Vitamin D supplementation could ease IBS symptoms

January 26 2018. A review published on January 25, 2018 in the *European Journal of Clinical Nutrition* adds evidence to a beneficial effect for vitamin D against unpleasant symptoms and diminished quality of life experienced by individuals with irritable bowel syndrome (IBS), a chronic, relapsing, functional bowel disorder whose cause is unknown. The syndrome is characterized by bloating, abdominal pain, diarrhea and constipation. Stress and dietary factors have been observed to worsen symptoms.

"IBS is a poorly understood condition which impacts severely on the quality of life of sufferers," noted lead researcher Dr Bernard Corfe of the University of Sheffield’s Department of Oncology and Metabolism. “There is no single known cause and likewise no single known cure." In their review, Dr Corfe and his associates note that four observational studies and three randomized controlled trials have examined the effects of vitamin D in irritable bowel syndrome. All observational studies uncovered vitamin D deficiency in a substantial proportion of people with IBS. Two of the intervention studies found improvement in IBS symptom severity and quality of life in association with vitamin D supplementation. The findings suggest that low vitamin D is common in IBS patients and that vitamin D supplementation could help improve symptoms. "The study provides an insight into the condition and, importantly, a new way to try to manage it," Dr Corfe stated. "It is evident from the findings that all people with IBS should have their vitamin D levels tested and a large majority of them would benefit from supplements.”

Despite improvements in cancer therapies, cancer is the leading cause of death worldwide. Many patients experience severe, unnecessary symptoms during treatment as well as at the end of life. Often, patients receive 'aggressive' care at the end of life that is discordant with their preferences. Palliative care is an approach that focuses on communication and quality of life, including treatment of physical, psychosocial, and spiritual suffering. This approach is appropriate for patients with life-limiting cancer, throughout the course of their disease. A growing body of evidence supports the integration of palliative care into routine cancer care, owing to the benefits in symptom control, quality of life, patient satisfaction, and resource utilization. Palliative care can be delivered in inpatient, outpatient, and home-based settings. The specialty and associated infrastructure is expanding rapidly with support from the international medical community. The ideal model of how to incorporate palliative care providers into the care of patients with cancer is yet to be defined; future research is needed to develop delivery systems and improve access to palliative care services. Through collaboration between oncologists and palliative care teams, there is hope of improving the quality of care for patients with both curable and life-limiting cancers.

