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THE ACTIVITIES OF COENZYME Q_{10} AND VITAMIN B_6 FOR IMMUNE RESPONSES

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SUMMARY Coenzyme Q_{10} (CoQ_{10}) and vitamin B_6 (pyridoxine) have been administered together and separately to three groups of human subjects. The blood levels of CoQ_{10} increased ($p<0.001$) when CoQ_{10} and pyridoxine were administered together and when CoQ_{10} was given alone. The blood levels of IgG increased when CoQ_{10} and pyridoxine were administered together ($p<0.01$) and when CoQ_{10} was administered alone ($p<0.05$). The blood levels of T4-lymphocytes increased when CoQ_{10} and pyridoxine were administered together ($p<0.01$) and separately ($p<0.001$). The ratio of T4/T8 lymphocytes increased when CoQ_{10} and pyridoxine were administered together ($p<0.001$) and separately ($p<0.05$). These increases in IgG and T4-lymphocytes with CoQ_{10} and vitamin B_6 are clinically important for trials on AIDS, other infectious diseases, and on cancer.

For almost 50 years, the essentiality of vitamin B_6 to immune responses has been known. In 1990, Chandra and Sudhakaran (1) recorded a comprehensive account of these decades of international investigations of the regulation of immune responses by vitamin B_6. In 1955, Stoerk (2), a colleague of Harris and Folkers, showed that a deficiency of vitamin B_6 caused a severe withering of the thymus in rats; the latter two investigators had described the first organic synthesis of pyridoxine only in 1939 and had the synthetic vitamin available for animal experimentation; Ott (3), Emerson (4). Stoerk had observed the thymus of such rats to be virtually free of lymphocytes. At the human level, Dobbelstein et al. (5) reported in 1974 that the lymphoid cells from vitamin B_6-deficient patients exhibited diminished cell-mediated immune responses. In 1984, Casciato et al. (6) reported that therapy with pyridoxine caused improvement in immunologic abnormalities in patients.

Vitamin B_6 as a coenzyme, pyridoxal 5'-phosphate (PLP), is apparently essential in the biosynthesis of coenzyme Q_{10} in the

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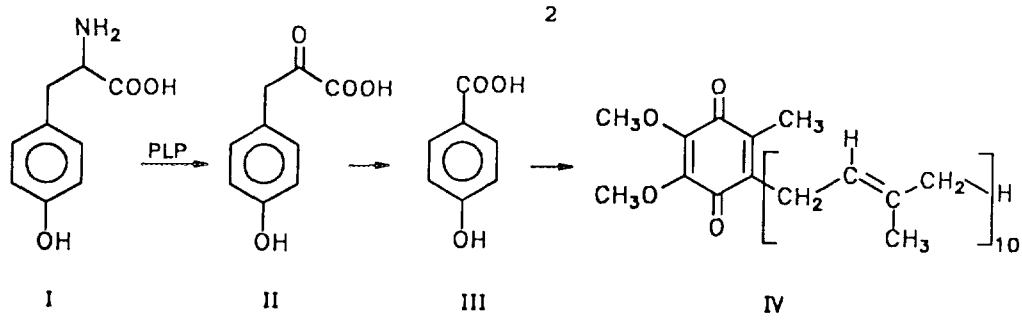
human body. Tyrosine, I, is converted into p-hydroxybenzoic acid, III, by enzymic mechanism apparently involving pyridoxal 5'-phosphate. Then, III is converted to coenzyme Q_{10}, IV, by a series



I II III IV

of sequential reactions, requiring other vitamins, as described by Friis et al. (7). Therefore, it is plausible that a human deficiency of vitamin B_6 could include a diminution in the biosynthesis of coenzyme Q_{10} in the human body, and cause metabolic dysfunctions or diseases due to the deficiency of coenzyme Q_{10}.

Due to the essential involvement of vitamin B_6 in the biochemistry of the amino acids, and the existence of the amino acids in the structures of the antibodies, it is relevant, in overview, that vitamin B_6 is indispensable for the immune responses of T-lymphocytes from the thymus and for the humoral antibody responses from B-lymphocytes from the bone marrow.

Because of the chemical relationship between coenzyme Q_{10} and vitamin B_6 in biosynthesis, and because of the essentiality of vitamin B_6 to the biochemistry of both the B-lymphocytes and the T-lymphocytes, we have studied, for the first time, the effect of the administration of coenzyme Q_{10} and vitamin B_6 together and separately to three groups of human subjects.

PROTOCOL OF STUDY Thirty-three human volunteers, 11 males and 22 females, ranging in age from 30 to 75, participated in this study. One group (N=13) was treated orally with 200 mg/day of CoQ_{10} and 300 mg/day of pyridoxine. Another group (N=11) was treated with 200 mg/day of CoQ_{10}, and another group (N=9) was treated with 300 mg/day of pyridoxine. Although it was recommended to the subjects that they take these two vitamins, appropriately, and daily, it is certain that compliance was not perfect everyday for two months, as based upon the blood levels of CoQ_{10} and the assay of EGOT. There were only two analyses of blood samples, the first as control and the second after two months. In general, compliance was regarded as "ordinary". The data are in Table I.

