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Nicotinic Acid and Prevention of Nutritional Panmyelophthisis in Rats.

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Recently attention has been focused from different angles on nicotinic acid and nicotinamide. The importance of nicotinic acid in tissue metabolism as a co-enzyme^{1, 2} and as an agent for promoting growth in bacteria^{3, 4} has been recognized. Furthermore, Funk⁵ stated that nicotinic acid, especially nicotinamide, produced in rats and pigeons kept on a diet devoid of the vitamin B₂ complex "a much larger food intake and better weight, as compared with the controls." Even in the absence of substantiating details, the latter observations made it probable that nicotinic acid might constitute a separate factor in the vitamin B₂ complex.

While in my own unpublished experiments nicotinic acid had no effect in acrodynia in rats (vitamin B₆ deficiency disease⁶) either on the skin manifestations or on the growth rate, Elvehjem and his coworkers⁷ have succeeded in demonstrating the specific anti-black-tongue activity of nicotinic acid and nicotinamide in dogs. The therapeutic effect of nicotinic acid is not confined to canine black-tongue; it has been shown^{6, 8} to apply equally well to human pellagra. Thus the long-assumed pathogenetic identity of these 2 diseases is finally proved. In the light of these observations nicotinic acid and its derivative, nicotinamide, can be accepted as the specific anti-black-tongue or pellagra-preventing factor. This conclusion bears out the circumstantial evidence presented in previous experiments,⁹ according to which vitamin B₆ and the P-P factor must represent different constituents of the vitamin B₂ complex.

¹ Euler, H. v., Albers, H., and Schlenk, F., *Z. physiol. Chem.*, 1935, **234**, I; 1936, **240**, 113.

² Warburg, O., Christian, W., and Griesse, A., *Biochem. Z.*, 1935, **279**, 143.

³ Knight, B. C. J. G., *Biochem. J.*, 1937, **31**, 731.

⁴ Mueller, J. H., *J. Bact.*, 1937, **34**, 429.

⁵ Funk, C., and Funk, J. C., *J. Biol. Chem.*, 1937, **119**, xxxv.

⁶ Cf. also Fouts, P. J., Helmer, O. M., Lepkovsky, S., and Jukes, T. H., *Proc. Soc. Exp. Biol. and Med.*, 1937, **37**, 405.

⁷ Elvehjem, C. A., Madden, R. J., Strong, F. M., and Woolley, D. W., *J. Am. Chem. Soc.*, 1937, **59**, 1767.

⁸ Smith, D. T., Ruffin, J. M., and Smith, S. G., *J. A. M. A.*, 1937, **109**, 2054.

⁹ Birch, T. W., György, P., and Harris, L. J., *Biochem. J.*, 1935, **29**, 2830.

Rats are not very sensitive to a deficiency of the P-P factor. The only symptom that became noticeable⁹ in rats fed for 4 months diets that produced blacktongue in dogs or pellagra in human beings was a subnormal growth rate. Skin lesions or other typically pellagra-like manifestations have never been encountered.

In vitamin studies it is more suitable to use as the experimental basis a disease arising from deficiency of only one vitamin factor rather than a disease due to a complex deficiency. Thus in research having to do with the isolation of vitamin B₆ it seemed desirable to supplement the B₆ free basal diet, containing only vitamin B₁ and riboflavin as components of the whole vitamin B group, with nicotinic acid, in order to eliminate a disturbing although apparently not imposing complication which might be due to a deficiency of nicotinic acid.

This change in the diet (1000 gm. of food¹⁰ mixed with 1 gm. of nicotinic acid*) took place on Nov. 4, 1937, and involved the 180† rats fed the vitamin B₆ deficient diet. All other experimental conditions, and in particular the ingredients of the diet, remained the same as heretofore. As was expected, no difference has been observed in the production or the progress of the rat acrodynia and in the rate of growth of the rats in the experiment. However, the addition of nicotinic acid to the diet surprisingly resulted in *complete suppression* of panmyelophthisis, a complication which was a common occurrence¹¹ in rats kept under the same nutritional conditions but without nicotinic acid. In the 8 weeks preceding the addition of nicotinic acid, 20 fatalities due to panmyelophthisis were observed, while in the 8 weeks following the change in diet not one animal died from this disease, and, with the exception of one case of anemia (remarkable for the absence of agranulocytosis), all symptoms characteristic of panmyelophthisis were conspicuously absent after the second week. The rat with anemia has shown complete recovery on the diet plus nicotinic acid without any further specific supplement.¹¹ Dis-

TABLE I.

	Deaths from panmyelophthisis during week							
	1	2	3	4	5	6	7	8
Before								
addition of nicotinic acid to the diet	3	1	3	5	2	2	2	2
After	0	0	0	0	0	0	0	0

¹⁰ György, P., *Biochem. J.*, 1935, **29**, 741.

* Kindly furnished by the S.M.A. Corporation, Cleveland.

† This number fluctuated slightly, owing to intercurrent deaths and addition of new animals during the experiment.

¹¹ György, P., Goldblatt, H., Miller, F. R., and Fulton, R. P., *J. Exp. Med.*, 1937, **66**, 579.

tribution of the 20 fatalities over the 8 weeks in question was fairly uniform (Table I).

In previous studies,¹¹ panmyelophthisis has been found to be a disease with seasonal predilections, but November and December represented months in which panmyelophthisis was a frequent complication. In the experiments described here, the total number of animals was essentially the same in the 2 periods before and after addition of nicotinic acid to the diet.

In view of these facts the observations here recorded seem to indicate in rats a close relationship between nicotinic acid and prevention of nutritional panmyelophthisis with all its manifestations.

Further experiments are required in order to establish definitely the prophylactic, and possibly also the therapeutic effect of nicotinic acid on the maturation of bone marrow.

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Preparation and Administration of Globulin from Rabbit Antipneumococcus Sera.

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Although rabbit antipneumococcus sera offer certain theoretical^{1, 2, 3} and practical⁴ advantages in pneumonia therapy their use has not been without danger, so that a simple, though incomplete, method of antibody purification might be of value. The following method of preparing globulin for therapeutic purposes has been in effective use at the Presbyterian Hospital and is novel only in the substitution of efficient centrifugation for dialysis in the removal of the sodium sulfate used for precipitating the globulin. Analyses, data on administration, and excerpts from patients' charts are given.

Sera and solutions were kept sterile; the water and 0.85% saline

¹ Goodner, K., Horsfall, F. L., Jr., and Bauer, J. H., *PROC. SOC. EXP. BIOL. AND MED.*, 1936, **34**, 617.

² Heidelberg, M., Pedersen, K. O., and Tiselius, A., *Nature*, 1936, **138**, 165; Heidelberg, M., and Pedersen, K. O., *J. Exp. Med.*, 1937, **65**, 393.

³ Heidelberg, M., and Kendall, F. E., *J. Exp. Med.*, 1937, **65**, 647.

⁴ Goodner, K., Horsfall, F. L., Jr., and Dubos, R. J., *J. Immunol.*, 1937, **33**, 279, and references given there.