Facial rash, arthralgia, mouth ulcers and hair loss are common clinical features of systemic lupus erythematosus, an autoimmune condition that, in severe cases, can cause end-stage kidney disease.

Systemic lupus erythematosus
clinical features and diagnosis

By Nina Brown, MBChB, MRCP, Stephen Hughes, MPharm, and Mike Venning, PGD, FRCP

Systemic lupus erythematosus (SLE or lupus) is a multisystem autoimmune disorder. Clinical manifestations can range from mild (ie, predominantly mucocutaneous and musculoskeletal symptoms) to severe and life-threatening (eg, involving the heart, lungs and kidneys).

Patients with SLE are typically diagnosed between the ages of 15 and 45 years and the condition occurs in around 11 times more women than men. The overall incidence in north America and northern Europe is around 4–5 per 100,000 people. However, there is substantial ethnic variation — SLE affects 10-times as many Afro-Caribbeans as Caucasians (prevalence 207 per 100,000 compared with 20 per 100,000, respectively).

Clinical features
SLE can be difficult to diagnose because patients frequently present with non-specific symptoms, such as fatigue, arthralgia and general malaise. Mouth ulcers, hair loss and a photosensitive facial rash (in a typical malar “butterfly” distribution across the cheeks) are more typical clinical symptoms of lupus.

Less often, patients present with substantial organ involvement, such as pericarditis, pleuritis or disease affecting the central nervous system (with seizures or other neurological symptoms).

Renal involvement is now thought to affect most patients with SLE. Known as lupus nephritis, renal SLE typically manifests as proteinuria. Untreated it usually progresses over time, with deteriorating renal function and increasing risk of end-stage renal disease.

SLE is a disease in which activity varies over the duration of the disease (ie, relapsing/remitting). Remission can be difficult to classify, with some studies accepting a reduction in disease activity and others requiring an absence of disease activity when a patient is not undergoing immunosuppressive treatment. The latter is difficult to achieve — recent clinical trials demonstrate that less than 16% of patients achieve a “major clinical response” from treatment over 12 months.

Disease flares can be precipitated by environmental factors; for some patients, the trigger is unknown. A disease flare is defined by the British Isles lupus activity group.

SUMMARY

Systemic lupus erythematosus (SLE) is an autoimmune condition that is more common in women than in men. Classic clinical features of the condition include facial rash (in a butterfly pattern across the cheeks), arthralgia, mouth ulcers and hair loss. In more severe cases, SLE can affect the kidneys (known as lupus nephritis) and the central nervous system (eg, cerebritis).

The severity of SLE varies. Although disease flares can be caused by environmental factors (such as exposure to ultraviolet light), for some patients the triggers are unknown.

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**Clinical Focus**

Condition has been confirmed in twin studies, which demonstrate 24–56% concordance in monozygotic twins; nevertheless, the lack of complete concordance indicates that environmental factors also contribute to the pathogenesis of disease.

Exposure to ultraviolet (UV) light is known to trigger disease activity, particularly the cutaneous manifestations of SLE. This possibly occurs through the direct alteration of DNA structure, or through an abnormal immune response to UV-mediated damage in the skin cells. The relationship between sun exposure and SLE is complex, with some evidence suggesting that vitamin D deficiency is linked with a predisposition to the development of several autoimmune diseases, including SLE. In mice, vitamin D has been shown to protect against SLE. It is thought that vitamin D might affect T cell differentiation and regulation, as well as B cell proliferation, but the use of vitamin D for the treatment of SLE requires further investigation.

Because SLE is more common in women, and disease flares occur frequently during pregnancy (see Box 1), female sex hormones, particularly oestrogen, have been linked with development of SLE.

