no latent diabetes, five had elevated serum triglyceride levels; their ages were: 22, 22, 33, 55 and 74 years.

In summary: elevated serum lipid levels can occur in latent diabetes and even in prediabetes, this being in line with Randle's hypothesis that in diabetes failure of lipid metabolism is the primary defect.

Dietary restriction of carbohydrate and fat and administration of heparin or thyroid extract led to normalisation of plasma lipid levels and of glucose tolerance with striking improvement in general condition and arrest to the progression of vascular lesions.

(Plasma insulin and growth hormone determinations with radioimmunological methods and assay of lipid mobilizing factor in these cases are in progress).

## **12. Effects of insulin on the metabolism of triglycerides**

GRIES, F. A., POTTHOFF, S. and JAHNKE, K., *II. Medizinische Klinik und Poliklinik, Medizinische Akademie Düsseldorf, Moorenstr. 5, Düsseldorf, Deutschland*

Insulin influences directly the turnover of triglycerides from serum lipoproteins. The half life of artificial radioactive labelled chylomicra is normal in well controlled diabetes mellitus, but longer in decompensated diabetic subjects. It can be normalized by i.v. injection of insulin. Thus it seems probable that insulin has an effect on the uptake of chylomicron fat by peripheral tissues.

This was proven by further experiments. Normal, ad libitum fed Sprague Dawley rats, alloxan diabetic rats, and other alloxan diabetic rats treated with insulin were injected with radioactive labelled chylomicra. 10 min. later the animals were killed and the radioactive fat contained in blood and several organs was measured. There were typical differences between the three groups. The radioactivity of blood was highest in the diabetic and lowest in the insulin treated rats. The most striking differences were seen in adipose tissue. There was little radioactivity in diabetic animals whereas after injection of insulin the uptake of labelled fat was increased about 4 times.

These findings make it probable, that the hyperlipaemia in diabetic acidosis is not only caused by fat mobilisation and increased synthesis of lipoproteins following high uptake of free fatty acids in the liver, but may also be considered as representing an impaired triglyceride uptake in peripheral tissues, especially adipose tissue.

## **\*13. Effect of some sugars on fat mobilization in health and diabetes**

KBATTAB, M., EL-MOFTY, A. and FAYEK, K., *Faculty of Medicine, Cairo University, Kasr El-Aini Street, 28 Cairo, Egypt, U.A.R.*

Glucose administration in normal individuals of average weight, in healthy but obese persons, and in diabetics resulted in varying degrees of diminution of the NEFA concentration, followed by a rise in the latter. Ketotics showed no drop of NEFA, reflecting the profound metabolic changes in these cases.

Glycerol administration produced the same effect as glucose except in some obese diabetics. This might be explained by the presence of some opposing humoral factor such as growth hormone.

Gluconolactone administration produced no effect in healthy persons. In thin diabetics a drop in NEFA and sugar occurred, while in obese diabetics a rise in blood sugar occurred, with no changes in NEFA. The possible explanations of such a sequence of events are discussed.

**\*14. Dietary fats and diurnal variations of blood lipids in juvenile diabetes**

LARSSON, Y. A. A., PERSSON, B. E. H. and STERKY, G. C. G., *Pediatric Department, Karolinska Institutet, Crown Princess Lovisa's Children's Hospital, Polhemsgatan 30, Stockholm, Sweden*

The diurnal variations of serum cholesterol, phospholipids and triglyceride, and of the free fatty acids as well as blood ketones in plasma have been studied in a series of 90 juvenile diabetics classified in six groups according to duration of diabetes: new patients and cases with a duration of 2, 5, 10, 15, and 20 years. In addition the effect on the blood lipids of treatment with a diet high in polyunsaturated fatty acids was especially analyzed in 27 patients.

