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Studies Find that Folate Reduces Risk of Colorectal Cancer and Adenomas

A couple of speculative reports caused a small panic when they suggested that taking folic acid – the form of the vitamin used in most supplements – could increase the risk of developing colorectal cancer. The idea was repeated by doctors, newspaper stories, and on the internet, and it was starting to become a medical urban legend.

But it's apparently false. Two new studies have found that both folic acid and folate (the form found in plants) are associated with a significant reduction in the risk of colorectal cancer.

Edward Giovannucci, MD, of Harvard University, and his colleagues drew on data from two large studies, which included more than 151,000 women and 51,000 men. Between 1980 and 2004, 2,299 of the subjects were diagnosed with colorectal cancer, and 5,655 were diagnosed with colorectal adenomas, a type of growth that could be either benign or precancerous.

People who had consumed relatively large amounts of folate or folic acid (from supplements or fortified foods) for 12 to 16 years were about 30 percent less likely to develop colorectal cancer. Similarly, high folate or folic acid intake for four to eight years was associated with a 30 percent lower risk of adenomas.

There was no relationship between folate or folic acid and a greater risk of colorectal cancer or adenomas.

Multivitamins also had benefits. People who took them for more than 15 years had a lower risk of colorectal cancer, while taking them for less time lowered the risk of adenomas.

In another study, Victoria L. Stevens, PhD, a researcher at the American Cancer Society, Atlanta, Georgia, and her colleagues analyzed data from studies of more than 56,000 women and 43,000 men. They found that both folate and folic acid were associated with lower risks of colorectal cancer, and that total intake of the vitamin was related to a 19% lower risk of the disease.

"Intake of high levels of total folate reduces risk of colorectal cancer; there is no evidence that dietary fortification or supplementation with this vitamin increases colorectal cancer risk," wrote Stevens and her colleagues.

One of folate's roles is in the regulation of our genes. The vitamin plays an essential role in the production of chemical units called "methyl groups," which attach to genes and then regulate their activity. This process is known to turn off many of the genes involved in promoting cancer.

References: Lee JE, Willett WC, Fuchs CS, et al. Folate intake and risk of colorectal cancer and adenoma: modification by time. *American Journal of Clinical Nutrition*, 2011;93: 817-825. Stevens VL, McCullough ML, Sun J, et al. High levels of folate from supplements and fortification are not associated with increased risk of colorectal cancer. *Gastroenterology*, 2011;141:98-105.e1. ❑

Perspectives

The Problem with Too Much Salt

The ancient human diet contained several times more potassium than sodium, and our bodies are better suited for metabolizing the former. The problem? Today's diets often provide 10 times more sodium than potassium.

High sodium intake in the form of salt is strongly associated with hypertension and heart disease, but some of the evidence is conflicting. Part of the reason is that researchers have focused more on sodium than the amount of potassium in diets.

A couple of recent studies seemed to upend the link between sodium and heart disease. These studies showed little relationship between sodium and heart diseases.

Then earlier this month, an article in the *Archives of Internal Medicine* looked at the relationship of both sodium and potassium to heart disease. The researchers showed that a high intake of sodium

More research summaries on next page

combined with low intake of potassium increased the risk of heart disease by more than two times and increased the risk of cardiovascular death by almost 50%. A high sodium-to-potassium ratio also boosted the risk of death from any cause by 50%, suggesting an even broader impact on health.

But what most people miss in this discussion is that most dietary sodium doesn't come from the salt shaker on your dining table. Rather, it's added to packaged and prepared foods before you even buy them. Packaging – that is, boxes, cans, bottles, jars, tubs, and bags – indicate that food has been processed. Processing usually reduces the nutritional value of foods while increasing both the salt and sugar content to seduce your taste buds.

