

# Alternative Medicine: A Review Article the Lupus Journey from the Diagnosis to Recovery and Beyond

Mohd. Wasiullah<sup>1</sup>, Piyush Yadav<sup>2</sup>, Vishal Prajapati<sup>3,\*</sup>, Pragati Yadav<sup>4</sup>

## Abstract

*Lupus, a chronic autoimmune disease, presents a complex and often volatile journey for patients, from diagnosis to recovery and beyond. The course is usually characterized by periods of acute flare-ups, followed by remissions, with different symptoms affecting different organ systems. This review delves into managing lupus with alternative medicine, highlighting how it can work alongside conventional treatments. It covers topics like diet, herbal remedies, acupuncture, and mind-body practices, all aimed at easing symptoms, reducing inflammation, and enhancing quality of life. In addition, it highlights the challenges and controversies surrounding alternative treatments, while emphasizing the importance of patient-centered care and integrative strategies. The journey from diagnosis to cure for lupus is multifaceted, and alternative therapies offer hope for better well-being when used in conjunction with conventional medicine.*

**Keywords:** Autoimmune disease, complementary therapy, holistic management, herbal treatments, lupus

## INTRODUCTION

Living with lupus can be unpredictable and challenging, impacting not just the body but also the mind and spirit. This autoimmune disease arises when the immune system mistakenly targets healthy tissues, leading to inflammation and potential damage to different organs [1]. This condition is known for its fluctuating nature, where periods of flare-ups can be followed by times of remission, making the path to recovery complex and unique for every individual. The journey typically begins with a diagnosis, often following a series of frustrating and sometimes misdiagnosed symptoms. As patients navigate the

emotional and physical hurdles of understanding the disease and its impact, they are also introduced to the realities of treatment and lifestyle adjustments. Yet, with medical advancements, a supportive care team, and a resilient mindset, many people with lupus can find ways to manage their symptoms, live fulfilling lives, and look toward the future with hope [2]. This exploration of the lupus journey aims to offer insight into the challenges faced, the strategies for recovery, and the ongoing process of living with lupus. Whether recently diagnosed or living with lupus for many years, the path to managing and thriving in the face of this condition is ongoing, full of learning, adaptation, and strength [3].

## EPIDEMIOLOGY OF LUPUS

Lupus is a chronic and complex autoimmune disease that predominantly affects women, with around 90% of cases occurring in females. It most commonly appears between the ages of 15 and 44,

### \*Author for Correspondence

Vishal Prajapati

E-mail: [vishalpraja16@gmail.com](mailto:vishalpraja16@gmail.com)

<sup>1</sup>Principal, Department of Pharmacy, Prasad Institute of Technology, Jaunpur, Uttar Pradesh, India

<sup>2</sup>Academic Head, Department of Pharmacy, Prasad Institute of Technology, Jaunpur, Uttar Pradesh, India

<sup>3</sup>Lecturer, Department of Pharmacy, Prasad Polytechnic, Jaunpur, Uttar Pradesh, India

<sup>4</sup>Scholar, Department of Pharmacy, Prasad Institute of Technology, Jaunpur, Uttar Pradesh, India

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though it can develop at any age [4]. Certain racial and ethnic groups, such as African American, Hispanic, Asian, and Native American populations, are more affected by lupus compared to Caucasians.

Globally, about 5 million people are estimated to live with the disease, while in the United States, roughly 1.5 million are affected. Research shows that African American women are two to three times more likely to develop lupus than white women, with Hispanic and Asian women also having higher rates. The reasons behind these disparities remain unclear but are thought to involve a mix of genetic, environmental, and hormonal factors [5]. The genetic predisposition to lupus is still being researched, and while certain gene variants have been linked to an increased risk of developing the disease, the exact mechanisms remain unclear. In addition to gender and ethnicity, environmental factors, such as exposure to ultraviolet light, infections, certain medications, and smoking have been suggested as potential triggers for lupus flare-ups or the onset of the disease in genetically predisposed individuals [6].

