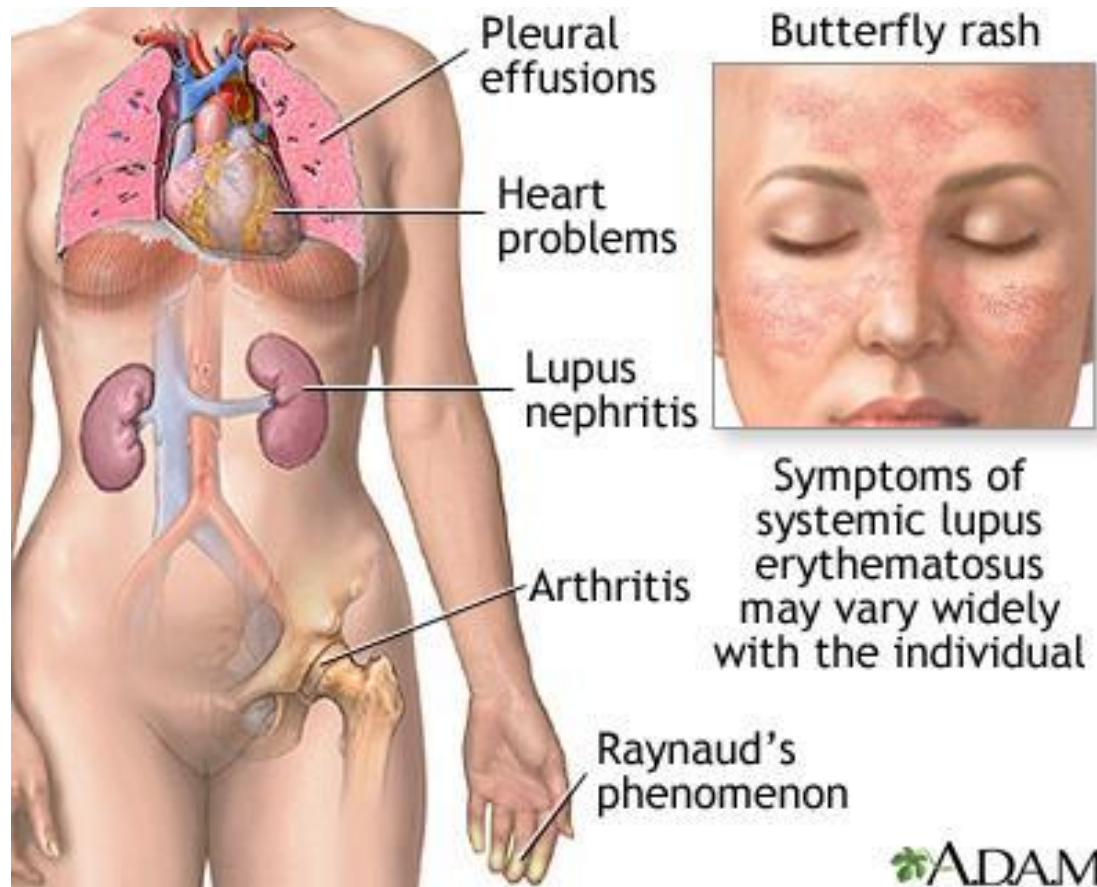


SYSTEMIC LUPUS ERYTHROMATOUS



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Systemic lupus erythematosus (SLE) is an autoimmune disease associated with autoantibody production. SLE is a multisystem disease.

The term “lupus” (Latin for wolf) was first used in the 13th century to describe erosive lesions that looked like skin that had been gnawed by a wolf.

EPIDEMIOLOGY

1. SLE occur most frequently in women of reproductive age (15–50 years old)
2. Rates are nine times higher in women than in men.
3. It is affected by ethnicity, which includes genetic, geographic,
4. cultural, social, and other aspects within a group.
5. Rates are higher in non - whites than in the white population.
6. It is most common in those of African origin.

ETIOLOGY

The exact etiology for SLE is unknown but many factors have been identified that appear to play a role in the disease.

Predisposing factors

1. Genetic influences :

- a. First-degree relatives of patients with SLE are 20 times more likely to develop the disease than those in a general population.
- b. The genetic predisposition to SLE is a result of the interplay of a combination of genes.
- c. The major histocompatibility complex (MHC) class II alleles HLA-DR2 and HLA-DR3 are known to be linked to SLE.

2. Epigenetic regulation of gene expression :

- a. Gene expression is regulated by deoxyribonucleic acid (DNA) methylation and histone modifications.
- b. These epigenetic changes can cause alterations that may influence SLE.
- c. Hydralazine and procainamide, two drugs that may induce lupus, inhibit DNA methylation.

3. **Environmental factors :**

- A. Cigarette smoke is phototoxic and associated with cutaneous lupus.
- B. Ultraviolet light can cause keratinocytes in the skin to release nuclear material that can further stimulate the immune system and autoantibody production by B cells.
- C. Viruses Epstein–Barr virus.
- D. Other include : infections, medications (eg, vaccines and biologics) psychological stress, silica dust, hydralazines, petroleum, solvents (eg, nail polish remover and metal cleaners), dyes, and pesticides.

4. **Hormones,** and

5. **Abnormalities in immune cells and cytokines**

PATHOPHYSIOLOGY

- Interaction between susceptibility genes and environmental factors results in abnormal immune responses by formation of various autoantibodies.
- Some of the important *antinuclear antibodies (ANAs)* or antinuclear factors (*ANFs*) against different nuclear antigens are as under:
 - I. Antinuclear antibodies (ANA)** These are the antibodies against common nuclear antigen that includes DNA as well as RNA. These are demonstrable in about 98% cases and are used as screening test.
 - II. Antibodies to double-stranded (anti-dsDNA)** This is the most specific for SLE, is present in 70% cases.
 - III. Anti-Smith antibodies (anti-Sm)** These anti bodies appear against Smith antigen which is part of ribonucleoproteins. It is also specific for SLE but is seen in about 25% cases.

iv) Other non-specific antibodies Besides above, there are several other antibody tests which lack specificity for SLE.

These are as follows:

- A. *Anti-ribonucleoproteins (anti-RNP)*** seen in 40% cases of SLE but seen more often in Sjögren's syndrome.
- B. *Anti-histone antibody***, which is antibody against histone associated with DNA in chromatin, is seen particularly in cases of drug-induced lupus than in SLE.
- C. *Antiphospholipid antibodies (APLA) or lupus anticoagulant*** are tests for thrombotic complications in cases of SLE.
- D. *Anti-ribosomal P antibody*** is antibody against protein in ribosomes and is seen in CNS lupus.

