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Good for the Body, N-Acetylcysteine May Also Treat Mood and Behavior Disorders

N-acetylcysteine (NAC) is one of the most remarkable nutritional molecules. It is a potent antioxidant, as well as a precursor to glutathione compounds, the most powerful family of antioxidants made by the body. NAC is widely used to treat Tylenol overdose and also to break up mucus in the lungs. Still other research has also found that NAC is a powerful immune stimulant and can significantly reduce flu symptoms.

As good as NAC is for the body, two recent case reports suggest that it might also be good for the mind. NAC normalizes the activity of neurotransmitters, including serotonin and dopamine.

In the first report, Vladimir Coric, MD, of Yale University, New Haven, Connecticut, treated a 58-year-old woman who had suffered from obsessive-compulsive disorder (OCD) since childhood. Her obsessive-compulsive behavior included fears of contamination, excessive hand washing, hoarding, and repetitive rituals. She had been treated with several medications, including fluvoxamine (Luvox), but with only limited success.

Coric and his colleagues began treating her with 600 mg of NAC daily, increasing the dose over six weeks to 3 grams daily. She continued to take 3 grams of NAC daily for another seven weeks, along with fluvoxamine.

"Over the course of NAC augmentation, Ms. A's sense of contamination gradually decreased such that she began to be much less disturbed by intrusive thoughts of being contaminated...She became better able to resist her compulsive washing rituals and was able to confront many obsessional triggers better than she had in many years...her symptoms remained improved at her 2-month follow-up visit," Coric wrote.

In a second report, Coric and his colleagues described a 25-year-old woman suffering from treatment-resistant depression, anxiety, borderline personality disorder, and regular acts of self-mutilation (lacerating her abdomen). The drug riluzole (Rilutek) helped, but it resulted in over-sedation and was discontinued. Within a week of discontinuing riluzole, the patient began cutting herself again.

Coric and his colleagues began treating the women with 600 mg of NAC twice daily, which significantly reduced her desire to lacerate herself. Although NAC was not as effective as riluzole, the patient did not engage in any self-mutilation for more than six months (when Coric and his colleagues submitted their observations for publication).

In separate research presented late last year at the annual meeting of the American College of Neuropsychopharmacology, held in San Juan, Puerto Rico, researchers described evidence that NAC can also reduce craving for cocaine, an addictive drug that mimics the neurotransmitter dopamine. Peter Kalivas, Ph.D., of the Medical University of South Carolina, reported that four 600 mg doses of NAC over 12 hours significantly reduced addicts' desire for cocaine.

References: Lafleur DL, Pittenger C, Kelmendi B, et al. N-acetylcysteine augmentation in serotonin reuptake inhibitor refractory obsessive-compulsive disorder. *Psychopharmacology*, 2006;184:254-256. Pittenger C, Krystal JH, Coric V. Initial evidence of the beneficial effects of glutamate-modulating agents in the treatment of self-injurious behavior associated with borderline personality disorder. *Journal of Clinical Psychiatry*, 2005;66(11):1492-1493. ❑

Perspectives...

High Cost for a Low-Benefit Study

In February, the *Journal of the American Medical Association* published three articles analyzing results from the $415 million Women's Health Initiative (WHI) study. The WHI tracked the health and eating habits of almost 50,000 women for eight years. Newspaper headlines announced that low-fat diets, which half the women followed, failed to reduce the risk of breast and colon cancer, heart attacks, or strokes.

Continues on next page

The WHI study demonstrated just how much good money can be wasted in flawed research. WHI grew out of the idea that all dietary fat was bad, and the plug should have been pulled on this study in the 1990s when other studies clearly showed that there are both good and bad dietary fats.

In keeping with the "all fat is bad" idea, women assigned to eat low-fat diets were never asked to distinguish between types of fat. As a result, olive oil was grouped with lard and trans fats. You don't have to be a nutritionist to know there's a difference.

Worse, and more confounding from a scientific perspective, the low-fat group didn't eat a low-fat diet. They were asked to reduce their fat intake to 20 percent of their calories, but less than one-third of the women were able to do this during the first year, and by the final year of the study, only one-eighth of the women continued eating a low-fat diet.

