Immunoreactive Insulin, Glucose Tolerance, and Carbohydrate Inducibility in Types II, III, IV, and V Hyperlipoproteinemia

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SUMMARY

The elevation of plasma glycerides by a high carbohydrate diet (carbohydrate induction) has been systematically correlated with glucose tolerance, insulin output and ponderal index in normals and in patients with different types of hyperlipoproteinemia. Carbohydrate inducibility (ΔTG) was similar in normals and patients with Type II hyperlipoproteinemia. Delta TG was nearly always much greater than normal in Type III, and was quite heterogeneous in type IV. The scatter in ΔTG values in Type V patients was extremely great. The basal triglyceride and ΔTG were positively correlated only in Type IV.

Abnormal glucose tolerance was present in approximately one third of Types II and III, one half of Type IV and 80 per cent of Type V patients.

Hyperinsulinemia was present in most Type V patients, while a majority of Type II and III patients had relatively normal insulin levels. Approximately one third each of the Type IV patients had low, normal, and abnormally high insulin levels. Increasing insulin and insulinogenic indices were correlated with increased ΔTG in the normal, but not in any of the patient groups. In the specific groups of hyperglyceridemic patients in this study, plasma insulin levels did not appear to be a primary determinant of the degree of carbohydrate induction. DIABETES *18*:739-47, November, 1969.

The phenomenon of "carbohydrate induction" of hypertriglyceridemia[1] refers to an increase in plasma triglyceride concentrations occurring when a diet very high in carbohydrate is substituted for either a normal diet or one in which most of the calories come from fat. The increase in glycerides with carbohydrate feeding has been observed in normal subjects and in patients with hypertriglyceridemia. The degree of carbohydrate induction has been correlated with glucose intolerance[2-5] and sometimes considered to be dependent upon hyperinsulinemia.[2,3,5]

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In this report we describe a systematic study of the intercorrelations of dietary responses to carbohydrate feeding, glucose tolerance, and plasma insulin in patients with familial Types II, III, IV, and V hyperlipoproteinemia[6] and in a small group of normal subjects. In general, the lipid abnormalities were found to be largely independent of abnormalities of carbohydrate metabolism.

MATERIAL AND METHODS

Patients with hyperlipoproteinemia

One hundred and seven patients with Types II, III, IV, and V hyperlipoproteinemia were studied. The patients had been classified according to a system employing paper electrophoresis, measurement of cholesterol and triglyceride concentrations, and preparative ultracentrifugation.[6] The diagnoses of hyperlipoproteinemia were made following a week or two of a normal diet, with weight stable. Each patient was judged to have primary hyperlipoproteinemia after hepatic[7] or renal disease,[8,9] hypothyroidism,[8,10] and other disorders known to produce hyperglyceridemia[11-15] were excluded. The patients were not preselected on the basis of obesity or glucose intolerance. All the available relatives of these patients had been sampled; of the seventy-six probands with Types II, IV, and V hyperlipoproteinemia,[6] one or more relatives of seventy also had the characteristic abnormal lipoprotein pattern. The remaining thirty-one patients had Type III hyperlipoproteinemia. This disorder is apparently recessive[6] and a first degree relative of only eighteen could be found with the identical lipoprotein anomaly. The other Type III probands had the "phenotypic" lipoprotein pattern and other clinical abnormalities of this type.[16] No patient had previously received insulin. Diabetes, when present, was controlled by diet; no patients were taking oral hypoglycemic agents at the time of this study.

