Thyroxine effects on parameters of glucose turnover in BHE rats fed menhaden oil

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The effect of hyperthyroidism on glucose turnover in BHE rats fed menhaden oil was studied. Thyroxine-treated rats had a greater glucose mass, a greater absolute glucose synthesis rate, less hepatic and muscle glycogen levels, and greater hepatic and peripheral fat cell lipogenic rates than nontreated rats. No differences in body weight gain were observed, nor were there differences in blood glucose levels, glucose space, or fractional reversible or irreversible glucose use. These observations suggest that thyroxine and menhaden oil were additive in their effects on glucose metabolism in BHE rats, which are genetically programmed to develop non–insulin-dependent diabetes mellitus.

Keywords: Glucose turnover; BHE rats; hyperthyroidism; fish oil

Introduction

In an earlier paper, we reported that feeding menhaden oil (MO) to BHE rats resulted in a decrease in hepatic and peripheral lipogenesis.[1] We have also shown that this diet affects hepatic mitochondrial respiration such that energetic efficiency (amount of adenosine triphosphate [ATP] produced per mole of oxygen consumed) was improved.[2] Further improvement was noted when MO-fed rats were injected daily with thyroxine (T_4). The diet effect was thought to be due to an increase in mitochondrial fluidity, whereas the T_4 effect was thought to be due to a change in activity in the components of the respiratory chain and coupling complexes. Thus, the diet and hormone effects were additive with respect to mitochondrial respiration.

BHE rats are characterized by their higher than normal rates of gluconeogenesis,[3] which can be potentiated by feeding a sucrose-rich diet[4] and/or a diet containing hydrogenated coconut oil.[5] The gluconeogenic process is not down-regulated in the fed animal[4] but continues at an unusually high rate. This feature of the BHE rat is analogous to that observed in the diabetic human. Studies of the T_4 effects on gluconeogenesis revealed that gluconeogenesis from nitrogen-containing substrates was decreased in cells from hyperthyroid BHE rats.[6] Studies of glucose turnover in rats fed corn oil and treated with T_4 revealed that T_4 treatment resulted in increases in fractional glucose turnover rates and fatty acid synthesis rates while serving to deplete hepatic glycogen stores.[7] Since feeding MO results in a decrease in hepatic lipogenesis and since this is an important aspect of glucose turnover, we speculated whether the T_4 effects described above would occur in MO-fed BHE rats. Thus, the present paper reports the results of an experiment using BHE rats fed a 6% MO diet and given daily injections of either T_4 or vehicle. Glucose turnover, lipogenesis, gluconeogenesis, and glycogen synthesis were measured using labeled glucose, tritiated water, and labeled alanine.

Materials and methods

Two groups of 10 BHE weanling male rats were used. They were housed in hanging wire mesh cages in a room controlled for temperature (21° ± 1°C), humidity (45% to 50%), and light (lights on, 6:00 AM to 6:00 PM). Food and water were always available. Food intakes and body weight gains were determined weekly. The animals were fed a diet containing 6% MO,* 64% su-

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*Gift of Zapata Hayne, Reedville, VA, USA.

Table 1 Fatty acid composition of menhaden oil

Fatty acid	Total fatty acids (mole %)
14:0	9
16:0	15
18:0	4
16:1	13
18:1	14
18:2	2
18:3	1
18:4	7
20:4	2
22:1	3
20:5	20
22:6	11

crose, 10% casein, 10% lactalbumin, 5% AIN Mineral Mix,[8] 4% fiber (Alphacel), and 1% AOAC vitamin mix.[9] The fatty acid composition of the MO is shown in *Table 1*. The diet ingredients, except for the MO, were purchased from ICN Nutritional Biochemicals, Cleveland, OH, USA. One group was injected daily with 10 μg T_4/100 g body weight during the last week of the experiment. The control group was injected with vehicle only. The 10 μg T_4 was divided into two doses administered at 12-hour intervals. The T_4 (Sigma Chemical Co., St. Louis, MO, USA) was dissolved in 0.005 M NaOH.

