Role of Dietary Fat in Health[1]

RICHARD J. JONES, Department of Medicine, Pritzker School of Medicine,
Division of Biological Sciences, University of Chicago, Chicago, Illinois 60637

ABSTRACT

Recent scientific evidence is reviewed which shows that some modest success at improving the morbidity due to atherosclerotic disease has been achieved by a diet lower in fat and cholesterol and higher in polyunsaturated fatty acids than the usual American diet. This has shown a group correlation with serum cholesterol reduction. The effect is small enough that no statistically significant improvement in overall mortality rate has yet been seen in groups studied. Many imponderables remain in the use of a high polyunsaturated fatty acids diet: not only is the optimal daily dietary intake uncertain, but its effects upon the body economy are just beginning to receive attention. While it seems reasonable to attempt nomalization of abnormal blood lipid patterns through dietary or pharmacological efforts in those individuals with acquired or inherited hyperlipidemias, the presently available data do not warrant major revision of the dietary pattern for the remaining 80-90% of the population.

INTRODUCTION

Perhaps the principal reason for discussing the role of fat in the American dietary is the current recommendations of the American Medical Association (1) and the Intersociety Commission for Heart Disease Resources (2). The latter body has made the most specific suggestions for adult nutrition with a view to minimizing the effects of atherosclerosis. They have suggested that, in addition to maintaining a caloric intake calculated to achieve and maintain an optimal body wt, cholesterol intake should be reduced to less than 300 mg from the present average of 600 mg/day, total fat intake should be reduced to less than 35% total calories and saturated fatty acids (SAFA) to less than 10% from the present 15-18%, while the monounsaturated and the essential polyunsaturated fatty acids (PUFA) should each achieve at least 10% calories. This implies a substantial increase in the latter from the present average of 3-5%. Without dwelling upon the theoretical relationship of dietary fat to blood lipids and finally to arterial wall lipids and the atherosclerotic process, I would like to review the applied research which supports the notion that a change in our dietary will reduce the incidence of heart attacks, strokes, and sudden death before going on to a review of the little we know about the role of dietary fat.

First, there is the evidence supplied by the Framingham Project and many other epidemiological studies relating the incidence of new heart disease and sudden death (which is presumed ca. 90% of the time to be due to a heart attack) to several risk factors (3). When each of the major risk factors is weighted according to its contribution to atherosclerotic disease complications (Fig. 1), the most important of these factors for our consideration, and also the most important factor in men, after age, is serum cholesterol. The serum cholesterol is a rough reflection of the total body pool of exchangeable cholesterol (4); and many lines of evidence, both clinical and experimental, suggest that the higher the blood cholesterol, the more severe and extensive is the arterial disease. At this point, however, we must point out that careful balance studies have not always found reductions in serum cholesterol to parallel a reduction in the total body burden. In fact, it was in the comparisons of cholesterol balance on a saturated fat diet vs a heavily polyunsaturated fat diet that the fall in serum cholesterol in the latter dietary period could not be accounted for in the fecal losses of cholesterol and its metabolic products but suggested a redistribution of cholesterol between blood and tissues (5). Nevertheless, several clinical studies on dietary prophyllaxis have found a correlation between reduced mortality from atherosclerotic complications and a reduced serum cholesterol for the group.

DIETARY PROPHYLLAXIS

There have been many clinical epidemiological studies attempted in which the progression of coronary disease, the major cause of death attributable to atherosclerotic complications was measured in two groups, one on a normal (high animal fat) diet and one on a cholesterol lowering diet. These studies have been well reviewed elsewhere (6-9), and, while all of them did not universally show benefit from a low animal fat diet, the larger more painstaking studies were able to show a significant difference in the two groups after 5 years.

