produce acid by the addition of 1 and 100 p.p.m. of NaF. Resistance to the action of fluoride on acid production varied among strains.

2. Continued exposure to 100 p.p.m. NaF lowered the ability of an actively acidogenic strain of lactobacilli to produce acid from glucose. This reduced acidogenic activity continued even in the absence of NaF. One p.p.m. of NaF had no demonstrable effect.

3. One hundred p.p.m. NaF inhibited the dehydrogenases of lactobacilli for 8 out of 9 substrates. The inhibition by 1 p.p.m. was much less.

15953

Effect of the Fat Content of Diets on Blood Sugar.

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The adverse effect of fat feeding on the carbohydrate tolerance of normal persons has been amply demonstrated. Staub[1] and Kageura[2] 25 years ago discovered the fact that healthy men, after being kept on carbohydrate-free meals for 2-3 days, responded to glucose feeding with "diabetic-like" blood sugar-time curves and glycosuria. Himsworth[3] obtained identical results with high fat diets even when including carbohydrates not in excess of 50 g per day. In these studies no attention was paid to the postabsorptive blood sugar level, but the data in the reports of these authors disclosed no rise above the normal level.

Changes in the postabsorptive glycemic level after fat feeding were first reported by F. M. Allen and his associates.[4] Their observations were made on epileptic persons who were fed 260 to 580 g of fat daily, with only 12 to 22 g of protein and 2.5 to 3.7 g carbohydrate. Periodically performed determinations of the plasma sugar showed marked and gradual increases, as for instance (in the most responsive subject) from the initial 135 mg % to 357 mg % in 7 weeks.

Allen's observations, and a number of other studies related to the subject, were carried out under rather extreme experimental conditions. Our interest lay in the effect of high fat diets which, at the time of our studies here reported, were (and very widely still are) prescribed to diabetic patients. Accordingly, the carbohydrate ration was 100-150 g, daily, with unrestricted protein consumption. We selected for the experiment healthy persons, whose carbohydrate tolerance was normal and whose eating habits fitted into a pattern which can be considered as representing the normal, average type. They customarily consumed 80-120 g protein, 80-120 g fat, and 200-300 g carbohydrate. For the experiment the protein was kept at the usual level, the fat was increased to 200-250 g, and the carbohydrate was limited to approximately 100 g. Just prior to changing to the high fat diet the sugar content of the venous blood was determined in the postabsorptive state. In most instances several determinations were made on consecutive days while the subjects were still on the normal diet in order to ascertain the extent of normal fluctuations of the fasting glycemic level. These were very slight, ranging from 0 to 3 mg %, provided that the subjects adhered to a fairly uniform though unmeasured diet.

Since rather slight changes in the blood sugar were to be detected, accuracy of the analytical procedure required special attention. At the time of these studies—1936 and 1938—we used the copper-iodometric

[1] Staub, H., *Z. klin. Med.*, 1922, **93**, 133.

[2] Kageura, N., *J. Biochem.* (Japan), 1922, **1**, 333.

[3] Himsworth, H. P., *Clin. Sci.*, 1933, **1**, 1.

[4] Weeks, D. F., Renner, D. S., Allen, F. M., and Wishart, M. B., *J. Metabol. Research*, 1923, **3**, 317.

TABLE I.
Changes in Postabsorptive Blood Sugar Level of Healthy Persons Under the Influence of High Fat Diets.

Subject	Duration of high fat diet, days	Mg glucose per 100 cc venous blood		Increase, mg %
		On normal diet	After high fat diet	
C.	2	85	96	11
H.	3	87	95	8
T.*	2	72	83	11
M.	3	86	91	5
G.	3	84	89	5
S.	3	87	100	13
R.C.	3	91	100	9
H.K.	2	85	91	6
K.	1	88	94	6
E.S.	2	98	99	1

* Carbohydrate ration was decreased to 50-60 g per day.

procedure of Shaffer and Somogyi[5] with the deproteinization method later described by Somogyi.[6] The results obtained represent true (fermentable) sugar. The accuracy of the technic was within 1-2 mg %; thus any change registered in the blood sugar level, which exceeded 2 mg %, was regarded as representing an actual change.

