macodynamic action. These groups are essential for the activity of the lactogenic hormone.

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THE EFFECT OF COCARBOXYLASE UPON METABOLISM AND NEURO-PSYCHIATRIC PHENOMENA IN PELLAGRINS WITH BERIBERI[1]

THE present communication is a report of observations on eight selected cases of pellagra with beriberi which were studied from chemical, neurological and psychiatric standpoints. Preceding and following the administration of cocarboxylase, each patient was studied repeatedly by the following methods: (1) Analysis of blood samples for metabolites, including sulfite combining substances. (2) Neurological examination, including chronaximetric measurement. (3) Estimation of the psychiatric status.

The intravenous administration of 50 milligrams of cocarboxylase (Merck) to persons who exhibited signs of an "active process" was followed, in every instance, by dramatic and rapid improvement. The bisulfite-binding substances decreased in quantity. The pathological signs of peripheral and cranial nerves, which had become increased in patients who were being treated with nicotinic acid and riboflavin, became less conspicuous or disappeared. The irritability of a number of muscles, measured in terms of their strength-duration curves, returned from underexcitability before treatment to normal values and in some cases even progressed to overexcitability. Correspondingly, the increased threshold of sensibility to touch and prick in arms and legs was reduced to normal, and the depressed pupillary and corneal reflexes improved quantitatively, often becoming normal.

Following the administration of cocarboxylase, some beneficial effect occurred, in some persons within an hour and in all persons within four hours. Improvement continued for from one to four days thereafter. Since the unbalanced diets of these persons remained essentially unchanged, in the absence of further therapy the patients tended to regress rapidly to their condition preceding treatment. A psychoneurotic syndrome which was recognized in these persons and which responded promptly to the administration of cocarboxylase will be described separately. In contrast, in the persons selected for control, there was no decrease of bisulfite-binding substances in the blood and no improvement in the neurological and psychoneurotic symptoms following cocarboxylase therapy.

The present study shows that the neuropathy accompanying pellagra represents a clinical entity (beriberi), distinct from a deficiency of nicotinic acid or of riboflavin. It shows also that cocarboxylase (pyrophosphate of thiamin) has a striking effect upon certain intermediate products of carbohydrate metabolism and induces improvement in the affected peripheral and cranial nerves. Furthermore, the decrease of bisulphite-binding substances in the blood is accompanied by a decrease or disappearance of certain neurological signs and of psychoneurotic symptoms.

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EVIDENCE FOR THE EXISTENCE OF A RESPIRATORY NEUROHORMONE

IN the course of studies on the pressor effects of acetylcholine, it was observed that amounts of acetylcholine which produce pressor effects and contraction of the nictitating membrane also increase the rate and depth of respiration for brief intervals. It was also observed that the larger the dose of acetylcholine the longer the duration of respiratory stimulation and the greater the depth of respirations. The pressor effect always outlasts the respiratory stimulation.

The minimum amounts of acetylcholine producing respiratory stimulation in atropinized dogs and cats are 0.15 to 0.2 mgm or more per kilogram, but in the presence of optimum amounts of eserine (about 1.5 mgm per kilogram) as little as 0.005 mgm of acetylcholine may produce respiratory stimulation. If 0.05 mgm of acetylcholine is used throughout in atropinized animals, the smallest dose of eserine which is required to produce respiratory stimulation from this amount of acetylcholine is 0.04 to 0.05 mgm per kilogram. In the same animals doses of epinephrine which produced blood pressure elevation and withdrawal of the nictitating membrane also caused a decrease but never an increase in the rate of respiration.

In five cats and eight dogs the carotid sinuses were removed and in some of these animals the vagi above the ganglia nodosa as well as the sympathetics above the superior cervical ganglia were sectioned. In these animals, which were treated with atropine and eserine,

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