

Clinical Studies

The Effect of a Low Fat Diet on the Serum Lipids in Diabetes and Its Significance in Diabetic Retinopathy*

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NUMEROUS studies on the influence of dietary fat and cholesterol upon the different serum lipids have been published. It has become clear that a great many variables are involved and failure to take these into consideration presents many pitfalls in interpretation of the results. One must distinguish between short term effects, such as alimentary lipemia, and long-lasting effects, such as are found in the different mean serum cholesterol levels of populations with different dietary fat intakes [7]. Animal fat versus vegetable fats, the importance of unsaturated fatty acids and the relative distribution of carbohydrates and proteins are other variables [2], as are reducing diets [3] and the duration of starvation [4].

As an indicator of the serum lipid changes, the serum cholesterol has been used in the great majority of cases up to the present time [5]; more recently the serum lipoproteins have been employed for this purpose [6-8]. Neutral fat, especially in low fat diets, has received scant attention [9,10]. Excellent reviews discuss these and other problems of lipid metabolism at length [2,11,12].

It has been found that a diet low in fat results in a decrease of serum cholesterol [9-11,13,14] and possibly of certain fractions of the beta-lipoproteins [7,9]. Reduction of the dietary cholesterol alone is not very helpful [1,11]. A low fat diet gives a decrease of triglycerides in approximately 80 per cent of cases only if an ample protein intake is permitted; a rise, however, is found in 20 per cent [9]. Low protein-low fat diets result in erratic changes of serum trigly-

cerides [10]. Administration of vegetable fat instead of animal fat lowers the serum cholesterol and the phospholipids [15]; this is probably owing to the unsaturated fatty acids which are present in vegetable fats [2,16]. Triglycerides do not show a consistent change when vegetable instead of animal fat is used [2].

The caloric balance also influences serum lipids in some way: a positive balance over a long period gives an elevation of the serum lipids but a doubled caloric intake in young men on a high fat diet is possible without such elevation if the excess energy is dissipated in physical exercise [17].

As compared with the abundant literature on the influence of dietary and other factors upon serum lipids, very little attention has been given to the significance of dietary fats for diabetes mellitus and its complications. When it was recognized early in the study of the disease that a disturbance in the utilization of carbohydrates was its main characteristic, prescribed diets contained a minimum of carbohydrates; the caloric balance was formed by fats. When insulin became available a more liberal intake of carbohydrates was permitted but fats still provided a considerable percentage of the daily food intake and the average diabetic diet at present contains from 80 to 110 gm. of fat daily [18].

It is a common clinical observation that atherosclerosis is more frequent in diabetic persons than in normal persons of the same age group [19,20]. Furthermore it is known that in poorly controlled diabetes all the serum lipids

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are increased [27]. Some authors, however, maintain that the serum lipids of properly controlled diabetes in patients taking the usual amount of dietary fats are normal [22,23]. Rabinowitch [24] stated, contrariwise, that diets low in fat and high in carbohydrates tended to decrease the serum cholesterol and might also prevent atherosclerosis. His diets, although considerably lower in fat than those generally used, still contained approximately 50 gm. of fat per day. The desirability of reducing the fat intake of diabetic subjects in certain clinical states has recently been discussed by Root [25]. Only one investigator, Singh [26], has described and advocated the use of a really low fat diet, but he mentioned no studies of the serum lipids nor were the effects of this program on diabetic retinopathy observed.

There are, however, a few incidental observations on the effects of a low fat diet in diabetes. Kempner, in 1945, during his studies on the effect of the "rice diet" in hypertensive disease, also observed patients with diabetes [13]. He noticed that they could be easily transferred to his low fat rice diet without requiring increased insulin and he described two cases in detail. In one the serum cholesterol dropped from 315 mg. per cent to 230 mg. per cent and a marked improvement of the retinopathy was noted. In the other patient no data on serum lipids were mentioned but considerable improvement of the retinopathy also was found. Similar results, but without details on fundi or serum lipids, were reported in three diabetic subjects by Watkin and co-workers in their extensive study of the significance of the rice diet in hypertension [10].

Nearly all serum lipid analyses reported in the literature have been made on the serum of fasting patients. Although this gives a good base line value it might obscure important changes in serum lipids occurring during the day. The high fat intake of most diabetic subjects can be expected to cause an elevation of triglyceride fat and cholesterol in the serum, and unless these daily fluctuations are recorded an incomplete picture of the behavior of the serum lipids will result. Failure to recognize the importance of such fluctuations might account for the opinions in the literature that deny the significance of fat intake for levels of the serum lipids in patients with diabetes.

The diurnal variation of serum lipids in diabetic patients was therefore studied and the effect of the daily fat intake on these patterns

was observed over a period of six to twenty-four months. The patients were in caloric equilibrium during the observation period and their diabetes previous to the experimental diet was properly controlled so that only minimal glycosuria was permitted. The effect of lowering the fat intake on the course of the diabetic retinopathy was also observed. No chemical data are available on the composition of the retinal exudates commonly seen in diabetes but it seems possible that they contain lipids and that reduction of transported lipids in the serum might therefore affect their formation.

METHODS

All subjects had diabetes with retinopathy. Some were taking insulin; in others the disease was controlled by diet alone. (Table 1.) All had been properly controlled, with infrequent slight glycosuria and no ketonuria for prolonged periods. Serial lipid studies were carried out in most cases, before starting the low fat diet, by examining blood samples at frequent intervals during the day. The patients were then requested to ingest a diet containing less than 20 gm. of fat daily (only the fat in the lean meat that they were permitted). The diet also contained 80 gm. of protein, and caloric equilibrium was maintained with carbohydrates to minimize changes in body weight. In most instances this meant the replacement of 80 to 110 gm. of fat by carbohydrates. Serial lipid studies were obtained three, six and twelve months after conversion to this diet in most cases. All patients were conscientiously observed to make sure that they followed the diet or to detect those who did not. Three admitted not having followed the diet as prescribed: one patient was seen to consume butter, eggs and milk freely, and he was dropped from the series; another admitted having neglected her diet; in the third case a private physician obtained this information although the patient had previously denied it. Before evidence of defection had been obtained, however, a rise in the serum lipids had aroused doubts about the reliability of these patients. Some of their lipid values have been included for comparison.

Although it was realized that our diet might interfere with the normal intake and absorption of fat-soluble vitamins, no dietary supplements of any kind were given.

Complete blood counts, hematocrit, urine, renal function (serum non-protein nitrogen, phenolsulphophthalein excretion), serum electrolytes, serum proteins and liver function tests were performed at intervals during the study. Color photographs of the fundi were made of each patient before dietary treatment began and at three-month intervals thereafter. Total fatty acids were determined according to the method of Man and Gildea [27]; free cholesterol according to Sperry and Schoenheimer, as

