The Nutrition Reporter™
© Jack Challem September 2002 Vol 13 No 9
The independent newsletter that reports vitamin, mineral, and food therapies

Rethinking the Glycemic Index: It May Be Better to Consider the "Glycemic Load"

Millions of people use the "glycemic index" to predict the effect of carbohydrates they eat – and for good reason. Some are diabetics trying to minimize dangerous blood-sugar swings. Others are trying to control blood-sugar levels to prevent diabetes. But views of the glycemic index are shifting, evidenced by several noteworthy scientific articles.

In theory, the glycemic index, proposed in 1981, measures how specific carbohydrate-containing foods raise blood sugar levels. But the glycemic index can often be perplexing. Two versions of it use glucose and white bread – highly refined, high-glycemic food products – as reference points for measuring other foods. Puzzling as well is how some foods stack up on the glycemic index. For example, table sugar ranks a mid-range 59, whereas carrots are a very high 92, leaving the impression that white sugar is healthier than carrots.

The glycemic index is based on how the blood sugar levels of test subjects respond to 50-gram servings of particular foods, such as bread, pasta, rice, fruits, and vegetables. Unfortunately, glycemic index rankings for meats and nonstarchy vegetables are rarely published.

More recently, some researchers have advocated a slightly different standard, the "glycemic load," based on the glycemic index multipled by the amount of carbohydrate in the food. For example, 50 grams of a baked potato ranks very high on both the glycemic index and the glycemic load, 85 and 20 respectively. (The numerical scale of the glycemic load is lower). But while carrots rank near the top of the glycemic index, they rank at the bottom of the glycemic load, ranging from 1 to 3. Thus, carrots *are* healthier than high-carbohydrate, high-glycemic foods, such as table sugar.

Other low-starch or nonstarchy fruits and vegetables also fare better on the glycemic load. Apples, apricots, cherries, grapefruit, oranges, papaya, peaches, pears, and plums rank in the middle of the glycemic index, but near the bottom of the glycemic load. Strawberries, which also rank in the middle of the glycemic index, rank only 1 on the glycemic load. Plain sausages, as well as peanuts, have a negligible effect on the glycemic load, and broccoli has no effect whatsoever.

So, how does this affect you? According to David S. Ludwig, MD, PhD, of the Harvard Medical School, the glycemic index and the glycemic load of the American (Western) diet has risen in recent years, the result of greater consumption of highly processed carbohydrates. In general, refined starchy foods tend to have a higher glycemic index and load, whereas nonstarchy vegetables and fruit, meats, and fish tend to have a lower glycemic index and load.

According to an article by Ludwig in the *Journal of the American Medical Association*, foods that rank high on the glycemic index and glycemic load set the stage for hunger pangs, overeating, overweight, diabetes, and heart disease. Here's why: After a high glycemic meal (e.g., containing bread, cereal, instant rice, or potato), blood-sugar levels can rise twice as high as after a low-glycemic meal. High-glycemic foods trigger a rapid insulin release, pushing blood-sugar levels too low and leaving a person hungry.

According to Ludwig, post-meal hypoglycemia, followed by hunger and more eating, is so common that it is considered normal. Furthermore, a high-glycemic meal leaves a person more sensitive to carbohydrates at the following meal.

Chronically elevated insulin levels set the stage for insulin resistance, which underscore diabetes. Ludwig argues that the rational alternative is to eat a low-glycemic diet that moderates both blood sugar and insulin levels.

References: Ludwig DS. The glycemic index. Physiological mechanisms relating to obesity, diabetes, and cardiovascular disease. *JAMA*, 2002;287:2414-2423. Foster-Powell K, Holt SHA, Brand-Miller JC. International table of glycemic index and glycemic load values: 2002. *American Journal of Clincial Nutrition*, 2002;76:5-56. □

N-Acetylcysteine Supplements May Benefit Some Women with PCOS

An estimated 10 percent of reproductive-age women suffer from polycystic ovary syndrome (PCOS). The condition is typically characterized by elevated levels of male hormones, excess facial hair, enlarged ovaries with many cysts, a lack of ovulation, and difficulty conceiving. Elevated insulin levels (hyperinsulinemia) and prediabetic insulin resistance occurs in more than half of women with PCOS, with hyperinsulinemia more common in obese than in thin PCOS patients.

