

ALTERNATIVE THERAPIES IN WOMEN'S HEALTH

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Vitamin C Supplementation for Coronary Heart Disease Protection in Women

*By Phyllis D. Light, LMT, AHG, BS,
andCarolynn J. Thomas, BSN, MSPH, RN*

THE CONTROVERSY OVER THE PRIMARY AND SECONDARY DISEASE prevention properties attributable to vitamin C, or ascorbic acid, continues unabated. Proponents hail vitamin C as an inexpensive and effective life insurance supplement. But long-range prevention studies focused on vitamin supplementation notoriously are inexact and obscured by the difficulty of accurately accounting for measurement of dietary intake and other confounders such as genetics, lifestyle, concomitant supplements and medications, and health behaviors. Still, a recently published, vigorous study affirming the cardioprotective nature of vitamin C supplementation in women has revived the traditional disagreements.¹

History and Function of the Supplement

Among the earliest controlled research studies, *A Treatise of the Scurvy*, published in 1754, began the journey of vitamin C research. James Lind studied 12 men aboard the *H.M.S. Salisbury* who suffered from scurvy, a condition common among sailors at sea for about a month. Scurvy symptoms include swollen and bleeding gums, open skin sores, dry skin, fatigue, bone lesions, and impaired wound healing. Lind concluded that a beneficial substance in citrus cured scurvy. Previous to this, lime juice was believed to possess beneficial properties and effects against scurvy, and Lind's study quantitatively supported these beliefs. But, despite this study's published results, the British Navy waited 40 years before officially requiring lime or lemon juice as a food staple on ships. Once this official action was taken, scurvy virtually disappeared, and hospital admissions of sick sailors dropped by 50%.^{2,3}

Vitamin C first was isolated in 1928 by the Hungarian biochemist and Nobel Prize winner Albert Szent-Györgyi, PhD.⁴ The body requires this water-soluble vitamin for the synthesis of collagen, the main structural component of blood vessels, bone, organs, tendons, ligaments, skin, and hair. (See *Table 1 for other functions.*) With the

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exception of humans, primates, bats, and guinea pigs, most mammals manufacture vitamin C. Humans require dietary vitamin C for healthy physiologic functioning.⁵

As an antioxidant, vitamin C protects low-density lipoprotein (LDL) cholesterol from oxidative damage; when LDL is damaged, oxidized cholesterol leads to heart disease.⁶ In addition, lipoprotein-a, a major component of arterial plaque, is reduced in the presence of vitamin C. In this way, vitamin C is believed to help maintain cardiovascular health by inhibiting the formation of lesions along blood vessel walls.⁶

Women and Heart Disease

Heart disease is the leading cause of death among American women, killing six times as many women as breast cancer.⁷ More than 250,000 women die each year from heart attacks, while another 32,000 women die of congestive heart failure. On average, women who smoke experience heart attacks 19 years earlier in life than non-smokers. Moreover, women with diabetes are two to three times more likely to experience heart attacks. Women have a significantly higher mortality rate from heart attacks than men, but receive only 33% of the performed angioplasties, stent procedures, and bypass

surgeries.⁷ For additional information on statistics and current research on women's heart disease, see www.americanheart.org.

Nurse's Health Study and Other Research on Vitamin C

In 1976, the largest cohort study of women, the Nurse's Health Study, began when approximately 121,700 female registered nurses between ages 30 and 55, living in 11 large U.S. states, completed a mailed questionnaire of lifestyle and medical history. Follow-up questionnaires were sent every two years to collect information on potential risk factors and identify newly diagnosed cases of coronary heart disease (CHD). Included in the questionnaires was a semi-quantitative food-frequency questionnaire to assess the intake of micronutrients and other dietary components. The final sample, after controlling for non-response and missing or extraneous data, was a cohort of 85,118 women who were followed for 16 years for the occurrence of CHD. This study had as its primary endpoint, incident CHD including any non-fatal myocardial infarction, or fatal coronary event diagnosed after the 1980 questionnaire but before June 1, 1996.¹

An intensive review of medical records was performed on incident cases to confirm diagnosis. After adjusting for age, smoking history, and several other coronary risk factors, the final analysis of the study revealed a CHD risk reduction of approximately 28% with vitamin C supplementation. This percentage also included adjusting for the intake of phytonutrients and other dietary antioxidants.¹

