

H A N D O U T O N H E A L T H

Systemic Lupus Erythematosus

**U.S. Department of Health and
Human Services
National Institutes of Health
National Institute of Arthritis and
Musculoskeletal and Skin Diseases**

For Your Information

This publication contains information about medications used to treat the health condition discussed in this booklet. When this booklet was printed, we included the most up-to-date (accurate) information available. Occasionally, new information on medication is released.

For updates and for any questions about any medications you are taking, please contact the U.S. Food and Drug Administration at 1-888-INFO-FDA (1-888-463-6332, a toll-free call) or visit their Web site at www.fda.gov.

This booklet is not copyrighted. Readers are encouraged to duplicate and distribute as many copies as needed.

Additional copies of this booklet are available from the National Institute of Arthritis and Musculoskeletal and Skin Diseases Information Clearinghouse, NIAMS/National Institutes of Health, 1 AMS Circle, Bethesda, MD 20892-3675, and on the NIAMS Web site on the Internet at <http://www.niams.nih.gov>.

Table of Contents

Defining Lupus **3**

Understanding What Causes Lupus **7**

Symptoms of Lupus **8**

Diagnosing Lupus **11**

Treating Lupus **14**

Lupus and Quality of Life **19**

Pregnancy for Women With Lupus **23**

Current Research **24**

Hope for the Future **30**

Additional Resources **31**

Information Boxes

Common Symptoms of Lupus **8**

Diagnostic Tools for Lupus **13**

Warning Signs of a Flare **21**

Preventing a Flare **21**

Tips for Working With Your Doctor **22**

Promising Areas of Research **28**






Systemic Lupus Erythematosus

This booklet is for people who have systemic lupus erythematosus, commonly called SLE or lupus, as well as for their family and friends and others who want to better understand the disease. The booklet describes the disease and its symptoms and contains information about diagnosis and treatment as well as current research efforts supported by the National Institute of Arthritis and Musculoskeletal and Skin Diseases (NIAMS) and other components of the Department of Health and Human Services' National Institutes of Health (NIH). It also discusses issues such as health care, pregnancy, and quality of life for people with lupus. If you have further questions after reading this booklet, you may wish to discuss them with your doctor.

Defining Lupus

Lupus is one of many disorders of the immune system known as autoimmune diseases. In autoimmune diseases, the immune system turns against parts of the body it is designed to protect. This leads to inflammation and damage to various body tissues. Lupus can affect many parts of the body, including the joints, skin, kidneys, heart, lungs, blood vessels, and brain. Although people with the disease may have many different symptoms, some of the most common ones include extreme fatigue, painful or swollen joints (arthritis), unexplained fever, skin rashes, and kidney problems.



Lupus can be effectively treated with drugs, and most people with the disease can lead active, healthy lives.

At present, there is no cure for lupus. However, lupus can be effectively treated with drugs, and most people with the disease can lead active, healthy lives. Lupus is characterized by periods of illness, called flares, and periods of wellness, or remission. Understanding how to prevent flares and how to treat them when they do occur helps people with lupus maintain better health. Intense research is underway, and scientists funded by the NIH are continuing to make great strides in understanding the disease, which may ultimately lead to a cure.

Two of the major questions researchers are studying are who gets lupus and why. We know that many more women than men have lupus.

Lupus is three times more common in African American women than in Caucasian women and is also more common in women of Hispanic, Asian, and Native American descent. In addition, lupus can run in families, but the risk that a child or a brother or sister of a patient will also have lupus is still quite low. It is difficult to estimate how many people in the United States have the disease because its symptoms vary widely and its onset is often hard to pinpoint.

There are several kinds of lupus:

- Systemic lupus erythematosus (SLE) is the form of the disease that most people are referring to when they say “lupus.” The word “systemic” means the disease can affect many parts of the body. The symptoms of SLE may be mild or serious. Although SLE usually first affects people between the ages of 15 and 45 years, it can occur in childhood or later in life as well. This booklet focuses on SLE.
- Discoid lupus erythematosus is a chronic skin disorder in which a red, raised rash appears on the face, scalp, or elsewhere. The raised areas may become thick and scaly and may cause scarring. The rash may last for days or years and may recur. A small percentage of people with discoid lupus have or develop SLE later.
- Subacute cutaneous lupus erythematosus refers to skin lesions that appear on parts of the body exposed to sun. The lesions do not cause scarring.
- Drug-induced lupus is a form of lupus caused by medications. Many different drugs can cause drug-induced lupus. Symptoms are similar to those of SLE (arthritis, rash, fever, and chest pain) and they typically go away completely when the drug is stopped. The kidneys and brain are rarely involved.

