Lupus and the Skin

A Patient's Guide to Skin Involvement in Lupus

LUPUS UK

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This booklet has been produced by LUPUS UK

LUPUS UK is the national charity supporting people with systemic lupus and cutaneous lupus and assisting those approaching a diagnosis.

For more information contact:

LUPUS UK, St James House, Eastern Road,
Romford, Essex, RM1 3NH

Tel: **01708 731251**
Email: **HeadOffice@LupusUK.org.uk**

www.LupusUK.org.uk

Reg. charity nos: 1200671

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Please contact National Office should you require further information on the sources used in the production of this booklet or for further information about lupus. LUPUS UK will be pleased to provide a booklist and details of membership.

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Introduction

Lupus is an autoimmune condition. In patients with autoimmune conditions, a part of the immune system 'misfires' and attacks normal cells in the body rather than helping to fight infections. Generally, lupus is not an inherited condition, but about 3-10% of patients will have a family history of lupus and the genetics are complex and not fully understood. It is important to recognise that lupus is not infectious or contagious and therefore skin problems, which are often visible to others, cannot be passed on or "caught" like an infection.

There are two main ways of classifying skin (cutaneous) lupus. Firstly, the skin lesions can be acute, subacute or chronic. Secondly, lupus skin disease can occur without disease elsewhere in the body or can occur as skin disease with lupus also affecting other organs (systemic lupus erythematosus, SLE).

Some skin lesions and rashes are very suggestive of a diagnosis of lupus (lupus-specific). However, patients with lupus can also have skin problems that are seen in other diseases and are not necessarily a sign of lupus when seen in isolation (non-specific for lupus). All forms of the disease can be aggravated by exposure to sunlight.

The disease can vary in severity and be mild in some patients, resolving spontaneously or easily treated with the use of creams. Other patients may have more severe disease, requiring treatment with drugs that are given orally or through a vein (intravenously). The severity of the disease in a single person can also wax and wane with time.

If you develop a new rash, you should go to your GP or consultant to get checked for appropriate diagnosis and treatment, as the new rash may not be related to lupus or may require different treatment to other skin involvement you have. If lupus of the skin is suspected, your GP is likely to refer you to a Dermatologist (skin doctor) who may then recommend a skin biopsy and blood tests. The biopsy is usually carried out under local anaesthetic and is done to rule out other conditions which can mimic skin lupus. The blood tests are carried out to look for potential disease elsewhere and also to look for proteins in the blood that support the diagnosis.

Cutaneous lupus without disease elsewhere

There are several forms of lupus of the skin which occur without people ever developing disease in other organs. A person can have one or more of the different forms of cutaneous lupus simultaneously or at different times of their life. A small minority of patients, perhaps up to 10%, with these forms of skin lupus can develop disease elsewhere in the future but there are currently no reliable ways of predicting which patients will progress. The forms of skin disease which can manifest solely in the skin are outlined below:

1. Discoid lupus erythematosus (DLE)

This form of skin lupus most commonly affects the head and neck, although it can occur anywhere on the body. On white skin, DLE presents as red scaly lesions (plaques) which can heal with scarring. On brown or black skin the redness may be harder to see and DLE can present as darker patches with scale and scarring. If scarring occurs it is permanent. The scalp can be affected and this can cause scarring and permanent hair loss if left untreated. In patients with black or brown skin particularly, there can be changes in the colour of the skin which can take a long time to resolve, even after the condition has been adequately treated. The skin can become darker (postinflammatory hyperpigmentation) or lighter (postinflammatory hypopigmentation), and there is no proven treatment for the colour change, other than waiting for it to naturally resolve. This can take many months or even years.

DLE can be associated with systemic symptoms suggestive of SLE in perhaps 5-20% of cases. Some patients have widespread discoid lupus affecting several sites on the body (generalised DLE), while some have a small number of plaques in a limited area (localised DLE). The risk of systemic lupus with localised DLE is about 5%, whereas patients with more generalised disease have a 10-20% risk of developing systemic lupus.

Figure 1: *Two patients with DLE of the cheek shown on opposite page. Note the redness of the rash is more visible in white skin (figure 1b) whereas in brown skin (Figure 1a) the rash appears darker:*

Figure 1a):

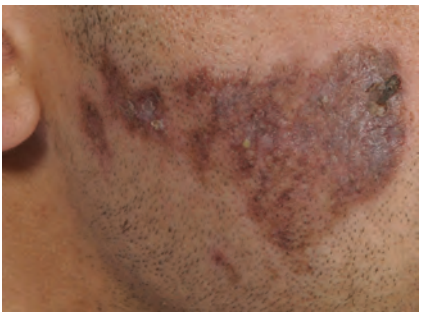


Figure 1b):

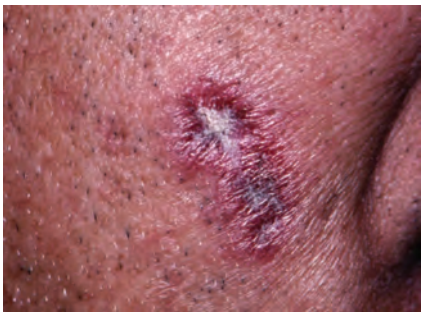


Figure 2: *Patient with postinflammatory hypopigmentation and ongoing active disease*

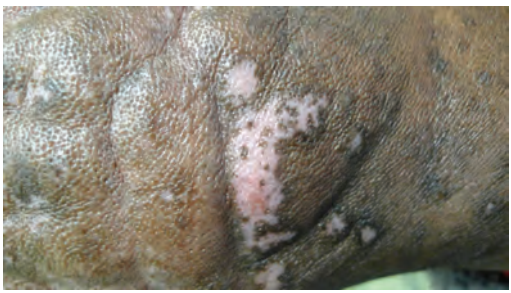
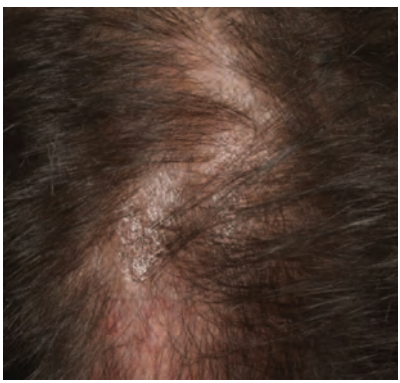


Figure 3: *A case of DLE of the scalp showing scaling on the crown*



2. Hypertrophic lupus erythematosus

In some patients, skin lesions can look warty and raised. On the hands the lesions can mimic viral warts, as in the picture below. Because the two can look different when looking under a microscope, a skin biopsy helps distinguish between viral warts and lupus.

