PROCEEDINGS OF THE SOCIETY FOR EXPERIMENTAL BIOLOGY AND MEDICINE **183**, 273–278 (1986)

Age and Thyroid Hormone as Factors in the Responses of BHE Rats to Starvation–Refeeding[1] (42418)

MOON-JEONG KIM, JU-SHIN PAN, AND CAROLYN D. BERDANIER[2]

Department of Foods and Nutrition, University of Georgia, Athens, Georgia 30602

Abstract. The interacting effects of thyroid hormone, age, and duration of starvation on the enzyme and liver lipid responses of BHE rats to starvation–refeeding were studied. Rats were starved for 2, 4, or 7 days and refed a 65% glucose diet for 2 days. The rats were either 150 or 420 days of age and injected daily with either saline or 10 μg thyroxine/100 g body weight. Neither age nor duration of starvation affected the glucose-6-phosphate dehydrogenase or malic enzyme activity or liver lipid response to starvation–refeeding. However, thyroxine treatment potentiated the response to starvation–refeeding in the 420-day-old rats when the duration of starvation increased from 2 to 7 days.

Starvation–refeeding is a widely used technique to increase hepatic lipogenesis in rats (1–13). In our hands, the technique consists of 48 hr of starvation followed by 48 hr of refeeding a 65% glucose diet. Lipogenesis is then assessed using the activities of the NADP-linked enzymes glucose-6-phosphate dehydrogenase (G6PD; EC 1.1.1.49) and malic enzyme (ME; EC 1.1.1.40) and/or the incorporation of ^{3}HOH into fatty acids. The large increase in enzyme activity, called the enzyme overshoot, is dependent on a large (and relatively sudden) influx of glucose from the diet; whether the role of glucose is direct or indirect is not known. There is an increase in *de novo* enzyme protein synthesis as well (3–5). *De novo* enzyme synthesis may be orchestrated by the glucocorticoid hormones (6–9) but other hormones such as insulin (4, 5, 8), thyroid hormone (10, 11) and the sex hormones (12) may be involved as well.

Adelman (13) reported that after 72 hr of starvation the early (8-hr refeeding) glucokinase response was dampened by age but that by 48 hr of refeeding the age differences in the enzyme response to starvation had disappeared. Subsequently, it was reported (14) that age affected tissue hormone binding which, in turn, might explain the early glucokinase response. Boll *et al.* (15) also reported a dampening effect of age on the responses of rats to starvation–refeeding while Szepesi *et al.* (16) did not. The latter group only measured the responses of rats after 48 hr of refeeding in two groups of rats differing in their initial body weight.

In an earlier report (17), we showed that young (~50 days of age) age-matched BHE rats had a larger enzyme overshoot and liver lipid response to starvation–refeeding than did Sprague–Dawley rats. Strain differences in enzyme activity and tissue lipids between meal fed and *ad libitum* fed Wistar and BHE rats have also been reported (18) as have differences in hepatic metabolism and insulin status (19–22). Adams, in an extensive study of the effects of diet and genetics on longevity (23), reported that BHE rats fed a variety of diets had length of lifespans ranging from 400 to 800 days while Wistar rats, bred and reared under the same conditions, fed the same diets, had lifespans ranging from 600 to 1000 days. The prevalence of disease in these two strains and the role of diet there on was also studied by Durand *et al.* (24, 25). These workers fed high sucrose, glucose, or starch diets and found that when fed sucrose, BHE rats had a median length of life of 469 days and when fed glucose or starch their median lengths of life were 602 and 616 days, respectively. Wistar rats fed these diets had median lengths of life of 626, 645, and 645 days, respectively. Whereas Wistar rats generally died from respiratory disease, BHE rats generally died from renal disease. The rats were not reared in a pathogen-free environment nor were their respective breeding colonies pathogen free. Nonetheless, re-

[1] Supported by Georgia Agricultural Experiment Station Project H779.

