Abstracts of Current Literature

DIETARY FATS AND SERUM LIPIDS

Recent work reported from the Rockefeller Institute has demonstrated no correlation between increases in dietary fat and postabsorptive concentration of triglyceride in plasma. In normal subjects the administration of diets low in fat and high in carbohydrate produced hypertriglyceridemia and increased levels of low-density plasma lipoproteins. These results appear to be at variance with those obtained in studies performed upon the Bantu. While these investigations are not comparable because of differences in the duration of feeding periods and other dietary factors involved, there is an indication that further research in this area is required.

The Influence of Diet on Serum-Triglycerides in South African White and Bantu Prisoners. A. Antonis and I. Bersohn. *Lancet*, 1: 3, 1961.

Many studies from South Africa have demonstrated that the white population eating the usual Western diet in which fats contribute 40 per cent of the calories has far more coronary disease than the Bantu whose diet has only about 15 per cent of calories from fat. In this study both racial groups were studied for long periods on controlled diets. There is a great deal of detail in this paper which will have to be read in the original by workers in this field.

The main conclusions were as follows: There was no racial difference in the response to diets. On the same basic diets the serum triglyceride levels were similar, both in amount and composition, and both groups responded similarly to manipulation of the diet.

After habituation to a low fat diet (15 per cent of calories) the ingestion of a diet in which 40 per cent of calories was derived from fat and which was rich in monoenoic and saturated fatty acids for a year resulted in a significant rise of previously low serum triglyceride levels. Change from a high fat to a low fat diet also produced a significant temporary increase in the level of serum triglycerides which only returned to base levels after three to six months. Fasting serum triglyceride fatty acid composition strongly resembled that of the dietary fat. It is suggested that the nature and proportion of fat in the diet may influence the rate of clearance of triglycerides from the blood stream, thereby affecting fasting serum triglyceride levels.

F. E. HYTTEN

The Effect of Test Feeds on the Plasma Lipids. K. J. Kingsbury, D. M. Morgan and P. C. Shervington. *Lancet*, 2: 1045, 1960.

When so much interest is at present focused on the effect of diet on plasma lipids, a simplified test is to be welcomed. The usual method of feeding the test fat for long periods with a rigidly controlled diet is difficult and tedious for both the investigator and the subject. In the method of assay described here a single 50 gm. feed of the fat under test is given after a period of fat deprivation, and changes in the plasma levels of glycerides, cholesterol and phospholipids are measured at one and a half, three and a half, five and a half, seven to nine and twenty-four hours.

The plasma changes, called the lipid response, are characteristic of the type of fat given, and its advantages as a method of investigation are discussed. The test "is not offered as an alternative to long-term experiment, but as a supplementary method especially useful for rapid biological assays." F. E. HYTTEN

Site of Origin of Plasma Triglyceride. S. O. Byers and M. Friedman. *Am. J. Physiol.*, 198: 629, 1960.

The plasma lipid concentrations six hours after injection with *p*-iso-octyl polyoxyethylene phenol polymer (Triton®) were compared in groups of seven to twelve rats subjected to surgery. When the gastro-

intestinal tract alone was removed, plasma lipids were the same as in the sham-operated control animals (except for a small cholesterol deficit). Although the rats deprived of liver but still retaining the gastrointestinal tract accumulated some triglyceride and cholesterol, the amount was small compared with that in the viscerectomized rat with a functioning liver, or the sham-operated control animals. When both liver plus gastrointestinal tract were removed, lipid values were the same as in normal rats not given Triton. The authors conclude that the liver is the major source of plasma triglyceride. AUTHORS

Effect of a Saturated Medium-Chain Triglyceride on Serum-Lipids in Man. S. A. Hashim, A. Arteaga and T. B. Van Itallie. *Lancet*, 1: 1105, 1960.

Since natural fats are complex in their effects on serum lipids, feeding experiments are difficult to interpret. In this study a synthetic fat, medium-chain triglyceride was used as the sole fat in feeding experiments. The medium-chain triglyceride preparation was a fraction of hydrolysed coconut oil comprising fatty acids of 6–12 carbons, reconstructed to triglycerides. Its effect was compared with feeding isocaloric amounts of corn oil and butter.

Compared to corn oil, medium-chain triglyceride induced a slight rise in serum total cholesterol. In the experiments in which medium-chain triglyceride was compared with butter, serum lipides increased when butter followed the administration of medium-chain triglyceride but fell when medium-chain triglyceride followed the ingestion of butter.

