

HEALTH AND STRESS

The Newsletter of The American Institute of Stress

Number 4

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THROWING THE BABY OUT WITH THE BATHWATER?

The Beta Carotene and Retinol Efficacy Trial (CARET) was recently halted after four years, because of disturbing evidence that participants receiving beta carotene and/or vitamin A supplementation were at significantly greater risk for lung cancer and premature death. Similar findings were reported in a 1994 Finnish study of smokers. The 12-year Physicians' Health Study of over 22,000 male doctors, most of whom were non-smokers, also revealed no health benefits from beta carotene supplements. They have now also been discontinued in this, as well as the ongoing Women's Health Study of 40,000 female health professionals. If beta carotene does not promote health, and could cause cancer, should it be discouraged, or even withdrawn?

On the other hand, more than 200 reports suggest that beta carotene and other antioxidant vitamins can be effective in preventing cancer and heart disease. In both the CARET and Finnish studies,

participants with high levels of serum carotenoids at the start of the study had a lower incidence of subsequent cancer, and beta carotene may have been given too late to see any effect in smokers. Another factor might be that all the formulations were colored with quinoline yellow, an artificial food dye with known carcinogenic properties. In addition, other confounding factors were not considered, including degree of exercise, exposure to cigarette smoke, air pollution, sunlight, radiation, pesticides, polyunsaturated fats, living at a high altitude, flying a lot, emotional stress, trauma, infections, and other influences that increase free radical production. The Finnish study followed the 1986 Chernobyl disaster, and the study group came from one of the first areas to receive a very heavy fallout. The CARET and Physician's Health Study have not been published, only a portion of the data was released to the press, and it is not clear whether the results will prove to be statistically significant. For example, the highest incidence of cancer in the Finnish study occurred in those drinking the most alcohol, but the available CARET data does not reveal how many of the participants drank, much less how much.

Everyone agrees that a diet high in fruits and vegetables provides protection from cancer and cardiovascular disease, but the assumption that this is

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*The Newsletter of
The American Institute of Stress*

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due to beta carotene or other specific antioxidants may not be valid. It is possible that beta carotene may merely be a marker for other powerful cancer fighting carotenoids and phytochemicals found in the same fruits and vegetables, including alpha-carotene, cryptoxanthin, lutein, zeaxanthin, lycopene, and various terpenes. All three of the negative studies cited used synthetic beta carotene, not the mix of natural occurring carotenoids which form the basis of most supportive epidemiological reports.

Can Antioxidant Vitamins Be Harmful?

Nevertheless, the findings are disturbing, and highlight other concerns about the current capricious and haphazard use of vitamins and other nutritional supplements. Almost half of all Americans currently take vitamins, usually on a daily basis, and the vast majority take multiple vitamins and minerals as well as other antioxidant products. Many take eight or more different pills and preparations, and some consume up to several hundred times the recommended daily dosages. However, it is not known whether this might suppress the body's

production of its own free radical scavengers, since in animal studies, the administration of vitamin E resulted in a shutdown in the production of natural antioxidants. In one study of 500 breast cancer patients, those having high vitamin E levels had more aggressive cancers, and lower levels of free radical by-products. This suggests that the cancer cells may have developed adaptive responses that provided them more protection from natural antioxidants. A similar tendency has been shown in prostate, lung and colon cancer. This has important implications, since most cancer patients usually take multivitamin preparations to improve their nutritional status, and in some instances, this might do more harm than good. Those taking large doses of vitamin E could be making their tumors more resistant to natural defense mechanisms. Taking mixtures of antioxidant vitamins might also prove counter productive. Beta carotene has been shown to reduce tissue levels of vitamin E, and megadoses of some antioxidants might also block the protective effects of others, causing fatigue or even more serious problems.

In one study, pregnant women whose vitamin A intake exceeded 10,000 IU a day, were over 60% more likely to have a baby with a significant birth defect, including cardiovascular disease and cleft palate, compared to the normal risk of 1 in 1,000. Some readily available vitamin A products contain 25,000 IU in a single capsule, almost 10 times the recommended daily dose. Chromium picolinate is an antioxidant, but when given in large amounts to laboratory animals, was found to produce chromosomal damage that could cause cancer.