The twenty-seven patients (fifteen males, twelve females) with Type II hyperlipoproteinemia had increased

beta lipoproteins.[6] The beta lipoprotein cholesterol in each exceeded > 210 mg. per 100 ml. Six of them also had triglyceride concentrations above the normal levels for age-matched controls[6] and concomitant minor increases in pre-beta lipoproteins. The thirty-one patients (twenty-two males, nine females) with Type III hyperlipoproteinemia were characterized by an abnormally broad beta lipoprotein band on paper electrophoresis and a beta migrating lipoprotein in the D < 1.006 fraction obtained after ultracentrifugation.[6,16] The thirty-six Type IV subjects (thirty-one males, five females) had hyperglyceridemia with an increased concentration of pre-beta lipoproteins. The thirteen patients (nine males, four females) with Type V hyperlipoproteinemia had both visible chylomicrons and increased pre-beta lipoproteins in plasma obtained after an overnight fast.

Normal subjects

Twenty-three normal controls were also studied and fell into two age groups (tables 1 and 2). The "young" normals included five males and eight females from eighteen to twenty-three years of age. The "middle-age" normals, recruited from local community health associations, included six females and four males whose ages ranged from forty to fifty-eight years. All of these had normal thyroid, renal, endocrine, and cardiovascular function as determined by routine inpatient examinations and normal fasting blood glucose levels. Cholesterol and triglyceride levels after a week of normal diet were well within levels used by this laboratory to define normal limits.[6]

Procedures

The patients and controls were admitted to the Clinical Center and were ambulatory throughout the study period. An index measurement of cholesterol and triglyceride was obtained at or before the time of admission, with the patients at a constant weight, off therapy, and on an ad libitum diet (table 1). All 130 subjects were then placed on a basal diet providing approximately 20, 40, and 40 per cent of calories as protein, carbohydrate, and fats, respectively. The fats provided a P/S ratio of approximately 2.0 and the diet contained less than 300 mg. cholesterol per day. This diet was continued for a minimum of one week. In seventy-five subjects (table 1) the basal diet was then replaced by one providing approximately 80 per cent of calories as carbohydrate (7 gm. carbohydrate/kg./day) and 1 per cent as fat. This high carbohydrate diet was fed for seven days. The carbohydrate consisted of mixed simple sugars, complex sugars, and starch. The cholesterol content was negligible. On both diets calories were continually adjusted to maintain weight within ± 0.5 kg.

On the fourth day of the high carbohydrate diet, an oral glucose tolerance test was carried out with administration of 100 gm. glucose in a prepared drink. Concentrations of plasma glucose[17] and serum immunoreactive insulin[18] were determined on the initial and

TABLE 1

Mean ± S.D.M. values for measured variables for all individuals given the high carbohydrate diet

Patient type	Number of patients	Index TG* (mg./100 ml.)	TG_B† (mg./100 ml.)	Index cholesterol	△TG‡ (mg./100 ml.)	Glc.§ (mg./100 ml.)	IRI‖ (μU./ml.)	MSI**	SI††	PI‡‡
Young normals	13	69±17	63±17	165±14	58±45	92±6	38±17	.42±.2	2.4±1.1	12.8±.4
Middle-aged normals	10	95±40	83±35	202±38	101±65	104±9	70±25	.71±.3	3.1±2.1	12.7±.4
II	8	148±79	141±44	367±51	117±64	106±9	79±53	.80±.5	3.0±2.3	12.6±.6
III	14	574±352	365±213	335±81	430±208	129±55	71±34	.64±.4	2.1±1.3	11.6±.9
IV	20	396±249	280±149	256±44	270±153	132±31	76±54	.64±.39	1.8±1.0	12.3±.5
V	10	1,873±1,143	1,535±1,648	307±122	35±1,087	126±23	118±50	1.1 ±.5	3.3±2.3	12.3±.4

*Index triglyceride.
†Basal triglyceride.
‡Carbohydrate induced increment in TG (highest TG during seven days high carbohydrate diet minus TG_B).
§Mean glucose.
‖Mean insulin.
**Modified Seltzer insulinogenic index.
††Seltzer insulinogenic index.
‡‡Ponderal index.