Thus the cholesterol-raising effect of butter cannot be wholly due to its content of medium-chain fatty acids, which do not themselves have this effect. Nor can the cholesterol-lowering effect of medium-chain triglyceride be explained in terms of the content of linoleic or other polyunsaturated fatty acids since they are not present in this preparation. The main similarities between medium-chain triglyceride and such cholesterol-lowering fats as corn oil are physical: a low melting point, a relatively high miscibility in water and increased solubility in organic solvents. It is possible that metabolic differences might exist.

F. E. HYTTEN

Perhaps the most important factor influencing the rate of absorption of fats is their melting point. This is probably of especial significance in gastrectomized patients in whom the mixing, melting and partial emulsification of fats in the stomach would be lacking.

The Effects of Chain Length on the Metabolism of Saturated Fatty Acids by the Rat. S. L. Kirschner and R. S. Harris, *J. Nutrition*, 73: 397, 1961.

Four C^{14}-carboxyl-labeled saturated fatty acids (butyric, caprylic, lauric, palmitic), each mixed with other triglycerides and safflower oil, were administered by stomach tube. Radioactivities of the breath of the rats and of the urine and colon contents were measured. Activity measurements of the fecal samples indicated significantly lower efficiency of absorption of palmitic acid (86 per cent) as compared with lauric (98 per cent) and caprylic and butyric (above 99 per cent). Rates of metabolism based on examination of the respired $C^{14}O_2$ were highest for butyric and caprylic acids, lowest for palmitic acid, with lauric acid intermediate. The high rates of metabolism of butyric and caprylic acids are believed to be in part due to their rapid transport to the liver via the portal rather than the lymphatic system, with resultant rapid oxidation instead of entering the fat depots. FRANK E. RICE

Several lipid-mobilizing factors have been described since the isolation of a peptide material from the pituitary gland by Seifter and Balder in 1957.

Fat-Mobilizing and Ketogenic Activity of Urine Extracts: Relation to Corticotrophin and Growth Hormone. T. M. Chalmers, G. L. S. Pawan and A. Kekwick. *Lancet*, 2: 6, 1960.

One of the most important new findings in the field of human fat metabolism has been that of a fat-mobilizing substance first described by Kekwick's group in 1958. In this paper there is a moderately detailed description of the extraction identification and properties of this substance isolated from the urine of fasting human subjects. It seems to be a polypeptide-like substance which causes transient hypoglycemia, ketonemia and increased mobilization and catabolism of fat in mice with depletion of body fat stores. At a concentration of less than 1 μg. per ml. the material is active *in vitro* in releasing free fatty acids from rat adipose tissue.

The fat-mobilizing substance is present in the urine of subjects on 1,000 calorie high fat or high protein diets but not in those on 1,000 calorie high carbohydrate diets. It is present in diffuse lipoatrophy and absent in lipodystrophy, present in diabetic ketosis, carcinomatosis and in postoperative subjects on low food intakes, but absent in late pregnancy and after brief exercise. In subjects with known pituitary deficiency or after removal of the pituitary, the substance does not appear in the urine. It is shown to be distinct from either growth hormone or corticotropin.

Final identification of this substance and a quantitative method of estimation will open up huge fields of important research. F. E. HYTTEN

The need for balanced food mixtures is well illustrated in the following study in which choline fed with fat prevented hepatic steatosis.

Demonstration of the Effect of Oral Fat with Choline within One Hour on Centrolobular Hepatic Cells of the Rat. E. A. Porta and W. S. Hartroft. *Gastroenterology*, 39: 758, 1960.

A method was devised to quantitate the amount of neutral fat accumulated in centrolobular hepatic cells of rats, using staining of frozen histologic sections with

oil red O and a statistical method for quantitating the fat droplets. The effect of choline on centrolobular fat accumulation after force feeding with corn oil was studied. Choline administered at the same time as the oil was found to depress centrolobular fat at the end of one hour after administration but not at two, three or four hours. Choline administered three hours after oil feeding had no effect. The authors conclude that to be effective choline must reach the liver at the same time as the oil. This is believed to be evidence in favor of the ingestion of well balanced food mixtures containing all known essential elements.

Since the effects of choline on the distribution of fat in hepatic lobules differs in the mouse, cat and monkey, as compared to the rat, it is not evident what results might be obtained in these species or in man.

JAMES B. HAMMOND

Influence of Prolonged Feeding of High-Fat Diets on the Number of Mast Cells in the Mesentery. J. Fodor, P. Fabry and Z. Lujdo. *Arch. path. Anat.*, 333: 582, 1960.

