THE EFFECT OF DIETARY THERAPY ON ABNORMAL CARBOHYDRATE AND FAT METABOLISM

D. J. DE LANGE, M.SC., H. S. MEŸ, M.SC. AND F. S. VIVIER, M.SC., *National Nutrition Research Institute, South African Council for Scientific and Industrial Research, Pretoria;* AND W. H. DAVIS, B.SC., M.MED., *Cardiac Clinic, Medical School, Pretoria*

The normal tolerance to glucose and the low fat fractions in the blood shown by the Bantu[1] in South Africa may be regarded as favourable in so far as they are associated with a very low death rate from coronary disease. The relatively low incidence of severe atherosclerosis and coronary disease in the Bantu can probably be ascribed to their diet and manner of life. The atheromatous lesions associated with abnormal carbohydrate and fat metabolism are frequently associated with incorrect eating habits of long duration, and available evidence indicates that White subjects, once they become habituated to the Bantu type of diet, take on many of the favourable metabolic features characteristic of these people.[1,2] This accords with the general belief that atherosclerosis is a metabolic disease which is preventable and up to a point reversible.[3]

In view of the possible relationship between atherosclerosis and abnormal carbohydrate and fat metabolism, it is important to know to what extent diet can improve the abnormal carbohydrate and fat metabolism found in so many White persons, especially those who have suffered an attack of coronary thrombosis. The present report deals with the effects of dietary therapy on 20 subjects with evidence of abnormal carbohydrate and fat metabolism.

The type of diet chosen was one devised by Rautenbach[4] for the treatment of diabetic patients, i.e. patients with an impairment in carbohydrate and fat metabolism resembling that of coronary thrombosis patients but much more severe in extent. The theoretical object of the diet was to cause a reduction in insulin requirement by reducing the total carbohydrate intake, and in adrenal activity by reducing the fat intake.

MATERIAL AND METHODS

A group of 20 test persons received dietary treatment for 8 - 12 months. Eleven had suffered an attack of coronary thrombosis and all showed deviations as far as sugar-tolerance curves and/or fat fractions in the blood were concerned. The diet provided approximately 1,800 calories per day, of which 65% was derived from carbohydrates (predominantly starch) and 25% from fat. The protein intake was limited to approximately 55 G/per day. The basic diet which was prescribed for all the subjects was modified where necessary to ensure that the overweight subjects lost no more than 5 - 8 lb./month. All the subjects regulated their own intake.

Tests were carried out at the start of the experiment and twice thereafter at intervals of 3 - 6 months. The concentrations of total fatty acids, essential fatty acids (linoleic and arachidonic acids) and cholesterol were determined in the fasting blood as previously described,[5] and a glucose-tolerance test was performed after the oral administration of 50 G of glucose.

RESULTS

The mean values for blood glucose obtained during the glucose-tolerance tests are shown in Fig. 1. The values are expressed as percentages of the levels obtained at the beginning of the test (fasting level). The three curves represent (*a*) the average values obtained before the dietary regimen, (*b*) those obtained 3 - 6 months after, and (*c*) those obtained 8 - 12 months after commencing dietary therapy.

The subjects showed on the average a reduced glucose tolerance at the start of the experiment, evidenced particularly by the delay in the return of the glucose concentration to the fasting level after glucose administration. The curves tended to become more abnormal after the subjects had been on the diet for 3 - 6 months but became normal after 8 - 12 months of dietary treatment.

