Vol. 192, No. 1, 1993 BIOCHEMICAL AND BIOPHYSICAL RESEARCH COMMUNICATIONS
April 15, 1993 Pages 241-245

SURVIVAL OF CANCER PATIENTS ON THERAPY WITH COENZYME Q_{10}

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Received February 23, 1993

SUMMARY - Over ca. 25 years, assays in animal models established the hematopoietic activities of coenzyme Q's in rhesus monkeys, rabbits, poultry, and children having kwashiorkor. Surprisingly, a virus was found to cause a deficiency of CoQ_9. Patients with AIDS showed a-"striking"-clinical response to therapy with CoQ_{10}. The macrophage potentiating activity of CoQ_{10} was recorded by the carbon clearance method. CoQ_{10} significantly increased the levels of IgG in patients.

Eight new case histories of cancer patients plus two reported cases support the statement that therapy of cancer patients with CoQ_{10}, which has no significant side effect, has allowed survival on an exploratory basis for periods of 5-15 years. These results now justify systematic protocols.

INTRODUCTION - The data and potentiality are updated herein on the therapy with coenzyme Q_{10} (vitamin Q_{10}) of patients with diverse forms of cancer, and with eight new case reports which emphasize an apparent increase in survival. This biomedical and clinical research is based entirely upon concepts of biochemical mechanisms which intrinsically support the immune system, and not upon concepts of the classical medicinal chemistry of anti-tumor drugs which are foreign to the human body.

HEMATOPOIETIC ACTIVITY OF COENZYME Q_{10} - Fitch and Folkers et al., 1965 (1) reported the first and very significant revelation of the hematopoietic activity of coenzyme Q_{10} in young rhesus monkeys which were anemic. They added that the hematopoietic activities of vitamin E and of the chromanol of hexahydrocoenzyme Q_4 were on the basis of the antioxidant activities of these two chromanols which could protect a level of CoQ_{10}. The anemia of this monkey model occurs under a dietary restriction and limitation in the biosynthesis of CoQ_{10}. Farley and Fitch et al., 1967 (2) reported the hematopoietic activity of hexahydrocoenzyme Q_4 in six anemic monkeys by positive reticulocytosis and elevation of hemoglobin levels. They considered that H_6CoQ_4 was substituting for the intrinsic CoQ_{10} of the monkey, because H_6CoQ_4 has coenzymatic bioenergetic activity.

0006-291X/93 $4.00

HEMATOPOIETIC ACTIVITY OF H_6CoQ_4 IN THE RABBIT MODEL - Ludwig et al., 1967 (3) reported that H_6CoQ_4 elicited a hematopoietic response in a rabbit model on an antioxidant-deficient diet by significantly effecting bone marrow cell maturation and myeloid precursor cells.

HEMATOPOIETIC ACTIVITY OF CoQ_{10} IN CHILDREN HAVING KWASHIORKOR - Majaj and Folkers, 1968 (4) reported that CoQ_{10} showed hematopoietic activity in children having marasmus or kwashiorkor (protein-calorie malnutrition) by the prolonged hematopoietic response of the peripheral blood and bone marrow. The CoQ_{10}-blood levels of four such anemic children ranged from 0.5-0.6 μg/ml.

HEMATOPOIETIC ACTIVITY OF H_6CoQ_4 IN POULTRY - Larsen and Enzmann et al., 1969 (5) reported that H_6CoQ_4 showed hematopoietic activity by maintaining levels of hemoglobin and packed cell volumes in chicks and turkey pullets, presumably by substituting for the intrinsic CoQ_{10} in the deficiency state.

VIRUS INDUCED DEFICIENCY OF CoQ_9 - Bliznakov and Folkers et al., 1975 (6) surprisingly found a deficiency of CoQ_9 (intrinsic to mice) following infection with the Friend leukemia virus. Significant increases in the deficiency of a CoQ_9-enzyme increased in the spleen and blood of infected animals as the infection progressed. One may consider again today whether the virus of AIDS contributes to a functional deficiency of CoQ_{10} by interfering with CoQ_{10}-enzyme(s) or with the biosynthesis of CoQ_{10}.

