Handout on Health: Systemic Lupus Erythematosus

This publication is for people who have systemic lupus erythematosus, commonly called SLE or lupus, as well as for their families and friends and others who want to better understand the disease. The publication 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 U.S. 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 publication, you may wish to discuss them with your doctor.

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What Is 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.

Typically, 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.

Who Gets Lupus?

We know that many more women than men have lupus. Lupus is more common in African American women than in Caucasian women and is also more common in women of Hispanic, Asian, and Native American descent. African American and Hispanic women are also more likely to have active disease and serious organ system involvement. 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. 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.

Understanding What Causes Lupus

Lupus is a complex disease, and its cause is not fully understood. Research suggests that genetics plays an important role, but it also shows that genes alone do not determine who gets lupus, and that other factors play a role. Some of the factors scientists are studying include sunlight, stress, hormones, cigarette smoke, certain drugs, and infectious agents such as viruses. Studies have confirmed that one virus, Epstein-Barr virus (EBV), which causes mononucleosis, is a
cause of lupus in genetically susceptible people.

Scientists believe there is no single gene that predisposes people to lupus. Rather, studies suggest that a number of 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.

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 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.
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.

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 occur on the face and ears, upper arms, shoulders, chest, and hands and other areas exposed to the sun. 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.

- **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. Most often, the only indication of kidney disease is an abnormal urine or blood test; however, some patients may notice dark urine and swelling around their eyes, legs, ankles, or fingers. 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, depression, 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. People with lupus are also at increased risk for atherosclerosis (hardening of the arteries).

- **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). People with lupus who have a type of autoantibody called antiphospholipid antibodies have an increased risk of 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 pain or other symptoms. Endocarditis can damage the heart valves, causing the valve surface to thicken and develop growths, which can cause heart murmurs. However, this usually doesn't affect the valves' function.

**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 you truly have 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 confirm a diagnosis of lupus or rule out other causes for a person's symptoms. 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 and other autoimmune diseases. Occasionally, it is also found 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.

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.

**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.
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 test (a test to measure inflammation) can provide valuable information. Another common test measures the blood level of a group of substances called complement, which help antibodies fight invaders. A low level of complement could mean the substance is being used up because of an immune response in the body, such as that which occurs during a flare of lupus.

**Treating Lupus**

Diagnosing and treating lupus often require a team effort between the patient and several types of health care professionals. Most people will see a rheumatologist for their lupus treatment. 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), cardiologists (doctors specializing in the heart and blood vessels), hematologists (doctors specializing in blood disorders), endocrinologists (doctors specializing in problems related to the glands and hormones), dermatologists (doctors who treat skin disease), and neurologists (doctors specializing in disorders of the nervous system). It is also important for people with lupus to have a primary care doctor—usually a family physician or internist (internal medicine specialist)—who can coordinate care between their different health providers and treat other problems as they arise.

The range and effectiveness of treatments for lupus have increased dramatically in recent decades, giving doctors more choices in how to manage the disease. Medications used in the treatment of lupus include the following:¹

¹All medicines can have side effects. Some side effects may be more severe than others. You should review the package insert that comes with your medicine and ask your
health care provider or pharmacist if you have any questions about the possible side effects.

**NSAIDs:** For people with joint or chest pain or fever, drugs that decrease inflammation, called nonsteroidal anti-inflammatory drugs (NSAIDs), are often used. Although 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.

2 Warning: Side effects of NSAIDs include stomach problems; skin rashes; high blood pressure; fluid retention; and liver, kidney, and heart problems. The longer a person uses NSAIDs, the more likely he or she is to have side effects, ranging from mild to serious. Many other drugs cannot be taken when a patient is being treated with NSAIDs, because NSAIDs alter the way the body uses or eliminates these other drugs. Check with your health care provider or pharmacist before you take NSAIDs. NSAIDs should only be used at the lowest dose possible for the shortest time needed.

**Antimalarials:** Antimalarials are another type of drug commonly used to treat lupus. These drugs prevent and treat malaria, but doctors have found that they also are useful for lupus. A common antimalarial used to treat lupus is hydroxychloroquine. 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.

