tides. Because of the nature of the precursor it is thought that most of the radioactivity was in the pyrimidine ring rather than in the carbons of the sugar.

The radioactivity data obtained from the resin are thought to be better than those from the paper because there was considerable residue after evaporating solutions from the paper with resulting self absorption. A negligible amount of residue was left after evaporating solutions from the resin.

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Effects of Vitamin B_{12} on Thiouracil Action in Rats.*† (18142)

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Vit. B_{12} has been demonstrated to counteract the deleterious actions of several substances administered in toxic quantities to rats. Thus, it has been shown to overcome the retardation of growth which follows administration of toxic amounts of thyroid powder or thyroprotein(1-4), diethylstilbestrol(4) and lactose(5). In addition, Popper *et al.*(6) have reported that vitamin B_{12} can prevent the acute hepatic injury which results from administering carbon tetrachloride to rats.

Thiouracil has been shown to cause a direct depression of thyroid hormone synthesis, thereby stimulating increased production of thyrotrophic hormone by the anterior pituitary with subsequent thyroid hypertrophy (7-8). The inhibition of thyroid function usually results in reductions in growth rate and food intake, although these may also be mediated in part through non-thyroid mechanisms(9). Would vit. B_{12} counteract any of these actions of thiouracil?

Procedure. Immature female rats of the Carworth strain, divided into 8 uniform groups of 10 each, were fed the following basal ration for 30 days: yellow corn meal, 35%; ground wheat, 25%; linseed oil meal, 10%; whole milk powder, 20%; alfalfa leaf meal, 6%; brewers yeast, 3%; and table salt, 1%. The following substances were added to the basal ration of each group of rats: 1, controls; 2, 40 μg of vit. B_{12}§ per kg; 3, 80 μg vit. B_{12} per kg; 4, 0.1% thiouracil; 5, 0.1% thiouracil and 40 μg vit. B_{12} per kg; 6, 0.1% thiouracil and 80 μg of vit. B_{12} per kg; 7, 0.1% thiouracil, and 40 μg of vit. B_{12} per kg during last 10 of 30 days; 8, 0.1% thiouracil, and 80 μg of vit. B_{12} per kg during last 10 of 30 days. Four hours prior to sacrifice, each rat was injected intraperitoneally with a tracer dose of radio-

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§ Crystalline vitamin B_{12} in the form of a triturate of NaCl was kindly furnished by Dr. D. F. Green of the Veterinary Division, Merck and Co., Inc., Rahway, N. J.

TABLE I. Effects of Vitamin B_{12} on Thiouracil Action in Rats.

Group	Treatment	Avg body wt		Avg daily food intake per rat, g	Avg thyroid wt		Radioactivity—avg counts per sec.		
		Orig., g	Final, g		Actual, mg	Per 100 g body wt, mg	Per thyroid	Per mg thyroid	Per 100 g body wt
1	Controls	60.3	135.2	9.2	12.5	9.3 ± 1.4*	25.2 ± 3.8*	2.1 ± .6*	18.9 ± 3.5*
2	40 μg B_{12}	60.4	147.7	9.7	12.2	8.3 ± 1.7	26.8 ± 6.7	2.3 ± .7	18.2 ± 5.0
3	80 μg B_{12}	60.7	153.8	10.1	14.5	9.4 ± 1.3	28.4 ± 7.8	2.0 ± .5	18.8 ± 5.8
4	Thiouracil	61.1	102.7	7.0	51.6	50.3 ± 10.5	3.4 ± 1.1	.07 ± .03	3.4 ± 1.2
5	Thiouracil + 40 μg B_{12}	60.1	136.6	8.8	13.6	10.1 ± 3.9	.3 ± .1	.03 ± .02	.2 ± .1
6	Thiouracil + 80 μg B_{12}	60.8	144.5	9.4	35.8	24.9 ± 5.4	.5 ± .2	.01 ± .00	.4 ± .2
7	Thiouracil + 40 μg B_{12} last 10 days	61.4	105.9	—	51.7	49.3 ± 12.7	3.3 ± 1.3	.08 ± .01	3.2 ± 1.3
8	Thiouracil + 80 μg B_{12} last 10 days	60.4	115.8	—	42.8	36.8 ± 5.8	1.4 ± .9	.03 ± .01	1.2 ± .7

* Standard error of mean $= \sqrt{\frac{\Sigma d^2}{n(n-1)}}$

active iodine (I^{131}) estimated to contain 0.2 μc of radioactivity. The thyroids were weighed, dried and counted separately under a thin end window counter. All rats were housed in a constant temperature animal room at 75° F.

