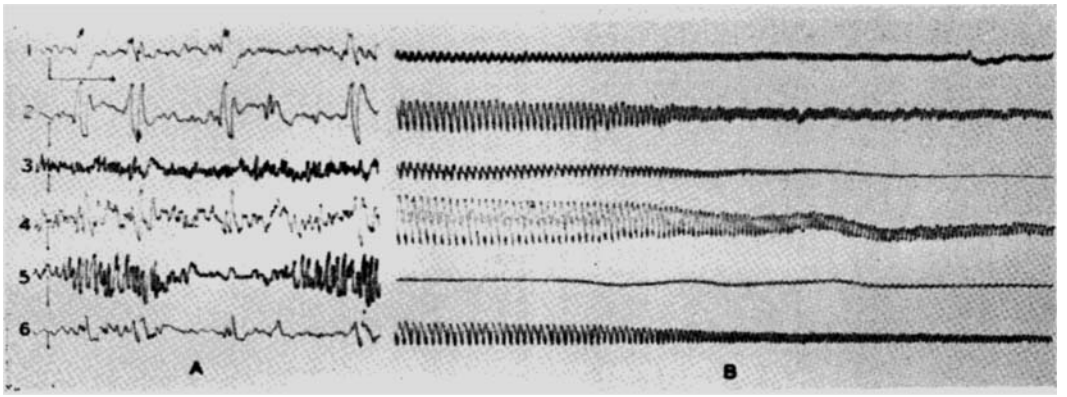

FIG. 1.

Dial cat. Right hypothalamus injected with 0.03 mg strychnine. A, control; B, during asphyxia, immediately after normal and convulsive potentials had been abolished. Note asynchrony in control and synchronous discharge in asphyxia.

1. Left ventrolateral thalamus (monopolar).
2. Right hypothalamus (monopolar) injected with strychnine.
3. Left motor cortex (bipolar).
4. Same site, monopolar.
5. Left auditory cortex (bipolar).
6. Same site, monopolar.

Calibration 100 microvolts and 1 second.

mic nuclei[2,4] do not act as pacemakers of cortical activity as long as the excitability of the cortex is unchanged.

2. In conditions such as asphyxia and anoxia which lead to a relative predominance of hypothalamic excitability the discharge of these subcortical nuclei determines the qualitative and quantitative activity in thalamus and cortex and leads to periods of complete synchrony of hypothalamic, thalamic and cortical activity.

[4] Gellhorn, E., and Ballin, H. M., *Am. J. Physiol.*, 1946, **146**, 630.

16841

Relation of Iodinated β-amylose (Tridine) to Some Thyroid Functions.

J. R. JAENIKE* AND E. S. NASSET.

From the Department of Physiology and Vital Economics, School of Medicine and Dentistry, University of Rochester.

The appearance of iodinated β-amylose, "Tridine",† a compound of carbohydrate and iodine, suggested a biological assay to determine whether it behaves like an inorganic salt of iodine or like other iodinated organic compounds such as thyroxin or thyroglobulin.

Methods. White albino rats were used throughout the experiment. All animals received ground dog biscuit‡ and water *ad libitum* for 5 to 7 days before any experiment was begun. During the experimental period the control group remained on this diet while

* At present interne in Medicine, Strong Memorial Hospital, Rochester, N. Y.

† According to the manufacturer, The Clairmint Chemical Co., 7 Lackawanna Avenue, Newark 2, N. J. "Tridine" is iodinated β-amylose and contains approximately 20% of iodine by weight. The Clairmint Chemical Co., defrayed part of the expense of this investigation.

‡ Purina Laboratory Chow.

TABLE I.
Effects of Tridine and Thyroxine on Thiouracil-induced Hypothyroidism.