In another report, taking large doses of vitamin E was found to reduce risk for prostate cancer, but resulted in a higher incidence of hemorrhagic stroke because of its anticoagulant effects. Under normal circumstances, vitamin C is an antioxidant, but in the presence of iron, it acts as an oxidizer, and can cause cardiac damage in patients with hemochromatosis, or others who have had multiple transfusions. Multivitamin-mineral pills containing iron, copper, and manganese, can generate billions of free radicals when large amounts of vitamin C are also taken.

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Which Antioxidant Vitamins Should I Take, And How Much?

Vitamins have traditionally been viewed as substances required in very minute amounts to prevent or treat specific deficiency diseases. Almost half of adult Americans erroneously believe they can get all the vitamins they need from their diet by adhering to the minimal daily requirements (MDR) or recommended dietary allowances (RDA). Taking any more would be a waste of money, since it would not be utilized and excreted as a waste product. These standards are established by the U.S. Department of Agriculture based on recommendations by the FDA, the National Academy of Sciences and other agencies. Although numerous scientific studies suggest that they are archaic, and there has been considerable public pressure, there are apparently no current plans to revise them. The Alliance for Aging research, a 10-year old non-governmental, non-profit group devoted to advance medical research on human aging, convened a special panel to study the issue. After carefully reviewing over 200 studies over the past twenty years dealing with antioxidant vitamin research, the experts concluded that "healthy adults should sharply increase their intake of selected antioxidant nutrients". They recommended a daily intake of 250 to 1000 mg of vitamin C, (as opposed to the RDA of 60 mg), and 100 IU to 400 IU of vitamin E, (RDA 30 IU), and 10 to 30 mg of beta carotene. However, no RDA has ever been established for beta carotene. In addition, none of the negative studies noted above were available at the time of the panel's report, and it is not clear if this might change their endorsement or opinion. As the Director of the Office of Special Nutritionals at the FDA commented, "This issue is going to get hotter before it gets resolved."

However, it is important to distinguish between the minuscule amounts currently endorsed for preventing or curing deficiency diseases, and much larger dosages, which have physiologic effects that are totally unrelated to these disorders. In 1955, it was found that niacin (vitamin B₃) could lower blood cholesterol levels, but in doses very

much higher than those needed to prevent pellagra. Linus Pauling made vitamin C a household word in the late 70's, by suggesting that it did much more than cure scurvy. He believed that taking doses hundreds of times higher than the official RDA of 60 mg could help prevent everything from the common cold, to cardiovascular disease and cancer, and increase longevity by 12-18 years. He was his own best advertisement, since he attributed his unusual physical and mental vitality well into his nineties, to an average intake of 18,000 mg of vitamin C daily for over 20 years. While originally scoffed at by the medical profession, Pauling's predictions have gained increasing support, and the public has subsequently been bombarded by extravagant promotional promises for megadoses not only of vitamin C, but other vitamins and herbals claiming antioxidant benefits.

A recent poll indicated that although most Americans had heard the term, few knew what antioxidants were, could not identify them correctly, or explain how they differed from other vitamins. The majority were not aware that antioxidants might play a role in preventing cancer, heart disease, and stroke. Almost 40% mistakenly thought that they had something to do with aiding digestion. More than 4 out of 5 were confused or skeptical about their ability to improve immune system function, and retard or reverse such stigmata of aging as wrinkled skin, cataracts, macular degeneration, and gray hair. The frenzy in this field has been fueled by the phenomenal potential commercial rewards. Some appreciation of this may be gained by the observation that one health food store chain has opened a new facility nearly every day for the last three years, and anticipated sales of 1 billion dollars in 1995! Vitamin C consumption rose 61% in 1994, sales of vitamin E and beta carotene doubled, and the public spent more than \$268 million for these three supplements alone. Some stores have over 1000 vitamins and herbs alone or in various combinations, and can create personalized one-month packs to fit any customer's specifications. Products that were once obscure, can now be readily found on the shelves of every supermarket and pharmacy, and most convenience stores.

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Are Fruits, Vegetables, And Herbals Better?