[2] To whom correspondence should be addressed.

0037-9727/86 $1.50

gardless of the conditions and the diets it was apparent that BHE rats had significantly shorter lifespans than did their Wistar cohorts. In view of this and the many reports of the increased hepatic lipogenic capacity of the BHE rat compared to the Wistar or Sprague–Dawley rat, the question arose of whether their previously reported (17) high enzyme overshoot and liver lipid response to starvation–refeeding would be dampened by age. Since BHE rats might also be functionally hypothyroid (25–27) and since thyroid hormone may play a role in the enzyme overshoot response to starvation refeeding (10, 11), we asked the question of whether exogenous thyroid hormone would affect the starve–refeed response. Lastly, since the duration of starvation has been shown to affect the overshoot response of young Wistar rats (28), the question of whether adult BHE rats would respond similarly arose. To answer these questions, adult 150- or 420-day-old male thyroid-treated or untreated BHE rats were either *ad libitum* fed or starved 2, 4, or 7 days and refed a 65% glucose diet for 2 days. Consistent with an earlier report (16), we found that age did not affect the overshoot response. We also found that thyroid hormone treatment increased the overshoot response in the 420-day-old rats starved for 4 or 7 days.

Materials and Methods. Male BHE[3] rats of 150 and 420 days of age were used. They were housed individually in hanging wire mesh cages in a room controlled for temperature (21 ± 1°C), humidity (40–50%), and light (lights on, 0600–1800 hr). Water was always available. The rats were weighed daily and their food intakes determined. The rats were randomly allocated into eight groups at each age. Half of each of these groups were given daily injections of thyroxine (10 μg/100 body wt; L thyroxine, Sigma Chemical Co., St. Louis, Mo.) while their cohorts were injected with isotonic saline. One group at each age with and without thyroxine treatment was fed *ad libitum* a 65% glucose diet (6–9, 11, 12, 17). Additional groups of rats, with and without thyroxine treatment at each age, were starved for 2, 4, or 7 days and then fed the glucose diet for 2 days. Thus, a total of 16 groups of rats comprised the experiment. The various groups and their treatments are listed in the tables.

At the end of the refeeding period, rats were killed by decapitation, the livers quickly excised, chilled, weighed, and used for the determination of G6PD and ME activity (29) and liver lipid (30). Significant differences in the means attributable to age, duration of starvation, thyroid hormone treatment, or to an interaction of any two or all three of the variables were identified using analysis of variance (31). A one-way analysis of variance was also used to determine significance of difference due to duration of starvation within each age group (31). Lastly, within each feeding treatment at each age, a Student *t* test was used to determine significant differences attributable to hormone treatment (32).

Results. As expected, the 420-day-old rats weighed more initially and at the end of the experiment than the 150-day-old rats (Table I). Both sets of rats, because they were adults and no longer actively growing as are the rats customarily used for starvation–refeeding experiments, did not gain an appreciable amount of weight when fed *ad libitum* the glucose diet. When the 150-day-old rats were starved for 7 days and refed, their final body weights were significantly less than rats fed *ad libitum* or when starved for 2 or 4 days and refed for 2 days. Administration of thyroid hormone resulted in all three starved–refed groups having similar final body weights. When the 420-day-old rats were compared, again the *ad libitum* fed, 2-day and 4-day starved–refed rats were similar and the 7-day starved–refed rats weighed significantly less than *ad libitum* fed or the 2-day starved–refed groups. The 4-day starved–refed group was intermediate and not significantly different from either the *ad libitum* fed or the 2- or 7-day starved–refed groups. This pattern was unchanged by thyroid hormone treatment.

Food intake, adjusted for body weight, was similar for the 150-day-old rats and was increased by thyroid hormone treatment when these rats were starved and refed. In the older rats food intake decreased when the rats were starved and refed and this decrease was reversed by thyroid hormone treatment. Analysis of variance of the data indicated that age

[3] UGA colony.