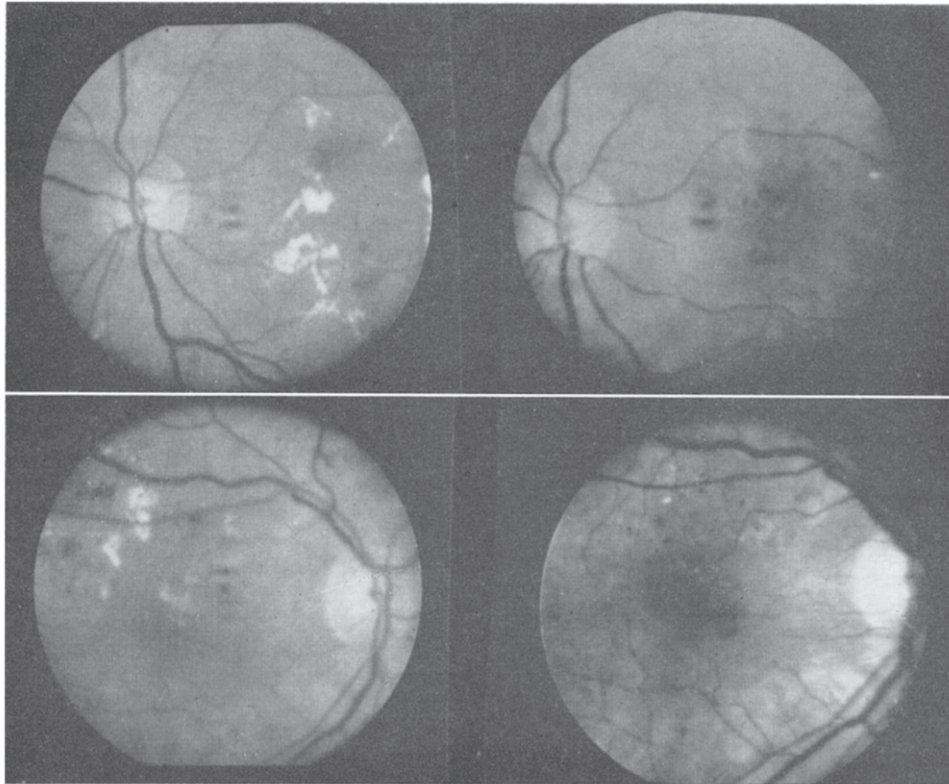


FIG. 1. Case 1. Fundi of right and left eye before institution of a low fat diet (left) and fifteen months later (right).

modified by Sobel and Mayer [28]; total cholesterol according to Sperry and Brand [29]. Phospholipids were determined as lipid P according to Fiske and Subbarow [30].

The free and total cholesterol are calculated in

milligrams per 100 ml. of serum; the fatty acids are expressed as milliequivalents per liter (normal limits, 5 to 20 mEq./L.) and the triglyceride fat is calculated as triglyceride fatty acids by subtracting the sum of cholesterol fatty acids and phospholipid fatty acids

TABLE I

DIABETIC HISTORY OF ALL CASES AND DAILY FAT INTAKE BEFORE THE EXPERIMENTAL DIET WAS STARTED

Patient and Case No.	Sex	Age at Onset of Diabetes (yr.)	No. of Years Patient was Diabetic	Minimum Number of Years of Retinopathy	Duration of Insulin Therapy (yr.)	Units of Insulin Per Day	Daily Fat Intake (gm.)
BN, I	F	34	35	?	10	50	80
BL, II	M	19	21	4	21	60	97
TR, III	F	58	4	4	0	0	80
TA, IV	F	36	20	1	2	30	100
IV, V	F	26	25	2	26	40	120
JH, VI	F	25	14	1	15	45	100
GN, VII	F	54	2	1	3	15	80
CO, VIII	F	62	2	1	0	0	100
TS, IX	F	42	13	2	1	20	75
WL, X	F	45	8	?	0	15	80
FT, XI	F	51	11	1	12	25	>100
ES, XII	M	47	3	1	0	10	>100

TABLE II
LABORATORY DATA BEFORE (1) AND AT THE END (2) OF THE LOW FAT DIET

Patient and Case No.	Low Fat Diet Started	Total Calories*	Weight (lb.)		Blood Pressure (mm. Hg)		Patency of Peripheral Arteries		Hemoglobin (gm. %)		Hematocrit (%)		Albuminuria		PSP† Excretion (%)		Serum Non-protein Nitrogen (mg. %)		Albumin Globulin (gm. %)	
			1	2	1	2	1	2	1	2	1	2	1	2	1	2	1	2	1	2
BN, I	Feb. 1954	1350	178	150	$\frac{240}{100}$	$\frac{170}{95}$	4/8	4/8	12	12.8	33	43	1+	1+	$\frac{15}{9}$..	56	70	...	$\frac{3.1}{2.7}$
BL, II	June 1954	2260	148	...	$\frac{200}{130}$	$\frac{185}{120}$	5/8	5/8	12	40	..	4+	4+	$\frac{5}{20}$..	45	..	3.2	...
TR, III	Feb. 1955	2200	180	183	$\frac{120}{70}$	$\frac{150}{80}$	6/8	6/8	12	13	40	41	0	0	$\frac{30}{35}$	$\frac{20}{10}$	59	37	$\frac{3.5}{2.7}$	$\frac{3.4}{3.1}$
TA, IV	April 1955	1800	161	153	$\frac{155}{75}$	$\frac{160}{80}$	4/8	2/8	13	11.5	34	35	1+	2+	$\frac{19}{12}$	$\frac{18}{5}$	44	39	$\frac{2.1}{2.8}$	$\frac{1.7}{2.8}$
IV, V	April 1956	2650	176	142	$\frac{130}{80}$	$\frac{125}{75}$	5/8	6/8	15	12	35	39	0	0	$\frac{22}{26}$	$\frac{28}{37}$	35	40	$\frac{3.2}{3.6}$	$\frac{2.9}{4.3}$
JH, VI	Sept. 1956	2500	112	112	$\frac{135}{90}$	$\frac{140}{85}$	7/8	7/8	14	14	..	45	0	0	$\frac{45}{30}$	7	33	22	$\frac{3.5}{3.6}$	$\frac{4.0}{3.0}$
GN, VII	Oct. 1956	1450	147	133	$\frac{160}{90}$	$\frac{170}{90}$	6/8	6/8	14	12.1	41	42	0	0	$\frac{33}{11}$	$\frac{43}{34}$	33	31	$\frac{3.0}{3.6}$	$\frac{4.0}{2.3}$
CO, VIII	Nov. 1956	2000	128	111	$\frac{200}{80}$	$\frac{250}{120}$	3/8	3/8	11	12.4	33	38	1+	0	$\frac{14}{3}$	$\frac{18}{10}$	37	42	$\frac{4.3}{2.6}$	$\frac{3.7}{3.8}$
TS, IX	Dec. 1956	1450	141	139	$\frac{120}{80}$	$\frac{125}{80}$	6/8	6/8	14	12.2	42	36	1+	0	$\frac{32}{20}$	$\frac{30}{28}$	33	36	...	$\frac{4.0}{2.1}$
WL, X	Dec. 1957	1400	138	134	$\frac{120}{90}$	$\frac{170}{100}$	6/8	6/8	15	13.4	47	42	0	0	$\frac{63}{18}$	$\frac{76}{11}$	32	35	$\frac{3.5}{4.3}$	$\frac{3.4}{4.2}$
FT, XI	Mar. 1957	1400	145	145	$\frac{150}{90}$	$\frac{195}{85}$	15	15	..	48	0	0	$\frac{45}{5}$..	29	46	$\frac{4.3}{3.4}$	$\frac{3.5}{3.0}$
ES, XII	Jan. 1957	2100	162	164	$\frac{220}{105}$	$\frac{245}{125}$	8/8	8/8	12.7	34	..	1+	1+	$\frac{34}{22}$	17	36	..	$\frac{2.7}{3.4}$...

* Total calories distributed in all cases: 80 gm. of protein, 10 to 20 gm. of fat. Balance: carbohydrates, except in Case XI (see text).
† Phenolsulfonphthalein.