**Corticosteroids:** Corticosteroids, such as prednisone, hydrocortisone, methylprednisolone, and dexamethasone, 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, by injection, or by intravenous (IV) infusion (dripping the drug into the vein through a small tube). Because they are potent drugs, the doctor will seek the
lowest dose required to achieve the desired benefit.

In an effort to minimize side effects associated with corticosteroids, 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.

**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 and mycophenolate mofetil, restrain the overactive immune system by blocking the production of immune cells. These drugs may be given by mouth or by IV infusion. The risk for side effects increases with the length of treatment.

**BLyS-specific inhibitors:** Belimumab, a type of agent referred to as a B-lymphocyte stimulator (BLyS) protein inhibitor, was approved by the U.S. Food and Drug Administration (FDA) in March 2011 for patients with lupus who are receiving other standard therapies, including those listed above. Given by IV infusion, belimumab may reduce the number of abnormal B cells thought to be a problem in lupus.

In studies conducted so far, African American patients and patients of African heritage did not appear to respond significantly to belimumab. An additional study of this patient population is planned to evaluate belimumab further in this subgroup of lupus patients. However, this difference in response to a treatment may be another indicator of the various ways that the disease affects different patients.

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. In addition to medications for lupus itself, in many cases it may be necessary to take additional medications to treat problems related to lupus such as high cholesterol, high blood pressure, or infection.

**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 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.

What You Can Do: The Importance of Self-Care

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 allow 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.

People with lupus should also be aware of their increased risk of premature cardiovascular disease. This makes healthy lifestyle choices such as eating well, exercising regularly, and not smoking particularly important for people with lupus.

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.

Staying healthy requires extra effort and care for people with lupus, so it becomes especially important to develop strategies for maintaining wellness. One of the primary goals of wellness for people with lupus is coping with the stress of having a chronic disorder. 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.

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.

### Pregnancy and Contraception for Women With Lupus

Although pregnancy in women with lupus is considered high risk, NIAMS-supported research suggests that most women with mild to moderate lupus can expect to have healthy pregnancies. 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 several 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.

For women with lupus who do not wish to become pregnant or who are taking drugs that could be harmful to an unborn baby, reliable birth control is important. Oral contraceptives (birth control pills) were once not an option for women with lupus because doctors feared the hormones in the pill would cause a flare of the disease. However, a large National Institutes of Health (NIH)-supported study called Safety of Estrogens in Lupus Erythematosus National Assessment (SELENA) found that severe flares were no more common among women with lupus taking oral contraceptives than those taking a placebo (inactive pill). As a result of this study, doctors are increasingly prescribing oral contraceptives to women with inactive or stable disease.

Research Highlights

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, and why are cases in these groups often more severe? 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) has a major focus on lupus research in its on-campus program in Bethesda, Maryland. By evaluating patients with lupus and their relatives, researchers at the National Institutes of Health (NIH) are learning more about how lupus develops and changes over time.

The NIAMS also funds many lupus researchers across the United States. To help scientists gain new knowledge, the NIAMS sponsored the development of a Lupus Registry and Repository that gathers 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.

The NIAMS also helped establish a registry to collect information and blood samples from children affected by neonatal lupus and their mothers. Information from the registry forms the basis of family counseling and tracks important data such as recurrence rates in subsequent pregnancies. The hope is that the registry will facilitate improved methods of diagnosis, as well as prevention and treatment for this rare condition.

In 2003, the NIH established the Lupus Federal Working Group (LFWG), a collaboration among the NIH Institutes, other Federal agencies, voluntary and professional organizations, and industries with an interest in lupus. The Working Group is led by the NIAMS and includes representatives from all relevant U.S. Department of Health and Human Services (HHS) agencies and other Federal departments having an interest in lupus.

Following are some recent areas of NIAMS/NIH lupus research:

**Genetics**

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

Genome-wide association studies have identified a number of genetic variations associated with lupus, although the functions
of identified variants and the contribution to the disease remain largely unknown. In most cases, lupus is thought to be caused by a combination of many genetic variations, each with modest effects. Recent studies, however, have pointed to the existence of rare variations with more substantial effects in certain subsets of lupus patients.

A number of genes associated with lupus risk and severity have been discovered. Some are linked to patient populations at high risk for lupus, including African American and Hispanic individuals.

