

Asthma

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Asthma is the most common chronic pulmonary disorder in the United States. The condition is characterized by hypersensitivity and inflammation of the lung's airway (bronchial) tissue, and asthma attacks can leave a person gasping for breath. While most cases are mild, more than 5000 deaths are attributed to asthma attacks each year, according to the American Academy of Allergy, Asthma and Immunology (AAAAI 2006).

The incidence of asthma cases has surged in recent years, although researchers aren't sure exactly why. According to some studies, up to 5 percent of the US population is affected by asthma, with half of these cases developing before age 10 (Kasper DL et al 2005). Asthma attacks can be triggered by allergies and environmental irritants. Scientists have also discovered links between asthma and other diseases and conditions, including gastroesophageal reflux disease (GERD) and obesity (Flaherman V et al 2006).

People with asthma usually rely on medications to control their condition. During severe asthma attacks, patients need "rescue medications," which are designed to restore airflow. When attacks aren't occurring, many asthmatics take "maintenance medications," or medications that have been shown to reduce the risk of acute asthma attacks. Both classes of medications have side effects, but because of the more severe side effects (such as high blood pressure) associated with rescue medications, the goal of conventional therapy is to prevent attacks with the right dosages of maintenance drugs.

Life Extension takes this philosophy one step further. Under the best circumstances, asthmatics could control their condition without the use of any medications, completely avoiding the side effects associated with prescription drugs. In recent years, researchers have learned a great deal about asthma and natural methods to inhibit the underlying inflammatory cascade that causes so much misery. Life Extension has also uncovered evidence that a common herbal extract, butterbur, is a highly effective asthma therapy. Finally, oxidative stress, which can wreak havoc with cells, has been linked to asthma, thus antioxidants have a definite role in therapy.

Lifestyle changes can also affect the frequency of asthma attacks and their severity. People who smoke are strongly encouraged to quit. Numerous smoking-cessation strategies are available, from nicotine replacement to group therapy. It may also help to reduce exposure to second-hand smoke and air pollution whenever possible. There is an increased risk of asthma among people who live in heavily populated urban areas. Finally, seeking treatment for diseases such as GERD and obesity may help reduce the severity of asthma.

UNDERSTANDING ASTHMA: INFLAMMATION AND OXIDATIVE STRESS

Asthma is primarily a disorder of the bronchial tubes, the airways that connect the windpipe (trachea) and the lungs. The bronchial tubes are surrounded by smooth muscle. The tubes themselves are lined with mucus glands and contain inflammatory immune-system cells called mast cells, lymphocytes, and eosinophils. When activated, these cells produce inflammatory mediators such as histamine and leukotrienes, which bind with receptors on cells within the bronchial tubes.

During an asthma attack, a cascade of events is launched that results in the production of histamine and leukotrienes. Leukotrienes are derived from the inflammatory arachidonic acid. These inflammatory mediators cause a host of changes in bronchial tissue: they trigger a dramatic increase in mucus secretion and a simultaneous rapid constriction of the bronchial smooth muscle, which narrows the bronchial tubes and reduces the amount of air that can pass through them. Over the course of the subsequent few hours, inflammatory cells move into the area, capillaries begin to leak fluid, and direct tissue damage occurs, triggering further inflammation and swelling. The net result is wheezing and coughing and eventual trapping of air in the alveoli (a tiny, thin-walled, capillary-rich sac in the lungs, or air sac) and smaller airways. This air trapping is most dangerous to the asthmatic because it progressively limits the amount of air that can be exchanged between the lungs and the blood stream, eventually causing rising carbon dioxide levels and falling oxygen levels. The increased muscular effort required to move air increases oxygen demand, tissue metabolism, and acid production, eventually resulting in exhaustion and, in extreme cases, respiratory collapse and arrest.