- Neonatal lupus is a rare disease that can occur in newborn babies of women with SLE, Sjögren's syndrome, or no disease at all. Scientists suspect that neonatal lupus is caused by autoantibodies in the mother's blood called anti-Ro (SSA) and anti-La (SSB). Autoantibodies ("auto" means self) are blood proteins that act against the body's own parts. At birth, the babies have a skin rash, liver problems, and low blood counts. These symptoms gradually go away over several months. In rare instances, babies with neonatal lupus may have a serious heart problem that slows down the natural rhythm of the heart. Neonatal lupus is rare, and most infants of mothers with SLE are entirely healthy. All women who are pregnant and known to have anti-Ro (SSA) or anti-La (SSB) antibodies should be monitored by echocardiograms (a test that monitors the heart and surrounding blood vessels) during the 16th and 30th weeks of pregnancy.

It is important for women with SLE or other related autoimmune disorders to be under a doctor's care during pregnancy. Physicians can now identify mothers at highest risk for complications, allowing for prompt treatment of the infant at or before birth. SLE can also flare during pregnancy, and prompt treatment can keep the mother healthier longer.

Understanding What Causes Lupus

Lupus is a complex disease, and its cause is unknown. It is likely that a combination of genetic, environmental, and possibly hormonal factors work together to cause the disease. Scientists are making progress in understanding lupus, as described here and in the “Current Research” section of this booklet. The fact that lupus can run in families indicates that its development has a genetic basis. Recent research suggests that genetics plays an important role; however, no specific “lupus gene” has been identified yet. Studies suggest that several different genes may be involved in determining a person’s likelihood of developing the disease, which tissues and organs are affected, and the severity of disease. However, scientists believe that genes alone do not determine who gets lupus and that other factors also play a role. Some of the factors scientists are studying include sunlight, stress, certain drugs, and infectious agents such as viruses.

In lupus, the body’s immune system does not work as it should. A healthy immune system produces proteins called antibodies and specific cells called lymphocytes that help fight and destroy viruses, bacteria, and other foreign substances that invade the body. In lupus, the immune system produces antibodies against the body’s healthy cells and tissues. These antibodies, called autoantibodies, contribute to the inflammation of various parts

**It is likely that
a combination of ...
factors work
together to cause
the disease.**

of the body and can cause damage to organs and tissues. The most common type of autoantibody that develops in people with lupus is called an antinuclear antibody (ANA) because it reacts with parts of the cell's nucleus (command center). Doctors and scientists do not yet understand all of the factors that cause inflammation and tissue damage in lupus, and researchers are actively exploring them.

Symptoms of Lupus

Each person with lupus has slightly different symptoms that can range from mild to severe and may come and go over time. However, some of the most common symptoms of lupus include painful or swollen joints (arthritis), unexplained fever, and extreme fatigue. A characteristic red skin rash—the so-called butterfly or malar rash—may appear across the nose and cheeks. Rashes may also

Common Symptoms of Lupus

- Painful or swollen joints and muscle pain
- Unexplained fever
- Red rashes, most commonly on the face
- Chest pain upon deep breathing
- Unusual loss of hair
- Pale or purple fingers or toes from cold or stress (Raynaud's phenomenon)
- Sensitivity to the sun
- Swelling (edema) in legs or around eyes
- Mouth Ulcers
- Swollen glands
- Extreme fatigue

occur on the face and ears, upper arms, shoulders, chest, and hands. Because many people with lupus are sensitive to sunlight (called photosensitivity), skin rashes often first develop or worsen after sun exposure.

Other symptoms of lupus include chest pain, hair loss, anemia (a decrease in red blood cells), mouth ulcers, and pale or purple fingers and toes from cold and stress. Some people also experience headaches, dizziness, depression, confusion, or seizures. New symptoms may continue to appear years after the initial diagnosis, and different symptoms can occur at different times. In some people with lupus, only one system of the body, such as the skin or joints, is affected. Other people experience symptoms in many parts of their body. Just how seriously a body system is affected varies from person to person. The following systems in the body also can be affected by lupus.

**Symptoms
can range
from mild
to severe and
may come and
go over time.**


- **Kidneys:** Inflammation of the kidneys (nephritis) can impair their ability to get rid of waste products and other toxins from the body effectively. There is usually no pain associated with kidney involvement, although some patients may notice swelling in their ankles. Most often, the only indication of kidney disease is an abnormal urine or blood test. Because the kidneys are so important to overall health, lupus affecting the kidneys generally requires intensive drug treatment to prevent permanent damage.

- **Lungs:** Some people with lupus develop pleuritis, an inflammation of the lining of the chest cavity that causes chest pain, particularly with breathing. Patients with lupus also may get pneumonia.
- **Central nervous system:** In some patients, lupus affects the brain or central nervous system. This can cause headaches, dizziness, memory disturbances, vision problems, seizures, stroke, or changes in behavior.
- **Blood vessels:** Blood vessels may become inflamed (vasculitis), affecting the way blood circulates through the body. The inflammation may be mild and may not require treatment or may be severe and require immediate attention.
- **Blood:** People with lupus may develop anemia, leukopenia (a decreased number of white blood cells), or thrombocytopenia (a decrease in the number of platelets in the blood, which assist in clotting). Some people with lupus may have an increased risk for blood clots.
- **Heart:** In some people with lupus, inflammation can occur in the heart itself (myocarditis and endocarditis) or the membrane that surrounds it (pericarditis), causing chest pains or other symptoms. Lupus can also increase the risk of atherosclerosis (hardening of the arteries).

