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Splanchnic Secretion Rates of Plasma Triglycerides and Total and Splanchnic Turnover of Plasma Free Fatty Acids in Men with Normo- and Hypertriglyceridaemia

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Abstract. Plasma triglyceride (TG) "turnover rates" were estimated in the fasting state in three different ways: splanchnic chemical TG secretion, splanchnic isotope TG secretion and plasma TG clearance. Forty-two men with a wide range of fasting plasma TG concentrations, from 0.53 to 16.50 mmol/l were investigated. A constant intravenous infusion of albumin-bound ^{3}H-labelled palmitate was given and blood was simultaneously sampled from the hepatic vein and an artery for determination of hepatic venous-arterial differences of labelled and unlabelled plasma TG. In addition total and splanchnic turnovers of plasma FFA were measured. Similar values were obtained for plasma TG "turnover rate" by the splanchnic chemical TG secretion and the plasma TG clearance method. The values for these two methods varied between 3 and 74 μmol/min. and m^2 body surface area, except for two cases who had considerably higher values. The splanchnic isotope TG secretion method gave lower values varying from 1 to 34 μmol/min. and m^2 body surface area. This method probably measures only that fraction of the splanchnic TG secretion which is derived from plasma FFA. No correlations were found among normotriglyceridaemic subjects between plasma total TG or VLDL-TG concentrations and plasma TG "turnover rates" measured by any of the three methods. For patients with hypertriglyceridaemia significant positive correlations were found between plasma VLDL-TG concentrations and plasma "turnover rates". The "fractional turnover rate" decreased with increasing TG levels in an apparently hyperbolic fashion. The results suggest an impaired plasma TG removal capacity in patients with hypertriglyceridaemia. In 7 out of 14 patients the plasma TG "turnover rates" were in the upper part of the normal range and seemed to have contributed to the hypertriglyceridaemia in these patients. Plasma FFA turnover rate ranged between 102 and 439 μmol/min. and m^2 body surface area. On the average splanchnic FFA mobilization and uptake were about 30 and 60 per cent respectively of total FFA turnover rate. Significant positive correlations were found for the interrelationships between the three plasma FFA total and splanchnic transport parameters. Significant positive correlations were found between the three plasma TG "turnover rates" and total and splanchnic turnover of plasma FFA in subjects with normal plasma TG concentrations. Some patients with hypertriglyceridaemia fell outside the intervals of 99 per cent confidence of the regression analyses for the normo-triglyceridaemic subjects. This group had higher TG "turnover rates" than "expected" from plasma FFA turnover rates and may represent a distinctive group of hypertriglyceridaemia from the point of view of pathogenesis. It was concluded that all patients with hypertriglyceridaemia who were investigated had decreased "fractional turnover rates" of plasma TG indicating a decreased removal capacity which might be a primary cause of the hypertriglyceridaemia although inflow of plasma TG seemed to be an essential contributing factor in half the number of patients.

Key words: Plasma triglycerides. Plasma free fatty acids. Palmitic-9,10-^{3}H acid. Turnover rate. Splanchnic plasma triglyceride secretion rate. Plasma triglyceride removal. Plasma triglyceride turnover (rate). Hepatic venous-arterial difference of triglyceride concentration. Plasma free fatty acid turnover (rate). Splanchnic mobilization of free fatty acids. Splanchnic uptake of free fatty acids.

Introduction

The albumin-bound free fatty acids (FFA) and the triglycerides (TG) of the very low density lipoproteins (VLDL) are the two main forms in which fatty acids are transported in blood in fasting man. This has been the subject of several reviews in recent years [1–5]. The splanchnic region plays an important part in regulating the plasma concentrations of both FFA and TG in man. Fatty acids are mobilized from splanchnic adipose tissue and this is an important source of plasma FFA [6]. The liver is the main site of synthesis and secretion of plasma TG during the fasting state ([3, 7]).

Increased concentrations of VLDL-TG in man, i.e. hypertriglyceridaemia, is an abnormality seen in patients with different kinds of hyperlipoproteinaemias. The lipoprotein patterns in hypertriglyceridaemia may be of types II B, III, IV or V [8]. Hypertriglyceridaemia occurs in many patients with clinical manifestations of atherosclerosis [9, 10] but also occurs in patients without symptoms. The pathogenesis of increased levels of VLDL-TG is not known. In principle however, they may result from either increased secretion into or decreased removal from plasma of TG. Both mechanisms may also operate together. We have developed methods for measuring splanchnic secretion rates of plasma TG and splanchnic turnover of FFA [6, 11, 12]. These methods have been used in this work to see if hypersecretion or decreased removal of plasma TG is the major cause of hypertriglyceridaemia in man.