TABLE I. EFFECT OF AGE, THYROID HORMONE, AND DURATION OF STARVATION ON BODY WEIGHTS AND FOOD INTAKES OF BHE RATS REFED A 65% GLUCOSE DIET

Treatment	150 days of age		420 days of age	
	Without thyroid	With thyroid	Without thyroid	With thyroid
Final body weight (g)				
Ad libitum	402 ± 12[a] (5)	414 ± 13[a] (5)	481 ± 14[a,y] (4)	445 ± 13[a] (4)
S2-R	365 ± 12[a] (6)	369 ± 22[b] (5)	478 ± 16[a,y] (3)	435 ± 17[a,y] (5)
S4-R	376 ± 17[a] (5)	354 ± 12[b] (6)	434 ± 20[a,b,y] (5)	401 ± 20[a,b,y] (4)
S7-R	319 ± 13[b] (6)	331 ± 18[b] (5)	392 ± 13[b,y] (4)	371 ± 9[b] (5)
Net body weight changes (g)				
Ad libitum	1 ± 5[a]	6 ± 5[a]	−6 ± 10[a]	−29 ± 9[a,x,y]
S2-R	−15 ± 4[b]	−22 ± 6[b]	−15 ± 2[a]	−34 ± 2[a,b]
S4-R	−40 ± 5[c]	−46 ± 3[c]	−50 ± 4[b]	−51 ± 3[b]
S7-R	−80 ± 8[d]	−98 ± 6[d,x]	−63 ± 8[b]	−83 ± 6[c,x,y]
Daily food intake (g/100 g body wt/day)				
Ad libitum	6.2 ± 0.2[a]	5.4 ± 0.3[a,x]	8.3 ± 0.6[a,y]	4.3 ± 0.3[a,x,y]
S2-R	6.3 ± 0.3[a]	7.0 ± 0.2[a]	5.2 ± 0.5[b,y]	5.5 ± 0.2[b,y]
S4-R	5.8 ± 0.1[a]	7.3 ± 0.2[b,x]	4.9 ± 0.2[b,y]	6.6 ± 0.1[c,x]
S7-R	6.0 ± 0.3[a]	7.4 ± 0.2[b,x]	5.1 ± 0.2[b]	7.1 ± 0.3[c,x]

Analysis of Variance

	Final body wt	Net body wt change	Daily food intake
Hormone	NS	*	*
Age	**	NS	**
Hormone × Age	*	NS	*
Treatment	**	**	NS
Hormone × Treatment	NS	NS	**
Age × Treatment	NS	**	**
Hormone × Age × Treatment	NS	NS	**

[a–d] Mean ± SE; number of rats in parentheses. Means with different superscripts (*a–d*) within a column for the parameter are significantly different ($P < 0.05$).

[x] The effect of thyroid hormone within the age and dietary treatment group is significant ($P < 0.05$).

[y] The effect of age within the thyroid and dietary treatment group is significant ($P < 0.05$).

* $P < 0.05$; ** $P < 0.01$; NS, nonsignificant by analysis of variance.

affected initial body weight, final body weight, and food intake. Duration of starvation affected the final body weight while thyroid hormone treatment affected the food intake. Significant hormone–age interaction effects were found on final body weight and food intake. Food intake was also affected by the interaction of thyroid hormone treatment and duration of starvation, the interaction of age and duration of starvation, and by the interaction of all three variables.

Relative liver size (RLS) was significantly less in starved–refed rats treated with thyroid hormone than in nontreated starved–refed rats (Table II). The duration of starvation did not affect RLS; however, the RLS of the starved–refed groups exceeded that of the *ad libitum* fed groups. Thyroid hormone treatment of the 150-day-old rats negated the starve–refeed effect on RLS but did not have this effect in the 420-day-old rats. Analysis of variance of the RLS data revealed that RLS was affected by age, hormone treatment, duration of starvation, and by the interactions of age and hormone treatment and of hormone and duration of starvation–refeeding treatments.

