FAT METABOLISM IN NEPHRITIS.

By A. HILLER, G. C. LINDER, M.D., C. LUNDSGAARD, M.D., AND D. D. VAN SLYKE, PH.D.

(*From the Hospital of The Rockefeller Institute for Medical Research.*)

It has been known for some time that in some cases of nephritis there is an increase in the blood lipoids, sometimes to the extent of 100 per cent or more above the normal. A review of the literature to 1917 has been given by Bloor (1). Later investigations confirmed these results. Epstein and Rothschild (2) thought the high lipoids in nephritis represented a condition of fat non-utilization. Bloor (1) regarded the abnormalities in blood lipoids in severe nephritis as the result of a retarded assimilation of fat in the blood, which he thought to be one manifestation of a general metabolic disturbance.

We have approached the subject by an attempt to discover whether the heaping up of lipoids in the blood is due to a retarded rate of fat combustion, or to a retardation of its deposition from the blood into the tissues. Fat metabolism experiments were planned, both on normal individuals and on nephritics with and without high blood lipoids.

Summary of Previous Literature.

The Effect of Fat Ingestion on the Total Metabolism.—Koraen (3) and Johansson and Koraen (4) concluded that there was no increase in metabolism as a result of the ingestion of fat. Gigon (5) did not always find an increase in the total metabolism, except when large amounts of fat were given, but he found an increase in the fat metabolism. Von Voit (6) stated that when 100 per cent of the basal requirement was fed to a dog in the form of fat, the total amount of protein and fat burned remained the same after ingestion of fat as during fasting. The fat ingested merely replaced the body fat in metabolism. Magnus-Levy (7), in experiments on dogs and on man, found an increase in total metabolism as a result of fat ingestion, and furthermore showed that the degree of increase was dependent on the amount of fat ingested. Rubner (8), Staehelin (9), Bartmann (10), Murlin and Lusk (11), and Benedict and Carpenter (12) all reported an increase in total metabolism after fat ingestion.

The Effect of Fat Ingestion on the Blood Lipoids.—Cholesterol: Increases in the blood cholesterol in the dog after fat ingestion were reported by Reicher (13) and by Terroine (14). No significant changes in blood cholesterol after fat ingestion in the dog were found by Bloor (15), Knudson (16), Bang (17), and Zucker (18).

Lecithin: Increases in blood lecithin after fat ingestion in the dog were reported by Reicher (13), Bloor (15), Knudson (16), and Zucker (18).

Fat and Fatty Acids: Increases in fatty acids or in neutral fats after fat ingestion in the dog were reported by Lattes (19), Reicher (13), Terroine (14), Bloor (15), Knudson (16), Zucker (18), Bang (17), and Eckstein (20). The only reports in the literature on human subjects are those of Neumann (21) and of Neisser and Braeuning (22), who reported an increase in fatty substances in the blood after fat ingestion determined by the ultramicroscopic method; those of Cowie and Hoag (23), who corroborated the results of Bloor on dogs by feeding cream to five children and three adults; and those of Bang (17), who found only slight changes in the fat content of the blood of human subjects after fat ingestion, as compared with the striking increase in the dog.

EXPERIMENTAL.

Methods.—The basal metabolism determinations were made by the Tissot spirometer method (24). The gas analyses were made with the Henderson modification of the Haldane gas analysis apparatus (25). The protein metabolism was determined by analysis of urinary nitrogen by the Kjeldahl method. When protein was present in the urine, this was removed by heating the urine and adding trichloroacetic acid until no further precipitation occurred. The mixture was diluted to a volume, filtered, and portions of the non-protein solution used for Kjeldahl determinations. All respiratory quotients given are non-protein.

The blood lipoids were determined by colorimetric and nephelometric methods. In the earlier experiments, Figs. 1, 3, and 11, in which the lipoids are recorded as total lipoid, the older method of Bloor was used (26). In the later experiments cholesterol and fatty acids were determined on plasma and on whole blood by the recent method of Bloor, Pelkan, and Allen (27). Lecithin determinations were made according to Randles and Knudson's modification of Bell and Doisy's method for the determination of phosphorus (28).

Fat Ingestion Experiments.—The basal metabolism of each subject was determined on a day previous to the day of fat ingestion, in order to familiarize the subject with the procedure, so that the factor of nervousness might be reduced as far as possible on the day of the experiment. On the day of fat ingestion the basal metabolism was determined as usual, during 10 minute periods, and blood was taken for the determination of lipoids. A meal consisting of butter (usually 1 gm. of butter per kilo of body weight) was then given. Various methods were employed to make the butter more palatable. The butter was served either in the form of balls coated with bran, or melted. 100 to 200 cc. of water were given if

TABLE I.

Metabolic and Blood Lipoid Changes after Fat Ingestion in Normal and in Nephritic Subjects.

Subject	Cal. Basal	Cal. Maximal	Cal. Increase	Incr. in metab. (%)	R.Q. Basal	R.Q. Minimal	Decr. R.Q. (%)	Tot. lip. Plasma Initial	Max.	Ch. mg	Ch. %	Chol. Plasma Initial	Max.	Ch. mg	Ch. %	Chol. Whole bl. Initial	Max.	Ch. mg	Ch. %	Lec. Plasma Initial	Max.	Ch. mg	Ch. %	Lec. Whole bl. Initial	Max.	Ch. mg	Ch. %	Fatty ac. Plasma Initial	Max.	Ch. mg	Ch. %
Normals.																															
G.L.	0.95	1.04	+0.09	+9.5	0.82	0.78	0.04	820	740	−80	−9.8	175	175	0	0.0													325	265	−60	−18.5
	0.97	1.07	+0.10	+10.3	0.76	0.72	0.04																								
J.P.	0.87	0.98	+0.11	+12.6	0.80	0.80	0.00	650	825	+175	+27.0	210	230	+20	+9.5													355	640	+285	+80.0
	0.94	1.03	+0.09	+9.6	0.77	0.76	0.01																								
C.L.	0.83	0.89	+0.06	+7.2	0.81	0.75	0.06					155	175	+20	+12.9													190	245	+55	+29.0
J.N.	1.06	1.06	0.00	0.0	0.76	0.70	0.06					160	160	0	0.0	150	150	0	0.0	190	205	+15	+7.9	275	285	+10	+3.6	380	385	+5	+1.3
R.B.	0.84	0.97	+0.13	+15.5	0.80	0.73	0.07					195	195	0	0.0	135	145	+10	+7.4	250	250	0	0.0	300	300	0	0.0	545	640	+95	+17.4
H.S.	1.02	1.06	+0.04	+3.9	0.76	0.76	0.00					195	210	+15	+7.7	180	165	−15	−8.3	220	220	0	0.0	295	295	0	0.0	360	440	+80	+22.2
Average				+8.5			0.035				+8.6				+5.0				−0.3				+2.6				+1.2				+21.9
Nephritics with normal blood lipoids.																															
H.L.	1.08	1.19	+0.11	+10.2	0.82	0.72	0.10					180	195	+15	+8.3													450	470	+20	+4.5
J.O'M.	1.25	1.40	+0.15	+12.0	0.81	0.77	0.04					240	240	0	0.0													550	550	0	0.0
Average				+11.1			0.07								+4.1																+2.2
Nephritics with high blood lipoids.																															
F.R.	0.94	1.00	+0.06	+6.4	0.88	0.80	0.08	990	1,070	+80	+8.1	410	450	+40	+9.9													1,040	1,270	+230	+22.1
J.D.	1.20	1.26	+0.06	+5.0	0.83	0.78	0.05					250	290	+40	+16.0													580	1,000	+420	+72.4
	1.16	1.39	+0.23	+19.8	0.87	0.81	0.06																								
M.F.	0.94	1.08	+0.14	+14.9	0.85	0.75	0.10					460	460	0	0.0	355	349	−6	−1.7	425	465	+40	+9.4	470	520	+50	+10.6	750	1,220	+470	+62.7
L.S.	0.89	0.96	+0.07	+7.9	0.78	0.75	0.03					620	730	+110	+17.7													965	1,105	+140	+14.5
	0.92	1.03	+0.11	+12.0	0.83	0.75	0.08					510	485	−25	−4.9													980	1,250	+270	+27.6
B.S.	1.26	1.39	+0.13	+10.3	0.82	0.75	0.07					580	570	−10	−1.7	380	375	−5	−1.3	430	510	+80	+18.6	415	465	+50	+12.0	950	1,620	+670	+70.5
Average				+10.9			0.067								+6.1				−1.5				+14.0				+11.3				+45.0

