# SYSTEMIC LUPUS ERYTHEMATOSUS

TUCOM
Dep. of Medicine
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Dr. Hasan I. Sultan
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## Learning objectives:

1. Define Systemic lupus erythematosus (SLE).
2. Review the pathophysiology and causes of SLE.
3. Clarify the clinical features of SLE.
4. Outline the investigations of SLE.
5. Review the Revised American Rheumatism Association diagnostic criteria for SLE.
6. Outline the treatment of SLE.
7. Show the prognosis of SLE.

# Systemic lupus erythematosus (SLE)

**SLE: Is a multisystemic autoimmune disease that results from immune system mediated tissue damage that involved the skin, joints, kidney, central nervous system, cardiovascular system, serosal membranes, and the hematologic and immune systems.**

**It is a rare disease with a prevalence that ranges from about 0.03% in Caucasians to 0.2% in Afro-Caribbeans. 90% of affected patients are female and the peak age at onset is between 20 and 30 years, with considerable increase morbidity and a mortality.**

## Pathophysiology

The cause of SLE is incompletely understood, but there is a form of interactions among genetic, immunological, environmental, and hormonal factors.

**Genetic factors:** There is a higher concordance in monozygotic twins and the disease is strongly associated with polymorphic variants at the HLA locus. In a few instances, SLE is associated with inherited mutations in complement components C1q, C2 and C4.

**Immunological factors:** 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, leading to polyclonal B- and T-cell activation and autoantibody production.

**Environmental factors:** that cause flares of lupus, such as UV light and infections (particularly viruses), increase oxidative stress and cause cell damage. Certain drugs, including procainamide and hydralazine, can induce a lupus-like syndrome, but the symptoms usually abate after discontinuing use of the drug.

The female preponderance of SLE implies a role for **hormonal factors** in the disease.

# Clinical features

1- **General:** Symptoms such as fever, weight loss and mild lymphadenopathy may occur during flares of disease activity, whereas others such as fatigue and low-grade joint pains can be constant and not particularly associated with active inflammatory disease.

2- **Arthritis:** Arthralgia is a common symptom, occurring in 90% of patients. Tenosynovitis may also occur ,but clinically apparent synovitis with joint swelling is rare. Joint erosions do not occur.

3- **Raynaud's phenomenon:** is common in SLE along with arthralgia or arthritis.

4- **Renal involvement:** is one of the main determinants of Prognosis. The typical renal lesion is a proliferative glomerulonephritis, characterized by heavy hematuria, proteinuria and casts on urine microscopy.

**5- Skin Rash:** is common in SLE and is classically precipitated by exposure to UV light. Many distinct types occur:

- The classic butterfly facial rash (up to 20% of patients). This is erythematous, raised and painful or itchy, and occurs over the cheeks with sparing of the nasolabial folds.
- A discoid rash characterised by hyperkeratosis and follicular plugging, with scarring alopecia if it occurs on the scalp.
- Diffuse, usually non-scarring alopecia, which may also occur with active disease.
- Urticarial eruptions.
- Livedo reticularis which is also a feature of antiphospholipid syndrome and can become frankly vasculitic, if severe.

