**Selected by
Andreas Michalsen
Berlin**

Latest Publications You Should Not Miss

Marcocci C, Kahaly GJ, Krassas GE, Bartalena L, Prummel M, Stahl M, Altea MA, Nardi M, Pitz S, Boboridis K, Sivelli P, von Arx G, Mourits MP, Baldeschi L, Bencivelli W, Wiersinga W, European Group on Graves' Orbitopathy: The course of mild Graves' orbitopathy. N Engl J Med 2011;364:1920–1931.

Background: Oxygen free radicals and cytokines play a pathogenic role in Graves' orbitopathy.

Methods: We carried out a randomized, double-blind, placebo-controlled trial to determine the effect of selenium (an antioxidant agent) or pentoxifylline (an antiinflammatory agent) in 159 patients with mild Graves' orbitopathy. The patients were given selenium (100 µg twice daily), pentoxifylline (600 mg twice daily), or placebo (twice daily) orally for 6 months and were then followed for 6 months after treatment was withdrawn. Primary outcomes at 6 months were evaluated by means of an overall ophthalmic assessment, conducted by an ophthalmologist who was unaware of the treatment assignments, and a Graves' orbitopathy-specific quality-of-life questionnaire, completed by the patient. Secondary outcomes were evaluated with the use of a Clinical Activity Score and a diplopia score.

Results: At the 6-month evaluation, treatment with selenium, but not with pentoxifylline, was associated with an improved quality of life ($P < 0.001$) and less eye involvement ($P = 0.01$) and slowed the progression of Graves' orbitopathy ($P = 0.01$), as compared with placebo. The Clinical Activity Score decreased in all groups, but the change was significantly greater in the selenium-treated patients. Exploratory evaluations at 12 months confirmed the results seen at 6 months. Two patients assigned to placebo and one assigned to pentoxifylline required immunosuppressive therapy for deterioration in their condition. No adverse events were evident with selenium, whereas pentoxifylline was associated with frequent gastrointestinal problems.

Conclusions: Selenium administration significantly improved quality of life, reduced ocular involvement, and slowed progression of the disease in patients with mild Graves' orbitopathy.

Salas-Salvadó J, Bulló M, Babio N, Martínez-González MÁ, Ibarrola-Jurado N, Basora J, Estruch R, Covas MI, Corella D, Arós F, Ruiz-Gutiérrez V, Ros E, PREDIMED Study Investigators: Reduction in the incidence of type 2 diabetes with the Mediterranean diet: results of the PREDIMED-Reus nutrition intervention randomized trial. Diabetes Care 2011;34:14–19.

Objective: To test the effects of two Mediterranean diet (MedDiet) interventions versus a low-fat diet on incidence of diabetes.

Research Design and Methods: This was a three-arm randomized trial in 418 nondiabetic subjects aged 55–80 years recruited in one center (PREDIMED-Reus, northeastern Spain) of the Prevención con Dieta Mediterránea (PREDIMED) study, a large nutrition intervention trial for primary cardiovascular prevention in individuals at high cardiovascular risk. Participants were randomly assigned to education on a low-fat diet (control group) or to one of two MedDiets, supplemented with either free virgin olive oil (1 liter/week) or nuts (30 g/day). Diets were ad libitum, and no advice on physical activity was given. The main outcome was diabetes incidence diagnosed by the 2009 American Diabetes Association criteria.

Results: After a median follow-up of 4.0 years, diabetes incidence was 10.1% (95% CI 5.1–15.1), 11.0% (5.9–16.1), and 17.9% (11.4–24.4) in the MedDiet with olive oil group, the MedDiet with nuts group, and the control group, respectively. Multivariable adjusted hazard ratios of diabetes were 0.49 (0.25–0.97) and 0.48 (0.24–0.96) in the MedDiet supplemented with olive oil and nuts groups, respectively, compared with the control group. When the two MedDiet groups were pooled and compared with the control group, diabetes incidence was reduced by 52% (27–86). In all study arms, increased adherence to the MedDiet was inversely associated with diabetes incidence. Diabetes risk reduction occurred in the absence of significant changes in body weight or physical activity.

Conclusions: MedDiets without calorie restriction seem to be effective in the prevention of diabetes in subjects at high cardiovascular risk.

Fung TT, van Dam RM, Hankinson SE, Stampfer M, Willett WC, Hu FB: Low-carbohydrate diets and all-cause and cause-specific mortality: two cohort studies. Ann Intern Med 2010;153:289–298.

Background: Data on the long-term association between low-carbohydrate diets and mortality are sparse.

Objective: To examine the association of low-carbohydrate diets with mortality during 26 years of follow-up in women and 20 years in men.

