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## IN THE NEWS

### **SAMe Improves Efficacy of Antidepressant Therapy**

The dietary supplement S-adenosyl-L-methionine (SAMe) improves symptoms of depression in people who had been nonresponsive or only partially responsive to antidepressant therapy, according to scientists at Harvard Medical School.\*

In a pilot study at Massachusetts General Hospital, 30 subjects who failed to respond after a month of treatment with Prozac®, Paxil®, Effexor®, or other standard antidepressant drugs were given 400 mg of SAMe twice a day for two weeks, followed by 800 mg of SAMe twice a day for four weeks. Participants were free to decrease the dose to 400 mg after consulting with their physician.

At the study's conclusion, half of the patients were found to have experienced significant improvement in depressive symptoms and 43% experienced a complete remission of symptoms. No serious adverse events were reported.

Research team leader Jonathan Alpert, MD, stated, "Some previous trials have suggested that SAMe might have effects comparable to some antidepressants, but there has not been sufficient research on oral SAMe preparations or comparisons with available antidepressants. This is the first study to look at the safety and efficacy of combining SAMe with antidepressant treatment after antidepressants had proven insufficient on their own. Patients and physicians have been using these combinations without good supporting data, and these results are an initial step toward compiling the necessary scientific evidence."

The National Institutes of Health is sponsoring a current and future trial of SAMe in depressed patients.

—Dayna Dye



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#### Reference

\* Alpert JE, Papakostas G, Mischoulon D, et al. S-Adenosyl-L-methionine (SAMe) as an adjunct for resistant major depressive disorder: an open trial following partial or nonresponse to selective serotonin reuptake inhibitors or venlafaxine. *J Clin Psychopharmacol.* 2004 Dec;24(6):661-4.

### **DHEA Supplements May Reduce Abdominal Fat**

Supplementing with dehydroepiandrosterone (DHEA) may help reduce abdominal fat that increases with age and is associated with insulin resistance and atherosclerosis, according to a recent study published in the *Journal of the American Medical Association*.\* DHEA, a hormone produced by the adrenal glands that declines with advancing age, had previously been found to shrink abdominal fat in laboratory animals, but its effect on humans has not been confirmed.

Dennis T. Villareal, MD, and John O. Holloszy, MD, of the Washington University School of Medicine in St. Louis randomly selected 28 men and 28 women aged 65 to 78 to receive 50 mg per day of DHEA or a placebo for six months. Visceral abdominal fat, which occurs within the abdomen, and subcutaneous fat, which exists under the skin, were measured by magnetic resonance imaging before and after the treatment period. Glucose and insulin responses were determined by administering oral glucose tolerance tests.



At the study's conclusion, participants who received DHEA had experienced significant losses in visceral and subcutaneous fat. Women who received DHEA lost an average of 10.2% of their visceral fat, while men lost an average of 7.4%. Subcutaneous fat loss averaged 6% for men and women. Those who received a placebo gained small amounts of both types of fat.

DHEA also improved insulin action. No significant adverse events were reported, and DHEA did not cause an elevation in the male subjects' prostate-specific antigen (PSA) levels.

The study authors concluded, "These findings provide evidence that DHEA replacement may partially reverse the aging-related accumulation of abdominal fat in elderly people with low serum levels of DHEAS [DHEA-sulfate]. They also raise the possibility that long-term DHEA replacement therapy might reduce the accumulation of abdominal fat and protect against development of the metabolic/insulin resistance syndrome."

—Dayna Dye

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#### Reference

\* Villareal DT, Holloszy JO. Effect of DHEA on abdominal fat and insulin action in elderly women and men: a randomized controlled trial. *JAMA*. 2004 Nov 10;292(18):2243-8.

## Broccoli Compound Halts Breast Cancer Growth

Sulforaphane, a compound found in broccoli and other cruciferous vegetables, is able to block cell growth in late-stage human breast cancer cells, according to a study recently reported in the *Journal of Nutrition*. Study authors Keith Singletary and Steven Jackson of the University of Illinois at Urbana-Champaign believe that sulforaphane could be used to prevent and treat breast cancer.

In 1992, researchers at Johns Hopkins University reported that sulforaphane induces enzyme systems that help the body defend itself against cancer-causing substances, which is effective during cancer's early stages. The current research sheds light on how the compound works in late-stage cancer.

Singletary and Jackson administered sulforaphane to cultured human breast cancer cells, and discovered that within 24 hours, the compound had significantly blocked cell division compared to controls. Sulforaphane also disrupted the cells' microtubules, which are necessary for the separation of duplicated chromosomes during cell division.

