Relation of Thyroid Status to Nitrogen Excretion Following Exposure to Thermal Radiation.* (20573)

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The well known negative nitrogen balance which follows severe burning has not yet been fully explained. The conclusion that it is a complex phenomenon, not related to any single biochemical event, appears to be justifiable when the reports of various investigators are considered(1-4). The increased excretion of steroids which accompanies the period of greatest nitrogen excretion(5,6) and observations relative to the thyroid(7,8) imply abnormal endocrine functions during the post-burn state. Endocrine involvement is to be expected in view of the alarm and stress reactions(9) which the organism undergoes with thermal trauma. Our experience that thyroid activity (as measured by radio-iodide uptake) of burned animals deviates from normal(10), and the study of Gribble and Peters(8) which suggested the increased nitrogen excretion to be related to altered thyroid status, demanded that these biochemical parameters be measured in intact animals with normal, hypo- and hyperthyroid status.

If the activity of the thyroid is related to the increased nitrogen excretion which follows thermal assault, then changes in nitrogen output in hypo- and hyperthyroid burned rats should differ from that of euthyroid burned animals. Euthyroid nitrogen excretion (post-burn) should approach that of the hyperthyroid rats, whereas nitrogen output of the hypothyroid beasts should show little change. The following study was made to test this hypothesis.

Experimental. Three groups of adult male rats, twelve rats per group, were selected for uniform body weight (190-210 g) and fed an 18% casein ration(11). One group received 0.5% desiccated thyroid (Armour) in the basal diet. The second group received 0.5% thiouracil, whereas the third group received no additions and served as controls. Paired feeding was employed throughout with the thiouracil-fed rats acting as the limiting group from the beginning. Three-day nitrogen balances were measured starting on the 21st day of these dietary regimes and on the 28th day. By this time all 3 groups were in comparable states of negative nitrogen balance as indicated in Table I. On the 34th day half of the animals in each group were shaved and burned by one minute exposure of 20% of the total body surface (midriff) to dry heat emitted from an array of six 150 watt electric lamps concentrically arranged. The caloric flux of this device has been estimated to be the order of 14-15 g cal per cm^2 per minute. After burning, a third 3-day nitrogen balance was then measured. Thyroid status of the 3 unburned groups was evaluated by I^{131} uptake at the end of the experiment. Methods of radioassay have been described elsewhere(10).

Results. As indicated in Table I, burned hyperthyroid rats excreted 50% more urinary nitrogen than did unburned hyperthyroid animals. Total nitrogen excretion of the burned rats of this group increased 19%, nitrogen bal-

TABLE I. Nitrogen Metabolism in Relation to Thyroid Status Pre- and Post Burning.
(All values as mg N/100 g body wt.)

Group	Period, day	Fecal N.	Urinary N.	N. balance
Hyperthyroid	21st–24th	588	577	–1089
Euthyroid	"	626	462	–1020
Hypothyroid	"	454	358	– 749
Hyperthyroid	28th–31st	399	173	– 536
Euthyroid	"	339	178	– 482
Hypothyroid	"	355	163	– 485
Hyperthyroid b*	34th–37th	644	366	– 925
" c	"	605	243	– 754
Euthyroid b	"	577	349	– 851
" c	"	474	151	– 544
Hypothyroid b	"	474	217	– 619
" c	"	560	184	– 654

* b = burned; c = control.

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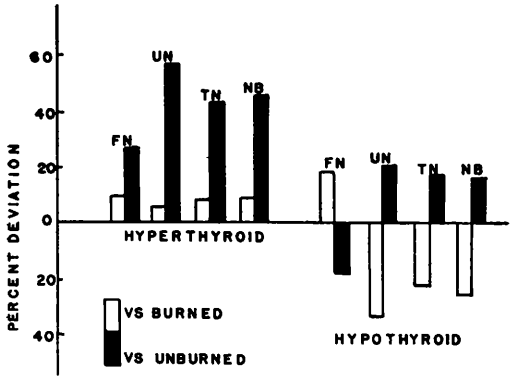

FIG. 1. Comparison of nitrogen excretion of hyper- and hypothyroid rats (burned) with euthyroid rats. FN, fecal nitrogen; UN, urine nitrogen; TN, total nitrogen; NB, nitrogen balance.

ance, 23%. Euthyroid burned rats excreted 131% more urinary nitrogen, 49% more total nitrogen, and nitrogen balance increased negatively 57%. The urinary nitrogen, total nitrogen and nitrogen balance of the burned hypothyroid rats varied +18%, —7% and —5% when compared to unburned hypothyroid controls. The deviations of hyperthyroid and hypothyroid rats from euthyroid animals is summarized in Fig. 1. The I^{131} uptake by the thyroids of the hypothyroid rats was about 3% of euthyroid (100%), whereas the uptake by the hyperthyroid animals was 6.9%. Only the burned euthyroid rats showed significant changes in I^{131} uptake (Table II). These results confirm the thyroid status of each group (12).

