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Thiamin Excretion Tests in Children with Paralytic Poliomyelitis.

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A most important question concerning the natural history of human poliomyelitis is: Why do most individuals infected with poliomyelitis virus escape paralysis, the contact with virus being expressed in them by the non-paralytic, abortive, or inapparent forms of the disease? One answer frequently given is that an immunity has been achieved as the result of previous repeated exposure to subinfective doses of virus, but there is no evidence that subinfective doses *(i.e.,* those which fail to initiate virus multiplication) give rise to immunity. Another possible explanation is that in individuals without previous contact with the virus, certain tissues may be unfavorable sites for optimum virus multiplication, thus presenting a barrier against further progression and dissemination.[1,2] It has been shown that with certain viruses and certain tissues the development of such constitutional barriers is related to growth and maturation of the host.[1,2] Furthermore, in mice the development of some of these barriers during the rapidly growing period may be prevented or retarded by either general malnutrition or specific dietary deficiencies of thiamin, riboflavin, and presumably other factors.[2,3]

Studies concerning the influence exerted by vitamins C and D on the course of experimental poliomyelitis have yielded various results.[4,5,6] However, more recent investigations have indicated (1), that vitamin C fails to modify the course of poliomyelitis produced in monkeys by the nasal instillation of virus,[7] and (2), that a deficiency of vitamin D is not essential for the spread of poliomyelitis virus along peripheral nerves.[8]

The possible role of a deficiency of the vitamin B complex or of one of its factors in determining whether the virus-host relationship shall take the form of paralytic or non-paralytic, abortive, or inapparent poliomyelitis deserves careful investigation. The present communication describes studies we have made in 7 patients with paralytic poliomyelitis who were tested for thiamin deficiency by the intravenous thiamin load test of Najjar and Holt.[9] The results obtained were of the same order as those found in normal children.

Procedure. All subjects had clinically typical paralytic poliomyelitis which developed while they were residing in or near Cincinnati during September or October, 1940 and 1941. The tests were performed usually within a day after admission to the hospital, so that a change of diet from that of the home can hardly be considered a factor. For 12 to 24 hr prior to the test the subjects were maintained on water and fruit juice, a regimen providing only minimal quantities of the B vitamins. The load tests were carried out as follows: following emptying of the bladder by catheterization 1 mg of thiamin hydrochloride ("Betaxin"—Winthrop) was injected intravenously. A second catheterization was carried out at the end of 4 hr to obtain the test specimen. In 3 subjects the excretion of thiamin was followed at half hour intervals after the injec-

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TABLE I.
Thiamin Load Tests in Patients with Paralytic Poliomyelitis.

Subject (Sex)	Age (Yrs)	Paralysis: Day of	Paralysis: Extent	Highest temp. on day of test (°F)	μg thiamin in urine excreted during test period following intravenous inj. of 1 mg thiamin: Observations in patients: 1st half hr	2nd half hr	3rd half hr	4th hr	Total 4 hrs	Range in normal control subjects (4-hr period followng test dose)*
C.W. (M)	15	3	Partial; arms, legs	99.9	180	74	24		278	
W.J. (M)	14½	5	Complete; left leg Partial; arms, right leg	99	231				231	109-236 (Avg 180)
T.D. (M)	14	4	Partial; right arm, legs	98.6				244	244	
G.S. (M)	7	3	Partial; right arm Complete; legs	99.5				95	95	
G.N. (M)	5	10	Partial; legs	101.2	101	74	24		199	150-246
A.G. (M)	2¼	8	Complete; left leg	99.7	139	18	7		164	(Avg 207)
N.W. (F)	1 11/12	4	Partial; left leg	100.5				311	311	260-338 (Avg 302)

*Najjar and Holt.[9]

tion for 1½ hr, these specimens being likewise obtained by catheterization. The urine specimens were preserved with an equal volume of 3% acetic acid and sent by air express to Baltimore. Thiamin was measured by the thiochrome method developed by Jansen[10] and modified by Hennessy and Cerecedo.[11]

Results. In Table I are given the figures for thiamin excretion in these patients, as well as figures for a series of normal controls of various age groups which were tested by Najjar and Holt[9] with this same load test. It will be noted that 6 out of the 7 poliomyelitis patients showed figures within the normal range, and the seventh patient excreted a quantity of thiamin which was only slightly below this. It would thus appear that thiamin deficiency was not a factor in the development of the paralytic form of the disease in these subjects.