Diagnosing Lupus

Diagnosing lupus can be difficult. It may take months or even years for doctors to piece together the symptoms to diagnose this complex disease accurately. Making a correct diagnosis of lupus requires knowledge and awareness on the part of the doctor and good communication on the part of the patient. Giving the doctor a complete, accurate medical history (for example, what health problems you have had and for how long) is critical to the process of diagnosis. This information, along with a physical examination and the results of laboratory tests, helps the doctor consider other diseases that may mimic lupus, or determine if the patient truly has the disease. Reaching a diagnosis may take time as new symptoms appear.

No single test can determine whether a person has lupus, but several laboratory tests may help the doctor to make a diagnosis. The most useful tests identify certain autoantibodies often present in the blood of people with lupus. For example, the antinuclear antibody (ANA) test is commonly used to look for autoantibodies that react against components of the nucleus, or “command center,” of the body’s cells. Most people with lupus test positive for ANA; however, there are a number of other causes of a positive ANA besides lupus, including infections, other autoimmune diseases, and occasionally as a finding in healthy people. The ANA test simply provides another clue for the doctor to consider in making a diagnosis. In addition, there are blood tests for individual types of autoantibodies that are more specific to people with lupus, although not all people with lupus test positive for these and not all people with these antibodies have lupus. These antibodies include anti-DNA, anti-Sm, anti-RNP, anti-Ro (SSA), and anti-La (SSB). The doctor may use these antibody tests to help make a diagnosis of lupus.



It may take months or even years for doctors to piece together the symptoms to accurately diagnose this complex disease.

Some tests are used less frequently but may be helpful if the cause of a person's symptoms remains unclear. The doctor may order a biopsy of the skin or kidneys if those body systems are affected. Some doctors may order a test for anticardiolipin (or antiphospholipid) antibody. The presence of this antibody may indicate increased risk for blood clotting and increased risk for miscarriage in pregnant women with lupus. Again, all these tests merely serve as tools to give the doctor clues and information in making a diagnosis. The doctor will look at the entire picture—medical history, symptoms, and test results—to determine if a person has lupus.

Other laboratory tests are used to monitor the progress of the disease once it has been diagnosed. A complete blood count, urinalysis, blood chemistries, and the erythrocyte sedimentation rate (ESR) test can provide valuable information. Another common test measures the blood level of a group of substances called complement. People with lupus often have increased ESRs and low complement levels, especially during flares of the disease. X rays and other imaging tests can help doctors see the organs affected by SLE.

Diagnostic Tools for Lupus

- Medical history
- Complete physical examination
- Laboratory tests:
 - Complete blood count (CBC)
 - Erythrocyte sedimentation rate (ESR)
 - Urinalysis
 - Blood chemistries
 - Complement levels
 - Antinuclear antibody test (ANA)
 - Other autoantibody tests (anti-DNA, anti-Sm, anti-RNP, anti-Ro [SSA], anti-La [SSB])
 - Anticardiolipin antibody test
- Skin biopsy
- Kidney biopsy

Treating Lupus

Diagnosing and treating lupus are often a team effort between the patient and several types of health care professionals. A person with lupus can go to his or her

family doctor or internist, or can visit a rheumatologist. A rheumatologist is a doctor who specializes in rheumatic diseases (arthritis and other inflammatory disorders, often involving the immune system). Clinical immunologists (doctors specializing in immune system disorders) may also treat people with lupus. As treatment progresses, other professionals often help. These may include nurses, psychologists, social workers, nephrologists (doctors who treat kidney disease), hematologists (doctors specializing in blood dis-

orders), dermatologists (doctors who treat skin disease), and neurologists (doctors specializing in disorders of the nervous system).

The range and effectiveness of treatments for lupus have increased dramatically, giving doctors more choices in how to manage the disease. It is important for the patient to work closely with the doctor and take an active role in managing the disease. Once lupus has been diagnosed, the doctor will develop a treatment plan based on the patient's age, sex, health, symptoms, and lifestyle. Treatment plans are tailored to the individual's needs and may change over time. In developing a treatment plan, the doctor has several goals: to prevent flares, to treat them when they do occur, and to minimize organ damage and complications. The doctor and patient should reevaluate the plan regularly to ensure it is as effective as possible.

Treatment plans are tailored to the individual's needs and may change over time.