Why the bronchial tubes become so sensitive in asthmatics is not fully understood, but research suggests that immune-system cells known as T cells play a central role. Some T cells induce inflammation to fight off a foreign threat, while others reduce inflammation once the threat has subsided. Conditions such as asthma, in which the body overreacts to threats, may be related to an imbalance or malfunction of these and other immune-system components (Tosca MA et al 2003; Howard TD et al 2002; Ray A et al 2000).

The idea behind nutritional supplementation is to disrupt this inflammatory cascade whenever possible. For example, omega-3 fatty acids have been shown to inhibit the production of arachidonic acid, which reduces the concentration of inflammatory leukotrienes (Wong KW 2005). Other nutrients, such as curcumin, interfere with other causative factors in the inflammatory cascade, such as inhibiting nuclear factor kappa beta and an enzyme that converts arachidonic acid to leukotriene B4.

It is very important that asthmatics take whatever steps are necessary to control their condition. Unchecked, asthma can cause permanent damage to the bronchial tubes, a situation known as airway remodeling. Under constant inflammatory stress, the bronchial tubes undergo structural change. The bronchial tubes thicken; the surrounding smooth muscle increases; the epithelium (the fragile layer of cells lining the bronchial tubes) sloughs off into the passageways; and mucus production increases. These changes can permanently reduce lung function and increase the frequency of asthma attacks (Larj MJ et al 2004; Nakagawa T et al 2004).

Scientists are also beginning to better understand the interaction between allergies, asthma, and oxidative stress. Oxidative stress occurs when highly reactive molecules, known as free radicals, interact with molecules within the body, especially DNA and mitochondrial membranes. Experimental evidence suggests that some pollutants, such as vehicle exhaust, may produce oxidative stress in the bronchial tubes (Gilmour MI et al 2006). Studies suggest that dietary supplementation with precursors of glutathione (an internal antioxidant), such as cysteine and alpha-lipoic acid, can enhance the pulmonary defenses, thus countering oxidative stress (Bridgeman MM et al 1991).

Interestingly, asthma and GERD seem to be strongly associated. GERD is a chronic condition in which partially digested stomach contents, including acid, flow backward into the esophagus. Heartburn and other symptoms usually result. Although the relationship between asthma and GERD is unclear, there is evidence for two related mechanisms. The irritation by acid of nerve receptors in the esophagus may produce a reflex irritability in the vagus nerve, producing increased sensitivity to cough-inducing stimuli in the lungs. Alternatively (or in addition), microscopic food particles and acid may be aspirated into the lungs from the refluxed material, triggering the initial round of inflammation that sets off the attack (Jiang SP et al 2005). Both mechanisms involve an initial inflammatory stimulus from the irritating stomach contents.

Good nutrition and eating habits are important in the prevention of GERD. For more information on how to treat GERD, see the chapter Gastroesophageal Reflux Disease.

DIAGNOSIS AND MEDICATIONS USED TO TREAT ASTHMA

There is no single means of diagnosing asthma. A patient's medical history, including any existing or former breathing difficulties, allergies, or skin conditions, such as eczema, are important clues. Family medical history is also important because asthma tends to run in families. Very often, patients have a history of chronic or recurrent cough for months or years before the diagnosis of asthma is finally made.

Physicians may perform pulmonary function tests to determine various parameters of lung function, such as total volume of air and the rate and force of expiration (breathing out). They may also perform a "bronchoprovocation" test, which involves the induction of a minor asthma attack by the use of histamine or some other substance.

Medication to treat asthma can be categorized as short-acting rescue medication or as maintenance medication. Rescue medications are designed to provide immediate relief from the symptoms of an asthma attack. Long-acting control medications reduce inflammation and prevent asthma attacks from occurring. Asthma experts agree that the major goal of medication is to optimize long-term control medications so that rescue medications, with their many side effects, can be minimized or eliminated (Simons FE 1999).