The source of these autoantibodies as well as hyper gammaglobulinaemia seen in SLE is the **polyclonal activation of B cells** brought about by following immunologic derangements:

- i) an inherited defect in B cells;
- ii) stimulation of B cells by micro-organisms;
- iii) T helper cell hyperactivity; and
- iv) T suppressor cell defect.

Two types of immunologic tissue injury can occur in SLE:

1. **Type II hypersensitivity** is characterised by formation of autoantibodies against blood cells (red blood cells, platelets, leucocytes) and results in haematologic derangement in SLE.
2. **Type III hypersensitivity** is characterised by antigen-antibody complex (commonly DNA-anti-DNA antibody; sometimes Ig-anti-Ig antibody complex) which is deposited at sites such as renal glomeruli, walls of small blood vessels etc.

PREDISPOSING FACTORS

GENES

High Hazard Ratios (≥ 6);

Deficiencies of C1q, C2, C4 (rare)
TREX1 mutations affecting DNA
degradation (rare)

Affecting Ag presentation or persistence,
e.g., phagocytosis of immune complexes
HLA-DRB1 (*1501, *0301), DR3, DQA2
CR2, FCGR2A/B

Enhance Innate Immunity, including production of IFNs
TNFAIP3, IRF5/TNPO3, IRF7/PHRF1, ITGAM, ICAMs

Alter Adaptive Immunity B and/or T Cell Signaling
BANK1, STAT4, MSHS, IZKF3, TCF7

GENES FOR LUPUS NEPHRITIS

HLA-DR3, STAT4, APOL1 (African Americans),
FCGR3A, ITGAM, IRF5, IRF7, TNFSF4 (Ox40L), DNASE1

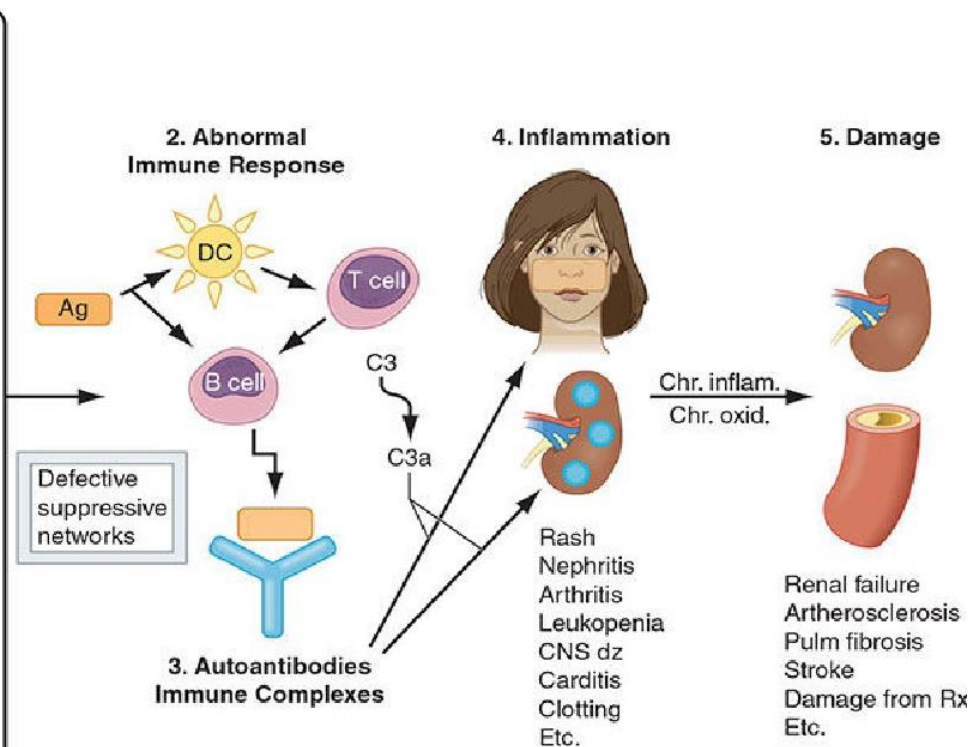
ENVIRONMENT/MICROENVIRONMENT

Ultraviolet Light, Smoking, Crystalline
Silica, ?EBV infection
Femaleness

EPIGENETICS

Hypomethylation of DNA: In CD4+T, B and monocytes
Some affect IFN production
Histone modifications: Some increase expression
of predisposing genes and/or IFN production
MicroRNA affecting gene expression

Mir-21, -146A, -155, -569, -30A, Let-7a



- Pathogenesis is related in large part to production of increased quantities and immunogenic forms of nucleic acids and other self-antigens, which drive autoimmune-inducing activation of innate immunity, autoantibodies, and T cells.
- Interactions between genes, environment, and epigenetic changes drive increased autophagy, Ag presentation, neutrophil NETosis, autoantibody formation with increased plasma cells, and production of pathogenic effector T cells in Th1, Th17, and Tfh subsets, with ineffective regulatory networks.

- The exact mechanism of autoantibody tissue destruction is unclear.
- Immune complexes form when autoantibodies bind to nuclear material and deposit in tissues.
- They activate the complement cascade, leading to an influx of inflammatory cells and tissue injury.
- Autoantibodies might also directly react with proteins in tissues.
- There are increased T helper cells type 2 and 17 and diminished number and function of T regulatory (Treg) cells.
- Cytokines, such TNF- α , interferon-gamma, and interleukin-10, produced by activated T cells can stimulate B cells.
- Cytokines play multiple roles in SLE and contribute to inflammation and tissue damage.
- Interleukin-10 stimulates B cell proliferation and autoantibody production in renal cells and may affect skin and joint symptoms.
- Increased T cell production of interleukin-17 correlates with disease activity and may contribute to kidney and other tissue damage.