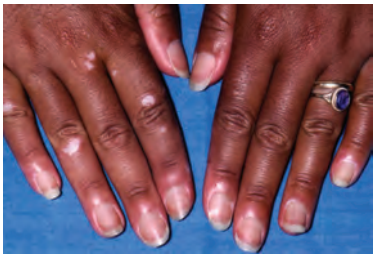


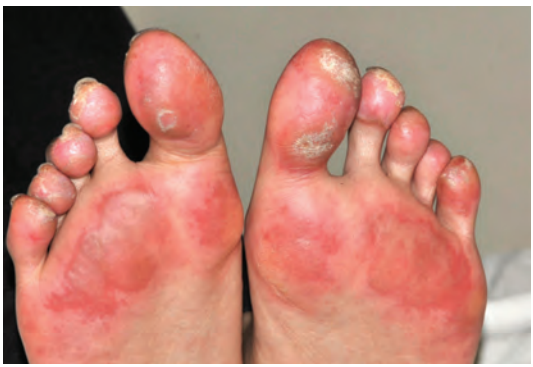
Figure 4: *Hypertrophic lupus erythematosus affecting the hands*

3. Chilblain lupus

This can occur with skin lupus alone or with systemic lupus. It tends to present with scaling and purple-red lesions on the tips of the fingers and toes. It can be painful and is often aggravated by cold weather, but it can persist for months after the weather improves. In severe cases it may cause breakdown of the skin (ulceration). About 15% of patients with chilblain lupus will develop systemic disease.

Chilblain lupus can be treated with steroid creams, a drug called nifedipine which belongs to a class of drugs called calcium channel blockers and often used for high blood pressure, or other medications used to treat skin lupus such as hydroxychloroquine (see section on treatment with tablets on page 17). Keeping your hands and feet warm during cold weather can also help.

Figure 5: *A patient with white skin and chilblain lupus affecting the feet. In brown or black skin the redness can appear more dark purple (violaceous) in colour*



4. Lupus panniculitis

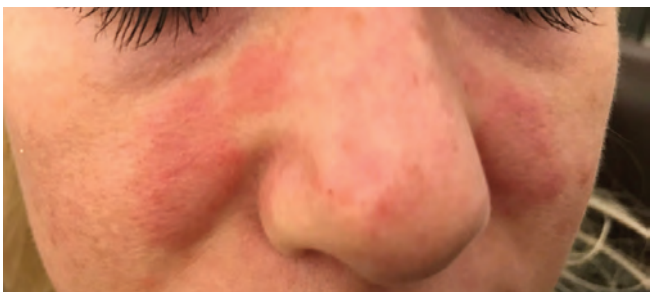
This is also known as lupus profundus. It presents with firm lumps underneath the skin, sometimes with overlying skin changes similar to those seen in discoid lupus. These lumps can heal with loss of fat in the affected area, causing indentation of the skin at the affected site. Patients with lupus panniculitis are thought to be at higher risk of developing systemic lupus.

Figure 6: *A patient with lupus panniculitis of the left side of the back. This can be difficult to see and is more obvious when feeling the skin which feels lumpy and hard*

5. Lupus tumidus

This presents with red, raised, nodular lesions that lack scaling, most commonly on the face. It is very rarely associated with systemic lupus. The lesions are often provoked by sun exposure and are located on sun exposed sites of the body. They resolve without scarring. Most patients with this form of skin lupus will respond to treatment with hydroxy-chloroquine (see page 17).

Figure 7: *A patient with lupus tumidus affecting the face*



6. Subacute cutaneous lupus (SCLE)

Patients with SCLE generally have a good prognosis, although perhaps 50% of such patients will experience some features of systemic lupus including fatigue, arthritis and fever. Severe disease of other organs is less common (approximately 10%).

Many patients with this form of lupus will have antibodies in their blood called anti-Ro and anti-La antibodies. SCLE can be caused by numerous drugs, so it is advisable to let your doctor know which medications you take to rule this out, because stopping the offending drug can lead to complete resolution of the disease.

SCLE is non-scarring and presents with a red, scaly, ring-like rash on the body that can be mistaken for widespread ringworm, particularly in sun-exposed sites. The redness is easier to see on white skin. On brown or black skin the affected areas may appear as dark brown rings with scale. As it heals, it may leave behind paler patches of skin (hypopigmentation) and dilated fine blood vessels (telangiectasia) on the surface of the skin which can take some time to resolve. SCLE can be localised to a few body sites or be widespread and dramatic. It can occasionally look very similar to psoriasis and present with red scaly plaques that have a silvery scale.

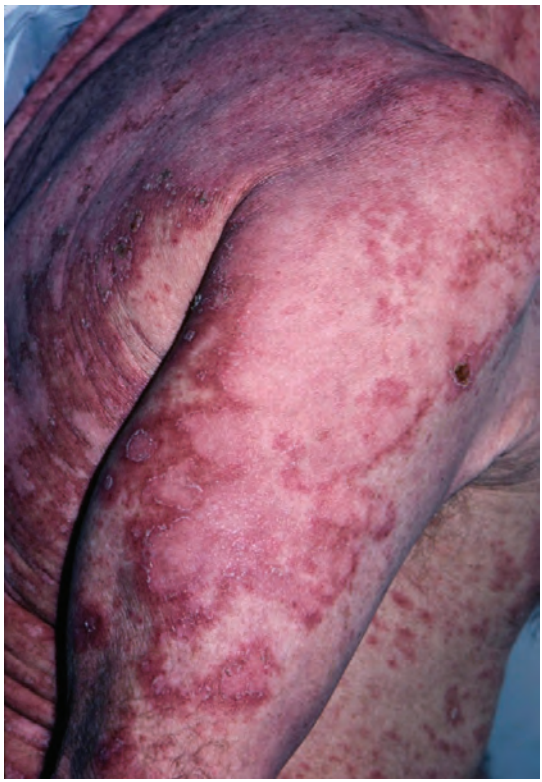


Figure 8: *A patient with subacute lupus erythematosus*

Neonatal lupus

Antibodies are proteins normally produced by the immune system as a response to infection, but in autoimmune conditions like lupus these proteins can attack a person's own cells causing lupus as a result. Anti-Ro antibodies can be seen in lupus but are also found in Sjogren's disease. Newborns can be affected by antibodies to Ro (SS-A) circulating in the mother's blood.