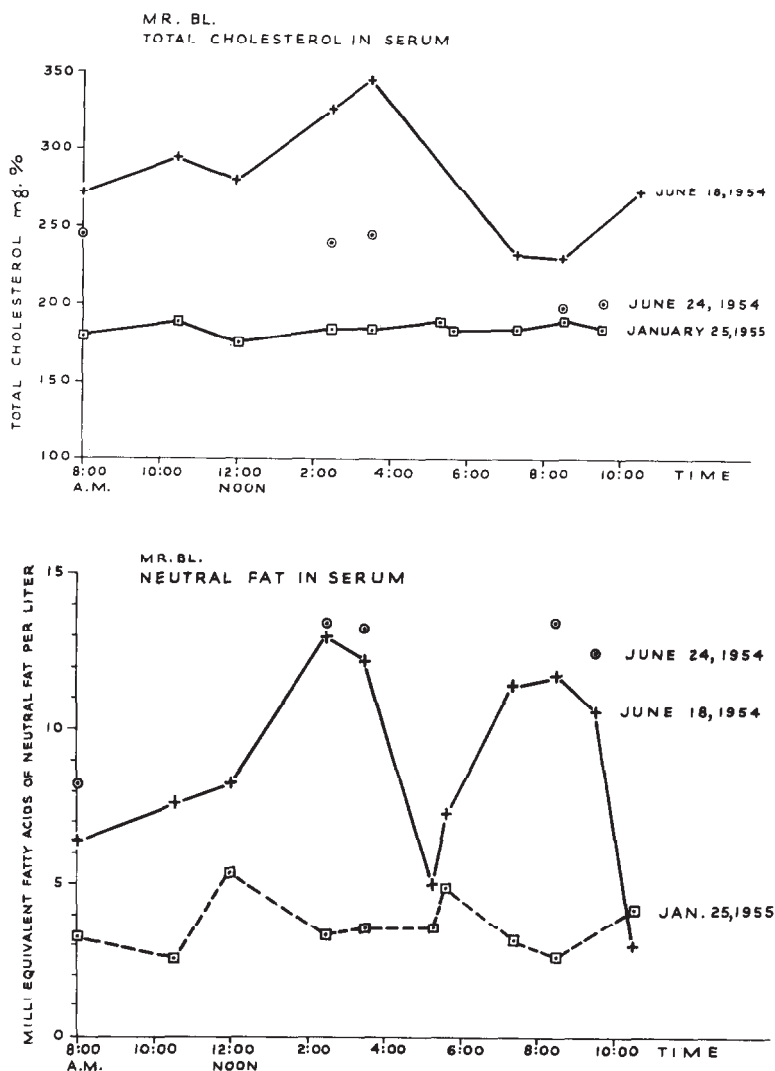


FIG. 2. Case II. Diurnal lipid curves before beginning the low fat diet and at intervals thereafter.

from total fatty acids [23] (normal limits, 3 to 10 mEq./L.).

RESULTS

Twelve patients, ten women and two men, were followed up for various periods of time between 1954 and 1957; seven of them are still under observation at the time of writing. Of the remaining five subjects, two have died, two did not care to continue the diet, and one withdrew from treatment. Of the original group eleven continued the low fat diet faithfully for periods of six months to two years.

The date of onset of diabetes as well as of

retinopathy is nearly always uncertain, because both diseases may exist for several years without subjective symptoms. Our estimates of duration are therefore only approximate. The majority of the subjects had had diabetes for more than ten years (Table 1) but there were two patients whose diabetes had been recognized for only three years who nevertheless had very marked diabetic retinopathy. All patients had previously been on the usual high fat diet. Nearly all had had 100 gm. or more of fat per day, and in the two patients who claimed a lower fat intake, it was evident on questioning that in preceding years they had eaten more fat.

TABLE III
SERUM LIPIDS OF PATIENT BNDCT.

Date	Serum Cholesterol		Serum Lipid P (mg. %)	Serum Total Fatty Acids (mEq./L.)	Serum Neutral Fat Fatty Acids (mEq./L.)
	Total (mg. %)	Free (mg. %)			
2/12/54	292	93	9.7	19	8.2
4/2/54	223	63	10.4	20	9.9
11/15/54	253	69	11.4	19	7.6
6/22/55	176	50	8.2	7.3	0
7/14/55	165	44	8.6	13	4.9
12/3/55	126	34	6.6	7.3	1.1

Four patients had hypertension. Most showed signs of peripheral arteriosclerosis but it was difficult to evaluate this precisely. In Table II we have tried to give some quantitative expressions to the degree of arteriosclerosis by determining the number of peripheral arteries of arms and legs (radial, ulnar, posterior tibial and dorsal pedal) in which a pulse could be palpated; $\frac{3}{8}$, for instance, means that three of the eight arteries mentioned were patent and five occluded. Four patients had mild anemia. Albuminuria was present in four; renal function was satisfactory in most patients but in two of them (Bl and Bndct) there was terminal elevation of the blood non-protein nitrogen. The serum proteins in most cases showed an elevated globulin with a decrease in albumin.

There was no important change in the clinical and laboratory findings of any patient during the period of observation and low fat diet with the exception of the rise in blood non-protein nitrogen in two patients. All but two maintained their body weight by exchanging the fats in their diet for carbohydrates. The replacement of 100 gr. of fat with carbohydrates was possible in all cases without raising the amount of insulin, by first withdrawing the fats and then permitting gradually increased amounts of carbohydrates. This surprising increase in glucose tolerance was also seen in the two patients who were not taking insulin and who therefore consumed up to 400 gr. of carbohydrates without requiring any. The effects of the diet on the serum lipids and the retinal changes observed will be described in detail for each patient.

CASE REPORTS

CASE I. Mrs. Bndct., a sixty-nine year old woman who had had diabetes for thirty-five years, had severe retinopathy with large exudates. At the beginning of AUGUST, 1959

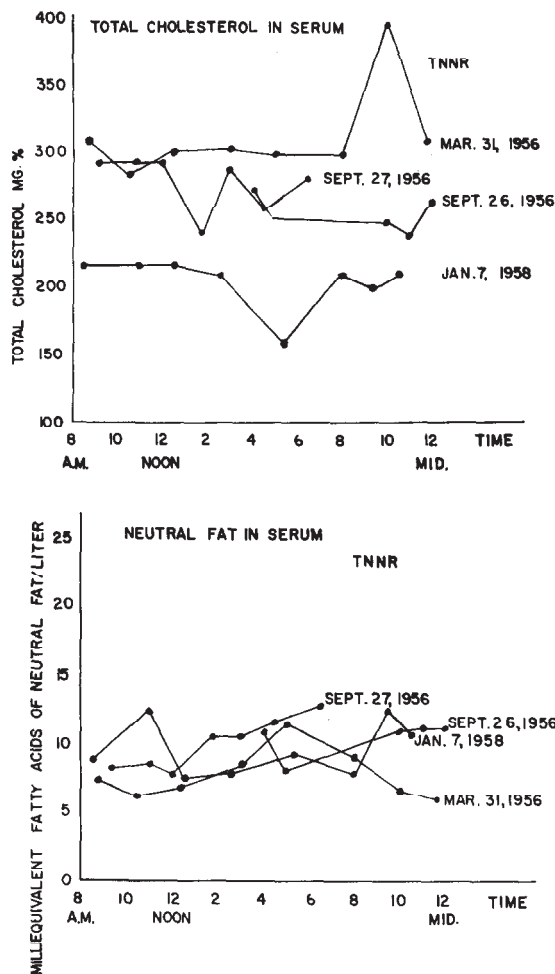


FIG. 3. Case III. Diurnal lipid curves before beginning the low fat diet and at intervals thereafter.

the clinical observation (Table III) her serum total cholesterol was 292 mg. per cent and the triglycerides 8.2 mEq./L. She started the low fat diet in February 1954 and during the next two years her serum lipids slowly decreased. Serial lipid studies during twenty-four-hour periods were unobtainable and her lipids represented fasting specimens. There can, however, be no doubt about the marked drop in serum lipids during the time of observation. The very low values obtained in December 1955 may be due to semi-starvation in her final months of life. She died of cardiac failure shortly thereafter. Photographs of the fundi showed a great reduction in the size of the exudates. Two years later the fundi were nearly clear. (Fig. 1.) This disappearance of the exudates occurred very slowly, the first changes becoming visible only after three to six months of dieting.