TABLE 2

Mean ± S.D.M. values for measured variables in all normals and patients

Patient type	Sex M	Sex F	Number of pts.	Age in yrs. Mean range	IRI* (μU./ml.)	Glc.† (mg./100 ml.)	PI‡	MSI§	SI‖
Young normals	5	8	13	19 (18-23)	38±17	92±6	12.8±.4	.42±.2	2.4±1.1
Middle-aged normals	6	4	10	49 (40-58)	70±25	104±9	12.7±.4	.71±.3	3.1±2.1
II	15	12	27	43 (18-65)	60±47	110±5	12.7±.9	.48±.4	2.2±1.8
III	22	9	31	43 (26-62)	57±32	118±40	12.1±.8	.56±.3	2.4±1.8
IV	31	5	36	42 (37-64)	65±46	129±31	12.5±.7	.56±.4	1.7±1.0
V	9	4	13	44 (27-51)	106±52	125±21	12.3±.6	.99±.6	3.0±2.3

*Mean insulin.
†Mean glucose.
‡Ponderal index.
§Modified Seltzer insulinogenic index.
‖Seltzer insulinogenic index.

30, 60, 90, 120, 180, and 240-minute samples during the glucose tolerance test. Fasting blood samples were drawn every other day during the basal diet period, and daily during the high carbohydrate diet. Triglyceride[19] and cholesterol[20] concentrations and lipoprotein electrophoretic patterns[21] were obtained on each sample.

All of the remaining fifty-five patients were changed from the basal diet to one moderately high in carbohydrate (300 gm./day). On the fourth day of this diet glucose tolerance tests were carried out. Thus glucose tolerance and insulin response were measured in all 130 subjects (table 2), and the response of plasma glycerides to seven days of carbohydrate feeding determined in seventy-five subjects (table 1).

Glucose tolerance tests were done in fourteen subjects on both the high carbohydrate and 300 gm. carbohydrate diets. Glucose tolerance tests and insulin responses obtained after the two preparative diets did not differ significantly.

Analytical procedures

All bloods for serum immunoreactive insulin measurement were drawn in glass syringes, allowed to clot at 4° C. and centrifuged in the cold. The serum was then stored frozen if not assayed immediately. The double antibody radioimmunoassay of Soeldner and Sloane[18] was used, employing I-125-labeled porcine insulin (Isoserve, 50 μc./μg.), standard porcine insulin 23.5 U./mg. (kindly supplied by Dr. O. Behrens, Lilly Pharmaceuticals, Indianapolis) and anti-insulin serum (Sylvana, Millpath, New Jersey) used at a dilution of 1:350. Under these conditions, the standard curve of binding of crystalline insulin to antibody was linear between 5 and 120 μU. of insulin per ml. Insulin was measured in duplicate samples and samples for standard curves were analyzed in triplicate. Variations between samples were less than 5 per cent. Recovery of known amounts of crystalline insulin added to serum samples was at least 90 per cent on each assay run. Standard samples of known insulin content were measured during each assay, and varied less than 6 per cent from assay to assay.

Definition of terms

The index cholesterol and triglyceride (table 1) represent the respective lipid concentrations measured initially when the patient had been eating a normal diet, holding steady weight, and taking no medication. TG_B is the triglyceride concentration on the final day of basal diet. Delta TG represents the difference between TG_B and the highest triglyceride concentration obtained during seven days of the high carbohydrate diet. In twenty-one of forty-two Types II, III, and IV patients and in nineteen of twenty-three normals, triglyceride reached a peak concentration before the final day of carbohydrate feeding. In seven normals and six patients the peak triglyceride concentration occurred by day five.

Glucose (Glc) is the arithmetic mean of plasma glucose concentrations measured during the four-hour oral glucose tolerance test. IRI is the arithmetic mean of insulin concentrations measured at the following intervals during the glucose tolerance test: 0, 30, 60,

90, 120, 180, and 240 minutes.

