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Evaluation of Nicotinic Acid Nutrition by Studies of Urinary Excretion.

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The adequacy of nicotinic acid nutrition in man is determined at the present time solely on the basis of clinical findings. Several investigators[1,2,3] have reported that there is little difference in the quantity of nicotinic acid and its derivatives excreted in the urine in a 24 hr period by normal persons and by patients with dietary deficiency. Perlzweig, Sarett and Margolis[2] have recently suggested that the urinary excretion following the administration of 500 mg of nicotinamide may serve as a test of nicotinic acid deficiency.

This report deals with observations made on 6 normal persons, 18 hospital patients without signs of deficiency disease and 10 patients with clinical findings indicating deficiency of one or more members of the B group of vitamins. Of this last group 7 had lesions of pellagra, 5, evidence of ariboflavinosis and one, thiamin deficiency. The quantity of nicotinic acid and its derivatives excreted in the urine in a 24 hr period was determined by the method of Perlzweig, Levy and Sarett[4] with minor modifications.[5] Nicotinic acid is excreted in a number of forms, a small percentage as nicotinamide, coenzyme and nicotinuric acid (acid hydrolyzable derivatives) and a large percentage as trigonelline, which must be determined separately. The method is very satisfactory for the determination of acid hydrolyzable derivatives and is the best available for the estimation of trigonelline, although in our experience only 40 to 50% of this compound added to urine can be recovered.

Since trigonelline is the main excretion product of nicotinic acid and since it is present in many foods, it is essential in studying nicotinic acid metabolism to place subjects on a diet low in trigonelline, which was done in this investigation.

In the 34 subjects studied, there was no difference in the amount of "nicotinic acid"† excreted in the urine in 24 hr by normal persons and by patients with and without clinical evidence of deficiency of the B vitamins. (Table I). The average output of trigonelline, however, was highest in the normal group, next in the patients without evidence of deficiency disease and lowest in patients with pellagra, ariboflavinosis and thiamin deficiency. The total 24 hr output of nicotinic acid derivatives averaged in normal persons 16.2 mg, in patients with deficiency 8.7 mg. While these findings suggest that there is a decreased excretion of trigonelline in nicotinic acid deficiency there is marked overlapping in the range of values in the 3 groups. The status of nutrition in a given patient therefore, cannot be determined by measuring the excretion in the urine for 24 hr.

Sixteen persons were given 300 mg of nicotinamide‡ orally and the quantity of nicotinic acid derivatives excreted in the urine during the subsequent 6 and 24 hr determined. Nicotinamide is excreted almost entirely as trigonelline (Table II). Normal persons excreted on an average twice as much trigonelline as did hospital patients in both

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1 Sarett, H. P., Huff, J. W., and Perlzweig, W. A., *J. Nutrition*, 1942, **23**, 23.

2 Perlzweig, W. A., Sarett, H. P., and Margolis, L. H., *J. Am. Med. Assn.*, 1942, **118**, 28.

3 Field, H., Melnick, D., Robinson, W. D., and Wilkinson, C. F., *J. Clin. Invest.*, 1941, **20**, 379.

4 Perlzweig, W. A., Levy, E. D., and Sarett, H. P., *J. Biol. Chem.*, 1940, **136**, 729.

5 Dann, W. J., and Handler, P., *J. Biol. Chem.*, 1941, **140**, 201.

† The term nicotinic acid is used to include all acid hydrolyzable derivatives.

‡ Nicotinamide furnished through the courtesy of Merck & Co.

TABLE I.
Urinary Excretion of Nicotinic Acid Derivatives in 24 Hours in Subjects on a Diet Low in Trigonelline.

Subjects		Nicotinic acid* (mg)	Trigonelline† (mg)	Total (mg)
Normal persons (6)	Range	0.9-1.5	11.1-21.1	12.3-22.1
	Avg	1.2	15.0	16.2
Patients without deficiency (18)	Range	0.6-3.0	2.5-25.2	3.5-26.6
	Avg	1.4	8.6	10.0
Patients with "B" deficiency (10)	Range	0.5-1.6	3.8-14.0	4.3-15.0
	Avg	1.0	7.7	8.7

*Acid hydrolyzable derivatives.
†Expressed as amount determined as nicotinic acid.

the 6 and 24 hr periods after the test dose. There was little overlapping of findings in the 2 groups. The output of trigonelline was slightly less in patients with vitamin B complex deficiency than in the other patients. The diet in all the patients had been somewhat inadequate. Since approximately 50% of the trigonelline excretion occurred in the first 6 hr after the test dose, as much information was obtained by measuring the 6 as the 24 hr output.

The extra excretion after the administration of 300 mg of nicotinamide was calculated by subtracting the total output in a control period of 24 hr from that found on the day of the test dose. Normal persons excreted 18 to 76 mg, hospital patients 0 to 41 mg, and patients with vitamin deficiency, 6 to 21 mg. The retention of nicotinamide appeared to be closely related to the degree of dietary deficiency.

Determination of the amount of trigonelline excreted in a 6 hr period after the administration of 300 mg of nicotinamide may serve as an index of nicotinic acid nutrition.

TABLE II.
Urinary Excretion of Nicotinic Acid Derivatives After the Oral Administration of 300 mg of Nicotinamide.

Test performed		Normal persons (6) Range	Avg	Patients without deficiency (6) Range	Avg	Patients with "B" deficiency (4) Range	Avg
Excr. after test dose 6 hr (mg)	N.A.*	0.8- 4.3	2.5	0.6- 4.8	2.0	0.2- 1.0‡	0.6‡
	Trig.†	17.1-39.6	25.9	7.5-17.8	13.0	10.1-14.7‡	12.4‡
	Total	18.7-43.9	28.4	8.1-22.6	15.0	10.3-15.7‡	13.0‡
Excr. after test dose 24 hr (mg)	N.A.*	2.0- 4.5	3.3	1.0- 7.4	3.4	0.8- 2.0	1.2
	Trig.†	27.3-83.9	49.6	17.4-39.7	27.1	11.1-31.5	20.4
	Total	30.1-88.4	52.9	19.2-47.1	30.5	11.9-33.5	21.6
Extra excr. after test dose (mg)	Total	17.8-76.1	36.7	0.0-40.7	21.7	5.6-20.5	13.7

*N.A—Nicotinic acid.
†Trig.—Trigonelline.
‡Six-hour output measured in only 2 patients.