Changes in lipoid content per 100 cc. of plasma and whole blood.

desired. Water ingested in such small amounts has no effect on the metabolism (29). Bran was used because it contains no material which is absorbed, and, therefore, does not enter into the metabolism. Intestinal activity alone does not enter into the changes in basal metabolism (30). Rubner (8) showed that a dog could eat bones without increasing his metabolism. The metabolism was determined by 10 minute periods, 1, 3, and 5 hours after the fat ingestion. Blood and urine samples were taken immediately following the initial basal metabolism, and the 3 and 5 hour metabolism periods. The subject was kept as quiet as possible during the entire period of the experiment in order to eliminate as far as possible all factors affecting the metabolism. No determinations of fat in the feces were made.

Control experiments were performed on six normal individuals. The results of these controls are shown in Figs. 1 to 8. Seven patients with nephritis of various types were examined. Two of these cases were patients with normal blood lipoids. One, shown in Fig. 9, was a case of nephrosclerosis with no signs of renal insufficiency. The other, Fig. 10, was a case of subchronic glomerulonephritis with marked renal involvement. Five of these patients, Figs. 11 to 19, were cases with increased blood lipoids. Three were suffering from nephrosis: L.S., B.S., and F.R., Figs. 16, 17, 18, 19, and 11; but the last of these was in a state of almost complete recovery. The remaining two patients, J.D., and M.F., Figs. 12, 13, 14, and 15, were cases of chronic glomerulonephritis. Control experiments were performed on two of these patients with high blood lipoids, Figs. 15 and 19. The procedure was the same as in the fat ingestion experiments, except that no fat was given, and the experiment was carried on only to the 3rd hour. We did not wish to fast the patient longer than necessary, and after the 3rd hour the significant increases had already occurred in the majority of experiments. In all cases in which edema existed, the basal metabolism was calculated on the patient's weight at the time of disappearance of the edema, when the weight became constant.

Table I gives a summary of all the experiments, with averages of the results. Table II gives the character of the diet of the patient, and the amount of fat given on the day of the experiment.

TABLE II.

Diet Previous to and on Day of Fat Ingestion.

Subject.	Body weight.*	Diet 10 days prior to fat metabolism experiment.					Basal requirement.		Amount of fat ingested.	Fat ingested in per cent of 6 hr. requirement.	Date of fat feeding.	Basal metabolic rate, deviation from Du Bois' average normal.†
		Total calories.	Per cent of basal requirement.	Calories per kilo.	Protein.	Fat.	24 hr.	6 hr.				
	kg.	*cal.*	*per cent*	*cal.*	*gm.*	*gm.*	*cal.*	*cal.*	*cal.*	*per cent*		
Normals.												
G. L.	66.0						1,550	387.5	460	118.6	Sept. 28, 1922	−11.4
J. P.	77.5						1,740	435.0	460	105.6	Oct. 3, 1922	−5.9
C. L.	90.4						1,800	450.0	460	102.2	" 10, 1922	−7.9
J. N.	58.0						1,490	372.5	446	112.7	May 2, 1923	−8.0
R. B.	77.0						1,600	400.0	460	115.0	Apr. 16, 1923	−10.8
H. S.	72.1						1,750	437.5	514	117.5	Mar. 26, 1923	−3.7

Nephritics.											
H. L.	51.1	1,850	137	36.2	55	60	1,350	337.5	383	113.5	Dec. 11, 1922	+3.0
J. O'M.	40.7	1,650	133	40.6	55	60	1,240	310.0	307	99.0	" 18, 1922	−18.3
F. R.	60.2	2,000	148	33.3	70	50	1,350	337.5	460	136.3	May 25, 1922	−22.3
J. D.	36.0	1,600	146	44.4	60	70	1,100	275.0	307	111.6	June 8, 1922	−25.6
	36.0	1,700	155	47.3	60	65	1,100	275.0	307	111.6	Oct. 17, 1922	−28.3
M. F.	48.0	1,700	155	35.4	50	70	1,100	275.0	345	125.5	Apr. 23, 1923	−19.0
L. S.	62.5	1,000	77	16.0	35	45	1,300	325.0	383	118.0	Oct. 30, 1922	−19.2
	62.5	1,600	123	25.6	70	55	1,300	325.0	383	118.0	Dec. 4, 1922	−18.7
B. S.	33.9	1,500	125	44.3	40	50	1,200	300.0	307	102.3	Apr. 3, 1923	−20.7
		1,600	139	47.2	70	30	1,150	287.5			" 26, 1923	−20.0

* Body weights recorded are weights after the disappearance of edema.
† Normal subjects show deviations up to ± 15 per cent from the average.

DISCUSSION.

