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Horm. Metab. Res. 11 (1979) 628–634

Effects of Hypo- and Hyper-Thyroidism on In Vivo Lipogenesis in Fed and Fasted Rats*

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Summary

Thyroidectomized rats (T) daily injected with either 0, 0.1, 1.8 or 25 μg of L-thyroxine/100 g body wt. were compared with intact controls (C). The appearance of radioacitvity in fatty acids 30 min after the i.p. injection of (3-^{14}C)pyruvate was reduced in adipose tissue and enhanced in liver of T+25, being no differences between the other groups and C. (^{14}C)-Fatty acids are reduced with 3 h of fasting only in the adipose tissue of T+1.8 and C, while 24 h produces a reduction in liver in the T+1.8, T+25 and C, and in adipose tissue in the T+1.8 and C animals. The highest percentage of radioactivity was observed in the liver glyceride glycerol fraction, being greater in T+25 than in the other groups. Fasting produces an increment in the (^{14}C)-glyceride glycerol fraction. being significant only in the hypothyroid animals in both liver and adipose tissue. The most sensitive parameter to fasting was the formation of (^{14}C)-non-saponifiable lipid in both the C and T+1.8 animals, while it does not change in T+0 or T+0.1, but is enhanced within 24 h in the adipose tissue of T+25. It is proposed that most of the observed changes are due to the other endocrine disfunction s which appear in hypo- and hyperthyroidism, as the *in vivo* results do not comply with *in vitro* effects of thyroxine on lipogenesis of others.

Key-Words: *Lipogenesis – Hypothyroidism – Hyperthyroidism – Adipose Tissue – Liver*

Introduction

The comparative contribution to the synthesis of different lipidic fractions in the organism differs between liver and adipose tissue; the response of either tissue to changes in the dietary condition of the animals being also different (*Borensztajn* and *Getz* 1972; *Jansen* 1966; *Jansen, Zanelli* and *Hutchison* 1966, 1967, 1968). Thyroid hormones are well known to affect lipid metabolism. Increased oxidation of cholesterol and fatty acids had been documented in thyrotoxic states (*Dayton* 1960; *Kritchevsky* 1962; *Myant* 1968; *Spirtes* 1953). However, the role of thyroid hormones in the regulation of lipogenesis has still to be established, as recently suggested by *Faas, Carter* and *Wynn* (1972, 1977).

[1] Postdoctorate research fellow of the Juan March foundation, Spain.

*Supported by a grant from the "comisión Asesora de Investigación Cientifica y Técnica, Presidencia del Gobierno", Spain

Received: 15 Aug. 1978 **Accepted: 29 Jan. 1979**

0018–5043/79 1132–0628 $ 03.00

Table 1 Effects of thyroidectomy and treatment with L-thyroxine in the rat

	Body weight[+] (g)	Liver weight (g)	Epididymal fat pad weight (mg)	Plasma protein bound iodine (μg/100 ml)
Intact controls	193 ± 4	10.6 ± 0.4	1343 ± 361	4.59 ± 0.25
Thyroidectomized + 0 μg L-T_4[++]	103 ± 7	4.6 ± 0.7	222 ± 27	0.23 ± 0.36
p[+++]	< 0.001	< 0.001	< 0.05	< 0.001
Thyroidectomized + 0.1 μg L-T_4	164 ± 8	6.5 ± 0.6	449 ± 78	0.68 ± 0.28
p	< 0.01	< 0.001	< 0.05	< 0.001
Thyroidectomized + 1.8 μg L-T_4	202 ± 8	10.3 ± 0.4	752 ± 149	4.46 ± 0.28
p	N.S.	N.S.	N.S.	N.S.
Thyroidectomized + 25 μg L-T_4	172 ± 5	11.9 ± 0.8	446 ± 87	9.55 ± 0.71
p	< 0.01	N.S.	< 0.05	< 0.001

+ Mean ± S.E. of 5 rats / group
++ Amount of L-thyroxine daily injected/100 g body weight for 40 days
+++ p values correspond to the differences of each group vs the intact controls (N.S. = not significant, i.e. $P > 0.05$)

