Systemic Lupus Erythematosus: A review of the disease and treatment options
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Abstract

Objective: To provide an up-to-date review of the etiology, epidemiology, clinical features, diagnostic findings, and treatment options for systemic lupus erythematosus.

Data Sources: A PubMed search of English language using a combination of words: elderly, systemic lupus erythematosus*, late onset systemic lupus erythematosus*, etiology, screening, diagnosis, or treatment to identify original studies, guidelines, and reviews on systemic lupus erythematosus, SLE, late onset systemic lupus erythematosus published between 2000 - present.

Study Selection and Data Extraction: Overall original studies, clinical reviews, references, and guidelines were obtained and evaluated on their clinical relevance.

Data Synthesis: The literature included guidelines and considerations for the etiology, diagnosis, screening, and management of systemic lupus erythematosus*, and late onset systemic lupus erythematosus.

Conclusion: Systemic lupus erythematosus (SLE) is a chronic autoimmune disorder whereby the exact etiology is unknown. SLE predominately affects younger women; however, it is reported to occur in up to 20% of patients 50 years or older. In patients with SLE, nearly every system in the body is affected with varying degrees of severity ranging from subclinical to fatal. The hallmark feature of SLE is the production of auto-antibodies directed primarily against nuclear antigens, but also against cytoplasmic components of cells. The diagnosis of SLE is based on criteria set by the American College of Rheumatology. Management is individualized and depends on presenting symptoms and reducing the likelihood of permanent damage to organs and tissues.
Key Words: Elderly, Geriatrics, Late onset Systemic Lupus Erythematosus, Systemic Lupus Erythematosus, Treatment.

Abbreviations

ACEI = Angiotensin Converting Enzyme Inhibitor, ACR = American College of Rheumatology, ALT= Alanine Transaminase, ANA = Antinuclear antibodies, Anti-DNA = Anti-deoxyribonucleic acid, Anti-dsDNA = Anti-double stranded deoxyribonucleic acid, Anti-La/SSB = Anti-La sjögren syndrome type B, Anti-RNP antibodies = Anti-ribonucleoprotein, Anti-Ro/SSA = Anti-Ro/Sjögren syndrome type A, Anti-Sm antibodies = Anti-Smith antibodies, AST = Aspartate Transaminase, CBC = Complete Blood Count, CH50=50% hemolytic complement, COX-1= Cyclooxygenase-1, COX-2 = Cyclooxygenase-2, EULAR = European League Against Rheumatism, GI = Gastrointestinal, IV = Intravenous, MTX = Methotrexate, NSAIDs = Non-Steroidal Anti-inflammatory Drugs, RF= Rheumatoid Factor, SLE = Systemic Lupus Erythematosus, SLICC = Systemic Lupus International Collaborating Clinic
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Introduction

Systemic lupus erythematosus (SLE) or lupus is a chronic, progressive, autoimmune disorder that affects multiple organ systems, with a broad range of clinical and laboratory manifestations.¹⁻³ The term lupus means wolf in Latin and is named as such due to facial lesions found in the disease process that are reminiscent of a wolf’s bite.⁴ This review will provide up-to-date information regarding the etiology, environmental and genetic influences, clinical features, diagnostic findings, and treatment options for SLE.

Etiology

While the etiology is unknown, there are several factors associated with the development of SLE (Table 1).¹,²,⁵⁻⁸ Unexplainably, SLE patients do not clear apoptotic cells appropriately.²⁻⁹ These cells release auto-antigens that may help drive the defective immune process.⁹ The complex interaction between environment and immunologic factors in genetically susceptible individuals leads to continued deregulation of the innate and adaptive immune pathways with evidence of auto-antibody secreting plasma cells and auto-antigen, hyper-reactive, memory B-cells.¹,⁷,¹⁰⁻¹³ Auto-antibodies often form long before clinical manifestations result in chronic, widespread tissue and organ damage.²,⁶,¹⁴,¹⁵ Patients with SLE experience acute exacerbations and remissions resulting in protean clinical and serologic manifestations.¹⁶,¹⁷ SLE may develop as a result of exposure to medications. It is estimated that 10% of patients diagnosed with SLE may have drug induced lupus, and over 80 drugs (Table 2) have been implicated in the disease development.⁷,¹⁶,¹⁸⁻²¹

