Antibodies to Ro/SS-A are found in people with either lupus or Sjogren's syndrome, and are almost always found in babies who are born with neonatal lupus. **Antibodies to Jo-1** are associated with polymyositis, while **antibodies to PM-Scl** are associated with certain cases of polymyositis that also have features of scleroderma. **Antibodies to Scl-70** are found in people with a generalized form of scleroderma, and **antibodies to the centromere** (a structure involved in cell division) are found in people with a limited form of scleroderma which tends to have a chronic course.

Complement

Laboratory tests which measure complement levels in the blood may also be helpful to the physician in making a diagnosis of SLE. Complement is a blood protein that destroys bacteria and also influences inflammation. Complement proteins are identified by the letter "C" and a number. The most common complement tests are **C3**, **C4**, and **CH50**. If the total blood complement level is low, or the C3 or C4 complement values are low and the person also has a positive ANA, some weight is added to the diagnosis of lupus. Low C3 and C4 complement levels in individuals with a positive ANA may signify the presence of active disease, especially kidney disease.

Biopsy

Sometimes examination of a tissue sample **(biopsy)** can be helpful in making a diagnosis. The biopsy is one of the best ways to evaluate an organ or tissue. The procedure involves removal of a small sliver of tissue, which is then examined under a microscope. The doctor can use the biopsy to identify the amount of inflammation and damage to the tissue. Further tests can be performed on the specimen to determine whether the problem is due to lupus or is caused by some other factor such as infection or medication. Almost any tissue can be biopsied. The most common sites biopsied in lupus are the skin and kidney. The results of the biopsy, like any other laboratory test, should be examined in combination with the individual's medical history and clinical findings.

Tests to Assess Disease Activity

When a person diagnosed with lupus develops new or recurring symptoms, laboratory testing of blood or urine can help determine if the symptoms are due to an increase in lupus activity. Disease activity correlates with a rise in:

- CRP (C-reactive protein) binding
- Sedimentation rate, or ESR
- Anti-DNA
- Liver and kidney function tests (AST, ALT, BUN, creatinine)
- CPK (muscle enzyme)
- Urine protein or cellular casts

Disease activity also correlates with a fall in:

- CBC (white blood cell count, hemoglobin, platelets)
- Complement components
- Serum albumin

Putting It All Together

The interpretation of all these tests, and their relationship to symptoms, can be difficult. When a person has many symptoms and signs of lupus and has positive tests for lupus, it is easier for physicians to make a correct diagnosis and begin treatment. It is more common for an individual to report vague, seemingly unrelated symptoms of achy joints, fever, fatigue, or pain, and to have negative or borderline test results. Fortunately, with growing awareness of SLE, an increasing number of physicians will consider the possibility of lupus in the diagnosis. While these tests are useful only when their strengths and limitations are understood, in the hands of skilled physicians these are important tools that assist in diagnosing lupus.

The Lupus Foundation of America

The Lupus Foundation of America (LFA) was established in 1977 to educate and support those affected by lupus and find the cure. The LFA supports research, education, awareness, patient services, and advocacy.

The Lupus Foundation of America is the only nationwide organization exclusively serving individuals, families and friends affected by lupus. The LFA has hundreds of local chapters and support groups throughout the United States, as well as international affiliates around the world.

The LFA is a grassroots, volunteer-driven organization. Contact the LFA or the chapter that serves your area to find out how you can become involved in our mission.

For information about lupus or to locate the chapter nearest you, visit our website at **www.lupus.org** or call toll-free **1-800-558-0121**.

Become a Lupus E-Advocate and help pass federal legislation that will benefit people with lupus. Send an e-mail message to **advocacy@lupus.org** and enter SUBSCRIBE in the subject line. You'll receive periodic advocacy updates and other breaking lupus news and information.