Basal Metabolic Rate.—The basal metabolic rate of the normals varied from −3.7 to −11.4 per cent from Du Bois' average normal standard, averaging −7.9 per cent (Table II). A few of these rates are slightly low according to the older standards of ±10 per cent, but all fall within the normal range as extended by Boothby (31) in his recent report of 8,614 determinations of basal metabolic rate. Of these, 127 were normals. He has concluded that although the great majority of normals fall within the ±10 per cent range, a sufficient number extend to a ±15 per cent range to make it necessary to extend the standard for normals to that zone, using the Du Bois standards for comparison. The hypertension case, H.L., Fig. 9 and Table II, had a normal rate of +3 per cent. All of the nephritic cases, Figs. 10 to 19 and Table II, had a lowered metabolic rate, ranging from −18.3 to −28.3 per cent. Whether the lowered metabolic rate found in all of our nephritics is a manifestation of the disease or not, we are not prepared to say. We think that the low metabolic rate may be due to the fact that all of our patients had been on a low caloric diet for some time, which is capable of depressing the rate of metabolism, as shown by Benedict in his reports on inanition and reduced diet (32). Our patients were all kept well above their basal requirement, as shown in Table II. The diets averaged 146 per cent of the 24 hour basal requirements, but this is low when compared to the ration of a normal individual who is up and about. Furthermore, most of our patients had been inactive and in bed for several months before the determination was made.

Effect of Fat Ingestion on Metabolism.—The metabolism of the normals after fat ingestion showed some variations, as shown in Figs. 1 to 8, and in Tables I and II. The increment in metabolism varied from 0 in one case, to 15.5 per cent, with an average of 8.5 per cent. This increase agrees fairly well with the results previously reported in the literature (3–12). The majority of investigators fed much larger quantities of fat than were used in our experiments, which accounts for their greater increment in the metabolism, as shown by Magnus-Levy (7). The amount of fat which our subjects ate varied between 99 and 136 per cent of the basal requirement for the 6 hours of the experiment,

as shown in Table II. The increase in metabolism in the nephritic cases varied from 5 to 19.8 per cent, averaging 10.9 per cent (Table I). There was no difference in the effect on total metabolism between normals and nephritics in their reaction toward fat ingestion.

Changes in Respiratory Quotient.—The respiratory quotients in two normals showed no significant change throughout the experiment. The remaining four showed a decided drop (Table I) which signified that fat was being burned to a greater extent after the fat ingestion than before. The nephritic cases showed the same decrease in respiratory quotient after fat ingestion, so that there was no marked difference in the degree and the kind of metabolism between normals and nephritics. That these changes are not due to natural variations in the course of the day is shown by control experiments on two patients, Figs. 15 and 19, in which there was no change in respiratory quotient and no increase in metabolism.

Effect of Fat Ingestion on Blood Lipoids.

Cholesterol.—The blood cholesterol curves are for the most part straight lines. The average increase in plasma cholesterol for normals was 5 per cent, and for nephritics 6.1 per cent (Table I). The changes in the cholesterol of whole blood averaged −0.3 per cent for normals and −1.5 per cent for nephritics. The changes are very slight, and nearly all fall within the limits of experimental error. The cholesterol picture does not agree with the earlier reports of Reicher (13) and Terroine (14), who found an increase in the cholesterol, but agrees with later reports by Bloor (15), Knudson (16), Bang (17), and Zucker (18), who found the blood cholesterol unchanged after fat ingestion, using the dog as a subject.

Lecithin.—The lecithin of both plasma and whole blood showed no change after fat ingestion in two normals, Figs. 7 and 8, and Table I. In one normal, Fig. 5 and Table I, the lecithin increased 7.9 per cent in the plasma and 3.6 per cent in the whole blood. These results do not corroborate those obtained when dogs were used as subjects. Reicher (13), Bloor (15), Knudson (16), Zucker (18), and Eckstein (20), all report an increase in blood lecithin during fat absorption in the dog. Different species do not always react in the same way, and

different animals in the same species do not always show the same reactions toward lipoids, as shown by Bang (17), by Neisser and Braeuning (22), and by Bloor (15). All lecithin observations in the literature were made on dogs. Our average increase in lecithin in three normals is 2.6 per cent for plasma, and 1.2 per cent for whole blood.

The nephritic cases with high lipoids showed greater increases than the normals. Determinations were made on two nephritics, M.F. and B.S., Figs. 14 and 18, and Table I. The average increase in lecithin was 14 per cent for plasma and 11.3 per cent for whole blood. Control experiments were performed on both of these patients, which showed no change in the lecithin of plasma or whole blood during a similar period when no fat was ingested.

Fatty Acids.—The increase in the fatty acids of the blood of normals after fat ingestion is slight. Of the six subjects used, one showed a decrease in the fatty acids of the plasma, four showed an increase varying from 1.3 to 29 per cent, and one showed an increase of 80 per cent (Table I). The latter subject, J.P., Figs. 3 and 4, was the only normal who showed any considerable increase in fatty acids. Similar results were obtained in two different experiments. In the first experiment, Fig. 3, the total lipoids were determined (26). In the second experiment, Fig. 4, fatty acids and cholesterol were determined separately (27), and the fatty acids present a curve almost as steep as some of the severe nephritic curves. The average increase in plasma fatty acids was 21.9 per cent. These results, which we have obtained on human subjects, with the one exception of J. P., are very different from the results obtained on dogs by Lattes (19), Reicher (13), Terroine (14), Bloor (15), Knudson (16), Zucker (18), Eckstein (20), and Bang (17), all of whom report a larger increment, varying between 50 and 245 per cent. Our results, however, agree very well with those reported by Bang (17) in his experiments on human subjects. He fed fat in the form of butter and cream, amounting to 150 gm. of fat. Of the twelve subjects, three showed no increase $1\frac{1}{2}$ hours after ingestion, three showed an increase of less than 20 per cent, the remaining six showed an increase varying between 28 and 67 per cent. The average increment was 28.4 per cent. The average increment for our six normals was 21.9 per cent (Table I). There are two possible reasons why our

results in the fatty acids should differ from the observations made on dogs, aside from the greater factor of difference in species. In the first place, in the majority of experiments performed on dogs, the fat was ingested in the form of olive oil (Bloor (15), Bang (17), and Zucker (18)). Bang (17) showed that when lard was fed to dogs no hyperlipemia appeared, when butter was fed there was often a hyperlipemia, but when olive oil was used, a hyperlipemia always occurred. He also found great variations in individual reactions of dogs toward ingested fat. Neisser and Braeuning (22) also stated that the amount of increase in blood lipoids varied with the kind of fat fed, and with the animal. If the same variations due to the kind of fat ingested hold good for men as well as for dogs, the fact that the dogs were usually fed on olive oil and our subjects were fed on butter would account for some of the differences in results. The variations found by Bang (17) in individual reactions in dogs undoubtedly also hold good in the case of men, as shown by the great variations exhibited in Bang's figures for men (17) and also by our case of J. P., Figs. 3 and 4, and Table I. In the second place, our subjects received much smaller amounts of fat than any of the animals reported. Reicher's dogs (13) received 5 or 6 gm. of fat per kilo of body weight; Bloor's dogs (15) received from 7 to 16 gm. per kilo; Knudson's (16) and Zucker's (18) about 5 gm. per kilo, and Bang's (17) about 3 to 5 gm. per kilo. Our subjects received about 1 gm. of butter per kilo, which is somewhat less than 1 gm. of fat per kilo. The dosage, therefore, averages about one-fifth of that given in the dog experiments, so one would expect less of an increase in the blood lipoids. Bloor (15) stated that the increased amount of fat in the blood might be due to the introduction of a quantity of fat greater than the temporary storehouse can take care of, with resulting accumulation. It is probable that the amount of fat which our human subjects received was within the limits of the amount which the average normal can dispose of, and that amount is probably removed from the blood as rapidly as it is taken up by it.