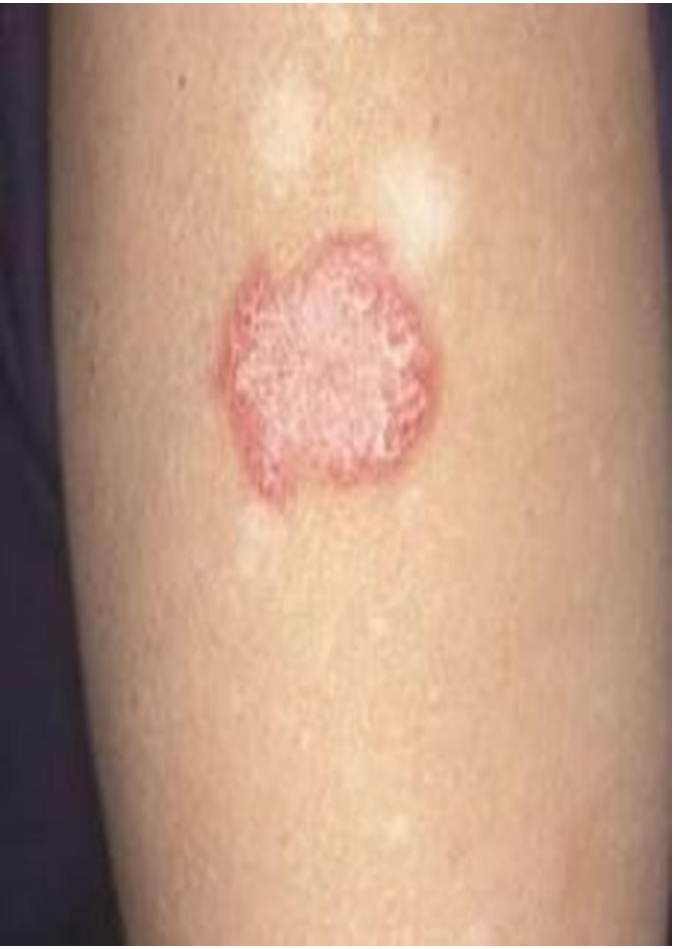
**6- Cardiovascular:** The most common manifestation is pericarditis. Myocarditis and Libman–Sacks endocarditis can also occur.

**7- Lung involvement:** is common and most frequently manifests as pleurisy or pleural effusion.

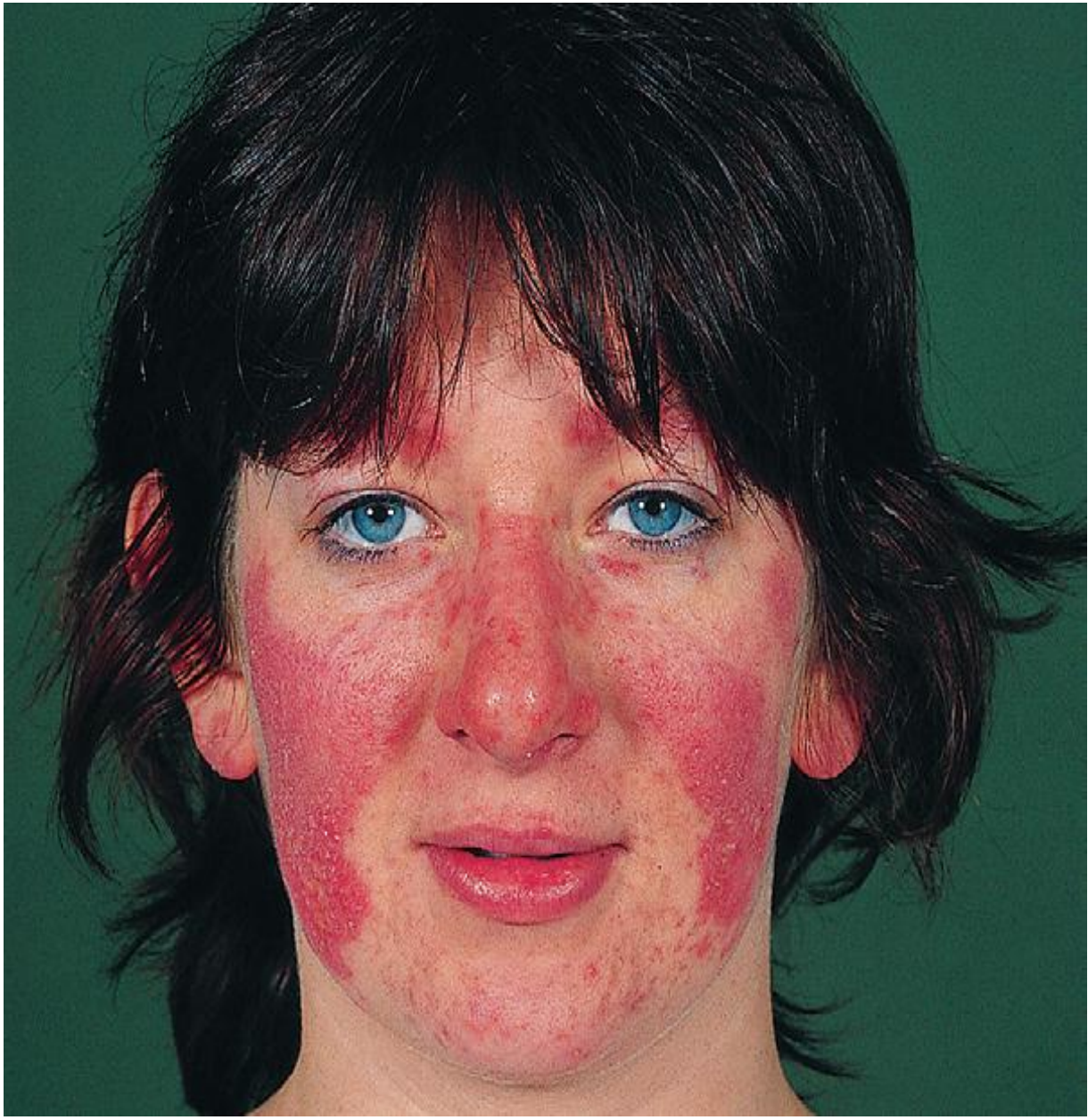
**8- Neurological:** More specific features of cerebral lupus include visual hallucinations, chorea, organic psychosis, transverse myelitis and lymphocytic meningitis.