After 4 weeks of feeding, the groups were subdivided into five weight-matched pairs. The various aspects of glucose turnover were determined in nonfasted rats. The first half of each group was anesthetized with sodium pentobarbital and injected via the femoral vein with 10 μCi[U-^{14}C]glucose and 100 μCi[6-^{3}H]glucose/100 g body weight (part 1). The tritiated glucose (Amersham International, Amersham, UK) and carbon-labeled glucose (ICN Radiochemicals, Irvine, CA, USA) were injected in an isotonic sterile solution. Tail blood samples were withdrawn at 15-minute intervals after tracer injection for a total of 105 minutes. The blood samples were collected in heparinized tubes and centrifuged (3,500 rpm for 10 minutes at 4°C), and the plasma was used for the determination of the specific activity of the glucose. After perchlorate deproteinization, the supernatant was applied to the top of a mixed bed ion exchange column (0.5 g Amberlite CG-120-Na^+ above 0.5 g of Amberlite CG 400 formate) according to the methods of Krebs et al.[10] The remaining 2 ml of eluate was evaporated to dryness to remove ^{3}HOH. The ^{3}H/^{14}C radioactivity of the dried eluates was determined after reconstitution in 1 ml H_2O and the addition of 10 ml toluene/Triton X-100 (3:1, vol/vol) containing 5 g of PPO (2,5-diphenyloxazole) plus 250 mg of POPOP (1,4-bis(5-phenyloxazole-2-yl)-benzene)/l as a scintillant. Radioactivity was determined in a liquid scintillation spectrometer (Beckman model 9200, Palo Alto, CA, USA) using the channels ratio method.

At the end of the blood collection period, the rats were killed by pneumothorax. Liver, gastrocnemius muscles, and epididymal fat pads were quickly excised, weighed, and flash frozen in liquid nitrogen. Liver and muscle were used for the determination of glycogen. Liver and fat pads were used for the determination of fatty acids. The specific activity of the glycogen was determined. Liver and muscle samples (approximately 1 g) were digested with 2.0 ml of 40% (wt/vol) KOH at 100°C. The glycogen was purified by the method of Cowgill and Pardee.[11] The glycogen was washed three times with alcohol. It was then hydrolyzed to glucose with 1 M H_2SO_4 for 2 hours at 100°C, and samples of the hydrolysate were used for the determination of glucose by glucose oxidase[10] and radioactivity as described earlier.

Glucose turnover rates were calculated from semilogarithmic plots of ^{14}C and ^{3}H glucose in the plasma versus time using the methods validated by Smith et al.[12] The radioactivity of each isotope was expressed as the fraction of the dose injected per 100 g body weight remaining in 1 μmol of plasma glucose at the time of sampling (fractional residual radioactivity). The glucose turnover rate (mg/min/100 g body weight) was estimated from a semilog plot of plasma glucose specific activity versus time. The plot yielded a straight line represented by the exponential equation $S = S_oC^{-kt}$ where S is the specific activity (dpm/μmol) of glucose in a blood sample, S_o is the extrapolated glucose value at zero time, and k is the first order rate constant or the fractional turnover rate (min^{-1}). This is 2.303 × slope of the decay curve. The fact that a straight line was obtained suggests that glucose turned over in an instantaneously mixing pool during the 105 minutes of observation.

The glucose synthesis or production rate, R (μmol/min/100 g body weight), is equal to Mk, where M is the blood glucose pool size (μmol/100 g body weight) and could be determined by the equation, M = injected radioactivity (dpm/100 g body weight) S_o. The glucose pool size is the product of glucose concentration, C (μmol/ml, average from seven time points), and the space occupied by the glucose pool (the pool space, V, ml/100 g body weight): R = kCV.

