Diurnal Fluctuations in Triglyceride, Free Fatty Acids, and Insulin during Sucrose Consumption and Insulin Infusion in Man

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ABSTRACT Serial changes in circulating triglyceride, free fatty acids (FFA), insulin, and glucose have been measured in human subjects fed sucrose as the sole source of calories for 2- or 3-day periods. The sucrose was given either during the day with overnight fasting (19 subjects) or as continual 3-hour meals during the day and night (seven subjects). Insulin was infused overnight in five additional subjects on the day–feeding regimen to determine the effect on triglyceride concentration.

The concentration of triglyceride increased during the study in all subjects, but there was a clear diurnal pattern in the response which was present even in the continual feeding studies. The rise in triglyceride occurred mainly overnight, and during the day there was frequently a fall in the concentration. The overnight increase was significantly less when insulin was infused. There were also diurnal fluctuations in FFA and insulin in both daytime and continual feeding regimens. The plasma FFA, like triglyceride, rose during the night and fell during the day while the insulin rose during the day and fell overnight.

Separate statistical analysis of the daytime and overnight changes revealed that the changes in triglyceride were significantly but negatively correlated with changes in insulin during both periods. The changes in triglyceride and FFA were positively correlated during the day but not significantly related during the night. The data show that when sucrose is eaten for 2 or 3 days, there is a general increase in triglyceride concentration upon which are superimposed major diurnal fluctuations in the concentrations of triglyceride, insulin, and FFA. It is suggested that the highly significant inverse relationship between changes in triglyceride and insulin may be mediated through an effect of insulin on triglyceride removal.

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INTRODUCTION

The relationships between plasma triglyceride, free fatty acids (FFA),[1] and insulin have been the subject of several reports. A positive correlation between plasma triglyceride and insulin levels has been found in man (1–3) while infusion of insulin (4) or tolbutamide (5) in fasted humans has been accompanied by falls in the triglyceride concentration. Triglyceride levels may also be lowered by feeding glucose (6) through mechanisms which may involve enhanced production of insulin and suppression of FFA turnover. The inflow of triglyceride from liver to plasma can be influenced experimentally by varying the concentration of plasma FFA (7) and in some studies in humans a relationship between the plasma triglyceride concentration and the plasma FFA turnover has been suggested (7, 8).

The plasma triglyceride concentration rises in response to an increase in dietary carbohydrate (9–11). In man this rise is clearly demonstrable within 1–2 days. We have examined the interrelationships between the changing concentrations of plasma triglyceride, FFA, insulin, and glucose during short periods of high–sucrose diets and the modifying influence of infusions of insulin on these changes.

METHODS

Dietary regimes. Sucrose was given as the sole source of calories for periods of 2 or 3 days in the form of lemonade. The appropriate consumption of calories was estimated from dietary history. Two separate dietary regimens were studied, and in each, meals were consumed in 10–15 min. No attempt was made to preserve basal conditions although physical activity was limited. (*a*) Day–feeding studies: the sucrose was provided in four equal amounts given at 9 a.m., 12 noon, 3 p.m., and 6 p.m., with overnight fasting. 19 individuals were studied, 11 normal males aged 17–51, 3 middle aged obese subjects (two males and one female), 3 untreated diabetics (2 middle aged males who developed di-

[1] *Abbreviations used in this paper:* FFA, free fatty acids.

abetes at maturity and one 16 year old female) and 2 women aged 54 and 59 with endogenous type IV hypertriglyceridemia (12). (*b*) Continual feeding studies: sucrose was fed every 3 hr in equicaloric amounts throughout the day and night for 48 hr, beginning at 9 a.m. on the first morning and concluding at 6 a.m. on the third morning. Seven subjects were studied, three normal males aged 18–28, two middle aged males with untreated diabetes acquired at maturity and a male aged 38 and a female aged 54 with endogenous type IV hypertriglyceridemia. (*c*) Day feeding plus insulin infusion: five subjects on the day-feeding regimen were given an intravenous infusion of glucagon-free insulin (Actrapid, Novo, Denmark) during the second night of study. The rate of infusion was 1.25–1.5 U/hr commencing at 7:30 p.m. and concluding the following morning at 9 a.m. The second night was chosen for the infusion because of the uniformity of the findings during the second 24 hr in the day-feeding studies. Subjects included two normal males aged 18 and 24, two middle aged women with endogenous type IV hypertriglyceridemia, and one untreated 12 year old male diabetic.