Fruits and vegetables seem to provide benefits that cannot be reduplicated by taking massive doses of individual vitamins or other constituents that have been arbitrarily selected. Unfortunately, fewer than 10% of us consume the servings of two fruits and three vegetables recommended daily. A recent nationwide survey found that nearly half of the respondents had eaten no fruit on a given day. Many others don't get proper nourishment because they skip meals, or rely on fast foods that have little nutritional value. Most people would rather pop a pill than change their diet. In addition, a recent survey showed that pregnant women can't get enough vitamins from their diet alone to prevent neural tube defects, and Pauling would have had to consume 255 oranges daily to obtain an equivalent amount of vitamin C. All of this has spurred an increased interest in natural herbal products containing multiple constituents that seem to have some synergistic effect. Plant and herbal preparations are the fastest growing product line of supplements, and have now surpassed vitamins. Over 32 million Americans took one or more herbal supplements in 1994, sales rose 31 percent between 1994 and 1995, and will exceed 2 billion dollars in 1995. The problem is that as long as no claims are made for cure, treatment or prevention, their manufacturers don't have to prove anything with respect to either how safe they are, or how well they work.

"Over 200 lbs. of vegetables in a bottle" claims one advertisement for a supplement allegedly composed of a blend of powdered vegetables, but the manufacturer couldn't provide any information about its phytochemical or antioxidant content. University researchers who specialize in food analysis and processing procedures, emphasize that current technology does not permit condensing huge volumes of produce into any pill, without losing large amounts of nutrients. One broccoli concentrate was found to contain only sulforaphane, a potential cancer fighting agent found in this and other dark green vegetables. However, you would have to swallow 100 pills at a cost of \$20, to get the

amount found in a single serving of broccoli, and you would miss the dozens of other beneficial phytochemicals, vitamins, minerals, and fiber. Several years ago, a government study reported that one quarter of the ginseng products contained none of the active ingredient, and a recent *Consumer's Report* found a 10-fold variation in potency in the ten ginseng preparations tested. A 1993 Duke University analysis of a dozen l-carnitine supplements, revealed that half had less than 60% of the amount advertised on the label, and that even pills in the same bottle had different dosages.

How Can We Insure Safety Or Prove Efficacy?

Some European countries have a much more scientific and safer approach, since plant medicines are regulated and dispensed as other pharmaceuticals. Germany has its special Commission E, composed of physicians, pharmacists, toxicologists and pharmacognosists, expert in medicinal plant chemistry, who apply the same rigorous safety and efficacy standards used for other prescription drugs. More than 80% of German physicians regularly prescribe plant medicines, and in Germany and France, approximately 40% of herbal purchases are reimbursed by insurance companies. The leading herbal is ginkgo biloba, which has been the subject of some 300 bona fide scientific studies, including over 40 double blind clinical trials, and recent sophisticated EEG and event related potential (ERP) mapping analysis. There is little financial incentive for U.S. pharmaceutical companies to conduct such evaluations, since it would be extremely difficult for them to obtain protective patents.

For example, melatonin mania is rampant, with sales now exceeding those for any nutritional supplement, including vitamin C. One melatonin marketer alone projected sales of more than 7 million bottles in 1995. All of this is quite amazing, since there are few if any long term human studies to confirm many of the claims. Melatonin is far and away the most potent antioxidant for the very toxic free hydroxyl radical. Although it appears to be safe in amounts thousands of times those usually recom-

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mended, many believe it should be subjected to the same scrutiny the FDA requires for other hormones and biologically active substances. Some animal studies have shown that supplemental melatonin administration decreases serotonin, which is already low in some forms of depression, and one human study suggests that high doses of melatonin may worsen depression. There is little information about the effects of melatonin on the actions of serotonin reuptake inhibitors like Prozac, knowledge about its possible interactions with other widely used medications, or how it could affect pregnancy, lactation, and puberty, much less possible hazards of long term use. There is absolutely no control over the production process, because melatonin is sold as a dietary supplement. This could have disastrous consequences, as was experienced several years ago, when over 30 died from taking tryptophan, a popular sleeping aid which is the precursor of melatonin. Numerous others suffered permanent neurologic damage, and while the problem was eventually traced to certain batches that had been contaminated during the manufacturing process, officials recalled all preparations because of concerns about tryptophan itself. Similar quality control problems could occur with melatonin, since while some products are synthesized, others are extracted from animal sources. Four out of six melatonin products that were recently analyzed were found to contain impurities that could not be identified.

