TABLE 378-2 CLASSIFICATION OF LUPUS NEPHRITIS (INTERNATIONAL SOCIETY OF NEPHROLOGY AND RENAL PATHOLOGY SOCIETY)

Class I: Minimal Mesangial Lupus Nephritis
Normal glomeruli by light microscopy, but mesangial immune deposits by immunofluorescence.
Class II: Mesangial Proliferative Lupus Nephritis
Purely mesangial hypercellularity of any degree or mesangial matrix expansion by light microscopy, with mesangial immune deposits. A few isolated subepithelial or subendothelial deposits may be visible by immunofluorescence or electron microscopy, but not by light microscopy.
Class III: Focal Lupus Nephritis
Active or inactive focal, segmental or global endo- or extracapillary glomerulonephritis involving ≤50% of all glomeruli, typically with focal subendothelial immune deposits, with or without mesangial alterations.
Class III (A): Active lesions—focal proliferative lupus nephritis
Class III (A/C): Active and chronic lesions—focal proliferative and sclerosing lupus nephritis
Class III (C): Chronic inactive lesions with glomerular scars—focal sclerosing lupus nephritis
Class IV: Diffuse Lupus Nephritis
Active or inactive diffuse, segmental or global endo- or extracapillary glomerulonephritis involving ≥50% of all glomeruli, typically with diffuse subendothelial immune deposits, with or without mesangial alterations. This class is divided into diffuse segmental (IV-S) lupus nephritis when ≥50% of the involved glomeruli have segmental lesions, and diffuse global (IV-G) lupus nephritis when ≥50% of the involved glomeruli have global lesions. Segmental is defined as a glomerular lesion that involves less than one-half of the glomerular tuft. This class includes cases with diffuse wire loop deposits but with little or no glomerular proliferation.
Class IV-S (A): Active lesions—diffuse segmental proliferative lupus nephritis
Class IV-G (A): Active lesions—diffuse global proliferative lupus nephritis
Class IV-S (A/C): Active and chronic lesions—diffuse segmental proliferative and sclerosing lupus nephritis
Class IV-G (A/C): Active and chronic lesions—diffuse global proliferative and sclerosing lupus nephritis
Class IV-S (C): Chronic inactive lesions with scars—diffuse segmental sclerosing lupus nephritis
Class IV-G (C): Chronic inactive lesions with scars—diffuse global sclerosing lupus nephritis
Class V: Membranous Lupus Nephritis
Global or segmental subepithelial immune deposits or their morphologic sequelae by light microscopy and by immunofluorescence or electron microscopy, with or without mesangial alterations. Class V lupus nephritis may occur in combination with class III or IV, in which case both will be diagnosed. Class V lupus nephritis may show advanced sclerosis.
Class VI: Advanced Sclerotic Lupus Nephritis
≥90% of glomeruli globally sclerosed without residual activity.

Note: Indicate and grade (mild, moderate, severe) tubular atrophy, interstitial inflammation and fibrosis, and severity of arteriosclerosis or other vascular lesions.

Source: JJ Weening et al: Kidney Int 65:521, 2004. Reprinted by permission from Macmillan Publishers Ltd., Copyright 2004.

TABLE 378-3 SYSTEMIC LUPUS INTERNATIONAL COLLABORATING CLINIC CRITERIA FOR CLASSIFICATION OF SYSTEMIC LUPUS ERYTHEMATOSUS

Clinical Manifestations	Immunologic Manifestations
Skin	ANA > reference negative value
Acute, subacute cutaneous LE	Anti-dsDNA
Chronic cutaneous LE	Anti-Sm
Oral ulcers	Antiphospholipid
Alopecia	Low serum complement
Synovitis	Positive direct Coombs test
Renal	
Prot/Cr ≥0.5	
RBC casts	
Biopsy[a]	
Neurologic	
Seizures, psychosis, mononeuritis, myelitis, peripheral or cranial neuropathies, acute confusional state	
Hemolytic anemia	
Leukopenia (<4000) or	
Lymphopenia (<1000)	
Thrombocytopenia (<100,000)	

[a]Renal biopsy read as systemic lupus qualifies for classification as SLE even if none of the other above features are present.

Interpretation: Presence of any 4 criteria (must have at least 1 in each category) qualifies patient to be classified as having SLE with 93% specificity and 92% sensitivity.

Abbreviations: ANA, antinuclear antibody; Cr, creatinine; LE, lupus erythematosus; Prot, protein.

Source: M Petri et al: Arthritis Rheum 64:2677, 2012. Because these criteria are new, currently ongoing clinical studies use prior American College of Rheumatology Criteria; see EM Tan et al: Arthritis Rheum 25:1271, 1982; update MC Hochberg: Arthritis Rheum 40:1725, 1997.

presence in an individual of multiple autoantibodies without clinical symptoms should not be considered diagnostic for SLE, although such persons are at increased risk.

INTERPRETATION OF CLINICAL MANIFESTATIONS

When a diagnosis of SLE is made, it is important to establish the severity and potential reversibility of the illness and to estimate the possible consequences of various therapeutic interventions. In the following paragraphs, descriptions of some disease manifestations begin with relatively mild problems and progress to those more life-threatening.

OVERVIEW AND SYSTEMIC MANIFESTATIONS

At its onset, SLE may involve one or several organ systems; over time, additional manifestations may occur (Tables 378-3 and 378-4). Most of the autoantibodies characteristic of each person are present at the time clinical manifestations appear (Tables 378-1 and 378-3). Severity of SLE varies from mild and intermittent to severe and fulminant. Approximately 85% of patients have either continuing active disease (while being treated) or one or more flares of active disease annually. Permanent complete remissions (absence of symptoms with no treatment) are rare. Systemic symptoms, particularly fatigue and myalgias/arthralgias, are present most of the time. Severe systemic illness requiring glucocorticoid therapy can occur with fever, prostration, weight loss, and anemia with or without other organ-targeted manifestations.

MUSCULOSKELETAL MANIFESTATIONS

Most people with SLE have intermittent polyarthritis, varying from mild to disabling, characterized by soft tissue swelling and tenderness in joints and/or tendons, most commonly in hands, wrists, and knees. Joint deformities (hands and feet) develop in only 10%. Erosions on joint x-rays are rare but can be identified by ultrasound in almost half of patients. Some individuals have rheumatoid-like arthritis with erosions and fulfill criteria for both RA and SLE ("rhupus"); they may be coded as having both diseases. If pain persists in a single joint, such as knee, shoulder, or hip, a diagnosis of ischemic necrosis of bone should be considered, particularly if there are no other manifestations of active SLE because its prevalence is increased in SLE, especially in patients treated with systemic glucocorticoids. Myositis with clinical muscle weakness, elevated creatine kinase levels, positive magnetic resonance imaging (MRI) scan, and muscle necrosis and inflammation on biopsy can occur, although most patients have myalgias without frank myositis. Glucocorticoid therapies (commonly) and antimalarial therapies (rarely) can cause muscle weakness; these adverse effects must be distinguished from active inflammatory disease.

CUTANEOUS MANIFESTATIONS

Lupus dermatitis can be classified as acute, subacute, or chronic, and there are many different types of lesions encompassed within these groups. Discoid lupus erythematosus (DLE) is the most common