OBSERVATIONS ON THE SIGNIFICANCE OF THE CHOLESTEROL CONTENT OF THE BLOOD PLASMA IN DIABETES MELLITUS*

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IN 1929 the writer[1] reported the results of a statistical investigation of the cholesterol content of the blood plasma in diabetes mellitus. The conclusions drawn were based upon a study of 2,000 observations in 385 cases. Plasma cholesterol was found to afford a reliable index of progress, and its determination was, therefore, regarded as a valuable aid in the management of this disease. Blood and urine sugar data, when used alone, had their limitations. In some cases, on discharge of the patient from the hospital, the diabetes appeared to be under ideal control, in that the blood sugars were normal and the urines were free of sugar with diets compatible with the individual's requirements; the blood plasma, however, contained excess quantities of cholesterol. These patients, as a group, when observed periodically for sometime, did not appear to do as well as those whose bloods contained normal quantities of cholesterol. The incidence of complications (infections, acidosis, neuritis, etc.) appeared to be relatively high and dietary indiscretions or complications resulted in hyperglycæmia not readily controllable with diet or insulin. Amongst those whose bloods contained normal quantities of cholesterol, but at a later date showed excess quantities, there appeared to be a relationship between the degree of control of the diabetes and the cholesterol content of the blood. It was then pointed out that, as with laboratory tests in general, in the interpretation of data, due consideration must be given to other conditions which might also lead to similar results; excess quantities of cholesterol may be found in clinical conditions other than diabetes (jaundice, cholecystitis, pregnancy, nephrosis, etc.). A similar study made in juvenile diabetes[2] led to similar conclusions, and, again, a relationship was found between the concentration of cholesterol in the plasma and the degree of control of the disease. The data fitted with the observation[3] that "increasing tolerance indicating a more or less constantly normal blood sugar usually results in maintenance of the blood fat at the normal level. . . ."

It must be here observed that the conclusions were statistical. They, therefore, may, or may not, and need not necessarily, apply to a given individual. Determination of plasma cholesterol has, however, since been a routine in every case of diabetes in this clinic and many thousands of data have accumulated, and, with additional experiences, there appears to be no reason for modifying the views expressed originally in the above mentioned reports. In the writer's opinion, a normal cholesterol content indicates that the fundamental disturbance of the metabolism of the diabetic is under control. Of course, control and severity are obviously not synonomous terms; severe diabetics are not infrequently seen with normal blood cholesterols; nor does a normal cholesterol imply that a mild diabetic may not meet with complications. It does, however, appear to indicate that, in spite of severity, the disease is under control and the individual is less susceptible to these complications; and as prognosis depends largely upon the latter, a normal cholesterol content indicates a favourable prognosis.

Judging from the literature, Joslin's clinic in Boston is the only other clinic for diabetes in which intensive cholesterol studies similar to our own are made as a routine. Practically simultaneously with our own publication, Hazel Hunt[4] reported the experiences of that clinic. Though the value accepted by Joslin for the upper limit of normality (0.230 per cent) is higher than our own (0.180 per cent) the conclusions drawn were somewhat similar; cholesterol appeared to be a more consistent guide to the real condition of the patient than the blood sugar; and absence of relationship was found between the severity of the diabetes and cholesterol, providing the disease was properly controlled.

Our experiences have also taught us that a person who develops acidosis and coma is

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not necessarily a *permanently severe* diabetic. A mild diabetic may, in spite of normal cholesterol, suddenly lose carbohydrate tolerance, because of an infection, develop acidosis and coma; but with a normal cholesterol, if the infection does not interfere with the action of insulin, that is, if the patient recovers from the coma, the diabetes will probably still be mild. A case met with recently in our clinic may be cited as an example.[5] This man (Hosp. No. 4661/31) was admitted to the hospital with severe acidosis and in early stages of coma. The coma was, apparently, precipitated by infection (cystitis). With insulin he recovered rapidly, was subsequently exposed to a prostatectomy, and discharged from the hospital on a diet compatible with his requirements without the use of insulin. He is still able to do without it; the blood sugars remain normal and the urines are free of sugar. Conversely, with an excess of plasma cholesterol, the diabetic, on recovery from coma, will probably be more severe; the patient will require more insulin and the tendency towards complications will be greater.

