Medical Management of Systemic Lupus Erythematosus

Case Study and Commentary, Diane L. Kamen, MD, MSCR, and Gary S. Gilkeson, MD

Systemic lupus erythematosus (SLE) is a potentially severe, frequently disabling autoimmune disease with multiorgan involvement and a typically waxing and waning course. SLE is often considered the prototypical autoimmune disease. It is characterized by the production of a vast array of autoantibodies and a variable clinical presentation that may include arthritis, skin disease, hematologic manifestations, central nervous system disease, early atherosclerosis, and often the development of glomerulonephritis [1]. SLE has the potential to affect virtually every organ.

The clinical symptoms and immunologic manifestations of SLE are diverse, and no 2 patients present the same way. Early diagnosis can be difficult because of the insidious onset of predominantly nonspecific constitutional symptoms (eg, fatigue and low-grade fever). The average delay between symptom onset and diagnosis is 2.5 years, with arthritis being the most frequent initial manifestation (34.5% of a large multiethnic cohort) [2].

The estimated prevalence of SLE varies between 15 and 51 cases per 100,000 in the U.S. population [3]. Multiple susceptibility genes as well as environmental factors contribute to the development of SLE. There is a complex pattern of inheritance, with concordance rates higher in monozygotic twins than in dizygotic twins but not 100%, suggesting the influence of environmental triggers of disease expression [4]. Characterizing the genetic basis of disease and discovering environmental triggers are active areas of research in SLE.

**CASE STUDY 1**

**Initial Presentation**

A 20-year-old African-American woman presents to her primary care physician complaining of fatigue, leg pain, and a rash.

**History**

The rash started approximately 1 year ago as pruritic sores on her scalp and scaly patches around her ears. Lotions and
over-the-counter hydrocortisone have been ineffective. Starting 2 weeks ago, the patient also noted pain and dependent swelling in her feet and ankles; the swelling improves with elevation. Upon questioning, the patient reports that she has noticed darkened urine but no dysuria. Fatigue has been present for several months.

The patient has no significant past medical or surgical history. Her father is healthy, and her mother has rheumatoid arthritis. The patient takes daily birth control pills and has no drug allergies. She currently smokes half a pack of cigarettes daily and has smoked for 7 years. The remainder of the review of systems is noncontributory.

**Epidemiology and Risk Factors**

SLE is considered primarily a disease of women of childbearing age, although males or females of any age can be affected. The typical age at diagnosis is between 15 and 45 years. The female-to-male ratio is 9:1. African Americans and Hispanic Americans have a threefold increased incidence of SLE, develop SLE at an earlier age, and have increased morbidity and mortality compared with whites [5,6].

SLE cases demonstrate familial clustering, and susceptibility has a genetic component. From 5% to 12% of first-degree relatives of SLE patients will themselves develop the disease during their lifetime. Several susceptibility loci as well as specific gene polymorphisms have been identified, although the relationships are complex and vary by ethnicity [7]. As in the case of this patient, there is also a higher incidence of other autoimmune diseases in family members of SLE patients. First-degree relatives of female patients with SLE have a 4 times greater risk of having an autoimmune disease compared with those without SLE [8].

Multiple environmental risk factors have been implicated as playing a role in triggering SLE. Studies of exposures such as ultraviolet light, medications, hormones, infectious agents, hair dyes, cigarette smoking, silica, and dietary factors have produced conflicting results, with no single factor explaining the excess risk [9–15]. The case patient currently smokes cigarettes, a factor that was shown in a meta-analysis of 9 case-control and cohort studies to have a small but statistically significant association with the development of SLE [16].

**Physical Examination**

Physical examination of the patient reveals a blood pressure of 170/110 mm Hg, pulse of 80 bpm, respiratory rate of 18 breaths/min, temperature of 99°F, and weight of 206 lb. Skin examination reveals 2 coin-shaped scarring patches of hair loss on the scalp and multiple erythematous plaques in the pinnae and around the ears. Head, neck, chest, cardiovascular, and abdominal examinations are otherwise unremarkable. Examination of the extremities reveals bilateral 2+ pitting edema of the feet and ankles, bland knee effusions, and tenderness of the proximal interphalangeal joints bilaterally.

