

Natural Medicine and Nutritional Therapy as an Alternative Treatment in Systemic Lupus Erythematosus

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Abstract

Systemic lupus erythematosus (SLE) is a multisystem autoimmune disorder without a known cure. Conventional medicine typically approaches the disease with a treatment plan that includes the use of corticosteroids, non-steroidal anti-inflammatory drugs (NSAIDs), antimalarial drugs, and chemotherapeutic agents. The results vary and safety is questionable. Conservative treatment methods, such as the use of vitamins, minerals, and fatty acids, have been shown to have an impact on the activity of the disease. Alternative medicine treatments, including the use of dehydroepiandrosterone (DHEA) and Chinese medicines, such as *Tripterygium wilfordii* Hook F (TwHF), have gained a growing interest recently and may prove to be viable treatment options in the future. The elimination of possible associated factors, such as food allergens and SLE-symptom eliciting foods like alfalfa seeds, have also been shown to affect disease activity. Conservative alternative medicine approaches have been shown to provide some benefit in SLE studies; however, the evidence is limited, and the overall effectiveness and long-term safety have not been established. More research must be conducted in this area to further establish firm treatment protocols which provide maximum therapeutic benefit and minimum treatment-related side effects.

(*Altern Med Rev* 2001;6(5):460-471)

Introduction

Systemic lupus erythematosus (SLE) is an autoimmune disease that imposes multiple complications on an affected individual, the family, and the healthcare provider who tries to control its manifestations. The etiology of this disease is unknown and its course often differs from patient to patient. To complicate matters further, SLE is often misdiagnosed or overlooked by healthcare providers.

The diagnosis of SLE is presently based on criteria promulgated by the American College of Rheumatology (ACR). The ACR defines the presence of Lupus in patients presenting with four of the eleven signs or symptoms outlined in Table 1.

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Table 1. ACR Criteria for Identifying Systemic Lupus Erythematosus

Skin criteria

Butterfly rash (lupus over the cheeks and nose)

Discoid rash (a thick, disk-like rash that scars, usually on sun-exposed areas)

Sun sensitivity (rash after being exposed to ultraviolet A and B light)

Oral ulcerations (recurrent sores in the mouth or nose)

Systemic criteria

Arthritis (inflammation of two peripheral joints with tenderness, swelling or fluid)

Serositis (inflammation of the lining of the lung (also called pleura) or the heart (also called the pericardium))

Kidney disorder (protein in urine samples or abnormal sediment in urine seen under the microscope)

Neurologic disorder (seizures or psychosis with no other explanation)

Laboratory criteria

Blood abnormalities (hemolytic anemia, low white blood cell counts, low platelet counts)

Immunologic disorder (blood testing indicating either a positive LE preparation, anti-DNA, false-positive syphilis test or a positive anti-Sm)

Positive ANA blood test

There are several classifications of lupus. Discoid lupus erythematosus is described as usually being limited to the skin and may, or may not, present with a positive anti-nuclear antibody (ANA) test. It is a cutaneous form of the disease; its symptoms include mucosal ulcerations of the nose, mouth and vagina, butterfly rash, loss of hair, thick scarring discoid lesions, skin pigmentation changes, hives and welts, and Raynaud's phenomena (color changes in the fingertips – red, white, or blue – as a response to stress and temperature change).¹

Drug induced lupus is a condition characterized by lupus-like symptoms that are a

result of an adverse reaction to a prescription drug. In most cases the symptoms disappear with discontinuation of the drug. Anticonvulsant drugs, such as carbamazepine, have been particularly found to induce lupus-like symptoms in patients.²

When the disease progresses and begins to involve one or multiple systems of the body, it achieves the diagnosis of systemic lupus erythematosus. SLE itself is divided into subtypes based on the severity of the disease. The non-organ-threatening type of the disease presents with symptoms of severe fatigue, dyspnea, fever, swollen glands and joints, muscle and joint pain, and rashes or other skin

conditions. The organ-threatening form of the disease presents with the above symptoms, as well as involvement of the heart, lungs, liver, and kidneys. The prognosis is less favorable than the non-organ-threatening form of SLE and it is often these complications that become terminal.¹