Bronchodilators are usually used as rescue medications (except when combined with steroids for long-term maintenance). They work by relaxing the bronchial muscles. These medications can be inhaled, injected, or taken orally. Bronchodilators are of three types:

- **Beta-2 agonists** (e.g., albuterol). Short-acting beta-2 agonists are meant only for immediate relief of symptoms and may be given in conjunction with a maintenance medication. Long-acting beta-2 agonists are sometimes prescribed as stand-alone maintenance medications. Numerous brands of beta agonists are on the market.
- **Anticholinergics**. These medications block the action of acetylcholine, a neurotransmitter. They produce effects similar to those of the beta-2 agonists, with a similar side effect profile.
- **Theophylline**. Chemically similar to caffeine, this drug is not a first-line treatment because it is not as effective as other medications. Theophylline use has been associated with vitamin B6 deficiency (Shimizu T et al 1996).

Although effective for short periods of time, bronchodilators can be stressful for the body. These medications mimic the action of adrenaline, which is released during the "fight or flight" response and causes dilation of the bronchial tubes. Side effects include rapid

heart rate, increased blood pressure, increased blood sugar levels, irregular heart rhythms, and a variety of other responses (Nizet TA et al 2004; Wraight JM et al 2004; Rodrigo GJ et al 2002).

In general, however, the goal of asthma therapy is to reduce the need for rescue medications by keeping patients stable on maintenance medications. Maintenance medications include the following:

- **Corticosteroids.** These medications reduce inflammation by down-regulating production of inflammatory cytokines. Corticosteroids usually require several hours to onset, with peak effects not seen for one to three days. These medications can be inhaled or administered via nasal spray but also may be taken orally or injected.

Commonly used inhaled medications include Beclovent® (beclomethasone), Pulmicort® (budesonide), and AeroBid® (triamcinolone). Nasally administered medications include Beconase® (beclomethasone), Rhinocort® (budesonide), Flonase® (fluticasone), and Nasonex® (mometasone).

Long-term use of systemic (oral or injected) corticosteroids is associated with cataracts and glaucoma, osteoporosis, muscle weakness, chemical-induced diabetes, hypertension, adrenal gland dysfunction, and edema. Corticosteroids also deplete the body of calcium, magnesium, potassium, and zinc and may lead to osteoporosis. Some of these nutrients should be supplemented during long-term corticosteroid therapy (Banov CH 2004). Inhaled corticosteroid medications produce far fewer side effects because of the low doses of steroids involved. These drugs are associated with local side effects, however, such as thinning of the oral or nasal mucus membranes and yeast infections.

- **Leukotriene modifiers.** These make up a relatively new class of drug that prevents or reduces inflammation by inhibiting the production or activity of leukotrienes. Leukotrienes are synthesized from arachidonic acid by lipoxygenase enzymes. Commonly used leukotriene modifiers include Singulair® (montelukast), Accolate® (zafirlukast), and Zylflo® (zileuton).
- **Mast cell stabilizers.** These medications prevent mast cells (a type of immune cell) from releasing histamines, which can lead to an allergic reaction or an asthma attack. Mast cell stabilizers are less effective than other medications and are not frequently prescribed. They are usually reserved for individuals who cannot tolerate the side effects of other asthma medications.

A new type of treatment targets a class of immunoglobulins called immunoglobulin E, which activates mast cells and other inflammatory cells that trigger asthma attacks. Several trials have demonstrated the promise of this product in allergic asthma activity and as a therapy that may help patients reduce or avoid corticosteroids (Boushey HA Jr 2001). It is designed for use in moderate to severe asthma only. Side effects, which may be serious, include allergic reactions, hypotension (low blood pressure), arthritis, and kidney failure.

BUTTERBUR: AN HERBAL APPROACH TO ASTHMA

Butterbur (*Petasites hybridus*) is a perennial shrub that has been used since ancient times to treat a variety of conditions. As far back as the 17th century, butterbur was used to treat cough, asthma, and skin wounds (MMWR 2001). Today, researchers have uncovered the mechanism of action that makes butterbur effective.