**Characteristic Musculoskeletal Features**

Joint pain is the most common presenting symptom of SLE. Joint involvement in SLE is typically symmetric and inflammatory in nature, characterized by joint swelling and stiffness in the morning, which improves with exercise. In contrast to rheumatoid arthritis, deformities and joint space erosions are less common in SLE. A Jaccoud-like arthropathy can be seen in SLE patients, with ulnar deviation, hyperflexion, and hyperextension deformities that are reducible. Also, patients often report pain that is out of proportion to the degree of synovitis seen on examination. Some SLE patients have articular disease and serologic features consistent with rheumatoid arthritis, a condition that has been referred to as “rhupus,” which is associated with rheumatoid factor positivity, elevated C-reactive protein, and an erosive polyarthritis with nonreducible deformities [17,18]. First-line therapy for a patient with arthritis as the primary manifestation of their SLE is nonsteroidal anti-inflammatory drugs.

Avascular necrosis (AVN) of bone is a major source of morbidity in SLE and often presents as painful motion localized to a single joint. The frequency of AVN has been reported at 10% to 12% and is most often seen in the femoral head, although the knees, shoulders, ankles, and wrists are often involved as well [19]. Corticosteroid use, the presence of arthritis, and use of cytotoxic medication are each independent risk factors for the development of AVN in SLE patients [20].

Patients with SLE may develop myopathy that is either inflammatory or related to medications, most commonly corticosteroids. These patients present with muscle weakness and myalgias. The inflammatory myositis of SLE is often more subtle, in both clinical presentation and in muscle biopsy findings, compared with what is seen in polymyositis [21].

**Clinical Spectrum of Lupus**

The clinical spectrum of lupus is wide and includes SLE, chronic cutaneous (discoid) lupus, subacute cutaneous...
lupus, drug-induced lupus, and neonatal lupus. It is estimated that cutaneous lupus is 2 to 3 times more prevalent than SLE [22]. In these patients, it is important to evaluate for systemic involvement and, if present, to treat accordingly.

The case patient has a discoid rash—a scarring skin lesion that is the hallmark of chronic cutaneous (discoid) lupus but that also can occur in SLE. In contrast, the annular lesions of subacutecutaneous lupus are nonscarring, highly photosensitive, associated with anti-Ro/SS-A antibodies, and are more often seen in Caucasian women [23]. In addition to a discoid rash, the case patient has evidence of systemic disease, with hypertension and edema that likely represents renal involvement, making SLE more likely. First-line treatment for SLE-related skin lesions includes sunscreen (and sun avoidance), antimalarial agents (eg, hydroxychloroquine), and topical corticosteroids.

Drug-induced lupus is an important consideration when a patient presents with new onset of lupus-like symptoms; more than 80 drugs have been associated with lupus. Typically, drug-induced lupus is a milder form of SLE, with arthralgias, myalgias, fever, pleurisy, and pericarditis, which usually resolve after discontinuation of the drug. Antinuclear antibodies (ANA) are present in 90% of cases of drug-induced lupus [24]. A higher frequency of positive antihistone antibodies may help distinguish drug-induced lupus from SLE. Drugs that have been proven to induce lupus include minocycline, hydralazine, procainamide, isoniazid, methyl dopa, chlorpromazine, and quinidine, none of which the case patient was taking [24].

How is the diagnosis of SLE made?

Diagnosis of SLE

Early diagnosis of SLE is made difficult by its highly variable clinical presentation. Many different diseases, particularly infections, malignancies, and drug effects can cause symptoms similar to those of SLE. What distinguishes SLE from many other disorders is the ability of SLE to cause abnormalities in multiple organs simultaneously. In this case, the patient has sufficient risk factors to warrant a screening test for SLE.

