Arteriosklerose

Ross R.
Atherosclerosis--an inflammatory disease.
N Engl J Med 1999 Jan;340(2):115-26

Kein Abstrakt verfügbar

Arteriosklerose und Therapie mit Coenzym Q10 (Literatur) bei Personen mit *Diabetes mellitus, Typ II*

Watts GF, Playford DA, Croft KD, Ward NC, Mori TA, Burke V.
Coenzyme Q(10) improves endothelial dysfunction of the brachial artery in Type II diabetes mellitus.
Diabetologia 2002 Mar;45(3):420-6
AIM/HYPOTHESIS: We assessed whether dietary supplementation with coenzyme Q(10) improves endothelial function of the brachial artery in patients with Type II (non-insulin-dependent) diabetes mellitus and dyslipidaemia. METHODS: A total of 40 patients with Type II diabetes and dyslipidaemia were randomized to receive 200 mg of coenzyme Q(10) or placebo orally for 12 weeks. Endothelium-dependent and independent function of the brachial artery was measured as flow-mediated dilatation and glyceryl-trinitrate-mediated dilatation, respectively. A computerized system was used to quantitate vessel diameter changes before and after intervention. Arterial function was compared with 18 non-diabetic subjects. Oxidative stress was assessed by measuring plasma F(2)-isoprostane concentrations, and plasma antioxidant status by oxygen radical absorbance capacity. RESULTS: The diabetic patients had impaired flow-mediated dilation [3.8 % (SEM 0.5) vs 6.4 % (SEM 1.0), p = 0.016], but preserved glyceryl-trinitrate-mediated dilation, of the brachial artery compared with non-diabetic subjects. Flow-mediated dilation of the brachial artery increased by 1.6 % (SEM 0.3) with coenzyme Q(10) and decreased by -0.4 % (SEM 0.5) with placebo (p = 0.005); there were no group differences in the changes in pre-stimulatory arterial diameter, post-ischaemic hyperaemia or glyceryl-trinitrate-mediated dilation response. Coenzyme Q(10) treatment resulted in a threefold increase in plasma coenzyme Q(10) (p < 0.001) but did not alter plasma F(2)-isoprostanes, oxygen radical absorbance capacity, lipid concentrations, glycaemic control or blood pressure.
CONCLUSION/INTERPRETATION: Coenzyme Q(10) supplementation improves endothelial function of conduit arteries of the peripheral circulation in dyslipidaemic patients with Type II diabetes. The mechanism could involve increased endothelial release and/or activity of nitric oxide due to improvement in vascular oxidative stress, an effect that might not be reflected by changes in plasma F(2)-isoprostane concentrations.

Dauermedikation
bei Personen in Behandlung mit *HMG-CoA Reduktase Hemmern* (*Statine)*

Sarter B.
Coenzyme Q10 and cardiovascular disease: a review.
J Cardiovasc Nurs 2002 Jul;16(4):9-20
This article provides a comprehensive review of 30 years of research on the use of coenzyme Q10 in prevention and treatment of cardiovascular disease. This endogenous antioxidant has potential for use in prevention and treatment of cardiovascular disease, particularly hypertension, hyperlipidemia, coronary artery disease, and heart failure. It appears that levels of coenzyme Q10 are decreased during therapy with HMG-CoA reductase inhibitors, gemfibrozil, Adriamycin, and certain beta blockers. Further clinical trials are warranted, but because of its low toxicity it may be appropriate to recommend coenzyme Q10 to select patients as an adjunct to conventional treatment.

Bargossi AM, Grossi G, Fiorella PL, Gaddi A, Di Giulio R, Battino M.
Exogenous CoQ10 supplementation prevents plasma ubiquinone reduction induced by HMG-CoA reductase inhibitors.
Mol Aspects Med 1994;15 Suppl:s187-93
The biosynthetic pathway of the CoQ polyisoprenoid side chain, starting from acetyl-CoA and proceeding through mevalonate and isopentenylpyrophosphate, is the same as that of cholesterol. We performed this study to evaluate whether vastatins (hypocholesterolemic drugs that inhibit HMG-CoA reductase) modify blood levels of ubiquinone. Thirty-four unrelated outpatients with hypercholesterolemia (IIa phenotype) were treated with 20 mg of simvastatin for a 6-month period (group S) or with 20 mg of simvastatin plus 100 mg CoQ10 (group US). The following parameters were evaluated at time 0, 45, 90, 135 and 180 days: total plasma cholesterol (TC), HDL-cholesterol, LDL-cholesterol (LDL-C), triglycerides (TG), apo A1, apo B and CoQ10 in plasma and platelets. In the S group, there was a marked decrease in TC and LDL-C (from 290.3 mg/dl to 228.7 mg/dl for TC and from 228.7 mg/dl to 167.6 mg/dl for LDL-C) and in plasma CoQ10 levels from 1.08 mg/dl to 0.80 mg/dl. In contrast, in the US group we observed a significant increase of CoQ10 in plasma (from 1.20 to 1.48 mg/dl) while the hypocholesterolemic effect was similar to that observed in the S group. Platelet CoQ10 also decreased in the S group (from 104 to 90 ng/mg) and increased in the US group (from 95 to 145 ng/mg). This study demonstrates that simvastatin lowers both LDL-C and apo B plasma levels together with the plasma and platelet levels of CoQ10, and that CoQ10 therapy prevents both plasma and platelet CoQ10 decrease, without affecting the cholesterol lowering effect of simvastatin.