NSAIDs: For people with joint or chest pain or fever, drugs that decrease inflammation, called nonsteroidal anti-inflammatory drugs (NSAIDs), are often used. While some NSAIDs, such as ibuprofen and naproxen, are available over the counter, a doctor's prescription is necessary for others. NSAIDs may be used alone or in combination with other types of drugs to control pain, swelling, and fever. Even though some NSAIDs may be purchased without a prescription, it is important that they be taken under a doctor's direction. Common side effects of NSAIDs can include stomach upset, heartburn, diarrhea, and fluid retention. Some people with lupus also develop liver, kidney, or even neurological complications, making it especially important to stay in close contact with the doctor while taking these medications.

Antimalarials: Antimalarials are another type of drug commonly used to treat lupus. These drugs were originally used to treat malaria, but doctors have found that they also are useful for lupus. A common antimalarial used to treat lupus is hydroxychloroquine (Plaquenil)*. It may be used alone or in combination with other drugs and generally is used to treat fatigue, joint pain, skin rashes, and inflammation of the lungs. Clinical studies have found that continuous treatment with antimalarials may prevent flares from recurring. Side effects of antimalarials can include stomach upset and, extremely rarely, damage to the retina of the eye.

* Brand names included in this publication are provided as examples only, and their inclusion does not mean that these products are endorsed by the National Institutes of Health or any other Government agency. Also, if a particular brand name is not mentioned, this does not mean or imply that the product is unsatisfactory.

It is dangerous to stop taking corticosteroids suddenly, so it is very important that the doctor and patient work together in changing the dose.

Corticosteroids: The mainstay of lupus treatment involves the use of corticosteroid hormones, such as prednisone (Deltasone), hydrocortisone, methylprednisolone (Medrol), and dexamethasone (Decadron, Hexadrol). Corticosteroids

are related to cortisol, which is a natural anti-inflammatory hormone. They work by rapidly suppressing inflammation. Corticosteroids can be given by mouth, in creams applied to the skin, or by injection. Because they are potent drugs, the doctor will seek the lowest dose with the greatest benefit. Short-term side effects of corticosteroids include swelling, increased appetite, and weight gain. These side effects generally stop when the drug is stopped. It is dangerous to stop taking corticosteroids suddenly, so it is very important that the doctor and patient work together in changing the corticosteroid dose. Sometimes doctors give very large amounts of corticosteroid

by vein over a brief period of time (days) (“bolus” or “pulse” therapy). With this treatment, the typical side effects are less likely and slow withdrawal is unnecessary.

Long-term side effects of corticosteroids can include stretch marks on the skin, weakened or damaged bones (osteoporosis and osteonecrosis), high blood pressure, damage to the arteries, high blood sugar (diabetes), infections, and cataracts. Typically, the higher the dose and the longer they are taken, the greater the risk and severity of side effects. Researchers are working to develop ways to limit or offset the use of corticosteroids. For example,

corticosteroids may be used in combination with other, less potent drugs, or the doctor may try to slowly decrease the dose once the disease is under control. People with lupus who are using corticosteroids should talk to their doctors about taking supplemental calcium and vitamin D or other drugs to reduce the risk of osteoporosis (weakened, fragile bones).

Immunosuppressives: For some patients whose kidneys or central nervous systems are affected by lupus, a type of drug called an immunosuppressive may be used. Immunosuppressives, such as cyclophosphamide (Cytoxan) and mycophenolate mofetil (CellCept), restrain the overactive immune system by blocking the production of immune cells. These drugs may be given by mouth or by infusion (dripping the drug into the vein through a small tube). Side effects may include nausea, vomiting, hair loss, bladder problems, decreased fertility, and increased risk of cancer and infection. The risk for side effects increases with the length of treatment. As with other treatments for lupus, there is a risk of relapse after the immunosuppressives have been stopped.

Other Therapies: In some patients, methotrexate (Folex, Mexate, Rheumatrex), a disease-modifying antirheumatic drug, may be used to help control the disease. Working closely with the doctor helps ensure that treatments for lupus are as successful as possible. Because some treatments may cause harmful side effects, it is important to report any new symptoms to the doctor promptly. It is also important not to stop or change treatments without talking to the doctor first.

Alternative and Complementary Therapies: Because of the nature and cost of the medications used to treat lupus and the potential for serious side effects, many

Because some treatments may cause harmful side effects ... report any new symptoms to the doctor promptly.


patients seek other ways of treating the disease. Some alternative approaches people have tried include special diets, nutritional supplements, fish oils, ointments and creams, chiropractic treatment, and homeopathy. Although these methods may not be harmful in and of themselves, and may be associated with symptomatic or psychosocial benefit, no research to date shows that they affect the disease process or prevent organ damage. Some alternative or complementary approaches may help the patient cope or reduce some of the stress associated with living with a chronic illness. If the doctor feels the approach has value and will not be harmful, it can be incorporated into the patient's

treatment plan. However, it is important not to neglect regular health care or treatment of serious symptoms. An open dialogue between the patient and physician about the relative values of complementary and alternative therapies allows the patient to make an informed choice about treatment options.