A discussion of past population-based research in vitamin C supplementation is presented in the literature.^{1,3,6,8} One study has shown that deficiencies in vitamin C intake are associated with increased CHD risk; however, several other studies have not proven a CHD reduction benefit associated with higher vitamin C intakes.⁷ The First National Health and Nutrition Examination Study (NHANES I) Epidemiologic Follow-up Study showed a 45% reduced risk of CHD in men and a 25% reduced risk of CHD in women corresponding to a higher (300 mg/d) intake of vitamin C.⁹ A large prospective epidemiologic study in Finnish men and women suggested a vitamin C-associated risk reduction of CHD in women but not in men.⁶ Singh et al studied 595 elderly subjects in urban India and found a vitamin C-associated CHD risk reduction.¹⁰ Studies such as these used varying doses of vitamin C, some quite low, and other antioxidant vitamins, including vitamin E. A recent meta-analysis on the role of vitamin C and antioxidant vitamins showed no evidence of CHD prevention.⁶

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Questions & Comments

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Table 1
Vitamin C functions

- Required for synthesis of collagen (critical for structural integrity of blood vessels, tendons, ligaments, bone, skin, wound healing)⁶
- Required for synthesis of neurotransmitter, norepinephrine (critical for brain function and mood)⁶
- Improves blood vessel dilatation (critical for blood flow to organs, especially heart and brain)¹⁶
- Required for the synthesis of carnitine (molecule that transports fats to mitochondria in cells for conversion to energy)⁸
- Required in metabolism of cholesterol to bile acids (critical for digestion and cholesterol processing)¹⁷
- Highly effective antioxidant (critical for the integrity of the immune system by protecting vital molecules in the body from damage; e.g., common cold virus)¹⁸
- Enhances nitric oxide synthase availability inside blood vessels (critical for protecting blood vessels from platelet aggregation and thrombus formation)⁶
- Facilitates the dietary absorption of iron¹⁸

A long-term prospective study to draw definitive conclusions on the benefit of vitamin C for primary prevention of CHD would be impractical and cost-prohibitive, especially in the context of the inherent limitations of study design and the complexity of making statistical adjustments for confounders such as other underlying conditions, dietary intake, varieties of supplementation including concomitant vitamin E and antioxidants, and measuring tissue saturation.¹¹

Dosing, Food Sources, and Supplements

Since the average half-life of ascorbic acid in human adults is 10-20 days, vitamin C has to be supplied regularly through diet or tablets to maintain an adequate pool in the body. Taking 100 mg/d adequately saturates the body pools, and the recommended daily allowance (RDA) for adults (> 19 yr) has gradually increased to 100-120 mg/d as new research elucidates advantages of this nutrient. In his editorial comment on the Nurse's Health Study, Balz Frei, PhD, director and endowed chair of the Linus Pauling Institute at Oregon State University, concludes that increasing the current RDA to 500 mg/d is warranted.¹¹ A scientific advisory panel to the U.S. government-sponsored Alliance for Aging Research recently recommended that all healthy adults increase their vitamin C intake to 250-1,000 mg/d, which may be adequate for preventive purposes.¹² Others contend that larger quantities may be beneficial to reverse processes in cancer, asthma, and heart disease.¹³

Certain conditions and activities—including smoking, diabetes, burns, infections, stress, wound healing, hormone therapy, and pregnancy—diminish the body's pool of vitamin C. Increased supplementation in those conditions is warranted to maintain a body pool sufficient to counteract ongoing losses.⁶

Rich dietary sources of vitamin C include citrus fruits, strawberries, cantaloupe, tomatoes, cabbage, broccoli, and dark-green leafy vegetables. As illustrated in Table 2, different fruits and vegetables vary in their vitamin C content. Over-the-counter vitamin C (L-ascorbic acid) is available in many forms, but research has shown that time-released formulations are absorbed better than regular vitamin C.¹⁴

Safety and Drug Interactions

Research demonstrates that vitamin C supplementation is safe and non-toxic. Excess vitamin C is eliminated via the kidneys. Doses of 6-10 g/d cause gastrointestinal problems and diarrhea in some people.

