glycosuria and diuresis. Thus there was no improvement in the diabetic state during the period of aureomycin administration as expressed by glycosuria and diuresis. The gain in bodyweight during this period in spite of increased glycosuria and diuresis can be explained by the fact that during this period the animals consumed more food. Obviously at least a part of the additional food was utilized. The cause for the increased food intake during aureomycin administration is not clear. It might be related to a possible specific metabolic effect of aureomycin.

The question of food utilization in chronic diabetic rats receiving aureomycin and the intermediary metabolic effects of aureomycin in diabetes are under investigation.

Summary. 1. Aureomycin given to chronic alloxan diabetic rats caused an average gain in body weight of 19.0 ± 2.9 g during 28 days. Control chronic alloxan diabetic rats gained 9.6 ± 2.0 g during the same period. 2. During aureomycin administration the animals consumed more food and had increased glycosuria and diuresis.

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The aureomycin was kindly supplied by the Lederle Co.

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Effect of Oral Thyroxine and Tri-Iodo-Thyronine on Radioactive Iodine Uptake and Serum Protein Bound Iodine in Normal Human Subjects. (20262)

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Studies of synthetic sodium-levo-thyroxine have shown that, as oral medication in dosage of about 0.5 mg or less daily, it is calorigenic and clinically active(1). In similar dosage it has been shown to reduce the uptake of radioactive iodine(2). Tri-iodo-thyronine, recently identified, synthesized, and demonstrated in human serum(3), also has been shown to be clinically effective(4), and to be several times as potent as thyroxine.

This report is on the effect of these medications, given orally, on the 24-hour uptake of a 5 microcurie tracer dose of radioactive iodine* before and at the end of a week of oral medication. The serum protein bound iodine was also determined.

Procedure. The subjects were normal volunteers at their usual activities as medical students or laboratory workers. Blood was drawn for serum protein bound iodine determinations and about 5 microcuries of carrier free radioactive iodine were given; 24 hours later, the accumulation in the thyroid gland was counted and compared with a dummy. The subjects were then provided with sodium-levo-thyroxine tablets,† in dosages from 0.025 mg to 0.5 mg to take once a day by mouth for a week. On the sixth and seventh days of the week, blood was drawn for serum protein bound iodine and the 24-hour tracer study again was repeated, after a

* Radioactive iodine received from Atomic Energy Commission, Oak Ridge.

† Generously provided by Dr. Robert P. Herwick of Baxter Laboratories, Morton Grove, Ill., by whom these studies were in part supported.

TABLE I. Effect of Oral Medication with Sodium-Levo-Thyroxine Given Once a Day for 7 Days to 17 Normal Subjects. A) before starting treatment; B) 6th day on treatment; C) 7th day after treatment discontinued; A') uptake before treatment; B') uptake on 7th day of treatment.

Dose, mg	Protein bound iodine, γ %			Cholesterol, mg %			I^{131} uptake, %	
	A	B	C	A	B	C	A'	B'
.025	5.2	5.0	5.0	400	318		16.7	26.0
	5.9	5.5	5.2	318	239	200	14.9	13.0
	4.9	5.7	4.2	284	326	207	30.1	28.5
	5.5	6.4		209	193		18.0	11.9
	4.8	5.7			230		21.0	29.6
.075	4.6	5.2		318	324		15.0	9.5
	3.8	4.3		253	235		27.0	9.4
.100	5.1	5.5	5.8	300	284	277	13.9	13.0
	5.5	6.0	5.3	270	290	308	31.6	22.6
	6.2	6.0	5.6	260	146	222	24.7	17.4
	5.7	5.4	4.5	230	264	276	27.0	4.0
	4.9	4.6		179	206		18.8	12.0
.200	4.6	7.1					28.0	20.7
.500	5.3	7.8					28.0	17.8
	4.9	11.0					25.0	15.3
	6.0	6.9					23.0	9.9
	4.3	6.8					26.0	12.6

background count and suitable adjustment of the tracer dose. A similar protocol was followed with tri-iodo-thyronine.‡ The tablets of this medication contained 0.035 mg. Studies were made at 6 levels of medication from 0.008 mg to 0.140 mg. It is important for future comparisons to note that the blood was drawn and the tracer given and counted within a few hours after ingestion of the medication.

