SYSTEMIC LUPUS ERYTHEMATOSUS

- SLE is a fluctuating multisystem disease with a diversity of clinical presentations.

- Abnormal immunologic function and formation of antibodies against “self” antigens underlie the pathogenesis of SLE.

- The hallmark of SLE is the development of autoantibodies to cellular nuclear components that leads to a chronic inflammatory autoimmune disease.

- The disease occurs predominantly in women, with a reported female-to-male ratio approaching 10:1.

- SLE is reported to be less prevalent in whites than in other ethnic groups, including blacks, Hispanics, Native Americans, and Asians.

- The etiology of abnormal autoantibody production and development of SLE is still unknown.

- Genetic, environmental, and hormonal factors all may play a role in loss of “self” tolerance and expression of disease.

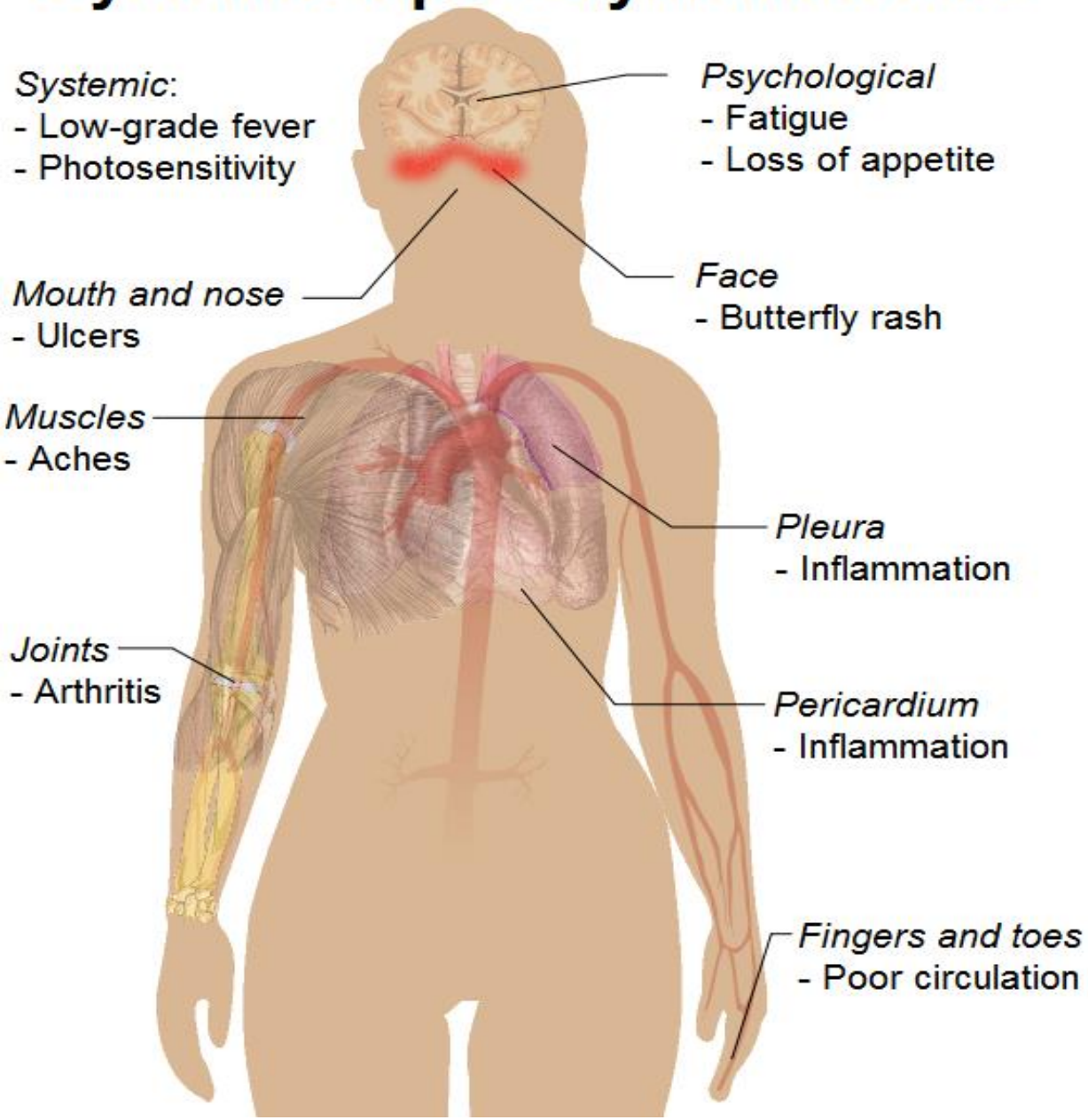
- A popular theory is that autoimmune disease such as SLE develops in genetically susceptible individuals after exposure to a triggering agent, possibly something in the environment.