Denmark has ordered melatonin withdrawn, it is available only on prescription in Great Britain and Switzerland, and Canada has banned both melatonin and chromium supplements. New Zealand just took a 500 mg vitamin C product off the market following evidence of contamination, and France requires a prescription for dosages of 500 mg or more. However, when the FDA moved to impose tougher new rules for supplements in 1993, Congress was bombarded with millions of letters and faxes and large protest demonstrations. This resulted in the present Dietary Supplement Health and Education Act, which has few restrictions to safeguard the public from products that might prove harmful. Because of concern over reported adverse

reactions and even deaths, Senator Kassenbaum attempted to introduce a revision last December that would require more safety research, or a physician's prescription. It was quickly withdrawn following well organized opposition from vested commercial interests and fanatic antioxidant enthusiasts. Ohio and Texas have imposed their own restrictions for certain nutritional supplements that have been shown to be harmful and even lethal. The very recent death of a healthy college student in New York City following consumption of a popular supplement that contained no label warnings despite known serious adverse reactions, may also lead to stricter state laws for some products, but there are no easy solutions, or criteria on where to draw the line. It will be necessary to steer a careful course between the Scylla of unrestrained self-treatment spurred on by sensationalism, and the Charybdis of ultra conservatism that could deny important benefits for millions. Nobody wants to throw the baby out with the bath water, but something needs to be done.

Paul J. Rosch, M.D., F.A.C.P.

Editor

Some of this information was contained in prior Newsletters and has been included here to provide a more balanced and informative report. An abbreviated version of the above will appear as a Guest Editorial in *Medical Tribune*.

Green Tea, Cardiovascular Disease, And Cancer

Green tea is consumed in copious amounts in the Orient, where it has been considered to confer a variety of health benefits for over 4,000 years. Allegedly, the Chinese Emperor Shen Nung, often called "The Divine Healer", discovered this tonic in 2737 B.C., when some tea leaves accidentally fell into a pot of water he was boiling. The cultured Mandarin word for tea is *ch'a*, but sailors and traders pronounced it as *t'e*, or *tay* in their dialects. It was introduced into Japan in 805 as a medicine, and since then, has been used for digestive disorders, headache, infections, and to prevent cavities. When the East India company first began the public

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sale of tea in London in 1657, it was advertised as a cure for "apoplexy, catarrh, colic, consumption, drowsiness, epilepsy, gallstones, lethargy, migraine, paralysis, and vertigo".

A very recent report appears to provide support for some of these claims. Apoplexy, drowsiness, seizures, headache, paralysis and dizziness, can all be manifestations of a stroke, or impending stroke. A 15-year study of 552 Dutch men, has now confirmed that those who drank more than 4.7 cups of tea daily, had a 70% reduced risk of stroke, compared to those who drank less than 2.1 cups. Tea is rich in flavonoids, which reduce the tendency for blood platelets to clump or cause clots. The researchers also found that men with a high flavonoid intake, had almost 75% lower risk for stroke, than those at the lower end of the scale.

Another constituent of tea, chemically classified as a catechin, can curtail cancer growth in laboratory animals, and some studies suggest that as little as one cup of green tea a week can reduce the risk of developing esophageal cancer. Researchers compared the tea drinking habits of patients with esophageal cancer with those of healthy controls. Regular tea drinkers, who also smoked and drank, showed a reduced risk of 20% risk for men, and 50% for women. For both men and women who did not smoke or drink, the reduced risk was about 60%, compared to controls. The more tea the participants drank, the lower their risk for esophageal cancer.

Other chemicals in tea can significantly lower lipid levels. In one study of 1,371 men, Japanese scientists found that those who drank the most green tea, had the lowest cholesterol and triglyceride measurements. Tea drinkers also had the highest levels of the cardioprotective cholesterol component, HDL, and the least amount of very damaging LDL low density lipoproteins. The greatest rewards were seen in those who drank a minimum of 10 cups daily. This could pose a problem for many working people, who would encounter difficulties in being able to conveniently prepare, consume, and eliminate such large quantities. Most Americans can't even find the time to follow the usual recommendations to drink at least 8 glasses of water a day. In addition, we tend to use black tea for our hot and iced tea drinks, since it is less astringent. This

usually comes from India, where the leaves are fermented, and may not provide as much protection because of this processing procedure.

