# The influence of thyrotropin-releasing hormone (TRH) on growth rate and thyroid activity in broiler chicks

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#### ABSTRACT

Twenty-eight-day old broiler chicks were used to determine growth rate and thyroid activity responses to various doses and routes of administration of synthetic thyrotropin-releasing hormone (TRH). In experiment 1, daily intramuscular (im.) injections of 2  $\mu$ g TRH/ chick over 10 or 20 days stimulated the relative body weight gain in cockerels by 5.7 and 10%, respectively, compared with saline injected controls. In experiment 2, TRH administered im. (2  $\mu$ g/chick) or orally (80  $\mu$ g/chick) over 10 days significantly increased (P  $\leq 0.01$ ) the relative body weight gain of cockerels by 20.3 and 29.6%, respectively and slightly improved feed conversion efficiency. No effect of TRH on the growth rate of female chicks was found. Treatment with TRH induced a marked increase of relative thyroid size, basal metabolic rate and plasma triiodothyronine and thyroxine levels. Our data confirmed earlier reports that improvement in growth rate of TRH-treated chicks appears to be mediated by thyroid hormones.

KEY WORDS: chicks, TRH, growth, thyroid activity

INTRODUCTION

In all vertebrates, except fish, the hypothalamic tripeptide thyrotropin-releasing hormone (TRH) is known to stimulate the synthesis and release of thyroid hormone i.e. triiodothyronine ( $T_3$ ) and thyroxine ( $T_4$ ), both indispensable for normal growth and development of young animals. Thus, administration of exogenous TRH may lead to augmented thyroid hormone levels and consequently to accelerated growth rates. In mammals, this growth-promoting effect has been demonstrated with intravenous (iv.) or intramuscular (im.) injections of TRH into cattle (McGuffey et al., 1977; Davis et al., 1977; Muir and Wier, 1987) and lambs (Davis et al., 1976).

The possible anabolic effect of exogenous TRH on birds has been tested in several experiments. The results of studies by Leung et al. (1984) indicated that daily iv. injection of 1 or 10  $\mu$ g TRH/chick for 17 days increased the growth rate

of 28-day old male chickens by about 12% compared with saline injected controls. Significant non-dose-related increase of plasma  $T_3$  and  $T_4$  concentrations were observed. Peak circulating hormone levels appeared 1 h after TRH injection (Leung et al., 1984; Kahl and Rząsa, 1980; Kühn et al., 1991). On the other hand in the experiment of Buonomo and Baile (1986) daily iv. injection of TRH for 21 days failed to stimulate the growth rate of cockerels, despite enhanced growth hormone (GH) secretion. It was also claimed that TRH injected iv. into adult birds is not thyrotropic but has a somatotropic effect and is responsible for the peripheral conversion of  $T_4$  into  $T_3$  (Kühn et al., 1991).

Most authors employed iv., im. or subcutaneous (sc.) routes of TRH administration. Because TRH is a small peptide, Burke and Vaughters (1984) tried to study the effect of its oral administration to chicks in either feed or drinking water. Although exogenous dietary TRH increased secretion of plasma GH, the growth rate of chicks was not affected. In contrast, Cogburn et al. (1989) reported that a large dose of TRH in feed given for 21 days stimulated the growth rate of chickens by 14% and plasma  $T_3$  level by 38% when compared with a control group.

The present study was designed to determine the effect of thyroid manipulation using synthetic TRH as an intrumuscular or oral active growth stimulant in growing broiler chickens.

#### MATERIAL AND METHODS

One hundred twenty seven twenty-eight day old nonsexed White Rock  $\times$  Cornish broiler chickens were used in two separate experiments. In both experiments chickens were divided at random into 3 groups, each of 21 or 22 birds, and kept on natural lighting schedule in individual cages with free access to standard diet and water. The standard ration contained 19.7% crude protein and 3100 kcal metabolizable energy/kg. During the 20 days of experiment the body weight and feed intake were recorded and feed conversion (g feed/g gain) calculated.