Two insulinogenic indices were calculated. One index was calculated by the method of Seltzer (SI) for the six cumulative area ratios of insulin:glucose[22] during the oral glucose tolerance test. The other was a modified index (MSI), calculated by dividing the total area under the insulin curve by the total area under the curve of glucose concentrations. The areas subtended by insulin and glucose concentration were calculated by smoothing and numerical integration. Ponderal index (PI)[23] was calculated for each patient at the end of the control dietary period.

Statistical analysis

Relationships between the measured variables were determined from simple correlation matrices. The correlation coefficients are summarized in table 3.

RESULTS

The mean (± 1 S.D.M.) values obtained for all variables in patients given the high carbohydrate diet (7 gm. carbohydrate/kg./day) are summarized in table 1. All of the patients with Types III, IV, and V had index triglyceride values above those arbitrarily defined as normal in our laboratory.[6] TG_B was measured after one week of the basal diet in the hospital and reflected the decrease in triglycerides often seen in hyperglyceridemic patients after hospitalization without specific change in diet. The mean TG_B was lowered 30 and 37 per cent, respectively, in Types IV and III, from index triglyceride levels.

Absolute carbohydrate induction

The degree of carbohydrate induction (ΔTG) expressed in absolute terms varied greatly between groups and between individuals in the same group (tables 1 and 4, figure 1). The mean ΔTG in the young normal group was 58 mg. per 100 ml. This was about half of the mean in the middle-age normal and Type II

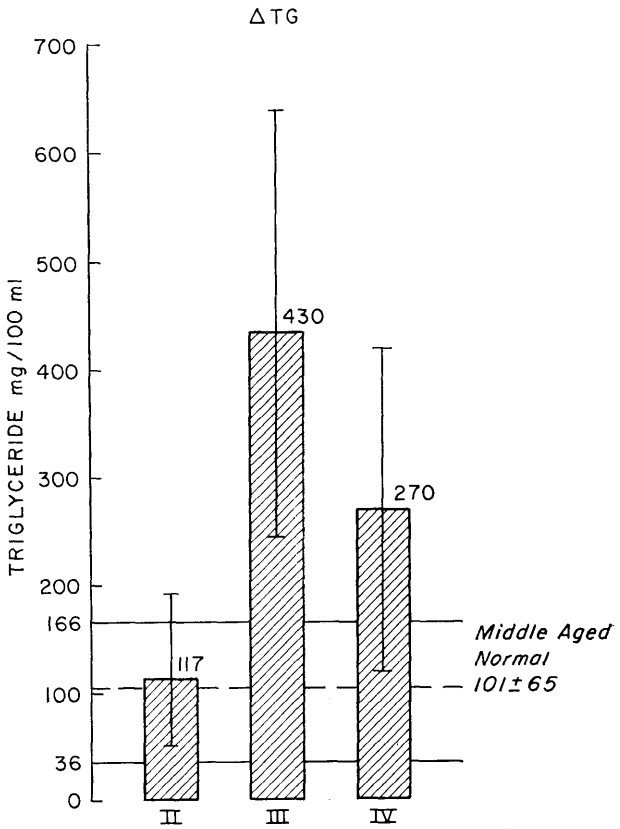

FIG. 1. Triglyceride response to high carbohydrate diets (> 7 gm. CHO/kg./day expressed as increment in triglyceride above the baseline (ΔTG).

TABLE 3

Correlations between measured variables in patients and normals given high carbohydrate diets

Group	No. of subjects	Glc/ΔTG	Glc/TG_B	IRI/ΔTG	IRI/TG_B	TG_B/ΔTG	MSI/ΔTG	SI/ΔTG	PI/ΔTG	PI/TG_B
II	8	*.714*†	.481	—.20	—.378	.482	—.267	—.677*	—.02	.150
III	14	.304	*.588*†	.05	—.277	.127	.02	.176	—.446	.07
IV	20	.090	.320	—.31	.382*	*.483*†	—.32	—.12	—.01	.112
V	10	.107	.256	.193	.161	—*.84*‡	—.02	.02	—.155	.205
Middle-aged normals	10	—.165	.286	*.632*†	.106	.236	*.632*†	.273	—.538	.266
Young normals	13	—.368	—.173	*.615*†	.547*	.417	*.658*†	*.745*‡	.195	.433

*p < .1.
†p < .05.
‡p < .01.