Mature albino rats of the Wistar strain weighing 200 gm. were fed one of the following diets for eight, sixteen or forty-three weeks, respectively: (1) a low fat diet containing 10.6 calories per cent, (2) a high fat diet containing 80 calories per cent, and (3) a high fat diet containing 80 calories per cent, 5 per cent being cholesterol. The fat used was beef suet. At necropsy, the number of mast cells present in the mesentery was determined by counting 3 × 50 fields of 0.012 sq. mm. As early as after eight weeks, and more so after sixteen weeks, the number of mast cells decreased after consumption of the high fat diets. After forty-three weeks, this decrease was statistically significant at the 1 per cent level.

M. SILBERBERG

Intravenous Lipids in Nutrition. A. J. D. Michel. *Presse méd.*, 11: 394, 1960.

With intravenous lipids a large amount of calories can be given in small volume. The emulsions are not excreted in the urine or feces, and they generally supply 1,600 calories per L. Thanks to the progress made in their manufacture and stabilization, we can look forward to the advantages of using them in parenteral nutrition.

H. GOUNELLE

NONESTERIFIED FATTY ACIDS

The resistance of many obese subjects to weight reduction by caloric restriction has led frequently to the suggestion that basic differences in energy metabolism must exist between normal and the obese persons. Some indication of these differences is indicated by the failure of nonesterified atty acid levels to rise during fasting in obese patients.

Effect of Fasting on Levels of Plasma-Nonesterified Fatty Acids in Normal Children, Normal Adults and Obese Adults. J. Corvilain, H. Loeb, A. Champenois and M. Abramow. *Lancet*, 1: 534, 1961.

One of the greatest recent advances in lipid metabolism and metabolism generally has been the recognition of nonesterified fatty acids as a fundamental importance in energy turnover. The level of plasma nonesterified fatty acids after fourteen hours' fasting was measured in 122 children aged four months to ten years, thirty normal adults aged eighteen to fifty years and fifteen obese adults aged eighteen to sixty years who were more than 25 per cent overweight by Life Insurance Standards.

The levels found were 699 ± 199 mEq. per L. for the children, 448 ± 140 for normal adults and 778 ± 156 for the obese adults. The adults and thirty-two children were further tested after a nineteen hour fast. The levels in the children rose from 643 ± 143 to 986 ± 235 mEq. per L., in the normal adults to 560 ± 157 and in the obese adults to 795 ± 185. Thus the children had a very marked increase with prolonged fasting, the normal adults a moderate further rise and the obese adults, no further rise. No reasons for these differences are known.

F. E. HYTTEN

Plasma Unesterified Fatty Acid Concentration in Fetal and Neonatal Life. C. M. Van Duyne and R. J. Havel. *Proc. Soc. Exper. Biol. & Med.*, 102: 599, 1959.

The concentration of unesterified (free) fatty acid in the plasma of fetal sheep and newborn infants is much lower than in the maternal plasma and is comparable with the low levels (of the order of 0.2 to 0.3 mEq. per L.) seen later in life after the administration of glucose and insulin. It rises after delivery concomitantly with a fall of plasma glucose.

These findings suggest a shift from glucose of fatty acid oxidation during the first few hours of life and provide further evidence for the concept that there is a reciprocal relationship between glucose and fatty acid oxidation.

G. WALKER

Effect of Previous Starvation on the Response of Plasma Lipids and Free Fatty Acids to a Fat Meal. M. J. Albrink and R. S. Neuwirth. *J. Clin. Invest.*, 39: 441, 1960.

Plasma free fatty acids (also known as NEFA or UFA) are a rapidly metabolized component of serum lipids. They are derived from the fat of adipose tissue and are an important form in which fat is mobilized, transported and made available for fuel during starvation. Free fatty acids in plasma increase during starvation.

In this study on eight human subjects, changes in plasma lipids were determined when a fat meal was administered at the end of a starvation period of several days. Starvation of from two to seven days caused an increased concentration of free fatty acids from an average of 0.38 (after overnight fast) to 1.85 mEq. per L. at the end of the fast. Variable increases in serum cholesterol and triglyceride were noted. However, when a meal identical in composition to the control meal was given as the first food after termination of the

starvation period, there was an abrupt decrease in the elevated concentrations of free fatty acids in five of six subjects. The abrupt fall when a fast is terminated by feeding fat is compatible with the hypothesis that fat metabolism becomes more efficient during starvation. This drop is in sharp contrast to the lack of response or even rise in the concentration of free fatty acids when a fat meal follows only a short fast.

Although changes in the concentration of free fatty acids are believed to be entirely due to changes in the rate of release from adipose tissue, others have shown that the nutritional status affects the removal rate of free fatty acids differently in different organs.

