

intraperitoneal injection of neoprontosil and certain other drugs of the sulfonamide group. This myocarditis is histologically similar to that observed in the hearts of humans dying after the administration of these drugs.

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Biotin and Scaly Dermatitis of the Chick.

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In a recent communication,¹ chicks raised on a heated diet² were reported to show symptoms of a severe dermatosis similar to the one described by Hegsted, *et al.*³ As shown in Tables I and II, the deficiency syndrome was readily obtained with chicks reared on diet X-5, which is ration K-11⁴ modified by the addition of 2 mg of 2-methyl-1,4-naphthoquinone per 10 kg of diet. The symptoms most frequently developed on the toes and feet, often in the cor-

TABLE I.
Effect of Biotin Concentrates on Growth and Scaly Dermatitis in Chicks.*

Depletion period Wt and symptomst			Daily doses, γ	Route‡	No. of chicks	Test period Wt and symptomst		
26th day, g	55th day, g	68th day, g				8th day, g	17th day, g	25th day, g
130 N	230 D	290 M	0	O	20	340 S	—	350 S
160 N	270 M	350 S	2.5	O	5	440 DH	530 C	550 C
130 N	220 M	260 S	1.25	O	5	330 DH	410 C	440 C
140 N	210 M	230 S	24	SC	4	290 DH	340 C	350 C
150 N	250 M	290 S	18	SC	4	360 DH	440 C	480 C
140 N	250 M	280 S	12	SC	4	360 DH	460 C	500 C
130 N	270 M	310 S	6	SC	4	410 DH	530 C	600 C
130 N	210 M	250 S	2.5	SC	3	340 DH	440 C	490 C

¹ Ansbacher, S., *Science*, 1941, **93**, 164.

² Ansbacher, S., *PROC. SOC. EXP. BIOL. AND MED.*, 1940, **44**, 248.

³ Hegsted, D. M., Oleson, J. J., Mills, R. C., Elvehjem, C. A., and Hart, E. B., *J. Nutrition*, 1940, **20**, 599.

⁴ Ansbacher, S., *PROC. SOC. EXP. BIOL. AND MED.*, 1941, **46**, 421.

TABLE II.
Effect of Crystalline Biotin on Growth and Scaly Dermatitis in Chicks.*

Depletion period Wt and symptomst			Doses			Test period Wt and symptomst	
25th day, g	42nd day, g	64th day, g	γ	No. of	Route†	8th day, g	16th day, g
110 N	200 D	270 S	10	3	O	330 DH	440 C
140 N	200 M	280 S	10	3	O	280 DH	460 C
150 N	250 D	390 S	3	5	IM	390 DH	450 C
120 N	210 D	320 M	5	3	IM	400 DH	590 C
100 N	140 M	220 S	10	3	IM	220 DH	360 C
100 N	200 D	230 S	10	3	IM	290 DH	410 C
120 N	210 D	300 M	10	3	IM	360 DH	460 C

*Chicks reared on diet X-5:

Heated [120°C, 1 week] grain [25 parts wheat middlings and 58 parts yellow corn] mixture

%

83

Salt mixture [Table I, *J. Nutrition*, 1939, **17**, 303]

2

Calcium carbonate

1

Cod liver oil containing 10 ml menadione

Casein [SMACO, vitamin-free] with added 80 mg thiamine hydrochloride, 80 mg riboflavin, 80 mg pyridoxine hydrochloride, 1 g calcium pantothenate, 1 g nicotinic acid, 1 g inositol, 3 g choline chloride and 3 g p-aminobenzoic acid per 1.2 kg

12

†Symptoms: N—None; D—Definite; M—Marked; S—Severe; DH—Definite Healing; C—Complete Healing.

‡Route: O—Oral; SC—Subcutaneous; IM—Intramuscular.

ners of the beaks and on the combs, occasionally on the eyelids, and were always most severe on the toes.

Biotin concentrates (SMACO) were found to possess growth-promoting property and curative effect (Table I), all the treated animals showing definite improvement within a period of 5 days and practically complete healing of the scaly dermatosis in about 2 weeks. Similar results (Table II) were obtained with crystalline biotin methyl ester,⁵ kindly supplied by Dr. Vincent du Vigneaud. It should be mentioned that the treated birds showed at the end of the test period a residual dermatosis on the toes, the extent of which was in many cases so slight that a careful examination was necessary to find it.

The data presented show conclusively that the scaly dermatosis observed in the chicks is a result of a simple⁶ dietary deficiency in biotin. Concentrates fed daily at a level equivalent to only 1.25% of biotin were effective. Severely depleted birds responded to crude preparations subcutaneously injected in daily doses equivalent to

⁵ György, P., Rose, C. S., Hofmann, K., Melville, D. B., and du Vigneaud, V., *Science*, 1940, **92**, 609.

⁶ György, P., *Arch. Dermat. and Syphil.*, 1941, **43**, 230.

as little as 2.5 γ of biotin. The scaly dermatosis was observed to be healed by the administration of the crystalline biotin ester. The minimum curative dose has not yet been determined and is probably less than 10 γ .

It is apparent from the experiments as a whole that the chick can be employed in a quantitative biological assay of biotin. Such a procedure is certainly more time-consuming than, *e. g.*, a yeast growth technic,⁷ but it is definitely more expedient than a bioassay with rats based upon a secondary⁸ deficiency disease brought about by egg-white injury.

Conclusion. Biotin-deficiency is brought about in the chick reared on a heated ration of low biotin content (0.1 γ /g). This deficiency is produced in the absence of dietary egg white which is essential for the development of the avitaminosis in the rat. Deficiency symptoms are completely cured by administration of crystalline biotin methyl ester. The chick can be used in a quantitative biological assay of biotin.

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Generalized Muscular Weakness as a Toxic Reaction to Digitalis.*

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Clark,¹ Cushny² and Neuschloss³ demonstrated that the efficiency of a nerve muscle preparation could be markedly impaired if ex-

⁷ Snell, E. E., Eakin, R. E., and Williams, R. J., *J. Am. Chem. Soc.*, 1940, **62**, 175.

⁸ György, P., Rose, C. S., Eakin, R. E., Snell, E. E., and Williams, R. J., *Science*, 1941, **93**, 477.

* This paper comprises part of a thesis submitted to the Graduate School of the University of Minnesota in partial fulfilment of the requirements for the degree of Doctor of Philosophy in Medicine.

¹ Clark, A. J., *Brit. Med. J.*, 1912, **2**, 687.

² Cushny, A. R., *The Action and Uses in Medicine of Digitalis and Its Allies*, Longmans, Green and Co., London, 1925.

³ Neuschloss, S. M., *Pflügers Arch. f. d. ges. Phys.*, 1922, **197**, 235.