Although SLE occurs in every age group and gender, the target population is women between the ages of 15 and 45. It is estimated that in the United States 80-92 percent of the lupus population is female. Drug-induced lupus appears to be the only non-gender biased form of the disease, with men being as equally susceptible as women. In addition, certain ethnic groups – American Indians, African Americans, and Asians – have a higher incidence of the disease compared to other nationalities, with Hispanics and Caucasians following. These prevalence trends also seem to exhibit variability based on geographic location. For example, China and the Philippines show a greater incidence than Japan. The incidence is nearly ten times greater in the American Sioux tribes compared to other American Indian tribes. Although these trends are inconsequential by themselves, when analyzing the global incidence it is apparent the disease is on the rise and controlling it is proving extremely difficult.¹

SLE poses a major obstacle to the healthcare community because the etiology and progression of the disease are so poorly understood. Conventional medicine, with variable success, approaches the disease with various forms of drug therapy. Corticosteroids, such as prednisone, are a staple in the treatment protocol, with prednisone being used to both suppress the aggressive autoimmune response and stabilize the resultant inflammation. Nonsteroidal anti-inflammatory drugs (NSAIDS) are readily prescribed to aid the corticosteroids. Antimalarials, such as hydroxychloroquine, are frequently used to subdue manifestations of the disease. Finally, cytotoxic drugs like methotrexate,

azathioprine, and cyclophosphamide are used with the objective of reducing steroid dosage.^{3,5}

Variable results are obtained from these conventional approaches and side effects often must be weighed against the actual manifestation of the disease. Prednisone has been found to cause a variety of side effects, such as musculoskeletal complications like avascular necrosis and Cushingoid symptoms.⁶ The gastrointestinal damage caused by the excessive use of NSAIDS is well documented. The cytotoxic drugs often fail to achieve remission and cause side effects such as cytopenia, hepatitis, nausea, vomiting, stomatitis, and central nervous system (CNS) disturbance.^{3,5}

With conventional medicine failing to make any significant breakthroughs, it is both appropriate and rational to determine if alternative medicine can make contributions to fill the void. At the present time, the use of vitamins, minerals, dietary fatty acids, and the elimination of symptom-inducing foods show great promise as possible treatment options for SLE. In addition, the use of DHEA and Chinese medicine already appear to exhibit therapeutic effects on SLE activity.

Conventional Approaches: Mechanisms and Side Effects

SLE has proven to be a difficult disease to understand and an even harder one to control. Conventional medicine typically utilizes a treatment approach similar to other autoimmune diseases, targeting the disease by the use of corticosteroids and/or NSAIDS. Prednisone, probably the most widely used corticosteroid, aims to suppress the resultant inflammatory response that accompanies SLE and many other autoimmune conditions. Prednisone has been shown to have effects on interleukins 1 and 2 (IL-1; IL-2). IL-2 plays a key role in the proliferation of T-cells. The spontaneous production of IL-1 is pro-inflammatory and may inhibit the utilization of IL-2 by T-cells. In one study, doses of 20-45 mg/

day of prednisone had a positive influence on the production of both IL-1 and IL-2. Furthermore, increased doses of prednisone reduced the spontaneous production of IL-1 that appears to be a characteristic of both active cases of SLE and those in remission. The addition of the oral cytotoxic drugs, cyclophosphamide and azathioprine, also demonstrated increased IL-2 and reduction of IL-1 production. These findings suggest the immunoregulation benefits of prednisone, and provide insight into the possible pathogenesis of SLE and the roles IL-1 and IL-2 play in the disease.⁴

Although corticosteroid administration may be beneficial as a treatment option for SLE, its use is not without significant risk. Prolonged prednisone use, or high doses (30 mg/day or greater), have been demonstrated to be a major risk factor for avascular necrosis.⁶⁻⁸ Musculoskeletal involvement is very common in SLE, and may include muscle atrophy or weakness, erosive arthritis, and osteoporosis. It is difficult to determine if these symptoms are a result of the disease or from corticosteroid usage. In either case, the use of prednisone is a modifiable risk factor and its use should be carefully monitored to reduce the possibility of it being a primary cause for musculoskeletal damage.⁶

