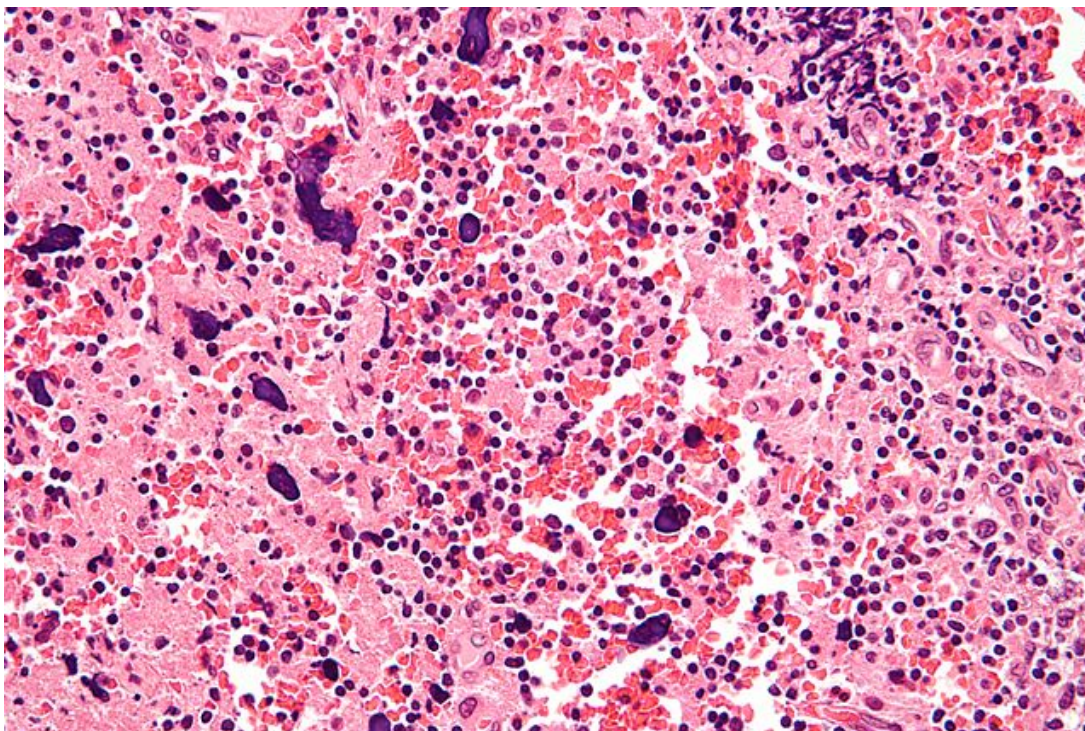


Pediatric Systemic Lupus Erythematosus (SLE) — Diagnostic Criteria and Life Expectancy

[See online here](#)

Systemic lupus erythematosus is a chronic inflammatory condition that is characterized by the clinical involvement of the skin, joints, kidneys, blood cells, and central nervous system. The main clinical features of the disease include malar rash, joint pain, fever, proteinuria, hypertension, anemia, lymphopenia, and seizures or psychosis. The disease is believed to be an autoimmune disorder and has been associated with the formation of autoantibodies such as an antinuclear antibody, anti-Smith, and anti-dsDNA.



Definition of SLE

Systemic lupus erythematosus in children (SLE) is a chronic inflammatory disease that is characterized by the formation of autoantibodies against nuclear and cytoplasmic antigens. SLE is a systemic condition that **affects the skin, joints, kidneys, blood cells, and the central nervous system**. SLE's natural history is characterized by a relapsing and remitting course. The diagnosis of SLE is confirmed by looking for a constellation of clinical and laboratory findings which are part of the American College of Rheumatology (ACR) criteria for SLE.

Epidemiology of SLE

Estimated incidence

The estimated incidence of SLE **can range between 1 to 10 per 100,000** depending on whether the researcher has included only definite SLE or also probable SLE cases in their definition. Likewise, the prevalence of SLE can also range from 5.8 to 130 per 100,000, again depending on the criteria used for the confirmation of the diagnosis.

Occurrence

In the United States, the Lupus Foundation of America estimated that there are at least 1.5 million cases of SLE. This figure is quite large and most likely includes milder forms of SLE and probable SLE in addition to definite SLE.

Pediatric SLE is more common in African Americans and Hispanics. A recent study of SLE prevalence in the white population has estimated a prevalence of 30.5 per 100,000. To better understand the effect of race and ethnicity on the frequency of SLE, another study has considered the ethnical differences in the prevalence of SLE. SLE prevalence among African Americans in this study was 105.8 per 100,000, whereas the prevalence of SLE in the white population was around 46 per 100,000.

Different Sexes and Ethnicities

SLE is also more common in females with a female to male ratio of 10:1. The estimated prevalence of SLE in African American females was 1 in 537. Asian women also appear to have a higher risk of SLE compared to white women.

