



## Module 1930

# Lupus: causes, symptoms and management

From this pharmacy CPD module you will learn about:

- Who is affected and how common the condition is
- The different forms and their causes and symptoms
- How it is diagnosed and treated
- Advice and information that pharmacists can offer patients

### JACOB WARNER, PHARMACIST

Lupus is the term commonly used to describe the most severe form of lupus erythematosus – systemic lupus erythematosus (SLE).<sup>1</sup>

Lupus erythematosus can be classified into two types: systemic and cutaneous. SLE can cause damage to internal organs, whereas the cutaneous form does not cause general ill health and is confined to the skin.<sup>2</sup> In some people both types can be present, with cutaneous lupus erythematosus appearing as a manifestation of SLE; however, cutaneous lupus erythematosus can occur independently.<sup>3</sup> Photosensitivity – an immune system reaction that is triggered by sunlight – is common to all forms and the exact cause is unknown.<sup>2,4</sup>

SLE is a chronic, multisystem, autoimmune disease characterised by immunological abnormalities, particularly the presence of antinuclear antibodies.<sup>5,6</sup>

Cutaneous lupus erythematosus is a photosensitive skin eruption that can be either localised or widespread.<sup>7</sup> It can be classified into three types: acute; subacute; and chronic (which includes discoid).<sup>3</sup>

This module will focus on the two most common types of chronic lupus erythematosus – SLE and discoid lupus erythematosus (DLE).

### Who does lupus affect?

SLE is more common in women of childbearing age, but is being increasingly recognised in European men and women over the age of 40 years.<sup>6</sup> Approximately 1 in 1,000 people in the UK were affected by SLE in 2012, and it is more common in people of south Asian and African-Caribbean descent.<sup>6</sup>

Genes may play a role in the development of SLE.<sup>8</sup> Some human leukocyte antigen DRB1 types are more common in SLE patients and patients with a defective C4 complement gene also develop a lupus-like illness.<sup>4</sup> Illness, injury and periods of stress are thought to trigger SLE, as well as environmental factors (such as UV light), viruses (such as the Epstein-Barr virus)

and some drugs.<sup>4,8</sup>

Drugs may account for up to 6% of cases of SLE. Patients taking some long-term medications may present with clinical and serological manifestations. Drugs implicated include procainamide (possibly due to its effect of inhibiting DNA methylation), minocycline, isoniazid, phenytoin, carbamazepine, terbinafine and sulfasalazine (possibly due to its sulfonamide component). Recent data also appears to show SLE linked with interferons and monoclonal antibodies against tumour necrosis factor-alpha. When the drug is discontinued, the clinical presentation usually resolves.<sup>5</sup>

DLE is also more common in women and usually presents in people aged 20-40 years. It affects between 17 and 48 people per 100,000 and is more common among those who smoke.<sup>9</sup> It is rare for multiple family members to have DLE, but it is recognised that some families carry genes that increase the risk of developing it.<sup>2</sup> Patients with DLE usually find sunlight triggers their condition and can make their rash worse.<sup>2</sup>

### Prognosis

SLE survival rates have improved vastly in recent years and if patients are diagnosed early and treated appropriately, the disease may go into remission.<sup>10</sup> However, while there have been significant advances in the treatment of SLE and its associated comorbidities, patients still die on average 25 years earlier than the mean in the UK. The most common causes of mortality include infection, cardiovascular disease and severe disease activity.<sup>5,6</sup>

Patients with DLE tend to develop scarring, hair loss and pigmentary changes as a result of the lesions and if treatment is not initiated early on in the disease. About 5% of patients may go on to develop SLE.<sup>7</sup>

### Symptoms

#### Systemic lupus erythematosus

SLE is a remitting and relapsing illness, with non-specific signs and symptoms contributing



SLE is a remitting and relapsing illness that presents with non-specific symptoms, such as a rash

to the well-recognised delay in diagnosis.<sup>4,6</sup> The average time from onset of symptoms to diagnosis is reported as approximately two years.<sup>5</sup> The disease course can vary greatly between patients and relapses can be mild or severe. Some patients will have predominantly haematological, renal, or central nervous system manifestations, with the pattern that dominates early on usually prevailing throughout the disease course.<sup>11</sup>