The course of lupus can vary widely between individuals, ranging from mild cases with few symptoms to severe, life-threatening conditions affecting multiple organs. Advancements in early diagnosis, better treatment options, and improved patient care, the prognosis for many people with lupus has significantly improved, and the overall survival rate continues to rise [7].

## Diagnosis Management and Active Criteria for SLE

### *Diagnosis of Systemic Lupus Erythematosus (SLE)*

The diagnosis of systemic lupus erythematosus (SLE) can be challenging due to the varied and nonspecific nature of its symptoms, which often overlap with other conditions. The diagnosis of SLE involves a combination of clinical evaluations, symptom assessments, and laboratory tests [8].

## CLINICAL FEATURES

### **SLE Symptoms Can Affect Virtually any Organ System, with the Most Common Being**

- *Skin*: Malar rash (butterfly-shaped rash across the nose and cheeks), discoid lupus, photosensitivity [9].
- *Musculoskeletal*: Joint pain, swelling, and arthritis.
- *Renal*: Lupus nephritis (kidney involvement).
- *Cardiopulmonary*: Inflammation of the pleura (pleuritis) and pericardium (pericarditis), along with a heightened risk of cardiovascular disease.
- *Hematologic*: Anemia, leukopenia, thrombocytopenia.
- *Neurological*: Seizures, psychosis, headaches.

### **Laboratory Testing**

- *Antinuclear Antibodies (ANA)*: ANA is a hallmark of SLE and is positive in about 95% of patients, though it can be present in other conditions or even in healthy individuals.
- *Anti-DsDNA (Double-Stranded DNA) Antibodies*: Strongly associated with SLE and closely linked to lupus nephritis.
- *Anti-Smith (SM) Antibodies*: Specific but less sensitive, highly suggestive of SLE [10].
- *Complement Levels (C3, C4)*: These can be low in active SLE, as the complement system is often consumed during inflammation.
- *Anti-phospholipid Antibodies*: Associated with increased risk of thrombosis (APS—antiphospholipid syndrome) [11].
- *Urinalysis*: To check for kidney involvement, such as proteinuria, hematuria, or cellular casts.
- *Diagnostic Criteria*: The diagnosis of SLE often relies on criteria from the American College of Rheumatology (ACR) and the Systemic Lupus International Collaborating Clinics (SLICC), both of which consider a mix of clinical symptoms and immunological markers.

### **ACR Criteria for SLE Diagnosis (1982, Updated 1997)**

A person must meet at least 4 out of 11 criteria to be diagnosed with SLE.

- Malar rash.
- Discoid rash.
- Photosensitivity.
- Oral ulcers.
- (nonerosive).
- Serositis (pleuritis or pericarditis).
- Renal involvement (proteinuria or cellular casts).
- Neurologic disorders (seizures, psychosis).
- Hematologic disorders (anemia, leukopenia, lymphopenia, thrombocytopenia).
- Immunologic abnormalities (e.g., anti-DSDNA, anti-SM, antiphospholipid antibodies).
- Positive ANA (if present at a titer of 1:80 or higher).

The SLE diagnosis is confirmed when a person meets at least 4 criteria, including at least one clinical and one immunological criterion.

### **SLICC Criteria for SLE Diagnosis (2012)**

To meet the criteria, a patient must have at least 4 criteria, with at least 1 clinical and 1 immunological criterion, or a biopsy-proven lupus nephritis and positive ANA or anti-DNA.

- *Clinical Criteria:* Include similar findings to the ACR criteria, such as malar rash, discoid rash, photosensitivity, oral ulcers, arthritis, serositis, renal involvement, neurological issues, and hematologic manifestations [12].
- *Immunologic Criteria:* Positive ANA, anti-DSDNA, antiphospholipid antibodies, low complement levels (C3, C4), or direct Coombs test [13].

## **MANAGEMENT OF SLE**

Management of SLE is multidisciplinary and aims to control symptoms, reduce flare-ups, prevent organ damage, and improve quality of life. Treatment plans are personalized to everyone, depending on the severity of the disease and the organs affected [14].

### **General Management Principles**

- *Patient Education:* Understanding the disease and managing symptoms is key. This includes avoiding sun exposure, managing stress, and understanding the need for regular follow-ups [15].
- *Regular Monitoring:* Regular laboratory tests (e.g., kidney function, complement levels) and clinical exams to monitor disease activity, complications, or medication side effects [16].

