

Vitamin E Deficiency and Seizures in Animals and Man

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SUMMARY: *Study of 100 children with grand mal convulsive disorders and 100 medically healthy children of matching age showed significantly lower plasma levels of vitamin E in the former (means 632.2 ± 17.3 and $822.5 \pm 21.8 \mu\text{g/dl}$ respectively; $p < 0.001$). This finding accords with the ability to prevent seizures in rodents by giving α -tocopherol before exposing them to a convulsion-inducing environment.*

RÉSUMÉ: *Une étude de 100 enfants souffrant d'épilepsie type grand mal comparés à 100 enfants du même âge médicalement normaux a révélé une baisse significative de la vitamine E chez les premiers (moyennes 632.2 ± 17.3 et $822.5 \pm 21.8 \mu\text{g/dl}$ respectivement, $p < 0.001$). Ce résultat est en accord avec le fait que le traitement préalable par α -tocopherol chez les rongeurs prévient les crises convulsives lorsque ce traitement est donné avant d'exposer les animaux à un environnement convulsivant.*

INTRODUCTION

Probably no vitamin has commanded more public attention or been the subject of more clinical controversy than vitamin E, a natural nutrient with no known toxic effect. However, its reported effects in relation to seizure-susceptibility (Behnke, 1940; Jerrett et al., 1973) appear to have attracted little notice.

The present study stemmed from the chance observation of a low plasma level of vitamin E in a mentally retarded child with seizures.

MATERIALS AND METHODS

Plasma vitamin E was assayed by a modification of the method devised by Bieri et al. (1970).

Preliminary experiments on blood of known vitamin E content were conducted to examine whether anticonvulsant drugs interfere with assay of the vitamin in plasma. Each sample was divided into four portions, high concentrations of diphenylhydantoin and phenobarbital were added, and the vitamin E content of each aliquot was re-assayed.

Two hundred children were studied: 100 had grand mal convulsive disorders (study group) and 100 were medically healthy (controls). They were subdivided by age, 2-6 years (52 in each group) and 8-12 (48 in each group), and their plasma vitamin E levels and serum cholesterol were determined.

STUDY PATIENTS

Their sole medication was anticonvulsant drugs, singly or in combination; all other drugs, particularly iron, were excluded. They had no gastrointestinal problems such as diarrhea or malabsorption, and no evidence of liver disease. The following data were taken from hospital records: anticon-

vulsant medication, dosages, and duration; degree of control of the epilepsy, serum anticonvulsant levels, electroencephalogram reports, and developmental assessment (including presence or absence of mental retardation).

CONTROL SUBJECTS

These patients had been admitted for minor surgical procedures. They were otherwise apparently healthy, with no medical problems and on no medication. Blood samples were taken from those withdrawn for routine tests.

RESULTS

As expected, assay of the experimental samples showed no change in vitamin E content after the addition of high or low concentrations of either anticonvulsant drug. (Vitamin E does not partition with these drugs and does not interfere in their chromatographic assay.)

Intergroup comparison showed virtually identical mean serum cholesterol values, but significantly different plasma vitamin E levels (Fig. 1). In the control group, these latter values were distributed normally and tended to increase with age throughout the range studied (Fig. 2A). In the study group, values were not significantly different from control between 2 and 6 years of age but levelled off at 8 years and then tended to fall slightly (Fig. 2B). Mean values in relation to age are shown in Fig. 3.

None of the other investigations yielded useful information. In particular, there was no correlation between dosage and duration of anticonvulsant therapy and its degree of control of the epilepsy in relation to plasma vitamin E levels. These findings have been reported in detail (Ogunmekan, 1977).

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FIGURE 1

Mean Plasma Levels of Serum Cholesterol and Plasma Vitamin E (\pm SE) in the Two Groups

	Study group	Controls	P
Serum cholesterol (mg/dl)	159.6 \pm 2.5	159.4 \pm 2.5	N.S.
Plasma vitamin E (μ g/dl)	632.2 \pm 17.3	822.5 \pm 21.8	< 0.001

N.S., not significant

FIGURE 3

Mean Plasma Vitamin E (\pm SE) in Relation to Age-group

	Controls	Plasma vitamin E (μ g/dl)		n	p
		n	Study Group		
2-6 yr	726.9 \pm 22.6	52	671.2 \pm 22.0	52	N.S.
8-12 yr	926.0 \pm 32.3	48	604.8 \pm 26.4	48	< 0.001

N.S., not significant

DISCUSSION

Exposure to 100% oxygen induces seizures in rats and mice (Jerrett et al., 1973) and can cause convulsions in man (Behnke, 1940), but Jerrett et al. (1973) found that they could prevent the seizures by prior administration of α -tocopherol, an anti-oxidant. In their experiments, seizures occurred in 100% of vitamin E deficient rats and in 50% of those fed a normal diet, but none developed in rats fed a diet containing an α -tocopherol supplement.