Methods

Subjects and Experimental Procedure

The subjects were 42 men between 25 and 65 years old and were either blood donors or patient volunteers. The patients came from the internal medicine outpatient department at either the Karolinska or Löwen-

strömska Hospital. No previous dietary modifications were made because of the study. All patients had had a fasting plasma TG concentration above 2 mmol/l at least once prior to the study. None had either overt diabetes mellitus (as judged by the absence of glucosuria and by a fasting blood sugar below 105 mg/100 ml), or any other endocrine disorder as judged by history and physical signs. For the purpose of analysis of data subjects were devided into "normal" and hypertriglyceridaemia on the basis of values for plasma TG concentration in the Stockholm population [13] (see further under Calculations and Definitions).

The procedure was performed in the morning after the over-night fast and has been described in detail [6]. During the study the subjects were at rest in the supine position. Catheters were introduced percutaneously first into a cubital vein of the left arm for infusion of albumin-bound tritiated palmitate and Indocyanine green, and then into an artery in the same arm for arterial blood sampling. The arterial catheter was kept patent by flushing with saline after the withdrawal of each sample.

An arterial blood sample (30 ml), called the zero sample, was taken for the determination of serum lipoproteins, plasma TG, cholesterol and FFA before the infusion of albumin-bound ^{3}H-9,10-palmitate (New England Nuclear Chemicals GmbH, Frankfurt) at a rate of 0.28 ml/min was started. The start of the infusion is referred to as zero time. Arterial blood samples (10 ml) were taken at 60 and 120 min. for determination of plasma TG concentration. At about 120 min. the hepatic vein was catheterized from a right cubital vein under fluoroscopic guidance. This catheter was connected to a slow rate saline infusion. No heparin was given during the study which lasted for about four hours. At 150 min. a primer dose of 15 mg Indocyanine green (Cardio-Green, Hynson Westcott & Dunning Inc., Baltimore) was given intravenously followed by a constant infusion at a rate of approximately 0.6 mg/min. At 180, 210 and 240 min. blood samples of 50 ml were taken simultaneously from the artery and the hepatic vein at the same rate, sampling generally lasting 1–2 min. The concentration of Indocyanine green, plasma FFA, TG and glycerol and ratio-activity of plasma FFA and TG were estimated on these samples. In each study two measurements (at 180 and 240 min.) were made of hepatic venous-arterial TG concentration and three measurements (at 180, 210 and 240 min.) were made of the same difference in TG radio-activity.

At the end of the study the blood plasma volume was determined using ^{131}I-albumin [14].

Analytical Methods

Blood samples were transferred to dry heparinized tubes and kept on ice until the study was completed. Plasma was separated from blood cells by centrifugation at about 250 g for 10 min. at 4° C and then either processes immediately or stored for a few hrs at 4° C.

FFA concentrations were determined on four replicates of each sample according the to method of Dole [15] with the modification described by Trout *et al.* [16]. Glycerol analyses were also made on four replicates of each sample according to Wielend's method [17].

For the determination of TG concentrations ten isopropanol extracts of each sample were prepared. On each extract glyceride glycerol together with the smaller amount of free glycerol was assayed in triplicate using a Technicon Auto Analyzer [18]. The plasma TG concentrations were obtained by substracting the corresponding free plasma glycerol [6]. Some technical modifications have been made since the original method was described [6]. A new fluormeter (Technicon model II) with higher sensitivity was used in this study. Several blanks and standards were run along with the samples to compensate for the drift of the autoanalyzer. Very exact automatic pipettes were used for the extraction procedure.

Plasma lipoprotein patterns were examined by paper electrophoresis [19]. The following lipoprotein fractions were separated by preparative ultracentrifugation [20]: the very low density lipoproteins (VLDL) the low density lipoproteins (LDL) and high density lipoproteins (HDL). TG and cholesterol [21] were measured in each fraction. In the patients, the top and bottom fractions obtained after ultracentrifugation at $d = 1.006$ were subjected to paper electrophoresis [10].

Indocyanine green concentration in plasma was measured on five replicates of each sample and splanchnic blood plasma flow was calculated according to the method of Winkler and Tygstrup [22]. The most lipaemic plasma samples had to be ultracentrifuged to eliminate the lipaemia before determining the indocyanine concentration.

For radio-assay ten replicate chloroform/methanol extracts of each sample were made and the lipid fractions separated by TLC [23]. The separated plasma FFA and TG fractions were counted in a Packard Tri-carb liquid scintillation spectrometer model 3375. The radio-activities of the samples were always more than 20 times background which was about 30 cpm. All samples were counted twice for 5 min each time.

All statistical analyses were performed according to Snedecor [24].

Calculations and Definitions

Turnover rates of plasma FFA were calculated according to Armstrong *et al.* [25].

Uptake and mobilization of FFA across the splanchnic area were calculated as described before [11].

