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Review Article

A Systemic Review of Lupus Erythematosus autoimmune disease Classification, Pathogenesis, and Diagnosis

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Abstract

Lupus is a systemic chronic inflammatory autoimmune disease that can present with a wide range of clinical symptoms. The four main types of lupus are neonatal and paediatric lupus erythematosus (NLE), drug induced lupus (DIL), discoid lupus erythematosus (DLE) and systemic lupus erythematosus (SLE). Due to aberrant immunological function and the generation of autoantibodies, which result in the development of immune complexes that may negatively impact healthy tissue, patients with lupus have a loss of self-tolerance. Immune abnormalities, environmental, hormonal, and genetic variables have been discovered, but the exact etiologic process remains unknown. There have also been confirmed correlations between the start of lupus and age, sex, region, and race. Microbiological and pharmaceutical methods for symptoms reduction, resolution, and enhanced quality of life should be part of the personalized management of this illness.

Keywords: autoimmune disease; lupus erythematosus; types of lupus; pathogenesis of lupus; diagnosis of lupus, management of lupus, b & t cells role in lupus

Introduction

Systemic lupus erythematosus (SLE) is a multisystem chronic autoimmune disease. it is more common in women of reproductive age as compared to males. [1]. There is a lack of clarity regarding the precise cause of this illness. Patients occasionally have flare-ups of differing intensity or periods when no symptoms or indicators are apparent. It has been shown, however, that a combination of hereditary and environmental variables can set off immunological responses that lead to the overproduction of pathogenic autoantibodies by B cells and the dysregulation of cytokines, which can cause damage to tissues and organs. The presence of antibodies against cytoplasmic and nuclear antigens is a characteristic of SLE [2].

Additionally, it is possible that SLE patients have other autoantibodies, such as anti-phospholipid, anti-cardiolipin, anti-Scl-70 (found in systemic sclerosis), anti-La, and anti-Ro which are present in Sjogren disease and others. This suggests a broad correlation between SLE and other autoimmune diseases [3]. Clinical symptoms of this illness range widely, from moderate cutaneous involvement to severe organ damage, including heart failure, pulmonary hypertension, and kidney failure. The most sophisticated and accurate categorization criteria to date are those employed by the American College of Rheumatology (ACR) and the European League Against Rheumatism (EULAR) [4]. SLE management is difficult and calls for a multidisciplinary strategy. The organs affected and the severity of the disorders determine the therapy plan. Even though the illness affects several systems, each person's course will differ based on the severity, frequency of flare-ups, and length of remission. The degree of substantial organ involvement—such as in the kidneys, lungs, or heart—may shorten life expectancy. If not, 80% to 90% of SLE patients may have an average life expectancy with close monitoring [5]. A comprehensive search of databases and search engines including Scopus, Embase, PubMed/NLM, Google Scholar and ResearchGate, was performed using appropriate keywords, including systemic lupus erythematosus, The review includes the pathogenesis, function of B cells and T cells in SLE, and the classification criteria of SLE. Additionally, articles that may be relevant to the pathogenesis, classification, and diagnosis management were included. The data derived from the literature search is combined with clinical knowledge and presented as an all-encompassing review.

Neonatal and paediatric lupus erythematosus (NLE)

NLE is a rare type of lupus that affects neonates. It is believed to be caused by autoantibodies from the mother that cross the placenta. Just over 1% of children individuals with positive maternal autoantibodies go on to develop NLE, though. The skin, liver, and heart are frequently involved in clinical manifestations. There have been reports of significant morbidity and death as well as cardiac manifestations; however, in most NLE patients who also be involved in other organs (such as the skin, liver, and blood), signs and symptoms have occasionally resolved on their own in 4-6 months. [6]

Drug induced lupus (DIL)

DIL is the result of an autoimmune reaction brought on by drug exposure. While different organ systems may be impacted, clinical symptoms often go away when the offending substance is stopped. [7]

Discoid lupus erythematosus (DLE)

Atrophic photosensitive dermatosis and chronic scarring are the hallmarks of DLE, which can develop into SLE or strike individuals already afflicted with SLE. It is believed that the cause is hereditary, and that women, African Americans, and those in their 20 – 40 years have the highest prevalence. Many times, a biopsy of a rash on the arms, face, neck, or scalp is used to make the diagnosis. Topical corticosteroids, chemical and physical sunblocks, and antimalarial medications are frequently used to control the clinical symptoms of DLE and prevent illness flare-ups. [8]

Systemic lupus erythematosus (SLE).

SLE is frequently referred to as just "lupus," its effects on several organ systems set it apart from other forms. In women of childbearing age, SLE is diagnosed in between 20 to 150 people per 100,000; however, individuals of any age, male or female, might be affected. it is commonly observed in Native Americans, Hispanics, Asians, and African Americans are the groups most likely to experience SLE. [4]

Epidemiology

Geographical differences are observed in the reported incidence and prevalence of SLE worldwide; North America has the highest incidence and prevalence, Africa the lowest incidence, and Australia the lowest prevalence. The therapy of the condition and its clinical outcome are significantly influenced by factors such as age, gender, and ethnicity. Although SLE is more common in women, men experience a more severe and rapid course of the disease, which leads to a poor prognosis. Genetic variations and environmental factors can be blamed for this discrepancy. The incidence rate for the Caucasian population is currently 6.73 cases per 100,000 people year, while the African-American population has 31.4 cases per 100,000 people annually. Black Americans had a prevalence rate of 517 per 100,000, compared to 134 per 100,000 for Caucasians and European Americans [9,10].