HYPERCHOLESTEROLÆMIA AND CAROTINÆMIA

For some as yet unknown reason diabetics tend to retain vegetable pigments more than non-diabetics and this accounts for the high incidence of carotinæmia in this disease. The condition known as *xanthosis diabetica* affords an example of the possible degree of retention of these pigments. The condition is not due entirely to the high vegetable content of the average diabetic diet. For example, of 59 patients with xanthosis diabetica reported by the writer,[6] 13 had never been on special diets prior to detection of this skin condition. Connor[7] also observed that the bloods of many diabetics contained larger quantities of carotin than the normal individual, though they were on practically normal diets. Diabetics with carotinæmia, as those with hypercholesterolæmia, do not appear to do well; large insulin dosage is common and the incidence of arteriosclerosis is high. Thus, of the above mentioned 59 patients with xanthosis, 44—an incidence of approximately 75 per cent—required insulin and 36—an incidence of about 61 per cent—had some evidence of arteriosclerosis; whereas, in the clinic, as a whole, only about 18 per cent were taking insulin and about 22 per cent had arteriosclerosis. The average duration of diabetes amongst the arteriosclerotics with xanthosis was about three years; whereas, amongst the arteriosclerotics in the clinic as a whole it was about five years.

In a statistical study, the writer found a relationship between carotinæmia and hypercholesterolæmia.[8] Such a relationship might, *a priori*, be expected, since plants contain substances (sterols) very closely allied chemically to cholesterol. That this, however, is not the only explanation is suggested from the finding of individuals with marked carotinæmia and no excess of plasma cholesterol and, conversely, individuals with marked hypercholesterolæmia and no undue carotinæmia.

The purpose of referring to the experiences with carotin and cholesterol was to suggest a relationship between these blood constituents and arteriosclerosis. Various explanations have been offered for the high incidence of cardiovascular disease in diabetes, but none has as yet stood the text of experiment. Hypercholesterolæmia has long been suspected, but the mechanism involved still requires elucidation. The writer made a suggestion based upon a study of the colloidal osmotic pressure of the blood in diabetes.[9] Though there was little direct evidence, the sum of all data (clinical and laboratory) then available tended to support the view that, in diabetics with hypercholesterolæmia a colloidal pressure greater than normal is constantly exerted in the capillaries. To overcome the latter, for purposes of renal excretion, a greater hydrostatic pressure is required; this increased pressure, though relatively small, when continued over a long period of time might have the same effect as more marked intracapillary pressure exerted over a short period of time. In animals, the latter, when produced either by injection of epinephrine or by sympathetic stimulation, is alleged to cause arteriosclerosis.

VITAMINES AND ARTERIOSCLEROSIS

An explanation of the high incidence of cardiovascular disease in diabetes may possibly be found in the newer experiences with vitamines, according to the following observations.

Firstly, sterols are practically universally distributed throughout biological media and, though little is known of their functions, some

definite information has been obtained with respect to one of them, namely, ergosterol. The latter is capable of absorbing ultra-violet light rays, and following exposure to these rays is so altered chemically and physically that it acquires physiological and pathological properties; in small doses it may prevent or cure rickets, but, when administered in excessive doses, it readily increases the calcium content of the blood and leads to hypercalcification of the skeletal and other body tissues.

Secondly, there is a very intimate association between cholesterol, sterols in general, and ergosterol; they are almost invariably found together. It, therefore, appears reasonable to assume that blood which contains excess quantities of cholesterol or carotin also contains excess quantities of ergosterol.

Thirdly, in the human being, the epidermal portion of the skin normally contains large amounts of cholesterol and a portion of the skin at least is normally exposed to ultra-violet light. This, as a matter of fact, is supposed to account to some extent for the protection against rickets. Both solar rays and artificial radiation are capable of producing the antirachitic factor. There is still some doubt as to whether all sterols, or certain forms only, possess this antirachitic property. For the present purpose, however, this is irrelevant, since, as stated above, wherever one finds cholesterol one may reasonably assume that ergosterol is also present.

Lastly, there is abundant evidence that the skin of the diabetic is relatively rich in sterols. In addition to chemical evidence (hypercholesterolæmia and carotinæmia), there is clinical evidence, namely, the pigmentations. Diabetic skin must, therefore, also be rich in ergosterol.

Combining these observations, therefore, it appears reasonable that the tissues of the diabetic, because of exposure of the skin to sunlight, are being bombarded continually with irradiated ergosterol and thus are exposed to hypercalcification. The high incidence of arteriosclerosis in the above mentioned group of diabetics with xanthosis is suggestive.

