

Dietary Thyrotropin-Releasing Hormone Stimulates Growth Rate and Increases the Insulin:Glucagon Molar Ratio of Broiler Chickens¹ (42969)

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Abstract. The effects of thyroid manipulation on growth, feed efficiency, and plasma hormone levels were determined in rapidly growing chickens. Beginning at 3 weeks of age, eight broiler cockerels were provided with control feed (CF) or feed containing either 1 ppm of triiodothyronine (T₃), 1 ppm of thyroxine (T₄), 0.3% propylthiouracil (PTU), or 5 ppm of thyrotropin-releasing hormone (TRH) for 3 weeks. Blood samples were taken at 4, 5, and 6 weeks for determination of plasma levels of growth hormone, insulin-like growth factor, T₃, T₄, insulin, glucagon, glucose, and nonesterified fatty acids. Dietary TRH increased ($P < 0.05$) the growth rate of chickens by 14% when compared with the CF group. Plasma growth hormone levels were reduced ($P < 0.05$) 65% by dietary T₃ and 33% by treatment with either T₄ or TRH when compared with the CF group. Plasma insulin-like growth factor levels were 16% lower ($P < 0.05$) in PTU-fed birds than the other treatment groups. Plasma T₃ levels were elevated ($P < 0.05$) 3-fold by dietary T₃ and 38% by TRH whereas plasma T₃ in the PTU group was 38% below the average of CF birds. Plasma T₄ levels were increased ($P < 0.05$) by 12-fold in T₄-fed birds, decreased 48% in TRH-fed birds, and nondetectable in birds treated with either T₃ or PTU. Compared with the other treatments, dietary PTU increased ($P < 0.01$) plasma insulin levels 4.3-fold whereas TRH provided a 2.7-fold increase in plasma insulin. Plasma glucagon levels were 26% higher ($P < 0.05$) in T₃-fed birds than those fed either T₄ or PTU. These observations indicate that thyroid activity plays an important role in regulating secretion of GH and the pancreatic hormones. Furthermore, our study demonstrates the potential use of TRH as an orally active growth promoter for poultry. [P.S.E.B.M. 1989, Vol 192]

Several studies have revealed distinct interactions between growth hormone (GH) secretion and thyroid function in birds. Chickens in which thyroid activity is depressed by goitrogen treatment (1, 2), autoimmune thyroiditis (3), or surgical/radioiodine ablation (4) have higher plasma GH levels than euthyroid birds. The sex-linked dwarf chicken has elevated levels of both GH and thyroxine (T₄) in plasma whereas triiodothyronine (T₃) concentrations are greatly re-

duced (5). Since the activity of hepatic 5'-monodeiodinase (5'-MDI) is very low in the sex-linked dwarf chick, Scanes *et al.* (5) have suggested that sex-linked dwarfism in chickens is due to the reduction in conversion of T₄ to T₃ in peripheral tissue rather than hypopituitarism. The depressed growth rate in two dwarf strains (sex-linked and autosomal dwarfs) of Leghorn chickens was restored to normal by either giving a daily injection of mammalian GH or by supplementing their diets with T₃ or T₄ (6, 7). However, dietary T₃ or T₄ failed to increase the growth rate of sex-linked dwarf broiler chickens (8). The importance of T₃ to the normal growth process was demonstrated by the ability of exogenous T₃, rather than GH therapy, to correct the growth deficit of hypophysectomized Leghorn chickens (9). In contrast, the addition of T₃ to the diet of normal broiler chickens actually depresses their weight gain and feed intake (10).

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The idea of thyroid involvement in regulation of growth in birds is further supported by the fact that injection of chickens or turkeys with thyrotropin-releasing hormone (TRH) produces a remarkable surge in GH secretion from the pituitary (11, 12). Daily intravenous injection of TRH for 17 days was found to stimulate the growth rate of broiler chickens by about 12% (13). In a novel experiment, Burke and Vaughters (14) showed that acute oral administration of TRH in either feed or drinking water of chickens provoked secretion of GH. Although this study raised the possibility of using TRH as an orally active growth stimulant, the addition of TRH to the drinking water of broiler chickens did not increase their growth rate despite elevated plasma GH levels (15). The purpose of this study was to determine the effect of thyroid manipulation, including dietary TRH, on the growth rate and plasma hormone levels of rapidly growing broiler chickens. Thyroid-active substances were added to the feed of chickens to induce hyperthyroidism (T_3 , T_4 , and TRH) or hypothyroidism (propylthiouracil, PTU). Brief portions of this work were presented earlier (16, 17).