SLE is primarily observed in women between the ages of 15 and 44 [11], making it one of the most gender-differentiated autoimmune disorders [10]. SLE is a prevalent diagnosis in women of reproductive age. Its etiology may be influenced by hormones, and it presents several medical and behavioural issues that impact family planning and pregnancy. The racial trends of SLE suggest that non-Caucasian people are the disease's primary victims. Compared to the Caucasian population, African American, Hispanic, and Asian groups in the US have higher rates of SLE. African-American women experience it three to four times more frequently [11].

Geography

According to a report filed by the National Arthritis Data Working Group, 250,000 Ameri-cans are thought to be affected with SLA.[13] When compared to Americans of Eastern Eu-ropean ancestry, the prevalence of SLE in the United States shows a clear elevation among Asian, Afro-American, Afro-Caribbean, and Hispanic Americans. [14,15] For instance, com-pared to Hispanic patients in Nogales, Arizona, where the rate is 100 cases per 100,000 per-sons, Caucasian patients in Rochester, Minnesota, had a prevalence of SLE of about 40 cases per 100,000 persons. [16,17] Compared to African-Americans in the United States, black people in Africa have a far lower incidence of SLE.[18] More research is also needed on the occurrence of SLE in different demographics (e.g., urban versus rural locations). Larger, pop-ulation-based research involving a broad patient base are necessary, according to epidemiolog-ic data derived from lupus registries. Due to various possible barriers, including different case definitions, limited source populations, and different demographic group aims, such data are currently missing. [19]

Sex and Age

Women with SLE are more likely to get it, especially those who are infertile. Studies have indicated that women who used oral contraceptives or hormonal therapies, or who menarched early, had a greater risk of systemic lupus erythematosus (SLE). This increased incidence may be related to hormones, specifically estrogen.[20] Men are at the same decreased risk as prepubertal or postmenopausal women. There is additional evidence linking Klinefelter's syndrome, a condition where males have an extra X chromosome, to an increased prevalence of SLE. This suggests that SLE may have a hormonal etiology. [21]

Pathogenesis

The exposome, or environmental influence, and the genome interact intricately in the patho-physiology of sickle cell disease (SLE) to produce an epigenetic modification that modifies the expression of genes that aid in disease progression. In genetically sensitive individuals, exposure to environmental variables including UVB radiation, viruses, and toxins causes a loss of immunological tolerance and abnormal activation of the immune system [22]. The in-troduction of self-antigens into the immune system, potentially due to heightened apoptotic cell count, starts a feedback loop between the innate and adaptive immune systems. The clini-cal picture of SLE is the resultant widespread tissue damage caused by the formation of auto-antibodies and immunological complexes, autoreactive T and B cells, complement activation, and cytokine release [23]. This review focuses on SLE's environmental influences, immuno-pathogenesis, and genetic susceptibility.

Environmental factors and their influence.

Epidemiological studies have clearly demonstrated the link between the occurrence of SLE and exposure to silica, cigarette smoke, oral contraceptives, ultraviolet B (UVB), specific medications, and Epstein-Barr virus (EBV) infection. Increased oxidative stress, inflammato-ry cytokine overexpression, systemic inflammation, and epigenetic changes are plausible bio-logical explanations for these correlations [24]. Here is a review of environmental exposure and its possible impact on the pathophysiology of SLE.

Particulate Exposure

According to experimental research, crystalline silica triggers intracellular antigen release and cellular death. Decreased regulatory T-cell activity, oxidative stress, and elevated pro-inflammatory cytokine activity are additional disease pathways. Exposure to silica is associat-ed with increased levels of immune complexes and serum autoantibodies in mouse models [25]. Nicotine, polycyclic aromatic hydrocarbons, carbon monoxide, and free radicals are among the harmful substances found in cigarette smoke that can cause oxidative stress and damage endogenous proteins and DNA. These exposures can also result in genetic mutations that can cause autoimmunity and increase the production of cytokines that promote inflamma-tion [26]. According to a meta-analysis of research on smoking and the risk of SLE, smokers were more likely than non-smokers to acquire SLE (OR 1.5; 95% CI 1.09, 2.08) [27].

Ultraviolet B Exposure

Reactive oxygen species are produced and pro-inflammatory cytokines like TNF-α, IL-1, IL-6, and IFN-α are expressed more often when exposed to UVB light. IFNs play a role in the development of UVB-induced inflammatory skin lesions in SLE patients. Additionally, UVB enhances the release of IL-8 and chemokine ligands (including CCL5, CCL20, and CCL22) and upregulates intracellular adhesion molecules (like ICAM-1 and LAF1), all of which at-tract immune cells to inflammatory regions [27]. UVB-induced DNA hypomethylation in CD4+ T cells, which encourages autoreactivity and autoantibody formation, is another factor in the development of illness. Moreover, exposure to UVB impedes the removal of apoptotic cells [28,29].