	Organ wt per 100 g body wt					Metabolic rate*	
	Pituitary mg	Thyroid mg	Adrenals mg	Kidneys g	Liver g	0 days	10 days
Group 1 (6)† Control	5.4 ±0.37	9.0 ±0.73	30.3 ±1.22	0.68 ±0.019	4.0 ±0.16	77.0	81.0 + 4.2%
Group 2 (6) 0.1% Thiouracil	6.3 ±0.33	15.9 ±0.51	26.0 ±1.14	0.75 ±0.023	5.2 ±0.25	82.6	67.0 —18.9%
Group 3 (6) 0.1% Thiouracil + 3% Tridine	6.5 ±0.36	13.2 ±0.73	26.5 ±0.73	0.77 ±0.080	4.1 ±0.26	76.8	64.2 —16.4%
Group 4 (6) 0.1% Thiouracil + Thyroxine	6.2 ±0.15	9.9 ±0.66	28.1 ±1.77	—0.74 ±0.016	3.7 ±0.14	—	79.3

* Calories/24 hr/kg¾.
† No. of animals.

the other groups received their medication in addition as a dietary supplement. The food intake was recorded and the animals were weighed every other day. The animal room temperature was maintained at 27° ±1°C.

At the beginning and termination of each experimental period the resting, fasting (24 hr) metabolic rates were determined by the use of a modified Haldane apparatus.[1] By the use of the preliminary fast and an alternate carbon dioxide absorbing jar which was switched on only when the rats were inactive it was possible to approximate the basal metabolic rate. The metabolic rates were calculated as calories per 24 hours per kilogram to the three-fourths power.

At the end of each experimental period, the animals were sacrificed and the pituitary, thyroids, adrenals, liver, and kidneys weighed and computed as weight of organ per hundred grams of body weight. Histological sections were taken when indicated and stained with hematoxylin and eosin.

Results. The mean results with their standard errors are given in the tables. Any change that could occur by chance in only 5% or less of the trials is considered significant.

Experiment I. Twenty-four adult (150 g) female rats were used in this series. After a preliminary period of 7 days, the metabolic rates were determined and medication begun. For this purpose they were divided into 4 groups of 6 animals each. Group 1 served as controls, Group 2 received 0.1% thiouracil in the food, Group 3 received 3% tridine and 0.1%thiouracil in the food, and Group 4 received 0.1% thiouracil in the food and 0.02 mg of *l*-thyroxine injected subcutaneously every other day. After 10 days a final metabolic rate determination was made and the animals sacrificed, the organs weighed, and histological sections taken of the thyroid and kidney of all animals. The data are assembled in Table I. Histologically, all the animals showed normal renal tissue. Group 1 showed normal thyroid tissue. Group 2 showed changes in the thyroid typical of thiouracil medication, namely, nearly complete disappearance of the colloid substance together with marked hyperplasia of the epithelial cells with a change from the cuboidal to the high columnar form. In Group 3 this picture was modified so that colloid was present and more abundant than in the previous group, but it was still subnormal in amount. There was also less evidence of epithelial hyperplasia, but it was present to a slight degree. Group 4 showed thyroid sections which were identical with the control group.

Tridine had no significant effect on the lowered metabolic rate of thiouracil-treated

[1] Anderson, J. T., and Nasset, E. S., *J. Nutrition*, 1948, **36**, 703.

TABLE II.
Effect of Tridine on Thyroxine-treated Adult Rats.

	Organ wt per 100 g body wt					Metabolic rate*	
	Pituitary mg	Thyroid mg	Adrenals mg	Kidneys g	Liver g	0 days	10 days
Group 5 (6)† Thyroxine	7.7 ±0.54	9.1 ±0.51	29.6 ±1.23	0.82 ± .014	4.2 ±0.11	79.8	91.5 +14.7%
Group 6 (6) Thyrox. + 1% Tridine	7.1 ±0.42	9.3 ±0.78	31.5 ±1.67	0.94 ±.030	4.5 ±0.11	79.0	90.5 +14.6%
Group 7 (6) Thyrox. + 3% Tridine	6.7 ±0.42	10.8 ±1.61	30.1 ±3.39	0.92 ±0.040	4.5 ±0.28	76.5	83.8 + 9.5%
Group 8 (6) Thyrox. + 5% Tridine	7.5 ±0.19	10.8 ±0.30	32.8 ±3.65	0.95 ±0.074	5.3 ±0.66	77.0	86.1 +11.8%

* Calories/24 hr/kg¾.
† No. of animals.
All rats received 0.02 mg thyroxine subcutaneously every other day.

rats. (The standard error of the metabolic rate determination is about 2.5% of the total value). The thyroid glands of Group 3 were significantly smaller than those in Group 2 (thiouracil alone) but it will be shown later that this is not a specific effect of tridine.

