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Curative Effect of Pantothenic Acid on Adrenal Necrosis.*

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During the past 2 years we have frequently observed adrenal damage in rats kept on purified rations similar to J29.[1] The glands exhibit a definite pinkish or even purple color and in severe cases are greatly enlarged. Histological examination of these glands showed the condition to be an hemorrhagic cortical necrosis similar to that reported by Daft and Sebrell[2] and described by Nelson.[3] These workers stated that the condition was due to a deficiency of a dietary factor present in the fuller's earth filtrate of liver extract. We found that several different liver extract fractions would prevent the condition, and since some of these fractions were low in pantothenic acid we felt that the active factor might be separate from this vitamin. When synthetic pantothenic acid became available we were able to study the active agent more thoroughly.

The basal ration used (J36) consisted of sucrose 76%, alcohol-extracted casein 18%, salts III[4] 4%, corn oil 2%, thiamin chloride, vitamin B_6, and riboflavin 300γ per 100 g of ration, nicotinic acid 2.5 mg per 100 g, and choline hydrochloride 30 mg per 100 g. Two drops of haliver oil were fed by dropper each week. Rats were placed on experiment at 3 weeks of age.

In several different series the adrenals from rats on the basal ration were compared with those from rats receiving 25, 50, or 100 γ of calcium pantothenate per day. In other groups similar levels of pantothenic acid were fed, but with food intake restricted to that of rats receiving no pantothenic acid. Additional choline and a liver extract

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1 Oleson, J. J., Elvehjem, C. A., and Hart, E. B., PROC. SOC. EXP. BIOL. AND MED., 1940, **43**, 161.

2 Daft, F. S., and Sebrell, W. H., *Pub. Health Reports*, 1939, **54**, No. 51, 2247.

3 Nelson, A. A., *Pub. Health Reports*, 1939, **54**, No. 51, 2250.

4 McKibbin, J. M., Madden, R. J., Black, S., and Elvehjem, C. A., *Am. J. Physiol.*, 1939, **128**, 102.

preparation were also fed. The rats were killed by decapitation, usually after being on experiment for 4 to 6 weeks, and the adrenals prepared immediately for histological study.

The results of the experiments are summarized in Table I. Of the

TABLE I.

Diet	Total No. of rats	Avg weekly gain g	Adrenals		
			Normal	Early necrosis	Advanced necrosis
J36 only	15	5.8	3	3	9
J36 (with choline at 200 mg/100 g)	7	8.5	1	0	6
J36 + calcium pantothenate at					
25 γ/day	3	9.6	3	0	0
50 "	10	15.8	10	0	0
100 "	13	15.6	13	0	0
As above with restricted intake	6	8.5	6	0	0
J36 + factor W concentrate = 0.2 g L.E.	7	18.8	7	0	0

15 rats receiving the basal ration alone, 3 had normal adrenals, 3 had adrenals showing hemorrhage or early necrosis, and 9 had adrenals which were severely necrotic. One of the normal cases was killed after only 2 weeks, so that the condition may not have had time to develop. All the others were killed between 4 and 6 weeks.

When calcium pantothenate was given at levels of 25, 50, or 100 γ per day the necrosis was completely prevented in all 32 cases. The food intake of 6 of these rats was restricted to that of rats on the basal ration alone, so that increased consumption could not supply more of any other factor to prevent the necrosis. Three of the 6 rats received 50 γ, and the other 3, 100 γ per day; the adrenals of all were normal.

In order to eliminate the possibility of the condition being a choline deficiency, 7 rats received the basal ration in which the choline level had been increased from 30 to 200 mg per 100 g. Of these 7 rats, 6 showed very severe adrenal necrosis at 4 and 6 weeks; the seventh had normal adrenals, but was killed after only 2 weeks. Choline seemed to aggravate rather than prevent the condition.

Liver extract which had been autoclaved in 1N sulfuric acid for 1 hour was fed to 7 rats at a level of 0.2 g per day. The adrenals of the rats were normal. Although the autoclaving destroyed most of the pantothenic acid in the liver extract, enough remained so that the rats received about 4 γ per day. This amount was evidently sufficient to prevent the occurrence of adrenal necrosis on our ration.

Summary. Rats receiving only our basal ration J36 showed an hemorrhagic cortical necrosis of the adrenals after 4-6 weeks. This condition was prevented by calcium pantothenate. Choline did not

prevent but rather aggravated the condition. Acid autoclaved liver extract prevented the condition, but its action may have been due to its pantothenic acid content.

The activity of pantothenic acid in the prevention of adrenal necrosis has been reported by Daft, F. S., Sebrell, W. H., Babcock, S. H. J., and Jukes, T. H., (*Public Health Rep.*, 1940, **55**, 1333) but due to an oversight the authors did not find their paper until after this note was submitted for publication.

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Effect of Testosterone Propionate on Regenerating Anal Fin of Adult *Platypoecilus maculatus* Females.*

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It has been found previously that administration of testosterone propionate to adult female poeciliid fishes masculinizes the anal fin but does not produce a typical male copulatory organ or gonopod (Regnier[1]—*Xiphophorus helleri;* Grobstein[2]—*P. maculatus, P. variatus*). The present experiments were performed to determine whether the incomplete masculinization may be due, in whole or in part, to lack of capacity of the reacting fin for gonopod formation.

Sixty-six adult *P. maculatus* females (9 months of age or older, 25 to 35 mm in length) were injected intraperitoneally with testosterone propionate during anal fin regeneration. In the 5 separate series that were run, both dosage and the interval between time of removal of the anal fin and beginning of injection were varied in an effort to obtain the most typically male response possible. Concentrations of 2.5, 5.0 and 25.0 mg/cc were used and injection was begun at intervals of 0, 5, 10, 12, 20, 24 and 56 days after removal of the anal fin. In all series but one 0.05 cc of solution was injected every fifth to seventh day until the response was completed.

Controls were of 3 types: 15 were untreated during anal fin regeneration, 10 were injected during regeneration with sesame oil,

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1 Regnier, M., *Bull. Biol.*, 1938, **72**, 385.

2 Grobstein, C., unpublished data.