The purpose of experiment 1 was to determine the effect of daily im. injection with 2  $\mu$ g TRH/chick for 10 or 20 days on growth rate, basal metabolic rate (BMR), thyroid size and plasma T<sub>3</sub> level. The birds of control group were injected with 0.5 ml saline solution for 20 days. On day 1, 5, 10, 15 and 20 blood samples were collected into heparinized syringes from the wing veins of 10 chickens of each group 1 h after TRH or saline injections. After centrifugation the plasma was stored at  $-20^{\circ}$ C until assayed for T<sub>3</sub> levels.

The BMR was determined on 10 chicks from each group on days 10 and 20 of the experiment on the basis of  $O_2$  and  $CO_2$  concentrations in expired air using a universal Type M.G.-4 diaferometer (Kipp and Zonen, Delft, Holland).

Chickens fasted for 12 h overnight were placed individually in a temperature-controlled box. Measurements of  $O_2$  and  $CO_2$  were done between 8.00 and 12.00 h in a thermoneutral environment. After the adaptation period the  $O_2$ consumption of each chick was recorded for 2 consecutive 10 min. readings. The results were extrapolated to a 1 h period and expressed as  $O_2$  ml/g body weight. At the end of the experiment the birds were weighed, killed by decapitation and sexed. The thyroid glands were dissected and weighed.

A more practical form of TRH administration was the subject of experiment 2. Ingestion of TRH was assessed in terms of its effect as an active growth and thyroid hormone stimulant in 28-days old male and female broiler chickens. As in the previous experiment, one group of chickens received TRH intramuscularly at a dose of 2  $\mu$ g/chick, the second group received 80  $\mu$ g/chick directly into the crop, control group received im. injection of saline solution for 10 days. During this time and for the following 10 days birds were fed to appetite the standard ration as in experiment 1. The samples of blood were collected as in experiment 1 and, additionally, on day 3. Both plasma T<sub>3</sub> and T<sub>4</sub> levels were measured. The growth performance data of chickens were determined as in experiment 1.

The TRH preparation used was synthetized in the Institute of Chemistry, University of Gdańsk. TRH was dissolved in physiological saline and stored at  $-10^{\circ}$ C in sterile ampoules.

Plasma  $T_3$  and  $T_4$  levels were measured using radioimmunoassay kits supplied by the Polish Institute of Nuclear Research, Centre of Isotope Production and Distribution.

Unfortunately, in both experiments, the average initial body weight of 28-days old control chickens differed from this of the corresponding TRH-treated groups. In order to minimize this effect the relative body weight gain i.e. gain of 48-days old chickens: initial body weight (%) was calculated.

The Duncan test was used for comparison of the means of these data only. The differences between plasma  $T_3$  and  $T_4$  levels, BMR and relative thyroid size of treated versus non-treated birds were compared using the Student-t test.

### RESULTS

#### Experiment 1

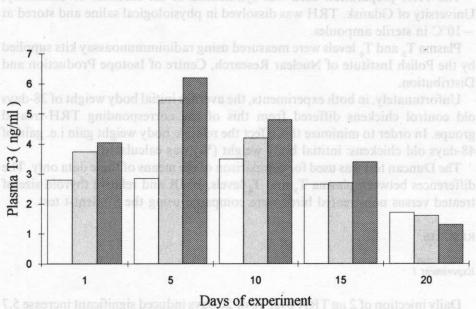
Daily injection of  $2 \mu g$  TRH over 10 or 20 days induced significant increase 5.7 and 10%, respectively, in relative body weight gain of male chickens as compared with control ones (Table 1). Feed efficiency in both, TRH-treated and control groups was similar. TRH injections into female chickens did not alter the relative growth parameters.

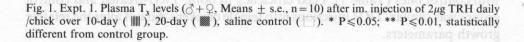
Group	s chaine a b	28	dy weight day g)	48	dy weight day g)	weigh	ve body t gain* %)	effic	eed eiency /g gain)
+inoque to	Male	n was i	istratio	ambs	нята	0.6110	ictical. 1	and our	A m
Control	itos no acti	447	$\pm 32$	1257	±36	181	±22	2.63	±0.15
TRH-10	eliond 15	518	±83	1508	±163	191	±28	2.56	$\pm 0.38$
TRH-20	HAT bo <sup>8</sup>	483	±88	1444	±194	199	±26	2.56	±0.40
	Female								
Control	14	525	±104	1325	±159	153	± 57	2.74	±0.25
TRH-10	nt fed to ap	512	±75	1338	±122	161	±25	2.89	±0.39
TRH-20	lloo ana 14 l	519	±104	1340	$\pm 208$	158	±28	2.78	±0.24