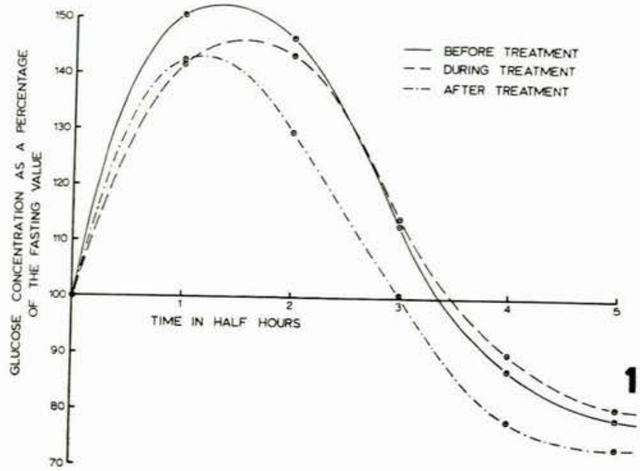

Fig. 1. Changes of glucose tolerance in patients undergoing dietary treatment.

The statistical analysis of the glucose-tolerance curves presented some difficulty, since to the best of our knowledge no test exists which is suited to this particular problem. As an approximate solution, the Friedman two-way analysis of variance was applied to the 1½-hour glucose readings on the curves. There was no significant difference at a 5% level between the three sets of values (5%<P<10%). The same test applied to the area under the glucose-tolerance curve demonstrated a highly significant over-all difference (P<1%). It is of interest to note that the sums of ranks in the Friedman test for the three periods were 46, 46 and 28 respectively, indicating that the areas under the first and second curves were similar but that they differed greatly from that under the third curve.

The average total fatty acid concentration in the serum of the 20 test persons, all of whom improved their glucose tolerance, dropped from 513 mg./100 ml. at the beginning to 317 mg./100 ml. at the end of the test period (Fig. 2). The serum-cholesterol concentrations also decreased, in some cases sharply and in others more gradually. The percentages of linoleic and arachidonic acids present in the total fatty acids increased from 20·7 - 26·0% and from 5·6 - 7·4% respectively (Fig. 2).

The two-tailed Friedman two-way analysis of variance was applied to the various fat fractions to test whether the dietary treatment had affected these entities in any way. The test showed that a highly significant difference existed between the three sets of values in respect of total fatty acids, cholesterol, linoleic acid and arachidonic acid. In the case of total fatty acid and cholesterol concentrations the final values were lower than the initial values while the opposite was true in the case of linoleic and arachidonic acid concentrations These differences were all statistically significant.

DISCUSSION

The dynamic equilibrium which exists between triglycerides and the tissue pool of free fatty acids is the result of two opposing processes, viz. esterification (lipogenesis) and lipolysis. The balance between these two processes controls the exchange of fatty acids between tissue triglycerides and the plasma. When the availability of glucose to the adipose tissues is low, the rate of lipolysis exceeds the rate of lipogenesis and free fatty acids accumulate in the plasma. Lipogenesis has been found to be markedly depressed in the adipose tissue of starved rats and also in the tissues of rats maintained on a high-fat, low-carbohydrate diet.[6, 7]

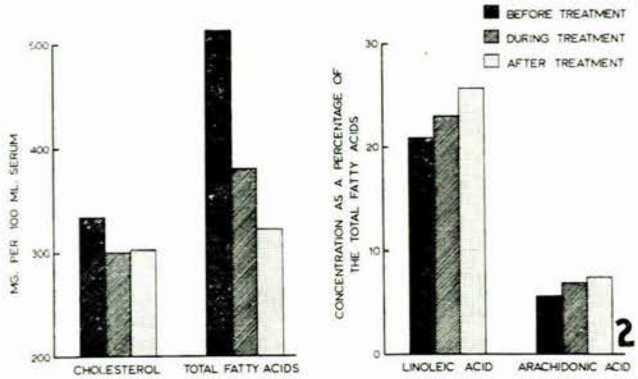

Fig. 2. Changes in the concentration of some serum lipids in patients undergoing dietary treatment.