Consistent with earlier reports (1–9, 11, 12, 16, 17, 28) starvation–refeeding elicited a twofold increase in enzyme activity above that observed in the *ad libitum* fed rats. Both G6PD and ME activities were greater in the starved–refed rats than in the ad libitum fed rats. Nei-

TABLE II. EFFECT OF AGE, THYROID HORMONE, AND DURATION OF STARVATION ON G6PD, ME, AND % LIVER LIPID RESPONSES OF BHE RATS TO REFEEDING A 65% GLUCOSE DIET

Treatment	150 days of age		420 days of age	
	Without thyroid	With thyroid	Without thyroid	With thyroid
Relative liver size, RLS				
Ad libitum	3.58 ± 0.31^{a} (5)	3.47 ± 0.20^{a} (5)	3.19 ± 0.24^{a} (4)	$2.94 \pm 0.11^{a,y}$ (4)
S2-R	5.07 ± 0.21^{b} (6)	$3.69 \pm 0.098^{a,x}$ (5)	4.43 ± 0.03^{b} (3)	$3.61 \pm 0.16^{b,x}$ (5)
S4-R	5.15 ± 0.19^{b} (5)	$3.93 \pm 0.19^{a,x}$ (6)	4.49 ± 0.26^{b} (5)	$3.72 \pm 0.08^{b,x}$ (4)
S7-R	5.19 ± 0.24^{b} (6)	$3.98 \pm 0.11^{a,x}$ (5)	4.60 ± 0.06^{b} (4)	$3.98 \pm 0.11^{b,x}$ (5)
Glucose 6 phosphate dehydrogenase (units/100 g body wt)				
Ad libitum	22.0 ± 4.4^{a}	30.4 ± 2.1^{a}	17.6 ± 2.9^{a}	18.7 ± 3.0^{a}
S2-R	46.6 ± 4.2^{b}	51.4 ± 3.4^{b}	38.8 ± 5.7^{b}	52.3 ± 7.1^{b}
S4-R	56.7 ± 3.2^{b}	56.9 ± 4.5^{b}	$39.1 \pm 2.9^{b,y}$	$69.2 \pm 6.0^{c,x}$
S7-R	50.8 ± 3.3^{b}	47.9 ± 3.5^{b}	$39.4 \pm 5.3^{b,y}$	$72.2 \pm 6.5^{c,x,y}$
Malic enzyme (units/100 g body wt)				
Ad libitum	9.5 ± 1.1^{a}	11.7 ± 1.3^{a}	6.6 ± 1.2^{a}	11.8 ± 1.8^{a}
S2-R	20.2 ± 2.2^{b}	$30.4 \pm 3.2^{b,x}$	14.8 ± 1.9^{b}	$35.9 \pm 4.5^{b,x}$
S4-R	23.5 ± 1.7^{b}	$42.0 \pm 4.1^{c,x}$	$15.3 \pm 1.8^{b,y}$	$50.1 \pm 5.6^{c,x}$
S7-R	21.1 ± 1.3^{b}	$31.3 \pm 3.3^{b,x}$	$14.7 \pm 2.4^{b,y}$	$51.8 \pm 3.7^{c,x,y}$
% liver lipid (% w/w)				
Ad libitum	6.32 ± 0.91^{a}	6.85 ± 0.78^{a}	5.16 ± 0.39^{a}	5.80 ± 0.17^{a}
S2-R	$7.53 \pm 0.44^{a,b}$	$12.23 \pm 0.68^{b,c}$	$7.46 \pm 0.75^{a,b}$	$10.94 \pm 1.02^{b,x}$
S4-R	8.63 ± 0.50^{b}	$14.57 \pm 0.73^{c,x}$	$6.69 \pm 0.67^{a,b}$	$16.53 \pm 0.66^{c,x}$
S7-R	9.29 ± 0.72^{b}	$15.91 \pm 0.84^{c,x}$	7.65 ± 0.36^{b}	$16.43 \pm 1.14^{c,x}$