The effect of intramuscular injection of 2  $\mu$ g TRH/chick for 10 or 20 days on the growth parameters of male and female broiler chicks Experiment 1

TABLE 1 TABLE 1

\* Relative body weight gain (%) = (body weight gain: initial body weight)  $\times$  100





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Crowner C	2	thyrc	kelauve thyroid size		10 day of experiment	xperiment			20 day o:	20 day of experiment	
sdnoio		(mg/1C we	(mg/100 g body weight)	body weight (g)	veight )	basal metabolic rate (ml O <sub>2</sub> /h/g)	.bolic rate ,/h/g)	) )	body weight (g)	basal mei (ml C	basal metabolic rate (ml O <sub>2</sub> /h/g)
Control TRH-10 TRH-20	19 21 22	6.09 7.86** 7.33	+ 2.43 + 1.52 + 1.54	944 1039 1046	+ + + + 27 10	1.27 1.55** 1.52**	$\pm 0.05$ $\pm 0.09$ $\pm 0.05$	1266 1455 1435	+ 35 + 37 + 58	0.95 0.93 1.20**	+0.04 +0.05 +0.01
** P ≤ 0.01	** P ≤ 0.01 statistically	different fi	different from control group.	roup.							
The effect of i and female br Experiment 2	The effect of intramuscula and female broiler chicks Experiment 2	lar (2 µg TF s	TABLE 3 The effect of intramuscular (2 μg TRH/day/chick) or oral (80 μg TRH/day/chick) TRH administration for 10 days on the growth parameters of male Experiment 2	) or oral (80 <i>µ</i>	ug TRH/day/	(chick) TRH	administra	tion for 10 d	lays on the <sub>i</sub>	growth paran	TABLE 3 neters of male
Certine Certine			Inital bod	Inital body weight	Final	Final body weight		Relative body	yb, **	Feed	p
	sci	=	i)	20 udy (g)		то цау (g)		weigin gain (%)		eniciency (g feed/g gain)	aucy g gain)
	Male										
Control		9	590	±120	1418	$\pm 192$		137B	$\pm 46$	2.80	$\pm 0.71$
TRH-im.		Ś	564	$\pm 101$	1496	+ 26		165^	±47	2.61	$\pm 0.29$
TRH-oral		9	533	<del>1</del> 90	1480	± 197		178A	±17	2.48	$\pm 0.42$
	Female										
Control		6	568	$\pm 112$	1423	$\pm 93$		150A	± 13	2.65	$\pm 0.19$
TRH-im.		15	532	$\pm 123$	1373	$\pm 189$	_	159A	±15	2.64	$\pm 0.35$
TRH-oral		14	529	± 82	1348	$\pm 164$		155^A	<u>+</u> 21	2.65	$\pm 0.18$

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The effect of im. daily injections of 2  $\mu$ g TRH/chick over 10 or 20 days on plasma T<sub>3</sub> level at days 1, 5, 10, 15 and 20 is shown in Figure 1. It can be seen that within the first 5 days of TRH injections there was a dramatic elevation in the plasma T<sub>3</sub> concentration. The mean plasma T<sub>3</sub> level in group TRH-10 and TRH-20 was higher than in control birds by 30 and 45% (P  $\leq 0.05$ ) on day 1, by 94 and 119% (P  $\leq 0.01$ ) on day 5 and 21 and 22% on day 10, respectively. The plasma T<sub>3</sub> concentration on day 15 was 35% higher (P  $\leq 0.05$ ) only in the group receiving prolonged TRH infusion. By day 20 of the experiment, plasma T<sub>3</sub> level in all birds declined and no differences between groups were noted.

BMR data, expressed as intake of ml  $O_2/h/g$  body weight measured after 10 and 20 days of the experiment, demonstrated that  $O_2$  consumption increased only during the period of TRH infusion (Table 2). In both experimental groups the  $O_2$  intake after 10-days injection period exceeded intake of the control birds by 20 to 22% (P  $\leq 0.01$ ). The consumption of  $O_2$  on the 20 th day of the experiment was higher by 26% (P  $\leq 0.01$ ) only in those chickens which received longer TRH treatment. The respiratory quotient (RQ) in fasting chicks for both experimental periods in all of the groups was 0.64 to 0.78 (mean 0.70  $\pm 0.012$ ).