In Table I are presented 9 cases in which high fat diet, administered for 2-3 days, caused a distinct rise in the postabsorptive blood sugar. As may be noted, the smallest increase was 6, the highest 13 mg %. In the 10th case (the last in Table I) no change had occurred in 2 days. This subject was a heavy eater, accustomed to consuming between 150 and 200 g of fat per day, with the consequence that the addition of an extra 100 g of fat for 2 days constituted a relatively less significant change in his diet and probably for this reason failed to affect his glycemic level. His postabsorptive blood sugar, as may be seen in Table I, was 98 mg % before the experiment. This was already abnormally high, most likely owing to overeating and heavy consumption of fat. (The normal variations range between 70 and 90 mg %, as shown by our statistical material (unpublished) comprising more than 1000 individuals with normal carbohydrate metabolism).

The change in the postabsorptive blood sugar is readily reversed by returning the subject from high fat to his normal diet. The 4 examples recorded in Table II illustrate the reversibility of the process. Return of the blood sugar to normal levels was effected when a high fat regime was followed by 3 days of low fat (60-70 g) diet; then again a rise took place in the blood sugar after another 2 days' course on a high fat regime. It is evident that the postabsorptive sugar level can be shifted back and forth by changing the dietary regime. Increase of the fat ration leads to an elevation, decrease of it to a lowering of the glycemic level.

TABLE II.
Reversibility of the Postabsorptive Blood Sugar Level of Healthy Persons by Changing Diets.

Subject	Mg glucose per 100 cc venous blood on		
	High fat	Low fat	High fat
R.C.	99	91	99
M.S.	98	88	100
H.H.	95	87	93
N.C.	96	85	95

In order to produce an increased blood sugar level by a high fat regime, the carbohydrate ration must not be decreased below 100 g per day; if it is decreased to about 50 g, the postabsorptive blood sugar may or may not increase. In some cases it does increase during the first or second day, but then it usually declines below the normal level. One of our subjects (Dr. T. in Table I who, with a fat ration of 200-250 g, received only 50-60 g of carbohydrate per day) showed a rise of blood sugar on the second

[5] Shaffer, P. A., and Somogyi, M., *J. Biol. Chem.*, 1933, **100**, 695.

[6] Somogyi, M., *J. Biol. Chem.*, 1945, **160**, 69.

TABLE III.
Changes in the Postabsorptive Blood Sugar Level of Diabetic Patients Under the Influence of Low Fat Diets.

Case No.	Date	Blood sugar mg %	Decrease in blood sugar mg %	Case No.	Date	Blood sugar mg %	Decrease in blood sugar mg %
1	5-21-36	174		16	2-13-36	208	
	26	129	45		3- 4	101	107
2	6- 8	122		17	3-26	204	
	11	102	20		4- 8	103	101
3	10-19	137		18	5- 6	245	
	26	114	23		13	153	92
4	11-17	161		19	7-16	264	
	25	85	76		25	168	96
5	3-23-37	123		20	9-18	342	
	26	112	11		25	269	73
6	7-28-38	158		21	11-13	201	
	8- 1	117	41		21	108	93
7	11-22	164		22	3-27-37	222	
	28	145	19		29	173	49
8	1-10-39	110		23	7-24	195	
	17	95	15		28	150	45
9	4-26	135		24	1-27-39	371	
	5- 3	103	32		30	323	48
10	5- 4	171		25	7-19	187	
	10	126	45		25	131	56
11	5-16	147		26	8- 2	255	
	24	119	28		5	181	74
12	7- 8	125		27	10-21	231	
	10	94	31		26	120	111
13	7-11	134		28	11-27	295	
	14	116	18		12- 1	207	88
14	10-17	152		29	3- 1-40	375	
	19	127	25		4	258	117
15	11- 6	111		30	4-27-35	247	
	8	84	27		6- 1	128	119

day of the regime, but a drop to the low level of 64 mg % during the next 2 days.