Analytical procedures. Samples of blood were collected several times during each 24 hr for measurements of plasma triglyceride (13), FFA (by the method of Dole and Meinertz using a single extraction and thymol blue as an indicator [14]), serum insulin[2] (15), and blood glucose (by the glucose oxidase method). In the day-feeding studies, blood was collected in the mornings before the first meal and subsequent samples were taken 1 hr after the completion of the meal. In the continual feeding studies, blood was collected 1 hr after the previous meal. The 1 hr postprandial triglyceride level had been found not to differ significantly from that immediately preceding the meal. Packed cell volume was estimated on all specimens; there was less than 4% variation during any study. Body weights varied by less than 0.9 kg.

Statistical analyses. Since studies of large populations have shown that the triglyceride concentration is not a normally distributed variable but rather is positively skewed (16), the triglyceride concentration has been expressed as the logarithm of its level in mg/100 ml for purposes of statistical analyses. The blood glucose level has also been expressed as the logarithm of its concentration in mg/100 ml so that the weighting by the diabetic subjects might be reduced.

RESULTS

Day-feeding studies. Fig. 1 *a* shows the triglyceride concentration in individual subjects measured at intervals during the first 48 hr of sucrose feeding. In some subjects measurements were made only during the first 24 hr whilst in others only during the second 24 hr. Although the triglyceride concentration increased in almost every subject at the end of 24 or 48 hr, diurnal variations were commonly noted. The triglyceride level tended to fall during the day reaching the lowest value at 11 p.m., 5 hr after the last meal. In several subjects with low fasting values, however, there was a small increase over this period. During the 2nd day when fasting levels were higher than on the first morning, the decrease from 9 a.m.–11 p.m. was more apparent. Over-all, the decrease in milligrams per milliliter was significantly correlated with the fasting values ($R = +0.74$, $P < 0.001$).

By contrast, the triglyceride concentrations rose in every subject during the period 11 p.m.–9 a.m. Considering both nights of study the magnitude of this elevation was positively correlated with the concentration at 11 p.m. ($R = +0.66$, $P < 0.001$).

The response to a 100% sucrose diet eaten in this manner was examined on the 3rd, 7th, and 15th day in two subjects fed diets containing 75–80% of the calories as carbohydrate for 15 days. A similar diurnal pattern in the triglyceride response was found on each occasion.

Fig. 1 *b* shows the corresponding FFA concentrations. FFA levels were suppressed by sucrose consumption, remaining low for at least 5 hr after the last meal. There was generally an overnight increase in the concentration but this was variable and even absent in several subjects.

Fig. 1 *c* shows the insulin concentrations. Although the magnitude of the response was highly variable the pattern was similar in all subjects. The concentration was elevated after eating sucrose and returned to basal levels overnight. The single flat response was obtained in a juvenile diabetic girl.

Table I *a* summarizes these results in terms of the means and coefficients of variation of triglyceride, FFA, insulin, and glucose at serial times during the study. Table 1 *b* presents the values of these parameters in the juvenile diabetic girl.

Since the changes in the triglyceride concentration appeared to be influenced by the magnitude of the concentration itself, these diurnal variations were analyzed as percentage changes. In this way any interrelationships observed between the fluctuations in the parameters measured would not simply reflect a correlation between absolute levels. The percentage changes in triglyceride concentration from 9 a.m.–11 p.m. and from 11 p.m.–9 a.m. have been computed to provide four values for each 48 hr study. These times were chosen because they most often provided the greatest differences between triglyceride levels. The diurnal fluctuations in the plasma FFA concentration have been calculated as the percentage difference between the fasting level at 9 a.m. and the mean of the daytime values (two or three fluctuations 1 hr postcibal). The diurnal variations in insulin have been described as the percentage difference between the mean of the daytime values and the mean of the three nighttime values obtained generally at 11 p.m., 4 a.m., and 9 a.m.

The relationship between the percentage changes in plasma triglyceride, FFA, and insulin from one 12 hr

[2] Human insulin used for standards in the immunoassay of serum insulin was kindly supplied by Dr. Mary Root of Lilly Research Laboratories, Indianapolis, Ind.