Chemical and isotope plasma TG secretion from the splanchnic region were calculated as described in detail previously [6, 12]. Calculation of the clearance of plasma TG from blood has also been described previously [6, 12]. With the exception of a few studies, measurements of chemical TG secretion and plasma TG clearance were made twice, and measurements of

isotope TG secretion were made three times during each study. Plasma TG "turnover rate" is used as a convenient term for both splanchnic plasma TG secretion rate and for plasma TG clearance rate when steady state conditions apply. Plasma TG "fractional turnover rate" is the ratio between the "turnover rate" and the VLDL-TG pool. The VLDL-TG pool is the product of plasma volume and plasma VLDL-TG concentration at zero-time.

The normal range of plasma TG values was defined, taking into consideration both age and sex, on the basis of values for plasma TG concentration found in the Stockholm population [13]. The upper limit of normal was taken as the mean value plus two standard deviations (logarithm values see page 70 table A 12 in ref. [13]).

Results

Subjects

The subjects are characterized in Table 1. Plasma cholesterol values varied between 150 and 430 mg/100 ml. Plasma TG concentrations ranged widely from 0.53 to 16.50 mmol/l. The lipoprotein analyses revealed that 20 subjects had "normal" patterns according to

Table 1. Characteristics of the Subjects studied

Subject	Diagnosis	Age years	Body weight kg	Body surface area m^2	Weight height index [a]	TG mmol/l	CH mg/100 ml	VLDL TG mmol/l	VLDL CH mg/100 ml	LDL TG mmol/l	LDL CH mg/100 ml	HDL TG mmol/l	HDL CH mg/100 ml	Type of lipoprotein pattern
R.E.	BD	35	83	2.06	1.00	0.53	170	0.17	3	0.24	96	0.15	70	N
P.L.	BD	25	73	1.88	0.97	0.57	—	0.18	5	0.21	98	0.10	57	N
E.S.	BD	26	76	2.07	0.84	0.66	150	0.33	5	0.27	101	0.11	57	N
R.M.	BD	43	79	2.00	0.98	0.80	—	0.30	7	0.44	198	0.14	50	N
F.G.	BD	29	73	1.93	0.92	0.83	231	0.34	7	0.33	113	0.20	112	H-α
R.S.	BD	29	78	1.98	0.99	0.86	191	0.55	5	0.25	127	0.18	46	N
K.H.	BD	62	84	2.06	1.04	0.87	—	0.39	10	0.35	163	0.11	49	N
G.B.	BD	42	78	2.09	0.85	1.00	222	0.44	9	0.38	132	0.18	70	N
P.N.	BD	38	82	1.91	1.19	1.01	—	—	—	—	—	—	—	—
L.N.	BD	30	83	2.11	0.94	1.04	164	0.27	3	0.21	57	0.13	96	H-α
R.M.	BD	36	65	1.80	0.87	1.06	202	0.38	7	0.35	123	0.10	66	N
G.J.	BD	56	60	1.62	1.00	1.12	180	0.28	10	0.31	99	0.11	88	N
N.H.	BD	29	62	1.66	0.98	1.12	183	0.58	18	0.26	108	0.08	40	N
B.P.	BD	43	62	1.82	0.78	1.23	216	0.38	7	0.38	148	0.22	71	N
B.L.	FH	54	83	2.08	0.98	1.38	212	0.63	32	0.34	124	0.03	53	III
O.S.	MI	55	71	1.85	0.99	1.59	270	0.89	24	0.44	197	0.20	49	N
I.E.	FH	44	67	1.72	1.05	1.69	207	0.79	18	0.51	155	0.22	44	N
B.A.	BD	53	94	2.04	1.34	1.76	213	0.77	12	0.33	132	0.21	72	N
L.E.	BD	40	59	1.59	1.02	1.78	—	1.13	14	0.34	125	0.10	43	N
K.L.	BD	44	66	1.83	0.87	1.90	—	0.88	16	0.27	86	0.17	45	N
H.M.	BD	27	75	1.90	1.01	2.05	201	1.10	26	0.35	128	0.20	51	N
K.M.	BD	49	62	1.65	1.00	2.14	233	0.95	22	0.67	—	0.15	23	N
E.J.	MI	52	82	1.98	1.08	2.32	—	1.64	29	0.40	163	0.17	57	IV
H.G.	AP	47	82	1.96	1.11	2.33	—	0.94	38	0.66	206	0.11	35	N
L.J.	BD	31	87	2.14	1.01	2.37	—	1.12	38	0.55	212	0.15	39	N
B.H.	CI	56	83	1.99	1.01	2.79	244	1.48	41	0.52	167	0.20	36	IV
E.H.	AP	65	78	1.90	1.10	2.93	254	1.68	39	0.52	189	0.14	39	IV
Y.I.	MI	53	64	1.74	0.93	2.96	—	1.26	32	0.98	264	0.27	33	II B
N.L.	AP	50	80	1.96	1.05	2.98	—	2.00	37	0.51	156	0.27	30	IV
K.O.	MI	47	72	1.84	1.03	2.98	174	2.17	43	0.35	105	0.26	36	IV
H.N.	MI	42	105	2.22	1.35	3.62	269	2.33	48	0.93	190	0.36	31	IV+Ex. b
A.A.	MI	43	80	1.98	1.03	3.62	311	2.35	45	0.63	231	0.18	35	II B
R.H.	XT	37	63	1.76	0.99	4.40	2.64	3.79	124	0.48	112	0.19	39	III
N.J.	MI	45	86	1.98	1.19	4.50	265	2.92	93	0.67	168	0.22	28	IV
A.H.	CI	61	66	1.75	0.97	4.52	252	3.81	75	0.46	137	0.12	20	IV
K.K.	XT	44	86	2.07	1.08	4.63	366	3.80	128	0.81	142	0.34	61	III
E.N.	HI	51	85	2.01	1.12	4.99	204	3.97	47	0.62	152	0.18	26	IV
G.H.	FH	35	92	2.10	1.18	6.35	206	5.50	75	0.64	112	0.21	33	IV
J.P.	MI	52	76	1.81	1.21	6.50	264	5.35	111	1.05	175	0.34	29	IV SPβ
T.J.	IC	52	70	1.81	1.02	8.92	361	6.29	229	0.39	94	0.14	16	IV
N.N.	MI	48	80	1.96	1.05	12.29	430	11.84	269	0.66	120	0.23	31	IV
H.H.	FH	41	80	1.95	1.07	16.50	361	15.00	247	0.46	48	0.27	—	IV SPβ