In the present study, the "in vivo" lipogenesis was studied in both liver and adipose tissue in thyroidectomized rats, treated with exogenous thyroxine during a prolonged period of time in order to obtain different thyroid status. These experiments were carried out in both fed, 3 and 24h fasted rats, to determine the sensitivity of the antilipogenetic effect of food deprivation. (3-^{14}C)-Pyruvate was used as substrate, since it enters the lipogenic sequence at a point beyond the pentose and glycolytic pathways, being well established that it is a good precursor for lipogenesis, even after starvation (*Aranda* and *Herrera* 1974; *Jomain* and *Hanson* 1968; *Kneer* and *Ball* 1968; *Patel, Jomain-Baum, Ballard* and *Hanson* 1971).

Materials and Methods

Young male Wistar rats, weighing 40–50 g, were fed on a medium-residue, low-iodine diet (0.04–0.09 μg of iodine/g) (*Escobar del Rey, Morreale de Escobar, Jolin* and *Lopez-Quijada* 1968), surgically thyroidectomized (*Zarrow* 1964), thereafter injected intraperitoneally daily with 0, 01., 1.8 or 25 μg of L-thyroxine/100 g body weight for a period of 40 days. Comparisons were made with age-matched intact male controls under the same diet supplemented with 1.7 μg of KIO_3/g, injected daily with 0.9 % NaCl, during the same period of time. Animals were housed in an air-conditioned animal quarter, maintained at 22–24 °C, with automatically controlled lights under a 12 hours-on /12 hours-off cycle, commencing at 11.00. All experiments were carried out at 11.00 and starvation was timed on the basis of the previous period of food deprivation by adequate removal of the food at pre-set times. During the starvation period the animals received distilled water *ad libitum*. Animals were i.p. injected with 0.5 ml of a solution containing 0.5 mmoles of sodium pyruvate and 1.09 x 10^7 DPM (The Radiochemical Center, Amersham, England) of (3-^{14}C)-pyruvate per 100 g of body weight. Rats were decapitated 30 min thereafter, and livers and epididymal fat pads removed, and rapidly frozen in liquid N_2. Lipids were extracted from weighed aliquots of the frozen tissues and purified in 2:1 v/v chloroform-methanol (*Folch, Lees* and *Sloane-Stanley* 1957). One aliquot of the lipid extracts was dried under N_2 and used for counting to determine the radioactivity in *total lipids*. Another dried aliquot was saponified in 5 M KOH in 95 % (v/v) ethanol for 2 h at 100 °C. Non-saponifiable lipids were extracted with heptane and the heptane-washed bottom was acidified with 5N H_2SO_4 and re-extracted with heptane for isolation of the fatty acids. Final heptane extracts were evaporated to dryness under N_2 at 40°C for counting. The radioactivity in the glyceride-glycerol was calculated from the difference between radioactivities in the total lipids, and the heptane extracts. Recovery experiments with (^{14}C)-tripalmitine or (^{14}C)-palmitate added to lipid extracts prior to saponification, indicated that more than 97 % of either labelled compound was recovered in the fatty acid fraction, and less than 0.9 % remained in the water soluble bottom after the saponification and heptane extraction. Free cholesterol was measured (*Crawford* 1958; *Zak, Dickenman, White, Burnett* and *Cherney* 1954) in aliquots of the non-saponifiable fractions and found to be 98.8 % of that determined in aliquots of initial total lipid extracts.

Results

Body, liver and epididymal fat pad weights

Although no difference in the body weight before thyroidectomy was observed among the groups of animals studied (47.56 ± 0.65 g, in all animals), at sacrifice the thyroidectomized rats (T+0) show significantly reduced body weight (Table 1), which was partially compensated by the daily injection of 0.1 μg of L-thyroxine (T+0.1), and completely normalized by the daily injection of 1.8 μg (T+1.8), when compared with the weights of intact controls. The thyroidectomized rats treated with 25 μg of L-thyroxine (T+25) showed a reduced body weight, due to a loss of lean mass more than to a change in the growth of the animals, as their body size (length between the snout and the beginning of the tail) did no differ from that of the intact controls (19.2 ± 0.2 cm *vs* 19.6 ± 0.3 cm, respectively). Liver and epididymal fat pad weights were also reduced in T+0 rats, and the difference with the controls were smaller in the T+0.1 group (Table 1). These parameters were completely normalized in T+1.8 animals, while in T+25 the epididymal fat pads weight was significantly reduced, al-