These experiments were prompted by observations previously made on diabetic patients who showed a substantial decrease in the fasting blood sugar level after being placed on diets which contained 200-300 g of carbohydrate and only 50 g of fat per day. The drop occurred often in 2-3 days, in other instances it required a week or more. Only patients whose diabetic condition was not very severe were thus studied; none who had ketosis was included in the series. This was a necessary condition, since no insulin treatment could be employed during the observations. For the same reasons patients who previously had been accustomed to treatment with large doses of insulin (25 units or more per day), were excluded. Patients with coronary artery disease and passive congestion of the liver were likewise ruled out, as it is known that in this condition the blood sugar may suddenly shoot up to high levels and just as rapidly recede after the correction of cardiac decompensation.

In Table III are recorded 30 examples representative of observations comprising over 400 cases. A substantial decrease of the fasting blood sugar is evident in all instances. In general, 2 factors influence the degree of change: In the first place, the greater the interval of time between 2 sugar determinations, the greater is the drop in the hyperglycemic level. The second factor is the initial glycemic level: the higher this is before the initiation of the low fat diet, the greater will be the drop during a given period.

The effect of low fat diet follows no uniform pattern; in fact it shows great individual variations. There are cases, for instance, in which a change from high fat, low carbohydrate to low fat (50 g), liberal carbohydrate (200-300 g) diet produces an increase in the fasting blood sugar. This is, however, a transitory change, for a few days later the predominating effect of low fat pre-

TABLE IV.
Initial Rise, Followed by Drop of Postabsorptive Blood Sugar Level of Diabetics after Changing from High Fat to Low Fat Diet.

No.	Patient	Date	Blood sugar mg %
1.	E.S.♀	April 22, 1936	325
		" 24	335
		May 8	276
		" 19	170
2.	P.R.♂	June 14, 1939	108
		" 15	124
		" 16	107
3.	G.L.♂	Jan. 8, 1940	187
		" 12	232
		" 16	190
		" 19	171
4.	M.S.♂	Aug. 22	151
		" 23	168
		" 26	140
		" 30	108
5.	M.Se.♂	Dec. 8, 1942	121
		" 9	147
		" 11	127
		" 12	109

vails and the blood sugar follows the usual declining course. Thus the initial rise can be misleading if one observes the changes of the blood sugar only for a few days after the change in diet. In Table IV are recorded a few cases which illustrate this phenomenon. The changes of the postabsorptive blood sugar level under the influence of diet are reversible in diabetic patients in the same way as in the normal: high fat rations, associated with restrictions of carbohydrates, augment the hyperglycemia, while low fat, liberal carbohydrate diets lead to a decrease of the blood sugar.

Summary. 1. Diets containing high fat rations and restricted amounts of carbohydrates increase the postabsorptive (fasting) blood sugar level. 2. This change takes place in healthy and diabetic individuals alike, with the difference that it is much more accentuated and obvious in the diabetic organism. Thus, the physiologic processes in the healthy and in the diabetic individual are qualitatively identical, but in the diabetic they are greatly exaggerated (Claude Bernard); in other words, the difference between the normal and the diabetic individual, in regard to the physiologic process described, is only of degree but not of kind.

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Effect of Rutin on Induced Proteinuria in Albino Rats.*

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Various reports have appeared in the recent literature concerning the ability of the flavone, rutin, to decrease capillary permeability. These publications are somewhat at variance with one another, and many of them deal with qualitative data. Since the permeability of the glomerular capillaries is one of the factors which influence the rate of protein excretion in the urine, and since it has been claimed that rutin changes capillary permeability, a quantitative study was undertaken to determine the effect of large doses of rutin on the rate of protein excretion following parenteral administration of bovine albumin to albino rats.

A total of 84 healthy albino rats, of both sexes, was selected at body weights of approximately 150 g each. These were separated into 4 groups, rats within each group being of the same sex. During the 72 hours of the experimental period following the initial administration of albumin all rats were kept in urine collection cages and were fed 10% dextrose in water containing 0.4% sodium chloride and vitamins of the B com-

* The bovine albumin used in these experiments was obtained through the courtesy of Dr. J. D. Porsche from the Armour Laboratories.

The rutin used was supplied by the Abbott Laboratories.