lipolysis is augmented by mass action as the concentration of substrate (triglyceride fat) increases. The findings of this study are consonant with the hypothesis that lipolysis plays a physiological role in removal of turbid fat particles from the blood and that unesterified fatty acid bound to protein may be a mechanism for transporting fat from blood to tissues. Heparin probably accelerates the activity of the lipolytic mechanism(5).

Summary. 1. During alimentary lipemia and lipemia produced by intravenous injection of fat emulsions there was a rise in the concentration of free fatty acid in serum. The free fatty acid was found in the non-turbid portion of serum (infranatant of high speed centrifugation). Injection of heparin produced an elevation of free fatty acid concentration which was greater in lipemic than in fasting subjects. A portion of this elevation after heparin was attributable to *in vitro* lipolysis. 2. It is suggested that lipolysis with free fatty acid formation may play a role in normal fat metabolism and transport.

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Effect of Triiodothyronine on Oxygen Consumption of Tissues Not Responsive to Thyroxine.* (21954)

S. B. BARKER.

From Department of Pharamacology, University of Alabama Medical Center, Birmingham.

The most prominent effect of thyroxine injection in experimental animals is an increase in metabolic rate. Corresponding increases in oxygen consumption have been obtained with such tissues as heart, liver, kidney, diaphragm, skeletal muscle and salivary gland removed from thyroxine-injected animals. In contrast, many other tissues do not participate in the metabolic stimulation, notably brain, spleen, testis, prostate, seminal vesicle, ovary, uterus, thymus and lymph node(1,2).

Since the discovery of triiodothyronine (TRIT) as a form of thyroid hormone even more potent than thyroxine(3), it has been proposed that the latter may be active only after partial deiodination to triiodothyronine (4). Evidence is accumulating that such a transformation does occur(5,6), although its obligatory character is far from established (7). It seemed possible that the lack of response of the tissues mentioned above, as far as thyroxine was concerned, might be due to

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TABLE I. Effect of Injections of L-Thyroxine or of L-Triiodothyronine on Tissue Metabolism of Thyroidectomized Rats.

Tissue	Thyroidect.,* control Qo_2	% change from control Qo_2		
		Thyroxine,* 2 mg/kg/d	TRIT,* .5 mg/kg/d	TRIT,† 2 mg/kg/d
Liver	1.02	+ 42.2	+ 44.1	+ 63.8
Diaphragm	.62	+ 43.2	+ 32.3	+ 47.7
Salivary gland	1.98	+ 24.7	+ 37.9	+ 49.1
Heart	.58	+152.4	+135.9	+200.3
Brain	1.34	− .7	− 1.5	+ 2.4
Spleen	1.42	− 4.9	+ 5.6	+ 1.6
Testis	.62	+ 12.9	+ 8.1	− 5.7
Seminal vesicle	.89	+ 1.1	− 4.5	− 3.8
Prostate	1.45	+ 6.2	− 6.2	+ 4.0
Ovary	1.49	+ 4.7	+ 3.4	+ 1.7
Uterus	1.12	− 11.6	− 14.3	+ 7.7
Thymus	1.14	+ 5.3	+ 3.5	+ 4.8
Lymph node	1.17	− .9	+ 11.1	+ 2.5
Gastric Sm. Mus.	.73	+ 2.7	.0	− 3.9

* Five ♂ and 5 ♀ in each of these groups.
† One ♂ and one ♀ in this group.

inability to carry out this transformation. The results of the present work show that, although TRIT is some 4 times as effective as thyroxine in increasing metabolism of several tissues, its results are not qualitatively different from those of thyroxine.

