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Niacin Deficiency in Rabbits and Response to Tryptophane and to Niacin.

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Tryptophane has been shown to be effective in curing niacin deficiencies in the rat,¹ the chick,² the mouse,³ and in the dog.⁴

Wooley and Sebrell⁵ showed that growing rabbits fed a purified diet containing 20% casein, required niacin for survival and growth. The only symptom attributed to niacin deficiency was anorexia.

The study reported below concerns the response of niacin-deficient rabbits to tryptophane as compared to niacin.

Experimental. Twenty-four male, New Zealand rabbits, about 3 months of age, in litters of from 2 to 8, and weighing between 1600 and 2000 g each, were placed in metal cages with wire mesh floors. The animals were divided into 4 groups of 6 each, separating the littermates. All of these rabbits were fed purified diet No. 673, previously described.⁵ Assays of the diet showed less than 0.05 μ g of niacin per gram.

After 8 weeks on the basal diet, the experimental animals were treated for 4 weeks as follows:

Group 1. Continued on basal diet.

Group 2. 400 mg *dl*-tryptophane per rabbit per day mixed into the food.

Group 3. 10 mg niacin per kg body weight per rabbit per day mixed into the food.

Group 4. Received both tryptophane and niacin as in Groups 2 and 3.

Two rabbits, one in Group 1 and one in Group 3, died before the study was completed.

The weight of each rabbit and the amount of ration consumed was recorded weekly. Hemoglobin and hematocrit determinations, and total leukocyte and differential counts

were made at the end of the 2 periods of observation.

All of the animals were sacrificed at the end of the experiment. The liver weights were recorded. Portions of the liver and hamstring muscles from each rabbit were analyzed for total nitrogen,* niacin and tryptophane. The niacin was determined by the author's modification of the method of Snell and Wright.⁶ The casein hydrolysate in the medium was increased to 10%, sodium acetate to 2%, and dextrose to 2.5%. The niacin standard curve contained from 0.2 to 2 μ g per tube. The tryptophane was determined by the method described by Wooley and Sebrell.⁷

Results. Weight gains and food consumption are recorded in Table I. Rabbits fed the basal diet ate an average of 250 g per week and lost an average of 90 g during the first 8-week period.

During the next period of 4 weeks, the rabbits that were continued on the basal ration showed a decline in appetite and a more rapid loss of weight. The animals that were fed niacin and those that were given tryptophane gained weight and ate increased amounts of ration at a similar rate. Those that received both showed greater weight gains and increases in food consumption than did the animals that received either of these supplements alone.

Blood changes are summarized in Table II. All of the rabbits were anemic at the end of 8 weeks on the basal ration. Most of them showed low leukocyte and granulocyte counts. At the end of the next 4 weeks, the rabbits

¹ Krehl, W. A., Teply, L. J., Sarma, P. S., and Elvehjem, C. A., *Science*, 1945, **101**, 489.

² Briggs, S. M., *J. Biol. Chem.*, 1945, **161**, 749.

³ Woolley, D. W., *J. Biol. Chem.*, 1946, **162**, 179.

⁴ Hundley, J. M., personal communication.

⁵ Wooley, J. G., and Sebrell, W. H., *J. Nutrition*, 1945, **29**, 191.

⁶ Snell, E. E., and Wright, L. D., *J. Biol. Chem.*, 1941, **139**, 675.

⁷ Wooley, J. G., and Sebrell, W. H., *J. Biol. Chem.*, 1945, **157**, 141.

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TABLE I.
Average Weight and Food Consumption.

No. of rabbits		Original wt	Deficiency period		Treatment period	
			After 8 wk, wt	Avg weekly food consumption	After 4 wk, wt	Avg weekly food consumption
5	Avg	1850	Group 1. No treatment given.			
			1780	248	1630	184
6	"	1760	Group 2. Treated with tryptophane.			
			1660	254	1990	316
5	"	1730	Group 3. Treated with niacin.			
			1600	260	1910	326
6	"	1790	Group 4. Treated with tryptophane and niacin.			
			1730	245	2190	398

TABLE II.
Blood Findings.