Lupus and Quality of Life

Despite the symptoms of lupus and the potential side-effects of treatment, people with lupus can maintain a high quality of life overall. One key to managing lupus is to understand the disease and its impact. Learning to recognize the warning signs of a flare can help the patient take steps to ward it off or reduce its intensity. Many people with lupus experience increased fatigue, pain, a rash, fever, abdominal discomfort, headache, or dizziness just before a flare. Developing strategies to prevent flares can also be helpful, such as learning to recognize your warning signals and maintaining good communication with your doctor.

It is also important for people with lupus to receive regular health care, instead of seeking help only when symptoms worsen. Results from a medical exam and laboratory work on a regular basis allows the doctor to note any changes and to identify and treat flares early. The treatment plan, which is tailored to the individual's specific needs and circumstances, can be adjusted accordingly. If new symptoms are identified early, treatments may be more effective. Other concerns also can be addressed at regular checkups. The doctor can provide guidance about such issues as the use of sunscreens, stress reduction, and the importance of structured exercise and rest, as well as birth control and family planning. Because people with lupus can be more susceptible to infections, the doctor may recommend yearly influenza vaccinations or pneumococcal vaccinations for some patients.



Women with lupus should receive regular preventive health care, such as gynecological and breast examinations. Men with lupus should have the prostate-specific antigen (PSA) test. Both men and women need to have their blood pressure and cholesterol checked on a regular basis. If a person is taking corticosteroids or antimalarial medications, an eye exam should be done at least yearly to screen for and treat eye problems.

Learning to recognize the warning signs of a flare can help the patient take steps to ward it off or reduce its intensity.

Staying healthy requires extra effort and care for people with lupus, so it becomes especially important to develop strategies for maintaining wellness. Wellness involves close attention to the body, mind, and spirit. One of the primary goals of wellness for people with lupus is coping with the stress of having a chronic disorder. Effective stress management varies from person to person. Some approaches that may help include exercise, relaxation techniques such as meditation, and setting priorities for spending time and energy.

Developing and maintaining a good support system is also important. A support system may include family, friends, medical professionals, community organizations, and support groups. Participating in a support group can provide emotional help, boost self-esteem and morale, and help develop or improve coping skills. (For more information on support groups, see the “Additional Resources” section at the end of this booklet.)

Warning Signs of a Flare

- Increased fatigue
- Pain
- Rash
- Fever
- Abdominal discomfort
- Headache
- Dizziness

Preventing a Flare

- Learn to recognize your warning signals
- Maintain good communication with your doctor

Learning more about lupus may also help. Studies have shown that patients who are well-informed and participate actively in their own care experience less pain, make fewer visits to the doctor, build self-confidence, and remain more active.

Tips for Working With Your Doctor

- Seek a health care provider who is familiar with SLE and who will listen to and address your concerns.
- Provide complete, accurate medical information.
- Make a list of your questions and concerns in advance.
- Be honest and share your point of view with the health care provider.
- Ask for clarification or further explanation if you need it.
- Talk to other members of the health care team, such as nurses, therapists, or pharmacists.
- Do not hesitate to discuss sensitive subjects (for example, birth control, intimacy) with your doctor.
- Discuss any treatment changes with your doctor before making them.

Pregnancy for Women With Lupus

Although a lupus pregnancy is considered high risk, most women with lupus carry their babies safely to the end of their pregnancy. Women with lupus have a higher rate of miscarriage and premature births compared with the general population. In addition, women who have antiphospholipid antibodies are at a greater risk of miscarriage in the second trimester because of their increased risk of blood clotting in the placenta. Lupus patients with a history of kidney disease have a higher risk of preeclampsia (hypertension with a buildup of excess watery fluid in cells or tissues of the body). Pregnancy counseling and planning before pregnancy are important. Ideally, a woman should have no signs or symptoms of lupus and be taking no medications for at least 6 months before she becomes pregnant.

Some women may experience a mild to moderate flare during or after their pregnancy; others do not. Pregnant women with lupus, especially those taking corticosteroids, also are more likely to develop high blood pressure, diabetes, hyperglycemia (high blood sugar), and kidney complications, so regular care and good nutrition during pregnancy are essential. It is also advisable to have access to a neonatal (newborn) intensive care unit at the time of delivery in case the baby requires special medical attention.

**Pregnancy
counseling
and planning
before pregnancy
are important.**

Current Research

Lupus is the focus of intense research as scientists try to determine what causes the disease and how it can best be treated. Some of the questions they are working to answer include: Why are women more likely than men to have the disease? Why are there more cases of lupus in some racial and ethnic groups? What goes wrong in the immune system, and why? How can we correct the way the immune system functions once something goes wrong? What treatment approaches will work best to lessen lupus symptoms? How do we cure lupus?