A number of drugs are known to lower vitamin C levels, thus requiring an increase in intake. Estrogen-containing medications, e.g., birth control pills and hormone replacement therapies, lower plasma and white blood cell levels of vitamin C. Frequent aspirin use can lower vitamin C levels.

Large doses of vitamin C can reduce the effectiveness of anticoagulant medications such as warfarin, requiring more intensive monitoring of blood levels and increased dosages to maintain therapeutic effectiveness and prevent blood clots. Persons on anticoagulants should limit their vitamin C intake to no more than 1,000 mg/d. Higher doses of vitamin C can interfere with the interpretation of certain laboratory tests (e.g., serum bilirubin, serum creatinine, and the assay for occult blood via guaiac testing of stool samples).⁵

Vitamin B₁₂ absorption can be reduced when taken simultaneously with vitamin C. This can be a concern when vitamin B₁₂ is taken for a medical reason such as anemia or as part of a protocol to reduce homocysteine levels. Elevated homocysteine levels have been identified as a risk factor of cardiovascular disease. Another major concern for heart patients is the concomitant use of antioxidants (1,000 mg/d of vitamin C, 800 IU/d of vitamin E, 100 mcg/d of selenium, and 25 mg/d of beta-carotene) could diminish the protective effects of statins.¹⁵

Conclusion

Although scurvy rarely occurs today, many researchers believe that a significant number of people suffer from chronic shortages of vitamin C. Poor nutrition, aging, lifestyle issues, environmental influences,

and continuous stress contribute to this chronic shortage. The protective and curative effects of this compound are not adequately appreciated, despite a number of studies. Therefore, no clear consensus on dose recommendations for primary prevention is lauded in conventional circles. However, in terms of CHD risk reduction in women, vitamin C experts support increased intake of ascorbic acid to doses between 250 mg/d and 1,000 mg/d.

Recommendation

Alternative medicine usage among women of all ages, races, and socioeconomic backgrounds has increased significantly as women continue to seek support in finding ways to maintain a healthy lifestyle.¹² National public health initiatives and advocacy groups have been much more active in educating and motivating women on the local level with programs such as “The Heart Truth for Women—Red Dress Program” supported by the U.S. Department of Health and Human Services (www.nhlbi.nih.gov/health/hearttruth/whatis/reddress.htm) and WomenHeart: The National Coalition for Women with Heart Disease (www.womenheart.org).

There is consensus that women can lower their heart disease risk with smoking cessation, blood pressure control, cholesterol reduction, weight maintenance, physical activity, and prevention and treatment of diabetes. The specific behavioral and medicinal methods of achieving such risk-factor reduction goals require the marrying of two approaches. Both conventional and alternative medicine must reach out to women and motivate change to effect a reduction in the numbers of women succumbing to heart disease. Although age and family history also influence risk, research shows that risk factor modifications can reduce heart disease risk by 82%.¹³

For women, the latest evidence supports the efficacy of supplementing their diets with 1,000 mg/d of time-released L-ascorbic acid to improve their heart health. This is one specific stepping stone toward reducing risk. Women must be more proactive in harnessing resources that can empower them toward risk factor reduction. ❖

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Table 2 USDA food composition data for vitamin C ^{5,14}		
Food	Serving	Vitamin C
Orange juice	3/4 cup (6 ounces)	75 mg
Grapefruit juice	3/4 cup (6 ounces)	60 mg
Orange	1 medium	70 mg
Strawberries	1 cup, whole	82 mg
Tomato	1 medium, raw	23 mg
Sweet red pepper	1/2 cup, raw	141 mg
Broccoli	1/2 cup, cooked	58 mg
Potato	1 medium, baked	26 mg

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Seasonal Affective Disorder: Is It Time to See the Light?

Source: Magnusson A, Boivin D. Seasonal affective disorder: An overview. *Chronobiol Int* 2003;20:189-207. Avery D. A turning point for seasonal affective disorder and light therapy research? *Arch Gen Psych* 1998;55:863-864.