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

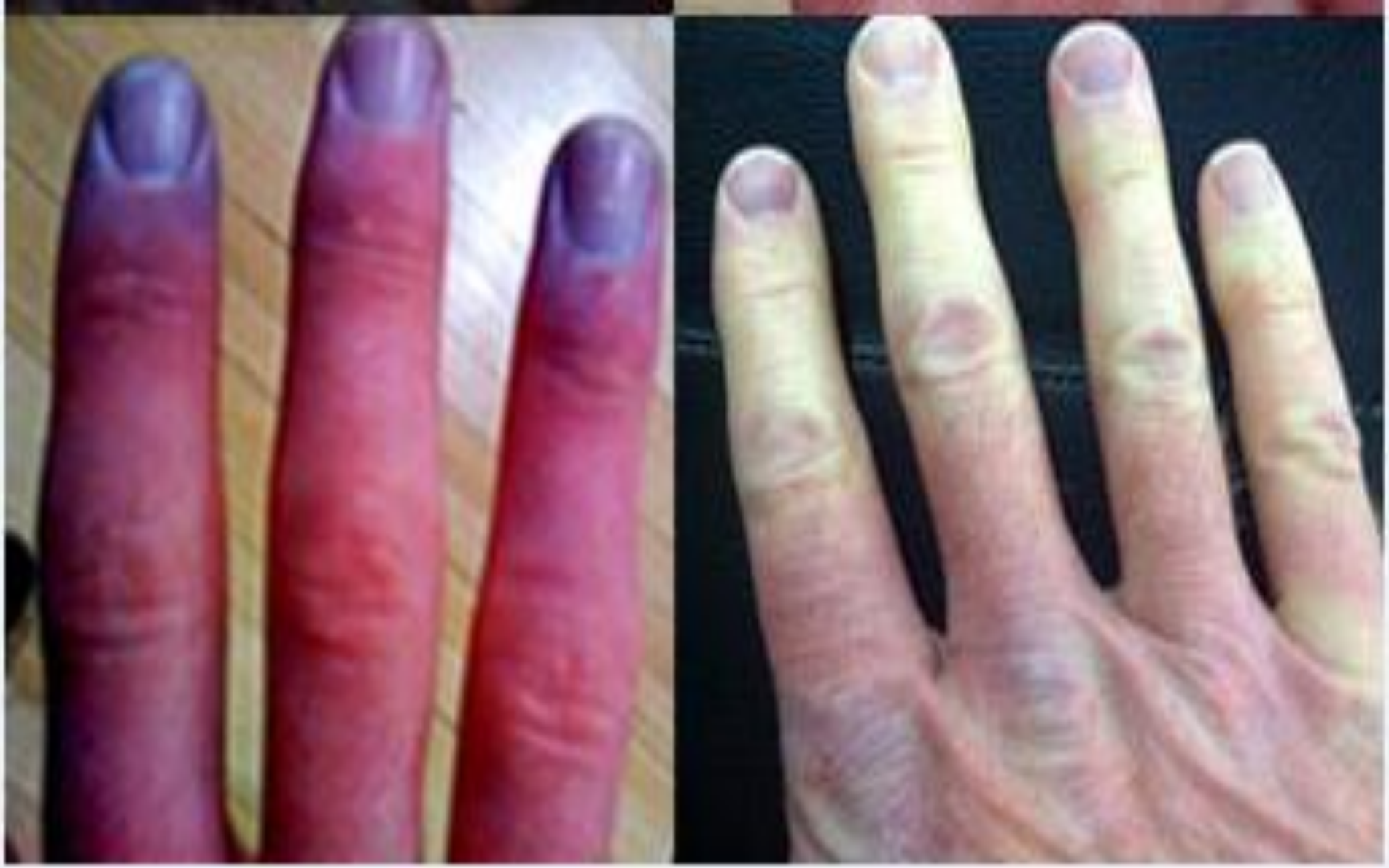
**10- Gastrointestinal:** Mouth ulcers may occur and may or may not be painful. Mesenteric vasculitis is a serious complication, which can present with abdominal pain, bowel infarction or perforation.



