

## Prevention Protocols

- Determining What Works
- Conventional Medicine Recommends Vitamin Supplements
- L.E.F.'s Prevention Protocol

It used to be thought that little could be done to postpone what nature has in store for us. Today, a growing scientific consensus indicates that individuals possess a great deal of control over how long they are going to live and what their state of health will be.

Mainstream medicine has relied on simple measures of preventing disease, such as controlling hypertension, yet many doctors are coming to the realization that additional steps can be taken to protect against premature aging and death.

In fact, the results of tens of thousands of scientific studies make it abundantly clear that following the proper lifestyle can add a significant number of healthy years to the average person's lifespan.

The premise of taking actions to maintain youthful health and vigor is based on findings from peer-reviewed scientific studies that identify specific factors that cause us to develop degenerative disease. These studies suggest that the consumption of certain foods, food extracts, hormones, or drugs will help to prevent common diseases that are associated with normal aging.

Therefore, the concept of disease prevention can be defined as the incorporation of findings from published scientific studies into a logical daily regimen that enables an individual to attain optimal health and longevity.

Taking aggressive steps to extend one's lifespan is a major commitment. This Prevention protocol provides practical information about what a person can do to take advantage of the consensus of scientific knowledge obtained from the most prestigious medical journals in the world.

### THE BASIS FOR DETERMINING WHAT WORKS

People seeking to reduce their risk of disease are often overwhelmed by the volume of technical data on the subject. For the past 23 years, the Life Extension Foundation has meticulously reviewed the published medical literature dating as far back as 1917. Life Extension personnel have dedicated the past 35 years to working with physicians and scientists to develop validated methods of preventing age-related disease.

Each year, the Foundation spends millions of dollars on research projects aimed at extending the healthy human lifespan. Since 1983, the Foundation has reviewed thousands of blood test results of members who have been following antiaging supplement, drug, and hormone-replacement programs.

Based on this vast accumulation of data, the Life Extension Foundation has designed a practical disease prevention protocol that is based solely on scientific principles.

Before you embark on a program to reduce your risk of degenerative disease, it is important for you to know about scientific studies conducted on humans that show these therapies really work. If you are not aware of these published studies, you may be unlikely to methodically follow a long-term disease prevention program.

### CONVENTIONAL MEDICINE RECOMMENDS VITAMIN SUPPLEMENTS

- FDA's Suppression of Folic Acid
- Vitamin C Controversy
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- Reducing Mortality
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For the greater part of the 20th century, mainstream medicine was openly hostile to the idea of healthy people taking vitamin supplements. This antivitamin position began to change in the 1990s as irrefutable evidence emerged that supplements could reduce the risk of age-related disease without inducing toxicity.

In the April 9, 1998, issue of the *New England Journal of Medicine*, an editorial was entitled "Eat Right and Take a Multi-Vitamin." This article was based on studies indicating that certain supplements could reduce homocysteine serum levels and therefore lower heart attack and stroke risk. This was the first time this prestigious medical journal recommended vitamin supplements (Oakley 1998).

An even stronger endorsement for the use of vitamin supplements was in the June 19, 2002, issue of the *Journal of the American Medical Association (JAMA)*. According to the Harvard University doctors who wrote the JAMA guidelines, it now appears that people who get enough vitamins may be able to prevent such common illnesses as cancer, heart disease, and osteoporosis. The Harvard researchers concluded that suboptimal levels of folic acid and vitamins B6 and B12 are a risk factor for heart disease and colon and breast cancers; low levels of vitamin D contribute to osteoporosis; and inadequate levels of the antioxidant vitamins A, E, and C may increase the risk of cancer and heart disease (Fairfield et al. 2002).

### **The FDA's Suppression of Folic Acid**

The Food and Drug Administration (FDA) has spent enormous resources trying to prevent people from supplementing with folic acid. The FDA argues against folic acid supplementation because the presence of folic acid in the blood could mask a serious vitamin B12 deficiency. In a study in the *Journal of the American Medical Association*, Losonczy et al. (1996) addressed the FDA's concerns by recommending that folic acid supplements be fortified with vitamin B12 as a prudent way of gaining the cardiovascular benefits of folic acid without risking a B12 deficiency.

