

Dermatitis on a Synthetic Ration Adequate for Growth and Reproduction in the Rat.

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The importance of pantothenic acid, pyridoxine, and the essential fatty acids for the prevention of dermatitis in the rat has been demonstrated by a number of investigators.¹⁻⁵ It is the purpose of the present communication to point out that in addition to the above still another dietary factor(s) is involved in the maintenance of normal tail epithelium.

Procedure and results. The basal ration consisted of sucrose 73.2, Vitamin Test Casein* 22, 1(-) cystine 0.3, and Sure's Salt Mixture No. 1 4.5.[†] To each kg of the above were added 5 mg thiamine hydrochloride, 5 mg pyridoxine, 10 mg riboflavin, 100 mg nicotinic acid, 100 mg calcium pantothenate, 150 mg para-aminobenzoic acid, 400 mg inositol, and 1 g choline chloride. Daily supplements of 150 mg corn oil (Mazola), 0.25 mg alpha-tocopherol, and an A-D concentrate‡ equivalent to 50 U.S.P. units of vitamin A and 5 U.S.P. units of vitamin D were also administered.

Twenty-eight male and female albino rats of the Wistar strain were weaned at 21 days of age, and litter mates divided into the following two groups: (1) maintained on the

synthetic ration listed above, and (2) maintained on a natural food ration supplemented once weekly with lettuce. Both males and females were bred at approximately 70 days of age. Females were placed with males of proven fertility, and pregnancy dated from the finding of sperm in the vaginal tract. Males, in turn, were bred to females maintained on a natural food ration adequate for growth, reproduction and lactation.

Growth. Both male and female rats on the synthetic diet were consistently heavier than litter mates receiving the natural food ration. Of 7 males raised from weaning on the synthetic diet, 5 were heavier than the largest natural food control. Similar results were obtained for females. At 100 days of age, males on the synthetic ration averaged 264 g as contrasted to 233 g for litter mates maintained on a natural food ration.

Reproduction. Five out of 7 males raised from weaning on the synthetic diet mated successfully the first time they were placed with estrus females at approximately 70 days of age. In every instance, litters of apparently normal young were born. Females raised from weaning on the synthetic diet exhibited regular estrous cycles as determined by vaginal smears. Four females were bred to normal males of proven fertility, and pregnancy dated from the finding of sperm in the vaginal tract. Young of normal birth weight were delivered at term, 2 litters of 11 each, and one of 8, that could not be distinguished from those born of natural food controls. A fourth litter consisting of 11 young of normal birth weight included 7 young born dead. In no instance did the mother nurse her young.

Dermatitis. Although the synthetic ration was adequate for promoting growth and reproduction in the albino rat, animals maintained on this ration exhibited a dermatitis

¹ Henderson, L. M., McIntire, J. M., Waisman, H. A., and Elvehjem, C. A., *J. Nutrition*, 1942, **23**, 47.

² Gyorgy, P., Poling, C. E., and Subbarow, Y., *Proc. Soc. Exp. Biol. and Med.*, 1939, **42**, 738.

³ Richardson, L. R., and Hogan, A. G., *Proc. Soc. Exp. Biol. and Med.*, 1940, **44**, 583.

⁴ Salmon, W. D., *J. Biol. Chem.*, 1941, **140**, cix, *Proc.*

⁵ Richardson, L. R., Hogan, A. G., and Itschner, K. I., *Missouri Agr. Exp. Sta. Res. Bull.*, 1941, **33**, 2.

* S.M.A. Corporation, Chagrin Falls, Ohio.

† Sure, Barnett, *J. Nutrition*, 1941, **22**, 499.

‡ Nopco Fish Oil Concentrate, assaying 800,000 U.S.P. units vitamin A and 80,000 U.S.P. units vitamin D per gram.

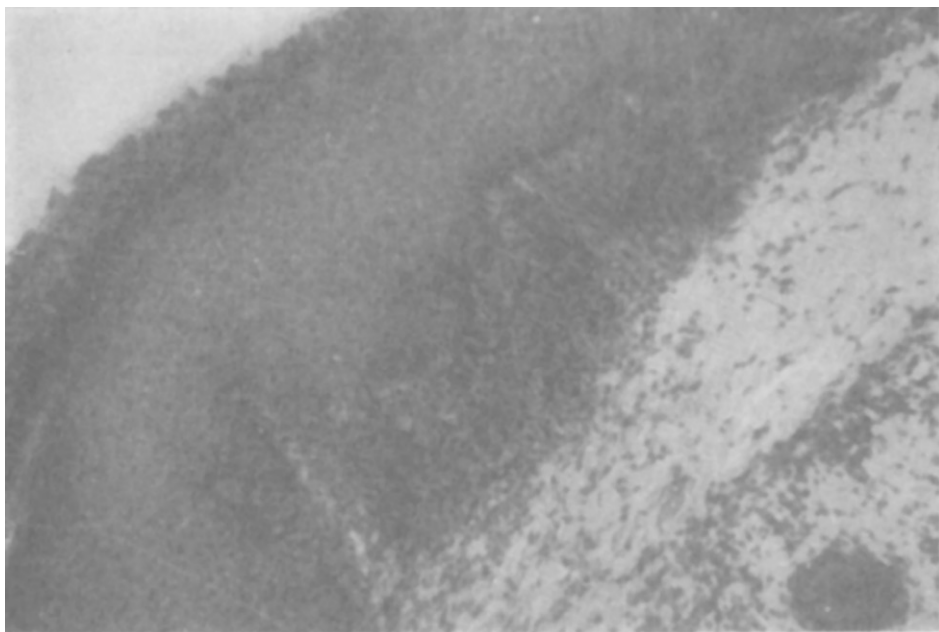


FIG. 1.
Tail of rat maintained on synthetic ration. Magnification 100 $\times$.