It has been suggested that a high-fat diet may stimulate secretion of the anterior pituitary hormones and thereby indirectly cause an increased production of adrenal cortical hormones.[8] The glucocorticoid effects of certain hormones on carbohydrate, lipid and protein metabolism are well established.[9] These effects include the stimulation of gluconeogenesis with its facilitating action on noradrenalin-induced lipolysis[10] and on the development of adrenalin-induced hyperglycaemia.[11] The effect on the adrenals of a high-fat diet could also explain the findings of Samuels *et al.*,[12] viz. that rats on a high-fat diet respond to an injection of glucose with a blood sugar rise about 50 mg./100 ml. greater than that of similarly treated animals maintained on a high-carbohydrate diet.

Carbohydrate metabolism is influenced by many hormones, of which the amount secreted is affected by certain nutritional regimes. It is therefore possible that the processes which govern carbohydrate metabolism, including insulin secretion, may be rendered inadequate by certain dietary patterns. The habitual high-fat, high-protein diet of Western peoples could be responsible for a pituitary-adrenal overactivity. Such overactivity causes an increase in appetite and digestive capacity and in the secretion of insulin. The development of a diabetic tendency in spite of increased insulin secretion could be explained by the increased utilization of insulin during lipogenesis or by the anti-insulin effect of most of the pituitary and adrenal hormones. In addition, a congenital weakness of the islets of Langerhans might prevent sufficient insulin from being secreted to meet the increased demands and may even cause a degeneration of the secretory cells.

In view of the probable deleterious effect of the Western-type diet, it was not surprising to find that the sugar tolerance of the subjects in the present series showed a progressive improvement when a low-fat diet was given which supplied a restricted amount of calories per day.

Carbohydrate metabolism is closely linked with fat metabolism and it is to be expected that a reduced glucose tolerance will be coupled with an increased fat fraction in the blood. If the defective carbohydrate metabolism is corrected, the high fat fraction can be expected to decrease to more normal levels. The average total fatty acid concentration in the blood of the 20 test persons, all of whom improved their tolerance to glucose (Fig. 1), fell from 513 mg./100 ml. at the beginning to 317 mg./100 ml. at the end of the test (Fig. 2). The latter values approximated those obtained for groups of people among whom coronary thrombosis seldom occurred.[13]

The cholesterol concentration in the serum of the test persons decreased sharply in some cases, but to a lesser extent in others, and occasionally even rose. This finding would appear to indicate that the cholesterol fraction in the serum of man is less rapidly affected by dietary treatment than the total fatty acid fraction.

The sharp increase in the total percentage of essential fatty acids present in the total fatty acid fraction of the serum was mainly the result of an increase in linoleic acid from 20·7 to 26·0% and in arachidonic acid from 5·6 to 7·4%. It is of interest that Lossow and Chaikoff[14] found an increased oxidation of linoleic acid in the body cells of diabetic rats. In our test persons therefore, whose glucose tolerance was decreased, it is possible that the initial low percentage of linoleic acid in the total fatty acid fraction may have been due to increased oxidation of this essential fatty acid. This effect is enhanced when in addition the intake of linoleic acid is low, a possibility which must be kept in mind in view of the high proportion of saturated fat consumed by most of the Western peoples.

The improvement in the arachidonic acid concentration of the fatty acid fraction seen in the present series may have been due to an improvement in pyridoxine status.[15] A 'conditioned deficiency' of pyridoxine may be caused by factors which increase the requirement for the vitamin. Silberg[16] has proved, for instance, that high-protein diets increase the pyridoxine requirements of mice. Kratzer and Williams[17] found that chicks fed a ration containing 30% linseed oil developed what appeared to be a pyridoxine deficiency, although the ration contained many times the amount of pyridoxine normally required by chicks. The work of Kotake[18] has indicated that the administration of large doses of the sodium salts of fatty acids to albino rats can result in a deficiency of pyridoxine. The high standard of living of the White population of the Republic of South Africa and other countries of the West results in excessive intakes of protein and fat which might therefore cause a relative pyridoxine deficiency. Such a relative pyridoxine deficiency would depress the conversion of linoleic acid to arachidonic acid, and might explain the low serum arachidonic acid values found in our series at the beginning of the test.