Abstract: Seasonal affective disorder (SAD) is a condition of regularly occurring depressions in winter with a remission the following spring or summer. In addition to depressed mood, the patients tend to experience increased appetite and an increased duration of sleep during the winter. The pathological mechanisms underlying SAD are incompletely understood. Certain neurotransmitters have been implicated; a dysfunction in the serotonin system in particular has been demonstrated by a variety of approaches. The role of circadian rhythms in SAD needs to be clarified. The phase-delay hypothesis holds that SAD patients' circadian rhythms are delayed relative to the sleep/wake or rest/activity cycle. This hypothesis predicts that the symptoms of SAD will improve if the circadian rhythms can be phase-advanced. There is some experimental support for this. SAD can be treated successfully with light therapy. Other forms of light treatments, pharmacotherapy, and other therapies are currently being tested for SAD.

Source: Eastman C, et al. Bright light treatment of winter depression. *Arch Gen Psych* 1998;55:883-889.

Abstract: Bright light therapy is the recommended treatment for winter SAD. However, the studies with the best placebo controls have not been able to demonstrate that light treatment has a benefit beyond its placebo effect. Ninety-six patients with SAD were randomly assigned to one of three treatments for four weeks. Depression ratings using the Structured Interview Guide for the Hamilton Depression Rating Scale, SAD version (SIGH-SAD) were performed weekly. There were no differences among the three groups in expectation ratings or mean depression scores after four weeks of treatment. However, strict response criteria revealed statistically significant differences; after three weeks of treatment morning light produced more of the complete or almost complete remissions than placebo. Bright light therapy had a specific antidepressant effect beyond its placebo effect, but it took at least three weeks for a significant effect to develop. The benefit of light over placebo was in producing more of the full remissions.

■ COMMENTS BY MARY L. HARDY, MD

MOST OF US FEEL LIKE WE GET THE "WINTER BLUES" to some degree, but seasonal affective disorder (SAD), defined in the DSM-IV as recurrent depression with a seasonal pattern, is a more serious condition. All the typical symptoms of depression are present (fatigue, change in appetite and sleep patterns, depressed mood), but they begin with the decrease in light in fall or early winter and resolve during the spring. SAD is most common among women of childbearing years. In the United States, SAD has been reported to be more prevalent the further north one lives. SAD has been documented internationally with prevalence rates varying from less than 1% to almost 10%.¹ In the United States, this can mean that as many as 10 million people suffer from SAD. Patients with SAD also are much more likely to suffer from other types of cyclic depression such as premenstrual dysphoric syndrome.²

Although the accepted therapy for SAD disorder since the 1980s has been exposure to bright light (2,000-10,000 lux) for 30 to 120 minutes per day during the winter, methodological questions limited the implementation and widespread acceptance of this recommendation.³ Two recent, well-designed studies in the *Archives of Psychiatry* both support the use of bright light therapy and demonstrate that morning exposure is superior to evening treatment. A placebo-controlled trial of 96 patients with SAD during the winter in Chicago was performed to compare an early morning light treatment vs. an evening light treatment to a dummy placebo treatment.⁴ Previous trials had used a low light source as a control for bright light therapy. This was not an ideal placebo, because patients could not be blinded and their expectation of benefit could distort the outcome. This trial used a dummy placebo that emitted negative ions and buzzed. Patients were told that infrared light was being tested and this deception seemed to correct for patient expectation. Therapy consisted of 1.5 hours exposure per day to a 6,000 lux light source beginning at either 6 a.m. or 9 p.m. for four weeks. Sixty-one percent of the morning-treated patients improved their depression rating by more than 50% compared to 50% of the evening patients and 32% of the placebo patients. Significant effects were not seen before three weeks of treatment in this study.

A second trial in the same issue of the *Archives of General Psychiatry* looked directly at the comparison of morning vs. evening light therapy.⁵ Fifty-one patients with SAD were matched with 49 control subjects in a crossover trial. Initially the patients were randomized to be exposed to either two hours per day of bright light therapy (2,500 lux) early (from 6-8 a.m.) or later (from 7-9 p.m.). After two weeks of initial therapy the groups

Seasonal Affective Disorder Resources

Mental Health Organizations

National Mental Health Association

Phone: (703) 684-7722

Web: www.nmha.org

Self-help Groups

Seasonal Affective Disorder Association

Web: www.sada.org.uk

National Organization for Seasonal Affective Disorder

Web: www.nosad.org

Vendors (This does not constitute a recommendation, nor does it represent all of the good companies available)