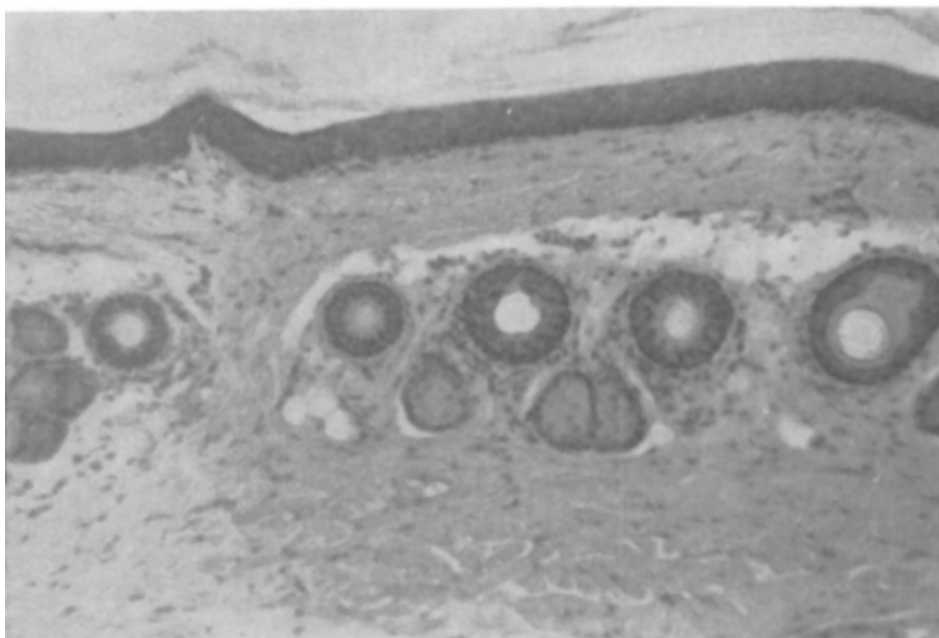


FIG. 2.
Tail of rat maintained on natural food ration. Magnification 100 $\times$.

of the tail that differed from that observed in pantothenic acid deficiency, pyridoxine deficiency, or deficiency of the essential fatty acids. During the sixth week on the synthetic diet, small reddish brown nodules appeared as intermittent elevations along the

surface of the tail, being more prominent in the proximal than the distal portion. Histologically the pathological picture approached that of an early granulomatous papule, with a hyperplasia of the epidermis to 4 or 5 times normal thickness, a marked irregularity of the basement membrane, and a leucocytic infiltration of subepidermal tissues particularly around the basement membrane and the epithelium of the hair follicles. (Figs. 1 and 2.) By the tenth week, approximately one-fourth of the animals exhibited small areas along the cheeks and lower jaw where fur had fallen out and hard reddish-brown scabs were visible. Superficially, however, with the exception of the tail lesions, the animals could not be differentiated from litter mate controls maintained on a natural food ration.

Attempts to cure the dermatitis with a single dietary supplement have been unsuccessful. Subcutaneous administration of a biotin concentrate[§] equivalent to 0.5 γ per day for a 3-week period had no effect on the alleviation of these symptoms. Similarly a solubilized liver extract rich in a factor necessary for the growth of *Lactobacillus casei*^{||} was also ineffective when incorporated as 2% of the ration for a period of one month. Administration of a natural food ration however resulted in a prompt remission of the dermatitis.

An interesting observation was the effect of alterations in the basal ration on the appearance of dermatitis. Fifteen litter mates of the above series (8 males and 7 females) were placed at weaning on a synthetic ration identical to the above but minus the corn oil. The sole source of essential fatty acids in the diet was accordingly that present in the purified casein. On this ration containing a total fat content, exclusive of the unsaponifiable vitamin A-D concentrate and alpha-tocopherol, of 0.04%, no evidence of

scaly skin or caudal necrosis was observed, although other evidence of essential fatty acid deficiency was present: retardation of growth; poor ovulation and delayed parturition in the female; sterility in the male. From the fourth to the seventh week on this fat free diet tail lesions were observed identical to those described for the basal ration; subsequent to the seventh week however, a gradual disappearance of dermatitis occurred. At 100 days of age tails of animals on the fat deficient diet were practically symptom free in contrast to the marked dermatitis observed in litter mates receiving an identical diet supplemented with corn oil.

In a subsequent series 16 albino rats of the Wistar strain were weaned at 25 to 30 days of age and divided into the following two groups: (1) consisting of 6 rats maintained on the basal ration listed above, and (2) consisting of 10 rats (5 males and 5 females) receiving a synthetic ration identical to that of Group I but deficient in inositol. At 100 days of age animals receiving the basal ration (Group I) exhibited a dermatitis of the tail indistinguishable from that observed in the previous experiment. Animals maintained on the inositol deficient diet (Group II) were free of dermatitis.

Inasmuch as sufficient pantothenic acid, pyridoxine, and essential fatty acids were present in the basal ration to insure a rate of growth not inferior to that observed in natural food controls, and inasmuch as both males and females were able to undergo apparently normal reproduction on the synthetic diet, it is felt that some dietary factor(s) other than the above is necessary for the prevention of dermatitis. Further experiments on the identity of this factor are now in progress.

Summary. A specific tail dermatitis is described distinct from that observed in pantothenic acid, pyridoxine or essential fatty acid deficiency. It is suggested that some dietary factor or factors other than the above is involved in the maintenance of normal tail epithelium.

[§] Biotin Concentrate No. 1000, S.M.A. Corporation, Chagrin Falls, Ohio.

^{||} Solubilized Liver Extract Fraction I. Wilson Laboratories, Chicago, Ill.