Vegetables and fruits are great natural sources of potassium, while also being low in sodium. So the research on sodium and potassium really points to two different types of eating habits: high-sodium diets reflect to the overconsumption of packaged, convenience, and fast foods, whereas high-potassium diets reflect eating habits that focus on a lot of vegetables and fruits. *–JC*

Taking Prenatal Multivitamins May Lower Autism Risk in Kids

Many different environmental factors seems to influence the risk of autism in children, and a new study suggests that women who take multivitamins before or during their pregnancy have a lower risk of having children who develop autism.

Rebecca J. Schmidt, PhD, of the University of California, Davis, and her colleagues studied 429 children with autism, ages two to five years, and compared them with 278 children with normal development.

Overall, children whose mothers took prenatal multivitamins for at least three months early in their pregnancy were 28 percent less likely to develop autism.

The risk of autism was particularly high – four and one-half times above normal – if the mothers did not take prenatal vitamins and if they also had a genetic variation known as MTHFR 677 TT. The MTHFR 677 TT variation interferes with the body's use of folic acid, which is critical for normal fetal development during the first few weeks of pregnancy.

Another genetic variation called COMT 472 AA in mothers was associated with a seven time increase in the risk of autism in their children, if the mothers did not take prenatal vitamins.

"Periconceptual use of prenatal vitamins may reduce the risk of having children with autism, especially for genetically susceptible mothers and children.

Reference: Schmidt RJ, Hansen RL, Hartiala J, et al. Prenatal vitamins, one-carbon metabolism gene variants, and risk for autism. *Epidemiology*, 2011;22:476-485. ❑

Sunlight and More Vitamin D Help with Rheumatic Diseases

Spending more time in the sun – what a team of researchers calls climatotherapy – results in significant increases in vitamin D and improvements in a variety of rheumatic diseases.

Marco Harari, MD, of the DMZ Medical Center Spa, in Dead Sea, Israel, and his colleagues treated 60 Norwegian women and men, with an average age of 62 years, for three weeks. The patients were divided into three groups: those with chronic pain syndromes, low back pain or fibromyalgia, and rheumatoid arthritis.

On admission, only 36.7% of the patients had optimal vitamin D levels, 40% had adequate levels, and 23.3% were deficient. The treatment protocol included daily sun exposure, soaking in the Dead Sea and mineral waters, mud applications, and fitness classes.

By the end of the 21-day study, the patients' vitamin D levels increased by an average of 25%. Overall, patients had a 60% decrease in pain.

Other research has shown that vitamin D plays a key role in the regulation of immunity, both in fighting infections and in modulating auto-immune reactions.

Reference: Harari M, Dramsdahl E, Shany S, et al. Increased vitamin D serum levels correlate with clinical improvement of rheumatic diseases after Dead Sea climatotherapy. *Israel Medical Association Journal*, 2011;13:212-215. ❑

High-Dose Alpha-Lipoic Acid, an Antioxidant, Aids in Weight Loss

Taking large amounts of alpha-lipoic acid can lead to a modest but meaningful amount of weight loss.

Alpha-lipoic acid plays a crucial role in mitochondrial bioenergetics, a process in which food molecules are burned for energy.

Ki-Up Lee, MD, of the University of Ulsan College of Medicine, South Korea, and his colleagues treated 360 obese men and women who also had high blood pressure, type 2 diabetes, or elevated cholesterol levels. The subjects, whose average age was 41 years, were asked to take 1,200 mg or 1,800 mg of alpha-lipoic acid or placebos daily for 20 weeks.

In both of the groups taking alpha-lipoic acid, the average weight declined significantly as early as four

weeks into the study. However, by the end of the study, only people taking 1,800 mg of alpha-lipoic acid daily mantained significantly greater weight loss compared with the placebo group.

People taking the larger amount of alpha-lipoic acid lost an average 3% of body weight, whereas those in the placebo group had a 1% loss of weight. Furthermore, many of the people taking 1,800 mg of alpha-lipoic acid lost more than 5% of their weight.

People taking alpha-lipoic acid used the R-lipoic acid form of the vitamin.