Two patients, H. L., nephrosclerosis, and J. O'M., subchronic glomerulonephritis, who showed normal blood lipoids, Figs. 9 and 10, and Table I, showed an increase in fatty acids of 4.5 and 0 per cent respectively, which comes well within our range for normals. The five patients with high blood lipoids, Figs. 11 to 19, and Table I,

however, showed much greater increases in plasma fatty acids than did the normals. The increase varied from 14.5 to 72.4 per cent, averaging 45 per cent. Since the normals averaged 21.9 per cent, the patients with high blood lipoids showed twice as great an increment as did the normals. Control experiments were performed, Figs. 15 and 19, to show that there was no significant change in blood lipoids in the course of the experiment when no fat was ingested.

Since the patients received approximately the same amount of fat per kilo of body weight as the normals, and yet showed a much greater increment in fatty acids and lecithin in the blood, the difference may lie in the ability of the organism to remove lipoids from the blood. The normal organism evidently has some mechanism, perhaps having some connection with the transport to and temporary storage in the liver, as suggested by Leathes (33), by which certain amounts of fat ingested are removed from the blood with a rapidity almost equal to that of their entrance into the blood. The increase in blood lipoids found in cases of nephritis may be due to some disturbance of this balancing mechanism, whereby the lipoids are much more slowly removed from the blood than under normal conditions. This disturbance apparently has no effect on the ability of the organism to burn fat, since the nephritic patients with high blood lipoids showed the same decrease in respiratory quotient as did the normals, which indicated that they had an equal ability to burn fats.

SUMMARY.

Determinations of the plasma lipoids and of the respiratory quotient and total metabolism (Tissot method) have been performed with nephritics and normal subjects before and after they ingested fat in the proportion of 1 gm. per kilo body weight.

After fat ingestion a greater increase of fatty acids and lecithin was noted in the plasma of nephritics with initially high blood lipoids than in the plasma of normal subjects or of nephritics without constant lipemia. In cholesterol no differences were found.

The nephritic patients with constant lipemia were able to burn fat as efficiently as normal individuals.

The accumulation of fat in their blood may be due to a disturbance in the mechanism for transferring lipoids from the blood to the tissue depots.

Explanation of Figures.

The abscissæ represent the number of hours after fat ingestion. The ordinates have a single scale which is used for all curves: For the metabolism curve, the ordinates represent calories per kilo per hour. For the lipoid curves the ordinates represent grams per 100 cc. of plasma or blood. The following signs are used to indicate the different curves.

●——● Calories per kilo per hour.

+——+ Non-protein respiratory quotient.

□ — —□ Whole blood fatty acids—per cent.

□——□ Plasma fatty acids—per cent.

△ — — △ Whole blood lecithin—per cent.

△——△ Plasma lecithin—per cent.

○ — — ○ Whole blood cholesterol—per cent.

○——○ Plasma cholesterol—per cent.

⊙——⊙ Total plasma lipoids—per cent.

Normal
G.L. Apr. 21 1922

60 gm. butter
=0.910 gm. per kg.

FIG. 1

Normal
G.L. Sept. 28 1922

60 gm. butter
=0.910 gm. per kg.

FIG. 2
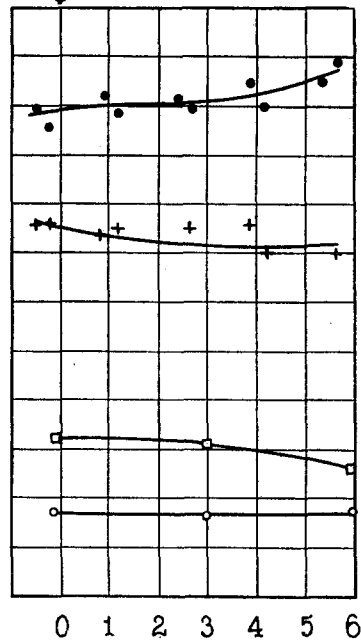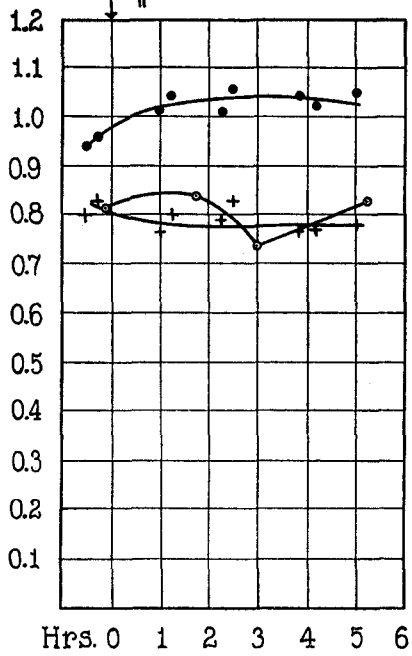
Normal
J. P. Apr. 25 1922

← 60 gm. butter
=0.77 gm. per kg.

FIG. 3
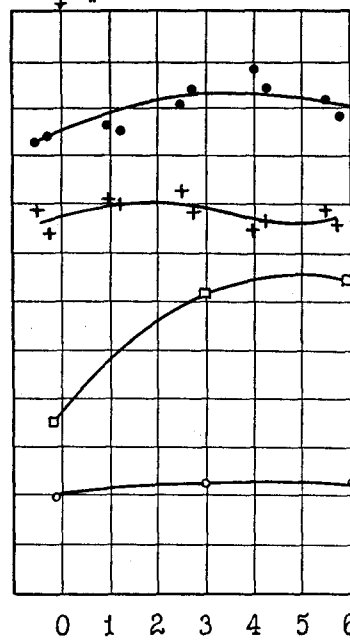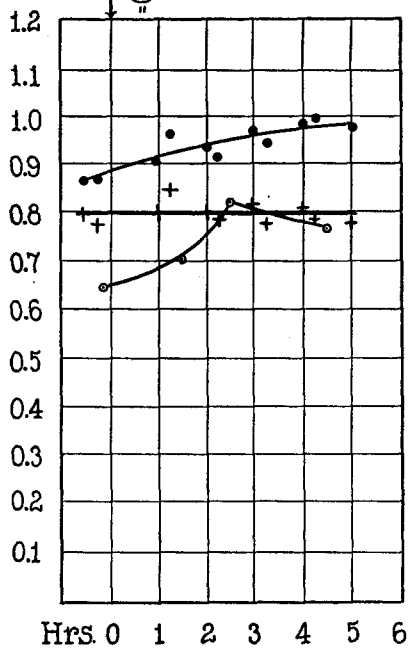
Normal
J. P. Oct. 3 1922

← 60 gm. butter
=0.77 gm. per kg.