Antibodies are passed from the mother to the fetus naturally, to enable babies to fight infections. However, disease-causing antibodies such as anti-Ro antibodies can also be transferred and are associated with two conditions. Firstly, there is a very low risk (2%) of the anti-Ro antibody causing damage to the baby's electrical heart rhythm, called heart block. Secondly, around 8% of women with anti-Ro antibodies may give birth to babies with a skin rash and occasionally other features such as transient low blood counts and liver tests, called neonatal lupus. The anti-Ro antibodies which cause neonatal lupus are cleared from the newborn's circulation at 6 months of age, as a result of which the skin rash and other abnormalities also clear because the anti-Ro antibodies are no longer present. The newborns of these mothers should have regular check-ups after birth.

The rash of neonatal lupus can appear at birth or several weeks later and can be made worse by exposure to sunlight. The rash often affects the head and neck and consists of scaly red plaques. It fades spontaneously and in most cases the skin changes resolve by 1 year of age, although the affected skin may show residual thinning (atrophy) and darkening of the skin for some time later. The condition usually needs no treatment but, if more severe, discussion with the paediatrician is advisable as steroid creams may be needed for a very short period but are ideally avoided.

There is some evidence that newborns with neonatal skin lupus are at slightly higher risk for developing non-lupus related autoimmune conditions but this is not common. Any symptoms should be monitored and reported to the GP or health professional.

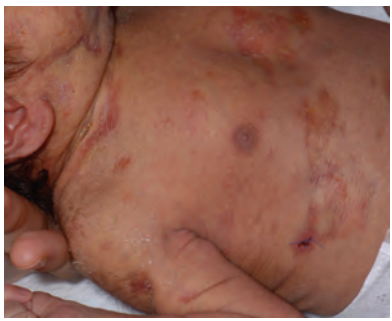


Figure 9: *A baby with neonatal lupus:*

Non-specific skin conditions that can occur in the context of lupus

1. Non-scarring alopecia

This is hair loss that is reversible as there is no scarring of the scalp. It can be seen in patients with SCLE and systemic lupus erythematosus, particularly if the lupus is active. In lupus, non-scarring hair loss can affect large areas of the scalp but can be reversible if the lupus is adequately treated.

There are many other causes of non-scarring hair loss and this is not a specific feature of lupus. In particular, stress, illness, and drugs can cause a type of hair loss called telogen effluvium where hair sheds at a faster rate.

2. Palmar erythema

This is redness of the palms. It can be seen in patients with lupus, but it is also a feature of many other diseases and is not specific to lupus. It does not require treatment and is often a sign of an overactive circulation due to an underlying inflammatory condition.

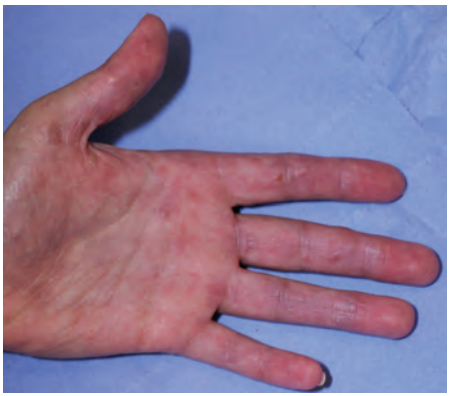
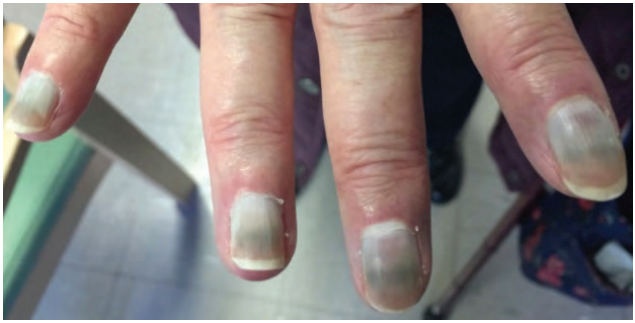


Figure 10: *A patient with palmar erythema*

3. Nail changes

Patients with lupus may develop changes in the nails which are not specific to lupus. These include redness and thickening of the cuticles of the nails, ridging of the nails, and pigmentation of the nails. Many other conditions can affect the nails, for example, psoriasis can cause nail pits, while fungal nail infections cause damage to the nails, and so if these problems occur, they may not be due to lupus. Some antimalarial medication (see page 17) also causes discolouration of the nails which usually occurs after many years on the drug but is difficult to eradicate, even when the drug is stopped as in the pictured case on the opposite page.

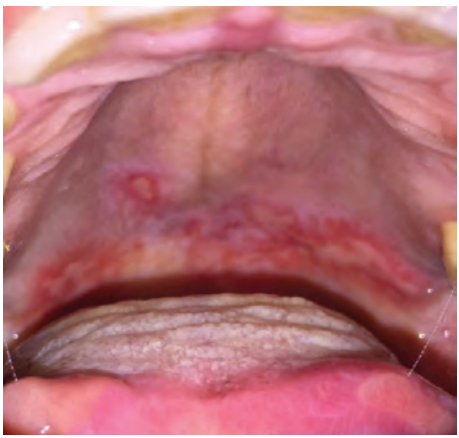
Figure 11: *Discolouration of the nails due to antimalarial medication*



4. Oral and nasal ulcers

Patients with lupus can develop ulcers (open sores) within the mouth or inside the nose. Most commonly, the roof of the mouth (hard palate) is affected. These are usually painless and often occur when the lupus is active. They can be treated with steroid pastes or pellets such as hydrocortisone buccal, rinses including steroid mouthwash (such as Predsol), or non-steroid mouthwashes including Difflam or chlorhexidine, or equivalent sprays. Medication used to treat lupus should also help to bring the condition under control and reduce the frequency of the ulcers. Whilst recurrent oral ulcers are a common feature of lupus, they are also seen in many other conditions and can have other causes including iron deficiency. Medications, some of which are used to treat lupus, including methotrexate (see page 18), can also cause mouth ulcers and this may need a change in medication or an increase in the frequency of folic acid supplements to help.