The first major effort at dietary prevention of coronary disease in a previously healthy population, designated as

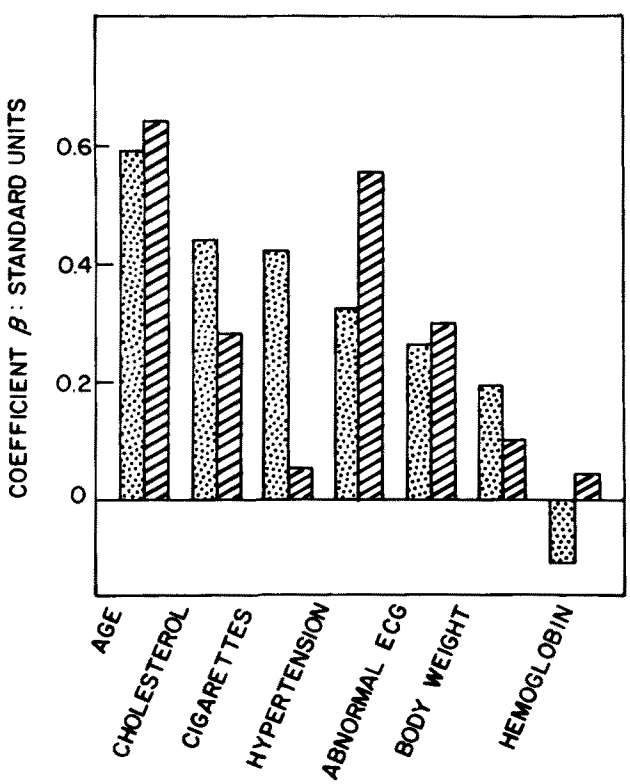

FIG. 1. A comparison of the standardized units of discriminant function coefficients for 7 risk factors in men and women as analyzed for the 12 year Framingham Project (3). Linear discriminant function, $y = \alpha + \Sigma \beta_i x_i$. ECG = electrocardiogram. ▨ = men ▩ = women.

[1]One of five papers presented at the symposium, "Status of Fat in Food and Nutrition," AOCS Fall Meeting, Chicago, September 1973.

TABLE I

Incidence of New Coronary Disease in Anticoronary Club Compared with Patients in Cancer Detection Clinics of New York City Department of Health (9)

	Anticoronary Club	Cancer Detection Clinics
Total number of men 40-59 years	941	457
New coronary events	17	32
Person years of experience	3,954	3,122
Incidence/100,000 person years	450	1,025

TABLE II

Norwegian Study Comparing Dietary Treatment with Control Diets in Male Myocardial Infarction Survivors (10)

End point	Conventional	Polyunsaturated fatty acids
Number of patients	206	206
Patients developing		
Sudden death	27	27
Myocardial infarction	54	34
New Angina Pectoris	29	10
Total relapses	90	64
Percent relapses	43.7	31.0

primary prevention, was that of the Anticoronary Club in New York City. Rinzler (9) reported on the experience with new development of heart disease in 1242 free living men 40-59 years of age. They pursued a diet in which 33% calories were derived from fat of which one-third of the fatty acids were saturated, one-third were monounsaturated, and one-third were polyunsaturated. After 10 years of annual review, the authors could compare the onset of new coronary disease in 941 subjects on this "prudent diet" with that in 457 men from a control group, male visitors to a cancer prevention clinic, who had been given no special dietary instruction. Table I shows that, in contrast to the control group, the members of the Anticoronary Club showed a fall of some 30 mgm% in serum cholesterol which was sustained for as long as they stayed in the project. Their adipose tissue, when sampled, showed ca. 100% increase in its burden of PUFA. Their 3954 person years of experience was associated with 17 new coronary events as compared to 32 new events in 3122 person years of experience in the control group. Thus, the dietary prophyllaxis could be said to have produced a halving of the incidence of coronary disease found in the control group. However, mortality rate in both groups was low (0.5% in the experimental and 1.7% in the control group) and, though in the desired direction, was not statistically significant.

Ca. 7 years ago, Leren (10) reported on his dietary study on men who survived a myocardial infarction. Ca. 408 such men were assigned randomly to a control group or a cholesterol reducing diet. The latter substituted unsaturated soybean oil for 72% fat in the Norwegian diet and accomplished a 17.6% (52 mgm%) reduction in serum cholesterol. Although no significant difference was found in sudden deaths between the two groups, or in total mortality, there was a significant difference in the number of recurrent myocardial infarctions and new symptoms of angina pectoris which favored the experimental group (Table II). In this study of secondary prevention, we again see in 5 years a halving of the incidence of new heart attacks and angina pectoris by using an appropriate diet. It was disturbing again that this improvement in heart attacks was not accompanied by a significant reduction in total mortality rate.

