

## Lupus

### A Multifaceted Disease

Lupus is an autoimmune disease that can affect many organ systems. In people who have lupus, antibodies are created by the body's immune system and directed against the body's own cells. Lupus affects the connective tissue, or the tissue that provides strength to joints, tendons, ligaments, and blood vessels. The severity of the disease ranges from minor to life-threatening complications that must be aggressively treated.

Lupus is a chronic condition. People with lupus tend to experience symptomatic periods, followed by periods of few symptoms or no symptoms at all. Total remissions are rare. Lupus flare-ups can be triggered by a number of factors, including exposure to ultraviolet (UV) light and toxins and a reduced antioxidant status.

The most common form of lupus is systemic lupus erythematosus (SLE). Other forms of lupus include cutaneous lupus, which affects the skin (and accounts for about 10 percent of all cases of lupus) and drug-induced lupus, which is caused by an inappropriate reaction to a drug or medication. Drug-induced lupus usually recedes when the drug is withdrawn. Because SLE is the most common form of lupus, and the most severe, this chapter will concentrate on SLE, and any reference to lupus in this chapter refers to SLE.

Any organ system that incorporates connective tissue can be affected by lupus, including the skin, kidneys, eyes, lungs, and the cardiovascular, vascular, musculoskeletal, nervous, blood, and gastrointestinal systems.

Like other autoimmune disorders, lupus is characterized by an abnormally activated immune response. Under normal conditions, the immune system is responsible for protecting the body from external invaders such as viruses and bacteria.

Those affected with lupus have abnormal sensitivity to T-cells and B-cells. These two kinds of white blood cells are overstimulated to attack the body's own tissues. Under normal circumstances, T-cells either attack and destroy "nonself" tissues directly, or identify them and produce chemicals (cytokines) that stimulate other immune cells to destroy the invader cells in a process called phagocytosis.

By contrast, B-cells normally identify nonself tissues and manufacture antibodies that recognize those specific antigens. When the antibodies attach to the antigen (forming an immune complex), they stimulate an immune response that attacks and destroys the invader. Afterward, the destroyed cell and the immune complex are removed from the bloodstream. When the immune reaction is completed, the number of antibodies created to target that specific antigen declines. If the antigen is recognized again, another immune response is stimulated.

In lupus, however, antibodies attack the patient's own tissues. These antibodies are called autoantibodies because they are directed at host tissues rather than outside molecules or cells. Many of the autoantibodies in lupus are directed against DNA and RNA or at protein complexes, which are incorrectly recognized as antigens in people with SLE. Finally, the normal removal system for antigens, autoantibodies, and immune complexes from the bloodstream is impaired, resulting in an inappropriate accumulation. If the accumulation persists for too long, clinical symptoms of the disease begin to appear.

It is estimated that 500,000 to 1.5 million people in the United States have lupus. About 90 percent of people with lupus are women of childbearing age, although men and children are affected as well. Lupus is more common in African Americans than in whites (Kasper DL et al 2004).

### CAUSES OF LUPUS

Lupus is considered a multigenic disease, meaning that it is caused by defects in multiple genes. Researchers have not identified a specific lupus gene, but have identified a number of genetic abnormalities that predispose people to developing lupus. It is likely that these multiple genetic defects each contribute a small amount to the abnormal immune responses seen in lupus. If enough of these genetic defects accumulate in the same person, the disease may develop.

A region of chromosome 16 has been associated with autoimmune disorders such as rheumatoid arthritis, psoriasis, and Crohn's disease. This suggests the existence of autoimmune genes that, when combined with other genetic defects, raises the likelihood of a person developing an autoimmune disorder.

Whether or not these genes are expressed (develop the lupus trait), and to what degree, relies on external and internal triggers. These triggers include stress, antioxidant levels, and exposure to toxic chemicals (Agisheva KN et al 1990; Bae SC et al 2002; Kasper DL et al 2004). Other triggers include infections (such as Epstein-Barr virus) that stimulate B-cell immune responses. In addition, lupus flare-ups may be more likely to occur in women who are taking estrogen-containing birth-control pills or conventional hormone replacement therapy (HRT) (Buyon JP et al 2005).