According to Dr. Singletary, "This is the first report to show how the naturally occurring plant chemical sulforaphane can block late stages of the cancer process by disrupting components of the cell called microtubules. We were surprised and pleased to find that sulforaphane could block the growth of breast cells that were already cancerous.

"The findings may be helpful in the development of new breast cancer prevention and treatment strategies. For example, it may be possible that ingesting [sulforaphane] in combination with certain natural compounds or drugs could enhance their anti-cancer effectiveness and reduce side effects.

—Dayna Dye

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#### Reference

\* Jackson SJ, Singletary KW. Sulforaphane inhibits human MCF-7 mammary cancer cell mitotic progression and tubulin polymerization. *J Nutr*. 2004 Sep;134(9):2229-36.

## Multivitamins Slow Progression of HIV

Micronutrients are known to potentiate the immune response, the body's sophisticated defense against infection and the target of the human immunodeficiency virus (HIV). In a collaborative study, researchers at the Harvard School of Public Health and the Muhimbili College of Health Sciences in Tanzania have shown that supplementing HIV-infected women with a multivitamin containing vitamin-B complex, vitamin C, and vitamin E significantly slowed HIV's progression to an advanced stage.\*

Multivitamin supplementation diminished the occurrence of known complications of HIV infection, including oral thrush, nausea, and diarrhea. By protecting the gastrointestinal tract, multivitamin supplementation may slow the onset of the metabolic wasting effect of HIV, the so-called lipodystrophy syndrome. Both CD4+ cell counts (a crucial measure of HIV disease status) and anti-inflammatory cytokine activity are increased in multivitamin users for up to five years. The researchers also showed that multivitamin users had a lower viral load than non-users.

Although HIV remains incurable, anti-retroviral medications are quite effective in managing its progression, and have transformed HIV from a virtual death sentence to a manageable chronic disease. Unfortunately, because of the cost of medications, less than 10% of those eligible for treatment actually receive it.

Although no substitute for the recommended therapeutic regimen used to treat advanced HIV, multivitamins can clearly play a significant role in the management of HIV by improving immune function. The benefits of optimal micronutrient usage are known to reduce one's risk for, and the severity of, other chronic diseases such as cardiovascular disease and cancer.

—Linda M. Smith, RN

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#### Reference

\* Fawzi WW, Msamanga GI, Spiegelman D, et al. A randomized trial of multivitamin supplements and HIV disease progression and mortality. *N Engl J Med.* 2004 Jul 1;351(1):23-32.

## IN THE NEWS

### Vitamin D Inhibits Breast, Prostate Cancer Cells

Alone or in combination with other chemotherapeutic agents, a naturally occurring form of vitamin D<sub>2</sub> inhibits the proliferation of breast and prostate cancer cells, according to a study recently published in the journal *Anticancer Research*.\*

Adequate levels of vitamin D metabolites are required for the normal regulation of calcium and phosphate levels. Mounting epidemiological evidence has also shown that vitamin D affords significant protection against cancer. This is of particular consequence to elderly adults, in whom vitamin D synthesis is reduced, vitamin D deficiency is commonplace, and peak incidences of a variety of cancers occur.

While very low amounts of vitamin D are required to maintain calcium and phosphate homeostasis, the much higher doses of vitamin D needed for cancer prevention can result in hypercalcemia (excessive blood levels of calcium) and potentially lethal toxicity. The mechanism by which vitamin D inhibits tumor cell growth involves the vitamin D receptor, which together with vitamin D exerts negative feedback control on cancer cell proliferation and differentiation, and promotes cell death. Not surprisingly, scientists are now developing vitamin D analogs that have decreased calcium-mobilizing activity and therefore can be safely used in humans at these higher, effective doses.

In their study, researchers at Bone Care International in Middleton, WI, found that naturally occurring vitamin D<sub>2</sub>, which is derived from plants and has low calcemic activity, is effective alone or in combination with traditional chemotherapeutic agents in inhibiting breast and prostate cancer cell lines in vitro. Vitamin D<sub>2</sub> was found to potentiate the effect of therapeutic agents such as doxorubicin, cisplatin, busulfan, etoposide, 5-fluorouracil, carboplatin, and paclitaxel. Because toxicity limits these chemotherapeutic agents, the combined effect with vitamin D<sub>2</sub> may enable dose reductions without loss of efficacy. Vitamin D<sub>2</sub> also augments the effect of tamoxifen, a well-tolerated anti-estrogen used as adjuvant therapy in the prevention of breast cancer recurrence. The addition of vitamin D to the existing arsenal of anti-tumor agents may have enormous therapeutic potential.