Reference: Koh EH, Lee WJ, Lee SA, et al. Effects of alpha-lipoic acid on body weight in obese subjects. *American Journal of Medicine*, 2011;124:85.e1-85.e8. ❑

Cutting Calories and Losing Weight Improves Sleep Apnea

Going on a very low-calorie diet and losing weight can lead to striking improvements in obstructive sleep apnea, according to a study by researchers at the Karolinska Institute in Stockholm, Sweden. The institute is the Swedish equivalent to the U.S. National Institutes of Health, which conducts research on a wide variety of diseases.

Sleep apnea is characterized by cessations in breathing while sleeping. Most of the people who suffer from it are overweight or obese, and they are at risk of developing many other health problems.

For one year, Kari Johansson, a PhD student, and her colleagues treated 63 men, ages 30 to 65 years, who were obese. Forty-four of the subjects completed the entire study.

The subjects were initially placed on a 550-calorie daily diet for seven weeks, followed by a two-week transition to a 1,500-calorie daily weight-maintenance diet for the rest of the study. The subjects were closely monitored, coached by a dietitian, and participated in monthly group therapy meetings.

The researchers tracked patients with an apnea-hypoapnea index, which reflected the total number of times in which breathing ceases during each hour of sleep. At the start of the study patients averaged 36 episodes of interrupted breathing per hour.

After being on the very low-calorie diet, the average number of sleep apnea episodes decreased by 21 per hour. The subjects had also lost an average of almost 40 pounds of weight.

After a year, the number of sleep apnea episodes averaged 17, down from 36 per hour. Weight loss at the end of the study averaged 26 pounds.

Patients with the most severe sleep apnea at the beginning of the study improved the most, as did those who lost the most weight.

Also after one year, half of the patients no longer needed to wear a type of mask to improve breathing while sleeping, and 10% of them had a complete remission of their sleep apnea.

Reference: Johansson K, Hemmingsson E, Harlid R, et al. Longer term effects of very low energy diet on obstructive sleep apnoea in sohort derived from randomised controlled trial: prospective observational follow-up study. *BMJ*, 2011;342:d3017. ❑

Selenium Supplements Lead to Improvements in Cholesterol

Taking selenium supplements can lead to reductions in total blood cholesterol and improvements in the "good" high-density lipoprotein (HDL) form of cholesterol.

Margaret P. Rayman, PhD, of the University of Surrey, United Kingdom, and her colleagues recruited 501 subjects, ages 60 to 74 years. The subjects were divided into four groups, which received 100, 200, or 300 mcg of high-selenium yeast supplements, or placebos, daily for six months.

People taking 100 mcg of selenium had an average 8.5 mg/dl decrease in their cholesterol levels, and those taking 200 mcg of selenium had an average 9.7 mg/dl decrease.

Those taking 300 mcg of selenium daily had just a 2.7 mg/dl decrease in their cholesterol. However, this group was the only one to have a significant increase in HDL cholesterol – an average of 2.3 mg/dl.

Reference: Rayman MP, Stranges S, Griffin BA, et al. Effect of supplementation with high-selenium yeast on plasma lipids. *Annals of Internal Medicine*, 2011;154:656-665. ❑

Folic Acid, Leafy Green Veggies Linked to Smarter Students

Swedish researchers have shown that students who have a relatively high intake of the B-vitamin folic acid get better grades at school.

Torbjorn K. Nilsson, MD, PhD, of Orebro University Hospital and his colleagues analyzed the grades and diets of 386 15-year-old boys and girls who were finishing their school year. After adding the grades from 10 core classes, the researchers found that the teenagers who had a higher dietary intake of folic acid also had higher academic scores.

The students did not eat fortified foods or take supplements during the study. Therefore, the most likely source of folic acid was leafy green vegetables.

According to Nilsson, teenagers are at risk of low folic acid intake and, consequently, higher homocysteine levels.

