CHANGES IN SERUM LIPID PATTERNS OF HEALTHY YOUNG MEN FED DIETS RICH IN LARD AND SUNFLOWER OIL

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ABSTRACT

The effects of sunflower oil and lard (40 percent of calories) on serum lipid patterns and cholesterol turnover was investigated in eight healthy young men. The 39-day metabolic trial consisted of 1) a 10-day stabilization period when a fat mix with a fatty acid composition representative of the average Canadian consumption was fed; 2) a 21-day experimental period when either the lard or sunflower oil diet was fed; and 3) a 7-day post-experimental period when the mixed fat diet was refed. Fasting venous blood samples were taken on days 4, 11, 18, 25, 32 and 39. Serum total cholesterol decreased ($P < 0.001$) 56 mg/100 ml on the sunflower oil diet and increased ($P < 0.001$) 26 mg/100 ml on the lard diet. Serum free and esterified cholesterol followed the pattern of total cholesterol as illustrated by the fact that the proportion of free and esterified cholesterol remained fairly constant within each group throughout the experiment. Although there were differences among the groups, serum cholesterol, serum lipid phosphorus and serum triglycerides followed similar patterns. There was little change in the fatty acid patterns of the serum phospholipids in response to dietary fat source. Little is known of the effects of dietary fat on the turnover of plasma cholesterol in normal, healthy men. Thirty-two days prior to the start of the study, each subject was infused with 50 microcuries of tritium labelled cholesterol and the decline in radioactivity in the plasma

was monitored during the study. The decrease of ^{3}H-cholesterol in the blood was twice as great on the sunflower oil diet as on the lard diet. However, there was no change in the slopes of the specific activity-time curve on the two diets which suggests that the rate of turnover of cholesterol differed on the two diets but synthesis and absorption of cholesterol remained constant. During the final seven days of the experiment when the mixed fat diet was fed, the effects of protein source on serum lipids was investigated. Two subjects from each of the lard and sunflower oil treatments consumed the same identical mixed fat diet of days 1 to 10, whereas the remaining four subjects consumed the same diet except that the soy protein was replaced by lean beef. Protein source was found to have no effect on any of the serum lipid parameters measured. The appreciable effects of sunflower oil and lard on serum lipid patterns is consistent with the hypolipidemic effect of polyunsaturated fatty acids and hyperlipidemic effect of saturated fatty acids although the recommendation of substituting animal fats with vegetable fats without considering the fat source is to be questioned.

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INTRODUCTION

The relation of angina pectoris to coronary atherosclerosis was recognized over two centuries ago. Myocardial infarction was first recognized clinically over a century ago. Today, syndromes characterized by cardiac pain are precisely diagnosed and treated (Altschule, 1974). Generally, when a disease is easily and satisfactorily treated, the pressure on scientists to elucidate the etiology and define preventive measures is minimal. But, when a disease is increasing in frequency - as is the case with coronary atherosclerosis - and when treatment of some of its manifestations is not satisfactory, the pressure for a solution is persistent and heavy.

Atherosclerosis, the leading cause of death in North America, is an entity characterized by the accumulation of cholesterol and other fatty substances in the walls of the large blood vessels (Gresham, 1972). From adolescence onwards, the disease is almost universally present in our population; persons with extensive disease become candidates for heart attacks and angina pectoris when the coronary arteries are involved, and for strokes when the cerebral arteries are involved. In North America, a male under 60 has one chance in five of developing atherosclerotic ischemic heart disease. Almost one-third of the initial heart attacks are fatal within a few hours and more than 60 percent before the victim receives medical attention. For the survivors the outcome is often gloomy (Brusis, 1971).

Clinical and epidemiological studies have indicated that the causes of atherosclerosis and the clinical events leading up to a heart attack are multifactorial (Epstein, 1972). These causes include genetic, cultural and environmental factors. Some of the cultural and environmental factors which are known to increase the risk of coronary heart disease (CHD) are under the control of the individual. These include dietary patterns (high intake of cholesterol, saturated fats and calories), sedentary living habits (Paffenbarger and Hale, 1975) and cigarette smoking. Other factors, which have been implicated but which are less well documented, are large coffee intakes (Paul, 1968), hardness of the drinking water, and emotional stress and tension (Schroeder, 1974). Some of the predisposing factors are not responsive to preventive intervention; men, for example, are more prone to CHD than pre-menopausal women. Diabetes mellitus, obesity and a positive family history of vascular disease also increase the risk of CHD (Kannel et al, 1967; Epstein, 1972).

The degree to which each of these factors has contributed to atherosclerosis has been confounded by many problems. Some of the factors are interrelated; obesity can be due to genetic factors or to an imbalance of caloric intake and energy expenditure (Katz et al, 1958); both can cause hypercholesterolemia. The complexity of the tissue and haemodynamical factors influencing the location and evolution of the atherosclerotic lesion (Altshule, 1974a), the difficulty at present to assess the presence and extent of

atherosclerosis in the living person and the lack of a satisfactory experimental animal model for atherosclerosis (Gresham, 1971), although work with primates appears promising (Jones et al, 1975), have added to the problem in elucidating and separating all the factors implicated in atherosclerosis.