The primary laboratory test for SLE is the ANA test, which is positive in more than 98% of patients. Its high sensitivity in SLE patients makes it a valuable screening test; however, its low specificity requires that other tests be performed to confirm the diagnosis. More than 100 different autoantibodies have been associated with SLE, but not all of these have been correlated with disease manifestations [25]. Studies of banked serum samples show that autoantibodies develop up to a decade prior to the diagnosis of SLE, raising the possibility of a predictive role [26].

The American College of Rheumatology has established criteria for the classification of SLE (Table 1). Any patient who presents with 4 or more of the 11 criteria, serially or simultaneously, and who has no alternative explanation for each manifestation is considered to have SLE for purposes of clinical studies [28]. Although designed for use in clinical trials, the presence of 4 of the 11 criteria is greater than 90% sensitivity and specificity for the diagnosis of SLE [29]. Rarely, a patient will present with a severe manifestation of SLE but fall short of having 4 criteria, and it is important to identify and treat these patients as well. Because of the usefulness of the American College of Rheumatology classification criteria in defining such a heterogeneous disease, many practitioners use the SLE criteria routinely in the clinical setting. Many disease manifestations, including alopecia, Raynaud’s phenomenon, vasculitis, and nervous system involvement (eg, aseptic meningitis, transverse myelitis, mononeuritis multiplex), however, are not included.

Diagnosis and Initial Therapy

A urinalysis is performed and shows greater than 300 mg/dL protein and 10 red blood cells per high-power field, with a few red cell casts. A complete blood count and metabolic profile are both unremarkable. C3 and C4 complement levels are both below normal. Erythrocyte sedimentation rate is elevated at 63 mm/hr; C-reactive protein level is normal. Serologic testing is positive for ANA antibodies at 1:320 titer homogenous pattern as well as double-stranded DNA antibodies. An anti-ENA panel is negative for anti-Sm, anti-RNP, anti-Ro/SS-A, anti-La/SS-B, and anti-Scl-70 antibodies.

In light of the patient’s discoid rash, arthritis, proteinuria, positive ANA result, and positive double-stranded DNA antibodies, the diagnosis of SLE is made. Treatment is initiated with prednisone (60 mg/day) and hydroxychloroquine (400 mg/day), and the patient is admitted to the hospital for blood pressure control and a renal biopsy.

• When should renal biopsy be considered for patients with SLE?

Indications for Renal Biopsy

Renal biopsy should be considered for any SLE patient who has clinical evidence of active nephritis, particularly at initial presentation, to help decide on whether or not to use more aggressive immunosuppression. A renal biopsy is appropriate in this case because the patient has red cell urinary casts, new proteinuria, and hypertension in the setting of SLE. Often asymptomatic proteinuria or hematuria is the presenting feature of nephritis, but clinical presentation does not always
reflect the degree of histologic change on renal biopsy. This patient had hypertension, proteinuria, hematuria with casts, and edema, suggesting the presence of proliferative and potentially rapidly progressive glomerulonephritis. Renal disease is the most important predictor of morbidity and mortality in SLE. Classification of lupus nephritis is based on histology obtained from the renal biopsy, and this classification has been shown to predict prognosis and is useful in directing therapy [30].

- **What are current treatment options for SLE and lupus nephritis?**

**Treatment**

Current therapies for SLE are limited. Treatments that have been approved by the U.S. Food and Drug Administration for SLE include only hydroxychloroquine, corticosteroids, and aspirin. Several immunosuppressive/cytotoxic drugs are also used and are felt to be beneficial for active disease, but patients are exposed to many toxicities over the course of treatment with these agents. Patients with SLE are often in a difficult situation of being dependent on corticosteroids and/or cytotoxic agents for control of their disease, while developing cumulative toxicities from their use.

