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JAMA: Carotenoids Can Prevent Heart Disease and Macular Degeneration

Two studies published in the *Journal of the American Medical Association* emphasized the role of carotenoids in reducing the risk of coronary heart disease and age-related macular degeneration (AMD).

Ironically, beta-carotene, the best known and most common dietary carotenoid, seemed to have minimal benefits. The coronary heart disease study looked at *total* carotenoid levels, whereas the AMD study discovered that two lesser known carotenoids, lutein and zeaxanthin, offered the most protection against the eye disease.

In the heart study, Dexter Morris, PhD, MD, of the University of North Carolina, Chapel Hill, followed 1,883 men with cholesterol levels above 265 mg per deciliter for 13 years. Of them, 282 either died from coronary heart disease or had a nonfatal heart attack.

The men with the highest blood levels of carotenoids had 36 percent fewer heart attacks and deaths compared with those with low levels of carotenoids. Nonsmoking men with the highest levels of carotenoids had 70 percent fewer heart attacks.

Morris wrote in *JAMA* (Nov. 9, 1994;272:1439-41) that "this study examined serum levels rather than dietary intake and total carotenoids rather than just beta-carotene. Beta-carotene represents only about one-quarter of total serum carotenoids and different carotenoids have varying amounts of antioxidant properties. Thus, total serum carotenoids may be more appropriate to measure than individual compounds."

In the other study, researchers at five eye centers in the United States looked at the role of carotenes and vitamins in preventing macular degeneration. They compared the diets of 356 case subjects with macular degeneration to 520 controls who had other types of eye diseases.

"Age-related macular degeneration (AMD) is the leading cause of irreversible blindness among persons older than 65 years," wrote lead investigator Johanna Seddon, MD, in *JAMA* (Nov. 9, 1994;272:1413-20). "Activities essential for independent living, including reading, driving, and writing, are most impaired by the loss of central vision due to this disease that affects the macula, the small central part of the retina."

AMD causes a partial loss of vision in about 13 million Americans and accounts for about one-third of the 900,000 cases of blindness in the United States.

Seddon, of the Massachusetts Eye and Ear Infirmary, Boston, noted that there has been no easy way to prevent

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Carotenoids, Vitamin E Protect Against Heart Attack When Cholesterol is High

Low levels of the carotenoids, particularly beta-carotene and lutein, increase the risk of heart attack among smokers. In addition, low levels of vitamin E increase the risk of heart attack among both smokers and nonsmokers if their blood cholesterol levels are high.

Those are the findings of a large-scale epidemiological study conducted at the Johns Hopkins University School of Medicine.

Debra Street, PhD, and George Comstock, MD, DrPH, analyzed nutrient levels in blood drawn from almost 26,000 people in 1974. During the 1980s, 123 of the study's participants suffered their first heart attack.

"Antioxidants are presently of interest for their potential role in inhibiting atherosclerosis, thus preventing some major clinical complications of atherosclerosis, such as myocardial infarction," the researchers wrote in *Circulation* (Sept. 1994;90:1154-61).

They analyzed the blood samples for four carotenoids (beta-carotene, lycopene, lutein, and zeaxanthin), vitamin E, and cholesterol. Next, they compared levels of these nutrients in those who had a heart attack and those who did not.

"Perhaps the most striking finding of the present study was that the association between low levels of serum carotenoids and subsequent myocardial infarction was observed only among smokers," the authors wrote.

Low levels of all the carotenoids, except for lycopene, were associated with a greater risk of heart attack. However, the correlation between low beta-carotene and heart attack was the strongest. People with the lowest levels of beta-carotene were "more than twice as likely" to suffer a heart attack.

Low vitamin E was not associated with heart attack risk unless cholesterol levels were greater than 240 mg per deciliter. Among people with high cholesterol levels, vitamin E was protective, perhaps by preventing the oxidation of the low-density lipoprotein form of cholesterol, the researchers suggested. □

Weighing the Need to Change the RDAs

Since their inception during World War II, the Recommended Dietary Allowances (RDAs) for vitamins and minerals have been intended to prevent serious deficiency diseases. Over the last decade or so, in light of the growing body of research on how vitamins can prevent heart disease and cancer, the RDAs have often been criticized for being too low.