When the important part played by pyridoxine in protein metabolism is borne in mind, particularly in regard to the mechanism of transamination, it seems not impossible that pyridoxine deficiency may prove to be the ultimate factor responsible for the pathological lesions which develop in the blood vessels in atheroma.[19] Nor would it be surprising to find that diet-induced intolerance to glucose could cause hyperlipaemia, accelerated blood-clotting,[20, 21] increased blood viscosity and aggregation of the red blood cells.[22]

SUMMARY

The influence of a calorie-restricted diet with a high proportion of carbohydrate and a moderate proportion of protein was studied for 8 - 9 months in 20 patients with abnormal carbohydrate and fat metabolism. A basic 1,800-calorie diet was prescribed for all the subjects but was modified where necessary to ensure that the overweight subjects lost no more than 5 - 8 lb./month. The tolerance to glucose, after a temporary deterioration in some cases, improved considerably in all the subjects during the 8 - 12 months of dietary therapy. The high initial total fatty acid concentration in the serum in each case decreased to what is considered a normal level on the prescribed diet. The lowered polyenoic fatty acid fraction of the serum total fatty acids increased gradually to a normal level as the tolerance to glucose improved and the concentration of the total fatty acids in the serum decreased.

We wish to acknowledge with gratitude the assistance of Dr. M. L. Neser in the preparation of the manuscript and to thank Mr. S. A. Fellingham of the NRIMS, CSIR, for the statistical analysis.

REFERENCES

1. Antonis, A. and Bersohn, I. (1960): Lancet, **1**, 998.
2. Walker, A. R. P. (1949): Nature (Lond.), **164**, 825.
3. Katz, L. N., Stamler, J. and Pick, R. (1956): Fed. Proc., **15**, 885.
4. Rautenbach, I. E. (1962): Personal communications.
5. De Lange, D. J., Meÿ, H. S. and Vivier, F. S. (1965): S. Afr. J. Lab. Clin. Med., **11**, 119.
6. Hausberger, F. X. and Milstein, S. W. (1955): J. Biol. Chem., **214**, 483.
7. Fetter, D. and Neidle, E. A. (1959): Metabolism, **8**, 762.
8. Vague, J. (1956): Amer. J. Clin. Nutr., **4**, 20.
9. Thorn, G. W., Reynold, A. E. and Cahill, G. F. (1959): Diabetes, **8**, 337.
10. Ramey, E. R. and Goldstein, M. S. (1957): Physiol. Rev., **37**, 155.
11. Schafrir, E. and Steinberg, D. (1960): J. Clin. Invest., **39**, 310.
12. Samuels, L. T., Reinecke, R. M. and Ball, H. A. (1942): Endocrinology, **31**, 42.
13. Waddell, W. R. and Field, R. A. (1960): Metabolism, **9**, 800.
14. Lossow, W. J. and Chaikoff, I. L. (1959): Proc. Soc. Exp. Biol. (N.Y.), **101**, 857.
15. Witten, P. W. and Holman, R. T. (1952): Arch. Biochem., **41**, 266.
16. Silberg, R. and Levy, B. M. (1948): Proc. Soc. Exp. Biol. (N.Y.), **67**, 259.
17. Kratzer, F. H. and Williams, D. E. (1948): J. Nutr., **36**, 297.
18. Kotake, Y. (1957): Clin. Chem., **3**, 432.
19. Rinehart, J. F. and Greenberg, L. D. (1949): Amer. J. Path., **25**, 481.
20. Fullerton, H. W., Davie, W. J. A. and Anastasopoulos, G. (1953): Brit. Med. J., **2**, 250.
21. Buzina, R. and Keys, A. (1956): Circulation, **14**, 854.
22. Cullen, C. F. and Swank, R. L. (1954): *Ibid.*, **9**, 335.