FIG. 4

Normal
J.N. May 2 1923

FIG. 5

Normal
C.L. Oct. 10 1922

FIG. 6
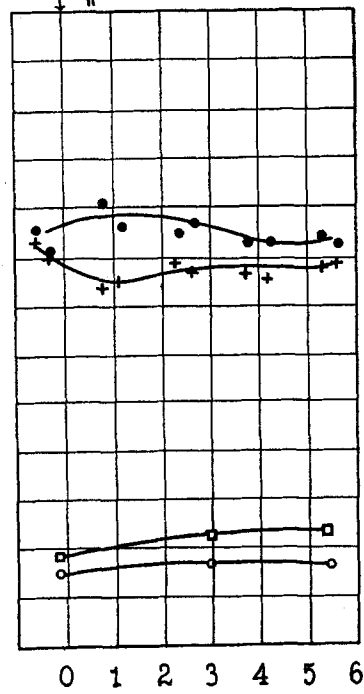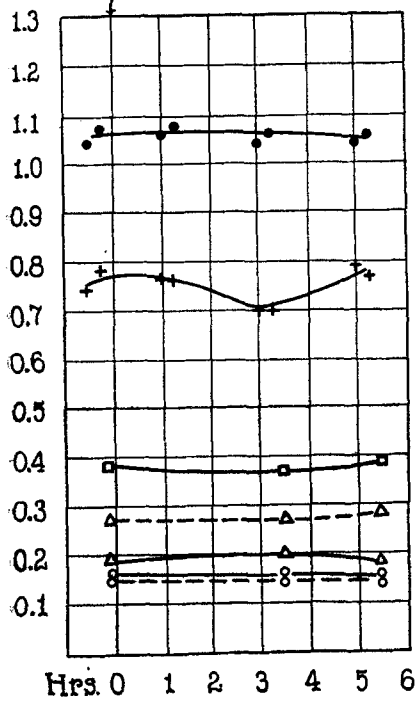
Normal
  R. B. Apr. 16 1923

Normal
  H. S. Mar. 26 1923

60 gm. butter
=0.78 gm. per kg.

67 gm. butter
=0.93 gm. per kg.

FIG. 7

FIG. 8

Hrs. 0 1 2 3 4 5 6

0 1 2 3 4 5 6
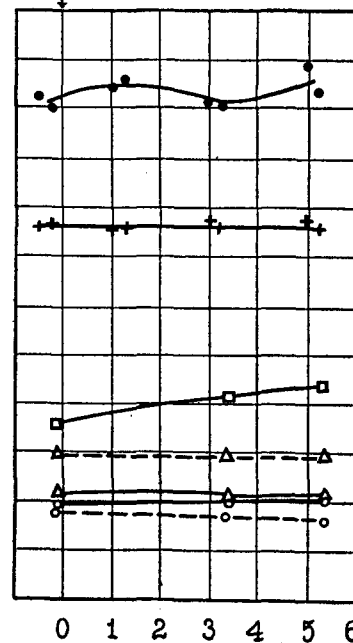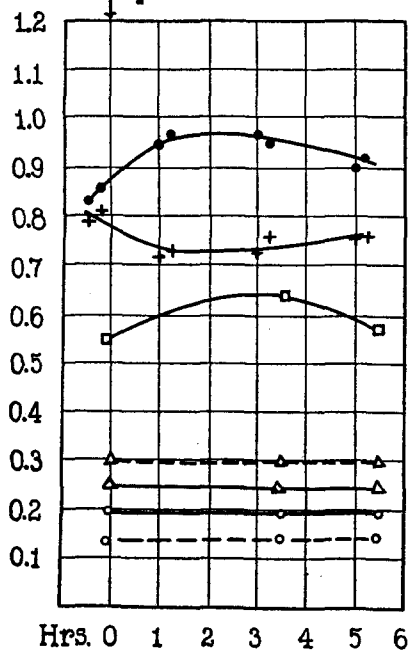
Nephritic with normal blood lipoids
H. L. Dec. 11 1922

Nephritic with normal blood lipoids
J. O'M. Dec. 18 1922

FIG. 9
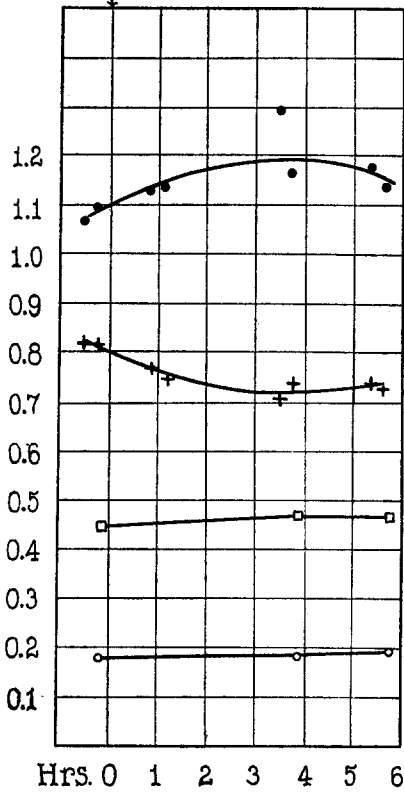
FIG. 10
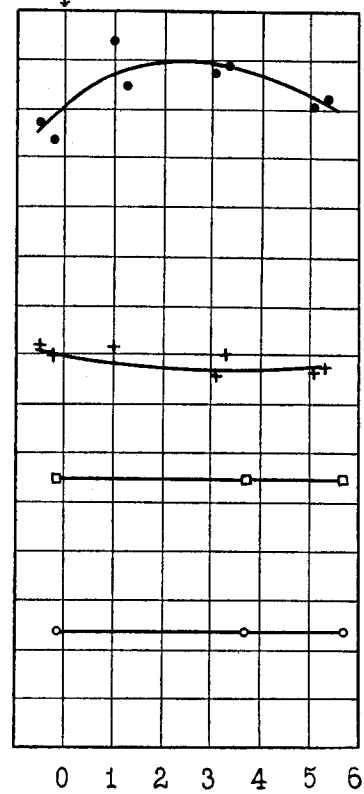
Nephritic with slightly high blood lipoids
F. R. May 25 1922