Epidemiology
SLE is most often initially diagnosed in young women of reproductive age but does affect those 50 years of age or older. Early diagnosis and treatment are important. The average time to reach a diagnosis is 2 years. However, in the late onset population, the average time to establish the diagnosis is often as long as 5 years. Improvements in diagnostic techniques as well as more intensive treatment methods have enhanced survival rates dramatically in recent years. The survival rate has improved from a 4 year survival rate of 50% in the 1950’s to the present day 20 year survival rate of approximately 80%. The prevalence of SLE in the United States population is 14.6-68 /100,000. About 10 - 20% of patients will be diagnosed with late onset SLE (first diagnosed age 50 years or older) and will often have more mild manifestations of the disease that may result in a delayed diagnosis. The female predominance may not be as significant in the late-onset populations. Systemic lupus erythematosus is 2 to 4 times more common among African Americans and other non-white populations.

Clinical Manifestations
Lupus often follows a characteristic pattern of relapse and remissions and typically develops over an extended period of time. It takes careful observation to make the diagnosis. The clinical presentation of SLE may be comprised of both systemic symptoms as well as specific signs of organ-system dysfunction. The incidence of clinical findings of early and late-onset SLE may vary (Table 3).

Common presenting findings of patients with SLE are fatigue, malaise, fever, anorexia, and weight loss. They may present with signs of systemic infection. Patients may also present with a number of dermatologic findings, including discoid and malar lesions, photosensitivity,
alopecia, periungual erythema, nailfold infarcts, and splinter hemorrhages. Thirty-five percent of patients with SLE will have some form of glomerulonephritis or nephrotic syndrome symptoms and signs on clinical examination, predicting a worse outcome. A renal biopsy is often suggested in patients with renal complications to fully understand the extent of its severity. Myalgias and muscle weakness are common. Up to 90% of patients with SLE present with symmetrical joint pain, that is typically a migratory polyarthropathy, distinguished from rheumatoid arthritis by its lack of joint destruction. The pathophysiology behind osteoporosis and the occurrence of fractures in SLE is multifactorial. It involves both disease and non-disease related factors, including complications of the treatment itself. The most common cardiac findings are pericarditis and pericardial effusion. Valvular abnormalities are frequent in patients with SLE, especially the mitral valve. Screening with transthoracic echocardiography may be indicated in patients with SLE, especially for those with identified risk factors such as corticosteroid use. SLE is also associated with an increased risk of coronary disease due to atherosclerosis. The mechanism for neuronal damage is consistent with the autoimmune nature of SLE. Anti-neuronal antibodies attack neurons causing damage and neurologic symptoms such as stroke, seizures and peripheral neuropathy. Cognitive dysfunction is a common neuropsychiatric manifestation of SLE as it is found in up to 80% of patients to a variable extent. Higher rates of anxiety and depression are found in patients with SLE. Depression occurs more commonly with changes in appearance and physical limitations due to complications or medication side effects. Health care providers should be alert for these manifestations.

Diagnosis
The clinical heterogeneity of SLE resulted in the development of classification criteria in 1982, and revised in 1997, by the American College of Rheumatology (ACR). The revision resulted in the establishment of 11 equally weighted criteria (Table 4), with 4 needing to be present for the formal diagnosis of SLE. A subspecialist in rheumatology or nephrology may diagnose a patient with only 3 criteria, if at least one is serologic and one is clinical. A patient can be described as having “latent” or “incomplete” lupus with as few as one criterion and additional common symptoms, such as fatigue, fever, alopecia or Raynaud’s phenomenon. Upon initial suspicion of SLE, the most important laboratory screening measure is the blood test for antinuclear antibodies (ANA). However, ANA is found in conditions other than SLE; therefore, more specific tests are needed to help confirm the diagnosis, such as anti-dsDNA (anti-double stranded DNA), anti-Sm (anti-Smith) and antiphospholipid antibodies. The anti-dsDNA and anti-Sm serological tests are considered definitive for lupus. Recent support has been given to monitoring specific B-cell subsets as biomarkers of disease activity.

In 2009, the Systemic Lupus International Collaborating Clinic (SLICC) revised the ACR’s classification criteria for SLE. The proposed classification “had better sensitivity than the ACR (94% vs. 86%), and roughly equal specificity (92% vs. 93%), and resulted in significantly fewer misclassifications (p = .0082).” If validated, the SLICC criteria may become the standard in the diagnosis of this disease.