Folkers K, Langsjoen P, Willis R, Richardson P, Xia LJ, Ye CQ, Tamagawa H.
Lovastatin decreases coenzyme Q levels in humans.
Proc Natl Acad Sci U S A 1990 Nov;87(22):8931-4
Lovastatin is clinically used to treat patients with hypercholesterolemia and successfully lowers cholesterol levels. The mechanism of action of lovastatin is inhibition of 3-hydroxy-3-methylglutaryl-coenzyme A reductase, an enzyme involved in the biosynthesis of cholesterol from acetyl-CoA. Inhibition of this enzyme could also inhibit the intrinsic biosynthesis of coenzyme Q10 (CoQ10), but there have not been definitive data on whether lovastatin reduces levels of CoQ10 as it does cholesterol. The clinical use of lovastatin is to reduce a risk of cardiac disease, and if lovastatin were to reduce levels of CoQ10, this reduction would constitute a new risk of cardiac disease, since it is established that CoQ10 is indispensable for cardiac function. We have conducted three related protocols to determine whether lovastatin does indeed inhibit the biosynthesis of CoQ10. One protocol was done on rats, and is reported in the preceding paper [Willis, R. A., Folkers, K., Tucker, J. L., Ye, C.-Q., Xia, L.-J. & Tamagawa, H. (1990) Proc. Natl. Acad. Sci. USA 87, 8928-8930]. The other two protocols are reported here. One involved patients in a hospital, and the other involved a volunteer who permitted extraordinary monitoring of CoQ10 and cholesterol levels and cardiac function. All data from the three protocols revealed that lovastatin does indeed lower levels of CoQ10. The five hospitalized patients, 43-72 years old, revealed increased cardiac disease from lovastatin, which was life-threatening for patients having class IV cardiomyopathy before lovastatin or after taking lovastatin. Oral administration of CoQ10 increased blood levels of CoQ10 and was generally accompanied by an improvement in cardiac function. Although a successful drug, lovastatin does have side effects, particularly including liver dysfunction, which presumably can be caused by the lovastatin-induced deficiency of CoQ10.

Ghirlanda G, Oradei A, Manto A, Lippa S, Uccioli L, Caputo S, Greco AV, Littarru GP.

Evidence of plasma CoQ10-lowering effect by HMG-CoA reductase inhibitors: a double-blind, placebo-controlled study.
J Clin Pharmacol 1993 Mar;33(3):226-9
Inhibitors of HMG-CoA reductase are new safe and effective cholesterol-lowering agents. Elevation of alanine-amino transferase (ALT) and aspartate-amino transferase (AST) has been described in a few cases and a myopathy with elevation of creatinine kinase (CK) has been reported rarely. The inhibition of HMG-CoA reductase affects also the biosynthesis of ubiquinone (CoQ10). We studied two groups of five healthy volunteers treated with 20 mg/day of pravastatin (Squibb, Italy) or simvastatin (MSD) for a month. Then we treated 30 hypercholesterolemic patients in a double-blind controlled study with pravastatin, simvastatin (20 mg/day), or placebo for 3 months. At the beginning, and 3 months thereafter we measured plasma total cholesterol, CoQ10, ALT, AST, CK, and other parameters (urea, creatinine, uric acid, total bilirubin, gamma GT, total protein). Significant changes in the healthy volunteer group were detected for total cholesterol and CoQ10 levels, which underwent about a 40% reduction after the treatment. The same extent of reduction, compared with placebo was measured in hypercholesterolemic patients treated with pravastatin or simvastatin. Our data show that the treatment with HMG-CoA reductase inhibitors lowers both total cholesterol and CoQ10 plasma levels in normal volunteers and in hypercholesterolemic patients. CoQ10 is essential for the production of energy and also has antioxidative properties. A diminution of CoQ10 availability may be the cause of membrane alteration with consequent cellular damage.

Mortensen SA, Leth A, Agner E, Rohde M.
Dose-related decrease of serum coenzyme Q10 during treatment with HMG-CoA reductase inhibitors.
Mol Aspects Med 1997;18 Suppl:S137-44
Coenzyme Q10 (ubiquinone) the essential mitochondrial redox-component and endogenous antioxidant, packaged into the LDL + VLDL fractions of cholesterol, has been suggested as an important anti-risk factor for the development of atherosclerosis as explained by the oxidative theory. Forty-five hypercholesterolemic patients were randomized in a double-blind trial in order to be treated with increasing dosages of either lovastatin (20-80 mg/day) or pravastatin (10-40 mg/day) over a period of 18 weeks. Serum levels of coenzyme Q10 were measured parallel to the levels of cholesterol at baseline on placebo and diet and during active treatment. A dose-related significant decline of the total serum level of coenzyme Q10 was found in the pravastatin group from 1.27 +/- 0.34 at baseline to 1.02 +/- 0.31 mmol/l at the end of the study period (mean +/- S.D.), $P < 0.01$. After lovastatin therapy the decrease was significant as well and more pronounced, from 1.18 +/- 0.36 to 0.84 +/- 0.17 mmol/l, $P < 0.001$. Although HMG-CoA reductase inhibitors are safe and effective within a limited time horizon, continued vigilance of a possible adverse consequence from coenzyme Q10 lowering seems important during long-term therapy.