Many of these benefits are believed to be due to the high content of polyphenols and flavonoids found in tea. The cardioprotective effects of alcohol have similarly been attributed to their high flavonoid content, and the alleged superiority of red wine in this regard, may be due to the fact that it contains both flavonoids and catechins. These ingredients are now being marketed as a "wine pill", to avoid the harmful effects of increased alcohol consumption. Perhaps a green tea tablet, or preferably a combination tea/wine capsule, could provide the benefits of both these beverages, without the associated risk of brain, liver, or kidney damage. In that regard, it is said that the Buddhists originally wanted to make tea drinking popular, to reduce the use of alcohol. Similarly, in the U.S., the phrase "tea drinker" is a synonym for "sober-headed", and a "teetotaler", (tee-totaler), now means anyone who abstains from alcohol.

Are Tea Drinkers Less Stressful?

Another factor to be considered, is that the lifestyles of tea drinkers may be more orderly and less stressful, as exemplified in the ritualistic Japanese tea ceremony. This had its origins in Zen Buddhism, and was popularized by the samurai, best known for their strict discipline, fearless courage, and undying loyalty. They would often commit *hara-kiri*, if their master died in battle, or even in bed. However, the samurai's creed involved much more than this. The warrior's life was seen as a moral progression which taught respect for all living things. The Japanese tea ceremony was designed to stimulate appreciation and respect for simple things, as well as other people, and, when properly practiced, promoted a sense of inner peace and calm. It involves an intricate ritual of meticulous preparation, pouring, and drinking of tea, that can take years to master. In England, the practice of taking "afternoon" or "high tea", was introduced in 1839 by the Duchess of Bedford, supposedly because tea relieved the feeling of weakness that regularly came over her around four or five in the

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afternoon. It has since become a British tradition that also requires learning the rules of proper etiquette and behavior, emphasizes politeness and consideration for others (tea and sympathy), and provides a period of quietude, tranquillity, and relief from the stresses of daily life.

Tea drinkers also seem to have healthier lifestyles than those who prefer coffee. One study of some 2500 men and women between the ages of 25 and 64, found that smoking, as well as meat and sausage intake, increased with coffee, and decreased with tea consumption. Conversely, eating fresh fruits, drinking juice or mineral water, and physical activity, tended to increase with tea drinking, and decrease with coffee.

British Medical Journal-February, 1995

Hospital Practice-June 15, 1995

Natural Healing Newsletter-October, 1995

Associated Press-March 24, 1996

Tea! Thou soft, thou sober, sage, and venerable liquid, thou innocent pretence for bringing the wicked of both sexes together in a morning; thou female tongue-running, smile-smoothing, heart-opening, wink-tipping cordial, to whose glorious insipidity I owe the happiest moment of my life, let me fall prostrate thus, and . . . adore thee.

Colley Cibber

Its proper use is to amuse the idle, and relax the studious, and dilute the full meals of those who cannot use exercise, and will not use abstinence.

Samuel Johnson

Do Your Own Bypass?

As we grow older, the progressive accumulation of atherosclerotic plaque can markedly restrict the flow of blood to vital structures such as the brain and heart. Two million Americans a year suffer from such serious blockage of the arteries in the legs, that a reaming out or bypass procedure is required. The 10% who are not candidates for any type of surgical correction, face persistent pain, skin ulcerations, and possible amputation of the affected area. However, in some instances, individuals spontaneously grow new blood vessels

around the obstructed area, essentially performing their own bypass procedure. Such new blood vessel growth, or angiogenesis, is frequently seen around certain malignant tumors, which release proteins that stimulate this process. Several years ago, scientists identified the gene responsible for manufacturing these growth factors, and have now been able to splice this into DNA. Theoretically, if this modified DNA were inserted into the smooth muscle cells on the inner lining of obstructed arteries, it could cause them to release growth factor, and stimulate the formation of new blood vessels around this area.