CASE II. Mr. Bl., forty-two years old, was totally blind, with irreparable changes in both eyes when he

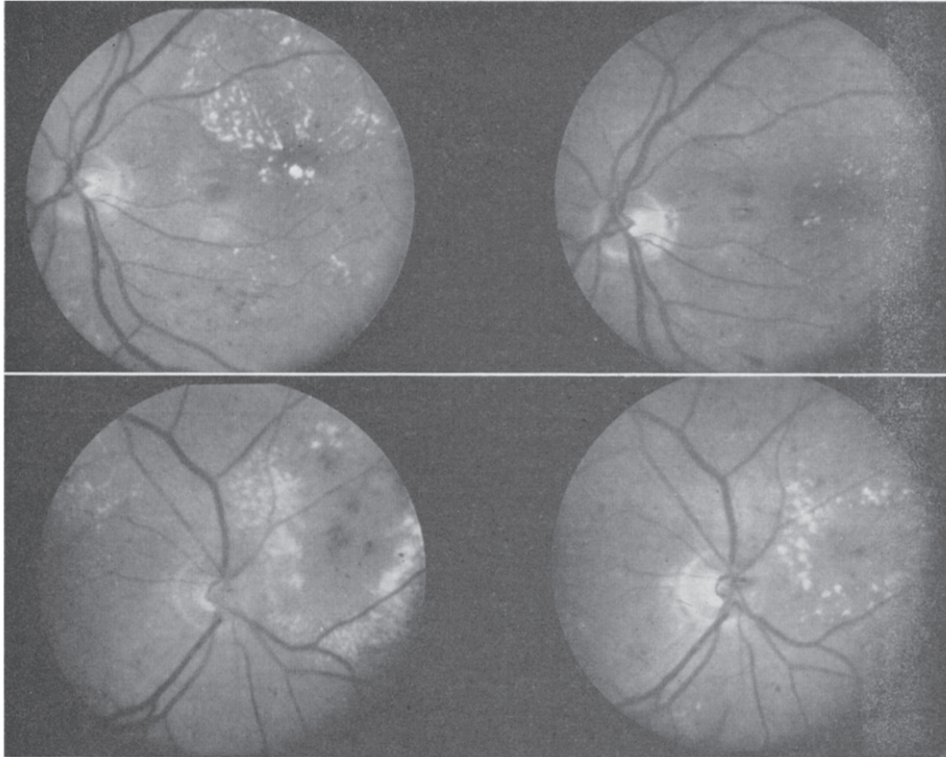


FIG. 4. Case III. Fundi of right and left eye before institution of a low fat diet (left) and five months later (right).

was first seen. His diabetes had always been carefully controlled. However severe retinopathy and Kimmelstiel-Wilson syndrome developed. He had marked peripheral arteriosclerosis, hypertension and reduced renal function. (Table II.) A low fat diet was instituted on June 19, 1954. Serial lipid studies during the day were made before this diet, one week after starting the diet, and seven months later. The values for serum total cholesterol and triglycerides are presented in Figure 2. Of special interest are the marked fluctuations in both triglyceride fat and cholesterol during the day. Note that after the patient had been on the low fat diet for one week the serum cholesterol and triglycerides were still clearly elevated, the last fraction showing high values at the same time of day as before. However, half a year later a considerable drop of the serum lipids was found and the values throughout the day plot out as a nearly horizontal line. Because the patient lived out of the state only incidental follow-up studies could be made, which showed little change. He died a year and a half later from cerebral hemorrhage.

CASE III. Mrs. Tnnr., sixty-two years old, had marked diabetic retinopathy with large exudates in both fundi. She did not use insulin with her regular diet or while on the low fat diet. Her serum lipids were only mildly elevated. During the first period of

observation they were drawn once a month at 1:00 P.M. A slight drop was observed during that period, from an average of 250 mg. of total cholesterol to 220 mg. and 14 mEq./L. of triglycerides to 7 mEq./L. After one year the patient was given a high fat diet (more than 100 gr. of fat daily) which was continued from February to September 1956. After that the patient resumed the low fat diet (less than 20 gr. daily) A slight drop in serum cholesterol occurred promptly and four months later the serum total cholesterol had dropped from a fluctuating 300 to 400 mg. per cent to a level of 200 mg. per cent. Little change had occurred in the neutral fat fraction of this patient. (Fig. 3.) The eyegrounds showed remarkable changes. During the first year of the low fat diet the large exudates almost completely disappeared. (Fig. 4.) Following reinstitution of the high fat diet new exudates developed, although after a considerable time lapse. They subsequently disappeared again when the fats were withdrawn.

CASE IV. Mrs. Tnna., fifty-six years old, had had diabetes for twenty years. Minimal retinopathy, consisting of small groups of tiny exudates, had been discovered recently. She also had a mild form of Kimmelstiel-Wilson syndrome. (Table II.) Her fasting lipids were elevated, the serum total cholesterol at one time being above 500 mg. per cent. Two months after

she started the low fat diet, a marked drop of the serum lipids was obtained. The patient then began eating fats again and the serum cholesterol rose to previous high values, to drop again under closer supervision. Concomitantly her serum triglycerides decreased somewhat. The values are of limited significance because the patient admitted to frequent lapses in her diet and refused to stay on any diet after a trial period of eight months. Thereafter her serum cholesterol again rose to high values (500 mg. per cent). A decrease in the number and size of the exudates was observed during the period of the low fat diet. One year later numerous large exudates had formed. This coincided with poor control of her diabetes and chronic heart failure.

CASE V. Mrs. Ivs., fifty-one years old, had had diabetes for twenty-five years and retinopathy for two years. Vascular abnormalities were preponderant in both eyegrounds, but she also had some exudates. No indication of Kimmelstiel-Wilson syndrome was apparent. After beginning her low fat diet the serum cholesterol dropped approximately 25 per cent and remained at the lower level for a year and a half. The serum triglyceride fat fraction, which was not elevated to begin with, remained unchanged. Serial lipid studies during the day at the beginning and end of this experimental period are shown in Figure 5. Photographs of the fundi showed disappearance of all small exudates of the left eye in eight months; the changes in the right eye during the last half year could be seen. The circle of minute exudates around the macula developed while the patient was on the low fat diet, probably after a hemorrhage, and disappeared subsequently. (Fig. 6.) In this patient the vascular disease of both eyes continued unabated for two years and she had several hemorrhages resulting in proliferative retinitis and decrease of eyesight. The discrepancy between vascular abnormalities and the development of exudates has been noticed to a lesser degree in other patients.

CASE VI. Miss Jhns., a thirty-eight year old woman had had diabetes for fourteen years, and a mild retinopathy for one year. Her serum cholesterol fractions were markedly elevated (total cholesterol 300 to 350 mg. per cent) but her triglyceride fat was normal. Following institution of the low fat diet the serum total cholesterol dropped to 200 mg. per cent or below, as illustrated in two daily curves with an eight-month interval. (Fig. 7.) These low values have been maintained for two years. The diabetic retinopathy cleared. In the course of the first year all exudates disappeared; some microhemorrhages recurred but were absorbed without apparent damage.

