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Use of Highly Purified Rations in the Study of Nicotinic Acid Deficiency.

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The corn meal used in modified Goldberger diets[1,2] for the production of canine blacktongue provides the animals with 0.1-0.12 mg per kilo per day of nicotinic acid.[3,4] Dogs ingesting such diets require, in addition, approximately 0.1 mg of nicotinic acid per kilo per day.[5] This agrees with the finding[6] that adult dogs require 0.2-0.225 mg per kilo per day of nicotinic acid when fed a purified diet low in nicotinic acid. Thus half the requirement of each dog is provided by the corn meal of the Goldberger diets.

Almost all dogs fed a modified Goldberger diet[1] have become acutely ill within 75 days and most of them have fallen ill within 40 days. It was thought that if dogs were fed a purified ration in which the nicotinic acid supplied was reduced to a minimum, the appearance of blacktongue should be considerably accelerated. The object was to continue the study of the physiological defects in acute deficiency rather than in intermediate stages.

Eleven adult mongrel dogs were fed a purified ration whose nicotinic acid content was held almost to its minimum possible level, less than 0.01 mg per kilo per day. The diet was identical with that of Schaeffer, McKibbin and Elvehjem[7] except that corn starch was substituted for half of the sucrose component. Each dog was housed in an individual cage; food, water intake and urine were measured daily.

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3 Teply, L. J., Strong, F. M., and Elvehjem, C. A., *J. Nutrition*, 1942, **23**, 417.

4 Sarett, H. P., *J. Nutrition*, 1942, **23**, 35.

5 Margolis, G., Margolis, L. H., and Smith, S. G., *J. Nutrition*, 1938, **16**, 541.

6 Schaeffer, A. E., McKibbin, J. M., and Elvehjem, C. A., *J. Biol. Chem.*, 1942, **144**, 679.

7 Schaeffer, A. D., McKibbin, J. M., and Elvehjem, C. A., *J. Nutrition*, 1942, **23**, 491.

Since no dog fell ill until the 63rd day, there were, seemingly, no advantages in using this costly diet. Four dogs became acutely ill after 63, 78, 85 and 98 days respectively, as judged by weight loss, anorexia, bloody diarrhea, thick, ropy salivation and the appearance of necrotic lesions of the cheeks, gums and throat. However, their state did not completely resemble that of blacktongue dogs on the Goldberger diet. Despite the acuteness of the deficiency syndrome the animals were not prostrate; they were alert and able to exercise. Moreover, each dog drank at least 500 cc of water daily, while dogs in blacktongue produced by Goldberger diets do not drink appreciable quantities of water despite their profound dehydration. There was no anuria, hemoconcentration or other evidence of dehydration although in all other respects the animals agreed with our concept of the nicotinic acid deficiency syndrome.

After 8 to 14 days in this condition, in which no therapeutic steps were taken, each dog spontaneously improved and 10 days later there was no evidence of blacktongue. Their subsequent behavior was identical with the description of blacktongue dogs produced on the Goldberger diet and treated with salt.[8] Appetite, weight and hemoglobin declined steadily.

Four dogs developed acute blacktongue on this ration after 89, 94, 145 and 187 days, respectively, and died within one week. Their condition was identical in all respects with that of the previous 4 dogs. They showed the classical signs of blacktongue but were not anuric, drank copious quantities of water and were not dehydrated or prostrate until a few hours before death. Their blood hemoglobin concentrations declined from original values of 15.2, 15.1, 14.8 and 13.5 g % to 12.3, 10.5, 10.0 and 7.4 g % respectively just before acute blacktongue and these levels did not rise appreciably during blacktongue. Their liver nicotinic acid concentrations were within the range found for blacktongue dogs on a Goldberger diet.[9] At autopsy the usual lesions were noted[10] and 2 showed signs of pneumonia which was probably due to aspiration of the Vincent's organisms which are responsible for the mouth lesions.[11]

The remaining 3 animals never developed blacktongue. For 5 months their appetites, body weight and blood hemoglobin steadily diminished. Thus, they resembled nicotinic acid deficient dogs who have been successfully treated with physiological saline.[8] One dog was permitted to decline and finally die in this deficient state. Just before death the animal had lost 65% of its weight and showed a hemoglobin concentration of 1.6 g %, hematocrit of 7% and red cell count of 1,020,000 per mm.^{3} The other 2 dogs were not permitted to decline this far and were saved for a study of the nature of the anemia.

This inconsistent behavior of dogs on a purified ration makes it difficult to evaluate the nature of the physiological defects in nicotinic acid deficiency. Certainly, their behavior is in marked contrast to that observed earlier on Goldberger diets.[8] Since the dehydration, lack of thirst and hemoconcentration characteristic of blacktongue produced by the ingestion of corn-meal-containing Goldberger diets are also seen in human pellagra, it seems not unlikely that the presence of corn meal *per se* may be an etiological factor in pellagra.

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10 Lillie, R. D., *Nat. Inst. of Health Bull.*, 1933, **162**, 13.

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