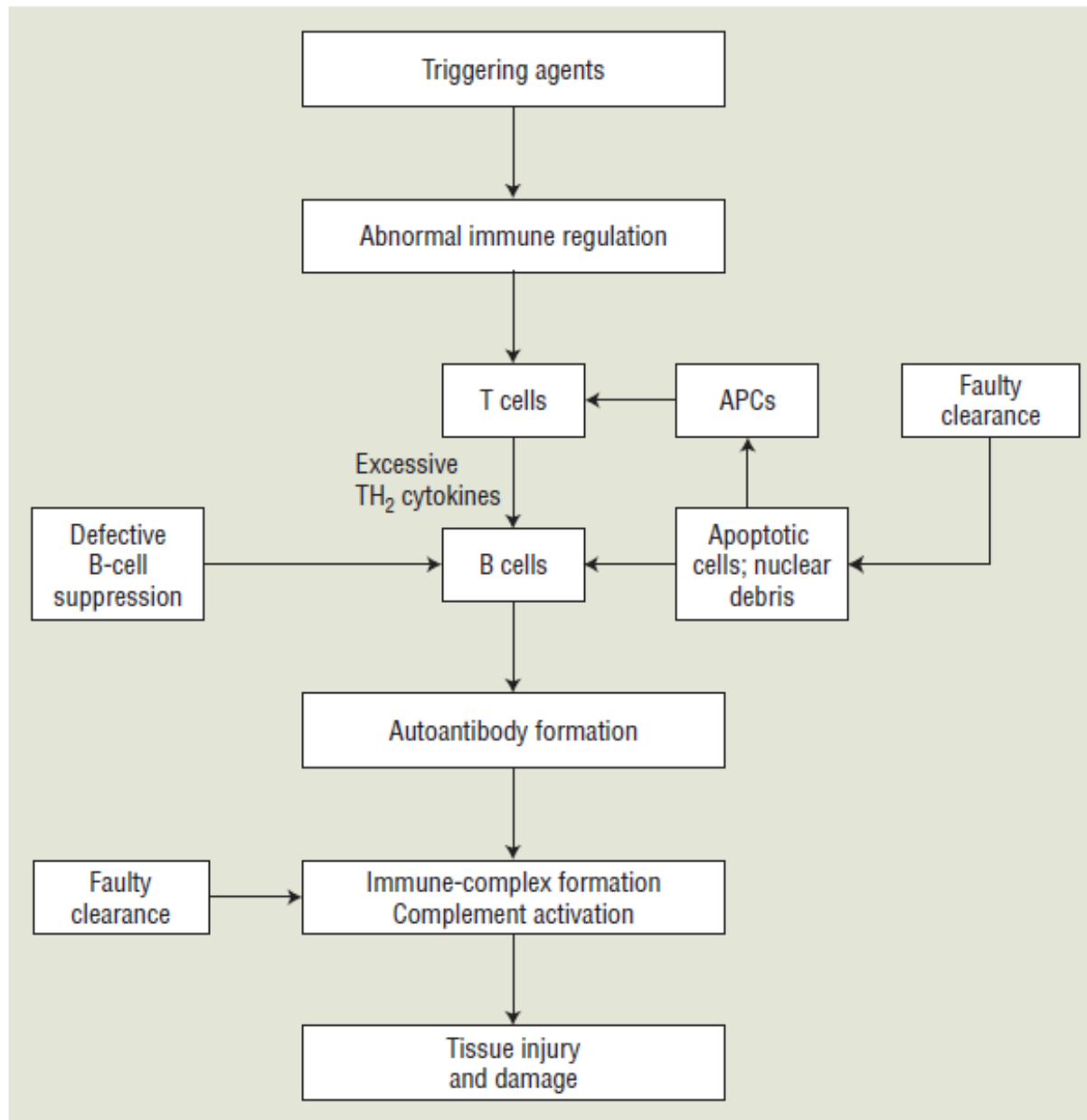


FIGURE 90-1. Pathogenesis of systemic lupus erythematosus. Environmental factors, such as infectious organisms, drugs, and chemicals, serve as triggering agents in genetically and hormonally susceptible individuals to induce a state of immune dysregulation. These abnormal immune responses lead to hyperactive T-helper type 2 lymphocyte and B-lymphocyte function. Suppressor T-lymphocyte function, cytokine production, faulty clearance mechanisms, and other immune regulatory mechanisms also are abnormal and fail to downregulate autoantibody formation from hyperactive B lymphocytes. The autoantibodies formed from this immune dysregulation become pathogenic, form immune complexes, and activate complement that leads to damage of host tissue. (APCs, antigen-presenting cells; TH₂, T-helper type 2.)

Initial risk factors

Genetic mutations:
HLA DR, IL-10, IRF-5,
Complement genes, ...

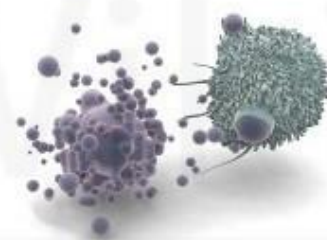


UV light



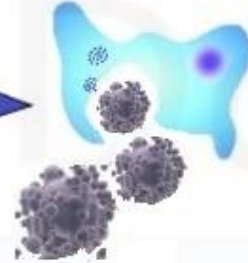
Viral infections:
Parvovirus B19
EBV

Increased number of cells
undergoing apoptosis

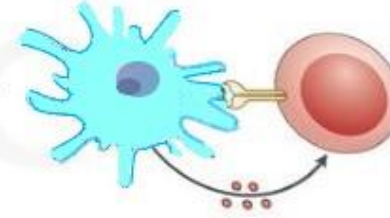


Apoptotic cells release nucleic
antigens and IFN

Uptake of self antigens by Dendritic
cells and dendritic cell maturation

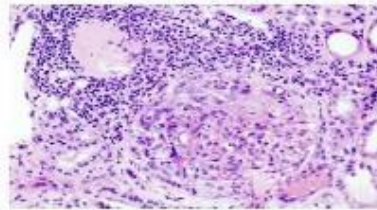


Antigen presentation and proinflammatory
cytokine secretion lead to T-cell activation

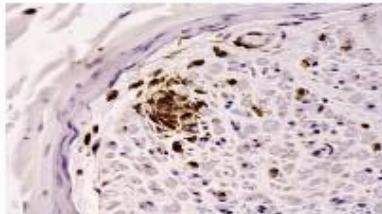


SLE pathophysiology

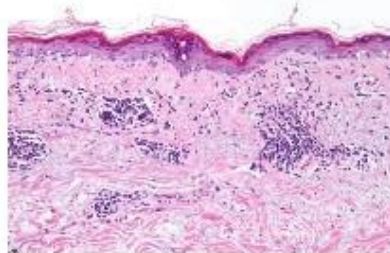
Glomerulonephritis



Vasculitis



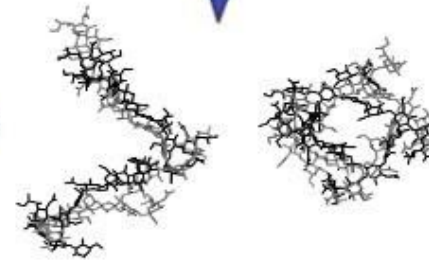
Dermatitis



Tissue destruction and complications:

Lupus nephritis
Cutaneous lesions
Lupus vasculitis
Lupus encephalitis
....