### **Pharmacological Treatment**

- *Non-steroidal Anti-Inflammatory Drugs (NSAIDs):* Primarily used to manage pain and inflammation in mild SLE cases, particularly for musculoskeletal symptoms.
- *Antimalarial Drugs (Hydroxychloroquine):* Often a cornerstone of treatment. These drugs reduce flares, control skin and joint symptoms, and may protect against organ damage, particularly in the kidneys and heart.
- *Corticosteroids (Prednisone):* Used to control acute flare-ups and more severe manifestations (e.g., lupus nephritis, CNS involvement). Steroids are tapered to the lowest effective dose.
- *Immunosuppressive Agents:* Drugs like azathioprine, mycophenolate mofetil, methotrexate, or cyclophosphamide are used for moderate to severe disease, especially when vital organs like the kidneys or lungs are involved.
- *Biologics:* Medications, such as belimumab (a monoclonal antibody that targets Blymphocyte stimulator) have been approved for treating active SLE and reducing flare-ups.
- *Anticoagulation Therapy:* For patients with antiphospholipid syndrome (APS) or those at high risk of clotting.

### Active Criteria for SLE

The disease activity in SLE is often assessed through tools like the SLE Disease Activity Index (SLEDAI) or British Isles Lupus Assessment Group (BILAG) index. These tools consider clinical manifestations and laboratory findings to quantify disease activity and help guide treatment [17].

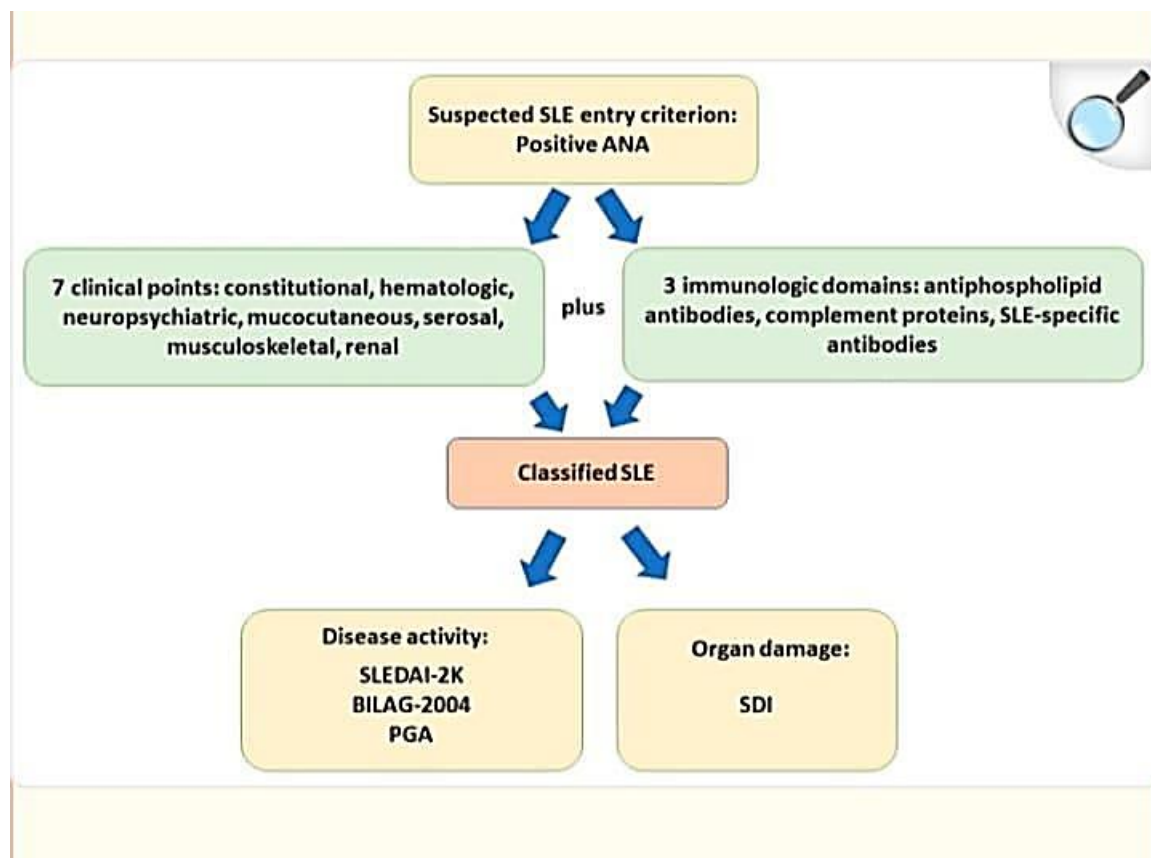
- *SLEDAI*: A score of 6 or higher generally indicates active disease.
- *BILAG*: Classifies disease activity into 5 grades, from A (severe disease) to E (no disease). These indices help clinicians assess whether the disease is in a flare or remission and tailor therapy accordingly [18].