All serum lipids have been implicated in atherosclerosis. Elevated serum cholesterol values appear to be a factor present in all forms of CHD, hence interest has been focused on serum cholesterol. Examination of atherosclerotic fatty streaks in human thoracic aorta have shown average cholesterol values five times those of normal aorta, and phospholipid values 1.5 times those in adjacent normal intimae (Insull and Bartsch, 1966). High fasting concentrations of plasma triglycerides have been shown to be a significant risk factor in atherosclerotic disease (Carlson and Boltiger, 1972) and it has been suggested that hypertriglyceridemia may have a risk independent of associated hypercholesterolemia (Albrink, 1973).

There have been many studies on man in which the diet has been closely regulated. These studies have shown that changes in the fat composition of the diet can bring about a change in serum lipid values. Diets high in saturated fats, containing high proportions of C12:0, C14:0 and C16:0 fatty acids, have been shown to elevate serum cholesterol values (Grande et al, 1972). On the other hand, saturated fatty acids of fewer than 12 carbon atoms (Keyes et al, 1965c) and stearic acid (Keyes et al, 1965c; Grande

et al, 1970; and Losier, 1972) have been found to have little effect on serum cholesterol values. Epidemiological studies have shown that populations who consume diets low in fat, such as those which characterize the Bantu, have little ahterosclerotic heart disease. But, these diets tend to be unpalatable and too extreme for North American society. Substitution of vegetable oils, rich in polyunsaturated fatty acids and low in saturated fatty acids and cholesterol, in place of animal fats can essentially achieve the same effect on serum lipids. This approach has offered a way to maintain a palatable high fat diet. Several controlled clinical trials have established the quantitative effects of saturated and polyunsaturated fat, as well as of dietary cholesterol on serum cholesterol in man (Hegsted et al, 1965; Keyes et al, 1965a; Keyes et al, 1965b; and Keyes et al, 1965c).

It has been suggested that to counteract the present incidence and mortality from CHD in North America, the diet must be modified to minimize elevations of serum lipids. However, many of the earlier studies implicating various fats were conducted with subjects who were fed forumula diets and who were not free-living individuals consuming mixed diets. Saturated fats are generally regarded as hypercholesterolemic although Losier (1972) found beef tallow, a fat high in stearic acid, to have a hypocholesterolemic effect. Thus, more precise information on the effects of specific fats and fatty acids is needed. However, if it is accepted, in general, that polyunsaturated fatty acids decrease serum cholesterol and that saturated fatty acids increase serum

cholesterol, the question arises as to how they bring about these effects; whether it is by increasing turnover of cholesterol or by a mechanism of redistribution of cholesterol between the various body tissues. The present study was undertaken to investigate the effects of lard, a saturated fat high in palmitic acid, and sunflower oil, a polyunsaturated fat high in linoleic acid, on cholesterol turnover and on serum lipid levels in healthy, free-living individuals consuming a mixed food diet.

REVIEW OF LITERATURE

The main features of cholesterol metabolism were elucidated in 1933 by Schoenheimer & Breusch who concluded that synthesis, absorption and destruction of cholesterol in mammals were controlled by a complex system of interrelated mechanisms in which cholesterol itself was a principal mediator. However, even today the means by which the regulatory mechanisms are integrated is poorly understood largely because adequate methodology for accurately quantitating sterol synthesis, absorption, excretion and degradation in the intact animal has been developed only recently. In addition, the miscibility of cholesterol among tissues and organs makes the dissection of control mechanisms in the various organs difficult. This review will attempt to summarize the current concepts of the measurement and regulation of cholesterol turnover.

Turnover, in the case of cholesterol, reflects the balance between input of cholesterol from endogenous tissue synthesis and from dietary sources, and the loss of cholesterol which occurs in the feces in the form of bile acids and neutral sterols. There have been several studies of cholesterol turnover. In addition to studies on cholesterol turnover, other studies have provided estimates of the flow of cholesterol among the body pools. Many of the studies have focused on assessing serum cholesterol levels because of the association between atherosclerosis and high serum cholesterol values. In general, the changes in plasma

cholesterol are thought to reflect the changes in other body tissues.

Studies in cholesterol turnover require considerable time because turnover is slow in some tissues. The measurement of cholesterol turnover demands steady state conditions in which there is a constant sterol intake and stable body weight. Cholesterol is lost almost exclusively in the feces. Fecal collections are problematic; total feces must be collected and corrections must be made for losses of neutral sterols due to bacterial degradation. Methods which measure the turnover of radioactive cholesterol in the plasma are more simple than chemical methods but do not yield the amount of information that direct quantitation of fecal sterols or a combination of both methods can give.