Results. The data on body growth, food intake and thyroid activity are summarized in Table I. The addition of 40 (Group 2) or 80 μg of vitamin B_{12} (Group 3) to the ration increased body growth and food intake above that in the control rats (Group 1), but thyroid weight and thyroid uptake of I^{131} were the same in all 3 groups. Thiouracil (Group 4) drastically reduced body growth, food intake and thyroid concentration of I^{131}, while thyroid weight was approximately five times that of the controls.

When vit. B_{12} was fed in amounts of 40 (Group 5) or 80 μg (Group 6) to the thiouracil-treated rats, the inhibitory effects of the drug on body growth were completely overcome throughout the 30-day period. Body growth in group 6 was even greater than in the controls, and food intake was increased in both groups. The ability of thiouracil indirectly to induce thyroid hypertrophy was completely or partially prevented by the vitamin, although thyroid uptake of I^{131} was even less than in the controls. When 80 (Group 8) but not 40 μg of vitamin B_{12} (Group 7) was added to the thiouracil ration during the last 10 of the 30-day experimental period, the inhibitory effect of the drug on body growth was partially overcome. Unfortunately, the food-intake data for these 2 groups were not available. While 80 μg of vit. B_{12} partially counteracted the ability of thiouracil to increase thyroid weight, the concentration of I^{131} by the thyroids was not increased.

Discussion. The data presented here indicate that vit. B_{12} can completely overcome the growth-retarding action of thiouracil in female rats. This can be explained partially, if not completely, by the ability of vit. B_{12} to increase food consumption in the thiouracil-treated rats. It should be recognized that since the thiouracil was incorporated into the ration, more of the drug was consumed by these vitamin-supplemented rats than by those which received thiouracil only. It is difficult to understand why vit. B_{12} should make thiouracil less effective in increasing thyroid weight but more effective in inhibiting uptake of I^{131} by the thyroid. If the vitamin increased the normal metabolism or excretion of thiouracil in the body, then the lessened ability of thiouracil to induce thyroid hypertrophy could be explained. On the other

hand, since vit. B_{12} increased the total thiouracil intake, it would appear logical to expect a greater thyroid inhibition than in the rats which received thiouracil without the vitamin. This would account for the lower concentration of I^{131} in the thyroids of the former as compared to the latter rats. On the whole, it seems reasonable to assume that thyroid uptake of a tracer dose of I^{131} is a better index of thyroid activity than thyroid weight. The former is believed to reflect direct thyroid secretory ability, whereas the latter reflects an indirect action on the thyroid by pituitary thyrotrophic hormone and does not definitely indicate either increased or decreased thyroid function.

It is interesting to consider whether vit. B_{12} can induce normal body growth in hypothyroid rats, as suggested by this study. Thus, vit. B_{12} completely counteracted the growth-retarding action of thiouracil, while the latter was still able to depress thyroid activity. It is possible that vit. B_{12} does not require the mediation of the thyroid to exert its anabolic effects on growth.

Summary. The effects of crystalline vit. B_{12} on thiouracil action was determined in immature female rats for a 30-day period. The vitamin completely counteracted the growth-inhibiting action of thiouracil, and this was accompanied by a considerable increase in food consumption. Although vit. B_{12} decreased the thyroid hypertrophy induced by thiouracil, the uptake of radioactive iodine (I^{131}) by the thyroids was even less than in the rats which received thiouracil only. It is suggested that vit. B_{12} may be able to induce normal growth in hypothyroid rats.

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Effects of Vitamin B_{12} on Normal Thyroid Function in Rats.*† (18143)

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Vitamin B_{12} can counteract the retardation of growth in young rats which results from administering toxic amounts of thyroid powder or thyroprotein(1-4). The mechanism by which vitamin B_{12} achieves this effect has not been explained, although Monroe and Turner(5) presented data indicating that the vitamin increases the catabolism of administered thyroxine in chicks. If this is so, then vitamin B_{12} may also favor the catabolism of endogenous thyroid hormone, in which case pituitary thyrotrophic hormone secretion would be stimulated with a subsequent increase in thyroid secretion rate. It was considered of interest therefore, to determine whether or not the administration of vitamin B_{12} would alter normal thyroid function in immature rats.

Procedure. Young male and female rats of the Carworth strain were placed on experiment for 20 and 30 days respectively. With the exception of 2 groups, all rats were fed the following basal ration: yellow corn meal, 35%; ground wheat, 25%; linseed oil meal, 10%; whole milk powder, 20%; alfalfa leaf meal, 6%; brewers yeast, 3%; and table salt,

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