Most cases of SLE occur in black women at the start of the childbearing age. **Hormonal factors and the use of oral contraceptives have been linked to an increased risk of SLE** onset and flares. Men with Klinefelter's syndrome are at an increased risk of SLE compared to men with a normal karyotype. Up to 20% of SLE cases are diagnosed within the first two decades of life.

Pediatric SLE is also becoming more commonly recognized and the estimated incidence in the United States of pediatric SLE is around 2.5 per 100,000. The prevalence of pediatric SLE in North America is around 25.7 per 100,000 when milder forms of the disease are accounted for.

Finally, it is worth noting that the female to male ratio of SLE onset in people older than 64 years is 1 to 1. This is most likely due to the lack of estrogen in the menopausal woman, which, as we have explained before, has been suggested to play a critical role in the onset of SLE in women.

Etiology of SLE

Pediatric SLE is an autoimmune disorder that is characterized by chronic **inflammation of multiple organs**. The exact cause or trigger of SLE is yet to be identified, but genetic predisposition plays a definite role.

Pediatric SLE, like any other autoimmune disorder, is characterized by a complex etiology rather than a single causative pathogen or exposure.

Note: Interaction between genetic predisposition and environmental exposures is believed to lead to autoimmune cellular proliferation and autoantibody production. HLA type DR3/2 have been linked to an increased risk of SLE. Additionally, polymorphisms in multiple genes related to immunoregulation have been suggested to be linked to an increased risk of SLE. Most of these genes are related to B-cell receptor pathway signaling.

Polymorphisms in BANK1, TNFAIP3, FAM167A, and KIAA15442 genes have been also linked to SLE. Congenital deficiencies of complement factors C4 and C2 are also associated with an increased risk of SLE.

The most recognizable exogenous exposures linked to SLE include ultraviolet light exposure, the use of exogenous hormones, pregnancy, and the Epstein-Barr Virus infection. Low birth weight, pre-term birth, exposure to silica dust, cigarette smoking and hormonal replacement therapy for postmenopausal women are also associated with an increased risk of SLE. **Breastfeeding appears to be protective from SLE.** Vitamin D deficiency increases the risk of autoimmune diseases including SLE.

Pathophysiology of SLE

When a genetically predisposed patient is exposed to one of the possible risk factors of SLE, he or she might develop autoimmune cellular proliferation and subsequent production of autoantibodies. The **production of hyperactive B-cells, the activation of T-cells, and an increased ratio of CD4:CD8 T cells are the main pathologic consequences** induced by the exposure to the environmental risk factor in patients who have a genetic predisposition for Pediatric SLE.

This impaired immune response is responsible for the production of autoantibodies against nuclear and cytoplasmic targets. These autoantibodies can cause impaired apoptosis and are responsible for the self-recognition of one's own cells as foreign by the immune system.

Clinical Presentation of SLE

The clinical presentation of pediatric systemic lupus erythematosus is **highly variable because of the systemic nature of the disease.** SLE can be a mild disease of main skin or joint manifestations or might be a fatal condition.

Pediatric SLE is characterized by malar rash, mucocutaneous ulcers formation, renal injury, proteinuria, fever, and lymphadenopathy. Pallor might be also seen because of hemolytic anemia in this group.

Women of childbearing age who present with fever, joint pain, and rash should be evaluated for probable SLE. The symptoms of SLE can be classified into constitutional, musculoskeletal, dermatologic, renal, neuropsychiatric, pulmonary, cardiac, hematologic, and gastrointestinal. The following table summarizes the main symptoms of SLE in adults:

Category	Symptoms	Comments
Constitutional	Fever Fatigue Joint Pain Weight Loss or Gain	Fever can be caused by active SLE or by a secondary bacterial infection.
Musculoskeletal	Arthralgia Muscle Pain Arthritis	Arthritis typically involves the hands, wrists, and knees. SLE arthritis might be asymmetrical. SLE characteristic hand deformities include swan neck deformities. SLE arthritis is usually not erosive.
Dermatologic	Malar Rash Photosensitivity Discoid Lupus	Malar rash is an erythema over the cheeks and nasal bridge, but not the nasolabial folds.

Renal	Nephrotic Syndrome Hypertension Hematuria Edema and Weight Gain	While 50% of SLE patients have clinically relevant kidney disease, almost all patients have evidence of microscopic involvement.
Neuropsychiatric	Seizures Psychosis	Neurologic manifestations rather than seizures and psychosis are very common in SLE but are not specific.
Pulmonary	Pleural Effusions Chest Pain Pulmonary Hypertension Interstitial Lung Disease: Progressive Exertional Dyspnea	Chest pain due to pleuritis is quite specific for SLE.
Cardiac	Pericarditis Myocarditis Pulmonary Hypertension Angina	Libman-Sacks endocarditis is a non-infectious disease that is seen in SLE and antiphospholipid syndrome.
Hematologic	Leukopenia Lymphopenia Hemolytic Anemia Thrombocytopenia	Lymphopenia is common in SLE which makes the patient immunocompromised.
Gastrointestinal	Pancreatitis Mesenteric Vasculitis Autoimmune Hepatobiliary Disease	Other gastrointestinal complications are usually caused by medication rather than active SLE.