Revised Criteria for Classification of Systemic Lupus Erythematosus[a]

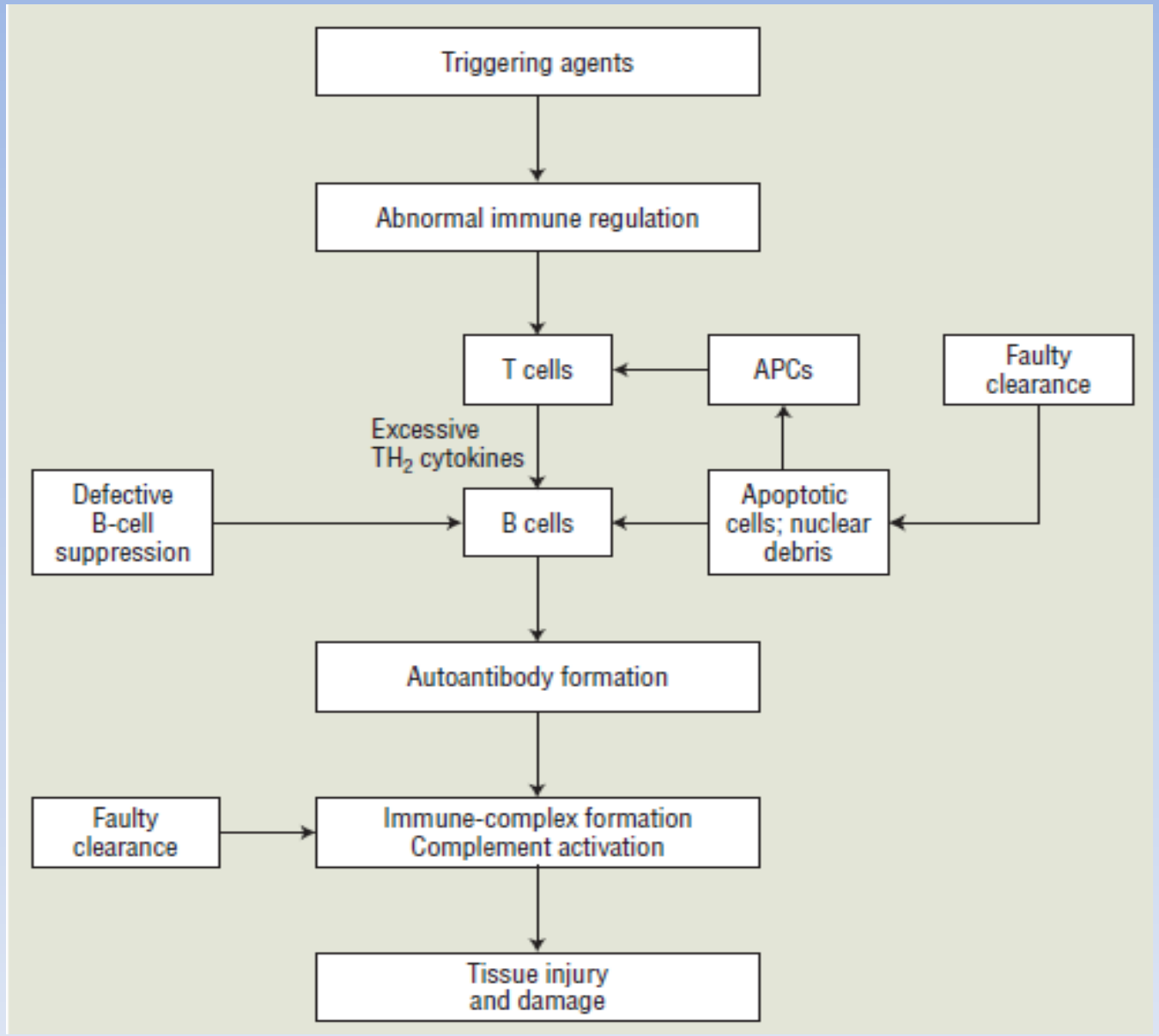
Criterion	Definition
Malar rash	Fixed erythema, flat or raised, over the malar eminences, tending to spare the nasolabial folds
Discoid rash	Erythematous raised patches with adherent keratotic scaling and follicular plugging; atrophic scarring may occur in older lesions
Photosensitivity	Skin rash as a result of unusual reaction to sunlight, by patient history or physician observations
Oral ulcers	Oral or nasopharyngeal ulceration, usually painless, observed by a physician
Arthritis	Nonerosive arthritis involving two or more peripheral joints, characterized by tenderness, swelling, or effusion
Serositis	Pleuritis—convincing history of pleuritic pain or rub heard by a physician or evidence of pleural effusion *or* Pericarditis—documented by electrocardiogram or rub or evidence of pericardial effusion
Renal disorder	Persistent proteinuria greater than 0.5 g/day or greater than 3+ if quantitation not performed *or* Cellular casts—may be red cell, hemoglobin, granular, tubular, or mixed
Neurologic disorder	Seizures—in the absence of offending drugs or known metabolic derangements, e.g., uremia, ketoacidosis, or electrolyte imbalance *or* Psychosis—in the absence of offending drugs or known metabolic derangements, e.g., uremia, ketoacidosis, or electrolyte imbalance
Hematologic disorder	Hemolytic anemia—with reticulocytosis *or* Leukopenia—fewer than 4,000/mm^3 total on two or more occasions *or* Lymphopenia—fewer than 1,500/mm^3 on two or more occasions *or* Thrombocytopenia—fewer than 100,000/mm^3 in the absence of offending drugs
Immunologic disorder	Anti-DNA; antibody to native DNA in abnormal titer *or* Anti-Smith (Sm) antigen; presence of antibody to Sm nuclear antigen *or* Positive finding of antiphospholipid antibodies based on (a) an abnormal serum level of immunoglobulin (Ig)G or IgM anticardiolipin antibodies, (b) a positive test result for lupus anticoagulant using a standard method, or (c) a false-positive serologic test for syphilis known to be positive for at least 6 months and confirmed by *Treponema pallidum* immobilization or fluorescent treponemal antibody absorption test
Antinuclear	An abnormal titer of antinuclear antibody by immunofluorescence or an antibody equivalent assay at any point in time in the absence of drugs known to be associated with "drug-induced lupus" syndrome