Diabetes mellitus, Typ II

Hodgson JM, Watts GF, Playford DA, Burke V, Croft KD.
Coenzyme Q10 improves blood pressure and glycaemic control: a controlled trial in subjects with type 2 diabetes.
Eur J Clin Nutr 2002 Nov;56(11):1137-42
OBJECTIVE: Our objective was to assess effects of dietary supplementation with coenzyme Q10 (CoQ) on blood pressure and glycaemic control in subjects with type 2 diabetes, and to consider oxidative stress as a potential mechanism for any effects. SUBJECTS AND DESIGN: Seventy-four subjects with uncomplicated type 2 diabetes and dyslipidaemia were involved in a randomised double blind placebo-controlled 2x2 factorial intervention. SETTING: The study was performed at the University of Western Australia, Department of Medicine at Royal Perth Hospital, Australia. INTERVENTIONS: Subjects were randomly assigned to receive an oral dose of 100 mg CoQ twice daily (200 mg/day), 200 mg fenofibrate each morning, both or neither for 12 weeks. MAIN OUTCOME MEASURES: We report an analysis and discussion of the effects of CoQ on blood pressure, on long-term glycaemic control measured by glycated haemoglobin (HbA(1c)), and on oxidative stress assessed by measurement of plasma F2-isoprostanes. RESULTS: Fenofibrate did not alter blood pressure, HbA(1c), or plasma F2-isoprostanes. There was a 3-fold increase in plasma CoQ concentration (3.4+/-0.3 micro mol/l, P<0.001) as a result of CoQ supplementation. The main effect of CoQ was to significantly decrease systolic (-6.1+/-2.6 mmHg, P=0.021) and diastolic (-2.9+/-1.4 mmHg, P=0.048) blood pressure and HbA(1c) (-0.37+/-0.17%, P=0.032). Plasma F2-isoprostane concentrations were not altered by CoQ (0.14+/-0.15 nmol/l, P=0.345). CONCLUSIONS: These results show that CoQ supplementation may improve blood pressure and long-term glycaemic control in subjects with type 2 diabetes, but these improvements were not associated with reduced oxidative stress, as assessed by F2-isoprostanes. SPONSORSHIP: This study was supported by a grant from the NH&MRC, Australia.

Herzinsuffizienz

Tran MT, Mitchell TM, Kennedy DT, Giles JT.
Role of coenzyme Q10 in chronic heart failure, angina, and hypertension.
Pharmacotherapy 2001 Jul;21(7):797-806
PURPOSE: Coenzyme Q10 (CoQ10) has a pathophysiologic role in many disease states. The purpose of this review is to provide recommendations regarding the safety, efficacy, and dosing of CoQ10 in the management of chronic heart failure (CHF), angina, and hypertension. DATA SOURCES: Literature pertaining to the safety and efficacy of CoQ10 specifically in cardiovascular indications was reviewed. We used relevant clinical trials, articles, reviews, and letters that were selected from a literature search of the MEDLINE database (1974-2000), Micromedex Healthcare Series, and the Natural Medicines Comprehensive Database. FINDINGS: Coenzyme Q10 administered orally has favorable actions in the described cardiovascular conditions and appears to be safe and well tolerated in the adult population. Issues concerning optimum target dosages, potential interactions, monitoring parameters, and the role of CoQ10 as a monotherapeutic agent need to be investigated further. Favorable effects of CoQ10 on ejection fraction, exercise tolerance, cardiac output, and stroke volume are demonstrated in the literature; thus, the use of CoQ10 as adjuvant therapy in patients with CHF may be supported. CONCLUSIONS: Coenzyme Q10 therapy in angina and hypertension cannot be substantiated until additional clinical trials demonstrate consistent beneficial effects. However, CoQ10 may be recommended as adjuvant therapy in selected patients with CHE At this time, CoQ10 should not be recommended as monotherapy or first-line therapy in any disease state.

Folkers K, Wolaniuk J, Simonsen R, Morishita M, Vadhanavikit S.
Biochemical rationale and the cardiac response of patients with muscle disease to therapy with coenzyme Q10.
Proc Natl Acad Sci U S A 1985 Jul;82(13):4513-6
Cardiac disease is commonly associated with virtually every form of muscular dystrophy and myopathy. A double-blind and open crossover trial on the oral administration of coenzyme Q10 (CoQ10) to 12 patients with progressive muscular dystrophies and neurogenic atrophies was conducted. These diseases included the Duchenne, Becker, and limb-girdle dystrophies, myotonic dystrophy, Charcot-Marie-Tooth disease, and Welander disease. The impaired cardiac function was noninvasively and extensively monitored by impedance cardiography. Solely by significant change or no change in stroke volume and cardiac output, all 8 patients on blind CoQ10 and all 4 on blind placebo were correctly assigned (P less than 0.003). After the limited 3-month trial, improved physical well-being was observed for 4/8 treated patients and for 0/4 placebo patients; of the latter, 3/4 improved on CoQ10; 2/8 patients resigned before crossover; 5/6 on CoQ10 in crossover maintained improved cardiac function; 1/6 crossed over from CoQ10 to placebo relapsed. The rationale of this trial was based on known mitochondrial myopathies, which involve respiratory enzymes, the known presence of CoQ10 in respiration, and prior clinical data on CoQ10 and dystrophy. These results indicate that the impaired myocardial function of such patients with muscular disease may have some association with impaired function of skeletal muscle, both of which may be improved by CoQ10 therapy. The cardiac improvement was definitely positive. The improvement in well-being was subjective, but probably real. Likely, CoQ10 does not alter genetic defects but can benefit the sequelae of mitochondrial impairment from such defects. CoQ10 is the only known substance that offers a safe and improved quality of life for such patients having muscle disease, and it is based on intrinsic bioenergetics.