Overall, the low-fat dieters ate almost the same amount of fat, fruits and vegetables, and whole grains as did the women who were allowed to eat whatever they wanted. So the differences between the low fat and anything-you-want-to-eat groups were negligible.

Did the study prove anything? It did find that a low-fat diet is very difficult to follow. The study never showed whether a healthy-fat diet might be better and easier to follow than a diet loaded with unhealthy fats – but then, you and I probably don't need $415 million to figure that out. *–JC*

Nucleic Acid Supplements, Once Passé, Turn Out to Be Good for the Gut

Back in the 1970s, nucleic acids – the building blocks of DNA and RNA – were touted as supplements that could slow the aging process and resist disease. But over the years, the value of nucleic acid supplements has been unclear and they've never had more than a niche following.

Now, research shows that supplements containing nucleic acids, sometimes called nucleotides and nucleosides, can protect the gut from damage. Based on these findings, nucleic acid supplements might help people heal after taking gut-damaging drugs, including nonsteroidal anti-inflammatory drugs, antibiotics, and proton-pump inhibitors.

Tania Marchbank, PhD, of the Imperial College of Medicine, London, and her colleagues conducted a serious of cell and animal studies using nucleotides comparable to those sold in health food stores.

Marchbank focused on the gut because cell turnover in the gastrointestinal tract is very rapid and requires large amounts of nucleotides. Although gut cells can make nucleotides from amino acids, they may need extra nucleotides for healing.

In experiments using human and rat intestinal cells, Marchbank tracked the movement of cells after injury. Normally, surviving cells migrate over damaged cells to begin the process of making new cells for healing. Cells treated with nucleotides increased their migration by two-fold, a sign consistent with increased healing.

In an animal study, Marchbank used a chemical to injure the guts of laboratory rats. However, rats given nucleotides – in amounts comparable to those people would take as supplements – had 60 percent less gastric damage.

Reference: Belo A, Marchbank T, Fitzgerald A, et al. Gastroprotective effects of oral nucleotide administration. *Gut*, 2006;55:165-171. ❑

Supplements Reduce Risk of Falls Among Older Women but Not Men

Until relatively recently, the conventional advice was to bone up on vitamin D and calcium to reduce the risk of fractures, particularly among older women. The reason, doctors believed, was that thinning bones led to falls and fractures.

But the latest findings have led to a twist in these recommendations: getting enough vitamin D and calcium reduces the risk of falls among older women. That's because vitamin D is also essential for maintaining normal muscle strength.

Researchers have long known that muscle weakness is one of the signs of vitamin D deficiency. Furthermore, vitamin D promotes protein synthesis, and muscle is made up largely of protein.

In the most recent study along these lines, Heike A. Bischoff-Ferrari, MD, of University Hospital, Zurich, Switzerland, and her colleagues tracked 199 men and 246 women who were 65 years of age or older. The men and women received either supplements containing 700 IU of vitamin C and 500 mg of calcium citrate malate, or placebos, daily for three years.

During the study, 55 percent of the women and 45 percent of men reported falling at least once. Among women taking the supplements, the overall risk of falling decreased by 46 percent. Among sedentary women taking the supplements, the risk of falling decreased by 65 percent, compared with women taking placebos.

Overall, the supplements did not influence the risk of falls among men, though there was a slight but statistically insignificant benefit for sedentary men.

Reference: Bischoff-Ferrari HA, Orav EJ, Dawson-Hughes B. Effect of cholecalciferol plus calcium on falling in ambulatory older men and women. *Archives of Internal Medicine*, 2006;166: 424-430. ❑

Early Consumption of Fries May Increase Later Risk of Breast Cancer

If you have a daughter or granddaughter of preschool age – that is, under five years old – be warned: feeding her French fries may significantly boost her risk of breast cancer later in life. That's the chilling finding of a study by researchers at Harvard Medical School.

Karin B. Michels, ScD, PhD, and her colleagues analyzed the eating habits of women participating in the Nurses' Mothers' Study, focusing on 582 women with breast cancer and 1,569 cancer-free subjects. The women's mothers filled out questionnaires recalling what foods their daughters ate as children.