Table 2 Effects of thyroidectomy and treatment with L-thyroxine on liver and epididymal fat pad (^{14}C)-lipids 30 min after the i.p. injection of 1.09 x 10^7 DPM of (3-^{14}C) pyruvate in fed and fasted rats

	Liver (^{14}C)-lipids+ (DPM/mg)			Epididymal fat pad (^{14}C)-lipids (DPM/mg)		
Time of Fasting (hours)	0	3	24	0	3	24
Intact controls	495 ± 102	645 ± 91	759 ± 162	52.7±12.6	25.9±3.9°	13.5±1.6°
Thyroidectomized + 0 μg L-T_4++	515 ± 109	523 ± 78	872 ± 105	25.3±13.3	40.6±13.0	29.8±5.0
p+++	N.S.	N.S.	N.S.	N.S.	N.S.	N.S.
Thyroidectomized + 0.1μg L-T_4	672 ± 141	713 ± 121	804 ± 134	41.8±16.5	47.5±6.6	24.6±4.8
p	N.S.	N.S.	N.S.	N.S.	<0.05	N.S.
Thyroidectomized + 1.8 μg L-T_4	601 ± 200	803 ± 114	747 ± 95	44.8±17.0	16.2±4.6°	15.5±2.6°
p	N.S.	N.S.	N.S.	N.S.	N.S.	N.S.
Thyroidectomized +25μg L-T_4	1123 ± 142	940 ± 125	750 ± 45	10.2±2.4	13.0±2.0	10.8±3.7
p	<0.05	N.S.	N.S.	<0.01	<0.05	N.S.

+ Mean ± S.E. of 5–10 rats / group
++ Amount of L-thyroxine daily injected / 100 g body weight for 40 days.
+++ p values correspond to the differences of each group vs. the intact controls (N.S. = not significant, i.e. $p > 0.05$)
° Differences between fasted and fed animals: o = $p < 0.05$.

though liver weights were similar to those of controls (Table 1). These differences are similar to those previously observed in animals under comparable conditions (*Aranda, Montoya* and *Herrera* 1972; *Llobera, Seibel* and *Herrera* 1978), and correspond to change in plasma PBI values (Table 1), showing the intense degree of hypothyroidism attained in the T+0 group, being milder in T+0.1 animals, and completely normalized in T+1.8, and the hyperthyroid state in the T+25 group.

(3-^{14}C)-Pyruvate conversion to total lipids

The appearance of labelled total lipids at 30 min after the injection of (3-^{14}C) pyruvate was greater in liver than in epididymal fat pads (Table 2). The thyroidectomy of the animals not treated with exogenous thyroxine (T+0) did not affect the label recovered in either tissue when animals were fed, as compared with intact controls. The injection of either 0.1 or 1.8 μg of thyroxine to the thyroidectomized animals (T+0.1 and T+1.8, respectively) had no effect on these relationships, whilst thyroidectomized animals treated with 25 μg of thyroxine (T+25) showed a significant enhancement in the appearance of ^{14}C-lipids in liver, and a reduced one in that of adipose tissue. Neither 3 nor 24 h of fasting altered the amount of radioacitvity found in the lipids of the liver in controls, T+0, T+0.1 and T+1.8 groups. In the T+25 animals, 3 and 24 h of fasting produced a non-significant reduction of the label in liver lipids, which eliminates the differences between this group and the controls, when fed. In adipose tissue, 3 h of fasting produces a significant reduction in the label found in lipids of intact controls and T+1.8 group, whilst in T+0, T+0.1 and T+25 animals there is no significant change in the ^{14}C-lipids observed with 3 or 24 h of fasting in the adipose tissue.