FIG. 11
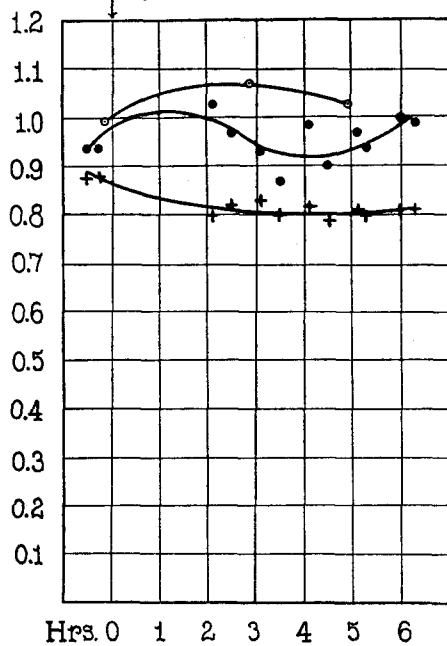
Nephritic with high blood lipoids
J. D. June 8 1922

Nephritic with high blood lipoids
Oct. 17 1922

=40 gm. butter
=1.116gm. per Kg.

FIG. 12

=40 gm. butter
=1.116gm. per Kg.

FIG. 13

1.3
1.2
1.1
1.0
0.9
0.8
0.7
0.6
0.5
0.4
0.3
0.2
0.1

Hrs. 0 1 2 3 4 5 6   0 1 2 3 4 5 6
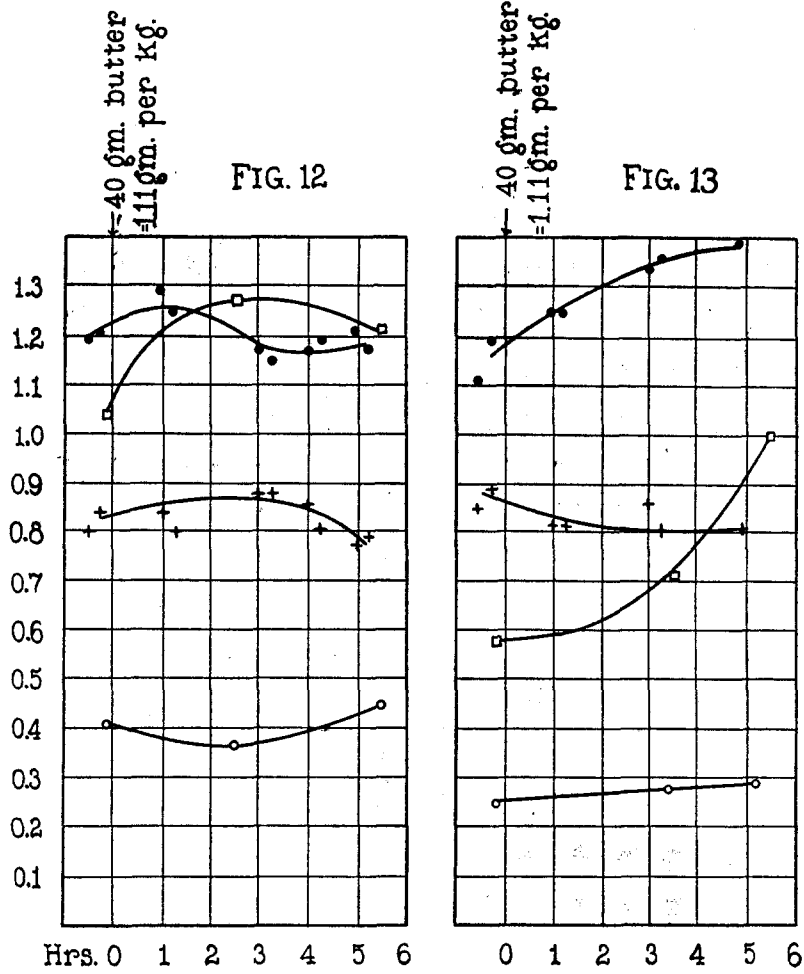
Nephritic with high blood lipoids
M. F. Apr. 23 1923

Control experiment
M. E. May 7 1923

FIG. 14

FIG. 15

-45 gm. butter
=0.94 gm. per kg.

No butter

Hrs. 0 1 2 3 4 5 6   0 1 2 3 4 5 6
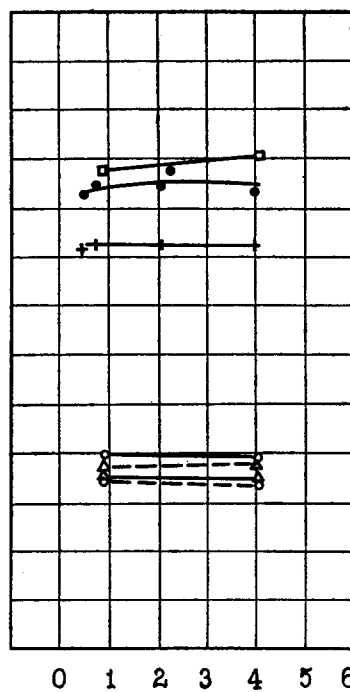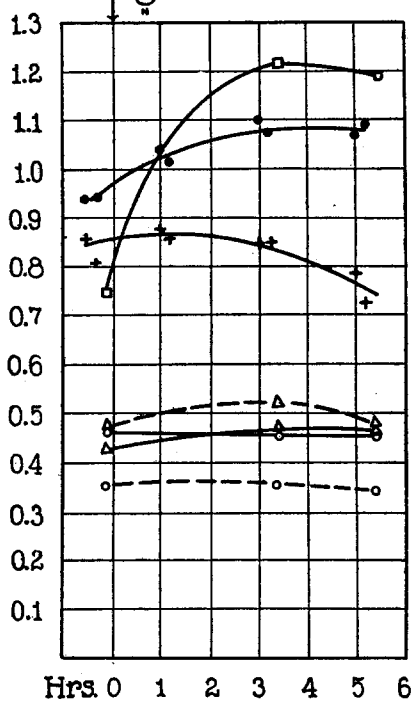
Nephritic with high blood lipoids
L.S. Oct. 30 1922