Figure 12: *Oral ulcers in a patient with active SLE*



5. Vasculitis

This is an inflammation of the blood vessels which can be localised to the skin or affect other organs. In white skin, it can appear as small purple lesions on the skin which do not turn white or paler (blanch) with pressure, or as red discolouration arranged in a fishnet pattern (livedo reticularis), or as deep red lumps underneath the skin. In brown or black skin the discolouration tends to be dark brown or purple as redness can be more difficult to see. In some patients, vasculitis may result in ulcers. Vasculitis has many other causes and in isolation is not diagnostic of lupus.

In lupus, vasculitis can be caused by direct effects on the blood vessels by proteins (primary inflammatory vasculitis) or it can be due to blockages of the vessels (vasculitis secondary to thrombosis). It is important to distinguish between inflammatory and thrombotic vasculitis, as the treatment for these two conditions is different. Over 40% of lupus patients have antiphospholipid antibodies ("sticky blood"), which are also commonly associated with livedo reticularis and thrombotic blood vessel changes. It is important to check for these in a simple blood test if the rash is present, particularly if there is also a history of recurrent miscarriages or thrombosis. A biopsy and blood tests can help doctors to differentiate between inflammation and thrombosis.

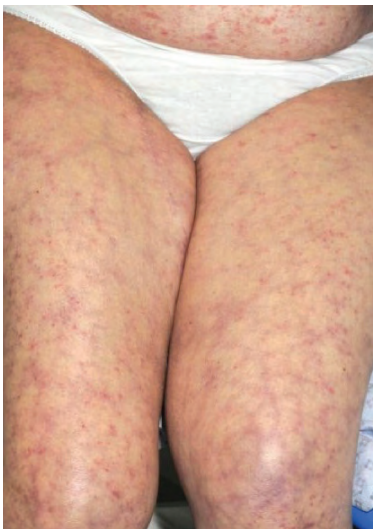
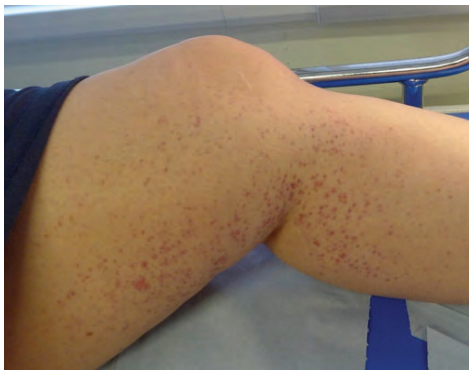


Figure 13: *The rash of livedo reticularis in white skin. In brown or black skin the rash can be dark brown or purple in colour.*

Figure 14: *Vasculitic rash in white skin*



6. Erythromelalgia

This is a condition characterised by burning pain and redness in the feet and/or hands that is worse in warm temperatures. Patients typically describe immersing their hands and feet in cold water to relieve their symptoms. This condition is not specific to lupus and is seen in patients with other conditions.

7. Skin issues as a side effect of medications used to treat lupus

Patients with lupus can also develop skin conditions due to medications used to treat the lupus. For example, oral steroids can cause stretch marks (striae) and thinning of the skin if used at high doses for prolonged periods of time. Oral steroids can also cause easy bruising and acne, which are reversible on reducing the dose of steroids or stopping the drug. Steroid dose reduction, for example during a flare of lupus, can sometimes make psoriasis flare as well if patients have this common skin condition. Methotrexate can cause mouth ulcers and these resolve on stopping the medication. Mepacrine can cause orange discolouration of the skin which is reversible on stopping treatment. Hydroxychloroquine can very occasionally cause an itchy, raised type skin rash (urticarial rash) after 2-4 weeks on the drug which necessitates stopping the drug. In addition, skin rash hyperpigmentation (darkening) of the skin, roof of the mouth, or nails can also occur with hydroxy-chloroquine, and although this can resolve over time on stopping treatment this is not always the case.

Skin problems occurring in systemic lupus erythematosus (SLE)

Although the manifestations of lupus already described, including discoid lupus and subacute lupus, can occur in isolation or less commonly with SLE, others are more usually associated with more widespread signs and symptoms consistent with systemic lupus erythematosus (SLE). There are criteria for diagnosing SLE, such as the American College of Rheumatology (ACR) guidelines, but because lupus can vary a lot between different people (is very “heterogenous”) these narrow criteria really only apply to clinical studies where similar types of lupus are often studied and so will miss many SLE patients. However, some symptoms are more commonly seen in SLE patients and would arouse a suspicion of SLE rather than localised skin lupus. These include joint

pains, hair loss, chest pains, headaches, and fevers, amongst others.

About half of patients with SLE will present with skin rashes, and up to 85% of patients with SLE will develop skin involvement at some point.

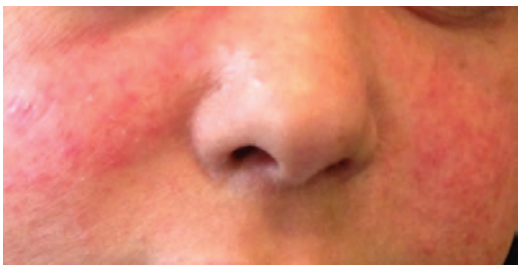
Photosensitivity-induced rash (Acute cutaneous lupus)

Sunlight sensitivity (photosensitivity) can cause an acute cutaneous lupus rash, often called a malar rash. There may be involvement of other sun-exposed sites. A malar rash usually occurs in active SLE. It is important to distinguish the lupus malar rash from other rashes which occur in the same areas and can look identical, such as rosacea and polymorphic light eruptions (PLE). The malar rash seen in lupus appears as redness and scale that tends to spare the skin creases that run from the nose to the edges of the mouth (nasolabial folds). Patients may also notice swelling of the skin (oedema) after exposure to sunlight. This can be especially striking on the face.

There may be a delay of several weeks between exposure to sunlight and the appearance of a rash, and patients often do not notice the correlation with sun exposure.

Exposure to sunlight can worsen disease in other organs. The reason for this is that UV rays penetrate the skin and change the behaviour of some immune cells, triggering a lupus flare. Treatment of the malar or other acute rash is to control the lupus with drugs outlined later and to practice sun-avoidance and use high factor sunscreen.