Differential diagnosis

As SLE has a spectrum of manifestations so it has to be differentiated from other disease conditions like:

- Pyrexia of unknown origin
- Arthralgia
- Renal diseases
- Skin disorders

Diagnostic Criteria of SLE

The most recent diagnostic criteria for SLE include **clinical, immunological, and hematological criteria.**

Clinical criteria

The clinical criteria of SLE include acute cutaneous lupus such as malar rash, chronic cutaneous lupus such as discoid rash, oral ulcers, nonscarring alopecia, synovitis involving two joints or more, pleurisy for one day, history of pleural effusions, pericarditis, proteinuria, seizures, psychosis, myelitis, mono neuritis multiplex or acute confusional state.

Hematological criteria

The hematological criteria of SLE include hemolytic anemia, leukopenia, lymphopenia, and thrombocytopenia. Immunological criteria for SLE are the presence of anti-dsDNA, anti-nuclear antibody, anti-Sm, lupus anticoagulant, false-positive RPR, low C3, or low C4.

The probability of SLE increases when more of the criteria are met.

Diagnostic Workup of SLE

Laboratory investigations are essential for the confirmation of the diagnosis of SLE as they provide critical information related to the diagnostic criteria.

Note: Hematologic workup of SLE include a complete blood count looking for leukopenia, lymphopenia, thrombocytopenia, and anemia.

Renal involvement can be confirmed by the presence of proteinuria (more than 0.5 g/day) or a 3+ result on dipstick testing. The presence of red blood cells casts can increase the certainty of the diagnosis.

Antinuclear antibodies titers above 1:160 are usually specific for SLE. Anti-dsDNA, anti-Smith antibodies, antiphospholipid antibodies, and the presence of lupus erythematosus cells are also specific immunologic findings of SLE. Anti-dsDNA and anti-Smith are the most specific autoantibodies for the diagnosis of SLE.

Erythrocyte sedimentation rate and C-reactive protein levels are usually elevated in SLE as in any other chronic inflammatory condition. **Liver function tests to exclude autoimmune hepatobiliary disease** complement levels to exclude early complement factors' deficiencies, and creatine kinase levels to exclude significant myositis and muscle damage are also indicated in patients with active SLE.

Radiography can reveal osteopenia of the affected joints or pleural effusions on chest X-rays. Echocardiography is useful in the assessment of the heart and the exclusion of heart failure. Brain magnetic resonance imaging might reveal white matter changes in patients with neuropsychiatric SLE manifestations. Cardiac magnetic resonance imaging is an excellent imaging modality for the detection of SLE related myocarditis.

Management of SLE

Treatment of systemic lupus erythematosus consists of non-steroidal anti-inflammatory drugs, antimalarial therapy, and short-term steroid therapy. If this approach fails to control the symptoms, or if the patient has major organ involvement, high-dose long-term steroid therapy is indicated. Cases that do not respond to steroid therapy might benefit from methotrexate, azathioprine or belimumab.

Patients with mild SLE without major organ involvement should be started on short-term corticosteroids and/or hydroxychloroquine. Non-steroidal anti-inflammatory drugs are indicated for pain control of the acute flares of SLE.

Immunosuppressive agents such as azathioprine, mycophenolate mofetil, and methotrexate should be given to patients with SLE that is refractory to steroid therapy. **Management of SLE psychosis or seizures is the same as the management of psychosis or seizures** in a non-SLE patient. If anti-psychotics and anti-epileptic drugs do not result in the resolution of psychosis and seizures respectively, one might consider immunosuppressive therapy.

Newer disease-modifying antirheumatic drugs (DMARD Therapy) have emerged as potential treatments for SLE. **Belimumab, a B-lymphocyte inhibitor, was found to reduce SLE activity** and decrease the number of flares. Rituximab which causes B-cell depletion might be ineffective in SLE.

Pregnancy is a risk factor for SLE flares; therefore, low-dose aspirin, prednisolone, and hydroxychloroquine should be continued during pregnancy. Mycophenolate mofetil, methotrexate, and cyclophosphamide should never be given to a pregnant woman who has SLE.

Prognosis

SLE has a tendency to damage organs. The 5-year survival rate for children is 90%. The most common cause of mortality are:

- Infections
- Nephritis

- Renal failure
- Neurogenic disease
- Pulmonary hemorrhage
- Complications of immunosuppressant drugs
- Cardiac failure in young adult years

References

[Systemic Lupus Erythematosus \(SLE\)](#) via emedicine.medscape.com

[Systemic Lupus Erythematosus](#) via webmd.com

[About Lupus](#) via lupusny.org

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