[a] Weight in kg/(height in cm-100). TG= triglycerides. CH=cholesterol. VLDL, LDL and HDL=very low, low and high density lipoproteins. BD=blood donor. FH=family history of ischemic heart disease. MI=myocardial infarction. AP= angina pectoris. CI=cerebral ischaemia. XT=Xanthoma tuberosum. HI=heart insufficiency. IC=intermittent claudication. N=normal. H-α=hyper-α-lipoproteinaemia. Ex. b.=extra band. SPβ=sinking pre-β-lipoprotein.

our "normal" values [26]. Two subjects had high concentrations of HDL or α-lipoproteins. Three patients had type III lipoprotein patterns [8] but one of these had normal values for total TG and cholesterol in plasma. Two patients had type IIB patterns and fourteen had type IV patterns. Of those patients with type IV patterns, one (H.N.) had an extra oil red staining band between the pre-β- and α-bands on paper electrophoresis. Two patients (T.J. and N.N.) with a type IV pattern had higher cholesterol/triglyceride ratios in VLDL than is generally seen. However, on paper electrophoresis the VLDL fraction had pre-β mobility and thus their lipoprotein abnormality cannot be regarded as type III pattern. Another two patients (J.P. and H.H.) with type IV patterns had pre-β-fractions recovered in the bottom fraction after ultracentrigufation at density 1.006 ("sinking pre-β").

Methodology

Since the original description of the method for the determination of hepatic venous-arterial differences of plasma TG concentrations [6, 11], certain technical improvements have decreased the analytical errors. The mean value of the analytical error for the determination of TG concentration in this study was less than 2 per cent, while earlier it was between 3 and 5 per cent (Table 2). The mean value of the error for the determination of TG radioactivity in the present study was 5.3 per cent in subjects with plasma TG concentration below 2 mmol/l and 3.4 per cent in patients with plasma TG above 2 mmol/l (Table 2). A statistically significant ($p<0.05$) hepatic venous-arterial difference in plasma TG concentration was found at least once in subjects with plasma TG concentrations below 2 mmol/l. As a matter of fact 33 out of 38 measurements of hepatic venous-arterial differences were significant in these 20 subjects. Of the 22 subjects with plasma TG values above 2 mmol/l, 19 had a least one significant hepatic venous-arterial difference and altogether 29 out of 43 were significantly positive. Hepatic venous arterial differences of plasma TG radio-activity were significant at least once in 41 of the 42 subjects and altogether in 81 out of 112 observations. To obtain an idea of the precision of a hepatic venous-arterial difference the frequency distributions of the standard errors of the means (SEM) for these differences in TG concentration and radio-activity are given in Table 2. The SEM for hepatic venous-arterial differences of plasma TG concentrations were less than 20 per cent of the difference in about half of the observations in subjects with TG concentration ≤ 2 mmol/l and less than 50 per cent in two thirds of the subjects with plasma TG values >2 mmol/l.

