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Effects of Dietary Thyroid Hormones on Growth and Serum T_3, T_4, and Growth Hormone in Sex-Linked Dwarf Chickens (41914)

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Abstract. Dwarf pullets fed with either T_3 or T_4 at 0.1, 1.0, and 10.0 ppm for 2 weeks showed no improvement in their body weight gain as compared with birds that were fed a control diet. Birds fed T_3 or T_4 at 10.0 ppm showed poorer growth, body weight gain, and feed efficiency than control birds. Pullets fed 1.0 ppm of T_3 showed significantly better feed efficiency than control birds. Serum T_3 concentrations were significantly higher when birds were fed 1.0 ppm of T_3 or 10.0 ppm of T_3 or T_4. Plasma T_4 concentrations were also higher in T_4 fed birds (1.0 ppm and 10.0 ppm), but were significantly lower in T_3 fed birds (1.0 ppm and 10.0 ppm) than in control birds. In birds fed T_3 or T_4 at 1.0-ppm and 10.0-ppm levels serum growth hormone concentrations were significantly lower as compared with control birds. In conclusion, exogenous T_3 and T_4 did not correct the sex-linked dwarfism of dwarf chickens. Such dwarfism is characterized by low circulating levels of T_3 and T_4.

The hormonal profile of the Snell's dwarf mouse is well characterized. This animal was first described by Snell (1) and since then its defect has been found to be hypopituitarism (2–5). Exogenous replacement of growth hormone (GH) (6, 7), prolactin (PRL) (6, 7), T_4 (7, 8), and somatomedins (9, 10) to Snell's dwarf mice enhances their growth rate. Phillips *et al.* (11) showed that Snell's dwarf mice do not lack the GH gene, but Cheng *et al.* (12) showed that the primary defect in Snell's dwarf mice was due to the deficiencies of GH precursor RNA and mRNA in total pituitary RNA. The genetics and morphological characteristics of the sex-linked recessive dwarf chicken were first described by Hutt (13). The carcass composition and the hormonal profile of the sex-linked dwarf chicken have recently been reported by us (14) and others (15, 16). The sex-linked dwarf chicken has higher circulating GH concentrations and lower T_3 concentrations in plasma than do normal fast growing chickens. The hypothyroidism is similar to that found in the Snell's dwarf mouse, but the high circulating GH in the chicken suggests that the endocrine basis of the dwarfism is different. Rajaratnam *et al.* (17) reported that the growth rate of the sex-linked dwarf chicken could be increased by feeding 0.05% Protamone (iodinated casein, contains 1% thyroxine activity), but van Tienhoven *et al.* (18) showed that 0.04% dietary Protamone did not correct the dwarfism. Recently, Marsh *et al.* (19) demonstrated that T_4 supplement could result in a significant increase in overall body weight gain in the sex-linked dwarf chickens. Since Scanes *et al.* (15) showed that diminished 5'-monodeiodinase activity in the sex-linked dwarf chickens resulted in reduced serum T_3 concentrations and functional hypothyroidism, the purpose of this present study was to define the effects of various dietary levels of T_3 and T_4 on growth and serum T_3, T_4, and GH concentrations in the dwarf chicken.

Materials and Methods. Sex-linked dwarf broiler breed pullets obtained from Hubbard Farms, Walpole, New Hampshire, were 4-weeks old when used in the present experiments. Birds were individually caged in a temperature (25°C) and light (14 hr light, 10 hr darkness) controlled room. Pennfield laboratory broiler bird's feed, Pennfield 180 (Pennfield, Lancaster, Pa.), was used, and the energy and protein levels are 1460 kcal/lb and 21.5%, respectively. Food and water were available *ad libitum*. Triiodothyronine (T_3) and thyroxine (T_4) were obtained from Sigma Chemical Company, St. Louis, Missouri, and the effects of T_3 and T_4 were examined in two separate experiments. Thyroid hormones were mixed into the diet with a AMF-glen 160 mixer, Model 74-57. Birds were randomly divided into four groups of eight or nine each in both experiments. Birds were fed with T_3 in the first experiment and

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TABLE I. EFFECTS OF DIETARY T_3 ON BODY WEIGHT GAIN, FEED CONSUMPTION, AND FEED EFFICIENCY IN DWARF PULLETS

	N	Body weight gain (g)[a]	Feed consumption (g)[a]	Feed efficiency (feed/gain)[a]
Control	9	425.0 ± 14.8	1035.0 ± 24.9	2.45 ± 0.06
T_3 (0.1 ppm)	9	410.0 ± 10.3	980.0 ± 24.5	2.39 ± 0.04
T_3 (1.0 ppm)	9	433.3 ± 17.2	989.4 ± 30.5	2.29 ± 0.03*
T_3 (10.0 ppm)	8	263.8 ± 8.2*	799.4 ± 14.1*	3.05 ± 0.09*

[a] Mean ± SEM.
* $P < 0.05$ as compared with control.

