## CHANGES IN THE LIPID RATIO OF THE DIET CAUSES IMMEDIATE ADAPTATION OF THE THYROID ECONOMY IN RABBITS

Department of Physiology<sup>1</sup> and Department of Animal Nutrition<sup>2</sup>, University of Veterinary Science, Budapest

## Introduction

It is well known from the literature (McBride and Cramer, 1978) that thyroid hormones influence lipid mobilization and distribution of fat in muscle fibers also in the rabbit as they do in other species (Langslow et al., 1984). The basically new results of the past ten years concerning peripheral thyroid hormone metabolism revealed that the composition of the diet may alter the amount of active thyroid hormone (triiodothyronine, T3) available for the different cells (for review see Larsen et al., 1981). These two facts make it plausible to suppose that a better understanding of the effect of diet composition upon thyroid economy is an economically important meat producing animal can help in raising ideas to improve the quality of feeding. The aim of the present paper was to demonstrate the possible pathways on which changes in the lipid ratio of the diet can influence thyroid economy in the meat rabbit, keeping the daily digestible energy intake at the same level.

#### Materials and Methods

4-5-month-old New Zealand White rabbits (body weight:  $2.96 \pm 0.09$  kg) were utilized in this experiment. The animals were fed according to the maintenance requirement i.e. 0.553 MJ DE per W<sup>0.75</sup> (DeBlas et al., 1985) and water was available continuously via automatic watering troughs. After a two-week adaptation period 10 animals were placed on a high lipid ratio diet (HLR) (see Table 1 and Table 2), another 10 animals remained on the original diet and served as controls (C). The chemical composition of the feeds were established according to A.O.A.C. (1975), the digestible energy content was calculated according to Fekete and Gippert (1986).

During the adaptation period and after it several blood samples were taken to monitor the serum thyroxine and triiodothyronine content (for details see Figures), 6, 11, 24 and 30 hours after and 24 hours before the introduction of the HLR diet 2 rabbits of each group were killed. Blood was taken by decapitation, liver, kidney and muscle (m. gluteus) were taken out and were snap-frozen on dry ice. Determination of deiodinase activity was carried out within a month after the experiment. This period of time did not influence enzyme activity according to our former experience (Rudas, 1986), T3 and T4 were determined by RIA (Pethes et al., 1978). The deiodination assay intailed the followings that are detailed elsewhere

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(Rudas, 1986): 1 g of the tissue was minced in  $4^{\circ}$ C phosphate buffer (pH 7.4, 0.05 mM). The activity of the deiodinase type-I was determined in the absence of propylthiouracyl (PTU) using 0.6 umol T4 as substrate and determining the corrected T3 produced. Type-II deiodinase activity was determined in the presence of 1 mM PTU.

Body weight of animals were checked every 3 days.

# Results and Discussion

The concentration of thyroxine in the blood serum (Figure 1) was not different in the two groups either before or after the introduction of the HLR diet. The values obtained during the experiment were within the range of the normal rabbit found by others (Slebodzinsky et al., 1983). There was a continuous drop in T4 concentration over the experimental period. This drop expressed at the end of the experiment and occured in both (C and HLR) groups. Since animals were in the same room during the experiment one should suppose that the well-known thyroxine decreasing effect of experimental stress (Ingbar et al., 1985) was responsible for this phenomenon.

The serum level of triiodothyronine was not different in the two groups before changing the diet (Figure 2). However 6 hours after the introduction of the HLR diet there was a sudden drop in the level of triiodothyronine in the HLR group in comparison to group C. The difference was statistically significant (p 0.05) and remained so for the rest of the experimental period. The figure also shows that the normal rhythmicity of the serum T3 level is not influenced by the HLR diet, that is the lower T3 level in the HLR group is parallel to that found in the control. This phenomenon, namely that diet induced changes in thyroid economy do not influence normal rhythmicity, is in accordance with other data in the literature on the human (Balsam and Leppo, 1984) and also with data obtained by this research group in chickens (Bartha et al., 1986, 1987).

Since the activity of type-II deiodination in the organs investigated was negligible, Table 3 shows only the results on type-I deiodination. Deiodination rate in the HLR group decreases dramatically 6 hours after introducing the dist in the liver and in the kidney. It is clear from the research efforts of the last years that the circulating level of the active form of thyroid hormones (T3) is basically influenced by those organs (liver and kidney) that can produce and discharge large amounts of T3 deiodinated from T4 into the circulation (so-called "exporter" or gans, see Silva and Larsen, 1983). The low T3 concentration parallel to normal T4 serum concentrations can be well interpreted as a results of the above (Table. 3) demonstrated very low level of deiodination in these exporter organs. The intriguing question, however, that asks for the trigger in these phenomena can not be answered at this point. The most plausible explanation for this sudden effect of diet composition upon peripheral deiodination of thyroid hormones might be that some gastrointestinal signal (of peptidic or other origin) reaches the liver (or also the kidney) right at the time when the ingestion of the altered feed occurs. This conception was raised by others (Decuypere et al., 1985), and it was further supported by this research group finding that gut glucagon might be the signal in chickens (Rudas and Newcomer, 1987) when thyroid economy responds to fasting and refeeding.

