Lab Tests

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SLE is a multi-system illness. It usually affects more than one organ. Although it commonly affects the skin (rashes), muscles and joints (pain), kidneys (abnormal urinalysis) and causes fatigue and malaise (“feeling miserable”), none of these symptoms are specific enough to make an absolute diagnosis of SLE (except for certain sun sensitive rashes). Therefore, in the appropriate clinical setting, laboratory testing is critical to confirming the diagnosis.

There are 3 goals in using laboratory testing in SLE:

- **Confirm** a diagnosis of lupus in patients whose clinical symptoms and signs suggest lupus. Laboratory tests are also helpful to distinguish lupus from other rheumatic diseases which may have similar symptoms and signs and to determine the extent of the organ involvement.
- **Monitor** the effects of treatment on the course of lupus. Some laboratory tests improve as the patient improves and worsen as the condition worsens (or even before there is a flare).
- **Distinguish** certain subsets of lupus. Some patients with lupus develop clinical problems not seen in all lupus patients and these symptoms and signs may be associated with certain laboratory abnormalities.

**Routine Clinical Tests**

These tests are commonly obtained for the screening of many medical illnesses and are not specific to SLE or any other disease. They can help determine the degree of the disease activity (mild to severe) and the presence of inflammation in various organs (e.g., kidney disease). Abnormalities in these routine tests are not specific enough to be diagnostic of lupus, but they may be helpful in monitoring the effects of treatment.

**Tests of Inflammation**

*Sedimentation Rate (ESR) and C-Reactive Protein (CRP)*

The ESR and CRP tests detect inflammation in the body from any cause (e.g., active lupus, infection, heart attack). Unfortunately, in some patients with active lupus, these tests are not very abnormal, so they are generally less helpful than in other inflammatory conditions, such as rheumatoid arthritis. Also, they are usually abnormal with infections, and cannot be used to distinguish a lupus flare from an infection in a lupus patient.

**Complete Blood Count**

*Hemoglobin and Hematocrit (to detect anemia), White Blood Cell Count, Platelet Count*

These tests are often abnormal in patients with active SLE. Patients with any inflammatory disease can be anemic when they are sick. However, some patients with active lupus develop a more severe anemia due to antibodies that directly attack and damage red blood cells (hemolytic anemia). Lupus is an illness which often causes a low white cell count or a low platelet count (seen in about 30% of patients). This can be a useful clue to the diagnosis of SLE in patients with multi-system conditions.
Urine Studies
*Urinalysis and Urine for Protein*

All patients with newly diagnosed SLE should have their urine tested. Kidney inflammation in lupus does not cause symptoms unless very severe or advanced. The presence of red blood cells and protein suggests active kidney inflammation from lupus (assuming there is no bladder or kidney infection).

Chemistry Panel
*Liver Tests (AST, ALT), Kidney Tests (BUN, Creatinine), Muscle Enzymes (CPK)*

Liver tests may be abnormal in patients with active SLE, especially if they are taking nonsteroidal anti-inflammatory drugs (NSAIDs), such as ibuprofen and others, for joint pain. These tests become normal when the lupus is treated. Abnormalities in the kidney tests suggest there is a reduction in kidney function which can be seen with acute kidney inflammation in lupus or with chronic kidney damage. Occasionally, muscle pain and weakness indicate muscle inflammation which will cause the CPK to be high. This will improve with treatment of the SLE.

Autoantibody Tests

The presence of autoantibodies [proteins (antibodies) which react with our own body constituents (antigens) in the blood or in cells] is the hallmark of SLE. The most characteristic of the autoantibodies are the antinuclear antibodies, which react with the constituents within the nuclei of all cells. The screening test for the presence of antinuclear antibodies is the fluorescent antinuclear antibody test (FANA or ANA). In general, these antibodies do not penetrate living cells so they are not necessarily directly damaging the tissues in lupus patients. However, they are characteristic laboratory markers in SLE.

FANA Test

This test is positive in almost all patients with active lupus (99%) and is a useful screening test. If it is negative, it is unlikely that the patient, if ill and untreated, has lupus. On the other hand, the test is not specific for lupus and can be positive in other connective tissue diseases (such as scleroderma and dermatomyositis), in some liver and lung diseases, in patients taking certain medications (procaainamide, hydralazine, isoniazid, etanercept, infliximab), in healthy relatives of lupus patients and in healthy elderly individuals. The specific constituents (antigens) in the nucleus to which the antibodies are directed (e.g. DNA, RNP, Sm, etc) are tested if the ANA is positive.