Treatment

There is no cure for SLE so early diagnosis and treatment to control dysfunction and complications are important. Management is individualized, depends on symptoms, and is directed at reducing the likelihood of permanent damage to organs and tissues. Treatment strategies in late onset SLE do not differ widely from those seen in younger patients.
disease course in late onset SLE is usually mild requiring less use of cytotoxic/immunosuppressive drugs and high dose corticosteroids for disease control. Guidelines were developed in 1999 by the ACR and in 2008 by the European League Against Rheumatism (EULAR) Task Force (Table 5). A major challenge in treating SLE is to inhibit clinically active disease without causing long term consequences. Clinicians should be aware of drug interactions and adverse reactions are possible. This is especially true in the older patient as they are more likely to be affected by multiple disease states and taking several medications. In addition, the pharmacokinetics and pharmacodynamics of drugs are often altered in the older patient. The safety profiles and monitoring recommendations for medications used in SLE are provided (Table 6).

Non-pharmacologic Management

Both the ACR and EULAR recommend non-pharmacologic treatment in the management of SLE. Patients should be counseled on lifestyle modifications, such as smoking cessation, weight control, and increasing exercise to limit co-morbidities of atherosclerosis, hypertension, and diabetes. Patients should minimize sun exposure by wearing appropriate clothing, applying topical sunscreens, and avoiding tanning beds. Screening for bone loss should be instituted and treatment commenced as needed. Patient education and psychosocial support are an important aspect of management. Information about SLE and specific problems of living with the disease should be combined with medical therapy to help alleviate depression and anxiety.

Unfortunately, challenges remain in increasing a patient’s quality of life. Clinicians should be alert to changes in psychosocial functioning and treated and/or referred for appropriate counseling as indicated.

Pharmacologic Management
Nonsteroidal Anti-inflammatory Drugs

Nonsteroidal Anti-inflammatory drugs (NSAIDs) are commonly used to relieve arthralgia, inflammation, serositis, and fever in patients with SLE. They can be used with or without low doses of steroids or antimalarial agents.\(^{41,46,47}\) NSAIDs inhibit the production of cyclooxygenase-1 (COX-1) and cyclooxygenase-2 (COX-2).\(^ {53}\) The inhibition of COX-1 decreases the production of prostaglandins that protect the lining of the gastrointestinal tract. The inhibition of COX-2 mediates the production of prostaglandins which moderates inflammation and pain. Therefore, NSAIDs that are selective COX-2 inhibitors, such as celecoxib, have reduced the occurrence of adverse gastrointestinal bleeding.\(^ {53}\) In a study of 50 SLE patients with predominance of musculoskeletal complaints and less severe organ involvement, celecoxib was found to be effective and safe.\(^ {54}\)

Regardless of their cyclooxygenase selectivity, NSAIDs may cause renal impairment, fluid retention, and interstitial nephritis.\(^ {47}\) Lupus nephritis is a risk factor for NSAID induced acute renal failure\(^ {55}\); therefore, NSAIDs should be used for the shortest effective period of time especially in patients with renal involvement, hypertension, or heart disease.\(^ {46,56}\)

Hydroxychloroquine

Hydroxychloroquine, an antimalarial drug, is frequently used as a first line treatment option for patients with mild SLE. It is effective in preventing the occurrence of new mild SLE manifestations.\(^ {15}\) A systematic review found antimalarials reduced lupus activity by more than 50% in pregnant and non-pregnant patients and a greater than 50% improvement in mortality.\(^ {51}\) Hydroxychloroquine also has been shown to have a beneficial effect on dyslipidemia.\(^ {57}\) Hydroxychloroquine inhibits Toll-like receptors that cause a down regulation of interferon-α and decreases the antigen processing for auto-antigen presentation.\(^ {58}\) The safety profile for
hydroxychloroquine is good. Retinal toxicity and macular damage can occur due to accumulation of the drug in ocular tissue;\textsuperscript{41, 47} therefore, the ACR recommends patients undergo a baseline eye examination before treatment and every 6 to 12 months thereafter.\textsuperscript{45} Hydroxychloroquine may be used during pregnancy.\textsuperscript{46}

Glucocorticoids

Systemic glucocorticoids are usually unnecessary in mild SLE, but low doses of prednisone 10 mg/day or less are used if the patient has cutaneous and musculoskeletal symptoms not responding to other therapies.\textsuperscript{45} Systemic glucocorticoids are used alone or in combination with other immunosuppressive agents for patients with significant organ involvement or refractory symptoms.\textsuperscript{41, 47}

Due to the long term adverse effects of glucocorticoid treatment, the shortest effective duration should be used.\textsuperscript{41, 47} Patients requiring long term glucocorticoid therapy should be monitored for the complications of hypertension, diabetes, myopathy, psychosis, and cataracts.