Some 2 dozen patients with severe peripheral vascular disease not suitable for any surgical correction are now being studied to test this hypothesis. A balloon catheter coated with a sticky solution of the modified DNA is inserted into the obstructed vessel until it reaches the obstructed area. The balloon is then inflated to coax the DNA growth factor into smooth muscle cells on the inner lining of the artery. If this proves successful, the procedure might also prove beneficial for some patients with blocked cerebral or coronary arteries, who are not candidates for surgical correction.

Another new approach to "man made" blood vessels, may come from new excimer laser technology that vaporizes tissue in its path, thus creating a new pathway. The procedure was recently used in experimental animals to create new channels through the entire thickness of the heart wall, and was well tolerated. Two to four months later, researchers occluded the coronary artery of these animals, as well as litter mates, to simulate a heart attack. Compared to the untreated controls, those with the new, laser created channels, showed much less heart muscle damage. These findings could be promising, since they demonstrate that channels can be created in the wall of the ventricle that remain open for at least 4 months. In addition, they appear to supply blood to damaged tissue directly from the contents of the heart itself, rather than new blood vessels. This might be helpful in the future, for some patients who cannot benefit from conventional corrective surgical procedures.

The Sciences-July/August, 1995

Business Wire-March 22, 1996

Book Reviews • Meetings and Items of Interest

Book Review

The New Wellness Encyclopedia, eds. The University of California at Berkeley Wellness Letter, Houghton Mifflin Co., New York, 1995, 611 pages, \$19.95

This large paperback compendium of information is designed to explain what you can do to help yourself to attain optimal health. The information is attractively presented in separate sections dealing with longevity, nutrition, exercise, self-care, and environment and safety. The discussion of vitamins, nutritional supplements, and antioxidants is clear and current. For example, evidence is presented that vitamin C protects against colds and cataracts, as well as cancer of the mouth, esophagus, stomach, pancreas, colon, lung, breast, and cervix. As the authors point out, many of these conclusions are based on studies of populations with low intakes of these nutrients, so it is not clear whether supplementation would have the same effect on people whose antioxidant intake is not deficient. The important role of oxidized LDL in the development of atherosclerotic plaque and the ability of certain antioxidants to prevent this is also explained.

The chapter devoted to stress provides the latest information on important mind/body links, ranging from the effects of stress on the immune system and the role of hostility in cardiovascular disease, to the important stress reducing effects of a strong social support, and the ability to express anger and other emotions. A variety of stress reduction strategies are reviewed, and their practical applications are explained in detail. A number of important topics not usually covered in offerings of this nature are also discussed, such as problems with memory and concentration, the importance of maintaining proper sleeping habits, how to protect your health while traveling abroad, optimal use of the changing health care

system, the significance of common laboratory tests and diagnostic procedures, and environmental safety hazards, including those posed by common appliances in the home. This useful guide also tells you what to do when you are sick, and almost every conceivable disorder is covered. There are numerous helpful charts, diagrams, illustrations, and tables, as well as a handy glossary to explain technical terms. The coverage of food contents is particularly comprehensive. Although there is no bibliography or lists for suggested reading, most of the sources one might want to consult for further information are identified in the text. This book is highly recommended to help you get on the road to developing a healthier lifestyle, and also to show you what to do to insure a speedier recovery if you become ill.

Meetings and Items of Interest

May 31-June 2 Mindfulness Meditation, Rowe Camp & Conference Center, Rowe, MA, call (413) 339-4216

June 6-9 1996 Symposium Medical Acupuncture Clinical Practice and Research, Sponsored by the Maricopa Medical Center, The Parc Fifty Five Hotel, San Francisco, CA, call (213) 937-5514

June 10-12 The Second Annual International Congress on Alternative & Complementary Medicine, Radisson Plaza Hotel at Mark Center, Alexandria, VA, call (800) 5BIOCON

June 21-24 ISSSEEM Sixth Annual Conference, Evolution of a New Paradigm: Science and Inner Experience, Boulder, CO, contact C. Penny Hiernu at (303) 278-2228

Aug. 12-16 Psychopharmacology and Its Role in Clinical Practice, write to: Seventeenth Cape Code Institute, Albert Einstein College of Medicine, 1308 Belfer Bldg., Bronx, NY 10461

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