B-cell activation
due to IFN, nucleic antigen, T-cell effect



Immune complexes formation and complement
fixation of immune complexes

CLINICAL PRESENTATION

Symptoms

1. Fatigue,
2. Depression,
3. Anxiety,
4. Photosensitivity,
5. Joint pain,
6. Headache,
7. Weight Loss,
8. Nausea/abdominal pain

Signs

1. Rash, Butterfly rash
2. Alopecia,
3. Fever,
4. Oral and nasal ulcers,
5. Arthritis,
6. Renal dysfunction,
7. Seizure, psychosis,
8. Pleuritis, pleural effusion,
9. Cardiovascular disease -
pericarditis/ myocarditis, heart
murmur, hypertension,
10. Anemia, leukopenia,
thrombocytopenia,
11. Lymphadenopathy,
12. Raynaud's phenomenon,
13. Vasculitis

Most common symptoms of
Systemic lupus erythematosus

Systemic:

- Low-grade fever
- Photosensitivity

Psychological

- Fatigue
- Loss of appetite

Mouth and nose

- Ulcers

Face

- Butterfly rash

Muscles

- Aches

Pleura

- Inflammation

Joints

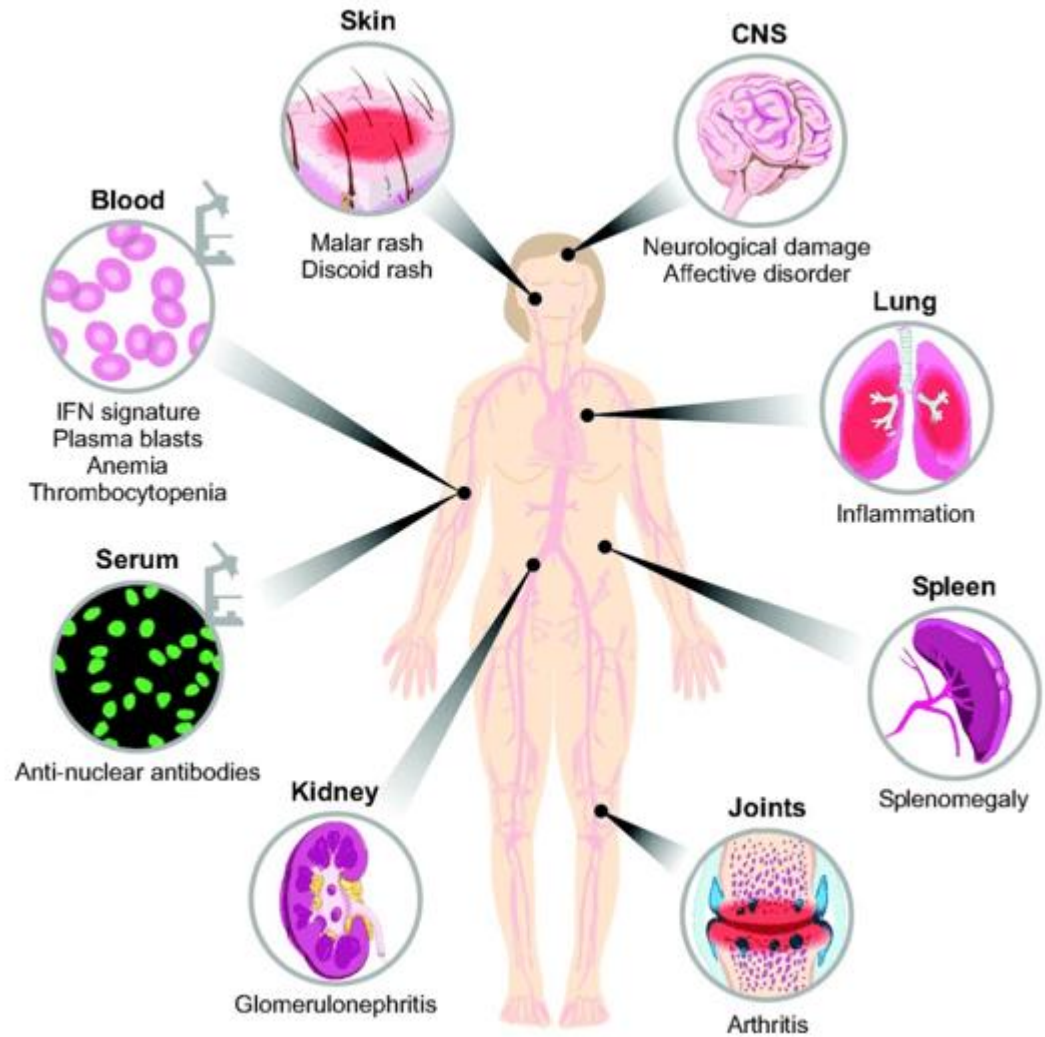
- Arthritis

Pericardium

- Inflammation

Fingers and toes

- Poor circulation



Diagnostic Tests

1. Serology: autoantibodies, antiphospholipid antibodies, complement;
2. Inflammatory markers: C-reactive protein, ESR;
3. Blood chemistries; CBP; urinalysis; lumbar puncture;
4. Renal biopsy

Table 1. SLICC Criteria

Clinical Features	Immunologic Features
Acute cutaneous lupus (maculopapular lupus rash, malar rash, photosensitive lupus rash, etc.)	High ANA concentration
Chronic cutaneous lupus (discoid rash, mucosal lupus, etc.)	High anti-dsDNA antibody concentration
Oral or nasal ulcers	Presence of anti-Smith
Nonscarring alopecia	Positive APA
Synovitis in ≥ 2 joints	Low complement (C3, C4, CH50)
Serositis	Direct Coombs test
Renal (urine protein or RBC casts)	Must have a total of 4 features with ≥ 1 clinical feature and 1 immunologic feature or Biopsy-proven LN with anti-dsDNA antibodies or ANA
Neurologic (seizures, psychosis, others)	
Hemolytic anemia	
Leukopenia or lymphopenia (without an identifiable cause)	
Thrombocytopenia (without an identifiable cause)	

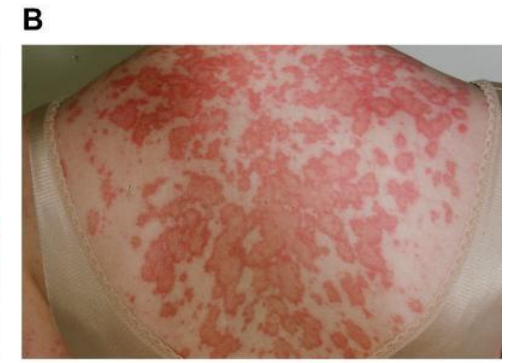
*ANA: antinuclear antibody; APA: antiphospholipid antibody; dsDNA: double-stranded DNA; LN: lupus nephritis; SLICC: Systemic Lupus International Collaborating Clinics; Sm: Smith.
Source: Reference 1.*

SLE flare: A flare is a measurable increase in disease activity in one or more organ systems involving new or worse clinical signs and symptoms and/or laboratory measurements.

