Lack of Influence of Vitamin B_{12} on Protein Catabolic Action of Cortisone.* (20025)

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The influence of vit. B_{12} on growth and N balance has been the subject of a number of studies. The growth of rats is enhanced by treatment with vit. B_{12} if the animals have free access to food(1). The fact that in rats fed a constant diet, vit. B_{12} fails to influence weight gain or N retention, suggests that the growth-enhancing effect in *ad lib.* fed animals is due to increased food intake and not to changes in the utilization and metabolism of foodstuffs(2). Similarly, in partially starved rats treatment with vit. B_{12} has no effect upon weight loss or N excretion(3). In *ad lib.* fed rats treatment with vit. B_{12} diminishes or prevents the growth retardation and weight loss caused by administration of thyroid hormone(4,5). If the food intake is kept constant, weight loss induced by thyroxine is not influenced by vit. B_{12}; however, under these conditions a significant improvement of N retention is found in spite of the uninfluenced weight loss(2). The growth retarding effect of cortisone is ameliorated by vit. B_{12} in *ad lib.* fed animals(6,7). In view of the fact that vit. B_{12} was found to decrease the N loss in thyroxine treated force fed rats, it was considered of interest to determine whether the vitamin would exert a similar effect upon N loss induced by cortisone.

Methods. Male rats, descendants of the Wistar strain, weighing between 180 and 250 g were used. All animals were tube fed a mixed diet described by Ingle *et al.*(8) twice daily. The animals were gradually adapted to tube feedings, after which they were fed a constant amount during the control and experimental periods. The amount of diet selected for each animal was sufficient to maintain weight or to permit a slight weight gain during the control period. The animals were kept in wire screened, individual metabolism cages in a constant temperature room (22-23°C). The 24-hour urine specimens were analyzed by a micro-Kjeldahl method. The urinary nitrogen excretion and weight of each animal were determined daily for a control period of 9 days, followed by an experimental period of equal length. During the experimental period 9 animals were treated with 3 μg of vit. B_{12} and 2.5 mg of cortisone acetate twice daily; 10 animals received 2.5 mg of cortisone acetate twice daily. All injections were given at the same time each day.

Results. Administration of 5 mg of cortisone daily caused the urinary N excretion to increase by 71 mg over that of the control period (Table I). The increase in the animals receiving 5 mg of cortisone and 6 μg of vit. B_{12} daily, was 64 mg. The difference is minimal, and statistically not significant. Nor did the weight loss of the animals receiving cortisone differ from that of the animals treated with vit. B_{12} in addition to cortisone.

Discussion. The weight loss and the increase in urinary nitrogen excretion induced by cortisone were not influenced by vit. B_{12} when the food intake was constant. This observation differs from that reported by Meites and Ogle(6), who showed that vit. B_{12} decreases, in part, the growth retarding effects of cortisone. The difference of the results of the two experiments is probably due to the different experimental conditions used. In our experiment the food intake was kept constant, and cortisone was administered for a short period, whereas in the experiment of Meites and Ogle the animals had free access to food, and were treated with cortisone for a longer period of time. The appetite as well as the food intake are known to increase in animals treated with vit. B_{12}(6). This appetite stimulating effect of vit. B_{12} might well account for the inhibition of the growth retarding effects of cortisone in *ad lib.* fed animals.

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TABLE I. Effect of Vit. B_{12} on N Excretion of Cortisone Treated Rats Force Fed Constant Rations. N excretion/24 hr.

Treatment (twice daily)	Control period,* mg	Treatment period,* mg	Diff., mg	"p" of diff.	Wt change, g/9 days
Cortisone, 2.5 mg	201	298	+97	.001	−13
	193	265	+72	"	−12
	197	269	+72	"	−19
	203	263	+60	"	−16
	201	277	+76	"	−18
	184	270	+86	"	−17
	181	255	+74	"	− 8
	151	224	+73	"	− 9
	184	238	+54	"	−10
	196	242	+46	"	− 7
Mean	189	260	71		−12.9
Cortisone, 2.5 mg + Vit. B_{12}, .3 mg	204	249	+45	.001	−10
	176	226	+50	"	− 8
	187	220	+33	"	− 8
	186	258	+72	"	−11
	202	280	+78	"	−15
	203	261	+58	"	− 8
	204	282	+78	"	− 8
	205	281	+76	"	−15
	210	292	+82	"	− 8
Mean	197	261	64		− 9

* Mean of 9 days.

Whereas vit. B_{12} does not decrease the nitrogen loss induced by cortisone, the same dose of the vitamin was shown in previous experiments to decrease the nitrogen loss induced by thyroxine(2). The reason for the difference of action of the vitamin on the nitrogen loss induced by cortisone, and by thyroxine respectively, is not known. Possibly the two hormones induce N loss by a different mechanism. The latter is but poorly understood in either instance; it has been suggested that the action of cortisone may be "anti-anabolic" rather than catabolic.

Summary. In rats receiving a constant food intake by tube feeding, the weight loss and N loss induced by cortisone is not improved by treatment with vit. B_{12}. This failure of vit. B_{12} to influence cortisone induced protein catabolism is in contradistinction to the N sparing effect of vit. B_{12} in thyroxine induced protein catabolism.

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