Tran MT, Mitchell TM, Kennedy DT, Giles JT.
Role of coenzyme Q10 in chronic heart failure, angina, and hypertension.
Pharmacotherapy 2001 Jul;21(7):797-806
PURPOSE: Coenzyme Q10 (CoQ10) has a pathophysiologic role in many disease states. The purpose of this review is to provide recommendations regarding the safety, efficacy, and dosing of CoQ10 in the management of chronic heart failure (CHF), angina, and hypertension. DATA SOURCES: Literature pertaining to the safety and efficacy of CoQ10 specifically in cardiovascular indications was reviewed. We used relevant clinical trials, articles, reviews, and letters that were selected from a literature search of the MEDLINE database (1974-2000), Micromedex Healthcare Series, and the Natural Medicines Comprehensive Database. FINDINGS: Coenzyme Q10 administered orally has favorable actions in the described cardiovascular conditions and appears to be safe and well tolerated in the adult population. Issues concerning optimum target dosages, potential interactions, monitoring parameters, and the role of CoQ10 as a monotherapeutic agent need to be

investigated further. Favorable effects of CoQ10 on ejection fraction, exercise tolerance, cardiac output, and stroke volume are demonstrated in the literature; thus, the use of CoQ10 as adjuvant therapy in patients with CHF may be supported. CONCLUSIONS: Coenzyme Q10 therapy in angina and hypertension cannot be substantiated until additional clinical trials demonstrate consistent beneficial effects. However, CoQ10 may be recommended as adjuvant therapy in selected patients with CHE At this time, CoQ10 should not be recommended as monotherapy or first-line therapy in any disease state.

Langsjoen PH, Vadhanavikit S, Folkers K.
Response of patients in classes III and IV of cardiomyopathy to therapy in a blind and crossover trial with coenzyme Q10.
Proc Natl Acad Sci U S A 1985 Jun;82(12):4240-4
Coenzyme Q10 (CoQ10), a biochemically established redox component of respiration including the coupled mechanisms of electron transfer and oxidative phosphorylation, is naturally present in the human myocardium. A double-blind and double-crossover trial has been conducted by administering CoQ10 and a matching placebo orally to two groups of patients having class III or IV cardiomyopathy (classification according to criteria of the New York Heart Association). Group A received CoQ10 and then placebo; group B received placebo and then CoQ10. Blood levels of CoQ10 and cardiac function were determined at 0 and 4 weeks (control stabilization period) and at 16 and 28 weeks (after the 12-week CoQ/placebo-treatment periods). For group A, significant increases in CoQ10 blood levels and cardiac function occurred during CoQ10 treatment and then decreased during crossover to placebo. For group B, there was no change in CoQ10 blood levels and cardiac function during placebo treatment, but increases in both parameters occurred in crossover to CoQ10. These patients, steadily worsening and expected to die within 2 years under conventional therapy, generally showed an extraordinary clinical improvement, indicating that CoQ10 therapy might extend the lives of such patients. This improvement could be due to correction of a myocardial deficiency of CoQ10 and to enhanced synthesis of CoQ10-requiring enzymes.

Langsjoen PH, Folkers K, Lyson K, Muratsu K, Lyson T, Langsjoen P.
Pronounced increase of survival of patients with cardiomyopathy when treated with coenzyme Q10 and conventional therapy.
Int J Tissue React 1990;12(3):163-8
During 1982-86, 43/137 patients with cardiomyopathy, Classes II, III and IV, had ejection fractions (EF) below 40%, and a mean EF of 25.1 +/- 10.3%. During treatment of these 43 patients with coenzyme Q10 (CoQ10), EF increased to 41.6 +/- 14.3% (p less than 0.001) over a mean period of 3 months (range, 2-4 months). At four subsequent periods up to 36 months. EF ranged from 43.1 +/- 13.3 to 49.7 +/- 6.4% (each period, p less than 0.001). The mean CoQ10 control blood level was 0.85 +/- 0.26 micrograms/ml which increased on treatment to 1.7 to 2.3 micrograms/ml for five periods up to 36 months (each period, p less than 0.001). The survival rates for all 137 patients treated with CoQ10 and for the 43 patients with EF below 40% were both about 75%/46 months. These two survival rates were comparable between 24 and 46 months, which is of extraordinary significance and importance when compared to survival of about 25%/36 months for 182 patients with EF below 46% on conventional therapy without CoQ10. The improved cardiac function and pronounced increase of survival show that therapy with CoQ10 is remarkably beneficial due to correction of CoQ10 deficiency in mechanisms of bioenergetics.