Nutrition can play an important role in lupus management, both in the prevention of flare-ups and in the management of inflammatory conditions that are associated with lupus. Specific nutrients can be utilized to improve cell communication, improve cell repair, and reduce oxidative stress (Brown AC 2000; Deluca HF et al 2001; Huang CM et al 2002; Linker-Israeli M et al 2001; Ozaki Y et al 2000). Deficiencies in key nutrients also create an environment that perpetuates inflammation and reduces a cell's ability to repair damage (Bhattacharya A et al 2003; Brooks WH 2002; Brown AC 2000; Deluca HF et al 2001; Huang CM et al 2002; Januchowski R et al 2004; Linker-Israeli M et al 2001; Ozaki Y et al 2000).

## POSSIBLE ORGAN DAMAGE RELATED TO LUPUS

Lupus can be associated with widespread organ damage that ranges from mild to very severe and life-threatening. The disease may initially affect one or several organ systems, with more becoming involved over time. In addition to the specific organ systems, lupus can cause generalized systemic symptoms including fever, weight loss, anemia, fatigue, and pain.

Some of the individual organ systems that may be involved with lupus include the:

- **Musculoskeletal system.** Many people with lupus have arthritis that varies from mild to disabling. Joint deformities, although relatively rare, can occur. Muscle weakness and inflammation (myositis) may also occur. People with lupus may develop bone density problems, especially if they are taking corticosteroid therapy. As with any patients who are at risk of osteoporosis, calcium and vitamin D3 should be prescribed first to prevent loss of bone mineralization (Adachi JD et al 1996). For more specific information on maintaining a healthy skeletal system, see the chapter Osteoporosis.
- **Skin.** Symptoms of lupus may include rash (especially the characteristic butterfly rash on the face) and other skin abnormalities.
- **Kidneys .** Swelling and inflammation of the kidneys is one of the most serious manifestations of SLE. Kidney inflammation (nephritis) is the leading cause of mortality in the first decade of the disease (Kasper DL et al 2004). A significant percentage of people with lupus have elevated levels of protein in their urine (proteinuria). Proteinuria occurs when the filtering system of the kidneys is damaged, either by high blood pressure, toxins, or inflammation. If the condition is not managed properly, end-stage renal disease may develop, requiring dialysis or transplantation.
- **Nervous system .** Neuropsychiatric lupus is an important and distinct subgroup of the disease. People with this form of lupus may have cognitive dysfunction and difficulty with memory and reasoning. Headaches are common. Additional complications include seizures, psychosis, and encephalitis.
- **Cardiovascular and vascular systems .** Researchers are continually uncovering more connections between lupus and heart disease. People with lupus may have transient ischemic attacks, strokes, and heart attacks, all related to their disease. Lupus is known to accelerate the atherosclerotic process, in which arteries are clogged with fatty plaque deposits. People with lupus experience elevated death rates from cardiovascular disease that cannot be explained by conventional risk factors alone (Tam LS et al 2005). Overall, people with SLE have a 5- to 6-fold increased risk of heart disease; younger women may experience a 50-fold increased risk (Bruce IN 2005). One contributing factor for this increased risk may be oxidative stress associated with lupus, which aggravates heart disease. This makes antioxidant status potentially very important for people with SLE (Tam LS et al 2005). People with SLE are more likely to have elevated blood pressure, diabetes, elevated cholesterol, elevated homocysteine, and metabolic syndrome (Afeltra A et al 2005; Bruce IN 2005). The following chapters may be of additional interest: Blood Clots, Coronary Artery Disease and Atherosclerosis, Hyperhomocysteinemia, Inflammation, and Stroke and Cerebrovascular Disease.
- **Lungs .** The most common lupus-related complication is swelling of the pleura, which is a thin sac in the upper chest that contains the lungs and is connected to the inner chest wall, diaphragm, and outer lining of the heart. There may be bleeding and swelling within the lungs.
- **Blood system .** Lupus is associated with anemia, leukopenia (low white blood cell count), and thrombocytopenia (low platelet count). Some people with lupus produce lupus anticoagulant, which reduces the blood's ability to clot and is associated with an increased risk of hemorrhage. For more information, see the chapter Blood Disorders.
- **Gastrointestinal system .** Nausea and diarrhea can occur during a lupus flare-up. In addition, the intestines themselves may be affected by swelling, perforations, bleeding, and sepsis.
- **Eyes .** Conjunctivitis is inflammation of the conjunctiva (the transparent membrane that covers the white of the eye and lines the eyelids). Swelling of the eyelids due to conjunctivitis is relatively common but rarely threatens vision in people with lupus. However, if the inflammation affects the retina rather than the eyelids, blindness may develop rapidly, over days or weeks. This requires prompt and aggressive medical intervention.