Epstein-Barr Virus Infection

In comparison to age-matched controls, SLE patients had significantly higher rates of EBV seropositivity [30]. Genetic deficiencies that lead to inadequate infection control and a higher frequency of latent EBV infection reactivation are possible explanations. In SLE patients, there is insufficient control over infection as evidenced by high viral loads, raised EBV IgA antibody levels, and deficient EBV-specific T cells. [31] Deficits in the complement pathway, IFN pathway components, and certain major histocompatibility complex (MHC) alleles are the main genetic predisposing factors. Furthermore, an increased number of EBV-infected cells during apoptosis will trigger an innate and adaptive immune response against released cellular antigens and EBV antigens due to extensive latent infection and reactivation. [32] Thus, inadequate management of EBV infection may play a role in the onset of SLE. Molecu-lar mimicry is another way that EBV may have a role in the development of SLE. SLE-associated autoantigens and antibodies against the EBV nuclear antigen (EBNA-1) cross-react. The immunological response to EBNA-1 in susceptible individuals causes the produc-tion of cross-reactive antibodies, which in turn causes epitope spreading and the eventual on-set of systemic lupus erythematosus (SLE). Additional viral linkages linked to SLE include the hepatitis B virus vaccination, parvovirus B19, and cytomegalovirus [33].

Drug Exposure

Procainamide, minocycline, isoniazid, hydralazine, and TNF-α inhibitors are among the medi-cations linked to the development of SLE. The two drugs that have the highest potential to cause SLE are procainamide and hydralazine, at 30% and 5% to 10%, respectively. Genetic predisposition, drug biotransformation, and epigenetic modifications in immune cells are some of the hypothesized pathways of medication-induced lupus. The main mechanism of acetyla-tion used in the metabolism of procainamide, hydralazine, and isoniazid is N-acetyltransferase enzymes. Following exposure to these medications, autoantibodies are more likely to accumu-late in slow acetylators who lack the N-acetyltransferase gene. [34] Furthermore, a few stud-ies have hypothesized a link between drug-induced lupus and the null complement alleles for HLA-DR2, HLA-DR3, C4A, and C4B. Additionally, these medications might disrupt com-plement component C3, which would prevent immune complexes from being cleared. Anoth-er possible mechanism of drug-induced lupus is called biotransformation, and it is centred on the oxidative metabolism of medicines in neutrophils. Myeloperoxidase, reactive oxygen spe-cies, and other toxic metabolites are thought to be released during the oxidative metabolism of procainamide and isoniazid, causing a cytotoxic effect. [35] It has been documented that immunological cells' epigenetic characteristics are changed by bio transformed medications and their metabolites. Procainamide and hydralazine both prevent T-cell DNA methylation, which raises the production of lymphocyte function-associated antigen 1 (LFA-1), which in turn triggers autoreactivity. Drug-induced lupus has also been linked to the innate immune response. Activated neutrophils release neutrophil extracellular traps (NETs), which are filled with cytosolic proteins and nuclear DNA. When autoantigen exposure triggers neutrophil muscarinic receptors, procainamide and hydralazine induce an autoimmune response that leads to the development of net neutrophil epithelial cells (NETs). [36]

Hormonal Influences

Sex hormones are known to have an impact on immune system performance and can either protect or induce the onset of SLE. Research has indicated that exposure to estrogen is linked to a higher risk of SLE. however, progesterone and testosterone provide protection by neu-tralizing the effects of estrogen. [37] Furthermore, sex hormones' impact on disease activity is demonstrated by their exacerbations during adolescence, pregnancy, and the postpartum phase. By boosting the generation of type 1 interferon (IFN), boosting the survival of auto-reactive B cells by the formation of anti-dsDNA antibodies, dysregulating T-reg cells, altering TLR pathways, and promoting the growth of dendritic cells, estrogen action may have a role in the development of disease [38].

Genetic Susceptibility

A genome-wide association study (GWAS) conducted over the past ten years has mapped over ninety SLE susceptibility loci, many of which are caused by additive single nucleotide polymorphisms. Furthermore, there have been reports of uncommon monogenic variants of SLE [39]. Of the 730 polymorphisms linked to SLE, 21 result in changes to amino acids, 484 are found in regions where genes are transcribed, and the remaining variants are intergenic, indicating a major impact on gene regulation rather than protein sequence [36]. Genes encod-ing products involved in lymphocyte signalling, type I interferon (IFN-I) signalling, and the clearance of immunological complexes (IC) contain or are close to the majority of SLE risk loci. The SLE risk genes that have been reviewed here are clustered into important disease pathways; nevertheless, because of their varied activities, these genes may contribute to the pathogenesis of the disease via a variety of methods [40].