Figure 15: *The classical malar rash in a white patient with active SLE. Note that in black or brown skin the redness can be more difficult to see.*



Raynaud's phenomenon

Patients with Raynaud's develop characteristic colour changes in their fingers and toes, usually with exposure to cold. The fingers and/or toes tend to become pale, then blue with some numbness and pain, and then finally red when the hands and feet are rewarmed. The cause of these

changes is a narrowing of the small blood vessels in the fingers followed by the vessels opening up again, but the reason why it happens is not clear. Raynaud's can occur on its own (primary Raynaud's) or be seen in association with many autoimmune conditions (secondary Raynaud's) and so is not specific to lupus but is found in about 15-40% of SLE patients.

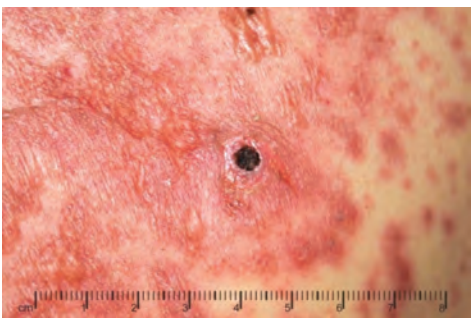
Secondary Raynaud's can cause a lack of blood supply in the hands or feet and lead to ulcers if it is severe. Urgent treatment is sometimes needed to prevent complications including loss of part of a digit. Other body sites can be affected, including the tip of the nose, the ears, and even very rarely the tongue.

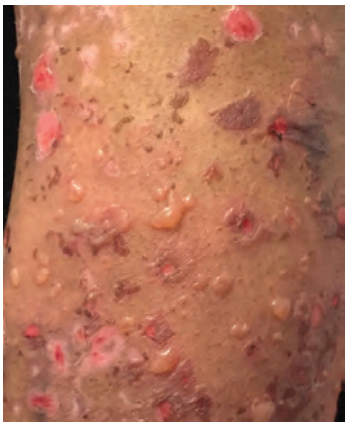
Treatments for Raynaud's open the blood vessels to increase blood supply. Some people find benefit with over-the-counter therapies such as ginger, vitamin C or vitamin E. However, for more troublesome cases, several drugs are used including GTN patches or ointment, tablets including nifedipine, losartan or fluoxetine, or intravenous therapy including iloprost which requires hospital admission. Newer treatments which have some evidence in small studies include sildenafil (Viagra) tablets or Botox injections.

Blisters

Blister formation accounts for less than 1% of skin lupus. Blisters in lupus patients can also be due to other causes, including drug rashes, and a skin biopsy may be required to differentiate between the various causes of blisters in lupus patients. Amongst the more severe blistering lesions, bullous lupus is a rare form of blistering systemic lupus which can cause scarring. It can affect the face, arms, trunk and legs. It can also be resistant to normal lupus treatments and require drugs such as dapsone, cyclophosphamide or rituximab.

Figure 16: *Two patients with active SLE and blistering rashes*





Factors affecting Cutaneous Lupus

Sunlight exposure

Both UVA and UVB rays can exacerbate skin lupus and we encourage patients to use sunscreens to protect against both. There can be several weeks between exposure to the sun and a flare of skin lupus so many patients who think they aren't sun sensitive actually are. Exposure to UV rays can cause damage to DNA in cells and this in turn leads to cell death. The accumulation of dead cells provokes a natural immune response. This can include the production of antibodies against components of the cells and the DNA within cells. These antibodies can then attack normal cells and cause the signs and symptoms of lupus. Patients with SLE seem to be more prone to DNA damage than the general population. In addition to this, patients with SLE seem less able to repair DNA damage than the general population, and the increased tendency to accumulate damaged DNA with UV exposure is thought to play a role in the development of lupus.

The ability of a sunscreen to protect against UVB is measured using Sun Protection Factor (SPF) and it is recommended that patients use a high factor (SPF 30 or 50), re-applying cream every 2 hours when it is very sunny (UV index report of 3 or more). The star rating of a sunscreen is an indication of its ability to protect against UVA. A sunscreen with at least a 4-star rating is recommended in photosensitive individuals. You can expect to need a shot glass (approximately 30ml) of sunscreen per application for the entire face and body. It is important to apply sunscreen on sunny days even if you are in the shade, as light can reflect from surfaces such as sand and water. Patients can also consider using UV protective clothing. Be mindful of expiry dates of sunscreens as most products will only last for 2-3 years.

Remember that UVA rays can penetrate through glass. In addition, UV light exposure can occur indoors from fluorescent lighting or halogen bulbs. Incandescent (tungsten) bulbs emit lower amounts of UV and are safer for patients with photosensitivity. High intensity discharge (HID) lamps, used in street lights and in large commercial areas such as supermarkets, are safe for patients with photosensitivity.

There are products such as films that can be applied to windows to protect photosensitive individuals from UV light, such as Dermagard and Llumar window film. These are polyester coatings applied to existing glass

which block more than 99% of UV light while still allowing clear vision through the glass. They can even be applied to car windows if needed.

In addition, a wide variety of medications have been associated with light-sensitivity. These include antibiotics such as doxycycline, blood pressure tablets including diuretics, and antidepressants such as venlafaxine. However, these reactions are likely to be rare and, in all cases, if there is concern a drug may have made your skin more light-sensitive or your skin rashes worse after starting a drug, consult your GP or lupus specialist.

Smoking

Smoking can make lupus skin disease worse. In addition, lupus is less likely to respond to some of the treatments we use for skin lupus, such as hydroxychloroquine. It is important to bear in mind that lupus increases heart disease risk, which is increased further with smoking.

Commonly used treatments for skin lupus

Creams (topical treatment)

Topical treatment (creams rather than tablets) can be used to treat a large number of patients with skin lupus. The mainstay of treatment is topical steroids. Steroids are hormones that are naturally produced by the body. Steroid creams come in different strengths and the more potent steroids can be very effective at preventing damage to skin caused by lupus (such as scarring and pigmentary changes) but run a higher risk of steroid-induced thinning of the skin (atrophy - see below). Topical steroids are classed as mild, moderately potent, potent, and very potent. The potency of a steroid cream is indicated in the information sheet provided with the medicine and is not reflected in the percentage of steroid on the label on the product packaging. Steroid creams can be named using trade names, which the manufacturers have given the product, or a generic name, which is the official name of the medicine, often indicated in small print on the packaging.