Most of the large-scale, prospective, randomized studies published in SLE have addressed lupus nephritis as the primary disease manifestation. Patients with proliferative glomerulonephritis (World Health Organization Class III or IV) usually cannot be adequately controlled with corticosteroids alone. Cyclophosphamide has been the mainstay of treatment in proliferative lupus nephritis, but recent trials using mycophenolate mofetil have shown efficacy with fewer adverse events [31,32]. The major toxicities of cyclophosphamide include bone marrow suppression, infection, hemorrhagic cystitis, bladder cancer, malignancy, and infertility. Despite improved therapies, severe lupus nephritis leads to renal failure requiring dialysis or transplantation in approximately 20% of patients over a 10-year period.

In recent years, there has been growing excitement about potential therapies for SLE with improved safety profiles. Several targeted biologic therapies for SLE are in various phases of clinical trials, including anti-CD20 antibody (rituximab) [33] and anti-B lymphocyte stimulator (BlyS) protein [34].
Common medications used in the treatment of SLE are listed in Table 2.

**Table 2. Common Medications Used in Systemic Lupus Erythematosus (SLE)**

<table>
<thead>
<tr>
<th>Medication/Class</th>
<th>Common Use in SLE</th>
<th>Serious Adverse Effects</th>
</tr>
</thead>
<tbody>
<tr>
<td>NSAIDs</td>
<td>Musculoskeletal manifestations, mild serositis, headache, fever</td>
<td>Renal and liver toxicity, GI bleeding, cardiovascular and central nervous system effects</td>
</tr>
<tr>
<td>Corticosteroids, topical</td>
<td>Skin rash</td>
<td>Skin atrophy, skin infection</td>
</tr>
<tr>
<td>Corticosteroids, oral</td>
<td>General manifestations of SLE</td>
<td>Hypertension, diabetes, osteoporosis, avascular necrosis, atherosclerosis, steroid myopathy, GI ulceration, increased infection risk, glaucoma, cataracts, Cushing’s syndrome</td>
</tr>
<tr>
<td>Corticosteroids, intravenous</td>
<td>Severe, life- or organ-threatening manifestations</td>
<td>Same as oral corticosteroids</td>
</tr>
<tr>
<td>Antimalarials (most commonly hydroxychloroquine)</td>
<td>Constitutional symptoms, musculoskeletal manifestations, skin rash, pleurisy, maintenance of remission</td>
<td>Ophthalmologic toxicity, hemolytic anemia with G6PD deficiency</td>
</tr>
<tr>
<td>Dehydroepiandrosterone</td>
<td>Mild manifestations of SLE, steroid-sparing agent</td>
<td>Hypertension, liver toxicity</td>
</tr>
<tr>
<td>Azathioprine</td>
<td>Steroid-sparing agent, maintenance of remission</td>
<td>Myelosuppression, increased infection risk, hepatotoxicity, lymphoproliferative disorders, drug hypersensitivity</td>
</tr>
<tr>
<td>Methotrexate</td>
<td>Arthritis, steroid-sparing agent</td>
<td>Myelosuppression, increased infection risk, hepatotoxicity, pulmonary infiltrates and fibrosis</td>
</tr>
<tr>
<td>Cyclophosphamide, oral daily or intravenous monthly</td>
<td>Severe, life- or organ-threatening manifestations</td>
<td>Myelosuppression, increased infection risk, bladder toxicity and carcinoma (higher risk with oral than with IV), gonadal toxicity</td>
</tr>
<tr>
<td>Mycophenolate mofetil</td>
<td>Lupus nephritis, steroid-sparing agent</td>
<td>Myelosuppression, increased infection risk</td>
</tr>
<tr>
<td>Cyclosporine</td>
<td>Alternative steroid-sparing agent</td>
<td>Myelosuppression, increased infection risk, hypertension, renal insufficiency</td>
</tr>
</tbody>
</table>

GI = gastrointestinal; NSAIDs = nonsteroidal anti-inflammatory drugs.

Common medications used in the treatment of SLE are listed in Table 2.

