# Systemic lupus erythematosus (SLE) or Lupus

## What is SLE?

LUPUS belongs to a group of disorders of our body's immune system, known as "autoimmune diseases". Normally, the immune system protects our body from harm, by producing antibodies, which attack invaders such as viruses and bacteria. In lupus, these antibodies attack one's own body tissues, causing inflammation and with time, damage, somewhat like an allergic reaction to oneself. This manifests as a multitude of symptoms including joint pains, skin rashes, muscle aches and fatigue.

The name "Lupus" (Latin for "wolf") dates back to medieval times, and refers to the classic rash that is seen in this condition, thought to resemble a wolf's bite. It is more correctly termed "Systemic Lupus Erythematosus", often abbreviated to "SLE": "Systemic" as it affects many parts or systems of the body and "Erythematosus" (Greek for "red") because of the characteristic red colour of the lupus rash.

Not everybody with lupus is affected the same way, which for the sufferer can be quite confusing and difficult to accept. Some people can have a mild form, limited to skin rashes and joint pains; whilst others have a serious and often, life-threatening form of the disease, involving vital organs such as the brain, kidneys and heart. In addition, the disease course can be quite unpredictable. Most patients go through periods where they are unwell (known as a flare) and quiet periods (remissions), whilst a few develop a more progressive, relentless form of the disease. This makes the condition difficult for doctors to recognise and a challenge to treat. To date, there is no cure for lupus, however if diagnosed in good time, there are many available therapies to improve symptoms, quality of life and longevity. People can live well with lupus if they actively work towards good health. Intense research is underway, and scientists are continuing to make great strides in understanding the disease, which may ultimately lead to a cure.

## Who gets Lupus?

A common misconception is that lupus only affects young women. Although most common in women between the ages of 20 and 40 years, lupus can occur in men as well as all age-groups, from childhood to later life. The disease is more common in some ethnic groups, mainly Blacks and Asians, and tends to be worse in these groups. The occurrence of lupus in South Africa is similar to that reported around the world, with kidney involvement being especially prominent. Lupus can run in families, but the risk that a child or a brother or sister of a patient will also have lupus is still quite low.

- *Lupus is 9x more common in women than men*
- *Lupus is two to three times more common in Black people*
- *Risk of giving lupus to your child is low*

## What causes Lupus?

Despite the major strides made by researchers into better understanding lupus, it remains unclear what causes lupus. The central problem is malfunctioning of the body's immune system. In a healthy state, our immune system produces certain fighter cells called lymphocytes and special proteins called antibodies which attack and destroy foreign substances such as viruses, bacteria and cancer cells. In lupus, these lymphocytes and antibodies attack healthy cells and tissues. When antibodies attack our own body cells they are known as autoantibodies. When autoantibodies attack the body's tissues, it results in inflammation, and if not stopped, damage to organs and tissues. It is unclear what is responsible for this "attack on self", but it is probably due to a combination of faults in our genetic code (a unique code that we are born with) and elements in our environment. Studies suggest that a number of different genes are involved in determining a person's likelihood of developing lupus, which tissues and organs are affected, and the severity of disease. Siblings, especially identical twins (with identical genetic code) of lupus patients, have a greater chance of developing lupus than the general population. The fact that this is not the case for every twin pair, suggests that genes alone is not enough to cause lupus. Environmental factors that seem to contribute to the development of lupus include sunlight, hormones, certain medications, and infectious agents such as viruses. Additionally, studies have shown that lupus patients are unable to remove damaged cells, and this debris collection could be the trigger for the immune attack.

## What are the signs and symptoms?

It is not easy to recognise lupus, even for doctors. Any organ system can be affected, in a variety of ways and usually in combinations that differ from one person to the next. Moreover, symptoms and signs come and go and new ones can develop through the years. Apart from the characteristic red skin rash that occurs over the cheeks and nose —the so-called "butterfly" or malar rash, symptoms are non-specific and often mimic other conditions. Table 1 lists the common features of lupus.
Almost every lupus patient complains about fatigue or tiredness at some stage during their illness. Changes in weight can be problematic, with weight loss and low appetite when the lupus is active, and weight gain with certain treatments or swelling from kidney problems. The skin can be very helpful in identifying lupus. Aside from the butterfly rash, rashes can occur over the rest

