LUPUS ERYTHEMATOSUS

A chronic autoimmune disease that mainly affects women of reproductive age and affects a wide range of organs.

⚠ Risk factor ♂ Male & Female

About Lupus erythematosus

Lupus erythematosus is a chronic inflammatory autoimmune disease that can affect many parts of the body, including the skin, joints, kidneys, blood cells, heart and lungs. Lupus is an auto-immune illnesses, which means that instead of the person’s immune system producing antibodies to fight and destroy disease-causing bacteria or viruses, it mistakenly attacks their perfectly healthy body tissues. Episodes of lupus tend to come and go throughout a person’s life, and the condition may cause periods of tiredness and pain. Lupus can be mild or life-threatening depending on which tissues are affected.

Lupus occurs in several types, including systemic lupus erythematosus (SLE), discoid and drug-induced. SLE is the most common type and causes the most difficulties.

Systemic lupus erythematosus (SLE)

Systemic lupus erythematosus (SLE) is a chronic autoimmune disease affecting almost all organ systems. It is characterized by exacerbations (or flares) of disease activity and disease damages. Several organs are also involved such as the brain, lungs, kidneys, heart, blood vessels, muscles, and skin. Common symptoms of SLE include fever, weight loss, glomerulonephritis (inflammation of the kidneys), alopecia (hair loss) and rash (Pic. 1). Other manifestations such as arthralgia (joint pain) and arthritis (joint inflammation) are frequently seen, with migratory arthritis affecting about 75% of patients (Pic. 2). Worldwide, the prevalence of systemic lupus erythematosus is 60 per 100,000 persons. SLE usually develops in the second and third decades of life, although it can present at any age.

Discoid lupus erythematosus

Discoid lupus erythematosus is a chronic skin condition of sores with inflammation and scarring favouring the face (Pic. 3), ears, and scalp and at times on other body areas. Discoid lupus can be generalised (diffusely affecting the skin of the whole body) or localised, presents with skin lesions localised above the neck, with favoured sites being the scalp, bridge of the nose, cheeks, above the lips and ears.

Drug-induced lupus erythematosus

Drug-induced lupus erythematosus is defined as a lupus-like syndrome temporally related to continuous drug exposure which resolves after discontinuation of the offending drug. These drugs cause an autoimmune response (the body attacks its own cells) producing symptoms similar to those of SLE. The diagnosis of lupus is based on a set of diagnostic criteria. Lupus is diagnosed if the patient fulfills 4 of these criteria:

- Malar rash – a rash over the cheeks and nose, often in the shape of a butterfly
- Discoid rash – a rash that appears as red, raised, disk-shaped patches
- Photosensitivity – a reaction to sun or light that causes a skin rash to appear or get worse
- Oral ulcers – sores appearing in the mouth
- Arthritis – joint pain and swelling of two or more joints
- Serositis – inflammation of the serous membranes, such as the lining of pleural or pericardial cavity
- Kidney disorder – pathological findings in the urine
- Neurological disorder – seizures or psychosis
- Blood disorder – low counts of any blood cell group
- Immunologic disorder – the presence of auto-reactive antibodies
- Abnormal antinuclear antibody (ANA) – the most commonly used test for lupus, however, it can be positive in a number of other diagnoses

The main aim of treatment is to control inflammatory disease activity and prevent flares of disease while in remission. Treatment almost always includes corticosteroids because of their anti-inflammatory properties. Based on the extent of organ involvement and the severity of the disease, other immunosuppressive drugs may be used, such as methotrexate, cyclophosphamide, azathioprine, or, most recently, biological agents such as intravenous immunoglobulins.

## Symptoms

### Systemic lupus erythematosus

A positive history of familial lupus, skin rashes (especially photosensitive skin rashes), arthritis, and fatigue may be suggestive of systemic lupus erythematosus. The most common symptoms of SLE include constitutional symptoms like fatigue, fever, myalgia (muscle pain), loss of appetite, sensitivity to sunlight, chest pain, swollen lymph nodes and weight changes. Other organ-specific symptoms mostly occur with disease progression. A typical symptom of SLE is facial butterfly-like rash (Pic. 1), but SLE may show a variety of symptoms in different organs depending on its complications. The early manifestations of systemic lupus erythematosus include common symptoms that may be seen in many other diseases as well – fever, joint tenderness, muscle weakness, muscle pain and weight changes, either weight loss due to gastrointestinal tract involvement and medications effect, or weight gain due to water retention in the body. In later stages of the disease, many various symptoms may be present due to multi-organ involvement.

### Discoid lupus

Localised discoid lupus erythematosus typically presents with skin lesions localised above the neck, with favoured sites being the scalp, bridge of the nose, cheeks, above the lips and ears as well as the arms. Discoid lupus may also involve the oral cavity, resulting in lesions such as ulcers or white spots.