Scientists have identified and isolated the compounds in butterbur that help reduce symptoms in asthma. Called petasins, these chemicals inhibit leukotrienes and histamines, which are responsible for symptom aggravation in asthma (Thomet OA et al 2002).

So far, a few research teams have examined butterbur's effectiveness in asthmatics, with encouraging results. In one open trial of 64 adults and 16 children and adolescents, asthma patients were treated for two months with butterbur extract, followed by an optional two-month open trial. They were measured throughout the study for the severity and frequency of asthma attacks. According to researchers, all the measured symptoms improved throughout the study, and 40 percent of patients were able to reduce their intake of traditional asthma medications (Danesch UC 2004).

Another study examined butterbur in conjunction with inhaled corticosteroid therapy. In this trial, 16 asthmatics were given butterbur or placebo while they continued their constant dose of inhaled steroid medications. Butterbur therapy, at 50 mg daily, was shown to reduce several measures of symptoms, leading researchers to conclude that butterbur is an effective adjunct therapy to corticosteroids. They called for further study of butterbur as a stand-alone therapy for mild asthmatics, who might be able to forgo their prescription medications (Lee DK et al 2004).

ANTIOXIDANT THERAPY

Researchers are also finding that antioxidants have the unique power to reduce lung and bronchial damage in people with asthma. The lungs are at particular risk for oxidative damage because their primary function is the exchange of oxygen and waste gases. Antioxidants protect the body's tissues by scavenging oxidant molecules and rendering them less harmful. Antioxidants can be

ingested, as in the case of vitamin C, or produced internally, as in the case of glutathione.

Nutritional approaches, although often slow to act in advanced disease, can enhance the effect of medical therapy by interfering with the inflammatory process and reducing oxidation, thereby potentially reducing the need for higher doses of medication. However, patients should always consult a physician before changing their diet or medication therapy.

Antioxidants (vitamins C, E, and A). A number of studies have suggested that consuming antioxidants such as vitamins C, E, beta-carotene, flavonoids, selenium, and other nutrients reduces the risk of bronchoconstriction associated with asthma.

For instance, studies have shown that vitamin C and possibly vitamin E supplementation can alleviate the severity of asthma symptoms (Ford ES et al 2004; Rubin RN et al 2004; Wijnhoven HA et al 2003; Trenga CA et al 2001; Fogarty A et al 2000; Hijazi N et al 2000; Seaton A et al 2000). Dietary supplementation with vitamin C and vitamin A (the substances that give fruits and vegetables their color) has also been associated with reduced susceptibility to asthma attacks. Other studies have demonstrated that vitamin C or E supplementation may be a valuable addition to the treatment of patients with allergic rhinitis (otherwise known as hay fever) and asthma.

Dietary supplementation of vitamin C has also been found to help a specific form of asthma called exercise-induced asthma (EIA). People with EIA are usually symptom free when not exercising. Studies have found that 1 or 2 g vitamin C daily diminished episodes of EIA. (Jaber R 2002).

Flavonoids. Flavonoids are the brightly colored pigments found in most fruits and vegetables. In plants, they assist with photosynthesis, but when consumed, they have antioxidant properties and have been associated with improved lung function. One study (Knekt P 2002) demonstrated that a high dietary intake of the flavonoids quercetin (found in wine, tea, and onions), naringenin (found in oranges and grapefruit), and hesperetin (found in oranges and lemons) was associated with a lower prevalence of asthma. It is interesting to note that quercetin has a chemical structure similar to cromolyn, a mast cell stabilizer sometimes used to treat asthma (Braunwald E et al 2001).