of the body, particularly areas exposed to the sun. Many lupus patients are sensitive to sunlight (photosensitive) and rashes can worsen after sun exposure. Mouth ulcers can be a sign of lupus, especially if the ulcers are painless. Hair-loss (alopecia) can occur, and for most it is reversible, however there are some patients who have scarring or irreversible hair-loss. A proportion of people with lupus complain of specific colour changes to their fingers (white then blue then red) when exposed to cold weather or stress. This is known as “Raynaud’s phenomenon” and is associated with lupus and other conditions like lupus. The joints are commonly involved in lupus. It could be just painful joints or there could be associated swelling or arthritis. Chest pain and shortness of breath can occur due to involvement of the heart, lungs, or the membranes which surround these organs (pleura or pericardium). There could be damage to the heart valves causing heart murmurs. A very noteworthy finding, is that lupus patients have a greater risk of developing atherosclerosis (hardening of the arteries) which can lead to heart attacks or strokes earlier in life. Inflammation of the kidneys (nephritis) is a major problem in lupus. There is usually no pain associated with kidney involvement and the only indication of a problem, is an abnormal urine or blood test; however, some patients may notice dark urine and swelling around their eyes, legs, ankles, or fingers. Because the kidneys are so important to overall health, lupus affecting the kidneys generally requires intensive drug treatment to prevent permanent damage. Lupus can also affect the brain and any part of the nervous system. Headaches, dizziness, depression, memory disturbances, vision problems, seizures, stroke, or changes in behaviour are just some of the many recognised ways that lupus affects the nervous system. Certain lupus sufferers have a tendency for their blood to clot, while others have a risk of bleeding.

Table 1: Common symptoms and signs of SLE

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| **Skin, mouth and hair**<br>**Rashes (sun-exposed areas + others)**<br>**Photosensitivity**<br>**Raynaud's phenomenon (see text)**<br>**Alopecia**<br>**Ulcers** | **Joints and muscles:**<br>Pain with/without swelling<br>Deforming arthritis resembling rheumatoid arthritis (in 5% lupus patients)<br>muscle weakness |
| **Kidneys**<br>**Dipstick test positive for blood/protein**<br>**Kidney failure**<br>**Body swelling (legs, eyes)** | **Heart and blood vessels**<br>High blood pressure<br>High risk heart disease<br>Shortness of breath, chest pain |
| **Brain and nervous system**<br>**Depression and anxiety**<br>**Stroke or paralysis**<br>**Migraine headaches**<br>**Fits** | **Lungs and pleura**<br>Effusions<br>Disease of lung tissue |
| **General**<br>**Fever, weight changes and fatigue**<br>**Anaemia (low blood)**<br>**Lymph nodes or glands** | **Other**<br>Tendency to form blood clots<br>Bleeding<br>Increased risk of infections |

## How is Lupus diagnosed?

Making a diagnosis of lupus is never easy. One of the most essential elements in diagnosing lupus, is the patient's account of their symptoms. If after a thorough physical examination and review of these symptoms the doctor suspects lupus, you will need to do a series of blood tests to confirm the presence of the disease. The most important blood test is known as antinuclear antibody or ANA. This test measures the presence of autoantibodies to the nucleus or "command centre" of our body cells. If you test positive for ANA you are more likely to have lupus. However, you can test positive and not have the condition. Therefore, if you have positive ANA, you may need to do other more specific tests to prove the diagnosis. These blood tests include antibodies to double stranded DNA (anti-dsDNA) and anti-Sm.
At this stage, you should be under the care of a rheumatologist, a doctor specialising in lupus.

Occasionally, blood tests may not be sufficient to make a diagnosis. In these circumstances, the doctor may order a biopsy of the skin or kidneys if those body systems are affected. Ultimately, the doctor must look at the whole picture: patient report, clinical signs and test results, in order to diagnose lupus.

Other laboratory tests are used to monitor the progress of the disease and to look for specific organ involvement. A complete blood count, blood chemistry, tests which show the presence of inflammation, urine testing and blood tests for components of the immune system that can be abnormal in active lupus, can provide valuable information. X rays and other imaging tests can help doctors see the organs affected by SLE.

