Effect of B-Complex Vitamins on Conditional Reflexes in Dogs

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The stimulus for my interest in the effect of vitamin deficiencies on behavior came from the work of Dr. Max Wintrobe about 1940. After witholding for several months some of the vitamin B-complex from pigs, he noted the development of ataxia and other neurologic symptoms as well as changes in the motor cells of the spinal cord.[1-4] But the methods of examination did not permit an adequate evaluation of behavioral changes.

The reverse effect—of stress on eating habits—had already been observed in my studies of neurotic dogs. Thus, in one such dog I had seen negativism, hyperacidity, and refusal of food in a stress situation.[5] Other dogs became depressed from emotional shocks and did not eat for four or five days, and one young dog taken away from its home practically starved itself in the laboratory, ate again when returned home, and finally died in the laboratory from grief and starvation. We have a dog ("V3"), born in the laboratory, who in a period of over five years (since 1950) has never accepted food when any person is standing nearby. This includes the *Diener* who has always fed the dog and has never been involved in the experimentation. Dog V3 developed a "catatonic" condition several years ago with *cerea flexibilitas*, immobility, and sexual impotency except under alcohol.[6]

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Concluding from the neuro-anatomic changes in Wintrobe's pigs that these neurologic changes would most likely be accompanied by impairment of the higher nervous activity measurable by the conditional reflex function, we undertook a study with Dr. Wintrobe on dogs.

METHODS AND OBSERVATIONS

Four dogs were subjected to a diet deficient in pantothenic acid or pyridoxine. These animals had been in the laboratory for several years during which time they elaborated conditional reflexes to different auditory stimuli connected with faradic shock to the foreleg (Fig. 1). When the animals had maintained a 100 per cent differentiation between two tones for some months they were given the deficient diet, which was quantitatively and qualitatively exactly the same as the control diet except that the vitamins, which had been given in capsules, were now omitted. After 4 to 15 days the animals showed disturbances in the conditional reflexes which became progressively worse; this disturbance consisted in failure to differentiate, notwithstanding repeated practice (Figs. 2 and 3). There were no observable behavioral or demonstrable neurologic changes (hopping, placing, tendon, or sexual reflexes). Return to the adequate diet restored the differentiation.

After several months of perfect differentiation the dogs were again put on the same deficient diet and there was again an impairment of conditional reflex equilibrium which was restored to normal a second time when the animals were returned to the adequate diet. Noteworthy was the loss of equilibrium between the conditional reflexes without any other observable changes in behavior of blood.