No. of rabbits		After 8 wk deficiency period				After 4 wk treatment period			
		Hemo-globin	Hemato-crit	Leuko-cytes	Granulo-cytes	Hemo-globin	Hemato-crit	Leuko-cytes	Granulo-cytes
5	Avg	9.5	27.4	Group 1. No treatment given.					
				8120	1680	8.9	25.8	6410	2230
6	"	9.3	27.3	Group 2. Treated with tryptophane.					
				6270	1725	11.9	37.4	9160	4090
5	"	9.4	28.4	Group 3. Treated with niacin.					
				5330	1790	11.7	34.1	8200	3270
6	"	10.1	29.4	Group 4. Treated with tryptophane and niacin.					
				7810	1540	13.2	38.7	9170	2910

that were continued on the basal diet were found to have still lower hemoglobin, hematocrit, and total leukocyte values. The granulocytes showed some increase, but did not reach the levels of the treated animals. The hemoglobin and hematocrit values, and the total leukocyte and granulocyte counts increased significantly in all of the treated groups.

The livers of the rabbits that were continued on the basal diet weighed less than did the livers of the supplemented animals.

The niacin content of the livers of rabbits fed the basal ration averaged 116 μg per g. This amount was from 43 to 70 μg less than the average amount found in the supplemented animals. The livers of the animals that received both tryptophane and niacin averaged the highest concentration of niacin.

The niacin content of the muscles of the rabbits in the various groups showed a different pattern from that of the livers. The muscles of the unsupplemented animals, and those of the rabbits that were fed tryptophane, showed similar assay values, *viz.* 88 and 93 μg per g. The muscles of the rabbits

that received niacin and those that received both niacin and tryptophane in their diets averaged higher values but they were similar to each other, *viz.* 130 and 128 μg per g, respectively.

The tryptophane and the nitrogen values of the livers and of the muscles of the rabbits in the experimental groups showed very little differences.

Summary. In the study reported above, it is shown that the exclusion of niacin from the ration of rabbits for 8 weeks was accompanied by a reduction of hemoglobin and the cellular components of the blood. After 12 weeks on this ration, there was a reduction of niacin concentration in the livers and the hamstring muscles.

After the animals had been on the niacin-deficient ration for 8 weeks, attempts to cure the deficiency by feeding tryptophane or, and niacin for 4 weeks were made. The addition of 400 mg *dl*-tryptophane per rabbit or 10 mg niacin per kg body weight to the daily ration of the animals was followed by increases in appetites. The responses in weight

TABLE III.
Assay of Livers.

No. of rabbits		Wt of livers	Niacin, μ g per g	% protein	Tryptophane % in protein
		Group 1. No treatment given.			
5	Avg	54	116	14.2	1.60
		Group 2. Treated with tryptophane.			
6	"	82	177	15.0	1.56
		Group 3. Treated with niacin.			
5	"	78	159	13.4	1.57
		Group 4. Treated with tryptophane and niacin.			
6	"	102	187	14.6	1.81

TABLE IV.
Assay of Muscles.

No. of rabbits		Niacin, μ g per g	% protein	Tryptophane % in protein
		Group 1. No treatment given.		
5	Avg	88	18.5	1.43
		Group 2. Treated with tryptophane.		
6	"	93	19.2	1.43
		Group 3. Treated with niacin.		
5	"	130	19.1	1.44
		Group 4. Treated with tryptophane and niacin.		
6	"	128	20.7	1.47

gain, hemoglobin, red and white blood cells were about equal when either of the substances were fed. The addition of both compounds to the ration resulted in greater responses. The niacin content of the livers of the rabbits that received either tryptophane or niacin supplements was approximately nor-

mal. The niacin in the muscles of the rabbits that were supplemented with niacin was found to be high, while the tryptophane animals had a niacin level similar to the concentration found in the muscles of the deficient rabbits.

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Effect of Hypophyseal Growth Hormone Upon Rats Fed Low Protein Diets.*

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In a current study¹ the degree of nitrogen retention produced by the hypophyseal growth hormone has been shown to depend on the dietary protein content. With diets contain-

ing 12, 18, 24 and 48% casein growth hormone produces prompt nitrogen retention and proportionate gain of weight. In this study adult female rats of the Long-Evans strain, aged 7 to 10 months, were each fed 12 g daily of a synthetic diet complete in all known dietary requirements with a protein content restricted to 6% alcohol-washed casein. This diet contains 0.1% choline

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¹ Gordan, G. S., Bennett, L. L., Li, C. H., and Evans, H. M., to be published.