In a thoughtful article in *Nutrition Reviews* (Aug. 1994;52:266-70), Paul Lachance, PhD of Rutgers University, and Lillian Langseth, DrPH, adjunct professor at the Columbia University School of Public Health, weighed the need to change the RDA concept from preventing deficiency conditions to one oriented toward the prevention of chronic disease.

"In their current form, the RDAs do not address functions of nutrients other than the prevention of deficiency and are not intended to represent optimal intakes," Lachance and Langseth wrote.

The impetus for changing the RDAs arises from many events, but two are especially noteworthy. One is that vitamin E reduces the risk of heart disease, but only in amounts above what is normally found in the diet. The other is that it took a "mind boggling" amount of data over 20 years to translate folic acid research into a public policy for preventing birth defects.

Some of Lachance and Langseth's observations:

• "The current RDAs are intended for 'practically all healthy persons.' It may be worthwhile to reconsider this aspect of the RDA concept. A large proportion of the general population cannot truly be described as 'healthy.' About 30% of Americans smoke, and many drink to excess. Others have diabetes, elevated cholesterol levels, or high blood pressure. After age 45, most people are not 'healthy' in the strict sense of the word and relatively few qualify as having no chronic or acute problem."

• "If the concept of the RDAs is to be updated, perhaps a name change is also in order. The Recommended Dietary Allowances have a prominent history, but their implications that the desired amounts of nutrients can and should be obtained solely from the diet may be outdated. Recent evidence suggests that for a few nutrients, it may be difficult or impossible to obtain optimal intakes from diet alone. Thus, in the future, recommended *nutrient* (such as from supplements) allowances may need to be distinguished from recommended *dietary* allowances."

• "Dr. Paul Lachance has proposed setting RDAs for vitamin C, vitamin E, and carotene equal to the amount of these nutrients found in an 'ideal' diet...an ideal diet would provide 5.2-6.0 mg/day of carotene, 217-225 mg/day of vitamin C, and 23-27 IU/day of vitamin E."

• "Perhaps special RDA accommodations could be made for... conditions that increase nutrient needs, such as cigarette smoking, excessive alcohol intake, or long-term polypharmacy in the elderly....Recent research indicates that the elderly have increased needs for several vitamins, including riboflavin, vitamin B6, vitamin B12, vitamin D, and folic acid."

• "The covers of the current edition of the RDA book describe it as 'the classic reference work for the nutrition, dietetic, and allied health professions...the most authoritative source of information on nutrient allowances for healthy people.' There is no question that past editions of the RDAs have earned these accolades. The challenge for the current FNB (the National Research Council's Food and Nutrition Board), and for those who will help with their work, is to maintain this standard of excellence during a time of rapid change in the science of nutrition." □

Solid Evidence: Boosting Calcium Intake Lowers Blood Pressure

More than 20 epidemiological and 80 experimental studies have shown an inverse relationship between calcium consumption and blood pressure. In general, the higher a person's calcium intake, the less likely he or she is to have hypertension.

In the journal *Hypertension* (April 1994;23:513-30), Daniel Hatton,PhD, and David McCarron, MD, of Oregon Health Sciences University, Portland, reviewed the findings of almost 300 scientific papers on calcium and blood pressure.

Ten years ago, McCarron startled the medical establishment by proposing that inadequate calcium intake was a key cause of hypertension. He noted in *Science* (June 19, 1984;224:1392-8) that elevated blood pressure was also associated with low levels of magnesium, potassium, *and* sodium.

"The increased risk of elevated blood pressure with lower calcium intake appears to be related to an apparent deficit in calcium metabolism that occurs in a subset of hypertensive individuals," Hatton and McCarron wrote in *Hypertension*.

They noted that the changes that occur in hypertensive people are mirrored in experimental animals. However, the benefits of calcium supplements in lowering blood pressure are more consistent in laboratory animals than in people. Still, most studies have found an inverse relationship between calcium intake and blood pressure.