Even though major medical journals (e.g., *New England Journal of Medicine*) long ago endorsed the use of folic acid to reduce cardiovascular disease (Malinow et al. 1998), the FDA still does not accept that folic acid has any benefit other than preventing a certain type of birth defect.

A study by Giovannucci et al. (1998) in the *Annals of Internal Medicine* showed how fatally flawed the position of the FDA is. Data from the famous *Harvard Nurses' Health Study* conducted at the Harvard Medical School showed that long-term supplementation with folic acid reduces the risk of colon cancer by an astounding 75% in women. The fact that there are 90,000 women participating in the *Harvard Nurses' Health Study* makes this finding especially significant. The authors of this study explained that folic acid obtained from supplements had a stronger protective effect against colon cancer than folic acid consumed in the diet. This new study helps to confirm the work of Dr. Bruce Ames, the famous molecular biologist who has authored numerous articles showing that folic acid is extremely effective in preventing the initial DNA mutations that can lead to cancer later in life. This Harvard report, showing a 75% reduction in colon cancer incidence, demonstrated that the degree of protection against cancer is correlated with how long a DNA-protecting substance (folic acid) is consumed. It was the women who took more than 400 mcg of folic acid a day for 15 years who experienced the 75% reduction in colon cancer, whereas short-term supplementation with folic acid produced only marginal protection.

There now exists a massive body of evidence that supplementation with folic acid can prevent both cardiovascular disease and cancer, yet the FDA has proposed rules that would prohibit the American public from even learning about these benefits. Colon cancer will kill 47,000 Americans this year. It is unfortunate that the FDA didn't "allow" these colon cancer victims to learn about folic acid in time.

### **The Vitamin C Controversy**

Does vitamin C cause kidney stones? Some doctors still believe it does, but a report from Harvard Medical School showed no increased risk of kidney stones when evaluating 85,557 women over a 14-year study period. This report, by Curhan et al. in the April 1999 issue of the *Journal of the American Society of Nephrology*, showed that women who consumed 1500 mg a day or more of vitamin C were no more likely to develop kidney stones than women who consumed less than 250 mg of vitamin C a day. The study did reveal that women who consumed 40 mg or more of vitamin B6 were 34% less likely to develop kidney stones compared to women taking fewer than 3 mg a day of B6 (Curhan et al. 1999). So now that kidney stone risk has been ruled out, let's look at some of the human studies showing positive benefits to vitamin C supplementation.

In the early 1990s, several large population studies showed a reduction in cardiovascular disease in those who consumed vitamin C. The media reported on some of these findings and this favorable publicity helped push a bill through Congress that prevented the FDA from banning high-potency vitamin C and other supplements.

The most significant report emanated in 1992 from UCLA, where it was announced that men who took 800 mg a day of vitamin C lived 6 years longer than those who consumed the FDA's recommended daily allowance of 60 mg a day. The study, which evaluated 11,348 participants over a 10-year period of time, showed that high vitamin C intake extended average lifespan and reduced mortality from cardiovascular disease by 42% (Enstrom et al. 1992).

A study by Nyyssonen et al. (1997) in the *British Medical Journal* evaluated 1605 randomly selected men in Finland ages 42-60 years from 1984-1989. None of these men had evidence of preexisting heart disease. After adjusting for other confounding factors, men who were deficient in vitamin C had 3.5 times more heart attacks than men who were not deficient in vitamin C. The scientist's conclusion was "vitamin C deficiency, as assessed by low plasma ascorbate concentration, is a risk factor for coronary heart disease" (Nyyssonen et al. 1997).

In a study in *The Lancet* (Khaw et al. 2001), researchers at Cambridge University in England looked at serum vitamin C and length of life. People who had the lowest levels of vitamin C were twice as likely to die when compared to those with the highest serum vitamin C levels. This study was based on the findings in more than 19,000 people. The question for those who want to achieve maximum health is: Do you want your blood to contain the lowest levels or the highest levels of vitamin C? Because being at the lowest level appears to double your risk of dying, we suggest that you consume fruits, vegetables, and supplements that are high in vitamin C.