Most common symptoms of

Systemic lupus erythematosus



Pathophysiology of SLE



CLINICAL PRESENTATION OF SYSTEMIC LUPUS ERYTHEMATOSUS

Sign/Symptom	Incidence (%)
☐ Musculoskeletal	
Arthritis and arthralgia	53–95
☐ Constitutional	
Fatigue	81
Fever	41–86
Weight loss	31–71
☐ Mucocutaneous	55–85
Butterfly rash	10–61
Photosensitivity	11–45
Raynaud's phenomenon	10–44
Discoid lesions	9–29
☐ Central nervous system	13–59
Psychosis	5–37
Seizures	6–26
☐ Pulmonary	
Pleuritis	31–57
Pleural effusion	12–40
☐ Cardiovascular	
Pericarditis	2–45
Myocarditis	3–40
Heart murmur	1–44
Hypertension	23–46
☐ Renal	13–65
☐ Gastrointestinal	
Nausea	7–53
Abdominal pain	8–34
Bowel hemorrhage (vasculitis)	1–6
☐ Hematologic	
Anemia	30–78
Leukopenia	35–66
Thrombocytopenia	7–30
☐ Lymphadenopathy	10–59

TREATMENT:

- Desired treatment outcomes for the patient with SLE are twofold: (a) management of symptoms and induction of remission during times of disease flare and (b) maintenance of remission for as long as possible between disease flares.