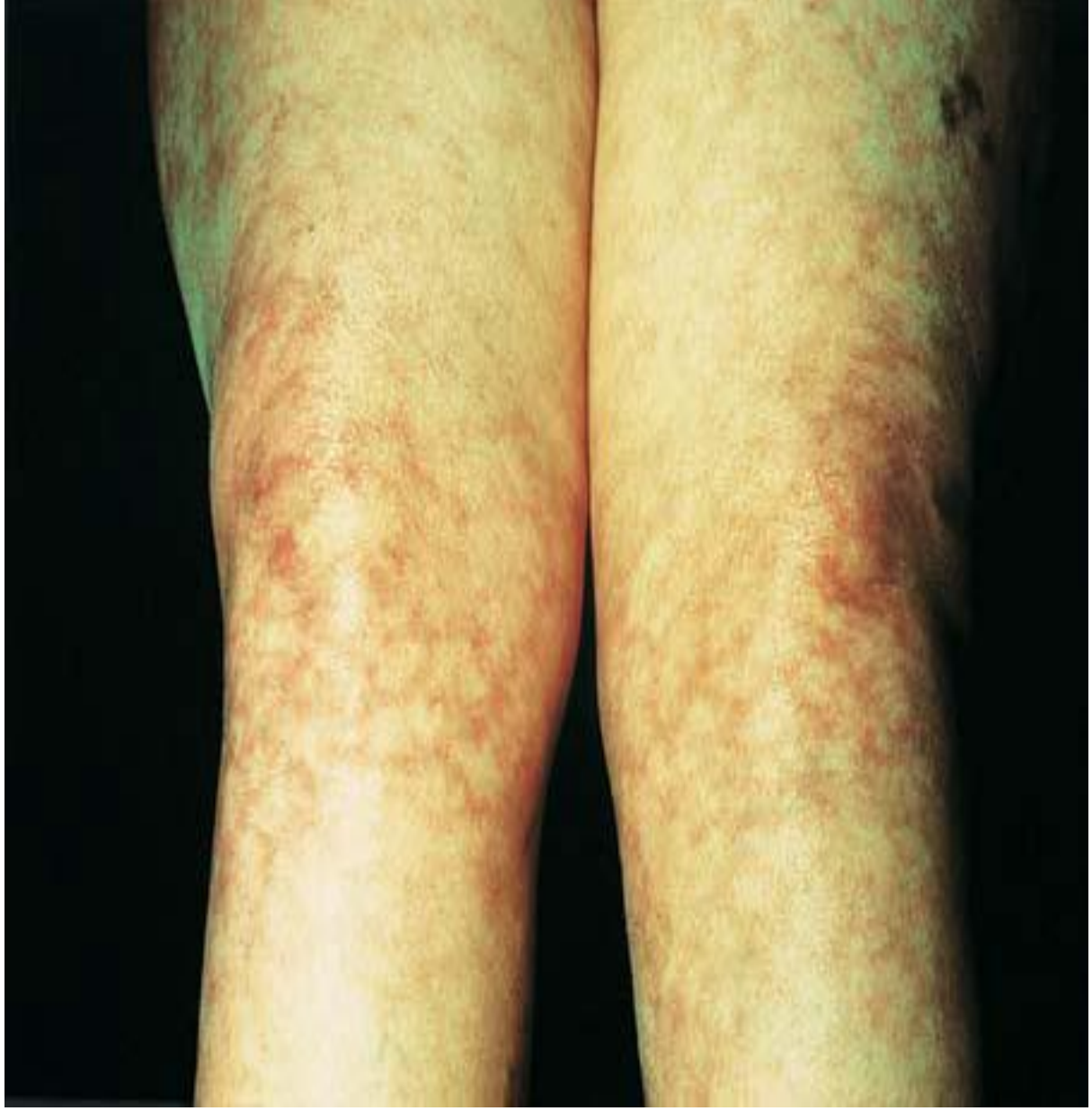
Discoid lupus presents with red, inflamed, coin-shaped patches of skin with a scaling and crusty appearance, most often on the scalp, cheeks, and ears. Hair loss may occur if the lesions are on the scalp