Methotrexate

Methotrexate (MTX), an antifolate, may be preferred in the management of resistant arthritis and cutaneous SLE.\textsuperscript{15} Methotrexate provides a significant advantage in patients with moderately active lupus by allowing lower steroid doses, and slightly decreasing lupus disease activity.\textsuperscript{59} In a recent prospective open label study, low dose MTX appears to be as effective as the antimalarial chloroquine, in patients with articular and cutaneous manifestations of SLE.\textsuperscript{60}

Cyclophosphamide

Cyclophosphamide, an alkylating agent, is the standard of care for lupus nephritis and is usually used in conjunction with corticosteroids.\textsuperscript{41, 61} It is also used with corticosteroids in patients with severe neuropsychiatric involvement.\textsuperscript{15, 62}
Mycophenolate

Mycophenolate exerts its immunosuppressive effect by inhibiting B- and T-cell proliferation.\(^{47}\)

In a systematic review and meta-analysis, mycophenolate in combination with corticosteroids was shown to be as effective as cyclophosphamide in the treatment of lupus nephritis and had less risk of leukopenia.\(^{63}\) Maintenance therapy, either with azathioprine or mycophenolate, is required for periods of remission and prevention of relapse after the initial control of lupus nephritis. In a 36-month, randomized, double-blind, double-dummy, trial comparing oral mycophenolate mofetil and oral azathioprine, mycophenolate mofetil was superior to azathioprine in maintaining a renal response to treatment and in preventing relapse in patients with lupus nephritis who had a response to induction.\(^{64}\)

Azathioprine

Azathioprine inhibits DNA synthesis and prevents lymphocyte proliferation in the immune system.\(^{15,41,47}\) It is used as a steroid-sparing agent in moderate to severe lupus and in the maintenance phase of lupus nephritis.\(^{15,47}\)

Belimumab

Belimumab, a human monoclonal antibody, blocks the biologic activity of B lymphocyte stimulator (BLyS/BAFF). This decreases the antibody levels in the body which may help reduce the autoimmune activity of SLE.\(^{41}\) Belimumab was approved by the FDA in 2011 for use in adults.\(^{7}\) In two phase III trials, BLISS-52 and BLISS-76, belimumab showed noteworthy improvements in patients with SLE after 52 weeks, but the advances were not statistically maintained at week 76.\(^{15}\) Belimumab demonstrated a steroid-sparing effect in these trials as well as a decreased rate of disease flares.\(^{65}\) To be included in the trial, patients had to meet the ACR criteria for SLE, and they had to have active disease. Patients also had to demonstrate a positive
ANA and be on a stable regimen of prednisone, NSAIDs, antimalarials, or immunosuppressive drugs for 30 days prior to the start of the trial. Exclusion criteria included severe active lupus nephritis, CNS lupus, and pregnancy. Exclusion criteria also included prior therapy within the last 3 months of IV cyclophosphamide, IV immunoglobulin, IV prednisone, or drugs that target B-lymphocytes.  

The safety profile for belimumab is good. Safety data from the BLISS trials demonstrated an adverse effect profile and infection rate similar to that of placebo in patients with a mean age of 40 +/- 12 years. There is no efficacy data in older patients. Patients on belimumab should not receive live vaccines 30 days before, or during treatment due to a decreased ability to mount an immune response.

Rituximab

Rituximab is a humanized chimeric mouse/human monoclonal antibody that targets the B-cell-specific antigen CD20. It leads to depletion of auto-reactive B-cells in the circulation of patients with SLE. Although not FDA approved, it is often used off label for severe refractory SLE. Unfortunately, placebo controlled trials in SLE failed to improve clinical outcomes.

