The Variable Effect of a Diet High in Unsaturated Fat in Hyperlipemic Subjects

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IT IS well known that a diet high in unsaturated fat will cause a decrease in serum cholesterol and other serum lipids in most persons with idiopathic hypercholesterolemia.[1-4] There also have been reports of the beneficial effect of a diet high in unsaturated fatty acids in the treatment of patients with hyperlipemia.[5-7] During the past four years chemical analyses of ultracentrifugally separated serum lipoprotein fractions performed in this laboratory have revealed three major patterns of lipid abnormalities. These patterns were first decribed by one of us (E. B.) in 1957,[8] and the two most common have recently been described in detail by Furman, Howard, Lakshmi and Norcia.[7] The most common abnormality has consisted of an elevation of total serum cholesterol in a clear serum, elevation of phospholipids and total lipids with the elevation of serum cholesterol occurring predominantly in the low density lipoprotein fraction (D 1.063 to 1.006). The second pattern observed consisted of an elevated total serum cholesterol in a cloudy or milky serum, elevated phospholipids and markedly elevated total lipids inferring an elevation of serum triglycerides. The elevated serum cholesterol in this pattern occurs predominantly in the very low density lipoprotein fraction (D <1.006). The third and least common pattern consists again of a rise in all lipid moieties with the rise in serum cholesterol occurring in both the low density and the very low density lipoprotein fractions. Brown and Page[9] also have described the effect of various dietary regimens in patients with similar serum lipid patterns.

It is the purpose of this report to present four patients with idiopathic hyperlipemia (types II and III) who responded in strikingly different manners to a diet high in unsaturated fat.

MATERIALS AND METHODS

Cholesterol determinations were made by the method of Zlatkis, Zak and Boyle[10] with the color reagent modification of Rosenthal, Pfluke and Buscaglia,[11] phospholipid determinations by the method of Zilversmit and Davis,[12] total lipid determinations by the method of Bragdon,[13] and ultracentrifuge analyses were performed by this laboratory's modification[14] of the method of Havel, Eder and Bragdon.[15]

CASE REPORTS

CASE I. This fifty-four year old white man (H. H.) was found to have hyperlipemia during a routine physical and laboratory examination and was referred to this laboratory for evaluation. His history revealed that he had had hypertension in the past which had disappeared without therapy. Family history revealed that his father had died of a myocardial infarct at sixty-four years of age. The patient admitted to a high intake of animal and dairy fat for many years. His initial blood lipid levels are listed in Table I. A serum protein electrophoresis performed at the same time was normal except for a slightly elevated beta globulin fraction. He was instructed in the use of a diet high in unsaturated fat and was told to eliminate solid fats and hydrogenated fats as much as possible from his diet and to use at least 4 tablespoons of edible corn or cottonseed oil per day. Two blood samples drawn during the next five months showed a significant

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decrease in all lipid values. No weight change occurred.

CASE II. This forty-eight year old mildly diabetic white man (R. C.) was found to have hyperlipemia at the time of a routine physical and laboratory examination. Family history revealed that his father had died of a coronary occlusion at the age of sixty-five years. This patient's initial serum lipid values are also listed in Table I. A two hour postprandial blood sugar determination was 170 mg. per 100 ml. with 1-plus glycosuria. He was instructed in the use of a diet high in unsaturated fat. During the next three months, however, his serum lipid values continued to rise on this diet therapy. On February 10, 1960, he was instructed in the use of a low fat diet which eliminated as much fat as possible from his diet. During the next two months there was a dramatic fall in his serum lipid values. No diabetic treatment was given. No weight change occurred.

CASE III. This forty-two year old white man (N. L.) was first seen in February 1959 for evaluation of hypercholesterolemia and hyperlipemia. His past history revealed that three months prior to admission he had had an episode of jaundice and hepatomegaly followed by lethargy and weight loss. This weight had been regained by the time of admission and during the following year he maintained his weight. He had also had episodes of profuse sweating during the preceding four years. He gave a history suggestive of chronic gallbladder disease with right-sided pain and intolerance to fatty and greasy foods. There was a history of some anginal type pain in the distant past but none in the recent past. His physical examination was essentially within normal limits except for a blood pressure of 150/100 mm. Hg and an enlarged liver which was felt 6 cm. below the right costal margin.

Laboratory studies performed at the time of his initial hospitalization on February 20 revealed a normal hemogram. Urinalysis showed a specific gravity of 1.037 associated with 2 to 3-plus albuminuria. Phenolsulfonphthalein excretion was 40 per cent in fifteen minutes and 75 per cent in one hour. Blood urea nitrogen was 17 mg. per 100 ml. and his serum protein electrophoresis revealed a normal protein pattern. Results of serum lipid studies made at this time are shown in Table I. The patient was considered to have a lipid defect of type III and was instructed in the use of a diet high in unsaturated fat. Nicotinic acid in the form of 4 gm. of potassium nicotinate was given daily. Lipid determinations made on May 11 revealed a slight decrease in total serum cholesterol and a rise in total lipids associated with an increase in low density lipoprotein cholesterol content. We believe that these values at this time indicated a rise in his serum triglycerides. One month later, on June 12, serum lipid studies revealed that his serum cholesterol values had returned to original levels with a continuing rise in total lipid values and very low density lipoprotein cholesterol content. This patient was not seen again for fourteen months, during which time, however, he continued to take potassium nicotinate daily and continued to adhere to his diet high in unsaturated fat. On August 24 his serum cholesterol level was elevated to 477 mg. per 100 ml. with a very large increase in total lipid values and very low density lipoprotein cholesterol content.