* https://www.nature.com/articles/nrclinonc.2012.211

**Daily Dose of Almonds, Dark Chocolate May Improve Lipid Profile**

Megan Brooks, December 04, 2017: Incorporating almonds, dark chocolate, and cocoa into a healthy diet may help reduce a risk factor for coronary heart disease (CHD). In a controlled trial, researchers found that eating nearly one-third cup of almonds a day—either alone or combined with almost one-quarter cup of dark chocolate and a little more than 2 tablespoons of cocoa a day—improved lipid/lipoprotein profiles, when compared with the average American diet absent of almonds and chocolate. Of note, say the researchers, the combined intake of almonds, dark chocolate, and cocoa led to a significant reduction in small dense LDL-cholesterol particles, a recognized risk factor for CHD. "It's important to put this into context:
The message is not that people should go out and eat a lot of chocolate and almonds to lower their LDL," lead researcher Dr Penny M Kris-Etherton (Penn State University, University Park, PA), said in a statement. "People are allowed to have about 270 discretionary calories a day, and when foods like almonds, dark chocolate, and cocoa are consumed together as a discretionary food, they confer health benefits unlike other discretionary foods such as frosted doughnuts," she said. "A take-home message is: choose your discretionary calories wisely. "Dark chocolate and almonds cannot substitute for an overall healthy dietary pattern," registered dietitian, who wasn't involved in the study, told the heart.org | Medscape Cardiology. "Yet choosing this approach toward that goal has benefits over a sugar-sweetened beverage or other option that offers only sugar and calories without the unsaturated fatty acids and flavanols that chocolate and almonds confer," she said. The study, which was funded by the Hershey Company and the Almond Board of California, was published November 29, 2017 in the Journal of the American Heart Association. Eating almonds or dark chocolate and cocoa regularly has been shown to have favorable effects on markers of CHD, but the combined effects have not been evaluated in a well-controlled feeding study, the researchers point out in their article. They investigated the individual and combined effects of dark chocolate, cocoa, and almonds on lipid, lipoprotein, and apolipoprotein concentrations, vascular health, and oxidative stress in 31 adults (13 female; mean age 46.3 years) who were overweight or obese (mean BMI 29.6 kg/m2) with elevated total cholesterol (TC, 210.0 mg/dL) and LDL cholesterol (138.3 mg/dL) but who were otherwise healthy. In this crossover study, participants consumed each of four isocaloric weight-maintenance diets: No "treatment" foods (average American diet). 42.5 g/day almonds (almond diet). 18 g/day cocoa powder and 43 g/day dark chocolate (chocolate diet). Almonds, cocoa powder, and dark chocolate (chocolate/almond diet). The diets were similar, except for the presence or absence of these treatment foods, which accounted for the major differences in the nutrient profile. Each diet period lasted for 4 weeks, followed by a 2-week compliance break. Compared with the average American diet, TC, non–HDL-C, and LDL-C after the almond diet were reduced by 4%, 5%, and 7%, respectively (P<0.05). The dual chocolate and almond diet reduced apolipoprotein B by 5% compared with the average American diet. For LDL subclasses, relative to the average American diet, the almond diet yielded a greater reduction in large buoyant LDL particles (-5.7 vs. -0.3 mg/dL; P=0.04), whereas the chocolate and almond diet provided a greater decrease in small dense LDL particles (-12.0 vs -5.3 mg/dL; P=0.04). However, neither almonds nor dark chocolate and cocoa affected markers of vascular health and oxidative stress. "Incorporating almonds, dark chocolate, and cocoa into a typical American diet without exceeding energy needs may reduce the risk of coronary heart disease," Kris-Etherton and colleagues conclude in their article. The researchers emphasize that these findings are specific to the patient population studied—overweight and obese middle-aged adults with elevated TC and LDL-C. That's clearly an important message here. Almonds can be part of a healthy diet. In an interview, bariatric dietitian cautioned that "no firm conclusions" can be drawn from this study about the value of eating almonds and chocolate on lipid profiles, adding that she "didn't find anything outstanding in the findings." She also was "surprised" that the diets were not particularly healthy, as they included croissants, pretzels, and white bread, "which are foods we would not recommend."

* References

Age-related declines in the immune system may better explain the increasing incidence of cancer with age than can simply the steady accumulation of genetic mutations. This new finding could affect cancer prevention and treatment, say the investigators. The research, which was published online in the Proceedings of the National Academy of Sciences of the United States of America on February 5, used a mathematical model to compare age-related changes in the incidence of over 100 cancers with age-related declines in the immune system and found that the model fit very well for more than 50 types of cancer.

The model was a better fit than the traditional model of accumulating genetic mutations and was better able to explain sex differences in the age-related increase in cancer incidence for specific forms of the disease.

Senior author, Thea Newman, PhD, School of Life Sciences, University of Dundee, United Kingdom, said in a release, "This is still very early days but if we are proven right then you could be talking about a whole new way to treat and prevent cancer."

She continued: "Nearly all of the mainstream research into cancer is based on how we can understand genetic mutations, target them and thereby cure the disease. "We're not debating the fact that mutations cause cancer, but are asking whether mutations alone can account for the rapid rise in cancer incidence with age when ageing causes other profound changes in the body."

Coauthor Clare C. Blackburn, PhD, Medical Research Council Centre for Regenerative Medicine University of Edinburgh, United Kingdom, added: "We believe that our findings are extremely relevant and show the need to take the immune system even more seriously in cancer research." However, an expert in the field approached for comment questioned the researchers' conclusions, pointing out that they relied on an outdated model of tumorigenesis and that not all cancer incidence rates simply increase with age, as implied by their model.

CANCER RISK INCREASE WITH AGE

Previous studies have shown that the incidence of cancer increases with age, with a median pivot age (signifying the crossover between a very low to relatively high risk) of 49.9 years across all cancer types.