## DIAGNOSIS AND CONVENTIONAL TREATMENT OF LUPUS

The diagnosis and treatment of lupus often depends on how serious the disease is and which organ systems are involved. Besides suppressing the autoimmune response with medications, physicians will attempt to treat individual problems of an affected organ system as they arise.

Further stimulating and/or boosting the immune system response in SLE may actually worsen the disease. People who have lupus must be under the supervision and care of a highly qualified physician who specializes in lupus treatment.

The diagnosis of lupus relies on the presence of characteristic symptoms of the disease, in addition to blood testing to detect the presence of autoantibodies. For a diagnosis of lupus to be made, at least four of the following criteria must be present (Cutolo M et al 2004; Kanda N et al 1999; Kasper DL et al 2004):

- **Butterfly rash.** Also known as malar rash. This rash is red, can be flat or raised, and covers the nose and cheeks.
- **Discoid rash.** Associated with discoid lupus erythematosus (DLE). The rash looks like raised circular patches of scaly skin. Some scarring may occur.
- **Sensitivity to sunlight.** Exposure to UV light causes a rash.
- **Oral ulcers.** Ulcers present in the mouth and nose.
- **Arthritis.** Joint inflammation involving tenderness, swelling, or fluid accumulation. This type of arthritis is related to inflammation rather than a wearing down of the joints.
- **Serositis.** Inflammation of the membranes lining the lungs or heart, or fluid collection between these membranes.
- **Kidney disorder.** Protein in the urine or other abnormal findings.
- **Neurological disorder.** Seizures or mental symptoms such as depression or psychosis.
- **Blood disorder.** Anemia from breakdown of red blood cells, or a low white blood cell count.
- **The presence of antibodies to double-stranded DNA.** A positive (elevated) anti-double-stranded DNA blood test.
- **The presence of antinuclear antibodies.** A positive (elevated) antinuclear antibody (ANA) blood test.

Once the diagnosis of lupus is made using these clinical criteria, a number of additional tests may be used to monitor the disease course and various organ systems. These might include a blood test for phospholipid antibodies, which can help predict the risk of blood clotting, in addition to a complete blood count (CBC), platelet count, urinalysis, and test of creatinine or albumin levels. These various tests help physicians track the activity of the disease in organ systems that are known to be involved and to detect previously uninvolved systems.

Conventional management of lupus aims at controlling flare-ups (usually with anti-inflammatory medications) and suppressing symptoms to prevent organ damage. The main conventional drugs used to treat lupus include:

- **Nonsteroidal anti-inflammatory drugs (NSAIDs).** These drugs, such as ibuprofen, are usually recommended for muscle and joint pain and for arthritis pain.
- **Acetaminophen or aspirin.** These are mild analgesics used to alleviate pain.
- **Corticosteroids.** Synthetically produced corticosteroids, such as prednisone, are used to reduce inflammation and suppress the immune system. These may be used topically for skin rashes or orally to treat other organ systems. In severe flare-ups, relatively large doses of corticosteroids may be prescribed for short periods.
- **Antimalarials.** These drugs, such as hydroxychloroquine sulfate, are prescribed for skin and joint symptoms of lupus. It may take months before the benefits of these drugs are evident.
- **Immunomodulating drugs.** These drugs, such as azathioprine and cyclophosphamide, suppress the immune system.
- **Biologic drugs.** These drugs include agents that block the production of specific antibodies, such as those against DNA, or agents that act to suppress the manufacture of antibodies through other mechanisms.