T_4 in the second experiment at 0.0, 0.1, 1.0, and 10.0 ppm for 2 weeks. These levels of T_3 and T_4 used in these experiments were based on previous findings reported by Singh *et al.* (20) and May (21). Body weights and feed consumption of each bird were recorded at the beginning and at the end of the experiment, and blood samples were collected via heart puncture at the end of the experiment. Serum samples were kept at −20°C until assayed for T_3, T_4, and GH concentrations.

Serum T_3 and T_4 concentrations were determined by the T_3 and T_4 clasp radioimmunoassay kits (Squibb, Princeton, N.J.), and serum GH concentrations were determined by a homologous RIA for chicken GH (22) with FLcGH-II as standard.

The data were examined by analysis of variance and the Student Newman–Keuls test, and differences were considered significant at $P < 0.05$.

Results. The effects of T_3 on body weight gain, feed consumption, and feed efficiency in the sex-linked dwarf pullets are shown in Table I. Birds which were fed T_3 at 0.1 and 1.0 ppm showed no significant changes in weight gain or feed consumption, but those fed at the 1.0-ppm level exhibited better feed efficiency as compared with control birds. Birds fed T_3 at 10.0 ppm showed poorer weight gain, lower feed consumption, and poorer feed efficiency when compared with control birds. The effects of the dietary T_3 on serum T_3, T_4, and GH concentrations are shown in Table II. Birds fed T_3 at 0.1 ppm showed no significant differences in serum T_3, T_4, and GH as compared with control birds, but birds which were fed T_3 at 1.0 and 10.0 ppm showed a significant increase in serum T_3 concentrations and a significant decrease in serum T_4 and GH concentrations.

The effects of dietary T_4 at 0.1, 1.0, and 10.0 ppm on body weight gain, feed consumption, and feed efficiency in sex-linked dwarf pullets are shown in Table III. Feed consumption was significantly lower in all T_4 fed birds, and birds fed T_4 at 1.0 and 10.0 ppm also showed a significantly lower body weight gain. The poorer weight gain in T_4 fed birds at 1.0 ppm could simply be due to poorer feed intake because there was no change in feed efficiency. The birds fed T_4 at 10.0 ppm showed a lower feed efficiency along with higher circulating T_3 and T_4 concentrations (Table IV). Serum T_3 was significantly higher in T_4 fed birds at 10.0 ppm,

TABLE II. EFFECTS OF DIETARY T_3 ON SERUM T_3, T_4, AND GH CONCENTRATIONS IN DWARF PULLETS

	N	T_3 (ng/100 ml)[a]	T_4 (μg/100 ml)[a]	GH (ng/ml)[a]
Control	9	133.4 ± 6.7	2.33 ± 0.10	57.2 ± 13.6
T_3 (0.1 ppm)	9	152.3 ± 10.8	2.07 ± 0.05	51.7 ± 12.9
T_3 (1.0 ppm)	9	333.6 ± 56.7*	1.17 ± 0.04*	10.3 ± 1.0*
T_3 (10.0 ppm)	8	1335.7 ± 265.5*	1.08 ± 0.06*	1.05 ± 2.7*

[a] Mean ± SEM.
* $P < 0.05$ as compared with control.

TABLE III. EFFECTS OF T_4 ON BODY WEIGHT GAIN, FEED CONSUMPTION, AND FEED EFFICIENCY IN DWARF PULLETS

	N	Body weight gain (g)[a]	Feed consumption (g)[a]	Feed efficiency (feed/gain)[a]
Control	9	466.1 ± 19.2	1098.9 ± 30.7	2.38 ± 0.05
T_4 (0.1 ppm)	9	427.2 ± 14.7	1018.3 ± 22.6*	2.39 ± 0.05
T_4 (1.0 ppm)	9	405.6 ± 12.3*	971.7 ± 20.9*	2.40 ± 0.04
T_4 (10.0 ppm)	9	356.7 ± 14.5*	905.6 ± 19.8*	2.56 ± 0.08

[a] Mean ± SEM.
* $P < 0.05$ as compared with control.

and serum T_4 concentrations were significantly higher at 1.0 and 10.0 ppm. Serum GH concentrations were also significantly lower in birds fed T_4 at 1.0 and 10.0 ppm (Table IV).