TABLE III

Nonfatal and Fatal Cardiovascular Events in Control and Experimental Dietary Groups (11)[a]

End point	Control	Experimental
Definite myocardial infarct		
by electrocardiogram only	4	9
overt	47	33
Sudden death	27	18
Cerebral infarct	25	13
Ruptured aneurysm	5	2
Amputation for gangrene	5	7
Miscellaneous	6	3
Total	119	85

[a]Los Angeles Veterans Administration study.

A subsequent study of secondary prevention in this country was that by Dayton and Pearce (11) who studied the development of new heart disease, strokes, other thromboembolic disease, and sudden death in inhabitants of a Los Angeles domiciliary care facility for aging military veterans who pursued either a normal diet or one calculated to lower the serum cholesterol. In the fat modified diet group, serum cholesterol levels were maintained at a level 31 mgm% lower than in the control groups. When all incidents of heart attack, stroke, and sudden death were tabulated after 8 years (Table III), a statistically significant reduction in total events was observed in the dietary group after exclusion of all subjects with preexisting atherosclerotic disease. In spite of this benefit in cardiovascular manifestations of disease, mortality rates were not different in the two groups. The experimental group, though it suffered less fatal cardiovascular disease, showed a greater incidence of fatal malignancy to make up the difference (12). This was a finding of borderline statistical significance, so that cancer could not be definitely implicated as a by-product of the diet. However, it did raise the specter of possible harm from the pursuit of a high vegetable oil diet.

More recently, in two Finnish mental hospitals, a crossover type of experiment was completed in which the diet of one, N, was changed so that most of the milk fat was replaced by soybean oil; the diet of the other, K, remaind essentially unchanged (13). After 6 years, their position was reversed and the second employed the modified diet, while N reverted to the usual high milk fat diet. Serum cholesterol determinations, measured at intervals in all residents, were lower in the hospital using the modified diet. During the first 6 years, a significantly lower incidence of electrocardiographic changes compatible with new infarction and also coronary deaths were seen in hospital N. During the second 6 year period, the mortality difference was less striking until allowance was made for differences in hospital admissions and discharges, then the rate of development of fatal coronary heart disease incidents/man year of exposure to the diet was significantly less in hospital K (Table IV).

Both of these last studies are remarkable, not because of the magnitude of the differences established, but because they showed any difference at all in these older people who were undoubtedly afflicted to a large degree by fairly advanced vascular disease at the outset. The hope is, of course, that if these fat modified diets were started earlier in life, they actually might serve to control the disease process and limit complications to a more significant degree.

DIETARY FAT

Many studies have shown that a reduction in animal fat content of the diet will reduce the serum cholesterol level. The displaced calories may be made up of carbohydrate,

protein, or vegetable oils. It has been traditionally assumed, on the basis of much former evidence, that diabetes mellitus (another important coronary risk factor) may be precipitated or aggravated, or a rise in serum triglycerides may occur, in the susceptible population placed on a high carbohydrate diet. On the other hand, there are many populations over the globe which have subsisted for generations without apparent problems on a low fat, high carbohydrate diet. The difficulty in making comparisons is that these people live in backward countries with poor medical surveillance and generally have a low life expectancy.

If one asks the question, "How necessary is fat to the human diet?" The answer is by no means agreed upon. It is true, of course, that the essential fatty acids (EFA) cannot be manufactured in the body nor can the fat soluble vitamins; but the fat soluble vitamins can be given in a very small volume, and the requirement for EFA is said to be no more than a few g/24 hr (14). As a matter of fact, one human volunteer was able to remain for 6 months on a low EFA fat diet with no adverse effects (15). The diet contained less than 2 g fat which incorporated the known fat-soluble vitamins. The volunteer noted an improved sense of well being and the disappearance of migraine headaches to which he had been subject for many years.