CASE IV. This forty-three year old white woman (V. L.) was discovered to have hyperlipemia in February 1956. Her history at that time revealed malaise and weakness. Her serum lipid values at that time are listed in Table I. She was placed on a low fat diet at that time by her physician. Lipid studies eight months later (October 3) when she was admitted to the Medical College Hospital, showed a decrease in the concentration of serum cholesterol and total lipids. Her serum was grossly milky at this time. While in the hospital she was placed on a very rigid low fat diet (less than 20 gm. daily); on her fifth hospital day after her cholesterol level had fallen to 270 mg. per 100 ml., she was started on a diet containing 80 gm. of corn oil per day in a skimmed milkshake in addition to the low fat diet. During the next eight hospital days her cholesterol level fell to 169 mg. per 100 ml. One month following discharge, during which time she utilized a diet high in unsaturated fat, she continued to maintain a low serum cholesterol level. During the next two years she voluntarily discontinued her diet high in unsaturated fat, and on October 10, 1958, her serum lipid level was markedly elevated, and ultracentrifuge fractionation revealed her lipid defect to be of the hyperlipemic variety. She was again instructed to use a diet high in unsaturated fat. During the next eight months her serum lipid levels fell to normal (Table I).

COMMENTS

It is our experience that a large majority of patients with essential hypercholesterolemia respond well to a diet high in unsaturated fat, and that those who do, respond with a decrease in serum lipids. Cholesterol determinations

TABLE I
Serum Lipid Values (mg./100 ml.)

Case No.	Date	Appearance of Serum	Total Cholesterol (mg./100 ml.)	Phospholipid (mg./100 ml.)	Total Lipid (mg./100 ml.)	Cholesterol			Treatment
						D < 1.063	D 1.063–1.006	D < 1.006	
Normal	...	Clear	160–240	160–240	600–900	50–70	100–140	10–30	...
I	2/3/60	Milky	495	592	3,456	68	80	292	Unsaturated fat*
	3/23/60	Cloudy	415	569	3,300	39	215	131	Unsaturated fat
	7/6/60	Slightly cloudy	254	355	2,100	27	104	124	Unsaturated fat
II	11/16/59	Cloudy	336	...	2,685	47	131	171	Unsaturated fat
	12/11/59	Cloudy	358	536	2,790	44	112	204	Unsaturated fat
	2/10/60	Milky	487	629	2,650	41	120	284	Unsaturated fat
	3/23/60	Cloudy	348	564	2,580	42	111	190	Low fat
	4/27/60	Cloudy	288	447	2,100	44	123	123	Low fat
III	2/20/59	Cloudy	374	...	1,980	62	177	126	Unsaturated fat
	5/11/59	Cloudy	342	...	2,148	58	143	141	Unsaturated fat
	6/12/59	Cloudy	374	...	2,820	67	142	149	Unsaturated fat
	8/24/60	Milky	477	...	4,230	22	70	344	Unsaturated fat
IV	2/10/56	...	800	...	4,000	...	...	...	Low fat
	10/3/56	Milky	514	...	2,366	...	...	...	Low fat
	10/8/56	Cloudy	270	...	1,341	...	...	...	Unsaturated fat
	10/16/56	Clear	169	...	733	...	...	...	Unsaturated fat
	11/14/56	Clear	195	...	1,033	...	...	...	...
	10/10/58	Milky	591	...	4,073	53	57	451	No diet
	6/11/59	Clear	235	...	...	76	113	39	Unsaturated fat

* Diet consisting of relative increase in unsaturated fat with concomitant decrease in saturated fat.

on ultracentrifugally separated serum lipoprotein samples, as noted in the introduction, would appear to divide patients into three distinct groups comparable to the three groups described by Brown and Page.[9] The elevated cholesterol content in the very low density lipoprotein fraction in most patients is an indication of disproportionately elevated serum total lipid levels as seen in hyperlipemia.

The data presented in this paper indicate that in certain types of hypercholesterolemia, particularly hyperlipemia with elevated triglycerides and elevated very low density lipoprotein cholesterol content, a diet high in unsaturated fat may actually aggravate the lipid defect and cause a rise in serum lipids, as shown in two patients (Cases II and III) described. Some patients (Cases I and IV), with a similar ultracentrifugally separated lipoprotein cholesterol distribution, may show a striking decrease in serum lipids while they are on a diet high in unsaturated fat. This is in agreement with Brown and Page[9] who described two patients with hyperlipemia who responded to a diet high in unsaturated fat, with a rise in their various serum lipids.

At the present time we have no explanation for this difference in response to a diet high

in unsaturated fat in patients with hyperlipemia. However, one can hypothesize that the metabolic defect in patients with essential hypercholesterolemia is such that they cannot utilize saturated fat to reduce cholesterol levels but are able to metabolize cholesterol more effectively with unsaturated fat in the diet. Our usual experience has been that patients with hyperlipemia are unable to utilize either saturated or unsaturated fat, and the effective diet therapy for these patients is usually a low fat diet. However, because of the difficulties inherent in a low fat diet due to unpalatability and restricted food choices, it would appear that a trial of a diet high in unsaturated fat is indicated in all patients with hyperlipemia, with close follow-up of the serum lipid levels to prevent an excessive rise in serum lipids before instituting a low fat regimen.

SUMMARY

Four patients with hyperlipemia are described. All had elevations of serum cholesterol with the major portion of this elevation occurring in the very low density ($D < 1.006$) lipoprotein fraction. In addition, total lipid values in all patients were disproportionately high inferring an elevation of serum triglycerides. All patients were placed on a diet high in unsaturated fat. Two of the four patients described herein had an increase in serum lipid values while adhering to this diet. These secondarily elevated levels returned to lower levels when a low fat diet was instituted. The other two patients had striking decreases in serum lipid values while on a diet high in unsaturated fat.

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