**Case Conclusion**

A nephrologist is consulted and performs a renal biopsy under ultrasound guidance. The biopsy reveals several hypercellular glomeruli, many with crescent formation. No necrosis is seen. Sections labeled with IgG, IgM, IgA, and C3 show positive immunofluorescence staining. On electron microscopy, subendothelial, subepithelial, and mesangial immune electron-dense deposits compatible with immune complexes were seen. The patient’s activity index is 13 out of 24 and her chronicity index 6 out of 12. The biopsy is consistent with class IV lupus nephritis; high-dose intravenous corticosteroids (1 g of methylprednisolone daily over 3 days) and intravenous monthly cyclophosphamide were initiated. Six months later, cyclophosphamide is changed to azathioprine for maintenance therapy and she is tapered off of prednisone. Other than persistent proteinuria, her SLE is fairly quiescent.

**CASE STUDY 2**

**Initial Presentation**

A 37-year-old white woman presents to the emergency department with exertional chest pain, nausea, diaphoresis, and shortness of breath.

**History**

The patient was diagnosed with SLE 10 years ago. Her initial manifestations of SLE included neuropsychiatric lupus with cognitive dysfunction, malar rash, positive ANA antibodies, and high-titer IgG and IgM antiphospholipid antibodies. The patient had been doing well on hydroxychloroquine, a daily aspirin, and low-dose prednisone (10 mg/day) until the day before she presented to the emergency department, when she developed the acute onset of left-sided chest pain while doing housework. She denies orthopnea, edema, fever, cough, or hemoptysis.

The patient has no previous cardiac history, but several first-degree relatives have known coronary disease. She denies any history of tobacco, alcohol, or illicit drug use. Review of systems is otherwise negative.

- Are patients with SLE at higher risk for cardiovascular disease?

There is a disturbingly high rate of cardiovascular disease among young SLE patients. SLE is an independent risk factor for atherosclerosis, and accelerated atherosclerosis is a major cause of morbidity and mortality among SLE patients.
The risk of coronary artery disease is increased 10-fold in SLE patients. In women aged 35 to 44 years, the estimated rate of myocardial infarction is 50-fold greater in those with SLE compared with control populations [35].

Evidence suggests that disease-related factors play a role in atherogenesis. In a case-control study that included 197 patients with lupus and 197 control subjects matched for age, gender, race, and hypertension status, the overall risk of atherosclerosis was 2.4 times higher in lupus patients compared with controls [36]. Logistic-regression analysis revealed an association between carotid plaque and duration of disease, a higher SLE damage/index score, and lack of immunosuppressive therapy.

Known cardiovascular risk factors such as hypertension, hyperlipidemia, hyperhomocysteinemia, diabetes, and obesity are very prevalent in SLE patients [37,38]. Even young patients with SLE should have routine screening for and management of these risk factors. But several studies have found that the “traditional” cardiovascular risk factors alone do not predict atherosclerosis in patients with SLE.

**Initial Evaluation**

Physical examination reveals tachycardia at a rate of 112 bpm and a blood pressure of 145/92 mm Hg. Findings on electrocardiography are consistent with an acute anteroseptal myocardial infarction. The patient’s CK-MB fraction and troponin I levels are elevated.

- Does this patient’s history of antiphospholipid antibodies affect her management?

**Antiphospholipid Antibody Syndrome**

Antiphospholipid IgG and IgM antibodies are associated with a higher risk of clotting and are independent predictors of vascular events [39]. They can be detected by testing for anticardiolipin antibodies, which are most often directed against β2-glycoprotein I. These antibodies may be found in healthy people without any excess thrombosis risk, so the syndrome is defined by the combined presence of a clinical abnormality (which involves a history of vascular thrombosis or pregnancy morbidity) with the laboratory abnormality. The clinical consequences of antiphospholipid antibody syndrome include venous and arterial thromboses and placental insufficiency in pregnancy resulting in fetal loss [40]. Despite the tendency to clot, these patients tend to have thrombocytopenia and, paradoxically, a prolonged partial thromboplastin time, which led to the term “lupus anticoagulant.”