Should this vitamine theory prove to be correct, the outlook of the diabetic appears to be better now than with former methods of treatment, in view of our experiences with the high carbohydrate-low calorie diet.[10 to 13] The most striking metabolic effect of this diet is, as has been shown previously, a rapid and sustained decrease of plasma cholesterol, both in insulin and non-insulin patients, regardless of the type or severity of the disease. The following is a reproduction of the Table showing the experiences with the first five hundred consecutive cholesterol determinations following institution of the new diet.

TABLE I.

CHOLESTEROL CONTENTS OF BLOOD PLASMA FOLLOWING HIGH CARBOHYDRATE-LOW CALORIE DIETS

Plasma cholesterol (per cent)	*First 250 analyses (Incidence)*	*Second 250 analyses (Incidence)*
-0.100	9	14
0.101 - 0.150	72	104
0.151 - 0.200	118	76
0.201 - 0.250	40	31
0.251 - 0.300	5	14
0.301+	6	11
Average	0.170	0.163

(Rabinowitch, I. M., *New Eng. J. Med.*, 1931, **16**: 799.)

More recent experiences differ in no way from those reported previously.

In the past it was very uncommon to see a diabetic, with the disease of five years' duration, without some evidence of arteriosclerosis, regardless of his age. Five years' experience with the new diet should, therefore, prove or disprove the value of this diet in the prevention of this complication.

The above observations emphasize the value of cholesterol determination in the management of the diabetic. Reference was made previously to a number of factors which must be considered in the interpretation of data. No consideration was, however, given to possible normal variations. All blood constituents made use of clinically (urea, sugar, creatinine, uric acid, etc.) vary more or less widely in the normal person, and cholesterol is no exception. In a recent paper, McEachern and Gilmour [14] record their observations in 28 normal fasting individuals. Blood analyses were made at hourly intervals for five hours. The findings were rather disturbing. Wide variations were noted; the maximum was 84, the minimum was 17, and the average was 41 mgrm. per 100 c.c. It would appear, there-

fore, that such wide variations would tend to minimize the value of this test.*

As stated before, the conclusions drawn from the cholesterol studies were statistical. Contrary to the general tendency in medicine, however, the writer has very much faith in such conclusions, providing proper statistical methods are employed and the results are properly interpreted. It is suggested that the generally prevalent skepticism in medicine is largely due to abuse of statistical methods by those not thoroughly familiar with technique, application or interpretation. Cholesterol studies afford an example of the use to which these methods may be put. Thus, maximum, minimum and average values alone, as given by McEachern and Gilmour, afford little indication of the significance of any series of measurements. Maximum and minimum values merely indicate *possibilities,* and an average, when given alone, that is, without its probable error, is of very little value; it affords no index of *probability,* since a few extreme values, high or low, may affect it very appreciably, especially in a *small* series of measurements. It may, therefore, be observed that the number of observations made by McEachern and Gilmour, compared with our own, was small. Thus:—

TABLE II.

	Number of observations	*Number of subjects*
McEachern and Gilmour..	140	28
Rabinowitch.....	2,000	385

A Frequency Distribution Table affords a better indication of conditions than maximum, minimum and average values alone; it yields information both as to *probabilities* and *possibilities.* As it is not only the total number of observations but the *wide* variations and their number which tend to affect an average in a small series of measurements, the importance of knowing the incidence of such variations is obvious. The writer, therefore, recalculated the data given by McEachern and Gilmour in Table II of their report and constructed such a Frequency Distribution Table, with the following results:—

TABLE III.

Cholesterol range mgrm. per 100 c.c.	*Number of cases*
-40	17
41 - 50	4
51 - 60	4
61 - 70	2
71 - 80	0
81+	1

It will be noted that the occurrence of wide variations was very uncommon; the maximum variation of 84 mgrm. applied to one only of the whole series of twenty-eight patients (Subject T. O.).

In Table IV of the same report are recorded half-hourly variations of plasma cholesterol of normal fasting individuals. These, again, indicate that wide variations were very uncommon; in the eight cases studied, the maximum variation was 46 mgrm. only (Subject B. A.); the minimum was 22 (Subject H. A.) and the average was 31 mgrm. per 100 c.c.

It is of interest here to note that, in spite of the variations found in normal subjects, the highest cholesterol value noted, when blood was obtained in the fasting state, was 0.218 per cent; 8 only of the 178 estimations (Tables II and IV) showed values above 0.200 per cent and the arithmetical mean of all values was 0.161 per cent. The latter agrees very closely with the writer's standard of normality, namely, 0.180 per cent. In other words, in spite of wide variations, the normal subjects showed normal, or nearly normal, values. If we accept Joslin's[15] upper limit of normality, namely, 0.23 per cent, *all* values were within the normal limits of variation. The experiences with cholesterols are, therefore, similar to those with blood sugar. The latter, as is well known, varies widely, ranging between 0.08 and 0.120 per cent; and a normal person, regardless of the variations has always a normal blood sugar when examinations are made in the fasting state.