Formation of (^{14}C)-fatty acids

The appearance of radioactivity in the fatty acid fraction after the injection of (3-^{14}C)-pyruvate in fed animals, was reduced in adipose tissue and enhanced in the liver of the T+25 animals, as related with values of intact controls there being no differences between the other groups of thyroidectomized rats and controls (Table 3). Fasting for a period of 3 h does not produce any difference in the formation of (^{14}C)-fatty acids in liver of either group, while in adipose tissue there is a significant reduction in the T+1.8 and control groups, with no change being observed in T+0, T+0.1 or T+25 animals. Fasting for a period of 24 h produces a significant reduction in the formation of (^{14}C)-fatty acids in liver in the T+1.8, T+25 and control groups, but with no changes in the T+0 and T+0.1 animals. The appearance of label in the fatty acid fraction is intensely reduced with 24 h of fasting in the adipose tissue of controls and T+1.8 rats, while in T+0, T+0.1 or T+25 group, there are no differences, as compared with values observed in these groups when fed

Formation of (^{14}C)-glyceride glycerol

Glyceride glycerol constitutes the lipidic fraction with the highest percentage of radioactivity in the liver in all groups (from 67.7 to 94.1 % of the label in the total lipids was found in the glyceride glycerol fraction in all groups). This fraction is greater in the liver of T+25 animals, than in other groups when fed, and after 3 h of fasting (Table 4). In other groups of thyroidectomized animals there appears to be no difference in their liver values as against in the intact controls. Fasting produces a progressive increment in the (^{14}C)-glyceride glycerol, which is only significant in the 24 h fasted T+0 animals, when compared with their fed values. In the T+25 group, 3 and 24 h of fasting produces a slight, but

Table 3 Effects of thyroidectomy and treatment with L-thyroxine on liver and epididymal fat pad (^{14}C)-fatty acids 30 min after the i.p. injection of 1.09 x 10^7 DPM of (3-^{14}C)pyruvate in fed and fasted rats

Time of Fasting (hours)	Liver (^{14}C)-fatty acids^{+} (DPM/mg) 0	3	24	Epididymal fat pads (^{14}C)-fatty acids (DPM/mg) 0	3	24
Intact controls	65±7	61 ± 14	32 ± 10^{o}	40 ± 12	15 ± 4^{o}	3 ± 1^{o}
Thyroidectomized + 0 μg L-T^{4++}	30±10	33 ± 9	23 ± 7	14 ± 12	6 ± 3	8 ± 3
p^{+++}	N.S.	N.S.	N.S.	N.S.	N.S.	N.S.
Thyroidectomized + 0.1 μg L-T^4	67±32	51 ± 19	58 ± 15	34 ± 14	31 ± 7	12 ± 3
p	N.S.	N.S.	N.S.	N.S.	N.S.	< 0.05
Thyroidectomized + 1.8 μg L-T^4	79±25	77 ± 14	17 ± 4^{o}	40 ± 16	10 ± 4^{o}	5 ± 1^{o}
p	N.S.	N.S.	N.S.	N.S.	N.S.	N. S.
Thyroidectomized + 25μ L-T^4	179±29	115 ± 29	57 ± 4^{o}	6 ± 2	9 ± 2	5 ± 2
p	< 0.05	N.S.	N.S.	<0.05	N.S.	N.S.

+ Mean ± S.E. of 5–10 rats / groups
++ Amount of L-thyroxine daily injected / 100 g body weight for 40 days
+++ p values correspond to the differences of each group vs. the intact controls (N.S. = not significant. i.e. $p > 0.05$)
o Differences between fasted and fed animals: o = $p < 0.05$.

not significant, decrease in the label found in the glyceride glycerol fraction which causes the differences to disappear in controls, when fed.

In the epididymal fat pads, the (^{14}C)-glyceride glycerol was significantly decreased in T+0 and T+25 groups, as compared with the fed controls. Fasting for periods of 3 or 24 h in T+1.8, T+25, and intact controls, does not produce any changes in this parameter. However, 3 h of fasting produces a significant increase in the formation of (^{14}C) glyceride glycerol in epididymal fat pads in T+0 and T+0.1 groups, and 24 h in the T+0 group.