The dietary habits of 250 families of the Hos tribe, an aboriginal tribe in Bi Har Province, India, were reported by Mitra (16). These families were found to use absolutely no fat in their cooking. Cooked food was only boiled or baked and fat intake was estimated at no more than 5 g/day/person. Although this primitive tribe could not be said to have been in the best possible health, for there were evidences of vitamin A deficiency and angular stomatitis, there was no eczema or other symptom attributable to EFA deficiency. Their energy was not at a low level. It can be concluded from these limited observations that the dietary needs for fat are largely culinary and gustatory. Although fat does have a high fuel value and great palatability, no one has demonstrated the need of adults for more than 5-10 g fat/day which could satisfy the requirements for essential fatty acids and fat-soluble vitamins (14).

On the other hand, if we are to pursue a low fat diet, the displaced animal fat calories cannot, for practical reasons, be made up in protein calories. Let us then take a hard look at this high vegetable oil diet which is being advocated as the simplest approach to controlling blood cholesterol. No populations have subsisted on such a diet for any length of time to provide actuarial experience as to the consequences; yet, this is precisely the diet which has been used in the four studies just quoted. Since it does seem to work as a hypocholesteremic diet, let us review the results of experimental studies which have explored the effect upon various biological parameters of employing a vegetable oil as compared with an animal fat in the diet.

TABLE IV

Effect upon Coronary Heart Disease Mortality of Cholesterol Lowering Diet in Two Finnish Mental Hospitals, K and N, for 2 Consecutive Six Year Periods (13)[a]

Group	Hospital N	Hospital K
	Mean cholesterol levels	
Diet	231	235
Control	272	269
	Total deaths	
Diet	115	60
Control	143	56
	Coronary heart disease death rate/1000 man years exposure	
Diet	5.7	7.5
Control	12.7	15.2

[a]During first 6 years, hospital N was on the high polyunsaturated fatty acid diet and K on the usual Finnish diet; during the second 6 years the hospital's diets were reversed, K was on the special diet, N had the control diet.

VEGETABLE OIL DIET

Schubert (17) discussed fat nutrition in childhood and made the point that the minimal dietary fat requirements in infancy have not been established. Pediatricians generally have assumed that human milk is the ideal food for infants. This contains ca. 54% calories from fat (5.4% as linoleic acid). Commercially available artifical formula diets used for infants contain ca. the same, 50% calories as fat, but have an increased percentage of calories from linoleic acid (11-22%). When such high polyunsaturated fatty acid diets are fed to premature infants, vitamin E deficiency has been produced. This is characterized by generalized edema, irritability, constipation, hemolytic anemia, and a characteristic seborrheic rash which are cleared by the administration of vitamin E. While the same vitamin E deficiency syndrome does not develop in healthy full term infants fed this formula, vitamin E levels develop which are much lower than in their counterparts given human milk for the same first 3 months of life. Concerning older children, the minimal requirements for vitamin E, linoleic acid, and cholesterol in the diet really have not been worked out.

Table V provides a partial list of several parameters that have been found to differ significantly in experimental animals or man when a polyunsaturated vegetable fat replaces a saturated animal fat in an otherwise adequate diet. Many of the observed effects seem beneficial: the reduction in the serum cholesterol level (18), the triglyceride response to dietary carbohydrate (19), the whole blood clotting time (20), and the platelet aggregation (21); and the enhancement of clearance of particulate lipid (22),

TABLE V

Parameters Influenced by Polyunsaturated Dietary Fat as Compared to a Saturated Dietary Fat (Eucaloric)

Reduced	Enhanced
1. Serum cholesterol level	1. Blood lipid clearance
2. Carbohydrate induced hypertriglyceridemia	2. Postheparin lypolysis
3. Blood coagulation time	3. Platelet survival
4. Platelet aggregation	4. Vitamin E. requirement
5. Eicosatrienoic acid (20:3) level	5. Arachidonic acid (20:4) level
6. Hepatic fatty acid synthetase	6. Membrane acetylcholinesterase adenosine triphosphatase
7. Renal cholesterol turnover	7. Hepatic microsomal enzyme activity
8. Learning under stress	8. Ceroid production

postheparin lipolytic activity (23), and platelet survival time (24) have all been documented and, according to present concepts, should be helpful in prevention of atherosclerosis or thrombosis. There are other influences, the beneficence of which are less certain. It is well known that the vitamin E requirement is increased in animals receiving a high PUFA diet (25) and that a vitamin E deficiency can be precipitated in premature infants (26). It also is known that diets rich in linoleic (n-6) (18:2) fatty acid stimulate an elevation of arachidonate, (n-6) (20:4) fatty acid, blood, and tissue levels and that conversely, a relative dificiency in the (n-6) (18:2) fatty acid provokes a rise inthe (n-9) (20:3) fatty acid (27). The significance of this change in the 20:3/20:4 ratio is not understood entirely, but it is a useful measure of linoleic acid deficiency and may be important in the structure and function of cell membranes and intracellular organelles.