The method for calculating glucose turnover as described above is based on the assumption that newly synthesized glucose is unlabeled and is released into the circulation at a steady rate. The validity of this assumption depends on the choice of isotope used to label the blood glucose. Some of the ^{14}C-labeled glucose is recycled, whereas the ^{3}H of carbon 6 of glucose is presumed to be lost during glycolysis and gluconeogenesis, and is thus less likely to reappear in the blood glucose.[12-14]

By comparing the turnover rates obtained with U-^{14}C-glucose with those obtained using ^{3}H-glucose, the rate of glucose carbon recycling from extrahepatic tissue to liver, i.e., Cori cycle, was calculated. This recycling is represented by the formula $R_{6H} - R_C$ and its percentage contribution to the blood glucose turnover is $100 \times (R_{6H} - R_C)/R_{6H}$, where R_{6H} and R_C represent tritiated and ^{14}C-labeled glucose, respectively.

The second half of each group was injected, again via the femoral vein, with 4 μCi L-[U-^{14}C]alanine/100 g body weight and 1 mCi ^{3}HOH/100 g body weight (part 2). Again, tail blood samples were drawn at 15-minute intervals for a total of 45 minutes, at which time heart blood was drawn followed by rapid excision of liver, gastrocnemius muscle, and epididymal fat pads. The blood plasma was used to determine radioactive glucose and total body water as described above. Blood plasma, liver, and fat pads were used for the determination of tritiated fatty acids.[15-18] Liver and muscle were used for the determination of ^{14}C-glycogen glucose. The appearance of ^{14}C glucose in the blood over time was taken as a measurement of the rate of gluconeogenesis by the liver. Means for each parameter were compared using the Student's *t* test.

Results

Table 2 shows that T_4 treatment had no effect on food intake, body weight, muscle weight, liver weight, or fat pad weight. This is consistent with our previous work with this dose of T_4 in BHE rats and indicates that we were within the physiologic range of T_4 levels in the body.

However, treatment with T_4 did affect the various parameters of glucose synthesis and use, as shown in *Table 3*. Rats treated with T_4 had a greater glucose mass and a greater absolute glucose synthesis rate, but no difference in the plasma glucose levels, fractional irreversible glucose turnover rate, or fractional glucose carbon recycling rate compared with control rats. These measurements of glucose turnover were conducted in nonstarved rats. The decay curves (*Figure 1*) of the specific activities of both ^{14}C-labeled and ^{3}H glucose were linear, while the blood glucose level was maintained virtually constant throughout the blood collection period. Because of these observations, either decay could have been used for the calculations. In fact, both were, and the calculated values were almost identical. Thyroxine-treated rats had greater rates of fatty acid synthesis in both liver and fat pads and less hepatic glycogen regardless of the precursor used (*Table 4*).

Table 2 Effect of thyroxine treatment on food intake, body weight, liver weight, and plasma glucose of BHE rats

	Treatment[a]	
	Control	T_4[b]
Food intake (g/100g body wt/day)	8.4 ± 0.3	7.9 ± 0.2
Initial body weight (g)	54 ± 1	54 ± 1
Final body weight (g)	225 ± 4	226 ± 4
Liver weight (g)	9.77 ± 0.24	10.48 ± 0.62
Muscle weight (g)	2.69 ± 0.06	2.83 ± 0.06
Epididymal fat pad weight (g)	2.30 ± 0.13	1.95 ± 0.14

[a] Values are mean ± SEM; N = 10.
[b] Rats were injected daily, with intraperitoneal T_4, 10 μg/100 g body weight.