T & B Cell Signalling

T & B-cell activation, proliferation, and interaction are regulated by adaptor molecules, kinas-es, and cytokines, which are encoded by susceptibility genes involved in abnormal T/B cell signalling in SLE. For instance, components involved in antigen presentation are encoded within the class II human leukocyte antigen (HLA) region [41]. An overactive immune re-sponse is caused by these molecules' increased surface expression. Alleles of HLA-DR2 and HLA-DR3 are linked to autoantibody production and susceptibility to SLE. Another gene that produces a tyrosine phosphatase that modifies B-cell receptor (BCR) and T-cell receptor (TCR) signalling, resulting in increased B-cell autoreactivity in SLE is protein tyrosine phos-phatase non-receptor type 22 (PTPN22). Comparably, another gene that codes for proteins is C-terminal Src kinase (CSK), which produces the tyrosine kinase C-Src as well as BANK1, which codes for a scaffold/adaptor protein linked to modified B-cell activation. ETS1, IKZF1, IKZF2, IKZF3, RAG1, RAG2, FASLG, FAS, SHOC2, and KRAS are transcription factors that control lymphocyte differentiation and proliferation and are encoded by the SLE susceptibility genes [42].

Role of T Cells

T cells are important in the pathophysiology of SLE because they secrete pro-inflammatory cytokines, which cause inflammation. They also trigger the production of autoantibodies by B cells and sustain the disease by accumulating autoreactive memory T cells. Nevertheless, T follicular helper (Tfh) cells are necessary for germinal centre formation, proliferation, isotype-switching, and somatic hypermutation; their ratios and functions are aberrant in patients with Tfh cells. Furthermore, these cells generate the cytokine IL-21, which promotes B cell devel-opment into memory B cells and plasma blasts that make antibodies. The interaction between Tfh cells and the OX40 ligand, which is expressed on myeloid antigen-presenting cells, drives the pathological growth of Tfh cells in SLE [43]. When circulating RNA-containing immune complexes activate TLR7, the OX40 ligand is stimulated to express. In SLE patients, this pathologic expansion of the TFH cell subgroup is linked to increased antibody production and tolerance loss [44,45].

Regulatory T (Treg) cells are a distinct group of T cells that, in healthy persons, decrease auto-reactive lymphocytes and inhibit the immune response while upholding self-tolerance. The action of IL2 is necessary for the formation of Treg cells. Treg cell formation and function are hampered in SLE by an unbalanced T cell cytokine profile marked by reduced IL2 [46]. Low amounts of the transcription factor activator protein 1 (AP-1), which ultimately promotes the development of SLE, result in reduced expression

of IL2 in T cells. Additionally, IL2 limits the expression of pro-inflammatory IL17, which high levels in SLE lead to local tissue dam-age [47].

Role of B Cells

B cells' production of autoantibodies and reaction to antigens have a role in the pathophysiol-ogy of SLE. The toll-like receptor (TLR) route, stimulation through beta cell-activating factor (BAAF), and B-cell receptor (BCR) mediated activation are the mechanisms linked to the abnormal activation of B cells. Tolerance is lost when B cells are stimulated via the TLR pathway. As shown in SLE patients, transitional B cells are sensitive to TLR9 stimulation and generate autoreactive marginal zone B cells. Cytokines, especially BAFF, can stimulate B cells, which can potentially impair B cell tolerance. Anti-dsDNA, anti-histone, and anticardi-olipin antibody levels are noticeably greater in SLE patients with high BAFF levels [43-47].

Moreover, B-cell receptor is an essential regulator of both positive and negative selection, and in healthy persons, B cell survival depends on ongoing BCR sensing. Serum IgM levels are greater and BCR-mediated B cell activation is more prominent in SLE patients with c-Src ty-rosine kinase (Csk) gene polymorphisms [48]. BCR-induced pro-apoptotic signals are bal-anced by pro-survival BAFF signalling. But in SLE, an imbalance of these signals results in a loss of tolerance, and the synthesis of autoantibodies ultimately advances the pathophysiolo-gy of the illness [49-52].

Role of the Complement System

Activation of the inflammatory cascade in organs with IC deposition, enhanced autoreactive CD+8 T cell activity, and reduced clearance of apoptotic debris and IC are only a few of the pathogenic pathways of SLE that complement deficiency is thought to speed up [53]. By al-tering their mitochondrial metabolism, C1q often aids in the elimination of immunological complexes and apoptotic debris while also preventing CD8+ T cells from responding to self-antigens. Autoantibodies and a lupus-like condition are observed in patients with C1q homo-zygous impairment, which is likely caused by the incapacity to eradicate apoptotic cells [54].

Clearance of Apoptotic Cells and Immune Complexes

An autoimmune reaction starts when self-antigens are exposed because of apoptotic cells' poor clearance. Furthermore, the inflammatory response may be exacerbated by the poor clearance of interferon (IC) resulting from autoantibodies attached to antigens. Relevant products for this system are encoded by HLA class III region genes; mutations in C4A, C4B, C1QA, C1QB, and C1QC have been linked to monogenic types of SLE [55].