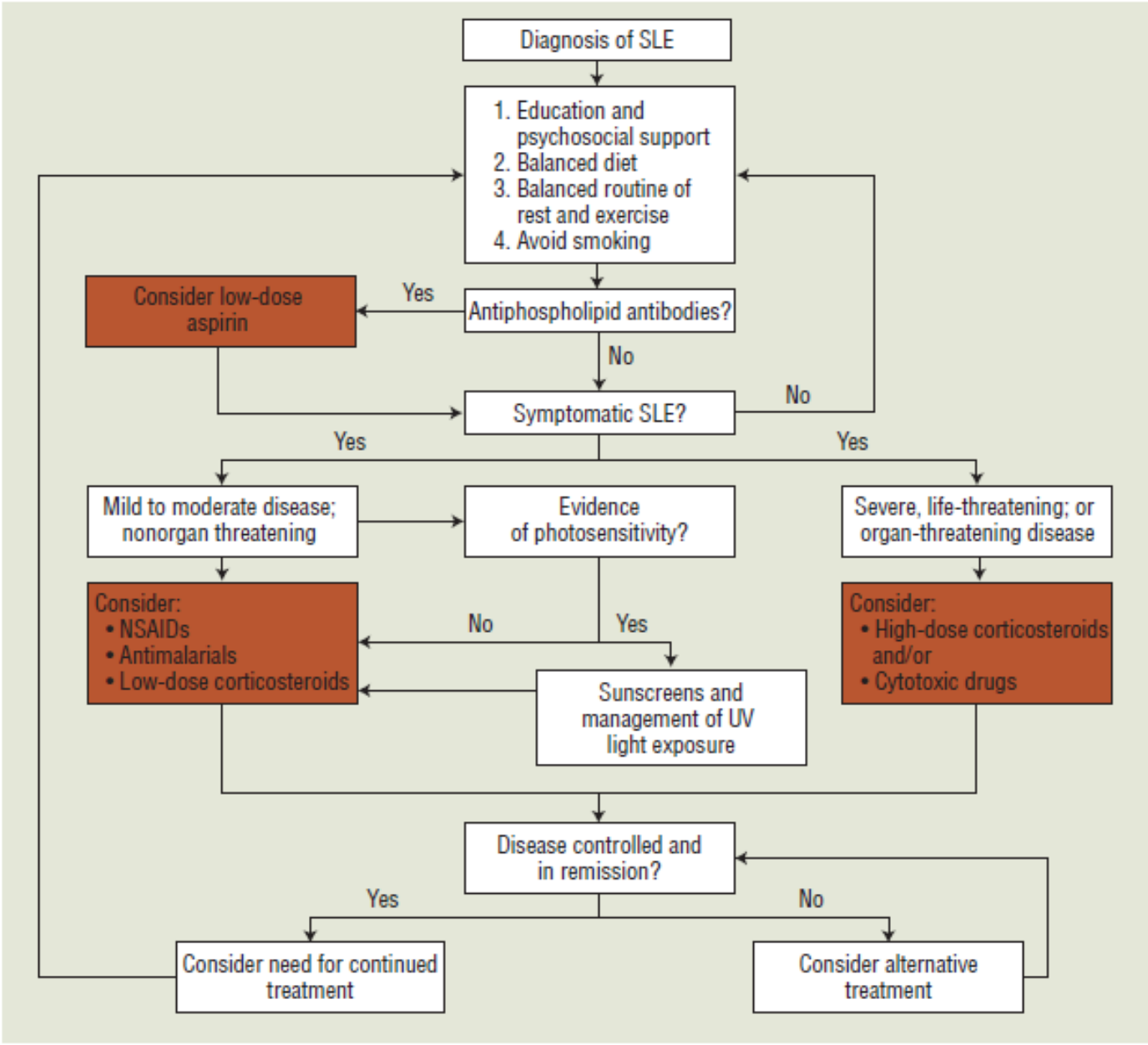
- A balanced routine of rest and exercise, while avoiding overexertion, is essential in managing fatigue.

- Avoidance of smoking may be particularly important because hydrazines in tobacco smoke may be an environmental trigger of lupus and likely contribute to accelerated CAD.