The titer (level) of the ANA (e.g. 1:640) is a measure of the amount of the antibody present. High titers make it more likely that the ANA is a true positive test (rather than a laboratory error or a borderline positive in a healthy individual – often positive up to a titer of 1:80). High titers do not necessarily point to a diagnosis of SLE. High titers can be seen in other conditions as well. The titer of the ANA is not usually helpful in monitoring disease activity in lupus patients. It may remain positive at high titers even when the lupus is in clinical remission.

The pattern of the ANA – homogenous (diffuse), speckled, peripheral (rim) – are generally not helpful except for the peripheral pattern which is seen almost exclusively in lupus patients.
Anti-DNA Antibodies

DNA is the building block of the genes in the nucleus of all cells. Antibodies to DNA are characteristic of patients with SLE. The presence of anti-DNA antibodies is highly specific for the diagnosis of SLE and is rarely found in other conditions, although it can occasionally be seen in patients taking certain medications. Anti-DNA antibody titers may be useful to monitor patients with SLE because they often drop when the lupus is in remission and rise again if it flares. It should be noted however that only 70% of lupus patients make anti-DNA antibodies, so the diagnosis of SLE can be made even if the test is negative.

Anti-Sm (Smith) Antibodies

The presence of Anti-Sm antibodies is highly diagnostic of SLE. Anti-Sm antibodies are found in only 30-40% of lupus patients and titers do not usually change with disease activity.

Anti-Ro/SSA Antibodies

This antinuclear antibody is found in patients with Sjogren’s syndrome and SLE. It occurs in about 40% of lupus patients. Its importance lies in its associations with certain subsets of lupus patients. One association is with sun sensitive skin rashes that occur in patients with subacute cutaneous lupus erythematosus (SCLE). These rashes may be extensive and widespread, but unlike discoid lupus rashes, do not lead to scarring. Anti-Ro/SSA is also associated with a condition known as the neonatal lupus syndrome. Mothers with anti-Ro/SSA antibodies (whether they have lupus, Sjogren’s syndrome, or no connective tissue disease) can have babies who temporarily develop photosensitive skin rashes or who are born with a congenital heart block (a slow heart rate). This is a rare condition.

Anti-histone antibodies

Anti-histone antibodies are seen in 60% of patients with SLE. They are also found in 90% of individuals with lupus caused by certain drugs such as procainamide and hydralazine.

Antibodies to phospholipids (APL)

Lupus Anticoagulant, Anti-Cardiolipin Antibodies, False Positive VDRL Test (test for syphilis)

Anti-phospholipid antibodies are directed against phospholipid antigens on platelets and other cells. They are not antinuclear antibodies and thus may be present in patients with a negative FANA test. Even though the name lupus anticoagulant sounds as though these antibodies might “thin the blood”, the presence of APL is associated with thrombosis (blood clots), not thin blood. APL may be found in 40% of lupus patients and in patients with other connective tissue diseases or in individuals with no other illness. These antibodies can occur in lupus patients even when the lupus is not clinically active or they can be associated with a number of serious clinical problems. These include recurrent miscarriages in pregnant women, mainly in the middle trimester; venous clots leading to thrombophlebitis and pulmonary embolism; arterial clots leading to strokes or gangrene.

Other Autoantibodies

There are other autoantibodies in SLE. Antibodies to ribonucleoprotein (RNP) are common but these are not diagnostically helpful because they are found in other diseases. Antibodies to ribosomal P proteins have been found in the blood of patients with neuropsychiatric lupus (brain
involvement). A newly approved test, antibodies to SR proteins, is positive in 50-70% of lupus patients.

**Complement Levels**

The complement system is important in immune reactions. When lupus is active, complement protein levels often drop. The most common complement proteins that are measured are the third (C3) and fourth (C4). Low C3 and/or C4 levels are common in active lupus and are of value in diagnosing SLE and in following response to drug treatment. Low complement levels are very common in lupus nephritis (kidney inflammation). They generally improve or return to normal as the kidney disease improves with medication.

**Other Tests**

There are other tests which are not considered laboratory tests, but which are also helpful in the diagnosis of SLE and discoid lupus and in determining the extent and severity of organ involvement. These include skin and kidney biopsies, x-rays, spinal taps and echocardiograms depending on the clinical features of the patients.

**Summary**

Patients with clinical symptoms and signs of a multi-system illness should undergo routine laboratory testing and testing for autoantibodies and complement levels, which can confirm the diagnosis of SLE with high accuracy. Furthermore, in known lupus patients, these tests can help define subtypes of SLE with unique clinical problems and can be useful in monitoring disease activity. The discovery of the usefulness of these tests has markedly improved our ability to diagnose and treat lupus patients.

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