S. O. WAIFE

Epinephrine, growth hormone and lipid-mobilizing factors appear to accelerate the release of fatty acids by affecting the rate of lipolysis. It is unlikely that epinephrine and growth hormone act in the same way to achieve this effect, since glucose uptake may be increased by the former and reduced by the latter hormone.

Response of Plasma NEFA Levels to Epinephrine Infusions in Normal and Obese Women. R. D. Orth and R. H. Williams. *Proc. Soc. Exper. Biol. & Med.*, 104: 119, 1960.

Ten obese women (mean weight 220 pounds) and nine control women (mean weight 127 pounds) were given infusions of epinephrine, 0.01 μg. per pound per minute, for thirty minutes. The plasma nonesterified fatty acid levels before infusion for the two groups were 653 and 625 μEq. per L., respectively, and at the end of the infusion, 1,115 and 1,112 μEq. per L. The mean increase in the blood glucose for the control subjects was 13 and for the obese subjects 30 mg. per 100 ml. It is concluded that there is no defect in the epinephrine-activated lipolytic system in obesity, but the authors do not discuss the fact that the actual dose of epinephrine infused was almost twice as great in the obese women as in the control women.

G. WALKER

Effects of Human Growth Hormone on Levels of Blood and Urinary Carbohydrate and Fat Metabolites in Man. D. H. Henneman and P. H. Henneman. *J. Clin. Invest*, 39: 1239, 1960.

Human growth hormone was administered to five patients with hypopituitarism, and various metabolic determinations were made. There was a prompt rise in plasma free fatty acids and in blood and urinary citrate and ketones. These changes preceded the detectable changes in protein metabolism by about twenty-four hours. With continued administration of human growth hormone, there was marked nitrogen retention, glucose intolerance, a sustained rise in plasma free fatty acids and citrate, elevation of blood pyruvate and decrease in blood lactate. When the hormone was given for more than two weeks, nitrogen excretion gradually returned toward normal levels; however, glucose intolerance continued.

S. O. WAIFE

Lipemia-Producing Activity of Pituitary Gland. Separation of Lipemia-Producing Component from Other Pituitary Hormones. D. Rudman, F. Seidman and M. B. Reid. *Proc. Soc. Exper. Biol. & Med.*, 103: 315, 1960.

A material which increases the plasma lipids in rabbits has been isolated from hog pituitaries by saline extraction, acetone precipitation and ion-change chromatography. It has no ACTH, GH, TSH, ICSH, FSH, prolactin, oxytocin or vasopressin activities, but is potentiated by ACTH. The material may contaminate certain commercial preparations of TSH and prolactin, which cause hyperlipemia when injected with ACTH, whereas hyperlipemia is not seen when purified TSH and prolactin are injected with ACTH.

A fat-mobilizing polypeptide found in the urine of fasting normal subjects by Chalmers et al. (*Lancet*, 2: 6, 1960) was not detected in the urine of fasting patients with hypopituitarism.

G WALKER

The direct utilization of fatty acids for energy productive by myocardium and other tissues has focused attention upon cellular mechanisms involved in the extraction of these substances from plasma.

Myocardial Metabolism of Fatty Acids. F. B. Ballard, W. H. Danforth, S. Naegle and R. J. Bing. *J. Clin. Invest.*, 39: 717, 1960.

In the fasting state, myocardial energy production is dependent primarily on fatty acids. The lipid fraction principally concerned with the transport and metabolism of fatty acids is the free fatty acid fraction. Studies in patients and in dogs indicate that in the postabsorptive state significant amounts of both esterified and free fatty acids were extracted by the myocardium. There was a proportionately greater usage of saturated than unsaturated fats by the heart. Ingestion of a fatty meal led to an increase in both plasma concentration and myocardial extraction of free acids. Esterified fatty acids account for more than half of the total fat extracted by the myocardium. The extraction is usually dependent on the arterial concentration.

S. O. WAIFE

Effects of Storage on Serum Non-Esterified Fatty Acid Concentrations. A. L. Forbes and J. L. Camlin. *Proc. Soc. Exper. Biol. & Med.*, 102: 709, 1959.

Lipolysis occurs in serum even when stored at minus 15°c. and is particularly marked when the triglyceride concentration is high. Nonesterified fatty acids are stable in refrigerated heptane extracts for at least ten days. If serum nonesterified fatty acid estimations cannot be performed immediately, valid results may still be obtained as long as the heptane extract is prepared with the least possible delay and is refrigerated.

G. WALKER