Symptoms can range from low-grade, aching pains with the presence of a rash, through to life-threatening severe symptoms that involve major organs. Typically they include:

- fatigue
- fever
- splenomegaly
- lymphadenopathy
- arthralgia
- weight loss
- mouth ulcers
- skin rashes that are sensitive to light



**Mouth ulcers are a symptom typical of SLE**

- chest pain
- headache
- muscle pain
- some hair loss
- Raynaud's phenomenon
- dry eyes and mouth.<sup>3</sup>

One of the key diagnostic factors is a malar, or butterfly, rash that appears across the face and spares the nasolabial folds, as well as a photosensitive rash and a discoid rash.<sup>5</sup> Major organ involvement is thought to develop within the first five years after disease onset and commonly affects the skin, joints, kidneys, lungs, nervous system, blood cells and the membranes lining the lungs or heart.<sup>4,12</sup>

The disease can present at any age, as a slowly or rapidly progressive active disease. If it is not promptly diagnosed, treated appropriately and monitored regularly it can be associated with the rapid accumulation of damage.<sup>6</sup>

In 1982, the American College of Rheumatology (ACR) established 11 abnormalities that may suggest a person has SLE; the requirement being that a patient may be classified as having SLE if four or more of these are present. The criteria are:<sup>4,12</sup>

- malar rash – a rash that is present over the cheeks
- discoid rash – patches of skin, sometimes circular, that are red and have scaling
- photosensitivity – skin that is very sensitive to sunlight
- oral ulcers – ulcers within the mouth or nose
- serositis – inflammation of the membranes that line the lungs or heart
- arthritis – two or more joints affected by stiffness and pain
- renal – protein leakage caused by inflammation of the glomerulus
- neurological – seizures or psychosis not caused by drugs or metabolic derangements
- haematological – low levels of haemoglobin, white blood cells or platelets
- immunological 1 – antibodies to native DNA,



**Arthritis (two or more joints affected by pain or stiffness) is one of the criteria used by the ACR in SLE diagnosis**

- Sm nuclear antigen or phospholipid
- immunological 2 – antinuclear antibodies (ANA).

However, not all patients who meet the ACR classification have SLE and not all patients diagnosed have four or more of these criteria, which can appear and disappear over time.<sup>6</sup> The Systemic Lupus International Collaborating Clinic (SLICC) index was introduced in 2012 and requires at least one clinical and one immunological criterion be met, as well as two others from an expanded list, making it more sensitive and allowing patients to be diagnosed earlier in the disease course.<sup>4,6</sup>

According to the British Society of Rheumatology (BSR) guidelines, published in

2017, in order to consider a diagnosis of SLE there needs to be a combination of clinical features and the presence of at least one relevant immunological abnormality.<sup>6</sup> The BSR guideline states that the ACR and SLICC classification criteria are not diagnostic criteria and do not cover all clinical manifestations of the disease, but they may be helpful when considering the diagnosis.

The BSR also advises that when considering a possible diagnosis of SLE, a detailed clinical history and examination is required in order to identify relevant clinical features, including assessment of haematological and renal parameters. Diagnosis should not be made without evidence of at least one autoantibody

or low complement level to support the diagnosis of an autoimmune disease, the BSR says.<sup>6</sup>

Multiple tests are usually performed when SLE is suspected, including urinalysis, full blood counts, erythrocyte sedimentation rates, antinuclear factor, serum complement levels and extractable nuclear antigen antibodies. The antinuclear antibodies (ANA) test is positive in almost all cases of patients with SLE, but is not diagnostic without clinical features, as ANA can also be present in other autoimmune conditions, such as systemic sclerosis, primary Sjögren's syndrome and polymyositis. If the anti-double-stranded DNA antibodies test is positive, it is highly likely that the person has SLE.<sup>4,13</sup>