Langsjoen PH, Langsjoen PH, Folkers K.
A six-year clinical study of therapy of cardiomyopathy with coenzyme Q10.
Int J Tissue React 1990;12(3):169-71
One hundred and forty-three cases of chronic, stable, non-secondary, non-hypertrophic cardiomyopathy, 98% of whom were in NYHA Classes III and IV, were given 100 mg of coenzyme Q10 orally in addition to their conventional medical programme in an open-label long-term study. Blood CoQ10 levels, clinical status, myocardial function and survival have been recorded now for almost 6 years. Mean control/CoQ10 levels of 0.85 micrograms/ml rose to 2 micrograms/ml in 3 months and remained stable at that level. Mean ejection fraction of 44% measured by systolic time interval analysis rose to 60% within 6 months and stabilized at that level with 84% of patients showing statistically significant improvement. Eighty-five percent of patients improved by one or two NYHA Classes. Survival figures were encouraging with an 11.1% mortality in 12 months and 17.8% mortality in 24 months, comparing favourably with several reports in the literature. There was no positive evidence of toxicity or intolerance in a total of 368.9 patient-years of exposure. Coenzyme Q10 is safe and effective long-term therapy for chronic cardiomyopathy.

Ma A, Zhang W, Liu Z.
Effect of protection and repair of injury of mitochondrial membrane-phospholipid on prognosis in patients with dilated cardiomyopathy.
Blood Press Suppl 1996;3:53-5
We have already proved that the mitochondrial membrane-phospholipid (MMP) injury changes of peripheral lymphocytes in patients with heart failure can be used as an injury indicator of myocardia, and are related to the long-term prognosis. In the present study, MMP localization of the peripheral lymphocytes was performed by modified Demer's tricomplex flocculation method, and we compared the changes, after classification, between the pre-treatment and the 12-week post-treatment, of coenzyme Q10 (Co.Q10) and captopril in 61 hospitalized patients with dilated cardiomyopathy (DCM). They were followed up for 16.1 +/- 7.8 months (mean). The results showed that compared with the placebo, Co.Q10 and captopril could significantly protect against and repair MMP injury and improve the heart function of patients with DCM after 12 weeks, and the 2-year survival rate rose significantly by 72.7% for Co.Q10, and 64.0% for captopril, vs 24.7% for placebo. As for Longrank test, X2 equals 4.660 and 6.318, respectively, with both $p < 0.05$. The aforementioned results indicate that MMP injury of peripheral lymphocytes can predict the prognosis of the patients with DCM, thus the protection and repairment of MMP injury can improve the life-quality and prolong the life-span of the patients.

Mortensen SA.
Perspectives on therapy of cardiovascular diseases with coenzyme Q10 (ubiquinone).
Clin Investig 1993;71(8 Suppl):S116-23
A defective myocardial energy supply--due to lack of substrates and/or essential cofactors and a poor utilization efficiency of oxygen--may be a common final pathway in the progression of myocardial diseases of various etiologies. The vitamin-like essential substance coenzyme Q10, or ubiquinone, is a natural antioxidant and has a key role in oxidative phosphorylation. A biochemical rationale for using coenzyme Q10 as a therapy in heart disease was established years ago by Folkers and associates; however, this has been further strengthened by investigations of viable myocardial tissue from the author's series of 45 patients with various cardiomyopathies. Myocardial tissue levels of coenzyme Q10 determined by high-performance lipid chromatography were found to be significantly lower in patients with more advanced heart failure compared with those in the milder stages of heart failure. Furthermore, the myocardial tissue coenzyme Q10 deficiency might be restored significantly by oral supplementation in selected cases. In the author's open clinical protocol study with coenzyme Q10 therapy (100 mg daily) nearly two-thirds of patients revealed clinical improvement, most pronounced in those with dilated cardiomyopathy. Double-blind placebo-controlled trials have definitely confirmed that coenzyme Q10 has a place as adjunctive treatment in heart failure with beneficial effects on the clinical outcome, the patients' physical activity, and their quality of life. The positive results have been above and beyond the clinical status obtained from treatment with traditional principles--including angiotensin-converting enzyme inhibitors.

Manzoli U, Rossi E, Littarru GP, Frustaci A, Lippa S, Oradei A, Aureli V.
Coenzyme Q10 in dilated cardiomyopathy.
Int J Tissue React 1990;12(3):173-8
The authors have tried to study the therapeutic efficacy of coenzyme Q10 (CoQ10) in patients with dilated cardiomyopathy (DCM). In fact, CoQ10 has been shown to be deficient in myocardial tissue biopsies taken from DCM hearts, compared to normal hearts. Thirty patients with histological diagnosis of DCM were orally treated with CoQ10 (100 mg/die) for 2 months. Before and after treatment a clinical examination with determination of NYHA class and an echocardiographic examination with determination of ejection fraction (EF) and of telediastolic (TDV) and telesystolic (TSV) volumes were performed, and blood was drawn for plasma CoQ10 determination. In seven patients the pretreatment endomyocardial level of CoQ10 was also assayed. Seven patients left the study because of poor therapeutic compliance. In 47% of patients the clinical symptomatology regressed, with improvement of NYHA class. The EF improved from 0.31 +/- 0.09 to 0.37 +/- 0.11 (p less than 0.001). The TDV passed from 262.2 +/- 85 ml to 203.3 +/- 83 ml (p less than 0.05), and the TSV from 166.13 +/- 75 ml to 126.9 +/- 56 ml (ns). The CoQ10 plasmatic levels improved in 95% of the patients: from 0.74 +/- 0.37 micrograms/ml to 2.27 +/- 0.99 micrograms/ml (p +/- 0.0001). The CoQ10 myocardial levels did not show univocal values, but the patients with lower myocardial levels seemed to have a better therapeutic response. These data suggest that the CoQ10 deficiency in DCM may be reversible and that the therapeutic effects depend on the basal plasmatic and myocardial levels. Therapy with coenzyme Q10 may be considered to be an efficacious aid in the traditional treatment of chronic cardiac failure.