MANAGEMENT

The nature and degree of severity of the disease determine when the signs and symptoms of lupus should be treated. Sun protection, a healthy diet and nutrition, exercise, quitting smok-ing, the right vaccinations, and the management of coexisting illnesses are general advice for all patients. NSAIDs, antimalarial medications, and corticosteroids are frequently used to treat the symptoms and signs of mild-to-moderate lupus patients. High-dose corticosteroids and immunosuppressive medications are used to assist manage the disease's progression as it advances and its clinical signs worsen. [56,57]

Nonsteroidal anti-inflammatory drugs (NSAIDs)

Nonsteroidal anti-inflammatory drugs can be used to treat aches, swelling, and pain related to the musculoskeletal system. These medications have anti-inflammatory, anticoagulant, and pain-relieving qualities that are helpful in treating common lupus-associated symptoms; never-theless, before prescribing NSAIDs to a patient with lupus, doctors should take the possibility of adverse effects into account. [55-57]

Antimalarial Medications

Certain antimalarial medications have shown promise in managing the different manifesta-tions of lupus and averting further flare-ups. Antimalarials may disrupt T-cell activation and suppress cytokine activity, while the precise mechanism is unknown. These substances may also prevent intracellular toll-like receptors from recognizing and binding foreign substances, which helps to trigger the immune system. [58] The most researched and often used medica-tion in this class is hydroxychloroquine (e.g., Sanofi Plaquenil), yet it has a risk of severe mus-cular and visual problems.

Steroids

Corticosteroids help with controlling immune system and blood pressure by acting as a natural hormone substitute for the adrenal gland. These medications lessen inflammation-related dis-comfort and edema, which can happen during a lupus flare-up. Corticosteroids should only be taken at the lowest dose and for as long as required to control an active aggravation of lupus due to their serious long-term adverse effects. [55,56]

Immunosuppressive Agents

Immunosuppressants are generally prescribed for more severe cases of lupus when antimalarial medications or high-dose corticosteroids have not been able to control the disease's symp-toms. They are also employed when preventing flare-ups and relapses and inducing and main-taining remission are crucial. High-dose corticosteroids may be administered with immuno-suppressants to manage flare-ups, reduce the dosage of each drug, or lessen the likelihood of side effects. Cyclophosphamide (Cytoxan, Bristol-Myers Squibb) and azathioprine (Azasan, Salix; Imuran, GlaxoSmithKline) are the most often utilized medicines in this class. Kidney issues associated with lupus have also been treated with mycophenolate (CellCept, Genen-tech/Roche). [55]

Monoclonal Antibodies

Belimumab

The first human monoclonal antibody was approved by the FDA in March 2011 to treat lu-pus. The first medication to be licensed for use in treating lupus patients in more than 50 years is belimumab (Benlysta, Human Genome Sciences/GlaxoSmithKline). Belimumab works by interfering with a protein required for B-cell activity (BLyS), which prevents B cells from be-coming activated. Belimumab, formerly known as LymphoStat-B, is advised for individuals with active SLE who are on standard therapy that includes immunosuppressants, NSAIDs, antimalarials, and/or corticosteroids. [54-59]

Additional Treatment Options

The use of stem cell transplantation to inject healthy cells into the body and aid in immune system reconstruction has piqued the curiosity of researchers. Clinical trials have examined DHEA and rituximab, both of which have improved patients' quality of life. While rituximab reduces the quantity of B cells and may be especially helpful in patients who do not respond to other commonly used immunosuppressants, DHEA is thought to aid in the control of sex hormones. [60]

Diagnosis

The diagnosis of SLE is based on observed signs and symptoms, laboratory tests, and diagnostic tests tailored to each patient. The American College of Rheumatology (ACR) classification criteria for systemic lupus erythematosus, updated in 1997, is a valuable tool for evaluating patients when SLE is suspected. [61] If a patient has at least four of the 11 criteria a diagnosis of SLE can be made in 95, which the specificity is 85% and the sensitivity is 85%.58 However, a study comparing the ACR criteria with the modified weighted criteria showed a higher sensitivity. weighted criteria (sensitivity, 90.3% vs. 86.5%; specificity, 60.4% vs. 71.9%).[62]

ANA testing is crucial in the diagnosis of SLE because nearly all individuals with the disease are ANA-positive.60 Although lower titers are frequently seen with rheumatoid arthritis than with SLE, positive ANA results are occasionally recorded in illnesses other than SLE (e.g., rheumatoid arthritis). Two autoantibodies that are quite helpful in the diagnosis of SLE are anti-dsDNA and anti-Smith (Sm). [63-65]

Complete blood count (CBC) with differential, a full metabolic profile, and a urinalysis to ascertain creatinine clearance and the existence of proteinuria or active sediment are frequent-ly carried out diagnostic laboratory analyses in addition to autoantibody testing. Further re-search is being done on the usefulness of testing complement levels (C3 and C4) as possible markers during SLE flares. [66] A patients signs and symptoms may be the focus of custom-ized diagnostic tests. Assessments of joint involvement, kidney size and impairment, pulmo-nary involvement, chest radiography, electrocardiography, and chest discomfort can all be made using radiography. [67]