A glance at any of the records of our diabetics, selected at random, also shows variations;

* Since this paper was submitted for publication, further observations on Variations of Blood Cholesterol were reported by Bruger and Somach (*J. Biol. Chem.,* 1932, **97:** 23). These authors found that the cholesterol content of the blood of normal individuals undergoes variations which are of the same magnitude as those found in pathological states. These authors state they were unable to explain the wide variations reported by McEachern and Gilmour; wider variations were found by the latter in 5 hours than observed by Bruger and Somach in 24 hours.

and these, it may be noted, are as a rule wider than those found by McEachern and Gilmour in normal subjects. An important observation, however, is that there is a fairly sharp line of demarcation between the normal and the pathological, providing that the data are obtained under *uniform conditions,* both with regard to technique and preparation of patient. According to our experience with many thousands of analyses, a change from the normal to the pathological or from the pathological to the normal level has invariably been the result of some condition to which the patient was exposed and which is generally recognized as a cause of alteration of carbohydrate tolerance (diet, insulin dosage, exercise, etc.). The following cases are cited as examples:—

TABLE IV.

(Hosp. No. 6286/27)

Date	*Cholesterol (per cent)*
Dec. 2	0.289
" 3	0.311
" 5	0.272
" 7	0.305
" 9	0.239

It will be observed that, in spite of wide variations, all values were definitely above the normal level.

In 1927, this patient was on a low carbohydrate-high fat diet, consisting of approximately 50 grm. carbohydrate, 150 grm. fat and 50 grm. protein. Though he looked and felt well and the blood sugars at no time showed any marked degree of hyperglycæmia, ranging between 0.137 and 0.181 per cent (a normal value was found on one occasion only) the plasma cholesterol reached and remained at a high level in spite of the wide variations. The following shows the records obtained in 1928:—

TABLE V.

Date	*Sugar (per cent)*	*Cholesterol (per cent)*
Jan. 17	0.143	0.537
Mar. 29	0.158	0.383
May 8	0.161	0.606
Sept. 10	0.181	0.505
Nov. 5	0.119	0.476

Until June 4, 1929, there were no further data. On that day, the blood sugar was 0.143 per cent, and the plasma cholesterol was still very high, namely, 0.582 per cent. The carbohydrate content of the diet was then increased to 75 grm. The results of the examination following this change of diet were as follows:—

TABLE VI.

Date	*Sugar (per cent)*	*Cholesterol (per cent)*
Sept. 16/29	0.188	0.416
Mar. 7/30	0.181	0.520
Oct. 14/30	0.156	0.333
June 6/31	0.181	0.370

It will be noted that there was a tendency towards a decrease of cholesterol. The carbohydrate content of the diet was then further increased to 100 grm. and, on November 2, 1931, the blood sugar was 0.151 per cent and the cholesterol was definitely lower, namely, 0.302 per cent. The diet was then changed to the new high carbohydrate-low calorie diet and consisted of 218 grm. carbohydrate, 45 grm. fat and 69 grm. protein. With this change of treatment, the cholesterol approached the normal level. Thus:—

TABLE VII.

Date	*Sugar (per cent)*	*Cholesterol (per cent)*
Dec. 5/31	0.166	0.268
Jan. 9/32	0.140	0.238

That the above results were not accidental is shown by the following case.

CASE 1

A. A. B. is a moderately advanced diabetic, but is able to maintain his height-weight relationship and keep his urine free of sugar and the blood sugar nearly normal without the use of insulin. When he was first seen (October 4, 1928), the blood sugar was normal, namely, 0.105 per cent, and the plasma cholesterol was 0.219 per cent. His diet then consisted of approximately 75 grm. carbohydrate, 175 grm. fat and 50 grm. protein. On January 10, 1929, the blood sugar was 0.137 per cent and the cholesterol was 0.333 per cent. Because of the increase of cholesterol, the diet was changed to 100 grm. carbohydrate. In spite of this change, the cholesterol remained at a high level. Thus:—

TABLE VIII.