Table I. Mean and S.D. of biological parameters

Biological Parameters	Stage	Group Q_{10}+ B_6	Q_{10} Only	B_6 Only
CoQ_{10} (μg/mL)	Baseline	0.72±0.29	0.80±0.27	0.77±0.18
	2-Month	1.89±0.70***	2.16±0.72***	0.82±0.25
B_6; Basal S.A.	Baseline	0.40±0.16	0.34±0.08	0.32±0.08
	2-Month	0.70±0.15***	0.34±0.10	0.66±0.13***
B_6; S.A. +PLP	Baseline	0.45±0.11	0.45±0.08	0.45±0.06
	2-Month	0.66±0.12***	0.44±0.09	0.62±0.10**
B_6 %Def.	Baseline	13.3±15.9	22.3±16.8	27.7±18.3
	2-Month	-5.2± 7.3***	24.1± 9.9	-6.2±10.9***
IgG (mg/dL)	Baseline	884± 194	1018± 276	757± 176
	2-Month	970± 180**	1104± 285*	790± 153
T4(%)	Baseline	52.3± 6.7	48.6±12.1	49.2± 7.6
	2-Month	59.5± 6.0**	59.4±11.6***	58.7± 9.8***
T8(%)	Baseline	22.3± 5.6	26.0± 9.3	22.7± 7.5
	2-Month	21.9± 5.4	23.6± 6.7	22.3± 5.0
T4/T8	Baseline	2.51±0.76	2.20±1.40	2.41±0.88
	2-Month	2.92±0.87***	2.95±2.07*	2.81±1.03*

Significantly different from baseline
(*:p<0.05, **:p<0.01, ***:p<0.001).

METHODS The level of CoQ_{10} in whole blood was determined as described by Ye et al. (8). The levels of T4- and T8-lymphocytes were determined as described by Parker et al. (9). The levels of IgG in serum were analyzed using the reagent kits and Immunochemistry Analyzer of Beckman Immunochemistry System, Fullerton, California.

The S.A. of EGOT was determined as described by Kishi and Folkers (10). Following the research of Brin et al.(11) on determining a deficiency of thiamine by the enzyme activity of a transketolase in hydrolysates of erythrocytes, Kishi and Folkers(10) determined a deficiency of vitamin B_6 by an assay of the glutamic oxaloacetic transaminase. Folkers (12) defined the principle of this enzymic methodology for the detection and measurement of a vitamin deficiency as follows: "the specific activity of a coenzyme-apoenzyme system is differentially assayed in the absence and in the presence of added coenzyme". A significant increase in the specific activity of the enzyme system in the presence of added coenzyme measures a deficiency of the coenzyme (Table I). The basal specific activity (S.A.) of the erythrocyte glutamic oxaloacetic transaminase (EGOT) is a measure of the functionality of vitamin B_6. The assay is then repeated in the presence of the coenzyme, pyridoxal 5′ -phosphate (PLP), which is a measure of a deficiency of the coenzyme in the enzyme system. The per cent deficiency of B_6 functionality is the assay with PLP less the assay without PLP, divided by the assay with PLP x 100.

DISCUSSION OF RESULTS The blood levels of CoQ_{10} significantly increased ($p<0.001$) over two months when CoQ_{10} and pyridoxine were administered together, and when CoQ_{10} was administered alone. The blood level of CoQ_{10} did not change when pyridoxine was administered alone.

As a measure of an effective blood level of vitamin B_6, the assay data of EGOT after two months of administration of pyridoxine were interpreted. The S.A. of EGOT had significantly increased ($p<0.001$) when coenzyme Q_{10} and vitamin B_6 were administered together, and when pyridoxine was administered alone. The S.A. of EGOT were maximal as recorded by Folkers et al. (13).

The blood levels of IgG, over two months, significantly increased ($p<0.01$) when CoQ_{10} and B_6 were administered together and significantly increased ($p<0.05$) when CoQ_{10} was administered alone, but did not significantly increase when pyridoxine was administered alone.

The blood levels of T-4 lymphocytes significantly increased ($p<0.01$) when CoQ_{10} and pyridoxine were administered together and significantly increased ($p<0.001$) when CoQ_{10} was administered alone and most notably, significantly increased ($p<0.001$) when pyridoxine was administered alone.

The blood levels of T-8 lymphocytes did not significantly increase over two months when CoQ_{10} and pyridoxine were administered together and separately.

The T4/T8 ratio significantly increased ($p<0.001$) over two months when CoQ_{10} and pyridoxine were administered together and significantly increased ($p<0.05$) when CoQ_{10} and pyridoxine were administered separately.

The failure, in this study, to record an increase in the levels of IgG when pyridoxine was administered alone may be because of erratic compliance or because the pyridoxine was administered for only two months. In a prior study of treating patients with the carpal tunnel syndrome with pyridoxine, a period of three months was required for statistically significant clinical improvement of the deficiency syndrome (14). A period of administration of two months of pyridoxine did suffice for an increase of T-4 lymphocytes in the thymus, but not for a humoral antibody response of B-lymphocytes in the bone marrow.

Langsjoen et al. (15) reported that the levels of CoQ_{10} in whole blood was significantly and severely depressed in patients with the acquired immune deficiency syndrome (AIDS). The blood

level of CoQ_{10} appeared to be lower in those exemplary patients having a more severe clinical disease of AIDS. Such patients have been on CoQ_{10} therapy for about three years with excellent clinical response and no evidence of opportunistic infection.

Folkers et al. (16) summarized clinical data on the survival of ten cancer patients on therapy with CoQ_{10}. Two such cases had experienced survivals for periods of 5-15 years.

The new data herein on the activities of CoQ_{10} and vitamin B_6 for immune responses are fundamental and strongly supportive of new protocols on treating AIDS and other infectious diseases and cancer with CoQ_{10} and with CoQ_{10} and vitamin B_6 together.

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