Cutaneous lupus erythematosus – Affecting skin

Three main types of cutaneous lupus erythematosus have been observed.

1. **Acute cutaneous lupus erythematosus** is seen in patients with SLE
 - a. Characterized by a photosensitive malar rash over the cheeks and nose with sparing of the nasolabial folds.
 - b. The arms and trunk may be involved.
 - c. The manifestations usually wax and wane without scarring.



2. **Severe SLE** is less common with the other forms of cutaneous lupus.
3. **Subacute cutaneous lupus erythematosus** is highly photosensitive
 - A. Manifested by annular or papulosquamous lesions that usually heal without scarring.
 - B. It can be accompanied by musculoskeletal complaints and patients have anti-rossa autoantibodies.
 - C. Subtypes of chronic cutaneous lupus erythematosus - common is discoid lupus.
1. **Chronic discoid lupus**
 - A. Confined to the head and neck
 - B. Chronic discoid lupus is associated with a lower incidence of arthritis, end-stage renal disease, and immunologic markers such as ana, anti-dsdna, and antiphospholipid antibodies.
 - C. It is more common in smokers and african americans.
 - D. It may be associated with scarring, scarring alopecia, malar rash, photosensitivity, oral ulcers, leukopenia, vasculitis, and chronic seizures.



Lupus nephritis Affecting kidneys

Neuropsychiatric lupus

1. About 50% of neuropsychiatric events appear within the first 2 years after the diagnosis of SLE.
2. Mild nonspecific neuropsychiatric findings such as headache, mood disorders, and mild cognitive dysfunction are common in SLE.
3. Findings more indicative of neuropsychiatric lupus include cerebrovascular disease (ischemic stroke and/or transient ischemic attack), anxiety, and seizures ; severe cognitive dysfunction, acute confusional state, peripheral neuropathy, and psychosis; and chorea, movement disorders, cranial nerve neuropathies, and aseptic meningitis abnormalities.
4. The diagnostic depending on the clinical presentation and preliminary findings - a thorough history and physical, lumbar puncture with cerebrospinal fluid analysis, EEG, serology, CBP, blood chemistries, neuropsychological assessment of cognitive function, nerve conduction studies, and MRI.

Cardiovascular lupus

1. Cardiovascular disease is a leading cause of death in patients with SLE.
2. Cardiac manifestations of SLE, such as pericarditis and myocarditis, patients with SLE are also at increased risk for accelerated atherosclerosis.
3. This is probably related to the chronic inflammation associated with the disease and adverse effects of the drugs (eg, high-dose corticosteroids) used to treat it.
4. Antiphospholipid antibodies and type I interferons may play a role in the pathogenesis.
5. Drugs such as hydroxychloroquine and mycophenolate mofetil may have a cardioprotective effect.

MANAGEMENT OF SLE

Treatment of SLE is determined by the

- Patient's symptoms,
- Organ involvement,
- Comorbidities, and
- Other patient-specific factors.

Goals of therapy

1. To prevent disease flares and involvement of other organs,
2. Decrease disease activity and prevent damage, maintain remission, reduce use of corticosteroids,
3. Improve quality of life, while minimizing adverse effects and costs.

General Approach

- Patients with SLE should be counseled lifestyle modifications such as protection from the sun, smoking cessation, exercise, and weight control.
- Immunization status should be assessed in consideration with immunosuppressive drugs.
- The effects of disease activity and treatment on pregnancy outcomes should be discussed.
- Mild symptoms can be managed with NSAIDs.
- Corticosteroids are used in low doses indefinitely as maintenance therapy.
- If the above therapy is ineffective or major organs are involved, immunosuppressive drugs are added.

Nonpharmacologic Therapy

1. Provide social and Psychological Support
2. Aerobic cardiovascular exercise may help decrease patients' risk for cardiovascular events and osteoporosis and may also improve fatigue and sleep disturbances, which are frequently experienced in SLE.
3. Photosensitivity is common in SLE, patients should wear protective clothing and hats and use sunscreens to protect themselves from the sun.
4. They should avoid tanning salons.
5. Patients with SLE should use sunscreens with high SPF values and apply them every 2 hours while in the sun.
6. Patients should be counseled to stop smoking. Smoking cessation is important, not only because it decreases cardiovascular risk, but because smoking can exacerbate SLE and diminish the effectiveness of antimalarials. Smokers also have a higher incidence of active rashes with skin damage and scarring.

