carried out as in the previous experiment except that the hourly insulin was given I.V. and the experiment continued for 15 hours. At the end of this time the control had required 22.2 g sugar, the amino acid rabbit 11.4 g, a difference of 10.8 g glucose compared to 2.5 g amino acids injected.

There can be no question of the action of this preparation of amino acids on the glucose utilization rates of hypophysectomized, and of insulin-injected rabbits. We are continuing our work in the attempt to determine what constituents are responsible for this action. Jacobs[5] found that cysteine diminishes the hypoglycemic action of insulin and believes this to be due to a specific action of the sulphydryl group. Our results could hardly be explained on this basis since the mixture we used contained no cysteine and very little cystine (0.3 to 0.5% of the total amino acid content).

Summary. A mixture of amino acids when injected intravenously into rabbits with high glucose utilization rates (from hypophysectomy, and from insulin) markedly reduced this glucose requirement.

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Effect of Vitamin B_1 and Vitamin B_2 Complex on the Loss of Weight Produced in Rats by Experimental Hyperthyroidism.

VICTOR A. DRILL. (Introduced by Ralph H. Cheney.)

From the Department of Biology, Long Island University, Brooklyn, New York.

Himwich, Goldfarb and Cowgill[1] reported that an increased amount of undifferentiated vitamin B_1 is needed during experimental hyperthyroidism, and Sure and Buchanan[2] found that vitamin B_1 has an antithyrogenic action. Later Drill[3] found that a large amount of yeast fed to rats receiving thyroxin will prevent a loss of liver glycogen. In this investigation a study was made on the effect of vitamin B_1 and of a yeast concentrate on the loss of weight produced by experimental hyperthyroidism.

Adult rats, weighing about 250 g, were all fed diet No. 8 *ad libitum*. This diet consisted of: salts, 4; cod liver oil, 4; Crisco,

5 Jacobs, H. R., PROC. SOC. EXP. BIOL. AND MED., 1938, **38**, 305.

1 Himwich, H. E., Goldfarb, W., and Cowgill, G. R., *Am. J. Physiol.*, 1932, **99**, 689.

2 Sure, B., and Buchanan, K. S., *J. Nutrition*, 1937, **13**, 513.

3 Drill, V. A., *J. Nutrition*, 1937, **14**, 355.

10; casein, 20; and cornstarch, 62 parts. Dried yeast (200 mg) was fed to each rat per day. This supplied 3.6 international units of vitamin B_1 and 4 Sherman-Borquin units of vitamin G (flavin) per day.

EXP. 1. Female rats were used in this experiment. Normal controls (5 rats), receiving diet No. 8 *ad libitum,* made a constant gain in weight. The thyroid fed controls (5 rats), received diet No. 8 *ad libitum* plus 100 mg of thyroid gland per day. The thyroid-fed controls were used to show that the amount of thyroid gland fed was sufficient to produce a continued loss in the weight of rats receiving a normal diet (No. 8). These rats showed a rapid decline in weight. Twelve test rats were also fed diet No. 8 plus 100 mg of thyroid gland per day for 17 days, during which time they lost an average of 23 g in weight. (See Table I for the average weight change of the rats.) On the seventeenth day a daily injection of 500 gamma of vitamin B_1 was begun in the test rats while they were still receiving thyroid gland. The female hyperthyroid rats injected with vitamin B_1 stopped losing weight, while the thyroid-fed controls, receiving thyroid gland but no injections of vitamin B_1, continued their rapid loss of weght. Although the test rats did not lose any more weight when injected with vitamin B_1, they did not regain any of their lost weight. On the thirtieth day of the experiment 5% of a brewer's yeast concentrate was included in diet No. 8 and fed to the test rats. An immediate gain in weight, as is shown in Table I, was then made. The rats continued to gain weight, while still receiving thyroid gland, up to the eighty-first day, at which time they were dissected for tissue studies. This experiment shows that vitamin B_1 and yeast concentrate, a rich source of the vitamin B_2 complex, enabled the test rats to regain their lost weight while thyroid gland was being fed. Vitamin B_1 alone did not enable the test rats to regain their lost weight.