After analyzing the data, Michels found that each weekly serving of French fries consumed as a preschooler increased the women's adult risk of breast cancer by 27 percent.

Michels wrote that "no other food or nutrient appeared as strongly correlated with adult breast cancer risk..."

Potatoes by themselves were not related to breast cancer risk, and French fries did not seem to reflect high intake of other types of fast foods.

Michels added that "the preparation of French fries, namely the use of frying fat high in saturated fats and trans-fatty acids, may be of relevance."

Reference: Michels KB, Rosner BA, Chumlea WC, et al. Preschool diet and adult risk of breast cancer. *International Journal of Cancer*, 2006;118: 749-754. ❑

High Blood Levels of Vitamin C Reduce Risk of Inflammation and Heart Disease

Relatively high blood levels of vitamin C – more than just dietary intake of the vitamin – seem to reduce several key risk factors for inflammation and heart disease.

S. Goya Wannamethee, PhD, and her colleagues from the Royal Free and University College Medical School, London, England, investigated dietary vitamin C intake, blood levels of the vitamin, and leading risk factors for heart disease in 3,258 men ages 60 to 79 years old. None of the men had been diagnosed with a heart attack, stroke, or diabetes.

Wannamethee found that men with the highest blood levels of vitamin C were most likely to have low blood levels of C-reactive protein (CRP) and tissue plasminogen activator (t-PA). CRP is a marker and promoter of inflammation, which is involved in heart disease and other disorders. High t-PA levels are a sign of endothelial dysfunction, or blood vessel stiffness, another risk factor for heart disease.

High dietary intake of vitamin C was also associated with level levels of CRP and t-PA, but the benefit was not as great as with high blood levels of vitamin C. That finding suggests that vitamin C was not simply a marker for foods that contain vitamin C and many other nutrients.

In addition, high blood levels of vitamin C were related to low levels of fibrinogen and blood viscosity, which would reduce the risk of blood clots. Dietary vitamin C was not associated with lower levels of fibrinogen and less blood viscosity.

Other studies have found that vitamin C is associated with greater longevity, and that vitamin C benefits people with high blood pressure, endothelial dysfunction, and coronary artery disease.

Reference: Wannamethee SG, Lowe GDO, Rumley A, et al. Associations of vitamin C status, fruit and vegetable intakes, and markers of inflammation and hemostasis. *American Journal of Clinical Nutrition*, 2006;83:567-574. ❑

Pycnogenol Supplements Found to Inhibit Cox-1 and Cox-2 Enzymes

Polyphenolic flavonoids, a family of antioxidants, have potent anti-inflammatory benefits and have been known, since the 1930s, to be synergistic with vitamin C. A recent study confirmed that Pycnogenol®, a proprietary complex of polyphenolic flavonoids, has significant anti-inflammatory effects – and explained at least some of its mechanisms.

In one experiment, Petra Högger , PhD, of Bayerische Julius-Maximilians University, Germany, and her colleagues asked five healthy men and women, ages 18 to 30 years, to take 200 mg of Pycnogenol daily for five days. Blood samples were taken before and after the Pycnogenol regimen.

Blood taken taken after the five-day Pycnogenol administration showed a significant decrease in the activity of Cox-1 and Cox-2, compared with blood taken before supplementation, in two of the five subjects. A modest decrease in Cox-1 and Cox-2 activity occurred in a third subject. Cox-1 and Cox-2 are key enzymes involved in the production of pro-inflammatory compounds, and the target of such drugs as Celebrex and Vioxx.

Högger and her colleagues then gave 10 subjects a single 300 mg dose of Pycnogenol. Blood samples taken 30 minutes later showed a significant decrease in Cox-1 and Cox-2 enzymes in nine of the 10 subjects. Högger noted that the Pycnogenol showed a "strikingly rapid bioavailability."