Prophylactic treatment with daily aspirin is often used in SLE patients with antiphospholipid antibodies but no history of a thrombotic event, although definitive evidence to support this practice is lacking. The case patient has had a myocardial infarction and therefore warrants full anticoagulation with heparin in the short term and warfarin in the long term, with a target international normalized ratio of at least 2.0 to 3.0. [41].

**Case Conclusion**

The case patient has a left heart catheterization with angiography revealing a high-grade stenosis of the left anterior descending coronary artery. Percutaneous transluminal coronary angioplasty with coronary stenting is performed without complication. Because her coronary ischemia is felt to be related to underlying antiphospholipid antibody syndrome, she remains on intravenous heparin until her international normalized ratio on warfarin is above 2.0.

**CASE STUDY 3**

**Initial Presentation**

A 29-year-old Hispanic woman with a 5-year history of SLE presents to her primary care physician for a routine follow-up visit and wishes to discuss plans for future pregnancy.

**History**

The patient’s disease has been well controlled for the past year, while her prednisone dose has been tapered down to now 7.5 mg/day. She is taking hydroxychloroquine, which has significantly improved her lupus-related rashes, fatigue, and arthritis. She has no history of renal disease. She recently stopped her birth control pills and would like to attempt pregnancy with her husband. Serologic testing shows a positive ANA and positive anti-Sm, anti-SSA, and anti-SSB antibodies.

- Is this patient at increased risk for pregnancy complications?

Women with SLE have a higher rate of spontaneous abortion, intrauterine fetal death, premature birth, and pre-eclampsia. Poor pregnancy outcomes are more common in women with increased disease activity during pregnancy; thus, medications such as hydroxychloroquine and azathioprine should be continued during pregnancy if required for disease control [42]. Certain other medications, such as methotrexate and cyclophosphamide, must be avoided if there is a chance of pregnancy because of their teratogenicity risk. Optimal pregnancy outcomes are achieved when SLE is in complete remission for 6 to 12 months [23].

Both the placenta and the fetus are at risk of becoming targets of maternal autoantibodies. There is a 2% risk of...
anti-Ro/SS-A and anti-La/SS-B antibodies crossing the placenta and causing neonatal lupus. The case patient should be counseled about the potential manifestations of congenital heart block, most often third-degree, and transient cutaneous, hepatic, and hematologic involvement [23].

It is also important to look for the presence of antiphospholipid antibodies, which can be associated with recurrent fetal loss. For women with antiphospholipid antibody syndrome and a history of fetal loss, preventive therapy with low-molecular-weight heparin plus low-dose aspirin has been shown to be effective in reducing the rate of spontaneous abortion rate [43].

Case Conclusion
The patient’s antiphospholipid antibody testing is negative. Her lupus is clinically quiescent so her prednisone is tapered by 2.5 mg every 2 weeks until she is on only hydroxychloroquine. Several months later she called the clinic to report a positive home pregnancy test. She was referred to high-risk obstetrics for close monitoring throughout her pregnancy.

SUMMARY
Although the prognosis for patients with SLE has improved over the past few decades, the disease remains one of substantial associated morbidity and mortality. As a consequence of the disease itself or medications used to treat it, patients acquire irreversible organ damage over time. The 10-year survival rate of all SLE patients is greater than 80%, but disabilities are common.

Paramount in the care of SLE patients is the need to monitor and treat disease activity as well as advise avoidance of potential disease triggers, including sulfa antibiotics, high estrogen–containing oral contraceptives, and direct sun exposure. It is also important for patients to stay up-to-date with routine health maintenance, including screening and prevention of osteoporosis, cardiovascular risk factor management, age-appropriate immunizations, and prompt treatment of infections, due to the propensity for life-threatening complications of these comorbidities.

A key role of the primary care provider is to be alert to the diagnosis of SLE, help manage routine health problems, and help monitor for drug toxicities. Due to the complexity of the diagnosis and treatment of SLE, close communication between the primary care provider and the rheumatologist is needed for the best patient care.

