Coenzyme Q10 is ineffective in Parkinson's disease

Clinical question Does coenzyme Q10 improve symptoms in patients with midstage Parkinson's disease?

Bottom line Coenzyme Q10, when added to stable drug regimens, is no better than placebo in improving symptoms of midstage Parkinson's disease. (Level of evidence = 2b)

Synopsis In this study, 131 patients aged 40 to 75 years with midstage Parkinson's disease (according to standardized definitions) using stable treatment regimens were randomly assigned to receive 3 months of nanoparticular coenzyme Q10 suspension (CoQ10; 100 mg three times a day) or placebo. The randomization process was concealed by using a central computer system. The researchers excluded patients taking multiple medications (including vitamin E, lipid-lowering medications, warfarin, clozapine, and metformin) and patients with secondary or atypical Parkinson's disease, hypothyroidism, epilepsy, psychosis, and those with levodopa-induced motor fluctuations or dyskinesias. The patients also needed to have been using stable drug regimens. The effectiveness of the CoQ10 was assessed by researchers masked to treatment assignment. The authors used intention to treat to assess the outcomes of interest, but with a twist. For patients who did not complete the study, the researchers carried forward the last known observation, which tended to favor the treatment group. The study only needed 53 patients in each group to have 95% power to detect clinically relevant differences (20% change in symptom scores). Approximately 80% of the patients completed the study. In addition to symptom scores, the researchers also measured CoQ10 levels. At the end of the study, the changes in symptom scores for patients receiving CoQ10 were not significantly different than those for patients receiving placebo. Since the last-observation-carried-forward approach tends to favor treatment groups, these findings seem pretty robust.

Storch A, Jost WH, Vieregge P, et al; German Coenzyme Q(10) Study Group. Randomized, double-blind, placebo-controlled trial on symptomatic effects of coenzyme Q(10) in Parkinson disease. *Arch Neurol.* 2007;64(7):938-944.

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Surgery is not recommended for asymptomatic HPT

Clinical question Does surgery benefit patients with asymptomatic hyperparathyroidism (HPT)?

Bottom line Observation is safe for patients with asymptomatic HPT. Surgery improves biochemical measures but does not improve quality of life. (Level of evidence = 1b–)

Synopsis Surgery is the standard of care for patients with symptomatic HPT. However, HPT is detected incidentally in many patients because of elevated serum calcium early in the course of disease; whether these patients might benefit from parathyroidectomy is not clear. In this study, 164 adults aged 50 to 80 years (mostly women) with serum calcium levels of 2.6 to 2.85 mmol/L were referred by their primary care physician. The patients were randomized to receive observation only or parathyroidectomy. Overall, patients in both groups had somewhat-worse-than-average quality of life (primarily on mental-health domains) measured by the SF-36 scale. However, there was no consistent or clinically important improvement in the surgical group as compared with the observation group after 2 years. Although parathyroid hormone and serum calcium levels not surprisingly decreased to the normal range in the surgery group, the serum calcium levels, creatinine levels, and BPs remained stable in the observation group.

Bollerslev J, Jansson S, Mollerup CL, et al. Medical observation, compared with parathyroidectomy, for asymptomatic primary hyperparathyroidism: a prospective randomized trial. *J Clin Endocrin Metabol.* 2007;92(5):1687-1692.

Probiotic yogurt prevents antibiotic-associated diarrhea

Clinical question Can a yogurt product prevent diarrhea in older, hospitalized patients treated with antibiotics?

Bottom line A probiotic yogurt drink containing active bacterial cultures decreased the likelihood of diarrhea following initiation of antibiotic therapy. (Level of evidence = 1b–)

Synopsis Researchers enrolled 135 patients with a mean age of 74 years (minimum age 50 years) who were admitted and required antibiotic treatment. The patients were treated for respiratory tract infection (50%), prophylaxis before or after surgery (25%), or for other infection; most were given antibiotics with a medium or high risk of causing diarrhea. Within 2 days of starting antibiotics, patients were randomly assigned (allocation concealed) to receive either a sterile placebo milkshake or a yogurt drink containing active cultures of *Lactobacillus casei, L casei imunitas, L bulgaricus,* and *Streptococcus thermophilus*. The 100 mL drinks were given on an empty stomach twice a day. Using intention-to-treat analysis, diarrhea (defined as more than two liquid stools a day for 3 days or longer) occurred in 12% of treated patients and 34% of control patients. Treated patients were also less likely to develop *C difficile* infection.

Hickson M, D'Souza AL, Muthu N, et al. Use of probiotic Lactobacillus preparation to prevent diarrhea associated with antibiotics: randomised double blind placebo controlled trial. *BMJ.* 2007;335(7610):80.

Levels of evidence in **Bottom line** are explained at www.infopoems.com/levels.html.
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Diet high in fiber/low in fat does not reduce risk of recurrent breast cancer

Clinical question Can a diet high in vegetables, fruit, and fiber and low in fat reduce the risk of recurrent breast cancer?