Hypertonie und Therapie mit Coenzym Q10 (Literatur) ohne Erfassung einer Vorerkrankung oder spezifischer Lebensumstände

Burke BE, Neuenschwander R, Olson RD.
Randomized, double-blind, placebo-controlled trial of coenzyme Q10 in isolated systolic hypertension.
South Med J 2001 Nov;94(11):1112-7
BACKGROUND: Increasing numbers of the adult population are using alternative or complementary health resources in the treatment of chronic medical conditions. Systemic hypertension affects more than 50 million adults and is one of the most common risk factors for cardiovascular morbidity and mortality. This study evaluates the antihypertensive effectiveness of oral coenzyme Q10 (CoQ), an over-the-counter nutritional supplement, in a cohort of 46 men and 37 women with isolated systolic hypertension. METHODS: We conducted a 12-week randomized, double-blind, placebo-controlled trial with twice daily administration of 60 mg of oral CoQ and determination of plasma CoQ levels before and after the 12 weeks of treatment. RESULTS: The mean reduction in systolic blood pressure of the CoQ-treated group was 17.8 +/- 7.3 mm Hg (mean +/- SEM). None of the patients exhibited orthostatic blood pressure changes. CONCLUSIONS: Our results suggest CoQ may be safely offered to hypertensive patients as an alternative treatment option.

Langsjoen PH, Langsjoen AM.
Overview of the use of CoQ10 in cardiovascular disease.
Biofactors 1999;9(2-4):273-84
The clinical experience in cardiology with CoQ10 includes studies on congestive heart failure, ischemic heart disease, hypertensive heart disease, diastolic dysfunction of the left ventricle, and reperfusion injury as it relates to coronary artery bypass graft surgery. The CoQ10-lowering effect of HMG-CoA reductase inhibitors and the potential adverse consequences are of growing concern. Supplemental CoQ10 alters the natural history of cardiovascular illnesses and has the potential for prevention of cardiovascular disease through the inhibition of LDL cholesterol oxidation and by the maintenance of optimal cellular and mitochondrial function throughout the ravages of time and internal and external stresses. The attainment of higher blood levels of CoQ10 (> 3.5 micrograms/ml) with the use of higher doses of CoQ10 appears to enhance both the magnitude and rate of clinical improvement. In this communication, 34 controlled trials and several open-label and long-term studies on the clinical effects of CoQ10 in cardiovascular diseases are reviewed.

Hypertonie
bei Personen mit *Diabetes mellitus, Typ II*

Hodgson JM, Watts GF, Playford DA, Burke V, Croft KD.
Coenzyme Q10 improves blood pressure and glycaemic control: a controlled trial in subjects with type 2 diabetes.
Eur J Clin Nutr 2002 Nov;56(11):1137-42
OBJECTIVE: Our objective was to assess effects of dietary supplementation with coenzyme Q10 (CoQ) on blood pressure and glycaemic control in subjects with type 2 diabetes, and to consider oxidative stress as a potential mechanism for any effects. SUBJECTS AND DESIGN: Seventy-four subjects with uncomplicated type 2 diabetes and dyslipidaemia were involved in a randomised double blind placebo-controlled 2x2 factorial intervention. SETTING: The study was performed at the University of Western Australia, Department of Medicine at Royal Perth Hospital, Australia. INTERVENTIONS: Subjects were randomly assigned to receive an oral dose of 100 mg CoQ twice daily (200 mg/day), 200 mg fenofibrate each morning, both or neither for 12 weeks. MAIN OUTCOME MEASURES: We report an analysis and discussion of the effects of CoQ on blood pressure, on long-term glycaemic control measured by glycated haemoglobin (HbA(1c)), and on oxidative stress assessed by measurement of plasma F2-isoprostanes. RESULTS: Fenofibrate did not alter blood pressure, HbA(1c), or plasma F2-isoprostanes. There was a 3-fold increase in plasma CoQ concentration (3.4+/-0.3 micro mol/l, P<0.001) as a result of CoQ supplementation. The main effect of CoQ was to significantly decrease systolic (-6.1+/-2.6 mmHg, P=0.021) and diastolic (-2.9+/-1.4 mmHg, P=0.048) blood pressure and HbA(1c) (-0.37+/-0.17%, P=0.032). Plasma F2-isoprostane concentrations were not altered by CoQ (0.14+/-0.15 nmol/l, P=0.345). CONCLUSIONS: These results show that CoQ supplementation may improve blood pressure and long-term glycaemic control in subjects with type 2 diabetes, but these improvements were not associated with reduced oxidative stress, as assessed by F2-isoprostanes. SPONSORSHIP: This study was supported by a grant from the NH&MRC, Australia.