In the March 9, 1999, issue of the American Heart Association's journal *Circulation*, elevated homocysteine levels were shown to cause rapid onset of endo-thelial (arterial lining) dysfunction (Chambers et al. 1999). This type of dysfunction reduces blood flow and can facilitate a lethal arterial spasm. Vitamin C inhibited arterial dysfunction by interfering with oxidative stress mechanisms. The doctors conducting the study stated that acute impairment of vascular endo-thelial function can be prevented by pretreatment with vitamin C.

In a double-blind study in the *Journal of the American College of Cardiology*, Watanabe et al. (1998) compared the effects of nitrate drugs in people receiving vitamin C to a placebo group not receiving vitamin C. The doctors administered nitrate drugs to healthy people and patients with coronary artery disease and then measured vasodilation response and cellular levels of cGMP, an energy substrate that is depleted by nitrate drugs. At day zero, all participants were measured to establish a baseline. After 3 days of vitamin C administration (2 grams 3 times daily), there was no change in either group. After 6 days of vitamin C therapy, an impressive 42% improvement in vasodilation response was observed, and a 60% improvement in cellular cGMP levels was measured in coronary artery disease patients receiving vitamin C compared to those receiving placebo. A similar improvement occurred in the healthy subjects taking vitamin C compared to the placebo group. The doctors concluded the study by stating that "these results indicate that combination therapy with vitamin C is potentially useful for preventing the development of nitrate tolerance" (Watanabe et al. 1998).

In another study in the *Journal of Clinical Investigation*, Bassenge et al. (1998) looked at the effects of nitrate drug therapy on human patients. Tolerance development was monitored by changes in arterial pressure, pulse pressure, heart rate, and activity of isolated patients. All patients experienced the deleterious effects of nitrate tolerance. However, when vitamin C was coadministered with the nitrate drugs, the effects of nitrate tolerance were virtually eliminated. The most significant improvement was a 310% improvement in the arterial conductivity test. The nitrate drugs induced a dangerous upregulated activity of platelets, but this too was reversed with vitamin C supplementation (Bassenge et al. 1998). The doctors who conducted this study indicated that vitamin C may be of benefit during long-term, nonintermittent administration of nitrate drugs in humans.

Chronic heart failure is associated with reduced dilating capacity of the endothelial lining of the arterial system. Scientists tested heart failure patients by high-resolution ultrasound and Doppler to measure radial artery diameter and blood flow. Vitamin C restored arterial dilation response and blood flow velocity in patients with heart failure. The scientists determined that the mechanism of action was that vitamin C increased the availability of nitric oxide, an important precursor to cGMP. This study was in the February 1998 issue of the journal *Circulation* (Rodes et al. 1998).

Also in 1998, another aspect of the effect of vitamin C on coronary artery disease was discovered. A study in the *Journal of the American College of Cardiology* (Vita et al. 1998) showed that low plasma ascorbic acid levels independently predict the presence of an unstable coronary syndrome in heart disease patients. According to the doctors, the study's results showed that the beneficial effects of vitamin C in treating coronary artery disease may result, in part, by an influence on arterial wall lesion activity rather than a reduction in the overall extent of fixed disease (Vita et al. 1998).

The published research findings suggest that vitamin C may reduce mortality in coronary artery disease patients, increase life span, and possibly eliminate the effects of nitrate tolerance in those taking nitrate drugs. Although not recognized in the medical establishment as a therapy for coronary artery disease, there now exists an accumulated wealth of evidence that vitamin C has beneficial effects in the treatment of heart-related illnesses.

Historically, mainstream medicine has ridiculed vitamin C supplementation. In today's modern world, conventional medicine says

that only 200 mg a day of vitamin C is needed, despite findings showing that high doses of vitamin C are required to produce optimal benefit. Meanwhile, the FDA continues to hold with the position that no more than 60-100 mg a day of vitamin C is needed.