Moreover, it is known that genetic predisposition and exposure to lifestyle and environmental factors lead to cancer via the accumulation of DNA mutations, with the traditional belief that five to six rare "driver" mutations are required in one cell to initiate cancer, termed the power law model. Because the incidence of many infectious diseases also increases with age, the researchers hypothesized that the age-related changes in cancer incidence may be better explained by the aging immune system than by solely the accumulation of mutations. They therefore developed a mathematical model based on two assumptions:

1. That potentially cancerous cells arise with equal probability at any age and
2. That there is an immune escape threshold related to T cell production, above which immunogenic cells can overwhelm the immune system and lead to a clinically detectable disease. For our model, we imagined a war between T cells and cancer cells, which the cancer cells win if they grow beyond a certain threshold," said lead author, Sam Palmer, PhD, School of Mathematical and Computer Sciences, Heriot-Watt University Malaysia, Putrajaya.
Mutations as Key Cause of Cancer

For comment, Medscape Medical News approached Cristian Tomasetti, PhD, from the Sidney Kimmel Comprehensive Cancer Center, Johns Hopkins University School of Medicine, Baltimore, Maryland, who has coauthored several recent papers suggesting that random mutations are responsible for most cancers. Those findings were widely reported in the media as showing that most cancer is "due to bad luck."

Dr Tomasetti said that he does not "consider their study sound."

"The power law does not represent the correct model for tumorigenesis; it is a more than 50-year-old model that captures only some aspects of the tumorigenesis process," he said.

"Therefore, a comparison between their model and the power law does not represent the appropriate analysis to conclude that their model is better at explaining the observed data than the current theory based on the gradual accumulation of somatic mutations."

He added: "With their theory, it is very difficult to explain why for various cancer types the incidence decreases at very old ages."

Dr Tomasetti also noted that a large literature supports the gradual accumulation of cancer mutations as a key cause of cancer.

Beta blockers safe for most patients with asthma or COPD?

January 05 2018. On December 7, 2017 in PLOS ONE, researchers Once upon a time in 1964, it was noted that propranolol, a nonselective beta-blocker, could precipitate severe bronchospasm in patients with asthma, especially at high doses. Additional small studies showed propranolol and other nonselective beta blockers could increase airway resistance. British guidelines advise avoiding beta blockers in asthma generally. As a result, beta blockers are often withheld from people with asthma or COPD who might benefit (i.e., those with congestive heart failure or past myocardial infarction). More recent evidence from better-quality studies suggests newer, cardioselective beta blockers appear safe and might even be beneficial in people with COPD, potentially reducing mortality and exacerbations. As for asthma, chronic use of cardioselective beta blockers doesn't seem to precipitate asthma attacks in mild or moderate asthma. A 2002 meta-analysis in Annals Internal Medicine showed that a single dose of beta blocker did reduce asthmatics' FEV1 by ~7.5% predicted, but this decrement went away with chronic use. They concluded "Cardioselective beta-blockers do not produce clinically significant adverse respiratory effects in patients with mild to moderate reactive airway disease ... cardioselective beta-blockers should not be withheld from patients with mild to moderate reactive airway disease." (That analysis did also conclude that nonselective beta-blocker use reduced FEV1, FVC, and bronchodilator response to β-agonist, but without noticeable increase in subjective respiratory symptoms or need for β-agonist inhalers.) A 2014 meta-analysis of 32 studies suggested more caution, reporting that 1 in 8 asthmatics exposed to selective beta blockers had an acute drop >20% in FEV1. That analysis could not report on chronic use of beta blockers, nor exacerbation risk. Chronic use of beta blockers, including nonselective beta blockers like nadolol, may actually improve bronchodilator response to albuterol, through as-yet undetermined effects. A very small randomized trial suggested that even nonselective beta blockers (propranolol) may be safer than previously believed for patients with mild to moderate asthma. Authors randomized 18 patients taking inhaled corticosteroids for mild to moderate asthma to receive propranolol up to 80 mg or placebo for 6-8 weeks in a crossover design study. Patients continued their inhaled steroids and were also given tiotropium, presumably as a safety measure. At trial's end, there were no significant differences between groups in airway hyperresponsiveness or asthma symptoms, although there was a 2.4% reduction in FEV1 predicted after chronic beta-blocker usage. Beta blockers are a key component of care for people who have had previous heart attacks or who have systolic heart failure. Three beta blockers have demonstrated a survival benefit in systolic heart failure: the cardioselective agents metoprolol XL and bisoprolol, and the non-cardioselective atenolol. It seems unlikely that the risks of worsening asthma or COPD outweigh the potential benefits of beta blocker use, in these patients.