Morero, et al., (28) was able to show that the kinetic constants for the reaction between red cell membrane acetylcholinesterase and acetylthiocholine were impaired and that membrane bound adenosine triphosphatase was altered in animals deficient in EFA. Enzymes of the endoplasmic reticulum of hepatocytes are of crucial importance in detoxification of many compounds. Norred and Wade (29) showed that addition of corn oil to a fat free diet stimulated microsomal enzyme reactions to ethylmorphine, hexobarbital, and cytochrome P-450. Suboptimal behavior of other enzymes important to mitochondrial phosphorylation and oxidation, to cytochrome oxidase activity, and to the activity of several dehydrogenases may be capable of correction by a PUFA diet (30,31), but no one seems to have looked at the possible dangers of overcorrection. Is there a point beyond which further addition of EFA make them not only nonessential but supraoptimal or even disadvantageous?

Although the evidence is rather preliminary and will need further documentation, a high PUFA diet has been shown to decrease cholesterol turnover selectively in rat kidney in vivo (32) and to inhibit (more than a saturated fat diet) fatty acid synthesis by the liver (33). Furthermore, studies on the ability of rats to learn maze patterns tentatively have shown subtle differences in learning ability depending upon the quality of dietary fat (34).

Perhaps the most serious potential hazzard in consuming a high PUFA diet resides in its possible enhancement of ceroid production. This lipofuscin, or aging pigment, is difficult to study chemically because it is so insoluble. It is thought to be a polymer of peroxidized long chain unsaturated fatty acids. It can be demonstrated histochemically and is reported by Hartroft (35) to be almost as ubiquitous in atherosclerotic plaques as cholesterol. In the experimental situation, it is more easily produced from polyunsaturated oils than from saturated fats and is apparently quite incapable of biodegradation. How important it may be in provoking arterial occlusion has not been established, but it does appear to be found with great consistency in the irreversible lesions of the arterial wall and, from what we do know about it, may be one of the most indestructible, nondegradable, insoluble contributors to that irreversibility.

Another important issue to be considered is whether the enhancement of hypertriglyceridemia by a low saturated fat diet, in which caloric intake is maintained by the substitution of carbohydrate, should be considered a serious disadvantage to health. In their initial report, Antonis and Bersohn (19) reported that most of their healthy Bantu volunteers adjusted to such a diet with a return to normal triglyceride levels in a period of less than 3 months. Most of their subjects of European extraction were slower in adapting to this diet and 30% did not return to normal levels even after 6 months. The question which never has been resolved in many confirmatory studies is whether these less adaptable people may not be precisely those individuals who are later destined to develop atherosclerotic disease.

The lipid patterns of young men proven to have coronary disease by angiography show that 80% have a high cholesterol, high triglyceride, or both (36). These are ca. equally divided into type II (hypercholesteremia) or type IV (hypertriglyceridemia) hyperlipoproteinemia. The latter all have high triglyceride levels, and ca. 40% show a diabetic glucose tolerance curve. Many, but not all of them will respond with a return to normal lipids if the carbohydrate intake is reduced with adequate caloric intake maintained by the addition of polyunsaturated vegetable oils. Studies of rather large numbers of patients placed on the American Heart Association recommended diet suggest that a hypertriglyceridemic response is quite rare and is a serious consideration in only a few subjects (37,38).