Formation of non-saponifiable (^{14}C)-lipids

The formation of non-saponifiable (^{14}C)-lipids from (3-^{14}C)-pyruvate constitutes the most sensitive parameter to fasting from those studied (Table 5). Actually, 3 h of food deprivation were enough to produce a significant decrease in this parameter, both in liver and adipose tissue in the intact controls (Table 5), this change being greater with a 24 h fasting period. A similar change was observed in T+1.8 animals. In T+25 animals, there is a such decrease in the appearance of label in the liver, in the non-saponifiable lipids, being already observed at 3 h of fasting. This is not, however, the case in adipose tissues, as values observed when fed were significantly lower than in controls, and fasting produces an increase, which is significant after 24 h of food deprivation, as related both to the values when fed and with those observed in controls at the time of starvation. Contrarily to the other groups, fasting does not alter the appearance of radioactivity in the non-saponifiable lipids in liver or adipose tissue from the hypothy-

Table 4 Effects of thyroidectomy and treatment with L-thyroxine on liver and epididymal fat pad (^{14}C)-glyceride glycerol 30 min after the i.p. injection of 1.09 x 10^7 DPM of (3-^{14}C) pyruvate in fed and fasted rats

Time of Fasting (hours)	Liver (^{14}C)-glyceride glycerol^{+} (DPM /mg) 0	3	24	Epididymal fat pads (^{14}C)-glyceride glycerol (DPM/mg) 0	3	24
Intact controls	335±102	524±83	681±153	6.0±1.0	6.6±0.6	6.2 ± 0
Thyroidectomized + 0 μg L-T$_4^{++}$	436± 46	443±62	816±103^{oo}	1.9±0.7	10.6±1.5^{o}	21.6 ± 2.5^{ooo}
p^{+++}	N.S.	N.S.	N.S.	< 0.05	<0.05	< 0.01
Thyroidectomized + 0.1 μg L-T$_4$	461± 68	458±80	704±116	7.1±1.9	13.3±1.5^{o}	12.4 ± 2.3
p	N.S.	N.S.	N.S.	N.S.	<0.001	N.S.
Thyroidectomized + 1.8 μg L-T$_4$	438±122	626±109	703± 90	5.2±1.1	7.3±0.9	9.0 ± 1.2
p	N.S.	N.S.	N.S.	N.S.	N.S.	N.S.
Thyroidectomized + 25 μg L-T$_4$	811±138	752± 99	650± 41	1.9±1.1	3.3±0.4	6.1 ± 1.8
p	< 0.05	N.S.	N.S.	< 0.05	<0.001	N.S.

+ Mean ± S.E. of 5–10 rats / group
++ Amount of L-thyroxine daily injected / 100 g body weight for 40 days
+++ p values correspond to the differences of each group vs. the intact controls (N.S. = not significant. i.e. $p > 0.05$)
o Differences between fasted and fed animals: o = $p < 0.05$; oo = $p < 0.01$; ooo = $p < 0.001$

Table 5 Effects of thyroidectomy and treatment with L-thyroxine on liver and epididymal fat pad (^{14}C)-non-saponifiable lipids 30 min after the i.p. injection of 1.09 x 10^7 DPM of (3-^{14}C) pyruvate in fed and fasted rats

	Liver (^{14}C)-non-saponifiable lipids+ (DPM/mg)			Epididymal fat pads (^{14}C)-non-saponifiable lipids (DPM/mg)		
Time of Fasting (hours)	0	3	24	0	3	24
Intact controls	83 ± 11	43 ± 7^{oo}	26 ± 7^{oo}	0.79 ± 0.20	0.26 ± 0.03^{oo}	0.08±0.03^{oo}
Thyroidectomized + 0μg L-T_4++	19 ± 5	23 ± 4	19 ± 7	0.20 ± 0.10	0.23 ± 0.11	0.35±0.08
p+++	< 0.01	< 0.05	N.S.	< 0.05	N.S.	<0.05
Thyroidectomized + 0.1 μg L-T_4	31 ± 12	15 ± 3	29 ± 8	0.44 ± 0.15	0.43 ± 0.06	0.40±0.06
p	< 0.05	< 0.05	N.S.	N.S.	< 0.01	<0.01
Thyoridectomized + 1.8 μg L-T_4	69 ± 11	46 ± 8	20 ± 5^{oo}	0.41 ± 0.13	0.18 ± 0.03^{o}	0.11±0.04^{o}
p	N.S.	N.S.	N.S.	N.S.	N.S.	N.S.
Thyoridectomized + 25 μg L-T_4	97 ± 11	50 ± 11^{o}	26 ±*4^{ooo}	0.11 ± 0.03	0.18 ± 0.03	0.27± 0.01^{oo}
p	N.S.	N.S.	N.S.	< 0.01	N.S.	<0.001