Corresponding author: Diane L. Kamen, MD, MSCR, 96 Jonathan Lucas, Ste. 912, Charleston, SC 29425.

Financial disclosures: None.

Author contributions: conception and design, DLK; drafting of the article, DLK; critical revision of the article, DLK, GSG.

www.turner-white.com

References
18. Fernandez A, Quintana G, Matteson EL, et al. Lupus arthropathy: historical evolution from deforming arthritis to rhu-
19. Gladman DD, Chaudhry-Ahluwalia V, Ibanez D, et al. Out-
comes of symptomatic osteonecrosis in 95 patients with sys-
20. Gladman DD, Urowitz MB, Chaudhry-Ahluwalia V, et al. Pre-
dictive factors for symptomatic osteonecrosis in patients with 
21. Gladman DD, Urowitz MB. Systemic lupus erythematosus 
position paper on the revision of the 1982 ACR criteria for
Primer on the rheumatic diseases. 12th ed. Atlanta: Arthritis 
Foundation; 2001.
explosion in systemic lupus erythematosus: more than 100
different antibodies found in SLE patients. Semin Arthritis 
26. Arbuckle MR, McClain MT, Rubertone MV, et al. Develop-
ment of autoantibodies before the clinical onset of systemic 
27. Hochberg MC. Updating the American College of Rheuma-
tology revised criteria for the classification of systemic lupus 
the classification of systemic lupus erythematosus. Arthritis 
29. Feletar M, Ibanez D, Urowitz MB, Gladman DD. The impact of 
the 1997 update of the American College of Rheumatol-
yogy revised criteria for the classification of systemic lupus 
erythematosus: what has been changed? Arthritis Rheum 
30. Weening JJ, D’Agati VD, Schwartz MM, et al. The classifica-
tion of glomerulonephritis in systemic lupus erythematosus 
32. Ginzler EM, Aranow C. Mycophenolate mofetil in lupus 
33. Looney RJ, Anolik JH, Campbell D, et al. B cell depletion as a 
novel treatment for systemic lupus erythematosus: a phase I/II 
dose-escalation trial of rituximab. Arthritis Rheum 2004;50: 
2580–9.
34. Stohl W. BlySfulness does not equal blissfulness in systemic 
lupus erythematosus: a therapeutic role for BLyS antago-
rates of myocardial infarction and angina in women with 
 systemic lupus erythematosus: comparison with the Fram-
36. Roman MJ, Shanker BA, Davis A, et al. Prevalence and cor-
relates of accelerated atherosclerosis in systemic lupus ery-
37. Costenbader KH, Wright E, Liang MH, Karlson EW. Cardiac 
 risk factor awareness and management in patients with sys-
38. Asanuma Y, Oeser A, Shintani AK, et al. Premature coronary-
artery atherosclerosis in systemic lupus erythematosus. N Engl 
thematosus in a multiethnic US cohort (LUMINA). XXIII. Base-
line predictors of vascular events. LUMINA Study Group. 
40. Merrill JT. Antibodies and clinical features of the antiphos-
pholipid syndrome as criteria for systemic lupus erythe-
41. Crowther MA, Ginsberg JS, Julian J, et al. A comparison of 
two intensities of warfarin for the prevention of recurrent 
thrombosis in patients with the antiphospholipid antibody 
42. Clowse ME, Magder LS, Witter F, Petri M. The impact of in-
creased lupus activity on obstetric outcomes. Arthritis Rheum 
43. Triolo G, Ferrante A, Ciccia F, et al. Randomized study of 
subcutaneous low molecular weight heparin plus aspirin 
versus intravenous immunoglobulin in the treatment of re-
current fetal loss associated with antiphospholipid antibod-
Medical Management of Systemic Lupus Erythematosus

**DIRECTIONS:** Each of the questions below is followed by 5 possible answers. Select the ONE lettered answer that is BEST in each case and circle the corresponding letter on the answer sheet.