Reference: Nilsson TK, Yngve A, Böttiger AK, et al. High folate intake is related to better academic achievement in Swedish adolescents. *Pediatrics*, 2011; doi10.1542/peds.2010-1481. ❑

Quick Reviews of Recent Research

• FDA warns that drugs can lower magnesium

Acid-blocking proton-pump inhibitor (PPI) drugs interfere with the absorption of vitamins B12 and C. In a safety announcement, the U.S. Food and Drug Administration (FDA) warned that the use of PPIs for more than one year also interferes with magnesium absorption. PPI drugs include Nexium, Prilosec, and Prevacid. In 2009, 21 million prescriptions were filled for these drugs. Low levels of magnesium can cause muscle spasms, irregular heartbeat, and seizures.

http://www.fda.gov/Drugs/DrugSafety/ucm245011.htm#Safety_Announcement

• Formula-feeding boosts prediabetes risk

Italian researchers studied 350 overweight or obese eight-year-old children. Children who were fed formula as infants had greater insulin resistance, a sign of prediabetes, compared with children who had been breast fed. The researchers concluded that "formula feeding seems to be associated with reduced insulin sensitivity and increased insulin secretion in overweight and obese children."

Manco M. *Journal of the American College of Nutrition*, 2011;30:29-39.

• Sugary soft drinks raise disease risk factors

Consuming any type of soft drink increases the risk of inflammation, diabetes, or heart disease, according to a study by researchers in Switzerland. The researchers recruited 29 healthy young men to participate in six three-week tests of different soft drink formulations. The daily 20-ounce (600mL) soft drinks provided one of the following during each phase of the study: 40 grams of fructose, 80 grams of fructose, 40 grams of glucose, 80 grams of glucose, or 80 grams of sucrose. One of the three-week tests focused on dietary advice to lower fructose consumption. Low-density lipoprotein (LDL) particle size was reduced – worsening a risk factor for heart disease – after consumption of the high-fructose and high-sucrose drinks. The other fructose-containing beverages resulted in similar changes. Fasting blood sugar and C-reactive protein levels also increased after consumption of the soft drinks.

Aeberli I. *American Journal of Clinical Nutrition*, 2011; doi 10.3945/ajcn.111.013540.

• Potato chips pack on the pounds

Researchers at Harvard University analyzed changes in dietary habits and weight gain in more than 120,000 American men and women between 1986 and 2006. They found that potato chips were associated with the greatest increase in weight, followed by all other forms of potatoes (e.g., fries) and sugar-sweetened soft drinks. Weight loss was associated with the consumption of vegetables, whole grains, fruits, nuts, and yogurt.

Mazaffarian D. *New England Journal of Medicine*, 2011; 364:2392-2404.

• Fish oils beneficial after heart procedure

Doctors from Krakow, Poland, treated 53 patients with balloon angioplasty and stents to improve blood flow through their arteries. Twenty-four of the patients were treated with aspirin and clopidogrel (Plavix) to prevent clots, and 30 patients were treated with these drugs plus 1 gram daily of omega-3 fish oils (which included 460 mg of EPA and 380 mg of DHA). Patients receiving the omega-3 fish oils had lower levels of thrombin, a clotting factor. They also formed clots with a different structure that allowed the body to break them down with greater ease.

Gajos G. *Arteriosclerosis, Thrombosis, and Vascular Biology*, 2011;31:1696-1702.

• Low vitamin D raises infection risk in infants

Infants with low levels of vitamin D are more likely to contract a serious lower respiratory infection called respiratory syncytial virus (RSV). The research, conducted in the Netherlands, found that infants were six times more likely to develop RSV during their first year of life if they had low levels of vitamin D.

Belderbos ME. *Pediatrics*, 2001: doi 10.1542/peds.2010-3054.

• Supplement reduces preeclampsia risk

Researchers in Mexico tested the effects of a nutrition bar fortified with L-arginine and antioxidants on 672 women at high risk of developing preeclampsia. Consuming two bars daily, providing 6.6 grams of L-arginine, 500 mg of vitamin C, and 400 IU of vitamin E led to a significant reduction in the risk of preeclampsia.

Vadillo-Ortega F. *BMJ*, 2011: doi 10.1136/bmj.d2901.

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