DEFICIENCY OF CoQ_9 IN SENESCENCE OF MICE - Bliznakov and Folkers et al., 1978 (7) reported a significant steep escalation of a deficiency of CoQ_9-enzyme activity in the thymus of three groups of aged mice; the thymus weight:body weight ratio significantly decreased in all three groups of aged mice.

PHAGOCYTIC ACTIVITY OF CoQ_{10} IN MICE - Bliznakov et al., 1970 (8) found that 48 hours after an iv. injection of an emulsion of CoQ_{10} that the phagocytic activity in rats was highly enhanced at a low dosage of 750 μg/rat. A 48-hour pretreatment with an emulsion of CoQ_{10} doubled the primary hemolytic antibody tighter at a dose as low as 150 μg/mouse. They concluded that their data pioneered the stipulation of the reticuloendothelial system (RES) by CoQ.

CoQ_{10} REDUCED PARASITEMIA CAUSED BY PLASMODIUM BERGHEI - Bliznakov, 1972 (9) recorded that CoQ_{10} increased survivors and prolonged survival, reduced parasitemia in blood-transferred Plasmodium berghei infection. Bliznakov and Folkers et al., 1975 (10) advanced the data showing a deficiency of a CoQ_9-enzyme in the spleen and blood of mice increased as infection by the Friend leukemia virus progressed.

CoQ_{10} ENHANCES HOST RESISTANCE IN ANIMAL MODELS - Bliznakov, 1976 (11) updated evidence which showed an increased resistance in animal models to bacterial and

protozoal infections, viral and chemically-induced neoplasia, particularly when CoQ_{10} was administered. Bliznakov concluded that the enhanced resistance was mediated by stimulation of the host defense system which requires cellular energy. The depression of the host defense system by chemical agents, by an oncogenic virus, and by senescence was reversed by CoQ_{10}.

CoQ_{10} ACTIVATES MACROPHAGES BY THE CARBON CLEARANCE METHOD - Hogenauer, 1981 (12) recorded the macrophage potentiating activity of CoQ_{10} in a particulate form by the intravenous route by the acceptable carbon clearance method. The macrophage potentiating activity of CoQ_{10} was paralleled by a protection of immune suppressed mice against lethal infections.

CoQ_{10} INCREASED LEVELS OF IgG IN PATIENTS - Folkers et al., 1982 (13) recorded significant increases of levels of IgG by oral capsules of CoQ_{10} in three patients with cancer, four with cardiovascular disease, and one with diabetes mellitus. The daily dosage of 60 mg was apparently too low.

DEFICIENCIES OF CoQ_{10} IN PATIENTS WITH AIDS AND EXPLORATORY THERAPY- Folkers et al., 1988 (14) reported the oral treatment of seven patients with AIDS with CoQ_{10}. Although compliance was poor, and the dosage was too low, the clinical results were encouraging and at times--"striking".

TWO CASE HISTORIES OF SURVIVAL OF CANCER PATIENTS ON CoQ_{10} - Folkers et al., 1993 (15) detailed two case histories of cancer patients with prolonged survival on therapy with CoQ_{10}. Briefly, the results are:

R.G., male, 48 years; diagnosed in 1977 as having inoperable bronchogenic carcinoma of the left lung; small cell type; massive mediastinal metastasis; diagnosis confirmed; started on CoQ_{10} in August, 1978. Negative bone scan in 1989. No evidence of cancer in October, 1992. Exceptional survival for 15 years, 1993.

B.R., female, 46 years; diagnosed as having extremely large and inoperable carcinoma of the rectum; posteriorly fixed to the sacrum; gross tumor remained after two ultimate operations; received CoQ_{10} for over three years with periodic chemotherapy; became disease free. It was concluded that CoQ_{10} may have made possible the extraordinary survival and a disease-free state, based on no evidence of tumor by CAT-scans, bone-scan and CEA levels.