The main concern with use of topical steroids, particularly where the skin is more fragile such as on the face and around the eyes, is thinning of the skin (steroid-induced skin atrophy). As these creams do not have many of the systemic problems associated with tablet steroids, these creams are the safest way to treat lupus effectively and steroid-induced atrophy is rare in patients managed by a specialist. Over-use

of steroids around the eyes is best avoided due to the risk of eye side effects (glaucoma, cataracts).

If patients have a small number of affected areas, doctors will sometimes treat the affected areas by injecting them with steroids.

In the UK, two steroid creams are available to buy over the counter. These are 1% hydrocortisone cream, which is mild, and clobetasone butyrate 0.05% cream, which is moderately potent. These creams should be avoided in children, in pregnancy, on more delicate skin sites such as the face and genital area, and on broken or infected skin unless this is under a doctor's supervision.

The more commonly prescribed steroid creams are listed below, with their potency indicated in the 3rd column (adapted from the National Eczema Society factsheet on topical steroids):

Trade name	**Generic name**	**Potency**
Hydrocortisone - strengths ranging from 0.1%-2.5%	Hydrocortisone- strengths ranging from 0.1%-2.5%	Mild
Betnovate- RD®	Betamethasone valerate 0.025%	Moderate
Eumovate®	Clobetasone butyrate 0.05%	Moderate
Haelan® (available as cream, ointment and tape)	Fludroxycortide 0.0125%	Moderate
Betacap® (scalp application)	Betamethasone valerate 0.1%	Potent
Betnovate®	Betamethasone valerate 0.1%	Potent
Diprosalic® (ointment and scalp preparation)	Betamethasone dipropionate 0.05%	Potent
Elocon®	Mometasone furoate 0.1%	Potent
Nerisone®	Diflucortolone valerate 0.1%	Potent
Synalar®	Fluocinolone acetonide 0.025%	Potent
Dermovate®	Clobetasol propionate 0.05%	Very potent
Etrivex® (shampoo)	Clobetasol propionate 0.05%	Very potent

Steroid creams should be applied so that the skin just glistens following application of the ointment or cream. A good guideline on how much steroid cream should be applied is the use of the fingertip unit. One fingertip unit (FTU) is the amount of cream or ointment that just covers the end of an adult finger from the tip to the crease of the first joint when squeezed from an ordinary tube nozzle
(see picture on opposite page).

Figure 17: *One fingertip unit (FTU) is the amount of cream or ointment covering the area from the tip of an adult finger to the first joint crease.*

One FTU is enough to cover an area of skin the size of two adult palms including the fingers. The amount of FTUs of cream or ointment required for each body site varies as shown in the table below:

Face and neck	2.5 FTU
One hand, front and back with fingers	1 FTU
Front of chest and abdomen	7 FTU
Back and buttocks	7 FTU
Entire leg and foot	8 FTU
Entire arm and hand	4 FTU

Some dermatologists will recommend the use of non-steroid ointments and creams containing calcineurin inhibitors, such as pimecrolimus or tacrolimus. These have an anti-inflammatory action and, unlike steroid creams, do not result in thinning of the skin. However, they occasionally cause a temporary (transient) local burning sensation or increased redness which tends to reduce with continued use. They are not licenced for use in lupus but are widely used by specialists.

Oral, intravenous or intralesional steroid treatment

Your doctor may prescribe a short course of oral steroids to bring your skin lupus under control. Oral steroids can cause side effects such as osteoporosis when used long-term at high doses, but daily doses of prednisolone of 7.5mg or below generally have far fewer side effects. Short courses of 8 weeks or less and steroids given through a drip (intravenously; IV) intermittently are also generally very safe. These short courses are often prescribed along with other tablets for lupus listed in the next few pages, because the other tablets can take weeks to have an effect, whereas steroids usually work within a few days. Occasionally, when patients have a very stubborn, persistent area of lupus, for example on the scalp, it can be injected directly with steroid (intralesional steroid).

Antimalarials

Hydroxychloroquine is a tablet that is generally well tolerated. The main concern regarding hydroxychloroquine in long-term use is problems with vision and the eye but, in general, with doses less than 5mg/kg body weight these problems are very rare. Your doctor will

advise you to have an eye check with an ophthalmologist at 5 years on the drug (earlier in some patients), but the drug is compatible with pregnancy and should not be stopped unless there are problems with it.

Mepacrine is less commonly used. It can be prescribed alone or in combination with hydroxychloroquine. Mepacrine generally does not affect the eye so it can be a good alternative in patients with eye problems or who don't tolerate hydroxychloroquine (for example, due to nausea). It can cause a mild orange discolouration of the skin, reversible on stopping the drug. It is not known if mepacrine is safe in pregnancy so is normally stopped before conception.

Chloroquine is another antimalarial medication. It is probably the most effective for skin lupus, but it has a higher risk of eye complications and so it is rarely used in the current era.

Oral immunosuppressive drugs: Methotrexate, Mycophenolate Mofetil, Azathioprine

These are well-established drugs in the treatment of lupus. All have been shown to help skin lupus in small studies as alternatives to, or in addition to, antimalarials. All are immune-suppressing drugs widely used for many autoimmune conditions. Mycophenolate and azathioprine are taken as daily tablets, while methotrexate is a weekly tablet or injection.

All of these drugs can increase the risk of infection which can be more severe when taking these drugs. It is important to ensure your GP provides access to vaccinations such as influenza and pneumonia, and precautions should be taken against unnecessary contact with people who are ill with colds, flu and other infections. If an infection occurs, the medication may need to be stopped temporarily. Blood tests monitoring is required for all of them. While all of them can be effective for the skin, the main advantage of azathioprine is that it is compatible with pregnancy, while mycophenolate and methotrexate must be stopped 3 months before conception.

Thalidomide

Studies show that in skin lupus resistant to other medications, thalidomide can be an effective treatment. In a study of 23 cutaneous lupus patients, 74% of those treated with thalidomide for a month or more showed complete resolution of their disease. In a more extensive analysis of several studies of 548 lupus patients, chronic forms of lupus skin disease responded in 90% of patients when thalidomide was used. However, the rate of adverse events was high at 24% of all patients.