Nephritic with high blood lipoids
L.S. Dec. 4 1922

FIG. 16

FIG. 17
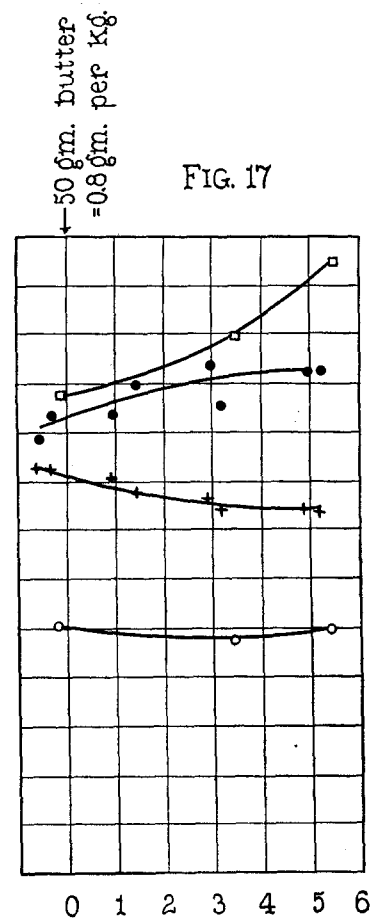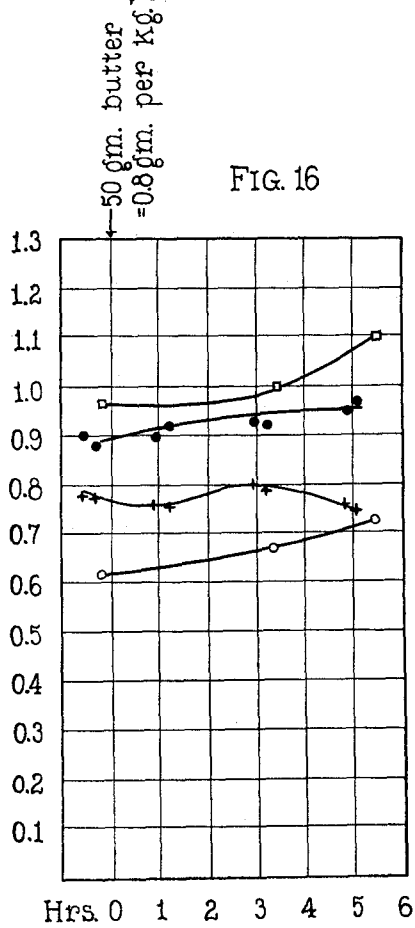
Nephritic with high blood lipoids
B. S. Apr. 3 1923

Nephritic with high blood lipoids
B. S. Apr. 26 1923
Control experiment

FIG. 18
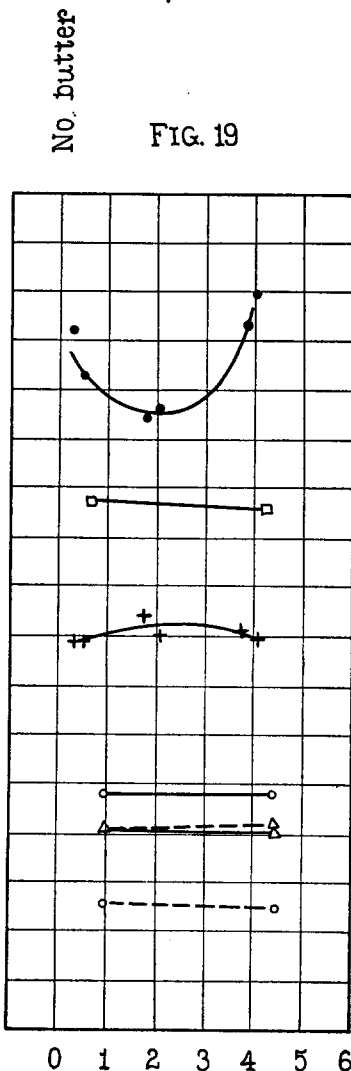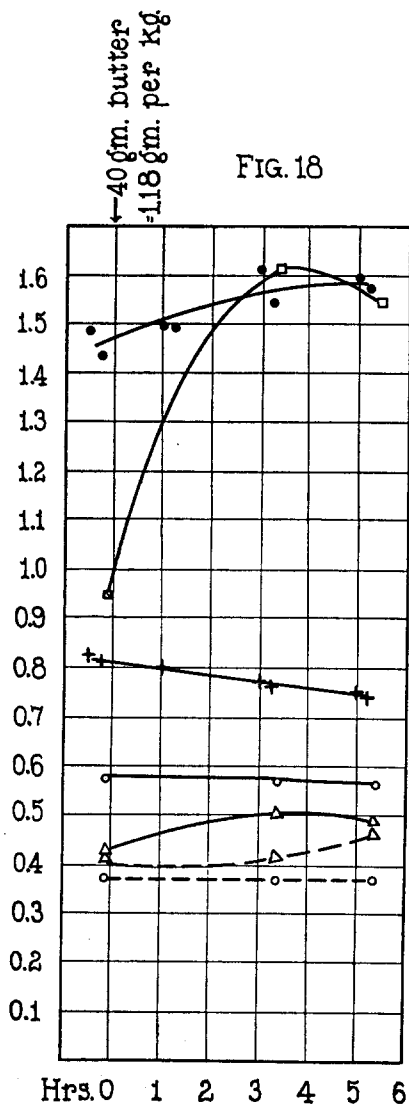
FIG. 19

At the time of the metabolism represented by the 1st hour in Fig. 19, the patient was very drowsy, and was almost asleep, which accounts for the dip in the curve at this point.

PROTOCOLS.

L. S.—Case of acute nephrosis. Male, 30 years. In September, 1922, following gastroenteritis, he became edematous and a considerable proteinuria was found. Investigation revealed a blood urea nitrogen of 0.12 gm. per liter, a plasma cholesterol of 5.50 gm. per liter, a phthalein output of 30 per cent in 2 hours, and a basal metabolic rate of +1 per cent. A diagnosis of nephrosis was made and a high protein diet prescribed. 2 weeks later the edema had greatly increased and become generalized, and there were occasional nausea and vomiting. The blood urea nitrogen was 0.39, the plasma cholesterol 4.6, and the basal metabolism −9.3. Thyroid was given without benefit. The urine progressively diminished in amount. There were no headaches, and no visual disturbances, but the vomiting increased and there was slight dyspnea.

On admission, October 6, 1922, he had great anasarca with hydrothorax and ascites. No retinal changes were present. Blood pressure 120/80; no cardiac hypertrophy; arteries healthy. The urine contained from 9 to 17 gm. of protein per liter; specific gravity 1,040; the deposit contained many casts, leucocytes, and a few blood cells. The blood urea nitrogen was 0.47 and urine urea nitrogen 13.0 gm. per liter. The plasma proteins were much depleted and the albumin-globulin ratio inverted. Wassermann reaction negative. Anemia slight.