Pharmacist’s Role

- Review the patient’s medications for drug induced lupus or for drug interactions (Table 2 and Table 7)
- Monitor for adverse reactions and therapeutic response
- Ensure the patient is current on inactivated influenza and pneumococcal vaccines
- Monitor vitamin D levels and bone mineral density
The majority of patients with SLE have insufficient levels of vitamin D. This may be due in part to less sun exposure, and medications used for the treatment of SLE.

Patients on long-term glucocorticoids should receive sufficient daily calcium and vitamin D and/or a bisphosphonate to minimize the degree of bone loss.73

- Review patient’s history to determine increased risk of NSAID-induced ulcers
  - The addition of a proton pump inhibitor or histamine-2 receptor blocker may be indicated

- Ensure that the patient is receiving daily supplemental folic acid to reduce side effects related to the gastrointestinal system74

- Confirm and make recommendations to ensure medications are administered correctly with regard to meals and in relation to other medications.

Conclusion

SLE is a chronic autoimmune disorder whereby the exact etiology of which is unknown. SLE predominately affects younger women; however, it is reported to occur in up to 20% of patients 50 years or older. In patients with SLE, nearly every system in the body is affected with varying degrees of severity ranging from subclinical to fatal. The hallmark feature of SLE is the production of hyper-reactive, memory B-cells. Auto-antibodies are directed primarily against nuclear antigens, but also against cytoplasmic components of cells. The diagnosis of SLE is based on criteria set by the ACR. The management of SLE is largely a suppression of the immune response, but should be individualized and dependent on presenting symptoms and disease progression.
References:


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44. Petri M. Systemic Lupus International Collaborating Clinic (SLICC).


54. Lander SA, Wallace DJ, Weisman MH. Celecoxib for systemic lupus erythematosus: case


65. Navarra SV, Guzman RM, Gallacher AE et al. Efficacy and safety of Belimumab in patients


74. Ortiz Z, Shea B, Suarez-Almazor ME et al. Folic acid and folinic acid for reducing side
Table 1. Factors Associated with the Development or Exacerbation of SLE

<table>
<thead>
<tr>
<th>Factor</th>
<th>Associated with</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sun exposure</td>
<td>Genetic influence</td>
</tr>
<tr>
<td>Smoking</td>
<td>Female hormones</td>
</tr>
<tr>
<td>Virus exposure (e.g. Epstein–Barr virus)</td>
<td>Immunizations</td>
</tr>
<tr>
<td>Stress</td>
<td>Occupational exposure (silica, mercury, etc.)</td>
</tr>
<tr>
<td>Diet</td>
<td></td>
</tr>
</tbody>
</table>

Sources: References 1, 2, 5-8.
Abbreviations: SLE = Systemic Lupus Erythematosus

Table 2. Medications that May Lead to the Development of SLE

<table>
<thead>
<tr>
<th>Drug Classification</th>
<th>Very Low Risk</th>
<th>Low to Moderate Risk</th>
<th>High Risk</th>
</tr>
</thead>
<tbody>
<tr>
<td>Antiarrhythmic</td>
<td>Propafenone</td>
<td>Quinidine</td>
<td>Procainamide</td>
</tr>
<tr>
<td>Antibiotic</td>
<td>Nitrofurantoin</td>
<td>Isoniazid, Minocycline</td>
<td></td>
</tr>
<tr>
<td>Antiepileptic</td>
<td>Phenytoin, Primidone\ Ethosuximide</td>
<td>Carbamazepine</td>
<td></td>
</tr>
<tr>
<td>Antihypertensive</td>
<td>Enalapril, Clonidine, Labetalol, Atenolol, Chlorthalidone, Hydrochlorothiazide</td>
<td>Captopril, Methyldopa</td>
<td>Hydralazine</td>
</tr>
<tr>
<td>Anti-inflammatory</td>
<td>Sulfasalazine</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Antipsychotic</td>
<td>Perphenazine, Lithium</td>
<td>Chlorpromazine</td>
<td></td>
</tr>
<tr>
<td>Antithyroid</td>
<td>Propylthiouracil</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Miscellaneous</td>
<td>Lovastatin, Levodopa\ Timolol ophthalmic drops</td>
<td></td>
<td>Infliximab, Etanercept, Adalimumab, Interferons</td>
</tr>
<tr>
<td>Biologic</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Sources: References 7, 16, 18-21.
Abbreviations: SLE = Systemic Lupus Erythematosus
Table 3. Clinical findings of early and late-onset SLE