A. METHODS OF MEASURING CHOLESTEROL TURNOVER

Nestel (1970) and Grundy & Ahrens (1969a) have reviewed the four major techniques for measuring cholesterol turnover in man. These include the chemical balance technique, isotopic balance methods, estimations based on analysis of radioactive cholesterol die-away curves in serum[1] and a combination of these methods.

Two types of isotopic balance methods have been used to distinguish between fecal products of endogenous and exogenous origin. The simplest method involves a single

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1. A plot which takes into account radioactive decay and biological turnover of the labelled compound.

intravenous injection of labelled cholesterol and the subsequent measurement of radioactivity in the plasma and fecal steroid fractions. The labelled cholesterol is administered at least 30 days prior to sampling to allow complete equilibration of the isotope among the various body tissues. The second approach, the steady state isotopic balance method, has been suggested as a means for calculating the amount of cholesterol absorbed. A constant amount of labelled cholesterol is ingested daily until a steady state is reached. Once a steady state has been reached, cholesterol turnover can be calculated.

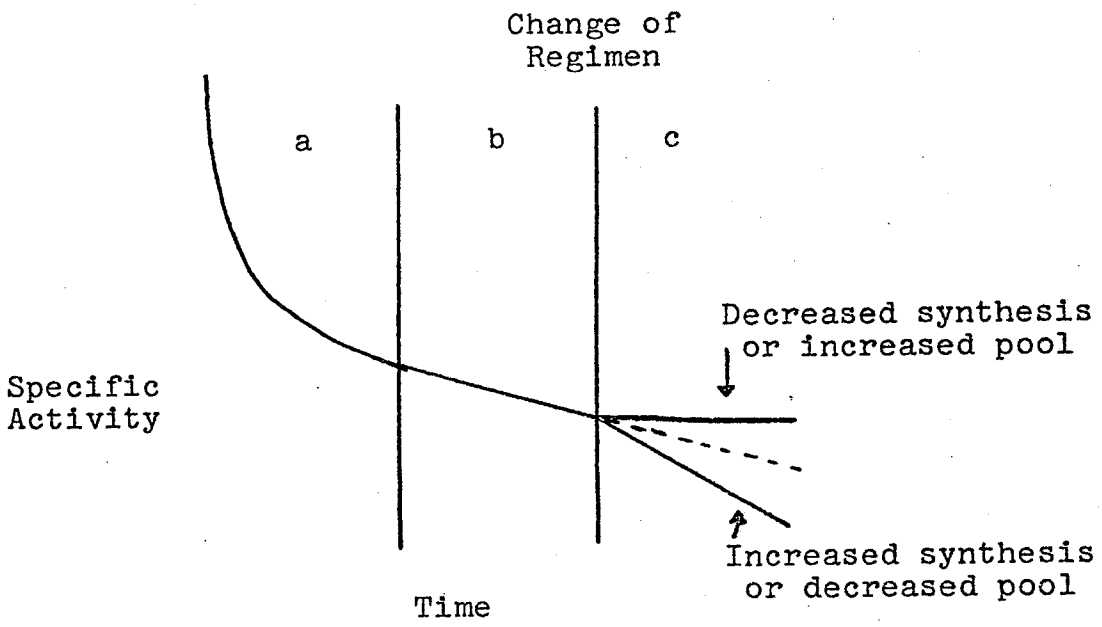
There have been several approaches for the measurement of cholesterol turnover by analysis of specific activity die-away time curves. One of the simplest techniques is the single intravenous injection of labelled cholesterol followed by monitoring of plasma radioactivity (Goodman and Noble, 1968). The limitation of this method is that no direct measurement of cholesterol synthesis and absorption is made.

Chobanian et al (1962) proposed a method for calculating the rate of total turnover of cholesterol on the basis of the die-away time curve of radioactive cholesterol. His approach reflected the turnover of a single pool of readily-miscible cholesterol excluding that in nerve tissue. This model did not account for the fact that the change in specific activity in serum cholesterol is not linear until 30 days following the injection of labelled cholesterol (Figure 1).

It is well documented that plasma cholesterol specific activity declines more slowly after the first few

FIGURE 1

SCHEMATIC LOG SPECIFIC ACTIVITY-TIME CURVE FOR SERUM CHOLESTEROL AFTER ADMINISTRATION OF A SINGLE DOSE OF RADIOACTIVE CHOLESTEROL



a = Period of Rapid Decay (non-linear fall off).

b = Period of Isotopic Equilibrium Between Readily Miscible Pools (linear fall-off).

c = After Change of Regimen.
(Pool is conceived of as all the body cholesterol except that in nervous tissue. Its size can be increased by decreased excretion, increased synthesis, or increased absorption of endogenous cholesterol. After a change in regimen, a decreased slope of the specific activity-time curve is due to decreased endogenous synthesis or increased pool size; increased slope is due to increased synthesis or decreased pool size.)

Grundy & Ahrens (1966).