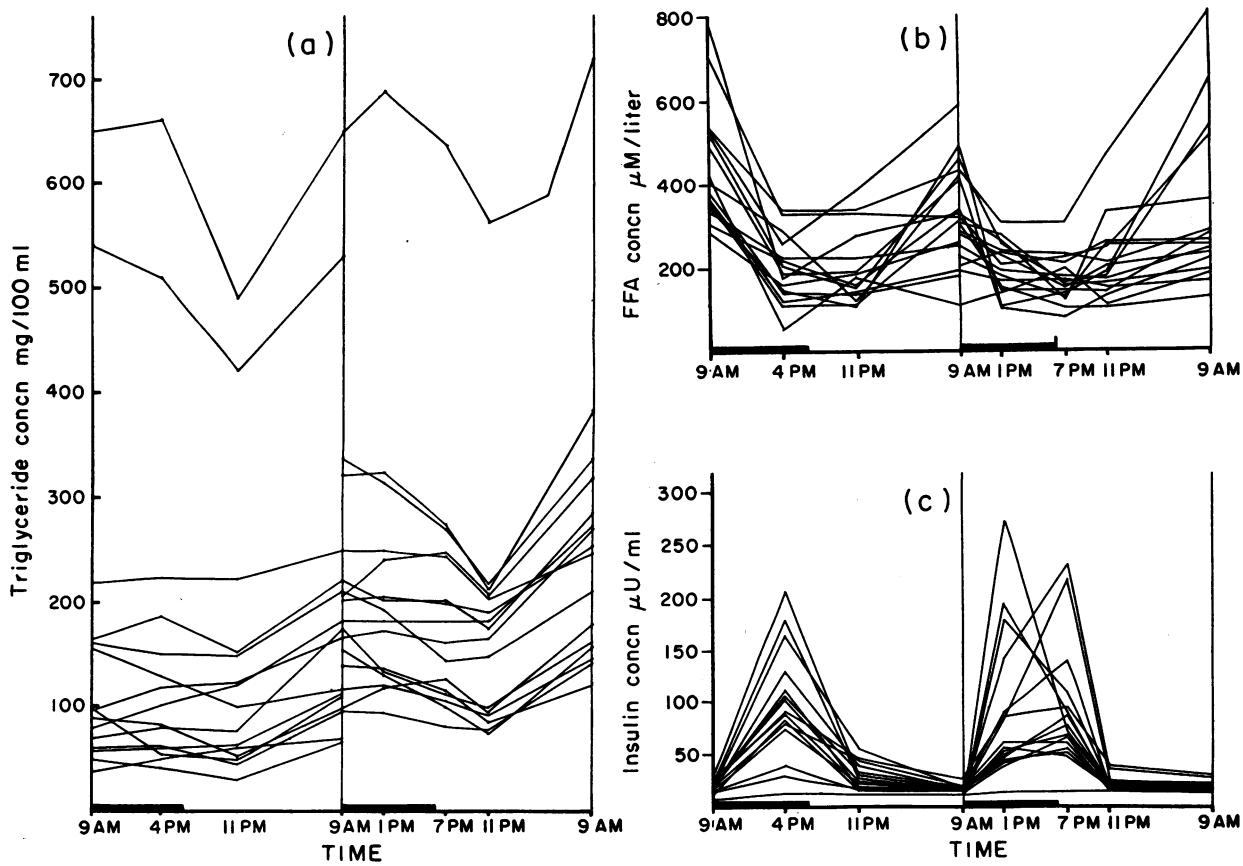

FIGURE 1 Day-feeding studies. Changes in the plasma triglyceride, FFA and insulin in 19 subjects on 100% sucrose diets. The horizontal bars indicate the periods during which the sucrose was eaten.

period to the next were then analyzed. The change in triglyceride was significantly, inversely related to the change in insulin ($R = -0.78$, $P < 0.001$); i.e., the percentage fall in triglyceride concentration that occurred during the day was related to the percentage increment in the mean insulin value over that same period. Conversely, the fall in the mean insulin value during the night was related to the overnight rise in triglyceride level. The percentage change in the triglyceride concentration was also significantly related, though directly, to the percentage change in the FFA level ($R = +0.45$, $P < 0.01$). The blood glucose levels were highly variable and not apparently related to the changes in triglyceride concentration.

Continual feeding studies. 48 hr of continual sucrose feeding every 3 hr produced increases in the plasma triglyceride of the same order as those found in the day–feeding studies (Fig. 2 *a*). During the second 24 hr the daytime increase was significantly less than the overnight increase ($P < 0.01$). The FFA and insulin levels are shown in Fig. 2 *b* and *c* respectively.