Date	*Blood* *Sugar (per cent)*	*Blood* *Cholesterol (per cent)*
May 16/29	0.192	0.416
Nov. 8/29	0.169	0.416
Feb. 21/30	0.126	0.302
July 10/30	0.133	0.302
Dec. 2/30	0.188	0.321
April 16/31	0.200	0.333

On April 16, 1931, the diet was changed to the high carbohydrate-low fat, namely, 254 grm. carbohydrate, 45 grm. fat and 75 grm. protein. On June 21st, the blood sugar was 0.143 per cent and the cholesterol decreased to 0.208 per cent! On this day, the diet was further increased to 272 grm. carbohydrate, 35 grm. fat and 78 grm. protein. At his last examination on July 24th, the blood sugar was normal, namely, 0.116 per cent and the cholesterol was 0.216 per cent.

During the entire period of observation, the urines have always been free of sugar. It will, therefore, be noted that at the time the diabetes was discovered the cholesterol was nearly normal; with the institution of treatment with a high fat and relatively low carbohydrate diet, the cholesterol gradually increased, though the urines were always free of sugar and the bloods showed no marked hyperglycæmia. With the institution of the high carbohydrate-low fat diet, the cholesterol approached the normal level. Incidentally, we have here another demonstration of the effects of the new diet without insulin in a diabetic who follows treatment carefully.

The following case shows the results of plasma cholesterol determinations made approximately monthly during a period of more than three years and, in spite of the fluctuations, these clearly indicate the course of events.

CASE 2

A male, aged 25 years, (No. 5053/28), was first admitted to our clinic on August 25, 1928. At that time, his diet consisted of approximately 150 grm. carbohydrate, 150 grm. fat and 60 grm. protein, and in order to keep the urine free of sugar and the blood sugar normal or nearly so he required 20 units of insulin twice a day, one-half hour before breakfast and one-half hour before the evening meal. In spite of the apparently good control of the diabetes, according to blood and urinary sugar data, the plasma cholesterol gradually increased; in August, 1928, it was 0.236 and on April 15, 1929, it was 0.396 per cent. Following increase of insulin dosage the cholesterol decreased, though it did not reach the normal level, according to the writer's standard; on October 28th, it was 0.216 per cent. In December of the same year, it again increased. On March 7, 1930, the diet was changed to the high carbohydrate-low fat consisting of 218 grm. carbohydrate, 56 grm. fat and 69 grm. protein. On June 11th, the diet was further increased to 236 grm. carbohydrate and on July 2nd to 254 grm. carbohydrate.

In spite of the variations, it will be noted here that, following institution of the high carbohydrate-low calorie diet, the blood cholesterol decreased to the normal level and has since been normal, except at one examination (April 2, 1931). Thus:—

TABLE IX.

(Hosp. No. 5053/28)

Date	*Plasma cholesterol (per cent)*	*Diet C.*	*F.*	*P.*	*Insulin (units)*
Aug. 25/28.....	0.236	150	150	60	20/0/20
Oct. 26/28.....	0.241	"	"	"	"
Nov. 16/28.....	0.260	"	"	"	"
Dec. 15/28.....	0.282	"	"	"	"
Jan. 11/29.....	0.340	"	"	"	"
Feb. 8/29.....	0.315	"	"	"	"
Mar. 8/29.....	0.273	"	"	"	"
Apr. 5/29.....	0.396	"	"	"	20/10/20
May 29/29.....	0.232	"	"	"	"
June 27/29.....	0.285	"	"	"	"
July 30/29.....	0.254	"	"	"	"
Aug. 27/29.....	0.242	"	"	"	"
Oct. 28/29.....	0.216	"	"	"	"
Dec. 26/29.....	0.321	"	"	"	"
Jan. 16/30.....	0.277	"	"	"	"
Mar. 7/30.....	0.252	218	56	69	"
June 11/30.....	0.120	236	"	72	"
July 2/30.....	0.145	254	"	"	20/0/20
Sept. 4/30.....	0.139	"	"	"	"
Oct. 2/30.....	0.111	"	"	"	"
Nov. 7/30.....	0.111	"	"	"	"
Dec. 30/30.....	0.160	"	"	"	"
Feb. 5/31.....	0.117	"	"	"	"
Apr. 2/31.....	0.241	"	"	"	"
May 14/31.....	0.166	"	"	"	"
July 7/31.....	0.184	"	"	"	"
Aug. 6/31.....	0.125	"	"	"	"
Sept. 15/31.....	0.122	"	"	"	"
Oct. 24/31.....	0.166	"	"	"	"
Nov. 17/31.....	0.166	"	"	"	"
Jan. 13/32.....	0.156	"	"	"	"

The bloods of persons in whom the diabetes is under ideal control show persistently normal values, in spite of wide variations. The following case is cited as an example.