Butterfly (malar) rash of systemic lupus erythematosus, sparing the nasolabial folds.



**Raynaud phenomenon manifests as recurrent symmetrical vasospasm of the fingers in response to cold exposure. characterized by pallor, cyanosis then congestion (redness), which is painful.**



**Livedo reticularis (systemic lupus erythematosus and anti-phospholipid syndrome).**

# Investigations

The diagnosis is based on a combination of clinical features

and laboratory abnormalities. To fulfil the classification criteria for SLE, at least 4 of the 11 factors must be present or have occurred in the past.

Patients should be screened for ANA and antibodies to extractable nuclear antigens. Patients with active SLE almost always test positive for ANA. Anti-dsDNA antibodies are characteristic of severe active SLE. Autoantibodies associated with SLE are shown in table in the next slide.

patients with active disease tend to have low levels of C3 and C4.

A raised ESR, leucopenia and lymphopenia are typical of active SLE, along with anaemia, haemolytic anaemia and thrombocytopenia.

# Autoantibodies in Systemic Lupus Erythematosus (SLE)

| Antibody | % | Clinical Utility |
|---|---|---|
| Antinuclear antibodies | 98 | Best screening test; repeated negative tests make SLE unlikely |
| Anti-dsDNA | 70 | High titers are SLE-specific and correlate with disease activity, nephritis and vasculitis |
| Anti-Sm | 25 | Specific for SLE; no definite clinical correlations |
| Anti-Ro (SS-A) | 30 | Not specific for SLE; associated with sicca syndrome, subacute cutaneous lupus, and neonatal lupus with congenital heart block |
| Antihistone | 70 | More frequent in drug-induced lupus than in SLE |
| Antiphospholipid | 50 | for cardiolipin, predisposes to clotting, fetal loss and thrombocytopenia |

# Revised American Rheumatism Association criteria for systemic lupus erythematosus

1- **Malar rash:** Fixed erythema, flat or raised, sparing the nasolabial folds

2- **Discoid rash:** Erythematous raised patches with adherent keratotic scarring and follicular plugging

3- **Photosensitivity Rash:** due to unusual reaction to sunlight

4- **Oral ulcers:** Oral or nasopharyngeal ulceration, which may be painless

5- **Arthritis:** Non-erosive, involving two or more peripheral joints

6- **Serositis:** Pleuritis (history of pleuritic pain or rub, or pleural effusion) or pericarditis (rub, ECG evidence or effusion)