A good steady state in plasma FFA concentration and radio-activity was achieved during each study. On the average ($\pm$ SD), plasma FFA concentration increased 0.05 ± 0.24 μmol/ml and hour, radioactivity increased 4 ± 24 cpm/ml and hour and specific radioactivity remained unchanged at 0 ± 54 cpm/μmol.

Table 2. Analytical errors expressed as coefficient of variation for plasma TG radio-activity and concentration and SEM on hepatic venous-arterial difference in per cent of hepatic venous-arterial difference for plasma TG radio-activity and concentration

Arterial TG concentration	Coefficient of variation %	Frequency distribution (number of observations) for SEM of hepatic venous-arterial difference in %					
		0—10	11—20	21—30	31—50	51—100	101—
≤2 mmol/l							
radioactivity	5.3±5.1	4	21	15	8	8	0
concentration	1.9±1.1	9	13	6	5	4	1
>2 mmol/l							
radioactivity	3.4±3.2	0	8	13	12	14	9
concentration	1.5±1.1	3	7	6	13	4	10

Coefficient of variation=standard deviation in per cent of the mean value.
For each plasma sample mean coefficient of variation and SEM values of TG concentration and radio-activity were calculated. The mean values of arterial plasma TG concentration were classed in two groups: ≤2 and >2 mmol/l. Within each range group the mean and SEM for coefficients of variation were calculated and SEM of hepatic venous-arterial difference were tabulated as shown in the table.

Plasma TG concentrations remained, on average, constant during the studies. For the subjects with plasma TG concentrations below 2.0 mmol/l the mean change ($\pm$ SD) was -0.003 ± 0.068 μmol/ml and hour and for the subjects with plasma TG concentrations above 2 nmol/l the mean change ($\pm$ SD) was -0.113 ± 0.121 μmol/ml and hour. This was calculated by linear regression analysis. On the basis of this it has been assumed that steady state conditions existed for all subjects.

There was a highly significant correlation between plasma FFA turnover rate expressed as μmol/min and as (a) μmol/min. and kg body weight ($r=0.97$) and as (b) μmol/min. and m^2 body surface ($r=0.92$). The same was true for TG "turnover rate" (r values between 0.97 and 1.00). In the presentation of the results we have chosen to express the "turnover rate" data in μmol/min. per m^2 body surface area.

Plasma Triglyceride Transport

Plasma TG Secretion and Clearance Rates. The individual values obtained by the three methods for plasma TG "turnover rate" are given in Table 3. The range for the chemical TG secretion and the plasma TG clearance methods was from 3 to around 80 μmol/min. and m^2 body surface area (Fig. 1), except for two cases which had considerably higher values by one of the methods. The corresponding range for the isotope TG secretion method was from 1 to 40 μmol/min. and m^2. The frequency distribution diagram (Fig. 1) reveals that the distribution of the values for plasma

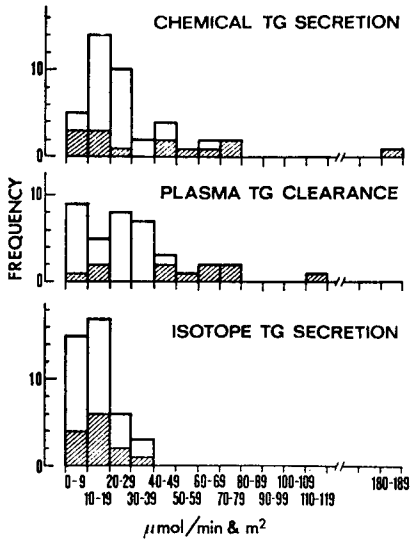

Fig. 1. Frequency (number of subjects) distribution of plasma TG "turnover rate" in normotriglyceridaemic (open bars) and hypertriglyceridaemic (hatched bars) subjects

TG "turnover rate" is skewed with the mean greater than the median. Fig. 1 shows that patients with hypertriglyceridaemia (see above for definition) can be found within the entire range of "turnover rates" for all three methods. However, for both the chemical TG secretion method and the clearance method there is clearly an overrepresentation of patients with hypertriglyceridaemia above 40 μmol/min. and m².

Comparisons of the Three Methods. The mean values for each subject obtained with the three methods for the determination of plasma TG "turnover rate" are plotted against each other in Fig. 2.

The chemical TG secretion method and the plasma TG clearance method gave, in general, similar values. The equation for the regression line is $y = 0.66x + 10$, r is 0.52 ($p < 0.001$) and S_b is 0.18. This equation is not significantly different from $y = x$.

The isotope TG secretion method gave values which were significantly correlated with those derived from both the chemical TG secretion method ($r = 0.48$, $p < 0.01$) and the plasma TG clearance method ($r = 0.71$ $p < 0.001$) up to 40 μmol/min. and m². However, when values above 40 μmol/min. and m² with the latter two methods are included, the relationship is not significant. Fig. 1 shows that in fact the isotope TG secretion method did not give values above 40.