EIGHT NEW CASE HISTORIES OF SURVIVAL OF CANCER PATIENTS ON CoQ_{10} -

W.F.C., male, 74 years, diagnosed with pancreatic carcinoma, October, 1992. He was seen at M.D. Anderson Cancer Center, and no treatment other than pain relief was recommended. His main complaints were back pain, loss of appetite, and weight loss. He has a history of two myocardial infarctions, but has no residual cardiac symptoms and takes no medications. He stopped smoking 25 years ago. His pretreatment CoQ_{10} level was 0.39 μg/ml. He was started on 266 mg of CoQ_{10} (from K. Folkers) daily in divided doses. Subjectively, he feels better, his weight loss has stopped and he is maintaining his weight. His appetite has returned and he feels that his pain is less (January, 1993).

E.K.C., female, 64 years, diagnosed with inoperable adenocarcinoma of both lungs. She has received both radiation therapy and chemotherapy and is felt to be in partial remission. She

has a 50 year-one pack a day smoking history. She has a history of angina and takes Beta Blockers and Nitroderm. Her pretreatment CoQ_{10} level was 0.55 μg/ml. She was started on 266 mg CoQ_{10} (from K. Folkers) in divided doses approximately five weeks ago. She is doing well (January 1993).

D.D.E., male, 67 years, 2½ year history of known laryngeal carcinoma which was treated initially with radiation therapy. He had many follow-up visits with negative biopsies; however, recently he had another positive biopsy. He was being evaluated for operative cord stripping when he was found to have primary squamous cell carcinoma of the right upper lobe of his lung. He was operated on and has had a successful right upperlobectomy, plus a cord stripping which was positive. He was started on CoQ_{10} at this time at a dose of 300 mg a day. He was rechecked approximately three weeks later and found to have a clinically positive lesion as a recurrence. He was referred to the Medical Center for evaluation. It was recommended that a total laryngectomy be done, but the patient refused. He underwent another cord stripping which was negative. He has been evaluated monthly and all subsequent biopsies have been negative. His follow-up from his lung cancer surgery has shown no evidence of recurrence (January, 1993).

E.V.J., female, 78 years (1993), cancer of the breast and a radical mastectomy (left side) in 1975. From 1975 to 1983 she had multiple blood and mammogram studies indicating the reoccurrence of cancer. Biopsy studies showed only benign tumors. In 1984 she developed Class III congestive heart failure, and was placed on CoQ_{10}. She has had no heart failure or positive test for cancer in the last nine years. She is active everyday in 1993.

E.M.J., male, 82 years, cancer of the colon which was surgically removed three years ago. One month after his surgery he had a heart attack which left him with poor cardiac function. For five months, his blood studies indicated the return of cancer. He was started on CoQ_{10} in 1990. His cardiac function significantly improved. He has not had a single positive blood test for active cancer since taking CoQ_{10}. He works everyday.

A.D., female, 56 years, after a bilateral radical mastectomy (6/4/79) was diagnosed with cancer. Cancer reoccurred in the left axillary region on 8/20/80. Adriamycin was started on 9/6/80 and discontinued 10/20/80 due to cardiotoxicity. Coenzyme Q_{10} was started 1/4/81 for the treatment of congestive heart failure (CHF) complicated by mitral valve insufficiency. Cardiac function improved significantly and the cancer appeared to be in remission. The mitral valve was replaced with a porcine valve (4/3/81). The patient remained on CoQ_{10} for ten plus years (4/4/92) without the reoccurrence of cancer or more than Class II CHF.

J.M., female, 52 years, diagnosed with lung cancer 10/4/83. Adriamycin was started (10/14/83) and discontinued (12/2/83) due to cardiotoxicity. Cardiac function deteriorated to Class IV congestive heart failure (CHF). The patient was placed on coenzyme Q_{10} for her heart failure (1/22/84), and remained on CoQ_{10} for 30 months, during which the CHF resolved to Class II and the cancer appeared to be in remission. Sixty days after stopping CoQ_{10} therapy, the patient was admitted to the hospital with shortness of breath and pulmonary edema. Death occurred on 9/22/86. Clinical findings were left heart failure, pulmonary edema, and cancer cells in both lungs.