To help answer these questions, scientists are developing new and better ways to study the disease. They are doing laboratory studies that compare various aspects of the immune systems of people with lupus with those of other people both with and without lupus. They also use mice with disorders resembling lupus to better understand the abnormalities of the immune system that occur in lupus and to identify possible new therapies.

The National Institute of Arthritis and Musculoskeletal and Skin Diseases (NIAMS), a component of the Department of Health and Human Services' National Institutes of Health (NIH), has a major focus on lupus research in its oncampus program in Bethesda, Maryland. By evaluating patients with lupus and their relatives, researchers oncampus are learning more about how lupus develops and changes over time. The NIAMS also funds many lupus researchers across the United States. Some of these researchers are studying the genetic factors that increase a person's risk for developing lupus. To help scientists gain new knowledge, the NIAMS also has established Specialized Centers of Research devoted specifically to lupus research. In addition, the NIAMS is funding lupus registries that gather medical information as well as

blood and tissue samples from patients and their relatives. This gives researchers across the country access to information and materials they can use to help identify genes that determine susceptibility to the disease.

Identifying genes that play a role in the development of lupus is an active area of research. For example, researchers suspect that a genetic defect in a cellular process called apoptosis, or “programmed cell death,” exists in people with lupus. Apoptosis is similar to the process that causes leaves to turn color in autumn and fall from trees; it allows the body to eliminate cells that have fulfilled their function and typically need to be replaced. If there is a problem in the apoptosis process, harmful cells may stay around and do damage to the body’s own tissues. For example, in a mutant mouse strain that develops a lupus-like illness, one of the genes that controls apoptosis is defective. When it is replaced by a normal gene, the mice no longer develop signs of the disease. Scientists are studying what role genes involved in apoptosis may play in human disease development.

**Scientists are
developing new
and better
ways to study
the disease.**

Studying genes for complement, a series of proteins in the blood that play an important part in the immune system, is another active area of lupus research. Complement acts as a backup for antibodies, helping them destroy foreign substances that invade the body. If there is a decrease in complement, the body is less able to fight or destroy foreign substances. If these substances are not removed from the body, the immune system may become overactive and begin to make autoantibodies.

Recent large studies of families with lupus have identified a number of genetic regions that appear to be associated with risk of SLE. Although the specific genes and their function remain unknown, intensive work in mapping the entire human genome offers promise that these genes will be identified in the near future. This should provide knowledge of the complex factors that contribute to lupus susceptibility.

Identifying genes that play a role in the development of lupus is an active area of research.

NIAMS-funded researchers are uncovering the impact of genetic, socioeconomic, and cultural factors on the course and outcome of lupus in Hispanics, African Americans, and Caucasians. Preliminary data show that African American and Hispanic lupus patients typically have more kidney damage compared with Caucasians. In addition, NIAMS-funded researchers found that African American lupus patients have more skin damage compared with Hispanics and

Caucasians, and that the death rate from lupus is higher in African Americans and Hispanics compared with Caucasians.

It is thought that autoimmune diseases, such as lupus, occur when a genetically susceptible individual encounters an unknown environmental agent or trigger. In this circumstance, an abnormal immune response can be initiated that leads to the signs and symptoms of lupus. Research has focused on both the genetic susceptibility and the environmental trigger. Although the environmental trigger remains unknown, microbial agents such as Epstein-Barr virus and others have been considered.

Researchers also are studying other factors that may affect a person's susceptibility to lupus. For example, because lupus is more common in women than in men, some researchers are investigating the role of hormones and other male-female differences in the development and course of the disease. A current study funded by the NIH is focusing on the safety and effectiveness of oral contraceptives (birth-control pills) and hormone replacement therapy in women with lupus. Doctors have worried about the wisdom of prescribing oral contraceptives or estrogen replacement therapy for women with lupus because of a widely held view that estrogens can make the disease worse. Oral contraceptives and estrogen replacement therapy do not, as once feared, appear to intensify lupus symptoms. Scientists do not know the effects of oral contraceptives on women with antiphospholipid antibody syndrome.

Patients with lupus are at risk of developing atherosclerotic vascular disease (hardening of the blood vessels that can cause heart attack, angina, or stroke). The increased risk is due partly to having lupus and partly to steroid therapy. Preventing atherosclerotic vascular disease in lupus patients is a new area of study. NIAMS-funded researchers are studying the most effective ways to manage cardiovascular risk factors and prevent cardiovascular disease in adult lupus patients.

In childhood lupus, researchers are evaluating the safety and effectiveness of drugs called statins that lower LDL (or bad) cholesterol levels as a method of preventing fat buildup in the blood vessels.

One out of five lupus patients experiences symptoms such as headaches, dizziness, memory disturbances, stroke, or changes in behavior that result from changes in the brain or other parts of the central nervous system. Such lupus patients have what is called “neuropsychiatric” lupus.

NIAMS-funded scientists are applying new tools such as

brain imaging techniques to discover cellular activity and specific genes that may cause neuropsychiatric lupus. By uncovering the mechanisms responsible for central nervous system damage in lupus patients, researchers hope to move closer to improved diagnosis and treatment for patients with neuropsychiatric lupus.

