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Experimental Evidence of an Additional Substance Essential to Mammalian Nutrition.

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It has become increasingly evident that one or more water soluble substances other than vitamins B (B_1) and G (B_2) were necessary for general mammalian nutrition. Further evidence appeared during the course of an experiment to study the effect of fairly high concentrations of vitamin G upon growth and reproduction. Litter mates had been divided between 3 diets planned to be both adequate and practically equal in all the known nutritional essentials except for the one variable, vitamin G. From previous experience it was expected that early growth would be improved by the higher concentrations of vitamin G.

It soon became apparent, however, that vitamin G had ceased to be the limiting factor since inferior growth attended the higher concentrations of that vitamin. At 140 days of age the average weight of the 4 males was 318, 269, and 250 gm., and that of the 6 females 239, 209, and 182 gm. for the 3 diets which contained successively increasing concentrations of vitamin G. This reversal was carried over to the young whose average weight at 28 days of age was 57 (35 cases), 47 (22 cases), and 29 (7 cases) gm. for the males, and 53 (31 cases), 43 (20 cases), and 30 (8 cases) gm. for the females, notwithstanding successively increasing amounts of vitamin G. The average gain in weight of representative young of the second generation from the 28th to 56th day of life was 119 (6 cases), and 89 (3 cases) gm. for the males, and 80 (6 cases), and 68 (6 cases) gm. for the females. The diet richest in vitamin G was not represented here.

When representative young from the 3 diets were fed Bourquin

and Sherman's[1] vitamin G deficient diet at 28 days of age, a striking reversal of their growth occurred. Those young which had grown poorly and were from mothers showing poor growth now grew the best. The average gain in weight from the 28th to 56th day was 9 (9 cases), 10 (10 cases), and 16 (9 cases) gm. for successive increases of vitamin G in the previous dietary.

It appeared, therefore, that growth had been previously inhibited on the diets richer in vitamin G by the deficiency of a substance present in the Bourquin and Sherman vitamin G deficient diet. The alcoholic extract of whole wheat seemed the most probable carrier of this nutritionally essential substance.

From a study of its properties and distribution, this substance may be identical with or closely allied to Reader's[2] vitamin B_4 and to the factor reported by Halliday.[3] It is present in whole wheat but only in lesser degree in skimmed milk powder since the poorest growth was obtained on the diet containing 70% skimmed milk powder by weight. It may be, therefore, the same factor which Halliday found in whole wheat but probably different from the factor which Coward[4,5] found to be potent in milk. Its presence in the whole wheat extract demonstrates its extractability by ethyl alcohol, 80% by weight. Reader reported that her vitamin B_4 was most readily extracted with 50% alcohol but to some extent by ether. Likewise, this substance must be relatively stable to heating at 78°C. for 2 hours in alcoholic solution. Reader has reported that the activity of her crystalline vitamin B_4 was destroyed by heating with alkali but not with acid, and that her crude vitamin B_4 was destroyed by 2 hours open heating at 95-97°C. to the extent of about 50%.

The concentration of this additional factor must have been fairly low in the diet attended by very inferior growth, but during the 6 months of the experiment no external symptoms other than lowered vitality appeared.

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[1] Bourquin, A., and Sherman, H. C., *J. Am. Chem. Soc.*, 1931, **53**, 3501.

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[3] Halliday, N., *J. Biol. Chem.*, 1932, **96**, 479.

[4] Coward, K. H., Key, K. M., and Morgan, B. G., *Biochem. J.*, 1929, **23**, 695.

[5] Coward, K. H., Key, K. M., Morgan, B. G., and Cambden, M., *Biochem. J.*, 1929, **23**, 913.