Analysis of Variance

	RLS	G6PD	ME	% liver lipid
Hormone	**	**	**	**
Age	**	NS	NS	NS
Hormone × Age	*	**	**	NS
Treatment	**	**	**	**
Hormone × Treatment	*	NS	**	**
Age × Treatment	NS	NS	NS	NS
Hormone × Age × Treatment	NS	*	*	NS

[a–c] Mean ± SE; number of rats in parentheses. Means with different superscripts (*a–d*) within a column for the parameter are significantly different ($P < 0.05$).

[x] The effect of thyroid hormone within the age group and feeding treatment is signficant ($P < 0.05$).

[y] The effect of age within the thyroid and feeding treatments is significant ($P < 0.05$).

* $P < 0.05$; ** $P < 0.01$; NS, nonsignificant by analysis of variance.

ther age nor duration of starvation affected the magnitude of the G6PD overshoot. However, age and duration of starvation did affect the level of enzyme activity. The 420-day-old rats starved for 4 or 7 days and refed for 2 days had lower G6PD activities than did the 4- or 7-day starved–refed 150-day-old rats. Age had little effect on G6PD activity in *ad libitum* fed untreated rats. With respect to ME activity, the 420-day-old rats tended to have less activity than the 150-day-old rats; however, these differences were significant only if the rats were starved for 4 or 7 days. When treated with thyroid hormone, the 420-day-old rats fed *ad libitum* had less G6PD activity than the 150-day-old rats. When starved and refed and T_4 injected, the 150-day-old rats had no further increases in G6PD activity although their ME activity when starved and refed increased. Thyroid hormone treatment of the 420-day-old rats increased G6PD activity in those rats starved for 4 or 7 days and ME activity in all three groups of starved–refed rats. Analysis of variance of these enzyme data showed signif-

icant hormone, hormone–age, and duration of starvation effects. G6PD activity was significantly affected by an interaction of all three variables while ME activity was affected by an interaction of the thyroid hormone and duration of starvation variables.

Liver lipid, as expected, increased with starvation–refeeding. The imposition of the thyroid hormone treatment served to increase the liver lipid levels in all three groups of starved–refed rats of both ages. As the duration of starvation increased, the liver lipid levels also increased slightly. The differences were not always significant. Analysis of variance of these data showed a significant effect of thyroid hormone treatment, duration of starvation, and an interaction of these two variables.

Discussion. The results of the present work are of interest because they show that the response to starvation–refeeding can be modified by thyroxine treatment, the duration of starvation, and age. According to Adelman (13), aging carries with it a reduced capacity to respond to a metabolic challenge. This conclusion was based on the glucokinase responses of rats of various ages during the first 8 hr of refeeding after 72 hr of starvation. Using the 48-hr starvation–48-hr refeeding treatment and measuring G6PD response, there were no differences in the enzyme overshoot response between the 150- and the 420-day-old rats. Both age groups evidenced a twofold increase in G6PD and ME activity when starved and refed. This was consistent with the results of an earlier study (16) using Wistar rats whose initial body weights were 125–200 and 275 g and larger but whose ages were not specified. Thus, the question of whether age dampens the BHE response to starvation–refeeding has been answered; it does not. However, if one were to compare the present results with those reported for young (~50 days of age) growing BHE starved–refed rats (17) who had a nearly 20-fold increase in enzyme activity following starvation–refeeding, one might answer in the affirmative. This then would be consistent with Adelman's report. He found that the age effect occurred primarily during the transition from the early rapid growth stage to adulthood (the first 6 months) rather than after adulthood has been obtained. In addition, time course studies of the G6PD response to starvation-refeeding (5) have shown that even in young rats the G6PD overshoot response is not evident until the second day of refeeding. Thus the G6PD response occurs in a different time frame from that of glucokinase (48 hr vs 8 hr) and is less affected by aging.