Table 3 Effect of thyroxine treatment on glucose turnover in BHE rats

	Treatment[a]	
	Control	T_4[b]
Plasma glucose (mg/dl)	131.7 ± 7.8	132.1 ± 6.3
Glucose mass (μmol/100g body wt)	517 ± 59	739 ± 65[c]
Glucose space (ml/100 g body wt)	5.47 ± 0.95	9.77 ± 1.90
Fractional irreversible glucose turnover rate (%min^{-1})	7.81 ± 1.12	9.72 ± 0.68
Absolute glucose synthesis rate (μmol/min/100 g body wt)	37.98 ± 2.06	71.50 ± 6.49[c]
Fractional glucose carbon recycling (Cori cycle) (%)	5.85 ± 1.99	14.14 ± 3.30

[a] Values are mean ± SEM; N = 5 for the control group; N = 4 for the T_4 group.
[b] Rats were injected daily with intraperitoneal T_4, 10μg/100 g body weight.
[c] Effect of T_4 treatment is significant ($P < 0.05$).

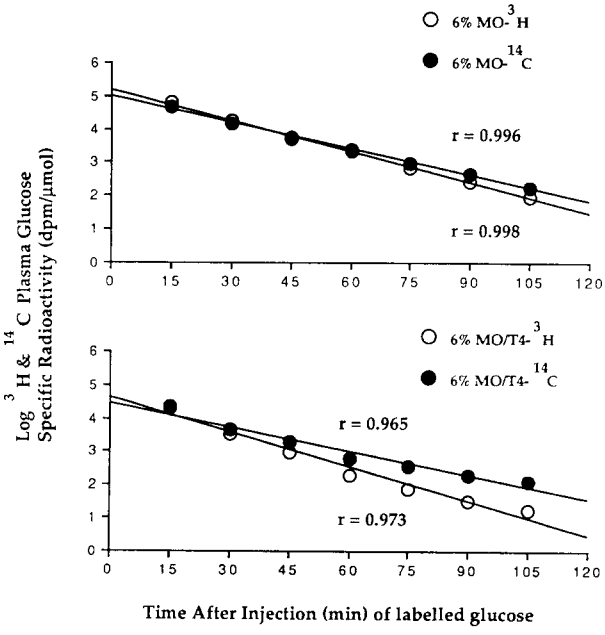

Figure 1 Semilogarithmic plot of plasma glucose-specific radioactivity in control and T_4-treated rats injected with D-[6-^{3}H]/[U-^{14}C]-glucose. Groups of five rats were injected intravenously with D-[6-^{3}H]/[U-^{14}C]-glucose at zero time. The dose of radioactivity was normalized to 100,000 dpm/100 g body weight for each isotope.

Muscle glycogen was significantly less in T_4-treated animals compared with control rats when injected with glucose, but no T_4 effects could be seen when labeled alanine served as the tracer. As with the labeled liver glycogen, the difference due to tracer incorporation was probably due to the difference in time between injection of the label and tissue harvest. When the labeled glucoses were given, the tissues were harvested 105 minutes later, whereas when labeled alanine was given, the tissues were harvested 45 minutes later. Since we know that metabolic rate is accelerated

Table 4 Tissue glycogen levels and fatty acid synthesis in thyroxine-treated and control BHE rats

	Treatment[a]	
	Control	T_4[b]
Liver glycogen (μmol glucose/g liver, wet wt)		
From part 1 (glucose) (killed at 105 min)	1,287 ±173	0.05 ± 0.02[c]
From part 2 (alanine) (killed at 45 min)	1,696 ± 175	472 ± 253[c]
Muscle glycogen (μmol glucose/g muscle, wet wt)		
From part 1 (glucose)	316 ± 19	202 ± 32[c]
From part 2 (alanine)	302 ± 11	335 ± 24
Specific activity in muscle glycogen (dpm/μmol glucose)		
U-^{14}C-glucose	1,111 ± 242	198 ± 47[c]
U-^{14}C-alanine	7.25 ± 0.87	6.83 ± 0.86
Hepatic (^{3}HOH) fatty acid synthesis (μmol acetyl U/g liver/45 min)	1.73 ± 0.1	5.5 ± 1.0[c]
Adipose (^{3}HOH) fatty acid synthesis (μmol acetyl U/g fat tissue/45 min)	1.0 ± 0.1	3.7 ± 1.2[c]

[a] Values are mean ± SEM; N = 5 for the control group; N = 5 for the T_4 group.
[b] Rats were injected daily with intraperitoneal T_4, 10μg/100 g body weight.
[c] Effect of T_4 treatment is significant ($P < 0.05$).