### Associated diseases

Lupus erythematosus is one of the group of connective tissue disease, which share many characteristic traits and may often overlap in one patient. All of these diseases have an auto-immune and inflammatory character and can have very variable clinical manifestations with various organ involvement. These diseases include rheumatoid arthritis (inflammatory disease affecting mainly small joints on the hands and feet), Sjögren’s syndrome (autoimmune disease affecting multiple glands), Raynaud’s phenomenon (episodes of spasms of arteries, that cause reduced blood flow) and scleroderma (autoimmune disease causing extensive scarring of various organs). Each of these diseases can present with symptoms very similar to lupus, such as skin lesions, joint pain, arthritis and mucous membranes inflammation, and may create overlap syndromes with lupus erythematosus.

### Complications

Common complications of lupus erythematosus include dermatitis (skin lesions and rashes), nephritis (kidney inflammation), and arthritis (joint inflammation). Skin involvement is very common and may have the form of localised patches of scarring and decoloration of skin, or may affect large portions of the body surface and produce red, itchy blisters that later turn into scars. Almost all systemic lupus patients present with joint pain and swelling, and some develop joint inflammation. Commonly affected are the joints of fingers, wrist, hands and knee joints.

### Risk factors

- family history of lupus
- female sex (lupus affects females 9 times more than males)
- reproductive age
- infections, such as EBV (Epstein-Barr virus)
- certain drugs, such as Chlorpromazine, Isoniazide, Methyldopa, Sulfasalazine or Procainamide
- smoking
- non-Caucasian race
- exposure to UV light

**How it can affect fertility**

**Female infertility**

Lupus erythematosus mainly affects women in their reproductive age. Menstrual alterations ranging from increased cycle flow, generally due to thrombocytopenia (low blood platelet count), to temporary amenorrhea (cessation of menstrual cycle) and premature menopause are fairly common in these patients. Ovarian failure, especially premature menopause, should be a constant concern in the management of patients with SLE. Therefore, premature interruption of estrogen (the primary female sex hormone) production may give rise to a higher risk of cardiovascular disease, osteoporosis and infertility, among other estrogen deficiency-related symptoms. Amenorrhea is the most common menstrual disorder in SLE and is associated with disease activity, stress and drugs used.

Cyclophosphamide is the immunosuppressive agent of choice for the treatment of various complications of SLE and, therefore, is the factor most highly associated with ovarian insufficiency. Gonadal toxicity (damage to sex glands) should be of great concern in premenopausal women who take cyclophosphamide. The frequency of ovarian insufficiency in SLE patients treated with this drug ranges from 11 to 59% in different studies and depends on the dose used, the age of the patient and methodological differences.

**Male infertility**

The reproduction potential of male patients is impaired by the disease directly in the testicular tissue or by immunosuppressive therapy. Infertility is an important issue for them nowadays due to better prognosis and quality of life. The evaluation of male subjects should rely on careful medical history, complete physical examination, semen analysis and sexual hormone profile. Although semen analysis is considered the hallmark of male infertility evaluation, standard seminal parameters do not detect abnormalities in up to 20% of sub-fertile males. The routine measurements do not reveal seminal defects at molecular levels that might be induced by reactive oxygen species, which are associated with male infertility.

Autoimmunity also affects fertility by the presence of ASA (anti-sperm antibodies). Immunologic infertility is characterized by the presence of antibodies against spermatozoa (sperm cells) in the serum and/or in the seminal plasma or on the sperm surface. The presence of multiple ASA can lead to the immobilization and/or agglutination (clumping) of spermatozoa, which blocks sperm-egg interaction. They can also prevent implantation or arrest embryo development. In SLE patients ASA have been found in up to 42% of the patients. Lastly, aneuploidies (abnormal cell divisions in the process of sperm cell maturation) are frequent and may also contribute for fertility impairment in SLE patient’s; therefore karyotype (examination of sperm cells’ chromosomes) should be evaluated to complete the fertility analysis of these patient’s, especially in those with severely compromised spermatogenesis.

**Prognosis**

The prognosis of systemic lupus erythematosus ranges from a benign illness to an extremely rapid progressive disease that can lead to a fulminant (rapidly progressing) organ failure and death. Without treatment, systemic lupus erythematosus will result in a very high mortality rate, with a report of higher than a 60% mortality rate during the mid-20th century. The presence of nephritis is associated with a particularly poor prognosis among patients with SLE; SLE is associated with a 10-year mortality of more than 50% among patients with nephritis. The increase in survival rate of patients and better prognosis may be due to increased disease recognition with more sensitive diagnostic tests, earlier diagnosis or treatment, the inclusion of milder cases, increasingly judicious therapy, and prompt treatment of complications. Although improvements in SLE diagnosis have led to better prognosis, the mortality rate among SLE patients is still 5 times higher than the normal population.

Although patients with SLE are as fertile as women in the general population, their pregnancies could be associated with complications. Also, certain drugs that may be used to treat more severe stages of lupus are associated with adverse effects on fertility. The drug cyclophosphamide is associated with an increased risk of
premature menopause and infertility, and the risk increases with dose and duration of administration.

**Gallery**

**Pic**  
A typical butterfly-like rash, also called malar rash, is a typical symptom seen in SLE patients.

**Pic**  
A graphic showing the various manifestations of systemic lupus.

**Pic**  
A photograph of a patient affected with discoid lupus, with the typical localization involving the face.

**Sources**
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