The observation of Schwartz *et al.* (33) that in Sprague–Dawley rats there is an age-related decline in hepatic enzyme response to thyroid hormone administration was not observed in BHE rats. In the present work, the 420-day-old rats responded as well as (in some instances better than) the 150-day-old rats to thyroxine treatment. In this instance, age did not dampen the ability of the rat to respond to this metabolic challenge. However, when one examines the data closely, one notes that response to the administration of thyroxine was age mediated. That is, the 420-day-old rats had slightly greater responses, especially when starved for 4 or 7 days prior to refeeding than did the 150-day-old rat. Perhaps, the old rats were less functional with respect to their thyroid status and therefore that this treatment "made them more normal." Such has previously been suggested for 50-day-old BHE rats used for studies of mitochondrial activity and hepatic gluconeogenesis (26, 27). Whether young or old adult rats of other strains would have a similar response is unknown. However, studies of the role of thyroid hormone in the glucocorticoid-mediated G6PD response to starvation–refeeding by Sprague–Dawley rats (11) suggests that thyroxine probably has an additive effect (to glucocorticoid) on the enzyme overshoot response and likely, if Sprague–Dawley rats were studied at 150 and 420 days of age, a similar effect might be observed.

The question of whether the duration of starvation would affect the enzyme overshoot response to starvation–refeeding has also been answered. Rats starved for 7 days had as much of an enzyme overshoot as did rats starved for 2 days. This is consistent with our earlier report using young rats of the Wistar strain (28).

The results of the present work, therefore, suggest that age does not always carry with it a reduction in the capacity of animals to respond to a metabolic challenge. Indeed, the present results compared to those reported by others suggest that the ability to respond to a metabolic challenge may differ depending on the nature of the challenge, the parameters

measured and the genetic background of the animal being studied.