Some medicines can cause SLE. Drug-induced SLE has a different autoantibody profile (it is associated primarily with anti-histone antibodies) and usually resolves when the causative drug is stopped. Drugs such as hydralazine and procainamide have been shown to alter.
the methylation status of DNA and potentially contribute to disease development.21

**Diagnosis**

As mentioned above, SLE can be difficult to diagnose because patients often present with non-specific symptoms, such as fatigue, arthralgia and general malaise. Criteria set out by the American College of Rheumatology (see Box 2) include a combination of clinical features and immunological markers, and can be used to aid diagnosis — patients who meet at least four of the 11 criteria are deemed to have SLE.24

**Prognosis**

Overall, the rate of mortality for patients with SLE is around 2.4 times higher than an age- and sex-matched population.25 Outcomes depend primarily on the degree and nature of organ involvement, with renal damage the strongest predictor of mortality.24

The severity of lupus nephritis can be classified on a scale from class I to class VI (with class VI being the most severe).27 Patients with class I and II disease generally have good long-term renal outcomes. Class IV is considered severe renal disease — class VI describes specific changes in patients who already have advanced disease. Other adverse prognostic markers in lupus nephritis include high creatinine at presentation, failure to achieve remission and renal flares.24, 28 Outcomes from lupus nephritis appear to be improving, with recent data reporting a 10-year survival rate of 98%.29

Although renal disease is the strongest predictor of mortality, the leading cause of death for patients with SLE is cardiovascular disease. Patients with lupus have a risk of cardiovascular disease that is up to 50-times higher than an age- and sex-matched population.31 The underlying mechanisms for this are thought to be a combination of increased traditional cardiovascular risk factors (such as hypertension) plus disease-related factors (such as systemic inflammation, altered immune profiles and side effects of treatment, in particular corticosteroids).32 Further evidence is required to establish how this risk can be best addressed with primary prevention.

**References**


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**Box 2: Simplified diagnostic criteria for systemic lupus erythematosus**

<table>
<thead>
<tr>
<th>CRITERION</th>
<th>DEFINITION</th>
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<tbody>
<tr>
<td>Malar rash</td>
<td>Fixed erythema, flat or raised, over the cheeks, tending to spare the nasolabial folds</td>
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<tr>
<td>Discoid rash</td>
<td>Erythematous raised patches with adherent keratotic scaling and follicular plugging (atrophic scarring can occur in older lesions)</td>
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<td>Photosensitivity</td>
<td>Skin rash caused by an unusual reaction to sunlight (determined by patient history or clinician observation)</td>
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<td>Oral ulcers</td>
<td>Oral or nasopharyngeal ulceration, usually painless</td>
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<tr>
<td>Arthritis</td>
<td>Non-erosive arthritis involving at least two peripheral joints, characterised by tenderness, swelling or effusion</td>
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<tr>
<td>Pleuritis or pericarditis</td>
<td>Either pleuritis (convincing history of pleuritic pain or clinical evidence of pleural effusion) or pericarditis (diagnosed using electrocardiogram or through clinical evidence of pericardial effusion)</td>
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<tr>
<td>Renal disorder</td>
<td>Either persistent proteinuria or cellular casts in the urine (e.g., from red blood cells or haemoglobin)</td>
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<tr>
<td>Neurological disorder</td>
<td>Either seizures or psychosis (that have no other precipitating causes, such as drugs or metabolic derangements)</td>
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<tr>
<td>Haematological disorder</td>
<td>Either haemolytic anaemia, leucopenia or thrombocytopenia</td>
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<tr>
<td>Immunological disorder</td>
<td>Presence of antibodies to double-stranded DNA (anti-dsDNA) or anti-Sm antibodies or a positive finding of antiphospholipid antibodies</td>
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<tr>
<td>Antinuclear antibody</td>
<td>Raised titre of antinuclear antibody in the absence of drugs known to be associated with drug-induced lupus</td>
</tr>
</tbody>
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32 Symmons DPM, Gabriel SE. Epidemiology of Dd in rheumatic disease, with a focus on RA and SLE. Nature Reviews Rheumatology 2011;7:399–408.