Design: Prospective cohort study of women and men who were followed from 1980 (women) or 1986 (men) until 2006. Low-carbohydrate diets, either animal-based (emphasizing animal sources of fat and protein) or vegetable-based (emphasizing vegetable sources of fat and protein), were computed from several validated food-frequency questionnaires assessed during follow-up.

Setting: Nurses' Health Study and Health Professionals' Follow-up Study.

Participants: 85,168 women (aged 34 to 59 years at baseline) and 44,548 men (aged 40 to 75 years at baseline) without heart disease, cancer, or diabetes.

Measurements: Investigators documented 12,555 deaths (2,458 cardiovascular-related and 5,780 cancer-related) in women and 8,678 deaths (2,746 cardiovascular-related and 2,960 cancer-related) in men.

Results: The overall low-carbohydrate score was associated with a modest increase in overall mortality in a pooled analysis (hazard ratio (HR) comparing extreme deciles, 1.12 (95% CI, 1.01 to 1.24); P for trend = 0.136). The animal low-carbohydrate score was associated with higher all-cause mortality (pooled HR comparing extreme deciles, 1.23 (CI, 1.11 to 1.37); P for trend = 0.051), cardiovascular mortality (corresponding HR, 1.14 (CI, 1.01 to 1.29); P for trend = 0.029), and cancer mortality (corresponding HR, 1.28 (CI, 1.02 to 1.60); P for trend = 0.089). In contrast, a higher vegetable low-carbohydrate score was associated with lower all-cause mortality (HR, 0.80 (CI, 0.75 to 0.85); P for trend ≤ 0.001) and cardiovascular mortality (HR, 0.77 (CI, 0.68 to 0.87); P for trend < 0.001).

Limitations: Diet and lifestyle characteristics were assessed with some degree of error. Sensitivity analyses indicated that results were probably not substantively affected by residual confounding or an unmeasured confounder. Participants were not a representative sample of the U.S. population.

Conclusion: A low-carbohydrate diet based on animal sources was associated with higher all-cause mortality in both men and women, whereas a vegetable-based low-carbohydrate diet was associated with lower all-cause and cardiovascular disease mortality rates.

Primary Funding Source: National Institutes of Health.

Stolarz-Skrzypek K, Kuznetsova T, Thijs L, Tikhonoff V, Seidlerová J, Richart T, Jin Y, Olszanecka A, Malyutina S, Casiglia E, Filipovský J, Kawecka-Jaszcz K, Nikitin Y, Staessen JA: Fatal and nonfatal outcomes, incidence of hypertension, and blood pressure changes in relation to urinary sodium excretion. JAMA 2011;305:1777–1785.

Context: Extrapolations from observational studies and short-term intervention trials suggest that population-wide moderation of salt intake might reduce cardiovascular events.

Objective: To assess whether 24-hour urinary sodium excretion predicts blood pressure (BP) and health outcomes.

Design, Setting and Participants: Prospective population study, involving 3,681 participants without cardiovascular disease (CVD) who are members of families that were randomly enrolled in the Flemish Study on Genes, Environment, and Health Outcomes (1985–2004) or in the European Project on Genes in Hypertension (1999–2001). Of 3,681

participants without CVD, 2,096 were normotensive at baseline and 1,499 had BP and sodium excretion measured at baseline and last follow-up (2005–2008).

Main Outcome Measures: Incidence of mortality and morbidity and association between changes in BP and sodium excretion. Multivariable-adjusted hazard ratios (HRs) express the risk in tertiles of sodium excretion relative to average risk in the whole study population.

Results: Among 3,681 participants followed up for a median 7.9 years, CVD deaths decreased across increasing tertiles of 24-hour sodium excretion, from 50 deaths in the low (mean, 107 mmol), 24 in the medium (mean, 168 mmol), and 10 in the high excretion group (mean, 260 mmol; P < 0.001), resulting in respective death rates of 4.1% (95% confidence interval (CI), 3.5–4.7%), 1.9% (95% CI, 1.5–2.3%), and 0.8% (95% CI, 0.5–1.1%). In multivariable-adjusted analyses, this inverse association retained significance (P = 0.02): the HR in the low tertile was 1.56 (95% CI, 1.02–2.36; P = 0.04). Baseline sodium excretion predicted neither total mortality (P = 0.10) nor fatal combined with nonfatal CVD events (P = 0.55). Among 2,096 participants followed up for 6.5 years, the risk of hypertension did not increase across increasing tertiles (P = 0.93). Incident hypertension was 187 (27.0%; HR, 1.00; 95% CI, 0.87–1.16) in the low, 190 (26.6%; HR, 1.02; 95% CI, 0.89–1.16) in the medium, and 175 (25.4%; HR, 0.98; 95% CI, 0.86–1.12) in the high sodium excretion group. In 1,499 participants followed up for 6.1 years, systolic blood pressure increased by 0.37 mm Hg per year (P < 0.001), whereas sodium excretion did not change (–0.45 mmol per year, P = 0.15). However, in multivariable-adjusted analyses, a 100-mmol increase in sodium excretion was associated with 1.71 mm Hg increase in systolic blood pressure (P < 0.001) but no change in diastolic BP.