Materials and Methods

Bird Management. Day-old broiler cockerels (Shaver \times Shaver strain) were obtained from a commercial hatchery (Cargill Hatchery, Dagsboro, DE) and maintained in a heated battery-brooder until 3 weeks of age. Birds were held under a 20-hr:4-hr light:dark cycle with brooder temperature maintained at 33°C for the first week and reduced by 3°C at weekly intervals. Brooding chicks were provided with a commercial broiler-starter ration (22% crude protein, 3100 kcal of metabolizable energy/kg feed) and water *ad libitum*.

Dietary Treatments. At 3 weeks, four birds were randomly assigned to each of 10 wire pens held in two controlled environment rooms. Five dietary treatments were randomly assigned to 10 pens of birds in a randomized complete block design with five pens in each replicate room. The basal ration or control feed (CF) was ground broiler-finisher ration (no. 122; Pennfield Corp., Lancaster, PA) that contained 19% crude protein and 3200 kcal of metabolizable energy/kg feed. The dietary treatments consisted of the incorporation of either 1 ppm of T_3 or T_4 , 0.3% PTU, or 5 ppm of TRH mixed into the basal ration. All thyroid-active substances were purchased from Sigma Chemical Co. (St. Louis, MO). The average daily weight gain (ADG) and feed consumption (ADFC) were determined per pen for the 3-week period. At the end of the experiment (6 weeks), each bird was bled and then killed to obtain liver weights. A 5-g sample of liver was taken for the *in vitro* determination of 5'-MDI activity (18).

Measurement of Plasma Hormones and Metabolites. A 4-ml blood sample was taken from each bird

at weekly intervals (4, 5, and 6 weeks). Specific double antibody radioimmunoassays were used to quantitate plasma levels of T_3 and T_4 (19), GH (20), insulin (21), and glucagon (22). The molar ratio of insulin:glucagon was calculated from plasma insulin and glucagon levels in each plasma sample assuming M_r of 5734 for insulin and 3483 for glucagon. Plasma levels of total insulin-like growth factor (IGF) peptide (i.e., both IGF-I and IGF-II) were determined by radioreceptor assay (23). The validation of this assay for quantitative measurement of IGF in chicken plasma has been described elsewhere (24). Plasma IGF levels in chickens are expressed as ng eq/ml since our radioreceptor assay utilizes recombinant-derived human IGF-I for standards and trace hormone. Colorimetric enzymatic assay kits were used to determine plasma levels of glucose (Sigma Chemical Co.) and nonesterified fatty acids (NEFA) (Wako Chemical Co., Dallas, TX).

Statistical Analyses. The experiment had a randomized complete block design with five dietary treatments replicated in two controlled environment rooms (blocks). Least squares regression analysis was used to test for the main effect of dietary treatment on ADG, ADFC, feed to gain ratio (FTG), body weight, relative liver weight, and 5'-MDI activity. All growth data were analyzed with the pen as the experimental unit since dietary treatment was applied to the pen. The plasma hormone/metabolite data were tested for the main effect of dietary treatment or week of age and their interaction on observations from individual birds. For statistical analyses, the final body weight and plasma hormone concentrations were transformed to the natural logarithm to account for heterogeneity of error variance (25). Fisher's least significant difference test was used to separate significant ($P < 0.05$) differences due to dietary treatment or week of age where appropriate (25). Plasma hormone data are presented as the main effects of dietary treatment which are averaged across 4, 5, and 6 weeks of age unless there was a significant interaction between dietary treatment and week of age.

Results

Growth and Feed Efficiency. The ADG of birds fed TRH was 14% higher ($P < 0.05$) than that of the CF group (Table I). The ADG of birds fed either 1 ppm of T_3 or 0.3% PTU was not different from that of CF birds, although the ADG of T_4 -fed birds was higher ($P < 0.05$) than that of T_3 and PTU groups. There were no significant differences in ADFC among dietary treatments. The feed efficiency of TRH-fed birds was about 18% higher ($P < 0.05$) than that of PTU- or T_3 -fed birds. The final (6 weeks) body weight of TRH-fed and T_4 -fed birds was higher ($P < 0.05$) than that of the CF birds (Table II). No difference in final body weight was found among birds given CF, T_3 , or PTU treatment.