TABLE 4

Delta TG and per cent triglyceride rise ($\Delta TG/TG_B$) on high carbohydrate diets (ΔTG mg./100 ml.) ($\Delta TG/TG_B$ per cent)

Group	Young normals		Middle-aged normals		II		III		IV		V	
	ΔTG	$\Delta TG/TG_B$	ΔTG	$\Delta TG/TG_B$	ΔTG	$\Delta TG/TG_B$	ΔTG	$\Delta TG/TG_B$	ΔTG	$\Delta TG/TG_B$	ΔTG	$\Delta TG/TG_B$
	—21	33.3	28	41	40	25	72	36	69	54	—2,445	—42
	17	30	46	52	52	37	174	48	88	64	—630	—23
	24	39	55	93	80	121	221	91	91	59	8	.7
	29	47	78	107	112	118	245	122	104	41	44	63.2
	35	52	87	76	118	76	294	37	142	131	75	18.2
	43	100	100	65	135	80	339	112	180	110	165	19.2
	53	79	101	326	170	129	424	78	189	58	317	25
	68	126	111	202	234	111	508	326	200	111	700	94
	69	172	154	175			532	224	206	35	1,900	211
	75	100	253	250			568	338	228	197		
	106	177					582	73	236	133		
	124	203					594	141	244	98		
	137	126					700	254	258	80		
							758	182	348	94		
									400	150		
									404	66		
									446	91		
									461	144		
									524	213		
									576	178		
Mean ±1 S.D.M.	58±45	99±59	101±65	139±96	117±64	87±40	430±208	147±103	270±153	105±52	35±1,087	41±76

patients. The mean ΔTG was considerably higher in Type IV (270 mg. per 100 ml.) and the highest mean was obtained in Type III patients (430 mg. per 100 ml.).

The cumulative distribution of ΔTG in both groups of normals was plotted and a normal distribution of this variable was obtained. For purposes of comparison an upper limit of normal was then arbitrarily chosen as the mean + 2 standard deviations of the ΔTG observed in the ten middle-age normals (231 mg. per 100 ml.). By this standard, ΔTG of almost all Type II's (seven of eight) and half of the Type IV patients (ten of twenty) was normal. Delta TG in ten of the fourteen Type III patients exceeded the highest ΔTG seen in the middle-aged normal group (table 4).

The scatter in ΔTG values in the ten Type V patients was extremely great, varying from —2,445 to +1,900 mg. per 100 ml. (table 4). This variability is inherent in the dual defect which characterizes these patients. The basal diet contained enough fat to maintain or sometimes increase their exogenous hypertriglyceridemia (chylomicronemia). When they were changed to the high carbohydrate diet, which contained almost no fat, the chylomicrons abruptly decreased and the triglyceride concentrations fell. Later pre-beta lipoproteins increased in all, but to a highly variable degree.

Relative carbohydrate induction

The triglyceride responses on the high carbohydrate diet were also evaluated in terms of the percentage rise of triglycerides ($\Delta TG/TG_B$). In Types II, III, and IV the mean percentage increase in triglycerides did not differ significantly from that of the middle-age normal group (by t test). Only in the Type IV patients was there a positive correlation ($p < .05$) between individual TG_B and ΔTG values (table 3). In the Type V patients there was a highly significant negative correlation ($p < .01$) between TB_B and ΔTG, reflecting the initial decrement in triglycerides following the change to the high carbohydrate diet.