+ Mean ± S.E. of 5–10 rats / group
++ Amount of L-thyroxine daily injected / 100 g body weight for 40 days
+++ p values correspond to the differences of each group vs. the intact controls (N.S. = not significant, i.e. > 0.05)
o Differences between fasted and fed animals: o = $p < 0.05$; oo = $p < 0.01$; ooo $p < 0.001$

roid animals, namely the T+0 and T+0.1 groups. The values observed in the liver of these groups when fed, were significantly lower than in their intact controls, this difference disappearing in animals fasted for a period of 24 h due to the decrease in the controls. In adipose tissue, the values of T+0 animals were significantly lower than in the controls, but after fasting (especially at 24 h of food deprivation), the T+0 and T+0.1 animals show significantly higher non-saponifiable (^{14}C)-lipids in their adipose tissue than their controls, principally due to the decrease in the latter group.

Discussion

After the injection of (3-^{14}C)pyruvate a substantial amount is rapidly converted into labeled glucose (*Herrera, Knopp* and *Freinkel* 1969). We have recently studied the rate of *in vivo* gluconeogenesis from (3-^{14}C)pyruvate in the same experimental situation as that used in the present study (*Llobera* and *Herrera,* unpublished results). Thus, the discussion below takes into consideration the effect that this recycling of the label may have on the actual amount of substrate measured in lipid fraction.

The high percentage of (^{14}C)-fatty acids formed in adipose tissue as related to the (^{14}C)-total lipids, contrasts with the preponderance of glyceride glycerol formation in liver. The response to fasting is also different for either parameter in both tissues, as there is a decrease in the formation of fatty acids in food deprived animals, while no change, or even an enhancement in the synthesis of (^{14}C)-glyceride glycerol from (3-^{14}C)-pyruvate. These changes are in agreement with those observed by other authors, using different lipogenic substrates (*Borensztajn* and *Getz* 1972; *Jansen, Hutchinson* and *Zanelli* 1966; *Jansen, Zanelli* and *Hutchinson* 1966). The formation of glyceride glycerol from pyruvate corresponds to a branch of the gluconeogenetic pathway. Actually, the use of gluconeogenetic substrates for glycerogenesis in the fasted state appears in the presence of a reduced utilization of glucose (*Balasse* and *Neef* 1973; *Cahill, Herrera, Morgan, Soldner, Steinke, Levy, Reychard* and *Kipnis* 1966; *Healt* and *Cormey* 1973; *Paul* and *Bortz* 1969) allowing an uninterrupted source of α-glycero-phosphate for the continuous esterification of fatty acids both in liver (coming from extrahepatic sources), and adipose tissue from the endogenous hydrolysis of glycerides. The appearance of labeled non-saponifiable lipids (presumably cholesterol) in adipose tissue is probably from intratissular synthesis, as the capacity of this tissue to synthesize cholesterol is already well documented (*Angel* and *Farkas* 1971, 1972; *Dietschy* and *Wilson* 1968; *Farkas, Angel* and *Avigan* 1973). The intense inhibition of the formation of non-saponifiable lipids in both liver and adipose tissue, indicates the high sensitivity to the nutritional state of the cholesterol synthesis. These data agree with those of *Kovanen* et al. (1975) showing with a more prolonged fasting period, an intense decrease in *in vivo* cholesterologenesis in both fat cell and liver. These findings contrast with those obtained in other peripheral tissues where cholesterol biosynthesis was found to be little influenced by caloric intake (*Dietschy* and *Siperstein* 1967; *Dietschy* and *Wilson* 1968).