Bottom line This study found no significant reduction in recurrent breast cancer or all-cause mortality in women previously treated for early-stage breast cancer who consumed a diet high in vegetables, fruit, and fiber, and low in fat. (Level of evidence = 1b)

Synopsis Plant-derived foods containing anticarcinogens may reduce the risk of recurrent cancer. These investigators randomized (concealed allocation assignment) 3,088 women, aged 18 to 70 years (mean age 53 years) and previously treated for early-stage breast cancer, to receive counseling about 1 of 2 dietary programs. The intervention group received intensive telephone counseling supplemented with 12 cooking classes and monthly newsletters in the first year, aimed at achieving a daily intake of five vegetable servings plus 16 ounces of vegetable juice, three fruit servings, 30 g of fiber, and 15% to 20% of total energy intake from fat. Women in the control group received printed materials describing a recommended daily intake of five servings of vegetables and fruit, a least 20 g of fiber, and less than 30% total energy intake from fat. Compliance with dietary intakes was assessed by 24-hour diet recalls conducted by telephone at random intervals for up to 6 years. Complete follow-up occurred for 95% of women for 7.3 years. Individuals assessing outcomes remained masked to treatment group assignment. At 4 years, the daily intake of vegetables, fruits, fiber, and energy from fat was statistically different in the intervention group compared with the control group (+65%, +25%, +30%, −13%, respectively). Using intention-to-treat analysis, there were no significant differences between the two groups in the risk of recurrent breast cancer or a reduction in all-cause mortality. The study was 82% powered to detect a 19% reduction in recurrent breast cancer in the intervention group.

Pierce JP, Natarajan L, Caan BJ, et al. Influence of a diet very high in vegetables, fruit, and fiber and low in fat on prognosis following treatment for breast cancer: the Women's Healthy Eating and Living (WHEL) randomized trial. *JAMA.* 2007;298(3): 289-298.

Celiac disease is common in patients with chronic gastrointestinal symptoms

Clinical question Can a case-finding strategy identify more patients with celiac disease (CD)?

Bottom line This study tells us that CD is relatively common in primary care practice, particularly in patients with GI symptoms, chronic fatigue, or thyroid disease. Patients with persistent symptoms should be evaluated for CD using the strategy described in this study, and the diagnosis should be confirmed either by intestinal biopsy or a successful trial of a gluten-free diet. (Level of evidence = 2c)

Synopsis CD is a relatively common cause of chronic GI symptoms and increases the risk of anemia, lymphoma, and osteoporosis. However, it often remains undiagnosed. In this study, the authors approached all adult patients presenting to a group of primary care physicians. Patients with at least one symptom or comorbidity associated with CD (including family history, anemia, recurrent abdominal pain or bloating, irritable bowel syndrome, chronic diarrhea, chronic fatigue, or autoimmune disorder) were asked to participate in the study by completing a detailed questionnaire and having blood drawn for CD serology. Of 2,568 patients who were approached to participate, 33% had none of the qualifying symptoms, 3% refused the questionnaire, and 26% refused the serology, leaving 976 (38%) for the study population. The initial blood test was for immunoglobulin A (IgA) anti-tissue transglutaminase (tTG) antibodies. Patients (n = 103) with a low value on this test (less than 0.5 units) had total IgA evaluated to rule out selective IgA deficiency. All results were normal. Thirty patients had an elevated tTG IgA (more than 7.0 units) and underwent testing for IgA endomysial antibodies; 22 had abnormal results on this test as well. Of this final group, 15 underwent small bowel biopsy and 17 adopted a gluten-free diet. We aren't told, however, whether the diet was successful. The most common initial reasons for screening were bloating (12 patients), thyroid disease (11), irritable bowel (7), and chronic diarrhea (6). Ultimately, CD was diagnosed in 11.6 per thousand visits, a rate much higher than that seen before the case-finding strategy was adopted.

Catassi C, Kryszak D, Louis-Jacques O, et al. Detection of celiac disease in primary care: a multicenter case-finding study in North America. *Am J Gastroenterol.* 2007;102(7):1454-1460.

Antibiotic prophylaxis may not decrease recurrent UTI risk in children

Clinical question Does antibiotic prophylaxis reduce the risk of recurrent urinary tract infection (UTI) in children?

Bottom line In a cohort of otherwise healthy children with a first UTI, antibiotic prophylaxis exposure was not associated with a reduced risk of recurrent UTI. Antibiotic exposure did, however, increase the risk of treatment-resistant pathogens. (Level of evidence = 2b)

Synopsis Although evidence of benefit is limited, clinicians commonly prescribe antibiotics to prevent recurrent UTIs in children. These investigators analyzed a cohort of children, aged 6 years or younger, with a first UTI from 27 primary care pediatric practices in the United States that share a

common electronic health record. To minimize lost data, researchers also searched both electronic and paper charts for information obtained from out-of-network hospitals and clinics. The authors do not state whether individuals assessing outcomes remained masked to the study hypothesis. However, independent data validation occurred by randomly comparing 5% of the abstracted information with the medical record. Agreement occurred with 95% of the data. Recurrent UTI was defined as a second positive urine culture obtained at least 2 weeks after completing therapy for the first UTI. From a total of 74,974 children seen for at least two clinic visits, 666 otherwise healthy children had a confirmed first UTI. Of these, 611 children underwent at least 24 days of follow-up. Nearly 90% of these children were female. Recurrent UTI occurred in 83 children (12% per year), with 51 (61%) of these recurrent infections caused by pathogens resistant to one or more antimicrobials. Using both univariate and multivariate analytic methods, factors associated with an increased risk of recurrent UTI included white race, aged 2 years or older, and grade 4 to 5 vesicoureteral reflux. Antibiotic prophylaxis exposure was not associated with a reduced risk of recurrent infection, but was significantly related to an increased risk of resistant infection.

Conway PH, Cnaan A, Zaoutis T, et al. Recurrent urinary tract infections in children: risk factors and association with prophylactic antimicrobials. *JAMA*. 2007;298(2):179-186.