**15. Zur Charakteristik der lipolytischen Aktivität des Fettgewebes bei Alloxandabetes**

LEITES, S. M. und DAVTYAN, N. K., *Department of Pathophysiology, Central Postgraduate Medical Institute, Vosstanya pl. 1/2, Moscow, U.S.S.R.*

Die lipolytische Aktivität des Fettgewebes der Ratte, des Kaninchens und des Menschen, die man durch Abgabe der höheren freien (nichtesterifizierten) Fettsäuren (NEFS) in das Inkubationsmedium registriert, wird durch Zugabe von Glukose gehemmt. Dieser Effekt wird durch Insulin aktiviert bei gleichzeitigem Eintritt der Glukose in das Fettgewebe. Bei Tieren mit experimentellem Alloxandabetes ist die Hemmung der Fettgewebslipolyse durch Glukose wesentlich abgeschwächt parallel mit der Verminderung der Glukoseutilisation. Das führt zur Erhöhung des NEFS-Spiegels des Serums bei Diabetes. Die Zugabe von Insulin zum diabetischen Fettgewebe aktiviert die Absorption von Glukose und die Triglyceridsynthese und dadurch wird die Abgabe von NEFS aus den Fettdepots vermindert.

In Versuchen in vitro und in vivo ist die aktivierende Wirkung des Adrenalins auf die Fettgewebslipolyse und den NEFS-Spiegel des Serums bei diabetischen Tieren wesentlich schwächer als bei den normalen. Die adipokinetische Wirkung von Somatotropin (STH) und ACTH ist bei diabetischen Ratten ausgeprägter als bei normalen. Die ausgeprägtere Aktivierung der NEFS-Mobilisation aus dem Fettgewebe bei diabetischen Tieren wird also durch den verminderten Eintritt von Glukose in das Fettgewebe und die Verstärkung des adipokinetischen Effektes des STH und ACTH bedingt. Die Wirkung des ACTH ist extrasuprarenal.

**Characteristic of lipolytic activity of adipose tissue in alloxan diabetes**

The lipolytic activity of the adipose tissue of rats, rabbits and man, determined by the measurement of the outflow into the incubation medium of higher free (nonesterified) fatty acids (NEFA), is inhibited by the addition of glucose. The inhibition effect is markedly activated by insulin and is accompanied by greater absorption of the glucose.

In experimental alloxan diabetes the inhibition effect of glucose on lipolysis is considerably weakened, parallel with a reduction in the absorption of the glucose. In diabetes this leads to a higher content of NEFA in the serum. An addition of insulin to the "diabetic" adipose tissue, enhancing the absorption of glucose and thereby activating the synthesis of triglycerides, reduces the outflow of NEFA from the adipose tissue and their content in the serum.

In experiments on diabetic animals and their tissues, it was found that adrenaline both in vitro and in vivo exerts a less pronounced activating influence on the lipolysis of adipose tissue and on the increase of NEFA in the serum in the diabetic animal than in normal animals. The adipokinetical effect of somatotropin (STH) and ACTH in diabetic animals is more pronounced than in normal animals.

Greater mobilisation of NEFA from adipose tissue of diabetic animals is thus determined by the reduced absorption of glucose by the adipose tissue and the enhanced adipokinetical effect of STH and ACTH. The effect of ACTH is extrasuprarenal.



**16. The effect of insulin and growth hormone on glucose metabolism by adipose tissue**

LEONARDS, J. R., *Western Reserve University, 2109 Adelbert Road, Cleveland 6, O., U.S.A.*

Male albino rats were injected with Raben type growth hormone (25 USP Units/Kg. body weight), crystalline pork zinc insulin (1-5 Units/Kg.) or saline, and sacrificed 5 min. to 2 hrs. later. Thin segments of their epididymal adipose tissue were incubated in bicarbonate buffer with 1 mg. per ml. of glucose and tracer amounts of glucose 1-C<sub>14</sub> and 6-C<sub>14</sub> in the absence or presence of insulin. In corporation of C<sub>14</sub> into CO<sub>2</sub>, glycogen, and lipid was determined. Growth hormone administered in vivo and the insulin in vivo or in vitro increased incorporation into all these products. However, quantitatively insulin favored incorporation into glycogen while growth hormone favored the appearance of C<sub>14</sub> in lipids and the conversion of glucose 6-C<sub>14</sub> to C<sub>14</sub>O<sub>2</sub>. In contrast to insulin added in vitro, insulin injection resulted in minimal increases in incorporation into glycogen. Under some conditions the effects of insulin and growth hormone were additive. These results indicate that the manner in which adipose tissue is exposed to insulin conditions its metabolic response and that stimulation of insulin secretion may not be the only immediate action of in vivo growth hormone on glucose metabolism. In addition these results cannot be explained solely by an action of insulin on the rate of glucose entry into the cell.