J.P., male, 63 years, with Class II congestive heart failure was diagnosed with cancer of the prostate 6/5/88. Coenzyme Q_{10} was started (7/6/88) to protect the heart during chemotherapy. A full course of chemotherapy was completed without increasing heart failure and with tumor suppression. CoQ_{10} therapy was stopped on 8-1-89 and sixty-four days later the patient was hospitalized with increasing heart failure and positive blood test for prostate cancer. CoQ_{10} therapy was resumed until 4/4/92 (17 months). The heart failure resolved to Class I and the cancer was in remission. The patient was hospitalized 84 days after stopping CoQ_{10} therapy with increasing heart failure and positive blood test for prostate cancer. The clinical condition deteriorated and death occurred on 9/16/92. The clinical findings were Class IV CHF, and cancer cells extending into the bladder and surrounding tissues in the lower abdomen.

DISCUSSION - Patients in heart failure were available who also had cancer and were treated with CoQ_{10} primarily for their heart failure, but with monitoring of their clinical status of cancer. One of these patients on CoQ_{10} revealed no symptom of heart failure or a positive test for cancer in nine years. Another patient had not even one positive blood test for active cancer during dosage on CoQ_{10} therapy for three years. Another patient remained on CoQ_{10} for ten years without the recurrence of cancer. Another patient having inoperable bronchogenic carcinoma of the left lung, small cell type and massive mediastinal metastasis has survived to January, 1993, for 15 years, with no evidence of cancer.

ACKNOWLEDGMENT - Appreciation is expressed to the Robert A. Welch Foundation of Houston, Texas.

REFERENCES

(1) C.D. Fitch, J.S. Dinning, F.S. Porter, K. Folkers, H.W. Moore, and J.L. Smith (1965) Arch. Biochem. Biophys. 112:488-493.
(2) T.M. Farley, J. Scholler, J.L. Smith, K. Folkers, and A. Fitch (1967) Arch. Biochem. Biophys. 121:625-632.
(3) F.C. Ludwig, R.M. Elashoff, J.L. Smith, J. Scholler, T.M. Farley, and K. Folkers (1967) Scand. J. Haematol 4:292-300.
(4) A.S. Majaj and K. Folkers (1968) Intern. J. Vitamin Res. 38:182-195.
(5) M. Larsen, J.R. Couch, F. Enzmann, L. Boler, H. Mustafa, and K. Folkers (1969) Intern. J. Vitamin Res. 39:4:447-456.
(6) E.G. Bliznakov, A.C. Casey, T. Kishi, H. Kishi, and K. Folkers (1975) Internat. J. Vit. Nutr. Res. 45:4:388-395.
(7) E.G. Bliznakov, T. Watanabe, S. Saji, and K. Folkers (1978) J. Med. 9:4:337-346.
(8) E.G. Bliznakov, A.C. Casey, and E. Premuzic (1970) Experientia 26:9:953-954.
(9) E.G. Bliznakov (1973) Proc. Natl. Acad. Sci. USA 70:2:390-394.
(10) E.G. Bliznakov, A.C. Casey, T. Kishi, H. Kishi, and K. Folkers (1975) Internat. J. Vit. Nutr. Res. 45:4:388-395.
(11) E.G. Bliznakov (1970) In: Biomedical and Clinical Aspects of Coenzyme Q, Vol. 1, K. Folkers & Y. Yamamura, eds., New York: Elsevier/North Holland Biomedical Press, pp. 73-83.
(12) G. Hogenauer, P. Mayer, and J. Drews (1981) In: Biomedical and Clinical Aspects of Coenzyme Q, Vol. 3, K. Folkers & Y. Yamamura, eds., New York: Elsevier/North Holland Biomedical Press, pp. 325-334.
(13) K. Folkers, S. Shizukuishi, K. Takemura, J. Drzewoski, P. Richardson, J. Ellis, and W.C. Kuzell (1982) Res. Commun. Chem. Path. Pharm. 38:2:335-338.
(14) K. Folkers, P. Langsjoen, Y. Nara, K. Muratsu, J. Komorowski, P.C. Richardson, and T.H. Smith (1988) Biochem. Biophys. Res. Commun. 153:2:888-896.
(15) K. Folkers, T. Hanioka, M. Williams, P. Quillin, and R. Iafelice (1993) The Relevance of a Deficiency of Coenzyme Q_{10} to Cancer. Submitted to Med. Chem. Res., February 1993.