The use of corticosteroids deserves special mention in the treatment of lupus, partly because corticosteroid therapy is so common in patients being treated for lupus. Prednisone, the most common corticosteroid used to treat SLE, has been shown to effect interleukins 1 and 2 (IL-1 and IL-2). IL-2 plays a key role in the proliferation of T-cells, while IL-1 inhibits the utilization of IL-2 by T-cells (Patavino T et al 2001).

The long-term use of corticosteroids is associated with significant risk and adverse effects. Specifically, adverse effects of glucocorticoid therapy include obesity, high blood pressure, dyslipidemia (an abnormality in—or abnormal amounts of—lipids and lipoproteins in the blood), and insulin resistance (Wake DJ et al 2004). Glucocorticoid excess leads to the accumulation of abdominal fat and other metabolic abnormalities known as metabolic syndrome (Bjorntorp P 2001). These changes increase the risk of premature atherosclerosis. In general, most physicians seek to limit a patient's exposure to long-term corticosteroid therapy and wean the patient off corticosteroids as quickly as possible because of the risk of serious adverse effects.

## THE HORMONE CONNECTION

Because lupus most often occurs in women of childbearing age, and flare-ups often occur during menstruation, some researchers have sought to uncover the link between lupus and sex hormones, especially estrogen. While progress has been made, the connection between lupus and estrogen remains highly controversial. It is known that people with lupus have elevated levels of estrogen metabolites and low levels of testosterone (Patavino T et al 2001). Women with lupus have shown reduced levels of progesterone (Folomeev M et al 1992).

Certain forms of estrogen are associated with inflammation, degenerative diseases, and estrogen dominance in people with lupus (Cutolo M et al 2004). Estradiol (the strongest form of estrogen) binds to receptors on T-cells and B-cells, increasing activation and survival of those cells, and predisposing women to prolonged attacks on their immune system (Grimaldi CM et al 2002).

Studies examining the role of estrogen in lupus have looked at HRT to see if the use of estrogen and progesterone contributes to lupus. In a study of 351 menopausal women with lupus, subjects were assigned to take either traditional HRT (consisting of conjugated equine estrogen at 0.625 milligrams per day [mg/day] and medroxyprogesterone at 5 mg/day for days 1 through 12 of each month) or a placebo. At the end of the study, the researchers found that the synthetic HRT increased the risk of mild to moderate flare-ups (but not the risk of serious flare-ups) in menopausal women with lupus (Buyon JP et al 2005).

Women with lupus should discuss the risks and benefits of estrogen therapy with their physicians because, based on these findings, there appears to be a risk that estrogen may exacerbate disease. In addition, extra caution is recommended because conventional HRT is associated with hypercoagulability (abnormally increased ability of blood to clot), which is already an issue in people with SLE who have antiphospholipid antibodies (Petri M 2001).

Bioidentical, natural hormone therapy has not been specifically studied in people with lupus, and the impact (positive or negative) of this type of therapy is unknown at this time.

### ***What You Have Learned So Far...***

- Lupus is an autoimmune disorder in which autoantibodies are generated against connective tissue. It can affect many organ systems. Symptoms range from mild to life-threatening.
- The most common form of lupus is systemic lupus erythematosus (SLE). Other forms of lupus include discoid lupus erythematosus (DLE) (which affects only the skin) and drug-induced lupus.
- Lupus affects more women than men. The disease is caused by multiple genetic defects that are expressed in conjunction with external triggers, such as exposure to sunlight and low levels of antioxidants.
- Most people with lupus have flare-ups and periods when symptoms subside or disappear. Physicians seek to control the symptoms and prevent organ damage to affected organ systems.
- Lupus is diagnosed by the presence of multiple factors. Mild lupus is generally treated with NSAIDs and other anti-inflammatory medications. More serious attacks, especially ones that threaten organ damage, are treated with glucocorticoids to reduce inflammation. Ideally, patients with lupus are weaned off glucocorticoids as quickly as possible.
- The connection between estrogen and lupus is highly controversial. Some studies have suggested that conventional estrogen therapy with strong, synthetic equine-derived estrogens contributes to flare-ups of lupus. No studies have been conducted on bioidentical estrogen therapy and lupus. Thus, menopausal women with lupus are advised to use great caution when it comes to estrogen replacement therapy.