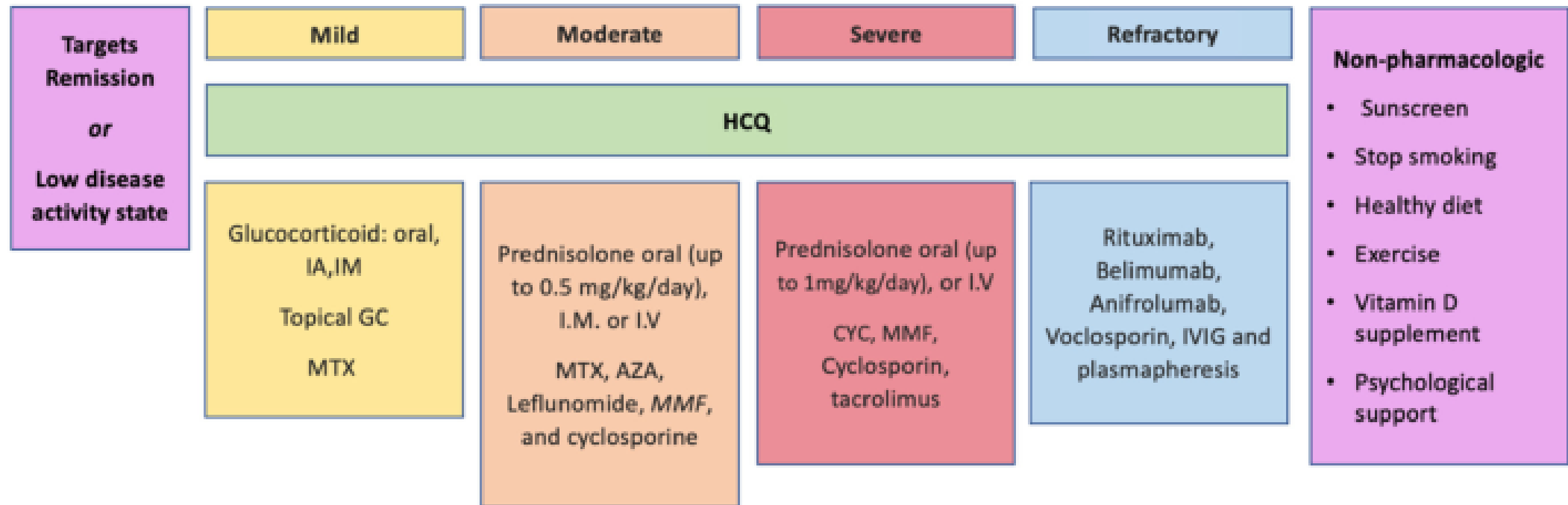
Pharmacologic Therapy

- Treatment is determined by the manifestation of SLE in individual patients.
- It consists of a combination of immunosuppression and symptomatic and supportive therapies.
- The only drugs approved by the FDA for treatment of SLE are aspirin, prednisone, hydroxychloroquine, and belimumab.
- The use of other drugs for SLE, even those considered “standard of care,” is considered to be “off-label” use.

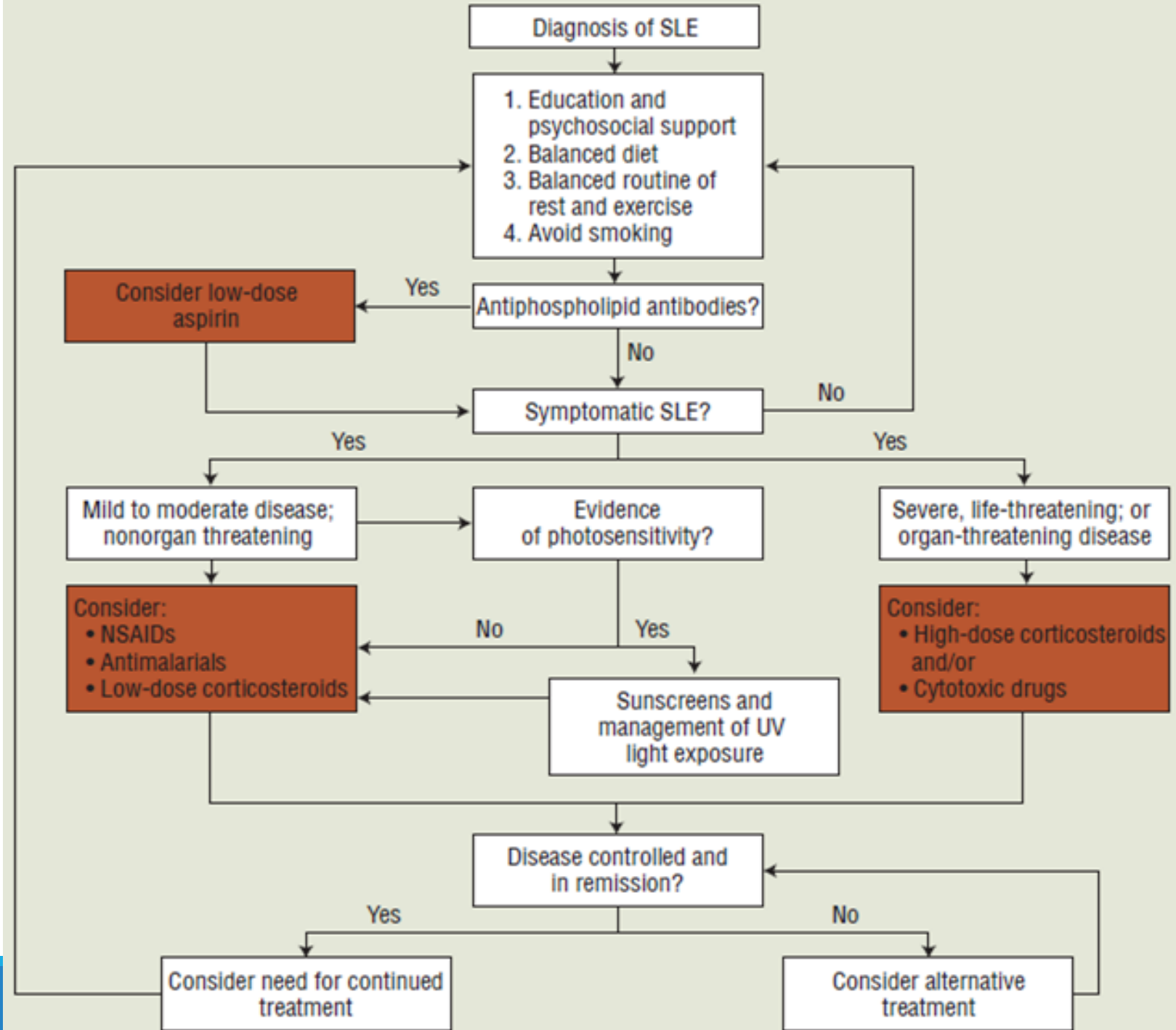
Drugs used in SLE

1. Glucocorticoids – Prednisolone, Methylprednisolone
1. NSAIDS
2. Antimalarials - Hydroxychloroquine
3. Biologics - Belimumab
4. Immunosuppressants – Cyclophosphamide, Mycophenolate mofetil, Azathioprine, Methotrexate
5. Tacrolimus
6. Leflunomide
7. IV IG