Results. Depression of the uptake of the second tracer dose was found with both medications as was to be expected. The effect of the smallest doses of tri-iodo-thyronine was greater than expected. This will require further titration of the lower dose ranges of both substances to approximate the comparative effectiveness in regard to this particular action of the thyroid hormone. It seems that tri-iodo-thyronine is about ten times as active as sodium-levo-thyroxine in this respect.

With the larger dosage of thyroxine, the serum protein bound iodine rose and on the effective small dosages of tri-iodo-thyronine it fell. (Tables I and II).

Comment. The depression of thyroid gland function as measured by radioactive iodine uptake indicated in this study may be due to an action of the medication in the gland itself, as occurs in antithyroid drug therapy, or it may be due to reduction in pituitary secretion of TSH. The latter site of action conforms to the theory that thyroid function is controlled by the level of thyroid hormone in the pituitary. The present work with tri-iodo-thyronine suggests that a fall in secretion of TSH was associated with a reduction in circulating protein bound iodine. The physiological paradox of reduced circulating thyroid hormone (PBI) during administration of thyroid hormone, *i.e.*, tri-iodo-thyronine, and apparent increase of thyroid hormone action, *i.e.*, depression of uptake, is accounted for by the high biological activity of the small quantities of iodine compound involved. Whether the action of tri-iodo-thyronine is on the tissues (elevation of basal metabolic rate), on the hypothalamus, on the anterior pituitary, or on the thyroid gland itself remains to be determined.

Summary. Sodium-levo-thyroxine in dosage of 0.075 mg, orally, usually reduced radioactive iodine uptake by the thyroid of normal human subjects; this was associated with a rise of protein bound iodine when a dosage of 0.2 mg or more was given. Tri-iodo-thyronine

‡ Generously provided by Dr. Arthur Heming of Smith, Kline, and French Laboratories, by whom these studies were in part supported.

TABLE II. Effect of Oral Medication with Tri-Iodo-Thyronine Given Once a Day for 7 Days to 25 Normal Subjects. A) before starting treatment; B) 6th day on treatment; C) 7th day after treatment discontinued; A') uptake before treatment; B') uptake on 7th day of treatment.

Dose, mg	Protein bound iodine, γ %			Cholesterol, mg %			I^{131} uptake, %	
	A	B	C	A	B	C	A'	B'
.008	4.6	3.9					18.8	2.7
	6.5	4.7					31.2	5.7
	4.8	3.5					31.6	5.9
	4.2	3.0					40.2	15.9
	3.6	2.9					18.8	6.2
.0175	4.7	4.3	5.7	276	276	295	22.0	13.3
	5.4	4.4	4.4	165	146	177	26.9	15.7
	5.0	4.0		259	227		21.0	2.3
	5.1	4.4	3.9	192	162	200	14.5	7.0
	5.0	4.1	3.8	565	543	520	21.3	4.6
	4.0	4.0	6.5	317	295	350	16.0	4.3
.035	4.2	4.2	6.4	234	212	235	17.0	2.7
	4.6	3.4	4.9	213	162	259	23.0	5.0
	5.4	2.7		260	343		20.0	10.0
.070	5.7	5.2		256	262		28.0	3.1
	3.8	5.0	3.8	244	192		20.0	5.0
	5.0	3.0	4.2	200	204	238	18.0	4.0
.105	4.0	4.9		312	294		13.0	6.7
	4.0	3.9	3.5	272	192	273	32.0	8.9
	4.4	2.9	4.3	192	227	224	13.0	2.0
.140	5.8	4.7		235	194		18.9	6.5
	6.4	4.9	5.1	214	322	228	19.4	6.5
	5.3	5.7	4.6	255	208	277	30.0	5.4
	4.6	5.1		200	208		14.0	8.6
	3.2			255			19.0	4.3

in dosage as low as 0.008 mg orally also reduces the uptake. This is associated with a decrease in serum protein bound iodine.

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Effect of Piromen on Survival of Irradiated Mice.* (20263)

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Piromen‡ stimulates a leukocytic response very similar to that produced by treatment with ACTH(1-3). The mechanism of Piromen stimulation is unknown, but it is believed that the drug affects directly or indirectly the adrenal cortex(4). There is evidence, how-

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‡ Trade name for a sterile non-protein, non-anaphylactogenic bacterial pyrogen. Furnished through the courtesy of Dr. William F. Windle, Baxter Laboratories, Morton Groves, Ill.