**17. Tolbutamide effects on glucose oxidation by human adipose tissue in vitro**

LINDSAY, R. W., HOLLIFIED, G. F. and OWEN Jr., J. A., *School of Medicine, University of Virginia, Charlottesville, Va., U.S.A.*

Recent studies by Antoniadou et al. (1) show that adipose tissue effects in vitro unbinding of "free" insulin from its "bound" serum protein complex; (2) postulate impairment of unbinding as an important pathogenetic factor in human diabetes; (3) describe an unbinding action of tolbutamide in vivo, thereby correcting this impairment. Conceivably, tolbutamide might do this via an effect on adipose tissue; if so, diabetic adipose tissue should manifest an exaggerated response to serum plus tolbutamide.

Two diabetic and five control patients had on successive days oral glucose and oral tolbutamide tolerance tests and fat biopsy. One-hour serum from each test was assayed for insulin-like activity, measuring glucose oxidation by rat adipose tissue (RAT). Human adipose tissue (HAT) was similarly incubated, with (a) beef insulin, (b) beef insulin + added tolbutamide (10 mg.%), (c) serum following glucose ingestion (GTS), (d) GTS + added tolbutamide (10 mg.%) and (e) serum following tolbutamide ingestion (TTS).

Results: (1) tolbutamide addition in vitro (a) did not enhance the response of any HAT to beef insulin, (b) questionably enhanced the response of diabetic HAT to GTS, and (c) had no effect on the response of normal HAT to GTS; (2) GTS and TTS displayed the same relative potencies on RAT and HAT regardless of whether the tissue donor was diabetic.

**\*18. The control of hyperlipidaemia in diabetic children**

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Elevated levels of total lipid, cholesterol, omega- and betalipoprotein lipid have been found at the time of diagnosis in 66% of diabetic children. With insulin treatment these levels rapidly fell towards normal. Serial determinations of the serum lipids for periods of up to five years after diagnosis show that with good insulin control the majority of children have maintained normal levels and when, during periods of poor control,

hyperlipidaemia has recurred it has responded promptly to insulin. In two children, however, in whom the initial hyperlipidaemia was very marked (total lipid over 2.0 g./100 ml.) elevated levels occurred in spite of good insulin control and were lowered by an unsaturated fat diet. Three children with similar marked initial hyperlipidaemia were given an unsaturated fat diet from the time of diagnosis and their serum lipids have remained normal. It is suggested that when gross hyperlipidaemia, present at the time of diagnosis, persists despite good control with insulin additional treatment with an unsaturated fat diet may be advisable.

#### **\*19. Metabolism of human fat**

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Subcutaneous fat from normal and diabetic people has been removed under light local anaesthesia from the buttock area. Pieces of fat weighing about 40 mg. have been individually incubated in a micro-incubation system (Keen et al.) with  $C^{14}$  labelled glucose. Glucose uptake, oxidation and incorporation into lipid have been studied quantitatively in the basal condition and in the presence of varying concentrations of insulin. Distinct differences in the in vitro behaviour of normal and diabetic fat have been demonstrated. An interesting phenomenon at very high insulin concentration, perhaps related to clinical insulin atrophy, has also been observed.

Keen, H., Field, J. B. and Pastan, I. H. A simple method for in vitro metabolic studies using small volumes of tissue and medium metabolism 1963, 12, 143.