## **DHEA: POTENTIAL UTILITY IN LUPUS**

Although conventional HRT with synthetic, equine-derived estrogen may exacerbate SLE as suggested by clinical trial data, there is some evidence that dehydroepiandrosterone (DHEA) supplementation may be helpful in treating people with SLE. People who have lupus are deficient in DHEA, possibly because of inflammation in the adrenal gland, which inhibits DHEA production (Chen CC et al 2004). DHEA has been shown to enhance the production of IL-2 and decrease anti-DNA antibodies in murine models of lupus (van Vollenhoven RF 2000).

In a double-blind, placebo-controlled trial of women with SLE, DHEA resulted in reduction of flare-ups, a reduction in prednisone dose, and decreased disease activity as measured on an SLE disease activity index. The dosage used in the study was 200 mg/day for 3 months. Patients reported a significant overall improvement. In addition, testosterone levels were increased (Chang DM et al 2004). Another study using 200 mg/day of DHEA found that women taking DHEA had fewer lupus flare-ups than did control subjects (Chang DM et al 2004).

DHEA has been proven to protect against the loss of bone density that often accompanies corticosteroid therapy. In another study of women with SLE on corticosteroid therapy, 200 mg/day of DHEA was shown to help maintain bone density (van Vollenhoven RF et al 1999) with minor adverse effects such as acne.

Similarly, people with SLE who have adequate levels of DHEA tend to have higher bone mineral density than those with low serum DHEA levels. Patients receiving corticosteroid therapy had lower DHEA levels in a dose-dependent manner (for example, the more corticosteroid taken, the lower the DHEA level) (Formiga F et al 1997).

Finally, DHEA has been shown to help increase testosterone levels in people with SLE. Numerous studies have shown that those with lupus have decreased testosterone levels. In one study of 25 premenopausal and 25 postmenopausal women, the women taking DHEA showed increased testosterone levels as well as decreased disease activity throughout the entire study (van Vollenhoven RF et al 1998).

## **REDUCING INFLAMMATION NATURALLY: THE ROLE OF FISH OIL**

Because inflammation is central to lupus, people with lupus should consider using anti-inflammatories to reduce symptoms. For more general information on inflammation, see the chapter Inflammation. A number of supplements (including fish oil and flaxseed) have been studied specifically in the treatment of people and animals with lupus.

The principal omega-3 polyunsaturated fatty acids are eicosapentaenoic acid (EPA) and docosahexaenoic acid (DHA). EPA and DHA are found in fish oil. They can also be derived from alpha-linoleic acid, which is found in flaxseed and walnuts. These fatty acids help build healthy cell membranes and improve membrane stability and have exhibited powerful immunomodulatory and anti-inflammatory properties. A number of studies have examined the role of these fatty acids in people and animals with lupus, with generally positive results.

In a study of people with lupus who had kidney inflammation, highly purified EPA was shown to decrease oxidative stress and alter the ratio of EPA and inflammatory arachidonic acid in favor of EPA (Nakamura S et al 2005). These results have been supported by animal studies showing that EPA and DHA decreased the release of inflammatory chemicals (Fernandes G et al 1996), and that fish oil can delay onset of lupus and other autoimmune disorders and prolong survival (Duffy EM et al 2004; Muthukumar A et al 2004; Simopoulous AP 2002).

Fish oil has synergistic effects with other nutrients. It has been shown to help regulate the activity of antioxidant enzymes in murine models of lupus, making the antioxidants more effective (Bhattacharya A et al 2003). Additionally, when given to mice in a mixture with evening primrose oil, it demonstrated effectiveness in alleviating lupus (Godfrey DG et al 1986).

Fish oil may be helpful in treating kidney disease associated with lupus. In some animal studies, proteinuria was prevented and survival was prolonged (Donadio JV Jr 1991). In a study of people with lupus who had kidney disease, fish oil was found to improve their condition (Clark WF et al 1989).