CASE VII. Mrs. Gddy., fifty-six years old, had had diabetes for two years with marked retinopathy including numerous large exudates. In the

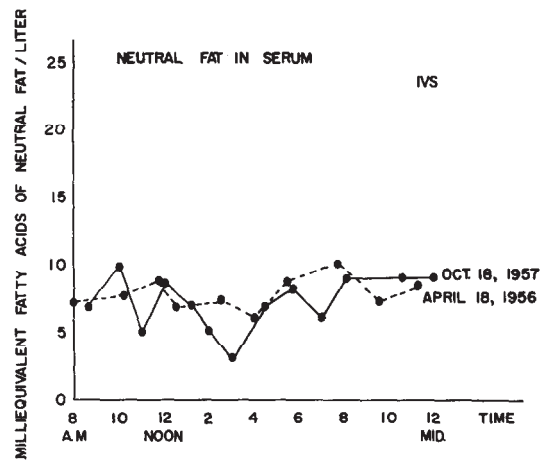
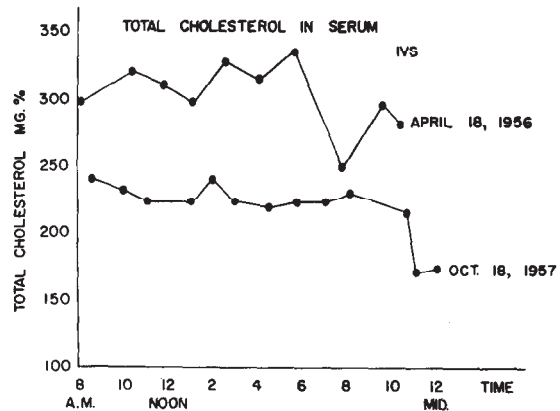


FIG. 5. Case v. Diurnal lipid curves before beginning the low fat diet and six months thereafter.

right fundus, halfway between the papilla and macula, an especially large mass of exudate was present, quite prominent above the level of the retina and apparently protruding into the vitreous body. Following institution of the low fat diet the behavior of her serum lipids was especially interesting when compared with the previous case. The serum triglyceride fraction showed the largest drop, although a decrease in serum total cholesterol also was observed. (Fig. 8.) At the same time a marked decrease in the size and number of exudates all through the fundus was noticed and even the previously described mass diminished slowly in size.

CASE VIII. Mrs. Cork, sixty-four years old, had had diabetes for two years and extensive retinopathy with a multitude of small exudates and many small retinal hemorrhages in both fundi. The serum lipids were markedly elevated. Both serum cholesterol fractions and the triglyceride fat dropped to normal levels following institution of the low fat diet. (Fig. 9.) The eyegrounds returned to normal in the course of one

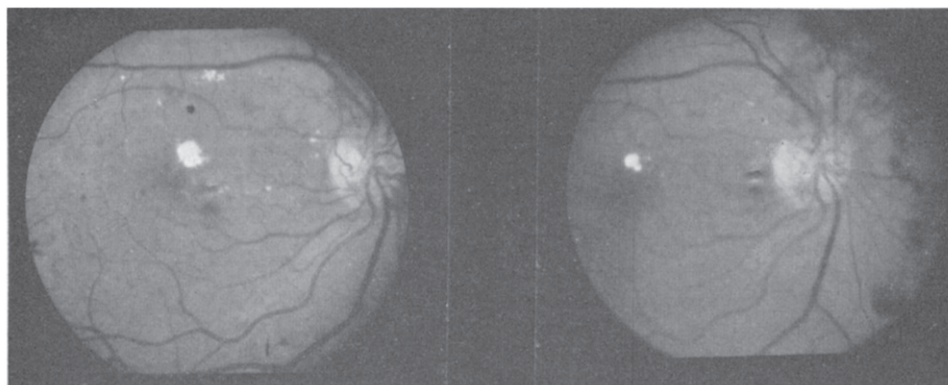


FIG. 6. Case v. Fundus of right eye before institution of a low fat diet (left) and eight months later (right).

year. (Fig. 10.) During the last months of this year her fat intake increased and the serum lipids rose. After resuming the strict low fat diet a rapid drop in serum lipids occurred.

CASE IX. Mrs. Tschl., a fifty-five year old woman who had had diabetes for thirteen years, showed mild retinopathy. Her serum cholesterol was elevated, approximately 300 mg. per cent. During the year that she followed the low fat diet this decreased to

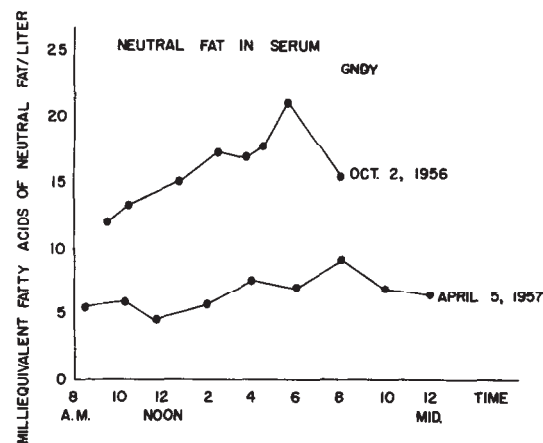
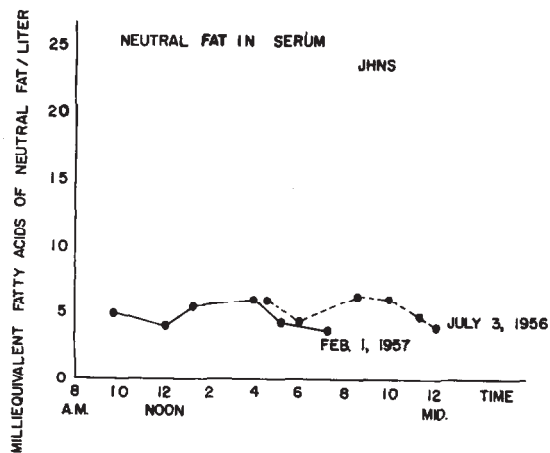
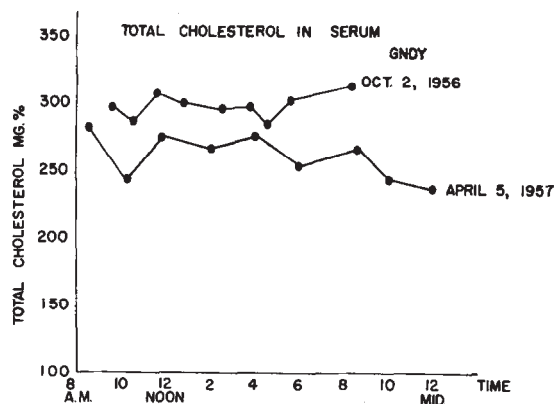
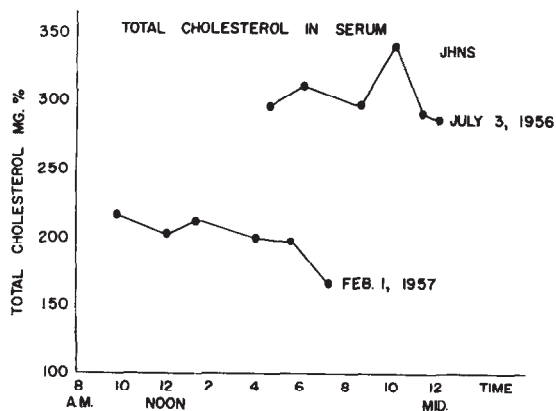


FIG. 7. Case vi. Diurnal lipid curves before beginning the low fat diet and seven months later.

FIG. 8. Case vii. Diurnal lipid curves before beginning the low fat diet and six months thereafter.

almost 200 mg. per cent. The triglyceride fat, if anything, increased slightly but remained below 10 mEq./L. The exudates in the right eye decreased during the first seven months. The left eye had a small retinal hemorrhage in December 1956 when she began the low fat diet. Three months later the hemorrhage had disappeared but in its place was a deposit of white material which subsequently disappeared during the next four months. (Fig. 11.)

CASE X. Mrs. Wills., a fifty-three year old woman who had had diabetes for eight years, presented a very mild retinopathy. Her serum lipids were within the normal range, the total cholesterol fluctuating throughout the day at approximately 250 mg. per cent. After starting the low fat diet her serum total cholesterol dropped to below 200 mg. per cent which was maintained for more than a year. A group of exudates in both eyes disappeared but in the right eye a circle of tiny new exudates appeared, perhaps in the wake of a hemorrhage. Similar new exudates in the left eye seemed to be related to previously observed hemorrhages. The larger exudates in the left fundus almost completely disappeared.