With the damaging properties of corticosteroids uncertain, most treatment plans opt for reducing their use, an objective often accomplished by using cytotoxic drugs. A study conducted at a large lupus clinic in Toronto, Canada, observed the trends in cytotoxic therapies used on their SLE patients.³ Azathioprine was the most widely used agent, followed by methotrexate, cyclophosphamide, and cyclosporin. The most common indication for using this therapy was to treat the inflammatory manifestations of the disease, with hopes of protecting the organ systems, and as a steroid-sparing agent to reduce the risk of harmful side effects. The determination of which agent to use depended primarily on the course of the disease. Methotrexate was used in SLE

most often with arthritis and least often with renal involvement. Cyclophosphamide was the agent of choice for active renal and neurological involvement. Indications for azathioprine were wide in spectrum and more generalized. At the conclusion of this study, 54 percent of the sample terminated the use of the cytotoxic agents, citing toxic side effects, remission, and failure to achieve any therapeutic affects from the medication as the major reasons. Side effects leading to termination included cytopenia, hepatitis, nausea/vomiting, hypersensitivity, and skin rashes. The positive findings of the study showed a decrease in prednisone dosage with all of the cytotoxic agents, mostly minimal, with the exception of azathioprine which accounted for the greatest dose reduction of the tested agents. Improvements were also found in most of the involved organ systems and remission was obtained in a small number of the study's patients.

Methotrexate's use has been increasing and its effectiveness has been the subject of several studies. Methotrexate demonstrated the ability to modulate the cytokine profiles of infected mice. Levels of tumor necrosis factor (TNF- α), IL-1, IL-2, IL-4, IL-10, and other chemical mediators were restored to levels similar to healthy mice.⁹ Methotrexate, however, did not demonstrate a significant effect on lowering corticosteroid doses in several studies.^{5,10} This inability to effectively reduce prednisone levels to clinical significance brings into question the use of the drug as an effective treatment option. Side effects also posed a problem in many of the patients taking the drug, and included stomatitis, central nervous system involvement, nausea/vomiting, and leukopenia. Altered liver function tests were also commonly present in the methotrexate patient profile.⁵

Conventional treatment for SLE often includes antimalarials (which act as cytokine inhibitors and circulating immune complex blockers). Hydroxychloroquine is the most widely used; its effectiveness was studied in

combination with quinacrine, another antimalarial drug. In this small study, five of six patients improved with this drug combination. The combination demonstrated the ability to lower prednisone necessity in most of the patients. Side effects were limited to yellowish skin discoloration, which was reversible on cessation of the treatment. It was not determined if the skin discoloration was a sign of liver toxicity or merely a change in skin pigmentation. Researchers suggested bone marrow and kidneys should be monitored as well, although they were not monitored in this study. This study demonstrated the potential of antimalarial combinations as an effective treatment option as opposed to use of either agent alone.¹¹

Natural Approaches to Lupus Treatment

Alternatives to conventional therapy treatments are becoming more popular due to the inability to find a cure for SLE and a growing desire for a treatment plan carrying a lower risk of adverse side effects.

DHEA

One alternative therapy gaining acceptance is the use of dehydroepiandrosterone (DHEA). DHEA is a steroid molecule manufactured by the cholesterol-pregnenolone pathway, and is an intermediate to androstenediol and androstenedione, which have the potential to become either estrone or testosterone. The physiological role of DHEA is not fully understood, but certain findings suggest it may play an instrumental role in the pathogenesis of SLE. As noted previously, this predominantly female-based disease is marked by abnormally high levels of estrogen metabolites and the inactivation of already low levels of testosterone. This suggests androgens may have an effect on controlling these hormone abnormalities.^{12,13} DHEA levels are also low in the serum of SLE patients, implying that steroids have a stronger link to the disease than

anticipated.¹⁴ With that in mind, the role of the hormone and its various properties has been explored in multiple studies.

DHEA was found to have various immunoregulatory effects, such as enhancing IL-2 production and the subsequent proliferation of T-helper 1 cells, and a decrease in anti-DNA antibodies in mouse models.¹⁵ A shift toward T-helper 1 dominance results in a decrease in pro-inflammatory cytokines.

DHEA supplementation was also shown to be beneficial in a double-blind, placebo-controlled study conducted by van Vollenhoven et al. DHEA, administered at a dose of 200 mg/day for three months to 28 females with SLE, resulted in a reduction in prednisone dosage, a lower occurrence of flare-ups, and a decrease in activity of the disease based on the SLE disease activity index. The same findings were not present with the placebo group, with the condition of the patients either staying the same or deteriorating. The exact mechanisms were not understood, but were believed to be related to testosterone levels and IL-2 production. DHEA may have regulated the abnormally low levels of these in the study group. The treatment was well tolerated with a low toxicity profile; however, side effects of acne and mild hirsutism occurred in a number of patients. Topical steroid treatment was beneficial in most cases and no patient dropped out of the study due to side effects.¹⁶