Discussion. Our results demonstrate that neither T_3 nor T_4 at the dose levels used has any growth promoting activity in the sex-linked dwarf chicken. This agrees with the findings of van Tienhoven *et al.* (18), but not those reported by Rajaratnam *et al.* (17). Previous investigators (17, 18) fed sex-linked dwarf chickens with Promatone which is iodinated casein having an equivalent of approximately 1.0% of thyroxine activity. Recently, Marsh *et al.* (19) showed that T_4 supplement in the diet could result in a significant increase in body weight gain in sex-linked dwarf chickens. Since all previous investigators (17–19) used white leghorn laying strain chickens, and we used broiler breeds meat strain chickens, the difference in the growth response could be due to the different strain of chickens used. Another possible reason why we did not observe any change in body weight gain is due to the short duration in our experimentation, and to the small number of chicks used in each treatment. It is also possible that the carcass composition might be altered due to thyroid hormones without any signs of growth in body weight gain.

The present findings along with previous reports about the hormone profile of the sex-linked dwarf indicate a different hormonal basis between the sex-linked dwarf chicken and the Snell's mouse. Snell's dwarf mice have hypopituitarism so exogenous replacement of GH, PRL, T_4, and somatomedins to animals could promote growth as discussed in the introduction. Also, Snell's mice are usually infertile. In contrast, van Tienhoven (18) showed that there were no significant differences in pituitary, thyroid, ovary, and oviduct weight between sex-linked dwarf and normal control chickens. Though the overall reproductive performance is significantly lower in the sex-linked dwarf chickens, they are not infertile, suggesting functional pituitary in sex-linked dwarf chickens. The sex-linked dwarf chickens were found to have a higher rate of GH synthesis in the pituitary (16) and higher circulating GH concentrations (14, 15). The pituitary content of GH was also reported to be similar in sex-linked dwarf and normal chickens (16, 23, 24).

The lower serum T_3 concentrations in the sex-linked dwarf were found to be due to the

TABLE IV. EFFECTS OF T_4 ON SERUM T_3, T_4, AND GH CONCENTRATIONS IN DWARF PULLETS

	N	T_3 (ng/100 ml)[a]	T_4 (μg/100 ml)[a]	GH (ng/ml)[a]
Control	9	164.5 ± 11.3	2.08 ± 0.16	156.6 ± 31.9
T_4 (0.1 ppm)	9	145.2 ± 6.6	2.08 ± 0.14	155.0 ± 30.0
T_4 (1.0 ppm)	9	162.5 ± 16.9	8.74 ± 0.83*	59.9 ± 8.1*
T_4 (10.0 ppm)	9	231.7 ± 28.9*	43.11 ± 3.31*	28.4 ± 2.2*

[a] Mean ± SEM.
* $P < 0.05$ as compared with control.

suppressed liver 5'-monodeiodinase activity (15), and Scanes *et al.* (15) proposed that the primary lesion in the sex-linked dwarf was at the level of peripheral monodeiodination of T_4. Since T_3 supplement did not improve body weight gain in our study, it appears less likely that the primary lesion in the sex-linked dwarf was at the peripheral monodeiodination of T_4. It is possible that the sex-linked dwarf could have low and/or absent T_3 receptors in the target tissue.

Though Scanes *et al.* (15) demonstrated the diminished 5'-monodeiodinase activity in the sex-linked dwarf, the significantly higher serum T_3 concentrations in the T_4 fed birds at 10.0 ppm suggest a small degree of conversion of T_4 to T_3. The difference between GH concentrations in the controls between the two experiments is not due to the inter-assay or intraassay variance or age difference because all the serum samples were examined in the same assay and the age of the birds in both experiments was the same. It is possible that the birds in the T_3 experiment are under stress because the GH concentrations in the control birds in the T_4 experiment are more similar to those we obtained from dwarf chickens at 6 weeks of age (13).

The relationship between thyroid hormones and growth hormones in the chicken is of interest. Our present findings that thyroid hormones significantly lower circulating GH concentrations agree with the recent reports of Harvey (25) and Harvey *et al.* (26), and they are different from results obtained in mammals. Thyroid hormones were shown to increase GH concentrations both *in vivo* and *in vitro* in rats (27, 28). Thus, the interaction of thyroid hormones and growth hormones in promoting growth in chickens is different from that in mammals.

Our preliminary study (Leung *et al.*, unpublished observations) showed that sex-linked dwarf chickens have fewer GH receptors than do normal chickens suggesting that the dwarfism in the sex-linked dwarf chicken could be due to the absence of GH receptors. Hoshino *et al.* (23) showed that sex-linked dwarfism could also be due to lower somatomedin activity. Since the high circuating GH concentrations are measured by radioimmunoassay, it is possible that the circulating GH in the sex-linked dwarf chicken is devoid of normal biological activity. Van Tienhoven *et al.* (18) observed that the sex-linked dwarf pullet has a higher incidence of "droplet cells" in the pituitary than do normal birds suggesting that the biological activity of the GH between normal and sex-linked dwarf chickens could be different.

In summary, present findings show that exogenous thyroid hormones could not promote growth in sex-linked dwarf chickens, and suggest that the lesion of the dwarfism could be lack of T_3 receptors at target level.

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