Drug Treatment of Systemic Lupus Erythematosus

Drug Class	Drug and Dose	Indication
NSAID	Various agents Antiinflammatory dose	Mild disease: fever, arthritis, skin rash, serositis
Antimalarial	Hydroxychloroquine 200–400 mg po daily Chloroquine 250–500 mg po daily	Mild disease: arthritis, skin rash, serositis
Corticosteroid	Prednisone 1–2 mg/kg/day po (or equivalent)	Initial control of severe disease
	<1 mg/kg/day (or equivalent)	Control of mild disease or maintenance after disease suppression with higher doses
	Methylprednisolone 500–1,000 mg IV daily × 3–6 day	Life-threatening disease
Cytotoxic	Cyclophosphamide 0.5–1 g/m^2 IV monthly for 6 months; then every 3 months for 2 years or for 1 year after remission Azathioprine 1–3 mg/kg po daily Cyclophosphamide 1–3 mg/kg po daily Mycophenolate mofetil 1–3 g po daily	Most commonly used in severe lupus nephritis; may be necessary for other severe disease manifestations

General approach in the management of SLE



Monitoring Adverse Effects of Drugs Commonly Used in Systemic Lupus Erythematosus

Drug	Toxicities to Monitor	Baseline Evaluation	Monitoring	
			System Review	*Laboratory*
Salicylates, NSAIDs	Gastrointestinal bleeding, hepatic toxicity, renal toxicity, hypertension	CBC, creatinine, urinalysis, AST, ALT	Dark/black stool, dyspepsia, nausea/vomiting, abdominal pain, shortness of breath, edema	CBC yearly, creatinine yearly
Corticosteroids	Hypertension, hyperglycemia, hyperlipidemia, hypokalemia, osteoporosis, avascular necrosis, cataract, weight gain, infections, fluid retention	Blood pressure, bone densitometry, glucose, potassium, cholesterol, triglycerides (HDL, LDL)	Polyuria, polydipsia, edema, shortness of breath, blood pressure, visual changes, bone pain	Glucose every 3–6 months, total cholesterol yearly, bone densitometry yearly to assess osteoporosis
Hydroxychloroquine	Macular damage	None unless patient is older than 40 years of age or has previous eye disease	Visual changes	Funduscopic and visual fields every 6–12 months
Azathioprine	Myelosuppression, hepatoxicity, lymphoproliferative disorders	CBC, platelet count, creatinine, AST or ALT	Symptoms of myelosuppression	CBC and platelet count every 1–2 weeks with changes in dose (every 1–3 months thereafter), AST yearly, Pap test at regular intervals
Cyclophosphamide	Myelosuppression, myeloproliferative disorders, malignancy, immunosuppression, hemorrhagic cystitis, secondary infertility	CBC and differential and platelet count, urinalysis	Symptoms of myelosuppression, hematuria, infertility	CBC and urinalysis monthly, urine cytology and Pap test yearly for life
Mycophenolate mofetil	Myelosuppression, hepatotoxicity, lymphoproliferative disorders, malignancy	CBC, hepatic function tests, renal function tests	Symptoms of myelosuppression, diarrhea, nausea/vomiting, dyspepsia, abdominal pain, dark/black stool or blood in stool	CBC weekly during first month, twice monthly during the second and third months, then monthly through the first year

- The mechanism of action of the **antimalarial drugs** is uncertain.

- It has been proposed that antimalarials interfere with T-lymphocyte activation.

- Other effects of antimalarials that may benefit patients with SLE include inhibition of cytokines, decreased sensitivity to ultraviolet light, antiinflammatory activity, antiplatelet effects, and antihyperlipidemic activity.

- Response to chloroquine occurs within 1 to 3 months, whereas the maximal effect of hydroxychloroquine may not occur for 3 to 6 months.

- Patients with clinical manifestations that are more serious or unresponsive to other drugs usually require corticosteroids.

- The goal of treatment with corticosteroids in SLE is to suppress and maintain suppression of active disease with the lowest dose possible.

- In patients with mild disease, low-dose therapy (prednisone 10 to 20 mg/day) is adequate.

- Azathioprine can be used as a “steroid-sparing” agent, allowing for the reduction of corticosteroid doses

- Cyclophosphamide may be of benefit to some patients with other serious, refractory manifestations of lupus, including neurologic manifestations.

- Reports of the use of other cytotoxic drugs for lupus in recent years include methotrexate, mycophenolate mofetil, mechlorethamine (nitrogen mustard), chlorambucil, and cyclosporine.

- Mycophenolate mofetil is an immunosuppressive agent that has become an established treatment of severe renal and nonrenal lupus refractory to conventional cytotoxic agents.

- Mycophenolate mofetil has been investigated as an alternative to cyclophosphamide for induction of remission.