### Discoid lupus erythematosus

Diagnosis of DLE is usually based on clinical features.<sup>9</sup> Typical presentation involves a rash on areas exposed to sunlight that is red, scaly, patchy and can sometimes be itchy and painful. The lesions may become hypertrophic and wart-like, and can cause hair loss if the scalp is involved.<sup>6</sup>

When the patches clear they may leave skin that is thin, scarred or of a different colour; however, the person's general health is usually not affected. A skin biopsy for histology is performed and blood tests conducted to check for systemic disease.<sup>2</sup> About 20% of patients with DLE have a positive ANA test and there may be low complement levels.<sup>9</sup> Blood tests should be repeated periodically to check for systemic disease.<sup>9</sup>

### Management of lupus

A variety of medications are used in the treatment of SLE; the medication chosen will depend upon the severity of the disease. Treatment is aimed at reducing inflammation and avoiding a flare-up, and may change over time depending on the disease.<sup>13</sup>

Usual treatment involves non-steroidal anti-



### Corticosteroids, such as prednisolone, are used in the management of the inflammatory symptoms

inflammatory drugs (NSAIDs), corticosteroids, antimalarials (such as hydroxychloroquine) and immunosuppressants (such as azathioprine and cyclophosphamide).<sup>6</sup> Belimumab and rituximab are two newer, biologic drugs that are used in the treatment of SLE.<sup>6</sup>

Mild SLE is considered as clinically stable with no life-threatening organ involvement and mainly involves mucocutaneous lesions, mild pleuritis and arthritis. For those with mild disease, hydroxychloroquine and methotrexate are recommended, along with short courses of NSAIDs for symptom control. Low-dose prednisolone (less than 7.5mg/day) may be required for maintenance therapy.

Topical preparations may be used for skin involvement and intra-articular injections for arthritis. Patients should also be advised about sun avoidance and the use of protective clothing to avoid UV radiation-induced lesions, as well as

the use of a UVA and UVB sunscreen.<sup>6</sup>

In moderate disease, higher doses of prednisolone (up to 0.5mg/kg/day) may be used, as well as using IM or IV doses of methylprednisolone. Immunosuppressive agents are usually required to suppress active disease; drugs such as methotrexate, azathioprine, mycophenolate mofetil and other calcineurin inhibitors can be used if response to hydroxychloroquine has been insufficient.

Two biologic drugs, belimumab and rituximab, may also be considered for refractory cases.<sup>6</sup> Belimumab works by inhibiting B-lymphocyte stimulator, which is responsible for stimulating antibody production, while rituximab works by targeting and depleting those cells that play a role in autoantibody production.<sup>10</sup>

Treatment of patients with severe SLE that is organ or life threatening involves high-dose prednisolone (up to 1mg/kg/day) to induce

remission, which may be used in combination with another immunosuppressive drug. Treatment depends on the underlying aetiology and may involve mycophenolate mofetil, cyclophosphamide or either of the biologic therapies mentioned earlier.<sup>6</sup>

Treatment of DLE involves topical ointments or creams. Potent steroids often help and topical calcineurin inhibitors, such as tacrolimus or pimecrolimus, are often used for the lesions. Hydroxychloroquine can be used and is sometimes combined with mepacrine, another antimalarial, if hydroxychloroquine is not clearing the lesions completely. In severe cases, azathioprine, mycophenolate mofetil or methotrexate may be used. Cosmetic camouflaging is an option if scarring occurs.<sup>2</sup>

### Research into future treatments

New therapies to control lupus activity are needed to reduce the requirement for treatment with corticosteroids. Several new treatments for SLE are undergoing clinical trials. For example:

- Rontalizumab is a humanised IgG1 anti-interferon alfa monoclonal antibody that has been associated with improvements in disease activity, reduced flare ups and decreased corticosteroid use.
- Voclosporin is a calcineurin inhibitor that has been granted fast track approval by the FDA in the USA for the treatment of lupus nephritis (inflammation of the kidneys caused by SLE) and is currently undergoing phase II trials in the UK.<sup>14</sup>
- Sifalimumab is a fully human IgG1 kappa monoclonal antibody that is being investigated for its use in severe SLE.<sup>5</sup>

### Advice and support for patients

Pharmacists are ideally placed to increase awareness of lupus erythematosus and provide patients with practical advice about how to best manage the condition and their medicines. Providing patients with information about their

disease and how to recognise flare-ups, as well as pointing them in the direction of available resources, encourages them to take responsibility for the management of the condition, which can help to improve outcomes.<sup>5</sup>

Lupus UK is the national charity for people living with lupus erythematosus. Its website has a wealth of information, including downloadable patient information leaflets and booklets covering a variety of topics.