A milk diet was given until the gastric symptoms had subsided, when bread, butter, and cereals were added. 30 gm. of urea were given daily and caused a slight increase in the output of urine without increasing the blood urea. On October 28, 2,600 cc. of fluid were aspirated from the right pleural sac. Improvement was fitful and by the end of October little progress had been made. At this time the first fat metabolism experiment was made.

From November 4 a diet containing 20 gm. of fat, 250 gm. of carbohydrate, and 60 gm. of protein was given, the protein being increased to 70 gm. on the 17th. The slow improvement continued unaltered until the 14th when a progressive increase in the output of water and chlorides began; this was followed by a dramatic fall in the blood urea to 0.17 on the 19th, while the urea feeding continued, and in body weight which reached 62 kilos on December 6. Plasma cholesterol on November 19 was 5.1 gm., and on November 24, 7.9 gm. By December 1 no edema remained and no fluid was present in the chest or abdomen. On November 24 in the middle of the diuresis the fat in the diet was increased to 40 gm. and the protein to 85 gm. without any change in the rate of improvement. On December 4 the second fat metabolism experiment was performed.

The subsequent history was uneventful and ended in an apparently complete recovery.

B. S.—Case of chronic nephrosis. Patient was a boy, 11 years old, who had had edema of the face and legs, and proteinuria since February, 1922. No cause was known. He felt perfectly well.

Admitted in November, 1922, he had a puffy face, and slight pitting of the right leg; the urine contained 4 gm. of protein per liter; the sediment was normal. The

plasma proteins were diminished, and the albumin-globulin ratio inverted. There were no vascular changes. Renal function tests elicited normal responses. The blood urea nitrogen was 0.07 gm. per liter. The edema disappeared, and he was discharged in December with a trace of protein in the urine.

In March he was readmitted with bilateral pleural effusion, ascites, and edema of the face and legs. Weight 40.6 kilos. On April 3 he was still in this condition; weight 39.5 kilos. Thyroid extract was given at the end of April, and was followed by improvement. On May 15 there were no signs of fluid and the weight was 34.5 kilos.

F. R.—Case of acute nephrosis. Female, 20 years. She was admitted in November, 1921, with moderate edema, proteinuria, a normal blood pressure, and normal blood urea. The plasma cholesterol was 7.9 gm. per liter, and the total fats 20 gm. per liter (old Bloor method). She developed a series of erythemata of obscure infective nature, and the edema greatly increased. In January and February the edema subsided while she was taking a high protein, low fat diet. In May, when the fat metabolism experiment was performed, she was convalescent; response to function tests was normal; the blood pressure was normal; and the urinary protein was reduced to a trace.

M. F.—Case of subacute glomerulonephritis. Female, 25 years old. Her ankles and legs became edematous in October, 1922. She remained at work until December, but the swelling steadily increased, and spread to the trunk and arms. Her vision became affected, but there were no symptoms of uremia.

Admitted January 4, 1923, she showed massive edema of the legs and lower part of the trunk, and moderate edema of the arms, face, and chest wall. Albuminuric retinitis was present in both eyes. Heart was not hypertrophied, but the blood pressure was 205/128. The pleuræ contained fluid. Urine: smoky, 3.5 gm. protein per liter, the deposit containing many casts and blood cells. Blood urea nitrogen 0.46 gm. per liter. Red blood corpuscles 3,520,000 and hemoglobin 62 per cent. Wassermann reaction negative.

On a milk diet and with daily sweat baths the edema diminished but the blood urea nitrogen rose to 0.80, and uremic symptoms developed. At the end of January she began to improve, her weight, blood urea, and blood pressure falling together, and by the middle of February she had no edema, no pleural effusion, and a blood pressure of 160/102. The urine remained smoky until March, and in May still contained numerous red blood corpuscles and casts. The blood urea nitrogen in April was 0.55 and the phthalein output 26 per cent in 2 hours. The red blood corpuscles had fallen to 2,200,000 and the hemoglobin to 47 per cent. She remained free from edema.

Weight on admission 65.8 kilos.

Weight after loss of edema 48 kilos.

J. D.—Case of subchronic glomerulonephritis. The patient, a boy of 14 years, developed edema in May, 1922, without any preceding illness or infection.

On admission there was marked general edema with effusions into the pleura and peritoneum. The area of cardiac dullness was enlarged, and the blood pres-

sure 135/90. The urine contained 4 gm. of protein per liter, a large amount of blood, and many casts. The blood urea nitrogen was 0.2 gm. per liter, and the phthalein output 46 per cent in 2 hours. Red blood corpuscles 4,100,000, and hemoglobin 65 per cent.

The edema rapidly subsided, and his weight fell from 50 kilos on May 19, to 38 kilos on June 9. By the beginning of June there were no signs of fluid in the chest or abdomen, and slight pretibial edema alone remained. The hematuria was persistent. He developed an increasing anemia, the red blood corpuscles being 2,400,000 in March, 1923. In February definite pathological changes were noted in the fundi. No nitrogen retention developed and his blood pressure fell to 120/70 soon after admission and did not rise again. The edema did not recur, although slight pretibial pitting persisted.

J. O'M.—Case of subchronic glomerulonephritis. The patient was a boy of 14 years. In September, 1922, his illness began with edema of the ankles; his urine contained albumin and blood. There was no history of an infection.

On admission on October 8 there was edema of moderate degree, the blood pressure was 116/70, and the area of cardiac dullness slightly increased. The urine contained 2 gm. of protein per liter, much blood, and many casts. The blood urea nitrogen was 0.4 gm. per liter. Wassermann reaction negative. Red blood corpuscles 3,800,000. Hemoglobin 55 per cent.

The edema rapidly disappeared, his weight falling from 47 kilos to 41 in 7 days. The blood urea nitrogen fell very slowly, being 0.26 gm. in January, 1923, and 0.19 in March. The anemia persisted. Renal function tests showed marked impairment. The urine continued to show protein and casts in large quantities, but the hematuria diminished considerably. The blood pressure did not rise, and no retinal lesions developed. He remained free from edema.

H. L.—Case of nephrosclerosis. The patient, a nervous woman of 29 years, had been ailing since March, 1922. In September raised blood pressure was discovered.

Admitted in November she presented a blood pressure of 215/130 without recognizable cardiac hypertrophy or arterial degeneration. There was a trace of protein in the urine. There were no retinal changes, no edema, and nothing abnormal in the urinary sediment. The blood urea nitrogen was 0.15 gm. per liter, and renal function tests (phthalein, iodide, urea feeding, dilution, and concentration) revealed no impairment of renal function. No focus of infection was found. Wassermann reaction negative. A salt-free diet with moderate amount of protein was given, and she received hot air baths and iodide medication. By the middle of December her blood pressure had fallen to 170.

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