EXP. 2. Male rats were used in this experiment. The diets, dosages, days of feeding and the number of rats were the *same* as in Experiment 1. As will be seen from Table I, the normal controls gained in weight, the thyroid-fed controls lost weight, and the test rats also lost weight and did not regain their lost weight when treated with vitamin B_1 and a yeast concentrate. Thus, a sex difference in response is present. The vitamin B_1 and yeast concentrate treatment enabled the female hyperthyroid rats to regain the amount of weight lost, while they were still receiving thyroid gland, whereas the male rats on the same dosage of thyroid gland did not recover their lost weight when treated.

TABLE I.
Average Gain or Loss of Weight of the Rats in Grams.

Days of Exp.	Experiment 1			Experiment 2			Days of Exp.	Experiment 3		
	Normal Controls	Thyroid-fed Controls	Test Rats	Normal Controls	Thyroid-fed Controls	Test Rats		Normal Controls	Thyroid-fed Controls	Test Rats
5	— 1g	—25	—21	+ 2	— 19	—20	5	+ 7	—28	—15
12	+ 5	—28	—21	+10	— 22	—25	10	+ 9	—29	—24
16	+10	—22	—20	+14	— 20	—29	14	+10	—34	—36*
17	+ 6	—25	—23*	—	— 30	—29*	17	+19	—38	—31
19	+ 5	—26	—17	+30	— 32	—21	21	+24	—56	—35
23	+ 5	—27	—22	+25	— 50	—24	24	+27	—67	—29
26	+ 5	—41	—21	—	— 74	—26	31	+26	—57	—31
30	+10	—59	—15†	+22	—102	—15†	35	+35	—69	—32
39	+17	—67	—10	+32	—122	—40	38	+37	—82	—31†
45	+22	—74	— 7	+31	—137	—50	42	+37	‡	—24
51	—	—86	— 6	—	‡	—	45	+40		—21
57	+24	‡	— 1	+26		—45	52	+45		—12
60	+33		— 6			‡	56	+44		+ 4
64	+29		— 4				58	+47		+ 6
70	+25		+ 1							
81	+32		+ 4							

*Daily subcutaneous injections of 500 gamma of vitamin B_1 begun.
†5% yeast concentrate added to diet No. 8 and fed to test rats in addition to the daily injection of 500 gamma of vitamin B_1.
‡The remaining rats were chloroformed and dissected.

EXP. 3. Male rats were used in this experiment. The same number of rats were used in each group as in Experiment 1. In this experiment the rats were fed 50 mg of thyroid gland per day, which is one-half of the former dosage. As will be seen from Table I, the normal controls, receiving only diet No. 8, gained in weight. The thyroid-fed controls, fed diet No. 8 plus 50 mg of thyroid gland per day, rapidly lost weight. The test rats also received diet No. 8 plus 50 mg of thyroid gland per day. These rats also lost weight. On the fourteenth day of thyroid feeding the daily injection of 500 gamma of vitamin B_1 was begun in the test rats. The injected rats stopped losing weight, but did not regain any of their lost weight until, as in Experiment 1, 5% of a brewer's yeast concentrate was included in diet No. 8 and fed to the test rats. The yeast concentrate was given to the test rats on the thirty-eighth day of the experiment, and a constant gain in weight was then made. Thus, male rats, which would not respond to vitamin B_1 and yeast concentrate treatment when receiving 100 mg of thyroid gland per day, responded when the dosage of thyroid gland was 50 mg per day.

When hyperthyroid rats are restricted to 12 g of food per day, they do not stop losing weight when vitamin B_1 is injected, even though there is no subnormal amount of vitamin B_1 in the tissues.[4] Thus caloric intake is an important factor in studying the gain of weight during experimental hyperthyroidism. This will be discussed at length elsewhere.

Conclusions. 1. Hyperthyroid rats which had lost weight and were still receiving thyroid gland regained their lost weight when *both* vitamin B_1 and the vitamin B_2 complex were administered. 2. A sex difference in response is present.

[4] Drill, V. A., *Am. J. Physiol.*, 1938, **122**, 486.