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### Saturating the Bladder

The most frequently voiced criticism about supplemental vitamin intake is that it produces "expensive urine," because water-soluble vitamins, such as vitamin C and the B vitamins, are rapidly excreted into the bladder within hours of ingestion. For years, the Life Extension Foundation has contended that these vitamins are beneficial in spite of their rapid excretion and that, moreover, it is desirable to have a bladder full of vitamins because certain vitamins inhibit chemicals that cause bladder cancer. In the September 1996 issue of the *American Journal of Epidemiology*, a study on the risk of bladder cancer in vitamin takers showed the following (Bruemmer et al. 1996):

- High intake of vitamin A and beta-carotene was associated with a 48% reduction in bladder cancer incidence compared to the lowest levels of vitamin A and beta-carotene intake.
- People taking higher amounts of vitamin C had a 50% reduced rate of bladder cancer. Those who took 502 mg or more of vitamin C a day had a 60% reduction in bladder cancer compared to those who took no vitamin C.
- For those who took multivitamin supplements for at least 10 years, the reduction in bladder cancer was 61% compared to people who took no vitamin supplements.
- High intake of fried foods was associated with double the risk of bladder cancer.

It appears from this study that even low-potency "one-a-day" supplements (which do not protect against other types of cancer) can at least protect against bladder cancer.

### Protecting Vision

Studies show that antioxidant supplements reduce the risk of cataracts. One study in the *American Journal of Epidemiology* (Rouhiainen et al. 1996) evaluated 410 men for 3 years to ascertain the association between serum vitamin E and the development of cortical lens opacities (cataracts). The men with the lowest level of serum vitamin E had a 3.7 times greater risk of this form of cataract compared to men with the highest serum level of vitamin E (Rouhiainen et al. 1996).

Although cataracts are usually treatable, a disease called wet macular degeneration is not. Those who eat spinach and collard greens have low rates of macular degeneration, and extracts from these vegetables thought to protect against this blinding disease are now available in dietary supplements that contain lutein and zeaxanthin.

### Keeping Arteries Clean

In a study reported in the *American Journal of Clinical Nutrition* (Bonithon-Kopp et al. 1997), antioxidant status was assessed and carotid artery occlusion was measured in 1187 men and women 59-71 years of age without any history of coronary artery disease or stroke. The results showed that the higher the level of vitamin E in red blood cells, the lower the risk of carotid atherosclerosis. In men with the highest levels of carotid atherosclerotic plaques, the lowest levels of vitamin E, selenium, and carotenoids were found. The scientists concluded by stating: "Our findings give some epidemiological support to the hypothesis that lipid peroxidation and low antioxidant status are involved in the early stages of atherosclerosis" (Bonithon-Kopp et al. 1997).

A study in the journal *Atherosclerosis* (Koscielny et al. 1999) showed that people who took a 900-mg of garlic supplement every day for 4 years had 5-18% less plaque buildup in their carotid arteries compared to the placebo group. The women in the study group actually showed a 4.6% decrease in carotid plaque volume over a 4-year period, whereas the placebo group showed a 5.3% increase in artery-clogging plaque.

There are more studies showing that atherosclerosis can be prevented than for any other degenerative disease. Because more people die or become disabled from vascular diseases than from any other cause, it would appear prudent to follow a program that would reduce one's risk of suffering a vascular-related heart attack or stroke.

### Are You Concerned about Cancer?

A well-justified fear of cancer is a major reason why people take dietary supplements. As has already been shown, there is a compelling body of evidence that cancer risk can be reduced by taking the proper supplements over an extended period of time.

An article in the *Journal of the American Medical Association* (JAMA) by Clark et al. (1996) showed that 200 mcg of supplemental selenium a day reduced overall cancer mortality by 50% in humans compared to a placebo group not receiving supplemental selenium. This 9-year study demonstrated that a low-cost mineral supplement could cut the risk of dying from cancer in half in certain individuals.

In the March 17, 1999, issue of the *Journal of the National Cancer Institute* (Zhang et al. 1999), associations between intakes of specific nutrients and subsequent breast cancer risk were investigated in 83,234 women who were participating in the *Harvard Nurses' Health Study*. Breast cancer risks were significantly lower in women who consumed alpha-carotene, beta-carotene, lutein/zeaxanthin, and vitamins A and C. Among premenopausal women who consumed moderate amounts of alcohol (a known risk factor in breast cancer), beta-carotene lowered risk. Premenopausal women who consumed 5 or more servings a day of fruits and vegetables had modestly lower risk of breast cancer than those who had less than 2 servings a day.