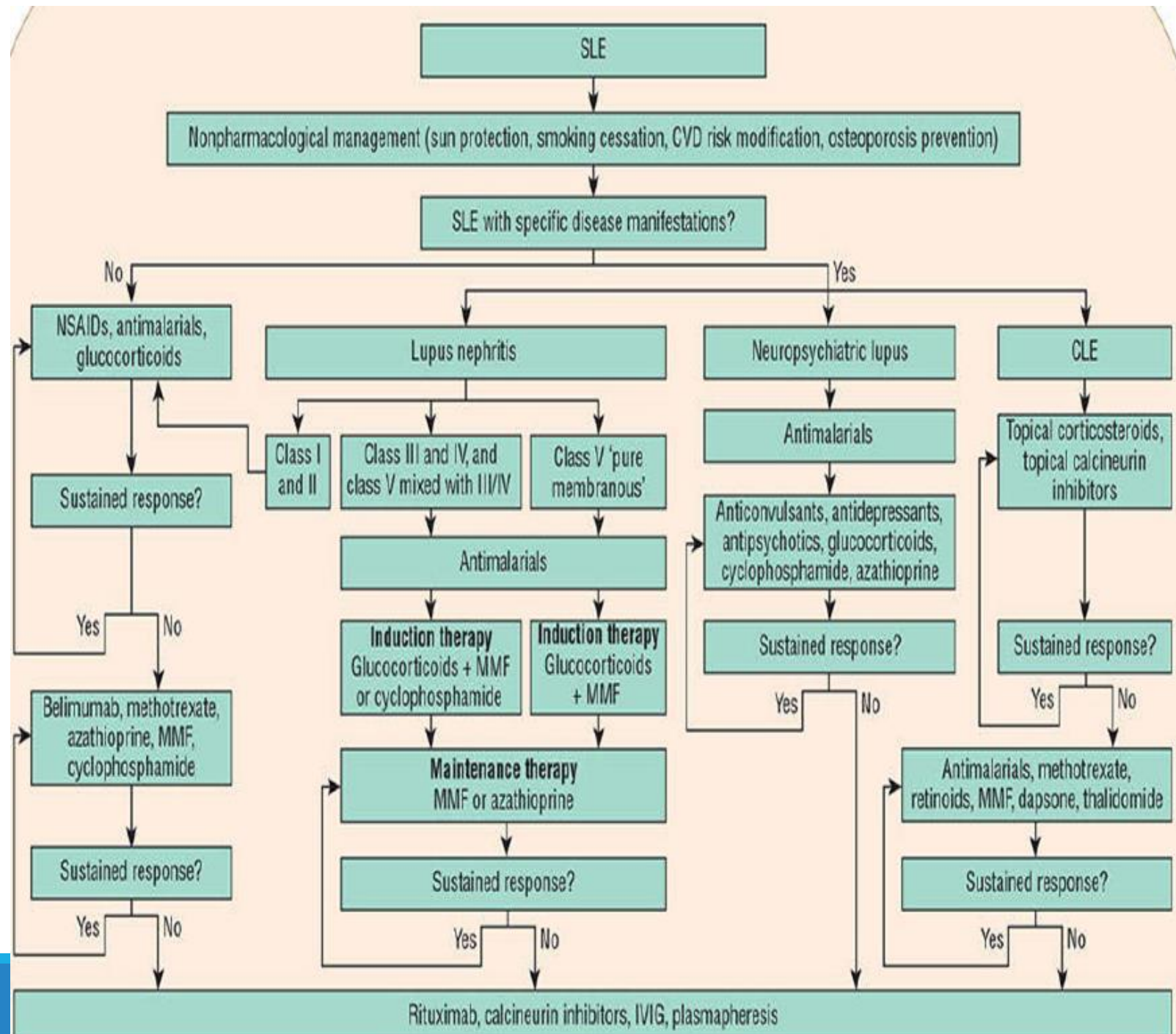
Algorithm for treat to target in lupus



General approach to the management of SLE.



Management of different manifestations of SLE



Management of different manifestations of SLE

Treatment of Specific organ system involvement in SLE

Musculoskeletal	First line treatment: HCQ. Second line treatment: MTX, Leflunomide, MMF. NSAIDS as symptomatic measures. GCs (low dose) can be added.
Cutaneous	First line treatment: HCQ ± topical GCs. Systemic GCs: severe cutaneous lupus Persistent skin lesion: methotrexate, mycophenolate, topical retinoids, MMF Dapsone: first-line SCLE and bullous SLE Belimumab: resistant CLE Pulsed-dye laser or surgery: localized, refractory lesions of CLE
Neuropsychiatric (NPSLE)	Inflammatory NPSLE: IV pulse steroid+ IV cyclophosphamide Ischemic NPSLE: Warfarin (+ve APS), Aspirin 100 mg/day (no APS).
Cardiac	Mild, acute or chronic pericarditis: NSAID Moderate, acute or chronic: GCs (0.5 mg/kg/day) Severe or constrictive pericarditis: methylprednisolone IV(1 g/day for 3 days) Recurrent pericarditis: colchicine (1 mg/day for at least 1month) Myocarditis with arrhythmia: pulses of GC (methylprednisolone 1 g/day for 3 days) followed by oral prednisone + HCQ Severe myocarditis arrhythmia: pulses of GC followed by oral prednisone + IV Cyclophosphamide. Maintenance therapy by MMF or Azathioprine. Gamma globulin in resistant case Endocarditis: GCs 1 mg/kg/day
Haematological	Thrombocytopenia: methylprednisolone IV(1 g/day for 3 days), AZA, MMF or cyclosporine Severe thrombocytopenia: cyclophosphamide or IVIG Refractory cases: plasmapheresis, rituximab or splenectomy Autoimmune haemolytic anemia: GC (1mg/kg/day). Resistant: pulse steroids, azathioprine, cyclophosphamide, splenectomy, IVIG, danazol, MMF and rituximab. Autoimmune leucopenia: Mild neutropenia ($>1.0 \times 10^9 < 2.0 \times 10^9$): no treatment neutropenia <1000: granulocyte-colony stimulating factor, GC 1m/kg/day. In refractory cases: Rituximab and stem cell transplantation

SLE Drugs indication and doses

TABLE 90-3

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) <1 mg/kg/day (or equivalent)	Initial control of severe disease Control of mild disease or maintenance after disease suppression with higher doses
Cytotoxic	Methylprednisolone 500–1,000 mg IV daily × 3–6 day	Life-threatening disease
	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	Most commonly used in severe lupus nephritis; may be necessary for other severe disease manifestations
	Azathioprine 1–3 mg/kg po daily	
	Cyclophosphamide 1–3 mg/kg po daily	
	Mycophenolate mofetil 1–3 g po daily	

IV, intravenously; NSAID, nonsteroidal antiinflammatory drugs; po, orally.