Glucose tolerance

Two separate criteria of abnormal glucose tolerance were used. The first (Fajans and Conn[24]) identified as abnormal the combination of a one-hour glucose level of 160 mg./100 ml. or above, plus a two-hour value of 120 mg./100 ml. or above. In borderline curves, a ninety-minute value of 140 mg./100 ml. or more was additionally required to identify abnormal glucose tolerance. The second criterion used was that of Bagdade.[25] The mean area circumscribed by the blood glucose time curve was determined by computer calculation (smoothing and numerical integration). Glucose area determinations that were greater than 2 S.D.M. above the mean determination for the pooled normal group ($N = 23$), were judged abnormal. There was excellent agreement between these two criteria. Abnormal oral glucose tolerance tests were observed by both methods

in nine of twenty-seven (33 per cent) of Type II, twelve of thirty-one (39 per cent) of Type III, nineteen of thirty-six (52 per cent) of Type IV and ten of thirteen (77 per cent) of Type V patients.

Insulin concentrations

Mean insulin concentrations for patients with Types II, III, and IV were similar to those of the middle-age normals (tables 1 and 2). The mean insulin level in the Type V patients was almost twice as high as values in other groups. A possible relationship between glucose and insulin concentrations during the oral glucose tolerance test was explored by using three different indices of insulin secretion. For two of these, the insulinogenic index calculated by the method of Seltzer[22] and the modified insulinogenic index, values deviating more than one standard deviation from the mean values of all the twenty-three normal controls combined were arbitrarily considered relatively high or low. In the third method plasma insulin responses were compared to glucose concentrations observed at corresponding times during the glucose tolerance test. Mean insulin concentrations obtained for all twenty-three normals at each individual time point during the GTT were used as a basis for intergroup comparison. Insulin output was considered to be relatively high when insulin levels at three points in time during the oral GTT were more than 1 S.D.M. above comparable mean levels for all normals. When the glucose tolerance test was abnormal, insulin output was considered to be relatively low if insulins at three or more points in time were below comparable mean values for normals. Fasting insulin levels were not considered in this third method of grading.

In all instances, the classification of insulin response as relatively normal, low or high was similar, regardless of which of these three methods were used. Insulin output in eighteen of twenty-seven Type II subjects was normal; seven were low and two high (figure 2). Seventeen of thirty-one Type III patients had normal, seven low, and seven high insulin responses. Thirteen of thirty-six Type IV patients had low insulin responses, fourteen were normal, and nine high. Ten of thirteen Type V patients had relatively high IRI; two were low, one normal.

Correlations between measured variables in patients and normals given high carbohydrate diets

In patients with Type II hyperlipoproteinemia there was a moderately significant ($p < .05$) correlation between Glc and ΔTG (table 3). Similar correlations were not obtained in any other group, or in normal

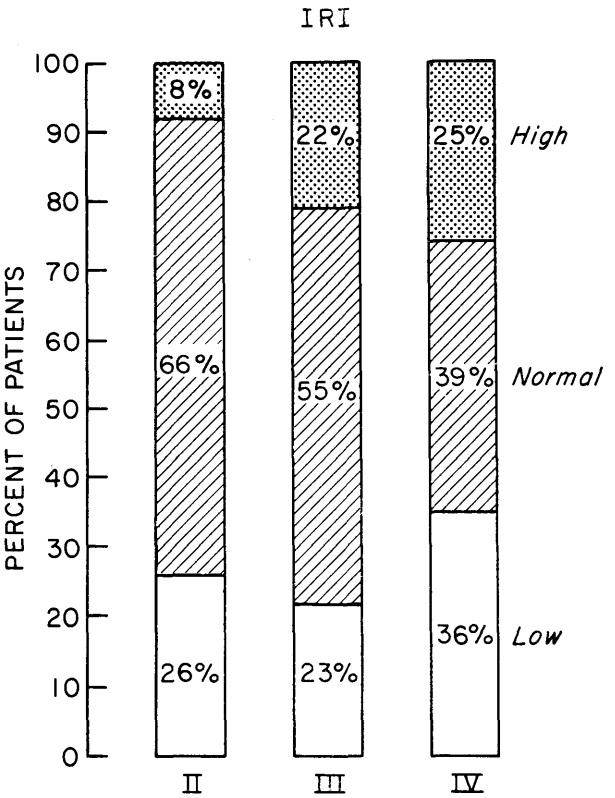

FIG. 2. Immunoreactive insulin (IRI) in Types II, III, and IV hyperlipoproteinemia.

subjects. In Type III patients, a positive correlation between Glc and TG_B was not coupled with a Glc: ΔATG correlation.