Table II presents the means and coefficients of variation of all prameters at serial times during the study. Although plasma FFA were markedly suppressed and remained low for the duration of the studies, some diurnal variation was observed in that the levels at 10 p.m. were significantly lower than those at 10 a.m. ($P < 0.01$). Similarly, although the insulin concentrations remained elevated throughout the day and night, the values at 10 a.m. on the second morning were significantly higher than those at either the preceding 10 p.m. ($P < 0.001$) or the following 10 p.m. ($P < 0.01$) despite the fact that the samples were obtained 1 hr after identical meals. In four of the subjects insulin concentration was also measured at 1 p.m. and 1 a.m. or 4 p.m. and 4 a.m. each day. The mean daytime level (10 a.m. and either 1 p.m. or 4 p.m.) was higher than the overnight level (10 p.m. and either 1 a.m. or 4 a.m.), although the difference was not statistically significant ($P = 0.08$). The blood glucose levels varied widely from subject to subject but the 1 hr postprandial values changed little in each individual.

TABLE I A

Day-Feeding Studies: Means and Coefficients of Variation of Parameters during 2 Days of 100% Sucrose Diet Consumed at 9 a.m., 12 Noon, 3 p.m., and 6 p.m.

	1st day*				2nd day‡				
	9 a.m.	4 p.m.	11 p.m.	9 a.m.	9 a.m.	1 p.m.	7 p.m.	11 p.m.	9 a.m.
Triglyceride, *log mg/100 ml*	2.07(0.05)	2.07(0.06)	2.02(0.05)	2.21(0.03)	2.33(0.02)	2.31(0.02)	2.27(0.02)	2.20(0.03)	2.40(0.02)
FFA, *μmoles/liter*	476(76)	207(53)	202(36)	341(45)	307(57)	199(17)	169(20)	206(36)	322(102)
Insulin, *μU/ml*	21(1.8)	100(28)	30(6.5)	21(1.2)	19(1.1)	92(55)	95(37)	21(3.2)	21(1.6)
Glucose, *log mg/100 ml*	1.96(0.01)	2.06(0.02)	2.01(0.02)	1.96(0.01)	1.95(0.01)	2.07(0.02)	2.13(0.02)	1.98(0.02)	1.96(0.01)

* Means of 15 values on 1st day.
‡ Means of 17 values on 2nd day.

TABLE I B

Day Feeding: Results in Subject with Juvenile Onset Diabetes

	1st day			2nd day				
	9 a.m.	4 p.m.	11 p.m.	9 a.m.	1 p.m.	7 p.m.	11 p.m.	9 a.m.
Triglyceride, *mg/100 ml*	156	120	103	115	118	118	115	145
FFA, *μmole/liter*	533	330	330	443	398	307	466	805
Insulin, *μU/ml*	11	17	17	15	18	18	16	15
Glucose, *mg/100 ml*	179	536	443	307	464	536	507	321

Insulin infusion studies. Table III presents the values of all parameters measured during the 2nd and 3rd days in the five subjects studied. The findings on the 1st day followed the pattern seen in all other day–feeding experiments. The response to insulin which was infused during the second night was similar in three of the five subjects in that the expected overnight rise in the triglyceride concentration appeared to be diminished. Fur-