CASE XI. Miss Fte., sixty-two years old, had had diabetes for eleven years and retinopathy for at least one year. Her serum total cholesterol was elevated, around 300 mg. per cent, and the triglyceride fat varied from 5 to 11 mEq./L. In the first two months of diet there was a slight fall in the serum cholesterol but a serial curve five months later again showed high values, above 300 mg. per cent. There was no improvement of the retinopathy. Miss Fte. finally acknowledged that she did not follow the low fat diet at all after the first few months and this failure is reported because it stresses the difficulty of being certain whether a patient follows a difficult diet without close supervision. Her case is also reported as a control study to show the persistence of the lipid pattern in a patient who remains on the usual fat intake.

CASE XII. In Mr. Esp., a fifty year old man who had had diabetes for three years with extensive retinopathy, the Kimmelstiel-Wilson syndrome also developed with marked hypertension. (Table II.) The patient was admitted with an acute appendicitis with complications, and the base line values for his serum lipids were therefore obtained after he had already followed a low fat diet for two months. His serum total cholesterol was 298 mg. per cent and triglycerides 10 mEq./L. Subsequent serum analyses one and five months later showed a serum total cholesterol of 247 and 243 mg. per cent and triglycerides of 4.9 and 3.6 mEq./L., respectively. The patient refused further blood studies and only one set of repeat photographs of the fundus could be obtained, approximately six months after he started the low fat diet. (Fig. 12.) A marked reduction of the exudates was noticeable.

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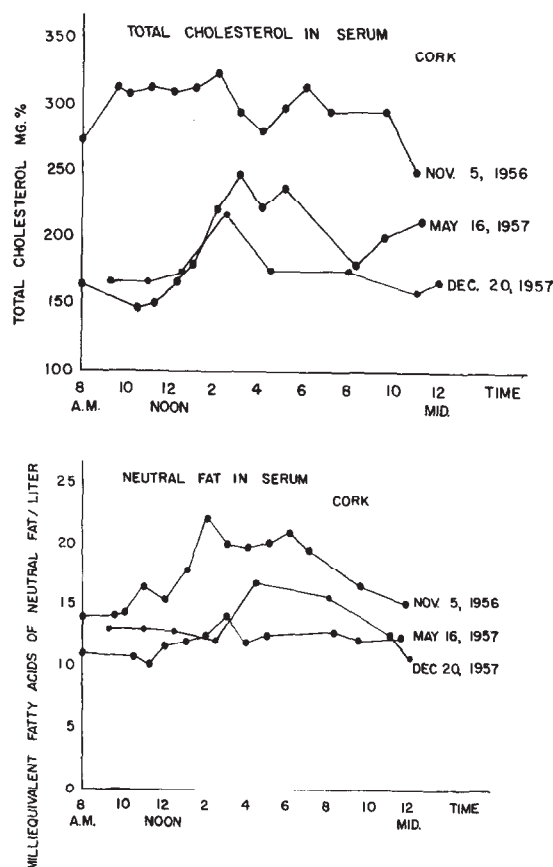


FIG. 9. Case VIII. Diurnal lipid curves before beginning the low fat diet and at intervals thereafter.

COMMENTS

Many authors in the past have observed that an increase in the ingestion of carbohydrates was followed by increased carbohydrate utilization [37] which continued even after insulin therapy was withdrawn [32]. In the presence of a high carbohydrate intake a change in the fat content of the diet did not appear to affect carbohydrate tolerance [32,33]; however in all these studies the minimum fat intake was apparently more than 40 gm. per day.

Our results are in close agreement with the incidental findings of Kempner's rice diet-hypertension studies [13], later corroborated by Watkin and colleagues [10]. Their diet was different from ours in that we permitted at least 80 gm. of protein while the rice diet had 20 to 30 gm. of protein and was also very low in salt. Since both high protein-low fat and low protein-low fat diets as well as our low fat-high carbohydrate-average protein diet have resulted in unchanged

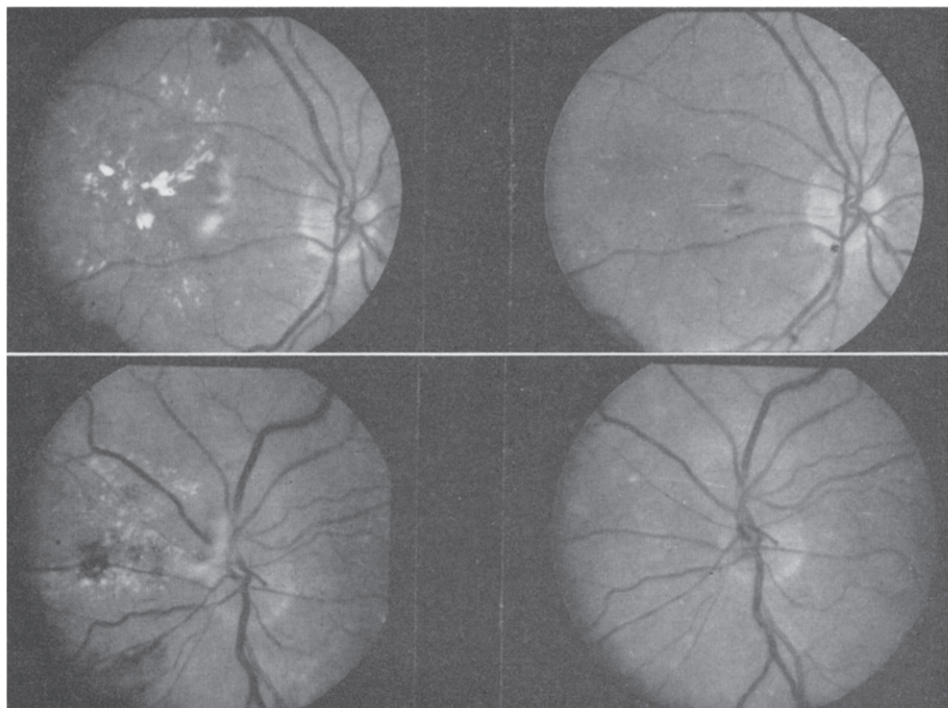


FIG. 10. Case IX. Fundi of right and left eye before institution of a low fat diet (left) and one year later (right).

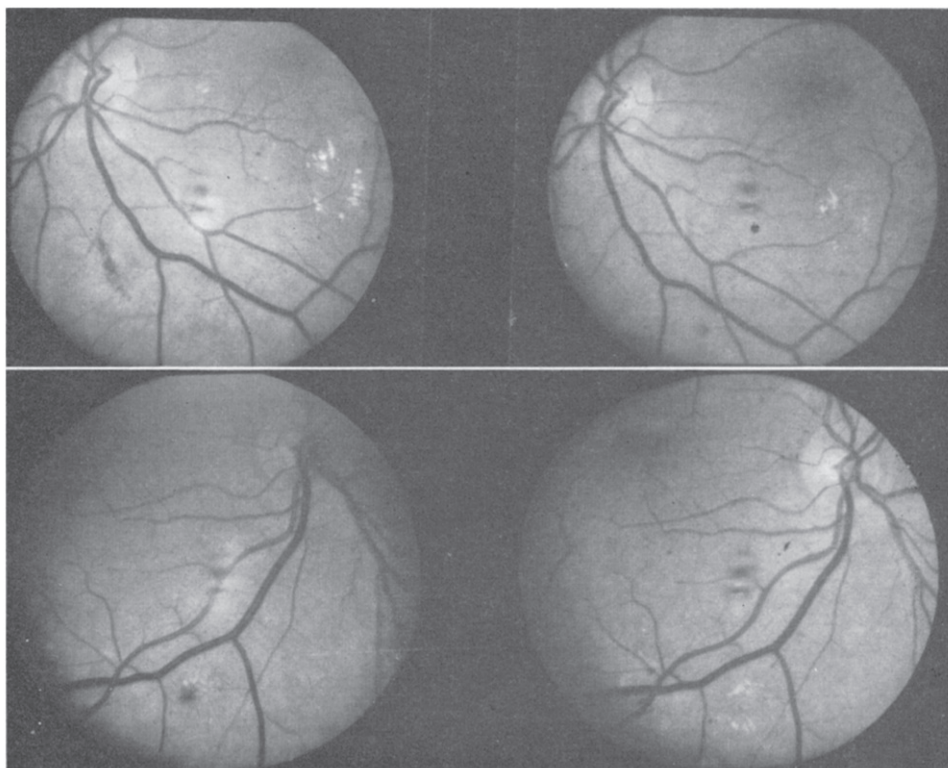


FIG. 11. Case IX. Fundi of right and left eye before institution of a low fat diet (left) and eight months later (right). Note the disappearance of the small hemorrhage and the residual exudate in the lower pair of photographs.