1. Tepperman HM, Tepperman J. The hexosemonophosphpate shunt and adaptive hyperlipogenesis. Diabetes 7:478–485, 1958.
2. McDonald BE, Johnson BC. Metabolic response to realimentation following chronic starvation in the adult male rat. J Nutr **87**:161–167, 1965.
3. Szepesi B, Freedland RA. Differential requirement for de novo RNA synthesis in the starved–refed rat: Inhibition of the overshoot by 8 azaguanine after refeeding. J Nutr **99**:449–458, 1969.
4. Szepesi B, Berdanier CD, Diachenko S, Moser PB. Effect of length of starvation, refeeding and 8 azaguanine on serum insulin and NADPH-linked dehydrogenases of rat liver. J Nutr **101**:1147–1152, 1971.
5. Szepesi B, Berdanier CD. Time course of the starve refeed response in rats: The possible role of insulin. J Nutr **101**:1563–1574, 1971.
6. Berdanier CD, Wurdeman R, Tobin RB. Further studies on the role of the adrenal hormones in the responses of rats to meal feeding. J Nutr **106**:1791–1800, 1976.
7. Berdanier CD, Wurdeman R, Tobin RB. Enzyme overshoot in starved-refed rats: Role of the adrenal glucocorticoid. J Nutr **108**:1457–1461, 1978.
8. Berdanier CD, Shubeck D. Interaction of glucocorticoid and insulin in the responses of rats to starvation-refeeding. J Nutr **109**:1766–1771, 1979.
9. Bouillon DJ, Berdanier CD. Role of glucocorticoid in adaptive hyperlipogenesis in the rat. J Nutr **110**:286–297, 1980.
10. Llobera M, Seibel MJ, Herrera E. Metabolic responses to short periods of starvation in hypo- and hyperthyroid male rats. Horm Metab Res **10**:319–324, 1978.
11. Nessmith S, Baltzell J, Berdanier CD. Interaction of glucocorticoid and thyroxine in the responses of rats to starvation-refeeding. J Nutr **113**:2260–2265, 1983.
12. Berdanier CD. Effects of estrogen on the responses of male and female rats to starvation–refeeding. J Nutr **111**:1425–1429, 1981.
13. Adelman RC. An age-dependent modification of enzyme regulation. J Biol Chem **245**:1032–1035, 1970.
14. Roth GS, Adelman RC. Age related changes in hormone binding by target cells and tissues: Possible role in altered adaptive responsiveness. Exp Gerontol **10**: 1–11, 1975.
15. Boll M, Bruckner E, Berndt J. Age related differences in dietary regulation of lipogenic enzymes in rat liver. Hoppe-Seyler's Z Physiol Chem **363**:103–106, 1982.
16. Szepesi B, Berdanier CD, Michaelis OE. Effect of age on the responses to starvation–refeeding in the rat. Proc Soc Exp Biol Med. **147**:195–200, 1974.
17. Berdanier CD, Venable L. Strain differences in response to starvation–refeeding. Nutr Rep Int **26**:955–960, 1982.
18. Berdanier, CD. Rat strain differences in response to meal feeding. Nutr Rep Int **11**:517–524, 1975.
19. Berdanier CD, Tobin RB, DeVore V. Studies on the control of lipogenesis: Strain differences in hepatic metabolism. J Nutr **109**:247–260, 1979.
20. Berdanier CD, Tobin RB, DeVore V. Effects of age strain and dietary carbohydrate on the hepatic metabolism of male rats. J Nutr **109**:261–271, 1979.
21. Berdanier CD. Metabolic characteristics of the carbohydrate sensitive BHE strain of rats. J Nutr **104**: 1246–1256, 1974.
22. Berdanier CD. The BHE strain of rat: An example of the role of inheritance in determining metabolic controls. Fed Proc **35**:2295–2299, 1976.
23. Adams M. Home Economics Research Report No. 24, Washington, D.C., U.S. Department of Agriculture, 108pp, 1964.
24. Durand AMA, Fisher M, Adams M. Histology in the rats as influenced by age and diet. Arch Pathol **77**: 268–277, 1964.
25. Durand AMA, Fisher M, Adams M. The influence of type of dietary carbohydrate effect on histological findings in two strains of rats. Arch Pathol **85**:318–327, 1968.
26. Berdanier CD, Shubeck D. Effects of thyroid hormone on mitochondrial activity in lipemic BHE rats. Proc Soc Exp Biol Med **166**:348–354, 1981.
27. Berdanier CD. Effects of thyroid hormone on the gluconeogenic capacity of lipemic BHE rats. Proc Soc Exp Biol Med **172**:187–193, 1983.
28. Szepesi B, Berdanier CD, Diachenko SK, Moser PB. Effect of length of starvation, refeeding and 8 azaguanine on serum insulin and NADP linked dehydrogenases of rat liver. J Nutr **101**:1147–1152, 1971.
29. Freedland RA. Effect of progressive starvation on rat liver enzyme activities. J Nutr **91**:489–495, 1967.
30. Bligh EG, Dyer WJ. A rapid method of total lipid extraction and purification. Canad J Biochem Physiol **37**:911–917, 1959.
31. Helwig JT, Council KA, eds. SAS Users Guide, Raleigh, N.C., SAS (Statistical Analysis Systems) Institute, Inc., pp113–241, 1982.
32. Dixon WJ, Massey FJ. Introduction to Statistical Analysis, New York, McGraw–Hill, 2nd ed., pp112–177, 1957.
33. Schwartz HL, Forciea MA, Mariash CN, Oppenheimer JH. Age-related reduction in response of hepatic enzymes to 3',5,3' triodothyronine administration. Endocrinology (Baltimore) **105**:41–46, 1979.

Received February 21, 1986. P.S.E.B.M. 1986, Vol. 183.
Accepted July 25, 1986.