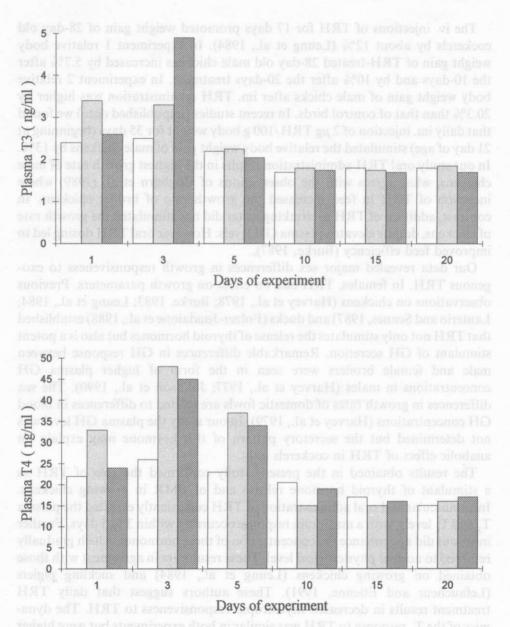
TRH injections were associated with appreciable thyroid enlargement. In birds treated with TRH over 10 or 20 days the thyroid size increased by 29 and 20.3%, respectively, compared with the control group (Table 2).

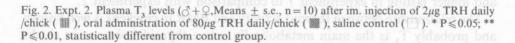
#### Experiment 2

Data on the effects of oral vs im. TRH administration on growth parameters of male and female chickens are presented in Table 3. TRH treatment over a 10-day period significantly ( $P \le 0.01$ ) influenced the relative body weight gain in males but not in females. Relative body weight gain of cockerels which received daily 2 µg TRH im. or 80 µg TRH orally increased by 20.3 and 29.6% respectively, in relation to control group. Feed efficiency of cockerels only was improved by 6.8 and 11.4%, respectively.

Both routes of TRH administration resulted in a immediate substantial increase in plasma  $T_3$  concentration (Fig. 2) at days 1 and 3, but from the day 5 it declined and on consecutive days of the experiment there were no differences among the groups. The plasma  $T_4$  level rapidly increased within days 1 to 3 of the TRH administration, remained elevated on day 5 and declined to the level of control over the next days of the experiment. Plasma  $T_4$  level in im. and orally TRH-treated groups surpassed this of control group by 53 and 10% (P  $\leq 0.01$ ) on day 1, by 83 and 75% (P  $\leq 0.01$ ) on day 3 and by 65 and 26% (P  $\leq 0.01$ ) on day 5, respectively. The changes in plasma  $T_3$  and  $T_4$  levels were generally more pronounced in chickens injected with TRH.

DISCUSSION





## DISCUSSION

The iv. injections of TRH for 17 days promoted weight gain of 28-day old cockerels by about 12% (Leung et al., 1984). In experiment 1 relative body weight gain of TRH-treated 28-day old male chickens increased by 5.7% after the 10-days and by 10% after the 20-days treatment. In experiment 2 relative body weight gain of male chicks after im. TRH administration was higher by 20.3% than that of control birds. In recent studies (unpublished data) we found that daily im. injection of 2  $\mu$ g TRH/100 g body weight for 35 days (beginning at 21 day of age) stimulated the relative body weight gain of male chickens by 13%. In our study oral TRH administration results in the highest growth rate of male chickens, what agrees with the observations of Cogburn et al. (1989) where inclusion of TRH in feed increased the growth rate of broiler chickens. In contrast, addition of TRH to drinking water did not stimulated the growth rate of chickens, despite elevated plasma GH levels. However oral TRH dosing led to improved feed efficiency (Burke, 1987).