SLE Drugs Adverse Effects with monitoring parameters

TABLE 90-4 Monitoring Adverse Effects of Drugs Commonly Used in Systemic Lupus Erythematosus

Drug	Toxicities to Monitor	Baseline Evaluation	Monitoring	
			<i>System Review</i>	<i>Laboratory</i>
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	Funduscopy and visual fields every 6–12 months
Azathioprine	Myelosuppression, hepatotoxicity, 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

Nonsteroidal Anti-inflammatory Drugs

Mechanism of Action

- Inhibit cyclooxygenase (COX) enzymes (COX-1 & COX-2), reducing prostaglandin synthesis.
- Decrease inflammation, pain, and fever by blocking prostaglandin-mediated pathways.
- COX-1 inhibition: Leads to gastric protection loss, platelet inhibition, and renal side effects.
- COX-2 inhibition: Reduces inflammation with fewer gastrointestinal effects but increases cardiovascular risks.

Indications

- Used as first line treatment for arthritis, Musculoskeletal complaints, fever and serositis

Adverse effects

- GI Bleeding, Hepatic toxicity, renal toxicity, HTN, CV Events, Aseptic meningitis

Corticosteroids

MOA

- Binds to glucocorticoid receptors → modifies gene transcription → suppresses inflammation.
- Reduces capillary permeability and polymorphonuclear neutrophil activity.
- Inhibits T-cell proliferation, induces apoptosis, and impairs lymphocyte function.
- Decreases antibody production by B-cells (delayed effect).
- Stabilizes lysosomal membranes, preventing further tissue damage.

Drug and doses

- Prednisone (oral) – Standard corticosteroid for SLE treatment.
- Methylprednisolone (IV) – Used for pulse therapy in severe cases.
- **Prednisolone and methylprednisolone** – Initial 0.1 to 1.5 mg/kg/day , Maintenance <10mg/day
- Hydrocortisone (topical) – For mild cutaneous manifestations.
- Dexamethasone (IV/oral) – Alternative for CNS lupus.
- Used to control flares and maintain low disease activity.
- Doses should be targeted to lowest effective dose for most forms of SLE.
- High doses are associated with infections, myopathy, psychological disturbances, osteonecrosis and stroke.

Adverse effects

Osteoporosis, Cataract, Glaucoma, DM, HTN, Dyslipidemia, Thinning of skin, Weight increases, Skin atrophy

Antimalarials

- The antimalarials chloroquine and hydroxychloroquine have long been used in treatment of SLE.
- Hydroxychloroquine is thought to have fewer adverse reactions and is the preferred drug.

MOA

- Hydroxychloroquine has anti-inflammatory, immunomodulatory, and antithrombotic effects.
- It reduces concentrations of inflammatory cytokines such as interleukins 1, 2, 6, 17, and 22, interferon alpha and gamma, and TNF- α .
- It alters antigen presentation and T-cell proliferative responses.
- It decreases activation of receptor which are involved in antiphospholipid syndrome.
- It reduces RBC Sludging, blood viscosity and platelet aggregation.
- It delays UV light absorption and may decrease the no. of skin antigen presenting cells.

- Hydroxychloroquine is used for skin and joint manifestations of SLE.
- It can prevent lupus flares and improve long-term survival.
- It has a beneficial effect on lipids and fasting blood glucose, decreases the risk of thrombosis in patients with antiphospholipid antibodies, and decreases infections.
- It can allow corticosteroid doses to be decreased.
- Patients receiving hydroxychloroquine often have disease flares when the drug is discontinued.
- Adverse effects with hydroxychloroquine are usually mild.
- Most common are GI and skin reactions and they usually improve with dose reduction.
- The main concern is retinal toxicity, but the incidence is low and may be less than that seen with chloroquine.

DOSE- Hydroxychloroquine – 200 – 400 mg OD

Immunosuppressive drugs

1. Cyclophosphamide

- It is used to treat SLE such as Lupus nephritis, CNS Lupus, Lung disease and Severe systemic vasculitis
- It is an alkylating agent that causes cross-linkage of DNA leading to cell death.
- It also reduces B cell and Ig G production and adhesion molecule and cytokines.
- **ADR** – Myelosuppression, opportunistic infection, hemorrhagic cystitis, bladder malignancy, infertility
- **Dose** – In above mention table slide no 26

2. Methotrexate

- It is an inhibitor of folic acid reductase which needed for DNA synthesis and cell growth.
- It is indicated for arthritis, skin disease and steroid sparing drug
- It is dosed once weekly in management of SLE
- ADR – Hepatitis, Hematologic, Pulmonary toxicity, Stomatitis
- **Dose** – In above mention table slide no 26

3. Azathioprine

- It is a purine analogue, inhibits DNA synthesis and prevents immune cell proliferation.
- It is used as an alternative to MMF, and less effective than cyclophosphamide
- It is indicated for SLE related arthritis, serositis, mucocutaneous manifestations, hematologic
- ADR- Myelosuppression, Hepatotoxicity
- **Dose** – In above mention table slide no 26

4. Mycophenolate Mofetil (MMF)

- It is hydrolyzed to mycophenolic acid which reversibly inhibits the enzyme inosine 5 monophosphate dehydrogenase, important for de novo synthesis of purine inhibits proliferation and differentiation of lymphocytes.
- The drug also has immunomodulating effects such as
 1. Induction of activated T cell apoptosis
 2. Inhibition of adhesion molecule expression
 3. Antiproliferative effect on fibroblast, dendritic cell and vascular SMC
- It is indicated in Cutaneous lupus, Arthritis, Hematologic manifestations.
- ADR – Nausea, vomiting, diarrhea, Red cell Aplasia.
- Contraindicated in Pregnancy.

Biologic Agents

- Autoantibody formation is an important feature of SLE, B Cell make logical target for SLE Therapy
- B-lymphocyte stimulator (BLyS) is a cytokine that is important for B cell survival, maturation, and differentiation.

1. Belimumab

- It is a fully human IgG1- λ monoclonal antibody that binds to soluble B Lymphocytes Stimulator (BLyS), which prevents BLyS from binding to receptors on B cells and promotes apoptosis of B lymphocytes.
- Belimumab is FDA-approved for treatment of autoantibody positive active SLE in addition to standard therapy.
- It is the first drug approved by the FDA in over 50 years for management of SLE.
- No Live vaccination should be given 30 days before and after the therapy.
- Premedication with acetaminophen, Diphenhydramine should be administered
- Contraindicated with other biologics and Cyclophosphamide
- ADR – Infusion reaction, Hypersensitivity reaction, Nausea, diarrhea, depression, fever, bronchitis, Insomnia, migraine.