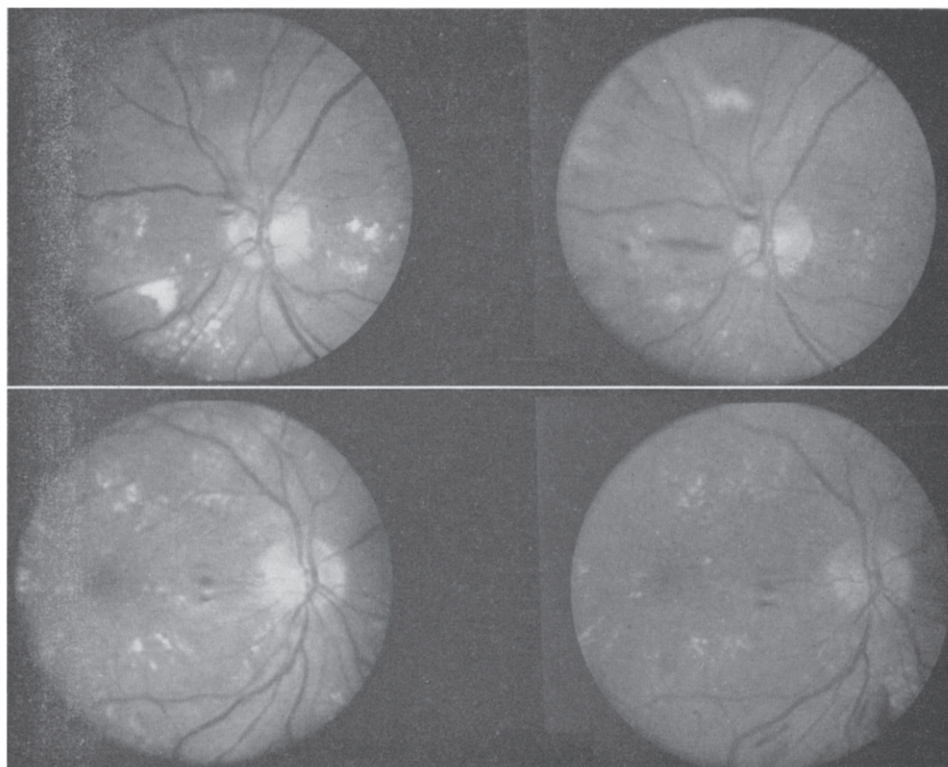


FIG. 12. Case xii. Fundi of right and left eye before institution of a low fat diet (left) and six months later (right).

or even decreased insulin requirements, it follows that either the reduction of fats or the increased amount of carbohydrates in the diet was responsible for the increased glucose tolerance in these diabetic patients.

All our subjects tolerated an increase of at least 135 gm. of carbohydrates without increasing the amount of insulin, and the same change in diet could be obtained in patients who did not require insulin. The mechanism of this phenomenon is not clear, but one can speculate that the low fat-high carbohydrate diet diminishes the fat deposits in the liver and improves glucose oxidation.

Due to limitations of space, it is not possible to report the hundreds of analyses made to show the variations of serum lipids in our patients on low fat diets. In lieu of these the graphs illustrating diurnal changes in serum total cholesterol and triglyceride fat, before and during the low fat diet, may give a sufficient idea of the variations observed.

The serum free cholesterol and cholesterol ester fractions changed more or less proportionally although the cholesterol esters comprised a slightly lower percentage of the total chole-

sterol than has been reported for normal persons. An illustration of the parallel changes of total and esterified cholesterol is given in Figure 13.

In order to summarize the percentage change during the low fat diet, averages of monthly lipid analyses of all patients, expressed as percentages of the base line values for serum total cholesterol, were compiled. (Fig. 14.) Those patients who initially had little elevation in serum total cholesterol reduced the percentage of reduction in total serum cholesterol disproportionately. Nevertheless an average drop of about 20 per cent is obtained and persists throughout the period of observation. This composite graph refers only to single monthly analyses, in contrast to the diurnal graphs. Furthermore the pretreatment value of each patient was compared with the value obtained after three months of treatment and the decrease in each case is represented in Figure 15. For convenience the cases have been arranged in order of their pretreatment levels of serum total cholesterol.

One patient, after having followed the low fat diet faithfully for several months, was found to have increased her dietary fat intake. Reinstitu-

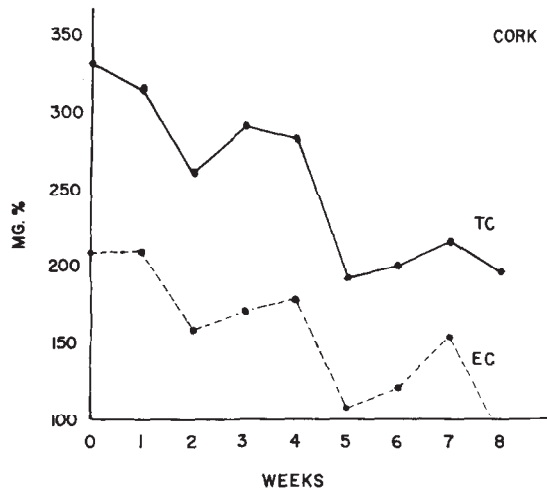


FIG. 13. Case VIII. Weekly fall in serum cholesterol. Weekly analyses demonstrate the effect of the low fat diet on the serum cholesterol of this patient. Note the parallel changes of serum total and esterified cholesterol.

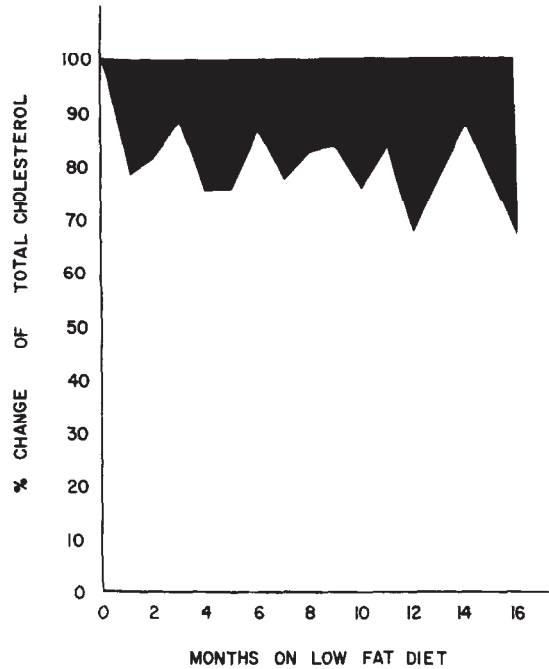


FIG. 14. Percentage fall in serum cholesterol of all cases combined. This curve represents the average monthly fall in serum cholesterol in all cases, expressed as percentage of the pretreatment level.