Relationship between Plasma TG Concentration and "Turnover rate". As VLDL-TG is the fraction of plasma TG which is believed to be the most active transport form, the relationship between TG "turnover rate" and VLDL-TG levels was analyzed. Since the values for plasma VLDL-TG concentration and for chemical TG secretion and plasma TG clearance were skewly distributed their logarithmic values have been plotted (Fig. 3). The relationship have also been studied further by correlation analysis (Table 4). There were no significant correlations in the case of the normal subjects. However, in patients with hypertriglyceridaemia significant correlations were found between logarithm values of VLDL-TG concentration and plasma TG "turnover rates" obtained with the

Table 3. Plasma TG "turnover rate" (μmol per minute and m² body surface area) and "fractional turnover rate" (per cent per minute)

Subject	"Turnover rate"			"Fractional turnover rate"		
	chemical TG secretion	isotope TG secretion	plasma TG clearance	chemical TG secretion method	isotope TG secretion method	plasma TG clearance method
R.E.	42	24±2	20	11.8	6.7	5.7
P.L.	16	13±4	6	4.9	3.8	1.7
E.S.	20	25±7	33	3.1	3.8	5.0
R.M.	5	6±2	9	1.0	1.4	2.0
F.G.	46	25±1	32	7.2	3.9	5.0
R.S.	20	9±0	13	1.6	0.7	1.0
K.H.	16	17±7	48	2.3	2.4	6.9
G.B.	61	30±13	23	6.7	3.3	2.6
P.N.	27	14	—	—	—	—
L.N.	25	14±4	26	4.6	2.6	4.8
R.M.	18	7±2	8	3.0	1.2	1.4
G.J.	13	4±2	5	2.2	6.7	0.9
N.H.	12	8±5	4	1.3	0.8	0.4
B.P.	33	30±7	30	4.7	4.3	4.3
B.L.	16	17±1	31	1.5	1.6	3.0
O.S.	24	9±1	20	1.8	0.7	1.5
I.E.	25	16±6	20	1.3	0.8	—
B.A.	36	13±1	37	2.3	0.8	2.4
L.E.	17	9±10	21	1.1	0.6	1.3
K.L.	17	21±3	31	1.0	1.3	1.9
H.M.	14	3	3	0.6	0.1	0.1
K.M.	22	9±3	13	1.4	0.6	0.8
E.J.	10	7±2	6	0.3	0.2	0.2
H.G.	8	10±3	22	0.6	0.7	1.5
L.J.	23	13±2	23	1.3	0.7	1.3
B.H.	8	6±2	14	0.3	0.2	0.5
E.H.	19	7±2	9	0.8	0.3	0.4
Y.I.	27	10±1	15	1.4	0.5	0.8
N.L.	42	17±4	38	1.3	0.5	1.1
K.O.	13	7±3	9	0.3	0.2	0.2
H.N.	7	11±3	15	0.2	0.3	0.4
A.A.	6	3	—	1.6	0.8	—
R.H.	14	21	72	0.3	0.4	1.3
N.J.	16	16±2	64	0.3	0.3	1.3
A.H.	21	18±23	43	0.4	0.3	0.7
K.K.	186	13±6	72	3.8	0.3	1.5
E.N.	43	1±6	—	0.6	0.0	—
G.H.	59	34±3	115	0.7	0.4	1.4
J.P.	73	15±1	48	0.8	0.2	0.5
T.J.	74	—	—	0.7	—	—
N.N.	42	23±5	66	0.2	0.1	0.3
H.H.	64	18±9	55	0.3	0.1	0.3

Chemical TG secretion and plasma TG clearance are expressed as mean values of determinations made at 180 and 240 min. and isotope TG secretion as mean values and standard errors of the means of determinations made at 180, 210 and 240 min in each study. Plasma TG "fractional turnover rates" have been calculated as the percentage ratio between the "turnover rate" and the plasma VLDL-TG pool assuming steady state conditions for plasma TG.

