Diet and triglyceride metabolism

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Triglyceride forms the major store of energy in the body and it is only recently that the role of the triglyceride metabolism has been considered to be other than harmless. A vast accumulation of triglyceride as adipose tissue has been long known to increase the stress and strain of other aspects of the individual's physiology because of the physical problems it creates. More recently it has become apparent that obesity is associated with biochemical problems, and a closer look at triglyceride metabolism indicates that there exist more subtle and possibly more sinister implications in these associated disorders of triglyceride metabolism. It is widely known from obesity and starvation studies that diet plays a major role in triglyceride metabolism, certainly in the quantitative sense, but there is the possibility that the quality of the diet can exert less striking, but nevertheless important, influences on triglyceride metabolism.

Dietary Fat

The studies of Lebedeff (1883), in which he fed either mutton tallow or linseed oil to dogs, were among the first to show that the triglyceride in the diet can be laid down practically unchanged in the adipose tissue. This has been confirmed in numerous reports on man, the most recent being from Finland (Miettinen, Turpeinen, Karvonen, Elosuo, and Paavilainen, 1972). In fact so consistent is this accumulation of dietary fat in the depots that needle biopsy and analysis of the fatty acid composition of adipose tissue can be used to check whether a patient is adhering to a dietary regime in which a certain triglyceride pattern is prescribed.

A high fat intake, in contrast to a high carbohydrate intake (see below), does not, however, give rise to a fatty liver and this, perhaps, is not surprising as most of the commonly consumed triglycerides are removed from the gut via the lymphatics. Nor does a high fat diet give rise to a raised level of serum triglycerides in the post-absorptive state, though obviously immediately after a fatty meal the serum is normally opaque with chylomicrons. This is not generally considered

to be disadvantageous but to be speculative, it would be of value to know how these postprandial elevations of serum triglyceride concentration affect processes such as the clotting mechanism (including platelet stickiness), blood viscosity, and even atherosclerosis, all of which may have an association with ischaemic heart disease.

Dietary Protein

The proteins in the diet play very little, if any, part in triglyceride metabolism. It is true that in protein deficiency in children the liver can accumulate triglyceride in very large quantities, but this only takes place when the protein deficiency is accompanied by a relative excess of carbohydrate (see below).

Dietary Carbohydrate

Scientific knowledge of the conversion of dietary carbohydrate to triglyceride is 120 years old (Lawes and Gilbert, 1850). The Strasbourg peasant was doubtless aware that his goose could carry out this conversion long before it was scientifically proven. More recently, a carbohydrate-induced hypertriglyceridaemia was first described in man (Ahrens, Hirsch, Oette, Farquhar, and Stein, 1961) and this condition seems to be fairly common (Wood, Stern, Silvers, Reaven, and Groeben, 1972).

In view of the important role of dietary carbohydrate in triglyceride metabolism, and especially the probable relationship between carbohydrate-induced hypertriglyceridaemia and atherosclerosis, it is perhaps not surprising that currently there is interest in the effect of different carbohydrates on triglyceride metabolism. This interest in the qualitative aspects of dietary carbohydrates is also encouraged by the knowledge that western communities seem to be eating less polysaccharides such as starch and more of the so-called 'refined' sugars, principally sucrose.

The two major sites of triglyceride metabolism in the body are the liver and adipose tissue. Though no triglyceride metabolism takes place in the blood

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much is written about the concentration of triglycerides in the plasma or serum, largely because blood is easily accessible. However, a change in level of serum triglyceride does not give any information about its cause; it could be an alteration in input or in output or both may be altered to a different extent. The effects of dietary carbohydrate on liver, adipose tissue, serum, and skin will be considered separately.

LIVER

As mentioned earlier, in protein deficiency in children an accumulation of triglyceride occurs in the liver when these children receive a relative excess of dietary carbohydrate along with their inadequate protein intake (Brock and Autret, 1952). This fat in the liver probably arises from the carbohydrate in the diet as no other source of energy is available. In animal experiments the extent of the accumulation of liver triglyceride has been found to be related to the type of carbohydrate in the diet; starch produced much less liver fat than an equal intake of sucrose (Macdonald, 1962; Allen and Leahy, 1966). In view of these experimental findings the nature of the carbohydrate consumed in clinical liver disorders, especially those in which there is an accumulation of hepatic triglyceride, may be important.

DEPOT FAT

There is no dispute about the quantitative role of dietary carbohydrate in the production of depot fat. There is, in contrast, a dearth of information on the qualitative aspects of dietary carbohydrate in the production of adipose tissue triglycerides largely, perhaps, due to the difficulty of measuring with a reasonable degree of precision the amount of depot fat in the body. In experiments on rats (Allen and Leahy, 1966) and baboons (Brook and Noel, 1969) it seemed that more depot fat resulted from dietary sucrose than from an equal quantity of starch. Similarly in very short term weight-losing regimens in man the amount lost was not the same with sucrose as with an isocaloric intake of a partial hydrolysate of starch (Macdonald and Taylor, 1973). If these preliminary findings are confirmed they raise the question whether the effect of various carbohydrates on the metabolic rate is always the same.