Table I. ADG, ADFC, and Feed to Gain Ratio of Broiler Chickens Fed Thyroid-Active Substances from 3 to 6 Weeks of Age

Treatment	ADG (g/bird)	ADFC (g/bird)	Feed to gain ratio (kg feed/ kg gain)
Control	50.1 ± 3.4b,c	104.8 ± 5.2a	2.10 ± 0.06a,b
1 ppm of T ₃	48.2 ± 2.0c	106.2 ± 3.6a	2.20 ± 0.02a
1 ppm of T ₄	56.0 ± 1.9a,b	115.8 ± 3.4a	2.07 ± 0.01a,b
0.3% PTU	47.7 ± 1.7c	108.6 ± 4.4a	2.28 ± 0.01a
5 ppm of TRH	57.0 ± 2.7a	107.4 ± 3.8a	1.89 ± 0.10b

Note. Each value represents the mean and SE of two pens (four birds/pen). Means within a column possessing a different letter are significantly ($P < 0.05$) different.

Table II. Final Body Weight, Relative Liver Weight, and Hepatic 5'-MDI Activity of Broiler Chickens Fed Thyroid-Active Substances from 3 to 6 Weeks of Age

Treatment	Body weight (kg)	Relative liver weight (% body weight)	5'-MDI ^a
Control	1.66 ± 0.06b	2.08 ± 0.07b	1.28 ± 0.05b
1 ppm of T ₃	1.61 ± 0.05b	2.37 ± 0.07b	1.66 ± 0.09a
1 ppm of T ₄	1.78 ± 0.13a	2.27 ± 0.11b	1.64 ± 0.13a
0.3% PTU	1.63 ± 0.07b	3.71 ± 0.17a	0.57 ± 0.05c
5 ppm of TRH	1.84 ± 0.04a	2.39 ± 0.09b	1.50 ± 0.07a,b

Note. Each value represents the mean and SE of eight birds. Means within a column possessing a different letter are significantly ($P < 0.05$) different.

^a Hepatic thyroxine 5'-MDI activity is expressed as ng of T₃ generated/(hr · mg protein).

The relative liver weight of PTU-fed birds was 63% higher ($P < 0.01$) than the average of the other treatment groups (2.28% body wt).

Hepatic 5'-MDI activity was depressed ($P < 0.01$) by 56% in birds fed 0.3% PTU for 3 weeks (Table II). In contrast, 5'-MDI activity was increased ($P < 0.05$) by 29% in birds fed 1 ppm of either T₃ or T₄ when compared with the average of the CF group. In general, hepatic 5'-MDI activity of broiler chickens was increased in the hyperthyroid state and depressed by hypothyroidism induced by PTU treatment.

Plasma Hormone and Metabolite Levels. Plasma GH levels were depressed ($P < 0.05$) 65% by T₃ treatment and 33% by treatment with T₄ or TRH when compared with the average GH level of CF birds over the 3-week period (22.5 ng/ml) (Fig. 1A). No difference was found in plasma GH levels between the CF group and PTU-treated birds. There was a main effect of week of age on plasma GH since the average GH level across all dietary treatments was 42% lower ($P < 0.01$) at 6 weeks than the average of 4 and 5 weeks (19.4 ng/ml).

Dietary PTU depressed ($P < 0.05$) plasma IGF levels 16% below the combined average of the other treatment groups (74 ng eq/ml) (Fig. 1B). The average plasma IGF level across dietary treatments was similar at 4 (68 ng eq/ml), 5 (74 ng eq/ml), and 6 (73 ng eq/ml) weeks.

Incorporation of 1 ppm of T₃ into the feed of growing broiler chickens increased ($P < 0.05$) plasma T₃ levels 3-fold when compared with the average plasma T₃ level (2.4 ng/ml) of the CF and T₄-fed group (Fig. 2A). Dietary TRH elevated ($P < 0.05$) plasma T₃ levels 38% above that of the CF group (2.4 ng/ml). In contrast, dietary PTU depressed ($P < 0.05$) plasma T₃ levels 38% below the CF average. The average plasma T₃ level across dietary treatments was similar at 4 (3.5 ng/ml), 5 (3.4 ng/ml), and 6 (3.2 ng/ml) weeks.