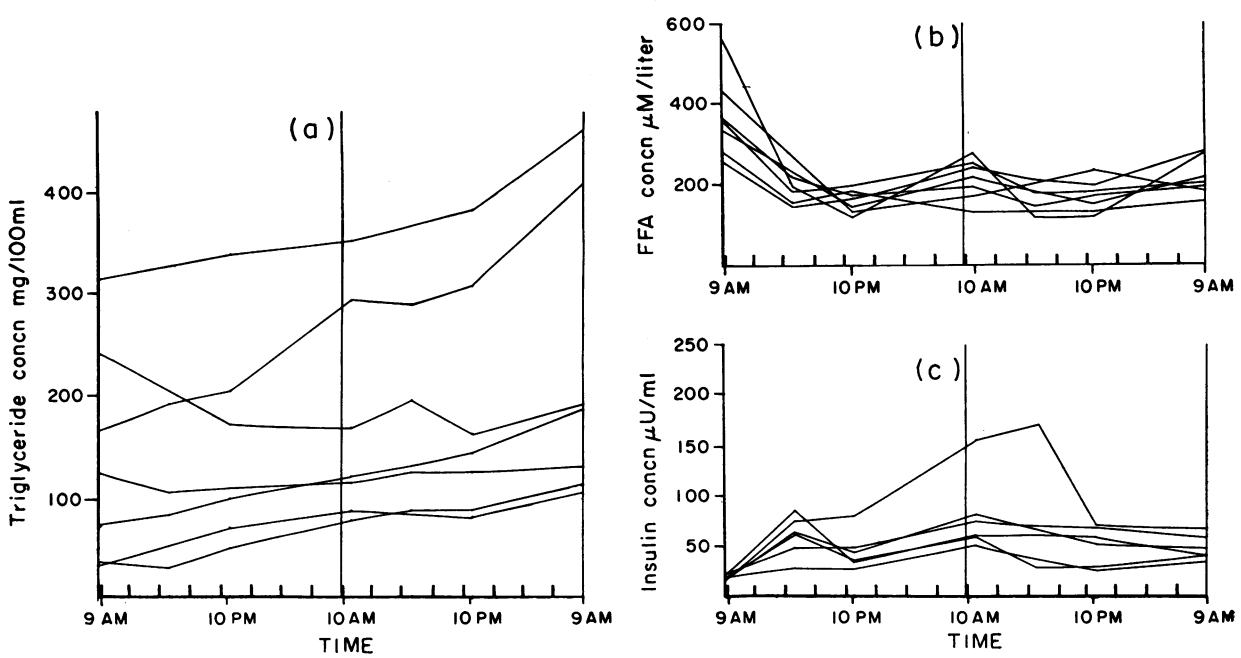

FIGURE 2 Continual-feeding studies. Changes in the plasma triglyceride, FFA, and insulin in seven subjects on 100% sucrose diets. The vertical bars indicate the time of each meal.

TABLE II

Continual-Feeding Studies: Means and Coefficients of Variations of Parameters during 2 Days of 100% Sucrose Diet Consumed every 3 hr from 9 a.m. on First Morning to 6 a.m. on Third Morning*

	1st day			2nd day		
	9 a.m.	1 p.m.	10 p.m.	10 a.m.	10 p.m.	9 a.m.
Triglyceride, *log mg/100 ml*	2.01(0.06)	‡	2.09(0.03)	2.17(0.02)	2.19(0.02)	2.28(0.02)
FFA, *μmole/liter*	391(19)	‡	168(3.0)	220(15)	173(11)	219(10)
Insulin, *μU/ml*	17(0.8)	63(11)	44(10)	81(21)	53(9.0)	49(4.4)
Glucose, *log mg/100 ml*	1.97(0.002)	2.02(0.008)	2.07(0.005)	2.08(0.010)	2.09(0.006)	2.03(0.006)

* Means of seven values.
‡ Incomplete data.

thermore the anticipated fall during the following day was not seen either. The infusion maintained a nocturnal concentration of insulin that was well above the basal level but not as high as during the day when sucrose was eaten at 3-hour intervals. The plasma FFA remained low during the infusion. The overnight rise in triglyceride concentration was not prevented in subject C. R., although the rise was not as great as that during the following night. The 12 year old untreated diabetic boy, W. C. in whom the triglyceride concentration rose during the first 24 hr, showed a marked response to the insulin infusion. The triglyceride level fell not only

TABLE III

Insulin Infusion Studies‡: Values of Parameters during the Second and Third Days of Study*

	2nd day				3rd day				
	9 a.m.	1 p.m.	7 p.m.‡	11 p.m.	9 a.m.‡	1 p.m.	7 p.m.	11 p.m.	9 a.m.
GF									
Triglyceride, *mg/100 ml*	110	85	67	52	75	93	87	86	153
FFA, *μmoles/liter*	312	240	191	140	140	161	140	161	211
Insulin, *μU/ml*	22	78	79	45	40	78	35	23	20
Glucose, *mg/100 ml*	85	126	132	92	68	129	102	98	98
IP									
Triglyceride	69	76	59	48	62	61	63	63	118
FFA, *μmoles/liter*	586	350	409	283	283	340	283	384	611
Insulin, *μU/ml*	15	48	56	33	38	49	38	15	19
Glucose, *mg/100 ml*	84	82	85	40	61	91	105	94	94
IF									
Triglyceride	693	719	648	625	623	705	679	623	712
FFA, *μmoles/liter*	166	217	116	142	166	116	142	166	243
Insulin, *μU/ml*	16	70	40	52	40	83	38	17	18
Glucose, *mg/100 ml*	79	116	116	50	76	144	129	87	82
CR									
Triglyceride	528	550	520	446	574	600	612	618	843
FFA, *μmoles/liter*	260	185	185	185	210	200	197	221	260
Insulin, *μU/ml*	20	73	95	62	74	82	73	40	20
Glucose, *mg/100 ml*	96	123	143	92	88	143	143	132	89
WC									
Triglyceride	89	105	104	94	94	81	66	52	61
FFA, *μmoles/liter*	182	131	157	131	131	308	334	283	409
Insulin, *μU/ml*	19	25	20	40	34	16	14	15	14
Glucose, *mg/100 ml*	197	281	264	203	114	169	161	209	129
Means and coefficients of variation									
Triglyceride, *log mg/100 ml*	2.28(0.08)	2.30(0.08)	2.23(0.09)	2.16(0.10)	2.24(0.09)	1.26(0.09)	2.24(0.10)	2.21(0.11)	2.36(0.09)
FFA, *μmoles/liter*	323(113)	234(33)	218(75)	174 (29.4)	180(25)	238(47)	225(44)	249 (42.7)	369(86)
Insulin, *μU/ml*	18 (0.4)	59 (6.6)	58(12)	46 (1.7)	45 (4.7)	56(11)	35 (4.3)	18 (0.5)	18 (0.3)
Glucose, *log mg/100 ml*	2.01(0.02)	2.13(0.02)	2.13(0.02)	1.89(0.05)	1.87(0.01)	2.12(0.01)	2.09(0.004)	2.06(0.01)	2.00(0.003)