Experiment II. Twenty-four adult (190 g) female rats were divided into 4 groups of 6 rats each and after an acclimatization period of 5 days, metabolic rates were determined and medication begun. All received 0.02 mg of thyroxine subcutaneously every other day. Group 5 received stock diet alone, while Group 6 received 1% tridine, Group 7 received 3% tridine, and Group 8 received 5% tridine, all mixed with the stock diet. After 10 days another metabolic rate determination was made, the animals sacrificed, and organ weights recorded. No histological sections were taken. Results are set out in Table II.

This experiment was designed to test the possible effect of feeding tridine (1, 3 and 5% of the diet) on hyperthyroidism produced by injection of thyroxine. The only significant change in all of these observations was an increase in the size of the thyroids of Group 8. All of the other organs as well as the energy metabolism were not significantly altered by tridine treatment. It is evident, therefore, that tridine in the dosages employed does not exhibit any marked antagonism to thyroxin.

Experiment III. It was of some interest to determine what influence the feeding of tridine might have on the growth of young animals. Twenty rats of both sexes about 4 weeks old were divided into 4 groups of 5 rats each and after a preliminary period of 5 days, the metabolic rates were determined and the animals started on the medication. Group 9 received stock diet, Group 10 received 1% tridine, Group II received 3% tridine and Group 12 received 5% tridine, all mixed with stock diet. After 18 days, the metabolic rates were again determined, the animals sacrificed, organ weights recorded, and histological sections of the thyroid gland taken. Table III shows the organ weights and the metabolic rates. Table IV shows weight gains, food consumption and efficiency of food utilization. There were no fatalities in any of the groups.

Histologically, the thyroid glands showed little deviation from the normal. There was slightly more colloid material present in those rats receiving 3% and 5% tridine than in the control and the 1% tridine group. There was, however, no evidence of epithelial hyperplasia. It is evident from Table III that the thyroid in Group 10 was significantly larger than the control (Group 9). The adrenal glands and the liver were significant-

TABLE III.
Tridine as a Dietary Supplement for Young Rats.

	Organ wt per 100 g body wt					Metabolic rate*	
	Pituitary mg	Thyroid mg	Adrenals mg	Kidneys g	Liver g	0 days	18 days
Group 9 (5)† Control	4.7 ±0.11	8.5 ±0.81	20.0 ±0.50	0.93 ±.028	6.2 ±0.11	98.0	88.6 — 9.6%
Group 10 (5) 1% Tridine	5.1 ±0.49	12.3 ±0.67	22.2 ±0.69	0.94 ± .032	6.7 ±0.19	99.5	88.1 —11.5%
Group 11 (5) 3% Tridine	4.6 ±0.24	9.9 ±0.96	23.8 ±0.47	0.97 ±.021	7.3 ±0.23	100.0	89.9 —10.1%
Group 12 (5) 5% Tridine	5.6 ±0.71	10.0 ±1.58	29.4 ±4.75	1.05 ±.104	6.7 ±0.71	99.0	80.3 —19.0%

* Calories/24 hr/kg¾.
† No. of animals.

TABLE IV.
Food Utilization in Young Rats as Affected by Tridine Supplement in the Diet.

	Avg wt		Avg gain g	Avg food intake g	G food eaten per g wt gained
	0 days g	16 days g			
Group 9 Control	56.0	136.4	80.4	200.9	2.5
Group 10 1% Tridine	53.6	118.4	64.8	172.4	2.7
Group 11 3% Tridine	50.8	104.6	53.8	147.6	2.7
Group 12 5% Tridine	50.8	76.4	25.6	112.9	4.5

ly larger in Groups 10 and 11. The energy metabolism was depressed significantly in Group 12 as compared with the other groups which exhibited only the normal decline in metabolic rate associated with maturation. Table IV shows that with all dosages of tridine there was a loss of appetite and a corresponding failure to gain weight. In Group 12 weight gained per gram of food eaten was very low and taken together with the depressed metabolism may be regarded as a sign of toxicity with possible impaired digestion and absorption of food. There was slight but inconclusive histological evidence of increased colloid production induced by tridine. There was, however, no increase in the metabolic rate to corroborate this finding. The maximum tridine intake was approximately 5.5 g per kilo per day.