Lupus Foundation of America, Inc.
2000 L Street NW, Suite 710
Washington, DC 20036
Information Request Line: 800-558-0121
www.lupus.org

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Laboratory Tests Used in the Diagnosis of Lupus

MORRIS REICHLIN, M.D.
Professor of Medicine and Member, Arthritis Immunology Program
University of Oklahoma Health Sciences Center

Vice-President of Research and Scientific Director
Oklahoma Medical Research Foundation
Oklahoma City, OK

LUPUS™
Foundation of America, Inc.

Because many symptoms of systemic lupus erythematosus (SLE) mimic those of other illnesses, lupus can be a difficult disease to diagnose. Diagnosis is usually made by a careful review of three factors:

- the individual's entire medical history;
- the individual's current symptoms; and
- an analysis of the results obtained in routine laboratory tests and some specialized tests related to immune status.

To make a diagnosis of SLE, an individual must show clinical evidence of a multi-system disease (i.e. has shown abnormalities in several different organ systems). The following are typical symptoms or signs that might lead to suspicion of SLE:

Skin	Butterfly rash across the cheeks; ulcers in the mouth; hair loss.
Joints	Pain; redness, swelling.
Kidney	Abnormal urinalysis suggesting kidney disease.
Lining membranes	Pleurisy (inflammation of the lining of the lung); pericarditis (inflammation of the heart lining); and/or peritonitis (inflammation around the abdomen). Taken together, these types of inflammation are known as polyserositis.
Blood	Hemolytic anemia (the red cells are destroyed by autoantibodies); leukopenia (low white blood cell count); thrombocytopenia (low number of platelets).
Lungs	Infiltrates (shadowy areas seen on a chest x-ray) that come and go
Nervous system	Convulsions (seizures); psychosis; nerve abnormalities that cause strange sensations or alter muscular control or strength.

If an individual has several of these symptoms, the physician will then usually order a series of tests to examine the functioning of the individual's immune system. In general, physicians look for evidence of autoantibodies. Although there is no one test that can definitely say whether or not a person has lupus, there are many laboratory tests which aid the physician in making a lupus diagnosis.

First, there are routine clinical tests which suggest that the person has an active systemic disease. These include the sedimentation rate (ESR) and C-reactive protein (CRP) which are frequently elevated in inflammation from any cause. Serum protein electrophoresis may reveal increased gammaglobulin and decreased albumin, and routine blood counts may reveal anemia and low platelet and white cell counts. Finally, routine chemistry panels may reveal kidney involvement by increases in serum blood urea nitrogen and creatinine, abnormalities of liver function tests, and increased muscle enzymes (such as CPK) if muscle involvement is present. These kinds of abnormalities alert the doctor to the presence of a systemic disease with multiple organ involvement.

Commonly used blood tests in the diagnosis of SLE are:

1) The antinuclear antibody test (ANA) to determine if autoantibodies to cell nuclei are present in the blood
2) The anti-DNA antibody test to determine if there are antibodies to the genetic material in the cell
3) The anti-Sm antibody test to determine if there are antibodies to Sm, which is a ribonucleoprotein found in the cell nucleus
4) Tests to examine the total level of serum (blood) complement (a group of proteins which can be consumed in immune reactions), and specific levels of complement proteins C3 and C4

The Antinuclear Antibody (ANA or FANA) Test

The **immunofluorescent antinuclear antibody (ANA or FANA) test** is a sensitive test for lupus, since it is present in 97 percent of those with the disease. When three or more typical clinical features are present, such as skin, joint, kidney, pleural, pericardial, hematological, or central nervous system findings as described above, a positive test confirms the diagnosis.