Flaxseed, in addition to being an alpha-linoleic acid, is a rich source of lignans, which make platelets less sticky, thus helping to reduce clotting and possibly reducing the risk of blood clots (Clark WF et al 1994). Flax lignans help reduce inflammation of the digestive tract and support a healthy balance of intestinal bacteria, as well as assist in the metabolism of hormones.

Finally, retinoic acids, a group of natural and synthetic vitamin A derivatives, have potent anti-inflammatory and immunomodulatory properties. Retinoic acids reduce inflammatory cytokine production. Animals with lupus receiving retinoic acid supplements experienced fewer symptoms, including reduced kidney inflammation and less swelling of the lymph nodes and spleen (Perez de

Lema G et al 2004). Immune cell activity was also reduced (Perez de Lema G et al 2004).

## ***Pregnancy and Lupus***

Because many women with lupus are of childbearing age, a frequent concern is whether or not they can successfully have children.

Fortunately, many women with lupus experience no flare-ups during pregnancy. However, there are some complications that can occur, and women with lupus who are considering pregnancy are strongly urged to consult their physician. The rate of miscarriage is about 2- to 3-fold higher in women with SLE (Kasper DL et al 2004). This is particularly true of women who have multiple disease-associated conditions, more advanced kidney disease, or antiphospholipid antibodies. Neonatal lupus is rare and is thought to be caused by maternal autoantibodies. Only about 1 percent of infants with positive maternal antibodies (antibodies from the mother with lupus) develop lupus.

## **ANTIOXIDANTS**

A low level of antioxidants has been shown to be associated with flare-ups. Antioxidants are valuable for their ability to reduce free-radical damage (Parke DV et al 1996). Dietary intake of antioxidants is decreased in people with SLE ( Bae SC et al 2002). Those with lupus exhibit significantly reduced levels of internally produced antioxidants such as glutathione and superoxide dismutase ( Bae SC et al 2002).

**Vitamin E.** Vitamin E helps stabilize membranes of lysosomes, or immune cells that contain destructive enzymes used to fight intruders. When membranes are unstable, these enzymes cause damage to surrounding healthy tissue. Vitamin E can help prevent the onset of autoimmune attacks by stabilizing membranes of lysosomes (Ayres S Jr et al 1978). The symptoms of mice with lupus that were treated with vitamin E greatly improved. The mice lived longer, immune cell activity was normalized, anti-DNA antibodies were reduced, and kidney function improved (Weimann BJ et al 1999).

**Selenium.** Selenium is a potent antioxidant that enhances cell repair. Fifty patients with lupus who had low glutathione levels were treated with selenium and vitamin E. The addition of these nutrients increased glutathione levels in 8 weeks (Juhlin L et al 1982). Selenium stimulates vitamin E in its role of immune and antioxidant regulation (Sprietsma JE 1999).

## **VITAMIN D**

People with lupus are frequently deficient in vitamin D. There are several reasons for this, including avoidance of the sun because of the photosensitivity that is associated with the disease (Becker A et al 2001; Huisman AM et al 2001). Persons with SLE are at increased risk of low bone mineral density and osteoporosis, partly because of a deficiency in vitamin D but also because of glucocorticoid therapy and disease-associated conditions such as chronic arthritis, reduced physical activity, and endocrine dysfunction (Bultink IE et al 2005; DiMunno O et al 2004).

Because of the risk of osteoporosis and the vitamin D deficiency associated with SLE, vitamin D and calcium supplementation are prescribed initially, especially for postmenopausal women and patients on glucocorticoid therapy (Franchimont N et al 2003; Sen D et al 2001).

In recent years, another interesting role for vitamin D in autoimmune disorders has emerged. Vitamin D has been found to exert profound effects on the immune system, including suppression of T-cell activation (Deluca HF et al 2001; May E et al 2004). Animal studies have shown that vitamin D, along with sufficient calcium intake, can either prevent or markedly suppress autoimmune diseases such as lupus. The mechanism of action may be related to the ability of vitamin D to stimulate IL-4, which suppresses inflammatory T-cell activity. Although studies are still ongoing, this suggests a possible important role for vitamin D in the future treatment of lupus and other immune system disorders (Deluca HF et al 2001).