Many insulin- and glucose-regulating supplements could potentially benefit PCOS. But a recent study has found that one supplement, N-acetylcysteine (NAC), may be especially helpful. NAC is well established as an antidote for Tylenol overdose, for breaking up lung mucous, and for reducing flu symptoms, and some research indicates that it can improve insulin function.

Anna Maria Fulghesu, MD, of the Universita Cattolica del Sacro Cuore, Rome, and her colleagues gave NAC to 25 PCOS patients, ages 19-33. Six other patients received placebos. Some of the women were obese, and some (but not all) had elevated insulin levels. Most patients received 1,800 mg of NAC daily for five to six weeks; obese patients received 3,000 mg of NAC daily.

The PCOS patients with elevated insulin levels had significant improvements after taking NAC. Their insulin levels decreased by about 14 percent and their insulin sensitivity improved, both positive signs. Other benefits included declines in testosterone and other male hormones, as well as significant reductions in total cholesterol and triglycerides.

None of these improvements occurred in PCOS patients with normal insulin levels who took NAC or in any of the patients taking placebos.

The researchers wrote that NAC "may be a new treatment for hyperinsulinemia in patients with PCOS....Lower NAC doses for a longer time (6 months or more) could be equally effective in improving the insulin disorders associated with PCOS."

Reference: Gulghesu AM, Ciampelli M, Muzj G, et al. N-acetyl-cysteine treatment improves insulin sensitivity in women with polycystic ovary syndrome. *Fertility and Sterility*, 2002;77:1128-1135. ▯

Folic Acid Can Offset Drug-Induced Increase in Homocysteine Levels

The drug methotrexate is commonly used to treat symptoms of rheumatoid arthritis. However, methotrexate interferes with the metabolism of folic acid, an essential B-vitamin, and it raises levels of homocysteine, increasing the risk of coronary heart disease – not a good tradeoff. So, could supplemental folic acid be of benefit?

Dutch researchers recently tracked the effect of methotrexate, as well as combinations of the drug combined with folic acid or folinic acid, in 113 patients over 48 weeks. At the beginning of the study, all of the patients had seriously elevated homocysteine levels, approximately 15 micromoles (mmol) per liter of blood.

Patients who started taking methotrexate (along with a placebo) had an average 3.6 mmol increase in homocysteine levels by the end of the study. Folic acid supplementation (1,000 mcg daily) blunted the rise in homocysteine levels. It also reduced the patients' original homocysteine levels by an average of 2.7 mmoles. Folinic acid supplementation (2,500 mcg daily) was not as effective, lowering homocysteine levels by only 1.6 mmol.

Reference: van Ede AE, Laan RF, Blom HJ, et al. Homocysteine and folate status in methotrexate-treated patients with rheumatoid arthritis. *Rheumatology*, 2002;41:658-665. ▯

Omega-3 Fatty Acids Improve Blood Vessel Tone, Reduce Risk of Restenosis

Either of the major omega-3 fatty acids – eicosapentaenoic acid (EPA) and docosahexaenoic acid (DHA) – found in fish and fish oil supplements can increase the flexibility of blood vessels.

Many studies have previously found that fish oil supplements, rich in both EPA and DHA, can reduce blood pressure, arrhythmias, and the risk of sudden cardiac death. In the current study, a team of international researchers tested the separate effects of EPA and DHA on "systemic arterial compliance."

Systemic arterial compliance refers to healthy flexibility in major blood vessels. In contrast, reduced arterial compliance, or stiffness, is a major factor in the development of hypertension and increased pulse pressure – both of which are, in turn, risks for coronary heart disease.

Paul Nestel, MD, of the Baker Medical Research Institute, Australia, and his colleagues asked 38 patients with abnormally elevated blood fats to take 3 grams of EPA, 3 grams of DHA, or a placebo daily for seven weeks. Patients with elevated blood fats commonly have reduced arterial compliance.

Patients consuming either of the omega-3 fatty acids benefited from significant increases in arterial compliance. Patients taking EPA had a 36 percent increase in arterial compliance, and those taking DHA had a 27 percent improvement. The improvements were related to slight reductions in systolic blood pressure and pulse pressure.

The patients taking EPA and DHA also had significant decreases in triglyceride, a blood fat that increases the risk of heart disease.

In a separate study, researchers tested whether fish oil capsules could reduce restenosis, or the redevelopment of heart disease, in patients undergoing balloon angioplasty.