Other bioflavonoids are reported effective in the treatment of asthma. Researchers recently looked at the effects of lycopene (the red pigment found in tomatoes and some fruits) on patients with EIA. More than half of patients (55 percent) showed improvement in the amount of air they could exhale (Neuman I et al 2000). Other studies found that pycnogenol (an extract of French maritime pine bark) appeared to reduce asthmatic symptoms (Rohdewald P 2002).

Ginkgo biloba. *Ginkgo biloba*, a flavonoid-rich extract of leaves of the *Ginkgo biloba* tree, may be an effective asthma therapy, according to the results of several studies (Mahmoud F 2000; Li MH et al 1997).

Vitamin B6. Only a limited number of studies have been conducted on vitamin B6 as it pertains to asthma (Sur S et al 1993). Although the results did not show a clear improvement in all asthma cases, researchers found that the asthma drug theophylline appeared to lower the blood level of vitamin B6. Theophylline is rarely prescribed in the United States. In cases when it is prescribed, a patient's vitamin B6 levels should be checked periodically to determine if supplementation is needed.

MINERALS AND FATTY ACIDS TO RELIEVE ASTHMA SUFFERING

Selenium. Studies have shown that individuals with chronic asthma may suffer from a selenium deficiency, increased oxidative stress, and decreased glutathione activity (Allam MF et al 2004; Fogarty A et al 2000). Selenium is an essential dietary mineral that plays a vital role in activating glutathione. In a recent study, women with relatively low blood selenium levels during pregnancy gave birth to infants with a higher incidence of asthma (Shaheen SO et al 2004). These results suggest that dietary supplementation with selenium may diminish the susceptibility to asthma.

Magnesium. Several studies have indicated that patients with asthma have lower levels of magnesium within the cells lining the airways. When daily magnesium supplementation was given to children with mild to moderate asthma, a significant decrease in the use of rescue beta-agonist inhalers was demonstrated (Bede O et al 2003). These results suggest that intracellular magnesium levels are associated with the severity of asthma and the frequency of asthma attacks. Maintaining normal magnesium levels appears to be an important component of asthma therapy.

Zinc. Zinc appears to affect apoptosis, or “programmed cell death.” All cells contain genetic code that determines when they should die. A defect may cause cells to die prematurely, leading to inflammation, which can trigger an asthma attack. Zinc may have a role in preventing premature cell death in the asthmatic lung, which might have a protective effect (Truong-Tran AQ et al 2003). However, more research is necessary to determine the role zinc might play in the lungs generally and asthma specifically (Richter M et al 2003).

Calcium and vitamin D. Steroid use, particularly oral or systemic, is associated with the development of osteopenia (reduced bone density) and eventual osteoporosis (a condition in which bones lose mass and density) (Braunwald E et al 2001; Gennari C 2001). When asthma patients are on long-term oral steroid therapy, supplemental calcium and phosphate are recommended to prevent osteopenia. Calcium citrate contains the highest available elemental calcium in capsule form (Gennari C 2001). Periodic bone densitometry evaluation is recommended for assessing the development of osteoporosis (Mortensen L et al 1998).

Preventing osteopenia involves the oral intake of 1200 mg elemental calcium along with supplemental vitamin D (1000 IU) daily. In the event that osteoporosis develops, a bisphosphonate is usually added to the therapy (Gennari C 2001).

Omega-3 and other polyunsaturated fatty acids. Omega-3 fatty acids, also known as fish oils, may play a role in the prevention of asthma by reducing the tendency toward inflammation. A study of the immune status of neonates showed that the neonatal production of inflammatory cells associated with asthma was significantly decreased in infants of supplemented mothers (Dunstan JA et al 2003).

The current literature is supportive of dietary omega-3 polyunsaturated fatty acid use as a means of modifying asthma susceptibility and severity. However, fish oil supplementation has been associated with a worsening of asthma in aspirin-sensitive asthmatics (Jaber R 2002). Therefore, it should not be used by this subpopulation of asthmatics. If asthma patients are unsure about their sensitivity to aspirin, they should check with their doctor before taking fish oil supplements.