Plasma T₄ levels were elevated ($P < 0.01$) 12.3-fold in birds fed 1 ppm of T₄ when compared with the average plasma T₄ level of CF birds (6.3 ng/ml) over the 3-week period (Fig. 2B). In contrast, plasma T₄ levels in TRH-fed birds were 48% lower ($P < 0.05$) than the average of the CF group. In T₃- and PTU-fed birds, plasma T₄ levels were below the limit of detection in the T₄ assay (i.e., less than 1.2 ng/ml). The average T₄ concentration across all dietary treatments was higher ($P < 0.05$) at 4 weeks (23.9 ng/ml) than that at 6 weeks (13.4 ng/ml).

There was a significant ($P < 0.01$) interaction between dietary treatment and week of age on plasma insulin levels. In particular, plasma insulin levels did not change across week of age in birds receiving CF (0.28 ng/ml), T₃ (0.24 ng/ml), or T₄ (0.42 ng/ml) treatments. However, plasma insulin levels increased

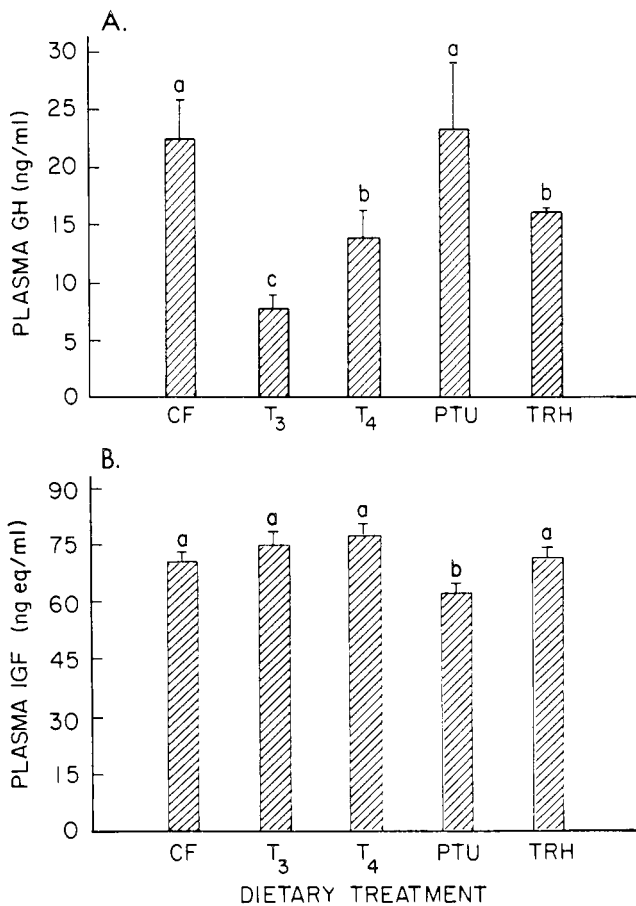


Figure 1. Plasma levels of GH (A) and IGF (B) in broiler chickens fed thyroid-active substances. Each value represents the mean and SE of 24 plasma samples; eight birds in each treatment group were bled at 4, 5, and 6 weeks. Treatment means possessing a different superscript are significantly ($P < 0.05$) different.

sharply after 1 week of treatment with either PTU (0.39, 1.2, and 2.0 ng/ml for 4, 5, and 6 weeks, respectively) or TRH (0.34, 0.94, and 1.03 ng/ml). Plasma insulin levels were elevated ($P < 0.01$) 4.3-fold by PTU treatment and 2.7-fold by dietary TRH when compared with the CF group, although 2 weeks of treatment were required before these changes were fully manifest.

Plasma glucagon levels were less responsive to dietary treatment than plasma insulin. Over the 3-week treatment period, plasma glucagon levels were similar for the CF (0.56 ng/ml), T₃ (0.62 ng/ml), T₄ (0.51 ng/ml), PTU (0.48 ng/ml), and TRH (0.53 ng/ml) groups. Plasma glucagon levels were 26% higher ($P < 0.05$) in T₃-fed birds than in those fed either T₄ or PTU.