* 100% sucrose diet consumed at 9 a.m., 12 noon, 3 p.m. and 6 p.m.
‡ Insulin infused on 2nd night from 7.30 p.m. to 9 a.m.

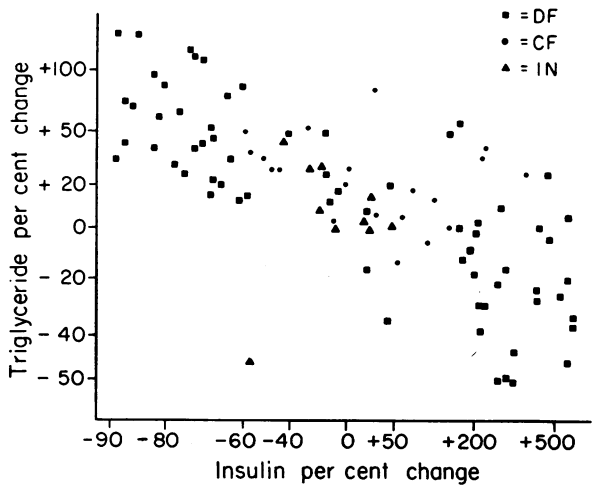

FIGURE 3 The relationship between the percentage changes in plasma triglyceride and insulin plotted on a log-log scale. DF, day-feeding studies; CF, continual-feeding studies; IN, insulin-infusion studies.

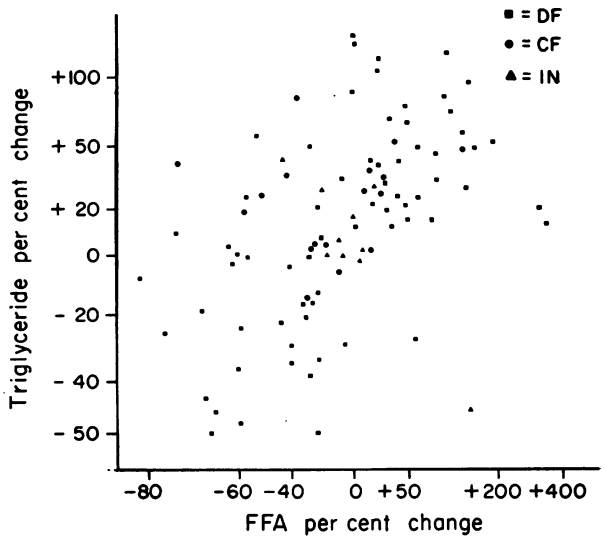

FIGURE 4 The relationship between the percentage changes in plasma triglyceride and FFA plotted on a log-log scale. DF, day-feeding studies; CF, continual-feeding studies; IN, insulin-infusion studies.

during the night of the infusion but continued to fall during the subsequent day after the infusion had been stopped. In this subject the plasma insulin concentration reached a peak of 93 μU/ml during the infusion, whereas it was never greater than 25 μU ml at other times.

Considering the five subjects together, the percentage increase in the triglyceride concentration during the night of the insulin infusion was significantly less than that during the following night ($P < 0.01$). Since it is possible that the increase would in any case have been greater on the third than on the second night regardless of the insulin infusions, the findings in these five subjects during the second night were compared with those obtained in the 17 subjects in the day–feeding studies (Fig. 1). The percentage increase in triglyceride concentration during the night of the infusion was found to be significantly less than that observed during the second night in the other 17 subjects ($P < 0.001$).