REFERENCES

1. Council Statement: J. Amer. Med. Assoc. 222:1647 (1972).
2. Intersociety Commission for Heart Disease Resources, Circulation 42:A55 (1970).
3. Truett, J., J. Cornfield, and W.B. Kannel, J. Chronic Dis. 20:511 (1967).
4. Goodman, D.S., and R.P. Noble, J. Clin. Invest. 47:231 (1968).
5. Quintao, E., S.M. Grundy, and E.H. Ahrens Jr., J. Lipid Res. 12:233 (1971).
6. Jones, R.J., "Atherosclerosis: Proceedings of the Second International Symposium," Springer-Verlag, New York, N.Y. 1970, p. 565.
7. Dayton, S., and M.L. Pearce, Amer. J. Med. 46:751 (1969).
8. Blackburn, H., and J. Willis, Minn. Med. 52:1185 (1969).
9. Rinzler, S.H., Bull. N.Y. Acad. Med. 44:936 (1968).
10. Leren, P., Acta Med. Scand. Suppl. 466:7 (1966).
11. Dayton, S. and M.L. Pearce, S.D. Hashimoto, W.J. Dixon, and W. Tomiyasu, Circulation 40:1. Suppl. II (1969).
12. Pearce, M.L., and S. Dayton, Lancet 1:464 (1971).
13. Miettinen, M., M.J. Karvonnen, O. Turpeinen, R. Elosuo, and E. Paavilainen, Lancet 2:835 (1972).
14. Davidson, S., R. Passmore, "Human Nutrition and Dietetics" Third Edition, Williams and Wilkins, Baltimore, Md., 1966, p. 109.
15. Brown, W.R., A.E. Hausen, G.O. Burr, and I. McQuarie, J. Nutr. 16:511 (1938).
16. MItra, K., Indian J. Med. Res. 30:91 (1942).
17. Schubert, W.K., Amer. J. Cardiol. 31:581 (1973).
18. Ahrens, E.H., Jr., D.H. Blankenhorn, and T.T. Tsaltas, Proc. Soc. Exper. Biol. and Med. 86:872 (1954).
19. Antonis, A., and I. Bersohn, Lancet 1:3 (1961).
20. Verstraete, M., Acta Cardiol. Suppl II:37 (1972).
21. Nordoy, A., Acta Med. Scand. 190:27 (1971).
22. Nestel, P.J., and P.J. Barter, Amer. J. Clin. Nutr. 26:241 (1973).
23. Struijk, C.B., W.M.T. Houtsmuller, H. Jansen, and W.C. Hülsmann. Biochim. Biophys. Acta 296:253 (1973).
24. Mustard, J.F., in "Evolution of the Atherosclerotic Pladue." Edited by R.J. Jones, University of Chicago Press, Chicago, Ill., 1963.
25. Whitting, L.A., N.Y. Acad. Sci. 203:192 (1972).
26. Hassan, H., S. Hashim, T.B. Van Itallie, et al., Amer. J. Clin. Nutr. 19:147 (1966).
27. Egwim, P.O., and F.A. Kummerow, J. Lipid Res. 13:500 (1972).
28. Morero, R.D., B. Bloj, R.N. Farias, and R.E. Trucco, Biochim. Biophys. Acta 282:157 (1972).
29. Norred, W.P., and A.E. Wade, Biochem. Pharm. 21:2887 (1972).
30. Johnson, R.M., J. Nutr. 81:411 (1963).
31. Tulpule, P.G., and J.N. Williams, J. Biochem. 217:229 (1955).
32. Rothfeld, B., A. Karmen, and A. Varady, Jr., Biochem. Med. 6:438 (1972).
33. Brickdorfer, K.R., P.B.P. Kari-Kari, I.H. Kahn, and J. Yudkin, Nutr. Metab. 14:228 (1972).
34. Cafrey, B., and M.Y. Patterson, Psychol. Rep. 29:79 (1972).
35. Hartroft, W.S., and E.A. Porta, Ceroid. Amer. J. Med. Sci. 250:324 (1965).
36. Heinle, R.A., R.I. Levy, D.S. Fredrickson, and R. Gorlin, Amer. J. Cardiol. 24:178 (1969).
37. Wilson, W.S., S.B. Hulley, M.I. Burrows, and M.Z. Nichaman, Amer. J. Med. 51:456 (1971).
38. Hall, Y., J. Stamler, D.B. Cohen, L. Mojonniere, M.B. Epstein, D.M. Berkson, I.T. Whipple, and S. Catchings, Atherosclerosis 16:389 (1972).

[Received October 8, 1973]