### LONG-TERM MANAGEMENT AND FOLLOW-UP

SLE is a chronic condition, and patients require long-term follow-up to manage disease activity, monitor for complications (such as cardiovascular disease, osteoporosis, and kidney disease), and adjust treatment as needed. Key areas of focus include.

#### Bone Health (Due to Steroid Use)

Cardiovascular health, including a higher risk of atherosclerosis and heart disease, is a significant concern in lupus. In summary, diagnosing and managing lupus requires a comprehensive approach that combines clinical evaluations, lab tests, and personalized treatment strategies to manage disease activity and minimize long-term complications. Consistent monitoring and a strong partnership between the patient and healthcare provider are crucial for achieving the best outcomes (Figure 1) [19].



**Figure 1.** Systemic Lupus Erythematosus (SLE).

### Pathogenesis of Systemic Lupus Erythematosus (SLE)

The development of Systemic Lupus Erythematosus (SLE) is complex, involving a mix of genetic, environmental, and immune system factors. Essentially, SLE is an autoimmune disease in which the immune system mistakenly targets the body’s own tissues, causing inflammation and damage to various

organs. While the exact processes remain unclear, several key factors play a role in the onset of SLE [20].

- *Genetic Predisposition:* Genetics plays a key role in the development of SLE. While there is a noticeable hereditary influence, the disease is not inherited in a straightforward Mendelian way. Multiple gene variants contribute to the risk, including genes related to immune regulation, inflammation, and apoptosis (programmed cell death).
- *HLA (Human Leukocyte Antigen) Genes:* Variants in the HLA class II region, particularly HLA-DR2 and HLA-DR3, are strongly associated with an increased risk of SLE.
- *Complement System Genes:* Genetic mutations in complement proteins (C1q, C3, C4) are linked to lupus, as these components are crucial in the clearance of apoptotic cells and immune complexes. Deficiency in complement proteins is associated with an increased risk of SLE.
- *Other Immune-Regulatory Genes:* Variants in genes involved in the regulation of T cells, B cells, and interferon signaling (e.g., IRF5, STAT4, BLK) have also been associated with lupus susceptibility.

### **Environmental Triggers**

Environmental factors play a critical role in triggering the onset or exacerbation of lupus in genetically predisposed individuals. These factors include:

- *Ultraviolet (UV) Radiation:* UV light can harm skin cells, causing the release of autoantigens that activate the immune system and trigger lupus flare-ups. Exposure to UV rays is known to aggravate skin symptoms of lupus, such as the malar rash.
- *Infections:* Viral infections, particularly with Epstein-Barr virus (EBV), have been linked to triggering lupus flare-ups. EBV may cause immune system dysfunction, contributing to the development of autoimmunity.
- *Drugs:* Some medications, like procainamide, hydralazine, and isoniazid, have been associated with drug-induced lupus. In these instances, the condition typically improves once the medication is stopped [21].
- *Smoking:* Smoking has been linked to a higher risk of developing lupus, as it can trigger immune system irregularities.