Before accepting this conclusion unreservedly it is necessary to consider certain other factors which may influence thiamin load tests. It has been shown[9] that with impaired renal function a test dose of thiamin is less rapidly excreted, the peak of excretion being reached only after 2 or 3 hr, instead of during the first half hour as in the normal subject. However, the total 4-hr thiamin excretion is not affected unless the renal impairment is extreme. In these poliomyelitis patients no tests of kidney function were made, but there was no evidence, from clinical examination or urinalysis, of any renal disease and the possibility of extreme renal impairment as an interfering factor may therefore be dismissed.

Deficiencies of other B factors may at times affect thiamin load tests, producing abnormal spilling and masking the retention of thiamin which occurs in thiamin deficiency. Najjar and Holt[9] observed abnormally high thiamin excretions in pellagra and in an experimental subject who was deprived of other B factors in addition to thiamin. Inability to utilize injected thiamin under these circumstances causes a characteristic alteration of the thiamin excretion curve; although exceedingly high in the first half hour, it falls promptly to zero, in contrast to the normal subject whose excretion of thiamin remains somewhat elevated for several hours. In order to find out whether this situation was present in the poliomyelitis patients, half-hourly excretion curves were run in 3 subjects. None of them showed the sharp drop to zero after the first half

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[11] Hennessy, D. J., and Cerecedo, L. R., *J. Am. Chem. Soc.*, 1939, **61**, 179.

hour. Specific evidence of nicotinic acid deficiency was sought in 2 other patients (G.S. and T.D.) whose urines were tested for the fluorescent factor F_2 shown by Najjar *et al.*[12] to be absent in nicotinic acid deficiency. These tests, performed on specimens obtained just before the thiamin injection, showed F_2 values of 7 and 20 units per hour respectively, values which preclude the possibility of nicotinic acid deficiency.

Thus, it would seem that nicotinic acid deficiency has not masked any thiamin deficiency in these paralytic patients, nor is nicotinic acid deficiency itself a prerequisite for the development of paralytic poliomyelitis.

It is possible that deficiencies of other B factors may contribute to the development of paralysis in this disease. In this connection it is of interest to call attention to recent evidence suggesting that in the nervous system of the pig certain changes attributed in other hosts to thiamin deficiency may be due to lack of other vitamin B factors such as pyridoxine and pantothenic acid.[13,14] Although the components of the B complex are usually found together in foodstuffs and the occurrence of a deficiency related to only one member of the vitamin B group is very rare,[15] it will, nevertheless, be necessary to determine the presence or absence of possible deficiencies of one or more of the other vitamin B factors before the relationship of the status of vitamin B nutrition to paralytic poliomyelitis can be completely evaluated.[16,17,18]

Summary. The results of thiamin excretion tests in 7 children having paralytic poliomyelitis did not differ in the main from those found in normal children. This finding indicates that the status of thiamin nutrition need not be a factor in determining whether infection by poliomyelitis virus shall result in the paralytic, or in one of the non-paralytic forms of the disease. Some evidence has also been obtained that nicotinic acid deficiency need not be a prerequisite for the development of the paralytic form of the disease. The role of other members of the vitamin B complex in relation to paralytic poliomyelitis remains to be investigated.

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Effect of p-Aminobenzoic Acid when Added to Purified Chick Diets Deficient in Unknown Vitamins.*

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Ansbacher[1] has reported that p-aminobenzoic acid is a growth-promoting factor for the chick. The basal diet which he used was a vitamin K deficient ration consisting largely of wheat middlings and yellow corn heated at 110° for about one week. Hammond, Miller and McClure[2] found that p-aminobenzoic acid is necessary for the

* Published with the approval of the Director of the Wisconsin Agricultural Experiment Station. Supported in part by grants from the Wisconsin Alumni Research Foundation and Swift and Company.

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2 Hammond, J. C., Miller, D., and McClure, H. E., *Poultry Sci.*, 1942, **21**, 185.