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Rôle of Para-Aminobenzoic Acid in Vitamin B-Complex Studies with Mice.*

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Shortly after Rubbo and Gillespie[1] published the isolation of p-aminobenzoic acid as the benzoyl derivative from yeast, one of us (S.A.)[2] reported that this aromatic amine has vitamin properties and should be classified as a factor of the vitamin B-Complex. Its anti-gray-hair activity was first demonstrated in the nutritional achromotrichia of the rat[2] and subsequently in the hydroquinone achromotrichia of the mouse.[3] Our more recent studies showed that it has a pronounced influence on tyrosinase activity[4] and is capable of modifying enzymatic melanin formation.[5] Subsequently Lipmann[6] suggested its possible rôle in pigmentation processes. Emerson[7] found that it cannot replace pantothenic acid and Sure[8] confirmed its vitamin character. He observed, namely, it to be identical in its effects with vitamin B_x which is necessary for lactation and reproduction. Incidentally, the anti-gray-hair vitamin was also named vitamin B_x by Lunde and Kringstad.[9] Finally, Lampen and Peterson[10] presented data showing p-aminobenzoic acid to be a typical B-vitamin, namely, a growth factor for certain organisms, and Sieve[11] described its beneficial effect in human† achromotrichia.

* Presented in part at Atlantic City, N. J., on September 11, 1941 (102nd Meet. of Am. Chem. Soc., Div. of Biol. Chem.).

1 Rubbo, S. D., and Gillespie, J. M., *Nature,* 1940, **146**, 838.

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

3 Martin, G. J., and Ansbacher, S., *J. Biol. Chem.,* 1941, **138**, 441.

4 Wisansky, W. A., Martin, G. J., and Ansbacher, S., *J. Am. Chem. Soc.,* 1941, **63**, 1771.

5 Martin, G. J., Wisansky, W. A., and Ansbacher, S., PROC. SOC. EXP. BIOL. AND MED., 1941, **47**, 26.

6 Lipmann, F., *J. Biol. Chem.,* 1941, **139**, 977.

7 Emerson, G. A., PROC. SOC. EXP. BIOL. AND MED., 1941, **47**, 448.

8 Sure, B., *Science,* 1941, **94**, 167.

† In clinical studies of asthma, one of us (S. A.) found that many asthmatics are greatly benefited by the oral administration of 100 mg of p-aminobenzoic acid t.i.d.

9 Lunde, G., and Kringstad, H., *Norsk Pelsdyrblad,* 1939, **13**, 500.

10 Lampen, J. O., and Peterson, W. H., *J. Am. Chem. Soc.,* 1941, **63**, 2283.

11 Sieve, B. F., *Science,* 1941, **94**, 257.

In the present communication we wish to report on the rôle of p-aminobenzoic acid in nutritional investigations with mice.

Black mice (Rockland Strain) were divided into 2 groups of 75 animals each, one of which was fed a basal diet (casein, 18; cerelose, 67; salts, 4; cod liver oil, 2; butter fat, 9) supplemented daily with 7 of the B-complex vitamins, namely, 25 γ of thiamine hydrochloride, 50 γ of riboflavin, 25 γ of pyridoxine hydrochloride, 500 γ of nicotinic acid, 1000 γ of choline chloride, 250 γ of calcium pantothenate, and 500 γ of inositol. Graying of the fur was noted in 75% of these animals within a period of from 2 to 4 weeks. The second group received daily 250 γ of p-aminobenzoic acid in addition to the 7 vitamins and the hair of all the animals remained black during the 9-week test period. Apparently, p-aminobenzoic acid has the same effect in mice as Labco Rice Polish Factor II, the chromotrichial potency of which has already been reported.[12]

The rôle of p-aminobenzoic acid in the nutrition of the mouse is further demonstrated by the data of Table I. When mice were fed the basal diet supplemented with the 8 B-complex vitamins, no growth, no alopecia and no achromotrichia was observed until death which occurred in the 75 animals used in from 8 to 13 weeks. When calcium pantothenate was omitted in the diet of another lot of 75 mice, a pantothenate-deficiency developed in about 80% of the animals, the symptomatology of which was identical with the one recently described by Woolley.[13] When the lipotropic[14] and

TABLE I.
Pantothenate-deficiency, Achromotrichia and Alopecia.

Complements to basal diet supplemented by 5* B-complex vitamins			
Calcium pantothenate γ	Inositol γ	p-Aminobenzoic acid γ	Symptoms
none	none	none	pantothenate-deficiency
,,	500	,,	,, ,,
,,	none	250	,, ,,
,,	500	250	,, ,,
250	none	none	achromotrichia
250	500	,,	,,
250	none	250	alopecia
250	500	250	none

*Thiamine hydrochloride (25γ), riboflavin (50γ), pyridoxine hydrochloride (25γ), nicotinic acid (500γ), choline chloride (1000γ).

12 Martin, G. J., *Science*, 1941, **93**, 422.

13 Woolley, D. W., PROC. SOC. EXP. BIOL. AND MED., 1941, **46**, 565.

14 Gavin, G., and McHenry, E. W., *J. Biol. Chem.*, 1941, **139**, 485.

spectacled-eye[15] factor inositol was omitted in the diet of another group of 75 mice, the typical[16, 17] alopecia appeared in about 80% of the animals. However, when inositol and p-aminobenzoic acid were omitted, the inositol-deficiency did not occur.[12] Since the addition of p-aminobenzoic acid to a heated vitamin K-deficient diet was observed[18] to result in an earlier incidence of avitaminosis, suggesting an inhibition of bacterial vitamin synthesis by the aromatic amine, it may be that inositol deficiency in mice on rations containing the amine is attributable to a bactericidal or bacteriostatic action of p-aminobenzoic acid. The report of Spink and Jermsta[19] "that the smaller concentrations of p-aminobenzoic acid in combination with a sulfonamide compound often appeared to inhibit growth more than was obtained with the sulfonamide compound alone," as well as preliminary bacteriological studies seem to substantiate this hypothesis.

Summary. Para-aminobenzoic acid has anti-gray-hair activity in the nutritional achromotrichia of the mouse. It is a dietary factor necessary for the demonstration of the anti-alopecia effect of inositol.

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Accelerated Hair Growth in the Rat After Adrenalectomy Cannot be Attributed to the Thyroid.

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It is difficult to provide an explanation for the rapid hair growth following adrenalectomy in the albino rat since the function or functions of the cortical portion of the adrenal are not well understood (previous experiments[1] indicate that it is the cortex which is involved). This unusual growth upon adrenalectomy might be due to the thyroid or thyroxin as the following suggests: Thy-

15 Pavcek, P. L., and Baum, H. M., *Science*, 1941, **93**, 502.

16 Woolley, D. W., *J. Biol. Chem.*, 1940, **136**, 113; 1941, **139**, 29; *Science*, 1940, **92**, 384.

17 Norris, E. R., and Hauschildt, J., *Science*, 1940, **92**, 316.

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

19 Spink, W. W., and Jermsta, J., PROC. SOC. EXP. BIOL. AND MED., 1941, **47**, 395.

1 Butcher, E. O., *Am. J. Physiol.*, 1937, **120**, 427.