Drug Class	Mechanism of Action	Commonly Used Agents and Dosage	Potential Adverse Effects	Common Monitoring Parameters
NSAIDs (including salicylates)	Block prostaglandin synthesis through inhibition of cyclooxygenase enzymes, producing anti-inflammatory, analgesic, and antipyretic effects	Various agents and dosages	Gastrointestinal irritation and bleeding, renal toxicity, hepatic toxicity, hypertension	Nausea, vomiting, abdominal pain, dark/tarry stool; baseline and annual CBC, SCr, LFTs, urinalysis
Corticosteroids	Multiple effects on immune system (e.g., blocking cytokine activation, tumor necrosis factor-α) and inhibiting interleukins, γ-interferon,	Prednisone PO 0.5–2 mg/kg per day Methylprednisolone IV 500–1,000 mg daily for 3 to 6 days (acute flare)	Weight gain, hypertension, hyperglycaemia, hyperlipidaemia, osteoporosis, cataracts, edema, hypokalaemia, muscle weakness, growth suppression, increased risk of infection, glaucoma	Baseline blood pressure, bone density, glucose, potassium, lipid panel; glucose every 3 to 6 months; annual lipid panel and bone density
Immunosuppressants	Multiple suppressive effect on immune system (e.g., reduction of T-cell and B-cell proliferation; DNA and RNA disruption)	Cyclophosphamide PO 1–3 mg/kg per day or 0.5–1 g/m^2 IV monthly with or without a corticosteroid Azathioprine PO 1–3 mg/kg per day Mycophenolate PO 1–3g daily	Myelosuppression, hepatotoxicity, renal dysfunction, infertility, increased risk of infection and cancer	Baseline and routine CBC, platelet count, SCr, LFTs, and urinalysis (depends on individual drug)
Antimalarials	Unclear; may interfere with T-cell activation and inhibit cytokine activity; also thought to inhibit intracellular TLRs	Hydroxychloroquine PO 200–400 mg daily	Macular damage, muscle weakness	Funduscopy and visual field examination at baseline and every 6 to 12 months

BLyS = B-lymphocyte stimulator protein; CBC = complete blood count; DNA = deoxyribonucleic acid; IV = intravenous; LFTs = liver function tests; NSAIDs = nonsteroidal anti-inflammatory drugs; PO = by mouth; RNA = ribonucleic acid; SCr = serum creatinine; TLRs = toll-like receptors; UTI = urinary tract infection.

Table 1: Commonly Used Medications in the Treatment of Systemic Lupus Erythemato-sus

Conclusion

The treatment and long-term complications of lupus have improved greatly over the past two decades, but there are still many unanswered questions about the disease. Ongoing studies and more randomized control trials are needed to develop targeted therapies. Treatment of chronic diseases, especially lupus, requires a great commitment and commitment. Poor medication adherence, monitoring and lack of reassessment of disease activity usually lead to poor outcomes, re-current relapses and resistance. Patients should be counselled about pathology, signs and symptoms, the need for regular monitoring, medication adherence, and preventive measures such as lifestyle modification, dietary modification, and regular exercise to control body weight and lipid levels and prevent cardiovascular disease complications.

References

1. Justiz Vaillant AA, Goyal A, Varacallo M (2022). Systemic Lupus Erythematosus. StatPearls Publishing, Treasure Island.
2. Karrar S, (2018). Cunninghame Graham DS: Abnormal B cell development in systemic lupus erythematosus: what the genetics tell us. Arthritis Rheumatol. 2018, 70:496-507.
3. Didier K, Bolko L, Giusti D, Toquet S, Robbins A, et al. (2018). Autoantibodies associated with connective tissue diseases: what meaning for clinicians? Front Immunol. 9:541.
4. Aringer M, Costenbader K, Daikh D, et al. (2019). European League Against Rheumatism/American College of Rheumatology classification criteria for systemic lupus erythematosus. *Arthritis Rheumatol.* 71:1400