All studies. Finally, the results obtained in all three studies (day-feeding, continual feeding, and insulin infusion) have been pooled and analyzed as above. The findings in this larger group resembled those of the day-feeding studies. Significant correlations were found between triglyceride and insulin ($R = -0.75$, $P < 0.001$, Fig. 3) and between triglyceride and FFA ($R = +0.32$, $P < 0.01$, Fig. 4). However, as the results obtained during the day and overnight have been pooled, these correlations will be over-emphasized by the extremes of change. Consequently the day and night periods have been examined separately. The second 24 hr of the day-feeding studies, including the five insulin infusions, were analyzed. Table IV summarizes the correlations. During the day significant correlations were found between percentage changes in triglyceride and insulin, triglyceride and FFA, and insulin and FFA. Overnight, a significant relationship between triglyceride and insulin persisted but the relationships between triglyceride and FFA and between insulin and FFA were no longer significant.

TABLE IV

Correlation Coefficients Between Percentage Changes in Triglyceride, FFA, and Insulin

	Number	TG vs insulin	TG vs FFA	Insulin vs FFA
Changes between day and night				
(*a*) Day feeding studies	68	-0.78, $p < 0.001$	$+0.45$, $p < 0.01$	-0.75, $p < 0.001$
(*b*) All studies	96	-0.75, $p < 0.001$	$+0.32$, $p < 0.01$	-0.64, $p < 0.001$
Changes during day	21	-0.67, $p < 0.01$	$+0.54$, $p < 0.05$	-0.51, $p < 0.05$
Changes overnight	21	-0.66, $p < 0.01$	$+0.09$, NS	-0.24, NS

DISCUSSION

The ingestion of glucose has been reported to lower plasma triglyceride in man (11) and rat (17). This may be mediated by changes in both insulin and FFA. Infusions of insulin in fasted humans decrease the rate of appearance of circulating FFA in plasma triglyceride in direct proportion to the decrease in FFA turnover (7). On the other hand, prolonged infusions of insulin in humans have produced falls in plasma triglyceride levels some hours after the cessation of the infusion when the concentration of FFA had already risen markedly (4). Bagdade, Porte, and Bierman (18) have shown that insulin lowers both endogenous and exogenous triglyceride levels in subjects with diabetic lipemia. Since insulin may stimulate the production of lipoprotein lipase in diabetic patients (18) as well as experimentally (19, 20), insulin may lower the triglyceride concentration by enhancing its removal.

In studies of prolonged carbohydrate intake, the triglyceride concentration as measured in the fasting state in the morning, has frequently been found to correlate positively with the insulin concentration, and it has therefore been suggested that the increased secretion of insulin might stimulate the production of triglyceride (2). Furthermore, a significant positive correlation has been found between serum triglyceride and serum insulin levels in a group of young patients with coronary heart disease; reduction in the insulin levels with phenformin was associated with a decrease in the triglyceride concentration (21). There is, however, little evidence that insulin stimulates the formation of plasma triglyceride, although insulin given in vivo does restore the capacity of the perfused liver to secrete triglyceride (22) and in rat liver slices insulin has been reported to stimulate the incorporation of ^{14}C–U-glucose into triglyceride fatty acids (23, 24).

Thus, whereas a positive correlation has been generally reported between plasma insulin and triglyceride concentrations in studies of prolonged carbohydrate intake, such a relationship has been found to be negative in our studies (Table IV). In the present study, advantage has been taken of the diurnal fluctuations in plasma triglyceride, FFA, and insulin throughout the 24 hr to investigate possible correlations in these changes. The highly significant negative correlations between the changes in insulin and the changes in triglyceride strengthen the likelihood that insulin influences triglyceride levels by stimulating removal rather than formation. The data are also consistent with suppression of triglyceride secretion from the liver.

Although both triglyceride and FFA levels showed qualitatively similar diurnal fluctuations in the day-feeding studies, the correlation between the changes in their concentrations was significant only during the day when both fell (Fig. 1). The changes overnight were not significantly correlated and in several subjects marked overnight rises in triglyceride occurred despite very small or no changes in FFA (Fig. 1). On the other hand, both daytime and overnight changes in triglyceride and insulin were correlated, though negatively, to a highly significant degree. It is therefore likely that insulin-induced suppression of FFA was not the only mechanism whereby insulin affected the triglyceride concentration.