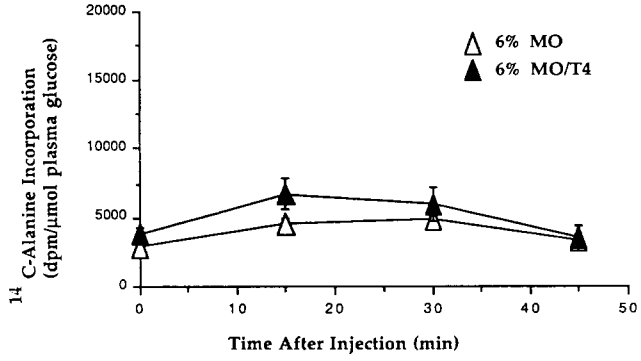

Figure 2 Time course of the incorporation of ^{14}C from L-[^{14}C]-alanine into plasma glucose. The L-[^{14}C]-alanine (4 μCi/100 g body weight) was administered by intravenous injection at zero time.

by T_4, this time difference in harvest could account for the difference in labeled hepatic and muscle glycogen from the different tracers. The time difference was necessary so that our estimates of tritiated water incorporation into fatty acids would represent de novo synthesis without the need for a large correction for fatty acid recycling.[16-18] Because of the glycogen-depleting effect of T_4 on hepatic glycogen, specific activity was not detectable from ^{14}C glucose. The time course of appearance of the labeled alanine in the blood glucose is shown in *Figure 2*. Little difference due to T_4 was observed in the blood levels of labeled glucose.

Discussion

In an earlier paper,[7] we reported that T_4 treatment of corn oil-fed rats resulted in no change in glucose mass and the absolute glucose synthesis rate while the irreversible glucose turnover and the glucose carbon recycling rates were increased. In the present work, T_4 treatment resulted in an increase in glucose mass, no change in irreversible glucose turnover rate, and an increase in glucose synthesis. The differences in results between the present and prior work suggest that the response to T_4 treatment might be determined by the type of fat fed to the animals. The MO-fed rats responded differently to T_4 than did the corn oil-fed rats.[7] This is seen in *Table 2*. Thyroxine treatment in the earlier experiment[7] resulted in a decrease in body weight gain and a decrease in liver weight. In the present work, T_4 was without effect on these parameters. This suggests that the rats were able to increase their energetic efficiency when treated with T_4 such that they did not reduce their body weight gain. This, in turn, suggests that the MO diet changed the internal milieu such than an increase in energy conservation was possible. In another paper,[2] we reported that the T_4 treatment effect was additive to that of MO with respect to hepatic mitochondrial respiration efficiency. Hepatic mitochondria from T_4-treated, MO-fed rats consumed less oxygen per mole of ATP produced than similarly treated rats fed corn oil or rats fed MO without T_4 treatment. Pryor et al.[19] have reported that when respiratory efficiency is increased, gluconeogenesis is decreased. Assuming that an increase in hepatic mitochondrial efficiency has occurred in the T_4-treated rats, as reported earlier,[2] we would have expected a decrease in incorporation of ^{14}C from alanine into glucose. However, this did not occur (*Figure 2*). Further, we expected to observe a decrease with T_4 treatment in the calculated absolute glucose synthesis rate (*Table 3*). The reverse was observed. According to the data in *Table 3*, the absolute glucose synthesis rate was nearly doubled by the T_4 treatment. However, one must take into consideration the fact that the absolute glucose synthesis rate consists not only of glucose synthesis from substrates such as lactate and alanine, but also of glucose which results from glycogenolysis. The T_4 treatment probably stimulated this process. Perusal of *Table 4* suggests that glycogen turnover was more rapid in the T_4-treated rats. This suggestion is based on the observation of differences in the amounts of glycogen in the rats killed at 45 and 105 minutes postlabel infusion. The T_4-treated rats killed at 45 minutes had more glycogen than did those killed at 105 minutes. Hepatic tissue from T_4-treated rats had little measurable glycogen, while muscle had less than two thirds that found in the control rats. Also of interest is the observation that T_4 treatment increased fatty acid synthesis in both liver and adipose tissue. Since the rats did not differ in their final body weights, one must assume that the energetic efficiency mentioned above for the hepatic mitochondria made possible sufficient ATP to support this process and that surplus energy could be stored as fat. However, equally possible is the supposition that sufficient ATP was available to support protein synthesis and growth at the expense of fat accumulation. Unfortunately, we