Our data revealed major sex differences in growth responsiveness to exogenous TRH. In females, TRH had no effect on growth parameters. Previous observations on chickens (Harvey et al., 1978; Burke, 1983; Leung et al., 1984; Lauterio and Scanes, 1987) and ducks (Folzer-Joudaione et al., 1988) established that TRH not only stimulates the release of thyroid hormones but also is a potent stimulant of GH secretion. Remarkable differences in GH response between male and female broilers were seen in the form of higher plasma GH concentrations in males (Harvey et al., 1977; Johnson et al., 1990). The sex differences in growth rates of domestic fowls are related to differences in blood GH concentrations (Harvey et al., 1979). In our study the plasma GH level was not determined but the secretory pattern of this hormone may explain an anabolic effect of TRH in cockerels only.

The results obtained in the present study confirmed the role of TRH as a stimulant of thyroid hormone release and of BMR in growing chickens. Intramuscular and oral administration of TRH consistently elevated the plasma  $T_3$  and  $T_4$  levels, with a maximum response occurring within 3 to 5 days. Further infusions did not enhance the concentration of these hormones, which gradually returned to normal physiological level. These results are in agreement with those obtained on growing chickens (Leung et al., 1984) and suckling piglets (Lefaucheur and Etienne, 1991). These authors suggest that daily TRH treatment results in decreased thyrotropin responsiveness to TRH. The dynamics of the  $T_3$  response to TRH was similar in both experiments but were higher and longer lasting in experiment 1 in comparison with experiment 2.

The relationship between thyroid activity and BMR in chickens is well known and probably  $T_3$  is the main metabolically active thyroid hormone in chicks

affecting the oxygen consumption (Bobek et al., 1977; Leung et al., 1985). Our study indicates that im. TRH treatment of chickens significantly increased BMR and thyroid size. The activation of the thyroid gland i.e. rises in  $O_2$  consumption and plasma  $T_3$  levels were associated with the time-course of TRH administration.

The both routes of TRH administration resulted in more pronounced increases of plasma  $T_4$  than  $T_3$  levels. It shows the predominance of the anabolic metabolism induced by the TRH experimental dose. Similarly, a more pronounced response of  $T_4$  in comparison to  $T_3$  levels was observed in TRH-treated suckling piglets (Lefaucheur and Etienne, 1991). On the other hand, the hyperthyroidism induced by high dietary TRH intake by growing chickens (Cogburn et al., 1989) or single high iv. dose into adult birds (Kühn et al., 1991) elevated only the plasma  $T_3$  concentration but not that of  $T_4$ . These authors supposed that the hyperthyroid state induced by high TRH doses increase peripheral conversion of  $T_4$  into  $T_3$ .

It may be concluded that both im. and oral TRH treatment effectively increase thyroid hormones concentrations in blood of growing broiler chicken but may improve the growth rate of male chickens only.

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#### STRESZCZENIE

#### Wpływ hormonu wyzwalającego tyreotropinę (TRH) na tempo wzrostu i aktywność tarczycy u kurcząt brojlerów

Badano wpływ zróżnicowanych dawek i metod podawania syntetycznego hormonu wyzwalającego tyrcotropinę (TRH) na tempo wzrostu i aktywność tarczycy u 28-dniowych kurcząt brojlerów. W doświadczeniu l wykazano, że domięśniowe wstrzykiwanie po 2  $\mu$ g TRH dziennie przez 10 lub 20 dni zwiększyło względne przyrosty masy ciała kogutków odpowiednio o 5,7 i 10% w porównaniu z kogutkami z grupy kontrolnej, otrzymujących injekcję soli fizjologicznej. Wyniki doświadczenia 2 wskazują natomiast, że wstrzykiwanie po 2  $\mu$ g TRH domięśniowo lub wprowadzenie 80  $\mu$ g TRH do wola przez 10 dni zwiększyło (P  $\leq$  0.01) względne przyrosty masy ciała kogutków odpowiednio o 20,3 i 29,6%. U kogutów obserwowano przy tym niewielką poprawę efektywności wykorzystania paszy. W obydwóch doświadczeniach nie wykazano wpływu TRH na wyniki tuczu kurek. Podawanie TRH zwiększyło względną masę tarczyc, tempo podstawowej przemiany materii oraz poziom trójjodotyroniny i tyroksyny w osoczu krwi. Przeprowadzone badania potwierdziły wcześniejsze doniesienia, że poprawa tempa wzrostu kurcząt może się odbywać za pośrednictwem hormonów tarczycy po podaniu TRH.