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Negative Effect of Chronic Morphinism on the Anorexia Characteristic of Vitamin B₁ Deficiency.*

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Certain observations made by Dr. Henry G. Barbour on dogs receiving repeated doses of morphine suggested that the anorexia exhibited by such animals might be due to some effect of the continued morphine administration on the organism's requirement for vitamin B₁. The perfection of a technic for studying in dogs the anorexia characteristic of lack of this vitamin made it possible to study this suggested relationship experimentally.

The method employed has been used successfully for many studies from this laboratory¹ and therefore need not be described here. Certain details pertinent to the investigation here reported should be mentioned, however. Our *Casein III*² B₁-free diet was used as the basal ration. At the beginning of a feeding trial the animal received several large daily doses of either dried yeast or wheat germ in order to "saturate" the tissues with the vitamin and in this way obviate any possible effect of the previous dietary regime. The number of days between cessation of such vitamin administration and the appearance of the characteristic anorexia was then noted, and the effect of a given dose of test substance in restoring the urge to eat then observed. Since the pure vitamin was not available at the time, several products were used. Although these differed in origin, they were alike in that they were good sources of vitamin B₁. Their values in this respect were determined by separate assay on pigeons.³ The test substances were dried yeast,[†] wheat germ,[‡] and an adsorbate similar to the international standard (1934) but made with Lloyd's reagent instead of ordinary fullers earth.[§] In

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¹ These are reviewed by Dann, M., and Cowgill, G. R., in the *Arch. Int. Med.*, 1938, **62**, 137.

² Cowgill, G. R., *Am. J. Physiol.*, 1923, **66**, 164.

³ Block, R. J., Cowgill, G. R., and Klotz, B. H., *J. Biol. Chem.*, 1932, **94**, 765.

[†] From the Northwestern Yeast Company, Chicago, Ill.

[‡] Embo, a product of General Mills, Inc., Minneapolis, kindly supplied by Dr. C. H. Bailey, Director of Research.

[§] Kindly supplied by Dr. H. W. Rhodehamel, Director of Research Laboratories, Eli Lilly Company, Indianapolis, Ind.

a few instances a concentrate,|| which could be given parenterally when necessary, was tried.

After each of the 3 widely different sources of the vitamin had been tested on 7 dogs under "normal" conditions, the animals were fed a stock diet and morphine administration begun.¶ The initial dose was 10 mg per kilo, which was increased as tolerance permitted, first to 20 mg per kilo, and finally to 30 mg per kilo. When tolerance for this greatest dose was so well developed that the dogs appeared to enjoy "normal" health, the animals were again fed the artificial B₁-deficient diet, the tissues saturated with vitamin B₁ as described above, and the same sources of the vitamin retested for their effects on the anorexia. Finally, wherever possible, following a long period during which the drug had been withdrawn and the animals appeared to have returned to an essentially "normal" state, the tests were repeated. These final trials were not possible in all cases because many dogs died suddenly for reasons not evident on gross examination or at autopsy.

The results yielded no evidence that chronic morphinism *per se* increases the dog's requirement for vitamin B₁.

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Influence of Ingestion of Raw and Desiccated Pancreas Upon Blood Lipids During Infection.*

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It has been shown that there is a definite lowering of the levels for the plasma lipids at height of an acute infection as compared with the values obtained during convalescence.¹ There is, however, a tendency for the lipid content of the blood plasma to rise very

|| Made according to the method of Stuart, E. H., Block, R. J., and Cowgill, G. R., *J. Biol. Chem.*, 1934, **105**, 463, and kindly furnished by Dr. H. W. Rhodhamel.

¶ I wish to thank Dr. Henry G. Barbour of the Laboratory of Pharmacology for supervising the morphinization of these animals.

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¹ McQuarrie, Irvine, and Stoesser, A. V., *PROC. SOC. EXP. BIOL. AND MED.*, 1932, **29**, 1281.