Conclusions: In this population-based cohort, systolic blood pressure, but not diastolic pressure, changes over time aligned with change in sodium excretion, but this association did not translate into a higher risk of hypertension or CVD complications. Lower sodium excretion was associated with higher CVD mortality.

Bäcker M, Lüdtke R, Afra D, Cesur O, Langhorst J, Fink M, Bachmann J, Dobos GJ, Michalsen A: Effectiveness of leech therapy in chronic lateral epicondylitis: a randomized controlled trial. Clin J Pain 2011;27:442–447.

Objectives: Leech therapy has been found to be effective in osteoarthritis of the knee and hand in previous trials. Chronic epicondylitis is a prevalent pain syndrome with limited treatment options. In this study, we tested whether leech therapy would be beneficial in the symptomatic treatment of chronic lateral epicondylitis.

Methods: Forty patients with manifestation of epicondylitis of at least 1-month duration were randomized to a single treatment with 2 to 4 locally applied leeches or a 30-day course with topical diclofenac. The primary outcome was change of pain sum score on day 7 calculated from 3 visual analog scales for pain during motion, grip, and rest. Secondary outcomes included disability (Disability of the Arm, Shoulder, Hand questionnaire), physical quality of life (Short Form-36), and grip strength. Outcomes and safety were assessed on days –3, 0, 7, and 45.

Results: Leeches induced a significantly stronger decrease of the pain score (143.7 ± 36.9 to 95.3 ± 45.1) compared with topical diclofenac (131.6 ± 29.6 to 134.7 ± 70.7 ; mean difference –49.0; 95% confidence interval, –82.9–15.1; P = 0.0075) after 7 days. On day 45, this group difference was reduced (–27.5; confidence interval, –60.8–5.8; P = 0.110) due to delayed pain relief with diclofenac. Functional disability showed a stronger decrease in the leech group, which was most prominent after 45 days (P = 0.0007). Quality of life increased nonsignificantly in the leech group. Results were not affected by outcome expectation.

Discussion: A single course of leech therapy was effective in relieving pain in the short-term and improved disability in intermediate-term. Leeches might be considered as an additional option in the therapeutic approach to lateral epicondylitis.

Johansson K, Hemmingsson E, Harlid R, Trolle Lagerros Y, Granath F, Rössner S, Neovius M: Longer term effects of very low energy diet on obstructive sleep apnoea in cohort derived from randomised controlled trial: prospective observational follow-up study. BMJ 2011;342:d3017.

Objective: To determine whether initial improvements in obstructive sleep apnoea after a very low energy diet were maintained after one year in patients with moderate to severe obstructive sleep apnoea.

Design: Single centre, prospective observational follow-up study.

Setting: Outpatient obesity clinic in a university hospital in Stockholm, Sweden.

Participants: 63 men aged 30–65 with body mass index (BMI) 30–40 and moderate to severe obstructive sleep apnoea defined as an apnoea-hypopnoea index ≥ 15 (events/hour), all treated with continuous positive airway pressure.

Intervention: A one year weight loss programme, consisting of an initial very low energy diet for nine weeks (seven weeks of 2.3 MJ/day and two weeks of gradual introduction of normal food) followed by a weight loss maintenance programme.

Main Outcome Measure: Apnoea-hypopnoea index, the main index for severity of obstructive sleep apnoea. Data from all patients were analysed (baseline carried forward for missing data).

Results: Of 63 eligible patients, 58 completed the very low energy diet period and started the weight maintenance programme and 44 completed the full programme; 49 had complete measurements at one year. At baseline the mean apnoea-hypopnoea index was 36 events/hour. After the very low energy diet period, apnoea-hypopnoea index was improved by -21 events/hour (95% confidence interval -17 to -25) and weight by -18 kg (-16 to -19 ; both $P < 0.001$). After one year the apnoea-hypopnoea index had improved by -17 events/hour (-13 to -21) and body weight by -12 kg (-10 to -14) compared with baseline (both $P < 0.001$). Patients with severe obstructive sleep apnoea at baseline had greater improvements in apnoea-hypopnoea index (-25 events/hour) compared with patients with moderate disease (-7 events/hour, $P < 0.001$). At one year, 30/63 (48%, 95% confidence interval 35% to 60%) no longer required continuous positive airway pressure and 6/63 (10%, 2% to 17%) had total remission of obstructive sleep apnoea (apnoea-hypopnoea index < 5 events/hour). There was a dose-response association between weight loss and apnoea-hypopnoea index at follow-up ($\beta = 0.50$ events/kg, 0.11 to 0.88; $P = 0.013$).