Immunsystem (Störungen des I.)
– bei Personen mit *Alter > 65 LJ*

Barbieri B, Lund B, LundstrÃm B, Scaglione F.
Coenzyme Q10 administration increases antibody titer in hepatitis B vaccinated volunteers--a single blind placebo-controlled and randomized clinical study.
Biofactors 1999;9(2-4):351-7
Persons involved in the study, 21 per treatment arm, were consuming ubiquinone (Q10), 90 mg/day, 180 mg/day or placebo, for two weeks prior to hepatitis B vaccination. After 30 days this vaccination was repeated. Q10 was given as soft gelatin capsules containing 30 mg each. The consumption was continued throughout the study conducted for 90 days. Clinical observations and laboratory tests were performed throughout the study and no adverse effects were observed in any of the groups. Already after 30 days the two groups receiving Q10 showed a slightly titer of antibodies to hepatitis B surface antigen then the placebo group. This difference escalated and the immunopotentiating effect of Q10 was even more clear-cut in the residual part of the study. In addition, a dose response did also seem to be present when comparing the 90 mg group with the 180 mg group. Statistics revealed that Q10 in the dose 180 mg/day is able to increase antibody response in vivo in humans vaccinated against hepatitis B with up to 57% ($p = 0.011$).

Leistungsfähigkeit
– bei Personen im *Leistungssport*

Ylikoski T, Piirainen J, Hanninen O, Penttinen J.
The effect of coenzyme Q10 on the exercise performance of cross-country skiers.
Mol Aspects Med 1997;18 Suppl:S283-90
Coenzyme Q10 supplementation (Bio-Qinon Pharma Nord, 90 mg/day) was studied in a double-blind cross-over study of 25 Finnish top-level cross-country skiers. With CoQ10 supplementation, all measured indexes of physical performance (AET, ANT and VO2Max) improved significantly. During verum supplementation, 94% of the athletes felt that the preparation had been beneficial in improving their performance and recovery time vs. only 33% in the placebo periods.

Mamma Ca

Lockwood K, Moesgaard S, Folkers K.
Partial and complete regression of breast cancer in patients in relation to dosage of coenzyme Q10.
Biochem Biophys Res Commun 1994 Mar;199(3):1504-8
Relationships of nutrition and vitamins to the genesis and prevention of cancer are increasingly evident. In a clinical protocol, 32 patients having -"high-risk"- breast cancer were treated with antioxidants, fatty acids, and 90 mg. of CoQ10. Six of the 32 patients showed partial tumor regression. In one of these 6 cases, the dosage of CoQ10 was increased to 390 mg. In one month, the tumor was no longer palpable and in another month, mammography confirmed the absence of tumor. Encouraged, another case having a verified breast tumor, after non-radical surgery and with verified residual tumor in the tumor bed was then treated with 300 mg. CoQ10. After 3 months, the patient was in excellent clinical condition and there was no residual tumor tissue. The bioenergetic activity of CoQ10, expressed as hematological or immunological activity, may be the dominant but not the sole molecular mechanism causing the regression of breast cancer.

Lockwood K, Moesgaard S, Hanioka T, Folkers K.
Apparent partial remission of breast cancer in 'high risk' patients supplemented with nutritional antioxidants, essential fatty acids and coenzyme Q10.
Mol Aspects Med 1994;15 Suppl:s231-40
Thirty-two typical patients with breast cancer, aged 32-81 years and classified 'high risk' because of tumor spread to the lymph nodes in the axilla, were studied for 18 months following an Adjuvant Nutritional Intervention in Cancer protocol (ANICA protocol). The nutritional protocol was added to the surgical and therapeutic treatment of breast cancer, as required by regulations in Denmark. The added treatment was a combination of nutritional antioxidants (Vitamin C: 2850 mg, Vitamin E: 2500 iu, beta-carotene 32.5 iu, selenium 387 micrograms plus secondary vitamins and minerals), essential fatty acids (1.2 g gamma linolenic acid and 3.5 g n-3 fatty acids) and Coenzyme Q10 (90 mg per day). The ANICA protocol is based on the concept of testing the synergistic effect of those categories of nutritional supplements, including vitamin Q10, previously having shown deficiency and/or therapeutic value as single elements in diverse forms of cancer, as cancer may be synergistically related to diverse biochemical dysfunctions and vitamin deficiencies. Biochemical markers, clinical condition, tumor spread, quality of life parameters and survival were followed during the trial. Compliance was excellent. The main observations were: (1) none of the patients died during the study period. (the expected number was four.) (2) none of the patients showed signs of further distant metastases. (3) quality of life was improved (no weight loss, reduced use of pain killers). (4) six patients showed apparent partial remission.