The molar ratio of insulin:glucagon reflects the progressive response of plasma insulin to PTU and TRH treatments since there was a significant ($P < 0.01$) interaction between dietary treatment and week of age (Fig. 3). In contrast, the insulin:glucagon molar ratio was maintained steadily across week of age in the CF, T₃ and T₄ treatment groups. The interaction was mainly due to the sharp increase in the insulin:glucagon molar

ratio after 1 week of treatment with either PTU or TRH. Dietary T₃ appeared to be more effective than T₄ in depressing the insulin:glucagon molar ratio. The

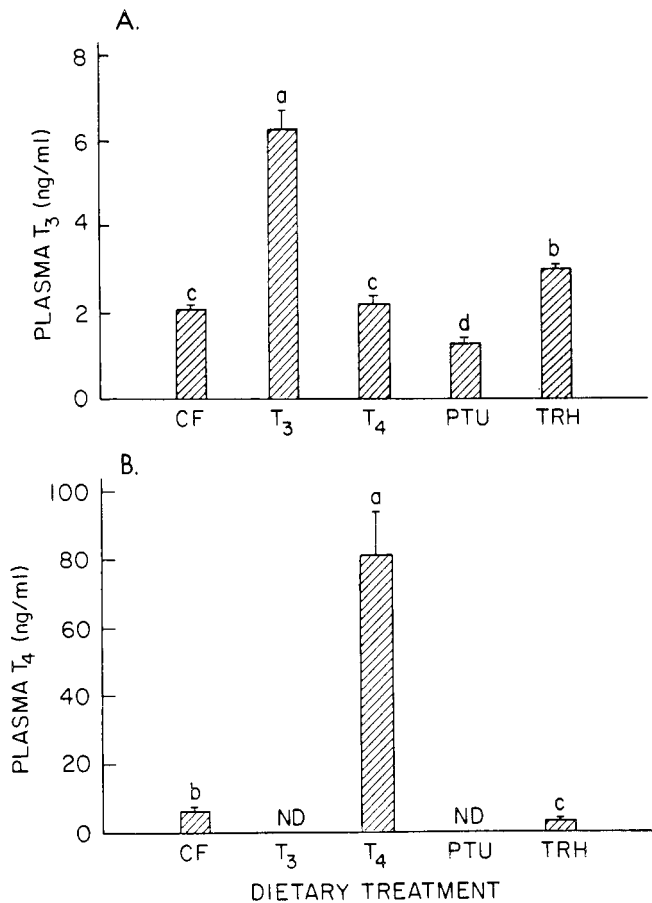


Figure 2. Plasma levels of T₃ (A) and T₄ (B) in broiler chickens fed thyroid-active substances. Each value represents the mean and SE of 24 plasma samples; eight birds in each treatment group were bled at 4, 5, and 6 weeks. Treatment means possessing a different superscript are significantly ($P < 0.05$) different.

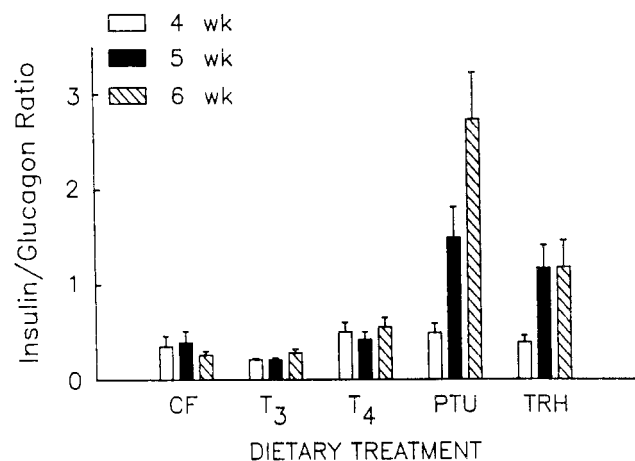


Figure 3. Molar ratio of insulin:glucagon in plasma of broiler chickens fed thyroid-active substances. Each value represents the mean and SE of eight birds. There was a significant interaction ($P < 0.05$) between dietary treatment and week of age.

average insulin:glucagon molar ratio of PTU-fed birds was 4.7-times higher and that of TRH-fed birds was 2.7-times higher than the average insulin:glucagon molar ratio of CF birds (0.33) across week of age.