In another study, van Vollenhoven et al explored the effects of DHEA in a double-blind, placebo-controlled clinical trial. SLE patients were randomly divided into a DHEA or placebo group for six months. All patients continued their prior adjunctive therapy of corticosteroids and immunosuppressives. Exact dosages of medications were not revealed in the study, but it is implied that differences among study participants were negligible. The researchers found that the placebo group demonstrated significant loss of bone density of the lumbosacral spine,

probably due to the effects of corticosteroid therapy. The test group received 200 mg/day of DHEA for six months and maintained bone density throughout the course of the study. This suggests DHEA may have an antiresorptive effect that may counteract bone damage caused by corticosteroids.¹⁷

Bone mineral density levels were also found to have a direct correlation to DHEA levels in a study conducted on 150 premenopausal SLE patients. Patients with adequate serum levels of DHEA had significantly higher bone mineral density levels compared to patients with low DHEA levels. Density mass was determined by measuring the femoral necks and the lumbar spine. The increased bone mineral density suggests DHEA acts as a protective mechanism against early bone loss and subsequent onset of osteoporosis. This study also showed serum DHEA levels had an inverse relationship with corticosteroid therapy. The patients receiving higher doses of prednisone appeared to have lower DHEA levels and decreased bone mineral densities compared to the control group. The same findings were not apparent with testosterone levels, bone mineral density, and steroid dosage, suggesting it was indeed DHEA possessing these properties and not another hormone along the pathway.¹⁸

The relationship between DHEA and SLE was further explored in a one-year study conducted on 50 SLE patients.¹⁹ Thirty-seven premenopausal and 13 postmenopausal women were given 200 mg DHEA once daily and monitored throughout the course of the study. Thirty-four patients were treated for six months, with 21 patients completing the full 12 months of the study. Patients showed an increase in serum levels of DHEA, DHEA sulfate, and testosterone in the first three months of therapy, and maintained these levels throughout the study with continued supplementation. More importantly, DHEA supplementation resulted in a decrease in SLE activity, based on measurements using the SLE

disease activity scores, and a reduction in prednisone doses. Although benefits were apparent, DHEA therapy was not without drawbacks. Sixty-two percent of the premenopausal woman in the study suffered acne as a side effect, and a smaller group had mild cases of hirsutism, consistent with the findings of van Vollenhoven. The postmenopausal women suffered acne at a lower frequency, but had a greater rate of breast tenderness, alopecia, and oily hair and skin compared to the premenopausal group. Acne, the most common side effect, was controlled in most of the woman by topical steroid treatments.

The role of DHEA was also explored to determine if it possesses antioxidant properties. Considering the amount of free radical destruction that takes place in SLE, any additional antioxidant protection would be beneficial. A study was conducted using rats that were fed either a vitamin E deficient diet supplemented with DHEA or a diet adequate in vitamin E with DHEA supplementation. The study found DHEA did possess the antioxidant property of decreasing iron-induced lipid peroxidation in the vitamin E deficient rats. This was not the case in the rats fed adequate vitamin E diets. It was believed antioxidant properties existed, but were masked by vitamin E, suggesting the antioxidant effect may not be evidenced unless there is a vitamin E deficiency. Although the vitamin E deficient rats showed some antioxidant activity, they also had an increase in weight loss and the presence of fatty enlarged kidneys, liver, and adrenal glands. DHEA may have the potential to scavenge free radicals, especially in conditions of inadequate vitamin E, but does not appear to spare vitamin E and prevent signs of a deficiency.²⁰

The Role of Essential Fatty Acids

Diet plays a key role in response to many diseases, including SLE. The role of essential fatty acids and dietary oils has been extensively examined using both mice and

human models. A study examined the effects of a mouse diet with varying amounts of calories and the addition of fish oils (omega-3 fatty acids) and corn oil (omega-6 fatty acids), and their effects on an induced antibody response. The mice were injected with sheep cells that induced an overactive immune response, the formation of plaque-forming cells, abnormal IL-1 and IL-2 activity, proteinuria, and subsequent death. Mice fed a diet containing fish oil had lower levels of proteinuria, decreased abnormal cytokine and interleukin activity, and better survival rates than mice fed corn oil diets. These findings may be linked to omega-3 fish oil's ability to inhibit the abnormal autoimmune activity of the B- and T-Lymphocytes and abnormal interleukin expression.²¹