Thalidomide has been associated with significant risks of birth defects in babies born to pregnant mothers who have taken the drug. It is usually avoided in women of child-bearing age but, if ever needed in this group, robust contraception (oral contraceptive, IUD for example) is mandatory. Thalidomide can cause nerve damage (peripheral neuropathy) which can lead to loss of sensation and weakness in 25% of patients. Your doctor may therefore recommend testing your nerve function before and during treatment with thalidomide.

Newer variants of thalidomide, including lenalidomide, may cause less nerve damage and are effective in small studies but relapse is common if the drug is stopped.

Dapsone

This drug is not classed as an immunosuppressant, but it does have anti-inflammatory effects. Small studies in lupus support its use. In a study of 34 patients, 18% showed complete resolution of skin disease with dapsone used alone or in combination with anti-malarial drugs. Another 41% showed improvement in their disease.

Your doctor will do a blood test to check your ability to metabolise Dapsone prior to prescribing it. Dapsone can cause anaemia, shortness of breath, and allergic reactions.

Acitretin

This is a retinoid drug which is rarely used in lupus but can be useful if the skin lupus is resistant to other medications. There are few studies, but one showed that in 14 patients with discoid lupus that is resistant to antimalarial treatments, half of whom also had systemic lupus, of the 13 patients who completed the study, 80% had a marked response.

Acitretin is used mainly in other scaly conditions including psoriasis and may be helpful for thin scaly skin lupus areas, especially as it seems to work in conditions where the keratin skin layer, which produces scaly skin, is overactive. However, if acitretin is used, patients need to avoid conception for 2 to 3 years after they stop treatment. For this reason it is not often used for women of child-bearing age.

Intravenous Immunoglobulin (IVIg)

IVIg is a purified and sterilised formulation of immunological defence proteins, mostly IgG. Injection of IVIg solution dampens the immune

system in several areas, allowing effective treatment for a variety of lupus manifestations including the skin and kidneys. It is often difficult to obtain because of restrictions on prescribing and the supply is limited because the solution is made from a large number of healthy volunteers' blood samples. The limited evidence so far suggests IVIg needs to be taken monthly for 6 months to be effective, but side effects are few.

Cyclophosphamide

Cyclophosphamide has been used for the treatment of lupus for over 50 years. It is generally reserved for more severe lupus not responsive to other therapies such as methotrexate or mycophenolate. Cyclophosphamide can also help severe lupus skin manifestations and is usually given through a drip (intravenously). Side effects include nausea. There is the potential for infertility with cyclophosphamide, but, at the doses normally used for lupus, the evidence indicates this is not common unless repeat courses need to be given.

Rituximab and belimumab

These intravenous drugs are reserved for more severe lupus, helping many aspects of lupus including the skin. Both are antibodies, rituximab being given intravenously (IV) and belimumab either IV or at home via subcutaneous injection. These drugs target immune cells called B-cells which play an important role in causing lupus. Rituximab removes B-cells from the circulation so they cannot do any harm, while belimumab blocks a blood chemical, BlyS, which normally allows B-cells to mature. Side effects can include an allergic reaction to the drug, largely prevented by the use of anti-allergy medication when giving either drug.

Newer therapies and strategies

Newer drugs have shown some benefit with skin lupus in clinical studies.

Anifrolumab, an antibody against the type 1 interferon receptor, has been effective in improving skin disease in studies and is licenced for use in the UK but funding concerns have limited its use and NICE approval for NHS use has not yet been gained. This may change in future.

Other drugs have shown some promise in early studies with a failure to replicate this in later studies meaning they are not licenced or funded for use in the UK at the present time. These include Janus Kinase (JAK) Inhibitors (baricitinib, tofacitinib) which are already used in conditions such

as rheumatoid arthritis. Ustekinumab targets the chemicals IL-12 and IL-23, important to the immune system, and is given three-monthly, with some case reports suggesting improvement of discoid lupus in some patients, though these results were not replicated in later more extensive studies. Injections of anti-TNF-α medication into lupus-affected skin has also shown promise in a recent small study. Despite the lack of effect in large clinical trials, it is likely there will be individuals who do respond to these therapies. Access to the medications in this setting remains challenging, however.

Summary of some of the treatments commonly used in lupus:

Drug	How long does this take to see benefit?	Comments	What are the precautions?	What are the commonest side effects?
Topical steroids	Within 1-4 weeks	Generally very safe if used as prescribed by a dermatologist	- Avoid prolonged use around the eyes (risk of cataracts and glaucoma). - Avoid prolonged use of potent steroids on the face, neck, genitals and body folds (skin flexures).	- Thinning of the skin with prolonged use of potent steroids. - Acne - Local skin infections
Oral steroids	Within 1-4 weeks	High doses should be used in short term only. Often very effective for rapid control of disease.	- Avoid live vaccines. - Care in patients with diabetes, glaucoma, active infection, osteoporosis or heart failure (can exacerbate). - Do not stop treatment abruptly if taking long term	At high doses for prolonged periods there is an increased risk of: - Thinning of the skin - Infection - High blood pressure - Diabetes - Osteoporosis - Gastric ulcers - Weight gain

Hydroxychloro-quine	At least 3 months	Safe in pregnancy		- Nausea - Itchy skin - Annual eye checks needed with use for more than 5 years
Mepacrine	At least 3 months	Can work well in combination with hydroxychloroquine. Generally very well tolerated.		Orange discolouration of skin and nails with long term use
Methotrexate	At least 3 months	Can be given orally or as an injection once a week. Regular blood monitoring required.	- Avoid in pregnancy and active infection - Avoid sun exposure whilst on treatment. - Avoid alcohol whilst on treatment.	- Nausea, gastroin-testinal symptoms. - Fatigue. - Increased risk of infection - Liver dysfunction - Oral ulcers
Mycophenolate mofetil	At least 3 months	Regular blood monitoring required. Men and women taking mycophe-nolate should avoid conception for 3 months after stopping treatment.	- Avoid in pregnancy - Avoid in active infection - Avoid sun exposure whilst on treatment	- Nausea, gastroin-testinal symptoms. - Increased risk of infection. - Shortness of breath. - Liver dysfunction.
Azathioprine	At least 3 months	Safe in pregnancy. Regular blood monitoring required.	TPMT (an enzyme) activity should be checked prior to commencing drug. Avoid sun exposure whilst on treatment	Effects on bone marrow. Increased risk of infection.