did not assess the composition of the bodies in this study so we do not know if such had occurred. Thyroxine has been shown to stimulate protein synthesis,[20] so this possibility is likely.

The real question now is, how can T_4 have these unique effects in MO-fed BHE rats? Usually, T_4 treatment results in a reduction in the rate of body weight gain. However, this did not happen in our work. Reed and Tarver[21] have reported that diet can influence the lipogenic response to T_4 in rat liver. They suggested that T_4 treatment increases the need for linoleic acid. This suggestion was based on their observation that the T_4 increased fatty acid synthesis with a decrease in growth. These effects were reversed when additional linoleic acid was provided. In the present work, dietary linoleic acid was minimal, but there was an abundance of omega 3 unsaturated fatty acids. We observed an increase in fatty acid synthesis, but no decrease in growth. It does not seem likely, therefore, that the T_4 effect on growth was mediated through its effect on linoleic acid. More likely, the additive effects of T_4 and MO on caloric efficiency were due to their combined effects on membrane fluidity. Both treatments result in an increase in membrane phospholipid fatty acid unsaturation, which increases membrane fluidity.[22-24] With more fluid membranes, metabolites and adenine nucleotides are exchanged more readily through the membranes while separate cellular compartments and processes dependent on these passages are facilitated. Clearly, this has happened in the present work. Glucose turnover has increased; so, too, has fatty acid synthesis. Both processes are dependent on membrane-mediated metabolite exchange.

Lastly, one must ask about the relevance of these findings in BHE rats. These rats are genetically programmed to develop non-insulin-dependent diabetes mellitus as they age. They also have a less active hepatic 5′-deiodinase activity.[25] It is possible that the diet and hormone effects on glucose metabolism shown in this study could correct some of this genetic tendency such that the age of onset of abnormal glucose tolerance could be increased. Further study will be needed before this suggestion can be accepted.

References

1 Berdanier, C.D., Johnson, B.J., and Buchanan, M. (1989). Interacting effects of menhaden oil and sucrose in the responses of two strains of rats to starvation-refeeding. *Nutr. Res.* **9,** 1167–1176

2 Kim, M-J.C., and Berdanier, C.D. (1989). Influence of menhaden oil on mitochondrial respiration in BHE rats. *Proc. Soc. Exp. Biol. Med.* **192,** 172–176

3 Berdanier, C.D. (1982). Rat strain differences in gluconeogenesis by isolated hepatocytes. *Proc. Soc. Exp. Biol. Med.* **169,** 74–79

4 Park, J.H.Y., Berdanier, C.D., Deaver, O.E., and Szepesi, B. (1986). Effects of dietary carbohydrate on hepatic gluconeogenesis in BHE rats. *J. Nutr.* **116,** 1193–1203

5 Wander, R.C., and Berdanier, C.D. (1986). Effects of type of dietary fat and carbohydrate on gluconeogenesis in isolated hepatocytes from BHE rats. *J. Nutr.* **116,** 1156–1164

6 Berdanier, C.D. (1983). Effects of thyroid hormone on the gluconeogenic capacity of lipemic BHE rats. *Proc. Soc. Exp. Biol. Med.* **172,** 187–193