- *96% of lupus patients are positive for ANA*
- *ANA can be positive in other conditions affecting the immune system and a proportion of healthy patients*
- *ANA testing should be done only if lupus is suspected based on the presence of symptoms and signs*

## How can lupus be treated?

Lupus cannot be cured but it can be controlled. Treatment depends on the type of symptoms you have and how serious they are. For instance, patients with muscle or joint pain, fatigue, rashes and other problems that are not dangerous, can receive "conservative" treatment. These options include non-steroidal anti-inflammatory drugs — referred to as NSAIDs. NSAIDs decrease pain and fever; and include ibuprofen, diclofenac and naproxen. They can cause serious side effects if used excessively like stomach bleeding or kidney damage. Always check with your doctor before taking any medications that are over the counter (without a prescription) for your lupus. When the lupus is more problematic, the doctor will use a group of anti-inflammatory drugs called corticosteroids; and depending on how serious or what organ is involved, the doses will vary from very small to very large. The doctor will usually prescribe this drug when the lupus is active and try to decrease and stop when disease is quiet. Higher doses and long term use can cause many complications including high blood pressure, diabetes, osteoporosis and weight gain to name a few. When the disease involves major organs like the kidney or brain or blood you might need very high doses of these steroids, sometimes given as an injection or infusion (drip). Doctors might introduce more potent drugs called immunosuppressive agents which can control the disease. Some such drugs that you might encounter are Imuran or Azathioprine, Cytoxan or Cyclophosphamide and Cellcept or MMF. Although very helpful, they can also have many undesirable side effects and complications. Doctors will monitor for these with blood and urine tests.

- *Corticosteroids should be used at the lowest dose and for the shortest period possible to decrease harmful side effects.*
- *Chloroquine benefits all patients with lupus.*

The most revolutionary drug in lupus treatment is Chloroquine (Plasmaquine) or Hydroxychloroquine. This drug was first introduced as an anti-malaria treatment for which it is still used today. It provides a host of benefits to all lupus patients including help with skin and joint involvement, reducing flares of lupus and protecting against blood clotting, to name a few. Where possible, all patients with lupus should be receiving this drug. There is a risk of eye damage with prolonged use, especially older patients and patients with kidney problems. Doctors advise an eye check prior to initiation and then annually after 5 years. With increased understanding of the immune system and its role in lupus development, scientists were able to develop a new type of medication known as “biologics”. Biologics are drugs that are made up fully or partly of human tissue and are designed to block the pathways in the immune system that cause lupus inflammation. These drugs include Rituximab and more recently Belimumab, a drug that recently has been used in the US and Europe. It is only available in South Africa through trials and its benefit in our population especially Black patients has not been established.

Most patients with lupus will receive more than one treatment at a time to control lupus and prevent damage to tissues. In addition to lupus medications, doctors will prescribe medications for associated problems such as high blood pressure, high cholesterol and patients who receive steroids, even low doses for more than 3 months will receive calcium and vitamin D supplements to protect bones from osteoporosis. Because treatment is lifelong, combination drug interactions and side effects can occur, regular monitoring is required to assess for compliance, drug toxicities and the presence of new organ involvement or complications.

Some people are hesitant to take medications because of the potential for side effects, and often seek advice or treatments from traditional healers, alternative health practitioners or home remedies. Although there may be some symptomatic or psychosocial benefits, there is no scientific proof that these treatments improve the disease process or prevent organ damage. If after consultation with your doctor it is determined that the alternative therapy is safe, it is important not to stop other medical treatment. Rather engage your doctor in your concerns, and make an informed choice about treatment options.

Lupus is not managed by a single medical practitioner but rather a team. This includes the rheumatologist as the primary decision maker, a family practitioner or physician, the rheumatology nurse, and other professionals depending on organ involvement. The patient is central to the management process and treatment must be tailored to their needs which may change over time. The treatment plan must include strategies to prevent flares, to treat them when they do occur, and to minimize organ damage and complications. Because some treatments may cause harmful side effects, it is important to report any new symptoms to the doctor promptly. It is also important not to stop or change treatments without talking to the doctor first.