The Sun Box Company

Phone: (800) 548-3968

Web: www.sunboxco.com

Northern Light Technologies

Phone: (800) 263-0066

Web: www.northernlight-tech.com

were withdrawn from light therapy for a week and then exposed to the alternate schedule. Melatonin levels also were measured weekly during the course of the trial. Early morning treatment was significantly more effective than evening therapy ($P < 0.001$). Remission was recorded in 37% of the morning-treated patients but in only 6% of the evening-treated patients. Early morning light also was more effective in normalizing the melatonin response in those patients. This trial showed positive results despite the relatively low intensity light and shorter duration of therapy. It would be expected from reading other studies that the percentage of positive responders would increase as treatment continued.

This therapy is well-tolerated by patients and the major difficulty is getting up early enough to have the 1.5 to 2 hour exposure before starting a regular workday. Limited evidence also suggests that early morning light exposure may be helpful in other types of episodic depression, which are problematic for women. Positive results have been reported in small trials of women with antepartum⁶ and postpartum depression,⁷ as well as late luteal phase dysphoric disorder.⁸

Implementation of therapy is facilitated by the wide variety of vendors and light sources currently available. (See resources.) Classically, patients would sit close to a powerful light box consisting of several tubes the size

of a florescent light bulb. These were bulky, expensive, and difficult to use outside of the house. Newer devices are more compact and convenient. Early clinical trial results show promise for an alarm clock that stimulates dawn by increasing the amount of light in the room in the 1-2 hours prior to arising. This device, if it proves to be as effective as a standard light box, could greatly improve patient compliance. Current devices cost between \$100-250.

In summary, for those patients who have an exaggerated response to winter darkness, we should consider light therapy. Recommended therapy consists of morning exposure to a light source of at least 2,000 lux for 30-120 minutes. Sources greater than 10,000 lux are less well tolerated and are more expensive. Therapy should be initiated at the earliest signs of negative effect on mood and stopped as the winter ends. Poor or no response in four weeks should trigger a re-evaluation of the therapy.

Light therapy is easy, well tolerated, and effective. For our patients who struggle with this insidious problem, this really could be the dawning of a whole new day. ❖

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CE Objectives

After reading *Alternative Therapies in Women's Health*, the health care professional will be able to:

1. evaluate alternative medicine and complementary therapies for women's health concerns;
2. identify risks and interactions associated with alternative therapies;
3. discuss alternative medicine options with patients; and
4. offer guidance to patients based on the latest science and clinical studies regarding alternative and complementary therapies.

CE/CME Instructions

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CE / CME Questions

1. Which of the following is true of vitamin C?
 - a. It protects low-density lipoprotein cholesterol from oxidative damage, which can lead to heart disease.
 - b. It reduces lipoprotein-a, which may help maintain cardiovascular health by inhibiting the formation of lesions along blood vessel walls.
 - c. Large doses of vitamin C can reduce the effectiveness of anticoagulant medications such as warfarin, requiring more intensive monitoring of blood levels and increased dosages to maintain therapeutic effectiveness and prevent blood clots.
 - d. All of the above
2. What is the leading cause of death among American women?
 - a. Auto accidents
 - b. Breast cancer
 - c. Heart disease
 - d. Lung cancer
3. What drugs lower vitamin C levels in the body?
 - a. Aspirin
 - b. Birth control pills
 - c. Hormone replacement therapies
 - d. All of the above
4. Which symptoms are present in persons with seasonal affective disorder?
 - a. Fatigue
 - b. Change in appetite and sleep patterns
 - c. Depressed mood
 - d. All of the above

Answers: 1. d, 2. c, 3. d, 4. d.

News Briefs

Unsafe Herbal Products Still Available on the Web

The U.S. Food and Drug Administration (FDA) issued warnings in 2001 about the safety of herbal products containing aristolochic acid. The products, however, are still available for sale on the Internet, says a recent letter to the editor of the *New England Journal of Medicine*.

FDA issued the alert after aristolochic acid was linked to kidney failure and cancer. Several other countries have even banned products containing the chemical. (The International Agency for Research on Cancer classifies products containing *aristolochia* species as human carcinogens.) The FDA, however, cannot take this step

because the law does not allow it to regulate herbs and other dietary supplements.