5. Stratta P, Mesiano P, Campo A, et al. (2009). Life expectancy of women with lupus nephritis now approaches that of the general population. Int *J Immunopathol Pharmacol.* 22:1135-41.
6. Elish D, Silverberg NB. (2006). Neonatal lupus erythematosus. Cutis 77:82–86.
7. Shmerling RH. (2005). Diagnostic tests for rheumatic disease: Clinical utility revisited. South Med J 98:704–711.
8. Prystowsky SD, Gilliam JN. (1975). Discoid lupus erythematosus as part of a larger disease spectrum: Correlation of clinical features with laboratory findings in lupus erythematosus. *Arch Dermatol* 111:1448–1452
9. Rees F, Doherty M, Grainge MJ, Lanyon P, Zhang W (2017).The worldwide incidence and prevalence of systemic lupus erythematosus: a systematic review of epidemiological studies. Rheumatology (Oxford). 56:1945-1961.
10. Weckerle CE, Niewold TB (2011). The unexplained female predominance of systemic lupus erythematosus: clues from genetic and cytokine studies. Clin Rev Allergy Immunol. 40:42-49.
11. McCarty DJ, Manzi S, Medsger TA Jr, Ramsey-Goldman R, LaPorte RE, et al. (1995). Incidence of systemic lupus erythematosus. Race and gender differences. Arthritis Rheum. 38:1260-1270.
12. Helmick CG, Felson DT, Lawrence RC, et al. (2008). Estimates of the prevalence of arthritis and other rheumatic conditions in the United States: Part 1. Arthritis Rheum 58(1):15–25.
13. Hochberg MC. (1985). The incidence of systemic lupus erythematosus in Baltimore, Maryland, 1970–1977. Arthritis Rheum 28:80–86.
14. Serdula MK, Rhoads GG. (1979). Frequency of systemic lupus erythematosus in different ethnic groups in Hawaii. Arthritis Rheum 22:328–333.
15. Uramoto KM, Michet CJ Jr, Thumboo J, et al. (1999). Trends in the incidence and mortality of systemic lupus erythematosus, 1950– 1992. Arthritis Rheum 42(1):46–50.
16. Balluz L, Philen R, Ortega L, et al. (2001). Investigation of systemic lupus erythematosus in Nogales, Arizona. Am *J Epidemiol* 154(11):1029–1036.
17. Symmons DP. (1995). Frequency of lupus in people of African origin. Lupus 4:176–178.
18. Lim S, Drenkard C, McCune W, et al. (2009). Population-based lupus registries: Advancing our epidemiologic understanding. *Arthritis Rheum* 61(10):1462–1466.
19. Costenbader KH, Feskanich D, Stampfer MJ, Karlson EW. (2007). Reproductive and menopausal factors and risk of systemic lupus erythematosus in women. Arthritis Rheum 56:1251–1262.
20. Buyon JP, Petri MA, Kim MY, et al. (2005). The effect of combined estrogen and progesterone hormone replacement therapy on disease activity in systemic lupus erythematosus: A randomized trial. *Ann Intern Med* 142:953–962.
21. Scofield RH, Bruner GR Namjou B, et al. (2008). Klinefelter's syndrome (47, XXY) in male systemic lupus erythematosus patients: Support for the notion of a gene–dose effect from the X chromosome. *Arthritis Rheum* 58:2511–2517
22. Justiz Vaillant AA, Goyal A, Varacallo M (2020). Systemic Lupus Erythematosus. StatPearls Publishing, Treasure Island; 1-10.
23. Karrar S, (2018). Cunninghame Graham DS: Abnormal B cell development in systemic lupus erythematosus: what the genetics tell us. *Arthritis Rheumatol.* 70:496-507.
24. Pan Q, Chen J, Guo L, et al. (2019). Mechanistic insights into environmental and genetic risk factors for systemic lupus erythematosus. Am *J Transl Res.* 11:1241-1254.
25. Brown JM, Archer AJ, Pfau JC, Holian A (2003). Silica accelerated systemic autoimmune disease in lupus-prone New Zealand mixed mice. *Clin Exp Immunol.* 131:415-421.
26. Monteiro BG,(2022). Pizarro CB: Environmental and occupational exposures in the develop-ment of systemic lupus erythematosus in adults: a narrative review. Rheumatology. 61-63.
27. Costenbader KH, Kim DJ, Peerzada J, Lockman S, Nobles-Knight D, et al. (2004). Karlson EW: Cigarette smoking and the risk of systemic lupus erythematosus: a meta-analysis. Arthritis Rheum. 50:849-857.
28. Pan Q, Chen J, Guo L, et al. (2019). Mechanistic insights into environmental and genetic risk factors for systemic lupus erythematosus. Am J Transl Res. 11:1241-1254.
29. Achtman JC, Werth VP (2015). Pathophysiology of cutaneous lupus erythematosus. Arthritis Res Ther. 17:182.
30. Yu C, Chang C, Zhang J (2013). Immunologic and genetic considerations of cutaneous lupus erythematosus: a comprehensive review. *J Autoimmun*. 41:34-45.
31. Berner BR, Tary-Lehmann M, Yonkers NL, Askari AD, Lehmann PV, (2005). Anthony DD: Phenotypic and functional analysis of EBV-specific memory CD8 cells in SLE. Cell Immunol. 235:29-38.
32. Su R, Li Z, Wang Y, et al. (2020). Imbalance between Th17 and regulatory T cells in patients with systemic lupus erythematosus combined EBV/CMV viraemia. Clin Exp *Rheu-matol.* 38:864-873.
33. Poole BD, Scofield RH, Harley JB, James JA Epstein-Barr virus and molecular mim-icry in systemic lupus erythematosus. Autoimmunity. 39:63-70.
34. Vaglio A, Grayson PC, Fenaroli P, Gianfreda D, Boccaletti V, (2018). Drug-induced lupus: traditional and new concepts. Autoimmun Rev. 17:912-918.
35. Rubin RL (2005). Drug-induced lupus. Systemic Lupus Erythematosus (Second Edition). Tsokos GC (ed): Academic Press, 535-547.
36. Petri M(2008). Sex hormones and systemic lupus erythematosus. Lupus. 17:412-415.
37. Deng Y, Tsao BP(2019). Genetics of human SLE. Dubois' Lupus Erythematosus and Related Syndromes (Ninth Edition). Wallace DJ, Hahn BH (ed): Elsevier, London; 54-68.
38. Laurynenka V, Kottyan LC, Weirauch MT, Kaufman KM, Harley JB(2021). Genetic predis-position to lupus across ancestries has >300 separable genetic contributions: what we know today. Lupus Sci Med.
39. Armstrong DL, Zidovetzki R, Alarcón-Riquelme ME, et al. (2022). GWAS identifies novel SLE susceptibility genes Ameer et al. Cureus 14(10): e30330.
40. Pan Q, Chen J, Guo L, et al. (2019). Mechanistic insights into environmental and genetic risk factors for systemic lupus erythematosus. Am J Transl Res. 11:1241-1254.
41. Mak A, Kow NY (2014). The pathology of T cells in systemic lupus erythematosus. *J Immu-nol* Res.
42. Al-Mayouf SM, Sunker A, Abdwani R, et al. (2011). Loss-of-function variant in DNASE1L3 causes a familial form of systemic lupus erythematosus. Nat Genet. 43:1186-1188.
43. Suárez-Fueyo A, Bradley SJ, Tsokos GC (2016). T cells in systemic lupus erythematosus. Curr Opin Immunol. 43:32-38.