The ANA test is positive in almost all individuals with systemic lupus, and is the most sensitive diagnostic test currently available for confirming the diagnosis of systemic lupus when accompanied by typical clinical findings. A negative ANA test is strong evidence against lupus as the cause of a person's illness, although there are very infrequent instances where SLE is present without detectable anti-nuclear antibodies. ANA-negative lupus can be found in people who have anti-Ro (SSA) or antiphospholipid antibodies. However, a positive ANA test, by itself, is not proof of lupus since the test may also be positive in:

1) other connective tissue diseases such as scleroderma, Sjogren's syndrome, rheumatoid arthritis, and thyroid disease, as well as liver disease and juvenile arthritis
2) individuals being treated with certain drugs, including procainamide, hydralazine, isoniazid, and chlorpromazine
3) viral illnesses such as infectious mononucleosis, and other chronic infectious diseases such as hepatitis, lepromatous leprosy, subacute bacterial endocarditis, and malaria
4) other autoimmune diseases, including thyroiditis and multiple sclerosis

The test can even be weakly positive in about 20 percent of healthy individuals. While a few of these healthy people may eventually develop lupus symptoms, the majority will never develop any signs of lupus or related conditions. The chances of a person having a positive ANA test increases as he or she ages.

Finally, as many as 30-40 percent of asymptomatic first degree relatives (siblings, parents, and children) of people with lupus may have a positive ANA test.

ANA Titers (number) and Patterns

ANA reports include a **titer** (pronounced TY-tur), and a **pattern**. The titer indicates how many times the lab technician had to dilute plasma from the blood to get a sample free of the antinuclear antibodies. For example, a titer of 1:640 shows a greater concentration of antinuclear antibodies than a titer of 1:320 or 1:160.

The apparent great difference between various titers can be misleading. Since each dilution involves doubling the amount of test fluid, it is not surprising that titers increase rather rapidly. In actuality, the difference between a 1:160 titer and a 1:320 titer is only a single dilution. This does not necessarily represent a major difference in disease activity. ANA titers go up and down during the course of the disease, and a high or low titer does not necessarily mean the disease is more or less active. Therefore, it is not always possible to determine the activity of the disease from the ANA titer.

A titer above 1:80 is usually considered positive. However, some laboratories may interpret different titer levels as positive, so one cannot compare titers from different laboratories.

The pattern of the ANA test can sometimes be helpful in determining which autoimmune disease is present and which treatment program is appropriate. The homogeneous (smooth) pattern is found in a variety of connective tissue diseases, as well as in people taking particular drugs such as certain anti-arrhythmics, anti-convulsants or anti-hypertensives. This pattern is also the one most commonly seen in healthy individuals who have positive ANA tests. The speckled pattern is found in SLE and other connective tissue diseases, while the peripheral (rim) pattern is found almost exclusively in SLE. The nucleolar (a pattern with a few large spots) pattern is found primarily in people who have scleroderma.

Because the ANA is positive in so many conditions, the results of the ANA test have to be interpreted in light of the person's medical history, as well as his or her clinical symptoms. Thus, a positive ANA alone is never enough to diagnose lupus. On the other hand, a negative ANA argues against lupus but does not rule out the disease completely.

A Positive ANA Does Not Equate to Having a Disease

The ANA should be looked at as a screening test. If it is positive in a person who is not feeling well and who has other symptoms or signs of lupus, the physician will probably want to conduct further tests for lupus. If the ANA is positive in a person who is feeling well and in whom there are no other signs of lupus, it can be ignored. If there is any doubt, a consultation with a rheumatologist should clarify the situation.

Other Autoantibodies

In those individuals with a positive ANA, additional tests can be done for certain particular antibodies that may better establish a diagnosis of SLE. The knowledge of which particular antibody is responsible for the positive ANA test can sometimes be helpful in determining which autoimmune disease is present. For instance, **antibodies to DNA** (the protein that makes up the body's genetic code) are found primarily in SLE. **Antibodies to histones** (DNA packaging proteins) are usually found in people with drug-induced lupus, but may also be found in those with SLE. **Antibodies to the Sm antigen** are found almost exclusively in lupus, and often help to confirm the diagnosis of SLE. **Antibodies to RNP** (ribonucleoprotein) are found in a number of connective tissue diseases. When present in very high levels, RNP antibodies are suggestive of mixed connective tissue disease, a condition with symptoms like those of SLE, polymyositis, and scleroderma.