The role of insulin in the disposal of circulating triglyceride was tested by infusing insulin overnight when the triglyceride concentration would otherwise have risen. Since it seemed important not to reduce the blood concentration of glucose to levels that would provoke symptoms, the plasma concentrations of insulin that were achieved during the overnight infusions were less than those that occurred during the day in response to the sucrose meals. Despite this, insulin appeared to reduce substantially the rise in triglyceride in the two normal subjects and in one of the two hypertriglyceridemic subjects (Table III). In the other hyperlipidemic subject a substantial increase was seen between 11 p.m. and 9 a.m. although this was less than during the subsequent night. The insulin was infused between 7:30 p.m. and 9 a.m. and when these periods are compared on consecutive nights, the increments in plasma triglyceride were much greater when insulin was not infused. In the fifth subject, a young diabetic, the infusion of insulin actually lowered the triglyceride concentration which had risen during the preceding night in response to sucrose. Interestingly, the infusions of insulin also appeared to prevent a further rise in the triglyceride concentration during the next 24 hr despite further sucrose ingestion. That this could in fact be ascribed to the insulin was suggested by the abolition of further glycosuria during the next 48 hr although no more insulin was given; heavy glycosuria had been present beforehand. In the five subjects the mean overnight rise in the triglyceride concentration during the insulin infusion, was significantly less than that seen in the other 17 subjects during the corresponding night.

The studies in the two previously untreated young diabetics were carried out in order to determine whether an increase in plasma triglyceride levels would occur in the absence of normal insulin secretion. Both subjects had presented with their first symptoms of diabetes some weight loss, polyuria, and thirst. A rise in triglyceride was seen during the first 24 hr in one subject and during the second 24 hr in the other despite very small changes in insulin levels. These two studies argue against a direct effect of insulin on triglyceride secretion and support rather a role in the removal of triglyceride.

The clear inverse relationship between changes in triglyceride and insulin levels which were seen in the daytime studies were not readily apparent with continual feeding. In the latter studies, the triglyceride concentration rose progressively while the insulin concentration remained elevated. However, during the second 24 hr, the rise in triglyceride was higher during the night than during the day, whereas the mean insulin levels were lower at 10:00 p.m., 1:00 a.m., and 4:00 a.m. than at 10:00 a.m., 1:00 p.m., and 4:00 p.m. in the four subjects in whom these measurements were made. Nevertheless, it is clear that with continual feeding, the amounts of insulin that were secreted did not prevent a rise in the triglyceride concentration. This does not exclude the possibility that greater secretion of insulin might have prevented the rise in triglyceride levels or that this rise would have been greater had the production of inuslin been less. The insulin infusion studies also showed that modest elevations in the plasma insulin concentration led to almost complete suppression of the overnight rise in triglyceride levels in some but not in all subjects. These studies, taken together, suggest that insulin is only one of several important factors that determine the plasma triglyceride concentration and that the extent to which insulin exerts this effect will depend on the amount of insulin secreted, the quantity of triglyceride presented for disposal, the responsiveness of the removal mechanisms, the secretion of opposing hormones, and other factors.

Superimposed on the over-all increase in triglyceride concentration following sucrose feeding, we found a marked diurnal pattern in the changes in triglyceride, insulin, and FFA concentrations. These diurnal fluctuations were most marked when sucrose was fed only during the daytime (Fig. 1) but since they were also observed, though to a lesser extent, with continual 24 hr feeding (Fig. 2) it is clear that these fluctuations are more than a simple reflection of the state of absorption.

Others have also reported diurnal changes in hormones and fuels that do not appear to be related merely to meals (25–27). The insulin responses during the continual feeding were significantly lower after an evening than after a morning meal. Exhaustion of insulin stores is an unlikely explanation since the response was again greater next morning. Malherbe, De Gasparo, De Hertogh, and Hoet have recently shown circadian variations in insulin levels in man, reporting significantly higher insulin responses in the morning to identical meals (28).

The many reports that have shown a positive correlation between insulin and triglyceride levels are not necessarily inconsistent with our studies. Firstly, since the daytime fall in triglyceride concentration correlated with both the fasting, early morning triglyceride concentration, and the subsequent day time rise in insulin, it is not surprising that the insulin response might also be significantly related to the fasting triglyceride level. However, the interpretations could differ; whereas we have argued that the fall in triglyceride concentration might imply insulin induced enhancement of removal mechanisms, others have regarded the positive correlations between triglyceride and insulin levels as evidence for enhanced triglyceride formation (2, 21). Secondly, longer periods of high carbohydrate intake might lead to some resistance to the action of insulin both with respect to glucose and triglyceride removal. High fasting triglyceride levels might then be expected to occur together with increased secretion of insulin, though the relationship need not be a causal one. Finally, there is the possibility that plasma triglyceride may stimulate insulin secretion; ingestion of triglycerides has been shown to stimulate insulin secretion in man (29).

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