Aleardo Maresta, MD, of Pisa, Italy, asked 339 patients to take fish oil capsules (containing 3 grams of EPA and 2.1 grams of DHA) or placebos daily for one month before undergoing balloon angioplasty. The patients continued to take these supplements for one month after angioplasty, after which they reduced the dose by half for another five months.

At that time, restenosis rates per blood vessel and per patient were approximately 25 percent lower among patients taking fish oil capsules, compared with those taking placebos.

References: Nestel P, Shige H, Pomeroy S, et al. The n-3 fatty acids eicosapentaenoic acid and docosahexaenoic acid increase system arterial compliance in humans. *American Journal of Clinical Nutrition*, 2002;76:326-330. Maresta A, Balduccelli M, Varani E, et al. Prevention of postcoronary angioplasty restenosis by omega-3 fatty acids: main results of the Esapent for prevention of restenosis Italian study (ESPRIT). *American Heart Journal*, 2002;143:e5 (electronic publication at www.mosby.com/ahj). □

JAMA Authors Cautiously Recommend Vitamins for Some Chronic Diseases

Conflicting studies can certainly be confusing. But a recent scientific review of vitamins in the *Journal of the American Medical Association* gave a cautious blessing to the use of some vitamin supplements.

Kathleen M. Fairfield, MD, and Robert H. Fletcher, MD, of the Harvard Medical School reviewed Medline-published clinical studies of nine vitamins or vitamin-like nutrients from 1966 through the beginning of 2002. The nutrients were folic acid, vitamins B6 and B12, vitamin E, provitamin A carotenoids and lycopene , vitamin A,
vitamin C, and vitamin K.

"Inadequate intake of several vitamins has been linked to chronic diseases, including coronary heart disease, cancer, and osteoporosis," they wrote.

Fairfield and Fletcher noted that while overt vitamin deficiencies were not common, "suboptimal" intake was. "For example, elderly patients are particularly at risk for vitamin B12 and D deficiency, alcohol-dependent individuals are at risk for folate, B6, B12, and thiamin [B1] deficiency, and hospitalized patients are at risk for deficiencies of folate and other water-soluble vitamins."

Folic acid and vitamins B6 and B12 can lower blood levels of homocysteine, considered a "major risk factor for coronary disease." Folic acid might also reduce the risk of colorectal and breast cancers.

The researchers also recommended supplementation with vitamin D. "Inadequate vitamin D levels are more common than previously thought, particularly among housebound and elderly people," They suggested that both vitamin D and vitamin K supplements might reduce the risk of osteoporosis.

However, Fairfield and Fletcher were reluctant to recommend supplementation with most of the other vitamins, including vitamins E and C.

Reference: Fairfield KM, Fletcher RH. Vitamins for chronic disease prevention in adults. Scientific review. *JAMA*, 2002;287:3116-3126. □

High Levels of Vitamin C May Reduce Risk of Stroke, Researchers Report

Men with low blood levels of vitamin C are more than twice as likely to suffer a stroke, compared with men who have high blood levels of the vitamin.

Jukka T. Salonen, MD, PhD, of the University of Kuopio, Finland, and his colleagues tracked the health of 2,419 middle-age men for a little over 10 years. During this time, 96 of the subjects had ischemic strokes and 24 had hemorrhagic strokes.

Overall, Salonen found that men with the lowest blood levels of vitamin C were almost two and one-half times more likely to have a stroke during the study's 10-year period, compared with men who had the highest vitamin C levels.

Low blood levels of vitamins translated to roughly 60 mg or less intake daily.

As vitamin C levels increased, the risk of stroke consistently decreased among the men. A 28.4 micromole per liter increase in vitamin C blood levels reduced the risk of stroke by 26 percent.

Men with hypertension and low vitamin C levels were 2.6 times more likely to have a stroke, and overweight men with low levels of the vitamin were 2.7 times more likely to suffer a stroke.

Vitamin C may reduce the risk of stroke by retarding oxidation of low-density lipoprotein (LDL) cholesterol and by improving the integrity of blood vessels in the brain.

Other studies have also found that vitamin C may reduce the risk of cardiovascular diseases, including stroke. At least two small clinical trials found that vitamin C supplements of 500 mg daily could significantly lower blood pressure.