#### **\*20. Role of polyunsaturated fatty acid in diabetic diet**

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1. In diabetic patients, serum lipids and red cell transketolase were increased and serum  $B_1$  level was decreased. 2. A single administration of 50 gm. of butter to healthy individuals resulted in a decrease in acetylation of PABA and  $\Delta 7$  p but an elevation of ip, lactic acid, pyruvic acid and NEFA levels. Administration of 100 gm. of protein to healthy persons resulted in an increase of NPN level and 17 KS, 17 KGS and 17 OHCS and catecholamine output in the urine. 3. Polyunsaturated fatty acid combined with V.B<sub>6</sub> and V.E administered to diabetics induced an increase in reduced glutathion and a decrease in cholesterol level. 4. Diabetics stabilized by basic treatments were given 200 excess calories in the form of various foodstuffs. The body weight was increased, giving an impression of improvement in the disease but the metabolism showed deterioration involving elevation of OGTT, lactic acid, citric acid, cholesterol and C/P levels and lowering of  $\Delta 7$  p, serum ILA level and urinary 17 KS output. The role of polyunsaturated vegetable oils in the diabetic diet was investigated. The importance of total calorific content of the diet was reemphasized. Alteration of fat within a given total calorie intake and use of a relatively high fat diet rich in polyunsaturated fatty acid deserves further study and consideration.

#### **21. Progressive hyperglycemia in experimental obesity of albino rats**

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There is no experimental proof that obesity leads to diabetes though their coincidence is common. In order to study their relationship experimental obesity was induced in male albino rats by PZ Insulin and a 40% fat diet. A control group was maintained on a standard diet and Insulin. Oral glucose tolerance (1 g./kg.) tests were performed regularly during a period of 12 months. Significantly higher fasting blood sugar was found in the obese group (ranging from 103-146, and 145-182 mg%) as compared with the control



group (ranging from 85-106 and 147-153 mg%) at 7 and 10 months respectively. Peak values 1 hour after glucose were significantly higher in the obese group (ranging from 137-192, 173-238, and 185-238 mg%) than in the control group (ranging from 138-154, 158-199, and 169-203 mg%) at 7, 10, and 12 months respectively. A fall in blood inorganic phosphate recorded 1 and 2 hours after glucose was significantly greater in the obese group at 10 months and blood level of pyruvic acid increased in both groups to 0.5 mg%, 3 hours after glucose, whereas lactic acid level increased significantly in the obese group (29.7 mg%) as compared to control group (13.8 mg%). The role of obesity in inducing hyperglycemic change will be discussed.

## **22. Fatty acid metabolism by human subcutaneous adipose tissue in diabetes mellitus**

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Subcutaneous adipose tissue was obtained by a biopsy procedure from normal males and from male subjects with recently discovered diabetes mellitus. The fat portions were incubated in Krebs-Henseleit bicarbonate buffer, with added albumin, glucose and palmitic acid-1-C<sup>14</sup>, or in the subjects' Edta-plasma with added palmitic acid-1-C<sup>14</sup>. A higher net release of glucose and FFA and a decreased incorporation of palmitic acid-1-C<sup>14</sup> in the glycerides were observed with diabetic adipose tissue. These changes appear to be more pronounced in juvenile diabetes. The derangement of fatty acid metabolism does not seem to be related to alterations of the glucose uptake in adipose tissue, as discussed earlier. (*Acta Med. Scand.* 174: 215, 1963).

## **23. Perfusion of the epididymal fat of the rat**

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A new technique is described for perfusing the epididymal fat tissue of the rat. During the two hour perfusion rapid utilization of glucose was observed, and this was further increased when insulin of the blood of fed rats was added.

Total Esterified Fatty Acid (TEFA) and Non-Esterified Fatty Acid (NEFA) concentrations increased in the circulating perfused blood during the control period. When insulin or blood from fed rats was added to the perfusate, TEFA remained constant while NEFA levels diminished significantly.

## **24. The metabolism of human adipose tissue in vitro. Some aspects of insulin action**

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Human adipose tissue incubated *in vitro* in Ringer bicarbonate buffer is insulin sensitive as far as glucose uptake is concerned, although no changes in CO<sub>2</sub> output have been detected, such as were observed in experiments with rat adipose tissue. Further evidence of a difference between human and rat adipose tissue metabolism has been obtained in experiments using human serum from normal individuals as the incubating medium. Under such conditions, crystalline beef insulin (Hoechst) added *in vitro* to human serum failed to increase glucose uptake, while an increase in the uptake was evident when the incubation was carried out with serum taken from the same subject either after intravenous tolbutamide administration or during a glucose tolerance test. The importance of the state of insulin in blood and its effects on adipose tissue metabolism, together with the differences between human and rat adipose tissue metabolism will therefore be discussed.