44. Nakayamada S, Tanaka Y (2021). Clinical relevance of T follicular helper cells in systemic lu-pus erythematosus. Expert Rev Clin Immunol. 17:1143-1150.
45. Tsokos GC, Lo MS, Costa Reis P, Sullivan KE (2016). New insights into the immunopatho-genesis of systemic lupus erythematosus. Nat Rev Rheumatol. 12:716-730.
46. Giang S, La Cava A(2016). Regulatory T cells in SLE: biology and use in treatment. Curr Rheumatol Rep. 18:67.
47. Mellor-Pita S, Citores MJ, Castejon R, Tutor-Ureta P, Yebra-Bango M, et al. (2006). Decrease of regulatory T cells in patients with systemic lupus erythemato-sus. Ann Rheum Dis. 65:553-554.
48. Jenks SA, Sanz I(2009). Altered B cell receptor signalling in human systemic lupus erythe-matosus. Autoimmune Rev. 8:209-213.
49. Möckel T, Basta F, Weinmann-Menke J, Schwarting A(2021). B cell activating factor (BAFF): structure, functions, autoimmunity, and clinical implications in systemic lupus erythematosus (SLE). Autoimmune Rev. 20:102736.
50. Shao WH, Cohen PL (2011). Disturbances of apoptotic cell clearance in systemic lupus ery-thematosus. Arthritis Res Ther. 13:202.
51. Pagani S, Bellan M, Mauro D, et al. (2020). New insights into the role of Tyro3, Axl, and Mer receptors in rheumatoid arthritis. Dis Markers. 1614627.
52. Jung JY, Suh CH (2015). Incomplete clearance of apoptotic cells in systemic lupus erythema-tosus: pathogenic role and potential biomarker. Int *J Rheum Dis.* 18:294-303.
53. Cook HT, Botto M (2006) Mechanisms of disease: the complement system and the patho-genesis of systemic lupus erythematosus. Nat *Clin Pract Rheumatol.* 2:330-337.
54. Leffler J, Bengtsson AA, Blom AM (2014). The complement system in systemic lupus ery-thematosus: an update. Ann Rheum Dis. 73:1601-1616.
55. Deng Y, Tsao BP (2010). Genetic susceptibility to systemic lupus erythematosus in the ge-nomic era. Nat Rev Rheumatol. 6:683-692.
56. (1999).American College of Rheumatology Ad Hoc Committee on Systemic Lupus Erythematosus Guidelines. Guidelines for referral and management of systemic lupus erythematosus in adults. Arthritis Rheum 42:1785–1796.
57. Bertsias GK, Ioannidis JPA, Arlinger M, et al. (2008). EULAR recommendations for the management of systemic lupus erythematosus. Report of a Task Force of the EULAR Standing Committee for International Clinical Studies Including Therapeutics. Ann Rheum Dis 67:195–205.
58. Katz SJ, Russell AS. (2011). Re-evaluation of antimalarials in treating rheumatic diseases: Re-appreciation and insights into new mechanisms of action. Curr *Opin Rheumatol* 23:278–281.
59. Benlysta (belimumab) (2011). for Injection, prescribing information. Rockville, Md.: Human Genome Sciences, Inc.
60. Ameer M, Chaudhry H, Mushtaq J, et al. (2022). An Overview of Systemic Lupus Erythematosus (SLE) Pathogenesis, Classification, and Management. *Cureus* 14(10): e30330.
61. Hochberg MC. (1997). Updating the American College of Rheumatology revised criteria for the classification of systemic lupus erythematosus (letter). *Arthritis Rheum* 40:1725.
62. Sanchez ML, Alarcon GS, McGwin G Jr, et al. (2003). Can the weighted criteria improve our ability to capture a larger number of lupus patients into observational and interventional studies? A comparison with the American College of Rheumatology criteria. Lupus 12:468–470.
63. Von Muhlen CA, Tan EM. (1995). Autoantibodies in the diagnosis of sys - temic rheumatic diseases. Semin Arthritis Rheum 24:323–358.
64. Mok CC, Lau CS. (2003). Pathogenesis of systemic lupus erythematosus. J Clin Pathol 56:481–490.
65. Brasington RD Jr, Kahl LE, Ranganathan P, et al. (2003). Immunologic rheumatic disorders. *J Allergy Clin Immunol* 111:593–601.
66. Borchers AT, Keen CL, Gershwin ME. (2007). Drug-induced lupus. Ann N Y Acad Sci 1108:166–182.
67. Birmingham DJ, Irshaid F, Nagaraja HN, et al. (2010). The complex nature of serum C3 and C4 as biomarkers of lupus renal flare. Lupus 19:1272–1280-1283.