**7- Renal disorder:** Persistent proteinuria > 0.5 g/day *or* cellular casts (red cell, granular or tubular)

**8- Neurological disorder:** Seizures or psychosis, in the absence of provoking drugs or metabolic derangement

**9- Haematological disorder:** Haemolytic anaemia *or* *leucopenia* (< 4 × 109/L) or lymphopenia* (< 1 × 109/L) or* thrombocytopenia* (< 100 × 109/L) in the absence of offending drugs

**10- Immunological disorder:** Anti-DNA antibodies in abnormal titre *or* presence of antibody to Sm antigen *or* positive antiphospholipid antibodies

**11- ANA disorder:** Abnormal titre of ANA by immunofluorescence

**A person has SLE if any 4 out of these 11 features are present serially or simultaneously.**

***On two separate occasions.**

# Management

The therapeutic goals are to educate the patient about the nature of the illness, to control symptoms and to prevent organ damage.

Patients should be advised to avoid sun and UV light exposure and to employ sun blocks cream (sun protection factor 50)= which blocks an estimated 98 percent of UV rays.

**1- Mild to moderate disease:** Patients with mild disease restricted to skin and joints can sometimes be managed with analgesics, NSAID and hydroxychloroquine (200–400 mg daily). Frequently, however, corticosteroids are also necessary (prednisolone 5–20 mg/day), often in combination with immunosuppressants such as methotrexate, azathioprine or mycophenolate mofetil (MMF).

- The monoclonal antibody belimumab (targets the β-cell growth factor) recently been shown to be effective in patients with active SLE who have responded inadequately to standard therapy.

**2- Life-threatening disease:** High-dose corticosteroids and immunosuppressants are required for the treatment of renal, CNS and cardiac involvement. A commonly used regimen is pulse methylprednisolone (10 mg/kg IV), coupled with cyclophosphamide (15 mg/kg IV), repeated at 2–3-weekly intervals for six cycles.

Mycophenolate mofetil has been used successfully in combination with high-dose steroids for renal involvement in SLE, with results equivalent to those of pulse cyclophosphamide but fewer adverse effects.

Belimumab in combination with standard therapy significantly decreases disease activity in SLE patients and is safe and well tolerated.

3- **Maintenance therapy:** Oral prednisolone 10–15 mg/day, azathioprine (2–2.5 mg/kg/day), methotrexate (10–25 mg/week) or MMF (2–3 g/day) should also be prescribed. The long-term aim is to continue the lowest dose of glucocorticoid and immunosuppressant to maintain remission.

Cardiovascular risk factors, such as hypertension and hyperlipidaemia, should be controlled and patients should be advised to stop smoking.

Patients with SLE and the antiphospholipid antibody syndrome, who have had previous thrombosis, require life-long warfarin therapy.

SLE patients are at risk of osteoporosis and hypovitaminosis D, and should be screened with biochemistry and DXA scanning accordingly.

## Prognosis

- Survival in patients with SLE in the United States is approximately 95% at 5 years, 90% at 10 years, and 78% at 20 years.
- Poor prognosis (~50% mortality in 10 years): renal impairment, hypertension, nephrotic syndrome, anemia, hypoalbuminemia, hypocomplementemia and male sex.

# Drug-Induced Lupus

This is a syndrome of positive ANA associated with symptoms such as fever, malaise, arthritis or intense arthralgias/ myalgias, serositis, and/or rash.

Has less female predilection than SLE, rarely involves kidneys or brain, is rarely associated with anti-dsDNA, is commonly associated with antibodies to histones, and usually resolves over several weeks after discontinuation of the offending medication.

The most frequent are the antiarrhythmics procainamide, disopyramide, and propafenone; the antihypertensive hydralazine; several angiotensin-converting enzyme inhibitors and beta blockers; the antithyroid propylthiouracil; the antipsychotics chlorpromazine and lithium; the anticonvulsants carbamazepine and phenytoin; the antibiotics isoniazid

# Thanks