A positive correlation ($p < .05$) between ΔTG and IRI was obtained for both normal groups, but not in any patient group (table 3). It will be noted (table 5) that of the Type IV patients with "normal" ΔTG as defined before, seven of ten were relatively hyperinsulinemic. None of these ten subjects had low insulin output. On the other hand, of the ten subjects who had abnormally high ΔTG, four had low insulin responses, and only two were hyperinsulinemic.

In addition to the significant positive correlation between IRI and ΔTG in both normal groups, the modified insulinogenic index and ΔTG were similarly correlated. The Seltzer index and ΔTG were also significantly correlated ($p < .01$) in the young normals. In none of the patient groups, however, were IRI or the several insulinogenic indices significantly correlated with ΔTG.

Ponderal index was not significantly correlated with any of the measured variables in the patient or normal groups.

TABLE 5

Glucose tolerance, insulin response and carbohydrate inducibility in Type IV subjects

ΔTG	Patient	Glucose tolerance	Insulin response	ΔTG
Normal*	1	Abnormal	High	69
	2	Abnormal	High	88
	3	Normal	Normal	91
	4	Abnormal	High	104
	5	Normal	Normal	142
	6	Abnormal	High	180
	7	Abnormal	High	189
	8	Normal	High	200
	9	Abnormal	High	206
	10	Normal	Normal	228
Abnormal†	11	Abnormal	Low	236
	12	Abnormal	High	244
	13	Abnormal	Low	258
	14	Normal	Normal	348
	15	Normal	Normal	400
	16	Abnormal	High	404
	17	Abnormal	Low	446
	18	Normal	Normal	461
	19	Abnormal	Low	524
	20	Normal	Normal	576

*ΔTG < mean + 2 S.D.M. of that obtained in middle-age normals (231 mg. per 100 ml.).
†ΔTG > mean + 2 S.D.M. of that obtained in middle-age normals.

DISCUSSION

There are a number of factors which make it difficult to agree upon a firm definition of "normal" carbohydrate induction. The present study and others previously reported[26-30] have involved the feeding of radical diets of somewhat different composition for different periods of time. There also seems to be inherent variability in the response of individuals even on the same regimen. As observed here, this includes some dependence of ΔTG upon age. Twenty-two of the twenty-three normal controls in this study exhibited a rise in plasma triglycerides of 24 to 253 mg. per 100 ml. within seven days after beginning a diet high in carbohydrate. In a previous study conducted in this laboratory[29] the mean ΔTG was 224; one subject had a ΔTG of 404 mg. per 100 ml. and it was suggested that the latter might have to be considered the "upper limit" of the normal response. In the present experiments, both the mean ΔTG and the maximum response were considerably lower. In general, our present data are in accord with a previous conclusion drawn from available studies by Bierman and Porte[30] that the mean glyceride concentration in a group of normals will be approximately doubled after changing the percentage of calories derived from carbohydrate from 40 to 80 per cent.

This study was undertaken to provide additional quantification of carbohydrate inducibility in patients with hyperlipoproteinemia and to determine whether carbohydrate inducibility correlated well with measures of carbohydrate metabolism. The present findings do not allow, however, for any generalization about carbohydrate induction, as defined here, to be applied to all patients with either endogenous (Type IV) or mixed endogenous and exogenous hyperglyceridemia (Types III and V). While ΔTG was nearly always much greater than normal in Type III, it was quite heterogeneous among Type IV patients. In some ΔTG, in absolute or in relative terms, was within the normal range (tables 4, 5). Only in Type IV patients was there a significant correlation between ΔTG and TG_B. The ΔTG was completely unpredictable in Type V.