Discussion. The data presented here indicate thyroid status to be related to the increased nitrogen catabolism which follows severe burning. This is in agreement with the findings of others(8) who have shown no significant differences in the nitrogen excretion of burned thyroidectomized rats. Their results are similar to those obtained with the hypothyroid rats in this study. The stimulation of thyroid activity following burning(10) does appear to bear some relation to the greatly increased nitrogen excretion. The fact that burned euthyroid rats excreted nearly as much nitrogen as the burned hyperthyroid rats suggests that these groups were catabolically equal. I^{131} uptakes by the thyroids of these two groups indicate the hyperthyroid group to have taken up much less iodide than did the burned euthyroid rats. This supports the hypothesis that nitrogen catabolism in the post-burn state is related to changes in thyroid activity. Thus the insignificant changes in the nitrogen catabolism of the burned hypothyroid rats should be an indication of a less active thyroid. This is apparent in view of the low uptake of radio iodide by the thyroids of the group, which was only 6.9% of that of the burned euthyroid rats. These studies do not rule out the probability of other endocrine functions being involved in initiating or perpetuating the abnormal protein catabolism of the post-burn state.

TABLE II. I^{131} Uptake by Thyroids of Burned and Unburned Rats.

Group	cpm/avg thyroid	% of euthyroid (unburned)
A. Unburned		
Hyperthyroid	139 ± 12*	6.9
Euthyroid	2015 ± 45	100
Hypothyroid	64 ± 7	3.2
B. Burned		
Hyperthyroid	210 ± 15	10.4
Euthyroid	3569 ± 59	177.3
Hypothyroid	54 ± 7	2.7

* Stand. error.

Summary. Protein catabolism in the post-burn state appears to be closely related to thyroid status. The post-burn nitrogen excretion of euthyroid rats approached that of hyperthyroid animals, whereas nitrogen catabolism of hypothyroid rats was practically unchanged.

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Effect of Sodium 5-Allyl-5-(1 methylbutyl) 2-Thiobarbiturate on Uptake of I^{131} by Rat Thyroid. (20574)

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Recent observations(1,2) indicated sodium ethyl(1-methylbutyl) thiobarbiturate (Pentothal), a commonly used anesthetic agent, to reduce the I^{131} uptake by rat thyroid to the extent of 89%. The reduced uptake was not found to be related to the anesthetic effect, since other anesthetics not containing a $-NH-\underset{\underset{SH}{|}}{C}=N-$ grouping did not impair I^{131} incorporation into the thyroid. It was decided to test another commonly used sulfur containing anesthetic(3,4), sodium 5-allyl-5 (1 methylbutyl) 2-thiobarbiturate (Surital) to determine its effect on the I^{131} trapping mechanism and particularly the chemical partition of I^{131} in the thyroid gland.

Methods. Eight adult male rats of the Wistar strain (180-205 g) were given Surital (40 mg/kg) intraperitoneally. Sixty minutes later, each animal was given intraperitoneal injections of 2 μc of carrier-free radioiodide (I^{131}) contained in one ml of physiological saline. In addition, 8 male rats of comparable weight were given I^{131} only to serve as controls. Four hours post administration of the I^{131}, the animals were sacrificed by a sharp blow on the head, the thyroids removed, stripped of adherent tissue. Mounting and radio assay technics have been described elsewhere(2). Results are expressed as counts per minute (cpm) per milligram of tissue. Thyroids from each group were pooled immediately following radio assay and digested in 3.5 N KOH for 8 hours on the water bath. The alkaline digests were fractioned with n-butanol by the method of Tong and Chaikoff(5) with minor modifications. The radioactivity of these fractions was determined under conditions of identical geometry. Counting was continued to give a statistical error of 2% or less. Results are expressed as the percentage of total recovered radioactivity from the thyroid hydrolysate.

Results. The data in Table I indicate that Surital markedly inhibits the uptake of I^{131} by the rat thyroid. Table II shows that although the total incorporation into the inorganic, di-iodotyrosine and thyroxine fractions was much lower in the Surital treated rats than in the controls, the ratio of I^{131} among these fractions is essentially the same.

Discussion. Obviously, the inhibition of I^{131} uptake in the presence of Surital is a reaction which prevents iodide from ultimately combining with thyro-protein, (a) by in-

TABLE I. Effect of Surital on I^{131} Incorporation into Rat Thyroid.*

	cpm/mg thyroid	% controls
Control animals	107.1 ± 11.8†	100.0
Surital-treated animals	10.4 ± 1.5	9.7

* Avg of 8 animals.
† Stand. error of the mean.

TABLE II. Partition of Recovered I^{131} in Alkaline Hydrolysates of Pooled Rat Thyroid Tissue.

Thyroid fraction	Control cpm	Control % of recovered I^{131}	Treated cpm	Treated % of recovered I^{131}
Iodide	2860	56.9	320	54.1
Di-iodotyrosine	1400	27.9	196	33.1
Thyroxine	760	15.2	76	12.8
Totals	5020	100.0	592	100.0