Rituximab	8-16 weeks	Given as an infusion	Avoid in active infection. Ideally patients should have covid vaccination 2-4 weeks before treatment	Increased risk of infection. Risk of infusion reaction. Malaise, nausea.
Cyclophosphamide	At least 4 weeks	Given orally or as an infusion	Avoid in active infection	- Nausea - Increased risk of infection - Cystitis (inflammation of the bladder, manifesting as blood in the urine) - Hair loss - Mouth ulcers - Liver dysfunction
IV Immunoglobulin (IVIg)	Within 6 weeks	Given as infusions given in succession over 2-5 days. Blood product made by pooling many blood donations so availability is limited and strictly controlled.	Avoid in IgA deficiency	- Nausea - Flu-like symptoms during the infusions.
Belimumab	Within 6 weeks	Given either as an IV infusion monthly in hospital or subcutaneous injection weekly at home	Ideally patients should have covid vaccination 2-4 weeks before injections start.	Injection reactions, increased risk of some infections but usually mild

Over the counter products and lupus

There is currently no evidence for the use of specific cosmetic products bought over the counter in treating lupus. Using a moisturiser regularly can help keep your skin hydrated and healthy; choose one that is fragrance-free. If your skin is very dry, creams and ointments are more effective than lotions. Avoid harsh soaps and consider using a soap substitute if your skin is dry and irritated.

Wellbeing and psychological factors

Patients with lupus with significant skin involvement have to cope with the lupus being active and taking treatment, but also the significant psychological burden of a visible component of lupus which affects interactions with other people including friends, family, and work colleagues, amongst others.

In some cases, skin lupus can lead to hyperpigmentation or scarring. Many patients can find this deeply distressing. Scarring of the skin is difficult to treat. Hyperpigmentation can take a long time to fade and can be complicated by important treatments such as hydroxychloroquine which also occasionally causes hyperpigmentation. Many patients find it helpful to use skin camouflage for hyperpigmentation and scarring. This is the use of specialist creams and powders which can cover the marks on the skin. These products are designed to be waterproof and can be used whilst playing sport or swimming. They can be prescribed on the NHS following a consultation at a specialised camouflage clinic. Patients with skin disease can be referred to a camouflage clinic on the NHS and can also self-refer via organisations such as Changing Faces (see page 25).

The psychological burden of skin involvement in lupus can contribute to the fatigue many lupus patients feel. In addition, patients with skin lupus have worse quality of life even when compared with other skin conditions such as acne and non-melanoma skin cancer. Factors associated with worse quality of life are more severe skin involvement, younger age, and distribution of lesions. Patients with skin lupus also more frequently have anxiety and depression. This impacts on quality of life, but there is now increasing recognition that medication may work more effectively if the underlying anxiety and depression are treated.

It is therefore essential to ensure that the treatment of skin lupus is

holistic. Medications allied to other strategies, including exercise to improve fatigue and counselling and cognitive behavioural therapy to improve anxiety, depression and quality of life, all help to ensure treatment has a more profound effect on improving well-being.

Places to find further information or support:

LUPUS UK

LUPUS UK offers advice and information to anyone who wants or needs it. We also help people to get in touch with other people with lupus through our Regional Groups, online patient forum, and National Contacts. You can reach us via:

- Helpline: **01708 731251**
- Website: **www.lupusuk.org.uk**
- Forum: **https://healthunlocked.com/lupusuk**
- Eclipse light-sensitivity information: **www.lupusuk.org.uk/eclipse**

Sunscreen

People with lupus who are light-sensitive are eligible to get sunscreen on prescription. This is because lupus meets the criteria set by the Advisory Committee on Borderline Substances (ACBS). Only certain sunscreens can be given on prescription because they must be approved by the ACBS.

Skin camouflage

Skin camouflage (sometimes called cosmetic camouflage) uses highly pigmented creams that are formulated to disguise scars, birthmarks, tattoos and skin conditions including rosacea, pigmentation and vitiligo. Skin camouflage products mimic normal skin tones and are significantly different from ordinary cosmetics.

Changing Faces has about 120 skin camouflage practitioners across England and Scotland, working out of GP surgeries, health clinics, hospitals, Red Cross and Changing Faces offices. The service is provided free of charge and they welcome donations. If you are a UK resident, you can ask your GP or other health or social care professional for a referral to the service. In some areas, you can refer yourself. They also have general information about products available on the high street and video guides. Visit **www.changingfaces.org.uk** or call **0300 012 0275**.

Hair loss support

It can be very challenging to adjust to a new appearance and everybody's coping strategies are different. Alopecia UK has a very helpful section on their website which provides information and advice for dealing with difficult situations, meeting new people and unhelpful thoughts. You can take a look here: **www.alopecia.org.uk/difficult-situations**. The charity also offers support groups and a range of information.

Hairpieces and extensions can be added into thin areas to create a fuller look. Make sure that the hair piece is not too tight because tension on weakened hair can also lead to hair loss. Wigs come in a wide range of styles, colours, lengths and material.

Wigs are available from the NHS but patients need to pay for them unless they qualify for help with charges. Up-to-date costs of NHS wigs and exemption criteria can be found here: **www.nhs.uk/nhs-services/help-with-health-costs/wigs-and-fabric-supports-on-the-nhs**

For private patients the price of the hair solutions can range from £150 to £1200 depending on the solution they require and what type of hair is used. Raoul wigmakers in London offer free, no obligation consultations for hair solutions. You can learn more about this on their website: **www.raoulwigmakers.co.uk**

Mental health & psychological support

It is very common for living with lupus to have an impact on your mental health. You are not alone. Your mental health is just as important as your physical health and you are not wasting anyone's time.

The NHS offers different mental health services, such as counselling and helplines. Sometimes you have to be referred by a GP, and sometimes you can refer yourself. You can find what services are available in your local area and how to access them on this website: **www.nhs.uk/nhs-services/mental-health-services**, by visiting your GP, or by calling **111**.

If you are feeling distressed and have an autoimmune diagnosis, you can receive free, ongoing emotional listening support with a volunteer at **The Wren Project**, a charity supporting people living with autoimmune disease. Self-refer here: **https://www.wrenproject.org/refer**

Notes

Publicity materials, leaflets, posters, a dvd for the newly diagnosed, media releases and more are always available from the charity's National Office for better awareness about lupus in clinics, hospitals and public places.

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