<table>
<thead>
<tr>
<th>Physical Findings</th>
<th>Serological Findings</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Early Onset SLE (age &lt; 50 y)</strong></td>
<td><strong>Late Onset SLE (age ≥ 50 y)</strong></td>
</tr>
<tr>
<td>Malar rash</td>
<td>Pulmonary manifestations</td>
</tr>
<tr>
<td>Photosensitivity</td>
<td>Serositis</td>
</tr>
<tr>
<td>Arthritis</td>
<td>Pericarditis</td>
</tr>
<tr>
<td>Alopecia</td>
<td>Pleurisy</td>
</tr>
<tr>
<td>Purpura / Cutaneous vasculitis</td>
<td>Sjögren’s syndrome</td>
</tr>
<tr>
<td>Raynaud’s phenomenon</td>
<td></td>
</tr>
<tr>
<td>Neuropsychiatric manifestations</td>
<td></td>
</tr>
<tr>
<td>Fever and lymphadenopathy</td>
<td></td>
</tr>
<tr>
<td>Nephritis / Nephrotic syndrome</td>
<td></td>
</tr>
<tr>
<td>Hematologic derangements</td>
<td></td>
</tr>
<tr>
<td>Increased frequency of anti-RNP antibodies and anti-Sm antibodies; low CH$_{50}$</td>
<td>Increased frequency of RF and ANA positivity; Increased frequency of the anti-nuclear autoantibodies, anti-Ro/SSA and anti-La/SSB positivity</td>
</tr>
</tbody>
</table>

Sources: References 18, 28, 30.
Abbreviations: ANA = Antinuclear antibodies, Anti-La/SSB = Anti-La/Sjogren syndrome type B, Anti-RNP antibodies = Anti-ribonucleoprotein, Anti-Ro/SSA = Anti/Ro Sjogren syndrome type A, Sm antibodies = Anti-Smith antibodies, CH$_{50}$=50% hemolytic complement, RF= Rheumatoid Factor, SLE = Systemic Lupus Erythematosus
Table 4 American College of Rheumatology Criteria for Diagnosis of SLE*

| Malar rash – butterfly shaped rash over the nose and cheeks; can be flat or raised |
| Discoid rash – a rash that appears as red, raised, disk-shaped patches |
| Photosensitivity – unusual reaction to sun or light that causes a rash to appear |
| Oral ulcers – sores, usually painless, appearing in the mouth or nasopharynx |
| Non-erosive arthritis – joint pain and swelling of two or more joints |
| Serositis – Pleuritis (inflammation around the lungs) or Pericarditis (inflammation around the heart) |
| Renal disorder – persistent protein (>0.5 gram/day) or any cellular casts in the urine |
| Neurological disorder – seizures or psychosis in the absence of offending drugs or known metabolic conditions |
| Hematologic disorder – hemolytic anemia, leukopenia, lymphopenia, or thrombocytopenia |
| Immunologic disorder – anti-DNA, Anti-Smith antibodies, or positive antiphospholipid antibodies on testing |
| Positive antinuclear antibody at any point in time in the absence of medications/drugs |

*Four of 11 criteria are needed for the formal diagnosis of SLE

Sources: References 12, 38, 39.

Abbreviations: Anti-DNA = Anti-deoxyribonucleic acid, SLE = Systemic Lupus Erythematosus
<table>
<thead>
<tr>
<th>Table 5 Treatment Recommendations Overview of SLE</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>American College of Rheumatology Committee</strong></td>
</tr>
<tr>
<td><strong>Mild SLE</strong></td>
</tr>
<tr>
<td>Nonsteroidal anti-inflammatory Drugs</td>
</tr>
<tr>
<td>Antimalariais (Hydroxychloroquine)</td>
</tr>
<tr>
<td>Oral glucocorticoids (low dose)</td>
</tr>
<tr>
<td><strong>Serious, Life Threatening, or Organ Threatening SLE</strong></td>
</tr>
<tr>
<td>High dose glucocorticoids</td>
</tr>
<tr>
<td>Immunosuppressive/cytotoxic agents (azathioprine, cyclophosphamide, and methotrexate)</td>
</tr>
<tr>
<td><strong>Lupus Nephritis</strong></td>
</tr>
<tr>
<td></td>
</tr>
</tbody>
</table>