Reference: Kurl S, Tuomainen TP, Laukkanen JA, et al. Plasma vitamin C modifies the association between hypertension and risk of stroke. *Stroke*, 2002;33:1568-1573. □

Quick Reviews of Recent Research

• Antioxidant combination may protect skin

A number of researchers have recommended "inside-out"protection against sunburn damage – that is, using sunscreens topically and taking antioxidants internally. In a study with human skin cells, researchers found that combinations of antioxidants were particularly effective in blocking damage from ultraviolet (UV) radiation. A combination of vitamins E and C and carnosic acid (from the herb rosemary) reduced levels of metalloproteinase 1 mRNA, a marker of UV skin damage. Although lycopene and beta-carotene did not lower metalloproteinase 1 mRNA levels by themselves, they did in combination with vitamin E. The researchers suggested that "combinations of natural compounds" might be useful in protecting against sunburn.

Offord EA, et al. *Free Radical Biology & Medicine*, 2002;32:1293-2002.

• Isoflavones reduce monthly breast pain

Cyclical mastalgia, a type of breast pain that is likely related to hormonal changes, affects many women just before their menstrual period. Researchers asked 18 women to take 40 mg or 80 mg isoflavones or placebos daily. Nine of the 12 women taking isoflavones had significant reductions in breast pain, whereas only two of the six women taking placebos improved. Women taking 80 mg daily of isoflavones had a 31 percent reduction in breast pain, and those who took 40 mg daily had a 44 percent reduction. Women taking placebos had a 13 percent reduction in mastalgia.

Ingram DM, et al. *Breast*, 2002;11:170-174.

• Beta-carotene may help kill leukemia cells

In a laboratory experiment, researchers exposed differentiated and undifferentiated leukemia cells to beta-carotene, using levels comparable to those found in supplements. Beta-carotene inhibited the growth of both types of leukemia cells, but it had a greater affect on undifferentiated cells. In addition, higher concentrations of beta-carotene were more effective than lower concentrations.

Palozza P, et al. *International Journal of Cancer*, 2002;97:593-600.

• Vitamin C, magnesium may aid lung function

Researchers compared dietary intake of vitamins and minerals to lung function in 2,633 men and women, ages 18-70. Nine years later, they repeated measurements in 1,346 people from the original group. After adjusting for smoking habits, the researchers found that higher intakes of vitamin C and magnesium were associated with stronger lung function. In a further analysis, vitamin C showed the strongest relationship to lung health.

McKeever TM, et al. *American Journal of Respiratory and Critical Care Medicine,* 2002;165:1299-1303.

• Heating increases lycopene availability in tomatoes

Heating foods can decrease levels of many nutrients. However, heating may increase bioavailability of carotenoids. In an experiment, heating tomatoes broke down the fibrous matrix containing lycopene, a carotenoid that may reduce the risk of prostate and other cancers. Heating significantly increased lycopene and total antioxidant activity in tomatoes. However, heating greatly reduced vitamin C levels.

Dewanto V, et al. *Journal of Agricultural and Food Chemistry*, 2002;50:3010-3014.

• Vitamin E can slow aging of brain

Using laboratory rats, researchers investigated how vitamin E and vitamin E deficiency might affect learning and brain aging. Cognition tests challenged the rats to remember the structure of a maze or the location of objects. Young rats fed vitamin E were better learners compared with either vitamin E-deficient or old animals. Extra vitamin E improved the learning abilities of young rats and protected them from memory loss.

Fukui K, et al. *Annals of the New York Academy of Sciences*, 2002;959:275-284.

• Alpha-lipoic acid may fight inflammation

White blood cells are a major mediator of inflammation. In an experiment, researchers exposed activated white blood cells to alpha-lipoic acid, a potent antioxidant. Alpha-lipoic acid reduced the cells' production of "intracellular adhesion molecule 1," which stimulates inflammation. Alpha-lipoic acid also reduced activity of the protein "nuclear factor kappa beta," which helps regulate inflammation-inducing genes.

Lee HA, et al. *Experimental Gerontology*, 2002;37:401-410.

The Nutrition Reporter™ (ISSN 1079-8609) is published monthly except for August and December and is distributed only by prepaid subscription. This issue, Vol 13 No 9, Phone: (520) 529-6801. Fax: (520) 529-6840. Email addresses: Jchallem@aol.com or jack@thenutritionreporter.com. The Nutrition Reporter™ is strictly educational and not intended as medical advice. For diagnosis and treatment, consult your physician. Subscriptions are $26 per year in the U.S.; either $33 U.S. or $48 CND for Canada; and $40 for other countries, payable in U.S. funds through a U.S. bank. The Nutrition Reporter is a trademark(TM) of Jack Challem.

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