"Of the published studies of calcium supplementation in humans, 24 reported a significant reduction in

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Cranberry Juice Reduces Urinary Infections

Cranberry juice has long been a folk remedy to treat urinary infections, which are most commonly caused by *E. coli*. Now, a well-controlled study demonstrates that cranberry juice can reduce urinary tract bacterial infections (bacteriuria) and associated white blood cells in the urine (pyuria).

The study, conducted by Jerry Avorn, MD, of the Harvard Medical School, compared the benefits of commercial cranberry juice to an identical looking and tasting placebo drink in 153 elderly women. The women were asked to drink at least 300 milliters (a large glass) of cranberry juice or placebo daily for six months. The placebo contained vitamin C to control that variable.

Urine samples from the second through sixth month of the study showed that women drinking the cranberry juice had a significantly lower incidence of bacteriuria and pyuria. Only 15 percent of the urine samples from the cranberry drinkers showed evidence of bacteriuria and pyuria, compared with 28.1 percent of those from the women taking the placebo, according to Avorn's article in the *Journal of the American Medical Association* (March 9, 1994;271:751-4).

"While asymptomatic bacteriuria in elderly women is commonly observed, it does not represent a condition with a negative prognosis or one that requires treatment," Avorn wrote. "However, demonstration of the capacity of cranberry beverage to reduce the occurrence of bacteriuria with pyuria in elderly women does lend credence to the belief that it contains a substance with biologic activity in relation to the urinary tract."

In a review article on the use of cranberry juice in treating urinary tract infections, James Fleet, PhD, of the Human Nutrition Research Center on Aging, Tufts University, noted that most researchers have believed that cranberry juice works by acidifying the urine. However, new research suggests that a compound in both cranberry and blueberry juice prevents bacteria from adhering to urinary epithelial cells.

"Out-of-hand dismissals of folk remedies are common in the cynical research communities," Fleet wrote in *Nutrition Reviews* (May 1994;52:168-70). "However, only well-designed studies relating the remedy to a measurable outcome can be used to support or dismiss such cures. This study provides a good example of how the research and medical communities should address the validity of folk remedies in the future." □

Fewer Fats, More Fiber Can Help Lower the Risk of Ovarian Cancer

Women who reduce their intake of saturated fat from meat, milk, butter, and other foods can dramatically reduce their risk of developing ovarian cancer. In addition, consuming more vegetable dietary fiber also reduces risk, according to a joint study by the Yale University School of Medicine and the University of Toronto.

Ovarian cancer is considerably more deadly than breast cancer, partly because it is difficult to diagnose in its early stages. About 20,000 American women develop the disease each year, and more than half of them die.

The study compared 450 Canadian women recently diagnosed with ovarian cancer with 540 women who were similar in age and lifestyle but free of disease.

The major risk factors included total caloric intake and saturated fat and egg consumption. Women who consumed large amounts of beta-carotene, other carotenes, dietary fiber, and vegetable fiber were the least likely to develop ovarian cancer.

Eating an additional 10 grams of saturated fat daily could raise a woman's risk of ovarian cancer by as much as 20 percent, while reducing saturated fat by 10 grams daily would lower the risk by 20 percent, according to Harvey Risch, MD, PhD, of Yale.

An increase of 6-10 grams of vegetable fiber daily was associated with a 30-40 percent reduction in the risk of ovarian cancer, Risch explained in the *Journal of the National Cancer Institute* (Sept. 21, 1994;86:1409-15).

There was no association between unsaturated fats and ovarian cancer.

"Whatever the mechanism of action, the present findings, if confirmed, suggest that ovarian cancer risk may be appreciably lowered by suitable modifications of the diet: reducing the intake of saturated fat (and perhaps eggs) and eating more vegetables," wrote Risch. □

Cow's Milk Again Linked to Juvenile Onset Diabetes

A Finnish study of 1,200 children has confirmed the association between cow's milk consumption and risk of insulin-dependent diabetes mellitus, also known as Type I diabetes.

S. M. Virtanen, PhD, of the University of Helsinki, found that children had a higher risk of developing diabetes when they began consuming cow's milk earlier in life and when they consumed large quantities of it.