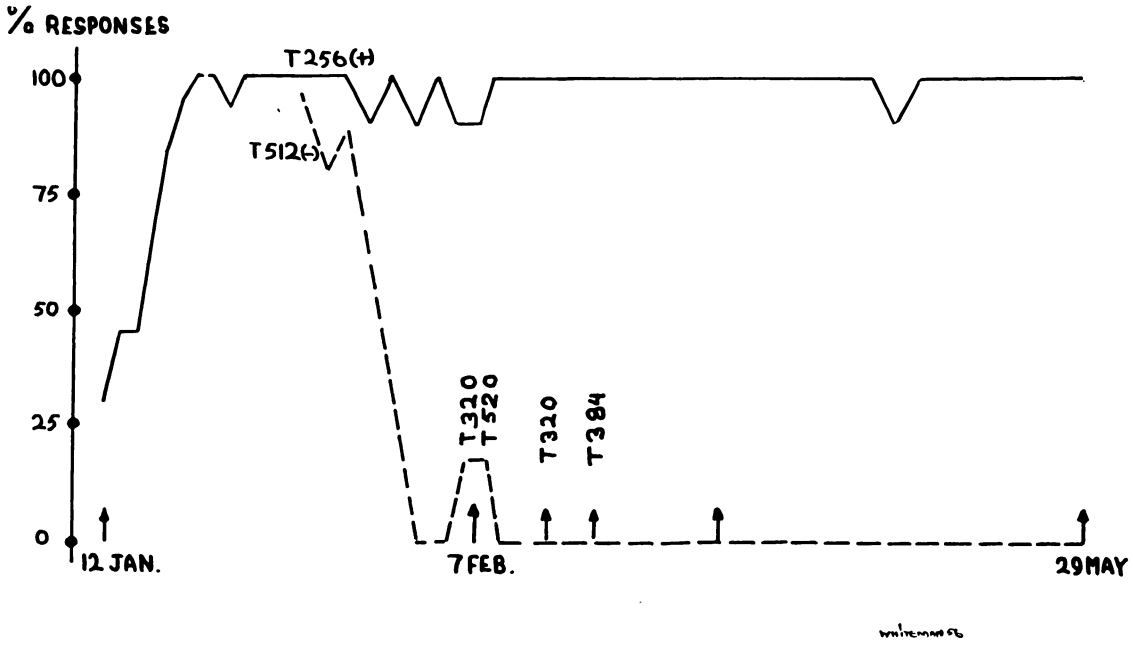

Fig. 1. Formation of excitatory conditional responses to T256+ (followed by shock) and inhibitory conditional responses to T512−, T320−, T520− and T384− (not followed by shock). Solid line shows the excitatory and the dotted line the inhibitory conditional responses. Perfect differentiation is 100 per cent for T256+ and 0 per cent for T512−.

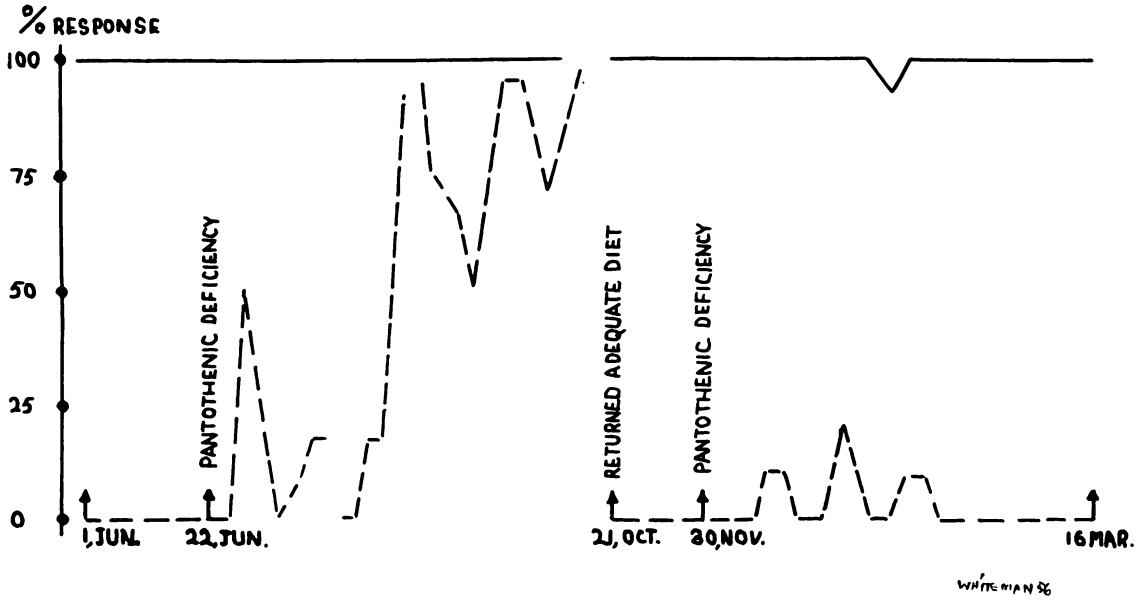

Fig. 2. Effect of pantothenic acid deficiency. Impairment of differentiation between T256+ (solid line) and T512− (dotted line) in four days after deficient diet. Perfect differentiation after return to an adequate diet. Subsequent deficient diet, November 30, causes less impairment.