* Beta blockers have not been proven beneficial in randomized trials for stable coronary artery disease (primary prevention in people without a previous myocardial infarction or who have risk factors). The theorized benefit among these patients drives the vast majority of beta-blocker prescriptions, but there is today no evidence-based imperative for this practice. So aside from asthma/COPD patients with prior heart attacks or systolic heart failure -- almost all of whom should receive beta blockers, as a rule -- this is a mostly academic debate.

* https://pulmccm.org/asthma-review/beta-blockers-safe-for-most-patients-with-asthma-ajrccm/
Case reports from our Egyptian Pharmaceutical Vigilance Center (EPVC)

Case Reports from Sohag-Toxic level dose with Digoxin

The Egyptian pharmaceutical Vigilance regional center in Sohag has received 14 ICSRs of toxicity with Digoxin administration and was manifested by nausea and vomiting in few cases. Seven of them for adult female patients, five for adult male patients, one for infant three months age and one for child male patient ten years old. All of the adult patients had administered Digoxin tabet as (0.25 mg per day) and both the infant and the child had administered Digoxin injection as (0.01 mg/ kg per day) not for long time (from a week to 6 months). Then their automatic analysis showed Digoxin level above 2 ng (toxic level); and since the normal level between (0.7 ng – 2 ng), then their physician stopped the administration of Digoxin.

Upon search, it was found that:

Digoxin toxicity: is indicated by nausea, vomiting, visual disturbances, and cardiac arrhythmias. Advanced age, low body weight, impaired renal function and electrolyte abnormalities predispose to toxicity.

Interpret the serum digoxin concentration in the overall clinical context, and do not use an isolated measurement of serum digoxin concentration as the basis for increasing or decreasing the LANOXIN dose. Serum digoxin concentrations may be falsely elevated by endogenous digoxin-like substances. If the assay is sensitive to these substances, consider obtaining a baseline digoxin level before starting LANOXIN and correct post-treatment values by the reported baseline level. Blood should be taken 6 hours or more after the last dose of digoxin. There are no rigid guidelines as to the range of serum concentrations that are most efficacious but most patients will benefit, with little risk of toxic symptoms and signs developing, with digoxin concentrations from 0.8 ng/ml (1.02 nmol/L) to 2.0ng/ml (2.56nmol/L). Above this range toxic symptoms and signs become more frequent and levels above 3ng/ml (3.84nmol/L) are quite likely to be toxic. However, in deciding whether a patient's symptoms are due to digoxin, the patent's clinical state together with the serum potassium level and thyroid function is important factors. Other glycosides, including metabolites of digoxin, can interfere with the assays that are available and one should always be wary of values, which do not seem commensurate with the clinical state of the patient.

References: Egyptian Pharmaceutical Vigilance Center (EPVC) newsletter. October 2016, vol.(7) issue (10)
NEW SHINGLES VACCINE: WHAT YOU NEED TO KNOW

In October 2017, the FDA approved a new shingles vaccine, called Shingrix. The CDC officially recommended that adults 50 and over get the new vaccine to prevent this painful, blistering disease instead of the previous one, Zostavax.

How is Shingrix different from Zostavax?
Shingrix is more than 90% effective at preventing shingles and a painful complication called postherpetic neuralgia (PHN) in all age groups. Zostavax only lowers the odds of getting shingles by 51%, and of PHN by 67%. It's even less effective in people ages 70 and older. The Zostavax vaccine has been around since 2006. It contains a live but weakened version of varicella zoster -- the virus that causes shingles and chickenpox. Shingrix has a dead version of the zoster virus. It also contains an adjuvant -- a substance that helps your body fight off the virus better. "It causes your immune system to produce more antibodies to fight shingles than the other vaccine produced. So your body has a stronger immune response to the Shingrix vaccine than to the Zostavax vaccine,"

How many doses of the vaccine do you need?
Two doses are needed, given 2 to 6 months apart. "That second dose is really important to make sure you get long-term protection," Hogue says.

What are the side effects?
Shingrix causes more side effects than Zostavax. "That's the price you pay for the boost in immune response," Schmader says. The main side effects reported in studies were soreness, redness, and swelling where you get the shot. Some people also got headaches or felt tired or achy after the shot. About 1 out of 10 people said the side effects were severe enough to disrupt their daily life. Yet most felt better within 3 to 5 days. “The side effects of the Shingrix are temporary, and usually last 2 to 3 days. While you may experience pain for a few days after getting Shingrix, the pain will be less severe than having shingles and the complications from the disease,“.


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