A study in the March 15, 1999, issue of *Cancer Research* (Gann et al. 1999) showed that the tomato extract lycopene was the most effective nutrient shown to protect against the development of prostate cancer. This study, started in 1982, followed 578 men for 13 years. Lycopene strongly reduced prostate cancer risk and more importantly, lowered the risk for aggressive cancer. This study confirmed many previous studies showing that lycopene can help prevent pancreatic, prostate, and a host of other cancers. A surprising finding revealed at the April 12, 1999, meeting of the American Association of Cancer Research showed that 30 mg of lycopene supplements a day slowed the growth of existing prostate cancer and lowered serum PSA readings by 20%!

Men with high intake of vitamin E were 35% as likely to develop colorectal adenomas as men with low vitamin E intake (Tseng et al. 1996). (Adenomas are neoplastic lesions that are considered precursors to colon cancer.) In a related study in the February 1999 issue of *Diseases of the Colon and Rectum* (Whelan et al. 1999), the use of multivitamins, vitamin E, and calcium supplements was found to be associated with a lower incidence of recurrent adenomas in 448 patients with previous neoplasia who underwent follow-up colonoscopy. This study found a protective effect against the recurrence of precancerous adenomas when any vitamin supplement was used. On this same subject, a report in the *American Journal of Epidemiology* (Tseng et al. 1996) showed that women with high folate intake were 40% less likely to develop adenomas of the colon than women with low folate intake.

But what if you already have cancer? Again, the research shows a prolongation of lifespan with proper supplementation.

In a study in *Cancer Letters* (Evangelou et al. 1997), animals with malignant tumors given high doses of vitamins C and E and selenium manifested a significant prolongation of the mean survival time. Complete remission of tumors developed in 16.8% of the animals. Low-dose administration of these vitamins failed to exert any beneficial effect on mean survival time of the animals. Results indicated that high doses (mega doses) of vitamins C and E in combination with other carefully selected antioxidants are probably needed in order to achieve sufficient prevention and treatment of malignant diseases. This study indicated that low-potency supplements are of little value.

Vitamin E succinate was shown to inhibit growth and induced apoptotic cell death of estrogen receptor-negative human breast cancer cells in a study in *Cancer Research* (Turley et al. 1997). These findings suggest that vitamin E succinate may be of clinical use in the treatment and possible prevention of human breast cancers.

The research clearly shows the risk of contracting cancer is reduced in those who supplement with adequate amounts of nutrients, such as selenium, folate, carotenoids, vitamins, and other plant extracts.

## **Reducing Mortality**

One of the most compelling reports that high-potency supplements extend lifespan in humans was by Losonczy et al. in the August 1996 issue of the *American Journal of Clinical Nutrition*. This study involved 11,178 elderly people, who participated in a trial to establish the effects of vitamin supplements on mortality. The study showed that the use of vitamin E reduced the risk of death from all causes by 34%. Effects were strongest for coronary artery disease, where vitamin E resulted in a 63% reduction in death from heart attack. In addition, the use of vitamin E resulted in a 59% reduction in cancer mortality. When the effects of vitamins C and E were combined, overall mortality was reduced by 42% (compared to 34% for vitamin E alone) (Losonczy et al. 1996). These results provided significant evidence about the value of vitamin supplementation, yet the media failed to report on it. What made this study so credible was that:

- It compared people who took low-potency "one-a-day" multiple vitamins to those who took higher-potency vitamins C and E supplements. Previous studies measuring the life expectancy of the "one-a-day" crowd did not show significant benefits, thereby causing most doctors to conclude there is no value in vitamin supplementation. In this new report, those taking "one-a-day" multivitamins did not do any better than people taking nothing at all, which supports the Life Extension Foundation's position that higher doses of antioxidants are required to reduce the risk of heart disease and cancer than those found in conventional supplements.
- It lasted 9 years! Most studies that attempt to evaluate the benefits of vitamin supplementation are for shorter time periods. It should be noted, however, that the famous *Harvard Nurses' Health Study* found that vitamin E reduced coronary artery disease mortality by more than 40% after only 2 years!
- It included 11,178 people, a larger group than most previous studies.