Experiment IV. Ten young (125 g) rats were used, 4 males and 6 females, equally divided into the 2 groups of 5. After a preliminary period of 5 days, metabolic rates were determined and medication was begun. Both groups received 0.1% thiouracil in the stock diet and in addition Group 13 received 3% tridine and Group 14 received 0.77% potassium iodide in the diet. These percentages represent equivalent amounts of iodine. After ten days a final metabolic rate was determined, the animals sacrificed, their organs weighed, and histological sections made of the thyroid glands. Results are recorded in Table V. Histological sections showed a modified thiouracil effect in both cases, the picture being similar to that of Group 3 in Experiment 1. In both groups there was a partial reversal of the thiouracil effect. There are no signifi-

TABLE V.
Comparison of Equivalent Amounts of Tridine and KI in Thiouracil-treated Rats.

	Organ wt per 100 g body wt					Metabolic rate*	
	Pituitary mg	Thyroid mg	Adrenals mg	Kidneys g	Liver g	0 days	10 days
Group 13 (5)†	5.4 ±0.32	13.7 ±1.13	18.8 ±2.55	0.99 ± .062	5.7 ±0.33	86.3	73.5 —14.8%
Group 14 (5)	5.7 ±0.73	12.5 ±1.78	18.9 ±2.57	0.86 ± .032	4.9 ±0.26	79.6	72.4 —10.0%

Group 13—0.1% Thiouracil in diet + 3% Tridine.
Group 14—0.1% Thiouracil in diet + 0.77% KI (≏ 3% Tridine in I).
* Calories/24 hr/kg¾.
† No. of animals.

cant differences between these groups in organ weights, energy metabolism or histological appearance of the thyroid gland. It is concluded that tridine exerts no unique effect which cannot be accounted for on the basis of its iodine content.

Discussion. It is evident from the results that tridine, in the animal body, behaves like an equivalent amount of inorganic iodine. Like KI,[2] tridine is capable of preventing partially the thyroid hyperplasia which accompanies thiouracil feeding. The low metabolic rate of thiouracil-treated rats is unaffected by feeding tridine as 3% of the diet. Moderate hyperthyroidism produced by the administration of thyroxin does not seem to be influenced significantly by the addition of tridine as a dietary supplement in concentrations of 1, 3 and 5%. From the fact that tridine is approximately equivalent, on the basis of iodine content, to KI in thiouracil-treated rats it may be concluded that the new compound is readily absorbed but it is not known whether it is hydrolyzed before absorption. Since starch is so readily digested it seems likely that β-amylose, a derivative of starch, should also be split to simpler units. It would be interesting to know whether ionic iodine is released in the lumen of the small intestine.

The deleterious effect of feeding tridine to growing rats is evidently closely related to an impaired appetite. The ingestion of tridine prevented maximal gains in weight. When the diet contained 5% of tridine the gain in weight was less than one-third of the control value and the food was very poorly utilized. It would be interesting to know whether this was due to non-absorption or to excessive waste after the foodstuffs had reached the blood stream.

Summary. 1. Iodinated β-amylose, tridine, prevents partially the thyroid hyperplasia caused by thiouracil. In this respect it acts like potassium iodide. Tridine, except in toxic concentrations has no effect on the metabolic rate.

2. In rats receiving thyroxin, tridine, in dosages of 1, 3 and 5% of the diet, has no significant effect on either the size of the organs or the metabolic rate.

3. In young rats all dosages of tridine (1, 3 and 5%) are deleterious with respect to consumption of food and gain in body weight.

4. In thiouracil-treated rats 3% tridine is indistinguishable in its effects from an equivalent (0.77%) amount of KI.

5. The data from the present series of experiments on 78 rats suggest that tridine when administered by mouth exerts its effect by virtue of its iodine content and when given in equivalent amounts cannot be distinguished from KI.

[2] Sadhu, D. P., *Am. J. Physiol.*, 1948, **152**, 150.