**Biomarkers**

Biomarkers are another significant area of lupus research. Biomarkers are defined as molecules that reflect a specific biological or pathological process, consequence of a process, or a response to a therapeutic intervention. Simply put, they can let the doctor know what is happening in the body—or predict what is going to happen—based on something reliably measurable in tissues, cells, or fluids. NIAMS-supported researchers are seeking to identify biomarkers that could be predictors of a flare in people with lupus.

**The Disease Process**

NIAMS-sponsored researchers are exploring possible triggers for lupus. One study found that biofilms, protective coatings that some bacteria develop, may be involved in the immune response leading to lupus. Another study revealed that TREML4, a protein found on certain immune cells, can cause the immune system to activate an inflammatory response. These findings may lead to new targets for treatments.

Investigators continue to uncover the role of viruses, hormones, systemic inflammation, and other factors in the initiation of lupus and disease flares. They are also attempting to understand the biological basis for sex differences in immune and inflammatory systems that contribute to the sex differences in the disease.

**Treatment**

Understandably, identifying and developing better treatments for lupus—and ensuring that patients receive the best treatments—are among the primary goals of lupus research.
Earlier studies from the NIH Intramural Research Program determined that treatment with immunosuppressive drugs (cyclophosphamide and prednisone) can prevent or delay kidney failure caused by nephritis, one of the most serious and life-threatening complications of lupus. Other NIH-supported research has shown that lupus patients treated with hydroxychloroquine were less likely to develop severe kidney disease, had lower disease activity, and used less steroid medication.

Today, NIAMS intramural investigators are exploring how lupus develops and how therapies impact the course of the disease. Investigators are also conducting therapeutic trials to test the safety and efficacy of novel lupus treatments.

In 2014, the NIH, pharmaceutical companies, and nonprofit organizations together created the NIH Accelerating Medicines Partnership (AMP). The goal of the AMP is to increase the number of new diagnostics and therapies for select diseases, including lupus, and to reduce the time and cost of developing them.

More information on research is available from the following resources:

- **NIH Clinical Research Trials and You** was designed to help people learn more about clinical trials, why they matter, and how to participate. Visitors to the website will find information about the basics of participating in a clinical trial, first-hand stories from clinical trial volunteers, explanations from researchers, and links on how to search for a trial or enroll in a research-matching program.

- **ClinicalTrials.gov** offers up-to-date information for locating federally and privately supported clinical trials for a wide range of diseases and conditions.

- **NIH RePORTER** is an electronic tool that allows users to search a repository of both intramural and extramural NIH-funded research projects from the past 25 years and access publications (since 1985) and patents resulting from NIH funding.

- **PubMed** is a free service of the U.S.
National Library of Medicine that lets you search millions of journal citations and abstracts in the fields of medicine, nursing, dentistry, veterinary medicine, the health care system, and preclinical sciences.

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 in the past. 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

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TTY: 301-565-2966
Fax: 301-718-6366
Email: NIAMSIinfo@mail.nih.gov
Website: https://www.niams.nih.gov

If you need more information about available resources in your language or another language, please visit our website or contact the NIAMS Information Clearinghouse at NIAMSIinfo@mail.nih.gov.

Other Resources

American College of Rheumatology
Website: http://www.rheumatology.org

Alliance for Lupus Research, Inc.
Website: http://www.lupusresearch.org

American Autoimmune Related Diseases Association, Inc.
Website: http://www.aarda.org (con información en español)
Arthritis Foundation
Website: http://www.arthritis.org

Lupus Clinical Trials Consortium, Inc.
Website: http://www.lupusclinicaltrials.org

Lupus Foundation of America
Website: http://www.lupus.org

Lupus Research Institute
Website: www.lupusresearchinstitute.org
(con información en español)

SLE Lupus Foundation
Website: http://www.lupusny.org

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by the NIAMS that provides health information and information sources. Additional information can be found on the NIAMS website at www.niams.nih.gov.

For Your Information

This publication may contain information about medications used to treat the health condition discussed here. When this publication was produced, 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:

U.S. Food and Drug Administration
Website: http://www.fda.gov
Toll free: 888-INFO-FDA (888-463-6332)

For updates and questions about statistics, please contact:

Centers for Disease Control and Prevention, National Center for Health Statistics
Website: http://www.cdc.gov/nchs
Toll free: 800-232-4636

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