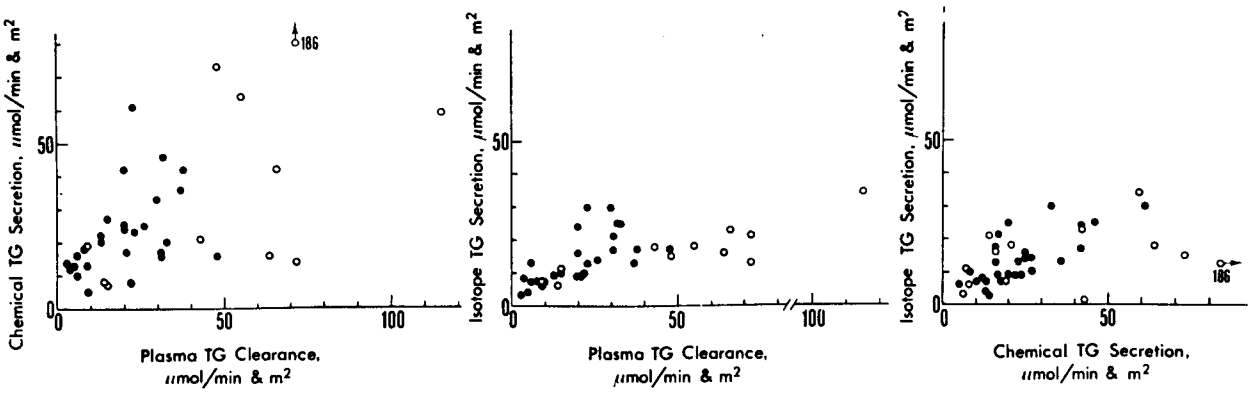

Fig. 2. Comparison between values for chemical and isotope plasma TG secretion and plasma TG clearance in normotriglyceridaemic (closed circles) and hypertriglyceridaemic (open circles) subjects

chemical secretion and the clearance method (log/log values).

Relationship between Plasma TG Concentration and "Fractional Turnover Rate". For each of the three methods the "fractional turnover rate" of plasma TG has been calculated (Table 3). The plots of TG concentration against the "fractional turnover rate" revealed a hyperbolic relationship with the "fractional turnover rate" decreasing as TG concentration increases (Fig. 4).

Total and Splanchnic Transport of Plasma FFA

Individual values for plasma FFA turnover rate, splanchnic FFA mobilization and uptake are presented in Table 5. The range for plasma FFA turnover rate was from 100 to around 500 μmol/min. and m² and a similar range was found for splanchnic FFA uptake. The range for splanchnic FFA mobilization was 5 to about 400 μmol/min. and m². No significant differences were found between "normals" and patients with hypertriglyceridaemia with regard to these FFA transport parameters. However, the mean values for splanchnic FFA uptake and mobilization were lower for hypertriglyceridemics than for "normals" (Table 6).

The *minimum* values for FFA mobilization and uptake were calculated assuming that all FFA taken up across the splanchnic area were of arterial origin (i.e. arterial FFA specific activities were used in the calculations). However, there is evidence that only a minor portion of plasma FFA is taken up at arterial specific activity. The *maximum* values for splanchnic FFA mobilization and uptake were calculated assuming that all FFA taken up across the splanchnic region had a specific activity equal to that of hepatic vein FFA. This assumes that the difference between arterial and hepatic vein specific activities depends only on the admixture of portal vein and hepatic artery blood. Since it is probable that the liver does account for

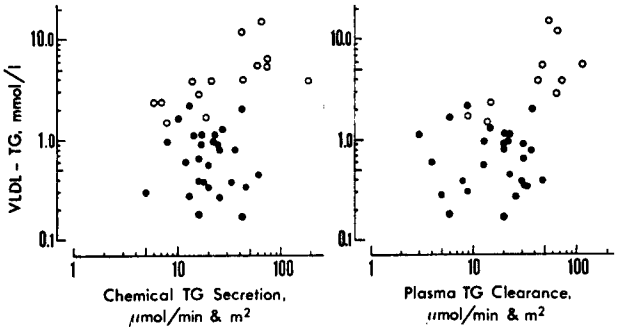

Fig. 3. Relationship between serum VLDL-TG concentration and plasma TG "turnover rate" in normotriglyceridaemic (closed circles) and hypertriglyceridaemic (open circles) subjects .Logarithmic scales

Table 4. Correlation coefficients for the relationships between plasma VLDL-TG (y) and values of the three methods for plasma TG "turnover rate" (x)

y/x	All subjects			Normotriglyceridaemia			Hypertriglyceridaemia		
	chemical secretion method	isotope secretion method	clearance method	chemical secretion method	isotope secretion method	clearance method	chemical secretion method	isotope secretion method	clearance method
log/log	0.45 $p<0.01$ [41]	−0.04 ns [40]	0.49 $p<0.01$ [38]	−0.08 ns [27]	−0.29 ns [27]	−0.01 ns [27]	0.65 $p<0.05$ [14]	0.44 ns [13]	0.68 $p<0.05$ [11]

ns=not significant. Figures within brackets indicate the number of subjects.