The average plasma glucose concentration of PTU-treated chickens was 11% higher ($P < 0.05$) than that of the other dietary treatment groups (269 mg/100 ml). The average glucose concentration across all treatment groups at 5 weeks (285 mg/100 ml) was higher ($P < 0.05$) than that at 4 weeks (266 mg/100 ml) but not different from the average at 6 weeks (278 mg/100 ml).

Plasma NEFA levels were consistently depressed ($P < 0.01$) in birds receiving the T_3 and PTU treatments (1.2 meq/liter) when compared with the average of the other treatment groups (1.8 meq/liter). There was a main effect ($P < 0.05$) of week of age on plasma NEFA levels since the average NEFA level at 6 weeks (1.8 meq/liter) was 20% higher than that at either 4 or 5 weeks (1.5 meq/liter).

Discussion

Our study clearly shows that dietary TRH stimulates the growth rate of broiler chickens. Leung *et al.* (13) demonstrated that daily iv injection of TRH (1 or 10 $\mu\text{g}/\text{bird}/\text{day}$) into broiler cockerels for 17 days increased their growth rate by 12%. Our study shows that a more practical treatment method, incorporation of TRH into feed, is capable of providing a similar growth response. In other studies, we have confirmed that dietary TRH in the range of 0.1–10 ppm stimulates the growth rate of broiler chickens (L. A. Cogburn and S. S. Liou, unpublished observations). In contrast, Burke (15) reported that administration of TRH in drinking water of chickens failed to alter growth rate, although plasma GH levels were elevated by TRH treatment. In an earlier study, Burke and Vaughters (14) demonstrated that oral administration of TRH in either feed or water of chickens was capable of provoking GH secretion. Daily iv injection of either TRH alone or in combination with GH-releasing factor for 21 days failed to stimulate growth or improve feed efficiency of broiler chickens despite enhanced GH secretion (26). The reason for these discrepancies in the response of chickens to exogenous TRH is not presently known. Direct measurement of TRH in blood following ingestion of TRH indicates that only 2–6% of an oral dose is actually absorbed from the gastrointestinal tract of the rat, dog, and human (27). Similarly, we have recently demonstrated that the bioavailability of TRH in chickens consuming 5 ppm of TRH in feed is about 2% (28). Therefore, we estimate that TRH-fed chickens in the present study were absorbing about 11 μg of TRH/day based on their ADFC of 107.4 g/bird. Burke (15) indicated that birds in his study consumed 60–120 μg of TRH/day in drinking water which probably means that only 1.2–2.4 μg of TRH/day was actually absorbed into the bloodstream. Perhaps the lack of growth response

in broiler chickens given TRH treatment via drinking water (15) was due to an insufficient daily dosage.

Treatment of euthyroid broiler chickens with dietary T_3 (1 ppm) from hatching to slaughter (0–7 weeks) usually reduces their growth rate and feed efficiency whereas the same level of T_4 is ineffective (2, 10, 29). Our study shows that dietary T_3 is not detrimental to growth rate and feed efficiency of broiler cockerels when fed only during the grower/finisher phase (i.e., 3–6 weeks). The higher final body weight of our T_4 -fed chickens is in agreement with May's (10) observation of a slightly higher growth rate in broiler cockerels fed 0.25–1 ppm of T_4 . The reduced weight gain and poorer feed efficiency of broiler chickens fed T_3 throughout their growth period (0–7 weeks) is usually accompanied by a marked depletion of body fat (29, 30). Hypothyroidism induced by treatment of chickens with either PTU or methimazole results in reduced growth rate, poorer feed efficiency, enlargement of the liver, and obesity (1, 2, 30, 31). These observations indicate that growth rate, feed efficiency, and body composition of chickens are dramatically altered by changes in thyroid activity.