High levels of IgA antibodies to cow's milk were specifically associated with an increased risk of diabetes. Other researchers have suggested that an immature immune system cannot distinguish between cow's milk proteins and certain pancreatic proteins, so it attacks both.

"Our results suggest that both the age at introduction of dairy products and the amount of milk consumed

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Carotenoids Protect Against Disease...

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macular degeneration. Nor is there an effective treatment for large numbers of patients.

"There is increasing speculation that dietary factors, particularly antioxidants, may prevent or impede the progression of AMD," she wrote. "The theory is biologically plausible. The outer retina, rich in polyunsaturated fatty acids, may be altered adversely by free-radical production and oxidation and, conversely, may be protected by nutrients that block this oxidative damage."

Seddon found that people who consumed a lot of carotenoids had a low risk of developing AMD. "After adjusting for other risk factors, individuals consuming the highest levels of carotenoids had a statistically significant 43% lower risk for AMD compared with those who consumed the lowest levels," she wrote.

An early analysis of the data found that beta-carotene, lutein, and zeaxanthin were associated with a "statistically significant" reduction in AMD risk. Further analysis revealed that lutein and zeaxanthin were the protective carotenoids.

Retinol (a form of vitamin A), vitamin C, and vitamin E in foods or supplements were not protective.

"Since we noted a statistically significant inverse association between the risk for AMD and carotenoid intake, we also evaluated individual foods containing carotenoids," wrote Seddon. "A strong, inverse association was seen for dietary intake of spinach or collard greens, with a statistically significant trend for a lower risk for AMD with a greater frequency of intake of these vegetables."

Perhaps not surprisingly, spinach and collard greens contain far more lutein and zeaxanthin than other carotene-containing foods. Carrots, high in beta- and alpha-carotene, are low in lutein and zeaxanthin.

Kale, mustard greens, and turnip greens are also high in lutein and zeaxanthin. However, subjects were not asked about their consumption of these foods.

Significantly, lutein and zeaxanthin are concentrated in the macula, whereas beta-carotene is almost completely absent. Lutein and zeaxanthin, which are yellow, filter out visible blue light, which can cause free-radical damage in the eye.

In an editorial in *JAMA* (Nov. 9, 1994;272:1455-6), Susan Hankinson, ScD, and Meir Stampfer, MD, DrPH, noted that "not all antioxidants are created equal...the substantial differences in the structure and biologic properties of specific antioxidants are likely to influence their ability to prevent a specific disease...Therefore, a null (negative) finding for one antioxidant on disease risk does not mean that other antioxidants could not be effective." □

Calcium Lowers Blood Pressure...

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blood pressure in at least a segment of the study population, and 13 reported no difference in blood pressure," wrote the researchers.

More recent analyses of these studies suggest that calcium supplements may provide the greatest benefits to specific groups of people, including African Americans, women with gestational hypertension, and salt-sensitive individuals. "Low calcium intake may be an especially important indicator because very low calcium diets (less than 400 to 600 mg / day) are most closely associated with elevated blood pressure, and work with experimental models indicates that low calcium diets elevate blood pressure," explained Hatton and McCarron.

The most consistent findings supporting the role of calcium supplements in lowering blood pressure come from studies that used large amounts of the mineral, the authors wrote.

Numerous mechanisms have been explored to explain how calcium lowers blood pressure. Among them:

- calcium relaxes smooth muscles,
- variations in calcium-regulating hormones influence blood pressure,
- calcium and sodium may influence the sympathetic nervous system, lowering or raising blood pressure,
- dietary calcium may change how other electrolyte minerals are metabolized, and
- calcium may affect neural function and the central nervous system.

"Nonvascular mechanisms must also be considered in expaining the role of dietary calcium in blood pressure regulation...studies...indicate that dietary calcium regulates sodium chloride appetite or intake. Low dietary calcium stimulates sodium chloride intake, and higher intakes of calcium suppress sodium chloride appetite," wrote Hatton and MacCarron. □

Milk, Diabetes...

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during childhood affect the levels of cow's milk antibodies..." Virtanen wrote in *Diabetologia* (April 1994;37: 381-7). □

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