## Controlling Aging

The National Academy of Sciences published three reports showing that the effects of aging may be partially reversible with a combination of acetyl-L-carnitine and lipoic acid (Hagen et al. 2002). One of these studies showed that supplementation with these two nutrients resulted in a partial reversal of the decline of mitochondrial membrane function while consumption of oxygen significantly increased. This study demonstrated that the combination of acetyl-L-carnitine and lipoic acid improved ambulatory activity, with a significantly greater degree of improvement in the old rats compared to the young ones. Human aging is characterized by lethargy, infirmity, and weakness. There is now evidence that supplementation with two over-the-counter supplements can produce a measurable antiaging effect.

The second study published by the National Academy of Sciences showed that supplementation with acetyl-L-carnitine and lipoic acid resulted in improved memory in old rats. Electron microscopic studies in the hippocampus region of the brain showed that acetyl-L-carnitine and lipoic acid reversed age-associated mitochondrial structural decay. In the third National Academy of Sciences study, scientists tested acetyl-L-carnitine and lipoic acid to see if an enzyme used by the mitochondria as biologic fuel could be restored in old rats. After 7 weeks of supplementation with acetyl-L-carnitine and lipoic acid, levels of this enzyme (carnitine acetyl-transferase) were significantly restored in the aged rats. Supplementation also inhibited free radical-induced lipid peroxidation, which enhanced the activity of the energy-producing enzyme in the mitochondria. The scientists concluded that feeding old rats acetyl-L-carnitine and lipoic acid can ameliorate oxidative damage, along with mitochondrial dysfunction.

## Hormone Replacement

Proper hormone replacement can produce an immediate improvement in the quality of life and also prevent many diseases. DHEA is one of several important hormones whose production in the body diminishes rapidly as people age past year 35. There now exists a wide body of evidence that supplementation with DHEA can prevent many degenerative diseases, while improving feelings of well-being and alleviating depression.

In the October 1996 issue of the journal *Drugs and Aging*, an overview of published studies by Watson et al. (1996) on DHEA revealed the following:

- In both humans and animals, the decline of DHEA production with aging is associated with immune depression, increased mortality, increased risk of several different cancers, loss of sleep, and decreased feelings of well-being.
- DHEA replacement in aged mice significantly normalized immune function to youthful levels.
- DHEA replacement has shown a favorable effect on osteoclasts and lymphoid cells, an effect that may delay osteoporosis.
- Low levels of DHEA inhibit energy metabolism, thus increasing the risk of heart disease and diabetes mellitus.
- Studies conducted on humans show essentially no toxicity at doses that restore DHEA to youthful levels.
- DHEA deficiency may expedite the development of some diseases that are common in the elderly.

Since this overview was published in 1996, hundreds of additional studies have substantiated DHEA's role as an antiaging hormone-replacement supplement. In a study published in *Biological Psychiatry* (Wolkowitz et al. 1997), DHEA was tested on middle-aged and elderly patients with major depression. DHEA was administered for 4 weeks in doses ranging from 30-90 mg a day. This level of dosing elevated DHEA serum levels to those observed in younger people. Depression ratings, as well as aspects of memory performance, significantly improved. This data suggested that DHEA may have antidepressant and promemory effects and corresponded with previous human studies in which DHEA supplementation (50 mg a day) significantly elevated mood in elderly people.

For specific information on antiaging hormone replacement, refer to the *Male Hormone Modulation Therapy, Female Hormone Replacement Therapy, and DHEA Replacement Therapy protocols*.

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### THE LIFE EXTENSION FOUNDATION'S PREVENTION PROTOCOL

If you are healthy now and want to stay that way, the Life Extension Foundation has designed protocols that incorporate the best-documented disease-preventing nutrients and hormones.

The Foundation's Prevention protocols consist of the 10 most important supplements for the average person to take every day to reduce risk of contracting the degenerative diseases of aging.

**Note:** *The Prevention protocol is for healthy people. Those seeking to treat an existing disease may refer to the many specific disease prevention protocols contained in this book.*

The following recommendations are listed in order of importance:

Life Extension's Top 10 Steps for Achieving Ultimate Health



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