Investigation of various possible causal factors to account for the low plasma levels of vitamin E in the study group has shown no correlation so far (Ogunmekan, 1977). Another possibility (not investigated) is that the low levels may reflect differences in rates of metabolism of the vitamin and anticonvulsant agents.

Studies are continuing of children with severe epilepsy refractory to treatment despite anticonvulsant drug

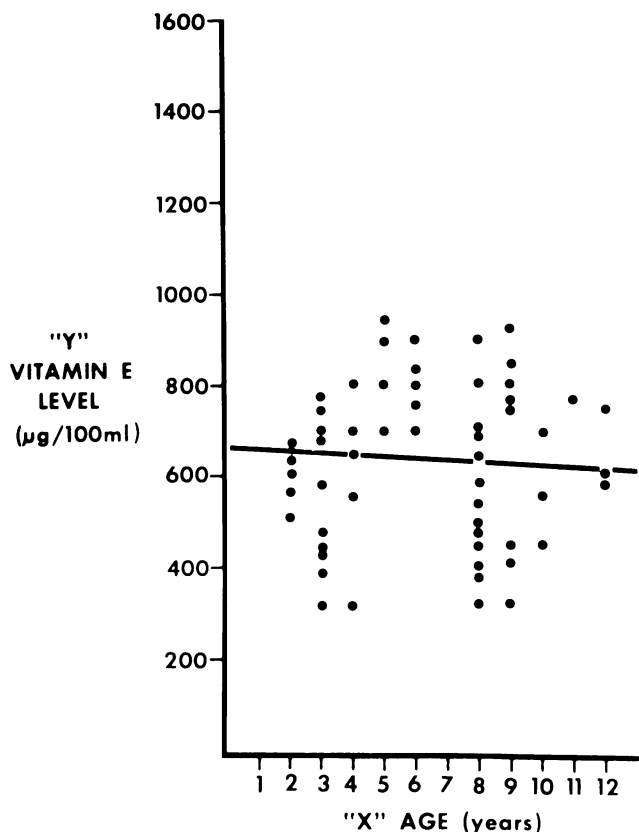


Figure 2A — Plasma vitamin E levels in relation to age in study group. Some dots represent more than one patient with identical levels.

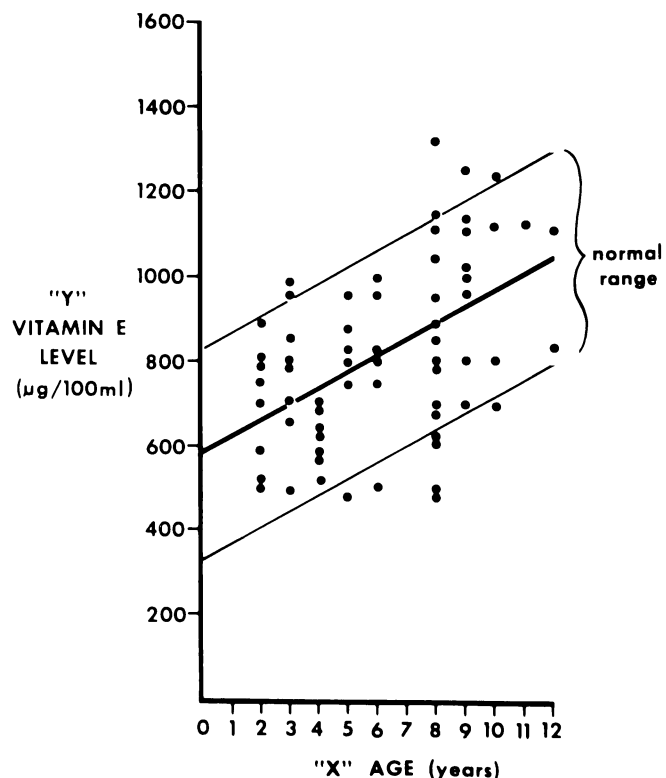


Figure 2B — Plasma vitamin E levels in relation to age in control group. Some dots represent more than one patient with identical levels.

blood levels usually considered to be in the therapeutic range. Supplements of α -tocopherol might improve seizure control in such patients.

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