—Linda M. Smith, RN

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#### Reference

\* Wigington DP, Urban CM, Strugnell SA, Knutson JC. Combination study of 1,24(S)- dihydroxyvitamin D<sub>2</sub> and chemotherapeutic agents on human breast and prostate cancer cell lines. *Anticancer Res.* 2004 Sep- Oct;24(5A):2905-12.

### High-Glycemic Diet Raises Colorectal Cancer Risk

Increased insulin levels resulting from a diet of high-glycemic foods markedly increased the risk of colorectal cancer in a large sample of American women, according to researchers at the University of California, Los Angeles.\*

Well-established research shows that daily consumption of more than five servings of fruits and vegetables high in soluble fiber affords significant protection against chronic diseases such as diabetes and heart disease, as well as cancers of the colon, breast, and prostate. The “fiber hypothesis” suggests that a diet rich in fiber favorably alters gastrointestinal absorption and digestion, by reducing direct carcinogen exposure, preserving antioxidant activity, decreasing tumor-promoting secondary bile acids, and increasing tumor inhibition via short-chain fatty acid synthesis.

The glycemic index measures the rate of carbohydrate absorption by the gastrointestinal tract. High-glycemic foods stimulate a rapid, heightened release of insulin, which has been suggested as a major risk factor for diabetes and cancer. Simple sugars such as pasta and white bread are absorbed rapidly and rank high on the glycemic index, whereas complex carbohydrates such as fruits, vegetables, and whole grains are absorbed slowly and rank low on the index.

The UCLA researchers sought to determine how increased insulin levels caused by a high-glycemic diet affected the risk of contracting colorectal cancer. They prospectively followed nearly 40,000 women for eight years, recording detailed dietary information and noting the incidence of colorectal cancer. The study demonstrated a significantly increased risk of developing colorectal cancer in those who followed a high-glycemic diet. The researchers attributed this enhanced risk to total and non-fiber carbohydrates in the diet. Blunting the pancreatic secretion of insulin with a diet of low-glycemic foods that are rich in soluble fiber—such as fruits, vegetables, nuts, legumes, and seeds—may pre-empt the development of cancer and metabolic diseases.

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## Reference

\* Higginbotham S, Zhang ZF, Lee IM, et al. Dietary glycemic load and risk of colorectal cancer in the Women's Health Study. *J Natl Cancer Inst.* 2004 Feb 4; 96(3):229-33.

## Low Chromium Tied to Heart Disease, Diabetes Risk

Men with both heart disease and diabetes were found to have low chromium levels compared to healthy control subjects, according to research recently published in the journal *Diabetes Care*.<sup>1</sup>

Holistically oriented practitioners have long used the mineral chromium picolinate in the management of their patients with type II diabetes and decreased insulin sensitivity. In 1997, researchers conducted a randomized, placebo-controlled study to determine whether the use of chromium supplements could produce metabolic improvements in 180 men and women with type II diabetes.<sup>2</sup> During this four-month study, the subjects took 100 mcg of chromium, 400 mcg of chromium, or a placebo each day. At the end of the trial, those taking chromium supplements saw a significant decrease in their fasting glucose levels, fasting insulin levels, and two-hour insulin levels, all of which pointed to improved insulin resistance.

In the newly published *Diabetes Care* study, men with both heart disease and diabetes were found to have low chromium levels via nail analysis. Researchers conducted cross-sectional analysis among men aged 40-75 years who had diabetes (688 patients), men who had diabetes and cardiovascular disease (198 patients), and healthy control patients (361 patients). In a concurrent case-control study, researchers examined 202 men with diabetes who developed heart disease against 361 healthy matched controls. The study authors study found that in both studies, men with diabetes and heart disease had lower levels of chromium when compared to healthy matched controls.

—Edward R. Rosick, DO, MPH, MS

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## References

1. Rajpathak S, Rimm EB, Li T, et al. Lower toe nail chromium in men with diabetes and cardiovascular disease compared with healthy men. *Diabetes Care.* 2004 Sep;27(9):2211-6.
2. Anderson RA, Cheng N, Bryden NA, et al. Elevated intakes of supplemental chromium improve glucose and insulin variables in individuals with type 2 diabetes. *Diabetes.* 1997 Nov;46(11):1786-91.

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