## **LIFE EXTENSION FOUNDATION RECOMMENDATIONS**

Individuals with lupus can benefit greatly from a healthy lifestyle. The Life Extension Foundation suggests:

- Get enough sleep.
- Eat a diet high in antioxidants and omega-3 fatty acids, including plenty of fish and nuts. Avoid excess calories, excess protein, and high levels of saturated fat and omega-6 fatty acids. Excessive quantities of nutrients such as zinc, iron, soy isoflavones (which have estrogen qualities), and alfalfa have been shown to aggravate lupus (Brown AC 2000; Zhao JH et al 2005).
- Exercise moderately. It improves antioxidant status.
- Limit exposure to the sun. UV light rays have been known to trigger flare-ups.
- Take probiotics to help reduce inflammation of the digestive tract and enhance digestion.

In addition to these common-sense steps, a number of nutrients might be considered to reduce inflammation, increase antioxidant levels, and suppress the overactive immune system. These include:

To increase antioxidant levels:

- **Vitamin C**—1000 to 2000 mg twice daily
- **Selenium**—200 micrograms (mcg) daily
- **Vitamin E**—400 international units (IU) daily
- **Superoxide dismutase**— (2000 mg of SODzyme and/or 100 to 300 mg of GliSODin daily)
- **Glutathione**—50 to 250 mg daily
- **N-acetyl cysteine** (a precursor to glutathione)—600 to 1200 mg daily

To improve immune system regulation and reduce inflammation:

- **EPA/DHA**—700 to 1400 mg EPA and 500 to 1000 mg DHA daily
- **Vitamin D3**—1000 IU daily (taken with calcium)
- **Vitamin A** —5000 IU daily (or 15,000 IU of beta carotene daily)

For people with lupus who have elevated homocysteine:

- **Vitamin B6**—200 to 750 mg
- **Folic acid**—800 to 2400 IU
- **Vitamin B12**—300 to 1200 IU

**DHEA**—15 to 75 mg daily. Have blood tested frequently to ensure adequate levels.

## LUPUS 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:

### DHEA

- Do not take DHEA if you could be pregnant, are breastfeeding, or could have prostate, breast, uterine, or ovarian cancer.
- DHEA can cause androgenic effects in woman such as acne, deepening of the voice, facial hair growth and hair loss.

### 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.

### Folic acid

- Consult your doctor before taking folic acid if you have a vitamin B12 deficiency.
- Daily doses of more than 1 milligram of folic acid can precipitate or exacerbate the neurological damage caused by a vitamin B12 deficiency.

### NAC

- NAC clearance is reduced in people who have chronic liver disease.
- Do not take NAC if you have a history of kidney stones (particularly cystine stones).
- NAC can produce a false-positive result in the nitroprusside test for ketone bodies used to detect diabetes.
- Consult your doctor before taking NAC if you have a history of peptic ulcer disease. Mucolytic agents may disrupt the gastric mucosal barrier.
- NAC can cause headache (especially when used along with nitrates) and gastrointestinal symptoms such as nausea and diarrhea.

## 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.

## SODzymes

- Do not take SODzymes if you are allergic to soy, corn, or wheat.

## 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 B6

- Individuals who are being treated with levodopa without taking carbidopa at the same time should avoid doses of 5 milligrams or greater daily of vitamin B6.

## Vitamin B12 (cyanocobalamin)

- Do not take cyanocobalamin if you have Leber's optic atrophy.

## 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 D

- Do not take vitamin D if you have hypercalcemia.
- Consult your doctor before taking vitamin D if you are taking digoxin or any cardiac glycoside.
- Only take large doses of vitamin D (2000 international units or 50 micrograms or more daily) if prescribed by your doctor.
- See your doctor frequently if you take vitamin D and thiazides or if you take large doses of vitamin D. You may develop hypercalcemia.

**Chronic large doses (95 micrograms or 3800 international units or more daily) of vitamin D can cause hypercalcemia.**

## 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.

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