Research has focused on both the genetic susceptibility and the environmental trigger.

Researchers are focusing on finding better treatments for lupus. A primary goal of this research is to develop treatments that can effectively minimize the use of corticosteroids. Scientists are trying to identify combination

therapies that may be more effective than single-treatment approaches. Another goal is to improve the treatment and management of lupus in the kidneys and central nervous

Promising Areas of Research

- Identifying lupus susceptibility genes
- Searching for environmental agents that cause lupus
- Developing drugs or biologic agents to treat lupus

system. For example, a 20-year study supported by the NIAMS and the NIH found that combining cyclophosphamide with prednisone helped delay or prevent kidney failure, a serious complication of lupus.

On the basis of new information about the disease process, scientists are using novel “biologic agents” to selectively block parts of the immune system. Development and testing of these new drugs, which are based on compounds that occur naturally in the body, comprise an exciting and promising new area of lupus research. The hope is that these treatments not only will be effective, but also will have fewer side effects. Preliminary research suggests that white blood cells known as B cells may play a key role in the development of lupus. Biologics that interfere with B cell function or block the interactions of immune cells are active areas of research. These targeted treatments hold promise because they have the advantage of reduced side effects and adverse reactions compared with conventional therapies. Clinical trials are testing the safety and effectiveness of rituximab (also called anti-CD20) in treating people with lupus. Rituximab is a genetically engineered antibody that blocks the production of B cells. Other treatment options currently being explored include reconstructing the immune system by bone marrow transplantation. In the future, gene therapy also may play an important role in lupus treatment.

**Scientists
are using novel
“biologic agents”
to selectively
block parts
of the immune
system.**



Hope for the Future

With research advances and a better understanding of lupus, the prognosis for people with lupus today is far brighter than it was even 20 years ago. It is possible to have lupus and remain active and involved with life, family, and work. As current research efforts unfold, there is continued hope for new treatments, improvements in quality of life, and, ultimately, a way to prevent or cure the disease. The research efforts of today may yield the answers of tomorrow, as scientists continue to unravel the mysteries of lupus.

For More Information

National Institute of Arthritis and Musculoskeletal and Skin Diseases (NIAMS)

National Institutes of Health

1 AMS Circle

Bethesda, MD 20892-3675

Phone: 301-495-4484 or

877-22-NIAMS (226-4267) (free of charge)

TTY: 301-565-2966

Fax: 301-718-6366

E-mail: NIAMSInfo@mail.nih.gov

www.niams.nih.gov

The National Institute of Arthritis and Musculoskeletal and Skin Diseases Information Clearinghouse is a public service sponsored by the NIAMS that provides health information and information sources. The clearinghouse provides information on lupus. Fact sheets, additional information, and research updates can also be found on the NIAMS Web site at www.niams.nih.gov.

Clinicaltrials.gov

The Department of Health and Human Services' National Institutes of Health, through its National Library of Medicine, has developed ClinicalTrials.gov to provide patients, family members, and members of the public current information about clinical research studies. You can search for trials by disease, location, treatment, or by funding organization at the Web site clinicaltrials.gov.

**American College of Rheumatology
Association of Rheumatology Health Professionals**

1800 Century Place, Suite 250

Atlanta, GA 30345

Phone: (404) 633-3777

Fax: (404) 633-1870

www.rheumatology.org

The American College of Rheumatology (ACR) is an organization of doctors and associated health professionals who specialize in arthritis and related diseases of the bones, joints, and muscles. The Association of Rheumatology Health Professionals, a division of ACR, aims to enhance the knowledge and skills of rheumatology health professionals and to promote their involvement in rheumatology research, education, and quality patient care. The association also works to advance and promote basic and continuing education in rheumatology for health professionals who provide care to people with rheumatic diseases.

Alliance for Lupus Research, Inc.

28 West 44th Street, Suite 1217

New York, NY 10036

Phone: (212) 218-2840 or (800) 867-1743 (free of charge)

www.lupusresearch.org

The Alliance for Lupus Research, Inc. (ALR), is a non-profit organization devoted exclusively to the support of promising research for the prevention, treatment, and cure of lupus. Through accelerated, focused, goal-oriented research programs, the ALR aims to promote basic and clinical sciences to achieve major advances leading to a better understanding of the causes of lupus.

American Autoimmune Related Diseases Association

22100 Gratiot Avenue

East Detroit, MI 48021

Phone: (586) 776-3900 or (800) 598-4668 (free of charge)

E-mail: aarda@aarda.org

www.aarda.org

The American Autoimmune Related Diseases Association (AARDA) is the only national nonprofit voluntary health agency dedicated to bringing a national focus and collaborative effort to the over 100 known autoimmune diseases through education, awareness, research, and patient services. By collaborating with the National Coalition of Autoimmune Patient Groups (NCAPG), AARDA supports legislative advocacy for autoimmune disease patients. AARDA provides free patient education information, physician and agency referrals, forums and symposia, and a quarterly newsletter.