Reference: Schafer A, Chovanova Z, Muchova J, et al. Inhibition of Cox-1 and Cox-2 activity by plasma of human volunteers after ingestion of French maritime pine bark extract (Pycnogenol). *Biomedicine and Pharmacotherapy*, 2006;60:5-9. ❑

Quick Reviews of Recent Research

• Supplements help patients with heart failure

Researchers treated 30 elderly patients with heart failure, first treating them medically and then adding either a high-potency multivitamin/multimineral supplement or placebo daily for nine months. The supplement included 150 mg of coenzyme Q10 and 200 mg of vitamin B1, both of which are helpful in heart failure, as well as moderately high doses of vitamins C and E. Patients taking the supplements had improved heart pumping function and a significant overall improvement in quality of life. Patients taking placebos either did not improve or deteriorated.

Witte KKA, et al. *European Heart Journal*, 2005; 26:2238-2244.

• Heart failure patients low in vitamin B1

In a study of 100 patients with congestive heart failure and 50 healthy subjects, researchers found that the patients were far more likely to be deficient in vitamin B1. One-third of the heart failure patients were deficient in vitamin B1, compared with only one-eighth of the healthy control subjects. Low urine levels of vitamin B1 reflected low blood levels.

Hanninen SA, et al. *Journal of the American College of Cardiology*, 2006;47:354-361.

• Fermented milk product lowers blood pressure

Ninety-four hypertensive patients, who were not taking medications, were asked to consume one of two beverages: (1) a fermented milk containing *Lactobacillus helveticus*, two types of tripeptides, potassium, calcium, and magnesium; or, (2) as a placebo, a fermented milk wth lower mineral levels and no tripeptides. The two tripeptides consisted of isoleucyl-prolyl-proline and valyl-prolyl-proline, which have been found in animal experiments to reduce blood pressure. After consuming a glass of the first beverage twice daily for 10 weeks, the subjects benefited from a 4 mm Hg decrease in systolic blood pressure and almost a 2 mm Hg drop in diastolic blood pressure. The researchers believe that the tripeptides inhibit the angiogensin-converting enzyme (ACE), a common target of medications for hypertension.

Jauhiainen T, et al. *American Journal of Hypertension*, 2005;18:1600-1605.

• Mediterranean-like diet reduces heart risks

Researchers asked 10 women and 12 men to eat either a Mediterranean-like diet or a more conventional Swedish diet for four weeks, then switch to the other type of diet for another four weeks. The Mediterranean diet, which is higher in omega-3 fats, led to an improved ratio between omega-6 and omega-3 fats, which are the healthier type. While on the Mediterranean diet, the subjects had a 10 percent decrease in white blood cells and a 15 percent decrease in blood platelet cells, changes that would reduce their risk of coronary artery disease. They also had a 13 percent decrease in vascular endothelial growth factor, another risk factor for heart disease.

Ambring A, et al. *American Journal of Clinical Nutrition*, 2006;83;575-81.

• Vitamin E might be helpful in prostate cancer

Based on animal experiments, researchers noted that the succinate form of vitamin E appears more effective in reducing prostate cancer growth, compared with other forms of the vitamin. In their review article, the researchers noted evidence that vitamin E succinate, selenium, and lycopene have a synergistic benefit in animal studies, but human clinical trials have not confirmed this effect.

Basu A, et al. *Nutrition Reviews*, 2005;63:247-255.

• Drinking tea may reduce ovarian cancer risk

Researchers studied the tea-drinking habits of more than 61,000 Swedish women, ages 40 to 76 years old. During an average of 15 years follow up, 301 of the women were diagnosed with ovarian cancer. Compared with women who rarely drank tea, those who occasionally consumed tea (at least once a month) were 18 percent less likely to develop ovarian cancer. Women who drank tea once a day had about a one-fourth lower risk of ovarian cancer, and those who drank two or more cups daily had almost half the risk. The researchers found that each additional cup of tea was related to an 18 percent lower risk of ovarian cancer. Tea is rich in antioxidant polyphenols, which are known to inhibit cancer cell growth. Some polyphenols have weak estrogen-like and estrogen-blocking effects, which might also have contributed to the lower risk among tea drinkers.

Larsson SC, et al. *Archives of Internal Medicine*, 2005;165:2683-2686.

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