### **IMMUNE DYSREGULATION**

A hallmark of SLE is immune system dysfunction, where the body's immune cells fail to distinguish between self and non-self, leading to the production of autoantibodies. Several immune pathways are involved in this dysfunction:

**Defective clearance of apoptotic cells:** One of the key features of SLE is the impaired clearance of apoptotic (dying) cells. Normally, apoptotic cells are removed by macrophages and dendritic cells, but in SLE, this process is inefficient. The buildup of cellular debris causes the immune system to mistakenly identify and attack the body's own tissues [22].

**Dysregulated T and B cell activity:** In SLE, there is an abnormal activation of both T cells and B cells:

- *T Cells:* Inappropriately activated helper T cells, particularly the Th1 and Th17 subsets, promote inflammation by releasing pro-inflammatory cytokines like IL-6 and TNF- $\alpha$ . These T cells also play a role in activating autoreactive B cells.
- *B Cells:* B cells generate autoantibodies that target self-antigens, including double-stranded DNA (DSDNA), histones, and ribonucleoproteins. These antibodies create immune complexes that accumulate in tissues, such as the kidneys (resulting in lupus nephritis) and joints, leading to increased inflammation and damage [23].

### **Plasmacytoid Dendritic Cells (PDCs)**

These cells are involved in the production of type I interferons (IFNs), which play a central role in driving the development of lupus. Overproduction of type I interferons leads to the activation of both T and B cells and promotes a pro-inflammatory environment.

### Formation of Autoantibodies and Immune Complexes

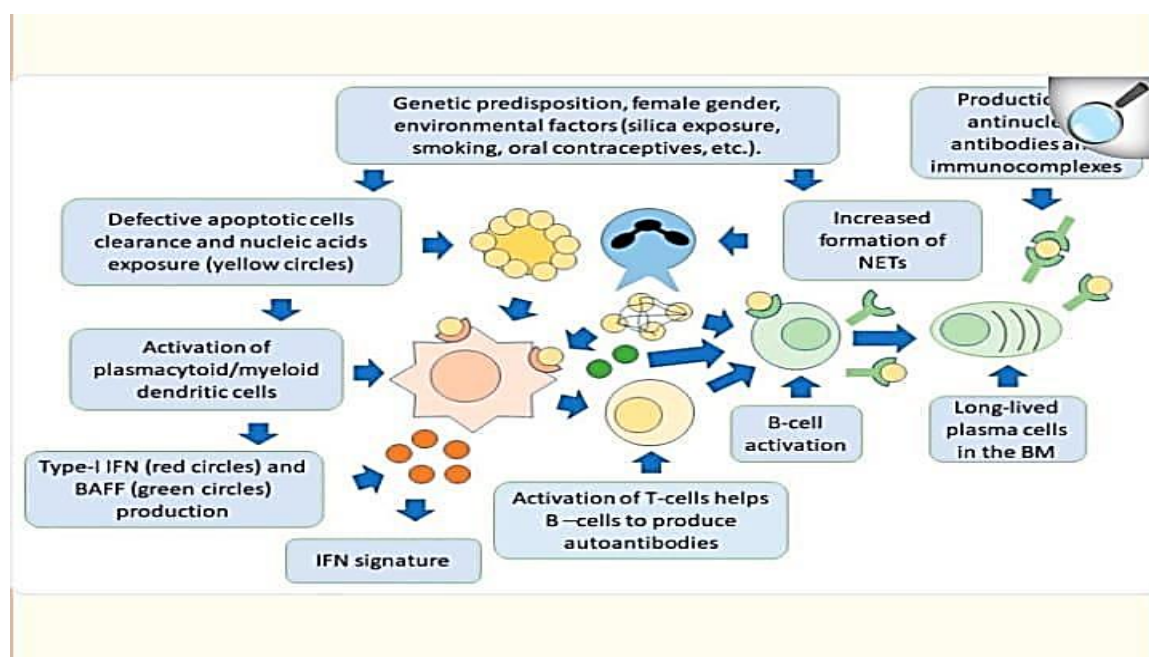
Autoantibodies are a hallmark of SLE and play a central role in its pathogenesis. The most observed autoantibodies in SLE include:

- *Anti-Nuclear Antibodies (ANA)*: These antibodies target components of the cell nucleus, including DNA, histones, and RNA. ANA are present in almost all patients with lupus, but their presence alone is not diagnostic.
- *Anti-DSDNA Antibodies*: These antibodies target double-strand DNA and are highly specific for SLE, particularly associated with lupus nephritis. Anti-Smith (SM) antibodies: Highly specific for SLE, these antibodies target small nuclear ribonucleoproteins (snRNPs).
- *Anti-Phospholipid Antibodies (APL)*: These include anticardiolipin antibodies and lupus anticoagulants, which raise the risk of blood clot formation (thrombosis) and are linked to antiphospholipid syndrome (APS). These autoantibodies form immune complexes that accumulate in various tissues, such as the kidneys, skin, and joints, causing inflammation and damage. In the kidneys, these immune complexes settle in the glomeruli, resulting in lupus nephritis, which can lead to kidney failure if not treated [24].

### Type I Interferon Pathway and Inflammatory Cytokines

A significant feature of SLE is the overproduction of type I interferons (IFN- $\alpha$  and IFN- $\beta$ ). These cytokines are typically produced by plasmacytoid dendritic cells (PDCs) in response to viral infections or cellular stress. In SLE, the production of type I interferons is aberrantly elevated, which plays a central role in.

This process involves enhancing the activation of T and B cells, boosting the production of autoantibodies, and triggering the release of additional inflammatory cytokines like TNF- $\alpha$ , IL-6, and IL-17, which further fuel inflammation and tissue damage. The activation of the type I interferon pathway is a key feature of lupus and plays a major role in disease activity. The development of SLE is driven by a mix of genetic factors, environmental triggers, and immune system dysfunction. Factors, such as impaired removal of apoptotic cells, excessive activation of T and B cells, the formation of autoantibodies, and the involvement of the type I interferon pathway all contribute to autoimmunity, inflammation, and tissue damage. Understanding these processes is essential for developing targeted treatments to manage the disease and prevent organ damage in those with SLE (Figure 2).



**Figure 2.** SLE of Pathogenesis.

## **The Role of Mitochondria in Systemic Lupus Erythematosus (SLE)**

Mitochondria are not only the powerhouses of the cell, responsible for generating ATP through oxidative phosphorylation, but also play a crucial role in cellular signaling, apoptosis (programmed cell death), and the regulation of inflammation. In the context of Systemic Lupus Erythematosus (SLE), mitochondria are increasingly recognized as central players in the pathogenesis of the disease, particularly due to their involvement in immune system activation, cellular damage, and the production of autoantibodies [25].

### **Mitochondria and Apoptosis**

Apoptosis, or programmed cell death, is a normal process that helps the body maintain tissue homeostasis and remove damaged or unnecessary cells. Mitochondria are crucial in apoptosis, as they control the release of proteins that initiate the cell's death process. In SLE, defective apoptosis is a key factor contributing to disease development.

**Impaired clearance of apoptotic cells:** In SLE, the normal process of clearing apoptotic cells is often impaired. When cells die prematurely and are not properly cleared, their contents (including mitochondrial DNA and other cellular debris) can leak out and stimulate the immune system. This contributes to the formation of autoantibodies against these “self” antigens, a hallmark of autoimmune diseases like SLE.

**Mitochondrial damage and exposure of autoantigens:** Mitochondrial dysfunction can lead to the release of mitochondrial components, such as mitochondrial DNA (mtDNA), cytochrome c, and other mitochondrial proteins, into the extracellular space. These molecules can act as danger signals (also called “damage-associated molecular patterns,” or DAMPs), which activate the immune system and promote the production of autoantibodies, particularly anti-DNA antibodies [22–24].