The omega-3 fatty acids eicosapentanoic acid (EPA) at 180 mg and docosahexanoic acid (DHA) at 120 mg were administered to 12 SLE patients. Six g/day omega-3 fatty acids resulted in a decrease in arachidonic acid and its resultant inflammation, which is usually high in SLE. Higher doses – 18 g/day – demonstrated an additional positive effect on cholesterol. Beneficial HDL levels were raised, while triglyceride and VLDL levels were lowered in the study group. LDL levels were not altered significantly, but the omega-3 fatty acids did show the potential to make an impact in controlling atherosclerotic plaquing, a problem not only for SLE patients, but the general population as well.²²

Kelley found that fish oil had an effect on suppressing macrophage activity and the production of cyclooxygenase metabolites that contribute to renal damage in a mouse lupus model. Life span was significantly longer in mice supplemented with fish oil, and symptoms of renal damage and lymphoproliferation were delayed compared to the control group. It should be noted that fish oil delayed the onset of the lupus symptoms, but the mice eventually succumbed to the same kidney problems and eventual death as the control group, although at a slower rate.²³

Another animal study also found fish oil supplementation offered an increased life span and renal protection; however, this study demonstrated a finding that was not recognized in the earlier studies. There was a significant difference in levels of the renal antioxidant enzymes catalase, glutathione peroxidase, and superoxide dismutase in the mice fed corn oil versus those fed fish oil. Fish oil-fed mice had higher renal levels of antioxidants, which suggests omega-3 fatty acids may protect the kidneys from free radical damage that manifest throughout the course of the disease. The corn oil-fed mice did not demonstrate this effect.²⁴

T-lymphocytes decline with age in mouse models, and this is believed to be universal in the presentation of SLE in both mice and humans. Researchers found no significant differences between T-lymphocyte activity in fish oil- and corn oil-fed mice. However, when the oils were combined with a calorie-restricted diet, the differences became apparent. The age-related decline in T-lymphocyte numbers was greatly reduced in the mice fed fish oil and the calorie-restricted diet. This was not the case with the corn oil group. This study supports the finding of other researchers that the onset of fatal kidney damage could be postponed by modulating the T-helper 1 and T-helper 2 ratios.²⁵

The antioxidant effects of omega-3 and omega-6 fatty acids were the focus of several studies by Venkatraman. In an initial study using a mouse-SLE model, mice fed a diet of vitamin E and fish oil showed greater antioxidant capacity compared to mice fed a vitamin E and corn oil diet.²⁶ A further study focused on the combination of vitamin E and omega-3 fatty acids to determine optimum dosage levels in experimentally-induced SLE mice. The SLE mice had elevated serum levels of anti-DNA antibodies, IL-4, IL-6, IL-10, IL-12, and TNF- α . (IL-4, IL-6 and IL-10 are involved in the humoral immunity response and IL-12 is involved in cell-mediated immunity.) Mice fed the fish oil diet and 75

IU of vitamin E demonstrated lower inflammatory cytokines, prostaglandin E₂ (PGE₂), leukotriene B₄ (LTB₄), and thromboxane B₂ (TXB₂). Mice fed a diet of fish oil and a higher dosage of 500 IU vitamin E demonstrated these same findings, as well as the additional benefits of lowering IL-6, IL-10, IL-12, and TNF- α . This study demonstrated that the combination of fish oil and vitamin E has an impact on many of the key mediators of SLE.²⁷

Flaxseed oil, comprised of 70-percent omega-3 fatty acids, has been shown to have a direct effect on the antibody profile of SLE patients. Anti-cardiolipin and anti-DNA antibodies are elevated in SLE patients and are used as diagnostic markers of the disease. It was found that mice fed diets supplemented with flaxseed oil had reductions in both antibodies. These findings were not noted in mice fed diets supplemented with other oil sources, including safflower, *Juniperus virginiana*, fish, corn, or soybean oils. Surprisingly, a high level of omega-3 fatty acid in the fish oil did not show the same result, suggesting the effects were directly related to another aspect of flaxseed oil besides the omega-3 content.²⁸