In summary present results show that fat mobilization, that is basically influenced by thyroid hormones in the rabbit (McBride and Cramer, 1978) can be modified by a regulatory loop consisting of the composition of the diet as a determining factor and by the peripheral metabolism of thyroid hormones as an adjusting mechanism. Data may suggest too, that there is a certain limit of the optimal fat supplementation of rabbit's diet,

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#### Figure legend

Figure 1: Blood serum thyroxine concentration in rabbits exposed to high lipid ratio (HLR) diet from the time point on indicated by the arrow. (O) = control diet. ( $\bullet$ ) = HLR, T4 = thyroxine, No statistically demonstrable difference occured as an effect of the diet,

Figure 2 : Blood serum level of triiodothyronine in rabbits exposed to high lipid ratio (HLR) diet from the time point on indicated by the arrow. (O) = control diet. ( $\bullet$ ) = HLR diet. T3 = triiodothyronine. -X - = p = 0.05.

Table 3 : 5°-deiodination (type-I) in different organs of rabbits kept either on control diet (C) or exposed to high lipid ratio diet (L) for 30 hours. Pairs of rabbits were bled and processed at the given time points in panel A, here data are averages of the two individual results. Panel B shows the summarized data between the 6th and 30th hours after introducing the new diet, so that statistical comparison can be made (mean + SEM)

			Pane	1 A		Panel B average of individual data durin 6-30 hours
Organs		hours	after	r diet 24	change 30	
		6	11			
liver	 c	35.7	26.3	26.5	35.9	31.12 + 5.6
	L	3.78	5.9	2.6	3.1	3.84 ± 0.87 ж
kidney	С	147.2	116.2	138.3	162,2	141 <b>.</b> 1 <u>+</u> 5 <b>.</b> 3
	L	80.7	$78_{\bullet}7$	80.1	108.5	86.8 <u>+</u> 15.1 x
muscle	С	2,39	2,84	1.97	2,11	$2_{\bullet}32 \pm 0_{\bullet}45$
	$\mathbf{L}$	1,98	2.47	2.11	2,21	2.19 + 0.15

407

		HL	
Ingredients, %			
wheat	42.5	30	
corn	10.0	7	
alfalfa meal (20 % CP)	-	40	
alfalfa meal (17 % CP)	30.0	-	
wheat bran	5 <sub>•</sub> 0	5	
sunflower meal, dehulled,			
solv. extr.	8 <b>.</b> 5	6	
meat meal	2.0	_	
sunflower oil	~	10	
mineral-vitamin suppl.	2.0	2	
Nutritive value			
DE, MJ/kg	11,08	$13_{\bullet}78$	
Crude protein, %	15, 80	15 <sub>0</sub> 00	
Digestible CP, %	10 <sub>0</sub> 00	11,10	
Ether extract, %	2,7	1 <b>2</b> ,10	

Table 1 : Composition of the experimental diets (C = control, HL = high lipid ratio)

# Table 2 : Daily energy and protein intake of the rabbits (C = control, HL = high lipid ratio)

	C	HL	Maintenance requirement <sup>2</sup>
Daily ration, g	113	91	
Energy intake, MJ DE/d	1 <b>,2</b> 5	1 <b>, 2</b> 5	1,25
CP intake, g/day	17.9	13 <b>.</b> 7	
DCP intake, g/day	11.3	10.1	8, 60
EE intake, g/day	3 <b>.</b> 0	11.0	min. 2,50
DEE intake, g/day	2,7	10,4	

 $CP = crude \text{ protein}, DCP = digestible CP, EE \approx ether extract,$ DEE = digestible ether extract

1





CHANGES IN THE LIPID RATIO OF THE DIET CAUSES IMMEDIATE ADAPTATION OF THE THYROID ECONOMY

# Rudas, P.<sup>1</sup> and Fekete, S.<sup>2</sup>

University of Veterinary Science, Budapest, Department of Physiology and Animal Nutrition<sup>2</sup>

The effect of the dietary lipid ratio was investigated in this experiment upon the serum level of thyroid hormones and on the deiodination activity of different organs in NZW rabbits in a short term experiment. At the beginning of the experiment half of the animals were provided high lipid ratio diet (HLR) 12.1 vs 2.7 % ether extract, the other half served as control (C). Serum thyroxine concentration did not change. T3 serum levels begin to drop significantly in group HLR as early as 6 hours after introducing high lipid in the diet and remained so until the end of the experiment.  $5^{\circ}$ -deiodination rate in the liver and in the kidney in animals of HLR group was highly significantly lower from 6 to 30 hours of the trial.

# CHANGEMENT DE L'ÉCONOMIE THYROIDIENNE DU LAPIN EN FONCTION DE LA TENEUR LIPIDE DE LA RATION

On a élevé la concentration de la matière grasse de l'aliment du lapin de 2,7 à 12,1 %. Cet changement n'a pas altéré la concentration de thyroxine du sang, mais celle de T3 a été significativement baissée déjà 6 heures apres le commencement du nouvel régime alimentaire et elle a restée sur ce niveau jusqu' au fin de l'essai. L'activité de 5'-deiodination dans le foie et les reins des animal du groupe ''huileux'' a été significativement plus basse de 6<sup>ème</sup> à 30<sup>ème</sup> heures de l'expérience.