Abnormalities of carbohydrate tolerance have previously been correlated with hyperglyceridemia and carbohydrate induction.[2,4,5] Although 39 per cent of the Type III, 52 per cent of the Type IV, and 77 per cent of the Type V patients had abnormal glucose tolerance tests, there were few significant correlations between carbohydrate inducibility and measures of glucose intolerance. The integral rise in glucose concentration after the oral glucose load (Glc) was directly correlated with TG_B in Type III, and with ΔTG in Type II patients (table 3). There were no highly significant correlations between ΔTG and the insulinogenic indices in the patient groups.

Circulating insulin levels have also been correlated with carbohydrate induction.[2,3] The mean absolute insulin (IRI) response to the oral glucose challenge was similar in normals and each patient group except Type V. A majority of the latter type had absolute hyperinsulinemia. IRI was quite variable in the Type IV patients; approximately one third were low, normal or high. Low IRI was particularly common in the Type IV patients who had increased carbohydrate inducibility (table 5). This is in contrast to previous studies[2,3] where no patients with endogenous hypertriglyceridemia and "abnormal ΔTG" were found to be hypoinsulinemic.

It is noteworthy that our patients with hyperglyceridemia included many with mature-onset diabetes. Their variable insulin responses are in accord with those previously reported in such diabetics by Seltzer et al.,[22] Yalow and Berson,[31] Buchanan[32] and Perley and Kipnis.[33]

There were consistent positive (and significant) correlations between IRI or the insulinogenic indices and ΔTG in both normal groups. There was no such

correlation in any of the groups of patients. Perhaps in normals insulin levels do affect triglyceride output from the liver, as has been demonstrated in vitro with liver slices.[34] When hyperglyceridemia is present, the situation may become more complex. Deficiencies in peripheral glucose metabolism may lead to less effective removal of glyceride from plasma.[35]

A third factor often related to hyperglyceridemia is relative obesity.[30] Basal glyceride concentrations decline with caloric restriction in most patients with hyperglyceridemia. Obesity exaggerates carbohydrate inducibility and carbohydrate intolerance.[30,35A,36] The means and ranges of the ponderal indices (PI) in our patients were very similar (tables 1, 2). Few were definitely obese, and the over-all sample may not have offered a wide enough range to test sufficiently the relationship of PI to ΔTG. PI did not correlate with the basal triglyceride levels or ΔTG. A similar lack of correlation had previously been reported in hyperglyceridemic patients by Reaven et al.[3] Other reports have directly related obesity to hyperglyceridemia,[5,35A] noting primarily the decrease in triglyceride concentrations during and following weight loss.[30,36-38]

These studies have thus examined the effects of highly experimental diets on glyceride concentrations in patients further selected by differences in lipoprotein patterns. It remains to be demonstrated unequivocally that altering the amount of carbohydrate in the diet over a practicable range of 30 to 50 per cent of total calories produces a sustained lowering of glycerides in such patients. There is a similar lack of firm data supporting a predictable and sustained effect of substitution of one type of carbohydrate for another.[39] From a practical standpoint, however, one is often forced to try relatively minor changes in dietary carbohydrate in the management of a patient with hyperglyceridemia. The identification of the several different types of hyperlipoproteinemia can be helpful in determining the degree of concern with dietary carbohydrate that is appropriate for a given patient. Moderate hyperglyceridemia in familial Type II hyperlipoproteinemia is very likely to have little dependence upon dietary carbohydrate; in Type III high carbohydrate intake will usually produce a profound elevation in triglycerides. Recommendations in Type IV patients can perhaps be made less empirical by further identification of those with low insulin output and glucose intolerance. They may represent a subgroup in which measures to improve glucose tolerance and elevate insulin levels have the greatest likelihood of leading to a decrease in triglyceride concentrations.[40-43]

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