Systemic lupus Erythematosus:

Epidemiology:

90% of affected patients are female and the peak age at onset is between 20 and 30 years.

SLE is associated with considerable morbidity and a fivefold increase in mortality compared to age- and gender-matched controls, mainly because of an increased risk of premature cardiovascular disease.

Pathophysiology:

The cause of SLE is incompletely understood but genetic factors play an important role.

This has led to the hypothesis that SLE may occur because of defects in apoptosis or in the clearance of apoptotic cells, which causes inappropriate exposure of intracellular antigens on the cell surface. This is supported by the fact that environmental factors that cause flares of lupus, such as ultraviolet light and infections, increase oxidative stress and cause cell damage.

Clinical features:

Clinical features in individual patients can be quite variable and range from mild joint and skin involvement to severe, life-threatening internal organ disease.

EULAR/ACR Criteria for the Classification of Systemic Lupus Erythematosus 2019:

Clinical domains	Points
Constitutional domain	
Fever	2
Cutaneous domain	
Nonscarring alopecia	2
Oral ulcers	2
Subacute cutaneous or discoid lupus	4
Acute cutaneous lupus	6
Arthritis domain	
Synovitis in at least two joints or tenderness in at least two joints, and at least 30 min of morning stiffness	6
Neurologic domain	
Delirium	2
Psychosis	3
Seizure	5
Serositis domain	
Pleural or pericardial effusion	5
Acute pericarditis	6
Hematologic domain	
Leukopenia	3
Thrombocytopenia	4
Autoimmune hemolysis	4
Renal domain	
Proteinuria >0.5g/24 hr	4
Class II or V lupus nephritis	8
Class III or IV lupus nephritis	10

Immunologic domains	Points
Antiphospholipid antibody domain	
Anticardiolipin IgG >40 GPL or anti-β2GP1 IgG >40 units or lupus anticoagulant	2
Complement proteins domain	
Low C3 or low C4	3
Low C3 and low C4	4
Highly specific antibodies domain	
Anti-dsDNA antibody	6
Anti-Smith antibody	6

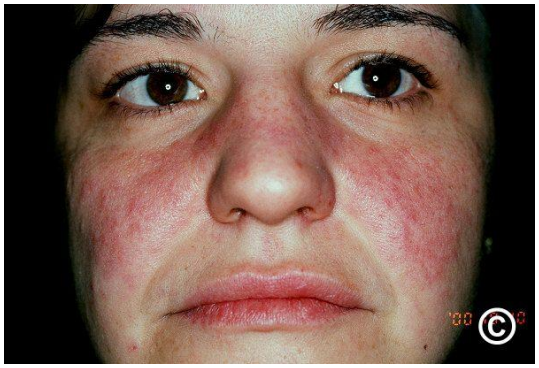
However, it should be emphasized that fulfillment of these classification criteria is not an absolute requirement for diagnosis.

It is clear that the most common presenting manifestations are constitutional symptoms (fever, fatigue, and/or weight loss), cutaneous

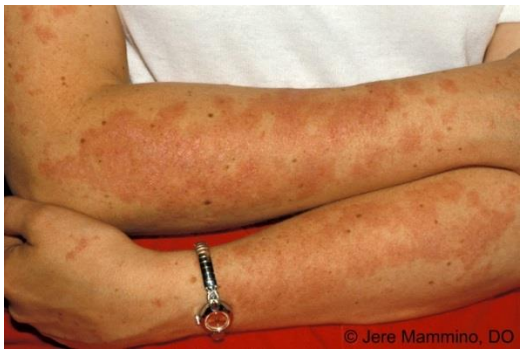
manifestations (e.g., malar rash), and articular manifestations (arthritis and/or arthralgia).

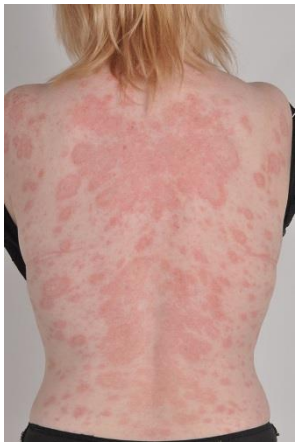
Acute Cutaneous Lupus Erythematosus: The hallmark feature of ACLE is localized to the malar region ("butterfly rash"). They do not appear on the nasolabial folds, which are sun-protected areas.