1. What is the most frequent initial clinical manifestation of systemic lupus erythematosus (SLE)?
   (A) Discoid rash
   (B) Joint pain
   (C) Seizure
   (D) Pleurisy
   (E) Raynaud’s phenomenon

2. Which of the following medications has NOT been associated with drug-induced lupus?
   (A) Procainamide
   (B) Hydralazine
   (C) Isoniazid
   (D) Minocycline
   (E) Losartan

3. Which of the following is NOT a characteristic finding in antiphospholipid antibody syndrome?
   (A) Thrombocytopenia
   (B) Spontaneous fetal loss
   (C) Arteriovenous malformation
   (D) Stroke
   (E) Venous thrombosis

4. Which antibody often present in SLE patients is associated with a higher risk of neonatal lupus?
   (A) Anti-Ro/SS-A antibody
   (B) Anti-double-stranded DNA antibody
   (C) Anti-RNP antibody
   (D) Anti-Sm antibody
   (E) Antiphospholipid antibody

5. In a lupus patient who presents with a painful, swollen, and warm joint while on high-dose corticosteroids, which of the following diagnoses is LEAST likely?
   (A) Avascular necrosis
   (B) SLE
   (C) Septic joint
   (D) Gout
   (E) Osteoporotic fracture
EVALUATION FORM: Medical Management of Systemic Lupus Erythematosus

Participants may earn up to 1 hour of category 1 credit by reading the article named above and correctly answering at least 70% of the accompanying test questions. A certificate of credit and the correct answers will be mailed within 6 weeks of receipt of this page to those who successfully complete the test.

Circle your answer to the CME questions below:

1. A B C D E
2. A B C D E
3. A B C D E
4. A B C D E
5. A B C D E

Please answer the following questions:

1. How would you rate this educational activity overall?
   __ Excellent __ Good __ Fair __ Poor

2. This article was fair, balanced, free of commercial bias, and fully supported by scientific evidence.
   __ Yes __ No

3. Please rate the clarity of the material presented in the article.
   __ Very clear __ Somewhat clear __ Not at all clear

4. How helpful to your clinical practice was this article?
   __ Very helpful __ Somewhat helpful __ Not at all helpful

5. What changes will you make in your practice as a result of reading this article?
   ___________________________________________________________
   ___________________________________________________________
   ___________________________________________________________
   ___________________________________________________________
   ___________________________________________________________

6. What topics would you like to see presented in the future?
   ___________________________________________________________
   ___________________________________________________________
   ___________________________________________________________
   ___________________________________________________________
   ___________________________________________________________

Please print clearly:

Name:_________________________________________________
MD/DO/Other: ________________________________________
Address: _______________________________________________
City: __________________________________________________
State:______________________________ Zip:______________
Phone:_________________________________________________
Fax: ___________________________________________________
E-mail: ________________________________________________

Are you a health care professional licensed to practice in the US/Canada who can use Category 1 AMA PRA CME credit to fulfill educational requirements?       ____ Yes       ____ No

Physicians are required to report the actual amount of time spent on the activity, up to the maximum designated 1 hour. The actual time spent reading this article and completing the test was ____________________.

Please mail or fax this sheet to:
Wayne State University, Division of CME
101 E. Alexandrine, Lower Level
Detroit, MI 48201
FAX: 313-577-7554

This activity has been planned and implemented in accordance with the Essential Areas and Policies of the Accreditation Council for Continuing Medical Education (ACCME) through the joint sponsorship of Wayne State University School of Medicine and the Journal of Clinical Outcomes Management. Wayne State University School of Medicine is accredited by the ACCME to provide continuing medical education for physicians.

Wayne State University School of Medicine designates this educational activity for a maximum of 1 category 1 credit towards the AMA Physician’s Recognition Award. Each physician should claim only those credits that he/she actually spent in the activity.

Release date: 15 July 2005
Expiration date: 30 July 2006