Borage oil. Borage oil, an herbal extract, contains a high percentage of a substance called gamma-linolenic acid (GLA). GLA is a type of fat that has been shown to regulate leukotrienes, biochemicals that can trigger asthma attacks. An asthma medication called zileuton works in much the same way.

Although more research must be done, borage oil, which contains GLA, may prove to be an attractive alternative as a dietary leukotriene-modifying therapy. Researchers found that daily supplementation of GLA had an impact on leukotrienes and warranted further study (Ziboh VA et al 2004).

Curcumin. Curcumin inhibits nuclear factor kappa beta, a major component for translating inflammatory stimuli into actions such as production of cytokines and changes in inflammatory cell function. Curcumin has been found to reduce the inflammatory responses of lymphocytes in human asthmatics, and in a laboratory animal model of asthma, treatment with curcumin reduced airway hyperresponsiveness (Kobayashi T et al 1997).

LIFE EXTENSION FOUNDATION RECOMMENDATIONS

Asthma is closely related to environmental health and allergies. People who suffer from allergies should obtain a high-quality high-efficiency particulate air filter in the home and avoid potential allergens whenever possible. Exercise may help improve lung function, but asthma patients should be aware that exercising in cold or polluted air (such as a winter morning run) can aggravate their condition.

Some asthma patients are given corticosteroids to reduce inflammation. Because these drugs can cause osteoporosis, people

taking any form of corticosteroid should also supplement with calcium and vitamin D to support strong bones. The following dosages are suggested:

- **Calcium**—1200 milligrams (mg) daily
- **Vitamin D**—1000 international units (IU) daily

Similarly, although theophylline is rare in the United States, it is sometimes prescribed for asthma. This drug has been shown to reduce levels of vitamin B6. For people taking theophylline, the following dosage of vitamin B6 is suggested:

- **Vitamin B6**—150 mg daily

Finally, all patients with asthma may be able to reduce their symptoms or reduce their medications by taking the following supplements that combat inflammation and target free radicals:

- **Butterbur**—50 to 150 mg daily
- **Vitamin C**—2000 to 3000 mg daily
- **Vitamin E**—400 IU daily, with at least 200 mg gamma tocopherols
- **Vitamin A**—5000 IU daily
- **Selenium**—200 micrograms (mcg) daily
- **Quercetin**—500 to 1000 mg daily (use only water-soluble quercetin)
- **Ginkgo biloba**—120 mg daily
- **Lycopene**—15 mg daily
- **Magnesium**—340 to 1000 mg daily
- **Zinc**—30 mg daily
- **EPA/DHA**—1400 mg EPA and 1000 mg DHA daily
- **GLA**—900 to 1800 mg daily
- **Curcumin**—800 to 1600 mg daily

PRODUCT AVAILABILITY

All the nutrients and supplements discussed in this section are available through the Life Extension Foundation Buyers Club, Inc. For ordering information, call anytime toll-free 1-800-544-4440, or visit us online at www.LifeExtension.com.

The blood tests discussed in this section are available through Life Extension National Diagnostics, Inc. For ordering information, call anytime toll-free 1-800-208-3444, or visit us online at www.LifeExtension.com.

ASTHMA SAFETY CAVEATS

An aggressive program of dietary supplementation should not be launched without the supervision of a qualified physician. Several of the nutrients suggested in this protocol may have adverse effects. These include:

Curcumin

- Do not take curcumin if you have a bile duct obstruction or a history of gallstones. Taking curcumin can stimulate bile production.
- Consult your doctor before taking curcumin if you have gastroesophageal reflux disease (GERD) or a history of peptic ulcer disease.
- Consult your doctor before taking curcumin if you take warfarin or antiplatelet drugs. Curcumin can have antithrombotic activity.
- Always take curcumin with food. Curcumin may cause gastric irritation, ulceration, gastritis, and peptic ulcer disease if taken on an empty stomach.
- Curcumin can cause gastrointestinal symptoms such as nausea and diarrhea.