Although iv injection of TRH (13) or acute oral dosing with TRH (14) typically increases plasma GH levels, our study shows that chronic treatment of chickens with TRH in feed actually depresses plasma GH levels. It is possible that the reduced levels of plasma GH in our TRH-fed chickens reflect diminished responsiveness of the pituitary to TRH stimulation since chickens quickly become refractory to repeated injections of TRH (32). On the other hand, endogenous GH secretion could be inhibited by the elevated plasma T_3 levels found in TRH-fed birds. This idea is supported by the observation that pretreatment of chickens with either T_3 or T_4 blocks TRH-stimulation of GH release (33). Plasma GH concentrations are reduced in a dose-related manner after a single injection of thyroid hormone, where T_3 is more potent than T_4 in depressing endogenous GH secretion (33). Dietary T_3 (1 ppm) also appears to be more inhibitory to endogenous GH secretion than the same dietary level of T_4 (30). In contrast, Leung *et al.* (2) reported that plasma GH levels were equally depressed by the addition of either 1 ppm of T_3 or T_4 to the feed of 4-week-old broiler cockerels. The present findings suggest that the enhanced growth response of TRH-fed chickens could be due to enhanced thyroid activity since plasma GH levels were reduced and IGF levels unaffected by TRH treatment. This idea is further supported by the fact that the administration of T_3 to hypophysectomized chickens (9) or T_4 to sex-linked dwarf chickens (7) is more effective than GH injections in restoring normal growth rate.

The only significant effect of thyroid manipulation on plasma IGF levels was the reduction of plasma IGF in PTU-treated cockerels. Our data confirm other reports of reduced levels of plasma IGF in goitrogen-

treated animals (30, 34). Daily iv injections of TRH (1 $\mu\text{g}/\text{kg}/\text{day}$) for 3 weeks (4–7 weeks) did not increase plasma levels of immunoreactive IGF-I despite consistently higher levels of plasma GH in TRH-injected chickens (26). Although plasma IGF levels were not significantly elevated in our T_4 -fed chickens, others have reported enhanced serum IGF levels after T_4 treatment in dwarf mice (35) and hypophysectomized rats (36). These findings support the idea that plasma IGF levels in normal chickens are not dependent upon the level of GH in circulation (37). In fact, Huybrechts *et al.* (38) have suggested that the low levels of immunoreactive IGF-I found in the sex-linked dwarf chicken are related to reduced T_3 levels because their plasma GH concentrations are greatly elevated.

In this study, plasma T_3 levels were increased 3-fold by 1 ppm of T_3 and apparently unaffected by the 12-fold increase in plasma T_4 levels brought about by dietary T_4 . Several workers have demonstrated that dietary T_4 stimulates 5'-MDI activity (i.e., the conversion of T_4 to reverse T_3) as evidenced by high levels of reverse T_3 in the plasma of T_4 -fed chickens (10, 29, 30). The normal levels of plasma T_3 in T_4 -fed chickens and the reduction of plasma T_4 usually observed in T_3 -fed chickens also support the consensus that T_3 is the metabolically active thyroid hormone of chickens (2, 10, 19, 29, 30). As expected, plasma T_3 levels were depressed in PTU-treated chickens and increased by dietary TRH. The absence of detectable T_4 levels in plasma of T_3 -fed birds suggests that exogenous T_3 inhibited secretion of T_4 from the thyroid gland. In PTU-treated birds, the absence of detectable T_4 levels in plasma indicates that thyroid secretion of T_4 was impaired by dietary PTU.

Our study shows that PTU treatment reduces 5'-MDI activity to one-half that of control chickens. In contrast, the hyperthyroidism induced by dietary thyroid hormones (or TRH) increases conversion of T_4 into T_3 . The elevation of plasma T_3 levels in euthyroid broiler chickens fed T_4 also suggests that 5'-MDI activity was stimulated (2). Our data do not support a recent report of reduced hepatic 5'-MDI activity in chickens fed 1 ppm of either T_3 or T_4 and increased 5'-MDI activity in chickens treated with methimazole (30). Other workers have demonstrated that hepatic 5'-MDI activity in birds (39) and mammals (40) is not affected by methimazole treatment whereas PTU is a strong inhibitor of hepatic 5'-MDI activity. Although 5'-MDI activity was greatly diminished, PTU-treatment birds were apparently able to maintain adequate plasma T_3 levels for growth by converting available T_4 into T_3 . Our study clearly shows that 5'-MDI activity in the chicken is stimulated by the hyperthyroid state and depressed by hypothyroidism. Increased conversion of T_4 into T_3 has also been demonstrated in the liver of the hyperthyroid rat (41). Injection of thyrotropin (TSH) into mice greatly increases 5'-MDI activity in

both the thyroid gland and liver (40). Accordingly, the increase in plasma T_3 and reduction of plasma T_4 levels observed in TRH-treated chickens suggest that 5'-MDI activity was enhanced without affecting T_4 secretion from the thyroid gland.