7 Kim, M-J.C., Pan, J-S., and Berdanier, C. (1989). Glucose turnover in BHE rats: effect of thyroid hormone. *Biochem. Arch.* (in press)

8 American Institute of Nutrition (1977). Report of the AIN Ad Hoc Committee on Standards for Nutritional Studies. *J. Nutr.* **107,** 1340–1348

9 Berdanier, C.D. (1974). Metabolic characteristics of the carbohydrate-sensitive BHE strain of rats. *J. Nutr.* **104,** 1246–1256

10 Krebs, H.A., Bennett, D.A.H., de Gasquet, P., Gascoyne, T., and Oshida, T. (1963). Renal gluconeogenesis: the effect of diet on the gluconeogenic capacity of rat kidney cortex slices. *Biochem. J.* **86,** 22–27

11 Cowgill, R.W., and Pardee, A.B. (1957). Glycogen. In *Experiments in Biochemical Research Technique* (R.W. Cogwill, A.B. Pardee, eds.), p. 158–160, John Wiley & Sons, New York

12 Smith, S., Cawthorne, M.A., and Simson, D.L. (1986). Glucose metabolism in the obese hyperglycemic (C57B1/6 ob/ob) mouse: the effects of fasting on glucose turnover rates. *Diabetes Res.* **3,** 83–86

13 Vernon, R.G., and Walker, D.G. (1974). Glucose metabolism in the developing rat: studies in vivo. *Biochem. J.* **127,** 521–529

14 Dunn, A., Chenoweth, M., and Schaeffer, L.D. (1967). Estimation of glucose turnover and the Cori cycle using glucose-6-t-^{14}C. *Biochemistry* **6,** 6–11

15 Dole, V.P., and Meinertz, H. (1960). Microdetermination of long chain fatty acids in plasma and tissue. *J. Biol. Chem.* **235,** 2595–2599

16 Lowenstein, J.M. (1971). Effect of (−) hydroxycitrate on fatty acid synthesis in vivo. *J. Biol. Chem.* **246,** 629–632

17 Fain, J.N., and Scow, R.O. (1966). Fatty acid synthesis in vivo in maternal and fetal tissues in the rat. *Am. J. Physiol.* **210,** 19–25

18 Jungas, R.L. (1968). Fatty acid synthesis in adipose tissue incubated with tritiated water. *Biochem. J.* **7,** 3708–3717

19 Pryor, J.H., Smyth, J.E., Quinlan, P.T., and Halestrap, A.P. (1987). Evidence that the flux control coefficient of the respiratory chain is high during gluconeogenesis from lactate in hepatocytes from starved rats. *Biochem. J.* **247,** 449–457

20 Towle, H.C., and Mariash, C.N. (1986). Regulation of hepatic gene expression by lipogenic diet and thyroid hormone. *Fed. Proc.* **45,** 2406–2411

21 Reed, E.B., and Tarver, H.J. (1976). Influence of diet on the lipogenic responses to thyroxine in rat liver. *Life Sci.* **17,** 1785–1798

22 Berdanier, C.D. (1988). Interaction of dietary fat type and thyroxine on the hepatic phospholipid fatty acids of BHE rats. *Nutrition* **4,** 293–296

23 McMurchie, E.J., Abeywardena, M.Y., Charnock, J.S., and Gibson, R.A. (1983). Effect of dietary lipids of the thermotropic behavior of rat liver and heart mitochondrial lipids. *Biochim. Biophys. Acta* **73,** 114–124

24 Hoch, F.L., Subramanian, C., Dhopeshwarkar, G.A., and Mead, J.F. (1981). Thyroid control over biomembranes. *Lipids* **16,** 328–335

25 McIntosh, M.K., Berdanier, C.D., and Cates, A-L. (1989). Studies on 5′deiodinase activities in rats differing in hepatic lipogenic potential. *FASEB J.* **3,** 1734–1740