Flaxseed oil was shown to be effective in lupus patients with nephritis. Serum levels of creatinine were reduced and creatinine clearance rates were improved with supplementation of flaxseed oil in quantities of 15-45 g/day. Thirty g/day seemed to be the most beneficial dosage, as 45 g/day was thought to raise protein levels in the urine. Thirty g/day also demonstrated the ability to lower total cholesterol by 11 percent and LDL cholesterol by 12 percent. Higher dosages showed similar effects, but less significant reductions. Blood viscosity was also reduced, which may improve proteinuria by decreasing glomerular capillary permeability.²⁹

Lupus nephritis patients have also demonstrated higher levels of platelet-activating factor (PAF), which is linked to renal damage and consequential proteinuria. Hall et al

conducted a study on mice with laboratory-induced SLE, exploring the effect of flaxseed oil. Mice fed a control diet consisting of mouse chow and no additional supplementation experienced irreversible platelet damage and premature death. The mice supplemented with flaxseed oil demonstrated platelet aggregation inhibition and subsequently had longer life spans. Proteinuria was also delayed by as much as four weeks compared to the control group. This study suggests that, although flaxseed may not prevent the inevitable manifestations of the disease, it prolonged the onset of damage from PAF and increased the life span of the study group mice.³⁰

Nutritional Status of Vitamins A and D

Supplementation with fat-soluble vitamins A and D may be indicated for patients with SLE. One study examined serum levels of active vitamin D (1,25(OH)₂D₃) in SLE, rheumatoid arthritis (RA), and osteoarthritis (OA) patients. Levels of 1,25(OH)₂D₃ were normal in RA and OA patients, but decreased in SLE patients. The best indicator of vitamin D status is believed to be 1,25(OH)₂D₃, which is known to play a key role in calcium homeostasis and immunoregulation by inhibition of lymphocyte activation and cytokine release. No correlation was found with corticosteroid use and 1,25(OH)₂D₃ levels, so the low serum levels were believed to be due to the disease itself. A possible explanation for the decreased vitamin D levels may be linked to the lack of sunlight exposure in most SLE patients due to their increased photosensitivity. The presence of deficiency suggests vitamin D supplementation may be indicated in this population.³¹

Supplementation of vitamin A at 100,000 IU daily for two weeks showed some beneficial immune responses in 10 women who participated in a study conducted by Vien et al. This high dose of vitamin A demonstrated no significant side effects and appeared to be

tolerated by the participants. The supplementation resulted in an increase in antibody-dependent cell-mediated cytotoxicity, natural killer cell activity, and IL-2 response. The long-term effects of vitamin A therapy and its impact on SLE have yet to be determined.³²

Antioxidants

Free radical damage plays a significant role in the pathogenesis of SLE. Several studies suggest antioxidant supplementation may improve the disease status of SLE patients. High levels of lipid peroxidases were found in SLE patients compared to healthy control patients³³ and low levels of antioxidants were found in the serum of SLE patients.³⁴ Comstock found that the antioxidants alpha-tocopherol, beta carotene, and retinol were lower in patients with SLE, as well as RA, suggesting free radical damage is an important component of the inflammatory disease process. This also suggests RA and SLE patients may require additional supplementation of antioxidants, such as vitamins A and E, and beta carotene.³⁴

The effects of antioxidants on mice and rats also have been studied. Rodents with MRL/ LPR (a lymphoproliferative disorder similar to SLE) were supplemented five times weekly with a mixture of 40 mcg beta carotene, 200 mcg alpha-tocopheryl acetate, 400 mcg vitamin C, and 0.132 mcg selenium in oil and compared to a control group of vitamin E-deficient rats. The study group showed a decrease in anti-double stranded DNA (anti-dsDNA) titers as well as a decrease in lymphoproliferation. This suggests antioxidants may be beneficial in the treatment of SLE.³² An additional study on mice found that selenium supplementation at four parts per million in drinking water improved natural killer cell activity and survival rates of mice with lupus. Those mice supplemented with lower or no selenium did not demonstrate this effect and consequently had shorter life spans.³⁵