Subacute Cutaneous Lupus Erythematosus: Subacute cutaneous lupus erythematosus (SCLE) is characterized by the presence of nonscarring, photosensitive lesions.

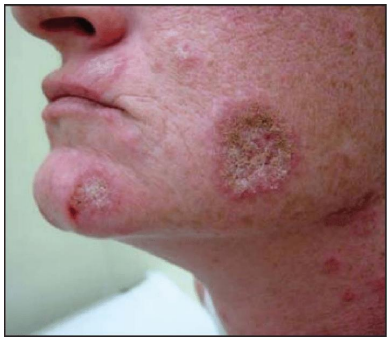


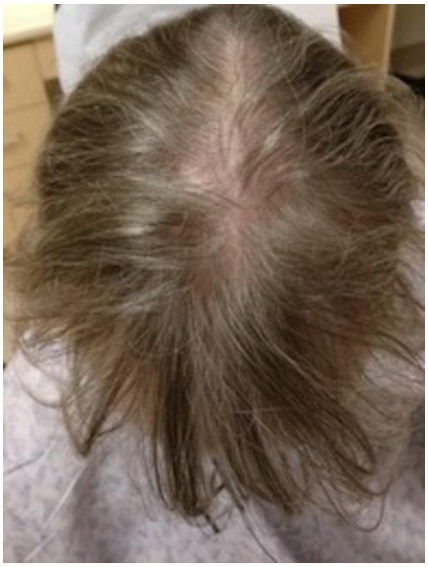
Chronic Cutaneous Lupus Erythematosus: Discoid lupus (DLE) is the most common subtype of CCLE.





Alopecia





Scarring alopecia is a common complication of discoid lupus. Nonscarring alopecia in patients with SLE can also be present.

Acute oral lupus lesions present as red macules, palatal erythema or petechiae, erosions, or ulcerations. These lesions are usually painless

Arthritis:

Arthralgia is a common symptom, occurring in 90% of patients, and is often associated with early morning stiffness. Tenosynovitis may also occur but clinically apparent synovitis with joint swelling is rare. Joint deformities may arise (Jaccoud's arthropathy) as the result of tendon damage but joint erosions are not a feature.

Kidney:

Renal involvement is one of the main determinants of prognosis and regular monitoring of **urinalysis** and **blood pressure** is essential.

The typical renal lesion is a proliferative glomerulonephritis, characterised by heavy haematuria, proteinuria and casts on urine microscopy.

It is estimated that as many as 90% of patients with SLE will have pathologic evidence of renal involvement on biopsy, but clinically significant nephritis will develop in only 50%.

Cardiovascular

The most common manifestation is pericarditis. The risk of atherosclerosis is greatly increased, as is the risk of stroke and myocardial infarction due to the adverse effects of inflammation on the endothelium, chronic glucocorticoid therapy.

Lung

Lung involvement is common and most frequently manifests as pleuritic pain (serositis) or pleural effusion. Other features include pneumonitis,

Neurological

Neuropsychiatric lupus (NPSLE) consists of a broad range of **neurologic** and **psychiatric** manifestations that can involve any aspect of the **central** or **peripheral** nervous system.

Headaches are reported in more than 50% of patients with SLE. Both migrainous and tension-type headaches have been described.

Steroid-induced psychosis is dose dependent and typically occurs within the first 2 weeks of treatment initiation.

CSF examination is important to rule out infection

Haematological:

Neutropenia, lymphopenia, thrombocytopenia and haemolytic anaemia may occur, due to antibody-mediated destruction of peripheral blood cells. The degree of lymphopenia is a good guide to disease activity.

Gastrointestinal:

Mouth ulcers may occur and may or may not be painful. Peritoneal serositis can cause acute pain. Mesenteric vasculitis is a serious

complication, which can present with abdominal pain, bowel infarction or perforation. Hepatitis is a recognized complication.

Investigations:

No clinical manifestation or laboratory test can serve as a definitive diagnostic test.