Sources: References 45, 46.
Abbreviations: SLE = Systemic Lupus Erythematosus
Table 6 Summary of adverse effects and recommended monitoring for medications used in the treatment of SLE

<table>
<thead>
<tr>
<th>Medication</th>
<th>Adverse effects</th>
<th>Monitor</th>
</tr>
</thead>
<tbody>
<tr>
<td>NSAIDs</td>
<td>Gastrointestinal bleeding, hepatic toxicity, renal toxicity, hypertension</td>
<td>CBC, creatinine, AST, ALT, blood pressure, monitor for bleeding</td>
</tr>
<tr>
<td>Glucocorticoids</td>
<td>Hypertension, hyperglycemia, hyperlipidemia, hypokalemia, osteoporosis, cataracts, fluid retention, glaucoma, infections</td>
<td>Blood pressure, cholesterol, glucose, potassium, bone mineral density</td>
</tr>
<tr>
<td>Hydroxychloroquine</td>
<td>Retinal and macular damage</td>
<td>Fundoscopic and visual fields, visual changes</td>
</tr>
<tr>
<td>Azathioprine</td>
<td>GI side effects, infections, Myelosuppression, hepatotoxicity, lymphoproliferative disorders</td>
<td>CBC, differential and platelet count, AST or ALT</td>
</tr>
<tr>
<td>Cyclophosphamide</td>
<td>Myelosuppression, malignancy, hemorrhagic cystitis, immunosuppression, severe infections, nausea, vomiting, reversible hair loss</td>
<td>CBC, differential and platelet count, urinalysis</td>
</tr>
<tr>
<td>Methotrexate</td>
<td>Myelosuppression, hepatic toxicity, pulmonary infiltrates or fibrosis, stomatitis</td>
<td>CBC, Hepatitis B and C serology in high risk patients, AST, albumin, bilirubin, creatinine, chest radiograph</td>
</tr>
<tr>
<td>Mycophenolate</td>
<td>Anemia, leukopenia, thrombocytopenia, infections, diarrhea, pancreatitis</td>
<td>CBC, differential and platelet count</td>
</tr>
<tr>
<td>Belimumab</td>
<td>Infections, bradycardia, hypotension, depression, leukopenia</td>
<td>CBC with differential</td>
</tr>
</tbody>
</table>

Sources: References 15, 41, 45, 47-51.
Abbreviations: ALT = Alanine Transaminase, AST = Aspartate Transaminase, CBC = Complete Blood Count, GI = Gastrointestinal, NSAIDs – Nonsteroidal Anti-inflammatory Drugs, SLE = Systemic Lupus Erythematosus
Table 7. Summary of drug interactions used in the treatment of SLE

<table>
<thead>
<tr>
<th>Medication</th>
<th>Drug Interaction</th>
</tr>
</thead>
<tbody>
<tr>
<td>NSAIDs</td>
<td>Lithium, Diuretics, Beta blockers, ACEI, Angiotensin Receptor Blockers</td>
</tr>
<tr>
<td>Glucocorticoids</td>
<td>No significant drug interactions</td>
</tr>
<tr>
<td>Hydroxychloroquine</td>
<td>No significant drug interactions</td>
</tr>
<tr>
<td>Azathioprine</td>
<td>Allopurinol, Febuxostat, Mesalamine, ACEI, Trimethoprim-sulfamethoxazole</td>
</tr>
<tr>
<td>Cyclophosphamide</td>
<td>No significant drug interactions</td>
</tr>
<tr>
<td>Methotrexate</td>
<td>Trimethoprim-sulfamethoxazole, NSAIDs</td>
</tr>
<tr>
<td>Mycophenolate</td>
<td>Cholestyramine, Antacids, and Phosphate Binders should not be administered at the same time</td>
</tr>
<tr>
<td>Belimumab</td>
<td>Drug interactions have not been formally studied</td>
</tr>
</tbody>
</table>

Sources: References 48-50, 69, 70.
Abbreviations: ACEI = Angiotensin Converting Enzyme Inhibitor, NSAIDs = Non-Steroidal Anti-inflammatory Drugs, SLE = Systemic Lupus Erythematosus