Arthritis Foundation

P.O. Box 7669

Atlanta, GA 30357-0669

Phone: (404) 872-7100 or (800) 568-4045 (free of charge),
or your local chapter (listed in the telephone directory)

www.arthritis.org

The Arthritis Foundation is the major voluntary organization devoted to supporting arthritis research and providing educational and other services to individuals with arthritis. It publishes free pamphlets and a magazine for members on all types of arthritis. It also provides up-to-date information on research and treatment, nutrition, alternative therapies, and self-management strategies for patients with lupus and other autoimmune diseases. Chapters nationwide offer exercise programs, classes, support groups, physician referral services, and free literature. For more information, call your local chapter, listed in the white pages of the phone book, or contact the Arthritis Foundation at the above address.

Lupus Clinical Trials Consortium, Inc. (LCTC)

47 Hulfish Street, Suite 442

Princeton, NJ 08540

Phone: (609) 921-6670

The LCTC is a nonprofit organization that encourages the identification and testing of promising new therapies for lupus. It provides infrastructure support grants to certain academic institutions to support their clinical research activities; encourages lupus clinical researchers from those institutions to share their expertise; supports and conducts educational efforts to show the need for lupus clinical research; and disseminates scientific insights to advance the discovery of new lupus therapies.

Lupus Foundation of America (LFA), Inc.

2000 L Street, N.W., Suite 710

Washington, DC 20036

Phone: (202) 349-1155 or (800) 558-0121

www.lupus.org

The LFA assists local chapters in providing services to people with lupus, works to educate the public about lupus, and supports lupus research. Through a network of more than 500 branches and support groups, the chapters provide education through information and referral services, health fairs, newsletters, publications, and seminars. Chapters provide support to people with lupus, their families, and friends through support group meetings, hospital visits, and telephone help lines.

Rheuminations, Inc.

221 East 48th Street, Ground Floor
New York, NY 10017
Phone: (212) 593-5180
Fax: (212) 593-5181
www.dxlupus.org

Rheuminations, Inc. is a private, nonprofit foundation committed to funding excellence in medical research to achieve a better understanding of the causes of lupus and to bring new treatments to market; to educate and to empower those who live with lupus and those who care for them; to establish a higher level of public awareness about the disease.

SLE Foundation, Inc.

330 Seventh Ave., Suite 1701
New York, NY 10001
Phone: (212) 685-4118 or
(800) 74-LUPUS (745-8787) (free of charge)
www.lupusny.org

The foundation supports and encourages medical research to find the cause and cure of lupus and improve its diagnosis and treatment. It also provides a wide variety of services to help patients with lupus and their families. In addition, this voluntary organization conducts a broad-based public education program to raise awareness of lupus and increase understanding of this serious, chronic, autoimmune disease.

Acknowledgments

The NIAMS gratefully acknowledges the assistance of Jill P. Buyon, M.D., Hospital for Joint Diseases, New York, New York; Patricia A. Fraser, M.D., Brigham and Women's Hospital, Boston, Massachusetts; John H. Klippel, M.D., The Arthritis Foundation, Washington, DC; Michael D. Lockshin, M.D., Barbara Volcker Center for Women and Rheumatic Disease, Hospital for Special Surgery, New York, New York; Rosalind Ramsey-Goldman, M.D., Dr.P.H., Northwestern University Medical School, Chicago, Illinois; George Tsokos, M.D., Uniformed Services University of the Health Sciences, Bethesda, Maryland; and Elizabeth Gretz, Ph.D., Barbara Mittleman, M.D., Susana Serrate-Sztein, M.D., and Peter E. Lipsky, M.D., NIAMS, NIH, in the preparation and review of this and earlier versions of this publication. Special thanks also go to the many patients who reviewed this publication and provided valuable input. An earlier version of this booklet was written by Debbie Novak of Johnson, Bassin, and Shaw, Inc.

The National Institute of Arthritis and Musculoskeletal and Skin Diseases (NIAMS), a part of the Department of Health and Human Services' National Institutes of Health (NIH), leads the Federal medical research effort in arthritis and musculoskeletal and skin diseases. The NIAMS supports research and research training throughout the United States, as well as on the NIH campus in Bethesda, MD, and disseminates health and research information. The National Institute of Arthritis and Musculoskeletal and Skin Diseases Information Clearinghouse is a public service sponsored by the NIAMS that provides health information and information sources. Additional information and research updates can be found on the NIAMS Web site at www.niams.nih.gov.





**U.S. Department of Health and
Human Services**

Public Health Service

National Institutes of Health

**National Institute of Arthritis and
Musculoskeletal and Skin Diseases**

NIH Publication No. 03-4178

September 1997

Revised August 2003