In the letter, researchers Lois Swirsky Gold, PhD, and Thomas H. Slone, MS, at the University of California at Berkeley, say the availability of the products on the Internet reveals a "serious flaw in the safety protection afforded the public." In 2003, they identified 19 products containing aristolochic acid and 95 products suspected to contain aristolochic acid for sale on U.S. web sites. These products and approximately 100 related web sites are listed at <http://potency.berkeley.edu/aristolochicacid.html>. These herbal products are sold for gastrointestinal symptoms, weight loss, cough, and immune stimulation.

“The failure to protect the public from the imminent hazard of aristolochic acid indicates that there is an urgent need to remove these products from the web and to develop a policy that addresses web sales of hazardous herbal products,” the researchers say.

Study Shows Drinking Black Tea Lowers Cholesterol

A recent study shows that drinking tea lowered low-density lipoprotein—the LDL “bad” cholesterol—for a small group of volunteers.

Results of the Agricultural Research Service (ARS) study were reported in the October 2003 issue of the *Journal of Nutrition*. The study was led by research chemist Joseph T. Judd, PhD, with the agency’s Diet and Human Performance Laboratory, one of seven laboratories at ARS’ Beltsville (MD) Human Nutrition Research Center. ARS is the U.S. Department of Agriculture’s chief scientific research agency.

The study assessed the effects of black tea consumption on blood lipid concentrations in adults with mildly high cholesterol. Seven men and eight women were given five servings of black tea per day for three weeks, and a tea-flavored water for another three-week period. In a third study period, caffeine was added to the tea-flavored water in an amount similar to that found in the tea.

Researchers found a 6-10% reduction in blood lipids in black tea drinkers in just three weeks. The study showed no effect on high-density lipoprotein, the HDL “good” cholesterol. The study’s authors concluded that drinking black tea, in combination with following a prudent diet moderately low in fat, cholesterol, and saturated fatty acids, reduces total and LDL cholesterol by significant amounts and may reduce the risk of coronary heart disease.

U.S. Study Shows Vitamins Save Health Care Costs

Giving vitamins to the elderly may save health care dollars, a recent study suggests. The study, conducted on behalf of Wyeth Consumer Health by health care consultant The Lewin Group, finds that vitamins could

improve overall health, making elderly people less likely to need drugs or hospital care. The study was launched with the aim of finding an inexpensive way to save money in health care.

The five-year estimate of potential savings (or cost offsets) resulting from improved immune functioning and a reduction in the relative risk of coronary artery disease through providing older adults with a daily multivitamin is approximately \$1.6 billion, the report says, according to Reuters. It also says that the five-year estimated cost offset associated with avoidable hospitalization for heart attacks is approximately \$2.4 billion.

The report concludes that over five years, it would cost \$2.3 billion to provide a daily multivitamin to older adults in the United States.

The group looked at a range of studies and reports. For instance, it studied the effects of taking vitamins on five diseases: coronary artery disease, diabetes, osteoporosis, prostate cancer, and colorectal cancer. The group also examined literature concerning the effects of multivitamins on immune functioning in older adults and the potential health care savings that might result from avoiding the hospitalizations, nursing home stays, and home health services associated with pneumonia, cellulitis, kidney and urinary tract infections, and septicemia.

Survey Finds CAM Services on the Rise

Hospitals were more likely to offer complementary and alternative medicine (CAM) services in 2002 than in 2001, according to the American Hospital Association Annual Survey of Hospitals for 2002.

The survey shows that the proportion of hospitals offering CAM services increased by 0.8 percentage points in 2002. About 16.5% of the 4,756 hospitals that answered the services questionnaire in the survey said they provide CAM, up from 15.7% of 4,773 respondents in 2001. Large hospitals reported the largest rise in CAM services, up 6.7 percentage points for hospitals with 300 to 399 beds and 10 percentage points for those with 400 to 499 beds. Hospitals with 25 to 49 beds were the only size category to see a decrease in CAM services, down three-tenths of a percentage point. ❖

In Future Issues:

Valerian for Insomnia
Alternative Therapies for Vaginitis
Touch Therapy for Pain
Glucosamine for Arthritis