EPA/DHA

- Consult your doctor before taking EPA/DHA if you take warfarin (Coumadin). Taking EPA/DHA with warfarin may increase the risk of bleeding.

- Discontinue using EPA/DHA 2 weeks before any surgical procedure.

Ginkgo biloba

- Individuals with a known risk factor for intracranial hemorrhage, systematic arterial hypertension, diabetes, or seizures should avoid ginkgo.
- Do not use prior to or after surgery.
- Avoid concomitant use of ginkgo with NSAIDs, blood thinners, diuretics, or SSRI's.
- Gastrointestinal symptoms (nausea and diarrhea) may occur.
- Allergic skin reactions may occur.
- Elevations in blood pressure may occur.

GLA

- Consult your doctor before taking GLA if you take warfarin (Coumadin). Taking GLA with warfarin may increase the risk of bleeding.
- Discontinue using GLA 2 weeks before any surgical procedure.
- GLA can cause gastrointestinal symptoms such as nausea and diarrhea.

Magnesium

- Do not take magnesium if you have kidney failure or myasthenia gravis.

Quercetin

- Quercetin can cause headache, mild tingling of the extremities, and gastrointestinal symptoms such as nausea.

Selenium

- High doses of selenium (1000 micrograms or more daily) for prolonged periods may cause adverse reactions.
- High doses of selenium taken for prolonged periods may cause chronic selenium poisoning. Symptoms include loss of hair and nails or brittle hair and nails.
- Selenium can cause rash, breath that smells like garlic, fatigue, irritability, and nausea and vomiting.

Vitamin A

- Do not take vitamin A if you have hypervitaminosis A.
- Do not take vitamin A if you take retinoids or retinoid analogues (such as acitretin, all-trans-retinoic acid, bexarotene, etretinate, and isotretinoin). Vitamin A can add to the toxicity of these drugs.
- Do not take large amounts of vitamin A. Taking large amounts of vitamin A may cause acute or chronic toxicity. Early signs and symptoms of chronic toxicity include dry, rough skin; cracked lips; sparse, coarse hair; and loss of hair from the eyebrows. Later signs and symptoms of toxicity include irritability, headache, pseudotumor cerebri (benign intracranial hypertension), elevated serum liver enzymes, reversible noncirrhotic portal high blood pressure, fibrosis and cirrhosis of the liver, and death from liver failure.

Vitamin C

- Do not take vitamin C if you have a history of kidney stones or of kidney insufficiency (defined as having a serum creatine level greater than 2 milligrams per deciliter and/or a creatinine clearance less than 30 milliliters per minute).
- Consult your doctor before taking large amounts of vitamin C if you have hemochromatosis, thalassemia, sideroblastic anemia, sickle cell anemia, or erythrocyte glucose-6-phosphate dehydrogenase (G6PD) deficiency. You can experience iron overload if you have one of these conditions and use large amounts of vitamin C.

Vitamin E

- Consult your doctor before taking vitamin E if you take warfarin (Coumadin).
- Consult your doctor before taking high doses of vitamin E if you have a vitamin K deficiency or a history of liver failure.
- Consult your doctor before taking vitamin E if you have a history of any bleeding disorder such as peptic ulcers, hemorrhagic

stroke, or hemophilia.

- Discontinue using vitamin E 1 month before any surgical procedure.

Zinc

- High doses of zinc (above 30 milligrams daily) can cause adverse reactions.
- Zinc can cause a metallic taste, headache, drowsiness, and gastrointestinal symptoms such as nausea and diarrhea.
- High doses of zinc can lead to copper deficiency and hypochromic microcytic anemia secondary to zinc-induced copper deficiency.
- High doses of zinc may suppress the immune system.

For more information see the Safety Appendix

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