In the present study it has been observed that differences in the thyroid status of the animals alter these relationships. Daily injections of 1.8 μg of L-thyroxine normalized all parameters studied in thyroidectomized animals showing that the observed effects are due to changes in the thyroid status and not to the removal of the thyroid gland. In hypothyroid animals, the appearance of label in both the fatty

acid and the non-saponifiable lipids was reduced in both liver and adipose tissue, and unlike the controls, fasting does not produce any change in this parameter in those animals. This is not due to a preferential use of pyruvate for other pathways, such as gluconeogenesis, as it has been previously shown that the enhancement of gluconeogenesis from pyruvate in the fasted state is slower in hypothyroid animals than in controls (*Llobera* and *Herrera*, unpublished results). From the present study it is not possible to determine the mechanism by which the decrease in the availability of thyorid hormones produce these effects, as they may well be the consequence of the other endocrine disfunctions which always accompany a deficiency in these hormones. Thus, for example, both T+0 and T+0.1 animals are shown to have low circulating levels of insulin and a reduced capacity of the pancreas to respond to insulinotropic agents (*Martinez, Llobera, Cornella* and *Herrera* 1977), that would contribute to the reduced lipogenetic capacity of these animals. The formation of glyceride glycerol from labelled pyruvate was not reduced in hypothyroid animals, especially in the fasted state, where this parameter is actually augmented both in T+0 and T+0.1 animals, in liver and adipose tissue. These results could be a consequence of either an enhanced glycerogenesis in these animals, or a reduced turnover of the newly formed glyceride glycerol. If glycerogenesis is parallel to gluconeogenesis, as has been shown in other conditions (*Aranda* and *Herrera* 1974), the augmented retention of labelled glyceride in these animals could correspond to a slower utilization of the newly formed glucose more than to an increased gluconeogenesis, as demonstrated in animals under similar experimental conditons (*Llobera* and *Herrera*, unpublished results).

The situation in hyperthyroid animals appears to be quite different from that of the other groups. In liver, both lipogenesis and glycerogenesis are enhanced in the fed state, with no change in the formation of non-saponifiable lipids. These effects do not comply with studies carried out *in vitro*, where it has been shown that thyroxine inhibits lipogenesis (*Faas, Carter* and *Wynn* 1972; *Myant* and *Iliffe* 1963). This discrepancy allows to suggest that the *in vivo* events are probably a consequence of secondary effects mediated by the other endocrine alterations which come together with the hyperthyroid situation. Actually, an increase in the activites of key lipogenic enzymes has been shown in hyperthyroid animals, (*Diamant, Gorin* and *Shafrir* 1972). The situation is quite different in the adipose tissue where the incorporation of (3-^{14}C)-pyruvate to either fatty acids, glyceride glycerol or non-saponifiable lipids, in the hyperthyroid animals were reduced. This is despite the fact, that it has been clearly shown that the activity of lipogenic enzymes are also enhanced in the adipose tissue of hyperthyroid rats (*Diamont* et al. 1972). This would probably be the result of a more rapid utilization of the newly formed lipids more than an inhibited lipogenesis, hindering the temporal retention of the synthesized labelled lipids. This interpretation agrees with the intensely enhanced lipolysis observed in these animals (*Fisher* and *Ball* 1967; *Montoya* and *Herrera* 1974; *Nikkila* and *Kekki* 1972), which would point to a short-life of the newly formed lipids, due to their rapid release in circulation for use in other tissues. This situation would be similar to that observed for liver glycogen, where glycogenolysis is greater than glycogenesis, despite the fact that both pathways are enhanced in these animals, disallowing the store of a normal concentration of glycogen in liver (*Llobera, Seibel* and *Herrera* 1978).

Contrarily to liver, adipose tissue lipogenesis is much less sensitive to fasting in the T+25 animals than in controls. This effect may be related to the fact that the circulating levels of insulin are unaltered with fasting in hyperthyroid animals (*Aranda* et al. 1972), and it is well known that adipose tissue, more than liver metabolism, is directly influenced by circulating insulin levels.

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