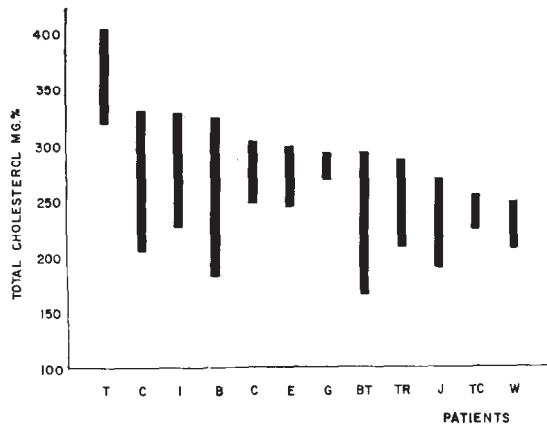


FIG. 15. Fall in serum cholesterol in each case. Each bar represents the fall in serum cholesterol during the first three months of the low fat diet in each case. Case C (Cork) is represented twice (see text).

tion of the strict diet was promptly followed by a renewed drop of her serum lipids; the changes obtained by weekly analyses are illustrated for total and esterified cholesterol in Figure 13. The importance of including diurnal series of lipid analyses in these cases has already been stressed and reported results have clearly supported this view, even if not all patients showed well defined alimentary peaks; this may be due to overlapping absorption from the different meals while the patients were on a high fat diet. From the graphs and other data we can conclude that diabetic patients who have either elevated serum cholesterol or triglyceride fractions, when trans-

ferred to a low fat diet, will show a reduction of whatever lipid fraction was elevated.

In all patients who adhered to the low fat diet the reduced serum lipid levels were maintained for the duration of the observation; in some cases more than two years. When no drop in serum lipids occurred or a subsequent rise was observed, it could be established that the patient had not adhered to the diet.

There is evidence of some correlation between triglycerides and glycemia. In non-diabetic healthy persons, Albrink [34] has demonstrated that the hyperlipemia which followed ingestion of 60 gm. of fat could be prevented by ingestion of 100 to 250 gm. of carbohydrates. For diabetic subjects this correlation has been described by Hirsch [35]. In our diabetic patients we found no evidence that glycemia, under the conditions of the diet, influenced the serum lipids (Fig. 16); considerable fluctuation of the blood sugar during the day occurred with a flat lipid curve. One patient (Tnna.) repeatedly had varying blood sugars with persistently high serum lipids. A low fat diet could still give a considerable rise in triglycerides of the serum if all the ingested lipids remained in circulation for a few hours. A difference in triglycerides of, say, 15 mEq./L. cor-

responds to only 12.8 gm. of triglyceride fat in 3 L. of serum. Apparently rapid deposition of fat occurs. Similarly, a low fat diet cannot affect the level of serum lipids merely through the lesser absorption of fat. This is obvious from the time required to reduce the serum lipids, which in our patients was several weeks. It seems therefore that the amount of ingested and absorbed fat itself plays a part in regulating the maintenance of serum lipid levels.

The laboratory tests of our patients before and during the dietary period showed little change. (Table II.) The results of the liver function tests have not been included in this table since they remained entirely normal. We have no reason to suspect, therefore, that our diet caused any liver damage during the period of observation.

While the diabetic patients were ingesting the low fat diet, changes in their retinae were observed which have been documented by black and white reproductions of Kodachromes. Diabetic retinopathy has two major components: vascular abnormalities (microaneurysms and hemorrhages) and the so-called exudates. Whatever their composition, these exudates are obviously due to passage of material from the small vessels. We have photographic evidence that they can develop in the wake of a hemorrhage (Fig. 11) but hemorrhages can disappear without leaving white exudates and they may form without a preceding hemorrhage; also, they do not all look alike and they may have a variable genesis and composition. Their natural history is not sufficiently known; small ones may come and go, but the disappearance of large ones that have developed in properly controlled diabetic patients is rare. Careful observation of the changes of these exudates in patients with diabetes, without specific treatment, is necessary for a better evaluation of our results.

With these reservations in mind we observed in eight of our ten patients, who had retinopathy with exudates, that regression of the exudates occurred. In two patients large exudates, up to several times the diameter of the optic disc, disappeared (Bndct., Tnnr.); in three patients agglomeration of many small exudates disappeared or decreased considerably in size and number (Cork, Gndy., Esp); in three who had few exudates to start with, the changes were more discrete but still clearly evident. In two patients the regression was not convincing, mostly because of the formation of tiny new exudates while the patient was on the low fat diet

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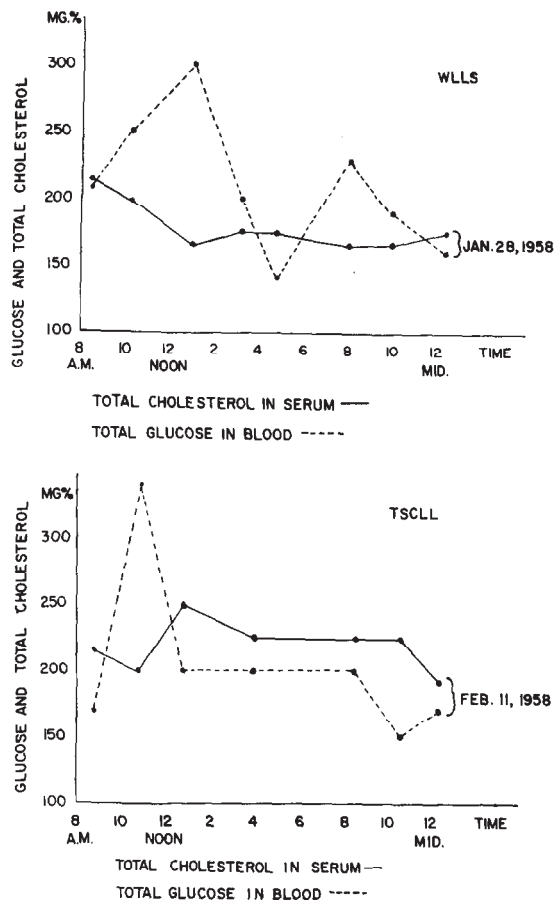


FIG. 16. Case IX (Tscll.) and X (Wlls.). Diurnal glucose and cholesterol curves. In both cases lack of correlation between diurnal values of glucose and cholesterol is seen.

(Tscll., Wlls.). Together with disappearance or reduction of the exudates, improvement of the retinal angiopathy was observed in one patient; this, however, was the exception and in most cases the vascular disease continued to manifest itself by microaneurysms and hemorrhages. While we do not postulate any immediate or indirect effects of the low fat diet on diabetic retinopathy we should like to draw attention to such a possibility.

On the basis of the information so far obtained, it seems justifiable to consider a strict low fat diet for diabetic patients who have elevated serum lipids and distinct retinopathy.

SUMMARY AND CONCLUSIONS

1. The effect of a diet containing only 20 gm. of fat per day was studied in a group of twelve patients with diabetes with retinopathy and elevated serum lipids.

2. We observed a striking increase in the glucose tolerance of these patients, which made it possible to increase the carbohydrates to at least 135 gm. per day, without increase of the insulin requirement. Patients who were controlled by diet alone did not require insulin after the transition to the low fat diet.

3. Of the eleven patients who followed this diet, lowering of the serum lipids was obtained in ten. This effect was maintained during the entire observation period of one to two years.

4. Of the ten patients who presented exudates in their fundi, marked decrease or disappearance was noticed in five; discrete but convincing reduction in three others. In two patients, whose exudates were minimal to start with, the changes were less convincing. In no patient who followed the low fat diet did new large exudates develop during the observation period.

5. Although no immediate or indirect relationship has been proved to exist between the observed lowering of the serum lipids and the disappearance of retinal exudates, such a relationship is suggested for further study.

6. It seems justifiable to consider a strict low fat diet in diabetic patients who present elevated serum lipids and distinct retinopathy.

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