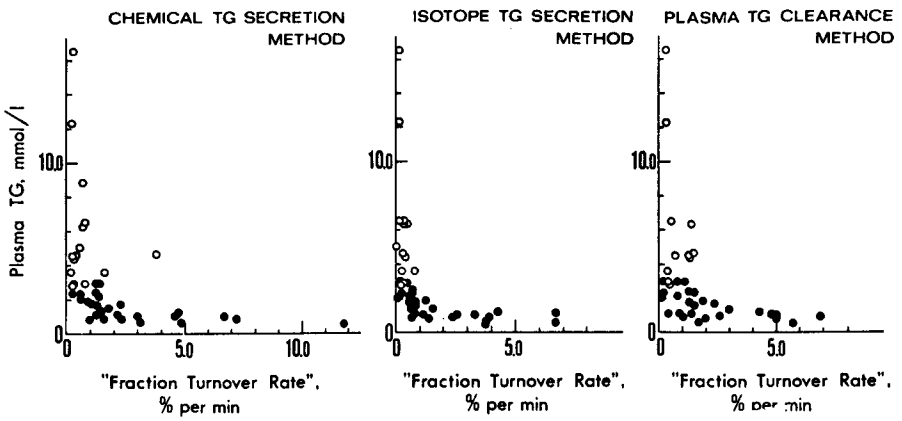

Fig. 4. Relationship between plasma TG concentration and plasma TG "fractional turnover rate" in normotriglyceridaemic (closed circles) and hypertriglyceridaemic (open circles) subjects

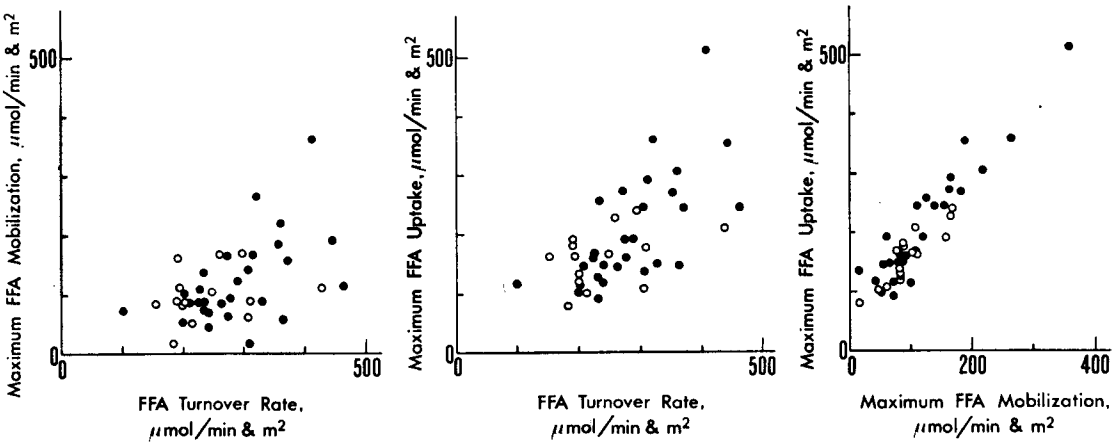

Fig. 5. Comparison between values for plasma FFA turnover rate, maximum splanchnic FFA mobilization and maximum splanchnic uptake in normotriglyceridaemic (closed circles) and hypertriglyceridaemic (open circles) subjects

most splanchnic FFA uptake, the maximum values for FFA uptake and mobilization have been used in the graphic presentation of results.

The interrelationship between plasma FFA turnover rate and splanchnic FFA uptake and mobilization are shown in Fig. 5. As expected, significant correlations were found between plasma FFA turnover rate and both, splanchnic FFA mobilization ($r=0.47$, $p>0.01$) and uptake ($r=0.63$, $p<0.001$), since both uptake and the mobilization constitute part of FFA turnover rate. On the average, splanchnic FFA mobilization and uptake were 38 and 66 per cent respectively of plasma FFA turnover rate. Furthermore, a very close correlation ($r=0.93$, $p<0.001$) was found between uptake and mobilization of FFA across the splanchnic area, which suggests the importance that FFA mobilization from splanchnic tissue can have for the flux of FFA to the liver.

Relationship between the Transport of Plasma TG and Plasma FFA.

A number of studies have shown that there is a correlation between plasma concentration of FFA and turnover rate of FFA. This was also the case in the present study ($r=0.63$). The following results are concerned only with relationships between FFA turnover rate and plasma TG transport.

Relationship between Plasma TG Concentration and Plasma FFA Transport.

For the material taken as a whole there was no significant relationship between plasma TG concentration and any FFA transport function: FFA turnover rate, maximum splanchnic FFA uptake or maximum splanchnic FFA mobilization. In addition there was no difference between subjects with normal TG levels and those with elevated TG levels (Table 6). However, for the patients with hypertriglyceridaemia, in contrast to the normo-triglyceridaemics, there was a positive relationship between TG concentration and FFA turnover rate ($r=0.67$, $p<0.01$) but not for maximum FFA mo-