Photosensitivity is a common trigger of all forms of lupus erythematosus; patients should be advised to dress appropriately to protect themselves from the sun and to use a sunblock that is effective against UVA and UVB rays, and has a sun protection factor of at least 15.<sup>5</sup>

Some patients may suffer from dry mucous

membranes, in which case lubricant eye drops or artificial saliva may prove beneficial.<sup>4</sup> A thorough oral care regimen, including regular visits to a dental practitioner, is recommended for all symptomatic patients with SLE. The use of lidocaine ointment may prove beneficial in the treatment of oral ulcers.<sup>5</sup>

Many of the drugs used to treat lupus erythematosus suppress the immune system, putting patients at increased risk of infection. Patients should be given general advice about maintaining a healthy and balanced diet, and advised to undertake regular, supervised exercise.<sup>5</sup>

Patients who smoke should be advised to quit – smoking has been shown to exacerbate cutaneous lupus erythematosus, as well as reduce the effect of hydroxychloroquine.<sup>5,6</sup>

## Lupus CPD planned learning

### What are you planning to learn?

I want to learn more about lupus erythematosus, including who is affected, how common the condition is, its different forms and their causes and symptoms. I also want to improve my knowledge of how lupus is diagnosed and treated, as well as the advice and information that pharmacists can offer to patients.

This learning will help me to improve my knowledge of SLE and to be able to confidently provide advice to patients and carers, to spot at-risk patients and know when to refer.

### How are you planning to learn it?

- I plan to read more about SLE on the Patient website at [tinyurl.com/lupus100](https://tinyurl.com/lupus100).
- I plan to read more about discoid lupus on the Patient website at [tinyurl.com/lupus101](https://tinyurl.com/lupus101).
- I plan to find reliable sources of information and support for patients with lupus, such as Lupus UK at [tinyurl.com/lupus102](https://tinyurl.com/lupus102) and NHS inform at [tinyurl.com/lupus103](https://tinyurl.com/lupus103).

### Give an example of how this learning has benefited the people using your services

A patient recently diagnosed with SLE asked for advice about protecting her skin from the sun, now that the weather is getting warmer. I was able to discuss UVA and UVB sunblocks and help her make a decision about which sun cream to buy. She also mentioned her eyes and mouth had been very dry. I explained this could be part of the lupus condition and suggested she make an appointment with her GP. I discussed maintaining good oral care and regular dental appointments, as well as signposting her to further sources of information.

## References

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## Take the 5-minute test online

1. Systemic lupus erythematosus (SLE) is more common in people of south Asian and African-Caribbean descent.  
**True or false**
2. Drugs that may cause SLE include minocycline, isoniazid, phenytoin, carbamazepine and sulfasalazine.  
**True or false**
3. Discoid lupus erythematosus (DLE) usually presents in people aged 40-60 years.  
**True or false**
4. DLE is more common in people who smoke.  
**True or false**
5. Patients with SLE die on average 15 years earlier than the mean in the UK.  
**True or false**
6. One of the key diagnostic factors of DLE is a butterfly rash that appears across the face.  
**True or false**
7. The antinuclear antibodies (ANA) test is positive in almost all cases of patients with DLE.  
**True or false**
8. For patients with mild SLE, hydroxychloroquine and methotrexate are recommended treatments.  
**True or false**
9. Antimalarials, such as hydroxychloroquine and mepacrine, are not suitable for use in the treatment of DLE.  
**True or false**
10. Patients with lupus erythematosus should use a sunblock effective against UVA and UVB, with a sun protection factor of at least 15.  
**True or false**

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