Dietary Considerations

Diet may play a significant role in the course of SLE. An interest in the use of non-sprouted alfalfa seeds as an anti-atherosclerotic and cholesterol-lowering agent prompted several studies in the past few decades. Clinical observations including pancytopenia and antinuclear antibody production in both primates and humans led researchers to believe alfalfa may be linked to SLE. In a study conducted by Bardana et al, 10 macaque monkeys were subjected to diets that selectively included the addition or absence of alfalfa seeds. It was found that the animals that ingested the alfalfa seeds developed a variety of health problems. The most mild of these was the slight presence of anti-dsDNA antibodies in the serum with no other clinical signs or symptoms. Changes of greater significance included extreme elevations in laboratory values of anti-dsDNA and ANA antibodies, signs of lethargy, anorexia, and a macular facial rash. The alfalfa seeds were withdrawn and most of the hematological factors reverted to normal with the exception of ANA and anti-dsDNA antibodies, thus suggesting the presence of SLE. The subjects were then reintroduced to a diet containing alfalfa seeds and the condition was immediately exacerbated. Lethargy, alopecia, edema, and atherosclerotic changes appeared in the first 30 days after reintroduction of alfalfa.³⁷

This prompted the researchers to further explore the relationship between alfalfa seeds and SLE. They concluded that the amino acid L-canavanine was the key constituent in alfalfa that causes the exacerbation of SLE signs and symptoms. L-canavanine is found in many legumes including soybean, alfalfa, and clover, as well as onions. However, cooking and autoclaving apparently destroy the lupus-eliciting effects without decreasing the lipid-lowering properties found in the foods.³⁸

Food allergies and sensitivities have been shown to have an adverse impact on rheumatoid arthritis, which is similar in many ways

to SLE in both treatment and flare-up activity.^{39,40} The discovery and elimination of possible food triggers may prove to be beneficial in SLE as well.

Traditional Chinese Herbal Medicine

Traditional Chinese medicine has approached SLE by using herbal remedies as a primary treatment option. *Tripterygium wilfordii* Hook F (TwHF), a vine-like plant that grows in southern China, is one of the most studied herbs in Chinese medicine for the treatment of SLE. TwHF has been found to inhibit IL-2, interferon-1, and PGE₂. More importantly, symptoms of fatigue, arthralgia, fever, and abnormal lab findings were normalized. Prednisone requirements were reduced by 50 percent by subjects taking TwHF.⁴¹ Although benefits were apparent with TwHF treatment, its usage was not without side effects. Common side effects included stomach upset, diarrhea, skin rash, and change in skin pigmentation. These effects were controllable with dosage adjustment and many symptoms ceased without intervention. However, other side effects of this herb were more serious and difficult to control, including reversible infertility in men⁴¹ and amenorrhea in women.⁴² Toxicity was also questionable with overdose being linked to myocardial and intestinal damage and renal failure. Although TwHF has been shown to have beneficial effects as a treatment for SLE, its dosage must be monitored closely to avoid toxic outcomes.⁴²

The effects of other herbs have been tested on mice with hopes of reducing the necessity for steroids. Chen et al tested the effects of several popular Chinese herbs, including *Atractylodes ovata*, *Angelica sinensis*, *Cordyceps sinensis*, *Ligustrum lucidum*, and *Codonopsis pilosula*. Extracts were prepared by decocting the dry herb with boiling water for 60 minutes and condensed to a concentration of 1 g/mL. The extracts were then mixed

with mouse chow and results were recorded. Of the herbs tested, *C. sinensis* proved to be one of the most effective at inhibiting anti-dsDNA antibodies and prolonging the life span of the affected mice. Although the effects were apparent, the actual mechanism causing these effects has yet to be determined.⁴³

Conclusions

SLE has proven to be a difficult disease to manage because little is known about its etiology. Finding an appropriate treatment has created difficulty for the healthcare provider. What is known is that SLE can affect any organ system in the body and every patient's response is unique. NSAIDs, corticosteroids, antimalarials, and cytotoxic agents can be beneficial to some patients and of little help to others. In addition, side effects often outweigh benefits and create complications of their own. Chinese medicine and DHEA may be viable alternatives as they have both demonstrated the ability to reduce disease activity and decrease prednisone necessity. However, long-term safety and appropriate dosage has not been established to date. Additional clinical trials and appropriately designed studies must be performed.

Antioxidant and omega-3 fatty acid supplementation have been shown to reduce free radical damage and inflammation, improve immunoregulation, and decrease cardiovascular and renal disease risk. Testing for food and drug allergies may benefit a certain population of SLE patients. Despite the inability to find a cure for SLE, research suggests alternative methods may benefit those who fail to respond to conventional drug-based therapies or who wish to offset the potential side effects of conventional medications. It is up to the patient and their healthcare provider to explore all treatment options, both conventional and alternative, in an attempt to most appropriately control the manifestations of SLE in an individual patient.

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