Methods. Both male and female albino rats of the Sprague-Dawley strain were used. All were thyroidectomized at least 4 weeks prior to being injected. As a reference material, L-thyroxine† was injected in a dose of 2 mg/kg/day for 4 days and the animals sacrificed on the fifth day. Preliminary studies indicated that an equimolar dose of L-triiodothyronine‡ produced a much greater elevation in metabolism of heart, liver, diaphragm and salivary gland than resulted from thyroxine. Since one-quarter of the equivalent dose gave approximately the same effect as thyroxine, this amount was used. The compounds to be injected were dissolved in a small amount of 0.1 N NaOH, which was diluted to a final concentration of 0.02 N and was made isotonic with NaCl. Some of the control animals were injected with an equivalent amount of the alkaline saline; since no differences were observed from the uninjected, all control animals were lumped together. Preparation of each of the various tissues was carried out as discussed previously(1,2). Oxygen consumption of each tissue was measured in a Krebs' Ringer phosphate medium with glucose (100 mg%) as substrate.

Results. Table I shows the average oxygen consumptions for the array of tissues studied from the control thyroidectomized animals and from those injected with thyroxine and triiodothyronine. Five males and 5 females were used in each category of control and thyroxine-injected or TRIT-injected. The averages of all tissues not sex-specific are therefore from 10 animals. It can be seen that, amongst the tissues used as references, liver and heart were increased about the same amount by both substances at the dose levels employed. Triiodothyronine accelerated salivary gland metabolism somewhat more, and diaphragm less than did thyroxine. Two additional rats are included which received 4 times as much triiodothyronine as the others, or a dose equimolar with the thyroxine. The oxygen consumption increases were greater in these 2, but not proportionally.

The remaining data in the Table deal with tissues previously found unresponsive to thyroxine, with one exception. These were again unaltered by thyroxine and in addition were not changed by either the 0.5 or the 2.0 mg dose of triiodothyronine. The one exception

† L-Thyroxine was obtained from the Travenol Laboratories, through the kindness of Dr. H. A. Fevold.

‡ L-Triiodothyronine was furnished by Dr. A. E. Heming of Smith, Kline & French Laboratories.

was gastric smooth muscle which had previously been reported as stimulated by thyroxine injection(1). When neither TRIT nor thyroxine influenced its metabolism in the present series, the original data of Barker and Klitgaard were carefully re-examined, but no explanation could be discovered for the discrepancy. Preliminary experiments with several other thyroxine analogs have yielded results similar to those shown here. This tissue now becomes consistent with other unresponsive structures also made up primarily of smooth muscle, such as uterus and seminal vesicle.

One may conclude from these data that, in the thyroidectomized rat, triiodothyronine produces qualitatively the same effects on tissue metabolism as thyroxine. As already mentioned, there is no clear evidence that formation of the triiodinated form from the tetraiodinated is an obligatory step in the tissue response to the latter. The present study discloses that, even if triiodothyronine is made available, some tissues do not respond. An interesting point to pursue would be to determine whether any of these resistant tissues is actually capable of deiodinating thyroxine.

Discussion. Unpublished observations of Klitgaard and Barker indicate that after injection of these amounts of thyroxine, the hormone is present in all tissues to about the same concentration, except for liver and kidney, where levels are much higher. Comparable data are not available for triiodothyronine. At much lower dose levels, both forms of the hormone have been shown to be present in many tissues of the animal body(8). The question of penetration of cells by thyroxine or TRIT has not been answered clearly although Gross *et al.*(8,9), have demonstrated considerable concentration of TRIT by parts of the brain, especially posterior pituitary.

Summary. 1. L-Triiodothyronine (TRIT) injected into thyroidectomized rats at a dose level equivalent to 0.5 mg L-thyroxine/kg body weight/day is capable of stimulating the oxygen consumption of liver, diaphragm, heart and salivary gland preparations to the same extent as 2 mg of L-thyroxine. 2. Neither 0.5 nor 2 mg TRIT injected/kg/day altered the metabolic rates of tissues found unaffected by 2 mg of L-thyroxine, including brain, spleen, testis, seminal vesicle, prostate, ovary, uterus, thymus, lymph node and gastric smooth muscle. 3. Even if thyroxine is converted to TRIT before exerting its effect on the metabolic rate the failure of these tissues to respond to thyroxine does not seem referable to any possible inability to carry out this deiodination.

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