## Special considerations

### Pregnancy, Hormones and Contraception

A commonly asked question, is whether or not it is safe to fall pregnant. Most women with lupus carry their babies safely to the end of pregnancy. There still exists a higher rate of miscarriage and premature births compared with the general population. This is seen especially in women who have certain antibodies known as antiphospholipid antibodies (antibodies that confer an increased risk of blood clotting in the placenta). Additionally, lupus patients with kidney disease have a higher risk of pregnancy associated high blood pressure which can also lead to pregnancy complications. One in twenty mothers with lupus have particular antibodies to structures known as Ro and La. These antibodies can be transferred to your baby and cause a lupus-like syndrome with a severe skin rash, or worse severe heart disease which may require a pacemaker to be fitted shortly after birth. We advise all patients to plan pregnancy in consultation with their doctor. The ideal situation would be when the disease is quiet, for at least 6 months, and patients should not be on any strong treatments which are potentially toxic to the unborn baby. Pregnancy should be treated as high risk with more frequent antenatal checks with close monitoring of mother and baby. Some women may experience a mild to moderate flare during or after their pregnancy. Medications that are safe in this period include steroids and chloroquine and azathioprine.

Until then, reliable birth control is important. An intrauterine device or loop contraceptive is the first choice, followed by injectable or oral contraceptives (preferably low oestrogen or progesterone only containing contraceptive pills). Oestrogen, the female hormone, has been implicated as a potential trigger for the development of lupus. This could explain why women are affected more often. Although not based on proof, there are fears that oestrogen treatment might trigger lupus to flare. Regardless of the method chosen, we advise condom use, not just as a second birth control measure, but also to prevent the transmission of sexually transmitted infections (STI's).

## Immunisations

Most are safe. However, “live vaccines” such as yellow fever, typhoid and polio vaccines are not advised if you are on immunosuppressive drugs. Always ask your doctor before being immunised. Doctors advise annual flu vaccines to reduce risk of serious infection and HPV vaccination before 25 years of age to protect from later cervical cancer, for which there exists an increased risk.

## Associated conditions

Certain conditions are seen more often in lupus patients than in the general population. These include Sjögren’s syndrome (disorder characterised by dryness of the eyes and mouth), overactivity or underactivity of the thyroid gland, rheumatoid arthritis and other disorders of the immune system. These conditions are investigated for by the doctors on a regular basis, especially if symptoms or signs are suggestive. Patients with lupus have an increased risk of atherosclerosis (thickening of blood vessels). This makes them high risk for strokes and heart attacks. In knowing this necessary lifestyle modifications to decrease risk of heart disease is important.

## What are the long-term prospects if I have lupus?

Treatment of lupus has improved, and people with the disease are living longer. Still, it is a chronic disease that can limit activities. Quality of life can suffer because of symptoms like fatigue and joint pain. Poor response to some treatments and inability to predict when lupus will flare can lead to depression, anger and loss of hope. People with lupus can take control of their disease by:

- Recognising the warning signs and precipitants of a flare: Increased fatigue, pain, a rash, fever, abdominal discomfort, headache, or dizziness can predict the onset of a flare. Precipitants include weather, stress, medications and foods.

## Preventing a flare:

- Avoid excess sun exposure. Sunlight can cause a lupus rash to flare and may even trigger a serious flare of the disease itself. When outdoors on a sunny day, wear a hat and use lots of sunscreen SPF > 30.
- Manage stress. This can be through exercise, meditation and time management strategies. A good support system is also important. This includes family, friends, medical professionals, community organizations, and support groups. Participating in a support group can provide emotional help, boost self-esteem and morale, and help develop or improve coping skills.
- Always check with your doctor before taking any new medications.
- Watch what you eat. People are very interested in whether diet therapy can help control lupus. Unfortunately, the evidence is very limited. There is more evidence to suggest that a diet low in saturated fat and supplemented by fish oil may be helpful.
- Regular medical checks: Good communication with your doctor. Doctors can react early to abnormalities noted on examination and laboratory tests. If new symptoms are identified early, treatments may be more effective.

- Preventing Infections: People with lupus can be more susceptible to infections. Avoid contact with patients who have active infection and get regular influenza or pneumococcal vaccinations.

- Take care of your general health: This includes regular gynaecological and breast examinations, blood pressure and cholesterol checks. People with lupus should be aware of their increased risk of premature cardiovascular disease. This makes healthy lifestyle choices such as eating well, exercising regularly, and not smoking particularly important.

## Take home messages

- Most people with lupus can live normal lives.
- Earlier recognition of symptoms will lead to earlier diagnosis and treatment, and ultimately better outcomes.
- To prevent serious problems, you should see your rheumatologist regularly. This lets your doctor keep track of your disease and change your treatment as needed.
- Stay informed. Ultimately, you are in charge of your lupus!