Our data do not support the notion that plasma GH levels regulate 5'-MDI activity in the chicken (42). Despite depressed plasma GH levels, hepatic 5'-MDI activity was highest in birds receiving the T_3 , T_4 , or TRH treatments. Furthermore, hepatic 5'-MDI activity is greatly depressed in the sex-linked dwarf chicken although plasma GH levels are very high (5). We have recently shown that plasma thyroid hormone levels and hepatic 5'-MDI activity in rapidly growing broiler chickens are unaffected by daily injection of natural or biosynthetic chicken GH (37).

The present study provides additional evidence that the thyroid hormones play an important role in regulating the secretion of insulin and glucagon from the pancreas. In particular, PTU treatment causes a dramatic elevation of plasma insulin levels presumably due to low levels of plasma T_3 (31, 43). The hypothyroidism induced by dietary PTU in chickens is characterized by a remarkable increase in the insulin:glucagon ratio, glycogenic and lipogenic hepatomegaly, and obesity (31). The PTU-treated chicken also has elevated plasma glucose levels and depressed levels of plasma NEFA. Our observation that plasma glucose levels were elevated in PTU-treated chickens despite a 4-fold increase in plasma insulin levels suggests that PTU causes insulin resistance. Raheja *et al.* (31) have suggested that the glycogen storage syndrome of PTU-treated chickens results from reduced activity of glucagon-dependent glucose-6-phosphatase. Based on our observations of a high insulin:glucagon molar ratio in hypothyroid (PTU-treated) chickens and a low insulin:glucagon molar ratio in plasma of hyperthyroid (T_3 -fed) chickens, we have proposed that plasma T_3 levels regulate the insulin:glucagon molar ratio and consequently fat deposition in the broiler chicken (43).

The low insulin:glucagon molar ratio normally found in birds indicates that their metabolism predominately operates in a catabolic mode (44). The increased insulin:glucagon molar ratio of PTU-treated chickens suggests predominance of the anabolic mode which is evidenced by increased accumulation of body fat (31). In contrast, the reduction of the insulin:glucagon molar ratio brought about by dietary T_3 increases metabolic and catabolic activity which results in depletion of body fat (29, 30, 43). The perturbation in plasma T_3 and T_4 levels that follows injection of insulin or glucagon into chickens has led to the speculation that the endocrine pancreas regulates thyroid hormone secretion (45). On the other hand, several studies on thyroid-manipulated chickens (31, 43) indicate that the reciprocal is true since metabolically active T_3 appears to inhibit insulin secretion while stimulating glucagon release. Our ob-

servation of elevated plasma insulin levels in TRH-fed chickens is supported by an earlier report of increased serum insulin concentrations in Holstein calves given daily injections of TRH (46). Hazelwood (44) has championed the concept that the insulin:glucagon molar ratio is the primary determinant of carbohydrate (and lipid) metabolism in birds. Our study on thyroid-manipulated chickens supports this view and provides additional evidence which indicates that plasma levels of T_3 determine the molar ratio of insulin:glucagon secreted by the pancreas.

The growth rate of broiler chickens is stimulated by dietary TRH. This improvement in growth rate of TRH-fed chickens does not appear to be mediated by GH or IGF. Dietary TRH increases plasma T_3 levels and the insulin:glucagon molar ratio whereas plasma levels of GH and T_4 are reduced. Hepatic 5'-MDI activity in chickens is enhanced by hyperthyroidism, induced by dietary T_3 or T_4 , and depressed in the hypothyroid state brought about by dietary PTU. In PTU-treated chickens, plasma levels of T_3 , T_4 and IGF are depressed while the insulin:glucagon molar ratio is greatly elevated. The thyroid hormones appear to play an important role in the growth process of chickens especially in regulating secretion of GH from the pituitary gland and determining the molar ratio of insulin:glucagon secreted by the pancreas.

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