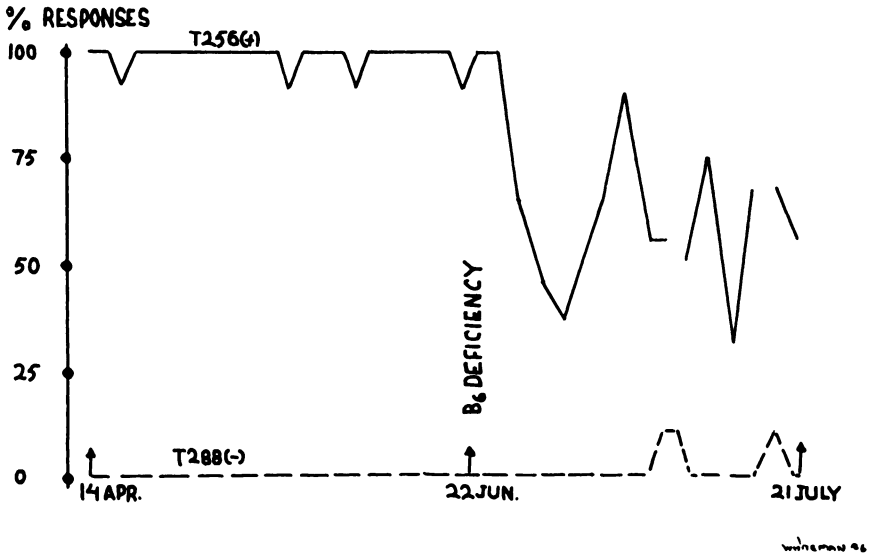

Fig. 3. Effect of pyridoxine deficiency. Note marked impairment differentiation within a few days after deficient diet, becoming worse during the next month.

DISCUSSION

Comparing the effect of this vitamin deficiency with other procedures we have used in the laboratory, the impairment in conditional reflex function is greater than that produced by 2 ml alcohol/kg although alcohol caused both marked neurologic changes including ataxia and personality modification. The effect is about the same as 3–5 mg/kg of morphine but morphine caused in addition a loss of equilibrium, drowsiness, and neurologic changes.[7] The loss of ability for differentiation is greater than that resulting from the exposure of the dog to an altitude of 18,000 feet for four hours and is equivalent to the effect of anoxemia caused by exposing the dogs to an altitude of 25,000 feet.[8] However, the impairment from anoxemia may last several months or may be irreversible, especially in old dogs, while the impairment from the vitamin deficiency is strictly temporary, being restored to normal within a few days after the return to an adequate diet.

Comparing the action of pantothenic acid deficiency with other agents, such as alcohol, morphine, mescaline, and anoxemia, this vitamin lack is almost entirely devoid of action on any measured function other than the conditional reflexes. This function, however, may be considered comparable to mental alertness and ability for learning. In hypothyroidism in humans we have shown that the conditional reflex function is markedly impaired, but that after thyroid extract administration it returns to normal parallel to blood cholesterol and basal metabolic rate.[9] Thus we may conclude that although a few days to a month of complete deprivation of pantothenic acid or pyridoxine may produce no neurologic or blood changes, this deficiency may seriously impair a mental function. This function is restored to normal, however, after a few days by the addition of the deficient vitamin to the diet.

REFERENCES

1. Wintrobe, M., Miller, J. L., Jr., and Lisco, H.: Relation of diet to occurrence of ataxia and degeneration in the nervous system of pigs. *Bull. Johns Hopkins Hosp.* 67: 377, 1940.
2. Wintrobe, M.: Thiamine deficiency in swine. *Bull. Johns Hopkins Hosp. 71*: 141, 1942.
3. Wintrobe, M.: Sensory neuron degeneration in pigs; protection afforded by calcium pantothenate and pyridoxine. *J. Nutrition* 24: 345, 1942.
4. Wintrobe, M.: Attempts to produce pernicious anemia experimentally. *New Eng. Med. Center* 3: 13, 1941.
5. Gantt, W.: *Experimental Basis for Neurotic Behavior.* Paul B. Hoeber, New York, 1944, p. 211.

6. GANTT, W.: Effect of alcohol on sexual reflexes of normal and neurotic male dogs. *Psychosom. Med.* 16: 174, 1952.
7. STEPHENS, J. H., and GANTT, W.: Effect of morphine on behavior. *Bull. Johns Hopkins Hosp.* 98: 245, 1956.
8. GANTT, W., THORN, G., and DORRANCE, C.: Anoxia on conditional reflexes in dogs. *Fed. Proc.* 8: 53, 1949.
9. GANTT, W., and FLEISCHMANN, W.: Effect of thyroid therapy on the conditional reflex function in hypothyroidism. *Am. J. Psychiat.* 104: 676, 1948.