### **Mitochondrial DNA (mtDNA) and Immune Activation**

Mitochondria have their own DNA, which is distinct from nuclear DNA and encodes a small number of genes crucial for mitochondrial function. In SLE, mtDNA has been identified as a major target for the immune system:

- *mtDNA as an Autoantigen:* When mitochondria are damaged or undergoing stress, mtDNA can be released into the cytoplasm or extracellular space, where it can be recognized by immune cells. This exposure of mtDNA is a strong inducer of autoimmunity, as it can trigger the production of autoantibodies against both mitochondrial and nuclear components.
- *Activation of Type I Interferon:* The release of mtDNA into the cytoplasm can trigger pattern recognition receptors (PRRs), like Toll-like receptor 9 (TLR9). TLR9 recognizes DNA from bacteria and damaged cells, including mtDNA, and its activation leads to the production of type I interferons (IFNs). In SLE, the elevated production of type I interferons plays a central role in driving immune dysregulation, amplifying the autoimmune response, and promoting inflammation [20–22].

### **Mitochondrial Dysfunction and Inflammation**

Mitochondrial dysfunction contributes to the inflammatory environment seen in SLE by several.

#### **Mechanisms**

- *Reactive Oxygen Species (ROS) Production:* Mitochondria are the primary site to produce reactive oxygen species (ROS), which are byproducts of cellular metabolism. In SLE, mitochondrial dysfunction leads to the excessive generation of ROS, contributing to cellular damage, inflammation, and tissue injury. ROS can also trigger pro-inflammatory pathways, such as nuclear factor-kappa B (NF- $\kappa$ B) and other inflammatory mediators, which further promote the disease process.
- *Mitochondrial Permeability Transition:* In response to cellular stress or damage, mitochondria undergo a process known as mitochondrial permeability transition (MPT), where the mitochondrial

membrane becomes more permeable, allowing pro-apoptotic proteins like cytochrome c to be released into the cytoplasm. This process contributes to cell death and the release of intracellular contents, including mitochondrial components, which can worsen the inflammatory response in SLE.

### Mitochondrial Dysfunction and Tissue Damage

Mitochondrial dysfunction also directly contributes to tissue damage in various organs affected by SLE, particularly the kidneys, heart, skin, and brain:

- *Lupus Nephritis*: In SLE, mitochondrial dysfunction in kidney cells, especially podocytes (the cells that form part of the kidney filtration barrier), contributes to glomerular injury and lupus nephritis. Mitochondrial stress leads to the generation of ROS, which causes podocyte injury and dysfunction, exacerbating kidney inflammation and damage.
- *Cardiac and Vascular Damage*: Mitochondrial dysfunction in endothelial cells (cells that line blood vessels) and cardiomyocytes (heart muscle cells) can contribute to the vascular abnormalities and increased cardiovascular risk seen in SLE. ROS production and impaired mitochondrial function lead to endothelial cell activation, promoting a pro-inflammatory and pro-thrombotic state, which can result in accelerated atherosclerosis and increased risk of heart attack and stroke.
- *Neuropsychiatric Lupus*: Mitochondrial dysfunction in neurons and glial cells may play a role in the neurological symptoms of SLE, including seizures, cognitive issues, and psychosis. Mitochondrial stress in the central nervous system (CNS) can trigger neuroinflammation and neuronal damage, contributing to the neuropsychiatric symptoms commonly observed in lupus [20–23].

### Therapeutic Implications: Targeting Mitochondria in SLE

Understanding the role of mitochondria in the development of SLE has led to the development of new treatment strategies focused on addressing mitochondrial dysfunction to decrease disease activity and tissue damage. Some of these potential therapies include:

- *Antioxidants*: Since excessive ROS production plays a major role in mitochondrial dysfunction and inflammation in SLE, antioxidants like N-acetylcysteine (NAC) could help reduce oxidative stress and prevent tissue damage. However, more clinical trials and research are necessary to evaluate their effectiveness.
- *Mitochondrial-targeted Therapies*: There is growing interest in developing drugs that specifically target.

### CONCLUSIONS

Mitochondria have a central and complex role in the development of SLE, driving immune system dysfunction, inflammation, and tissue damage. Mitochondrial dysfunction can lead to the release of autoantigens (like mtDNA), activation of immune cells, excessive ROS production, and ultimately, the exacerbation of disease symptoms. Understanding these mechanisms provides new opportunities for therapeutic interventions targeting mitochondrial function and oxidative stress in SLE, with the potential to improve disease outcomes and reduce long-term organ damage.

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