Instead, SLE is diagnosed on the basis of a constellation of characteristic symptoms, signs, and laboratory findings in the appropriate clinical context.

The hallmark serologic feature is the presence of ANAs, the ANA test is highly sensitive; it is positive **in more than 95%** of people with SLE. Other tests (e.g., anti-Ro/SS-A) usually confirm the presence of lupus associated in negative ANA.

Anti-dsDNA antibodies are present in no more than **50% to 60%** of patients with SLE, so their absence does not exclude the possibility of SLE. However, the presence of these antibodies is highly specific for SLE and therefore can be very helpful in establishing a definitive diagnosis. Complement consumption arising from immune complex disease may lead to hypocomplementemia in patients with SLE.

Titers of anti-dsDNA antibodies correlate with disease activity.

Urinalysis:

A urinalysis with microscopy is essential in the screening and monitoring of lupus nephritis. Hematuria, pyuria, dysmorphic red blood cells, red blood cell casts, and white blood cell casts may all be present.

Accurate measurement of proteinuria is critical because proteinuria is a very sensitive indicator of glomerular damage. Although the gold standard tool is an accurately collected 24-hour urine protein. Thus many clinicians are currently using the random spot urine protein-to-creatinine ratio for convenience.

Although easy to measure, serum creatinine is a fairly insensitive indicator of early decline in glomerular filtration rate (GFR).

Renal Biopsy:

When a patient with SLE has clinical or laboratory features that suggest the presence of nephritis, a renal biopsy should be performed to confirm the **diagnosis**, evaluate the **degree** of disease activity, and determine an appropriate course of **treatment**.

Treatment:

Systemic lupus erythematosus (SLE) activity usually follows the flare pattern, which is characterized by a relapsing remitting course.

Treatment in SLE should aim at remission or low disease activity and prevention of flares in all organs, maintained with the lowest possible dose of glucocorticoids.

Hydroxychloroquin (HCQ) is recommended for all patients with SLE, unless contraindicated

- Mucocutaneous: Mild malar rash and other photosensitive rashes usually respond to prophylaxis from sun exposure. Topical glucocorticoid (GCs) reduce redness and scaling, systemic anti-

malarials can be used alone or in combination with oral GCs (as much as 20 mg/day).

- In mild lupus arthritis, initial therapy is anti-malarials.

In persistent or aggressive disease, utilization of DMARDs is advocated, particularly Methotrexate.

- Lupus Nephritis (LN)
  Current therapeutic strategies in LN include an initial induction phase, aimed at substantially improving disease activity followed by a maintenance phase. Mild to moderate flares (stable Cr, subnephrotic proteinuria) may be treated with GC in combination with Azathioprine or mycophenolate. For severe nephritic flares, (re-)institution of cytotoxic therapy with monthly pulses of IV cyclophosphamid and IV methyleprednisolon.
- Central Nervous System Disease: (GCs alone or in combination with azathioprine for mild to moderate cases, or IV cyclophosphamid for severe ones.
  Antiplatelet or anti-coagulation therapy is recommended for events related to anti-phospholipid antibodies (APAs).
  Immunosuppressive therapy is usually not warranted for cognitive dysfunction in SLE
- Hematologic Disease: Mild cytopenias require no specific therapy other than regular monitoring.
  In more severe cases (platelet count < 50 × 103/mm3 or active bleeding, neutrophil count <1000/mm3), GCs are the mainstay of treatment. Steroid-sparing agents azathioprine can be added during steroid tapering.
- Cardiovascular disease: Patients with SLE should undergo regular assessment for traditional and disease-related risk factors for cardiovascular disease. Based on their individual cardiovascular risk profile, patients with SLE may be candidates for preventative

strategies as in the general population, including low-dose aspirin and/or lipid-lowering agents.

Lupus in Pregnancy:

Pregnancy may increase disease activity and precipitate the appearance of flares (13% to 74%). Pregnancies in patients with lupus, especially in patients with a history of LN or positive APA, are considered high risk for maternal and fetal complications, including preeclampsia, pregnancy loss, and pre-term birth.

Read more in:

Davidson's Principles and Practice of Medicine, 23rd edition

Kelley & Firestein's Textbook of Rheumatology, 10th edition