SERUM

Immediate effects

During an overnight fast the endogenous triglyceride level in the serum rises (Schlierf, Reinheimer, and Stossberg, 1971). After the consumption of glucose this level falls (Albrink, Fitzgerald, and

Man, 1958) and there is some evidence that the insulin released in response to the glucose increases the activity of lipoprotein lipase and hence increases the rate of removal of the serum triglyceride (Perry and Corbett, 1964). The fall in serum triglycerides after the ingestion of sucrose (Mann, Truswell, and Pimstone, 1971) or giving intravenous fructose (Jourdan, 1969) is much less than after giving glucose. This is consistent with the view that insulin release stimulated by glucose but not by fructose is responsible for the fall in serum triglycerides immediately after a meal.

Longer-term effects

There are few studies of the long-term effects on serum triglyceride levels. It is known that peoples who subsist on a high carbohydrate intake do not in the long term have raised fasting serum triglyceride levels (Antonis and Bersohn, 1960). In a study where a high carbohydrate diet was given for 39 weeks it was found that the level of triglyceride in the fasting serum rose at first and then returned to normal (Antonis and Bersohn, 1961). To complicate the picture it is now known that there are individuals who are carbohydrate-sensitive, in that their fasting triglyceride level rises when they consume a high carbohydrate diet (Fredrickson, Levy, and Lees, 1961). The conflicting results in this area could thus, to some extent, be due to heterogeneity in carbohydrate sensitivity among the subjects studied.

Most of the prospective studies on the role of various types of dietary carbohydrate on serum triglyceride levels have been carried out for relatively short periods of time, and have often meant giving the subjects much greater amounts of the particular carbohydrate under study than would normally be consumed, so that the results can only suggest the *possibility* of metabolic effects with normal levels of consumption.

In all, about eight groups of workers from all over the world have reported that in man different carbohydrates have different effects on lipid metabolism as judged by the level of fasting serum triglycerides. Several studies have shown that a diet containing large quantities of sucrose, when given to young men, is associated with higher levels of fasting serum triglyceride than when starch or glucose is given. A similar response has been found in experimental animals. It seems that the fructose moiety of sucrose is a factor in this difference (Macdonald, 1966a) because diets containing fructose are associated with a rise in the serum triglyceride level, whereas replacing fructose by glucose abolishes such a rise. Furthermore, the incorporation of ^{14}C -fructose into serum triglyceride is greater than that of ^{14}C -glucose (Macdonald, 1968).

Though no detailed study has been made in subjects with hypertriglyceridaemia of the effect of the various carbohydrates on triglyceride metabolism, there are some findings which suggest that the 'carbohydrate-sensitive' individuals are more sensitive to sucrose than to glucose and its polymers (Roberts, 1971; Kuo and Bassett, 1965).

SOME FACTORS MODIFYING THE EFFECTS OF DIETARY CARBOHYDRATES ON TRIGLYCERIDE METABOLISM

In any study of a dietary component, the effect of factors which could modify the metabolic response to that component must always be considered. Such factors could either reduce or exaggerate any modification of metabolism that is produced.

Sex

The increase in serum triglyceride seen in men on high sucrose diets is not found in premenopausal women but is found in postmenopausal women (Macdonald, 1966b). Similar differences in response were found with fructose, but not with glucose (Macdonald, 1966a). In animal primates the rise in the fasting serum triglyceride concentration brought about by sucrose is prevented when male animals are given oestradiol (Coltart and Macdonald, 1971). There is some evidence that suggests that the difference in the response seen in young women is due to their greater ability to remove triglyceride from the serum (Kekki and Nikkila, 1971).

Whether this difference in response to sucrose and fructose by young women is of any clinical importance is not known, but it is of interest to recall that premenopausal women have a low incidence of ischaemic heart disease.

Nature of the dietary fat accompanying the carbohydrate

Under normal circumstances the carbohydrates and fats in the diet make approximately equal contributions to the energy intake. When experiments are carried out keeping dietary carbohydrates and fats approximately isocaloric the rise in fasting serum triglyceride level associated with sucrose and with fructose is prevented or even reversed when the carbohydrate is accompanied by sunflower seed oil but not when accompanied by cream (Macdonald, 1972). Similar findings have been reported in hyperlipidaemic patients (Antar, Little, Lucas, Buckley, and Csimas, 1970).

This striking effect of sunflower seed oil, a polyunsaturated fat, means that in any study on the effects of dietary carbohydrate the type of fat in the diet is also important.

Nature of the dietary nitrogen accompanying the carbohydrate

The rise in fasting serum triglyceride in man on a high sucrose diet is of a similar order whether the protein in the diet is sodium caseinate, calcium caseinate, egg albumen, or gelatin. When, however, the nitrogen source is a balanced mixture of amino acids, the serum triglyceride response is considerably enhanced. That this is not due to the amino acids alone is shown by the absence of any rise in triglyceride when sucrose is replaced by glucose (Coles and Macdonald, 1972). The precise metabolic mechanism underlying these findings is not known.

SKIN

The skin is another site of triglyceride metabolism that can be influenced by the diet. It used to be taught that alteration in the level of carbohydrate in the diet could influence the 'greasiness' of the skin. Some evidence for this is the finding that the amount of lipid on the surface of the skin is partly dependent on the type of carbohydrate consumed. A high intake of sucrose in men raised the triglyceride on the surface of the skin, whereas dietary starch had the reverse effect (Llewellyn, 1967).

Summary

It is clear that the diet plays a part in triglyceride metabolism. The extent of this cannot be clearly defined, nor can the influence of diet in the disorders of triglyceride metabolism be assessed. There are certainly enough facts to suggest that an excess of a dietary component may be as important as a deficiency in causing disease, and in the state of an unbalanced dietary intake the effects on triglyceride metabolism could be critical.

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