CASE 3

(No. 6228/30) a male, aged 16 years. Data were obtained at approximately monthly intervals:

TABLE X.

(Hosp. No. 6228/30)

Date	*Cholesterol (per cent)*
Sept. 19/31.....	0.161
Oct. 24/31.....	0.164
Nov. 21/31.....	0.117
Dec. 12/31.....	0.151
Jan. 9/32.....	0.157

PLASMA CHOLESTEROL IN INSULIN WASTERS

Cholesterol determinations appear to be of value especially, in estimation of progress of insulin wasters—persons in whom insulin, when administered subcutaneously, acts as though given intravenously; the blood sugars decrease rapidly, but, with equal rapidity, return to the originally high level. Such persons

may suffer severe hypoglycæmic reactions shortly after an evening dosage of insulin, but, in spite of such reactions, have marked hyperglycæmia the following morning. Ideally, such diabetics should be given insulin in small doses at frequent intervals rather than in relationship to meals; and, wherever it is possible, this is the practice in this clinic; the insulin is given every 6 or 8 hours. We have about 20 such cases. In some the plasma cholesterol is normal, while in others, it is increased; and it is of interest to note that those with normal cholesterols appear to do well, in spite of persistent and marked hyperglycæmia and glycosuria. Some of these patients have been observed for years. In spite of glycosuria and fasting blood sugars ranging between 0.2 and 0.6 per cent, they feel well, perform their ordinary duties, maintain their expected body weights, and are, apparently, not unduly subject to complications. It would obviously be a fallacy to judge the severity of the diabetes in these cases by the difficulty with which hyperglycæmia and glycosuria are controlled. The following case is cited as an example:—

CASE 4

(Hosp. No. 3964/26) female, aged 61; duration of disease, 5 years. This patient is superintendent of a very active hospital, does not tire unduly, and on two occasions only has been off duty for a few days because of mild illness (respiratory and tooth infection). The following are the results of examinations made at different intervals during the last two years:—

TABLE XI.

Date	Blood sugar (per cent)	Cholesterol (per cent)
Jan. 9/30.....	0.454	0.157
Feb. 19/30.....	0.357	0.159
July 2/30.....	0.400	0.181
Sept. 11/30.....	0.384	0.249
Dec. 19/30.....	0.400	0.216
May 16/31.....	0.454	0.277
July 25/31.....	0.370	0.216
Nov. 9/31.....	0.344	0.208
Feb. 20/32.....	0.500	0.204

It will be noted that, in spite of the persistently marked hyperglycæmia, the plasma cholesterol was normal or only moderately increased.

Age might be considered a contributing factor; in diabetics at 60 the diabetes tends to be milder than at younger ages. The following case is, therefore, cited as another example:—

CASE 5

(Hosp. No. 6550/29) female, aged 25; duration of diabetes three years; a school teacher actively on duty. Hyperglycæmia and glycosuria have apparently had no effect on her general health. Here, again, with very few exceptions, we note normal or nearly normal plasma cholesterol values. Thus:—

TABLE XII.

Date	Blood sugar (per cent)	Cholesterol (per cent)
Nov. 1/30.....	0.500	0.196
Dec. 6/30.....	0.370	0.256
Jan. 24/31.....	0.476	0.192
Mar. 7/31.....	0.625	0.181
Apr. 25/31.....	0.416	0.200
May 30/31.....	0.500	0.287
Sept. 12/31.....	0.500	0.268
Nov. 28/31.....	0.370	0.222
Dec. 19/31.....	0.370	0.179
Mar. 12/32.....	0.416	0.160

Citation of more cases would be merely repetition of data. The purpose of this communication is to again emphasize the value of determination of plasma cholesterols in the estimation of progress and prognosis of the diabetic. Though wide variations may be noted in the diabetic, as in a normal person, the fluctuation of values does not minimize the value of the test. Repeated experiences have shown that there is a fairly sharp line of demarcation between the normal and the diabetic. Wide as the fluctuations may be in the normal, the values reported by McEachern and Gilmour clearly indicate that all values, including the maximum noted, were still below that generally regarded as definitely pathological; and, diabetics exceed this level only when the disease is not under control.

Attention is drawn to the marked hyperglycæmia and glycosuria met with in insulin-wasters, and which appear, at least up to the present time to have been compatible with good health, providing that the plasma cholesterol was either normal or only slightly increased.

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