Conclusion: Initial improvements in obstructive sleep apnoea after treatment with a very low energy diet can be maintained after one year in obese men with moderate to severe disease. Those who lose the most weight or have severe sleep apnoea at baseline benefit most. Longer term effects of very low energy diet on obstructive sleep apnoea in cohort derived from randomised controlled trial: prospective observational follow-up study.

Moe SM, Zidehsarai MP, Chambers MA, Jackman LA, Radcliffe JS, Trevino LL, Donahue SE, Asplin JR: Vegetarian compared with meat dietary protein source and phosphorus homeostasis in chronic kidney disease. Clin J Am Soc Nephrol 2011;6:257–264.

Background and Objectives: Patients with advanced chronic kidney disease (CKD) are in positive phosphorus balance, but phosphorus levels are maintained in the normal range through phosphaturia induced by increases in fibroblast growth factor-23 (FGF23) and parathyroid hormone (PTH). This provides the rationale for recommendations to restrict dietary phosphate intake to 800 mg/d. However, the protein source of the phosphate may also be important.

Design, Setting, Participants and Measurements: We conducted a cross-over trial in nine patients with a mean estimated GFR of 32 ml/min to directly compare vegetarian and meat diets with equivalent nutrients prepared by clinical research staff. During the last 24 hours of each 7-day diet period, subjects were hospitalized in a research center and urine and blood were frequently monitored.

Results: The results indicated that 1 week of a vegetarian diet led to lower serum phosphorus levels and decreased FGF23 levels. The inpatient stay demonstrated similar diurnal variation for blood phosphorus, calcium, PTH, and urine fractional excretion of phosphorus but significant differences between the vegetarian and meat diets. Finally, the 24-hour fractional excretion of phosphorus was highly correlated to a 2-hour fasting urine collection for the vegetarian diet but not the meat diet.

Conclusions: In summary, this study demonstrates that the source of protein has a significant effect on phosphorus homeostasis in patients with CKD. Therefore, dietary counseling of patients with CKD must include information on not only the amount of phosphate but also the source of protein from which the phosphate derives.

Yeh GY, McCarthy EP, Wayne PM, Stevenson LW, Wood MJ, Forman D, Davis RB, Phillips RS: Tai Chi exercise in patients with chronic heart failure. A randomized clinical trial. Arch Intern Med 2011; 171:750–757.

Background: Preliminary evidence suggests that meditative exercise may have benefits for patients with chronic systolic heart failure (HF); this has not been rigorously tested in a large clinical sample. We sought to investigate whether tai chi, as an adjunct to standard care, improves functional capacity and quality of life in patients with HF.

Methods: A single-blind, multisite, parallel-group, randomized controlled trial evaluated 100 outpatients with systolic HF (New York Heart Association class I–III, left ventricular ejection fraction $\leq 40\%$) who were recruited between May 1, 2005, and September 30, 2008. A group-based 12-week tai chi exercise program ($n = 50$) or time-matched education ($n = 50$, control group) was conducted. Outcome measures included exercise capacity (6-minute walk test and peak oxygen uptake) and disease-specific quality of life (Minnesota Living With Heart Failure Questionnaire).

Results: Mean (SD) age of patients was 67 (11) years; baseline values were left ventricular ejection fraction, 29% (8%) and peak oxygen uptake, 13.5 ml/kg/min; the median New York Heart Association class of HF was class II. At completion of the study, there were no significant differences in change in 6-minute walk distance and peak oxygen uptake (median change (first quartile, third quartile), 35 (-2 , 51) vs. 2 (-7 , 54) meters, $P = 0.95$; and 1.1 (-1.1 , 1.5) vs. -0.5 (-1.2 , 1.8) ml/kg/min, $P = 0.81$) when comparing tai chi and control groups; however, patients in the tai chi group had greater improvements in quality of life (Minnesota Living With Heart Failure Questionnaire, -19 (-23 , -3) vs. 1 (-16 , 3), $P = 0.02$). Improvements with tai chi were also seen in exercise self-efficacy (Cardiac Exercise Self-efficacy Instrument, 0.1 (0.1, 0.6) vs. -0.3 (-0.5 , 0.2), $P < 0.001$) and mood (Profile of Mood States total mood disturbance, -6 (-17 , 1) vs. -1 (-13 , 10), $P = 0.01$).

Conclusion: Tai chi exercise may improve quality of life, mood, and exercise self-efficacy in patients with HF.