Lockwood K, Moesgaard S, Yamamoto T, Folkers K.
Progress on therapy of breast cancer with vitamin Q10 and the regression of metastases.
Biochem Biophys Res Commun 1995 Jul;212(1):172-7
Over 35 years, data and knowledge have internationally evolved from biochemical, biomedical and clinical research on vitamin Q10 (coenzyme Q10; CoQ10) and cancer, which led in 1993 to overt complete regression of the tumors in two cases of breast cancer. Continuing this research, three additional breast cancer patients also underwent a conventional protocol of therapy which included a daily oral dosage of 390 mg of vitamin Q10 (Bio-Quinone of Pharma Nord) during the complete trials over 3-5 years. The numerous metastases in the liver of a 44-year-old patient "disappeared," and no signs of metastases were found elsewhere. A 49-year-old patient, on a dosage of 390 mg of vitamin Q10, revealed no signs of tumor in the pleural cavity after six months, and her condition was excellent. A 75-year-old patient with carcinoma in one breast, after lumpectomy and 390 mg of CoQ10, showed no cancer in the tumor bed or metastases. Control blood levels of CoQ10 of 0.83-0.97 and of 0.62 micrograms/ml increased to 3.34-3.64 and to 3.77 micrograms/ml, respectively, on therapy with CoQ10 for patients A-MRH and EEL.

Männliche Unfruchtbarkeit und Therapie mit Coenzym Q10 (Literatur) ohne Erfassung einer Vorerkrankung oder spezifischer Lebensumstände

Lewin A, Lavon H.
The effect of coenzyme Q10 on sperm motility and function.
Mol Aspects Med 1997;18 Suppl:S213-9

In sperm cells, the majority of coenzyme Q10 (CoQ10) an energy promoting agent and antioxidant, is concentrated in the mitochondria of the midpiece, so that the energy for movement and all other energy-dependent processes in the sperm cell also depend on the availability of CoQ10. The reduced form of CoQ10-ubiquinol also acts as an antioxidant, preventing lipid peroxidation in sperm membranes. The objective of the study was to evaluate the effect of CoQ10 on sperm motility in vitro, after incubation with 38 samples of asthenospermic and normal motility sperm, and to evaluate the effect of CoQ10 administration in vivo in 17 patients with low fertilization rates after in vitro fertilization with intracytoplasmic sperm injection (ICSI) for male factor infertility. All 38 sperm samples from patients registered in our infertility clinic had normal concentrations and morphology. Of these, 16 patients had normal motility (mean 47.5%) and 22 patients were asthenospermic (mean motility 19.1%). Sperm samples were divided into four equal parts and incubated for 24 h in: HAM's medium alone, in HAM's medium with 1% DMSO and HAM's with 5 microM or 50 microM CoQ10. While no significant change in motility after incubation was observed in the samples with initial normal motility, a significant increase in motility was observed in the 50 microM CoQ10 subgroup of sperm from asthenospermic men, with a motility rate of 35.7 +/- 19.5%, as compared to 19.1 +/- 9.3% in the controls ($P < 0.05$). The 17 patients with low fertilization rates after ICSI were treated with oral CoQ10, 60 mg/day, for a mean of 103 days before the next ICSI treatment. No significant change was noted in most sperm parameters, but a significant improvement was noted in fertilization rates, from a mean of 10.3 +/- 10.5% in their previous cycles, to 26.3 +/- 22.8% after CoQ10 ($P < 0.05$). In conclusion, the administration of CoQ10 may result in improvement in sperm functions in selective patients. Further investigation into the mechanisms related to these effects is needed.

Morbus Parkinson

Shults CW, Oakes D, Kieburtz K, Beal MF, Haas R, Plumb S, Juncos JL, Nutt J, Shoulson I, Carter J, Kompoliti K, Perlmutter JS, Reich S, Stern M, Watts RL, Kurlan R, Molho E, Harrison M, Lew M, . Effects of coenzyme Q10 in early Parkinson disease: evidence of slowing of the functional decline. Arch Neurol 2002 Oct;59(10):1541-50

BACKGROUND: Parkinson disease (PD) is a degenerative neurological disorder for which no treatment has been shown to slow the progression. OBJECTIVE: To determine whether a range of dosages of coenzyme Q10 is safe and well tolerated and could slow the functional decline in PD. DESIGN: Multicenter, randomized, parallel-group, placebo-controlled, double-blind, dosage-ranging trial. SETTING: Academic movement disorders clinics. PATIENTS: Eighty subjects with early PD who did not require treatment for their disability. INTERVENTIONS: Random assignment to placebo or coenzyme Q10 at dosages of 300, 600, or 1200 mg/d. MAIN OUTCOME MEASURE: The subjects underwent evaluation with the Unified Parkinson Disease Rating Scale (UPDRS) at the screening, baseline, and 1-, 4-, 8-, 12-, and 16-month visits. They were followed up for 16 months or until disability requiring treatment with levodopa had developed. The primary response variable was the change in the total score on the UPDRS from baseline to the last visit. RESULTS: The adjusted mean total UPDRS changes were +11.99 for the placebo group, +8.81 for the 300-mg/d group, +10.82 for the 600-mg/d group, and +6.69 for the 1200-mg/d group. The P value for the primary analysis, a test for a linear trend between the dosage and the mean change in the total UPDRS score, was.09, which met our prespecified criteria for a positive trend for the trial. A prespecified, secondary analysis was the comparison of each treatment group with the placebo group, and the difference between the 1200-mg/d and placebo groups was significant (P =.04). CONCLUSIONS: Coenzyme Q10 was safe and well tolerated at dosages of up to 1200 mg/d. Less disability developed in subjects assigned to coenzyme Q10 than in those assigned to placebo, and the benefit was greatest in subjects receiving the highest dosage. Coenzyme Q10 appears to slow the progressive deterioration of function in PD, but these results need to be confirmed in a larger study.